

# SPECIAL DELIVERY

NEWS FROM SINGAPORE'S ACADEMIC TERTIARY HOSPITAL FOR WOMEN AND CHILDREN

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# KKH INVENTION POWERS SMART PAIN RELIEF SYSTEM

Hospital and biomedical start-up develop commercially-viable labour pain relief devices.



Dr Sng Ban Leong, Deputy Head and Senior Consultant, Department of Women's Anaesthesia, KKH, demonstrates the use of the EPIVA smart infusion pump to deliver epidural pain relief to a patient.

More women can now look forward to responsive and personalised pain relief during labour, with the development of a clinically-proven analgesia delivery system invented by KK Women's and Children's Hospital (KKH).

The hospital is collaborating with Innovfusion, a medical device start-up in Singapore, to translate the technology behind the invention into a range of commercially-available smart infusion pumps that can customise a personalised pain relief regimen for patients.

"Labour pain often escalates and worsens as labour progresses, requiring an individualised, flexible analgesic regimen.

To create a more satisfactory birthing experience for the mother while safeguarding maternal and fetal well-being, we came up with an interactive technology that could administer the optimal amount of analgesia tailored to the patient's needs at any point in time," says Dr Eileen Lew, Head and Senior Consultant, Department of Women's Anaesthesia at KKH.

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A patient self-administers epidural analgesia at the touch of a button, using CI-PCEA technology.

#### THE SCIENCE BEHIND THE SYSTEM

Computer-integrated patient-controlled epidural analgesia (CI-PCEA) has been available to patients at KKH since 2009. Nearly 90 percent of patients rate their labour epidural experience as excellent or good.

The patented technology empowers patients in labour to determine the timing and frequency of their analgesia delivery, and to self-administer the pain-relief medication into the epidural space at the touch of a button.

A proprietary clinical algorithm analyses the patient's pain relief needs based on their analgesic demand over the past hour, and automatically adjusts the basal infusion rate of analgesia accordingly. This helps to reduce the incidence of breakthrough pain – failure of the regimen to provide adequate pain relief, necessitating unscheduled epidural supplementation – without increasing medication consumption or side effects.

# TRANSLATING RESEARCH INTO BETTER PAIN RELIEF FOR WOMEN IN LABOUR

The KKH-Innovfusion collaboration aims to produce three smart infusion pumps for the delivery of labour analgesia and anaesthesia. These include: EPIVA, for the delivery of epidural analgesia; INTRAVA, for the delivery of intravenous analgesia, and DIVA, for the management of blood pressure during elective Caesarean delivery under spinal anesthesia. The smart pumps will be based on clinically-tested prototypes by KKH, and powered by a proprietary algorithm developed by the Department of Women's Anaesthesia at KKH.

The first smart infusion pump, EPIVA, has been launched in January 2015. Designed for the customised delivery of epidural analgesia based on KKH's algorithm, the device is able to administer programmed relief medications in a bolus fashion – i.e. in discrete amounts, rather than the conventional method of a continuous basal infusion.

EPIVA is currently undergoing further research at KKH, as part of a Collaborative Outcomes with Labour Epidural Use Study (COLEUS). Preliminary trial results have found that that the higher driving pressure from the pump's bolus administration results in an improved uniform spread of analgesia in the epidural space. This leads to better pain relief, resulting in higher levels of maternal satisfaction with the same amount of pain relief medications.

#### CLINICAL TRIAL: IMPROVING THE BIRTH EXPERIENCE FOR MOTHERS

COLEUS aims to further investigate the clinical efficiacy of this epidural delivery system developed at KKH in comparison with conventional patient-controlled epidural analgesia (PCEA).

The systems will be trialed on about 3,000 first-time mothers with full-term pregnancies, who will be assessed on the degree of maternal satisfaction, quantity of analgesia used, as well as the well-being of the newborn.

"Women who experience increased pain during labour may also experience lower successful patient bolus demands when using PCEA, and may be at higher risk of dysfunctional labour, requiring obstetric intervention such as Caesarean or instrumental delivery," says Dr Sng Ban Leong, Deputy Head and Senior Consultant, Department of Women's Anaesthesia, KKH, and lead researcher for COLEUS.

"By improving our abilities to detect, intervene and hopefully prevent a mother's pain during labour, in the long term, we hope to be able to reduce maternal distress and anxiety," says Dr Sng.

COLEUS is funded by National Medical Research Council, Singapore, and is carried out by a multidisciplinary team comprising researchers from the Department of Women's Anaesthesia, Division of Obstetrics and Gynaecology, Mental Wellness Service, and Delivery Suite at KKH, and Duke-NUS Graduate Medical School. The clinical trial also includes industrial partner support from Innovfusion.



# TRANSFORMING THE EPIDURAL EXPERIENCE

Patient care and safety in obstetric epidural analgesia

Dr Sng Ban Leong, Deputy Head and Senior Consultant, Department of Women's Anaesthesia, KK Women's and Children's Hospital



Labour pains can be some of the worst pains a woman may experience in her lifetime. At KK Women's and Children's Hospital (KKH), the Department of Women's Anaesthesia provides anaesthesia, critical care and pain management services for women. The department also specialises in obstetric anaesthesia, which includes providing epidural analgesia during labour, regional anaesthesia for caesarean delivery and critical care for high risk obstetric conditions.

The gold standard of pain relief during labour is the provision of epidural analgesia. This involves the infusion of pain-relieving drugs directly into the epidural space – the outermost part of the spinal canal – via a small catheter. Epidural analgesia provides effective pain relief with minimal or no sedation, allowing the mother to participate fully during the labour and delivery process.

#### **RESEARCH FINDS MOTHERS' TIMING IS BEST**

At KKH, the majority of first-time mothers request for epidurals early in the labour process. Past studies have suggested that the timing of an epidural may affect the duration of labour, as well as the likelihood of needing a Caesarean section.

To better enable women to make informed choices on pain relief during childbirth, in 2014, the department led a research investigation into the timing of epidural administration, establishing that the right time to administer an epidural is when the patient requests for it.

Researchers from KKH, Duke-NUS Graduate Medical School, Singapore Clinical Research Institute and a medical student from NUS Yong Loo Lin School of Medicine, Singapore, collaborated on a



Cochrane systemic review comparing the effects of early and late epidurals during labour. The team reviewed data from nine studies involving 15,752 first-time mothers who were randomly assigned to 'early' or 'late' groups. During labour, those in the 'early' group were given epidurals when they were less than four to five centimetres dilated, while those in the 'late' group waited until they were four to five centimetres or more dilated.

The review found that those who had early epidurals were no more or less likely to need a Caesarean section than those who had late epidurals. Earlier epidurals also made no difference to the likelihood of needing an assisted birth involving forceps or suction, or to the amount of time spent in the second, 'pushing' stage

The findings of the review provide evidence-based assurance to mothers and healthcare providers that if the mother requests for epidural early in labour, this would not lead to adverse outcomes reported by some studies.

The medical evidence also supports guidelines by the American College of Obstetricians and Gynaecologists in 2006, which suggested that maternal request is a sufficient medical indication for pain relief during labour.

### PATIENT-CONTROLLED **EPIDURAL WINS MATERNAL**

At KKH, patients in labour are also empowered with greater autonomy over their pain control, with the use of patientcontrolled epidural analgesia (PCEA). This allows patients to self-administer additional pain medications into the epidural space at the press of a button, individualising the pain relief experience. The use of PCEA may also potentially result in fewer amounts of pain medications consumed during labour. Since 2012, nearly 90 percent of patients administered with PCEA have reported their labour epidural experience as excellent or good.

Innovative epidural delivery systems such as the computer-integrated patientcontrolled epidural analgesia (CI-PCEA), and automated mandatory bolus epidural administration techniques - have been investigated at KKH with promising results. The department is currently conducting a further clinical trial -Collaborative Outcomes with Labour Epidural Use Study (COLEUS) - to evaluate these systems' effectiveness in delivering an optimal pain relief experience. COLEUS is funded by National Medical Research Council, Singapore.

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#### CARE FRAMEWORK STRENGTHENS MATERNAL SAFETY

The department provides round-the-clock pain relief support for birthing patients, and administers about 400 epidurals for labour and delivery pain each month. Epidural pain relief is maintained using low dose concentrations of local anaesthetics with opioids, to provide a high quality of analgesia with reduced motor blockade – the loss of motor function – in the lower body.

However, a small proportion of women who receive epidural analgesia for labour pain may still continue to experience residual motor blockade for some time after delivery. This can cause weakness in the lower limbs, and may lead to a risk of falls in the immediate postnatal period.

To reinforce patient safety and reduce the risk of falls after delivery, the hospital has in place a rigorous care framework to identify and monitor women at high risk of post-delivery residual motor blockade. This is implemented by a multidisciplinary team consisting of medical professionals from the department, and the hospital's Delivery Suite, obstetric wards and Acute Pain Service.

Key measures of the care framework include:

#### 01

#### **ASSESS**



Assessing patients for residual motor blockade immediately after delivery, using a modified Bromage scale, which reflects the level and extent of motor blockage.

#### 02

#### TRANSPORT



Transporting patients who are experiencing residual motor blockade via wheeled bed; these patients are not permitted to be transported by wheelchair, or walk, until their blockade has resolved.

#### 03

#### REGISTER



Registering patients on a dedicated observation chart, to alert nurses and reviewing anaesthetists to provide heightened monitoring and assessment for residual weakness and numbness.

Each month, seven to 13 women are identified to experience residual motor blockade for some time after delivery, and receive close monitoring via this care framework.

#### **EDUCATING FOR EXCELLENCE IN OBSTETRIC ANAESTHESIA**

As the largest major obstetric anaesthesia teaching centre in Singapore, the department provides supervision and training for the SingHealth Anaesthesiology Residency Program (SHARP) and National Healthcare Group Residency Program. The hospital is a constant training ground for obstetric anaesthesia residents, who each undergo training for two to three months. To improve the interaction and communication between residents and faculty, debates and case-based discussions are also incorporated into the curriculum to hone residents' critical analysis and decision-making skills.

Placing patient safety as the highest priority, the department has developed training modules emphasising progressive competency in epidural analgesia, through epidural simulation training. Residents are assessed through competency-based learning and procedural skills tests under direct supervision by specialist faculty anaesthetists. This rigorous education helps to equip residents to advance the standards and possibilities of obstetric care into the future.

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Dr Sng Ban Leong's research interests include obstetric epidural analgesia, closed-loop systems, chronic post-surgical pain and the use of supraglottic airway for general anaesthesia in Caesarean section. He has received a National Medical Research Council (NMRC) Clinical Trials Grant for obstetric epidural delivery system research, NMRC Transition Award for chronic pain research and SingHealth Foundation Grant for vasopressor delivery system research.

In addition to his roles at KKH, Dr Sng is also Assistant Professor at Duke-NUS Graduate Medical School, and a Clinician-Scientist Mentor and Core Faculty for the SingHealth Anaesthesiology Residency Program.

### **OF BLISTERS AND SCALES**

Deciphering genetic skin conditions

Dr Chong Jin Ho, Associate Consultant; Dr Liew Hui Min, Associate Consultant; Dr Sharon Wong Mun Yee, Associate Consultant; Dermatology Service, KK Women's and Children's Hospital

Inherited genetic skin disorders, or genodermatoses, present most commonly at birth, during infancy, or in early childhood. While rare, they can occur with varying degrees of severity, ranging from mild disease to severe, life-threatening conditions. To provide optimal clinical outcomes, at KK Women's and Children's Hospital (KKH), patients with genodermatoses are managed in a multidisciplinary clinic jointly run by dermatologists, geneticists and paediatricians. In recent years, the clinic has seen eight to ten new cases of genodermatoses annually. This article discusses three of the more prevalent genodermatoses: epidermolysis bullosa (EB), congenital ichthyoses and incontinentia pigmenti (IP).

#### **EPIDERMOLYSIS BULLOSA**

EB is caused by mutations in various structural proteins of the skin. To date, more than 1,000 mutations in 14 genes have been documented. The mode of inheritance can be autosomal dominant or autosomal recessive. The condition is rare, with incidence ranging from 1:20,000 to 1:100,000.

#### Clinical features

EB is characterised by skin fragility, and a tendency to blister following even minimal mechanical friction or trauma. Erosions and blisters may also occur on the skin or mucous membranes.

EB is classified into four major types, according to the depth of skin at which blistering occurs. EB simplex presents with blistering within the epidermis (Figure 1); Junctional EB presents with blistering at the basement membrane zone; Dystrophic EB presents with blistering in the upper dermis; and Kindler syndrome presents with blistering in multiple levels, within and/or beneath the basement membrane zone.

Each type of EB can present with varying degrees of severity. Blisters and erosions usually occur at or shortly after birth. In milder cases, symptoms may only occur later in childhood or adulthood.

Distribution of blisters may be localised to sites of trauma, or may be generalised in severe cases. Other findings can include milia, atrophic scarring, granulation tissue, dystrophic or absent nails, and oral ulcers.



Figure 1. Epidermolysis bullosa simplex, which accounts for 70 percent of cases of EB.

The eyes, gastrointestinal, genitourinary and respiratory tracts may also be involved.

The disease tends to be milder in EB simplex - which accounts for approximately 70 percent of EB cases. Junctional EB usually has more severe involvement, especially Herlitz junctional EB, which has a very high mortality rate; most patients do not survive past infancy. Those who do experience chronic recurrent blistering, scarring, pseudosyndactyly, and often systemic involvement. Junctional and dystrophic EB are also associated with an increased risk of skin cancers

#### Management

Management of EB remains challenging and involves a multidisciplinary approach. No cure exists for the condition as yet; treatment is aimed at protecting the skin, preventing new blister formation, and treating complications. Wound prevention and care is crucial to prevent infection and aid healing; caregivers should be educated on the use of appropriate dressings and analgesia.

#### **CONGENITAL ICHTHYOSIS**

Congenital ichthyoses are hereditary disorders of cornification, caused by either abnormalities of intercellular junctions, or intercellular lipids within superficial epidermis. This leads to increased epidermal cell turnover, resulting in abnormal skin shedding, scaly, thickened skin and increased trans-epidermal water loss.

Congenital ichthyoses are classified into syndromic or non-syndromic types (Figure 2), with the latter being far more common. The incidence, inheritance, and clinical features of non-syndromic congenital ichthyoses are summarised in the table over the page.



Figure 2. Epidermolytic ichthyosis, a non-syndromic congenital ichthyose characterised by verrucous scale and blisters.

Continued from page 5..

#### Non-syndromic congenital ichthyoses

CONDITION	ICHTHYOSIS VULGARIS	X-LINKED RECESSIVE ICHTHYOSIS	EPIDERMOLYTIC ICHTHYOSIS	LAMELLAR ICHTHYOSIS	CONGENITAL ICHTHYOSIFORM ERYTHRODERMA
Incidence	1:250	1:2,000-6,000	1:300,000	1:300	0,000
Inheritance	Autosomal semi-dominant	X-linked recessive	Autosomal dominant		somal ssive
Onset	Two months	Majority by one year	At birth		only referred to dion baby
Clinical features	Fine to large scales	Large, brown scales	Verrucous scales, blisters	Large, plate-like scales;	Fine white scales; overlying erythema
Distribution	Generalised, sparing the flexures	Accentuates at neck, abdomen, back, and front of legs	Generalised, especially at the flexures	Gene	ralised
Comments	Hyperlinear palms; increased incidence of atopic dermatitis and keratosis pilaris	Associated with corneal opacities	Prone to secondary Staphylococcus aureus infection	Associated with ectropion, alopecia and nail dystrophy	Associated with ectropion and alopecia. Can be associated with neurologic abnormalities

#### Syndromic congenital ichthyoses

Syndromic congenital ichthyoses are associated with extracutaneous abnormalities, such as sparse and brittle hair.

The main syndromes associated with congenital ichthyoses include Netherton, as well as Refsum disease, Conradi, Sjogren-Larsson, congenital hemidysplasia with ichthyosiform erythroderma and limb defects (CHILD) and keratitis-ichthyosisdeafness (KID) syndromes.

Netherton syndrome is an autosomal recessive condition associated with atopy and trichorrhexis invaginata – a hair shaft

abnormality also known as 'bamboo hair'. Patients present during the neonatal or early infantile period with generalised scaling erythroderma. Failure to thrive, hypernatremic dehydration due to fluid loss through the skin, diarrhoea and cutaneous infections can also occur. Other syndromes may be less commonly seen.

#### Management

Management for congenital ichthyoses involves bathing with a soap-free cleanser, and frequent application of topical emollients. Keratolytic agents and topical or systemic retinoids may help to soften the scales and reduce itching.

Secondary bacterial infections may be treated with topical or systemic antibiotics, and vitamin D supplementation should be considered to prevent rickets – which can result from the lack of ultraviolet ray absorption by the skin.

Patients must take steps to prevent overheating, as temperature regulation may be affected due to sweat gland occlusion.

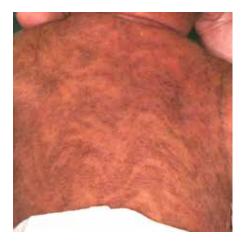


Figure 3. Stage two incontinentia pigmenti with hyperpigmented verrucous plaques arranged in lines of Blaschko.

#### **INCONTINENTIA PIGMENTI**

IP is an X-linked dominant disorder that is lethal in male embryos. The diagnosis of IP relies on the characteristic clinical cutaneous findings associated with abnormalities of dentition (hypo-, ano- or microdontia), hair (alopecia or woolly hair), nails (ridging, pitting or onychogryposis) and eyes (retinal detachment). The characteristic skin lesions evolve through four stages from infancy to adulthood (Figure 3).

Stage one is characterised by erythema, followed by blistering, usually in a linear distribution. This appears within the first two weeks of life, and clears within months. Stage two is characterised by linear, warty, hyperkeratotic plaques, and lasts for several months. Stage three is characterised by hyperpigmented streaks and whorls in the lines of Blaschko, usually fading in adolescence, leading to stage four. This final stage is characterised by linear hypopigmented atrophic streaks, which last throughout adulthood. Cognitive delays or intellectual disability are occasional associations.

Management for IP focuses on early detection and intervention for manifestations of the disorder, which can help to prevent complications such as blindness.

#### **DIAGNOSING GENODERMATOSES**

Today, the widespread availability of more sensitive diagnostic investigations means that many genodermatoses can be diagnosed at a molecular level. Technologies such as immunofluorescence (IF) mapping and next-generation DNA sequencing, allow clinicians to identify culprit gene mutations.

Despite technological advances, detective work remains a requisite for the clinician, as diagnostic variables differ between genodermatoses and their subtypes. Diagnoses often require investigations into the patient's clinical history, including family history and history of consanguinity, in addition to physical manifestations.

The diagnosis of EB is usually made on clinical history, including family history and history of consanguinity, and physical manifestations.

To confirm the diagnosis, skin biopsies may be performed for IF mapping to determine the level of skin cleavage and likely proteins involved.

Genetic tests may then be pursued to identify the gene mutation for more accurate molecular diagnosis and to inform prenatal genetic counselling.

For congenital ichthyoses, skin biopsy and genetic studies are helpful for diagnosis. The clinical presentation can vary, especially for syndromic congenital ichthyosis, therefore further investigations should be ordered accordingly. For instance, hair shaft examination is useful for the diagnosis of Netherton syndrome.

In the case of IP, diagnosis is based on clinical findings and molecular genetic testing of the IKBKG gene - the only gene known to be associated with IP. Targeted mutation analysis to identify the common 11.7-kb IKBKG deletion is the first line genetic test, followed by sequencing of the complete IKBKG gene if the individual is not found to have inherited the common deletion.

Family history consistent with X-linked inheritance, or a history of multiple miscarriages, also supports the diagnosis. IP is lethal in males, and females can be carriers of the defective gene. Thus, genetic counselling and prenatal testing for future pregnancies is recommended.



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Dr Chong Jin Ho is an Associate Consultant with the Department of Paediatrics at KKH. He has a special interest in dermatology, and completed a Diploma in Practical Dermatology with Cardiff University, United Kingdom.



Dr Liew Hui Min graduated from University of Dundee in Scotland and completed her medical training in the United Kingdom, obtaining her Membership of the Royal College of Physicians in 2007. She further pursued training in dermatology at King's College Hospital in London. Dr Liew's current subspecialty interests include paediatric and women's dermatology.



Dr Sharon Wong is an Associate Consultant with the Department of Paediatrics at KKH. She is a member of the Royal College of Paediatrics and Child Health, and holds a Diploma in Practical Dermatology with Cardiff University, United Kingdom. Dr Wong has a special interest in paediatric dermatology, and is currently pursuing further subspecialty training in St. John's Institute of Dermatology, London.

# A HANDS-ON APPROACH TO BREAST CANCER

Dr Tan Yia Swam, Associate Consultant, Breast Department, KK Women's and Children's Hospital

Breast cancer is the number one cancer affecting women worldwide. Cancer occurs when the body's cells become damaged, and are no longer able to repair themselves. These damaged cells grow in an uncontrolled manner, and can spread throughout the body. Generally, five to ten percent of patients with breast cancer have a genetic cause, which may be inheritable. However, more than 80 percent of patients with breast cancer develop the disease despite not having a family history.

Detection of cancer in the early stages is key to improving one's survival rate. According to the Singapore National Registry of Diseases Office, patients whose breast cancers are detected in stages zero to one have a five-year survival rate of 88 to 95 percent.

# AWARENESS AND VIGILANCE IS KEY

#### **Breast self-examination**

To facilitate early diagnosis and intervention for breast cancer, all women are recommended to conduct monthly breast self-examinations (BSE) from 20 years, keeping a lookout for signs of breast abnormality.

Such signs can include nipple bleeding or discharge, rash at the nipple or areola region, lumps in the breast tissue or near the underarm area, and changes in the size, shape and skin consistency of the breasts. Women who experience any of these symptoms should seek medical advice promptly.

#### Breast screening mammogram

As breast cancer may be asymptomatic in its early stages, women are also recommended to undergo yearly breast screening via a mammogram from 40 years, even if they have no symptoms of the disease. A mammogram is a painless X-ray examination which can help to identify abnormal structures such as cysts, calcifications and tumours within the breast. Yearly mammograms should be continued until 50 years, after which they should be conducted once every two years.

Patients should be referred for tertiary evaluation if they present with any of the above signs from BSE, or an abnormal imaging result. It is important to reassure patients that breast pain, on its own, is not a sign of breast cancer.

# REASSURANCE AIDS MENTAL PREPARATION

While BSE and screening are crucial to detect possible indications of breast cancer, further tertiary evaluation is required to make a definitive diagnosis of breast cancer, and determine a suitable course of management. However, lack of awareness about this process can cause undue anxiety to a patient.

#### Patient counselling

Reassurance from the attending primary physician – that a referral to seek tertiary evaluation does not necessarily mean that the patient has breast cancer – and being informed of the probable patient journey, is crucial to help prepare the patient physically and psychologically for their appointment at the referral centre.

The KK Breast Centre at KK Women's and Children's Hospital (KKH) is a major referral centre for the tertiary evaluation and management for a range of breast conditions, in particular, breast cancers. In 2014, the Centre provided care and management for over 18,000 patients with breast conditions, of which about two percent were new patients with breast cancer.





42-year-old Sophia receives a letter from her polyclinic, informing her of an abnormal imaging result from a recent screening mammogram. The letter refers her to the KK Breast Centre for further evaluation by a breast specialist.



#### **EXAMINATION AND DISCUSSION ON THE FIRST APPOINTMENT**

During her first appointment at KKH, Sophia is seen by a surgeon with the KK Breast Centre. The surgeon discusses her overall health status and risk factors for breast cancer, as well as conducts a physical examination of her breasts. The surgeon also arranges for a supplementary ultrasound scan.



#### REVIEW AND ADVICE ON THE SECOND APPOINTMENT

At Sophia's second appointment, the surgeon explains that the supplementary scan had detected an abnormality, and recommends that Sophia undergo a biopsy. Sophia is worried about having an abnormal result. However, the surgeon explains that not all abnormal results are indicative of cancer; the abnormality may be a benign lump, or microcalcification, and a biopsy is an important step to definitively determine if the breast abnormality is cancerous.

Sophia undergoes a breast biopsy, and the tissue sample is sent to the laboratory at KKH for microscopic examination.



#### RESULT AND DIAGNOSIS ON THE THIRD APPOINTMENT

A week later, Sophia returns to the KK Breast Centre for a discussion of the biopsy results with her surgeon. The results indicate that her breast condition is benign. The surgeon informs Sophia that she does not have breast cancer. As such, she does not require treatment or further tertiary management.

#### PARTNERING PATIENTS ON THEIR JOURNEY

Like Sophia's, some breast conditions may be benign, and may not require treatment or management.

In the event a patient is diagnosed with breast cancer, their attending surgeon will recommend the necessary treatment plan. This can include one or more of the following: surgery, chemotherapy, targeted therapy, endocrine therapy or radiation therapy.

The patient would also need to undergo staging scans to assess whether the cancer has spread to other parts of the body. A holistic treatment plan be up to six months in duration, after which the patient would be regularly followed-up by relevant medical specialists.

The KK Breast Centre has a dedicated multidisciplinary team of medical specialists and breast care nurses who provide medical and nursing care, counselling and education to help cancer patients throughout their cancer management journey and recovery process.

The hospital also runs the Alpine Blossoms Support Group, which is guided by healthcare professionals, with the aim to provide tailored holistic care for every patient with breast cancer.



#### TIPS FOR A AN APPOINTMENT AT THE KK BREAST CENTRE:

- Bring along your personal identification and referral letter
- Bring along any available breast images and reports that you have from a different clinic
- Do not apply powder on your chest, breast or underarm area
- Wear clothing that is convenient to remove, as you will need to remove the clothes above your waist
- A mammogram is not painful; however, you may experience slight discomfort



#### WHAT IS A BREAST BIOPSY?

A breast biopsy involves removing a small sample of tissue or fluid from the breast. The sample is sent to a laboratory to be checked for the presence of breast cancer. Biopsies may be done using several methods:

Fine needle aspirate - This is done with a small needle, such as that used when drawing a blood sample.

Core needle biopsy - This is done using a larger needle, and requires local anaesthesia. Patients may experience some discomfort and temporary bruising after the procedure. Simple analgesics such as paracetamol may be prescribed by the doctor.

Vacuum-assisted biopsy - This is recommended in certain situations, where the patient has a small group of microcalcifications, or a lump suitable for removal with vacuum-assisted biopsy. A special vacuum device is attached to the needle for removal of the lump. Sometimes, a metal clip is left at the site, to guide the surgeon should further surgery be necessary.

Open biopsy – This is a minor surgery performed under general anaesthesia. A small cut is made to remove a small tissue sample.



Dr Tan Yia Swam graduated from NUS Yong Loo Lin School of Medicine. She completed specialty training in General Surgery, and became a Fellow of The Royal College of Surgeons of Edinburgh in the United Kingdom. Dr Tan has a special interest in patient care and public awareness for breast cancer. She is also a council member of the Singapore Medical Association (SMA), as well as editor of SMA News.

# WHEN IT'S MORE THAN A VULVAR LUMP

Diagnosis and management for vulvar cancers

Dr Namuduri Rama Padmavathi, Staff Physician, Department of Gynaecological Oncology, KK Women's and Children's Hospital

#### HISTOLOGY

Vulvar cancers are a form of gynaecological cancer. Globally, the most common vulvar cancer is squamous cell carcinoma, which occurs in 85 to 90 percent of cases. Other common vulvar cancers include melanoma (6%), Bartholin's adenocarcinoma (4%), basal cell carcinoma (fewer than 2%) and sarcoma (fewer than 1%)¹. Vulvar cancers exhibit three common modes of spread: direction extension to adjacent structures, such as the vagina and urethra; lymphatic extension to regional or pelvic lymph nodes; and haematogenous spread to the liver and lungs, usually in the advanced stage of disease.

While vulvar cancers predominantly affect women aged 60 to 70 years, the median age of diagnosis has been decreasing over the past several decades<sup>2</sup>. A global trend of younger women presenting with squamous carcinoma of the vulva has been well documented. In addition, human papillomavirus (HPV) also appears to be increasingly common in younger women with vulvar carcinoma<sup>3</sup>. This may be associated with increasing HPV prevalence in areas around the world.

At KK Women's and Children's Hospital (KKH), vulvar cancers constitute one to two percent of all gynaecological cancers. From 1995 to 2014, the most commonly seen vulvar cancers are squamous cell carcinoma (86), Paget's disease (55), basal cell carcinoma (13) and melanoma (8). Other less common vulvar cancers include high- and low-grade sarcoma, granular cell tumour, sebaceous carcinoma, angiomyofibroblastoma and tumours with malignant potential.



While presentation varies according to stage of disease, the most common symptoms of vulvar cancer include: vulvar itching; irritation, pain or lump. The following indications should arouse suspicion in the examining physician, and necessitate referral for diagnostic biopsy:

- All irregular, fungating masses, non-healing ulcers, lumps, suspicious pigmented lesions and persistent warts in post-menopausal women
- Change in the appearance of vulvar epithelium with hypopigmentation or hyperkeratosis, characterised by leucoplakea
- Areas of lichen sclerosus with bleeding, ulceration and lumpiness

The histological diagnosis of vulvar cancer is based on biopsy results.

#### **MANAGEMENT**

Early vulvar cancer

Pretreatment evaluation includes computed tomography scans of the chest, abdomen and pelvis, to determine extent of spread of the disease. Excision with a ten millimetre margin will be required if the cancer lesion is smaller than two centimetres in diameter, and inguino-femoral lymphadenectomy will be required if stromal invasion is larger than one millimetre in diameter. Should the cancer lesion exceed two centimetres in diameter, radical local excision or radical vulvectomy, as well as inguino-femoral lymphadenectomy will be required.

#### Advanced vulvar cancer

Management for resectable advanced tumours includes radical excision, radical vulvectomy and inguinofemoral lymphadenectomy. Adjuvant local vulvar radiotherapy is required if resection margins are involved; surgical margin is less than eight millimetres; there is perineural and/or perivascular tumour involvement; or there is deep stromal invasion. Adjuvant groin and pelvic radiotherapy is required if the inguinofemoral lymph nodes are involved. Management for unresectable advanced tumours or fixed and ulcerated groin nodes includes concurrent chemotherapy and adjuvant radiation therapy.

Careful patient counselling is necessary to address intra- and post-operative issues, which can include the need for reconstructive surgery, or psychosexual complications, wound breakdown, introital stenosis, urinary or faecal incontinence and lymphoedema.

Post-operative care includes careful drying of the surgical site, the use of a bed cradle to allow air circulation around the wound, strict adherence to perineal hygiene using regular sitz baths, retention of the surgical drains until lymphatic leakage has completely ceased. Thromboprophylaxis and antibiotic prophylaxis are also prescribed to prevent infection and blood clots.

All treated vulvar cancers should be followed up in the gynecology cancer center for assessment of post-treatment complications and for recognition and treatment of recurrences.

#### **Prognosis**

Inguinal and femoral lymph node involvement is the most significant prognostic factor for survival in patients with vulvar cancer. The five-year survival rate in vulvar cancers with lymph node involvement is 25 to 40 percent, in contrast to 80 percent for cases which do not involve the lymph nodes.



#### SIGNS AND SYMPTOMS OF COMMON VULVAR CANCERS

TYPE	CLINICAL PRESENTATION	RECOMMENDED ACTION FOR GENERAL PRACTITIONERS	
Squamous cell carcinoma	A lump or growth on the vulva; colour or architectural changes in the vulvar skin, or growths that resemble a wart or ulcer.	Any suspicious-looking growths or other lesions, such as lumps, plaque, warty change or changes in skin texture, should be referred for a biopsy.	
Paget's disease	The primary lesion is an erythematous and scaly plaque, resembling eczema; usually well-delineated with crusting, weepy with erosions and even ulcerations. The labia majora and mons pubis are commonly involved.	Any pruritic erythematous or eczematous lesion of vulva unresponsive to topical steroids and antifungals should be referred for a biopsy.	
Bartholin's adenocarcinoma	Enlarged Bartholin's gland which is fixed and indurated; common in post-menopausal women.	Should not be treated as Bartholinitis or Bartholin's cyst; should be referred for further evaluation.	
Basal cell carcinoma	Presents as nodule, ulcer or plaque. Sometimes mistaken for warts or skin tags that itch, and bleed on scratching.	Any vulvar lesion with uncertain diagnosis must be referred for a biopsy.	
Sarcoma	Very rare. Presents as fast-growing vulvar masses that are fixed to underlying structures.	Any hard, fixed and fast-growing vulvar mass requires prompt referral to seek tertiary management.	
Melanoma	Lesions suspicious for early melanoma are characterised by the 'ABCD' symptoms:  Asymmetrical; Border irregularity; Colour changes or variegate with shades of red, blue and black;  Diameter greater than six millimetres.  Features of advanced-stage melanomas include bleeding, ulceration, pain and tenderness.	Should be referred to an oncologist for review.	

#### **RISK FACTORS FOR VULVAR CANCERS**

#### 01. HUMAN PAPILLOMAVIRUS (HPV)

High-risk HPV has been shown to be responsible for 60 percent of vulvar cancers

#### 02. ADVANCED AGE

Vulvar cancers are most common in women over 70 years

#### 03. LICHEN SCLEROSUS

Carries a five percent risk of becoming cancerous

- 04. HIGH-GRADE VULVAR **INTRAEPITHELIAL NEOPLASIA (VIN)**
- 05. IMMUNOSUPPRESSION
- 06. SMOKING
- 07. PRIOR HISTORY OF **CERVICAL CANCER**
- 08. EXTRAMAMMARY **PAGET'S DISEASE**
- 09. MELANOMA IN SITU

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Dr Namuduri Rama Padmavathi obtained her Doctor of Medicine in Obstetrics and Gynaecology from the University of Health Sciences in India, and is a member of the Royal College of Obstetricians and Gynaecologists in London. She further completed a graduate diploma in dermatology from National University of Singapore. Dr Padmavathi has a special interest in vulvar, gynaecological and dermatological diseases, including vulvar cancer and research involving vulvar disease.

# RESEARCH TO HELP IVF PATIENTS CONCEIVE

Happily married with a newborn son, Dr Ryan Lee is working hard towards delivering the joy of parenthood to more patients undergoing in vitro fertilisation (IVF).

"Trying for a baby is a tremendously mental and emotional process. Unfortunately, a proportion of couples who undergo IVF do not fall pregnant, even after several tries," says Dr Lee, a resident with the Department of Reproductive Medicine at KK Women's and Children's Hospital (KKH).

Supported by a research grant from the KKH Health Endowment Fund, Dr Lee is investigating the effect of clinically-induced local endometrial injury (LEI) on improving pregnancy outcomes for couples who experience recurrent implantation failure after IVF.

The study is being conducted in collaboration with scientists from the Singapore Immunology Network and Singapore-MIT Alliance for Research and Technology (SMART).



"By better understanding the changes to the endometrial cavity implicated in LEI, we hope to ultimately improve the overall success rate of IVF for the benefit of all patients."

#### Dr Ryan Lee

Resident

Department of Reproductive Medicine, KKH

#### SUPPORT RESEARCH FOR WOMEN AND CHILD HEALTH

The KKH Health Endowment Fund (KKHHEF) supports research investigations such as Dr Ryan Lee's, to advance better diagnoses, treatments and cures for women and children.

The KKHHEF also provides financial support for medical treatment to patients in need at KKH, and funds education and disease prevention programmes.

For more information on how you can support research for women and child's health through KKHHEF, please contact Christine at +65 6394 2329 or email development@kkh.com.sg.

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#### Paediatric Surgery Forum

#### GP Forum for Paediatric Health 2015

Date : 23 May 2015 (Saturday) Time : 1.00pm to 5.00pm

Fee : \$10 per pax (includes lunch and tea refreshment)

Venue: KKH Auditorium, Training Centre, Level 1, Women's Tower

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



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