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Children's Hospital
SingHealth

IN THIS ISSUE

COLLABORATING TO CONQUER

*Plastic surgery, Neurosurgery and
ENT specialists join together to
rescue a baby with a life-threatening
cranial condition.*

SPECIAL DELIVERY

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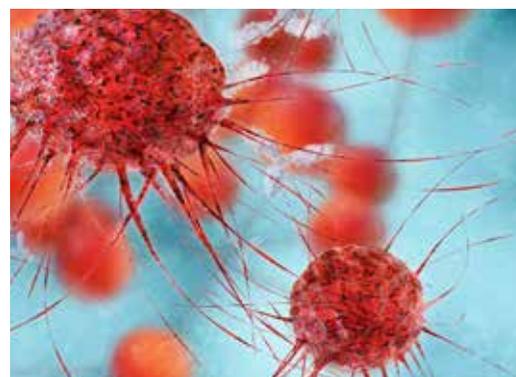
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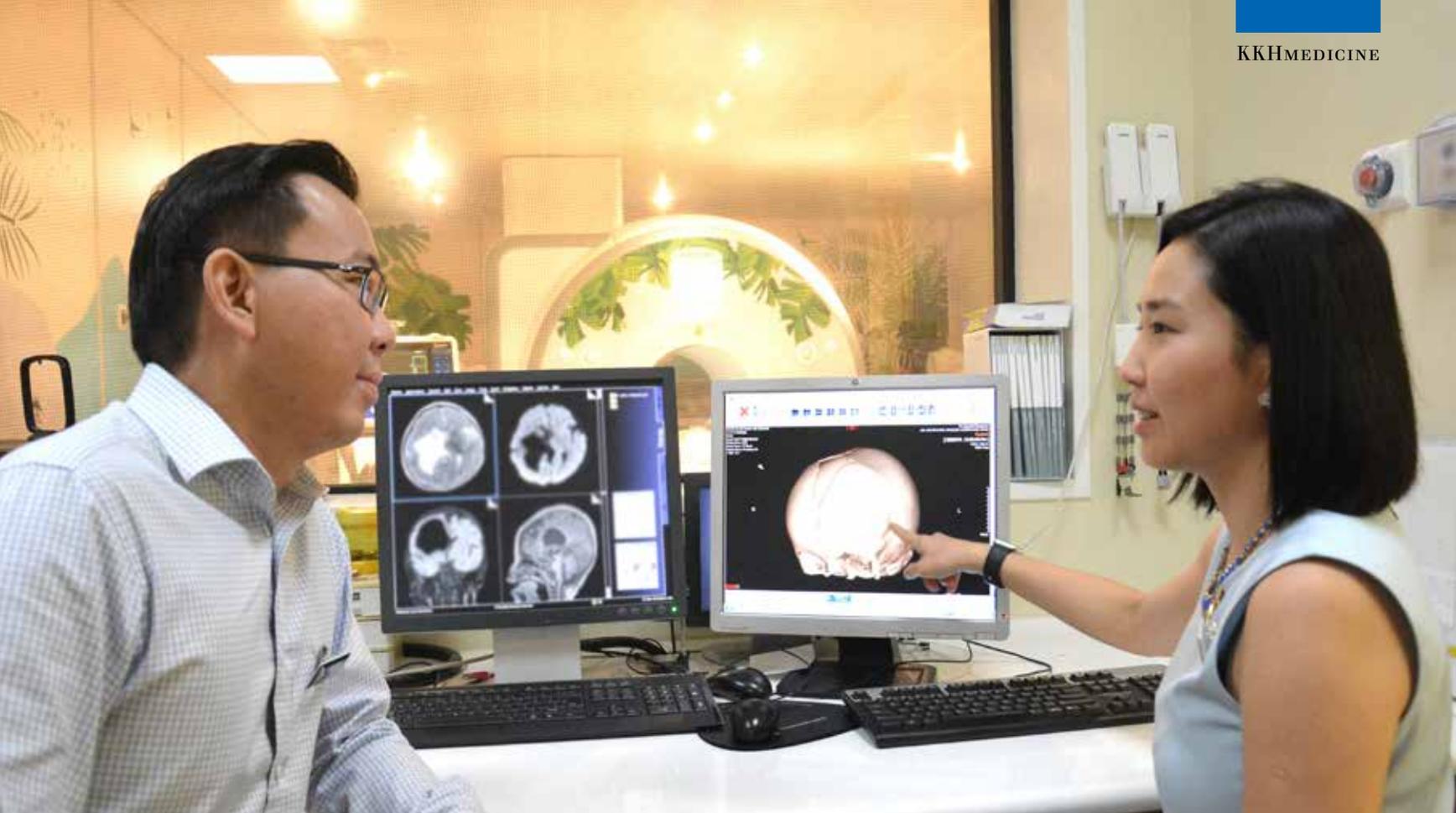
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Special Acknowledgements

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Dr David Low and Dr Gale Lim examine diagnostic images of an infant skull revealing craniosynostosis.

Collaborating To Conquer

Plastic surgery, Neurosurgery and ENT specialists join together to rescue a baby with a life-threatening cranial condition.

By Rebecca Tse

“With craniosynostosis, the sutures between the bony plates in the baby’s skull fuse too early, preventing the skull from growing normally. This compromises the cranial vault volume, severely impedes growth, and may lead to increased intracranial pressure.”

Dr David Low,
Head and Consultant, Neurosurgical Service, KKH

In September 2015, a multidisciplinary surgical team at KK Women’s and Children’s Hospital (KKH) carried out what is believed to be the first posterior cranial vault distraction in Singapore to rescue a 15-month-old toddler with multi-sutural craniosynostosis.

Born at 38 weeks gestation via lower segment caesarean section, Patient X was diagnosed at two months with Type I Pfeiffer Syndrome – a genetic disorder characterised by the premature fusion of certain skull bones (craniosynostosis).

“With craniosynostosis, the sutures between the bony plates in the baby’s skull fuse too early, preventing the skull from growing normally. This compromises the cranial vault volume, severely impedes growth, and may lead to increased intracranial pressure,” says Dr David Low, Head and Consultant, Neurosurgical Service, KKH, who was Patient X’s neurosurgeon.

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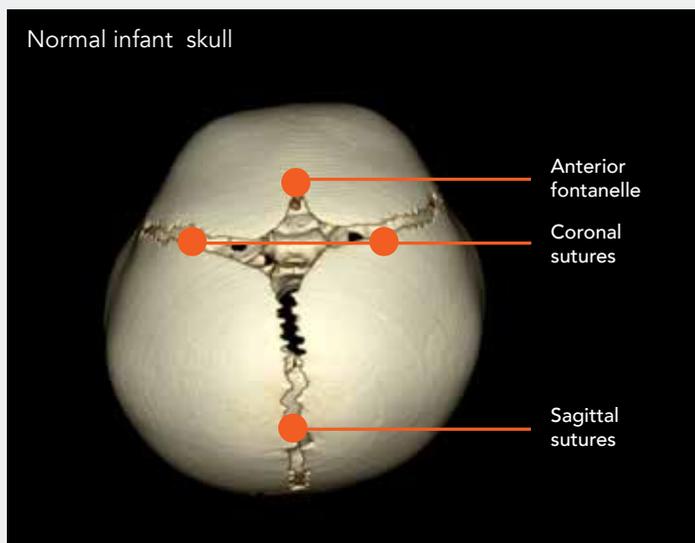
BACKGROUND

Patient X was initially asymptomatic. Her developmental milestones were normal and she had no drug allergies; her immunisation schedule was also up to date. However, at about 12 months, Patient X was found to have papilloedema. Computed tomography and magnetic resonance imaging scans of her brain confirmed the following diagnosis:

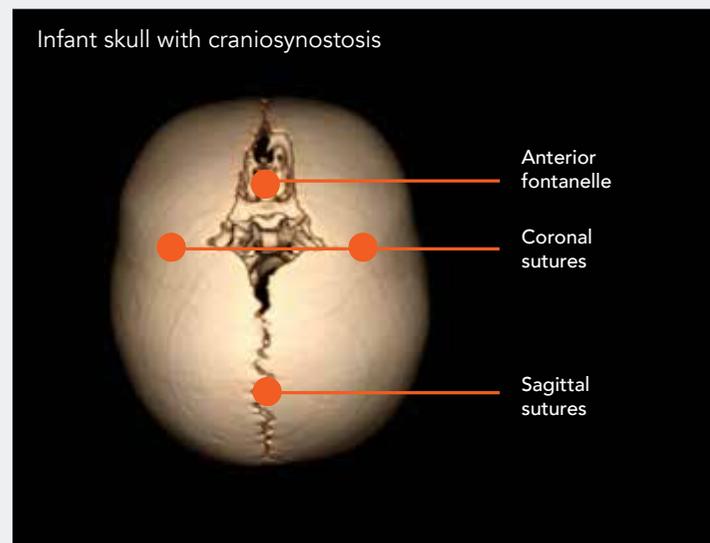
- Craniosynostosis with premature complete fusion of the coronal and right lambdoid sutures, and partial fusion of the left lambdoid suture.
- Small-sized posterior fossa with herniation of the cerebellar tonsils
- Syringohydromelia and dilation of the lateral and third ventricles
- Partial fusion of C4 to C7 vertebrae with rudimentary intervertebral discs
- Minimal hydrocephalus

These resulted in raised intra-cranial pressure, further complicated by severe proptosis and optic nerve compression, and concomitant Chiari malformation. Sleep studies also confirmed a diagnosis of moderate obstructive sleep apnoea.

“Due to abnormal oro-facial structures, which effectively reduce the volume of the ear, nose and throat canal, children with syndromic craniosynostosis are at high risk of respiratory difficulty. Otitis media with effusion is also common, leading to conductive hearing loss,” says Dr Alex Tham, then-Resident, Department of Otolaryngology, KKH, who attended to Patient X under the purview of Dr Annette Ang, Senior Consultant, Department of Otolaryngology, KKH.



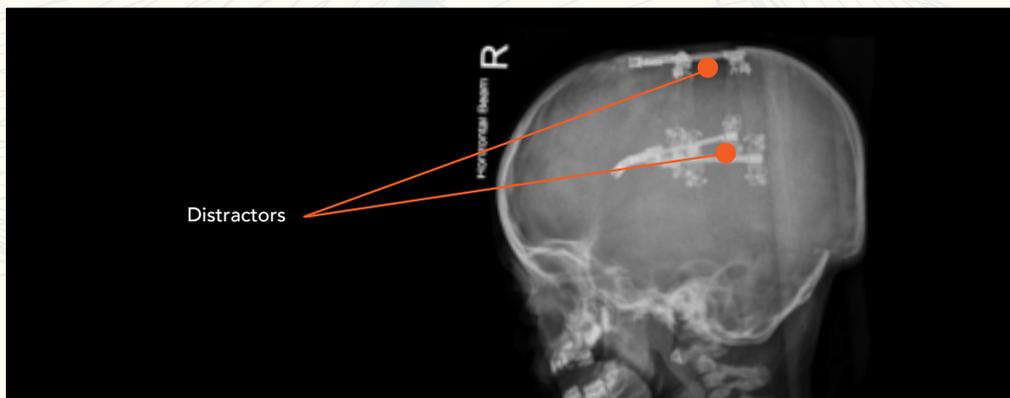
Sutures and fontanelles in the normal infant skull.



Prematurely fused coronal sutures in the skull of an infant with bi-coronal craniosynostosis.



The worldwide incidence of craniosynostosis is 1 in 2,500 and can be classified broadly into syndromic and non-syndromic cases. Since 2005, KKH has managed more than 60 cases of craniosynostosis, of which one third are syndromic.



Metal distractors placed along an infant's skull are used to gradually stretch the soft tissue and bone, allowing for expansion of the infant's intracranial space.

RECOMMENDATION

Patient X's multidisciplinary care team, which comprised neurosurgical, reconstructive and otolaryngology specialists, put forward a joint decision for a posterior cranial vault distraction. This surgical procedure would cut and expand the back of the patient's skull, gradually stretching the bone and skin to enlarge the intracranial space and create new bone.

Expert guidance was provided by Dr Por Yong Chen and Dr Vincent Yeow, both Senior Consultants with the Department of Plastic, Reconstructive & Aesthetic Surgery, KKH. Dr Por is also Head of the department, and Director of the KKH Cleft and Craniofacial Centre.

“Without early intervention, Patient X's prematurely fused skull would have been too small to safely accommodate the child's growth. This would eventually have led to irreversible brain and optic damage.”

Dr Gale Lim
Consultant, Department of Plastic,
Reconstructive & Aesthetic Surgery, KKH

PROCEDURE

At 15 months, Patient X underwent a posterior cranial vault distraction, with the following operative findings:

- Complete fusion of the coronal and right lambdoid sutures, and partial fusion of the left lambdoid suture
- Large emissary veins at the suboccipital region
- Right otitis media with effusion
- Hypertrophy of bilateral inferior turbinates

The following procedures were carried out:

- Large occipital-parietal craniotomy to provide relief to the tight posterior cranial vault
- Barrel stave osteotomies to the occipital bone inferiorly to aid remodelling
- Three posterior cranial vault distractors were anchored to the bone on either side of osteotomies
- Examination of both ears with right myringotomy and grommet tube insertion
- Distraction was commenced two days after surgery, and completed three months later without complication



A posterior cranial vault distraction provides the greatest intra-cranial volume expansion in comparison to other procedures (e.g. frontal-orbital advancement, total cranial vault remodelling). A distraction also results in sustained traction and less relapse from soft tissue recoil.

This mode of intervention carries lower risks of complication and/or relapse, which are significant considerations when treating syndromic craniosynostosis.

OUTCOME

Post-operatively, Patient X recovered uneventfully with marked improvement of her head shape and optic disc swelling, and resolution of frontal bossing. “Without early intervention, Patient X's prematurely fused skull would have been too small to safely accommodate the child's growth. This would eventually have led to irreversible brain and optic damage,” says Patient X's reconstructive surgeon Dr Gale Lim, Consultant, Department of Plastic, Reconstructive & Aesthetic Surgery, KKH.

“However, through early surgical planning and teamwork from various medical specialties, these were prevented. Patient X now has the chance to grow and develop normally like any child.”

The worldwide incidence of craniosynostosis is one in 2,500 and can be classified broadly into syndromic and non-syndromic cases. Since 2005, KKH has managed more than 60 cases of craniosynostosis, of which one third are syndromic.

UNCOVERING

The Secrets Of Growing Up Healthy

A Singapore study of pregnant women has found links between low levels of maternal vitamin D, higher fasting glucose concentrations and a higher likelihood of caesarean section delivery.

By Dr See Ling Loy



A research coordinator from the GUSTO study collects an oral sample from a child.

Vitamin D deficiency is common among pregnant women worldwide, and has been found to be associated with an increased risk of pre-eclampsia, gestational diabetes mellitus, preterm birth, and other tissue-specific conditions. Generally, mothers are prescribed with multivitamins containing vitamin D ranging from 200IU to 400IU during pregnancy. However, the status of maternal vitamin D in Singaporean women has not been intensively studied until recently.

Using data from GUSTO* (Growing Up in Singapore Towards healthy Outcomes), a national birth cohort study, we examined the maternal plasma vitamin D status of 940 mothers of Chinese, Indian and Malay ethnicity late in their second trimester of pregnancy (26-28 weeks' gestation) – looking for associations of their vitamin D status with glucose tolerance, risks of gestational diabetes and caesarean delivery. Plasma 25-hydroxyvitamin D (25OHD), the major circulating form of vitamin D, was used as the determinant of vitamin D status in our study.

VITAMIN D SENSITIVITY DIFFERS AMONG ETHNIC GROUPS

Studying the vitamin D status of this multi-ethnic cohort of 940 women, we discovered that:

4 in 10

pregnant women had inadequate plasma levels of vitamin D in the second trimester, with substantially higher rates found in Malay and Indian women compared to Chinese women.

By ethnicity,

the association between inadequate vitamin D status and higher glucose concentrations was found to be significant only in Malay women, while the odds of having emergency caesarean section were approximately two times greater in Chinese and Indian women with vitamin D inadequacy.

Overall,

maternal vitamin D inadequacy was associated with higher fasting glucose concentrations, and a trend towards higher likelihood of emergency caesarean delivery.

* GUSTO (Growing Up in Singapore Towards healthy Outcomes) is a large-scale long-term study of 1,176 Singaporean mothers who completed their entire pregnancy in 2009 and 2011. By studying maternal-fetal health from birth until nine years of age, the study aims to better understand the impact of genetic and environmental factors on neurodevelopment and metabolic disease, with the goal of finding ways of preventing the onset of diseases in later years.

IMPACTS ON PREGNANCY OUTCOMES

The association of vitamin D inadequacy and higher maternal fasting glucose could impose a negative impact on child health. Higher maternal fasting sugar, even without gestational diabetes, has been shown to be a strong predictor of fetal C-peptide level and body fat, which are linked with impaired metabolic outcomes in children.

These findings suggest varying threshold effects of vitamin sensitivity on pregnancy outcomes among ethnic groups. However, the reasons behind ethnicity variations in the responses to vitamin D levels remain unclear. Further investigations on biological components, social, nutritional practices and cultural differences are required to explain the mechanism of ethnicity disparity in vitamin D effects.

Nevertheless, the present findings are important to provide evidence for clinical recommendations regarding potential screening of vitamin inadequacy during prenatal care and the need for vitamin D supplementation in at risk groups. More studies are needed to confirm the recommendation of vitamin D supplement intake, period of starting and dosage.

Breaking new ground in maternal-fetal health research, Singapore's largest pre-pregnancy study is also currently underway.

The Singapore PREconception Study of long-Term maternal and child Outcomes (S-PRESTO) study is examining the effects of nutrition, lifestyle, mental health and other environmental factors in Singaporean mothers-to-be on the eventual health and socio-emotional outcomes of mother and child.

Medical and lifestyle data is obtained from participating couples through questionnaires and bio-sampling, from preconception, through pregnancy and up until the child is two years old. Data of the child's lifestyle, feeding patterns, body composition and core neurodevelopment is also measured.



Members of the S-PRESTO research team

PREVENTING DISEASES AND DISORDERS IN CHILDREN

S-PRESTO aims to identify the critical windows during early human development and related mechanisms that link maternal and perinatal health and nutrition with child development. In the longer term, this data will be invaluable to develop more effective approaches to intervene and prevent metabolic diseases and neurodevelopmental disorders.

One year since its launch in February 2015, S-PRESTO has garnered more than 316 women participants at preconception stage, of which 36 women are currently pregnant and four have safely delivered.

The GUSTO, maternal vitamin D and S-PRESTO studies are the collaborative efforts of KK Women's and Children's Hospital, Singapore Institute for Clinical Science (SICS) of the Agency for Science, Technology and Research (A*STAR), the National University of Singapore (NUS) and the National University Health System (NUHS).

The studies are supported by the National Research Foundation Singapore under its Translational and Clinical Research Flagship Programme and administered by the Singapore Ministry of Health's National Medical Research Council.

JOIN SINGAPORE'S LARGEST PRE-PREGNANCY STUDY

S-PRESTO is seeking couple participants who meet the following criteria:

- Women aged between 18 to 45 years old
- Currently residing in Singapore and intending to reside in Singapore for the next five years
- Planning for pregnancy
- Of Chinese, Indian or Malay ethnicity
- Intending to receive antenatal care and deliver at KKH



If you are interested in joining S-PRESTO, please visit www.s-presto.sg or call 1800-SPRESTO (1800-777 3786).

References:

1. Loy SL, Lek N, Yap F, Soh SE, Padmapriya N, et al. Association of Maternal Vitamin D Status with Glucose Tolerance and Caesarean Section in a Multi-Ethnic Asian Cohort: The Growing Up in Singapore Towards Healthy Outcomes Study. *PLoS ONE* 2015; 10(11): e0142239. doi: 10.1371/journal.pone.0142239



Dr Loy See Ling, Research Fellow, KK Research Centre, KKH

Dr Loy See Ling completed her Bachelor of Science (Dietetics) and Doctor of Philosophy (Human nutrition) in Malaysia. She has a special interest in early nutrition and its effects on later health, in particular obesity and diabetes. Dr Loy is currently investigating preconception and pregnancy prospective cohort studies in Singapore – namely the 'Growing Up in Singapore Towards healthy Outcomes' (GUSTO) study and 'Singapore PREconception Study of long-Term maternal and child Outcomes' (S- PRESTO) study.

Curing Childhood Cancer:

Are We There Yet?

by Dr Prasad Iyer

Cancer is life-threatening and so is its treatment. Despite this, survival outcomes for children with cancer are one of the biggest success stories in modern medicine.

The worldwide incidence of childhood cancer currently hovers at approximately 15 to 20 new cases per 100,000 children per year. In Europe and most parts of the world, the incidence of childhood cancers has risen by between 0.5 and 1.1 percent per year over the last two decades. Fortunately, this trend has not been seen in Singapore.

Encouragingly, the five-year rate of survival for all children with cancer has also increased, and currently stands at 75 to 80 percent. This reflects an overall improvement in survival rates for all types of childhood cancers, due in large part to better use of existing drugs in tailoring treatment, better supportive care and improved understanding of the disease.

Overall, leukaemias constitute the largest group amongst children with cancer. Dramatic improvement is particularly notable in acute lymphoblastic leukaemia (ALL), which is the most common paediatric malignancy.

In the mid-1970s, the five-year survival rate of children with ALL was 10 percent; this has risen to almost 90 percent currently. Therefore, modern clinical trials on ALL now focus on decreasing treatment intensity – thereby reducing toxicity whilst maintaining or improving cure rates.

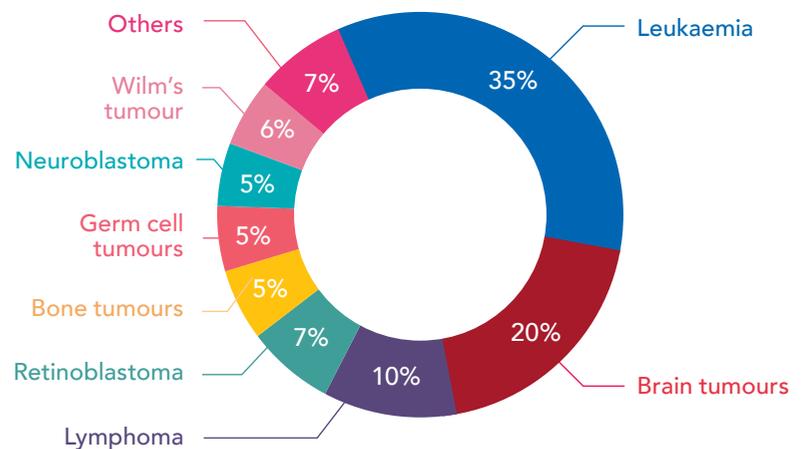
In contrast, survival outcomes for childhood sarcomas have plateaued in the last few decades. Despite advances in modern medicine, the median survival for children who are

diagnosed with diffuse intrinsic pontine glioma (DIPG), a type of brain tumour, remains less than one year from diagnosis.

One of the key challenges facing today's multidisciplinary paediatric oncology team is striking a balance between

treatment-related toxicity and achieving better cure rates. Survivors of paediatric cancer also require medical help to battle long-term toxicities such as cardiomyopathy, endocrinopathies, fertility problems and secondary malignancy.

Main types of cancer in Singaporean children



TREATING CHILDHOOD CANCER AT KKH

KK Women's and Children's Hospital (KKH) manages up to 70 percent of all children with cancers in Singapore – children with leukaemias, lymphomas and brain tumours being the most common. The care provided to these patients includes state-of-the-art assessment, current chemotherapy protocols and surgical techniques as well as comprehensive supportive care.

Management requires coordinated efforts from a wide range of healthcare professionals, including clinicians, surgeons, nurses, pathologists, radiologists, physiotherapists, occupational therapists, dietitians, pharmacists, speech/language therapists, psychologists, medical social workers and other subspecialists.

Haploidentical bone marrow transplantation is carried out at KKH for children and teenagers.

A fifteen-year-old boy was diagnosed with an extremely rare but aggressive form of acute leukaemia. Treatment was challenging, as the cancer did not respond to strong first-line chemotherapy, and the patient developed serious complications. After second-line chemotherapy, the patient underwent a haploidentical bone marrow transplant using stem cells from his mother. He is now cured of his disease and leads a normal life.

This form of treatment allows patients to accept donor stem cells which only half match their human leukocyte antigen (HLA) tissue type, such as stem cells from a parent or child.

This technique, in our experience, causes fewer side effects – resulting in a shorter hospital stay as compared to the traditional methods of bone marrow transplantation. Haploidentical bone marrow transplantation is useful to treat relapsed and high-risk malignancies as well as benign haematological, myeloproliferative conditions and immunodeficiency syndromes where time is of essence or there is non-availability of a matched donor in the stem cell registry.

To further advance the care of children and adolescents with brain and solid tumours, KKH formed a partnership with Viva Foundation for children with Cancer and St. Jude Children's Research Hospital, USA, in 2015. The VIVA-KKH Paediatric Brain and Solid Tumour Programme aims to improve clinical care and advance bench-to-bedside translational clinical research by establishing a molecular pathology programme.

GENOMICS: THE FUTURE OF CANCER

The landscape of cancer treatment will continue to evolve as we better understand cancer cells through genomics.

Already, technological advances – such as next-generation genetic sequencing methods – have identified numerous cancer-specific genetic changes in several paediatric and adolescent cancers that can be exploited as targets for novel therapies.

Precision medicine, which tailors therapy to the individual according to mutations detected within their cancer cells, is also being piloted in trials that will mature over time and add to the tools on hand.

Monoclonal antibody therapy for neuroblastoma and ALL are examples of modern immune-based therapies that are becoming increasingly available as additions to, and in some cases, alternatives to the traditional treatment modalities such as chemotherapy, surgery and radiotherapy. While in many cases, these therapies have shown dramatic responses in the

setting of refractory or relapsed cancer; much remains to be learned about how to integrate these therapies into existing upfront treatment regimens.

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- 1) Saletta F, Wadham C, Ziegler DS, et al (2014). *Molecular profiling of childhood cancer: Biomarkers and novel therapies.* *BBA Clinical*, 1, 59-77.
- 2) Bhattacharyya R, Tan AM, Chan MY, Jamuar SS, Foo R and Iyer P (2016). *TCR $\alpha\beta$ and CD19-depleted haploidentical stem cell transplant with reduced intensity conditioning for Hoyeraal-Hreidarsson syndrome with RTEL1 mutation.* *Bone Marrow Transplant*, 2016 doi: 10.1038/bmt.2015.352.

REFER A PATIENT FOR ASSESSMENT

Doctors can refer patients to the paediatric Haematology/Oncology Service at KKH for assessment, by contacting the hospital at +65 6294 4050.

! WARNING SIGNS OF CHILDHOOD CANCER

1. Pallor, bruising or bleeding, general bone pain
2. Lumps or swelling – especially if painless and without fever or other signs of infection
3. Unexplained weight loss or fever, persistent cough or shortness of breath, sweating at night
4. Eye changes – white pupil, new-onset squint, visual loss, bruising or swelling around the eye(s)
5. Abdominal swelling
6. Headaches, especially if unusually persistent or severe, vomiting (especially early morning or worsening over days)
7. Limb or bone pain, swelling without trauma or signs of infection

Prompt recognition of warning signs and early referral to a cancer centre are paramount in obtaining good outcomes as late diagnosis often causes significant increase in morbidity and mortality.



Dr Prasad Iyer, Consultant, Haematology/Oncology Service, Department of Paediatric Subspecialties, KKH

A paediatric and adolescent oncologist, Dr Prasad Iyer has had the great privilege of honing his clinical skills in three countries. He trained in the United Kingdom for 12 years and was conferred the Fellowship of the Royal College of Paediatrics and Child Health (FRCPC). He also trained in paediatric oncology in Newcastle for a further four years. Dr Iyer has special interests in leukaemia, lymphoma, solid tumours and bone marrow transplantation. In addition to clinical work, Dr Iyer also enjoys teaching the next generation of medical students and junior doctors.

Postmenopausal Bleeding – A Sign Not To Be Ignored

By Dr Sonali P Chonkar and Dr Rajeswari Kathirvel

With the average life expectancy of a Singaporean woman increased to about 84.9 years¹, nearly one third of a woman’s life is spent in the postmenopausal phase.

Menopause is said to have occurred when a woman has not had any periods for one year, and can usually be expected within the age range of 42 to 58 years. Women entering menopause should be counselled to remain alert for postmenopausal bleeding (PMB) – which is any vaginal bleeding that occurs one year after a woman’s final period.

A FIRST SIGN OF ENDOMETRIAL CANCER

While there is no sinister cause for PMB in the vast majority of patients, the symptom can be the first sign of cancer in about 10 percent of women. Table 1 shows some of the common causes of PMB.

Table 1:
Causes of Postmenopausal Bleeding²

Atrophic endometritis and vaginitis	60 – 80%
Exogenous oestrogens	15 – 25%
Endometrial hyperplasia	5 - 10%
Endometrial carcinoma	10%
Endometrial/cervical polyps	2 – 12%

It is noteworthy that 90 percent of women with endometrial cancer present with PMB indicating abnormal uterine bleeding. Endometrial cancer is the most common gynaecological cancer found in Singaporean women, with approximately 417 cases diagnosed annually³.

Investigation of PMB is therefore very important – indeed it is one of the most common reasons for which women are urgently referred to KK Women’s and Children’s Hospital (KKH).

Four Women, Four Different Causes

We examine the cases of four women who presented to KKH with PMB:



PATIENT A

Age 60s

Presentation: Blood stains on the toilet bowl and underwear

Examination	Diagnosis	Illustration
<ul style="list-style-type: none"> Clinical examination showed atrophic vulvovaginitis Pap smear revealed an atrophic smear with no malignant cells Ultrasound revealed significantly thickened endometrium of about 16mm Hysteroscopy found fluffy polypoidal endometrium 	<ul style="list-style-type: none"> Histology confirmed the patient had stage 1B endometrial adenocarcinoma. The patient underwent surgery to remove her uterus, cervix, ovaries and fallopian tubes. She also underwent a bilateral pelvic lymph node dissection and sentinel node sampling, and subsequently underwent vault radiotherapy. 	 <p style="font-size: small;">Figure 1. Hysteroscopy showing polypoidal endometrium</p>



PATIENT B

Age 50s

Presentation: Minimal vaginal spotting lasting for two days, followed by recurrent episodes of vaginal spotting six months later. Vaginal dryness but denied postcoital bleeding.

Examination	Diagnosis	Illustration
<ul style="list-style-type: none"> Clinical examination showed atrophic vulva and vagina Ultrasound revealed a normal endometrial thickness of 3mm Hysteroscopy found atrophic cavity 	<ul style="list-style-type: none"> Histology confirmed a scanty endometrium of basal type. The patient was treated with topical vaginal oestrogens. 	 <p style="font-size: small;">Figure 2. Hysteroscopy showing atrophic endometrium</p>

LEARNING POINTS FOR MANAGING WOMEN WITH PMB

PMB can be due to a wide variety of reasons, including benign and malignant causes. Even with minimal spotting, normal clinical examination and a probably thin endometrium, it is possible for PMB to be indicative of cancer.

A detailed history of all women presenting with PMB is essential, including the age of menopause, amount, type and duration of bleeding, history of hormone replacement therapy or selective oestrogen receptor modulators (e.g., Tamoxifen), pap smears

and medical history. A local examination of vulva and vagina, followed by a speculum examination of the cervix and bimanual pelvic examination should be performed. Even if a possible cause for PMB such as a cervical polyp is found, further investigations should still be undertaken.

A pap smear should be performed if not done recently. A transvaginal ultrasound scan of the pelvis must be performed to assess the endometrial thickness. An outpatient endometrial biopsy with pipelle/ explora or a hysteroscopy, dilatation and curettage should also be performed to establish the cause of the PMB.

THE PROS AND CONS OF INVESTIGATIVE METHODS

Transvaginal pelvic ultrasound (TVS)

- Endometrial polyps are usually seen as hyperechoic lesions with regular contours within the endometrial cavity surrounded by a thin hyperechoic halo. (97% sensitive, 74% specific; finding a single feeder vessel increases specificity to 95%).
- Endometrial hyperplasia is often seen as thickened hyperechoic and often cystic endometrium. Focal lesion is absent along with negative sliding sign and obvious feeding vessel. Endometrial thickness < 5 mm is less likely to be associated with the development of endometrial cancer.
- In atrophic endometritis, the ultrasound findings may be normal or may include thickened, heterogenous endometrium with intra-cavitary fluid with or without signs of intrauterine gas.
- For women on hormone replacement therapy, the endometrial lining is thicker; a cut-off value of > 8 mm should be observed for offering endometrial biopsy.

Outpatient endometrial biopsy – pipelle/explora

- 99% sensitive for detection of endometrial cancer
- Higher insufficient biopsy rate. For endometrial thickness <5mm, there is only a 27% chance of obtaining an adequate sample. Focal lesions may be missed.
- Not useful if the patient is on Tamoxifen
- Biopsy artifacts – increased difficulty in visualising gland architecture

Hysteroscopy, dilatation and curettage

- Gold standard; allows visualisation and sampling.
- 100% sensitive and 97% specific for endometrial polyps; also aids removal.
- 98% sensitive and 96% specific for evaluation of endometrial cavity in endometrial hyperplasia/malignancy.



PATIENT C

Age 70s

Presentation: Intermittent postmenopausal spotting for one month

Examination	Diagnosis	Illustration
<ul style="list-style-type: none"> • Clinical examination, bedside ultrasound and colposcopy was normal • Pap smear was suspicious for adenocarcinoma 	<ul style="list-style-type: none"> • A Pipelle's endometrial biopsy confirmed a malignant mixed mullerian tumour. • The patient underwent surgery to remove her uterus, cervix, ovaries and fallopian tubes. • She also underwent a pelvic lymph node dissection, para aortic node dissection and infracolic omentectomy. 	 <p>Figure 3. Colposcopy showing normal cervix</p>



PATIENT D

Age 50s

Presentation: PMB resembling light period for two days

Examination	Diagnosis	Illustration
<ul style="list-style-type: none"> • Clinical examination showed a cervical polyp that was avulsed and sent for histology • Ultrasound showed an endometrial thickness of 4mm 	<ul style="list-style-type: none"> • The patient's PMB resolved since the removal of the polyp. 	 <p>* Figure 4. Clinical examination showing a cervical polyp</p>

*Source: Dr Ahmed Ismail, Gynaecology Consultant, Queens Clinic, London (www.queenswaygynaecologyclinic.com)

The treatment method for women with PMB can vary greatly depending on the cause of bleeding.

ATROPHIC ENDOMETRITIS AND/OR VULVOVAGINITIS

In the case of atrophic endometritis and/or vulvovaginitis, topical oestrogens can be used without the need for progestogen therapy. Long-term treatment may be required as symptoms frequently recur after cessation of treatment.

POLYPS

Cervical polyps should be removed. As coexisting endometrial and cervical polyps are present in 24 to 27 percent of women, an ultrasound of the pelvis must be performed and further management planned accordingly.

Symptomatic endometrial polyps should be removed. If the polyp is asymptomatic and smaller than 18 mm in diameter, the risk of malignancy is low⁴. Thus the decision to remove the polyp should be balanced against the operative risks of removal⁵.

ENDOMETRIAL HYPERPLASIA

Left untreated, endometrial hyperplasia has the risk of progressing to endometrial cancer. The risk of malignancy, and therefore management, depend on whether the hyperplasia is simple or complex, and on the presence or absence of cellular atypia. These are outlined in Table 2.

Table 2.
Malignant risk of endometrial hyperplasia⁶

	Simple	Complex	Mean time for progression to cancer
No atypia	1%	3%	9.5 years
Atypia	8%	29%	4.1 years

Treatment options for endometrial hyperplasia include expectant management, hormonal therapy or surgery. The risk of endometrial cancer is reduced by three-to-five fold with the use of progestogens versus being left untreated. In the case of complex hyperplasia, lower regression rates are achieved with oral progestogens (66-69%) as compared to the levonorgestrel intrauterine system (LNG-IUS) (90-92%), but no difference was noted with simple

hyperplasia in both groups⁷. The surgical option is particularly recommended for women with complex atypical hyperplasia.

Malignancy of the genital tract on confirmation by biopsy should be referred to the gynaecological oncologist for further management.

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IN SUMMARY

1. PMB should always be investigated since 10 percent of women with PMB will have endometrial carcinoma.
2. The most common cause of PMB is atrophic vaginitis or endometritis.
3. Speculum examination should always be performed to rule out local lesions.
4. TVS can be used as an initial investigation.
5. There is still controversy about the cutoff value for endometrial thickness. The traditional ≤ 4 mm cut-off has a high negative predictive value for malignancy, and endometrial biopsy is unnecessary unless in cases of recurrent bleeding.
6. Endometrial biopsy is recommended if endometrium thickness is more than 4 mm, if endometrial thickness cannot be measured on TVS, or if recurrent bleeding occurs.
7. Hysteroscopy and endometrial biopsy remain the gold standard for women with PMB and for all symptomatic women on Tamoxifen.



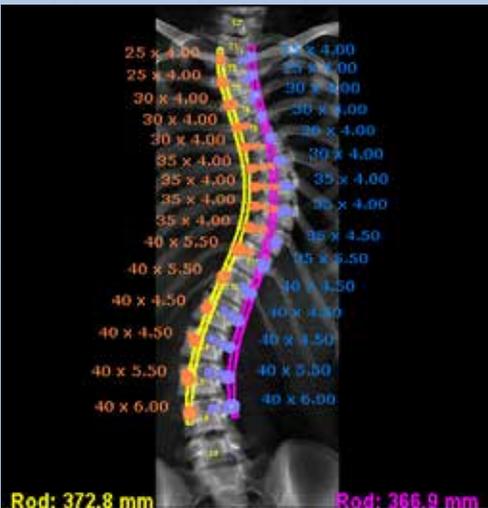
Dr Sonali P Chonkar, Staff Physician, Department of Obstetrics and Gynaecology, KKH
 Dr Sonali P Chonkar completed her MBBS and MD in OBGYN from Mumbai, India, and obtained her MRCOG in the United Kingdom. She has won several awards for excellence in medical education, most recently the 2014 SingHealth Golden Apple Award for outstanding Medical Educator. Dr Chonkar also serves as Deputy for the OBGYN clerkship, Duke-NUS Medical School.



Dr Rajeswari Kathirvel, Associate Consultant, Department of Obstetrics and Gynaecology, KKH
 An obstetrician and gynaecologist with special interests in high-risk pregnancy, Dr Rajeswari Kathirvel completed her MBBS in India and obtained her MRCOG in the United Kingdom, where she further underwent specialist training. In addition to her clinical work, Dr Rajeswari has a passion for teaching, and currently serves as Deputy Lead for Obstetrics and Gynaecology with the Lee Kong Chian School of Medicine.

LENDING THE SURGEON A HAND

Computerised pre-operative mapping and guidance is helping surgeons conduct spinal surgery with robotic precision and accuracy.



Robot-generated pre-operative plan for a patient with scoliosis

Under a pilot trial, surgeons at KK Women's and Children's Hospital (KKH) are using computerised pre-operative mapping and robotic guidance to conduct spinal surgery to correct scoliosis in children. To date, four patients have undergone the procedure.

"KKH very successfully performs up to 35 surgeries each year to correct severe scoliosis in children," says Associate Professor Kevin Lim, Chairman, Division of Surgery, KKH. "To provide even better care for our young patients, we are keen to examine the benefits of computerised pre-operative mapping and robotic guidance of screw placement through this pilot."

"Thus far, computer-mapped and robot-guided screw placement has been swift and



Robotic-guided screw placement during spinal surgery

accurate, with no need for a second attempt. We hope to see time savings as well, as shorter surgical procedures lower the risk of infection."

Scoliosis is an unnatural curvature of the spine that is common in children. The condition has an incidence rate of two percent in Singapore, and is most often seen in healthy children and adolescents aged ten years or more.

Surgical intervention is often the only viable treatment option for patients with severe scoliosis (spinal curvature greater than 45-50 degrees). This generally involves spinal fusion, where spinal vertebrae are instrumented with metallic implants and surgically fused, immobilising part of the spine.

The pilot trial began in November 2015 and is expected to conclude before June 2016. It is being conducted using the Renaissance® Guidance System.

3rd REHABILITATION AND RESPIRATORY SYMPOSIUM 2016

Optimising ventilation and oxygenation for critically ill patients

This symposium will address the education needs of paediatric and neonatal healthcare providers involved in the care of critically-ill patients.

Participants will gain insights on the various therapies required by patients with cardio-respiratory failure. Therapies include ECMO, mechanical ventilation, air flight transport, airway management and home care.

Date:	24 June 2016 (Friday)
Time:	7.30am to 4.30pm
Fee:	Free Admission (Open to Healthcare Professionals Only)
Venue:	KKH Auditorium, Training Centre, Level 1, Women's Tower

* CNE / CME points will be accredited.

For more details, please call 6394-8746 (Monday to Friday, 8.30am to 5.30pm) or log on to www.kkh.com.sg/events

KKH Warns Of Increase In Child Submersion Incidents

“It only takes a split second for someone to lose their child – so there should always be due care and vigilance by a supervising adult whenever a child is in or near water.”

Dr Arif Tyebally,
Department of Emergency Medicine, KKH

Statistics from the Department of Emergency Medicine at KK Women’s and Children’s Hospital (KKH) are showing an upward trend of submersion incidents involving children from 2011 to 2015 - with one in ten cases resulting in death.

Pre-school aged children were most vulnerable to submersion injuries, with the data revealing:

75
percent

of those with submersion injuries were children aged six years and below;

More than
50
percent

of submersion injuries occurred in condominium pools, with one in five of the incidents occurring during a pool party;

50
percent

of the drowning deaths in children were contributed from pool party fatalities

40
percent

of the submersion incidents occurred from Friday to Sunday, between 4pm and 8pm.

RECOMMENDATIONS ON PREVENTION OF SUBMERSION INCIDENTS INVOLVING CHILDREN

- Undivided attention should be given to children in the bath, swimming or when playing near bodies of water
- Extra vigilance during pool parties
- Presence of lifeguards
- Timely and effective implementation of cardiopulmonary resuscitation (CPR)
- Restriction of unsupervised access to bodies of water, for example, four-sided fencing
- Air-filled or foam toys should not be used as safety devices
- Keep pails/ buckets empty and turned over when not in use, particularly when there are toddlers in the vicinity.

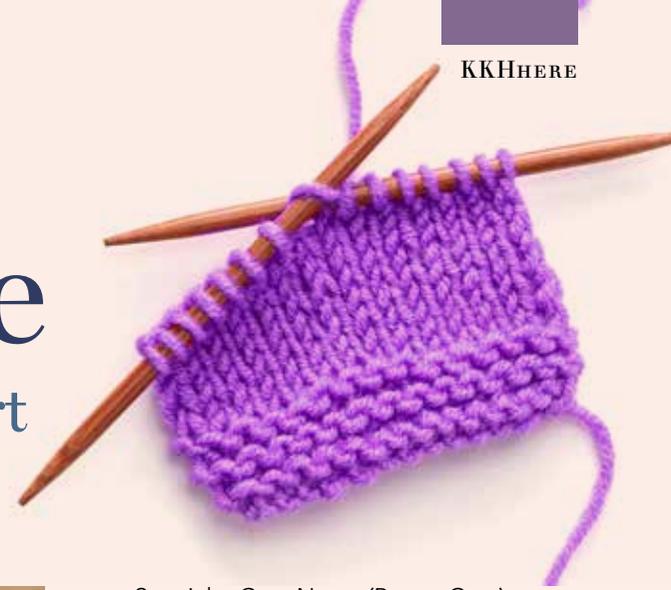
The majority of paediatric submersion cases in Singapore are treated at KKH. From 2011 to 2015, the hospital treated 104 children with submersion injuries – of which nearly two-thirds were boys. Patients ranged from infants less than one year, to children up to 15 years. Ten children died, and two survived their submersion ordeal but suffered hypoxic brain damage due to oxygen deprivation.

“The upward trend of submersion incidents involving children in recent years is disturbing as we know that all these incidents could have been prevented,” said Dr Arif Tyebally, Deputy Head and Consultant, Department of Emergency Medicine, KK Women’s and Children’s Hospital.

“Drowning deaths can occur within minutes and even if the child survives, there may be permanent brain damage. It only takes a split second for someone to lose their child so there should always be due care and vigilance by a supervising adult whenever a child is in or near water.”

A Stitch In Time

Breast cancer survivors knit to support patients with breast cancer.



Specialty Breast Care Nurse Teresa Ng (centre) with volunteer knitters from the Yarn Wonders project.

“Many of the volunteer knitters have themselves experienced breast cancer and triumphed over the disease. It really sends a powerful message to women with breast cancer – that they are not alone on this journey, and there is hope and life after cancer.”

Ms Teresa Ng
Assistant Director, Nursing, KKH

A group of volunteers and breast cancer survivors is bringing colour into the lives of patients fighting breast cancer – armed with multi-hued balls of yarn.

Each year, 150 to 200 women with breast cancer undergo surgery at KK Women’s and Children’s Hospital (KKH). To support these women through their cancer management

journey, volunteers and members of the KK Alpine Blossoms Breast Cancer Support Group are knitting sling bags designed to carry a wound drainage container, which is worn at the surgical site for one to two weeks post-surgery.

“The fight against breast cancer can be immensely challenging for patients physically, emotionally and psychologically,”

says Specialty Care Nurse (Breast Care) Teresa Ng, who is also an Assistant Director of Nursing at KKH.

“The gift of a hand-knit bag and personal message touches a precious life and provides much-needed encouragement,” she adds.

Dubbed the ‘Yarn Wonders Project’, each hand-knit sling bag can be sponsored at \$20 each, and sponsors will be able to pen their well wishes, or a personal message of encouragement, on a card to be gifted to the patient together with the bag.

All sponsorship proceeds from the project will go towards the KKH Health Endowment Fund (KKHHEF), which provides financial assistance for the medical needs of disadvantaged patients.

“Many of the volunteer knitters have themselves experienced breast cancer and triumphed over the disease. It really sends a powerful message to women with breast cancer – that they are not alone on this journey, and there is hope and life after cancer,” says Ms Ng.

Since March 2016, 137 sling bags have been knitted for distribution to patients who have undergone surgery for breast cancer. The group aims to knit 400 bags over a two-year period.



Support breast cancer care at KKH

If you are interesting in supporting the Yarn Wonders Project, or in volunteering to knit or sponsor a sling bag, please contact Ms Doris Seow Li Yuen at +65 6394 5815 or Seow.Li.Yuen@kkh.com.sg.



Professor Phua Kong Boo, Emeritus Consultant, Gastroenterology Service, KKH, with a patient.



PATIENTS. AT THE HEART OF ALL WE DO.



**KK Women's and
Children's Hospital**
SingHealth

ABOUT KK WOMEN'S AND CHILDREN'S HOSPITAL

Founded in 1858, KK Women's and Children's Hospital (KKH) is a recognised leader in Obstetrics, Gynaecology, Paediatrics and Neonatology. The 830-bed academic medical institution is Singapore's largest tertiary referral centre for high-risk women's and children's conditions. More than 600 specialists adopt a multi-disciplinary and holistic approach to treatment, and harness compassion, 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.



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