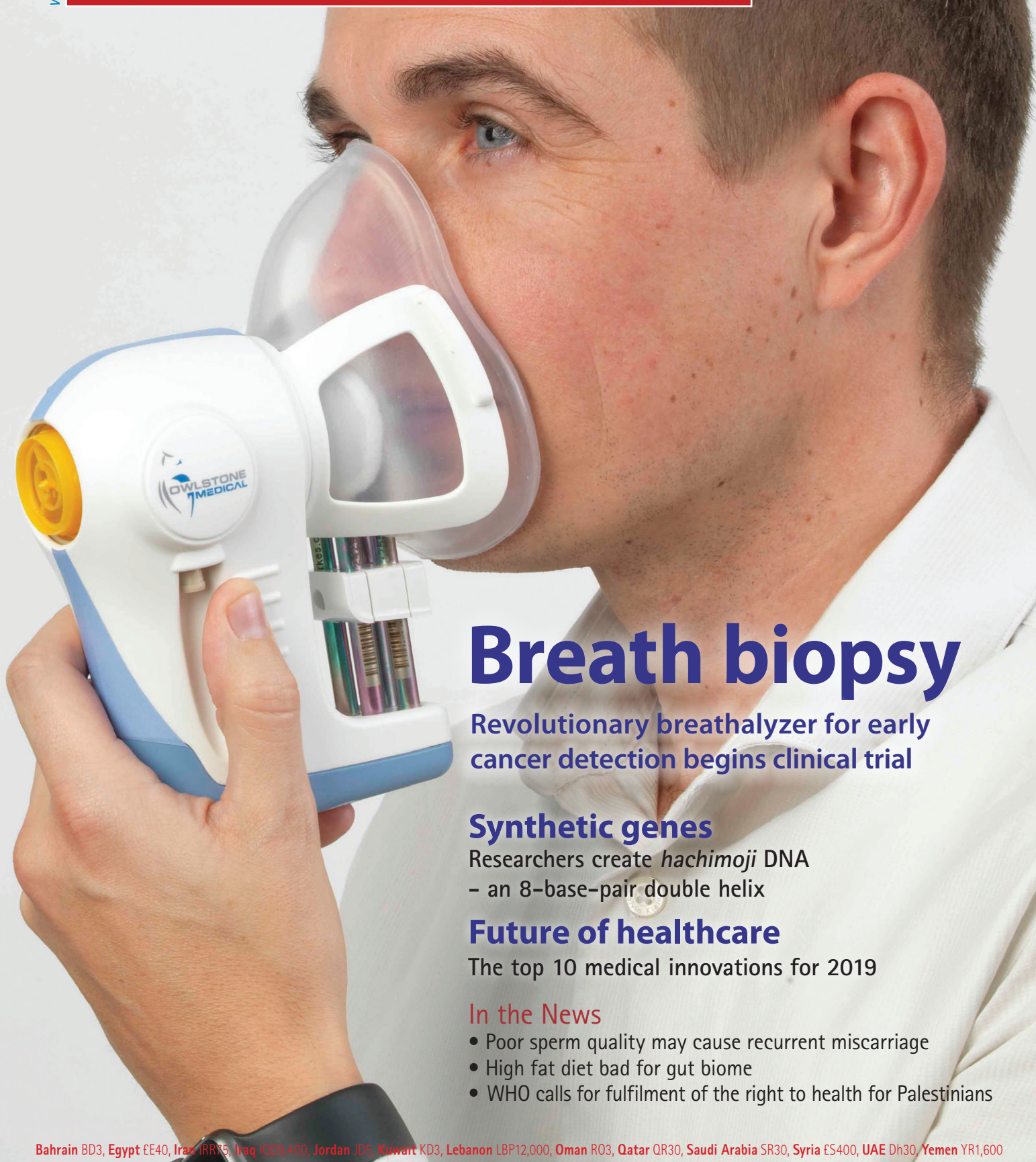


# Middle East HEALTH

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March - April 2019



## Breath biopsy

Revolutionary breathalyzer for early cancer detection begins clinical trial

## Synthetic genes

Researchers create *hachimoji* DNA  
- an 8-base-pair double helix

## Future of healthcare

The top 10 medical innovations for 2019

## In the News

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- High fat diet bad for gut biome
- WHO calls for fulfilment of the right to health for Palestinians

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# Prognosis

## Synthetic DNA

In a major research breakthrough, scientists have managed to synthesize synthetic DNA that has eight base pairs instead of the normal four we know. They are calling it *Hachimoji* DNA – from the Japanese: “hachi” meaning “eight” and “moji” meaning “letter”. This feat of molecular engineering is unprecedented and opens the door to completely new genetic systems and research into ways life could structure itself in environments we haven’t yet imagined. The advance offers new possibilities in many fields, including medical research and data storage. Read about this breakthrough in this issue.

The Arab Health exhibition in Dubai earlier this year was huge. We spoke to several exhibitors about their new products and solutions, too many to report on them all – so in this issue we cover a select few. We will publish a few more reports in the next issue. Artificial Intelligence (AI) was one of key themes running through the event, with many leading medical device manufacturers showcasing their AI innovations.

Also in this issue, we focus on Oncology and look at a number of recent developments in the field. Of particular interest, is the launch of a clinical trial to test a breath biopsy for multiple cancers. The breath test analyses molecules that could indicate the presence of cancer at an early stage and has the potential to revolutionize the way we detect and diagnose cancer in the future. The clinical trial will first look at patients with suspected oesophageal and stomach cancers and will then expand to prostate, kidney, bladder, liver and pancreatic cancers.

Also in Oncology, we look at the world’s first genetic sequencing of precancerous lung lesions that could pave the way for very early detection and new treatments.

In news from the World Health Organisation, we look at a report that indicates road traffic deaths are continuing to rise, with an annual 1.35 million fatalities. The WHO ‘Global status report on road safety 2018’ highlights that road traffic injuries are now the leading killer of children and young people aged 5-29 years. You can read more about this in the ‘News from the WHO’ section of *Middle East Health*.

Callan Emery

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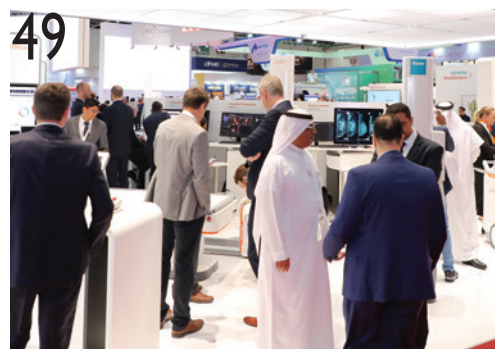
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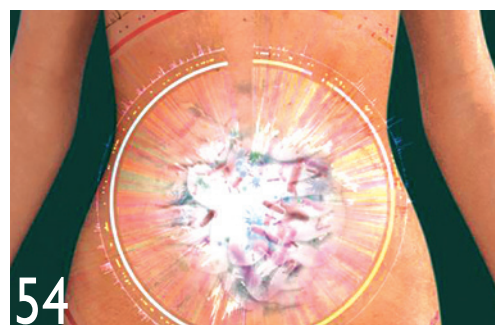
Cover image: Owlstone's ReCiva breathalyzer device.  
Credit: Owlstone Medical Ltd.



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# middle east monitor

## Update from around the region

### CMC Dubai partners with Siemens for diagnostic equipment

Clemenceau Medical Center in Dubai Healthcare City (CMC-DHCC) has entered a strategic partnership with Siemens Healthineers who will equip the medical center with interventional radiology, cardiology and diagnostic equipment, including 3T MRI, PET/CT, CT, and flat panel X-ray systems for women's health, trauma, and operating rooms.

Included in the partnership is the digitization of CMC-DHCC and the connection of the equipment to Siemens Healthineers' Picture Archiving and Communication System (PACS) and Cardiovascular Information System (CVIS).

Speaking about the new partnership, Dr Mounes Kalaawi, founding CEO of Clemenceau Medical Center (Beirut) and Chairman of Clemenceau Medicine International, said: "Our network of hospitals integrates the latest technologies with excellent patient care and hospitality services. Through our strategic alliances and partnerships, we extend our reach and accomplish more. Siemens Healthineers has a strong presence in Dubai and will provide CMC-DHCC with a competitive edge with their continuous support."

In addition to equipping the hospitals with state-of-the-art medical technology, Siemens Healthineers will also provide technical support, coupled with application training to assist in the continuous education and skill development of medical staff.

Ole Per Maloy, Managing Director, Siemens Healthineers, Middle East and Southern and Eastern Africa, commented: "As a technology partner, our goal is to support our customers with holistic solutions for complex challenges in the hospital environment. We are very pleased to enter this alliance with Clemenceau Medical Center, a leading name in the industry, and we are very confident that with our products, solutions and their skilled specialists, we create a winning pair that will together deliver high-value care to support more patients in the UAE",

The 110-bed CMC-DHCC is expected to open June 2019. Through Clemenceau Medicine International the Clemenceau Medicine Network extends from Clemenceau Medical Center in Beirut (CMC Beirut) to the upcoming medical centers in Dubai (CMC-DHCC) and Riyadh (CMC Riyadh).

### Dubai Health Authority and Philips Middle East to implement breast cancer screening program

Dubai Health Authority and Philips Middle East are collaborating on the implementation of a comprehensive breast cancer screening program at five primary healthcare centers and key hospitals.

Philips' breast cancer screening program streamlines population-based screening and gives caregivers the opportunity to focus on cancer cases that are tested positive and require attention as well as enabling a larger cross-section of the population to be screened

H. E. Humaid Al Qutami, Director General of the DHA said: "Our vision is to reduce the national cancer mortality rate through early detection. Through this collaboration, the public healthcare system will benefit from Philips' knowledge of population-based screening, while adapting it to the UAE's unique cultural requirements."

Breast cancer is the most commonly diagnosed cancer in women (24.2%, or about one in four of all new cancer cases diagnosed in women worldwide are breast cancer.) In the UAE, breast cancer is responsible for 24% of all cancer-related deaths among women.

Ozlem Fidanci, CEO, Philips Middle East and Turkey said: "The earlier a tumor is diagnosed, the greater the chances of survival. With figures suggesting the incidence of cancer cases will double in the region by 2030, we are happy to collaborate with the National Health Agenda to reduce the mortality rate. As Philips, we want to support physicians and patients with more than public awareness and technology, by offering an integrated approach and a range of different care pathways."

The program includes a continued med-

ical education module for radiologists and radiographers to be certified by the Dutch National Expert and Training Centre for Breast Cancer (LRCB) while benefitting from Philips' clinical expertise.

### Emirati son saves father by donating part of his liver

A UAE national with liver failure is recovering well after life-saving surgery, following his son's decision to donate a section of his own liver for the operation.

The living related liver transplant was one of the three living organ donations conducted back-to-back at Cleveland Clinic Abu Dhabi in October 2018, in a busy week that saw a total of six multi-organ transplant operations conducted at the hospital.

One of the most complex forms of transplant surgery, living related liver operations involve surgeons taking a section of a related donor's healthy liver and transplanting it into the sick patient.

Living donors in the UAE should be related to the patient, and in many cases a son or daughter donates part of their healthy organ to a parent. Following the first living related liver transplant in the hospital in July 2018, the specialist transplant team has continued to work with patients and their families to help them understand the range of options available.

Dr Antonio Pinna, Staff Physician in the Digestive Disease Institute at Cleveland Clinic Abu Dhabi who led the surgical team, explains: "A liver transplant is the last resort on the treatment spectrum and finding deceased donors can be a challenge. By adding living related transplant options, we are increasing the range of treatments available and also providing hope for patients in final stage organ failure.

"Over a short period of time, the team were able to operate on three patients who received liver donations from relatives, and a fourth patient who received a deceased donor liver. In each case, the patients and the living donors are recovering well," he added.

Waleed Ahmed Al Hadrami, the donor, said: "When I found out how sick my father was and that the only thing that



would save his life was a liver transplant, I didn't need to think about it – of course I would share my liver with him.”

He added: “At first, I was apprehensive about the procedure but as soon as I met the doctor, saw the level of expertise and technology, and the professional approach, I felt at ease. It felt good to be able to be able to do this for my father.”

The patient, Ahmed Al Hadrami, a father of nine, is recovering well. He commented: “I am so pleased that I had a transplant here in Abu Dhabi with my family around me. It has helped my recovery a lot and ensured the operation did not disrupt our family life too much. I did consider undergoing surgery abroad but when we discussed it, the most practical option was to have the surgery at Cleveland Clinic Abu Dhabi.

“Our leaders have done a remarkable thing by bringing this hospital to the United Arab Emirates,” he added.

Dr Bashir Sankari, Chair of the Surgical Subspecialties Institute at Cleveland Clinic Abu Dhabi, said: “Our transplant program continues to evolve, with the support of partner hospitals and the nation's medical authorities, and building on the transplant expertise of Cleveland Clinic in the US. It provides the sickest and most complex patient cases with the gift of life through transplant.”

From January 2019, UAE residents have been able to download the Hayat app and register as potential donors after their death.

Cleveland Clinic Abu Dhabi is the only multi-organ transplant facility in the UAE. The hospital completed its first living related donor kidney transplant in April 2017 and has subsequently performed heart, liver and lung transplants. The facility employs a highly-skilled team of surgeons and caregivers who collectively have performed thousands of transplants throughout their varied medical careers.

## **GSK launches Medzy chatbot in UAE to help patients use antibiotics correctly**

GSK has launched Medzy, a UAE-focused



chatbot, to help patients use antibiotics more responsibly. This is in response to results of research commissioned by GSK, which revealed significant gaps in antibiotic awareness and best practice amongst patients in the UAE, which could contribute to the growing threat of antimicrobial resistance (AMR).

The research used both qualitative and quantitative insights from doctors, pharmacists and patients in the Emirates, and identified several behaviours and factors which affect patients' adherence to antibiotic use. Some of the concerning factors, which may be contributing triggers of AMR, include:

- 54% of people find it difficult to remember to take antibiotics
- Almost three out of ten people believe they should stop taking antibiotics when they feel better, rather than finishing their course as prescribed
- Patients have a tendency to guess the next steps they need to take if they fail to take a dose. Some patients will take a double dose to compensate for a missed dose
- Advice from family, friends and the online community is often considered a key source of reliable information, meaning that patients often self-diagnose first, rather than visit the doctor

In response to these gaps, GSK has developed Medzy, an interactive UAE-centric patient engagement chatbot, implemented through Facebook Messenger. Medzy, which is an abbreviation of

“medication made easy”, was brought to life through close collaboration and testing with UAE patients, doctors and pharmacists, whose challenges and needs have played a role in shaping the technology.

The patient-friendly chatbot provides simple-to-understand information including, but not limited to:

- What antibiotics are, when to take them and how they work
- What AMR is, its causes, long term effects and prevention tips
- How to care for someone who is taking antibiotics
- Reminders for patients to take their medication
- Dosage and treatment length
- Formulation of medication, ingredients and side effects
- Safe disposal and storage
- A way for users to report any side effects.

Commenting on the development of Medzy, Sameh Elfangary, General Manager at GSK in the Gulf, said: “As a global leader in the antibiotic space, we are committed to tackling AMR through the promotion of appropriate use of antibiotics. When the data confirmed that almost 30% of UAE patients do not complete their course of antibiotics but also tend to seek advice from family, friends or online over a trained healthcare professional, the need became clear for an informed, patient-friendly solution that people can easily access, understand and incorporate into their daily lives.



“We see Medzy as a personal assistant for patients, dedicated to helping them manage their antibiotic use, offering simple but practical advice that could ultimately help slow down the process of AMR.”

Dr Farheen Ali, Diplomate of the American Board of Internal Medicine and Infectious Diseases, added: “As doctors, increasing patient awareness about antibiotic resistance and understanding their role is paramount to us, as is making it as easy as possible for patients to stick to what we prescribe. The research commissioned by GSK validates many of the challenges doctors in the UAE face, and calls for amplified awareness in the form of a helpful intervention, such as Medzy. We look forward to seeing in a year from now how, for those using the digital solution, Medzy has helped raise awareness levels and positively impacted patients’ adherence to prescriptions.”

- Medzy is currently available in English and will be launched in Arabic in the near future. The tool can be accessed at: [www.facebook.com/medzybygsk](http://www.facebook.com/medzybygsk)

## Medcare Women & Children Hospital awarded JCI accreditation

The Medcare Women & Children Hospital has recently been awarded the Joint Commission International (JCI) accreditation, reflecting the hospital’s high standard of patient safety and quality care. Based in Dubai, the Medcare Women & Children Hospital provides dedicated and specialised care in a range of more than 27 specialties including paediatrics, neonatal care, obstetrics and gynaecology, and women health.

The JCI organization is a recognised world leader in healthcare accreditation working to improve patient safety and quality of health in the international community.

Medcare issued a statement saying, achievement of this accreditation reflects Medcare’s commitment to attaining the highest standards in healthcare provision. It reinforces its initiative to enhance the patient-centric healthcare journey by

ensuring that patients’ safety and well-being comes first. Moreover, this is the third Medcare hospital to achieve the accreditation, showcasing consistency in delivering optimal outcomes throughout its network.

A team of international JCI inspectors spent four days in Medcare Women & Children Hospital to assess the facility, with a focus on service quality and patient safety. The fundamental principles of the hospital were evaluated through various forms of testing such as interviews with doctors and patients, and outcomes were matched with the JCI 6th Edition Standards for Hospitals. Based on these findings, the hospital was granted the JCI accreditation.

Andre Daoud, Group Chief Executive Officer (CEO) of Medcare said: “At Medcare, we are committed to encouraging the highest standards in preventive, curative and rehabilitative healthcare. It is our vision to champion clinical excellence and create a seamless and unique experience for the patient, keeping safety and wellbeing at the heart of our strategy. This accreditation reflects a strong team effort, showcasing the ways in which our staff work diligently to provide a better healthcare journey.”

## Physician highlights treatment gap for adolescent and younger adult cancer patients

A leading US cancer doctor is calling for more focus on adolescent and younger adult cancer patients, those between the ages of 15 and 40, who make up the majority of the Middle East’s population.

Poor lifestyle choices, namely smoking and a lack of proper diet and exercise, continue to contribute most significantly to the region’s growth in cancer patients. It has been long-established that smoking leads to lung cancer, and obesity is now strongly believed to lead to a range of cancers, including those of the colon and breast.

“The region’s largest number of cancer suffers are being overlooked or inadequately treated, and the reasons are simple,” said



Rabi Hanna, M.D., Department of Pediatric Hematology Oncology and Blood and Marrow Transplantation at Cleveland Clinic Children’s.

“Most adolescents and young adults are provided the same treatments as much older adults, even when we now know that the disease biology is different in younger patients. In addition, because they tend to be busy with school or work or parenting, young cancer sufferers are less likely to take part in critically important clinical drug trials that could yield breakthrough treatment options.”

Literature shows that adolescent and younger adult (AYA) patients affected with paediatric cancers such as Acute Lymphoblastic leukaemia benefit from more aggressive treatment protocols. The US National Institutes of Health has highlighted the gap in their care and noted how they lag behind children or adults in term of survival improvement and enrolment in cancer clinical trials. They refer to it as the “AYA gap”.

Dr Hanna added that, in addition to sending adolescent and young adult cancer patients to existing centres already experienced in treating this age group, regional physicians should provide them with far greater psycho-social support in the treatment of their diseases. **MEH**

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# worldwide monitor

Update from around the globe

## Prevention, screening, treatment package could avert 15 million Hep C infections by 2030

A comprehensive package of prevention, screening, and treatment interventions could avert 15.1 million new hepatitis C infections and 1.5 million cirrhosis and liver cancer deaths globally by 2030 – equal to an 80% reduction in incidence and a 60% reduction in deaths compared with 2015, according to the first study to model hepatitis C interventions globally published in *The Lancet*.

The estimates suggest that the interventions modelled in the study would reach the elimination targets set by the World Health Organization (WHO) to reduce the number of new hepatitis C infections by 80%, but narrowly miss the target to reduce mortality by 65% – which would instead be reached by 2032.

“Even though it narrowly falls short of the WHO targets for 2030, the impact our estimates suggest would be a tremendous stride forwards,” says Professor Alastair Heffernan, Imperial College London, UK, who led the research. “Eliminating hepatitis C virus is an extremely challenging aim that requires improved prevention interventions and screening, particularly in high-burden countries such as China, India, and Pakistan. Across the globe, these options are currently well below the levels we estimate are needed to have a major impact on the epidemic. Research into how to improve this in all settings, as well as increased funding, will be needed if we are to reach these targets.”

Globally, it is estimated that 71 million individuals are chronically infected with hepatitis C virus, and 10-20% will develop liver complications including cirrhosis and cancer – which were responsible for over 475,000 deaths in 2015. In recent years, the number of deaths from viral hepatitis infection has risen.

Transmission is most commonly as-

sociated with blood transfusions, unsafe healthcare-related injections, and injection drug use. The first two causes of infection have declined globally, but remain an issue in lower income countries. However, infection from injecting drug use is the primary cause in countries where all other causes have been mostly eliminated.

In 2014, direct-acting antivirals were developed, which provide greatly improved cure rates along with reduced side effects and shorter duration of treatment, meaning that more patients can successfully complete treatment than before.

As a result, in 2016, all 194 member states of the WHO have committed to eliminating viral hepatitis as a public health threat. These targets include reducing mortality by 65% and reducing new infections by 80% by 2030, compared with 2015 rates. This is to be achieved by preventing transmission (by improving blood safety and infection control measures, and extending harm reduction services for people who inject drugs), and expanding testing, and increasing treatment with direct-acting antivirals (DAAs) for those already infected.

In the new study, the authors created a model of the global hepatitis C epidemic in 190 countries using data on demography, people who inject drugs, current treatment and prevention programmes, historic trends, prevalence and mortality rates. Using this they estimated the effects of four interventions – implementation of comprehensive blood safety and infection control measures; expansion of harm reduction services (such as opioid substitution therapy and needle and syringe programmes) for people who inject drugs; provision of treatment for all people as soon as they are diagnosed with hepatitis C infection; and expansion of hepatitis C testing, so 90% of people with hepatitis C are diagnosed and offered treatment by 2030.

The authors note that reducing the global burden of hepatitis C depends on the progress made in just a few countries.

Infections and deaths averted, after implementation of the comprehensive package of interventions, are concentrated in a small number of countries, in particular China, India, Pakistan, and Egypt, which are the countries that contribute most to projected new infections by 2030.

“Achieving such reductions requires a massive screening programme and demands a rapid increase in new treatment courses in the short term – namely, 51.8 million courses of direct-acting antivirals by 2030. In the following 20 years, by contrast, the total number required is a much more modest 12 million courses. The reduced treatment requirement after 2030 indicates that rapid testing and treatment scale-up is a means to control the epidemic in the long term, though this must be done within the context of improved hepatitis C prevention measures as well,” adds Professor Tim Hallett, Imperial College London, UK.

• Read *The Lancet* report –  
doi: 10.1016/S0140-6736(18)32277-3

## Cancer Research UK, AstraZeneca open functional genomics centre

Cancer Research UK and AstraZeneca will open a new centre in the UK, dedicated to realising the full potential of functional genomics in the discovery and development of new drugs for patients with cancer.

“This new centre will be a huge asset to the UK cancer research community and will accelerate the development of new treatments for people with cancer,” said Professor Greg Hannon, director of the Cancer Research UK Cambridge Institute.

This partnership will explore in more detail the function and interaction of genes and proteins in cancer, and apply new genome-altering technologies such as CRISPR, to create sophisticated models of the disease for research.

The Joint Cancer Research UK - AstraZeneca Functional Genomics Centre will be a dedicated world-class resource for AstraZeneca and Cancer Research UK’s

academics and alliance partners working at all stages of translational research, from target discovery and validation, to assessing novel drug combinations.

By combining the experience and expertise of both organisations in cancer biology and functional genomics, including CRISPR technologies, it's hoped that this state-of-the-art facility will help deliver new treatments to patients much faster.

Building on the transformative potential of CRISPR for gene editing and understanding cancer biology, this centre will be a major driver for the use of CRISPR in drug discovery and development in the UK with research expected to get underway this year. The centre is being established with the expert guidance of Professor Greg Hannon, director of the Cancer Research UK Cambridge Institute. He said: "This new centre will be a huge asset to the UK cancer research community and will accelerate the development of new treatments for people with cancer.

"After two decades of effort, we're making fast progress but we're still only just beginning to tap into the full potential of CRISPR and to understand how this is applied alongside other functional genomics approaches. As we develop high-quality standardised techniques through the centre, we can create more sophisticated and powerful biological models of disease, handle larger and more complex data sets, and identify successful cancer drug targets with better accuracy."

Dr Iain Foulkes, Cancer Research UK's executive director of research and innovation, said: "As we move into an era of personalised medicine, we've reached a turning point in our ability to harness powerful technologies in the pursuit of targeted cancer therapies. We hope that this will translate into urgently needed new therapies for patients with hard to treat cancers, such as lung, pancreatic, oesophageal and brain tumours."

The Functional Genomics Centre will be a hub of expertise in genetic screens, cancer models, CRISPR tool design and

computational approaches to big data.

These techniques can be used to understand the genetic changes contributing to cancer development and to identify and validate potential drug targets. CRISPR technologies are also improving our ability to model disease systems, allowing researchers to accurately predict how these new treatments will work in patients, and identify genetic drivers of drug resistance.

The centre will be housed in the Milner Therapeutics Institute at the University of Cambridge and operationalised through Cancer Research UK's Therapeutic Discovery Laboratories - the charity's in-house drug discovery unit focused on establishing drug discovery alliances with industry. The specialist staff employed by both organisations at the centre will facilitate collaborative projects.

Dr Mene Pangalos, Executive Vice President, Innovative Medicines & Early Development, AstraZeneca, said: "The best science doesn't happen in isolation which is why AstraZeneca is committed to advancing innovative science through collaboration. This new centre of excellence with Cancer Research UK will combine our expertise in functional genomics and CRISPR technology to identify new biological pathways driving disease and will accelerate the development of new cancer medicines for patients."

### **World Bank gives \$80m to boost Ebola response**

The World Bank Group and the Pandemic Emergency Financing Facility (PEF) have approved a total of up to US\$80 million in grants and credits to support over half the estimated cost of an escalated six-month Ebola response effort being mounted by the government of the Democratic Republic of Congo (DRC) and international partners. The escalated campaign is estimated to cost about \$148 million and covers the period from February through the end of July 2019.


The World Bank Group, on February 28, made \$60 million of grants and cred-

its available through the International Development Association (IDA), its fund for low-income countries.

The Pandemic Emergency Financing Facility (PEF), an innovative financing mechanism created by the World Bank Group together with Japan, Germany and Australia, approved up to a \$20 million grant from its Cash Window within three days of receiving a request from the DRC government. Half of this amount will be released immediately to support frontline response, with the balance to be released within a month or sooner according to operational need.

"This 10th Ebola outbreak has been the worst that our country has faced so far, and this renewed financial commitment from the World Bank Group and the PEF allows us and our partners to concentrate fully on fighting Ebola and protecting the health of our citizens," said Dr Oly Ilunga Kalenga, Minister of Health of the DRC. "The situation is very challenging, but we are determined to increase our already strong efforts to contain the outbreak."

"Our priority is to halt this outbreak of Ebola and limit the devastation it causes to families and communities. [This] commitment ensures that lifesaving work can be urgently scaled up, and that lack of funding is not a constraint," said World Bank Group Interim President and CEO Kristalina Georgieva. "Our investments also help DRC and its neighbours to build strong health systems that protect their people and economies from the long-term damage that pandemics can cause."

The DRC has been fighting the current Ebola outbreak since August 2018, and over 480 deaths have been confirmed in the North Kivu and Ituri provinces, as of February 28. The World Bank has so far provided most of the financing for the Ebola response efforts from August 2018 through February 2019. It has also provided technical support to the strengthen the DRC health system and invested in pandemic preparedness in the nine countries bordering the DRC in case the outbreak crosses borders. 

# Top 10 medical innovations for 2019



Michael Roizen M.D., Chief Wellness Officer at Cleveland Clinic

Alternate therapies for pain. The use of artificial intelligence in healthcare. Expanded window to treat stroke patients. These are some of the innovations that will enhance healing and change healthcare in the coming year, according to a distinguished panel of doctors and researchers.

The list of up-and-coming technologies was selected by a panel of Cleveland Clinic physicians and scientists, led by Michael Roizen, M.D., Chief Wellness Officer at the Ohio, US-headquartered organization.

“Healthcare is ever changing and we anticipate that innovations such as cancer immunotherapy and pharmacogenomics will significantly transform the medical field and improve care for patients at Cleveland Clinic and throughout the world,” said Dr Roizen.

Here, in order of anticipated importance, are the Top 10 Medical Innovations of 2019:

## 1. Alternative therapy for pain: Fighting the opioid crisis

The opioid crisis has been declared a public health emergency. Today,

chronic pain is the leading cause of opioid prescription. Though several clinically validated alternative therapies for chronic pain exist, none have curtailed the crisis. Now, innovation and potential for hope comes by way of pharmacogenomic testing, which uses a patient’s genetic makeup to predict an individual’s metabolism of drugs, including some opiate-based drug. Pharmacogenomic testing can be used to avoid adverse reactions and eliminate unnecessary and ineffective prescriptions, replacing them with more effective medications. Pharmacogenomics can also be used to predict who may have little or no pain relief to some opiate-based analgesics. Such patients might otherwise finish their prescription quickly and return for a new prescription earlier than expected. Pharmacogenomics can reduce or eliminate the stigma of “drug-seeking” that might be unfairly ascribed to such patients and provide the opportunity to tailor medication therapy. In 2019, with increased access to genetic testing, pharmacogenomics is poised to make significant inroads into precision medicine and potentially an end to the crisis.

## 2. The advent of AI in healthcare

Once thought as a futuristic threat to humankind, artificial intelligence is now a part of everyday life. In healthcare, AI is changing the game with its applications in decision support, image analysis and patient triage. Today, artificial intelligence is helping physicians make smarter decisions at the point of care, improving the ease and accuracy of viewing patient scans and reducing physician burnout. For instance, machine learning algorithms have the ability to highlight problem areas on images, aiding in the screening process



and quickly making sense of the mountains of data within a physician’s EMR system. With AI’s continued integration into healthcare, caring for patients has become a matter of working smarter, not harder.

## 3. Expanded window for acute stroke intervention

When it comes to stroke intervention, a timely response is critical. Prolonged lack of blood flow following a stroke can cause irreversible destruction, often resulting in disability. In many cases of stroke, intervention methods can be deployed to save tissue. But until now, intervention of a stroke has only been recommended within a limited window of time. Released this past year, new guidelines suggest an expanded window for treatment. This lengthened timeframe is anticipated to lower the risk of disability and provide opportunity for recovery to an increased number of future stroke patients.

## 4. Advances in immunotherapy for cancer treatment

Cancer immunotherapy, or biologic therapy, is a technique that uses the body’s own immune system to fight cancer. While immunotherapies for cancer have existed for some time, the worldwide work toward a cure for cancer continues to highlight new and novel immunotherapeutic targets. Scientists are creating life-changing new

cancer treatments through the concepts of joint therapy and engineered T-cells. With the near daily discovery of new immunotherapeutic targets and biomarkers, it is the hope that effective therapies will soon exist for all tumour profiles.

### **5. Patient-specific products achieved with 3D printing**

Utilizing 3D printing technology, medical devices can now be matched to the exact specifications of a patient. Designed to be more compatible with an individual's natural anatomy, devices modelled from patient-specific dimensions have shown greater acceptance by the body, increased comfort and improved performance outcomes. The versatility provided by 3D printing gives medical practitioners the ability to provide patients the most advanced care, while simultaneously minimizing the risk of complication in patients that meet specific medical requirements. Currently, the most significant work in this space includes external prosthetics, cranial/orthopaedic implants, and customized airway stents for diseases narrowing the airway. Work in prosthetics and other bodily implants is also gaining speed with some cleared for the commercial market. The technology has also been found helpful in surgical planning. To date, the technology has been used for many complicated heart surgeries, and even the Cleveland Clinic's most recent total face transplant. With its widening healthcare applications, 3D printing is increasing the attention to detail in patient care.

### **6. Virtual and mixed reality for medical education**

Virtual and mixed reality involve the use of computer technology to create simulated and hybrid environments. Popular for their gaming applications, virtual and mixed reality, with their fu-

touristic affect, never fail to dazzle audiences. But VR/MR technology is much more than a game. These reality systems have recently caught the eye of healthcare professionals eager to sharpen their skills. Now popular for medical education, VR/MR programs provide simulation training that serves to enhance traditional medical schooling. With this immersive style of learning, VR/MR training appeals to all types of learners: audio, visual and kinaesthetic. Education via simulation is a productive step toward the system's most adept and confident healthcare providers.

### **7. Visor for prehospital stroke diagnosis**

Though less common than ischemic strokes, haemorrhagic strokes – during which blood escapes from a ruptured blood vessel in the brain – are responsible for nearly 40 percent of stroke deaths. Rapid diagnosis is necessary for effective treatment, as uncontrolled bleeding can lead to swelling of, and damage to, the brain. To speed diagnosis, healthcare professionals are using new, advanced technologies such as the haemorrhage scanning visor, which can detect bleeding in the brain. An efficient diagnostic tool, the visor for prehospital haemorrhage scanning serves to speed up diagnosis and the ever-important time to treatment.

### **8. Innovation in robotic surgery**

Most surgeries performed today are the shortest and least invasive that science will allow. This adaptation in surgical methodology is brought about in part by the integration of robotics. Robots in the operating room provide surgeons with guidance for extreme precision in surgery. Today, surgical platforms are highly advanced and are being used anywhere from spine to endovascular procedures. Shortened recovery time and limited pain after surgery are just a few of the patient benefits seen with minimally invasive robotized surgery. Continued ad-

vancement in the field has led to more precise and effective surgeries with improved surgical outcomes.

### **9. Mitral and tricuspid valve percutaneous replacement and repair**

Cardiac surgery today is less invasive and more routine and effective than its historic counterpart. Performed percutaneously – via a catheter through the skin – many cardiac procedures no longer require an open heart surgery approach. Two such procedures performed this way include replacements and repair of both the mitral and tricuspid valves. Hot on the trail of aortic valve percutaneous intervention, recent percutaneous mitral and tricuspid valve intervention has yielded significant positive outcomes while filling a void in the field of heart surgery. The exploration of this technology in a greater patient population is ongoing, but with promising post-op results, the innovation has significant implications for the future of cardiac care.

### **10. RNA-based therapies**

Akin to DNA-based gene therapies, RNA-based therapies are the newest innovation in labs nationwide and have shown immense potential. Interfering with genetic data at the ribonucleic acid (RNA) level gives scientists the ability to intercept a patient's genetic abnormality before it is translated into functioning (or non-functioning) proteins. Today, the most popular and successful mechanisms of RNA therapy include antisense nucleotides and RNA interference. These new therapies are being explored in a variety of rare genetic diseases such as Huntington's disease, as well as in cancer and neurologic diseases, with the hope of treatment by way of alternate genetic data. These new mechanisms of action are opening windows for progress and innovation in therapeutics. **MEH**

# the laboratory

Medical research news from around the world



## Poor sperm quality may cause recurrent miscarriage

Multiple miscarriages may be linked to the poor quality of a man's sperm, suggests new research.

The early-stage study, from scientists at Imperial College London, investigated the sperm quality of 50 men whose partners had suffered three or more consecutive miscarriages.

The research, published in the journal *Clinical Chemistry*, revealed that, compared to men whose partners had not experienced miscarriages, the sperm of those involved in the study had higher levels of DNA damage.

The study team hope these findings may open new avenues to finding treatments to reduce the risk of miscarriage.

Recurrent miscarriage affects around one in 50 couples in the UK, and is defined as the consecutive loss of three or more pregnancies before 20 weeks' gestation.

Until recently recurrent miscarriage was thought to be caused by health issues with the mother, such as infection or immune problems.

However, doctors are now realising sperm health may also play a role, explained Dr Channa Jayasena, lead author

of the research from Imperial's Department of Medicine: "Traditionally doctors have focused attention on women when looking for the causes of recurrent miscarriage. The men's health – and the health of their sperm, wasn't analysed.

"However, this research adds to a growing body of evidence that suggests sperm health dictates the health of a pregnancy. For instance, previous research suggests sperm has an important role in the formation of the placenta, which is crucial for oxygen and nutrient supply to the foetus."

In the new research, the team analysed the sperm of 50 men who were patients at the Recurrent Miscarriage Clinic at St Mary's Hospital in London, part of Imperial College Healthcare NHS Trust.

They then compared the results to the sperm health of 60 male volunteers whose partners had not suffered miscarriage.

The analysis revealed sperm from men with partners who had suffered recurrent miscarriage had twice as much DNA damage compared to the control group.

The research team suggest this DNA damage may be triggered by so-called reactive oxygen species.

There are molecules formed by cells in semen (the fluid that contains sperm cells) to protect sperm from bacteria and infection. However, in high enough concentrations the molecules can cause significant damage to sperm cells.

The results from the study revealed sperm from men whose partners had suffered miscarriage had a four-fold increase in the amount of reactive oxygen species compared to the control group.

The research team are now investigating what may trigger high levels of these reactive oxygen species.

Dr Jayasena explained: "Although none of the men in the trial had any ongoing infection, such as chlamydia, which we know can affect sperm health. It is possible there may be other bacteria from previous infections lingering in the prostate gland, which makes semen. This may lead to permanently high levels of reactive oxygen species."

He added there is increasing evidence obesity can lower sperm health, possibly because high levels of body fat can trigger an increase in reactive oxygen species. Therefore the team are analysing the metabolic health of the 50 men in the study, and assessing weight and cholesterol levels.

The men whose partners had suffered miscarriage were also slightly older than the control group, with an average age of 37 compared to 30, and were slightly more overweight. The team are now investigating whether these factors may have affected the levels of reactive oxygen species.

Dr Jayasena concluded: "Although this is a small study, it gives us clues to follow. If we confirm in further work that high levels of reactive oxygen species in semen increase the risk of miscarriage, we could try to develop treatments that lower these levels and increase the chance of a healthy pregnancy.

"It has taken medicine a long time to realise sperm health has a role to play in miscarriage ' and that the cause doesn't lie solely with women. Now we realise both partners contribute to recurrent miscarriage, we can hopefully get a clearer picture of the problem and start to look for ways of ensuring more pregnancies result in a healthy baby."

## High fat diet linked to unfavourable changes in gut bacteria and inflammatory triggers

A high fat diet is linked to unfavourable changes in the type and numbers of gut bacteria – collectively known as the microbiome – as well as a rise in inflammatory triggers in the body, finds the first study of its kind, published online in the journal *Gut*.

These effects may sow the seeds for the development of metabolic disorders, such as diabetes, and heart disease and stroke over the longer term, warn the researchers.

The findings may be particularly im-





portant for countries where dietary habits are becoming more ‘Westernised’ in tandem with increasing levels of population wealth, they add.

Previous experimental research suggests that a high fat diet creates an imbalance in gut bacteria and makes the gut ‘leaky’, while observational studies suggest that diet is strongly linked to the volume and type of bacteria in the gut.

The researchers wanted to see if different levels of dietary fat might alter gut bacteria in healthy young adults from China, where dietary habits are moving from a traditional low fat, high carb diet, to one relatively high in fat and low in carbs.

The researchers split 217 healthy 18 to 35-year olds of normal weight into three dietary groups by altering the ratio of carbs – white rice and wheat flour – and fat, mostly soybean oil – but otherwise, keeping fibre and protein content the same.

The three diets were: low fat, equivalent to 20% of energy intake; moderate fat, equal to 30 per cent of energy intake; and high fat, accounting for 40% of energy intake.

Each participant stuck to their particular diet for six months, and its impact on their gut bacteria and inflammatory triggers was assessed in blood and faecal samples taken at the start and end of the six months.

After six months participants in all three groups had lost weight, with those on the low fat diet losing the most. But certain changes, with potential implications for long term health, were evident in the samples from the high fat diet group.

Although there were no major changes in the overall volume of gut bacteria among the three groups, the numbers of beneficial bacteria that produce short chain fatty acids, including butyrate, had increased in the low fat diet group.

Butyrate is a key energy source for bowel cells and has anti-inflammatory properties.

By contrast, the numbers of these beneficial bacteria had fallen in the high fat diet group, while numbers of ‘unhelpful’ bacteria that have been found in the guts of people with type 2 diabetes, for example, had increased.

Certain bacteria, such as *Blautia* species, which were associated with lower cholesterol levels, were abundant among those on the low fat diet. *Bacteroides* species, which were associated with higher cholesterol levels, were more common among those on the high fat diet.

What’s more, the higher fat diet was associated with significant and potentially detrimental changes in long chain fatty acid metabolism, resulting in higher levels of chemicals that are thought to trigger inflammation. The opposite was true for the low fat diet.

The researchers emphasise that sampling was only done at the start and finish of the trial, and a more complete picture of microbial changes would have emerged with more frequent sampling.

And as all three groups lost weight, it’s not entirely clear whether the weight loss prompted the changes seen, or vice versa, and as the study participants were all young, healthy, and of normal weight, the findings might not be more widely applicable, they add.

But the findings do seem to illustrate the need to curb dietary fat intake, they suggest.

“Compared with a lower fat diet, long-term consumption of a higher fat diet appears to be undesirable... for young healthy adults whose diet is in transition from the traditionally consumed lower fat, higher carbohydrate diet to one characterised by an appreciably higher fat content,” the researchers conclude.

But their findings might also have implications for other countries, they suggest. “These findings might also have relevance in developed countries in which fat intake is already high,” they add.

- doi: 10.1136/gutjnl-2018-317609

## In mice, researchers find cause of, cure for brain injury associated with gut condition in premature infants

Using a mouse model of necrotizing enterocolitis (NEC) – a potentially fatal

condition that causes a premature infant’s gut to suddenly die – researchers at Johns Hopkins say they have uncovered the molecular causes of the condition and its associated brain injury. The discovery enabled the team to combine efforts with colleagues studying brain inflammation and to identify potential drugs that reverse the brain injury in mice.

While the exact causes of NEC in newborns were unclear, the disease is known to occur in premature infants who are fed formula and suffer other stressors, such as bacterial infections. So the team developed a mouse model of NEC by separating newborn mice from their mothers and feeding them formula, subjecting them to a low oxygen chamber twice a day for four days as a stressor and making sure they had similar gut bacteria by feeding them stool from a child who had developed severe NEC. According to David Hackam, M.D., Ph.D., the Garrett Professor and Chief of Pediatric Surgery, a professor of surgery, pediatrics and cell biology at the Johns Hopkins University School of Medicine, not only did these mice develop NEC, their brains also showed the same injury as seen in humans and impaired brain function when older. At this point, they were ready to figure out what was causing NEC-associated brain injury in these mice.

First, they looked at whether the immune cells of the brain, so-called microglia, were activated in these NEC mice, which would signify some sort of inflammation. Indeed, the microglia were activated. Others had shown that a protein called TLR4, which binds to bacteria in the gut, is also able to activate microglia in the brain. So they genetically engineered mice to not contain TLR4 on the microglia and gave these mice NEC. The researchers found that these mice did not develop NEC-associated brain injury, suggesting that TLR4 is the cause of that injury.

The team then sought to understand what it is about this gut condition that leads to brain injury. Their previous research had revealed that TLR4 protein was also



in the gut. According to Dr Hackam, TLR4 is present in the developing foetal gut at high levels. Those levels drop in full-term infants after delivery. Infants born prematurely, however, maintain high levels of TLR4 in their gut. TLR4 in NEC guts cause cells to release another protein, HMGB1. The team engineered mice to lack HMGB1 and then gave them NEC. These mice showed less microglial activation in the brain than nonengineered mice with NEC, implying that, indeed, the HMGB1 generated by TLR4 in an inflamed gut is the cause of NEC-associated brain injury.

The work originated through a chance conversation. “One of the cool things about Johns Hopkins is that it’s full of smart people studying all kinds of things. One of the first people I met when I came here in 2014 was Sujatha Kannan, who was studying brain injury in rabbits and had recently shown that an anti-inflammatory applied to the brain of rabbits could prevent cerebral palsy,” says Dr Hackam. So, Dr Hackam and Dr Kannan Rangaramanujam teamed up to see if this would work in NEC mice. They fed nanoparticles containing antioxidants and tagged with a fluorescent molecule to mice with NEC and examined mouse brains to see where the glowing molecules accumulated.

Sure enough, the brains glowed in the same brain regions where activated microglia are found. Additionally, these brains contained fewer activated microglia, suggesting that the nanoparticle drugs could protect the brain from NEC-associated brain injury.

“We really had to change our thinking from NEC being not only a gut condition to really being a gut-brain condition,” says Dr Hackam. “While this condition manifests more immediately in the gut, neonatologists should also focus on a brain-protective strategy, which could include surgery sooner, gut rest and antibiotics.

“This is a devastating disease, but now that we more clearly understand the molecular underpinnings,” says Dr Hackam,

“we are eager to see if it holds true in other models and in patients, so that we have a real chance at ultimately doing better for these babies and their parents.”

## Researchers find new IVF technique PICSi does not increase likelihood of having baby

Treating male infertility using a new IVF technique called PICSi, which is already offered in some private clinics, does not increase the likelihood of having a baby, according to the results of a randomised controlled trial.

During the PICSi treatment, sperm were selected to fertilise eggs based on whether they could bind to hyaluronan, a substance normally found surrounding the surface of eggs.

In a trial involving over 2,700 couples across the UK, researchers looked at the difference that hyaluronan made to the success rate of treatment for male infertility following injection of PICSi-selected sperm into the egg.

Led by the University of Leeds, the study found no meaningful difference in full-term live births using the new PICSi technique, with a success rate of around one in four couples for both the PICSi and the standard ICSI treatment.

Published in *The Lancet*, the study was the largest randomised controlled trial assessing whether or not PICSi would lead to more live births than current techniques, providing vital evidence to help guide both clinics and couples who are making decisions about treatment for male infertility.

Although PICSi treatment did not significantly increase the number of live births, the researchers found that it significantly reduced the number of miscarriages by 39% overall (4.3% of couples on PICSi experienced miscarriage compared with 7.0% on ICSI).

The couples involved in the trial were randomly assigned to either the standard ICSI treatment, or the new PICSi treatment, which costs more and is already offered in some fertility clinics, despite the lack of evidence that it increases success rates.

Lead author Dr David Miller, Andrologist at the University of Leeds, said: “ICSI treatment is currently used by millions of couples around the world and is becoming the dominant treatment for infertility in many places, so any improvements that can be made to the technique have the potential to create a widespread positive impact.

“Our findings, however, suggest that more work is needed to refine and improve PICSi before it can be more widely recommended to treat infertility.

“This trial has paved the way for further research to focus on miscarriage and look into exactly how and why hyaluronan-selected sperm can reduce the incidence of this devastating outcome.”

Co-author Professor Yakoub Khalaf, Medical Director and Consultant Gynaecologist at Guy’s and St Thomas’ NHS Foundation Trust, said: “Couples can be put under pressure to consider add-ons and other techniques that give them added hope and expectations of successful treatment, but it is important that there is good evidence to support their use.

“We hope these new findings can help couples who are considering IVF to decide which treatments to choose.

“IVF success rates have remained at roughly 25% of all treatment cycles for the past decade, so it is vital that we keep developing new effective techniques aimed at improving success rates.”

PICSi treatment is different to the commonly offered IVF treatment add-on ‘embryo glue’, as PICSi involves pre-selecting sperm based on whether or not they bind to hyaluronan. ‘Embryo glue’ involves the fertilised embryos being coated in hyaluronan to increase their chances of implanting in the womb.

IVF is used to treat both female and male infertility, which each account for around half of referrals to IVF clinics for assisted conception. In treating male infertility, embryologists manually choose the best sperm with which to fertilise an egg, by sight for ICSI and by hyaluronan binding for PICSi, as the sperm would be less able to cause pregnancy naturally.

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# Researchers develop *hachimoji* DNA – a synthetic 8 base pair double helix

In a research breakthrough funded by NASA, scientists have synthesized a molecular system that, like DNA, can store and transmit information. This unprecedented feat suggests there could be an alternative to DNA-based life, as we know it on Earth – a genetic system for life that may be possible on other worlds.

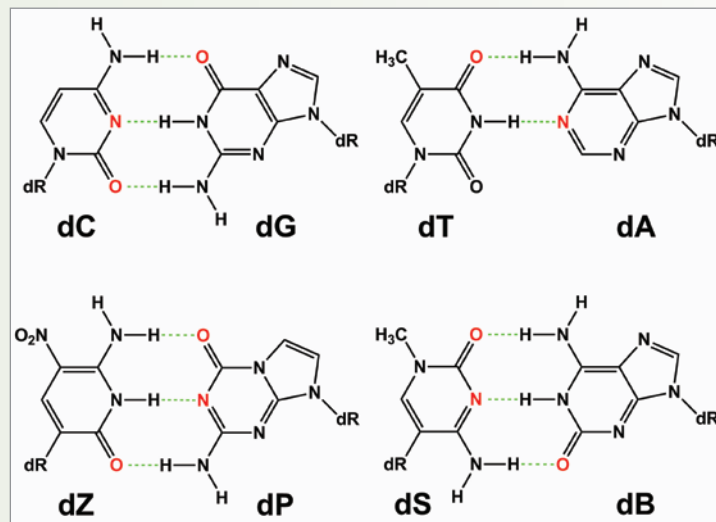
This new molecular system, which is not a new life form, suggests scientists looking for life beyond Earth may need to rethink what they are looking for. The research appears in February 22, 2019 issue of Science Magazine: “*Hachimoji DNA and RNA: A genetic system with eight building blocks*”.

DNA is a complex molecule that stores and transmits genetic information, is passed from parent to offspring in all living organisms on Earth, and its components include four key ingredients called nucleotides – all standard for life as we know it. But, what about life on other worlds?

“Life detection is an increasingly important goal of NASA’s planetary science missions, and this new work will help us to develop effective instruments and experiments that will expand the scope of what we look for,” said Lori Glaze, acting director of NASA’s Planetary Science Division.

One way to imagine the kinds of foreign structures found on other worlds is to try to create something foreign on Earth. A team of researchers, led by Steven Benner at the Foundation for Applied Molecular Evolution in Alachua, Florida, successfully achieved the fabrication of a new informational molecular system that is like DNA, except in one key area: The new molecule has eight informational ingredients instead of four.

The synthetic DNA includes the four nucleotides present in Earth life – adenine, cytosine, guanine, and thymine – but also four others that mimic the structures of the informational ingredients in regular DNA. The result is a double-helix structure that can store and transfer information.



Base pairings in hachimoji DNA (left) and hachimoji RNA (right). The natural bases are in the upper row; the unnatural, synthetic bases are in the lower row. Hydrogen bonds are dashed green lines, with acceptor atoms in red.

Benner’s team, which collaborated with laboratories at the University of Texas in Austin, Indiana University Medical School in Indianapolis, and DNA Software in Ann Arbor, Michigan, dubbed their creation “hachimoji” DNA (from the Japanese “hachi,” meaning “eight,” and “moji,” meaning “letter”). Hachimoji DNA meets all the structural requirements that allow our DNA to store, transmit and evolve information in living systems.

“By carefully analyzing the roles of shape, size and structure in hachimoji DNA, this work expands our understanding of the types of molecules that might store information in extraterrestrial life on alien worlds,” said Benner.

Scientists have much more to do on the question of what other genetic systems could serve as the foundation for life, and where such exotic organisms could be found. However, this study opens the door to further research on ways life could structure itself in environments that we consider inhospitable, but which might be teeming with forms of life we haven’t yet imagined.


“Incorporating a broader understanding of what is possible in our instrument design and mission concepts will result in a more inclusive and, therefore, more effective

search for life beyond Earth,” said Mary Voytek, senior scientist for Astrobiology at NASA Headquarters.

One of NASA’s goals is to search for life on other planets like Mars, where there was once flowing water and a thick atmosphere, or moons of the outer solar system like Europa and Enceladus, where vast water oceans churn under thick layers of ice. What if life on those worlds doesn’t use our DNA? How could we recognize it? This new DNA may be the key to answering these questions and many more.

This work also interests those interested in information as part of life.

“The discovery that DNA with eight nucleotide letters is suitable for storing and transmitting information is a breakthrough in our knowledge of the range of possibilities necessary for life,” said Andrew Serazin, president of Templeton World Charity Foundation in Nassau, The Bahamas, which also supported this work. “This makes a major contribution to the quest supported by Templeton World Charity Foundation to understand the fundamental role that information plays in both physics and biology”.

• You can read more about this breakthrough in Science  
doi: 10.1126/science.aat0971 

# NEWS FROM THE World Health Organisation



## International push to improve food safety

Greater international cooperation is needed to prevent unsafe food from causing ill health and hampering progress towards sustainable development, world leaders said at the First International Food Safety Conference, in Addis Ababa, on February 12, organized by the African Union (AU), the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Trade Organization (WTO).

A follow-up event, the International Forum on Food Safety and Trade, which will focus on interlinkages between food safety and trade, is scheduled to be hosted by WTO in Geneva (23-24 April). The two meetings are expected to galvanize support and lead to actions in the key areas that are strategic for the future of food safety.

Food contaminated with bacteria, viruses, parasites, toxins or chemicals causes more than 600 million people to fall ill and 420,000 to die worldwide every year. Illness linked to unsafe food overloads healthcare systems and damages economies, trade and tourism. The impact of unsafe food costs low- and middle-income economies around \$95 billion in lost productivity each year. Because of these threats, food safety must be a paramount goal at every stage of the food chain, from production to harvest, processing, storage, distribution, preparation and consumption,

conference participants stressed.

“The partnership between the African Union and the United Nations has been longstanding and strategic,” said African Union Commission chairperson Moussa Faki Mahamat. “This food safety conference is a demonstration of this partnership. Without safe foods, it is not possible to achieve food security,” he said.

“There is no food security without food safety,” agreed FAO Director-General José Graziano da Silva during his remarks. “This conference is a great opportunity for the international community to strengthen political commitments and engage in key actions. Safeguarding our food is a shared responsibility. We must all play our part. We must work together to scale up food safety in national and international political agendas,” he said.

“Food should be a source of nourishment and enjoyment, not a cause of disease or death,” said Dr Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization. “Unsafe food is responsible for hundreds of thousands of deaths every year, but has not received the political attention it deserves. Ensuring people have access to safe food takes sustained investment in stronger regulations, laboratories, surveillance and monitoring. In our globalized world, food safety is everyone’s issue.”

“Food safety is a central element of public health and will be crucial in achieving the 2030 Sustainable Development Goals,” WTO Director-General Roberto Azevedo said. “Trade is an important force to lift people out of poverty... when we reconvene in Geneva in April we will consider these issues in more depth,” he added.

Technological advances, digitalization, novel foods and processing methods provide a wealth of opportunities to simultaneously enhance food safety, and improve nutrition, livelihoods and trade. At the same time, climate change and the globalization of food production,

coupled with a growing global population and increasing urbanization, pose new challenges to food safety. Food systems are becoming even more complex and interlinked, blurring lines of regulatory responsibility. Solutions to these potential problems require intersectoral and concerted international action.

A central theme of the conference is that food safety systems need to keep pace with the way food is produced and consumed. This requires a sustained investment and coordinated, multi-sectoral approaches for regulatory legislation, suitable laboratory capacities, and adequate disease surveillance and food monitoring programmes, all of which need to be supported by information technologies, shared information, training and education.

## WHO calls for fulfilment of the right to health for Palestinians

Every cancer patient has the right to health. This means being able to access quality and acceptable health care and to enjoy the conditions of life that support staying healthy. Restrictions to accessing essential health services are one of the major barriers to the right to health for Palestinians living in the West Bank and Gaza Strip. Restrictions affect cancer patients at a vulnerable point in their lives, when they need specialist care and services for diagnosis and treatment. The World Health Organization calls for the protection and fulfilment of the right to health for all Palestinians.

After being diagnosed with cancer, patients in Gaza may often have to wait for months before being able to receive treatment. Getting a permit to access the health care needed outside can be a stressful and unpredictable process, and many apply multiple times before being able to exit. Even then, some patients are never able to secure the permits they need to access care.

The ability of Gaza’s hospitals to provide adequate diagnosis and treatment



to cancer patients is severely limited due to chronic shortages of medicines and lack of medical equipment. Nuclear medicine scanning needed for staging cancers, radiotherapy equipment and some specialized surgeries are unavailable. More than half of essential chemotherapy drugs were at less than a month's supply throughout 2018.

Many patients need health care elsewhere in the occupied Palestinian territory or abroad. But to leave the Gaza Strip for treatment, they must obtain a permit from Israeli authorities. This process can take up to several months, and even then some patients may be unsuccessful in securing access to travel for health care. In 2018, 39% of patient applications for permits to exit Gaza for health care were unsuccessful.

64-year-old Samira was diagnosed with uterine cancer in 2016. She underwent surgery but then required follow-up treatment unavailable in Gaza. Doctors referred Samira for radiotherapy to East Jerusalem. It took her more than 6 months and 5 permit applications to finally exit Gaza in June 2018. "All this time I was suffering from abnormal bleeding. It was a matter of life and death. Why was I denied a permit?" she says.

Proper cancer diagnosis and effective treatment are essential to improve the prognosis of patients and their chance of survival. The 5-year survival rate for breast cancer can exceed 80% if early detection and essential treatment services are available and accessible. In Gaza, however, it is significantly lower – only 65% of women with breast cancer survive 5 years after diagnosis.

Khadijah, a 32-year-old mother of 4, noticed something unusual with her breast in December 2017. Soon doctors confirmed she had breast cancer. In January 2018, Khadijah applied for a permit to go to Augusta Victoria Hospital in East Jerusalem for a specialized investigation – to see whether the cancer had spread and if so, how far. Her permit was denied. She started receiving chemotherapy in Gaza, but for optimal treatment surgery was needed. In July, Khadijah reapplied for a permit, and

again was denied. She decided to change her treatment destination to Egypt. Khadijah's second attempt to leave Gaza to Egypt was finally successful. She had surgery in August 2018, 7 months after diagnosis.

## Nearly 30 million sick and premature newborns in dire need of treatment every year

Nearly 30 million babies are born too soon, too small or become sick every year and need specialized care to survive, according to a new report by a global coalition that includes UNICEF and WHO.

"When it comes to babies and their mothers, the right care at the right time in the right place can make all the difference," said Omar Abdi, UNICEF Deputy Executive Director. "Yet millions of small and sick babies and women are dying every year because they simply do not receive the quality care that is their right and our collective responsibility."

The report, *Survive and Thrive: Transforming care for every small and sick newborn*, finds that among the newborn babies most at risk of death and disability are those with complications from prematurity, brain injury during childbirth, severe bacterial infection or jaundice, and those with congenital conditions. Additionally, the financial and psychological toll on their families can have detrimental effects on their cognitive, linguistic and emotional development.

"For every mother and baby, a healthy start from pregnancy through childbirth and the first months after birth is essential," said Dr Soumya Swaminathan, Deputy Director General for Programmes at WHO. "Universal health coverage can ensure that everyone – including newborns – has access to the health services they need, without facing financial hardship. Progress on newborn health care is a win-win situation – it saves lives and is critical for early child development thus impacting on families, society, and future generations."

With nurturing care, these babies can live without major complications. The

report shows that by 2030, in 81 countries, the lives of 2.9 million women, stillborns and newborns can be saved with smarter strategies. For example, if the same health team cares for both mother and baby through labour, birth and beyond, they can identify problems early on.

In addition, almost 68% of newborn deaths could be averted by 2030 with simple fixes such as exclusive breastfeeding; skin-to-skin contact between the mother or father and the baby; medicines and essential equipment; and access to clean, well-equipped health facilities staffed by skilled health workers. Other measures like resuscitating a baby who cannot breathe properly, giving the mother an injection to prevent bleeding, or delaying the cutting of the umbilical cord could also save millions.

According to the report, the world will not achieve the global target to achieve health for all unless it transforms care for every newborn. Without rapid progress, some countries will not meet this target for another 11 decades. To save newborns, the report recommends:

- Providing round-the-clock inpatient care for newborns seven days a week.
- Training nurses to provide hands-on care working in partnership with families.
- Harnessing the power of parents and families by teaching them how to become expert caregivers and care for their babies, which can reduce stress, help babies gain weight and allow their brains to develop properly.
- Providing good quality of care should be a part of country policies, and a lifelong investment for those who are born small or sick.
- Counting and tracking every small and sick newborn allows managers to monitor progress and improve results.
- Allocating the necessary resources, as an additional investment of US\$ 0.20 cents per person can save 2 of every 3 newborns in low- and middle-income countries by 2030.

Almost three decades ago, the Convention on the Rights of the Child guaranteed every newborn the right to the highest



# NEWS FROM THE World Health Organisation

standard of health care, and it is time for countries around the world to make sure the legislative, medical, human and financial resources are in place to turn that right into a reality for every child, the report says.



*Survive and Thrive: Transforming care for every small and sick newborn*  
[www.who.int/maternal\\_child\\_adolescent/documents/care-small-sick-newborns-survive-thrive](http://www.who.int/maternal_child_adolescent/documents/care-small-sick-newborns-survive-thrive)

## Traffic accidents leading killer of children and young people

A new report by the World Health Organization (WHO) indicates road traffic deaths continue to rise, with an annual 1.35 million fatalities. The WHO 'Global status report on road safety 2018' highlights that road traffic injuries are now the leading killer of children and young people aged 5-29 years.

"These deaths are an unacceptable price to pay for mobility," said WHO Director-General, Dr Tedros Adhanom Ghebreyesus. "There is no excuse for inaction. This is a problem with proven solutions. This report is a call for governments and partners to take much greater action to implement these measures."

The WHO Global status report on road safety 2018 documents that despite an increase in the overall number of deaths, the rates of death relative to the size of the world population have stabilized in recent years. This suggests that existing road safety efforts in some middle- and high-income countries have mitigated the situation.

"Road safety is an issue that does not receive anywhere near the attention it deserves – and it really is one of our great opportunities to save lives around the world," said Michael R Bloomberg, Founder and CEO of Bloomberg Philanthropies and WHO Global Ambassador for Noncommunicable Diseases and Injuries. "We know which interventions work. Strong policies and enforcement, smart road design, and powerful public awareness campaigns can save millions of lives over the coming decades."

In the settings where progress has

been made, it is largely attributed to better legislation around key risks such as speeding, drinking and driving, and failing to use seat-belts, motorcycle helmets and child restraints; safer infrastructure like sidewalks and dedicated lanes for cyclists and motorcyclists; improved vehicle standards such as those that mandate electronic stability control and advanced braking; and enhanced post-crash care.

The report documents that these measures have contributed to reductions in road traffic deaths in 48 middle- and high-income countries. However, not a single low-income country has demonstrated a reduction in overall deaths, in large part because these measures are lacking.

In fact, the risk of a road traffic death remains three times higher in low-income countries than in high-income countries. The rates are highest in Africa (26.6 per 100 000 population) and lowest in Europe (9.3 per 100 000 population). On the other hand, since the previous edition of the report, three regions of the world have reported a decline in road traffic death rates: Americas, Europe and the Western Pacific.

Variations in road traffic deaths are also reflected by type of road user. Globally, pedestrians and cyclists account for 26% of all road traffic deaths, with that figure as high as 44% in Africa and 36% in the Eastern Mediterranean. Motorcycle riders and passengers account for 28% of all road traffic deaths, but the proportion is higher in some regions, e.g. 43% in South-East Asia and 36% in the Western Pacific.



Global status report on road safety 2018  
[www.who.int/violence\\_injury\\_prevention/road\\_safety\\_status/2018](http://www.who.int/violence_injury_prevention/road_safety_status/2018)

## New WHO-ITU standard aims to prevent hearing loss among 1.1 billion young people

Nearly 50% of people aged 12-35 years – or 1.1 billion young people – are at risk of hearing loss due to prolonged and excessive exposure to loud sounds, including music they listen to through personal audio devices. Ahead of World Hearing Day (3 March), the World Health Organiza-

tion (WHO) and the International Telecommunication Union (ITU) issued a new international standard for the manufacture and use of these devices, which include smartphones and audio players, to make them safer for listening.

"Given that we have the technological know-how to prevent hearing loss, it should not be the case that so many young people continue to damage their hearing while listening to music," says Dr Tedros Adhanom Ghebreyesus, WHO Director-General.

Over 5% of the world's population – or 466 million people – has disabling hearing loss (432 million adults and 34 million children); impacting on their quality of life. Overall, it is suggested that half of all cases of hearing loss can be prevented through public health measures.

The Safe listening devices and systems: a WHO-ITU standard recommends that personal audio devices include:

- "Sound allowance" function: software that tracks the level and duration of the user's exposure to sound as a percentage used of a reference exposure.
- Personalized profile: an individualized listening profile, based on the user's listening practices, which informs the user of how safely (or not) he or she has been listening and gives cues for action based on this information.
- Volume limiting options: options to limit the volume, including automatic volume reduction and parental volume control.
- General information: information and guidance to users on safe listening practices, both through personal audio devices and for other leisure activities.

WHO recommends that governments and manufacturers adopt the voluntary WHO-ITU standard. Civil society, in particular professional associations and others that promote hearing care, also has a role to play in advocating for the standard and in raising public awareness about the importance of safe listening practices so that consumers demand products that protect them from hearing loss. The WHO-ITU toolkit for implementation of the global standard for safe listening devices provides practical guidance on how to do this. MEH

# Diabetes patients should be prescribed monitored physical activity



Catherine Heath

Patients with type 2 diabetes should be prescribed physical activity to control blood sugar and improve heart health. That is one of the recommendations in a position paper<sup>1</sup> of the European Association of Preventive Cardiology (EAPC), a branch of the European Society of Cardiology (ESC). The paper is published 15 January 2019 in the *European Journal of Preventive Cardiology*, a journal of the ESC.

“Sedentary lifestyles and unhealthy diets are the most important drivers of the increasing number of patients with type 2 diabetes and cardiovascular problems such as heart attacks,” said first author Dr Hareld Kemps, a cardiologist at Máxima Medical Centre, Veldhoven, the Netherlands. “Diabetes doubles the risk of mortality, but the fitter patients become the more that risk declines. Unfortunately, the majority of patients do not engage in exercise programmes.”

One in 11 adults worldwide have diabetes, of which 90% is type 2 diabetes. Nearly all patients with type 2 diabetes develop cardiovascular complications, which are the leading causes of death in this group.

The paper provides practical recommendations for doctors on how to motivate patients to incorporate physical activity into their daily routine, set achievable and measurable goals, and design individualised exercise training programmes to meet those goals.

“Just advising patients to exercise, which is what doctors typically do, is not enough,” said Dr Kemps. “Patients

must be assessed for comorbidities, risks related to exercise, and personal preferences. This will be cost effective in the long run so we have to wake up policy makers and healthcare insurers to pay for it. That needs clinicians to take the lead and call for programmes to be reimbursed.”

## Personalised exercise plan

Patients should see their doctor for a personalised plan, and those with health insurance should ask if exercise programmes are covered, said Dr Kemps. “There are also steps patients can take without needing to see a doctor first, such as interrupting sitting time and doing moderate exercise like walking and cycling.”

Long-term adherence can be improved by setting early achievable goals that are measurable, and adapting exercise plans to patients’ preferences. Remote guidance also looks promising, with patients monitoring themselves with smartwatches then sending data to a health professional for feedback.

Practical and specific goals tend to be motivational, said Dr Kemps. “For an elderly person this could be climbing the stairs in their home or walking to the supermarket – achievements that will really improve their quality of life. Being able to use less medication because of better glycaemic control is also an incentive.”

As for clinical targets, cardiorespiratory fitness and glycaemic control are the top two. Both improve with exercise training, the changes can be measured, and they are directly related to wellbeing, morbidity and mortality. Exercise also helps to lower blood pressure and harmful blood lipids.

Just advising patients to exercise, which is what doctors typically do, is not enough.

Dr Kemps noted that weight loss might not be the best target for exercise training. “It’s difficult to lose weight with exercise only and if that is the main target patients may become demotivated and stop exercising,” he said. “Weight loss is important, but it needs to be part of a multidisciplinary intervention that includes nutrition.”

As for the type and intensity of exercise, this needs to be personalised to each patient. High intensity interval training – for example alternating moderate and vigorous walking – is most effective at boosting fitness and controlling blood sugar, but may be unsafe for patients who develop arrhythmias (abnormal heart rhythm) during exercise or have ischaemia (restricted blood flow to the heart).

Dr Kemps said: “I can’t stress enough how effective even small increases in activity can benefit patients with type 2 diabetes and heart problems. Interrupting sitting with brief bouts of walking improves glucose control, while two hours of brisk walking per week reduces the risk of further heart problems.”

• doi: 10.1177/2047487318820420



# Researchers launch trial to test breath biopsy for multiple cancers

Researchers have launched a clinical trial to develop a breath test, analysing molecules that could indicate the presence of cancer at an early stage. This is the first test of its kind to investigate multiple cancer types.

Owlstone Medical, a global diagnostics company developing a breathalyzer for applications in early disease detection and precision medicine, and Cancer Research UK, launched the PAN Cancer trial for Early Detection of Cancer in Breath.

Researchers in the trial are using Owlstone Medical's Breath Biopsy platform to collect samples, including from healthy individuals as trial controls, to analyze volatile organic compounds (VOCs) in the breath. The trial aims to identify VOCs that can be used as breath-based biomarkers to detect and differentiate different cancer types, thereby improving early detection.

This approach holds great promise as cancer cells display altered metabolism even at the very earliest stage of disease, affecting the pattern of the VOCs exhaled. By identifying the changing pattern of VOCs early, the Breath Biopsy technology could detect cancer at the earliest stage of disease, when treatments are more effective and more lives can be saved.

The Breath Biopsy platform includes ReCIVA, a proprietary sample collection device that can take stable breath samples anywhere, the world's only commercial Breath Biopsy Laboratory located in Cambridge, UK, and the development of the world's largest Digital Breath

Biobank matched to patient phenotype.

Owlstone Medical is deploying the platform to address some of the key challenges of 21st century healthcare. The focus is on the early detection of disease with an emphasis on cancer, with clinical trials underway to develop breath tests for the early detection of lung and colorectal cancer, and on precision medicine through partnerships with large pharmaceutical

Technologies such as this breath test have the potential to revolutionize the way we detect and diagnose cancer in the future.

companies including AstraZeneca and GlaxoSmithKline to enable therapeutics to be deployed more effectively. Owlstone Medical's technology is currently in use at over 100 sites worldwide.

Dr David Crosby, head of early detection research at Cancer Research UK, said: "Technologies such as this breath test have the potential to revolutionize the way we detect and diagnose cancer in the future. Early detection research has faced an historic lack of funding and industry interest, and this work is a shining example of Cancer Research UK's commitment to reverse that trend and drive vital progress in shifting cancer diagnosis towards earlier stages."

Professor Rebecca Fitzgerald, lead trial investigator at the Cancer Research UK Cambridge Centre, said: "We urgently need to develop new tools, like this breath test, which could help to detect and diagnose cancer earlier, giving patients the best chance of surviving their disease. Through this clinical trial we hope to find signatures in breath needed to detect cancers earlier – it's the crucial next step in developing this technology. Owlstone Medical's Breath Biopsy technology is the first to test across multiple cancer types, potentially paving the way for a universal breath test."

## Recruitment

The trial is recruiting 1,500 patients at Addenbrooke's Hospital in Cambridge, UK, who have been referred from their GP with these specific types of suspected cancer. Prior to other diagnostic tests, breath samples will be collected using Owlstone Medical's ReCIVA Breath Sampler and processed in Owlstone Medical's Breath Biopsy laboratory in Cambridge.

The clinical trial will first look at patients with suspected oesophageal and stomach cancers and will expand to prostate, kidney, bladder, liver and pancreatic cancers in the coming months. Research is anticipated to run through 2021, and if the technology proves to accurately identify cancer the team hope that Breath Biopsy could in the future be used routinely in GP practices to determine whether to refer patients for further diagnostic tests.



# COLORECTAL CANCER ISN'T JUST TREATABLE. IT'S BEATABLE.

Early detection often allows for more treatment options. One such option is a minimally invasive surgical approach that can improve patient outcomes and also reduce cost.



## 10X SMALLER SCAR ON AVERAGE<sup>1,2,†</sup>

†Compared to patients who have open surgery.

## 19% MORE LIKELY TO SURVIVE 10 YEARS AFTER SURGERY<sup>3,‡</sup>

‡Compared to patients who have open surgery.

## 12% REDUCTION IN HOSPITAL COSTS ON AVERAGE<sup>4,5</sup>



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Billy Boyle, co-founder and CEO at Owlstone Medical, said: “There is increasing potential for breath-based tests to aid diagnosis, sitting alongside blood and urine tests in an effort to help doctors detect and treat disease. The concept of providing a whole-body snapshot in a completely non-invasive way is very powerful and could reduce harm by sparing patients from more invasive tests that they don’t need.”

“Our technology has proven to be extremely effective at detecting VOCs in the breath, and we are proud to be working with Cancer Research UK as we look to apply it towards the incredibly important area of detecting early-stage disease in a range of cancers in patients.”

Almost half of cancers are diagnosed at a late stage in England. This highlights the importance of early detection, particularly for diseases like oesophageal cancer where only 12% of oesophageal cancer patients survive their disease for 10 years or more. **MEH**

## What is Breath biopsy?

Breath Biopsy represents an entirely new way to measure the chemical makeup of breath by measuring volatile organic compounds (VOCs), gaseous molecules that can be sampled quickly and non-invasively from breath, and enabling whole-body sampling. These compounds are produced as the end product of metabolic processes within the body, meaning that underlying changes in metabolic activity can produce particular patterns of VOCs characteristic of specific diseases.

VOCs originating from all parts of the body are captured in breath, making Breath Biopsy applicable to a wide range of diseases including cancer, inflammatory disease, infectious disease, metabolic disease, cardiovascular disease and respiratory disease. The nature of Breath Biopsy, and VOC biomarkers, make them perfectly suited to addressing two of the major challenges of healthcare today: early detection and precision medicine.

Breath collection is carried out using Owlstone Medical’s ReCIVA Breath Sampler, which ensures reliable, reproducible collection of VOCs. Subjects breathe a controlled supply of air, and samples of their exhaled breath are captured and stabilized on Breath Biopsy Cartridges, which can then be shipped for analysis with Owlstone Medical’s Breath Biopsy analytical platform, using mass spectrometry or FAIMS to determine their VOC profile. Advanced data analytic techniques can then be applied in order to pinpoint the VOCs of interest.

# Noninvasive liquid biopsies rapidly, accurately determine response to cancer treatment

Results of two clinical studies have added to evidence that blood-based liquid biopsies can accurately track lung cancer treatment responses by measuring circulating tumour DNA (ctDNA) during immunotherapy and related treatments.

“There is an unmet clinical need for real-time, noninvasive detection of tumor response to targeted and immune checkpoint blockade treatments,” says Victor Velculescu, M.D., Ph.D., co-director of cancer biology at the Johns Hopkins Kimmel Cancer Center. “Our studies suggest that tests using blood samples will change the way cancer patients will be treated by helping to evaluate therapeutic responses more quickly and accurately, and avoid unneeded toxicity or ineffective treatments.”

The new studies, described in the December 2018 issues of the journal *Cancer Research*, showed that tracking responses to treatment by measuring ctDNA was a more accurate way of assessing tumour growth



Drew Hays

or shrinkage than traditional imaging techniques.

In a study of 28 adult patients with advanced nonsmall cell lung cancer (NSCLC), blood samples were taken prior to anti-EGFR (epidermal growth factor receptor) or anti-HER2 (human epidermal

growth receptor 2) treatments – which target cancer growth – and at intervals thereafter.

All of the patients were seen at hospitals affiliated with The Johns Hopkins University or University of California San Diego, and were treated with osimertinib, mavelertinib, afatinib or erlotinib. Blood samples were analyzed to detect ctDNA shed by tumours into circulating blood and to track tumour burden during therapy by detecting gene mutations as well as chromosomal changes in tumour cells.

As early as a week after receiving treatment, 16 patients with molecular response to treatment had nearly complete elimination of ctDNA that could be detected in their blood samples. Eight nonresponders to the therapy had limited changes in ctDNA levels and significantly shorter progression-free survival. Overall, patient response to treatment could be detected four weeks earlier and was more accurate than CT imaging.

The researchers also say that ctDNA **▶**

analyses of patients with stable CTs or nonmeasurable disease using imaging had improved prediction of clinical outcomes compared to patients with CT imaging.

“These results indicate the potential value of early assessment of responses to targeted therapies especially when CT imaging results are in the gray area between objective response and actual disease progression,” says Alessandro Leal, M.D., a graduate student at the Kimmel Cancer Center.

The early detection of changes using ctDNA preceded responses seen in subsequent scans and allowed mutation changes in the tumours to be tracked. With these results, the study showed that measuring ctDNA for an advanced cancer can be accurate and noninvasive than with repeat CT imaging.

“Noninvasive liquid biopsies identifying tumour-specific changes provide an opportunity for widespread implementation of monitoring approaches for different cancer types in a variety of clinical settings,” says Jillian Phallen, Ph.D., postdoctoral fellow at the Kimmel Cancer Center.

### Second study

In a second study of 38 patients with NSCLC, scientists including Valsamo Anagnostou, M.D., Ph.D., assistant

professor of oncology at the Johns Hopkins University School of Medicine and a member of the Kimmel Cancer Center, measured ctDNA and immune blood cell changes to determine responses to anti-PD-1 therapy, which boosts the immune response against cancer cells.

Nine patients with a clinical response to immunotherapy had a complete reduction in ctDNA levels shortly after the initiation of therapy. In contrast, 10 nonresponders showed no significant changes or increase in ctDNA levels. Molecular response, as measured by ctDNA levels, more accurately predicted overall survival for these patients – patients without a molecular response had shorter progression-free and overall survival than molecular responders. Overall, tumour responses to the therapy that were detected using ctDNA were found nearly nine weeks earlier than with conventional imaging.

Anagnostou and colleagues also investigated changes in the immune cells in the blood of these patients. Expansion of immune cells mirrored the ctDNA reduction during therapeutic response, suggesting that ctDNA reduction in circulating blood was in line with an effective immune response.

Anagnostou says the researchers also validated their findings in a group of early stage NSCLC patients who received anti-

PD1 therapy prior to removal of their tumours. The researchers found that ctDNA molecular responses accurately captured the effect of immunotherapy. The authors also showed that reduction in tumour size after immunotherapy correlated with reductions in ctDNA levels.

“Conventional imaging does not always or quickly capture the unique timing and pattern of response to immunotherapy, highlighting the urgent need to develop biomarker-driven approaches such as measuring ctDNA in blood samples,” Anagnostou says. “Early detection of disease progression on immunotherapy opens a window of opportunity in which changes in liquid biopsies may allow patients with resistance to be rapidly identified and redirected to receive alternative therapies.”

Together, these studies show that noninvasive liquid biopsy analyses of ctDNA changes during therapy are feasible and offer a more rapid and accurate assessment of treatment response than CT imaging. Velculescu cautions that more testing will be necessary to affirm the value of the results and to see if this method works for other types of cancer. He says he hopes the studies will spur development of new therapies by being able to diagnostically measure tumor loads more accurately. **MEM**

## Molecular profiling for very early lung cancer detection

The world’s first genetic sequencing of precancerous lung lesions could pave the way for very early detection and new treatments, according to a new study led by University College London (UCL) researchers.

Before lung cancer develops, precancerous lesions are found in the airway, but only half of these will actually become lung cancer, while others will disappear or remain benign without becoming harmful. Under the microscope, the lesions look the same, making it difficult to know which lesions to treat.

In this study, published in *Nature Medicine*, researchers have for the first time, discovered the differences between the lesions that will become invasive and those that are harmless, and they

can accurately predict which lesions will become cancerous.

“Our study helps to understand the earliest stages of lung cancer development, by figuring out what’s going on inside these cells even before they become cancerous,” said the study’s lead author, Professor Sam Janes (UCL Division of Medicine and University College London Hospitals, UCLH).

“Using this information, we may be able to develop screening tests, and new treatments that could stop cancer in its tracks.”

The researchers were studying biopsies of preinvasive lung cancer lesions of patients who were seen at UCLH. They conducted tests including gene expression profiling, methylation profiling, and

whole-genome DNA sequencing on 129 biopsy samples from 85 patients.

On average, the patients were followed up for over five years post-biopsy, to see which patients developed lung squamous cell carcinoma, one of the two most common subtypes of lung cancer.

The research team identified differences in genomic features such as mutations, gene expression and chromosomal instability, finding enough differences that they could predict with near-perfect accuracy which lesions would develop into cancer by checking the lesion’s molecular profile.

### No consensus

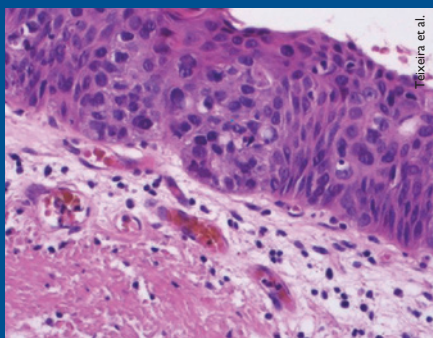
Precancerous lesions are detected by bronchoscopy, a minimally invasive test

that is often done on people with chronic cough or a history of lung cancer.

There is no consensus on treatment for precancerous lung lesions; in some countries, patients with such lesions undergo surgery, while elsewhere, patients are monitored and only treated if clear signs of cancer appear.

While bronchoscopy isn't offered to everyone at risk of lung cancer, the researchers say their findings could help to develop a simpler blood test to pick up the same molecular signals that are linked to early cancer development.

"If we can use this new understanding of cancer development to create new



Precancerous lung lesion, viewed by white light bronchoscopy (left) and autofluorescence bronchoscopy (right).

diagnostic tests, it may one day be invaluable in picking up cancer early,

enabling people to access treatment much earlier in the disease process," said co-first author Dr Adam Pennycuik of the UCL Division of Medicine.

The study could also help lead to new treatments. Some of the genes that are expressed differently in lesions that will become cancerous, have previously been identified as potential drivers of lung cancer.

"We are now continuing our research to further understand how these genes are driving cancer progression, and to see which ones could be targeted by new drug treatments," said co-first author Dr Vitor Teixeira, UCL Division of Medicine. **MEH**

## Researchers to trial innovative oral chemotherapy

An experimental chemotherapy drug that can be taken orally is moving into early phase clinical trials as part of a new partnership between Athenex, Cancer Research UK's Combinations Alliance and the NIHR Clinical Research Network Industry Alliance, announced in January.

This unique industry-academic initiative will be run through the Experimental Cancer Medicine Centres (ECMC) and the NIHR Clinical Research Network.

The partnership will enable researchers to investigate Athenex's innovative experimental drug Oraxol, the first oral formulation of the chemotherapy drug paclitaxel, in combination with other cancer treatments.

Paclitaxel is very effective at blocking the growth of cancer and is widely used for a range of cancer types, but currently it can only be given intravenously through a drip.

Oral delivery of paclitaxel is made possible by Athenex's novel orally administered gastrointestinal tract P-glycoprotein pump inhibitor, HM30181A.

HM30181A is a unique technology that enables oral absorption of a wide range of anticancer drugs, which can currently only be given intravenously due to poor oral absorption. It works by blocking the action of a protein on the surface of the gastrointestinal (GI) tract, increasing the amount of chemotherapy that reaches circulation in the bloodstream, to levels

**This exciting partnership will enable us to accelerate the development of a treatment that not only has the potential to improve patient outcomes, but also quality of life.**

where it can have a therapeutic effect on a patient's tumour.

Being able to take this type of chemotherapy orally opens up the opportunity for patients to have their treatment at home, rather than travelling to hospital regularly, and may reduce treatment delivery costs for health services.

Oraxol was recently awarded PIM (Promising Innovative Medicine) designation by the MHRA (Medicines and Healthcare products Regulatory Agency). Athenex already has a strong presence in North America and Asia; this partnership is part of a broader plan to move into Europe.

Rudolf Kwan, Athenex's Chief Medical Officer, said: "Oraxol marks a significant step forward for the development of oral chemotherapies, potentially changing the way a large proportion of cancer patients receive chemotherapy treatment. By working with Cancer Research UK's Combinations Alliance and NIHR Clinical Research Network, our goal is to develop

Oraxol in combinations that would not otherwise be possible, bringing new treatment options to more cancer patients."

The clinical trials managed by this partnership will be academically sponsored and delivered with additional support and oversight from Cancer Research UK and NIHR Clinical Research Network.

Dr Ian Walker, Cancer Research UK's director of clinical research, said: "This exciting partnership will enable us to accelerate the development of a treatment that not only has the potential to improve patient outcomes, but also quality of life.

"We look forward to exploring how this drug can be used in combination with other treatments and hope that it can play a part in addressing the urgent need for new treatments for patients with hard to treat and rare cancers."

Prof Matt Seymour, who leads for cancer research in the NIHR Clinical Research Network, said: "This is a good example of the UK's unique environment for bringing together academic researchers, industry innovators and the NHS, to join forces and design clinical research trials for more of our patients. I welcome this new alliance. Most anticancer drugs need to be given by injection in hospital, but programmes like this allowing effective drugs to be taken in tablet form at home, could potentially improve our patients' experience, and may open up opportunities for more sustained treatment, to keep cancers under better control." **MEH**

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# Anticancer vaccines gain new lease of life with personalisation techniques

Anticancer vaccines have gained a new lease of life with techniques to personalise them to individual patients. Cutting edge developments in this re-energised field were revealed at the ESMO Immuno-Oncology Congress in December in Geneva, Switzerland.

The original anticancer vaccines, launched in the late 1990s, were based on shared tumour antigens and failed to induce a potent immune response. After decades of disappointing results, a number of advances have sparked a renewed interest in the field. These include new technologies and prediction algorithms to personalise vaccines, and the introduction of checkpoint inhibitors for combination therapy.

Dr Michal Bassani-Sternberg, Group Leader, Immunopeptidomics, Hi-TIDE Laboratory, Department of Oncology, University of Lausanne, Switzerland, and the Ludwig Institute for Cancer Research in Lausanne, said: “The ‘modern anticancer vaccines’ session at the ESMO Immuno-Oncology Congress was timely since there is again a flurry of activity around anticancer vaccines. We can now customise vaccines for each patient based on the genomic information in their tumour, and the early results are promising.”

Personalisation has been made possible with high-throughput next generation sequencing. This technology identifies mutations that are unique to a patient’s tumour and are not found elsewhere in the body, meaning that a vaccine mounts a cancer-specific immune response. Algorithms can predict which neoantigens should be targeted for vaccination.

Dr Bassani-Sternberg said: “We have a good way to fish out and propose targets for vaccination. The first trials were published last year and showed that the se-

lected targets were immunogenic, meaning that vaccination induced immune responses or amplified existing immune responses against these neoantigens. In addition, the vaccines worked well with checkpoint inhibitors. We now need to see if vaccination against neoantigens leads to tumour regression in a larger cohort of patients.”

Neoantigens were explored in a dedicated session at the ESMO Immuno-Oncology Congress and were discussed in the session on modern anticancer vaccines, which also described the role of other vaccine targets. These include oncogenic proteins such as HER2, pathogens like the human papilloma virus (HPV), and prostate-specific antigens. These shared antigens are also being tested in combination with checkpoint inhibitors.

Dr Bassani-Sternberg said the combination of modern anticancer vaccines and checkpoint inhibitors appears to generate the most effective immune response.

“Vaccines can induce new responses in patients with ‘cold tumours’ which lack immune cells, thus making the environment receptive to checkpoint inhibitors,” she said.

Numerous questions remain unanswered, such as when to vaccinate patients. Should this be immediately after surgery, when there are few tumour cells left, or beforehand? Should vaccines be administered against primary tumours and metastases? Will it be necessary to give new vaccines every few months as tumours evolve naturally and in response to treatment? How and when should vaccines be combined with other therapies? And while the choice of neoantigen seems crucial, decisions are also needed on the formulation (protein-

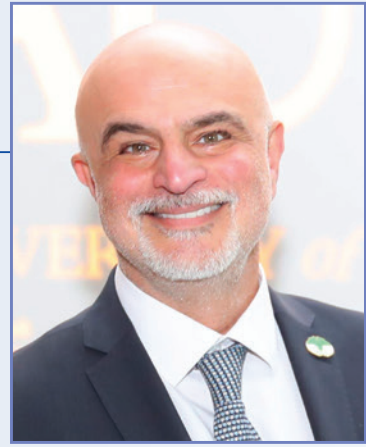
We can now customise vaccines for each patient based on the genomic information in their tumour, and the early results are promising.

based, RNA, cell-based), delivery vehicle (liposomes, virosomes, emulsions), route of administration (intranodal, intradermal), and adjuvants.

But despite these questions, vaccination appears feasible. The technology to develop vaccines is available and getting better, the vaccines are safe and immunogenic, and there is openness from the regulators to testing vaccines in clinical trials.

Dr Bassani-Sternberg said: “We are counting on new technologies that have now matured. Next generation sequencing has made identification of vaccine targets more efficient, reliable, and cheaper. The algorithms to interpret this data are benchmarked and validated for predicting which targets are most likely to be immunogenic. Sequencing technologies are only going to get better and prediction tools will become even more accurate.”

“There is great hope for vaccines,” she continued. “And they have the potential to benefit most patients because almost all tumours have targets that could be vaccinated.” MEH



Dr. Ali Taher, Professor of Hematology and Oncology and Director of The Naef K. Basile Cancer Institute at the American University of Beirut Medical Center.

American University of Beirut Medical Center

# Naef K. Basile Cancer Institute leads fight against cancer in Lebanon

The fight against cancer requires a team dedicated to keeping patients strong enough in their battle against one of the most devastating diseases, cancer. The Naef K. Basile Cancer Institute (NKBCI) at the American University of Beirut Medical Center (AUBMC) is a leading institute for adult cancer in Lebanon and the region. Their commitment to patients goes beyond the delivery of sophisticated care; the institute respects the individual needs of all those who seek their care and work to empower patients with the knowledge and support they require to successfully win their battle.

“Our patients are at the heart of what we do. We believe that all patients, of all demographics, deserve the best treatment modalities. It is our mission to reduce the burden of cancer in Lebanon and the region through the application of state-of-the-art medical knowledge and technology and the development of integrated and advanced programs in patient care, research, education, and prevention,” states Dr. Ali Taher, Professor of Hematology and Oncology and Director of NKBCI.

The new facilities in the Halim and Aida Daniel Academic and Clinical Center (Daniel ACC) contain a spacious patient and family reception area, with a friendly environment. Today, the state-of-the-art facility has established itself as a multidisciplinary center comprised of a specialized team of oncologists and doctors from different specialties who work hand in hand on providing comprehensive cancer prevention, diagnosis, and treatment.

Our faculty and staff are a group of national, regional, and international leaders in clinical and translational research. “We are, in fact, the first to develop subspecialized programs for the management of brain, breast, gastrointestinal, genitourinary, head and neck and lung cancers, in addition

to having a Palliative and Supportive Care Program, a benign and malignant hematology program, and Stem Cell Transplantation Unit,” added Dr. Taher.

At NKBCI, the well-being of all their patients comes first. This is why, they have taken the extra mile of joining efforts with TIES (Trust, Inspiration, Encouragement and Strength), an NGO that organizes inspirational activities and a variety of entertaining activities, to help patients divert their attention from sickness and focus on their inner power. Through their collaboration they were able to establish a psychosocial program that supports patients throughout their stay at the center and helps them alleviate their emotional distress.

Cancer represents a heavy burden on patients as well as on other entities in the community like the Lebanese Ministry of Public Health. As such, NKBCI plays a vital role in supporting its patients through the Cancer Support Fund (CSF) which was established in March 2018 by Hala Dahdah Abou Jaber and Dr. Taher to support needy adult cancer patients.

NKBCI consists of four major service units: Ambulatory Chemotherapy Treatment Unit (Outpatient), Inpatient Unit, Stem Cell Transplant Unit, and Radiotherapy Unit. They also have a Data Management and Clinical Research Unit that manage all current cancer research and ongoing clinical trials at the institution.

The history of the institute dates back to a generous donation made by the Naef K. Basile Foundation, following the death of Dr. Naef Basile, a Lebanese-American obstetrician-gynecologist whose lifelong wish was to give back to his country of birth, through the establishment of the NKBCI in 1995. Since its establishment, the institute has taken the challenge of advancing itself further through setting

programs that help detect cancer in its early stages leading to improved patient outcomes.


The Bone Marrow Transplant Program is JACIE accredited and has performed the first unrelated donor stem cell transplantation in Lebanon in addition to over 100 stem cell transplants per year.

Other unique services are available at the Radiation Therapy Department whose advanced equipment provides their patients with the best quality radiation treatment with reduced side effects. The team at the Department has also performed the first radiofrequency ablation of a breast mass in Lebanon.

Nursing care at NKBCI is also led by a specialized group of oncology nurses (AUBMC is the first Medical Center with MAGNET designation in the Middle East region) and dedicated oncology pharmacists.

To extend its care beyond Lebanon, NKBCI has brought international care standards to AUBMC and accordingly, they have set strong affiliations with both regional and international cancer Centers of Excellence, such as King Hussein Cancer Center (KHCC), MD Anderson Cancer Center (MDACC), and Memorial Sloan Kettering Cancer Center (MSKCC). This collaboration is in areas like advanced research and international tumor boards to discuss complex patient conditions, participate in scientific conferences as well as being more involved in Fellowship training programs.

“Advancing cancer care is a big responsibility and we, at NKBCI, are continuously seeking every opportunity to provide our patients with the latest technologies, specialized physicians and healthcare providers as well as community activities with. What unites us is an overall goal of intervening early, providing optimal cancer care, and improving outcomes for patients,” said Dr. Ali Taher. MEH



The Naef K Basile Cancer Institute at AUBMC offers a **holistic, advanced, and state-of-the-art oncology patient-centered care** that encompasses **physical, social, and psychological health treatments.**

For more information, please contact us at 00961-1-350000 ext: 7903

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Our lives are dedicated to yours





## The new Genetic-Oncology Clinic in Cook Children's identifies genetic risks of cancer for patients

Most of us know someone who has had cancer. That's because we are all at risk for developing the disease. Usually it's by chance. But in some cases, cancer develops because of our genetics and that means some of us are predisposed to developing different types of cancer.

The people who are already predisposed to developing the disease not only have a greater risk of developing cancer but also passing those genes on to their children.

Because of the advances in genetic testing and the importance of detection of those inherited cancer predispositions, Cook Children's has started the Genetic-Oncology Clinic.

"We are trying to educate families and patients to increase awareness," said Kelly Vallance, M.D., MPH. "But also to catch the cancer early, know the warning signs and find the way we are able to intervene and give these kids the normal lives they deserve. We do that by catching it early and teaching them what to look for."

The Genetic-Oncology Clinic provides care and counseling to children and their families with a predisposition to cancer. The program, one of only a few in the country, is a collaboration among pediatric oncologists, geneticists and genetic counselors who provide education, guidance, therapy and routine cancer surveillance studies when indicated for children with a predisposition to cancer.

Patients range from newborns to adults through the Life After Cancer Program at Cook Children's.

"Research coming out now recommends

Research coming out now recommends that almost all pediatric solid tumor patients, as well as certain leukemia patients, have genetic testing done to see if they are at increased risk for developing secondary malignancies.

that almost all pediatric solid tumor patients, as well as certain leukemia patients, have genetic testing done to see if they are at increased risk for developing secondary malignancies," said Heather Jernigan, a hematology and oncology clinic nurse and the nurse coordinator of Genetic-Oncology Clinic since it started a year and a half ago. "We know that almost every patient who gets cancer treatment is at risk for developing secondary malignancies. What we are learning is that with some patients with genetic predisposition syndrome that risk increases."

Becky Althaus was a catalyst to making the clinic a reality. Althaus worked with Mary Kukulich, M.D., medical director of Genetics, 40 years ago. The two of them worked together for about 19 years and Althaus said that's where she was taught about genetics. She already had a masters in nursing, and then became certified as a genetics counselor, earned her Ph.D. in genetics and a nurse practitioner. She went

on to help start genetic-oncology programs in three different locations before coming full circle by joining Cook Children's and working with Dr. Kukulich again.

"Between 10 to 14 percent of all pediatric cancers have a genetic component, so that means they have a genetic predisposition," Althaus said. "Because of that we really need to be testing most children who are diagnosed with cancer."

Genes are passed from parents to offspring and specify traits. Humans have approximately 20,000 genes. A mutation is a change in the DNA sequence that can occur in one of two types of genes:

- Somatic mutations occur in body and cells and are not passed on. They weren't born with a predisposition.
- Germline mutations occur in the eggs and sperm and can be passed on to offspring. This is a hereditary gene, meaning the child was born at risk for cancer at the moment of conception.

The Genetic-Oncology Clinic sees patients who are at risk for having cancer passed on to them genetically. That can mean their siblings or other family members could be at risk for developing the same cancer, or that the patients may eventually pass the gene on to their own children.

Explore Cook Children's Genetic-Oncology Clinic here:

[cookchildrens.org/genetic-oncology](http://cookchildrens.org/genetic-oncology)

• For more information or to refer a patient, please visit: [cookchildrensinternational.org](http://cookchildrensinternational.org)

Phone: +1-682-885-4685

E-mail: [international@cookchildrens.org](mailto:international@cookchildrens.org) 





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**When it comes to your child's health care, you want one thing... *the best.***

And sometimes finding the best pediatric specialty care means traveling outside of the country. Located in Fort Worth, Texas, Cook Children's has been serving patient families for 100 years. Just minutes from the Dallas-Fort Worth International Airport, Cook Children's is a renowned integrated pediatric health care system in the United States.

At Cook Children's, each child's team of caregivers is connected to a system of pediatric specialists, clinics, and award-winning medical center. Children see the same specialists every day while an international care coordinator focuses on all the family's needs. From flight scheduling to accommodations to recreation, our dedicated international team handles every detail.



# Researchers develop comprehensive new way to predict breast cancer risk

Scientists have created the most comprehensive method yet to predict a woman's risk of breast cancer, according to a study by Cancer Research UK published in *Genetics in Medicine*.

They have developed a way of calculating the risk of developing the disease by combining information on family history and genetics with other factors such as weight, age at menopause, alcohol consumption and use of hormone replacement therapy.

Although individually some of these things have a small impact on the likelihood of developing the disease, researchers found that by considering all of them at once, plus family history and genetics, they can identify groups of women who have different risks of developing breast cancer.

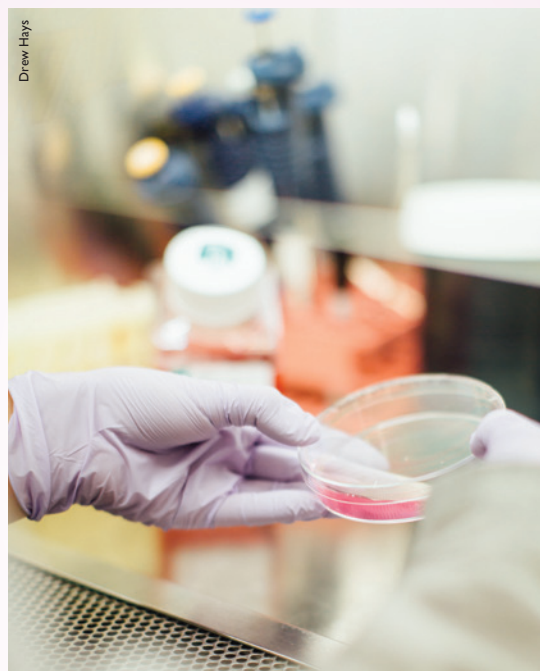
Importantly, for the first time, researchers have taken into account more than 300 genetic indicators for breast cancer. This makes calculating the risk much more precise than ever before.

From this, the researchers have created an online calculator for GPs to use in their surgeries.

Some GPs, practice nurses and genetic counsellors are testing this tool before it is considered for wider use. Doctors are prompted to answer a series of online questions about their patient including their medical and family history, whether they have any known genetic alterations linked to cancer, their weight and whether they drink alcohol.

In the future, information like this could help to tailor breast cancer screening depending on an individual's risk. For example, it could help determine what age they are first invited for breast screening or how regularly they are invited to receive it.

The risk calculation could also help



people to make decisions about preventative therapy – such as identifying women at high risk who may benefit from taking the drug tamoxifen – as well as encouraging women to think about the ways they could reduce the risk themselves, for example trying to keep a healthy weight.

Professor Antonis Antoniou, lead author at the University of Cambridge, said: “This is the first time that anyone has combined so many elements into one breast cancer prediction tool. It could be a game changer for breast cancer because now we can identify large numbers of women with different levels of risk – not just women who are at high risk.

“This should help doctors to tailor the care they provide depending on their patients' level of risk. For example, some women may need additional appointments with their doctor to discuss screening or

prevention options and others may just need advice on their lifestyle and diet.

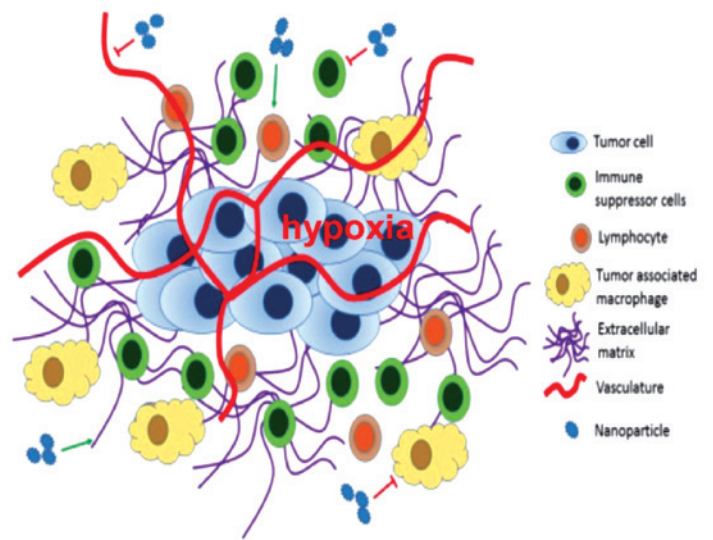
“We hope this means more people can be diagnosed early and survive their disease for longer, but more research and trials are needed before we will fully understand how this could be used.”

Dr Richard Roope, Cancer Research UK's GP expert, said: “Research like this is hugely exciting because in the future it will enable us to offer much more tailored care which will benefit patients and make best use of the services that we have available.

“Although having an increased risk of breast cancer means a woman is more likely to develop the disease – it's by no means a certainty. A woman at high risk may never get breast cancer just as a woman at low risk still could. But any woman with concerns should speak to her GP to discuss the options.” **MEH**

It could be a game changer for breast cancer because now we can identify large numbers of women with different levels of risk – not just women who are at high risk.

# Hostility of tumour microenvironment: a major challenge facing the immunotherapy war on cancer



■ By Professor S Chouaib  
Vice Chancellor - Research & Director of  
Thumbay Research Institute of Precision  
Medicine, Gulf Medical University.

Cancer is one of the deadliest diseases in the modern world. The past five years has witnessed dramatic advances in the cancer treatment through immunotherapy. Recently, the field of cancer immunotherapy, after years of failure, has seen unprecedented clinical responses, rapid drug development, and first-in-kind approvals from the U.S. Food and Drug Administration.

Newly approved immunotherapies include drugs that can manipulate the immune system and methods to genetically engineer patients' own T lymphocytes to recognize and attack their tumours (*Middle East Health*, May-June 2018). One extremely promising means to achieve anti-cancer immunity is to block the immune checkpoint pathways. However, it remains unclear why only a subset of individuals respond to treatment and how to better achieve sustained remissions. Hundreds of clinical trials are under way to see whether improved responses can be attained by combination therapy approaches.

Clearly, despite the advances being made, several obstacles still exist for the field of cancer immunotherapy. These include the inability to predict treatment efficacy and patient response; the need for additional biomarkers and; the development of resistance to cancer immunotherapies.

Future advances in cancer immunotherapy are expected to overcome and resolve many of these challenges. One of these challenges, which is attracting a lot of attention, is due to the conflict between the immune system of the host and the tumour microenvironment (TME).

It should be remembered that tumours are not autonomous masses of cells, but function as organs composed of many interdependent cell types. It is characterized by an irregular microvascular network and regions of chronically and transiently hypoxic cells. Among the metabolic changes, hypoxia plays a key role in sculpting the tumour microenvironment. It has become clear that solid tumours put up significant opposition by creating a microenvironment deficient of oxygen and glucose, thus depriving T cells of energy and pushing them to exhaustion. Clearly, the tumour microenvironment serves an important role in suppressing the antitumor immunity by its significant immune suppressive function. Therefore, future designs of immunotherapies should integrate the manipulation of the tumour microenvironment.

## Neoplastic cells

The response of neoplastic cells to immunotherapy is not solely dependent on the qualitative and/or quantitative features of the T cells and the complexity of the genomic aberrations they harbour, but is also regulated by numerous dynamic properties of the TME.

The TME consists of tumour cells, tumour-infiltrating immune cells, cancer-associated fibroblasts, the tumour vasculature and the extracellular matrix, which collectively can promote tumour transformation, protect the tumour from host immunity, support tumour growth and invasion, foster therapeutic resistance and, provide niches for dormant metastases to thrive.

The crosstalk between stroma cells and malignant cells within this environment crucially determines the fate of tumour progression, its hostility and heterogeneity.

It is also becoming clearer that the metabolic environment of the TME serves as a significant barrier to achieving greater treatment efficacy.

In considering the importance of metabolic programming in cancer cell and immune cell behaviour, we can revise our understanding of therapeutics in use today. Accordingly, promoting the elimination of solid tumours will require tools to relieve the defective metabolic reprogramming of intratumoral T cells imposed by the immunosuppressive TME. Tumour microenvironment-induced tumour heterogeneity is another obstacle to the success of cancer immunotherapy and there is increasing evidence demonstrating that the differences in the outcomes of cancer immunotherapy are attributed to the heterogeneity of the tumour and its microenvironment.

The results of clinical trials indicate that there are a number of patients with cancer who do not have a good response to monotherapy approaches. Therefore, combination strategies are required to achieve optimal therapeutic benefits.

In this regard, targeting the tumour microenvironment may provide a novel strategy for immunotherapy, break down the resistance of conventional cancer therapy and produce the foundation for personalized precision medicine.

One challenge is to consider the TME in the design of more integrative immunotherapy approaches based on boosting the immune system, tolerizing the microenvironment and controlling its complexity and heterogeneity.

Clearly more attention should be paid to the tumour as a whole and not just the epithelial component. Immunotherapies can be more effective by combining it with agents that modulate the tumour microenvironment. Its targeting may provide a novel strategy for immunotherapy – and produce the foundation for personalized precision cancer treatment. MEH



# Baylor St. Luke's esteemed doctor treats out-of-state patient

## Why Michele Hemstreet took a flight of faith

Michele Hemstreet and her family are used to moving around. Having a husband whose job allowed them to live abroad and in several different states taught Michele and her family how important it is to establish roots and embrace each new beginning. Making friends and developing a comfortable community were the family's typical first steps, but in 2013, the move from Illinois to North Carolina had Michele searching for something completely different.

In 1986, Michele was diagnosed with non-Hodgkin's lymphoma. Being only 26 years old with a one-year-old baby, Michele emphasizes "[the diagnosis] was a lot to take in and process at such a young age". After the cancerous mass was removed, the doctors began radiation. "They radiated my neck where the cancer was found and my chest," says Michele about her cancer treatment. For almost 30 years after her diagnosis and treatment, Michele led a normal, active life. However, in 2012, when visiting her doctor for a routine appointment, he recommended she take a standard healthy heart scan. Unexpected to both of them, the results revealed Michele's heart was affected by moderately severe aortic stenosis.

Her doctors confirmed the condition of her heart was due to the radiation she had experienced nearly 30 years prior. After having a stent put in by her trusted team of doctors in Illinois, her impending move to North Carolina had her searching for a new doctor as she knew the stent was only a temporary fix. "I wanted to find someone who specialized in radiated tissue," says Michele, knowing that her request was very specific. Michele was able to find a doctor with that exact "area of expertise": Dr. Juan Carlos Plana. Michele met with him a few times before he moved to Baylor St. Luke's Medical Center in Houston, and though that was far from her new address

in North Carolina, Michele took the flight of faith to continue seeing him.

"I felt that I was in good hands," says Michele when thinking back to her initial visit. "Although I could have opted to see another doctor in Cleveland, I already felt comfortable in his care. Dr. Plana's expertise in the area of radiation induced heart disease made the decision to follow him to Houston the right one for me." In 2017, after battling breast cancer alongside her heart condition, Dr. Plana worked with a team of cardiac specialists necessary for the complexity of Michele's case to ensure a successful aortic valve replacement.

Prior to her surgery, Michele's symptoms had become more complicated making her visits to Baylor St. Luke's more frequent. "One of the reasons I come back to [St. Luke's] is for the quality of care and their ability to deal with complicated cases," says Michele. Now, both Michele and her husband, Mark are retired and feel settled in their home in North Carolina. And though each appointment requires a flight to Texas, the confidence Michele has in Dr. Plana has made it all worth it. **MEH**



Dr Juan Carlos Plana consults with patient Michele Hemstreet

# New diagnostic technique reveals a protein biomarker that accurately differentiates bladder cancer from benign inflammation

Label-free digital pathology using infrared (IR) imaging with subsequent proteomic analysis for bladder cancer (BC) has revealed the first protein biomarker (AHNAK2) for BC. AHNAK2 differentiates between chronic cystitis (inflammation of the bladder) and a non-muscle invasive-type BC (carcinoma in situ) which is challenging to diagnose. A report in the *American Journal of Pathology* describes this new diagnostic procedure, which is label-free, automated, observer-independent, and as sensitive and specific as established histopathological methods.

Distinguishing benign inflammatory conditions in the bladder from low-grade and advanced cancers can be difficult, especially since some BC treatments induce inflammation.

“We developed this label-free digital pathology annotation system by IR imaging to support the pathologist, similar to driver assistance in cars. This technique in combination with a proteomics approach allowed us to identify AHNAK2 as an important new biomarker for BC, and the results encourage us to transfer this label-free digital technique to other pathologies,” explained Klaus Gerwert, PhD, Chairman of the Department of Biophysics and the PURE (Protein Research Unit Ruhr within Europe) consortium at Ruhr University Bochum, Germany.

Using label-free Fourier transform IR (FTIR) imaging, investigators were able to classify unaltered tissue thin sections by colour to identify regions of interest. “The resulting index colour images automates tissue classification, including cancer type, subtype, tissue type, inflammation status, and even tumour grading,” noted Prof Dr Gerwert.

In an analysis of 103 freshly-frozen samples that included confirmed diagnoses for 41 cystitis, 19 low-grade

carcinoma, and 43 high-grade carcinoma, FTIR imaging showed a specificity of 95%, sensitivity of 95%, and an accuracy of 95% compared to stained images reviewed by a trained pathologist. The technique also differentiated cancerous from healthy tissue as well as low- from high-grade carcinoma.

Laser capture microdissection was then used to obtain homogenous tissue samples for protein analysis by proteomics. By comparing tissue from patients with inflammatory bladder (cystitis) to samples from patients with invasive, high-grade urothelial carcinoma, the investigators identified three potential biomarkers, with the protein AHNAK2 found to be the best performing candidate biomarker.

In a large cohort that included 310 freshly-frozen, paraffin-embedded tissue samples (51 high-grade cancers, 67 carcinoma in situ [CIS], 84 low-grade cancers, and 108 patients with severe cystitis), AHNAK2 measurement achieved 97% sensitivity and 69% specificity in differentiating between severe cystitis with reactive urothelial atypia (RUA) vs CIS. It also displayed high sensitivity in distinguishing low versus invasive high grades and low grades vs CIS.

“In our study, AHNAK2 was identified and verified in two steps as a candidate biomarker for BC,” said Barbara Sitek, PhD, Deputy Director, Medizinisches Proteom-Center (MPC), Ruhr University, Bochum, Germany. “AHNAK2 has already been proposed as a potential prognostic biomarker for clear renal cell and pancreatic cancers and is part of a urinary mRNA panel for the diagnosis of BC and prediction of tumour aggressiveness.”

The investigators believe AHNAK2 could be a very helpful tool for detecting

This technique in combination with a proteomics approach allowed us to identify AHNAK2 as an important new biomarker for BC, and the results encourage us to transfer this label-free digital technique to other pathologies.

CIS recurrence or persistence, particularly because misdiagnosis of CIS can delay treatment of an aggressive malignancy or could lead to unnecessary treatment or bladder removal.

BC is the second most common urogenital malignancy, with about 430,000 new cases diagnosed worldwide in 2012. About 75% of newly diagnosed patients have non-muscle invasive, mostly low-grade BC, and about 25% have high-grade BC at the stage of infiltration of smooth muscle. The presence of acute or chronic inflammation (urocystitis) with RUA can complicate diagnosis, especially when patients with BC have been purposely treated with pro-inflammatory agents. The current gold standard for tumour grading and staging of BC is the visual inspection of stained tissue thin sections by a pathologist; immunohistochemistry is also used but can be difficult to interpret.

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common cancer in women, with an estimated 570,000 new cases diagnosed worldwide in 2018, of which around 85% occur in less developed regions. HPV, a group of more than 150 viruses, is responsible for the majority of cervical cancers. Proven methods are available to screen for and treat cervical pre-cancers, and broad-spectrum HPV vaccines can potentially prevent up to 84-90% of cervical cancers.

Nevertheless, large disparities exist in cervical screening and HPV vaccination coverage between countries. In low- and middle-income countries (LMICs), overall screening rates in 2008 were as low as 19%, compared to 63% in high-income regions; whilst by 2014 less than 3% of females aged 10-20 years in LMICs received the full course of HPV vaccination in 2014, compared to over a third in high-income countries.

The authors analysed high-quality registry data from the International Agency for Research on Cancer to predict future trends in cervical cancer if further action is not taken. They then used a dynamic model to calculate the impact of scaling up HPV vaccination and cervical screening on the cervical cancer burden globally, and in 181 countries of all levels of development, between 2020 and the end of the century.

### Modelling

The modelling focused on the deployment of vaccination and screening in low- and medium- income countries rather than detailed modelling of all the more recent improvements in countries with high levels of development, which may have underestimated timing to elimination in individual countries with high levels of development.

The researchers also predicted the earliest date when rates of cervical cancer might fall enough to achieve elimination (considering a possible elimination threshold of less than 4 cases per 100,000 individuals). The average worldwide age-standardised rate of cervical cancer in 2012 was 12 per 100,000.

Results showed that rapid vaccination scale-up to 80-100% coverage globally by 2020 using a broad-spectrum HPV

vaccine could prevent 6.7-7.7 million cases – but more than half of these would be averted after 2060.

If, in addition, cervical screening were scaled-up to high coverage by 2020 (with all women offered screening twice in their lifetime and 70% coverage globally), this could prevent an additional 5.7-5.8 million cases of cervical cancer in the next 50 years, and substantially speed up elimination.

Such efforts could result in cervical cancer being eliminated as a public health problem, with average rates across countries falling to less than 4 cases per 100,000 by 2055-59 in countries with very high levels of development (including the USA, Finland, the UK and Canada); 2065-69 for countries with high levels of development (including Mexico, Brazil, and China); 2070-79 for countries with medium levels of development (including India, Vietnam, and the Philippines); and 2090-2100 onwards for countries with low levels of development (such as Ethiopia, Haiti, and Papua New Guinea)<sup>[3]</sup>.

However, rates of less than 4 cases per 100,000 would not be achieved by the end of the century in all individual countries in Africa (eg, Kenya, Tanzania, and Uganda) even if high coverage vaccination and twice lifetime cervical screening could be achieved by 2020.

The authors note several limitations, including that their predictions are constrained by a lack of high-quality cancer incidence data over time, particularly in developing countries. They also note that the model assumed lifetime duration of vaccine protection and did not fully account for geographical differences in sexual behaviour, which might affect the accuracy of the estimates. They also assumed in their rapid scale-up scenarios that very high global vaccination coverage rates (of 80% or higher) would be achievable worldwide – but successfully providing two doses of the HPV vaccine with appropriate spacing is likely to be challenging, particularly in less developed regions. Finally, the rapid scale-up scenario examined in the study did not account for cultural, logistical, and financial barriers to scaling up screening in low-resource settings.

Despite the enormity of the problem, our findings suggest that global elimination is within reach with tools that are already available, provided that both high coverage of HPV vaccination and cervical screening can be achieved.

### References:

[1] This scenario assumes that 80-100% vaccination coverage is achieved for girls aged 12–15 years, and that all women are offered screening twice in their lifetime scaled up to 70% coverage globally.

[2] The more gradual scale-up scenario assumes delivery of 20–45% vaccination and 25–70% once lifetime screening coverage by 2030, increasing to 40–90% vaccination and 90% once lifetime screening coverage by 2050.

[3] The main results quoted are averaged across levels of development for each category of country, and individual country results will vary from the average. Importantly, a select few countries such as Saudi Arabia and Syria appear to already be at very low risk and it has been postulated that this is related to low exposure to HPV or the other co-factors of HPV infection. The authors point out that these countries will not ‘achieve’ elimination via active control by implementation of HPV vaccination. There are limitations in the registry data in many countries so this could be underreporting, and many countries are going through a westernisation transition which means that this could change in the future if countries do not consider the need to intervene. MEH



# The effects of anaesthesia in the brains of children

Two recent studies look at the effects of anaesthesia in children. One study published in *The Lancet* notes that anaesthesia is unlikely to have a lasting effect on the developing brains of young children. The second study by Mayo Clinic and published in *Anesthesiology* finds that there is no evidence anaesthesia lowers intelligence in young children. *Middle East Health* looks at these two studies in turn.

According to a study published recently in *The Lancet*, researchers find that a single hour of general anaesthesia in early infancy – longer than is necessary to perform the most common types of minor surgeries in childhood – does not result in measurable neurodevelopmental or behavioural problems up to the age of 5 years. The study was the first randomised trial of its kind involving 722 infants in seven countries.

The trial provides the strongest evidence to date that one brief exposure to anaesthesia is safe in young children. Nevertheless, the authors caution that most (84%) study participants were male and more research is needed to confirm the findings in girls and children with multiple and prolonged exposure to anaesthesia.

“Nearly half the general anaesthetics given to infants are used for less than one hour, therefore our findings should reassure health professionals and the millions of parents whose young children undergo surgical or diagnostic procedures with anaesthetic drugs

worldwide every year,” says Professor Andrew Davidson, Murdoch Children’s Research Institute, Australia, who led the study.

“Parents and clinicians may want to delay necessary procedures – particularly in very young children. These findings mean children no longer need to be subjected to the potential medical and developmental risks of delaying surgery, and anaesthetists do not have to avoid general anaesthetics in favour of less well established anaesthetic techniques.”

The study is the first randomised trial to investigate whether exposure to general anaesthesia in infancy (aged 60 weeks of postmenstrual age or younger), a time of high brain vulnerability, negatively impacts the growing brain at age 5.

During the first 3 years of life, around 1 in 10 children in developed countries – equating to millions of children every year – undergo surgical, medical, and diagnostic procedures under general anaesthesia including hernia repair, tonsillectomy, imaging, and endoscopies.

## Debate

For over a decade, the potential neurotoxicity of commonly used anaesthetic drugs in children has been debated. In 2017, the US Food and Drug Administration warned that prolonged or repeated anaesthesia in children younger than 3 years of age might affect brain development. However, this warning was based largely on animal studies which showed increased cell death in developing animals.

So far, research in humans has been limited to observational studies that have reported conflicting findings, and are unable to conclude whether anaesthesia itself is causing problems, or if other factors such as the underlying medical conditions that make surgery necessary, or the surgical procedure itself, might be to blame.

To provide more evidence, the General Anaesthesia compared to Spinal anaesthesia (GAS) study recruited 722 children undergoing surgical repair of inguinal hernia (one of the most common operations of early childhood) at 28



hospitals in Australia, Italy, the USA, the UK, Canada, the Netherlands, and New Zealand between February 2007 and January 2013. Participants were randomly assigned to general anaesthesia (363 children) or awake-regional (local) anaesthesia (which does not cause brain injury in animal models; 359 children).

In 2016, interim results found that neurodevelopmental outcomes at age 2 years did not significantly differ between the general anaesthesia and awake-regional groups.

Here, the researchers report the final results of the GAS trial at 5 years of age – a time when intelligence testing is strongly predictive of future achievement. Child psychologists used standard measures to assess the children's IQ score, memory, attention, executive function (skills that help with memory, impulse control, and planning), and behaviour.

Due to deviations from the treatment protocol (some children in the awake-regional group also had to be given a general anaesthetic) and loss to follow up, only 205 of 363 children in the awake-regional group and 242 of 359 children in the general anaesthesia group were included in the final analysis. The average duration of general anaesthesia was 54 minutes.

Results showed no significant difference in IQ scores between the children exposed to general anaesthesia (average IQ score 98.87) and awake-regional anaesthesia (99.08), after adjusting for age at birth and country, and accounting missing data. There were no significant differences in a range of other tests of neurocognitive function.

The authors note several limitations, including that there were a substantial number of deviations from the treatment protocol in the awake-regional group because children had to be given general anaesthesia, and a number of children were lost to follow up over the 5 years. They also point out that although several general anaesthetics are commonly used in children, participants in the trial only received sevoflurane, which could limit the generalisability of the findings. Additionally, 5 years of age may be too young to detect some executive functions and social-emotional skills which do not develop until later in life.

#### Comment

Commenting on the implications of the findings, Dr James O'Leary from the

University of Toronto in Canada says that the study provides the “strongest evidence to date” that a single, brief exposure to general anaesthesia during infancy is not harmful to neurodevelopment. However, he cautions: “Adverse neurodevelopment in childhood results from interactions among multiple risk and protective factors, including healthcare-related, genetic, familial, and environmental factors. Consequently, potential contributing factors other than general anaesthesia (eg, type of surgery, sex [84% of study participants were male]) should be considered when interpreting and generalising these findings. Perhaps most importantly, the study results cannot be extrapolated to children who undergo prolonged or repeated exposures to general anaesthesia or receive multiple anaesthetic drugs for the same surgical procedure... Whether anaesthesia causes neurological injury in patients under these conditions remains to be established.”

Associate Professor Nicola Disma, Chair of the Paediatric Scientific Sub-Committee at the European Society of Anaesthesiology, Director of Clinical Research, Department of Anaesthesia, Istituto G. Gaslini, Genova, Italy, commented: “This study, one of the largest ever completed on anaesthesia in children, has provided conclusive results that are reassuring for both patients and doctors: a single exposure to general anaesthesia of about one hour in early infancy does not cause a clinically significant adverse neurodevelopmental outcome at 5 years of age. These results have a positive impact on millions of young patients undergoing anaesthesia every year. In fact, one hour of anaesthesia is even longer than is necessary to perform the most common types of surgeries in childhood.

“The consortium that has produced this work represents an extraordinary example of international collaboration, and in future, with further trials, may be able to address remaining unresolved questions on the effects of prolonged anaesthesia in the developing brain.”

#### Does anaesthesia lower intelligence in young children?

A Mayo Clinic study finds no evidence that children given anaesthesia before their third birthdays have lower IQs than those who did not have it. A more

complex picture emerges among people who had anaesthesia several times as small children: Although their intelligence is comparable, they score modestly lower on tests measuring fine motor skills, and their parents are more likely to report behavioural and learning problems. The findings are published in *Anesthesiology*.

The U.S. Food and Drug Administration warned in 2016 that prolonged or repeated sedation before age 3 may affect brain development. The warning was based largely on data from animals, which may or may not apply to children.

Mayo researchers studied 997 people born from 1994 through 2007 in Olmsted County, Minnesota, the home of Mayo Clinic's Rochester campus. They were grouped according to the anaesthesia exposures they had before their third birthdays: 206 had two or more; 380 had one; and 411 had none. Ear, nose and throat procedures were the most common surgeries.

The researchers used the Rochester Epidemiology Project medical records database, brain function testing at ages 8-12 or 15-20, and parent reports to assess behaviour and brain function. Beyond their anaesthesia exposure, the three groups of patients were matched to be as similar as possible.

Intelligence, memory, and several other measures of brain function were similar among the groups.

However, those with multiple exposures to anaesthesia had modest declines in fine motor skills, such as the ability to draw figures with a pencil, and how quickly they processed information when reading. Their parents reported more learning and behavioural problems, such as difficulty reading; behaviours consistent with attention deficit hyperactivity disorder; breaking rules; or displaying aggression, anxiety or social withdrawal.

Parents whose children had anaesthesia once under age 3 reported more problems with mental skills known as executive functions - skills that help with memory, impulse control, planning and flexibility - but not with other behaviours.

“For the majority of kids undergoing surgery, the results overall are reassuring,” says lead author David Warner, M.D., a pediatric anesthesiologist at Mayo Clinic Children's Center. “About 80 percent of kids who need surgery under age 3 only need one, and it's relatively brief.”


Several other studies also show little evidence that a single anesthetic is associated with significant harm.

“Although we do have some concerns about the children who are receiving multiple anesthetics, it’s important to note that our results don’t allow us to conclude that anaesthesia itself is causing problems,” Dr. Warner says, adding that other factors, such as the conditions that make surgery necessary, could contribute. “However, the fact that we found some problems in some of these children means that research in this area needs to continue, including further analysis of our data.”

In the meantime, in most cases the benefit

of surgery outweighs any risk, Dr. Warner says. However, the potential for problems may need to be part of the decision-making process when parents and surgeons discuss surgery, he adds.

### References:

1. The full text of *The Lancet* study is available here: [www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)32485-1/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32485-1/fulltext)
2. Anesthesia and Neurodevelopment in Children: Perhaps the End of the Beginning *Anesthesiology* 4 2018, Vol.128, 700-703.  
doi:10.1097/ALN.0000000000002121 



## In case of Open Foetal Surgery, researchers recommend use of anaesthesia in foetuses from 21 weeks of gestation

Although the problem of whether foetuses are able to feel pain or not is still controversial, experts at the University Hospital Virgen del Rocío in Seville have recently published a study in which they confirm that from the second trimester of pregnancy, the future baby already shows signs of pain when given a harmful stimulus or as a response to stress. In response to this confirmation, the researchers indicate the need to anaesthetise the foetus during open foetal surgery, OFS.

There is a school of thought that believes that in the case of foetal interventions, it is sufficient to administer anaesthesia to the mother as this passes to the foetus through the umbilical cord. Now, the experts have shown that this might not be sufficient and that from 21 weeks, the foetus can feel pain, so it also needs to be anaesthetised.

“At the Hospital Virgen del Rocío, we have spent a decade doing open foetal surgery. In 2007, we did the first intrauterine spina bifida operation in Europe, and in only one case was the foetus unable to receive intravenously administered anaesthesia from the start of the operation. It was at that moment that our monitoring teams detected anomalies in the behaviour of the foetus, which led us to believe that this was effectively a reaction to

the stress caused by the pain. We quickly put in place the anaesthesia protocol and the spinal reconstruction was possible and the post-op period passed without any problems,” explains Doctor Javier Márquez Rivas, head of the Infant Neurosurgery Unit and the Neurosurgery Service at the hospital.

For her part, Doctor María J. Mayorga Buiza, paediatric anaesthetist and first signatory of the article, adds that one of the key aspects of anaesthesia in open foetal surgery is to help uterine relaxation, to keep foetal circulation stable and, once surgery is complete, to offer adequate management of the patient to avoid contractions among other complications, which helps to reduce the incidence of premature birth in these cases.


Open foetal surgery (OFS) is still a serious procedure for the mother and the foetus. In such cases, anaesthesia given directly to the foetus can be provided by different means, but in the opinion of these experts, direct administration is “obligatory” for reduce foetal stress and also release the incidence of foetal mortality.

Even though current models do not prove the perception of foetal pain before the third trimester and there is little evidence of the effectiveness of direct foetal analgesic and anaesthetic techniques, it is a confirmed fact that

foetal mortality is higher than 20% in the case of non-anaesthetised foetuses. This rate drops to 0% in operations carried out until now at the University Hospital Virgen del Rocío in Seville.

“The response of foetal stress to harmful stimulation that our monitoring teams observed in this case, does not completely prove that the foetus can feel pain. However, it is very improbable that there can be a perception of pain without a response to stress, and so these signals are often used as a substitute pain indicator,” explains the University of Seville researcher and co-author of this study, The Applied Physics professor Emilio Gómez González.

The research team that Professor Gómez Gonzalez leads works on the development of optical and neurophotonic techniques which are capable of evaluating the state and characteristics of the areas where surgery is taking place during complicated procedures.

“To advance in the area of anaesthesia is to advance in surgery. Formerly, there were patients who died from pain, therefore, the better our knowledge and training in anaesthesia and the greater the abilities of the monitoring teams, the more complex surgery can be,” says Doctor Mayorga Buiza. 




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# Commercial vested interests prevent action on greatest threat to human health

Leaders must take a hard line against powerful commercial interests and rethink global economic incentives within the food system in order to tackle the joint pandemics of obesity, undernutrition and climate change, according to a major new report by The Lancet Commission on Obesity. A key recommendation from the Commission is the call to establish a new global treaty on food systems to limit the political influence of Big Food. *Middle East Health* reports.

Malnutrition in all its forms, including undernutrition and obesity, is by far the biggest cause of ill-health and premature death globally. Both undernutrition and obesity are expected to be made significantly worse by climate change<sup>[1]</sup>.

The report follows the publication (17 Jan) of the Lancet-EAT Commission, which provided the first scientific targets for a healthy diet within planetary boundaries<sup>[2]</sup>. Now, the new report analyses the wider systems underpinning the global obesity pandemic, and identifies solutions to address decades of policy failure.

Over the past two decades, obesity, undernutrition and climate change have been viewed as separate, and policy responses have been unacceptably slow due to reluctance of policy makers to implement effective policies, powerful opposition by vested commercial interests, and insufficient demand for change by the public and civil society. Undernutrition is declining too slowly to meet global targets, no country has reversed its obesity epidemic, and comprehensive policy responses to the threat of climate change have barely begun.

“Until now, undernutrition and obesity have been seen as polar opposites of either too few or too many calories. In reality, they are both driven by the same unhealthy, inequitable food systems, underpinned by the same political economy that is single-focused on economic growth, and ignores the negative health and equity outcomes. Climate change has the same story of profits and power ignoring the environmental damage caused by current food systems, transportation, urban design and land use. Joining the three pandemics together as The Global Syndemic allows



us to consider common drivers and shared solutions, with the aim of breaking decades of policy inertia,” says Commission co-chair, Professor Boyd Swinburn of the University of Auckland.<sup>[3]</sup>

Led by the University of Auckland (New Zealand), the George Washington University (USA), and World Obesity Federation (UK), the new Lancet Commission is the result of a three-year project led by 43 experts from a broad range of expertise from 14 countries<sup>[4]</sup>.

The new Commission defines The Global Syndemic as the global interactions of the pandemics of obesity, undernutrition and climate change, which are linked through common drivers and shared solutions. Driving The Global Syndemic are food and agriculture policies, transportation, urban design and land use systems, which in turn are driven by policies and economic incentives that promote overconsumption and inequalities.

Among the actions recommended, the Commission calls for the establishment of a Framework Convention on Food Systems (FCFS) – similar to global conventions for tobacco control and climate change – to restrict the influence of the food industry in policy making and to mobilise national action for healthy, equitable and sustainable food systems.

Economic incentives must be redesigned, and US\$5 trillion in government subsidies to fossil fuel and large agricultural businesses globally should be redirected towards sustainable, healthy, environmentally friendly activities. Additionally, a global philanthropic fund of \$1 billion must be set up to support civil society in advocating for change.

“The prevailing business model of large international food and beverage companies that focus on maximising short-term profits leads to overconsumption of nutrient-poor food and beverages in both high-income countries and increasingly in low and middle-income countries. The coexistence of obesity and stunting in the same children in some countries is an urgent warning signal – and both will be exacerbated by climate change. Tackling The Global Syndemic requires an urgent rethink of how we eat, live, consume, and move, including a radical change to a sustainable and health-promoting business model fit for the future challenges we face today,” says Dr Richard Horton, Editor-in-Chief, The Lancet.<sup>[3]</sup>

#### **The Global Syndemic: common drivers require shared solutions**

The Global Syndemic represents a synergy of pandemics that co-occur in time and

Until now, undernutrition and obesity have been seen as polar opposites of either too few or too many calories. In reality, they are both driven by the same unhealthy, inequitable food systems, underpinned by the same political economy that is single-focused on economic growth, and ignores the negative health and equity outcomes.

place, interact with each other, and share common underlying societal drivers. For example, food systems not only drive the obesity and undernutrition pandemics but also generate 25-30% of greenhouse gas emissions (GHGs), and cattle production accounts for over half of those. Car-dominated transportation systems support sedentary lifestyles and generate between 14-25% of GHGs. Underpinning all of these are weak political governance

systems, the unchallenged economic pursuit of GDP growth, and the powerful commercial engineering of overconsumption.

The outcomes of obesity, undernutrition, and climate change also interact. For example, climate change will increase undernutrition through increased food insecurity from extreme weather events, droughts, and shifts in agriculture. Likewise, foetal and infant undernutrition increases the risk of adult obesity. Climate change may also affect prices of basic food commodities, especially fruit and vegetables, potentially increasing consumption of processed foods.

“We must recognise these connections and implement double-duty actions that address both obesity and undernutrition and triple-duty actions that influence multiple parts of the syndemic simultaneously,” says Commissioner Professor Corinna Hawkes, City University London (UK)<sup>[3]</sup>. Guidelines for a sustainable diet, the restriction of commercial influences, the right to wellbeing legislation, and policies for healthy, equitable, environmentally sustainable, economically prosperous food systems would all have an impact across obesity, undernutrition and climate change (ie, triple-duty, or triple-win actions). Additional examples would include:

- Reducing red meat consumption through taxes, redirected subsidies, health and environmental labelling, and social marketing would lead to healthier diets for cancer and obesity prevention, more land for efficient, sustainable agriculture, providing opportunities to reduce undernutrition, and lower GHG emissions from agriculture.

- Supporting active transportation through infrastructure, taxes and subsidy shifts, and social marketing strategies would lead to increased physical activity and less sedentary time, with an impact on obesity prevention, cheaper transport access to healthy food and employment, potentially reducing poverty and undernutrition, and lower GHG emissions from transportation.

“These actions also need to align with a healthier economy” says Hawkes. “We need far-sighted policy makers and private sector leaders to drive forward actions that produce benefits for obesity, undernutrition, economy and sustainability.”<sup>[3]</sup>



### Commercial vested interests: a powerful driver of The Global Syndemic

Economic power has been increasingly concentrated into fewer, larger companies. Key strategies used by the food industry to obstruct obesity prevention policies have included adopting self-regulation to pre-empt or delay state regulation, public relations efforts portraying industry as socially responsible while undermining and contesting the strength of scientific evidence, direct lobbying of government decision-makers, and framing nutrition as a matter of individual responsibility.

“With market power comes political power, and even willing governments struggle to get policies implemented against industry pressure. New governance dynamics are needed to break the policy inertia preventing action. Governments need to regain the power to act in the interests of people and the planet and global treaties help to achieve this. Vested commercial interests need to be excluded from the policy table, and civil society needs to have a stronger voice in policy-making. Without disruptive change like these, we will continue on with the status quo which is driving The Global Syndemic,” says Commissioner Tim Lobstein, World Obesity Federation, London (UK)<sup>[3]</sup>.

Attempts to include sustainability in national dietary guidelines in the USA and Australia failed as a result of food industry pressure to remove sustainability from the terms of reference. In the USA, subsidies for fossil fuels keep petrol prices artificially low, encouraging car use and disincentivising investment in active and public transportation. In 2016-17, the sugary drinks sector spent \$50 million to

lobby against local initiatives to reduce soda consumption, and research funded by the sector is five times less likely to find an association between sugary drinks and obesity compared to other studies.

The food industry’s obstructive power is further enhanced by governance arrangements that legitimise industry participation in public policy development, and the power that big corporations have to punish or reward governments by relocating investment and jobs. Furthermore, outlawed marketing practices in one country have been introduced or sustained in non-regulated countries. In Nepal, Ghana, South Africa, and Mongolia marketing for sugary drinks is common around schools, and school entrances in ways that would not be acceptable in high-income countries.

Regulatory approaches to product reformulation (eg. salt and sugar reduction), labelling and marketing to children are needed because industry-led, voluntary approaches have not been effective. Quasi-regulatory approaches that are government-led but still voluntary (such as Public Health England’s sugar reformulation programme) may prove more successful, but clear methods of accountability and sanctions for failures to meet targets are needed.

A Framework Convention on Food Systems modelled on tobacco and climate change treaties

The WHO Framework Convention on Tobacco Control (FCTC) and the United Nations Framework Convention on Climate Change (UNFCCC) provide valuable models for a global approach to tackle the negative health and environmental effects of the food system.

We need far-sighted policy makers and private sector leaders to drive forward actions that produce benefits for obesity, undernutrition, economy and sustainability.

The Commission calls for a new Framework Convention on Food Systems (FCFS) to link the powerful players around food systems into a common agreement, enabling governments to add elements of public health, social equity and environmental protection.

Based on Article 5.3 of the FCTC, a new FCFS would explicitly exclude the food industry from policy development. Such a commitment would recognise the fundamental and irreconcilable conflict that exists between some food and drinks industries' interests and those of public health and the environment; that all parties must be transparent and accountable when dealing with industry or working to further their interests; and that no fiscal advantages or inducements to produce food and beverage products that damage human and environmental health should exist.

"Although food clearly differs from tobacco because it is a necessity to support human life, unhealthy food and beverages are not. The similarities with Big Tobacco lie in the damage they induce and the behaviours of the corporations that profit from them. A Framework Convention on Food Systems would help empower individual nations against vested commercial interests, redirect the vast subsidies that currently benefit unhealthy industries, and provide full transparency," says author Professor William H. Dietz, George Washington University, Washington DC (USA).<sup>[3]</sup>

#### **Subsidies that foster ill health must be redirected**

In 2015, global subsidies from governments to the fossil fuel industries were about \$5.3 trillion per year, and nearly half a trillion US dollars went to agricultural subsidies (mostly for beef and dairy, as well as grains used in animal feed or ultra-processed foods) in the top 21 food-producing countries every year.

As industries continue to increase their profits, the costs of the environmental and health damage linked to their products are overwhelmingly borne by current

and future generations of tax payers. The Commission argues that these subsidies should be redirected to incentivise healthy and environmentally sustainable agriculture. Furthermore, the costs of products such as red meat and petrol should reflect the costs of their damages to the environment.

New business models fit for the challenges of the 21st century are needed to incentivise sustainable businesses in support of the public good, and broaden the business focus to explicitly include benefits to health, society and the environment.

#### **Civil society: a much-needed disruptive force**

Effective strategies to address the Global Syndemic will be unlikely to succeed without a broader base of support. The recent withdrawal of the USA from the Paris Climate Change Agreement demonstrates the fragility of agreements that might change based on the politics of the countries involved. Yet, despite the administration's decision, 2700 leaders from US cities, states, and businesses representing 159 million people and \$6.2 trillion in GDP have continued efforts to mitigate greenhouse gas emissions.

Mobilisation of civil society was crucial in driving commitment for a sugary drinks tax in Mexico. Despite strong resistance from the beverage industry aimed at watering down the proposed measures, a 10% tax was added to sugary drinks. Within two years, consumption of sugary drinks was reduced by 7.6%.

The Commission calls for \$1 billion from philanthropic and other sources to support 100 countries to apply Mexico's approach to implement food and nutrition policies.

"The past few years have seen renewed activism at the local level, whether in cities, communities, or in particular issues. As with other social movements, such as campaigns to introduce sugary drink taxes, efforts to address the Global Syndemic are more likely to begin at the community, city, or state level, and subsequently build to a national or global

level. Support for civil society is crucial to break the policy deadlock and the systems driving the Global Syndemic," adds Professor Dietz.<sup>[3]</sup>



The Global Syndemic of Obesity, Undernutrition, and Climate Change: The Lancet Commission report - Boyd A Swinburn et al.

<https://tinyurl.com/y7lewrff>

#### **References:**

[1] Key data on obesity, undernutrition and climate change:

- Excess body weight is estimated to affect 2 billion people worldwide, causing 4 million deaths, at a cost of \$US2 billion annually, or 2.8% of the world's GDP.

- At the same time, stunting and wasting affect 155 million and 52 million children worldwide, 2 billion people suffer from a micronutrient deficiency, and 815 million people are chronically undernourished. In Africa and Asia, undernutrition costs 4-11% of GDP.

- Estimates of the future economic costs of climate change are 5-10% of the world's GDP, with costs in low-income countries that may exceed 10% of their GDP.

- Food production is one of the largest contributors to climate change. Agriculture contributes 15-23% of all greenhouse gas emissions, comparable to transportation. When land conversion, food processing, and waste are taken into account, it can be as high as 29%.

[2] EAT-Lancet Commission [www.thelancet.com/commissions/EAT](http://www.thelancet.com/commissions/EAT)

[3] Quotes direct from authors and cannot be found in the text of the Commission.

[4] The Lancet Commission on Obesity was formed following the publication of two Lancet Series on Obesity in 2011 and 2015. The Commission is under the auspices of The Lancet, the University of Auckland, George Washington University, and the World Obesity Federation, and is comprised of 26 Commissioners from 14 countries, supported by 17 Fellows.

# OKI printers are first to have integrated DICOM

## Can print directly on to blue film

OKI, a leader in printing innovation, was at Arab Health to showcase their range of advanced printers with integrated DICOM for printing medical images. We spoke to Javier Lopez, General Manager, Industry Vertical Propositions at OKI, about their printers and how they are changing the way printing is done in a clinical environment.

Lopez explained that their printers are the first to combine the quality of an LED printer with integrated DICOM software, so printing can be done directly from medical equipment without the need for conversion software or external print servers. This also enables printers to be conveniently placed directly at the image source.

The printers can be connected to several imaging modalities simultaneously and can print in A3 or A4 paper format.

A key feature that sets them apart

from other printers is that they can print directly on to blue film, bypassing the need for sublimation of the blue film which is required with other printing devices. This capability significantly improves efficiency and reduces costs substantially.

“The capability to print on blue film without a DICOM server is totally unique,” Lopez said. “Our printers can do this because the DICOM software is embedded in the printer.

“These are the first LED printers with embedded DICOM software and with this innovation we are changing the way medical image printing is done in the clinical environment,” he said.

OKI printers print in high-definition colour and are ideal for non-diagnostic printing of X-rays, nuclear medicine images and scans from CT, MRI and ultrasound.

As well as printing medical images, they can also be used for standard office printing, which reduces the need for multiple printers and cuts down on the cost of consumables.

Lopez added that the printer can also print 1.2 metre long banners to enable printing an image with a ratio of 1:1. This is particularly useful for posters and educational materials.

The company has three medical printers – ES6410 DMe, ES8431 DMe and Pro9431 DMe.

The Pro9431 DMe has a print resolution of ProQ4800 and the other two, ProQ2400. All three print in colour and mono.

• For more information, visit: [www.oki.com/me](http://www.oki.com/me) MEH



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OKI's ES6410DM printer



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## DICOM Medical Printers A First in Digital Printer Technology

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To find out more visit [www.okime.ae/dicom](http://www.okime.ae/dicom)



# LG shows off their range of high resolution medical monitors and durable X-ray detectors

At this year's Arab Health we spoke to LG about the products they were exhibiting. LG is well known around the world for its consumer tech products, such as TVs. However, they are less well known as a company that manufactures medical tech products. They are relatively new to this field, but are well positioned to see success on the back of their globally respected brand. They are sticking to what they know and with their expertise in developing and manufacturing innovative TVs, they are using this knowledge to manufacture a range of high resolution medical monitors and X-ray detectors.

Commenting on the new range of solutions, LG Electronics MEA President, James Lee, said: "At LG, we believe that technology has the power to change lives. We have an extensive history in producing monitors and our advanced technology is recognized worldwide. We are proud to be able to service the local industry with our advanced imaging solutions. LG hopes to make it easier for medical professionals to provide high quality service and attention at every stage of care. We will continue to introduce differentiated medical imaging solutions and are committed to finding new ways to help people work better and live healthier."

Michael Park, Vice President and task leader at LG, explained that their displays have been enhanced for the operating room. The LG Ultra HD Monitor (Model: 27HJ710S) and Full HD Surgical Monitor (Model: 27HK510S) enable surgeons to see the finer details during surgery with their enhanced colour reproduction and Deep Red colour spectrum technology, which enables surgeons to correctly distinguish between blood and lesions, which are similar in colour.

The surgical monitor carefully measures and sets every grayscale tone to create a monitor compliant with DICOM Part 14. In addition, LG's surgical monitors offer stabilized brightness settings. They are

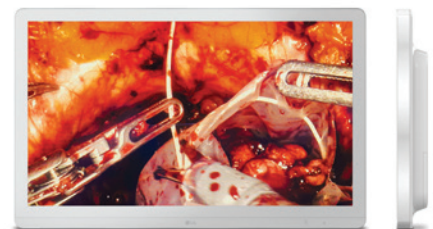


27-inch 8MP IPS Display. It meets the demands of X-ray, MRI and CT scanning by displaying consistent shading and accurately illustrating colour and grey tones. It is designed to showcase multiple imaging applications and allows various test results to be shown on the same screen. Additionally the monitor has a 178-degree wide viewing angle which enables wide-angle viewing without compromising clarity and ensuring minimal colour shift. This monitor also meets the standards of DICOM Part 14.

LG was also showcasing their X-ray detectors – wired (Model: 17HK700G-W) and wireless (Model: 14HK701G-W). Both X-ray detectors are light weight and have a durable carbon-fibre housing to suit various environments and needs. LG's DXD technology creates digital files from the scanner and shares them with a PC within 3 seconds in wired and 6 seconds in wireless mode.

Park explained that their filmless X-ray detectors are ideal for use with mobile or handheld X-ray devices. They had on a display an innovative handheld X-ray device which with their X-ray detector enables easy mobile X-ray use, in ambulances for example.

Park explained that with their global



presence they are well placed to ensure supply and service of their medical devices worldwide.

"Our products are the same quality as the leading medical manufacturers, but we have a very competitive price point," Park noted.

He added that they are looking for distribution partners for the Middle East market. Interested distributors can contact the LG Middle East head office in Dubai. [MESH](#)



## AI solutions take centre stage at Siemens

At this year's Arab in Dubai, Siemens Healthineers showcased its products and solutions under the motto "We enable you to deliver high-value care". The company noted that all their innovations are designed to enable healthcare providers worldwide to increase value by empowering them to expand precision medicine, transform care delivery, improve patient experience and digitalize healthcare.

The company's suite of AI-powered tools and digital solutions that are transforming care delivery formed the centerpiece of their showcase.

Bernd Ohnesorge, President Europe, Middle East and Africa at Siemens Healthineers, said: "The ability to collect and process large amounts of data has a huge impact on the whole healthcare system. In this digital transformation, we believe that industry knowledge and experience are crucial when turning data into actionable insights. Thanks to our close relations with healthcare professionals, we understand their challenges and needs. We systematically combine these insights with our in-depth knowledge in medical technology and data analytics to engineer solutions that help healthcare providers efficiently deliver the right treatment at the right time for every patient."

Some of the products Siemens Healthineers exhibited included AI-Rad Companion Chest CT, AI-Pathway Companion and an all new in-bore infotainment system.

**AI-Rad Companion Chest CT** is a software assistant that brings artificial intelligence (AI) to computed tomography (CT). Siemens Healthineers first intelligent software assistant for radiology – and the first application of the company's new AI-Rad Companion platform – identifies anatomies and potentially disease-relevant changes. Teams of Siemens Healthineers scientists trained the underlying algorithms based on extensive clinical datasets. Using CT images of the thorax, the software can differentiate between the various structures of the chest, highlight them individually, and mark and measure potential abnormalities. This applies equally to organs such as the heart and lungs, the aorta and the vertebral bodies. And the companion goes even one step further: The software automatically turns the findings into a quantitative report and thus helps increase productivity and quality in radiology.

The **AI-Pathway Companion** is a clinical decision support system based on artificial intelligence that supports physicians in making diagnostic and therapeutic

decisions along the clinical pathway. While numerous applications in the healthcare market make the workflows of individual clinical or administrative departments more efficient, the AI-Pathway Companion is designed to help optimize the processes along clinical pathways and thus support personalized as well as standardized patient management. The AI-Pathway Companion can provide physicians in multi-disciplinary disease boards with the clinical status of each patient, based on data integration and artificial intelligence, and can make recommendations for next steps to accelerate diagnostic and treatment decisions.

The **in-bore infotainment system** substantially improves patient satisfaction in MRI exams with the revolutionary Innovision system that allows patients to watch their favourite show during an MRI exam. It is available for all 70-cm bore systems and reduces the anxiety that can result in motion artifacts which can lead to the scan process having to be stopped. A specially designed pillow transmits clear audio signals and attenuates scanner noise substantially. The planned display makes the inside of the scanner seem larger, which can be beneficial to patients suffering from claustrophobia. [MEH](#)

# GE showcases products built on Edison platform for development of AI

At Arab Health, GE Healthcare showcased a range of new applications and smart devices built on Edison – a platform that helps accelerate the development and adoption of Artificial Intelligence (AI) technology and empower providers to deliver faster, more precise care.

Edison is part of GE Healthcare’s \$1 billion and growing digital portfolio and will serve as a “digital thread” for its existing AI partnerships and products. Clinical partners will use Edison to develop algorithms, and technology partners will work with GE Healthcare to bring the latest advancements in data processing to Edison applications and smart devices.

Edison also offers a cutting-edge service that allows data to be traced during the development of an algorithm. This tool, which reflects GE Healthcare’s commitment to safe, ethical and effective use of AI, could boost clinicians’ trust in the technology and radically simplify a developer’s ability to create compliant AI applications. The AI capabilities are just one of the more than 100 Edison services available to GE Healthcare and ultimately third-party developers. Other services include security, visualization, utilization management and auto-prototyping.

Elie Chaillot, President & CEO of GE Healthcare, Eastern Growth Markets, commented: “With digitization as a top priority for regional governments, Edison presents a strong opportunity for public and private healthcare providers here to leverage the potential of AI for transformational change. Helping connect patients and providers faster, the new apps and smart devices based on Edison complement the e-health strategy to achieve more efficient patient care.”

GE Healthcare presented the following Edison applications and Edison-powered devices:

- **AIRx** is an AI-based, automated workflow tool for MRI brain scanning



designed to increase consistency and productivity. AIRx is designed to provide automated slice prescriptions to help reduce previously redundant, manual steps. AIRx is intended to produce images that have less variability between technologists and between scans, to help lower the chances for a patient to be recalled due to incorrect slice placement. An increase in consistency is particularly important when doing longitudinal assessments for diseases like Alzheimer’s and Multiple Sclerosis. AIRx features a pre-trained neural network model that leverages deep learning algorithms and anatomy recognition based on a database of over 36,000 images sourced from clinical studies and reference sites.

- **Critical Care Suite** on Optima XR240amx is designed to identify cases with the critical condition of pneumothorax at the point-of-care to enable prioritization of image review. Critical Care Suite will employ a suite of AI algorithms, such as pneumothorax detection, designed to identify this potentially life-threatening

condition in chest X-Rays with high accuracy (>0.95 AUC). The AI algorithms are hosted on the mobile X-Ray system – a first of its kind AI-embedded imaging device – designed to share the output through an onscreen notification. When a pneumothorax condition is identified, the point-of-care notification alerts the clinical team, enabling prioritization of image review. The AI results are sent to PACS for review of the critical findings by a radiologist.

- **Automated Lesion Segmentation on LOGIQE10** increases productivity through automation. Ultrasound users experience significant ergonomic challenges due to repetitive exam steps. Automated Lesion Segmentation helps eliminate the need for the user to measure lesions manually, by segmenting an identified breast, thyroid or liver lesion and automatically providing a trace of the lesion and corresponding area. This feature also helps ensure consistency among different users, or even the same user, for documentation and follow-ups. **MEH**

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# Agenda

## Selected schedule of regional medical meetings, conferences and exhibitions



Event	Date / City	Contact
<b>■ March 2019</b>		
Patient Experience Excellence Congress	18-19 March 2019 Riyadh, KSA	<a href="http://www.pxec.biiconferences.com">www.pxec.biiconferences.com</a>
World Congress on Depression	18-19 March 2019, Dubai, UAE	<a href="https://depressioncongress.neurologyconference.com">https://depressioncongress.neurologyconference.com</a>
Middle East Heart Congress	18-20 March 2019, Dubai UAE	<a href="https://heart.cardiologymeeting.com">https://heart.cardiologymeeting.com</a>
12th Conference on Orthopaedics and Sports Medicine	18-19 March 2019, Dubai, UAE	<a href="https://orthopaedics.healthconferences.org/">https://orthopaedics.healthconferences.org/</a>
3rd Middle East Pharma Excellence Congress	19-20 March 2019, Dubai, UAE	<a href="http://www.menapharmaexcellence.com">www.menapharmaexcellence.com</a>
Middle East Pharmaceutical Cold Chain Conference	19-20 March 2019, Dubai, UAE	<a href="http://www.pharmacoldchainme.com">www.pharmacoldchainme.com</a>
Recent Medical Advancements: A 360° Approach to Patient Management Conference	21-22 March 2019, Dubai, UAE	<a href="https://go.evnt.com/350838-0?pid=5569">https://go.evnt.com/350838-0?pid=5569</a>
2nd World Congress on Nutrition and Obesity Prevention	21-22 March 2019, Dubai, UAE	<a href="mailto:nutrition@nutritionalconference.com">nutrition@nutritionalconference.com</a>
2nd Annual Health Systems Workshop Presented by Dubai Harvard Foundation & WHO	March 31 – April 1, 2019 Dubai, UAE	<a href="http://dhfmr.hms.harvard.edu/events">http://dhfmr.hms.harvard.edu/events</a>
<b>■ April 2019</b>		
12th World Conference on Human Genomics and Genomic Medicine	8-9 April 2019 Abu Dhabi, UA	<a href="mailto:rohit.casper@healthcarevents.com">rohit.casper@healthcarevents.com</a>
The Dubai International Paediatric Neurology Congress	11-13 April 2019 Dubai, UAE	<a href="https://go.evnt.com/317586-0">https://go.evnt.com/317586-0</a>
The RAK International Psychiatry Congress	19-20 April 2019, Ras Al Khaimah, UAE	<a href="https://go.evnt.com/350779-0">https://go.evnt.com/350779-0</a>
Basic Diabetes	19 April 2019 Al Ain, UAE	<a href="http://www.icldc.ae/event/basic-diabetes#Home">http://www.icldc.ae/event/basic-diabetes#Home</a>
Dubai International Conference on Infectious Diseases and Vaccination	25-27 April 2019 Dubai, UAE	<a href="http://www.dic-id.com">www.dic-id.com</a>
The International Pediatric Dermatology Congress	25-27 April 2019 Dubai, UAE	<a href="https://go.evnt.com/317586-0">https://go.evnt.com/317586-0</a>
The 6th Annual GCC Healthcare Innovation Congress	30 April - 1 May 2019 Dubai, UAE	<a href="https://go.evnt.com/294132-0">https://go.evnt.com/294132-0</a>

## Selected schedule of regional medical meetings, conferences and exhibitions

Event	Date / City	Contact
<b>■ June 2019</b>		
6th International Conference on Rare Diseases and Orphan Drugs	17-18 June 2019 Dubai, UAE	<a href="mailto:rare-diseases@memeetings.net">rare-diseases@memeetings.net</a>
International Conference on Vaccines and Immune Response	17-18 June 2019 Dubai, UAE	<a href="mailto:immuneresponse@mehealthevents.org">immuneresponse@mehealthevents.org</a>
<b>■ July 2019</b>		
14th World Congress on Healthcare and Medical Tourism	18-19 July 2019 Abu Dhabi, UAE	<a href="https://healthcare.global-summit.com/middleeast/">https://healthcare.global-summit.com/middleeast/</a>
<b>■ September 2019</b>		
The 5th Annual MENA International Orthopaedic Congress	19-21 September 2019 Dubai, UAE	<a href="https://go.evnt.com/349042-0">https://go.evnt.com/349042-0</a>
<b>■ October 2019</b>		
XXIV World Congress of Neurology - WCN 2019	27-31 October 2019 Dubai, UAE	<a href="https://go.evnt.com/323182-5">https://go.evnt.com/323182-5</a>



### 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](mailto:editor@MiddleEastHealthMag.com)

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# Almost 2000 unknown bacteria discovered in the human gut

Researchers at EMBL's European Bioinformatics Institute and the Wellcome Sanger Institute have identified almost 2000 bacterial species living in the human gut. These species are yet to be cultured in the lab. The team used a range of computational methods to analyse samples from individuals worldwide.

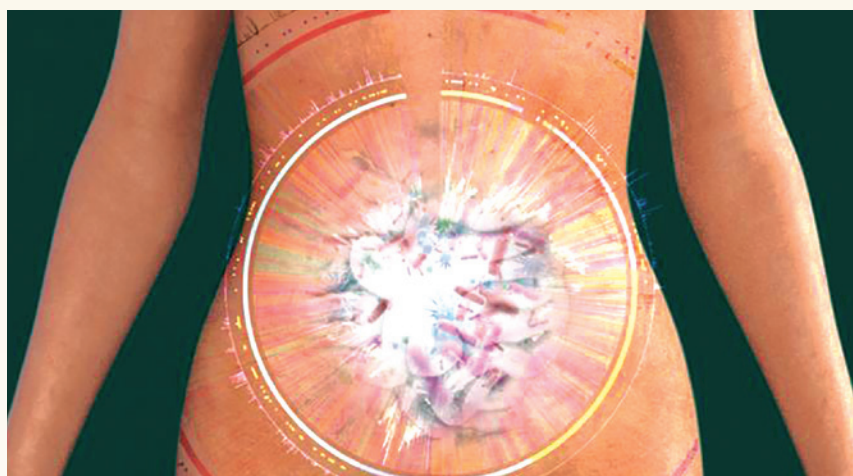
The results, published in the journal *Nature*, highlight that although researchers are possibly getting closer to creating a comprehensive list of the commonly found microbes in the North American and European gut, there is a significant lack of data from other regions of the world.

The human gut is home to many species of microbes, collectively referred to as the gut microbiota. Despite extensive studies in the field, researchers are still working on identifying the individual microbial species that live in our guts and understanding what roles they play in human health.

## 'Reconstructing' bacteria

There are many reasons why some microbial species that are part of the gut microbiota have remained unknown for so long, such as a low abundance in the gut or an inability to survive outside it. By using computational methods, researchers were able to reconstruct the genomes of these bacteria.

"Computational methods allow us to understand bacteria that we cannot yet culture in the lab. Using metagenomics to reconstruct bacterial genomes is a bit like reconstructing hundreds of puzzles after mixing all the pieces together, without knowing what the final image is meant to look like, and after completely removing a few pieces from the mix just



EMBL-EBI researchers and collaborators used computational tools to identify almost 2,000 previously unknown gut bacteria species.

to make it that bit harder," says Rob Finn, Group Leader at EMBL-EBI. "Researchers are now at a stage where they can use a range of computational tools to complement and sometimes guide lab work, in order to uncover new insights into the human gut."

## Geographical diversity

The research highlighted how the composition of gut bacteria differs around the world, and how important it is for the samples that we study to reflect this diversity.


"We are seeing a lot of the same bacterial species crop up in the data from European and North American populations," continues Finn. "However, the few South American and African datasets we had access to for this study revealed significant diversity not present in the former populations. This suggests that collecting data from underrepresented populations is essential if we want to achieve a truly comprehensive picture of the composition of the human gut."

## Blueprint of the human gut

"Computational methods allow us to get

an idea of the many bacterial species that live in the human gut, how they evolved and what kind of roles they may play within their microbial community," says Alexandre Almeida, Postdoctoral Fellow at EMBL-EBI and the Wellcome Sanger Institute. "In this study, we leveraged the most comprehensive public databases of gastrointestinal bacteria to identify bacterial species that have not been seen before. The analysis methods we used are highly reproducible and can be applied to larger, more diverse datasets in the future, enabling further discovery."

"Research such as this is helping us create a so-called blueprint of the human gut, which in the future could help us understand human health and disease better and could even guide diagnosis and treatment of gastrointestinal diseases," says Trevor Lawley, Group Leader at the Wellcome Sanger Institute.

• doi: 10.1038/s41586-019-0965-1 





## Interview

# Advanced, innovative treatment at Germany's Prostate Center Northwest

The world's largest centre for robot-assisted prostatectomy



*Middle East Health* speaks to **Dr Jörn Hinrich Witt**, Senior Consultant of the Urology, Paediatric Urology and Urological Oncology Clinic at the Northwest Prostate Centre in Gronau, Germany, about the centre and some of the innovative surgical techniques they use for prostate cancer surgery.

more than 25 urologists in the team. We have consultants specialized in all kinds of surgical treatment of urooncologic diseases (prostatectomy, partial nephrectomy, nephroureterotomy, cystectomy with the urinary diversion). To optimize oncological results and to minimize the trauma for the patients these procedures are usually performed robotically. We have also specialized urologists for endourologic procedures (TUR-P and endoscopic stone therapy). Another focus of the centre is reconstructive urology and female urology (neurogenic bladder dysfunction, continence problems, erectile dysfunction, urethra reconstruction and fistula surgery).

**MEH: How many foreign patients visited the centre in 2018?**

**JHW:** We have patients coming from all continents to our centre. In 2018 there were more than 500 foreign patients. We have several Arabic speaking staff members as well as an interpreter team to serve patients from the Arab world.

**Middle East Health:** Can you give a bit of background about the Prostate Center Northwest?

**Dr Jörn Hinrich Witt:** The Prostate Centre Northwest was established in 2004 and we started with robot-assisted surgery in the beginning of 2006. The Prostate Center Northwest is a certified by the German Cancer Society as a prostate cancer centre. It is also a certified Training Center for robotic surgery. We have five da Vinci robots for clinical use and one training robot.

**MEH:** Can you tell us about the medical staff at the centre?

**JHW:** The Prostate Center Northwest is a part of the Department of Urology, Pediatric Urology and Urologic Oncology. We treat all kinds of the urologic diseases with special focus on urologic oncology (prostate, kidney, bladder), reconstructive and female urology, benign enlargement of the prostate as well as stone therapy. Overall, we employ more than 140 staff members in our centre with

**MEH:** For patients from the Arab world who are considering seeking treatment at the centre, do you have a ‘medical tourism-like’ process to assist them with remote diagnosis, admissions, translation, etc?

**JHW:** For the Arab world, we work with DeMeGate to serve the patients in the best way. All needed information about the disease will be gathered and translated by DeMeGate and this will then be sent to our foreign patient service to evaluate the situation and initiate a treatment concept. This will then be discussed with the patient during an outpatient visit, by phone or by WebEx/Skype-conference. Referring doctors are also welcome to contact us directly or via DeMeGate. DeMeGate will also help the patient with all requirements for their travel (planning the trip, visa, translation service, etc). We have vast extensive experience with foreign patients, so our centre is very well prepared to serve patients from different countries and different cultures in the best way.

**MEH:** Regarding prostate cancer treatment, what expertise is available at the centre that sets it apart from other prostate cancer treatment centres?

**JHW:** Prostate Center Northwest is the world’s largest centre for robot-assisted prostatectomy. We have unsurpassed experience with more than 15,000 procedures, and with our well-trained consultants, our standardized processes and our quality management, we are able to achieve oncological results as well as functional results (continence and potency) far above the level of other institutions.

**MEH:** What different prostate cancer treatments are available at the centre? Are non-surgical treatments available?

**JHW:** According to the cancer diagnosis, we can do all useful prostate cancer treatment forms (focal and partial treatment of the prostate or radiation therapy by our radiation oncologists). In case of systemic disease, we also offer all the latest systemic treatment forms (androgen deprivation therapy, chemotherapy, targeted therapy and combined approaches).

**MEH:** Can all surgical treatments be carried out using the da Vinci robot?

**JHW:** Regarding localized or local advanced prostate cancer, invasive bladder cancer or most of the upper urinary tract, and



Prostate Cancer Northwest surgeons at work using the da Vinci surgical robot

kidney cancers, can be treated robotically. Also, benign indications (e.g. very large prostate) and many kinds of reconstructive surgery can be performed robotically.

**MEH:** What are the benefits of using the da Vinci robot?

**JHW:** Robot-assistance is the best surgical tool for complex surgical procedures. It provides 3D-vision for the surgeon and degrees of freedom like an open surgery. The image system allows 10-20 times magnification for very precise surgery. Because robot-assisted surgery is minimally invasive, all typical problems of open surgery (wound infection, thrombosis, embolism) are significantly reduced. The da Vinci robotic is an exceptional tool, but the surgeon is the key and has to be well-trained and should have a high level of experience. In our centre all consultants do surgery in high volume and are highly trained and internally reviewed on regular base.

**MEH:** I understand you have introduced the innovative transperineal

fusion biopsy technique for the precise diagnosis of prostatic tumours – can you explain what this is and how it benefits patients?

**JHW:** The traditional systemic prostate biopsy is in the end a blind random biopsy from different parts of the prostate. This is the reason that there is a relatively high chance to miss the cancer. Using a transperineal fusion biopsy leads to much higher accuracy and better cancer diagnosis. The technique includes a multi-parametric MRI of the prostate before the fusion biopsy. With the optimized result of the biopsy the treatment can also be better planned.

**MEH:** Is there anything else you’d like to add regarding developments in prostate cancer treatment at the centre?

**JHW:** The treatment has changed significantly over the past 20 years. We are continuously working hard to optimize oncological and functional results. In selected patients we offer local treatment forms like High Intensity Focused Ultrasound and vascular-targeted photodynamic therapy. **MEH**

# *Grandpa's doctor has a real Robot...*



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