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September - October 2020

Human Germline

International commission says technology not sufficiently advanced for heritable human genome editing

Equitable Access

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ACL injury

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Prognosis

Human Genome Editing

While the world continues to be focussed on the COVID-19 pandemic, we must not lose sight of other important developments in healthcare. One of these, which came to light on 3 September, is the publication of an extremely important document by the International Commission on the Clinical Use of Human Germline Genome Editing. The document states, in essence, that we do not yet have sufficiently advanced technology to carry out human genome editing without being absolutely sure that we will not make unwanted mutations to the human germline – and, as such, the commission says that heritable human genome editing should not be used to create a pregnancy. Their recommendations will be key to the regulations on the procedure expected to be issued by the WHO later this year. You can read about the commission's report in this issue of *Middle East Health*.

Also, in this issue, in an exclusive interview, we speak to Dr. Bandar Alknawy, CEO of the Ministry of National Guard – Health Affairs, Saudi Arabia about an influential global digital health summit that was held in Riyadh recently. Dr Alknawy, who is also president of King Saud Bin Abdulaziz University for Health Sciences, noted that there are six key priorities for the use of digital technology in healthcare, including crisis and risk communication, and health data governance. Read this interesting interview in this issue to find out about the other priorities and the potential benefits digital tech implementation can have for healthcare.

We receive a lot of news from Cleveland Clinic Abu Dhabi, one of the leading healthcare facilities in the region. It was particularly heart-warming to see that the nurses at the hospital have recently been honoured with the prestigious Lantern Award for nursing. Nurses play such an important role in healthcare, but often don't get the recognition they deserve.

With the exponential growth of vital information that clinicians are expected to know, clinical decision support systems are becoming an indispensable tool to assist with their diagnostic and other clinical decision-making. So, we are pleased to see the adoption of these systems increase throughout the region. Most recently the UpToDate system from Wolters Kluwer has been taken up by the MOH directorate in Al Ahsa, Saudi Arabia and the Dubai Health Authority in the UAE. Patients will be the ultimate beneficiaries.

Stay well

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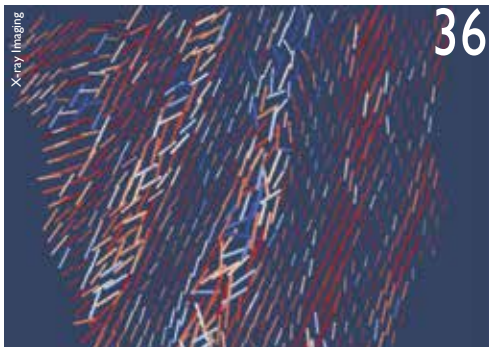

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middle east monitor

Update from around the region

Cleveland Clinic Abu Dhabi honoured with prestigious Lantern Award for nursing

Cleveland Clinic Abu Dhabi, part of Mubadala's healthcare network, has been awarded the Emergency Nurses Association's prestigious Lantern Award, one of only two hospitals outside the US to be named as the first-ever international recipients of the prestigious honour.

The Lantern Award is given by the Emergency Nurses Association, a global membership organization of more than 40,000 emergency nurses, in recognition of emergency departments that demonstrate exceptional performance and deliver the highest level of care to patients. The three-year award is given to only a handful of top-performing facilities each year, with just 28 of the more than 5,000 emergency departments in the United States receiving the award in 2019.

In addition to quality of care, emergency departments are evaluated for their commitment to innovation in terms of nursing practice, leadership, education, advocacy and research to qualify for the award. Cleveland Clinic Abu Dhabi has placed innovation at the core of its mission and was the first facility in the UAE to employ advanced nursing roles including nurse practitioners and physician assistants.

"At Cleveland Clinic Abu Dhabi, our nurses are the foundation of everything we do. Not only do they provide the highest possible level of patient care, they also play an active role in helping us improve every step of the patient journey," said Sue Behrens, Chief Nursing Officer, Cleveland Clinic Abu Dhabi.

Nurses at Cleveland Clinic Abu Dhabi play a vital role in its research efforts and work to implement new processes and procedures in the Emergency Department and across the hospital to improve patient care and outcomes. The Lantern Award is named in honour of Florence Nightingale, who is credited with changing nursing from an untrained job to a skilled, science-based profession. MEH

UAE's National Reference Laboratory opens new testing facility, adds new tech

As part of an expansion drive, Mubadala Healthcare's National Reference Laboratory (NRL) has opened a second COVID-19 testing facility, while simultaneously introducing an advanced virus-detection system and adopting new technology for delivering test results in record time.

Working closely with the Dubai Health Authority (DHA), NRL constructed the new COVID-19 laboratory at its Dubai facilities in under three weeks. Having passed its DHA inspection, the new laboratory is already accepting samples from hospitals and clinics across Dubai and the Northern Emirates, and has a scalable infrastructure to allow for capacity to be ramped up to meet demand.

Abdul Hamid Oubeisi, Chief Executive Officer of NRL, said: "Our world-class COVID-19 laboratory in Abu Dhabi has already delivered more than 240,000 test results. Advanced equipment and a highly skilled scientific team are needed to process these results accurately within a quick turnaround time. Through knowledge-sharing and by leveraging the expertise already gained, the process of establishing a similar laboratory in Dubai proved seamless.

"The key motivation for our ongoing expansion is that we cannot simply react to situations like the COVID-19 pandemic. Instead, we must continually increase our knowledge and upgrade technology to support the community with its immediate needs, as well as beyond the pandemic.

"We recently launched antibody testing to complement conventional COVID-19 testing, and we are also adopting two new forms of technology at our Abu Dhabi laboratory. The first enables us to deliver test results for infections within 45 minutes to three hours for critically ill patients, which increases efficiency in providing care for the most vulnerable segments of the UAE population. The second new technology is genomic sequencing, which has a multitude of public health benefits."

The rapid sample-processing system is one of only a few in the region and is best used in critical cases where time is of the essence. Its sensitive detection can drive appropriate treatment decisions and infection control, while the fully integrated automated platform offers superior accuracy. It performs nucleic acid extraction and reverse transcriptase polymerase chain reaction (RT-PCR), providing results for multiple syndromes, including COVID-19, in under three hours.

The Abu Dhabi laboratory's new genomic sequencing technology, on the other hand, has longer-term benefits as it

is a powerful tool for monitoring diseases and providing information about viral transmission in general.

This helps researchers to identify genetic changes in a virus when it spreads and assists in the development of treatments and vaccines that target specific features of a virus. It can also offer insights into the effectiveness of treatments and future vaccines as the virus continues to mutate. In addition, the knowledge produced can help in tackling future pandemics.

Oubeisi added: "We will continue to work closely with the government, health authorities and other parties to investigate the potential of extending our services in any way that they can benefit the UAE population or economy. There is currently a lot of potential to help employers in their decision-making, and we are also exploring ways to adapt our newly acquired technologies for broader use in the future." MEH

Amana Healthcare offers post-Covid rehab program

Amana Healthcare, a leading provider of post-acute care services, has launched a first-of-its-kind therapy program to rehabilitate patients who have been left with serious health issues and impairments after recovering from COVID-19.

Drawing on the Mubadala Healthcare provider's established expertise working with long-term care patients and offering specialized rehabilitation for conditions such as strokes and traumatic brain injuries, spinal cord injuries, the new program is being deployed as part of its broader efforts to mitigate the effects of the global pandemic.

While an immediate priority in hospitals at the outset of the pandemic has been to save the lives of patients with severe complications from COVID-19, with the network's hospitals declared free from COVID-19 attention is now turning to rehabilitation for discharged patients. To this end, Amana has devised a four-stage process that helps to restore the physical and cognitive functions that are often diminished in the aftermath of the disease, particularly over long periods of care in an ICU.

Deborah Pierce, Director of Rehabilitation at Amana Healthcare

Dr Jason Gray, Senior Director for Clinical Operations at Amana Healthcare, said: "COVID-19 can confine patients to medium- to long-term care in an ICU or acute hospital setting. Recovery brings new challenges, such as regaining breathing functions, physical movement, muscle strength, and healthy body weight and composition. Cognitive functions such as attention, memory and mood may also present psychological challenges. This is when the rehabilitation phase begins, and where Amana's post-COVID-19 rehabilitation program comes in."

Amana's post-acute rehabilitation (PAR) service is led by an in-house team of multidisciplinary (MDT) specialists which include physical medicine and rehabilitation physicians, physiotherapists, occupational therapists, respiratory therapists, dietitians, rehab nurses and social workers.

Deborah Pierce, Director of Rehabilitation at Amana Healthcare and a New Zealand-trained physiotherapist, emphasizes that the four stages of the program coalesce with the input of different professional disciplines.

She said: "The four rehabilitation stages cover ICU step-down rehabilitation and ventilator weaning; specialized inpatient rehabilitation; home or tele/video rehabilitation; and specialized outpatient rehabilitation. An assessment is made as to whether all four stages of the program are necessary; from here, we can deliver the correct therapy to assist in returning the patient to pre-illness levels of function, activities and life roles.

"Our objective is to help patients get back to their pre-COVID life," added Pierce. "Some patients need help getting off a ventilator but for many patients the challenge is to regain strength, mobility and independence after spending weeks immobile or comatose in a hospital bed. This is done by Amana's MDT team, and the program begins in Amana's rehabilitation facilities and continues in the patient's home."

Currently, inpatient referrals to Amana facilities come through those acute hospitals treating COVID-19 in the UAE. In contrast, outpatient tele/video rehabilitation and home rehabilitation can also be accessed directly by patients who have been discharged to their homes, or who have self-managed at home to date, but whose rehabilitation needs are yet to be addressed. This growing emphasis on telemedicine and homecare indicates a developing trend in the endeavour of overcoming the virus. MEH

Physicians stress importance of early diagnosis, treatment for Parkinson's

Physicians at Cleveland Clinic Abu Dhabi, part of Mubadala's healthcare network, are calling attention to Parkinson's disease and the role that early diagnosis and exercise can play in managing the condition.

Parkinson's disease is a neurological movement disorder characterized by tremors, slowness of movement, stiff muscles and unsteady walking. While there is no cure for the disease, medication and surgery can help to manage the condition and enable patients to enjoy better health for longer.

While the condition is most common in people over 60, a growing number in the Middle East are being diagnosed decades earlier. With the incidence of Parkinson's disease cases worldwide expected to double by 2040, experts are keen to highlight ways to control symptoms and slow the progression of the disease.

"As Parkinson's disease progresses, it can inhibit a person's ability to function and live independently. Although we have medications and surgical treatments to help control symptoms, natural measures are also

available. If you're active, you can control the disease, reduce your reliance on medication and avoid the need for surgery," says Dr. Shivam Om Mittal, a neurologist specialized in Parkinson's disease and movement disorders at Cleveland Clinic Abu Dhabi.

Although effective in controlling symptoms, medication and surgery do not alter the progression of the disease. However, research conducted by Cleveland Clinic in the United States has demonstrated that regular exercise can slow the advancement of Parkinson's disease. Patients who were placed on an eight-week high-intensity exercise program developed significantly improved motor function. The hospital is now conducting research into the precise link between exercise and slowing the disease.

"I have patients who do tai chi, yoga and swim. I've even had patients that run marathons and go cycling or hiking. Those patients do very well with just minimal medication. The role of medication is to keep patients active, allowing them to focus on controlling the disease. The key to this is early diagnosis," said Dr. Mittal.

Diagnosing Parkinson's disease requires a comprehensive medical evaluation that most patients don't seek out until their symptoms become very noticeable. Even then, they can struggle to get diagnosed. In more advanced cases, treatment focuses on reducing symptoms, allowing patients to be more active.

Roudha Yusuf, now 53, struggled to get a diagnosis and adequate treatment when she first noticed her symptoms 17 years ago. Despite travelling to the United States and Germany, her symptoms progressed to the point that she was unable to sit up or stand independently and was bedridden for almost 2 years.

Following a comprehensive evaluation by Cleveland Clinic Abu Dhabi's multidisciplinary movement disorder team, a treatment plan was devised to help control her symptoms and regain some of the movement she lost. Following her medical treatment, she was able to walk without any support.

"I was very sick, I felt I was almost dead. Thanks to the team at Cleveland Clinic Abu Dhabi who cared for me, I am much better now. This disease has taken a lot from me, but I can now walk, live my life and care for my family again," said Roudha.

For Dr. Mittal, Roudha exemplifies the importance of early diagnosis and treatment of Parkinson's disease. Catching the disease in its earliest stages, where symptoms can be as simple as a loss of smell or dream enactment at night, can make a tremendous difference.

"Roudha's story is a powerful message for patients with Parkinson's disease. With proper diagnosis and treatment, she was able to go from bed-ridden to up and walking. Although her disease had progressed a great deal, helping her to regain her movement means she can focus on using exercise and proper diet to control her illness. There is a light at the end of the tunnel and, with proper care and management, you can take your life back from this disease," said Dr. Mittal.

MOH Directorate in Al Ahsa partners with Wolters Kluwer to deliver evidence-based patient care with UpToDate

Wolters Kluwer, Health announced that the Ministry of Health Directorate in Al Ahsa, Saudi Arabia, has chosen UpToDate, the company's flagship clinical decision support (CDS) solution, to deliver evidence-based care across the city.

Al Ahsa City is the first directorate in the Kingdom to provide UpToDate region-wide to physicians, nurses and pharmacists across 12 hospitals and 60 primary care

centers, in a concerted effort to equip all clinicians with a leading CDS resource that will help to minimise medication errors, enhance patient safety and deliver the best possible healthcare services.

UpToDate is used by over 1.9 million clinicians around the world to make care decisions based on the latest evidence and recommendations by leading experts around the world. On a broader level, it promotes healthcare excellence which is in line with Saudi Arabia's 2030 vision to offer the best healthcare services in the world.

Mohamad Al-Omar, Director of Academic Affairs in Al Ahsa Directorate explained: "Implementing a CDS solution within all our facilities was one of the highest priorities for Al Ahsa Directorate. Reducing medication errors, enhancing patient safety while increasing our staff's medical knowledge throughout our facilities were our main strategic goals."

"UpToDate is a critical tool for all our practitioners in Al Ahsa City. Its ease-of-use in getting the right knowledge quickly, providing world-class care tailored to individual patients, as well as the wide-range of covered specialties and pharmacy drug monographs available, are among the many reasons we have chosen UpToDate."

Alaa Darwish, Country Manager for Middle East, Turkey and Africa, for Clinical Effectiveness at Wolters Kluwer, Health said: "It is an honour to partner with the MOH Directorate in Al Ahsa to make UpToDate available to doctors, pharmacists and nurses across the city."

"As the only clinical decision support tool associated with improved patient outcomes, UpToDate is an invaluable evidence-based resource that clinicians use every day to make the right decisions for patients and deliver the highest quality, safe healthcare services. In these difficult times of the COVID-19 pandemic it is even more critical to equip healthcare professionals with the latest evidence and recommendations from world-leading experts."

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worldwide monitor

Update from around the globe

WHO African Region declared free of wild polio

The WHO African Region has been declared free of wild polio by the Africa Regional Certification Commission after four years without a case. With this historic milestone, five of the six WHO regions, representing over 90% of the world's population, are now free of the wild poliovirus, moving the world closer to achieving global polio eradication.

Only two countries worldwide continue to see wild poliovirus transmission: Pakistan and Afghanistan.

"Ending wild polio virus in Africa is one of the greatest public health achievements of our time and provides powerful inspiration for all of us to finish the job of eradicating polio globally," said WHO Director-General Dr Tedros Adhanom Ghebreyesus. "I thank and congratulate the governments, health workers, community volunteers, traditional and religious leaders and parents across the region who have worked together to kick wild polio out of Africa."

Strong leadership and innovation were instrumental in stopping the wild poliovirus in the region. Countries successfully coordinated their efforts to overcome major challenges to immunizing children, such as high levels of population movement, conflict and insecurity restricting access to health services, and the virus's ability to spread quickly and travel across borders.

In addition, the continued generosity and shared commitment of donors – including governments, the private sector, multilateral institutions and philanthropic organizations – to achieving a polio-free world helped build the infrastructure that enabled the African region to reach more children than ever before with polio vaccines and defeat wild polio.

"During a challenging year for global health, the certification of the African region as wild poliovirus-free is a sign of hope and progress that shows what can be accomplished through collaboration and perseverance," said Rotary International President Holger Knaack. "Since 1996, when Nelson Mandela joined with Rotary, the Global Polio Eradication Initiative, and governments of the African region we've achieved something remarkable. This milestone tells us that polio eradication is possible, as long as the world remains committed to finishing the job."

The resources and expertise used to eliminate wild polio have significantly contributed to Africa's public health and outbreak response systems. The polio programme provides far-reaching health benefits to local communities, from supporting the African region's response to COVID-19 to bolstering routine immunization against other vaccine-preventable diseases.

While this is a remarkable milestone, we must not become complacent. Continued commitment to strengthening immunization and health systems in the African region is essential to protect progress against wild polio and to tackle the spread of type 2 circulating vaccine-derived poliovirus (cVDPV2), which is present in 16 countries in the region. Pockets of low immunity mean such strains continue to pose a threat and the risk is magnified by interruptions in vaccination due to COVID-19, which have left communities more vulnerable to cVDPV2 outbreaks.

The Global Polio Eradication Initiative calls on countries and donors to remain vigilant against all forms of polio. Until every strain is eradicated worldwide, the incredible progress made against polio globally will be at risk. MEH

New COVID-19 Law Lab to provide vital legal information and support for the global COVID-19 response

The COVID-19 Law Lab was launched on 22 July. This initiative gathers and shares legal documents from over 190 countries across the world to help states establish and implement strong legal frameworks to manage the pandemic. The goal is to ensure that laws protect the health and wellbeing of individuals and communities and that they adhere to international human rights standards.

The new Lab <*www.COVIDLawLab.org*> is a joint project of United Nations Development Programme (UNDP), the World Health Organization (WHO), the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the O'Neill Institute for National and Global Health Law at Georgetown University.

The COVID-19 Law Lab is a database of laws that countries have implemented in response to the pandemic. It includes state of emergency declarations, quarantine measures, disease surveillance, legal measures relating to mask-wearing, social distancing, and access to medication and vaccines. The database will continue to grow as more countries and themes are added.

It will also feature research on different legal frameworks for COVID-19. These analyses will focus on the human rights impacts of public health laws and help countries identify best practices to guide their immediate responses to COVID-19 and socioeconomic recovery efforts once the pandemic is under control. It builds off the work of the UHC Legal Solutions Network, which was established to help countries achieve universal health coverage through the implementation of rights-based legal frameworks.

Well-designed laws can help build strong health systems; evaluate and approve safe and effective drugs and vaccines; and enforce actions to create healthier and safer public spaces and workplaces. Critically, they are key to effective implementation of the WHO International Health Regulations: surveillance; infection prevention and control; management of travel and trade; and implementation of measures to maintain essential health services.

"Laws and policies that are grounded in science, evidence and human rights can enable people to access health services, protect themselves from COVID-19 and live free from stigma, discrimination and violence," says Achim Steiner, UNDP Administrator. "The COVID-19 Law Lab is an important tool for sharing good practices on laws and policies."

The COVID-19 pandemic has seen a vast increase in urgent legislative action to control and reduce the pandemic.

"Strong legal frameworks are critical for national COVID-19 responses," said Dr. Tedros Adhanom Ghebreyesus, WHO Director-General. "Laws that impact health often fall outside the health sector. As health is global, legal frameworks should be aligned with international commitments to respond to current and emerging public health risks. A strong foundation of law for health is more important now than ever before."

However, laws that are poorly designed, implemented, or enforced can harm marginalized populations, entrench stigma and discrimination, and hinder efforts to end the pandemic.

Winnie Byanyima, Executive Director of UNAIDS, said: "To ensure responses to the pandemic are effective, humane and sustainable, governments must use the law as a tool to uphold the human rights and dignity of people affected by COVID-19."

"We need to track and evaluate how laws and policies are being used during the pandemic to understand what works," said Dr. Matthew M. Kavanagh, faculty in Georgetown University's Department of International Health.

Katie Gottschalk, Executive Director of the O'Neill Institute for National and Global Health Law at Georgetown University Law Center added, "We must learn lessons from the early stage of pandemic policies to implement the most effective laws going forward – the COVID-19 Law Lab allows us to do just that." MEH

World Mental Health Day event to call for increased investment

On World Mental Health Day, 10 October, the World Health Organization, with partner organizations, United for Global Mental Health and the World Federation for Mental Health, will call for a massive scale-up in investment in mental health.

Mental health is one of the most neglected areas of public health. Close to 1 billion people are living with a mental disorder, 3 million people die every year from the harmful use of alcohol and one person dies every 40 seconds by suicide. And now, billions of people around the world have been affected by the COVID-19 pandemic, which is having a further impact on people's mental health.

Yet, relatively few people around the world have access to quality mental health services. In low- and middle-income countries, more than 75% of people with mental, neurological and substance use disorders receive no treatment for their condition at all. Furthermore, stigma, discrimination, punitive legislation and human rights abuses are still widespread.

At the so-called 'Big Event for Mental Health' on World Mental Health Day, the WHO will, for the first time, host a global online advocacy campaign on mental health. The WHO will showcase the work that its staff are doing around the world to reduce mental illness and the harmful use of alcohol and drugs. World leaders and mental health experts will join the WHO Director-General to talk about their commitment to mental health and what more must be done.

"World Mental Health Day is an opportunity for the world to come together and begin redressing the historic neglect of mental health," said Dr Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization. "We are already seeing the consequences of the COVID-19 pandemic on people's mental well-being, and this is just the beginning. Unless we make serious commitments to scale up investment in mental health right now, the health, social and economic consequences will be far-reaching."

Countries spend on average only 2% of their health budgets on mental health. Despite some increases in recent years, international development assistance for mental health has never exceeded 1% of all development assistance for health. This is despite the fact that for every US$ 1 invested in scaled-up treatment for common mental disorders such as depression and anxiety, there is a return of US$ 5 in improved health and productivity.

Dr Ingrid Daniels, President of the World Federation of Mental Health, said: "It is nearly 30 years since the first World Mental Health Day was launched by the World Federation for Mental Health. During that time, we have seen an increasing openness to talk about mental health in many countries of the world. But now we must turn words into actions. We need to see concerted efforts being made to build mental health systems that are appropriate and relevant for today's – and tomorrow's – world."

- For more information, visit:

United for Global Mental Health – *www.unitedgmh.org*

The World Federation for Mental Health – *https://wfmh.global/* MEH

Vaccinations decline during COVID-19 pandemic

The World Health Organization and UNICEF has warned of an alarming decline in the number of children receiving life-saving vaccines around the world. This is due to disruptions in the delivery and uptake of immunization services caused by the COVID-19 pandemic. According to new data by WHO and UNICEF, these disruptions threaten to reverse hard-won progress to

reach more children and adolescents with a wider range of vaccines, which has already been hampered by a decade of stalling coverage.

The latest data on vaccine coverage estimates from WHO and UNICEF for 2019 shows that improvements such as the expansion of the HPV vaccine to 106 countries and greater protection for children against more diseases are in danger of lapsing. For example, preliminary data for the first four months of 2020 points to a substantial drop in the number of children completing three doses of the vaccine against diphtheria, tetanus and pertussis (DTP3). This is the first time in 28 years that the world could see a reduction in DTP3 coverage – the marker for immunization coverage within and across countries.

"Vaccines are one of the most powerful tools in the history of public health, and more children are now being immunized than ever before," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General. "But the pandemic has put those gains at risk. The avoidable suffering and death caused by children missing out on routine immunizations could be far greater than COVID-19 itself. But it doesn't have to be that way. Vaccines can be delivered safely even during the pandemic, and we are calling on countries to ensure these essential life-saving programmes continue." MEH

WHO survey: 90% of countries report disruptions to essential health services during COVID-19 pandemic

The World Health Organization (WHO) has published a first indicative survey on the impact of COVID-19 on health systems based on 105 countries' reports. Data collected from five regions over the period from March to June 2020 illustrate that almost every country (90%) experienced disruption to its health services, with low- and middle-income countries reporting the greatest difficulties. Most countries reported that many routine and elective services have been suspended, while critical care – such as cancer screening and treatment and HIV therapy – has seen high-risk interruptions in low-income countries.

"The survey shines a light on the cracks in our health systems, but it also serves to inform new strategies to improve healthcare provision during the pandemic and beyond," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General. "COVID-19 should be a lesson to all countries that health is not an 'either-or' equation. We must better prepare for emergencies but also keep investing in health systems that fully respond to people's needs throughout the life course."

Services hit across the board: Based on reports from key informants, countries on average experienced disruptions in 50% of a set of 25 tracer services. The most frequently disrupted areas reported included routine immunization – outreach services (70%) and facility-based services (61%), non-communicable diseases diagnosis and treatment (69%), family planning and contraception (68%), treatment for mental health disorders (61%), cancer diagnosis and treatment (55%).

Countries also reported disruptions in malaria diagnosis and treatment (46%), tuberculosis case detection and treatment (42%) and antiretroviral treatment (32%). While some areas of health care, such as dental care and rehabilitation, may have been deliberately suspended in line with government protocols, the disruption of many of the other services is expected to have harmful effects on population health in the short- medium- and long-term.

Potentially life-saving emergency services were disrupted in almost a quarter of responding countries. Disruptions to 24-hour emergency room services for example were affected in 22% of countries, urgent blood transfusions were disrupted in 23% of countries, emergency surgery was affected in 19% of the countries.

Disruption due to a mix of supply and demand side factors. 76% of countries reported reductions in outpatient care attendance due to lower demand and other factors such as lockdowns and financial difficulties. The most commonly reported factor on the supply side was cancellation of elective services (66%). Other factors reported by countries included staff redeployment to provide COVID-19 relief, unavailability of services due to closings, and interruptions in the supply of medical equipment and health products.

Adapting service delivery strategies. Many countries have started to implement some of the WHO recommended strategies to mitigate service disruptions, such as triaging to identify priorities, shifting to on-line patient consultations, changes to prescribing practices and supply chain and public health information strategies. However, only 14% of countries reported removal of user fees, which WHO recommends to offset potential financial difficulties for patients.

The pulse survey also provides an indication of countries' experiences in adapting strategies to mitigate the impact on service provision. Despite the limitations of such a survey, it highlights the need to improve real-time monitoring of changes in service delivery and utilization as the outbreak is likely to wax and wane over the next months, and to adapt solutions accordingly.

To that end, WHO will continue to work with countries and to provide supportive tools to address the fallout from COVID-19. Given countries' urgent demand for assistance during the pandemic response, WHO is developing the *COVID19: Health Services Learning Hub*, a web-based platform that will allow sharing of experiences and learning from innovative country practices that can inform the collective global response. WHO is also devising additional surveys at the sub-national level and in health facilities to gauge the longer-term impact of disruptions and help countries weigh the benefits and risks of pursuing different mitigation strategies.

on the WEB Survey: Rapid assessment of continuity of essential health services during the COVID-19 pandemic
https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2020.1

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KEY NOTES

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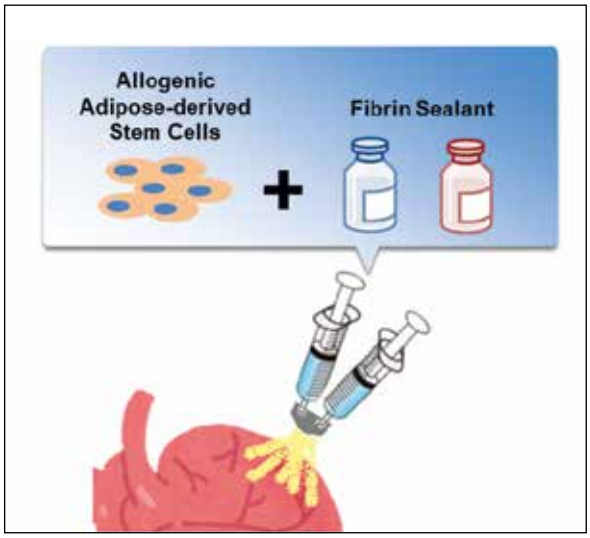


ADSCs are spread over the surface of the heart via cell spray in fibrinogen and thrombin solutions.

Doctors trial stem cell spray for heart failure treatment

A team of researchers led by Professor Sawa Yoshiki of Osaka University Hospital who developed a method of spraying mesenchymal stem cells onto the heart, have been testing the product, ADR-002K, in a Phase 1 trial at Osaka University Hospital. Details of this technique are published in *Transplantation*.

Heart disease is a leading cause of death globally. The prognosis of serious heart failure with ischemic cardiomyopathy (ICM) is particularly poor, but definitive therapy has not been established.

In order to treat serious heart failure, stem cell administration through coronary artery catheterization and intramyocardial injection of stem cells using a needle were performed, but there were concerns regarding the adverse effects and effectiveness of these medications.

In order to overcome these issues, a treatment method that involves skeletal myoblast cell sheet transplantation was developed and its effectiveness was proven to a certain extent; however, because it required the use of a cell processing center (CPC), it was difficult to put into practice at medical institutes without a CPC.

In a joint research project with ROHTO Pharmaceutical Co., using high-quality human allogeneic adipose-derived mesenchymal stem cells (ADSCs), this team developed a simple and convenient cell administration technique, which can be prepared in an operating room and available at low cost. Since this regenerative medicine technique does not require a CPC, it can be widely used at medical institutions.

ADR-002K is a cell spray method-based product and is composed of ADR-002 as its main component and a biological adhesive solution as its sub-component. This clinical trial is being conducted in order to confirm the safety and feasibility of ADR-002K methodology for patients with ischemic cardiomyopathy who undergo coronary artery bypass surgery.

- *https://journals.lww.com/transplantjournal/Fulltext/2018/12000/Cell_Spray_Transplantation_of_Adipose_derived.14.aspx*

New blood, new hope: Transfusions protect the brain from stroke damage, research finds

Muscle weakness permeates through one side of your body and your speech slurs. It's a stroke. And you need to be rushed to the emergency room.

Doctors replace your blood with the blood of a healthy person who's never suffered a stroke.

This blood swap lessens damage to your brain, and any neurological deficits from the stroke are nil.

This is not mere wishful thinking. It is a potential breakthrough in stroke therapy based on mice research by West Virginia University neuroscientists.

In the study, led by Xuefang "Sophie" Ren, research assistant professor in the Department of Neuroscience, the team found that blood substitution therapy rescues the brains of mice from ischemic damage. Their article is published in *Nature Communications* – *https://doi.org/10.1038/s41467-020-17930-x*

"What we were able to demonstrate is that if you remove part of the blood from a subject undergoing stroke, and replace that blood from a subject that's never had a stroke, the outcomes of that stroke are profoundly improved," said Ren, who's also director of the WVU Experimental Stroke Core.

The study is believed to be the first to show that blood replacement therapy leads to improved stroke outcomes in mice, a potential next step for stroke therapy in humans.

Most strokes (ischemic) occur when the blood supply to the brain is interrupted, usually by a blockage of the arteries leading to the brain.

While there is no known single medication for stroke, the only FDA-approved treatment for ischemic strokes is tPA, or tissue plasminogen activator, which dissolves the clot and improves blood flow. However, tPA typically must be administered within three hours of the stroke.

Ren's research indicates that blood transfusions can take place beyond that limited window – up to seven hours - and still have a positive impact. Replacing 20 percent of the blood in a mouse was enough to show a profound reduction in damage to the brain. The average adult holds around one-and-a-half gallons of blood in the body.

"The idea is to change the immune response that happens after stroke," Simpkins said.

Researchers explained that following a stroke, the makeup of a patient's blood changes, causing disruptions in the brain and how the body responds. Neutrophils, a type of white blood cell that helps lead the immune system's response, play a role in increasing the levels of an enzyme called MMP-9, which can lead to blood-brain

barrier leakage and degeneration in brain tissue.

Blood replacement therapy removes inflammatory cells and decreases neutrophils and MMP-9 levels following a stroke, the study concluded.

"The immune system doesn't recognize much of what's happening when there's a stroke," Simpkins said. "So the neutrophils go to the brain and try to clean up the damage that happens. But there's too much in the brain and those same neutrophils release MMP-9, which then exacerbates the damage.

"What we learn is that stroke is simply not a cerebral vascular event. It's a whole-body event. Both the brain and the body get signals that something's going on in the brain and as the immune system responds to try to help, it actually worsens the outcome. Therefore, by removing the blood and replacing it with the blood of those that have not experienced stroke, we get good outcomes."

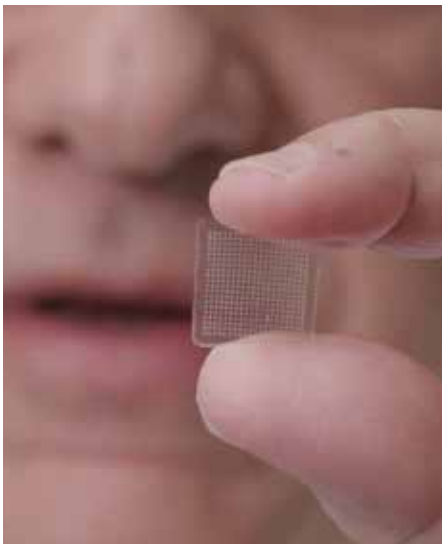
Currently, blood-based therapies are emerging as treatments to combat aging and fight neurodegenerative diseases, the researchers noted.

Now, blood replacement therapy is a proven strategy that targets the pathological systemic responses to stroke, Ren said, and could reduce the mortality of stroke patients.

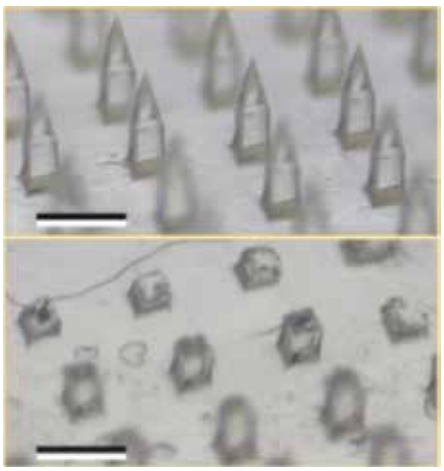
Researchers develop new microneedle array combination vaccine delivery system

Researchers at the University of Pittsburgh School of Medicine have developed a new vaccine delivery system for vaccines using live or attenuated viral vectors: a finger-tip sized patch that contains 400 tiny needles, each just half of one millimetre. Their progress is reported in the *Journal of Investigative Dermatology* – https://doi.org/10.1016/j.jid.2020.03.966

The needles, made from sugar and the specific cargo being delivered, comprise a three-dimensional (3D), multicomponent dissolving microneedle array (MNA). While feeling like having Velcro pressed against the skin, the vaccine would penetrate the upper level of the skin, absorb moisture from the skin, and then dissolve and release molecules that prompt the immune system to make antibodies to attack the virus. In addition to antibody production, this technology has the potential to improve cellular immune responses in patients and expand global immunization capabilities. It is clear evidence of the broad reach and contribution of skin scientists, even extending into pandemic vaccine design.



Microneedle Array Vaccine: The vaccine is delivered into the skin through a fingertip-sized patch of microscopic needles.



Dissolvable MNAs incorporating Ad.OVA ± Poly(I:C) were fabricated using a spin-casting method, applied to the mouse skin for 10 minutes, and then removed. Images of MNAs **(a)** before and **(b)** after the application were obtained using optical stereomicroscopy. Bar = 500 μm.

Explaining the importance of this work, lead author Louis D. Falo, Jr., MD, PhD, Professor and Chairman of the Department of Dermatology, University of Pittsburgh School of Medicine and UPMC, Pittsburgh, PA, USA, said: "We are developing this new delivery technology because while traditional vaccines are often effective in inducing antibody responses, they frequently fail to generate the cellular responses that are essential to prevent or treat many cancers or infectious diseases."

The skin is an ideal vaccination site because it contains an immune network that is highly responsive and encourages the generation of strong and long-lasting immunity.

Dissolvable MNAs are designed to mechanically penetrate the superficial cutaneous layers, rapidly dissolve upon insertion into the skin, and deliver uniform quantities of biocargo to a defined 3D space within the skin. This enables localized delivery of low amounts of drugs or vaccines to achieve high concentrations in this specific skin microenvironment.

Using in vivo mouse models, investigators generated the 3D multicomponent dissolvable vaccine platform combining a live adenovirus-encoded antigen with an added component, polyinosinic:polycytidylic acid (poly I:C), an immunostimulant used to simulate the skin immune system. This successfully induced both antibody responses and stronger cellular immune responses.

Induction of antigen-specific cellular immunity is a point of emphasis in the vaccine field, as evidenced by recent efforts to generate "universal vaccines" for mutable infectious diseases like influenza, HIV, and coronaviruses by targeting infected cells.

"Remarkably," says Dr. Falo, "the MNA vaccine platforms incorporating both antigen-encoding adenovirus and poly I:C augmented the destruction of targeted cells significantly compared to MNA-delivery of the same adenovirus alone." The research-

ers also found that the MNAs integrating both poly I:C and adenovirus retained their immunogenicity after one month of storage at 4 C. MNA-delivered vaccines also have advantages in their ease of fabrication, application, and storage compared to other vaccine delivery platforms.

"Our results suggest that multicomponent MNA vaccine platforms uniquely enable delivery of both adjuvant and antigen-encoding viral vectors to the same skin microenvironment, resulting in improved immunogenicity including cellular immune responses," comments Dr. Falo. "This MNA delivery approach could improve the effectiveness of adenoviral vaccines now in development for the prevention of coronavirus disease (COVID-19)."

The authors note in their paper that the "dissolving microneedle arrays (MNAs) with obelisk-shaped needles that incorporate adenovectors with or without Poly(I:C) were manufactured using their previously described MNA fabrication strategy (Korkmaz et al., 2015). Their MNAs are designed for human applications and are currently being used in phase I clinical trial for the treatment of cutaneous T-cell lymphoma. Their fabrication methods are flexible to rapidly modify the microneedle and array designs for application-driven optimization." MEH

Cleveland Clinic records second successful birth from transplanted uterus

An ongoing clinical trial by Cleveland Clinic to assess the efficacy of uterus transplants from deceased donors is celebrating the second successful birth, after Michele, a young Pennsylvania woman, gave birth to Cole, a perfectly healthy boy.

The trial aims to enrol 10 subjects. Since its launch in 2015, the Cleveland Clinic team has completed eight uterus transplants. Six have been successful and have resulted in 2 births of healthy babies. Two more are on the way.

A team of healthcare workers from more than 12 specialties spent four years preparing Michelle to become a mother. During this time, several potential donors were screened. A suitable match was found, and a successful uterus transplant was performed at Cleveland Clinic in January last year. It was followed by six months of observation to ensure that the uterus and Michelle were ready to become pregnant. Michelle became pregnant after her first embryo transfer, and had her baby delivered by Caesarean section in March this year.

Dr Cristiano Quintini, transplant surgeon

To explain more about how uterine transplants work, transplant surgeon Cristiano Quintini, MD and his colleagues – maternal-foetal medicine specialist Uma Perni, MD and Director Emeritus of Transplantation Andreas Tzakis, MD, PhD, who spearheaded bringing uterus transplantation to Cleveland Clinic in 2015 – answer some frequently asked questions.

Q: Why are you conducting the trial for deceased-donor uterine transplants?

A: We want to establish that Uterus Transplants can be performed safely and successfully, in order to become a treatment option for women with absolute uterine factor infertility (UFI).

By using deceased donors, we avoid any risk to a potential living donor.

It is a very exciting time because we are finally seeing the amazing and life-changing outcomes this transplant can have.

Q: What causes uterine factor infertility?

A: Most candidates were born without a uterus. This is a fairly common condition seen in 1/500 female births. These are otherwise healthy women. In few cases the uterus is removed during the reproductive age for life threatening bleeding, benign or malignant tumours.

Q: What does the process entail?

A: The first step is an evaluation to make sure a transplant can be done safely. The second step is to produce and store embrya, which will be used for future pregnancies. The third step is to place the patient on the waiting list and search for an appropriate donor.

Baby Cole, successfully delivered from a transplanted uterus.

When an appropriate donor is available, our recovery team goes to the donor hospital and recovers the uterus, which is transported back to Cleveland Clinic for implantation. The recipient receives immunosuppressive medications to prevent her immune system from rejecting the new uterus. Immunosuppression is needed from the time of the transplant and until the goal: one or two healthy babies are delivered. Our gynaecological specialists perform the embryo transfer 6 months after successful transplant. The pregnancy and delivery are followed by our high-risk pregnancy team who ensure that pregnancy and delivery are carried out safely. The transplanted uterus is removed when the delivery is successfully completed.

Q: How is uterus transplant pregnancy different from a traditional pregnancy?

A: From our experience and that of others worldwide, these pregnancies resemble natural pregnancies of women who had a transplant. Thousands of kidney, liver, heart, and lung recipients have delivered their babies, while they are immunosuppressed. We know there is an increased risk of high blood pressure and preeclampsia. Delivery is accomplished with a Caesarean-section.

Q: What happens after the baby is born?

A: The uterus is removed after the woman delivers one or two babies, depending on her preference. This minimizes the amount of time she needs to be on immunosuppressant medications. MEH

New molecule repairs cartilage, relieves symptoms of osteoarthritis

A newly discovered molecule has been found to provide long-lasting regeneration of bone and cartilage defects, as well as symptom relief, and could potentially play a role in treating osteoarthritis, according to early research in animals led by Queen Mary University of London.

Cartilage overlies bones to enable frictionless movement in the joints. Although bone heals well, cartilage often fails to repair after injury. This leads to further cartilage loss and osteoarthritis. It is the most common cause of disability for which there is no cure, costing around 1.5 to 2 per cent of GDP for Western countries. Cartilage regeneration is therefore a priority in medicine.

In the research, published in the journal *Science Translational Medicine*, the team studied a molecule called 'agrin' and discovered that it repairs cartilage by recruiting and activating adult stem cells present in the joint.

These mechanisms are the same as the ones the body uses when it is first developing the skeleton in the embryo. This study shows that supporting these mechanisms is an effective way to support the healing of lesions which are too big to heal in normal conditions.

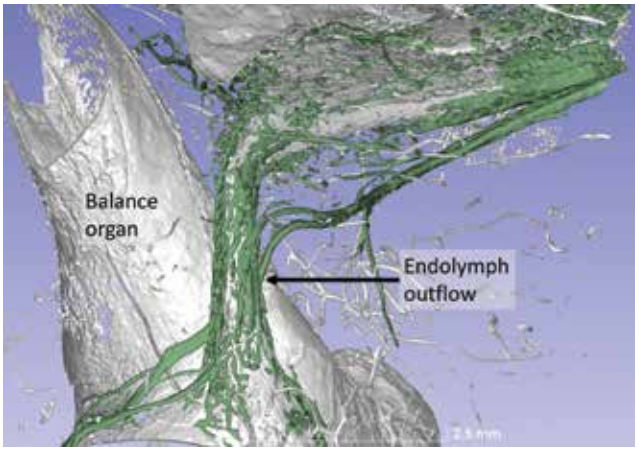
In experiments in mice, a gel containing agrin was injected into joint surface defects, and after eight weeks, found to induce long-lasting regeneration of bone and cartilage, more so than in a control group that received the gel, but without agrin.

Cartilage and bone repair was also better after six months in sheep that had received the agrin-containing gel, compared to a control group. These sheep also spent more time playing and less time resting throughout the study, suggesting that the improved repair was associated with improved function.

Commenting on the research, Professor Francesco Dell'Accio from Queen Mary University of London, said: "We've shown that it's possible to repair joint defects, for the moment at least in animals, not just in the bone but also in the cartilage. One single administration of this molecule is sufficient to trigger a cascade of events in the joints, which, once started, are then self-maintained. Not only does it achieve structural repair, but we've shown that it gives symptomatic relief in animals extremely rapidly."

The capacity of agrin to induce long-term cartilage regeneration after a single administration makes it an excellent candidate for clinical use, however, the researchers say they are still several years away from being able to begin clinical trials in humans.

- **doi:** https://doi.org/10.1126/scitranslmed.aax9086



A synchrotron X-ray of the balance organ of the human inner ear shows a kidney-shaped canal with a diameter of just approx. 0.5 mm. The inner ear has been reconstructed three-dimensionally in a computer program, and the surrounding bone has been made transparent. The green-coloured vessels surrounding the canal are thought to absorb and clean the fluid in the inner ear. It is believed that disruption of this function may cause Ménière's disease.

Advanced X-ray technology tells us more about Ménière's disease

The organ of balance in the inner ear is surrounded by the hardest bone in the body. Using synchrotron X-rays, researchers at Uppsala University have discovered a drainage system that may be assumed to play a major role in the onset of Ménière's disease, a common and troublesome disorder. These results are published in the journal *Scientific Reports*.

Ménière's disease is manifested in sudden onset of severe dizziness (vertigo) attacks, hearing impairment and tinnitus. Accumulation of excess fluid in the inner ear is thought to cause the disorder.

The researchers behind the new scientific article have investigated the organs in the human inner ear, which are very difficult to study. This part of the ear is enclosed by the body's hardest bone. Using synchrotron X-ray imaging, an advanced and powerful form of computer tomography, the scientists were able to study the organ of balance with its surrounding blood vessels. Since the technology generates energy too high for use on living humans, donors' temporal bones were used.

The images of the inner ear were reconstructed to make a three-dimensional model using computer software. Inside the hard bone the researchers discovered a drainage system that is thought to explain how the fluid in the inner ear is absorbed. This discovery may bring about an improved understanding of how and why Ménière's disease arises.

The synchrotron imaging investigation was carried out in Saskatoon, in the Canadian province of Saskatchewan. The study was conducted jointly with Dr Sumit Agrawal and Dr Hanif Ladak, who are researchers in London, Ontario, Canada.

The study is also part of The Human Vestibular Aqueduct, Endolymphatic Duct and Sac: A Morphological Study Using Micro-CT, Super Resolution Immunohistochemistry and Synchrotron Phase Contrast Imaging, a thesis publicly defended by Charlotta Kämpfe Nordström, an otologist at Uppsala University's Department of Surgical Sciences, on 7 May 2020.

- **doi:** 10.1038/s41598-020-65110-0

172 countries engaged in COVID-19 Vaccine Global Access Facility

As of 24 August, 172 economies were engaged in discussions to potentially participate in COVAX, a global initiative aimed at working with vaccine manufacturers to provide countries worldwide equitable access to safe and effective vaccines, once they are licensed and approved. COVAX currently has the world's largest and most diverse COVID-19 vaccine portfolio – including nine candidate vaccines, with a further nine under evaluation and conversations underway with other major producers.

COVAX, the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator, is co-led by the Coalition for Epidemic Preparedness Innovations (CEPI), Gavi, the Vaccine Alliance, and the World Health Organization (WHO) – working in partnership with developed and developing country vaccine manufacturers. It is the only global initiative that is working with governments and manufacturers to ensure COVID-19 vaccines are available worldwide to both higher-income and lower-income countries.

In order to be able to secure enough doses of vaccines to protect the most vulnerable populations, such as health workers and the elderly, the next step for the partnership is to confirm potential self-financing participants' intent to participate by 31 August and to turn these into binding commitments to join the COVID-19 Vaccine Global Access Facility (COVAX Facility) by 18 September, with first upfront payments to follow thereafter, and no later than 9 October.

"Equal access to a COVID-19 vaccine is the key to beating the virus and paving the way for recovery from the pandemic," said

GAVI/Adrian Brooks

Stefan Löfven, Prime Minister of Sweden. "This cannot be a race with a few winners, and the COVAX Facility is an important part of the solution – making sure all countries can benefit from access to the world's largest portfolio of candidates and fair and equitable distribution of vaccine doses."

The COVAX Facility is a Gavi-coordinated pooled procurement mechanism for new COVID-19 vaccines, through which COVAX will ensure fair and equitable access to vaccines for each participating economy, using an allocation framework currently being formulated by WHO. The COVAX Facility will do this by pooling buying power from participating economies and providing volume guarantees across a range of promising vaccine candidates, allowing those vaccine manufacturers whose expertise is essential to large scale production of the new vaccines, to make early, at-risk investments in manufacturing capacity – providing participating countries and economies with the best chance at rapid access to doses of a successful COVID-19 vaccine.

"In order to save lives in this pandemic, we must make sure that COVID-19 vaccines are available to all countries, including the most vulnerable," said Dag-Inge Ulstein, Norway's Minister of International Development.

The success of COVAX hinges not only on countries signing up to the COVAX Facility, but also filling key funding gaps for both COVAX R&D work and a mechanism to support participation of lower-income economies in the COVAX Facility.

"COVID-19 is an unprecedented global health challenge that can only be met with unprecedented cooperation between governments, researchers, manufacturers and multilateral partners," said Dr Tedros Adhanom Ghebreyesus, Director-General of WHO. "By pooling resources and acting in solidarity through the ACT Accelerator and the COVAX Facility, we can ensure that once a vaccine is available for COVID-19, it's available equitably to all countries."

Vaccine research

CEPI is leading COVAX vaccine research and development work, which aims to develop three safe and effective vaccines which can be made available to countries participating in the COVAX Facility. Nine candidate vaccines are currently being supported by CEPI; seven of which are currently in clinical trials. Governments, vaccine manufacturers (in addition to their own R&D), organisations and individuals have committed US$1.4bn towards vaccine R&D so far, but an additional US$ 1bn is urgently needed to continue to move the portfolio forward.

A further nine candidate vaccines which complement the current CEPI portfolio are currently being evaluated for inclusion in COVAX. Furthermore, COVAX will consider procuring vaccines that complement the portfolio from any producer in the world; conversations are already underway with a number of additional manufacturers not receiving R&D support from CEPI to procure their vaccines if they are successful. Maximising the portfolio of vaccines increases the probability of success as individual vaccines historically have a high failure rate.

"In the scramble for a vaccine, countries can act alone – creating a few winners, and many losers – or they can come together to participate in COVAX, an initiative which is built on enlightened self-interest but also equity, leaving no country behind," said Richard Hatchett, CEO of CEPI. "Only by taking a global view can we protect those most at risk around the world from the terrible effects of this disease. COVAX can deliver the vaccines that could end the pandemic, but it needs countries to step forward both to join the COVAX Facility, and also to address the serious funding shortfalls, including for R&D. The decisions that are taken now about COVID-19 vaccines have the power to change our future. We must be courageous and ambitious in striving for a multilateral solution."

> Equal access to a COVID-19 vaccine is the key to beating the virus and paving the way for recovery from the pandemic. This cannot be a race with a few winners, and the COVAX Facility is an important part of the solution – making sure all countries can benefit from access to the world's largest portfolio of candidates and fair and equitable distribution of vaccine doses.

$3 per dose

A collaboration between Serum Institute of India (SII), Gavi and the Bill & Melinda Gates Foundation announced earlier in August will ensure up to 100 million doses of AstraZeneca or Novavax's candidate vaccines, if successful, will be available to low- and middle-income economies through the COVAX Facility at just US$3 per dose. The arrangement also provides an option to secure additional doses if COVAX sees a need for it. Separate agreements between Gavi, CEPI and AstraZeneca, announced in June, guarantee a further 300 million doses of their candidate vaccine, if successful, for the COVAX Facility.

In addition, in June Gavi launched the COVAX Advance Market Commitment (AMC), a financing instrument aimed at supporting the participation of 92 lower and middle income economies in the COVAX Facility. The COVAX AMC has raised more than US$600 million against an initial target of securing US$2 billion seed funding from sovereign donors as well as philanthropy and the private sector, needed by the end of 2020. Funding the COVAX AMC will be critical to ensuring ability to pay is not a barrier to accessing COVID-19 vaccines, a situation which would leave the majority of the world unprotected, with the pandemic and its impact continuing unabated.

80 higher-income economies, which would finance the vaccines from their own public finance budgets, have so far submit-

The full list of CEPI-supported COVAX candidate vaccines

- Inovio, USA (Phase I/II)
- Moderna, USA (Phase III)
- CureVac, Germany (Phase I)
- Institut Pasteur/Merck/Themis, France/USA/Austria (Preclinical)
- AstraZeneca/University of Oxford, UK (Phase III)
- University of Hong Kong, China (Preclinical)
- Novavax, USA (Phase I/II)
- Clover Biopharmaceuticals, China (Phase I)
- University of Queensland/CSL, Australia (Phase I)


GAVI/Victoria Ivleva

ted Expressions of Interest ahead of the 31 August deadline for confirmation of intent to participate. They will partner with 92 low- and middle-income countries that will be supported by the AMC if it meets its funding targets. Together, this group of 172 countries represents more than 70% of the world's population. Among the group are representatives from every continent and more than half of the world's G20 economies.

"The momentum we are witnessing behind this unprecedented global effort means there could be light at the end of the tunnel: A vaccine is our best route to ending the acute phase of the pandemic and the COVAX effort is the best way to get there," said Dr Seth Berkley, CEO of Gavi, the Vaccine Alliance. "For higher-income countries it represents a win-win: not only will you be guaranteed access to the world's largest portfolio of vaccines, you will also be negotiating as part of a global consortium, bringing down prices and ensuring truly global access. Signing up to the COVAX Facility gives each country its best chance at protecting the most vulnerable members of their populations – which in turn gives the world its best chance at mitigating the toll this pandemic has taken on individuals, communities and the global economy. To make this end-to-end vision a reality, we need countries to make end-to-end commitments: funding R&D, signing up to the Facility, and supporting the COVAX AMC."

The COVAX Facility is coordinated by Gavi, the Vaccine Alliance, and forms a key part of COVAX – the vaccines pillar of the ACT Accelerator, a ground-breaking global collaboration involving vaccine manufacturers to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines. The overall aim of COVAX is to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world. It will achieve this by sharing the risks associated with vaccine development, and where necessary investing in manufacturing upfront so vaccines can be deployed at scale as soon as they are proven to be safe and effective, and pooling procurement and purchasing power to achieve sufficient volumes to end the acute phase of the pandemic by 2021.

The goal of COVAX is by the end of 2021 to deliver two billion doses of safe, effective vaccines that have passed regulatory approval and/or WHO prequalification. These vaccines will be offered equally to all participating countries, proportional to their populations, initially prioritising healthcare workers then expanding to cover vulnerable groups, such as the elderly and those with pre-existing conditions. Further doses will then be made available based on country need, vulnerability and COVID-19 threat. The COVAX Facility will also maintain a buffer of doses for emergency and humanitarian use, including dealing with severe outbreaks before they spiral out of control.

on the WEB COVAX facility
https://www.gavi.org/covid19/covax-facility

COVAX countries

The 80 countries that have submitted expressions of interest to the Gavi-coordinated COVAX Facility include 43 that have agreed to be publicly named: Andorra, Argentina, Armenia, Botswana, Brazil, Canada, Chile, Colombia, Croatia, Czech Republic, Dominican Republic, Estonia, Finland, Greece, Iceland, Iraq, Ireland, Israel, Japan, Jordan, Kuwait, Lebanon, Luxembourg, Mauritius, Mexico, Monaco, Montenegro, New Zealand, North Macedonia, Norway, Palau, Portugal, Qatar, Republic of Korea, San Marino, Saudi Arabia, Seychelles, Singapore, South Africa, Switzerland, United Arab Emirates, United Kingdom of Great Britain & Northern Ireland, Venezuela.

In July the Gavi Board agreed on the 92 economies that will be supported the COVAX Advance Market Commitment (AMC). The full list is as follows:

- **Low income:** Afghanistan, Benin, Burkina Faso, Burundi, Central African Republic, Chad, Congo, Dem. Rep., Eritrea, Ethiopia, Gambia, The Guinea, Guinea-Bissau, Haiti, Korea, Dem. People's Rep., Liberia, Madagascar, Malawi, Mali, Mozambique, Nepal, Niger, Rwanda, Sierra Leone, Somalia, South Sudan, Syrian Arab Republic, Tajikistan, Tanzania, Togo, Uganda, Yemen, Rep.,
- **Lower-middle income:** Angola, Algeria, Bangladesh, Bhutan, Bolivia, Cabo Verde, Cambodia, Cameroon, Comoros, Congo, Rep. Côte d'Ivoire, Djibouti, Egypt, Arab Rep., El Salvador, Eswatini, Ghana, Honduras, India, Indonesia, Kenya, Kiribati, Kyrgyz Republic Lao PDR, Lesotho, Mauritania, Micronesia, Fed. Sts., Moldova, Mongolia, Morocco, Myanmar, Nicaragua, Nigeria, Pakistan, Papua New Guinea, Philippines, São Tomé and Principe, Senegal, Solomon Islands, Sri Lanka, Sudan, Timor-Leste, Tunisia, Ukraine, Uzbekistan, Vanuatu, Vietnam, West Bank and Gaza, Zambia, Zimbabwe
- **Additional IDA eligible:** Dominica, Fiji, Grenada, Guyana, Kosovo, Maldives, Marshall Islands, Samoa, St. Lucia, St. Vincent and the Grenadines, Tonga, Tuvalu.

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Sharon McCutcheon

Researchers show children are silent spreaders of SARS-COV-2

In the most comprehensive study of COVID-19 paediatric patients to date, Massachusetts General Hospital (MGH) and Mass General Hospital for Children (MGHfC) researchers provide critical data showing that children play a larger role in the community spread of COVID-19 than previously thought.

In a study of 192 children ages 0-22, 49 children tested positive for SARS-CoV-2, and an additional 18 children had late-onset, COVID-19-related illness. The infected children were shown to have a significantly higher level of virus in their airways than hospitalized adults in ICUs for COVID-19 treatment.

"I was surprised by the high levels of virus we found in children of all ages, especially in the first two days of infection," said Lael Yonker, MD, director of the MGH Cystic Fibrosis Center and lead author of the study, "Paediatric SARS-CoV-2: Clinical Presentation, Infectivity, and Immune Reponses," published in *The Journal of Pediatrics*. "I was not expecting the viral load to be so high. You think of a hospital, and of all of the precautions taken to treat severely ill adults, but the viral loads of these hospitalized patients are significantly lower than a 'healthy child' who is walking around with a high SARS-CoV-2 viral load."

Transmissibility or risk of contagion is greater with a high viral load. And even when children exhibit symptoms typical of COVID-19, like fever, runny nose and cough, they often overlap with common childhood illnesses, including influenza and the common cold. This confounds an accurate diagnosis of COVID-19, the illness derived from the SARS-CoV-2 coronavirus, says Yonker. Along with viral load, researchers examined expression of the viral receptor and antibody response in healthy children, children with acute SARS-CoV-2 infection and a smaller number of children with Multisystem Inflammatory Syndrome in Children (MIS-C).

Findings from nose and throat swabs and blood samples from the MGHfC Pediatric COVID-19 Biorepository carry implications for the reopening of schools, daycare centers and other locations with a high density of children and close interaction with teachers and staff members.

"Kids are not immune from this infection, and their symptoms don't correlate with exposure and infection," says Alessio Fasano, MD, director of the Mucosal Immunology and Biology Research Center at MGH and senior author of the manuscript. "During this COVID-19 pandemic, we have mainly screened symptomatic subjects, so we have reached the erroneous conclusion that the vast majority of people infected are adults. However, our results show that kids are not protected against this virus. We should not discount children as potential spreaders for this virus."

Asymptomatic

The researchers note that although children with COVID-19 are not as likely to become as seriously ill as adults, as asymptomatic carriers or carriers with few symptoms attending school, they can spread infection and bring the virus into their homes. This is a particular concern for multi-generational families with vulnerable older adults in the same household.

In another breakthrough finding from the study, the researchers challenge the current hypothesis that because children have lower numbers of immune receptors for SARS-CoV2, this makes them less likely to become infected or seriously ill. Data from the group show that although younger children have lower numbers of the virus re-

ceptor than older children and adults, this does not correlate with a decreased viral load. According to the authors, this finding suggests that children can carry a high viral load, meaning they are more contagious, regardless of their susceptibility to developing COVID-19 infection.

The researchers also studied immune response in MIS-C, a multi-organ, systemic infection that can develop in children with COVID-19 several weeks after infection. Complications from the accelerated immune response seen in MIS-C can include severe cardiac problems, shock and acute heart failure.

"This is a severe complication as a result of the immune response to COVID-19 infection, and the number of these patients is growing," says Fasano, who is also a professor of Pediatrics at Harvard Medical School (HMS). "And, as in adults with these very serious systemic complications, the heart seems to be the favourite organ targeted by post-COVID-19 immune response," he adds.

Understanding MIS-C and post-infectious immune responses from paediatric COVID-19 patients is critical for developing next steps in treatment and prevention strategies, according to the researchers. Early insights into the immune dysfunction in MIS-C should prompt caution when developing vaccine strategies, notes Yonker.

The researchers emphasize infection control measures, including social distancing, universal mask use (when implementable), effective hand-washing protocols and a combination of remote and in-person learning. They consider routine and continued screening of all students for SARS-CoV-2 infection with timely reporting of the results an imperative part of a safe return-to-school policy.

"This study provides much-needed facts for policymakers to make the best decisions possible for schools, daycare centers and other institutions that serve children," says Fasano. "Kids are a possible source of spreading this virus, and this should be taken into account in the planning stages for reopening schools." MEH

Europe's largest initiative is launched to accelerate therapy development for COVID-19

CARE (Corona Accelerated R&D in Europe) a new consortium supported by the Innovative Medicines Initiative (IMI) public-private partnership was launched 18 August 2020 to accelerate the discovery and development of urgently needed medicines to treat SARS-CoV-2, the virus that causes COVID-19.

With a grant totalling €77.7 million, the CARE consortium is Europe's largest such initiative.

It is funded by cash contributions from the European Union (EU) and cash and in-kind contributions from 11 European Federation of Pharmaceutical Industries and Associations (EFPIA) companies and three IMI-Associated Partners.

CARE is a five-year project bringing together 37 partners from Belgium, China, Denmark, France, Germany, the Netherlands, Poland, Spain, Switzerland, the UK and the US, and is led by VRI-Inserm (French National Institute of Health and Medical Research, Paris, France), Janssen Pharmaceutica NV, one of the Janssen Pharmaceutical Companies of Johnson & Johnson (Beerse, Belgium), and Takeda Pharmaceuticals International AG, (Zurich, Switzerland). It integrates partners' COVID-19 projects ongoing since February 2020.

"The COVID-19 pandemic has emerged as the largest global health threat to humanity in this century, requiring the global scientific community to join forces in unprecedented ways," said Professor Yves Lévy, Executive Director of the VRI-Inserm and CARE coordinator. "Beyond the scientific excellence of the different teams involved in this very ambitious project, CARE is bringing together 37 partners in an alliance pooling their expertise and know-how around an ambitious five-year work plan to develop therapeutics against the current COVID-19 pandemic. We are very grateful for the financial support provided by the Innovative Medicine Initiative that will enable us to implement this plan"

Uniting some of the most innovative and experienced scientists from all relevant areas in a unique collaborative spirit, CARE will maximize synergies with other initiatives such as the Gates Foundation-supported COVID-19 Therapeutics Accelerator, MANCO , SCORE , and the ECRAID network, to accelerate the path to providing solutions for the current COVID-19 pandemic as well as future coronavirus outbreaks. After testing in the laboratory, the project will advance the most promising drug candidates to clinical trials in humans.

As a member of the CARE consortium, Boehringer Ingelheim will be leading the work stream of the consortium focusing on the development of virus neutralizing antibodies. Furthermore the company will provide antiviral molecules from its legacy HIV and HCV portfolio and small molecule candidates from a complete screen of its molecule library.

Clive R. Wood, Ph.D., Corporate Senior Vice President and Global Head of Discovery Research at Boehringer Ingelheim said: "The CARE consortium aims to unleash the power of open science and collaboration in the service of society. We will work quickly and decisively in an unprecedented spirit of co-operation with our partners in academia and industry to defeat the unprecedented menace of COVID-19 and other serious coronavirus diseases."

CARE project leader Marnix Van Loock, Senior Scientific Director and R&D Lead of Emerging Pathogens, Global Public Health, Janssen Pharmaceutica NV, said: "We are very excited to launch the CARE consortium and collaborate with other leading experts to urgently identify new medicines against SARS-CoV-2 and other coronaviruses that may have the potential to cause epidemics,.

As part of this initiative, we look forward to applying learnings from an ongoing collaboration on COVID-19 with the Rega Institute for Medical Research, part of KU Leuven, to screen a drug repurposing library of thousands of existing drug compounds."

Kumar Saikatendu, Ph.D., Director, Global Research Externalization, Takeda said: "It is humbling to see such a large collection of the best scientific minds in Europe come together to solve this complex problem with such urgency. COVID-19 is a once in a lifetime scientific challenge for our generation. CARE aims to create effective therapies with a positive safety profile for current and future coronaviral outbreaks. We hope to move fast and have a meaningful impact in a timely manner."

CARE aims to create effective therapies with a positive safety profile for the COVID-19 pandemic (drug repositioning), and develop new drugs and antibodies specially designed to tackle the SARS-CoV-2 virus.

The consortium builds on three pillars:

- Drug repositioning, by screening and profiling compound libraries contributed by partners with the aim of rapidly progressing molecules to advanced stages of clinical testing.
- Small-molecule drug discovery based on *in silico* screening and profiling of candidate compounds directed against SARS-CoV-2 and future coronavirus targets.
- Virus neutralizing antibody discovery using fully human phage and yeast display, immunisation of humanised animal models, patient B cells and *in silico* design.

Closely integrated with these pillars are work streams focusing on the refinement of candidate compounds through a comprehensive medicinal chemistry campaign, systems biology research and pre-clinical and clinical evaluation of molecules from all three pillars. The systems biology work package will investigate the viral pathophysiology to increase our understanding of the interplay between virus infection stages and human immune responses. It will identify disease markers, to inform therapy development and improve clinical trial design and monitoring of Phase 1 and 2 trials investigating new therapeutics developed by CARE. MEH

Study shows SARS-CoV-2 spreads further in indoor environments with low humidity

The airborne transmission of SARS-CoV-2 via aerosol particles in an indoor environment seems to be strongly influenced by relative humidity. This is the conclusion drawn by researchers from the Leibniz Institute for Tropospheric Research (TROPOS) in Leipzig and the CSIR National Physical Laboratory in New Delhi from the analysis of 10 of the most relevant international studies on the subject.

In addition to the usual measures, such as social distancing and masks, they recommend controlling the indoor air by increasing the humidity to above 40% – which is particularly pertinent for the Middle East where indoor environments are climate controlled with air-conditioning which has a tendency to dry out the air.

A relative humidity of 40 to 60 percent could reduce the spread of the viruses and their absorption through the nasal mucous membrane. To contain the COVID-19 pandemic, it is therefore important to implement standards for indoor air humidity in rooms with many people, such as hospitals, open-plan offices or public transport, writes the research team in the scientific journal *Aerosol and Air Quality Research*.

Researchers from India and Germany are recommending, in addition to the previously customary measures such as spacing and masks, the room air should also be controlled so that the air humidity does not fall below 40 percent.

For a long time, the main transmission route of viral droplets was considered to be direct human-to-human contact, because of infected people sneezing or coughing and secreting the virus. Because these drops are relatively large and heavy, they fall very quickly to the ground and can only cover very short distances in the air. The recommendation to keep a minimum distance of 1.5m to 2m (social distancing) is based on this assumption. Recently, however, COVID-19 outbreaks have also been recorded, which seem to be due to the simultaneous presence of many people in one room. A safety distance of 1.5m is apparently insufficient when infected and healthy people are together in one room for a long time. For example, Dutch researchers have now been able to prove that tiny drops of 5 micrometres in diameter, such as those produced when speaking, can float in the air for up to 9 minutes.

In July, 239 scientists from 32 countries, including the chemist Prof. Hartmut Herrmann from TROPOS, appealed to the

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World Health Organization (WHO) to focus more closely on the long-lived infectious particles suspended in the air. In order to contain the spread via the aerosol particles floating in the air, the researchers recommend not only continuing to wear masks but also, and above all, good indoor ventilation.

Physicists at TROPOS and the CSIR National Physical Laboratory in New Delhi have been studying the physical properties of aerosol particles for years in order to better estimate their effects on air quality.

"In aerosol research, it has long been known that air humidity plays a major role: The more humid the air is, the more water adheres to the particles and so they can grow faster. So, we were curious: what studies have already been conducted on this," explained Dr. Ajit Ahlawat from TROPOS.

They evaluated a total of 10 of the most relevant international studies between 2007 and 2020 by other researchers who investigated the influence of humidity on survival, spread and infection with the pathogens of influenza and the corona viruses SARS-CoV-1, MERS and SARS-CoV-2. The result: Air humidity influences the spread of corona viruses indoors in three ways: (a) the behaviour of microorganisms within the virus droplets, (b) the survival or inactivation of the virus on the surfaces, and (c) the role of dry indoor air in the airborne transmission of viruses. Although, low humidity causes the droplets containing viruses to dry out more quickly, the survivability of the viruses still seems to remain high. The team concluded that other processes are more important for infection.

"If the relative humidity of indoor air is below 40 percent, the particles emitted by infected people absorb less water, remain lighter, travel further through the room and are more likely to be inhaled by healthy people. In addition, dry air also makes the mucous membranes in our noses dry and more permeable to viruses," Dr. Ahlawat said.

At a higher humidity, the droplets grow faster, fall to the ground earlier and can be inhaled less by healthy people. "A humidity level of at least 40 percent in public buildings and local transport would therefore not only reduce the effects of COVID-19, but also of other viral diseases such as seasonal flu. Authorities should include the humidity factor in future indoor guidelines," said Dr. Sumit Kumar Mishra of CSIR - National Physical Laboratory in New Delhi.

For countries in cool climates, the researchers recommend a minimum indoor humidity. Countries in tropical and hot climates, on the other hand, should take care that indoor rooms are not extremely undercooled by air conditioning systems. When air is extremely cooled, it dries out the air and the particles in it, making people inside the room feel comfortable. But the dry particles will remain in the air for longer duration.

• doi: *https://doi.org/10.4209/aaqr.2020.06.0302*

UAE-based COVID-19 vaccine Phase III trials extended to Bahrain

Abu Dhabi-based G42 Healthcare has extended the world's first Phase III trials of an inactivated COVID-19 vaccine to a new centre in Bahrain with the first volunteers being vaccinated in the Kingdom.

The new phase of the #4Humanity trials will reinforce the ongoing collaboration between public health bodies in the UAE and Bahrain in combating the impact of the COVID-19 pandemic and increase the number of individuals who will participate in the trials.

In total, up to 6,000 volunteers are being sought for the new centre that will be the third in the ongoing trials after those in the UAE at the Abu Dhabi National Exhibition Centre in Abu Dhabi and Al Qarain Health Center in Sharjah.

This is an extension of the ongoing 4Humanity program by G42 Healthcare, the phase III clinical trials of the inactivated vaccine developed by Sinopharm CNBG in China that commenced in the UAE on 16 July.

The Phase III clinical trials follow the success of the Phase I and Phase II trials conducted by Sinopharm in China, which resulted in 100% of the volunteers generating antibodies to SARS-CoV-2, the virus that causes COVID-19, after two doses in 28 days. The new centre for the Phase III trials is open to individual volunteers aged between 18 and 60 living in Bahrain and will last for six to twelve months, with the volunteers required to be available for follow ups during this time.

G42 Healthcare CEO Ashish Koshy said: "It was always part of our original plan to open several centres to ensure the broadest impact and opportunity for individuals to participate and join the 4Humanity campaign. There has been a hugely enthusiastic response from the Ministry of Health and other public health bodies in Bahrain to work with us on the trials and to encourage their communities to volunteer in the trials.

"The expansion will also help to boost the overall numbers of people participating in the test to enable similar numbers to other international trials underway in nations with much larger populations."

The trials in the UAE are being managed by G4 Healthcare in partnership with the Department of Health - Abu Dhabi, the UAE Ministry of Health and Prevention (MOHAP) and Abu Dhabi Health Services Company. They are being conducted following the international guidelines stipulated by the World Health Organization and the United States Food & Drug Administration.

Odour-sensing cells in nose may be key entry point for SARS CoV-2

Scientists at Johns Hopkins Medicine, experimenting with a small number of human cell samples, report that the "hook" of cells used by SARS-CoV-2 to latch onto and infect cells is up to 700 times more prevalent in the olfactory supporting cells lining the inside of the upper part of the nose than in the lining cells of the rest of the nose and windpipe that leads to the lungs. These supporting cells are necessary for the function/development of odour-sensing cells.

The findings, from a preliminary study of cells lining both the nose and trachea, could advance the search for the best target for topical or local antiviral drugs to treat COVID-19, and offers further clues into why people with the virus sometimes lose their sense of smell.

A summary of the findings appears in a letter published August 19 in the *European Respiratory Journal*.

Scientists have known that SARS-CoV-2 latches on to a biological hook on the surface of many types of human cells, called an angiotensin-converting enzyme 2 receptor (ACE2). The receptor reels in essential molecules.

In a bid to explore the ACE2 link to COVID-19 in more detail, Andrew Lane, M.D., professor of otolaryngology–head and neck surgery, and director of the Division of Rhinology and Skull Base Surgery at the Johns Hopkins University School of Medicine, Mengfei Chen, Ph.D., a research associate in Lane's lab, and others on his team took a close look at ACE2 levels in nasal tissue specimens from 19 adult men and women with chronic rhinosinusitis (inflammation of nasal tissue) and in tissues from a control group of four people who had nasal surgeries for issues other than sinusitis.

The researchers also studied tissue samples of the trachea from seven people who underwent surgery for abnormal narrowing of the trachea.

Cells from children were not examined for this study, in part because they tend to have low ACE2 levels in the cells lining the nose, which may contribute to generally less severe illness among children infected with the SARS-CoV-2 virus. None of the study participants had been diagnosed with COVID-19.

The scientists used a high-resolution imaging technique called confocal microscopy to produce very sharp images of cells lining the nasal and tracheal airways. They used fluorescent stains to identify ACE2 receptors.

They found high levels of ACE2 among nasal cells that give structural support called sustentacular cells. These cells are located in an area called the olfactory neuroepithelium, where odour-sensing neurons are found. The researchers say this area of the nose may be particularly vulnerable to infection and might be the only infected site even when there are no symptoms. Because of this, they urge people to wear masks and wear them correctly.

For the study, depending on the biopsy sample, cells in the olfactory neuroepithelium had a 200-fold to 700-fold increase in ACE 2 proteins compared with other samples from the nose and trachea. Because the cells with high levels of ACE2 are associated with odour sensing, the researchers suggest that infection of these cells may be the reason some people with COVID-19 experience loss of smell.

Two of seven trachea specimens had low levels of ACE2 receptors, and the amount of those receptors was similar between study participants with and without chronic rhinosinusitis.

Because the cells lining the nose may prove to be a key entry point for SARS-CoV-2, Lane says there may be ways to target those particular cells with topical antiviral drugs or other therapies directly to that area. MEH

Report: International commission says heritable human genome editing should not be used to create pregnancy

The announcement in 2018 by a Chinese researcher that twins had been born after germline editing he had performed on early embryos led to an outcry in the scientific world about the medical, moral and ethical implications of such research. This led to the establishment of the International Commission on the Clinical Use of Human Germline Genome Editing which has now issued a report on the subject which is set to inform the World Health Organisation on its regulatory guidance expected later this year. *Middle East Health* reports.

Human embryos whose genomes have been edited should not be used to create a pregnancy until it is established that precise genomic changes can be made reliably without introducing undesired mutations to the human germline – a criterion that has not yet been met by any genome editing technology, says a new report by an international commission of the U.S. National Academy of Medicine, U.S. National Academy of Sciences, and the U.K.'s Royal Society.

Heritable genome edits can be passed down to future generations, raising not only scientific and medical considerations but also a host of ethical, moral, and societal issues. Extensive societal dialogue is needed before any country decides whether to permit clinical use of heritable human genome editing – making alterations to genetic material of human eggs, sperm, or any cells that lead to their development, including the cells of early embryos – with the intention of establishing a pregnancy.

If a nation decides that heritable human genome editing (HHGE) is permissible, initial uses should be limited to the prevention of serious monogenic diseases, which result from the mutation of one or both copies of a single gene – for example, cystic fibrosis, thalassemia, sickle cell anaemia, and Tay-Sachs disease, the report says. For these cases, HHGE should only be considered when prospective parents who are at known risk of transmitting a serious monogenic disease have no option or extremely poor options for having a biologically related child who is not genetically affected without the editing procedure, due to genetic circumstances or the combination of genetic circumstances and fertility issues.

"Any initial uses of HHGE should proceed incrementally and cautiously, and provide the most favourable balance of potential benefits and harms," said commission co-chair Richard Lifton, president of the Rockefeller University, New York City. "For the prevention of serious monogenic diseases, the commission has defined a responsible clinical translational pathway from rigorous preclinical research that determines whether and how editing can be performed efficiently and with high accuracy, to clinical application. Countries would then decide whether an editing application is permissible, informed by preclinical data as well as broad discussion of social and ethical issues. The report provides guidance on essential elements of national and international scientific governance and oversight."

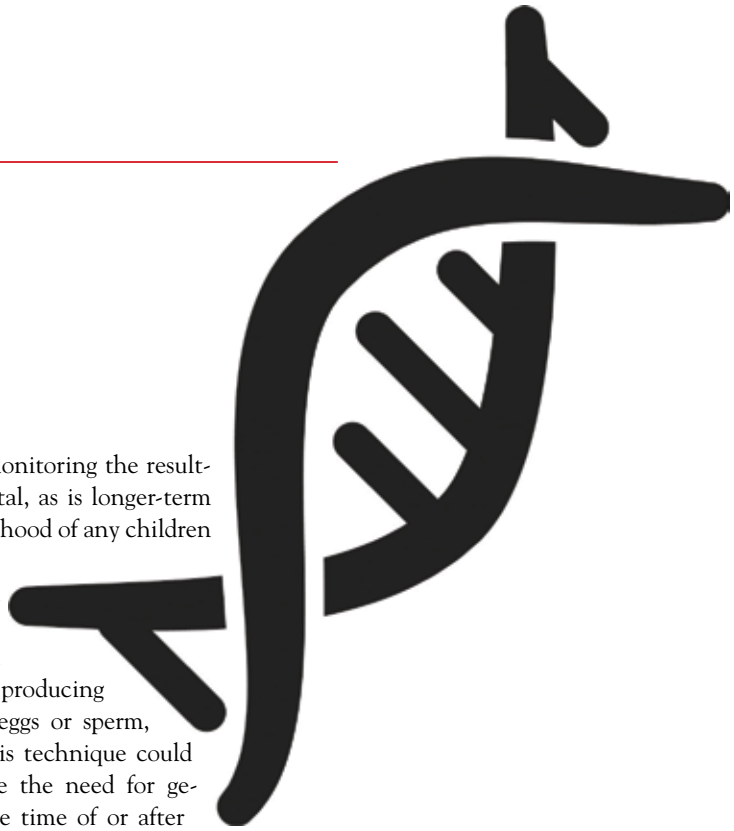
At this time, it is not possible to define responsible translational pathways from research to clinical application for other potential uses of HHGE, the report says. The uses, circumstances, and considerations differ widely, as do the technical advances that would be needed to make additional clinical uses feasible.

"Should they ever be used, it is vitally important that these technologies are used

For the prevention of serious monogenic diseases, the commission has defined a responsible clinical translational pathway from rigorous preclinical research that determines whether and how editing can be performed efficiently and with high accuracy, to clinical application.

for medically justified interventions, based on a rigorous understanding of how the pathogenic variant leads to disease," said commission co-chair Kay Davies, professor of genetics at the MDUK Oxford Neuromuscular Centre at the University of Oxford. "More research is needed into the technology of genome editing in human embryos, to ensure that precise changes can be made without undesired off-target effects. International cooperation and open discussion of all aspects of genome editing will be essential."

The International Commission on the Clinical Use of Human Germline Genome Editing, was formed in the aftermath of the 2018 International Summit on Human Genome Editing held in Hong Kong,



where a researcher from China announced that twins had been born following editing he had performed on early embryos, despite broad agreement in the scientific and clinical communities that it was premature and irresponsible to undertake heritable human genome editing.

The commission – comprising 18 members from 10 nations with expertise in genome editing technology; human genetics and genomics; psychology; reproductive, paediatric, and adult medicine; regulatory science; bioethics; and international law – was tasked with developing a framework for scientists, clinicians, and regulatory authorities to consider when assessing potential clinical applications of heritable human genome editing. The commission's goal was to define specific criteria and standards that would be required before HHGE could be considered for clinical use. The resulting report will inform the World Health Organization's expert advisory committee on human genome editing, which is developing appropriate governance mechanisms for both heritable and non-heritable human genome editing research and clinical uses. The WHO advisory committee is expected to issue its guidance later this year.

A translational pathway

The translational pathway described in the report for initial clinical use of HHGE identifies a number of requirements for preclinical evidence that should be met to demonstrate with high confidence that embryos have been correctly edited as intended, before any attempt is made to establish a pregnancy with edited embryos. The in vitro development of edited human embryos should also be evaluated prior to establishing a pregnancy to ensure that they meet developmental milestones, comparable to those of unedited embryos resulting from current in vitro fertilization practices. A biopsy should demonstrate that the intended edit is present in all biopsied cells, with no evidence of unintended edits. If, after rigorous evaluation, regulatory approval to establish a pregnancy is granted, monitoring the resulting pregnancy is vital, as is longer-term follow-up into adulthood of any children born.

Research should continue to evaluate the potential use of stem cells in producing functional human eggs or sperm, the report says. This technique could reduce or eliminate the need for genome editing at the time of or after fertilization. However, this type of HHGE should be carefully evaluated, as it raises its own distinct medical, ethical, and societal issues. The technique would need to be approved for use in assisted reproductive technology before editing such germ cells could be considered for clinical use.

Scientific governance and oversight

Each nation that considers developing HHGE will draw on its own regulatory infrastructure and oversight authorities, but all countries in which HHGE is being researched or conducted should have mechanisms and regulatory bodies in place to oversee progress toward potential clinical uses, prevent unapproved uses, and sanction misconduct, the report says.

In addition, before any clinical use of HHGE, an independent, multidisciplinary International Scientific Advisory Panel should be established to continuously assess the state of the scientific evidence regarding safety and efficacy of both human genome editing and associated assisted reproductive technologies. The panel should assess whether preclinical requirements have been met, review data on clinical outcomes from any regulated uses of HHGE, and advise on risks and benefits of other potential applications. Furthermore, it is very important that an international mechanism be established through which concerns about the ethics of research or conduct of heritable human genome editing that deviates from established guidelines or recommended standards can be reported to relevant authorities and publicly disclosed.

> More research is needed into the technology of genome editing in human embryos, to ensure that precise changes can be made without undesired off-target effects. International cooperation and open discussion of all aspects of genome editing will be essential.

In order to proceed with any HHGE applications that go beyond the initial uses as described by the commission, the commission recommends the creation of an international body with appropriate standing and diverse expertise to make recommendations concerning any proposed new category of use, and to advise on scientific and clinical benefits and risks. Informed by the work of the International Scientific Advisory Panel, this body should enable and convene ongoing discussions on the societal issues surrounding potential new applications of HHGE.

on the WEB Heritable Human Genome Editing
https://www.nap.edu/catalog/25665/heritable-human-genome-editing

Interview

Summit seeks to accelerate innovative multi-sector digital health collaboration

The Kingdom of Saudi Arabia hosted the Riyadh Global Digital Health Summit on 11 & 12 August. The summit brought together leaders of healthcare systems, public health, digital health, academic institutions and businesses to discuss the vital role of digital health in the fight against Covid-19 and future pandemics. The virtual summit was organised by the Ministry of National Guard and the G20 Saudi Secretariat and in collaboration with Saudi Center for International Strategic Partnerships. *Middle East Health* speaks to **H.E. Dr. Bandar Alknawy**, CEO, Ministry of National Guard – Health Affairs, President, King Saud Bin Abdulaziz University for Health Sciences, President, Riyadh Global Digital Health Summit.

H.E. Dr. Bandar Alknawy, CEO, Ministry of National Guard – Health Affairs, President, King Saud Bin Abdulaziz University for Health Sciences, President, Riyadh Global Digital Health Summit

The Riyadh Global Digital Health Summit covered a broad range of digital health innovations from Digital Epidemiology to Digital Public Health to Telehealth and its Role in combatting pandemics, such as Covid-19. It concluded with the issuing of a "Riyadh Declaration" that sets out a roadmap for accelerating digital health innovations to fight the current and future pandemics.

***Middle East Health*: What do you consider to be the most pressing need in healthcare in KSA that can be alleviated through digital innovation? Is it, for example, the collection of data for epidemiological purposes, the provision of healthcare through telehealth services or the communication of public health information to the population in the kingdom, or some other area?**

■ **Dr. Bandar Alknawy:** The Riyadh Global Digital Health Summit concluded with the announcement of the 'Riyadh Declaration' – nine recommendations, based on seven core principles, that will address six key priorities. Those are, in no particular order of importance: crisis and risk communication; health data governance, policy and regulation and its use in practice; establishing applied health intelligence; adoption of interoperable digital technology, scalability, and sustainability; enhancing the quality and effectiveness of digital technology for improved patient and population outcomes; and research and innovation.

***MEH*: What do you consider the highlights of the summit and why are these most relevant to the situation in KSA?**

■ **Dr. Bandar Alknawy:** For me, there were too many highlights to pick just one. We learnt that the global pandemic was predictable from as early as January 2020 and that there is no correlation between temperature or humidity and the growth of the virus. We heard how South Korea has used technology to gain full compliance from the public to support social distancing, quarantining and preventative measures. As well as how, in the UK, the NHS's strategy for collecting, storing and displaying data online helped the public make data-driven decisions about areas to avoid.

I thought Bernardo Mariano from the World Health Organisation hit the nail on the head by stressing that the "new normal, post-pandemic" will require more multisector partnership, like that which the RGDHS seeks to foster.

***MEH*: Following the presentation of a number of digital health tools / strategies / innovations at the summit, which ones do you think KSA should prioritize and why?**

■ **Dr. Bandar Alknawy:** From the dialogue during the summit, I am very proud that Saudi Arabia is one of the pioneering countries in the field of digital health and the adoption of technology in general. As part of Vision 2030, Saudi Arabia is investing heavily in developing the capacity, the capability and the infrastructure in the digital health arena. This was evident in the recent successful use of digital health solutions in the fight against the COVID-19 pandemic and also the successful management of the Hajj pilgrims. Another recent example of the strong leadership focus on this area, is His Majesty, King Salman, the Custodian of the Two Holy Mosque's approval of the national strategy for Artificial Intelligence.

Perhaps one area of more focus is the responsibility of health and care organisations and the medical workforce to be equipped with the knowledge, skills and training in data and digital technologies to face current and future healthcare challenges.

***MEH*: Further to the previous question: What do you envisage as being the main challenges in KSA to implementing these digital technologies and what can be done to overcome these challenges?**

■ **Dr. Bandar Alknawy:** The health sector in Saudi Arabia had made a huge stride in implementing digital technologies. For example, since 2015 we at the Ministry of National Guard – Health Affairs have co-developed, enhanced and implemented a state-of-the-art electronic patient record system (EPR) that underpins our comprehensive clinical care model across all sectors, whether it is primary care or specialised services, and all regions. This helped massively in improving our efficiency and our ability to provide effective and integrated care, and it enabled our healthcare workers to exchange clinical information safely and promptly. This enabled us to envision more advanced solutions, as we are currently working in collaboration with our South Korean partners on the use of Artificial intelligence solutions in five main areas, including epilepsy and early detection of cancer. It is essential for Saudi Arabia's healthcare system to move to electronic patients records in all hospitals and health and care organisations, and this will be a cornerstone for any further innovative application of digital technology in healthcare.

***MEH*: From a public health perspective, which digital health innovations, if implemented, do you believe will have the most immediate effect in improving the health of the people of KSA?**

■ **Dr. Bandar Alknawy:** It was evident from the summit there are exciting developments in the field of wearable technologies. These will allow healthcare professionals to have more capacity in monitoring and reducing the risk to public health, not only during the current crisis but also in the management of chronic diseases like obesity, hypertension and diabetes. I think developing our care models and our public acceptance of these technologies will be a key factor in advancing the healthcare systems of the future.

***MEH*: Over the long-term, which digital health innovations do you think are most important to mitigating future pandemics? How will they do this?**

■ **Dr. Bandar Alknawy:** As many of RGDHS's speakers highlighted in their excellent presentations and during Q&A sessions, Covid-19 does not recognise borders. Nor will future pandemics. The challenges created are experienced in every country.

So, what is of utmost importance is that, whatever digital health innovations are employed by healthcare systems, solutions are globally collaborative and connected so they are as effective as possible in defeating this pandemic and preventing future ones.

It was highlighted during the summit, and the subsequent Riyadh Declaration, that there is a need for establishing very robust public health data sharing across the globe. This will enable health system preparedness at national and international levels and will provide the early warning systems required to contain potential pandemics at an early stage. We support the WHO work in this field, and we call for more investment in the global digital health infrastructure to realise this much-needed initiative.

***MEH*: The Riyadh Declaration drawn up at the Summit sets out a road map for accelerating the implementation of digital healthcare. Can you please give a bit of detail about this declaration? Why was it drawn up? Will this apply to specific digital innovations only, if so which ones?**

■ **Dr. Bandar Alknawy:** The Riyadh Declaration declaration is a call to action to create the infrastructure to share good digital health evidence-based practices, and real-time high-quality data that encompasses local and global levels, to enable more health systems and countries to have actionable insights. It was a joint work by a diverse group of international experts in digital health, health and care leadership and public health. The Riyadh Declaration is a well-developed set of recommendations and key principles in order to ensure digital health is well placed in the fight against current and future pandemics.

Digital and data technology will promote the coordinated development of shared global public health policies and resilient health and care systems in order to perform better in future pandemics and other health challenges.

The Riyadh Declaration does not specify one type of innovation, however it highlights the importance of global connectivity in enhancing the preparedness for fighting current and future pandemics.

***MEH*: A potential vaccine for Covid-19 is still several months away. Do you think there is time enough to implement certain digital technologies that can have a mitigating impact on Covid-19, before a vaccine is rolled out? Which digital technologies do you think are best suited to this and why?**

■ **Dr. Bandar Alknawy:** The COVID-19 virus continues to mutate, like future viruses will, so we as humans have to also change our tactics. And fast. So RGDHS attendees agree that adopting Digital Health as quickly as possible is the best way forward, until a vaccine is available and beyond that time.

Certainly, two of the Riyadh Declaration's recommendations can be implemented in the short term, with no time to waste. They are working with global stakeholders to confront mis/disinformation propagation through social media platforms and mass media. As well as maintaining, continuing to fund, and innovating surveillance data systems as a core part of the connected global health system for rapid preparedness and optimal global response.

***MEH*: Is there anything important you'd like to add?**

■ **Dr. Bandar Alknawy:** Coronavirus has tested the capabilities of healthcare systems across the globe and the virus shows little sign of slowing down. But management of its impacts is improving, and countries are now turning to recovery plans that balance individuals' future safety with societies' economic needs.

In all walks of life, the pandemic has undoubtedly accelerated awareness of, and appreciation for, technological solutions. Digital technology has already had a pervasive impact on the identification, management and modelling of the Covid-19 spread, as well as on public health and wellbeing during the pandemic.

So, to achieve unprecedented advancements in Digital Health, healthcare professionals must now seize this opportunity to build on previous strides forward and advocate for accelerated digitalization as a core part of countries' recovery plans.

Because, for patients and consumers, the healthcare sector's greater embrace of innovation will mean more efficient services, for more people, at lower cost.

But this challenge requires global collaboration – to share the latest research, discuss and explore new ideas, and prevent further devastating impacts of this crisis and future ones.

That's why Saudi Arabia hosted the Riyadh Global Digital Health Summit (RGDHS). MEH

Emerging from COVID-19: Saudi Arabia's experience with MERS supports its successful pandemic response

Ensuring the well-being of residents and pilgrims is a primary pillar of Saudi Arabia's healthcare strategy. Saudi Arabia's successful experience in managing MERS-CoV, is testament to its agility in responding to public health emergencies.

The Kingdom of Saudi Arabia's successful response to the recent COVID-19 comes on the back of its experience in handling the more deadly MERS coronavirus

The successful response to the pandemic is particularly important as the nation prepares to host the G20 Riyadh Summit in November, with HRH King Salman bin Abdulaziz, the Custodian of the Two Holy Mosques, announcing in the wake of the extraordinary virtual meeting of the G20 in March that "a global response" is crucial to address the "COVID-19 pandemic and the challenges to healthcare systems and the global economy."

Saudi Arabia walked the talk in this regard: Despite also facing oil price volatility, alongside the challenges of the pandemic, the Kingdom took concerted efforts to overcome the crises from all fronts. The country responded to the pandemic head-on, scoring across all four phases of the preparedness and response framework – prevent, detect, contain and treat.

Overcoming challenges

Saudi Arabia had one of the most challenging environments in managing the crisis, with some unique circumstances to navigate. In addition to being the most populated nation in the Arabian Gulf, Saudi Arabia also has a large population of expatriates from across the world who live and work in the Kingdom. Any crisis preparedness and response framework, therefore, had to address not just Saudi nationals but this diverse demography.

Second, as the birthplace of Islam, Saudi Arabia welcomes pilgrims from across the world to the two Holy Cities of Makkah and Madinah, which required taking bold and swift measures to ensure the safety of not just residents but also of pilgrims.

Even before a single case of COVID-19 was reported in the Kingdom, Saudi Arabia suspended pilgrimages. Access to the two Holy Cities was barred as early as February 26, 2020 – long before many nations had even considered lock down, and prior to the World Health Organisation assessing that COVID-19 could be characterised as a pandemic. As of March 23, almost a month later, 174 countries, territories or areas introduced or updated travel restrictions.

The impact of early travel restrictions has been significant in achieving better outcomes in managing the spread of the virus. A study <*https://doi.org/10.1080/10255842.2020.1759560*> undertaken on the impact of mobility versus the spread of the pandemic indicate that "the Wuhan travel ban came too late" while in "Europe, travel restrictions were implemented a week after every country reported cases of COVID-19… and as a consequence, no European country was protected from the outbreak." The foresight of the Kingdom enabled it to be among countries that did not report an uncontrollable outbreak.

Responding to the COVID-19 crisis with a clear plan of action, Saudi Arabia implemented extensive measures, with the Ministry of Health taking the lead on managing the response to the pandemic through reliance on the advanced digital healthcare structure in place, as well as the fast-paced mobilization of more than 25 hospitals and care resources in the early phases of the pandemic, in order to contain the outbreak and to prevent exponential growth of cases that could burden the healthcare system. Measures were also taken to increase capacities as well as the production of PPE and medical supplies.

Food security was ensured with well-stocked supermarkets, even as reports of

hoarding were making headlines in other nations.

Underpinned by decisive policy making, strong governance and its robust healthcare system serving as the backbone of care, the Kingdom successfully navigated the crisis, and is today on the road to the 'new normal' with the phased opening of the economy.

Detection programme

At the outset of the pandemic, on March 30, 2020, HRH King Salman bin Abdulaziz decreed that coronavirus treatment must be available and at no cost to anyone in need of medical care, including those who reside in the Kingdom illegally with no legal ramifications.

Reporting to HRH Prince Mohammad bin Salman bin Abdulaziz, Crown Prince, Deputy Prime Minister and Minister of Defense, a high-level multisectoral committee, headed by the Minister of Health, was established, immediately. The committee continues to meet daily to evaluate the situation and to take timely action, underpinned by the leadership's hands-on guidance.

Updates were communicated to the public, with the cooperation of other entities, to promote transparency and build trust. The messages were carefully calibrated to reach every segment of the audience – young and old, and all the various nationalities living in the Kingdom.

Initially, the polymerase chain reaction (PCR) testing capacity in the Kingdom was about 1,000 tests per day and has increased to 95,000, with the daily average performed tests reaching 65,000.

The Kingdom also ramped up testing in multiple phases once restrictions on movement were eased by opening free mass testing drive-through test centres in the Kingdom's largest cities, including Mecca, Medina, Riyadh, Jeddah, Dammam and Aseer, as well as activating (Tetamman) Clinics – functioning as fever clinics – in over 230 locations in Primary Healthcare Centres and hospitals across the Kingdom for patients with symptoms.

In parallel, the National Laboratory at the Saudi Centre for Disease Prevention and Control (SaudiCDC) was the initial reference centre for the advanced clinical laboratory tests. The Kingdom has since expanded its laboratories that provide COVID-19 PCR testing, from 1 to 51 labs covering all regions.

From a capacity perspective, the kingdom has significantly expanded its ability to admit patients, both critical and non-critical, adding to its intensive care capacity more than 2,500 fully equipped beds in a period of three months, which is more than 30% of the ICU capacity that has been built over the years.

In parallel, skilled healthcare workers are being recruited and thousands of healthcare workers and volunteers are being trained or retrained to assist with the care of patients if need be. Additionally, clinical and therapeutic protocols are being monitored by dedicated specialized teams to ensure swift and timely updates.

New technologies have also been utilised to care for the critically ill, such as the oxygen helmet and the high flow nasal cannula, which have produced encouraging results, allowing for many patients to avoid intubation and mechanical ventilation.

Saudi Arabia has also started its phase I clinical trial on a vaccine candidate for MERS-CoV as well as the MIRACLE trial which has been ongoing to evaluate antiviral therapeutics in severely infected MERS patients – now to be expanded to include COVID-19 patients.

The road to the new normal

The Kingdom implemented drastic containment measures, notably the closure of schools, universities and commercial outlets, prohibited public gatherings and suspended operations in many government agencies. Complete lockdowns were imposed on major cities, and, smaller cities were subject to part-time curfews – all the decisions made after public health assessments. Flexible working hours and work-from-home routines, as well as mandating the use of face masks in public continue to support the Kingdom's focus on the pandemic management – all to successful results.

Currently, COVID-19 mortality rates within the kingdom is approximately 0.9%, which is considerably lower than the global rate. At this stage of the pandemic, the observed death rate globally is 4-5%. Variations in the rate of COVID related deaths between countries and regions are not fully understood. However, quick access to healthcare, early intervention, and supportive care seems crucial in reducing COVID-19 related deaths.

Furthermore, the mortality rate, while low, should also be viewed in the context of population risk factors related to lifestyle diseases such as diabetes, obesity and cardiovascular diseases. The diabetes prevalence rate of 18.3% in the Kingdom constitutes a major risk factor for COVID-19 patients. Comorbidity is an additional complexity the Kingdom faced while still managing to sustain low mortality rates.

The success of the approach is highlighted by the Kingdom returning to normalcy in just 73 days. Commercial activities have returned to normal, with all safety protocols in place, and the Ministry of Health assessing the situation, especially in relation to pilgrimage to the Holy Cities, which is being reviewed periodically.

The Kingdom has also lifted the ban on domestic flights. Mosques, malls, recreational facilities and restaurants have opened. This followed the systematic approach of tracking indicators such as readiness of the health system to tackle the pandemic, managing community spread, the efficiency of the healthcare system and performance effectiveness.

The successful response of Saudi Arabia in managing the crisis serves as a roadmap in healthcare crisis management for the world. MEH

Omnicell to provide medication management solutions for Saudi's new Imam Abdulrahman Bin Faisal University Hospital

Omnicell, a leading provider of supply and medication management solutions and adherence tools for healthcare systems and pharmacies and its partner Gulf Medical, has announced a new partnership with Imam Abdulrahman Bin Faisal University Hospital in Eastern Province, Saudi Arabia. Omnicell solutions are set to manage Inpatient Pharmacy Automation throughout the facility. This will support the hospital's drive to embrace world-class healthcare digitization in line with the Kingdom's Vision 2030, while further extending Omnicell's provision of medication management expertise in the region.

Iman Abdulrahman Bin Faisal University Hospital, a new 500-bed education healthcare facility, is due to open in early 2021. As part of its integrated strategy to set new standards in healthcare services, the hospital will incorporate the following portfolio of automation solutions from Omnicell:

- **Automated Dispensing Cabinets** – to enable smarter and safer medication management
- **Controlled Substance Dispenser** – to increase control and security of controlled substances, high-risk and high-value medications
- **Anaesthesia Workstation** – to enable anaesthesia providers instant access to medications and tighter control in the operating room
- **Anywhere RN Software** – a mobile medication station which allows nurses remote access to medication management
- **Unity Platform** – a comprehensive inventory management system for the supply and dispensing of medication via a single, shared database

These solutions will support pharmacists by automating and scheduling tasks related to medication preparation and distribution. It will reduce the burden on wider healthcare teams by ensuring they provide the right medication, of the right dose, at the right time.

Dr Abdul Salam Al-Asseri, associate professor and chief of pharmaceutical care services at Imam Abdulrahman Bin Faisal University Hospital, says: "With the dynamic advances in pharmacy practice, and with the shift in focus to patient-centred care, automation has become integral in the workplace as it will spare more time for pharmacists to spend on counselling and other patient services. It is always my priority to ensure optimum patient outcomes in an efficient manner. As such partnering with Omnicell will provide a large scale of automated solutions which can help our pharmacists to focus more on patient care and to be deeply involved with the clinicians on the floor. My administration and I look forward to investing in this partnership as the hospital prepares to open its doors for the first time early next year."

Ivor Matthews, Omnicell Sales Director International – Indirect Markets, adds: "Our solutions significantly reduce the potential for errors and minimise the administrative burden on healthcare professionals, freeing them up to spend more time on face-to-face patient care. Both Omnicell and our partner Gulf Medical are thrilled to join forces with Imam Abdulrahman Bin Faisal University Hospital and support its commitment to healthcare digitization, as set out in the Kingdom of Saudi Arabia's Vision 2030."

Omnicell technology has been supporting healthcare providers in the Middle East for 17 years, including King Faisal Specialist Hospital (KSA), National Guard Health Affairs (KSA) and Dubai Health Authority (UAE). Its proven and streamlined range of products and services aim to reduce medication dispensing errors, improve patient safety, drive efficiency and allow healthcare professionals to spend more time on face-to-face patient care. MEH

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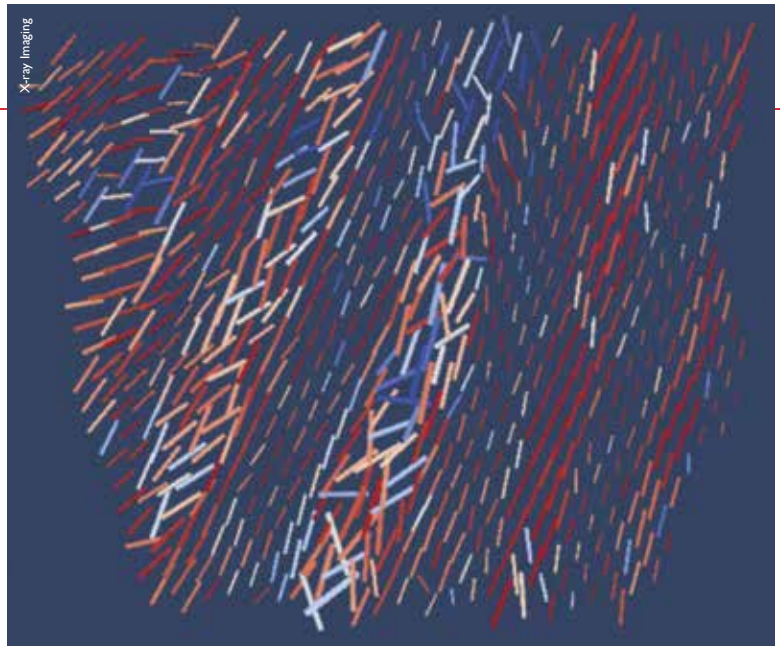
3D X-ray reveals novel structures inside bones



An international research team using new X-ray techniques to describe the architecture of healthy human bones has uncovered a hitherto unknown structure in bone tissue.

The human bone is a wonderful and fantastic biological material. Bone tissue is highly specialised, with a structure optimised for specific functions in the body. Healthy bones are strong, they have a high carrying capacity, and they are hard to break.

The internal structure of bones is of great international interest to researchers, and a better understanding of the fundamental biomaterial structures would make it possible to prevent various bone diseases. It could also facilitate the development of completely new materials, with unprecedented properties. However, the structure of the bones is simply too complex for us to be able to come close to imitating it.

An international team of researchers from Aarhus University, the European Synchotron in France (ESRF), the Swedish Chalmers University and the Paul Scherrer Institute in Switzerland have now uncovered a previously unknown substructure in bone tissue by means of a new X-ray technique. The discovery and the technique open up new approaches to the study of the underlying architecture of bone tissue, and help to create a better understanding of biomaterials.

The study is presented in the scientific journal, *Science Advances*.

3D image of the crystals in bones

If you cut into a bone, we know that the inner architecture of healthy bone tissue is constructed of basically two types of tissue: the so-called collagen fibrillations, which are primarily made up of protein. They comprise the bearing capacity of the mechanical properties of bone, with a microscopic, thread-like structure woven together with nanocrystals of minerals containing calcium.

Together, the two tissue types constitute a twisted hierarchical structure with the ability of the fibrillations to withstand stretching forces and bending, and the hardness and resilience of nanocrystals. It is this twisted structure that provides bones with their mechanical properties, and which researchers have been trying to understand for many years.

"The challenge until now has been that we have no method to demonstrate the orientation of the nanocrystals in the bone tissue," explains Associate Professor Henrik Birkedal from iNANO and the Department of Chemistry at Aarhus University.

The international team has succeeded in finding the solution by improving the X-ray technique known as tensor tomography, and by creating an accurate 3D map of the crystals in the tissue.

"In recent years, significant technological and scientific progress has made this new method possible. By means of more powerful synchrotron radiation, it is possible to improve the method, and to challenge the previous assumption about bone tissue," explains Manfred Burghammer from the research facility ID13 at the ESRF, who has been the research director of the project together with Birkedal.

The improved method makes it possible to see how the nanocrystals are actually located in the structure. This has already revealed a disparity with previous knowledge about bones that has been built up through many years of research. The bone structure is not uniformly structured as previously assumed, because there are deviations in the orientation of the nanocrystals.

"Frankly, we were a little shocked to find the deviation from the models," says Birkedal. "It's been a really cross-disciplinary, international collaboration with participants from physics, chemistry and health sciences, and we were all pleasantly surprised by the discovery."

Surprise findings

The new 3D images surprised the research group, because they conflict with fundamental theories that bones are built up in a predominantly uniform hierarchical structure.

"Admittedly, it's too early to give an unambiguous explanation of what hides behind the deviation we have demonstrated, but it has given science a new method of looking into the underlying structure of bones," says Tilman Grünewald from the ESRF.

The discovery potentially questions fundamentally a number of the models of bone tissue and the mechanical properties of bones that, among other things, have been used to describe the process of bone formation.

"Bones and other biomaterials, like sea shells, have a mechanical and structural characteristic that is closely linked to their structure. The better we understand this, the closer we can get to being able to imitate nature's building methods, for example. Our study has given us a new tool to reveal a few more of the secrets of nature, and this work is now underway," says Birkdal. MEH

Reference:
Mapping the 3D orientation of nanocrystals and nanostructures in human bone: Indications of novel structural features, *Science Advances*.
– **doi:** 10.1126/sciadv.aba4171

SternMed – German manufacturer of medical devices

German company SternMed is a fast-growing medical device manufacturer. Their products are user-friendly and produced specifically for the complex demands of the day-to-day practice in the fields of Diagnostic Imaging, OR Solutions and Patient Care.

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- lighting systems, surgery tables, anesthesia machines, ESUs
- patient monitors, infusion and syringe pumps and medical ventilators

X-ray systems

Radiology is a fundamental part of modern medicine. In this medical field, electromagnetic radiation is used to image abnormalities in the tissue or bone structure. X-rays are part of radiology and continue to be the most important imaging method in radiology.

Within SternMed's product range the company offers seven X-ray devices covering all essential technologies and specifications for all medical fields – from digital, analog, mobile, ceiling suspended, light-weight devices to the fully motorized Xenox M100 Plus.

The SternMed team believes that "having access to a proper health care is the right of every person in the world and we make it possible". Customer satisfaction is their top priority.

SternMed's vision is to make quality healthcare accessible worldwide by delivering essential and cost-effective medical equipment with German-quality standards. With the ISO 13485:2016 certification from TÜV Nord, SternMed shows that their company processes meet the highest German standards. MEH

Argonne scientists fashion new class of X-ray detector

New perovskite-based detectors can sense X-rays over a broad energy range

By **Jared Sagoff**

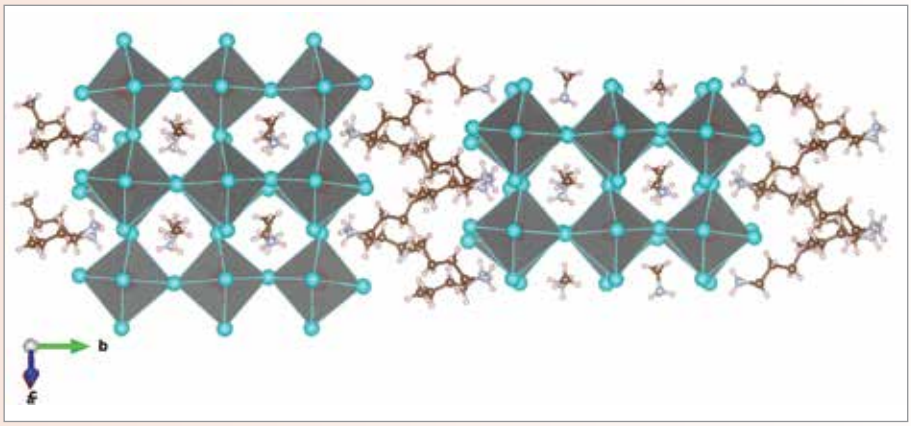

Image by Dave Tsai/Los Alamos

Two-dimensional (Ruddlesden-Popper phase layered perovskites (BA)2(MA)2Pb3I10 with three layers of inorganic octahedral slab and bulky organics as spacers.

Getting an X-ray at the dentist or the doctor is at best a little inconvenient and at worst a little risky, as radiation exposure has been linked to an increased risk of cancer. But researchers may have discovered a new way to generate precise X-ray images with a lower amount of exposure, thanks to an exciting set of materials that is generating a lot of interest.

Scientists at the U.S. Department of Energy's (DOE) Argonne National Laboratory and Los Alamos National Laboratory have identified a new class of X-ray detectors based on layered perovskites, a semiconducting material also used in some other types of applications such as solar cells and light-emitting diodes. The detector with the new material is 100 times more sensitive than conventional, silicon-based X-ray detectors.

"This new material for detecting X-rays could soon find its way into a variety of different everyday environments, from the doctor's office to airport security lines to research labs," said Argonne X-ray physicist Joseph Strzalka, who helped to characterize the perovskite material at Argonne's Advanced Photon Source (APS), a DOE Office of Science User Facility.

The perovskite materials work because they are deposited as a sprayed-on thin film, a production method that helps to reduce cost compared to having to grow a large silicon single crystal.

The new perovskite detectors can also detect X-rays over a broad energy range, especially at higher energies. This is because the perovskite contains heavy elements, such as lead and iodine, which tend to absorb these X-rays more readily than silicon. The potential even exists for the perovskite technology to be used as a gamma-ray detector, provided the films are made a little bit thicker and a small external voltage is applied.

"The perovskite material at the heart of our detector prototype can be produced with low-cost solution process fabrication techniques," said Hsinhan (Dave) Tsai, an Oppenheimer postdoctoral fellow at Los Alamos National Laboratory. "The result is a cost-effective, highly sensitive and self-powered detector that could radically improve existing X-ray detectors, and potentially lead to a host of unforeseen applications."

The development and analysis of the perovskite material was a close collaboration between Argonne APS (beamline 8-ID-E) and a Los Alamos team lead by device physicist Wanyi Nie. The material and thin film was created at Los Alamos and brought to Argonne to perform grazing incidence wide-angle X-ray scattering, which gives information about the crystallinity of the thin film. According to Strzalka, the technique shows how the crystal is oriented in the thin film, which relates to the performance of the detector.

Strzalka and Nie were also interested in how the charge transport properties of the film related to the crystal structure and temperature. By using a special stage that allowed the researchers to change the temperature of the sample and make electrical contacts during the measurement, they were able to understand the current generation and transport processes induced in the sample by the X-ray exposure.

"Our instrument at the beamline provides a versatile platform for different kinds of in-situ measurements, including keeping the sample in a vacuum environment while maintaining its temperature and also performing charge transport measurements," Strzalka said.

According to Strzalka, perovskites may continue to offer important breakthroughs. "The perovskite area is really hot right now, and users come to us to say 'can we do this and can we do that,' and it's really pushing us to develop our capabilities," he said.

Reference:
Highly sensitive and robust thin film X-ray detector using 2D layered perovskite diodes – *Science Advances*
doi: 10.1126/sciadv.aay0815

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Lexicomp® and UpToDate® are key components for achieving highest standards at Saudi Arabia's International Medical Centre

International Medical Center (IMC) strives to provide the highest standards of medical care and is considered to be one of Saudi Arabia's top hospitals. The IMC vision is to pioneer a unique approach of healing the body, mind, and soul by applying the best global healthcare standards and pursuing divine ethics. IMC is committed to high-quality patient care and continues to invest in IT infrastructure and new technologies that optimise the use of clinical systems and accuracy.

Evidence-based clinical resources support care quality & medical knowledge

IMC selected Lexicomp and UpToDate, the flagship drug reference and clinical decision support solutions from Wolters Kluwer to support medication therapy decisions at the point of care and medication order reviews. IMC prioritizes training and education of all medical staff including physicians, pharmacists, and nurses, and provides access to solutions that help them keep medical knowledge up to date.

This is where IMC saw the value of Lexicomp and UpToDate, and the reason why IMC ultimately decided to adopt the solutions as their evidence-based information resources. With new drug research and medical evidence published at a rapid rate, pharmacists and clinicians at IMC recognize that it is an ongoing challenge for them to stay current. Lexicomp and UpToDate provide instant access to the latest drug usage and information at the point of care. This helps ensure that clinicians have access to the very latest guidelines and drug information that is reviewed and validated by medical experts.

In addition to supporting pharmacist and physicians, IMC also educates residents. One of IMC's key missions is to train and educate professional medical human resources for the country. All residents at IMC are strongly encouraged to use online resources such as Lexicomp and UpToDate to keep themselves updated with fast-changing medical knowledge.

> Our pharmacists and clinicians rely on Lexicomp and UpToDate to provide current, evidence-based care. As the landscape of HealthIT continues to evolve, we look forward to having them incorporated with our EMR system. – Dr. Ali Y. Saber, Manager of Pharmaceutical Care at International Medical Centre.

Creating a custom formulary for busy clinicians on-the-go

Through its Referential Monograph Customization service, Wolters Kluwer works with healthcare providers to create their own easily searchable online formularies and integrate hospital-specific policies and drug lists with trusted Lexicomp drug information. Custom databases combine the evidence-based clinical information in Lexicomp with institution-specific information on drug availability and regulations.

IMC is able to update its own policies, guidelines, and formulary availability data using a user-friendly program – Lexicomp Information Management System (LIMS). Using LIMS, IMC has been able to select special fields to be displayed in its customized drug monographs, such as Saudi Arabia Brand Names, Prescribing Privileges, Drug Specific Identifiers, IMC Guidelines and IMC Pregnancy Category.

IMC since made these custom databases available to their clinical teams wherever and whenever they need it through Lexicomp Mobile Apps. With the smartphone mobile version, the IMC formulary, as well as Lexicomp, have become accessible to all clinicians 'on-the-go'.

> As internationally recognized and authoritative resources, we consider Lexicomp and UpToDate to be the most trusted evidence-based drug information and clinical decision support solutions. – Dr. Dina S. Al-Sanafawi, Infectious Diseases Clinical Pharmacist at International Medical Center.

Looking ahead

IMC readily embraces new technologies to improve quality of care and has implemented an electronic medical record (EMR) system for clinicians to access patient charts at the point of care. The next step in the innovation journey is to integrate clinical decision support resources into the EMR. MEH

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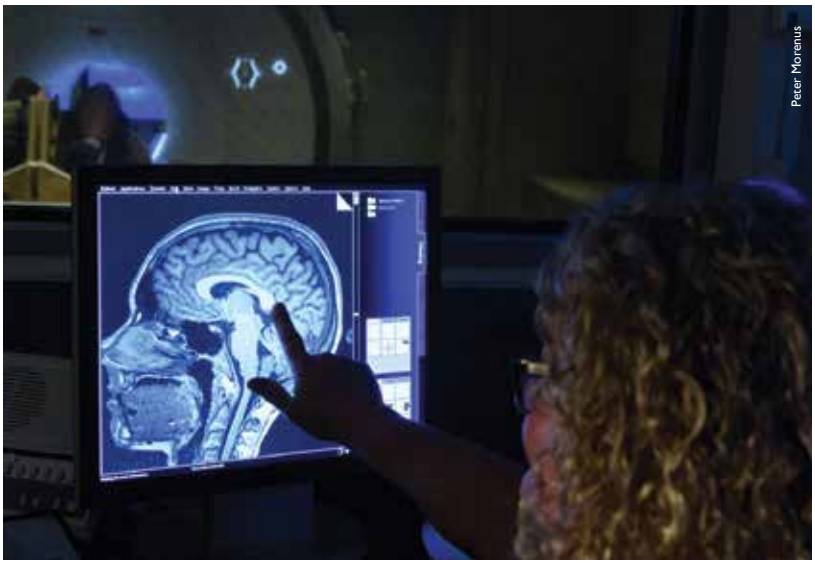
More than a knee injury: ACL tears cause harmful changes in our brain structure



Elisa Medeiros observes a functional MRI test in the fMRI at the Phillips Communication Sciences Building, University of Connecticut.

It's known that some joint function is often permanently lost after anterior cruciate ligament (ACL) reconstruction, and re-injury is common even with intensive physical therapy, but it's unclear why.

New research from the University of Michigan School of Kinesiology shows structural changes in the brains of patients who underwent ACL reconstruction. These changes hinder recovery and may contribute to performance deficits and re-injury, says study co-author Lindsey Lepley, U-M assistant professor of athletic training.

Lindsey Lepley and colleague Adam Lepley, clinical assistant professor of athletic training, took MRI brain scans of 10 ACL-reconstructed patients. The scans showed that part of the corticospinal tract—the pathway that scuttles messages from brain to muscles – had atrophied in the patients.

The corticospinal tract runs from front to back through both hemispheres of the brain. The side of the tract that controls the ACL-reconstructed knee was about 15% smaller than on the uninjured side, the researchers say.

Think of the altered corticospinal tract as a traffic tunnel that narrows, letting fewer cars pass through, they say. In the ACL reconstructed patients, less information gets from the brain to the muscle because less information can travel along the smaller tract.

"In essence, the brain not only alters the way it communicates with the rest of the body, joints, muscles, etc., but the structural makeup of the basic building blocks of the brain are also changed after ACL injury," Adam Lepley said. "We think that this is a protective mechanism, in which our body is trying to limit unwanted movement around a joint injury … and can be applied to not just ACL injuries, but other musculoskeletal injuries as well."

Adam Lepley, assistant professor of kinesiology , left, and Elisa Medeiros, technician, prepare a model patient for functional MRI testing to assess brain activation during a knee flexion and extension task at the Phillips Communication Sciences Building, University of Connecticut, on July 17, 2017.

Another recent study shows that downstream neural activity in the quadriceps is impaired during sport-like movements after ACL surgery, which suggests that poor brain structure and communication can lead to reduced functioning, the researchers say.

The bottom line for patients and clinicians is that a knee injury is not just about knees – other areas, like the brain structure, are negatively impacted, too.

"It means that during treatment, a systemic approach should be taken not just to improve range of motion or swelling at the injured joint, but also consider other impairments like poor movement patterns and muscle activation in order to get better outcomes," Lindsey Lepley said. "There is evidence of using visual retraining, different motor learning modalities like external focus of attention and biofeedback, which can help 'rewire' the brain to help the body adapt to a new normal." MEH

Human Growth Hormone treatment after ACL injury may prevent loss of muscle strength

After experiencing an anterior cruciate ligament (ACL) injury, a common sports injury in the knee, many athletes find they can't return to play with the same vigour as before their injury. This may change following a new study, published in *The American Journal of Sports Medicine*, which finds human growth hormone (HGH) treatment after ACL reconstructive surgery may prevent the loss of muscle strength in the knee.

"While modern surgical techniques can reconstruct ACLs in a minimally invasive way, the associated muscle atrophy can be a greater challenge to overcome," says Asheesh Bedi, M.D., senior author of the study, chief of sports medicine and shoulder surgery at Michigan Medicine and director of the Michigan Center for Human Athletic Medicine and Performance (MCHAMP).

"Residual atrophy can slow or limit the safe return to the prior level of competition, and contribute to risk of re-injury and even arthritis."

HGH, a hormone within the body, helps cells and tissues grow and regenerate. HGH supplements are banned by the World Anti-Doping Agency, and in collegiate and professional sports.

"When you hear of athletes taking HGH drugs when they are healthy, it's considered doping because they are essentially trying to overproduce the hormone and bulk their muscles and tissues as a competitive advantage," says Christopher Mendias, Ph.D., ATC, the lead author of the study, an adjunct associate professor of orthopaedic surgery at Michigan Medicine and an associate scientist in the Arthritis and Tissue Degeneration Program at the Hospital for Special Surgery.

Bedi and Mendias hypothesized that administering HGH supplements to injured athletes may activate HGH within the body to target the ACL tear and prevent the knee muscles from losing strength.

"Even after rehabilitation, many patients have muscles that are 30% to 40% weaker when they return to sports compared to their pre-surgery strength," Mendias says.

Trial criteria

The researchers examined 19 male athletes, ages 18 to 35, with ACL tears who were scheduled for ACL reconstruction surgery at Michigan Medicine. The study participants were randomly assigned to self-inject HGH or a placebo solution into their lower abdominal muscles twice daily over a six-week period, beginning one week prior to surgery. The research team excluded collegiate, professional or elite athletes from the study because of the substance ban, as well as patients with diabetes, as developing type 2 diabetes is a side effect of HGH supplements.

Prescription HGH is only available for treating growth hormone deficiency syndromes and can't be used off-label without approval from the U.S. Food and Drug Administration. By obtaining an investigational new drug exemption from the FDA, the research team was able to administer the drug to study enrolees.

The research team found the HGH injections did appear to have an effect after measuring knee muscle strength and volume, patient-reported outcomes, such as pain and symptoms, and analyzing biomarkers in blood samples from the injured athletes versus individuals without an ACL tear.

"While HGH did not appear to affect muscle volume or our patient-reported outcome scores, we found a 29% higher knee extension strength in our patients that had performed the HGH injections compared to those in the placebo group," Bedi says.

Examining the blood analyses revealed other signs of muscle and cartilage change. Patients who performed the HGH treatments had a 2.1-fold increase in circulating insulin-like growth factor 1 (IGF1), a protein similar to insulin that plays an important role in muscle growth. In addition, their blood samples indicated a 36% lower level of matrix metalloproteinase–3 (MMP3), an enzyme that breaks down proteins during growth processes in the body. MMP3 was an indirect biomarker of cartilage wear down in the study.

"We observed a consistent reduction in MMP3 in the HGH group from the first through the 12th post-operative weeks," Mendias says. "This finding suggests a potential protective effect of HGH after ACL reconstruction and that we should look more closely at its potential for cartilage healing in further studies."

Future use in sports?

Bedi and Mendias hope the results of this study allow for a reevaluation of the World Anti-Doping Agency and sports agencies' ban on HGH.

"Perhaps athletes could petition for a Therapeutic Use Exception, which allows a banned substance for a medically-appropriate reason, to prevent loss of muscle strength after ACL reconstruction," Mendias says. "Treatment occurs during a time when athletes are not playing due to their injuries. The goal is to prevent muscle weakness, not make athletes stronger than they were before their injuries. Any small performance-enhancing effects of human growth hormone seem to wear off quickly after stopping the medication, and does not offer a competitive advantage."

The research team notes that further studies into HGH are needed.

"We hope to build upon this research with future studies that include larger cohorts of athletes with broader demographics," Bedi says.

Mendias adds: "Further studies would also allow us to petition the FDA to approve the addition of orthopaedic injuries as an on-label indication for the drug." MEH

Reference:
The Use of Recombinant Human Growth Hormone to Protect Against Muscle Weakness in Patients Undergoing Anterior Cruciate Ligament Reconstruction – The American Journal of Sports Medicine. https://doi.org/10.1177/0363546520920591

New hope for ACL injuries: Adding eccentric exercises could improve physical therapy outcomes

A new study in rats by researchers at the University of Michigan challenges conventional wisdom about which exercises are most beneficial during post-injury physical therapy following anterior cruciate ligament (ACL) injuries. The findings suggest that adding eccentric exercises could dramatically increase muscle volume and improve outcomes for patients.

People with ACL injuries can lose up to 40% of the muscle strength in the affected leg – with muscle atrophy remaining a big problem even after ACL reconstruction and physical therapy.

Eccentric exercises contract the muscle during lengthening – think of the downswing of a bicep curl or walking downhill. Those exercises are much more effective at growing muscle than concentric exercises, where muscles shorten while producing force – think of the upswing of a bicep curl, said Lindsey Lepley, U-M assistant professor of kinesiology.

Historically, the lengthening component of eccentric exercises has been thought to cause muscle damage during physical therapy, so they're omitted, Lepley said. But concentric exercises alone don't achieve the muscle growth required to get patients to pre-injury muscle strength. This holds true for all sports-related muscle strains and injuries requiring physical therapy, not just the ACL reconstructions.

"Our group has long believed that incorporating eccentrics into PT is beneficial to muscle," said Lepley, whose earlier research found that incorporating eccentric exercise into an ACL rehabilitation program increased strength by 30%, compared to concentric exercise alone.

"The catch is that in order to combat this outdated notion that eccentrics are dangerous, we need to directly evaluate the immediate effects – hence the purpose of this study."

This study found that a single, 15-minute bout of eccentric exercise to novice muscle (a muscle unexposed to prior eccentric exercise) in rats was better than concentric exercise at promoting growth, with very limited injury, Lepley said. Muscle and the mechanisms governing function are highly conserved across species, she said.

> Our goal is to translate our findings from the bench-top to the sidelines. We want this information to get to clinicians and patients who have had musculoskeletal injuries to promote lifelong health and wellness.

In the study, Lepley and colleagues had rats run uphill or downhill on specially designed rodent treadmills. They then examined the muscle fibres for injuries and protein synthesis indicative of muscle growth.

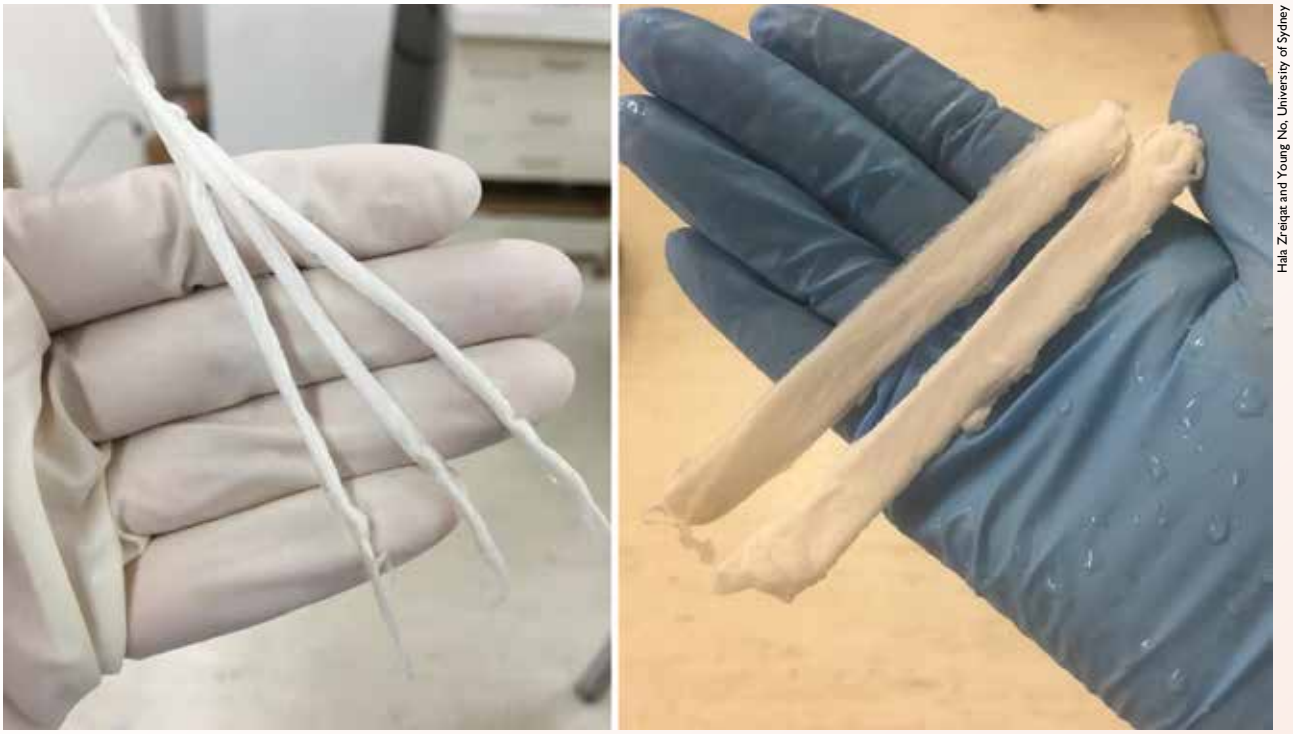
The researchers found only one damaged fibre in 9,000-plus muscle fibres, and that was in the concentric (uphill) exercise group. They also found a significant increase in protein markers associated with muscle growth in the eccentric group after exercise, compared to the concentric group.

Next, researchers hope to test the direct effect of eccentric exercise on muscle after ACL injury, using a noninvasive rodent model of ACL that mimics human injury, Lepley said.

"Our goal is to translate our findings from the bench-top to the sidelines," Lepley said. "We want this information to get to clinicians and patients who have had musculoskeletal injuries to promote lifelong health and wellness."

The study appears in the April issue of the *Journal of Athletic Training*. JAT has also developed a podcast for clinicians that explains the research. MEH

Reference:
Morphology and Anabolic Response of Skeletal Muscles Subjected to Eccentrically or Concentrically Biased Exercise – *Journal of Athletic Training*
https://doi.org/10.4085/1062-6050-174-19



Hala Zreiqat and Young No, University of Sydney

Synthetic fibre-reinforced hydrogels can be produced into different sizes and shapes

Researchers develop new synthetic scaffolds for tendon and ligament repair

University of Sydney biomedical engineers have collaborated with Columbia University and the University of Erlangen-Nuremberg to develop a synthetic material to assist in the regeneration of injured tendons and ligaments.

Worldwide, the costs of tendon and ligament rupture repair and surgery revision represent tens of billions of dollars of the clinical orthopaedic market.

A team of biomedical engineering researchers from the University of Sydney, working with the Regenerative Engineering Laboratory at Columbia University and the FAU Erlangen-Nurnberg Institute of Medical Biotechnology (Germany), are hoping to improve the outcomes of tendon and ligament repair by developing a new synthetic scaffold for their regeneration.

Led by School of Biomedical Engineering researchers Professor Hala Zreiqat, working with postdoctoral researcher Dr Young No, the researchers are the first to develop and patent novel fibre-reinforced hydrogel scaffolds, a synthetic substance that has the ability to mimic and replace human tendon and ligament tissue.

"Ruptures to tendons and ligaments mostly occur in accidents and when playing sport," said Professor Zreiqat, who is also the Director of the Australian Research Centre for Innovative BioEngineering and part of the Sydney Nano Institute.

"Worldwide and particularly in Australia, there is an immense clinical need for the development of readily available, off-the-shelf, mechanically strong synthetic tendon scaffolds.

"Conservative methods using immobilisation casts and movement restricting splints and braces often require several weeks of rehabilitation to achieve minimal functional recovery, while current implants carry a higher risk of rejection and infection.

"Our technology hopes to fast-track the restoration of tendons' and ligaments' mechanical function and support the growth of collagen tissue, without compromising the body's biological response."

Tested on patellar tendon models in rats, the synthetic scaffold has been developed with a stress resistance and water volume similar to real tendons and ligaments, allowing for the improved in-growth of collagen tissue.

"Until now, synthetic scaffolds have come with a significant risk of implant failure, as well as poor biological tissue integration and abrasion," said Zreiqat.

"Human tendons and ligaments are 70% water – they are complicated structures that include blood vessels, nerves and lymphatic vessels and perform the task of linking bone to muscle and moving the body.

"For synthetic scaffolds to be accepted by the body, their physical and chemical architecture must align with human tendons and ligaments."

The researchers now hope to investigate the long-term behaviour of these scaffolds in both internal and external bodily conditions, as well as to observe tissue integration and biomechanics in larger animal models. MEH

Reference:
High-Strength Fiber-Reinforced Composite Hydrogel Scaffolds as Biosynthetic Tendon Graft Material – *ACS Biomaterials Science & Engineering*
https://doi.org/10.1021/acsbiomaterials.9b01716

Diagnosis Related Groups: Understanding the system and how it can ensure more competitive medical costs and increased efficiency

By **Georges Chidiac,**
EVP, General Manager, Damana

Healthcare tariffs and how they are calculated have been a constantly evolving topic in countries that operate a private healthcare system. With the current global health crisis stretching the sector even further, it has become more apparent that standardised systems for patient care could help increase efficiency and the financial burden for all parties.

Diagnosis Related Groups (DRGs) is a patient classification system that standardises prospective payments to hospitals and encourages cost containment initiatives. First implemented in the United States more than 30 years ago, DRGs group patients in respect of diagnosis, necessary treatment and length of hospital stay. Before this categorisation, hospitals would be inclined to maximise the length of stay and over-utilise services to inflate costs.

The overarching benefit of the DRG system is that it fosters increased efficiency and transparency in costs per service, while reducing average length of hospital stay. Under this system, insurers pay hospitals a predetermined amount for a patient's care based on a variety of metrics as well as a cost base rate and relative weight. Cost base rate factors in the overall average hospital charge, while the relative weight assesses the weight of resources that are pulled from a hospital to perform the procedure, mainly driven by its complexity.

There are, according to figures from the US Centers for Medicare and Medicaid Services (CMS), approximately 740 categories of DRGs. Among the most common groups are natural births, caesarean section, neonate with significant problems, heart failure, angina pectoris, specific cerebrovascular disorders, psychoses, pneumonia, joint replacement, rehabilitation, kidney and urinary tract infections. Evolution of the system means some outpatient surgeries are now categorised under DRGs.

Optimising healthcare processes

DRGs look at several personal factors, such as age, sex, primary diagnosis, secondary diagnosis, previous procedures, comorbidities and complications, and more. Each category covers the costs of physician care, nursing care, technician services, therapies, radiology, laboratory, pharmaceuticals, room, meals. Through this process, costs can be directly related to the diagnosis of the patient, thus ensuring that healthcare processes are optimised. Exceptions must be considered with complex situations as two patients with the same condition may require different procedures.

While the system is designed to enhance efficiency and transparency, one counter argument is that the system creates financial incentives for early discharges. There is a view that occasionally certain policies are not in full accordance with the clinical benefits of the patient.

However, correctly implemented, DRGs can help effectively control costs, a welcome benefit for any industry in the current climate, and particularly for a health insurance sector that has felt financial strain and witnessed rising costs in the wake of COVID-19.

Regionally the implementation of DRGs is still in its early stages, although since 2010 Abu Dhabi has been at the forefront of a successful adoption of the system in all its healthcare facilities. Neighbouring emirates including Dubai have also began to ensure that DRGs are an integral part of the healthcare reimbursement system.

At SAICOHEALTH we have long been advocates of DRGs. Our teams work alongside providers to ensure that analysis of cost patterns can create amicable budget positions for hospitals and insurance providers.

Following a turbulent year for the healthcare industry, it is important to understand that the structure and transparency that DRGs offer will be vital for the future of healthcare billing. The success of further implementation relies on key factors including curated data from a sufficient data pool to better understand what the ecosystem would look like once the DRG transfer has occurred. Success will also be dependent on the ongoing support of authorities, medical institutions, and further data analysis to standardise medical costs.

Trust and open communications between all parties will light the way to standardised costs and resource allocation and, ultimately, quality patient care. MEH

About the author

Georges Chidiac has more than 14 years' experience in the regional insurance industry with a focus on budget administration; product development and market distribution; reinsurance structuring; cost containment as well as team leadership.
Chidiac is an industry thought leader and regularly shares his expertise on all insurance verticals at conferences across the region.
He holds a BA of Business administration and management from the Saint Joseph University in Lebanon.

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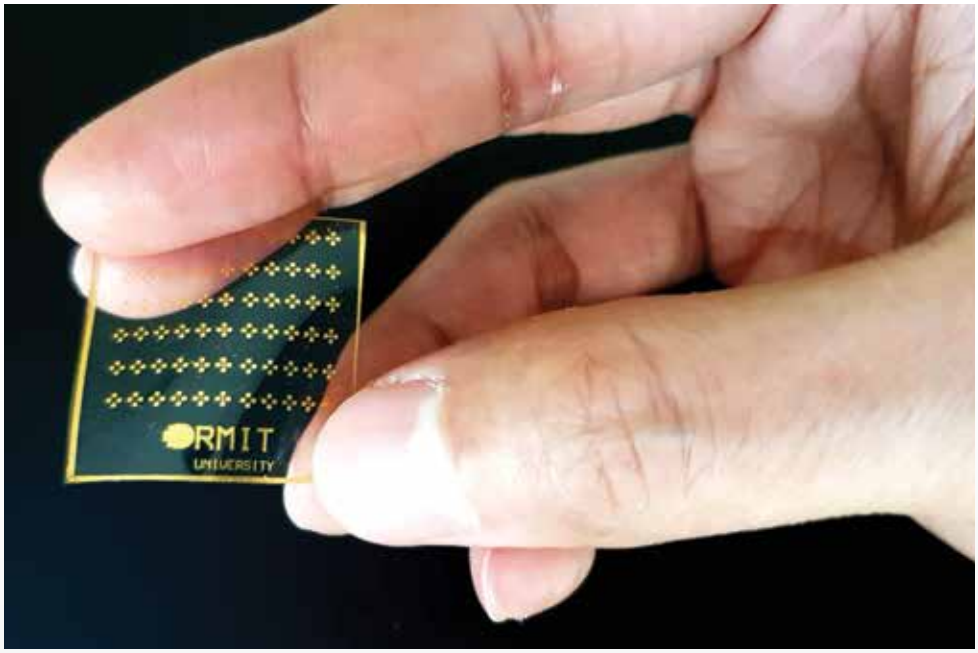

New electronic skin can react to pain like human skin

Researchers have developed electronic artificial skin that reacts to pain just like real skin, opening the way to better prosthetics, smarter robotics and non-invasive alternatives to skin grafts.

The prototype device developed by a team at RMIT University can electronically replicate the way human skin senses pain.

The device mimics the body's near-instant feedback response and can react to painful sensations with the same lighting speed that nerve signals travel to the brain.

Lead researcher Professor Madhu Bhaskaran said the pain-sensing prototype was a significant advance towards next-generation biomedical technologies and intelligent robotics.

"Skin is our body's largest sensory organ, with complex features designed to send rapid-fire warning signals when anything hurts," Bhaskaran said.

"We're sensing things all the time through the skin but our pain response only kicks in at a certain point, like when we touch something too hot or too sharp.

"No electronic technologies have been able to realistically mimic that very human feeling of pain – until now.

"Our artificial skin reacts instantly when pressure, heat or cold reach a painful threshold.

"It's a critical step forward in the future development of the sophisticated feedback systems that we need to deliver truly smart prosthetics and intelligent robotics."

How the electronic skin is made

The new research, published in *Advanced Intelligent Systems* and filed as a provisional patent, combines three technologies previously pioneered and patented by the team:

- **Stretchable electronics:** combining oxide materials with biocompatible silicone to deliver transparent, unbreakable and wearable electronics as thin as a sticker.
- **Temperature-reactive coatings:** self-modifying coatings 1,000 times thinner than a human hair based on a material that transforms in response to heat.
- **Brain-mimicking memory:** electronic memory cells that imitate the way the brain uses long-term memory to recall and retain previous information.

The pressure sensor prototype combines stretchable electronics and long-term memory cells, the heat sensor brings together temperature-reactive coatings and memory, while the pain sensor integrates all three technologies.

PhD researcher Md Ataur Rahman said the memory cells in each prototype were responsible for triggering a response when the pressure, heat or pain reached a set threshold.

"We've essentially created the first electronic somatosensors – replicating the key features of the body's complex system of neurons, neural pathways and receptors that drive our perception of sensory stimuli," he said.

"While some existing technologies have used electrical signals to mimic different levels of pain, these new devices can react to real mechanical pressure, temperature and pain, and deliver the right electronic response.

"It means our artificial skin knows the difference between gently touching a pin with your finger or accidentally stabbing yourself with it – a critical distinction that has never been achieved before electronically." MEH

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