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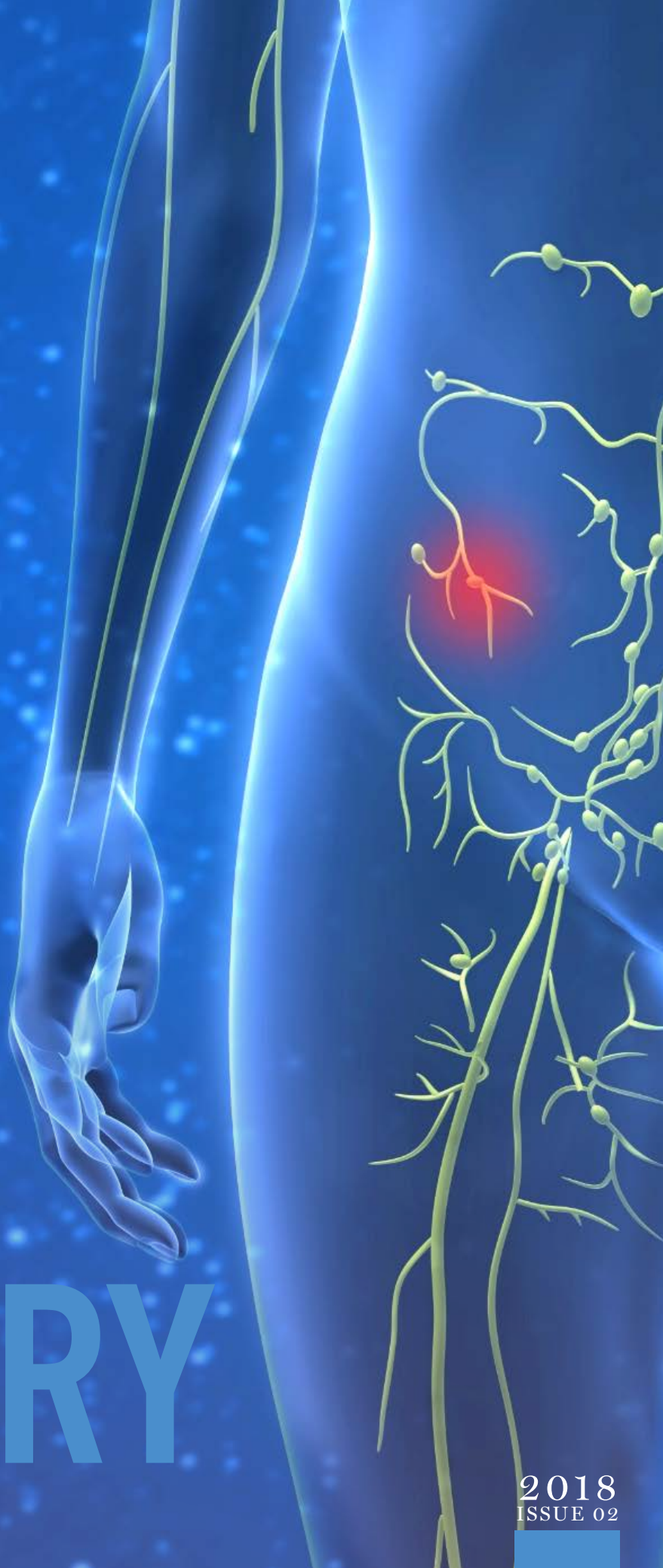
KKH  
160  
Years

1858-2018  
Celebrating Our Heritage,  
Shaping The Future

IN THIS ISSUE

## THE WAY FORWARD FOR ENDOMETRIAL CANCER

*Sentinel lymph node mapping using indo-cyanine green and near-infrared imaging has been shown to maintain a high detection rate while reducing the risk of morbidities associated with systematic bilateral pelvic lymphadenectomy in women with early-stage endometrial cancer.*



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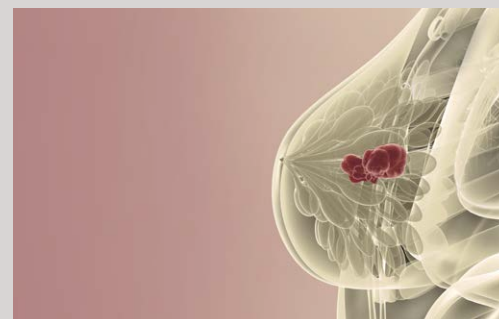
*KKH provides timely intervention and care for young patients with citrin deficiency, an autosomal recessive inborn error of metabolism with a high prevalence in Asia, to help them achieve optimal growth and development.*



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*KKH and AMKFSC Community Services Ltd organise Singapore's first Integrated Child Health and Social Congress to enhance awareness of the early formative years of a child's life, and cross-sector coordination of services and collaboration to support children from vulnerable families.*



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### **REMEMBERING A BELOVED HEALER, CHAMPION AND EDUCATOR**

*Colleagues and friends of the late Associate Professor Joseph Manuel Gomez (1952 - 2017) pay tribute to his dedication in providing compassionate and life-saving care for premature and sick neonates, and his tireless efforts towards improving clinical quality and patient safety at KKH.*

# The Way Forward For Endometrial Cancer:

## Sentinel Lymph Node Mapping Using Indo-Cyanine Green and Near Infrared Imaging

*A unique novel method for surgical staging of endometrial cancer, sentinel lymph node mapping using indo-cyanine green and near-infrared imaging has been shown to maintain a high detection rate while reducing the risk of morbidities associated with systematic bilateral pelvic lymphadenectomy in women with early-stage endometrial cancer.*

By A/Prof Timothy Lim

**U**terine cancer is the fourth most common cancer affecting women in Singapore, and its incidence has been increasing steadily over the last decade. Approximately 380 women are diagnosed with uterine cancer in Singapore every year, of which 60 per cent are seen and managed by the Department of Gynaecological Oncology at KK Women's and Children's Hospital (KKH).

Endometrial cancers account for 80 to 90 per cent of all uterine cancers globally, and more than two thirds of patients are found to have early-stage cancers. In KKH, about 180 patients are diagnosed with Stage I to Stage II endometrial cancers annually, according to the International Federation of Gynecology and Obstetrics (FIGO) 2009 criteria. The current standard treatment for women in Singapore with early-stage

endometrial cancers is a total hysterectomy (removal of the uterus), bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes) and a systematic bilateral pelvic lymphadenectomy (complete removal of lymph nodes from the pelvis). Surgical staging is also carried out to guide adjuvant treatment decisions, define recurrence risk and facilitate assessment of prognosis.

Approximately 10 per cent of women with cancer that is clinically confined to the uterus (i.e. no evidence of distant spread on computed tomography or magnetic resonance imaging scans) are found to have pelvic lymph nodes metastases – where cancer cells are found to have spread to the pelvic lymph nodes. Where the pelvic lymph nodes are found to be positive for cancer, this has been shown to confer a less ideal prognosis. Such patients are upstaged to

a diagnosis of Stage IIIC cancer, and would need to undergo adjuvant treatment such as chemotherapy and radiotherapy. Systematic bilateral pelvic lymphadenectomy has been associated with significant morbidity such as lower limb lymphoedema, pelvic lymphocyst formation and transient neuralgias in up to 20 per cent of patients.

### AN ENHANCED MODALITY OF SURGICAL STAGING

The sentinel lymph node (SLN) is the first node in a regional lymphatic basin that receives the lymph flow from the primary tumour, and its histological status may accurately predict the status of the regional lymphatic basin. Hence, SLN mapping and biopsy has been mooted as a useful modality for assessing lymph node involvement and triaging patients who would benefit from adjuvant treatment. This can help to prevent

Continued from page 3...

a complete pelvic lymphadenectomy and its associated morbidity in a significant number of patients – particularly those with early-stage cancer.

The traditional method for SLN mapping involves the use of a blue dye (patent blue or methylene blue) as well as radioactive tracers such as technetium-99 (Tc-99). However, using radioactive tracers necessitates a pre-operative nuclear medicine injection and lymphoscintigram, which are associated with additional costs and patient discomfort.

In recent years, SLN mapping using ICG-NIR (indo-cyanine green and near-infrared imaging) has emerged as an attractive alternative, and has been found to have similar rates of mapping success to that of radiocolloid Tc-99 combined with blue dye in many studies<sup>1,2</sup>.

Indo-cyanine green (ICG) dye is very safe, with a one in 42,000 risk of anaphylactic reaction. The fluorescent dye, which is injected into the cervix during the SLN mapping process, relies on a fluorimetry-capable camera and appears blue when excited by a light source in the near-infrared (NIR) range.

As light in the NIR range has a wavelength range of 700 to 900 nanometres and is

*SLN mapping and biopsy has been mooted as a useful modality for assessing lymph node involvement and triaging patients who would benefit from adjuvant treatment.*

*This can help to prevent a complete pelvic lymphadenectomy and its associated morbidity in a significant number of patients – particularly those with early-stage cancer.*

invisible to naked eye, it does not alter the surgical field when used. Laparoscopic systems are available where the fluorescence in the dye can be activated by a button on the NIR camera head. This turns the lymphatic channels and lymph nodes bright blue during the surgical staging of cancer (Figure 1), enabling a lymph node to be quickly and accurately identified (Figure 2)

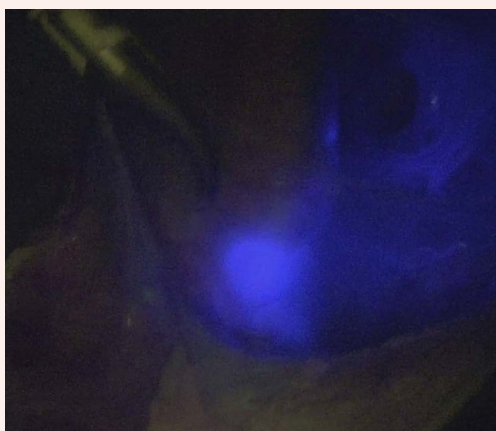
and a biopsy to be performed – where the lymph node is retrieved to examine its histological status (Figure 3).

A recent large study in the United States (FIRES Trial)<sup>3</sup> in 340 women with presumed early endometrial cancer found that SLN mapping using ICG-NIR yielded a detection rate of about 86 per cent and the negative predictive value was 99.6 per cent.

The false-negative rate was 2.8 per cent (i.e. 35 in 36 SLNs were positively identified), which is much lower compared to SLN mapping by radiological means.

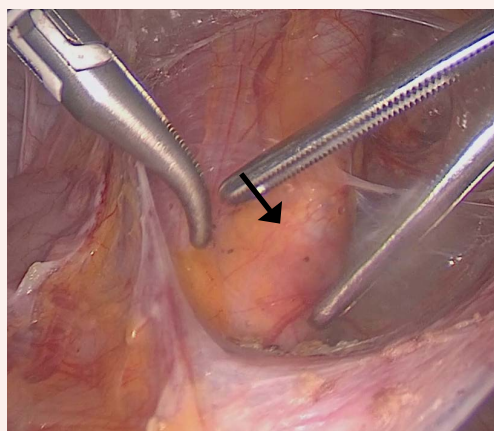
In another multicentre study in the United States<sup>4</sup>, 412 patients undergoing endometrial cancer staging using an SLN mapping with blue dye and ICG-NIR were found to have fewer overall number of lymph nodes removed, but a similar or higher rate of detection of Stage IIIC disease.

A third recent study from Sweden<sup>5</sup> involving 188 patients found a lower incidence of leg lymphoedema (1.3% versus 18%,  $p=0.0003$ ) and lower incidence of pelvic lymphocyst (2.3% versus 13.3%,  $p=0.02$ ) in patients undergoing SLN mapping and biopsy using ICG-NIR in comparison to systematic pelvic lymphadenectomy.



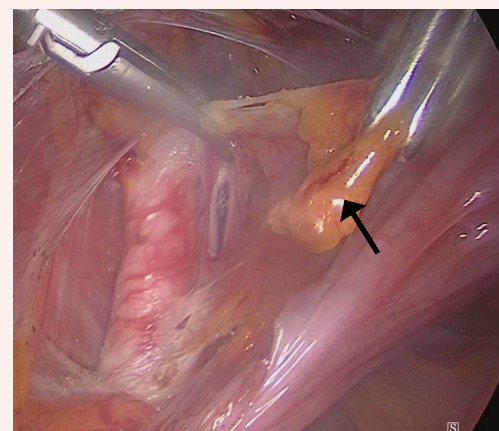
**Figure 1.**

The location of a sentinel lymph node (in bright blue) is identified with a near-infrared camera system.



**Figure 2.**

The location of the sentinel lymph node (black arrow) is identified on the left external iliac artery in the pelvis.



**Figure 3.**

A sentinel lymph node biopsy is performed, where a sentinel lymph node (black arrow) is retrieved to examine its histological status.

## A WAY FORWARD IN MANAGING EARLY STAGE ENDOMETRIAL CANCER

At KKH, a pilot evaluation of SLN mapping using ICG-NIR was conducted in 35 patients with clinically early-stage endometrial cancer who underwent laparoscopic staging surgery. ICG was injected at the three and nine o'clock positions of each patient's cervix after a laparoscopic entry into the peritoneal cavity was made. The SLN was first biopsied, followed by systematic pelvic lymphadenectomy.

The mean lymph node count was 21 nodes and the mean number of SLNs biopsied was three nodes per patient. The overall SLN detection rate was 97 per cent (34 in 35 patients) and the rate of bilateral mapping – the successful identification of SLNs on both sides of the pelvis – was 88.6 per cent (31 in 35 patients).

It was found that two patients (5.7%) had positive bilateral pelvic lymph nodes, two patients (5.7%) had positive SLNs and no patients had false-negative SLNs. Four patients (11.4%) were upstaged to Stage II or Stage IIIC1 endometrial cancer. The results obtained from the evaluation were similar to that in recently published

international data, and showed that SLN biopsy is a feasible alternative to systematic pelvic lymphadenectomy for surgical staging of endometrial cancer.

Following the pilot, the Department of Gynaecological Oncology at KKH officially introduced SLN mapping and biopsy using ICG-NIR to all patients diagnosed with endometrial cancer in August 2017. KKH is the first cancer centre in Singapore to offer this new modality of cancer staging for endometrial cancer and, to date, has conducted this procedure in more than 100 patients laparoscopically and more than 16 patients via open surgery.

Since 2014, the United States National Comprehensive Cancer Network (NCCN) guidelines have reflected emerging data regarding the role of SLN mapping in endometrial cancer management. The guidelines now include SLN biopsy using ICG-NIR as a consideration in the surgical staging of apparent uterine-confined malignancy, and the cervical injection technique is considered useful and validated.

Since May 2017, the Society of Gynaecologic Oncology in the United States has also endorsed the use of SLN mapping using ICG-NIR in patients with low grade

(Grade 1 or 2) endometrial cancer following the NCCN SLN mapping algorithm guidelines; however, patients should be counselled regarding the potential risk for missed occult disease using SLN biopsy for cancer staging.

Based on international data, the risk of missing occult disease is less than five per cent; this is lower than the risk associated with indirect methods such as radiological imaging. In our pilot evaluation, the risk approaches zero per cent if performed in carefully selected patients.

*KKH is the first cancer centre in Singapore to offer this new modality of cancer staging for endometrial cancer and, to date, has conducted SLN biopsy and mapping using ICG-NIR in more than 100 patients laparoscopically and more than 16 patients via open surgery.*

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Associate Professor Timothy Lim, Head and Senior Consultant, Department of Gynaecological Oncology, KK Women's and Children's Hospital

Associate Professor Timothy Lim is the Deputy Chairman of the Division of Obstetrics and Gynaecology at KKH. Heading the Department of Gynaecological Oncology, A/Prof Lim holds a strong interest in cervical cancer prevention, sentinel lymph node techniques, fertility sparing cancer surgery as well as advanced laparoscopic cancer surgery. A/Prof Lim is also the Academic Deputy Vice Chairman of Research for the SingHealth Obstetrics and Gynaecology Academic Clinical Programme.

# Citrin Deficiency: A Differential Diagnosis

Dr Christina Ong and Dr Ting Teck Wah

**C**itrin deficiency is an autosomal recessive inborn error of metabolism (IEM) which can manifest in three distinct age-dependent clinical phenotypes. In the neonatal age group, it can present as neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD), characterised by prolonged cholestatic jaundice and possible liver dysfunction. In childhood, it can present as failure to thrive and dyslipidemia caused by citrin deficiency (FTTDCD), characterised by poor weight gain. In adulthood, citrin deficiency can present as citrullinemia type 2, characterised by neurologic and psychiatric symptoms.

As a normal newborn metabolic screening result does not exclude the diagnosis of NICCD, it is crucial for healthcare providers to maintain a high level of suspicion for infants presenting with prolonged (i.e. more than 14 days for full term infants and more than 21 days for preterm infants) conjugated jaundice, infantile cholestasis and positive urinary reducing substance (URS) tests. Additionally, a small percentage of infants with NICCD will develop citrullinemia type 2; hence ongoing health surveillance into adulthood is essential.

## WHAT CAUSES CITRIN DEFICIENCY?

Citrin deficiency is associated with mutations in the *SLC25A13* gene. Mutation in *SLC25A13*

affects the function of aspartate/glutamate carrier 2 (AGC2) in the inner mitochondrial membrane. AGC2 transports aspartate into the cytosol, which is then used to generate arginosuccinic acid in the urea cycle. Aspartate in the cytosol also helps with the oxidation of nicotinamide adenine dinucleotide and hydrogen (NADH), and subsequently NADH-reduced equivalents can be transported into the mitochondrial matrix for adenosine triphosphate (ATP) synthesis by the respiratory chain complex.

When AGC2 is not working well, the urea cycle is disrupted. It can also cause NADH to accumulate in the cytosol which may result in energy shortage in the cell, especially in hepatocytes, where AGC2 is highly expressed. NADH build-up also inhibits the metabolism of galactose, a simple sugar, due to impairment of the uridine diphosphate galactose 4'-epimerase enzyme, resulting in elevated levels of galactose in the urine (galactosuria) and blood (galactosemia).

In the western population, classic galactosemia in infants is often associated with reduced levels of gal-1-phosphate-uridylyltransferase (GALT) enzyme activity. However, in East-Asian races, the prevalence of classic galactosemia is very low, whilst galactosemia due to NICCD is more common, as NICCD has a high prevalence in Asia. The carrier frequency for citrin deficiency in China is reported to be one in 65 while the carrier frequency in Singapore is reported to be one in 41.

## SCREENING AND DIAGNOSIS FOR NICCD

In recent years, KK Women's and Children's Hospital (KKH) is seeing an increasing number of paediatric patients presenting with NICCD. Paediatric patients with NICCD usually present with conjugated jaundice beyond two weeks of age, possibly accompanied by pale stool or poor weight gain. NICCD may not be detected by expanded newborn screening tests, which screen for IEM via a few drops of blood taken from the baby's heel at birth, as derangement of the amino acid profile may not have yet taken place.

A simple but effective way to screen for citrin deficiency is to test for URS. Patients with citrin deficiency will test positive due to increased levels of galactose in the blood and the urine. A liver function test will also typically show raised bilirubin levels, consisting mostly of conjugated bilirubin and elevated alkaline phosphatase.

In addition, the patient's plasma amino acid profile will usually indicate elevated levels of citrulline and amino acids such as threonine, methionine and tyrosine. Blood galactose levels will also be high but the activity of the GALT enzyme will be normal.

The diagnosis of NICCD is confirmed by performing sequencing and deletion / duplication analysis of the *SLC25A13* gene.

## MANAGEMENT FOR PATIENTS WITH NICCD

In KKH, paediatric patients with NICCD are managed by a multidisciplinary team of doctors from the Genetics Service and Gastroenterology Service, dietitians and genetics resource nurses. Patients are started on a lactose-free soy milk or special amino acid-based formula, which helps to alleviate the secondary galactosemia.

They are also given medium chain triglyceride (MCT) oil supplements, which have been shown to help energy production in patient cases reported by Japanese researchers. Patients who present with liver failure are given supportive management whilst their liver function improves.

Within a few weeks of treatment, patients demonstrate remarkable improvement in jaundice and liver function. After they are discharged, patients with NICCD continue to receive support from the genetics resource nurses, and are followed up in the citrin deficiency clinic at KKH. Newly established in 2018, the specialised clinic is held once every three months, and enables each patient to meet with the multidisciplinary team during a single clinic session.

Early diagnosis of citrin deficiency is crucial in enabling timely intervention to prevent complications, and help patients to achieve optimal growth and development.

Primary care providers play an important role in the early detection of infants who present with prolonged conjugated jaundice, and referring suspected cases for early tertiary assessment.

All infants with prolonged conjugated jaundice should have total and direct bilirubin tests performed. If the level of conjugated bilirubin is more than 20  $\mu\text{mol/L}$ , the infant should be referred early to the paediatric gastroenterologist or paediatric jaundice clinic for workup.

Other causes of conjugated hyperbilirubinaemia, including anatomical causes such as biliary atresia and choledochal cyst, will need to be ruled out. The paediatric gastroenterologist will also perform infective and metabolic screening tests as clinically indicated.

Citrin deficiency is suspected if the metabolic workup reveals the abnormalities described above and is confirmed by genetic testing.

## RESEARCH FOR THE EARLY DETECTION OF NICCD

Based on the current medical knowledge, it is not possible to predict the likelihood that an infant with NICCD will progress to develop complications later in life. The citrin deficiency team at KKH aims to pursue research into key factors determining the clinical presentation of citrin deficiency in neonates, and the efficacy of early intervention in altering the course of the condition.

Utilising genetic-based screening in Singapore as an adjunct tool in an upcoming research study, the team aims to detect citrin deficiency in newborn babies before the onset of symptoms. This will involve screening the newborns for common mutations in *SLC25A13* found in Singapore, using deoxyribonucleic acid (DNA) extracted from the drops of blood taken at birth for expanded newborn screening tests.

The research findings will be greatly beneficial to deepen the medical understanding of citrin deficiency, and enable the provision of more effective management and treatment for patients with the condition.

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*Dr Christina Ong graduated from the Imperial College School of Medicine, London, and received her post-graduate general paediatric and paediatric gastroenterology training at several major teaching hospitals in London. Dr Ong is currently on the specialist register for paediatric medicine and paediatric gastroenterology in Singapore and the United Kingdom, and has a special interest in inflammatory bowel disease, food allergies, gastrointestinal disorders, feeding difficulties and childhood nutrition.*



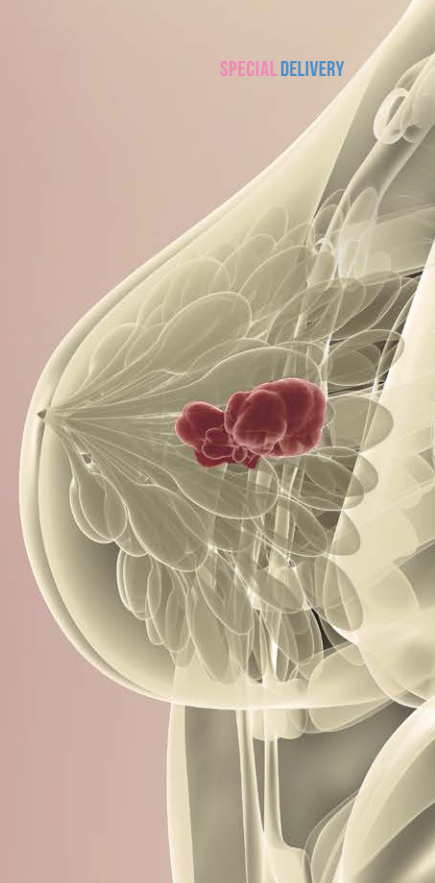
*Dr Ting Teck Wah, Consultant, Genetics Service, KK Women's and Children's Hospital*

*Dr Ting Teck Wah graduated from the National University of Singapore in 2006 and completed his paediatric medicine specialist training in 2014. His research interests are in the area of inborn errors of metabolism and genetics of neurodevelopmental delay. In 2017, Dr Ting completed his fellowship in the metabolic department of The Royal Children's Hospital Melbourne, Australia.*

# Minimal Scar Mastectomy – A Novel Mastectomy Technique

*Minimal scar mastectomy, a novel technique of nipple-sparing mastectomy without reconstruction, is enabling patients with breast cancer to conserve their nipple-areolar complex with minimal post-surgical scarring.*

By Dr Lim Geok Hoon



**B**reast cancer is the top cancer affecting women worldwide, and develops when cells in the breast begin to grow out of control.

In Singapore, it is estimated that one in 14 women develop breast cancer before the age of 75<sup>1</sup>.

Since March 2017, minimal scar mastectomy (MSM), a novel technique of nipple-sparing mastectomy without reconstruction, has been introduced at KK Women’s and Children’s Hospital (KKH) for select patients with breast cancer.

Arising from a combination of nipple-sparing mastectomy and the round block technique (an oncoplastic technique), MSM provides patients an alternative to the long transverse chest scar associated with traditional mastectomy (Figure 1A), with a more cosmetically pleasant concealed scar (Figure 1B).

MSM also enables the preservation of the nipple-areolar complex (Figure 1B) which has been shown to improve the psychological well-being of patients<sup>2</sup>.

## NIPPLE PRESERVATION MASTECTOMY WITHOUT RECONSTRUCTION

Every year, the KK Breast Department manages 300 to 400 women newly diagnosed with breast cancer. Treatment usually takes on a multidisciplinary approach, and can

### COMPARISON OF POST-SURGICAL RESULTS

**TRADITIONAL MASTECTOMY**  
(Image has been blurred)



**Figure 1A.** A long transverse scar associated with traditional mastectomy.

**MINIMAL SCAR MASTECTOMY**  
(Image has been blurred)



**Figure 1B.** A well-concealed scar around a patient’s areola (blue arrow) after undergoing minimal scar mastectomy.

comprise any combination of surgery, chemotherapy, radiotherapy, hormonal therapy and immunotherapy, depending on the extent and characteristics of the cancer. In most cases of treatable breast cancer, surgery of the breast is usually required, and would involve either breast conservation combined with radiotherapy, or a mastectomy with or without reconstruction. Axillary lymph node surgery may also be needed.

Traditionally, to spare the nipple during mastectomy, reconstruction would be mandatory to support the overlying breast skin envelope after the mastectomy was performed. This would involve the use of implants or the patient’s own tissue, usually from the back or abdomen, which can increase the duration and costs associated with the surgery.



During MSM, the skin around the areola is pre-operatively outlined to estimate the amount of breast skin to be removed. Thereafter, this excess breast skin is removed and mastectomy is performed using an incision around the areola, while preserving the nipple-areolar complex. The areolar wound is then closed in the same fashion as the round block technique.

This is possibly the first described surgical technique that is able to preserve the nipple-areolar complex in a mastectomy without the need for reconstruction.

Should the patient choose to go for reconstruction in future, the cosmetic outcome will also be better compared to those who had undergone a traditional mastectomy, since the transverse scar associated with the latter was avoided.

To date, MSM has been performed in four patients since its implementation at KKH, and the results have been encouraging. No complications have been reported post-operatively, and patients have been satisfied with the outcome of the surgery. It was also found that the length of hospitalisation following the surgery and the cost of MSM are comparable to that of a traditional mastectomy without reconstruction.

### A PROMISING TREATMENT OPTION FOR ASIAN WOMEN

The eligibility criteria for MSM includes small breasts, with no evidence of cancer involving the nipple-areolar complex or

a large area of breast skin. They would also need to have opted for mastectomy without reconstruction, and have the desire to conserve their nipple-areolar complex.

Patients who smoke, or have droopy breasts, breast cancer involving or in close proximity to the nipple or skin, connective tissue disease and/or diabetes, are advised against undergoing MSM, as these conditions may compromise the blood supply of the nipple, which may lead to complications following the surgery.

Potential complications associated with MSM include widening of the areola and necrosis (death) of the nipple-areolar complex. These are expected to be minimal and uncommon, and may occur in less than five per cent of patients who undergo MSM.

As MSM is highly similar to nipple-sparing mastectomy, with the only difference being the lack of reconstruction in MSM, the recurrence rate of breast cancer in patients who opt for MSM is similarly expected to be comparable to traditional mastectomy.

### A PERSONAL CHOICE

Although mastectomy with reconstruction will inevitably result in a better cosmesis compared to without reconstruction, the decision to embark on reconstruction remains a very intimate one.

In Singapore, the majority of patients with breast cancer choose to undergo mastectomy without reconstruction.

Up to 74 per cent of patients with breast cancer undergo a mastectomy<sup>3,4</sup>, of which about 75 to 88 per cent of these patients will not opt for a breast reconstruction<sup>4,5</sup>.

Between 2005 and 2017, the mastectomy rate among patients with breast cancer seen and managed by KKH was about 65 per cent, of which more than 70 per cent of these patients did not opt for reconstruction.

Given the high mastectomy rate without reconstruction, as well as a higher prevalence of women with smaller breasts in the Asian population<sup>6</sup>, MSM can certainly add to the surgical armamentarium for this group of breast cancer patients, allowing suitable patients to conserve their nipple-areolar complex with less scarring.

#### REFER A PATIENT

Patients diagnosed with breast cancer who are considering to undergo a minimal scar mastectomy can contact KKH at **+65 6294 4050** for a consultation at the KK Breast Centre.



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*Dr Lim Geok Hoon, Senior Consultant, KK Breast Department, KK Women's and Children's Hospital*

*Dr Lim Geok Hoon believes that a good cosmetic breast result is as paramount as a safe oncological outcome. As a result, Dr Lim pursued a year-long fellowship in the United Kingdom to train in breast cancer genetics and oncoplastic surgery. An adjunct assistant professor with the Duke-NUS Medical School, Dr Lim has published in several publications, which mainly focus on surgical oncoplastic techniques that are most applicable to Asian women. In 2015, Dr Lim also founded the Singapore Breast Oncoplastic Surgery Symposium (SBOSS) to increase regional awareness of oncoplastic breast surgery.*

# Remembering A Beloved Healer, Champion And Educator

*In memory of the late Associate Professor Joseph Manuel Gomez (1952 - 2017)*

**F**or close to three decades, the late A/Prof Joseph Manuel Gomez dedicated his life to providing compassionate care to vulnerable premature and sick infants and their families at KK Women's and Children's Hospital (KKH).

At the time of his passing in 2017, A/Prof Gomez had been serving as Head, Neonatal Intensive Care Unit (NICU); Director, Medical Informatics; and Chairman, Medication Safety Committee at KKH, working tirelessly to improve clinical quality and patient safety.

"Kind, gracious, and an exemplary role model, teacher and mentor to many, A/Prof Gomez made an impact on countless lives through his dedicated, compassionate care for the tiny, fragile premature infants and their families; as well as through his passionate advocacy for patient safety and clinical quality, shares A/Prof Chan Yoke Hwee, Chairman, Division of Medicine, KKH. "He remains close to our hearts and dearly missed."

## COMPASSIONATE HEALER

A familiar and reassuring figure in the NICU, A/Prof Gomez's love and dedication for sick infants was evident in his unwavering commitment to their care. "To A/Prof Gomez, every baby is precious and he would always say that he will go all out to save a baby however he can," recalls Assistant Director Nursing, Ms Annie Goh, who worked alongside A/Prof Gomez in the NICU for over 20 years.

"If a baby became very sick, he would stay by their bedside till they became better.

"If you had been the baby's parents, I think you would have felt assured that your baby was in good hands."

A/Prof Gomez led the expansion of the KKH NICU into the largest state-of-the-art facility of its kind in Southeast Asia in 2013. To introduce life-saving interventions for vulnerable infants with complex conditions, he spearheaded several key initiatives, such as high frequency oscillatory ventilation and inhaled nitric oxide therapy, and the neonatal and paediatric Extracorporeal Membrane Oxygenation (ECMO) programme, which provides critical and life-sustaining heart and lung support for infants with heart failure.

He was also the primary KKH collaborator for the neo.nEURO.network trial on therapeutic whole body cooling for babies with neonatal Hypoxic Ischaemic Encephalopathy, setting the standard of care for babies at KKH who require whole body cooling.

## STALWART SAFETY ADVOCATE

"A/Prof Gomez aspired to deliver the best care to every patient, benchmarked against international standards. Steady and systematic, he was always looking for better ways to improve clinical care outcomes based on accurate data collection and the latest evidence-based guidelines," shares Dr Chua Mei Chien, Head, Department of Neonatology, KKH.

Ms Pang Nguk Lan, Director, Quality, Safety and Risk Management, KKH, agrees.

"When it came to safety, there was no compromise with A/Prof Gomez. He would frequently conduct spontaneous audits of daily processes in the NICU. After which, he would lead the team in brainstorming areas for review and improvement for better staff and patient safety," says Ms Pang. "He never looked to fault-find, but led us in considering how to resolve issues at the core and improve our systems of care."

"Although he was a gentle and humble man, A/Prof Gomez was very strict about upholding hand hygiene practices to ensure a sterile and clean environment for the babies in the NICU," reminisces Ms Goh. "He was very meticulous in hand washing and hand hygiene, and often stood with his arms folded in the NICU to avoid touching the babies and equipment unnecessarily. We liked to tease him about looking like Sir Stamford Raffles' statue, but we understood that he did this to protect the babies."

"Under A/Prof Gomez's guidance, we were able to maintain a zero sepsis rate in very low birth weight infants in the NICU," adds Dr Quek Bin Huey, Head, NICU, KKH.

"A/Prof Gomez always strived towards zero morbidity, and he always led by example."

## CHAMPION FOR CLINICAL QUALITY

Serving as Director, Medical Informatics at KKH (2009-2017), A/Prof Gomez led the implementation of the Closed Loop Medication Management (CLMM) and Inpatient Pharmacy Automation System to revolutionise the hospital's inpatient medication and administration process.

## ABOUT A/PROF JOSEPH MANUEL GOMEZ



### POSITIONS HELD

- **Head and Senior Consultant**  
Neonatal Intensive Care Unit  
Department of Neonatology, KKH  
(2006 – 2017)

- **Director**  
Medical Informatics, KKH  
(2009 – 2017)
- **Chairman**  
Medication Safety Committee, KKH  
(2005 – 2017)  
  
Electronic Medical Records Clinical  
Documentation Committee, KKH  
(2016 – 2017)
- **Deputy Director**  
KKH Extracorporeal Membrane  
Oxygenation (ECMO) Programme, KKH  
(2011 – 2017)
- **Co-Chairman**  
Closed Loop Medication Management  
/ Inpatient Pharmacy Automation  
System/ Knowledge-Based Medication  
Administration Workgroup, KKH  
(2009 – 2017)
- **Co-Chairman**  
Medication Infusion Device Evaluation  
Committee, KKH  
(2016 – 2017)  
  
Clinical Core Design Team for  
Closed Loop Medication  
Management, SingHealth  
(2008 – 2017)  
  
National Medication Safety Taskforce,  
Ministry of Health  
(2010 – 2017)

### NATIONAL AWARDS

- **National Health IT Excellence Award – Champion for Health IT Excellence (2015)**
- **National Outstanding Clinical Quality Champion Award (2017)**

“It was truly enjoyable working alongside A/Prof Gomez on the implementation of the CLMM,” shares Ms Irene Quay, Head, Pharmacy Department. “He united the various healthcare disciplines with the common vision of harnessing automation technology to improve healthcare efficiency, and elevating patient safety with a systems approach.”

As advisor to the Nursing Informatics workgroup, A/Prof Gomez provided guidance on improving communication and clinical workflows across medical specialties. He was instrumental in the implementation of a digitised medical records system at KKH.

“He was a leader who believed and dared to dream for better care, leveraging on information technology,” shares Serene Chin, Deputy Director, Integrated Health Information Systems. “We will continue to live the legacy of the learning and blameless culture that he had advocated.”

### CARING EDUCATOR

Generous with his time and knowledge, A/Prof Gomez was extensively involved in teaching medical students, nurses and advanced specialist trainees in the NICU. “As a mentor, A/Prof Gomez was not only

concerned about imparting medical knowledge to his students, but also teaching them the right values. He was serious with the students, but also soft-spoken and patient, and would go the extra mile to explain in great detail,” shares Ms Goh. “As a result, the medical students were always comfortable with him.”

Dedicated to improving neonatal and perinatal care, A/Prof Gomez also visited many hospitals in Southeast Asia to conduct training in neonatology, medication safety and quality improvement. He was also an active member of the Singapore International Foundation Singapore Volunteer Overseas Programme.

## IN HONOUR OF A/PROF GOMEZ

### J.M. Gomez Faculty And Development Fund In Patient Safety And Clinical Quality

To honour A/Prof Gomez’s life-long commitment to patient safety and clinical quality, and continue his legacy of care for generations to come, the ‘J.M. Gomez Faculty Development Fund in Patient Safety and Clinical Quality’ was established in 2017. Administered by the SingHealth Duke-NUS Paediatrics Academic Clinical Programme, it supports research and education programmes, as well as training opportunities, in the critical areas of patient safety and clinical quality.

“A/Prof Gomez’s sudden passing was a great loss to all of us at KKH, to the medical community, and to patients. His exemplary contribution in healthcare and the way he touched lives will continue to remain in all our hearts,” shares A/Prof Chan. “Through the fund, we hope to develop and support clinical expertise in an area essential for clinical excellence and which A/Prof Gomez had championed all his life.”

For more information about the J.M. Gomez Faculty Development Fund in Patient Safety and Clinical Quality, please contact **Caroline Tham** at [development@kkh.com.sg](mailto:development@kkh.com.sg).

# KKH Clinician Scientists Clinch NMRC Awards

At the recent National Medical Research Council (NMRC) Awards Ceremony and Research Symposium 2018, clinician scientists Dr Mahesh Sangrithi and Dr Yeo Joo Guan from KK Women's and Children's Hospital (KKH) were amongst more than 60 clinician scientists who were recognised for transformative research to bring about impactful health outcomes and advance the delivery of healthcare in Singapore.

"KKH is committed to improving and optimising our patients' health, and we are honoured that the efforts of Dr Sangrithi and Dr Yeo have been recognised by the NMRC," says Associate Professor Sng Ban Leong, Director, KK Research Centre, KKH. "This support further boosts our capabilities to continue to embark on translational research that will benefit our healthcare delivery to women and children."

## PRIMARY INVESTIGATOR

**Dr Yeo Joo Guan**

Consultant, Division of Medicine, KKH

## AWARD

**Transition Award**

National Medical Research Council

## RESEARCH PROJECT

Interrogation of Childhood Onset Systemic Lupus Erythematosus Immunome for the Elucidation of Disease Mechanisms

## COLLABORATOR

**Associate Professor Thaschawee Arkachaisri**

Head and Senior Consultant, Rheumatology and Immunology Service

## MENTOR

**Professor Salvatore Albani**

Senior Consultant and Senior Clinician Scientist, Division of Medicine, KKH



## ELUCIDATING DISEASE MECHANISMS OF CHILDHOOD-ONSET DISEASES

"Research allows us to address unmet medical needs and find solutions to questions that currently do not have answers," says clinician scientist Dr Yeo Joo Guan, who is also a consultant with the Division of Medicine at KKH.

Dr Yeo is pursuing research into childhood-onset systemic lupus erythematosus (SLE), the most severe type of a group of rheumatic disorders common in Singapore – for which he was recognised with a Transition Award at the NMRC Awards Ceremony and Research Symposium 2018.

"The lack of a holistic understanding of the lupus immunome is a critical unmet need," shares Dr Yeo. "The pathogenesis of SLE involves multiple derangements that

*"The mapping of the disease mechanisms will also provide vital information for the development of better therapy against systemic lupus erythematosus, and possibly other autoimmune diseases."*

Dr Yeo Joo Guan  
Consultant  
Division of Medicine, KKH

disturb the fine balance between immunity and regulation. Traditional approaches, which focus on the role of one cell type or molecule at a time, are inadequate for the study of a multi-factorial disease like SLE."

Taking a multi-dimensional approach, Dr Yeo and team interrogate different parts of the lupus immunome simultaneously utilising mass cytometry to characterise a large number of immune markers at the single cell level.

The cell populations responsible for the disease or worsening of the condition (flare) are subsequently identified, prioritised based on their strength of association with disease activity, and characterised to identify target cells of interest for further interrogation to elucidate the pathogenic pathway.

"This approach has the immediate translational potential of identifying cell populations useful for the prediction of disease outcome. The mapping of the disease mechanisms will also provide vital information for the development of better therapy against SLE, and possibly other autoimmune diseases," says Dr Yeo.

"I am fortunate to be able to draw on the experience and expertise of my collaborator, and mentor, in the areas of research, rheumatology and immunology.

"In the longer term, we hope to better understand the aspect of immunocompetence during the development of the paediatric immune system, and transform the way diagnosis and therapy for paediatric rheumatological diseases is practised."

## INVESTIGATING THE BIOLOGY OF SEX CHROMOSOME DISORDERS AND INFERTILITY

For Dr Mahesh Sangrithi, winner of a Clinician Scientist Award (Investigator Category) at the recent NMRC Awards Ceremony and Research Symposium 2018, "The best moments are when you make significant and novel conclusions from experiments that can have an impact on the understanding of human illness."

The consultant with the Department of Reproductive Medicine at KKH was recognised for his research into sex chromosome aneuploidy-associated infertility to better understand the mechanisms underlying the influence of the X chromosome on gene expression and methylation in germ cells.

"Germ cells develop differently in males and females and give rise to sperm and eggs respectively. Our research has shown that the sex chromosome complement of germ cells can influence their identity; germ cells with sex chromosome aneuploidy display imbalanced X chromosome dosages, and a mismatch in X chromosome number and phenotypic sex can also distort the 'identity' of these germ cells," explains Dr Sangrithi.

This phenomenon can be seen in common chromosomal abnormality disorders such as Turner's syndrome (females with one X chromosome) – and Klinefelter syndrome (males with XX chromosomes); these syndromes are also associated with infertility.

"Our findings revealed more information about the stages of female and male germ cell development, and suggest that the mismatch between the number of X chromosome and gonadal sex may be causal in germ cell loss in sex chromosome infertility," shares Dr Sangrithi.

Working towards an in-depth analysis of germ cell identity, Dr Sangrithi's team has established the first research wet lab for obstetrics and gynaecology in SingHealth.

"This Reproductive Biology and Stem Cells laboratory, housed at the Academia, will enable the team to harness a combination of approaches, such as mouse models and RNA-, bisulphite- and ChIP-sequencing, to generate high-resolution expression and epigenetic maps of germ cells," says Dr Sangrithi.

"It is a real pleasure and honour to be working alongside distinguished researchers from KKH, Genome Institute of Singapore and Francis Crick Institute,

in pursuit of the answers to fundamental questions regarding how the human body works.

"The more we are able to uncover about the biology underlying germ cell identity, the better we will be able to inform and manage patients with sex chromosome aneuploidy syndromes, and infertility in general."

*"Our findings revealed more information about the stages of female and male germ cell development, and suggest that the mismatch between the number of X chromosome and gonadal sex may be causal in germ cell loss in sex chromosome infertility."*

Dr Mahesh Sangrithi  
Consultant  
Department of Reproductive Medicine, KKH

### PRIMARY INVESTIGATOR

#### Dr Mahesh Sangrithi

Consultant, Department of Reproductive Medicine, KKH

### AWARD

#### Clinician Scientist Award (Investigator Category)

National Medical Research Council

### RESEARCH PROJECT

Sex Chromosome Aneuploidy associated infertility: A paradigm for investigating the determinants of germ cell 'identity'

### CO-INVESTIGATORS

#### Dr James Turner

Senior Group Leader, Francis Crick Institute, United Kingdom

#### Professor Ng Huck Hui

Executive Director, Genome Institute, Singapore

### COLLABORATORS

#### Associate Professor Bernard Chern

Chairman, Division of Obstetrics and Gynaecology, KKH

#### Associate Professor Jerry Chan

Senior Consultant, Department of Reproductive Medicine, KKH



# Collaborating to Deliver Integrated Care for Children

*KKH and AMKFSC lead Singapore's first integrated child health and social congress*



Prof Alex Sia, CEO, KKH and Dr Ang Seng Bin, Chairman, AMKFSC, present a token of appreciation to guest-of-honour, Mr Sam Tan (right), Minister of State, Ministry of Foreign Affairs and Ministry of Social and Family Development.

In June 2018, KK Women's and Children's Hospital (KKH) and AMKFSC Community Services Ltd (AMKFSC), with support from Temasek Foundation Cares (TFC) and Early Childhood Development Agency (ECDA), organised Singapore's first Integrated Child Health and Social Congress to enhance awareness of the early formative years of a child's life, and the importance of cross-sector coordination of services and collaboration in the delivery of services to support children from vulnerable families.

Themed *Building the Child beyond Neurons for a Resilient Nation*, the two-day congress was graced by Mr Sam Tan, Minister of State, Ministry of Foreign Affairs and Ministry of Social and Family Development, and brought together more than 200 professionals from the health, social and early childhood sectors to discuss the importance of the first thousand days of life and mitigating the impact of adverse childhood experiences to influence positive outcomes.

"This congress is a significant milestone in our efforts to reach out to professionals serving the health, social and early childhood sectors. Each of these sectors are equally important and instrumental in providing a holistic, integrated and coordinated approach to support children from vulnerable families in enhancing the chances of better outcomes," shares Associate Professor Winnie Goh, Senior Consultant, Division of Medicine, KKH.

## **EARLY OUTCOMES FROM THE KIDS 0-3 PROGRAMME ANNOUNCED**

A highlight of the congress was the early outcomes of the KKH-led Temasek Foundation Cares Kids Integrated Development Service 0-3 (KIDS 0-3) programme, shared by A/Prof Goh, who also leads the programme.

Led by KKH, in partnership with AMKFSC, and funded by TFC, the programme was piloted in July 2014 to optimise the developmental potential of young children from vulnerable families through a multi-layered and integrated community health and social care support system. It includes home visitations and centre-based activities coordinated by a cross-sector, multidisciplinary team. The programme has, to date, supported 150 pairs of mother and child.

From July 2016, the KIDS 0-3 programme has also received funding support from ECDA under the KidSTART pilot, so that more children are able to benefit from the home visitation programme. "These encouraging results are a nod to the community capabilities that we have built to support vulnerable families and bring about better outcomes for their children," says A/Prof Goh. "Moving forward, we will



A/Prof Winnie Goh, Programme Lead, KIDS 0-3 programme and Senior Consultant, Division of Medicine, KKH, shares about the KIDS 0-3 programme.

continue to recruit more mothers and families into the programme, and consolidate the services and support provided to these vulnerable families.”

“We will also ensure that as the child reaches the age of three, an individualised transition plan is in place to connect families in the programme to other existing services in the community. This will enable integration of the children into preschools and kindergartens.”

**SIGNIFICANT OUTCOMES FROM THE KIDS 0-3 PROGRAMME**

**CHILD HEALTH**

There were significant improvements in the immunisation rate of children in the programme. Additionally, birth weights of children born to mothers enrolled in the programme antenatally were better than those recruited postnatally.

**CHILD DEVELOPMENT**

97 per cent of children in the programme were assessed to have normal cognitive ability. This is significantly higher compared to other study findings among children from families with challenging socio-economic backgrounds.

**CHILD BEHAVIOUR**

A smaller number of children in the programme were found to have emotional and behavioural problems compared to other studies in Singapore using the same measurement tool.

**FAMILY FUNCTION**

Parents have shown an increased ability to help their children learn, and to find the right resources when they need help.

**PARENT-CHILD INTERACTION/BONDING**

About 96 per cent of parents in the programme were able to demonstrate appropriate parent-child interactions in the affection and responsiveness domains. This is important as appropriate parent-child interactions correlated with better learning outcomes in the children.

**INAUGURAL PAEDIATRIC RESPIRATORY AND SLEEP MEDICINE SYMPOSIUM**

Join us at the Inaugural Paediatric Respiratory and Sleep Medicine Symposium to gain insights on the management of a wide range of respiratory and sleep conditions in children.

The three-day symposium will include a paediatric sleep medicine workshop on the first day, and a series of plenary lectures by a panel of internationally and locally-renowned speakers over the next two days will cover a comprehensive range of paediatric respiratory problems, with a focus on up-to-date, evidence-based management guidelines.

Hands-on sessions on polysomnography, pulmonary function tests and home ventilation for technology-dependent children will also be available.

**Who should attend:** Paediatricians, paediatric pulmonologists, residents, respiratory specialist nurses, and allied health professionals (respiratory/sleep technologists, respiratory physiotherapists, and more).

**Date:** 8 to 10 March 2019 (Friday to Sunday)

**Time:** 8.00am to 5.30pm

**Venue:** KKH Auditorium (Training Centre), Level 1, Women’s Tower

\* CME points will be awarded.



# CELEBRATING 160 YEARS OF TRANSFORMING CARE for Women and Children

Since 1858, KK Women's and Children's Hospital has embarked on an ongoing journey to transform care and advance medical innovation, research and education, evolving from humble beginnings as a general hospital to become Singapore's tertiary referral centre for women and children today.

In 2018, as KKH commemorates 160 years of heritage in serving the community and caring for women's and children's health, we remain committed on our mission to deliver excellent, holistic and compassionate care for generations of women and children to come.

► Read Issue 1, 2018 to see *Our First 100 Years (1858 - 1957)*

## RAISING THE BAR (1958 - 1977)

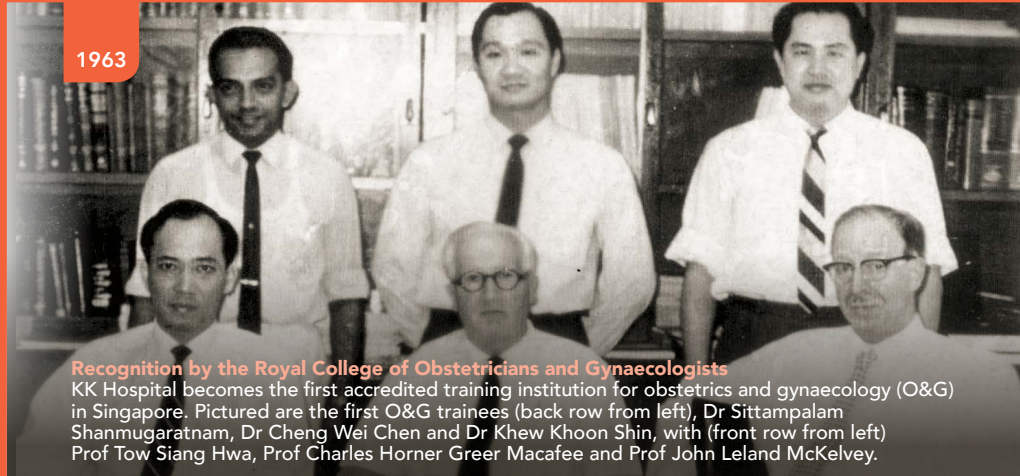
1958



### Improving care for infants

Incubators are introduced at Kandang Kerbau Hospital (KK Hospital) in 1958, in a special nursery for babies born prematurely. The introduction of such technology helps to improve the survival rate for newborns and sick babies.

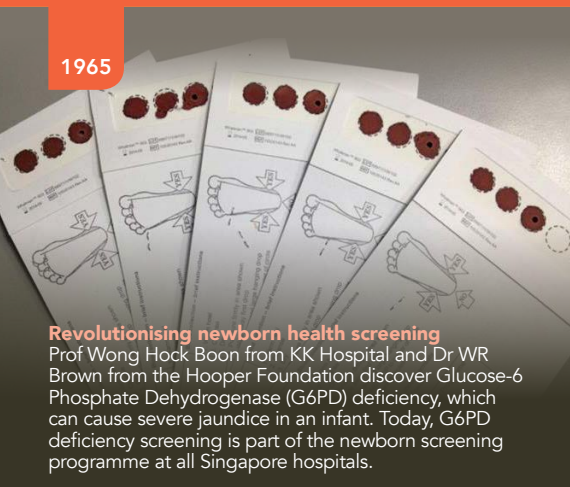
1963



### Recognition by the Royal College of Obstetricians and Gynaecologists

KK Hospital becomes the first accredited training institution for obstetrics and gynaecology (O&G) in Singapore. Pictured are the first O&G trainees (back row from left), Dr Sittampalam Shanmugaratnam, Dr Cheng Wei Chen and Dr Khew Khoon Shin, with (front row from left) Prof Tow Siang Hwa, Prof Charles Horner Greer Macafee and Prof John Leland McKelvey.

1965



### Revolutionising newborn health screening

Prof Wong Hock Boon from KK Hospital and Dr WR Brown from the Hooper Foundation discover Glucose-6 Phosphate Dehydrogenase (G6PD) deficiency, which can cause severe jaundice in an infant. Today, G6PD deficiency screening is part of the newborn screening programme at all Singapore hospitals.

1966 to 1976



### The largest maternity hospital in the world

KK Hospital sets the world record in 1966 for being the world's largest maternity hospital with a record birth of 39,835 babies born that year – a record it subsequently holds for ten years.

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

KK Women's and Children's Hospital (KKH) is Singapore's largest tertiary referral centre for Obstetrics, Gynaecology, Paediatrics and Neonatology. Founded in 1858, the 160-year-old academic medical institution specialises in the 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 830-bed 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.