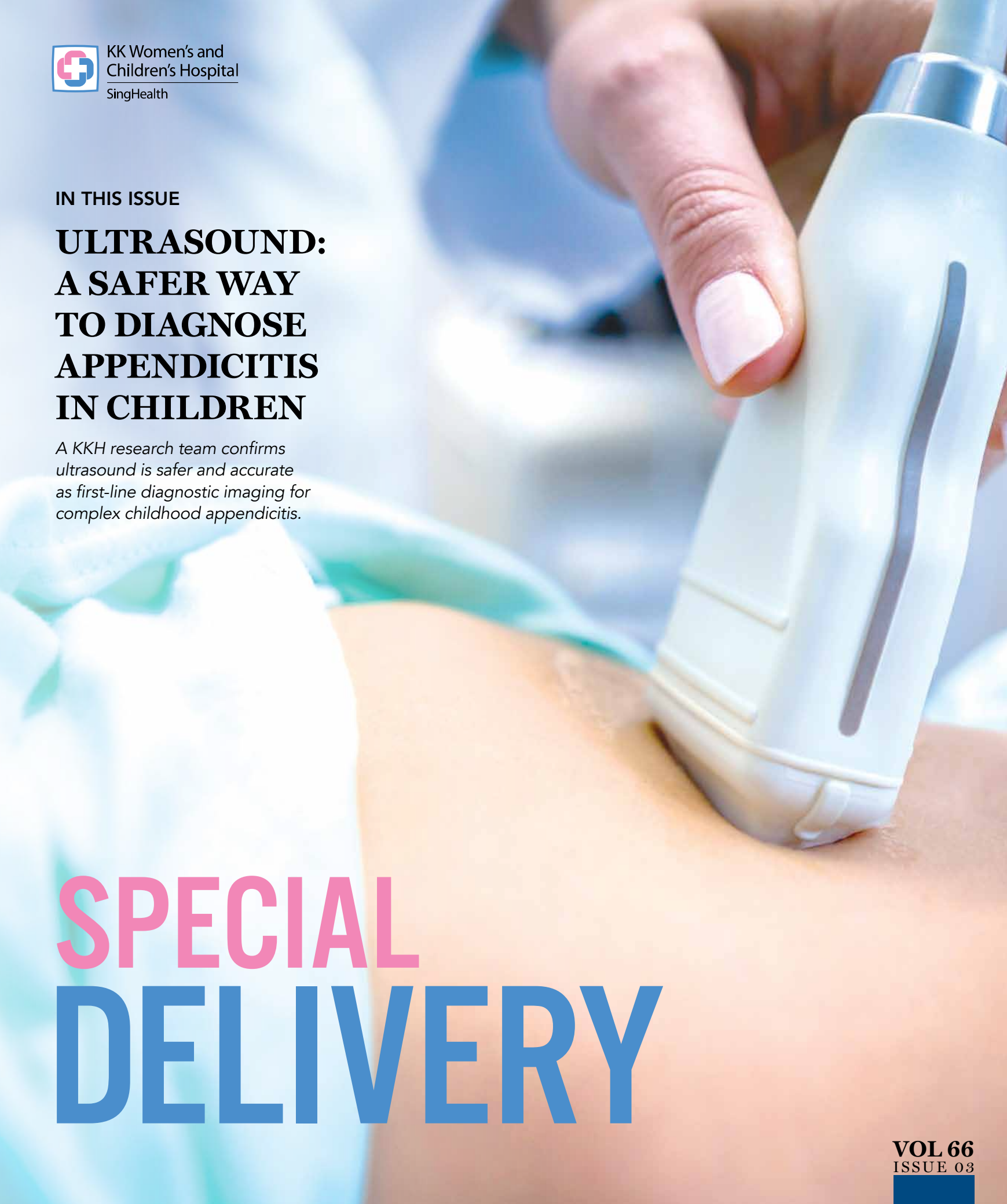
KK Women's and Children's Hospital
SingHealth



IN THIS ISSUE

## ULTRASOUND: A SAFER WAY TO DIAGNOSE APPENDICITIS IN CHILDREN

*A KKH research team confirms ultrasound is safer and accurate as first-line diagnostic imaging for complex childhood appendicitis.*

# SPECIAL DELIVERY

VOL 66
ISSUE 03

If you would like to discontinue receiving Special Delivery or receive it at a different address, please contact us at corporate.communications@kkh.com.sg or +65 6394 8048.





MICA MCI (P) 085/11/2016 REG NO 198904227G



## CONTACT INFORMATION

KK Women's and Children's Hospital
100 Bukit Timah Road, Singapore 229899
Tel: +65 6-CALL KKH (6-2255 554)
Fax: +65 6293 7933

Website: www.kkh.com.sg
Email: corporate.communications@kkh.com.sg

We are on facebook. 'Like' us for updates and news about KKH. www.facebook.com/KKH.sg

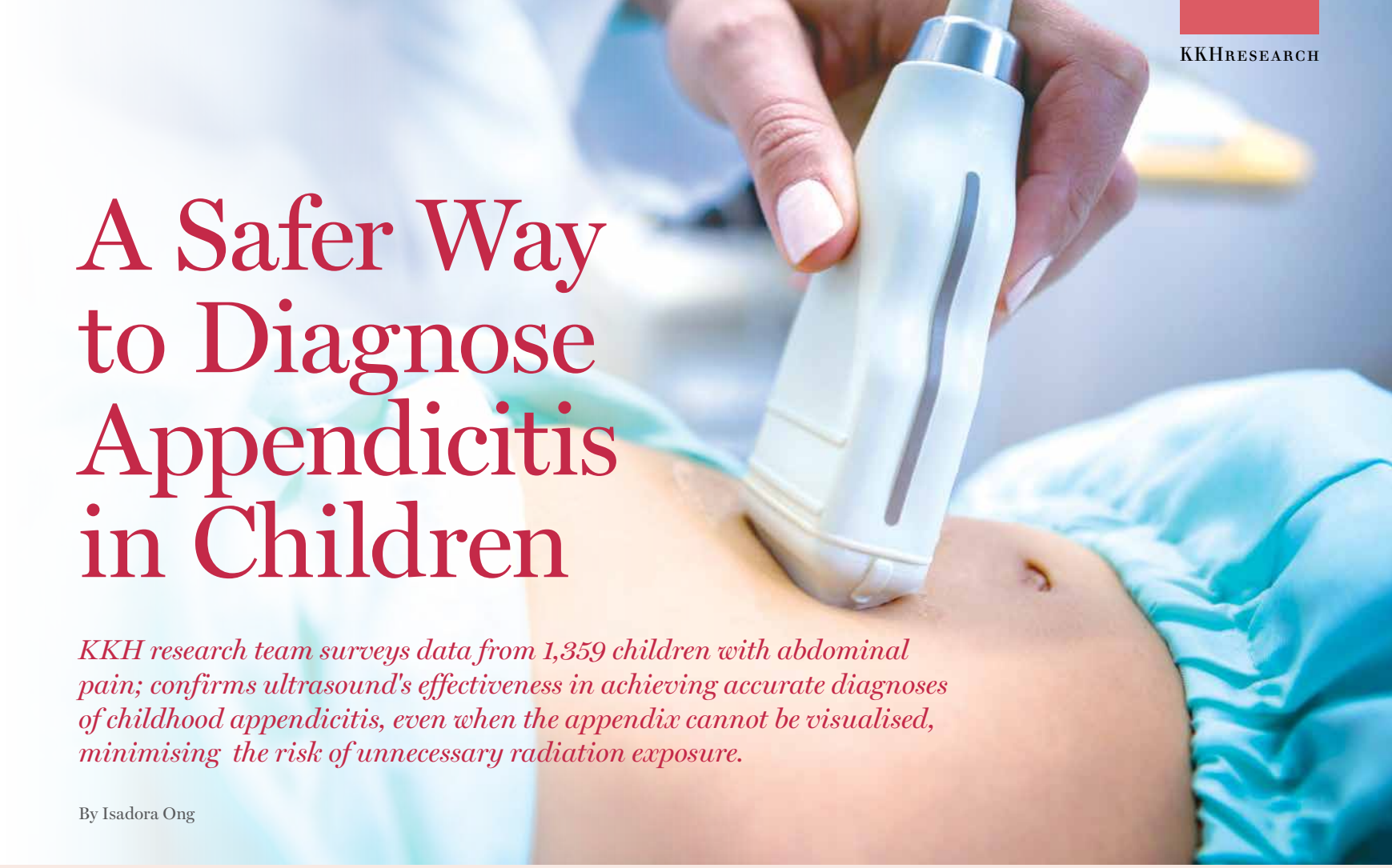

# CONTENTS

*News from Singapore's Academic Tertiary Hospital For Women And Children*









# A Safer Way to Diagnose Appendicitis in Children

*KKH research team surveys data from 1,359 children with abdominal pain; confirms ultrasound's effectiveness in achieving accurate diagnoses of childhood appendicitis, even when the appendix cannot be visualised, minimising the risk of unnecessary radiation exposure.*

By Isadora Ong

Acute appendicitis is the most common surgical emergency in children and adults, and can result in extreme inflammation and perforation of the appendix, necessitating prompt surgical removal (appendicectomy).

As the condition can be challenging to differentiate from other causes of acute abdominal pain, diagnostic imaging is routinely used as an adjunct to clinical examination for suspected cases of appendicitis.

Surveying data from 1,359 children who were admitted to KK Women's and Children's Hospital (KKH) for abdominal pain from January to December 2013, clinician researchers from KKH and Yong Loo Lin School of Medicine found that the high sensitivity and specificity of ultrasound enabled accurate diagnoses of appendicitis even in cases where the appendix was only partially or not visible.

"This is a significant new finding, as scans with an incompletely or non-visualised appendix are often thought to be unhelpful in diagnosing or ruling out appendicitis," says Principal Investigator, Dr Shireen Nah, Staff Physician, Department of Paediatric Surgery, KKH.

"As ultrasound is radiation-free, prioritising it as a first line of diagnostic imaging also allows us to minimise the risk of unnecessary radiation exposure for the child during the screening process," Dr Nah adds.

In cases where the appendix could not be visualised on ultrasound or definitively categorised as normal or abnormal, the observation of secondary signs suggestive of inflammation in the right lower quadrant of the abdomen was greatly valuable in informing the interpretation of the scan, resulting in high diagnostic sensitivity (82.4%), specificity (99.3%), positive predictive value (99.3%) and negative predictive value (97.9%).

These secondary signs included hyperaemia, presence of thickened echogenic periappendiceal or intra-abdominal fat, extraluminal fluid collection, free fluid, presence of an appendicolith and non-compressibility of the appendix.

> *"As ultrasound is radiation-free, prioritising it as a first line of diagnostic imaging also allows us to minimise the risk of unnecessary radiation exposure for the child during the screening process."*
>
> Dr Shireen Nah
> Staff Physician,
> Department of Paediatric Surgery, KKH



Continued on page 4...

Continued from page 3...

## ULTRASOUND APPEARANCE OF THE APPENDIX AND SECONDARY SIGNS SUGGESTING INFLAMMATION

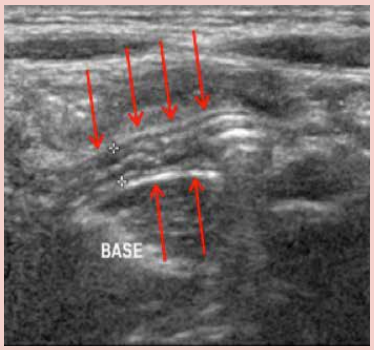



**Figure 1A.** An appendix is identified (red arrows) with normal diameter and no abnormal inflammatory changes surrounding it.

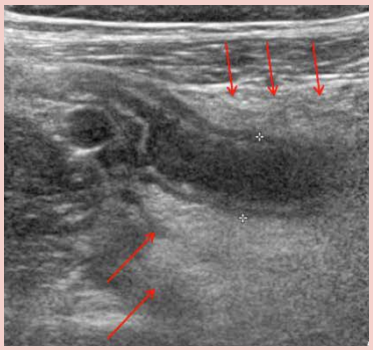


**Figure 1B.** Echogenic fat (red arrows) around a distended appendix is observed.

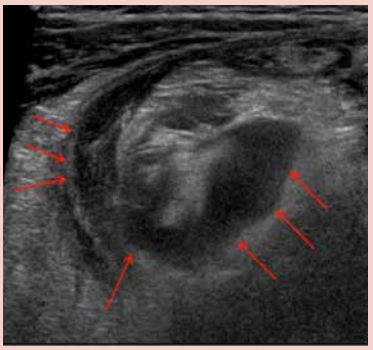


**Figure 1C.** A right lower abdominal mass composed of inflamed echogenic fat and pockets of fluid (red arrows) is observed.

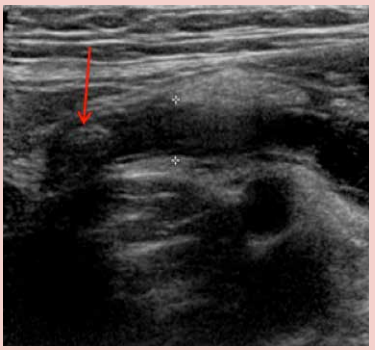


**Figure 1D.** An appendicolith (red arrow) within the distended appendix is identified with surrounding inflamed periappendiceal fat.

Excluding children who underwent ultrasound for other causes of abdominal pain, the use of supplementary computed tomography (CT) imaging to confirm a diagnosis of appendicitis was only necessary in 23 (3.5%) of 641 children who underwent ultrasound for suspected appendicitis.

"Altogether, these enabled us to maintain a low negative appendicectomy rate (2.2%) comparable to that of other leading medical centres, and a minimal risk of missed diagnosis, while preventing unnecessary surgical intervention and anaesthesia in children," said Dr Nah.

## ULTRASOUND IMAGING SAFER FOR CHILDREN WITH SUSPECTED APPENDICITIS

Appendicitis shares many of its common symptoms – such as abdominal pain, nausea with or without vomiting, loss of appetite and slight fever – with other causes of acute abdominal pain, such as genitourinary disorders and intussusception.

Furthermore, about 40 per cent of children who have appendicitis exhibit atypical or non-specific signs and symptoms. As a result, physical examination and clinical history notwithstanding, diagnostic imaging is necessary for an accurate diagnosis of appendicitis.

CT has traditionally been the imaging modality of choice for suspected appendicitis, due to its reliability in clearly visualising the appendix in a large number of patients, even those with a high body mass index. However, CT is associated with relatively high levels of radiation.

Although the dosage is kept as low as possible in paediatric centres, the dose-response relationship between ionising radiation exposure from paediatric CT scans and the risk of malignancy in children has been well-documented.

In contrast, ultrasound is non-invasive and radiation-free, making it a preferred alternative for the diagnostic imaging of children. It can be carried out repeatedly – even at the patient's bedside if needed – with minimal harm to the patient.

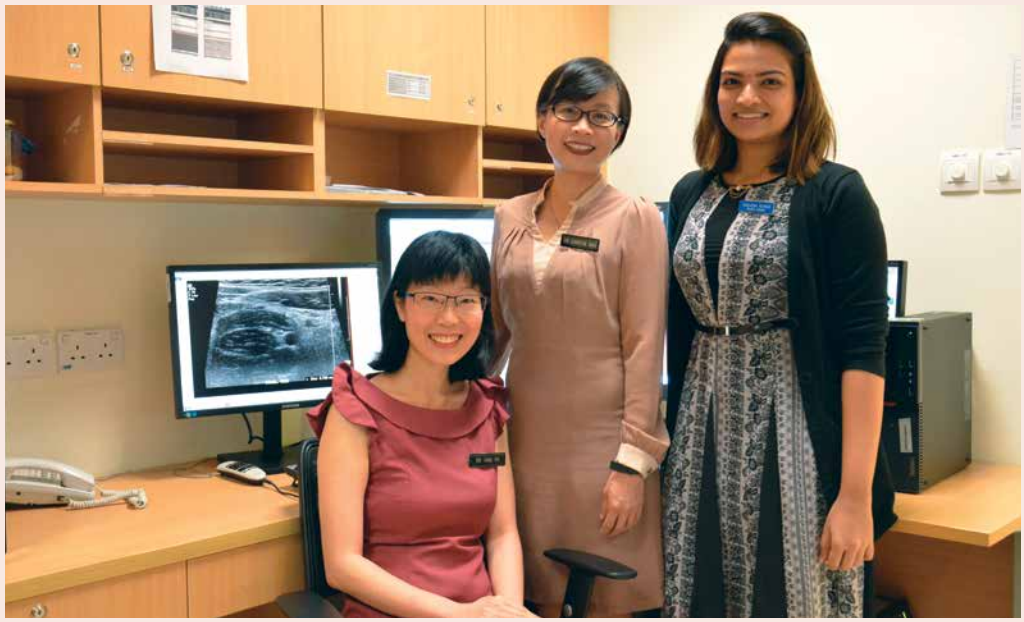
"We are constantly exploring ways to minimise the risks our patients are exposed to and to help them achieve optimal treatment outcomes," says co-investigator Dr Tang Phua Hwee, Senior Consultant, Department of Diagnostic and Interventional Imaging, KKH.

"The results of the study confirmed that ultrasound imaging can indeed be highly accurate in diagnosing appendicitis in children even when the appendix is not completely visualised, and that clinicians may safely use ultrasound results to supplement clinical assessment."

*"Altogether, these enabled us to maintain a low negative appendicectomy rate (2.2%) comparable to that of other leading medical centres, and a minimal risk of missed diagnosis, while preventing unnecessary surgical intervention and anaesthesia in children."*

Dr Shireen Nah
Staff Physician,
Department of Paediatric Surgery, KKH

"Moving forward, we are looking into faster, less invasive methods of diagnosing appendicitis and reviewing protocols to streamline the diagnosis process and increase accuracy. We are also extending research into alternatives for management of appendicitis, including non-operative treatment," Dr Nah adds.



Principal investigator, Dr Shireen Nah, Staff Physician, Department of Paediatric Surgery, KKH (centre), and her co-investigators Dr Tang Phua Hwee, Senior Consultant, Department of Diagnostic and Interventional Imaging, KKH (left), and Ms Sanjena Kumar, Medical Student, Yong Loo Lin School of Medicine, National University of Singapore.

*"We are constantly exploring ways to minimise the risks our patients are exposed to and to help them achieve optimal treatment outcomes."*

Dr Tang Phua Hwee
Senior Consultant,
Department of Diagnostic and Interventional Imaging, KKH

## TIPS FOR ASSESSING APPENDICITIS IN CHILDREN

### TIPS FOR COMMUNITY HEALTHCARE PRACTITIONERS

- When performing physical assessment, it is important to remember that, while the base of the appendix has a fixed position, the tip of the appendix is variable in position.
- If the inflamed appendix is in the pelvis, it can irritate the rectum, leading to tenesmus and resulting in a spurious history of diarrhoea.
- If the appendix irritates the bladder, the child may have symptoms attributed to a urinary tract infection, with frequency and dysuria.
- When appendicitis is suspected in a child, he/she should be referred for tertiary assessment at a specialist centre with paediatric surgical expertise.

### TIPS FOR PARENTS

- Children who experience sudden onset of pain in the right lower abdomen that is persistent for more than a few hours, especially if accompanied with a fever, should be brought immediately for assessment by a community healthcare practitioner.
- In some cases, the appendix may perforate (burst) due to extreme swelling. This can potentially lead to inflammation throughout the abdomen and blood infection that may be life-threatening.
- The likelihood of appendix perforation is much higher in children than in adults; thus timely assessment and treatment is important.

# Missing Connections in the Brain

*Researchers uncover a novel disease entity – Developmental Split-Brain Syndrome – with implications for brain organisation and neurodevelopment.*

By Isadora Ong

*"In contrast, individuals with developmental split-brain syndrome are born without a corpus callosum, and lack connection between the right and left sides of the brain and central nervous system from birth."*

Dr Saumya Jamuar
Consultant,
Genetics Service, KKH

A team of researchers has discovered a new genetic disorder – developmental split-brain syndrome – characterised by agenesis of corpus callosum, underdevelopment of the brain stem, and clinical manifestations of horizontal gaze palsy, intellectual disability and scoliosis.

The syndrome is caused by homozygous mutations in the gene *deleted in colorectal carcinoma (DCC)*, which is responsible for forming common connections, known as commissures, in the brain.

During normal fetal development, the right and left side of the brain develop independently but share commissures to allow for cross-transmission of electrical impulses. Both brain hemispheres are connected by the main and largest bundle of commissural neurons – the corpus callosum – which helps to coordinate brain function and activity, depth perception, hearing and walking in the individual.

"In contrast, individuals with developmental split-brain syndrome are born without a corpus callosum, and lack connection between the right and left sides of the brain and central nervous system from birth," explains Dr Saumya Jamuar, Consultant, Genetics Service, KK Women's and Children's Hospital (KKH), who led the study during his tenure as a clinical fellow at Harvard Medical School.

"Through a network of international collaborators, we identified three families from Mexico, the United States and Saudi Arabia, whose children remarkably shared this central defect, amongst other similar clinical and radiological features."

Structural magnetic resonance imaging of the brain of the affected children showed agenesis of corpus callosum (Figure 1E) and

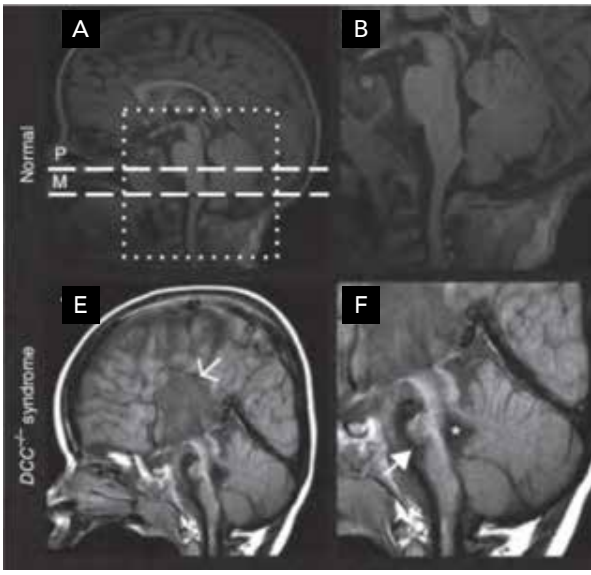



**Figure 1.** MRI scans of a child without developmental split-brain syndrome (images A, B, C and D), in comparison to a child with the syndrome (images E, F, G and H).

an underdeveloped brainstem (Figure 1F), leading to a midline cleft of the medulla with an unusual but characteristic butterfly appearance (Figure 1H).

Diffusion tractography further revealed a disorganised network of not just the commissural fibres, but also the associational, and subcortical fibres (Figure 2B). Fewer fibres were visualised in the affected individuals, with particular depletion of associational and commissural fibres.

## DISCOVERING THE LINK TO THE *DCC* GENE

Dr Jamuar analysed the DNA of the three affected families to delineate the genetic basis of the disease, mapping it to homozygous mutations in the *DCC* gene.

"While the *DCC* gene has been demonstrated in animal models to be responsible for guiding neurons across the midline in the brain, and thus key to the formation of connecting brain tracts, no human had ever been reported with such features," says Dr Jamuar. "These were the first known human cases."

## IMPLICATIONS OF A SPLIT IN BRAIN ORGANISATION

Whilst rare, the phenomenon of split brain has been intensely studied with implications on brain organisation.

Explicit connections between split brains and neurodevelopmental disorders, including autism and Asperger syndrome, have also been established.

"Split-brain syndrome is often seen in adults and children who have undergone surgical transection of the corpus callosum to manage refractory epilepsy. In these patients, the left and right brain behave as independent organs, developing separate concepts and impulses to act.

"This syndrome can create interesting dilemmas – where one side of the brain may favour an activity while the other side may not – providing a unique perspective into understanding how the brain functions as two separate organs," shares Dr Jamuar.

"However, as the surgery is performed in mature brains, the effect of lack of connections between the sides of the brain from an embryological perspective is still unknown."

## IMPROVING THE OUTCOME OF PATIENTS WITH RARE GENETIC DISEASES

With the discovery of developmental split-brain syndrome, patients with symptomatic clinical and radiological features and their families can now be identified and recommended to undergo screening for mutations in the *DCC* gene.

An accurate diagnosis will enable affected patients and their families to be educated on the prognosis and future complications, and engaged on opportunities for management and therapeutics for the syndrome.

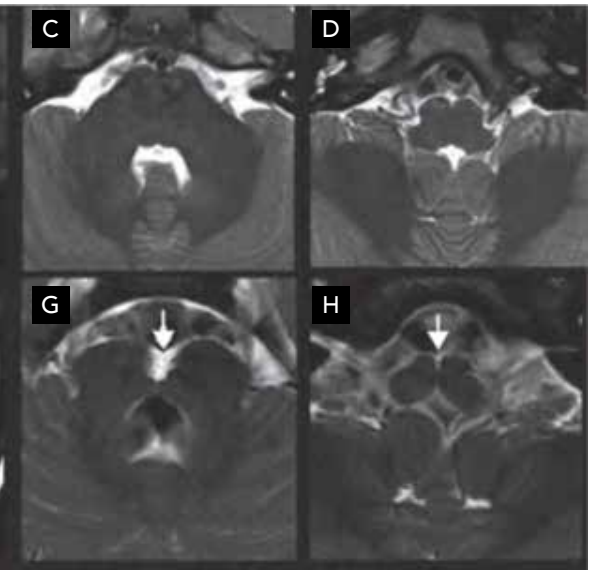
Biological relatives at risk of mutations in the *DCC* gene can also be recommended for genetic testing to confirm their genetic variant and assess their risk of inheriting the syndrome. If they are found to be carriers of this gene mutation, they can receive appropriate counselling on the implications of future reproductive decisions.

"The study findings may also have implications in improving our understanding of how the brain develops, and common disorders such as scoliosis and squint," Dr Jamuar adds.

"We will continue to search for more patients who may have aberrations along the same genetic pathway, and look forward to discovering answers to longstanding mysteries faced by some patients and their families around the world."

## MOVING FORWARD

Since his return from Harvard Medical School, Dr Jamuar has initiated the Singapore Undiagnosed Disease Endeavour for Kids (SUREKids) programme at KKH, in partnership with Agency for Science, Technology and Research (A*STAR) and National University Hospital. The programme has recruited over 300 families, and has successfully diagnosed more than 100 families. Some of these families have benefitted from targeted therapeutic interventions initiated on the basis of the genetic findings.



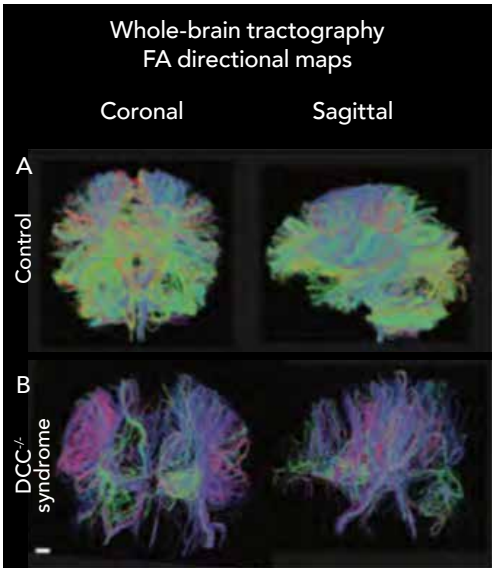




**Figure 2.** Comparison of whole-brain tractography of a child without developmental split-brain syndrome (Control) and a child with the syndrome ($DCC^{-/-}$ syndrome).

*This study was led by Dr Saumya Jamuar, under the supervision of Prof Christopher A. Walsh, an Investigator of the Howard Hughes Medical Institute (HHMI) and Chief of the Division of Genetics at Boston Children's Hospital (BCH), and A/Prof Timothy Yu, Department of Pediatrics, Harvard Medical School. During the study, Dr Jamuar was a clinical fellow at Harvard Medical School and is now Consultant, Genetics Service, KKH.*

*A paper outlining the study findings, entitled 'Biallelic mutations in human DCC cause developmental split-brain syndrome', was published online in Nature Genetics on 27 February 2017, in Volume 49 Issue 4 April 2017.*

# Innovating for the Future

*To improve the lives and health of future generations, clinician researchers and scientists at KK Women's and Children's Hospital (KKH) are pioneering innovative ways to advance women's and children's health outcomes.*

*Supported by $7 million in centre grants from the National Medical Research Council, researchers from KKH, in collaboration with National Dental Centre Singapore, SingHealth Polyclinics and National Healthcare Group Polyclinics, are exploring key areas which impact women's and children's health and wellbeing, including auto-immunology, childbirth and persistent pain, genetics, metabolic syndromes and endometriosis.*

By Rebecca Tse

## INVESTING IN INTEGRATIVE TRANSLATIONAL RESEARCH

Leading the charge is a new Integrative Translational Research Programme which aims to enhance KKH's core research capabilities to better pursue healthcare applications with significant impact and benefit to the healthcare system and population.

"In seeking answers to clinically relevant questions of benefit to women's and children's health, we are collaborating with fellow healthcare institutions, academic research institutions and med-tech industries to launch transdisciplinary streams of enquiry into research areas including the genetics of childhood disorders, obstetric anaesthesia and pain management, stem cells and biomarkers and molecular signatures, among many others," says Associate Professor Sng Ban Leong, Director, KK Research Centre, and Head and Senior Consultant, Department of Women's Anaesthesia, KKH.

"The programme will enable us to achieve greater synergy in translational research by facilitating greater centralisation and coordination across KKH's various research capabilities, resources and platforms. It will also provide a robust structural framework for the integration of research, education and mentorship of more clinician scientists," says A/Prof Sng, who also leads the Integrative Translational Research Programme.

One such research bearing fruit is the discovery of a potential dual regulatory mechanism responsible for inactive disease in childhood-onset systemic lupus erythematosus (SLE), by Dr Yeo Joo Guan, Associate Consultant, Division of Medicine, KKH. The research was done in collaboration with Associate Professor Thaschawee Arkachaisri, Head and Senior Consultant, Rheumatology & Immunology Service and with mentorship from Professor Salvatore Albani, Senior Consultant and Senior Clinician Scientist, Division of Medicine, KKH.

"Childhood-onset SLE is the most severe type of systemic vasculitides – which is the most common group of rheumatic disorders in Singapore. It is associated with renal, neurological and haematological sequelae and significant morbidity," says Dr Yeo.

"In patients with inactive lupus disease, a unique immune signature was found with an increase in both the regulatory B and regulatory T follicular cells. Further, the regulatory B cell population express a unique combination of surface markers – which we are currently examining for the dual translational potential to be used as a predictor of clinical fate and a future therapeutic target in lupus."

Under the new Integrative Translational Research Programme, KKH also welcomes three new core research programmes in translational omics and biomarkers, medical technology, and epidemiology and health services research. These will join the existing genomics, translational immunology and bioimaging core research platforms in driving more effective, safer and patient-centred care through personalised medicine.

"These new research cores will enable us to better investigate diseases at the molecular and metabolic level, personalise patient management, and enhance healthcare efficiency and safety through the integration of medical technology into clinical pathways. We are also pursuing epidemiology and health services research to optimise perinatal care through health technology assessment, identifying health specific outcomes, and provide a cost-effective healthcare system," adds A/Prof Sng.

**Associate Professor Sng Ban Leong**

Director,
KK Research Centre and
Head and Senior Consultant,
Department of Women's Anaesthesia, KKH

# BUILDING SINGAPORE'S FIRST RESEARCH ECOSYSTEM FOR METABOLIC HEALTH IN WOMEN AND CHILDREN

**IPRAMHO Executive Committee members** – Dr Tan Ngiap Chuan, Director of Research, SingHealth Polyclinics (left); Prof Tan Kok Hian, Head and Senior Consultant, Perinatal Audit and Epidemiology Unit, Department of Maternal Fetal Medicine (centre); Dr Ang Seng Bin, Head & Consultant Family Physician, Family Medicine Service, KKH (right); and Dr Tang Wern Ee, Head, Clinical Research Unit, National Healthcare Group Polyclinics (not pictured).

To lower the risk of metabolic disease in future generations, KKH is also establishing Singapore's first Integrated Platform for Research in Advancing Metabolic Health Outcomes in Women and Children (IPRAMHO), in partnership with SingHealth Polyclinics and National Healthcare Group Polyclinics.

Metabolic syndromes are a group of conditions – increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels — that occur together, increasing the risk of heart disease, stroke and diabetes.

"Obesity and diabetes are two of the most urgent metabolic health issues. Singapore has one of the highest incidences of gestational diabetes mellitus (GDM) in the world, with recent KKH studies showing that about 15 to 20 per cent of pregnant women have GDM," says IPRAMHO lead, Professor Tan Kok Hian, Head and Senior Consultant, Perinatal Audit and Epidemiology Unit, Department of Maternal Fetal Medicine, KKH.

"To combat and reverse these trends in our population, IPRAMHO will be Singapore's first collaborative ecosystem for advancing research in metabolic health, with dedicated teams pursuing methodologies such as translational medicine and implementation science, health systems, primary care, behavioural science and human factors, as well as women's and children's health epidemiology."

## TRANSLATING RESEARCH INTO INNOVATION AND INTERVENTION

To track and manage metabolic health for women and children, IPRAMHO seeks to develop a seamless, integrated model of care, including a national registry, and optimised implementation of effective population prevention strategies and diabetes and weight reduction programmes, supported by evidence-based collaborative joint research.

"Going beyond exploring the developmental origins and pathways of metabolic health, our research will focus on the psychosocial, mental and structural pathways of interaction between patients and care providers at the tertiary, primary and community level," adds Prof Tan.

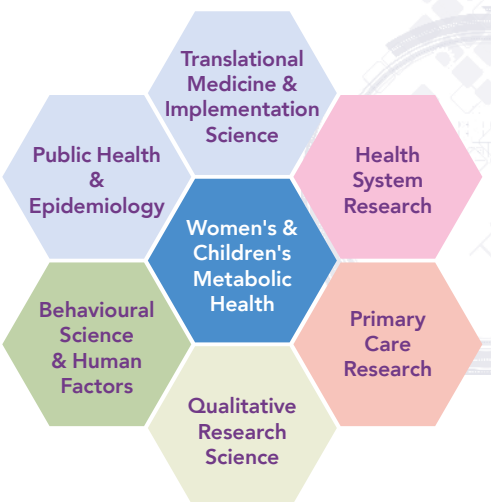
"Our goal is to revolutionise the way medical professionals and health systems engage with patients and women and children at risk for obesity and diabetes in managing their day-to-day health, and allowing us to develop evidence-based, effective, affordable and scalable interventions."

## BUILDING LONG-TERM CAPACITY AND CAPABILITY

In the long term, IPRAMHO will function as a centralised research and training hub, spurring industry partnerships, collaborations with global healthcare leaders, and seed grants for research into medical technology, healthcare innovation, nutrition and dietetics. It will also provide a strong core to build a pipeline of researchers, clinician-scientists and innovators.

"By looking at women's and children's health starting from the womb, and optimising the continuum of care from pregnancy to childbirth, neonate to infant, child, adolescent and eventually adult, we are laying the foundations for transformation of our nation's health, and bettering the future of our generations to come," says Prof Tan.

## IPRAMHO RESEARCH METHODOLOGIES




Continued on page 10...

Continued from page 9...

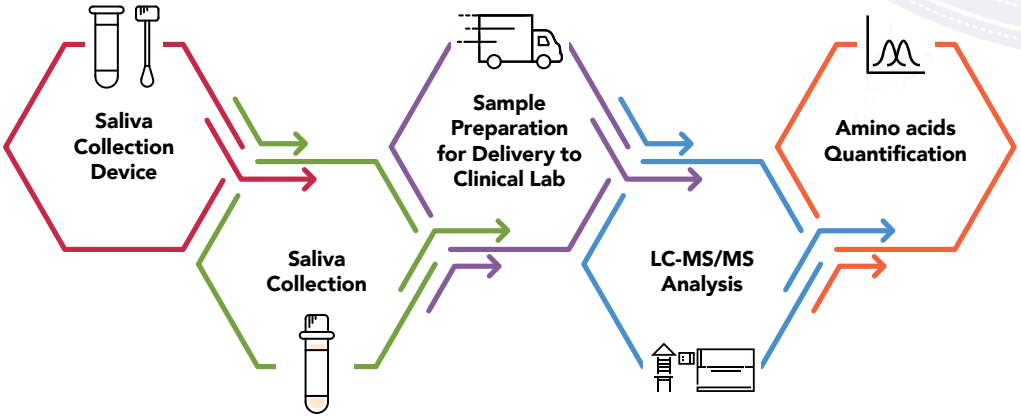
# INNOVATING TO CREATE BETTER PATIENT EXPERIENCES

National Dental Centre Singapore (NDCS) and KKH scientists are developing a painless, non-invasive and convenient solution to save patients with Maple Syrup Urine Disease (MSUD) and Phenylketonuria (PKU) from a lifetime of blood tests, and enable them to better manage their health at home.

"Metabolic disorders MSUD and PKU are caused by enzyme deficiencies, which lead to elevated levels of phenylalanine and branched-chain amino acids (BCAAs) in the blood and tissues. While these amino acids are essential for the body's normal growth and metabolism, they can cause neurological and psychomotor abnormalities if allowed to accumulate unchecked in the body," says co-investigator Dr Tan Ee Shien, Senior Consultant, Genetics Service, KKH, who is also Director of the KKH Newborn Screening Programme.

> *"Blood tests are invasive and especially painful and traumatic for infants and young children. The high frequency of blood testing and visits to the hospital that these necessitate can lead to needle phobia in the patient, and also represent a significant source of stress and economic burden for parents."*
>
> Ms Jasmine Goh
> Genetics Specialty Care Nurse,
> Genetics Service, KKH

## COMPONENTS OF THE PROPOSED FIVE-STEP SOLUTION




People with MSUD and PKU require life-long treatment to monitor and maintain the amino acids at acceptable levels in the body. This involves dietary restrictions coupled with frequent and regular blood testing. Excluding episodes of intercurrent disease or acute metabolic decompensation, a patient diagnosed with MSUD or PKU at birth will undergo about 950 blood tests throughout their lifetime.

"Blood tests are invasive and especially painful and traumatic for infants and young children. The high frequency of blood testing and visits to the hospital that these necessitate can lead to needle phobia in the patient, and also represent a significant source of stress and economic burden for parents," says Ms Jasmine Goh, Genetics Specialty Care Nurse, Genetics Service, KKH.

These factors can lead to non-adherence for regular blood testing, which may result in serious complications due to poor control of the patient's phenylalanine or BCAA levels.

To overcome these barriers and encourage patients to adhere to regular amino acid monitoring, the team is developing a five-step solution. Patients will be provided saliva collection kits to collect saliva samples at home. The samples are then delivered to the clinical laboratory to undergo LC-MS/MS (liquid chromatography coupled with tandem mass spectrometry) analysis and amino acid quantification.

"Saliva contains phenylalanine and BCAAs – albeit at lower concentrations than blood – making it a potential diagnostic fluid. Importantly, saliva can be self-collected painlessly, non-invasively and conveniently, making it a stress-free experience for patients and caregivers," says Dr Ho Meng Fatt, Principal Investigator, Department of Research, NDCS.

> *"In the longer term, this will pave the way for the development of non-invasive diagnostic and therapeutic monitoring tests in the area of lifelong medical conditions."*
>
> Dr James Lim
> Chief Scientific Officer,
> Department of Pathology and Laboratory Medicine, KKH

The team is currently looking into the development of a method to stabilise amino acids in saliva for delivery to the clinical laboratory.

"The end result will be a new solution for the therapeutic monitoring of amino acids in PKU and MSUD patients that is non-invasive, painless, convenient, and more cost effective than the current method of testing. The new solution is applicable not only in our local healthcare setting, but across all other healthcare institutions globally," says Dr Tan.

"In the longer term, this will pave the way for the development of non-invasive diagnostic and therapeutic monitoring tests in the area of lifelong medical conditions," adds co-investigator Dr James Lim, Chief Scientific Officer, Department of Pathology and Laboratory Medicine, KKH.

# COMBATING THE RISK OF DIABETES IN OBESE CHILDREN

Joining the nationwide effort against diabetes, KKH and NDCS researchers are teaming up to better predict the risk of diabetes and other metabolic complications in obese children and adolescents through salivary amino acid profiling.

Insulin resistance has been shown to predict the development of glucose intolerance (impaired fasting glucose, impaired glucose tolerance and Type 2 diabetes mellitus), and associated complications such as dyslipidaemia and hypertension. Recent studies have shown that circulating plasma levels of branch-chain amino acids (BCAA) and aromatic amino acids have been correlated with measures of insulin resistance and can potentially be surrogate markers to predict the risk of diabetes.

## PREDICTING INSULIN RESISTANCE

"We hope to study the utility of saliva as an accurate measure of the BCAA profile. By identifying these biomarkers in plasma and saliva, we can potentially predict insulin resistance. We may someday be able to use saliva to determine the likelihood of future diabetes risk in obese children and adolescents," says Primary Investigator Dr Oh Jean Yin, Deputy Head, Department of Paediatrics and Senior Consultant, Adolescent Medicine Service, KKH.

The team aims to collect saliva samples from 115 overweight and severely overweight children and adolescents attending the KKH Paediatric Weight Management Clinic who are between six to 18 years old and exhibit clinical indications requiring blood tests for metabolic screening.

A minute amount of blood will be taken from existing samples collected during patients' routine fasting blood tests, and both blood and saliva samples will be analysed to measure serum and saliva concentrations of BCAAs. Data from the study will be used to examine the association between elevations in the fasting concentration of plasma BCAAs, measures of insulin resistance and the severity of childhood obesity.

While insulin resistance often develops in adolescence, the presence of obesity worsens the process, as children and adolescents with a higher body mass index (BMI) have a higher risk of cardiometabolic complications such as dyslipidaemia, hypertension, hyperinsulinaemia and glucose intolerance. It is estimated that 10 to 25 per cent of obese children have impaired glucose tolerance that may not be clinically apparent for many years.

## IDENTIFYING CHILDREN AT RISK

Efforts to identify children and adolescents at risk of the development of atherosclerotic cardiovascular disease and Type 2 diabetes mellitus using BMI, waist circumference, systolic blood pressure, serum triglycerides and HDL cholesterol and glucose tolerance have long been debated to have their limitations because of the influence of age, gender and race, stage of puberty.

"We hypothesise that plasma and salivary levels of BCAAs such as leucine, isoleucine and valine may be more reliable biomarkers in predicting the future risk for cardiometabolic disease in obese adolescents, even before early disease is present," says Dr Oh.

Based on the findings of the first-phase study, a follow-up collaborative study is also planned to examine the subset of patients with elevated BCAA levels but no baseline insulin resistance every six months for up to two years, to monitor for possible future development of insulin resistance.

These findings will have significant clinical relevance, where salivary BCAA as a clinical tool may be an extremely acceptable method for screening children and adolescents at risk of development of Type 2 diabetes mellitus.

"The development of such alternative, painless methods of screening children and adolescents enhances our ability to identify at-risk groups early, and enables us to implement more targeted and effective weight management and lifestyle interventions for these children," says Dr Oh.

KKH clinical research coordinator, Ms Foo Chuan Ping, simulates collecting a saliva sample from a study participant.

*Members of the KKH-NDCS research team include: Principal Investigator, Dr Oh Jean Yin, Deputy Head, Department of Paediatrics and Senior Consultant, Adolescent Medicine Service, KKH; and co-investigators Dr Ho Meng Fatt, Principal Investigator, Department of Research, NDCS; Dr Kumudhini Rajasegaran, Head and Senior Consultant; Dr Elaine Chew, Consultant; Dr Alison Snodgrass, Consultant, Adolescent Medicine Service; Dr Siew Jia Xuan, Consultant, General Paediatrics Service; and Dr Saumya Jamuar, Consultant, Genetics Service, KKH.*

*The investigators of this study also gratefully acknowledge the generous support of the Tan Cheng Lim Research and Education Fund.*

## Hydrotherapy at KKH is Giving Children and Women

# The Freedom to Move

At KK Women's and Children's Hospital (KKH), hydrotherapy is being used to enhance and complement conventional land- and gym-based therapy for women and children with conditions such as neurodevelopmental delay, cerebral palsy, muscle dystrophy, chronic pain, osteoarthritis and sports injuries.

Hydrotherapy is the use of water as a medium to carry out therapeutic exercises to reduce pain, improve physical strength and function, and enhance quality of life after sustaining an injury or disability. Studies have observed better compliance and adherence to hydrotherapy compared to land therapy, as patients tend to experience less pain and more ease of movement[1].

"The buoyancy and resistance of the water provides a unique environment for rehabilitation," explains KKH Senior Physiotherapist, Ms Lindsey Jean Ross Weller. "In the water, patients with physical restrictions – such as low muscle tone or weakness, disabilities, injuries and even paralysis – are able to safely and comfortably perform exercises that are not achievable while on land. This enhances their rehabilitation, improving their strength and cardiovascular fitness, as well as flexibility, balance, coordination and mobility."

The hydrotherapy pool at KKH is equipped with a ramp and a commode wheelchair for easy access into the water for patients who are unable to stand. Three different pool depths also allow patients to experience therapy at different body weight loads.

### MANAGING PAIN

Hydrotherapy is conducted in heated water, 32 to 34 degree Celsius, as warmth helps to ease tight muscles and enhance relaxation, which reduces pain. Hydrostatic pressure also increases venous return and circulation, which can also help to ease oedema and further reduce pain. These can help to increase range of motion, and bring relief to patients who suffer from chronic and acute pain.

"We have patients of all ages who struggle to walk or do any land-based therapy, and are also unable to visit the public pool independently. Some suffer from chronic pain due to neuromuscular conditions such as fibromyalgia and osteoarthritis. Hydrotherapy provides a healthy and sustainable way to manage their pain and maintain strength and fitness, as it gives them the benefits of rehabilitation and exercise while reducing the pressure and body weight loading on their limbs," adds Ms Weller.

At KKH, hydrotherapy is provided by certified physiotherapists; all patients will be assessed to ensure there are no contraindications prior to commencing hydrotherapy, and regularly monitored to determine their goals and suitability.

### PAEDIATRIC HYDROTHERAPY

Hydrotherapy is particularly beneficial for children with gross motor delay and global developmental delay, enabling them to build and maintain muscle strength and tone, and improve limb functionality and walking ability.

For children who are unable to walk or crawl due to neuromuscular conditions, hydrotherapy may be their only opportunity to experience freedom and independence of movement. The child can learn how to swim, stand and walk in the water with the appropriate flotation device. Hydrotherapy can even be used to maintain lung function and inspiratory muscle strength through games which encourage them to blow bubbles or blow objects in the water.

Moreover, water provides a tactile, auditory and visually stimulating environment that can be especially beneficial for children with sensory integration disorders. Therapy conducted using this medium can enhance their ability to perceive their surroundings

Senior Physiotherapist, Ms Lindsey Jean Ross Weller, helps eight-year-old Garren with hydrotherapy exercises to improve muscle strength and joint stability.

through their senses, and coordinate their limbs to respond more effectively to the stimulus.

## ANTENATAL AQUA WORKOUT

"The benefits of hydrotherapy can also be applied through antenatal aqua workout to relieve pregnancy-related aches and pains, and help women maintain and even improve cardiovascular fitness during pregnancy," says Ms Weller. "Maintaining a regular and moderate exercise routine during pregnancy helps to prepare them for labour. It also improves insulin sensitivity, which can have a beneficial effect on blood sugar levels and help to reduce blood pressure."

The Rehabilitation Centre at KKH conducts the only antenatal aqua classes in Singapore that are run by physiotherapists. The physiotherapist is able to modify exercises to suit the physical condition of each participant, ensuring that they do not strain their muscles or injure themselves.

"The effect of warm water helps to reduce stiffness, spasm and pain caused by tight or aching muscles during pregnancy. The buoyancy of the water also reduces the effect of gravity, allowing the woman to exercise more freely and easily in the water even with a big tummy," Ms Weller added.

Under the supervision of a physiotherapist, pregnant women, even those who are not able to swim, can safely engage in exercises to improve strength in specific muscles, such as pelvic floor control, and reduce pain due to muscle strain, such as in the lower back.

### *REFER A PATIENT*

*Polyclinics and community healthcare practitioners can contact KKH at +65 6294 4050 to refer patients for consultation and assessment on their suitability to commence hydrotherapy.*

*Antenatal aqua classes at KKH are open to the public. For more information, please contact the KKH Patient Education Centre at +65 6294 4050 or email pec@kkh.com.sg.*

## CASE STUDY: HYDROTHERAPY FOR EIGHT-YEAR-OLD CHILD WITH HYPOTONIA AND A TRACHEOSTOMY

Eight-year-old Garren has hypotonia and hypermobile ligaments, in addition to a tracheostomy to help with his breathing. He also has global developmental delay. Garren's parents experienced difficulty carrying out water-based therapy for him at a public pool due to a fear of the public not being accustomed to children with special needs, and water being accidentally splashed into his tracheostomy by other pool users, which would cause him to experience breathing difficulties and expose him to possible infection.

Garren has been undergoing regular hydrotherapy at KKH for nearly two years. Each 30-minute session comprises exercises to strengthen the muscles of his trunk and limbs, and enhance his joint stability, flexibility and range of motion – all of which are crucial in enabling him to sit upright and walk with less assistance.

Hydrotherapy also provides sensory stimulation to improve his body awareness. This is beneficial for his overall strength and mobility, and to improve his sitting or standing balance.

Hydrotherapy is also a source of enjoyment for Garren, as it provides freedom of movement and pleasant stimulation for his senses.

*References:*

1. *Declerck, M., Verheul, M., Daly, D and Sanders, R (2016) Benefits and enjoyment of a swimming intervention for youth with cerebral palsy: an RCT Study, Pediatr Phys Ther, 28:162-169.*

*This article acknowledges the inputs of the Physiotherapy Department, KKH.*

# Better Care for Mothers and Babies

*Pioneering programmes at KKH are opening new avenues to boost mothers' health and give babies a better start to life.*

With the vision to provide excellent, holistic and compassionate care for women and children, KK Women's and Children's Hospital (KKH) continually seeks better and more effective ways to improve patients' lives. Ongoing efforts received a welcome boost in late 2017, with collaboration between KKH and Temasek Foundation Cares to introduce pilot programmes to help optimise detection and care for women with gestational diabetes mellitus, and launch Singapore's first donor human milk bank programme to provide breast milk to premature and sick babies in Singapore.

## NEW CARE MODEL FOR PREGNANT WOMEN WITH GESTATIONAL DIABETES

In Singapore, up to one in five women are at risk of gestational diabetes mellitus (GDM), a condition that puts them at increased risk of developing high blood pressure during pregnancy, experiencing preterm labour, maternal complications and developing Type 2 diabetes mellitus (T2DM) in their lifetime.

Despite the risks, about 90 to 95 per cent of women with GDM do not undergo regular check-ups to monitor their diabetes condition after delivery to ascertain if their condition has resolved, or maintain a routine of screening for T2DM at least once every three years.

To improve detection, care and support for this vulnerable group, in September 2017, KKH and Temasek Foundation Cares introduced the 'Temasek Foundation Cares GDM Care' programme, which aims to pilot a novel model of care encouraging all pregnant women receiving antenatal care in KKH to undergo GDM screening, and receive appropriate antenatal and postnatal care and follow-up to track and manage their diabetes condition.

The $1.09 million programme aims to benefit about 5,400 women with GDM and their families over a three-year period.

"The incidence of GDM is rising globally due to an increasing average age for childbearing, as well as an increased prevalence of diabetes in the population, exposing both mother and baby to increased health and mortality risks," explains programme lead, Professor Tan Kok Hian, who is also Head and Senior Consultant, Perinatal Audit and Epidemiology Unit, Department of Maternal Fetal Medicine, KKH.

"Children born from pregnancies affected by GDM tend to be big babies weighing more than four kilogrammes at birth, putting them at higher risk of suffering birth trauma and a lack of glucose in the bloodstream which can lead to long-term negative health effects. They also have higher risks of developing obesity and T2DM later in life," Prof Tan adds.

Under the pilot, all expectant mothers in KKH are offered routine GDM screening between 24 and 28 weeks of gestation. Expectant mothers with GDM are also guided by a team of Diabetes Care Navigators in observing a care plan for optimal management of the condition, to achieve the best outcomes for both mother and child.

Educational support will be provided to patients and their families during pregnancy and after delivery to encourage healthier lifestyles and minimise the health risks arising from a pregnancy affected by GDM. If the condition persists after delivery, they can be referred to a network of care partners for further evaluation and follow-up management of their condition.

Subsidies will also be provided to women who require further financial assistance to optimise care for themselves and their families.

"The Temasek Foundation Cares GDM Care programme is truly a welcome boost to our ongoing efforts to enhance care and improve health for women and children. Through the early detection, timely intervention and close follow-up care afforded by this structured care and education programme, we are closer to optimising prevention and management of diabetes and its associated health risks for our future generations," says Prof Tan.

Diabetes Care Navigator and Nurse Clinician, Asmira Bte Mohamed Rahim, guides a pregnant patient on the self-administered finger-prick test to monitor her blood sugar levels.


Guest of Honour, Madam Halimah Yacob (centre) at the launch of Singapore's first donor human milk bank, with (from left) A/Prof Ng Kee Chong, Chairman, Medical Board, KKH; Prof Alex Sia, CEO, KKH; Mr Richard Magnus, Chairman, Temasek Foundation Cares; Prof Ivy Ng, Group CEO, SingHealth; Ms Woon Saet Nyoon, Chief Executive, Temasek Foundation Cares; and Dr Chua Mei Chien, Head and Senior Consultant, Department of Neonatology, KKH.

# SINGAPORE'S FIRST DONOR HUMAN MILK BANK OPENS AT KKH

In August 2017, KKH launched Singapore's first donor human milk bank programme to provide a ready supply of safe, pasteurised human breast milk donated for vulnerable premature and sick neonates whose mothers are not able to provide enough breast milk to support their babies' needs.

Funded by Temasek Foundation Cares, the $1.37 million three-year pilot programme aims to recruit approximately 375 healthy and eligible mothers, who are willing to donate their excess breast milk, to benefit 900 babies receiving neonatal care in KKH, Singapore General Hospital* and National University Hospital*.

"Breast milk is the best form of nutrition for babies, containing white blood cells and antibodies that protect the baby against infections and improve their chances of survival. The fat globules in breast milk enable better brain and vision development. This makes breast milk especially beneficial for premature and sick newborns, who have immature and weak digestive systems that make them prone to feeding intolerance.

"Providing safe, pasteurised donated breast milk to these vulnerable babies allows them to benefit from this ideal source of nutrition while also significantly improving their chances of development and recovery," says Dr Chua Mei Chien, Director, Temasek Foundation Cares Donor Human Milk Bank Programme, and Head and Senior Consultant, Department of Neonatology, KKH.

The first of its kind in Singapore, the KK Human Milk Bank will collect, screen, process and store breast milk received from donors, following strict international guidelines for laboratory testing, processing and storage of the pasteurised milk, before it is dispensed for use. Eligible donors will be required to undergo a stringent donor screening process and blood tests, as well as education on the handling and storage of the breast milk prior to donation.

Every year, about 350 very low birth weight infants receive neonatal intensive care in Singapore's public hospitals. Despite best efforts to support breastfeeding, up to 80 per cent of sick neonates in the Neonatal Intensive Care Unit and Special Care Nursery receive formula milk meant for premature babies, either totally or partially, during their hospital stay due to inadequate supply of breast milk from their own mothers.

"As a Baby-Friendly Hospital Initiative-certified hospital, we are committed to improving neonatal and infant health and supporting mothers in their endeavours to breastfeed before birth by providing breastfeeding education, during their hospital stay and after they are discharged," adds Dr Chua.

"This precious supply of ready, safe, pasteurised donor breast milk will be greatly beneficial in helping us to reduce the risk of potential complications in the babies, while optimising their immunity, development and overall health."

* *Available to these hospitals after the first year of operation.*

## Be a KKH Volunteer!

To find out more about volunteering opportunities at KKH, please visit **www.kkh.com.sg/volunteer** or email **volunteer@kkh.com.sg**

**Playing games** – KKH volunteer Tan Li Shuang completes a puzzle with a patient during a ward play session. Ward play supports hospitalised children through challenging times during their stay in the hospital by offering fun and familiar activities which can provide them with distraction and comfort.

PATIENTS. AT THE HEART OF ALL WE DO.

KK Women's and Children's Hospital
SingHealth

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
OBSTETRICS & GYNAECOLOGY

SingHealth DukeNUS ACADEMIC MEDICAL CENTRE
PAEDIATRICS

KKH HEALTH FUND
Part of SingHealth Fund

### ABOUT KK WOMEN'S AND CHILDREN'S HOSPITAL

Founded in 1858, KK Women's and Children's Hospital (KKH) is a recognised leader and Singapore's largest tertiary referral centre for Obstetrics, Gynaecology, Paediatrics and Neonatology. The 830-bed academic medical institution leads in patient-centred management of high risk conditions in women and children. More than 500 specialists adopt a compassionate, multi-disciplinary and holistic approach to treatment, and harness medical innovations and technology to deliver the best medical care possible.

Accredited as an Academic Medical Centre, KKH is a major teaching hospital for all three medical schools in Singapore, Duke-NUS Medical School, Yong Loo Lin School of Medicine and Lee Kong Chian School of Medicine. The Hospital also runs the largest specialist training programme for Obstetrics and Gynaecology and Paediatrics in the country. Both programmes are accredited by the Accreditation Council for Graduate Medical Education International (ACGME-I), and are highly rated for the high quality of clinical teaching and the commitment to translational research.

**GIVE HOPE**

**MAKE POSSIBLE**

**LIFE-GIVING BREAKTHROUGHS**

Because every woman and child deserves good health

**www.kkh.com.sg/GIVE**