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Endometriosis as a systemic disease: What's the relevance

Endometriosis is now considered a systemic disease with systemic hormonal, po-inflammatory, pro-angiogenic, immunologic, and genetic process rather than a disease predominantly affecting the pelvis. Endometriosis affects metabolism in liver and adipose tissue, leads to systemic inflammation, and alters gene expression in the brain that causes pain sensitization and mood disorders. Recent clinical evidence also discuss how endometriosis interacts with cardiovascular risk factors and cardiovascular disease (CVD). The full effect of the disease is not fully recognized and goes far beyond the pelvis. Recognition of the full scope of the disease will facilitate clinical diagnosis and allow for more comprehensive treatment.

In this lecture, we discuss the latest understanding of endometriosis as a systemic disease with multiple manifestations outside the parameters of classic gynecological disease. Modern approaches to this disease include early identification through clinical diagnosis, recognition of associated systemic manifestations, judicious use of imaging, and long-term management of all aspects of the disease. Hormonal therapy and surgery are aimed at treating pelvic disease, but both approaches have associated failure rates, and do not completely address the systemic effects of this disorder. Dienogest, as the 4th generation progestin with local systemic effect, could potentially contribute to the better management of endometriosis progression.

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12

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APAC Consensus: Early diagnosis and management in endometriosis

The diagnosis and treatment of endometriosis has recently undergone considerable changes with an increasing focus on patient-centered care that includes more frequent clinical management, including use of questioning and imaging, and early medical treatment. In 2019, clinicians with expertise in the diagnosis and treatment of endometriosis within APAC region met to critically evaluate available evidence at the time, including international guidelines and consensus reports on clinical diagnosis and early medical management of endometriosis and their applicability to current clinical practices, with a predominant focus within Asia.

This lecture will provide an overview of this APAC Consensus that was presented in the recent international SEUD Conference in December 2021 which incorporated an algorithm to emphasize the importance of early clinical diagnosis and early medical management for endometriosis in Asia. Additionally, this lecture will also discuss how this APAC consensus is in alignment with the most updated ESHRE 2022 Guidelines on Endometriosis Management, including the role and duration of medical treatment post-surgical intervention.

龍震字 L3

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The application of new generation FemiLift laser on GSM and SUI Treatment

GSM (Genito-Urinary Syndrome of Menopause) is becoming an increasing concern for women worldwide. According to the North American Menopause Society, by the year 2025 the number of postmenopausal women is expected to rise to 1.1 billion, more than half of which will likely experience vulvovaginal symptoms that significantly impact their lifestyle, emotions and sex life.

The shift in hormones that occurs with menopause can cause the lining of the vagina to become thinner, drier, less elastic and inflamed. FemiLift rejuvenates the vaginal lining, increasing the thickness of the vaginal walls and restoring natural lubrication. The treatment reduces uncomfortable symptoms such as itching, burning and friction and helps improve sexual function.

Alma FemiLift is a state-of-the-art, minimally-invasive outpatient solution that incorporates CO2 technology to provide optimal care for various feminine concerns. The procedure is fast, painless and completely safe, and provides highly effective results. It's a versatile solution that enables medical practitioners to treat various feminine indications quickly and effectively. Procedures are conducted in an outpatient setting, and do not require anesthesia or downtime, ensuring that women can resume their routine – and regain their confidence – soon after.

FemiLift opens up your clinic to a wide range of patients, varying in age and stage in life, broadening your reach – and adding real value to your practice.

The benefits of alma femilift:

- *Fast, homogeneous treatments
- *Minimally invasive
- *Outpatient treatment co2 technology: Clinically proven
- *Optimal For collagen remodeling
- *Safe, easy & effective
- *Immediate results
- *Hygienic, single use probe

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Beneficial of FemiLift Laser of Labiaplasty

Labiaplasty, a surgery with growing demand as more and more women find that there is an answer to their problems by surgical relief of functional and cosmetic appearance. Procedure may involve simply reducing large or hanging labia, matching asymmetric labia, or tightening or filling the labial area. Using linear surgical technique approach with CO2 laser is relatively simple and can greatly enhance the patient's confidence with satisfactory results.

Another fast-growing industry will be non-surgical female rejuvenation procedure in office procedure, easy yet effective. Alternatives for the management of uro-vulvo-vaginal disorders, not only innovation in the treatment of womens' intimacy disorders, but A REAL FEMININE REVOLUTION.

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Endometrial cancer screening: current status and where to go?

After decades of efforts in cancer research, the improvements in the incidence and survival of most cancers are encouraging. However, one of the exceptions is endometrial cancer (EC), the most common gynecologic cancer, for which both the incidence and mortality rates are increasing. According to GLOBOCAN 2018, approximately 382,000 cases of EC were reported and nearly 90,000 deaths were caused by EC in 2018. The number of women with newly diagnosed EC is estimated to grow by 52.7%, reaching 544,178 in 2040. The mortality rate of EC is increasing and is estimated to increase at an average of 16% every 5 years from 2018 to 2040.

Abnormal uterine bleeding is the most frequent symptom of endometrial cancer, but many other disorders give rise to the same symptom. Even when bleeding occurs in postmenopausal women, only 10% of cases are caused by an endometrial cancer. The choice of the ideal detection strategy depends upon the sensitivity, specificity, probability of accuracy, and cost. Transvaginal ultrasound (TVU) is used to exclude endometrial cancer. The cut-off value for TVU in symptomatic premenopausal women and those taking hormone replacement therapy is lower because of variations in endometrial thickness under the influence of circulating female steroid hormones. Endometrial samples obtained by suction curettage in an outpatient setting may have a higher sensitivity and specificity compared with TVU. However, the failure rate of this invasive procedure can be up to 54%. The clinical guidelines recommend fractional dilatation and curettage (D & C) under anesthesia if the endometrial sampling is inadequate or inclusive for diagnosis. Thus, many patients undergo repeated invasive evaluations by endometrial sampling or D & C, which is inconvenient, stressful, and costly. The diagnostic accuracy of hysteroscopy can achieve an overall sensitivity of 86.4% and specificity of 99.2% in both pre- and postmenopausal women. However, there is debate over the best cut-off value for endometrial thickness diagnosed with TVU that should warrant endometrial sampling or hysteroscopy. Cytology from cervical scrapings have also been used for detecting endometrial cancers, but the rate of abnormal results ranges from 32.3% to 86.0% for type I endometrial cancer and 57.1% to 100% for type Il endometrial cancer. There is a need for a better method for endometrial cancer screening.

Studies on epigenetic silencing have revealed a role of DNA methylation in carcinogenesis. DNA methylation may occur early in carcinogenesis and is sufficiently stable for analysis. The application of DNA methylation as a biomarker for cancer detection or patient stratification has been increasing. However, research on EC epigenomics, especially for screening purposes, is relatively limited. Our previous comprehensive methylomics study illustrated a methylation panel of BHLHE22/CDO1/CELF4 genes for predicting EC risk using cervical scrapings. The proof-of-concept real-time polymerase chain reaction (PCR)-based detection of methylated BHLHE22/CDO1 genes has been further prototyped in a retrospective cohort with a sensitivity of 84.8% and a specificity of 88.0% for the diagnosis of EC. A multicenter, two-stage confirmatory study was conducted to validate the cancer-detection performance of MPap, including BHLHE22/CDO1/age/BMI. In stage 1, the sensitivity, specificity, and positive and negative predictive values of MPap were 92.9% (80.5-98.5%), 71.5% (64.8-77.5%), 39.8% (82.9-100.0%), and 98.0% (94.3-99.3%), respectively, for 249 patients. These values were validated in stage 2, where they were 92.5% (82.9-100.0%), 73.8% (67.6-79.4%), 40.2% (30.8-50.5%), and 98.1% (95.8-100.0%), respectively, for 245 patients. MPap outperformed transvaginal ultrasound in all these aspects.

MPap uses the infrastructure for cervical cancer screening and provides a feasible alternative for endometrial cancer detection. This is the first study to validate the utility of MPap using cervical scrapings with least physical injury in routine clinical practice. Further validations in different populations and in various clinical dilemmas such as breast cancer patients with tamoxifen treatment, asymptomatic women with hereditary cancer gene mutations, or fertility sparing in early endometrial cancer patients, may broaden the use of this molecular screening of endometrial cancer in the future.

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Female Obesity and Its Management

杜思德

彰化基督教醫療財團法人彰化基督教醫院

根據學者專家 20 歲以上人群肥胖發生率的調查統計表明·發胖者占調查總人數 21.7%·其中男性佔 46.1%·女性佔 53.9%·在一般人群中·女性肥胖人數明顯比男性多。

而 Liraglutide 是一種與人體腸道荷爾蒙 GLP-1 結構類似的注射藥物。GLP-1 可以經由作用於身體的重要器官,包含屬於中樞神經系統的下視丘,增加飽足感,對於胃部則有延緩胃部排空的效果,使食物停留在胃部的時間拉長,較不會感覺到飢餓,因此使用 liraglutide 有效減少食物總量的攝取、減輕體重,而我們也可以由臨床使用 liraglutide 3.0 mg 的 SCALE 一系列研究得知其效果與安全性。而 Liraglutide 3.0 在台灣是唯一具有體重控制適應症的 GLP-1 注射藥物,如何正確使用 on label 的藥物於體重管理以保護醫療照護者與病患為一重大課題。

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詹德富 *L7*

高危險妊娠案例分享-(1)子癲前症早期診斷與治療(2)早產診斷、管理與治療

高危險妊娠是在妊娠期間,母親和胎兒有潛在的危險,導致胎兒或母體的健康,可能因此發生不良於懷孕結果的狀況,甚至生命安全受到影響。根據目前的統計結果顯示,高危險妊娠佔所有懷孕婦女的比例約 15-20%,因素可能與母體本身有關,包含疾病史,重要器官的功能異常、年齡,體重,生活型態等等。也可能來自妊娠因子,包含多胞胎,胎兒異常,妊娠高血壓,妊娠毒血症,妊娠糖尿病,胎盤異常,早產,等等的因子。

子癲前症是發生妊娠時的嚴重高血壓, 定義為血壓>140/90 mmHg·並且伴隨蛋白尿以及/或孕婦急性腎損傷、肝功能異常、神經學特徵、溶血、血小板減少症或胎兒生長遲滯。子癲前症在世界盛行率約3-8%, 發生率約3-5%,然而在開發中國家有更高的子癲前症發生率。子癲前症是造成胎兒及母體併發症其中之一的主因・14%的孕婦死亡與子癲前症有關。子癲前症的發展與胎盤有關,因此移除胎盤是治療子癲前症的唯一方法。歐洲心臟病學會指引建議使用可溶性血管內皮生長因子受體1(sFlt-1)/胎盤生長因子(PlGF)比值:若sFlt-1/PlGF比值<38·代表孕婦未來一週內臨床上疑似子癲前症的孕婦,發展子癲前症機率極低。

藉由定期產檢,早期與中期判別高危險妊娠因子並加以掌握是必要的;因應高齡化生產與少子 化的趨勢,政府也擬將增加補助未來產檢次數與檢測項目。經過多年醫界與學會的努力,高危險妊 娠門診的建立,國內周產期照護網絡也逐漸完善,進一步減少了高危險妊娠可能帶來的不良生產結 果。再者,已於民國105年實施至今的「生產事故救濟條例」,除了協助醫療人員精實通報與建立完整 救濟制度以外,更保護醫療人員,減少因生產事故產生的各種糾紛。

早產及妊娠高血壓是造成胎兒或母親常見併發症的原因之一,嚴重還會危害孕婦與胎兒生命安全。國內的早產率約佔10%,而妊娠高血壓則是國內孕產婦死亡或子宮切除的主因之一,兩者都對母胎健康或社會帶來許多醫療成本及社會照護支出。因此,無論是孕產婦與家人對高危險妊娠有足夠的認知,或者是醫療人員對於早產現象及妊娠高血壓即早一步預防,掌握與處置的訓練,都能夠大幅減少懷孕過程中的風險傷害及衝擊,對於國內母胎安全與生育品質的提升,將有長足的影響是值得重視的議題。早產現象的治療的安全及有效的催產素受體抑制劑即將取得健保給付,提升醫療照護品質,並嘉惠患者。

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維生素 B6 補充對孕吐的重要性

The importance of Vitamin B6 supplementation for morning sickness

孕期噁心嘔吐 (Nausea and vomiting of pregnancy, NVP) 是女性在懷孕初期很常見的症狀,其盛行率高達 80%。典型的孕吐症狀發生在懷孕第四週至第十六週之間,約有 10%的婦女症狀會持續至懷孕第二十週。孕吐會造成孕婦龐大的生理及心理壓力,影響生活品質,增加醫療保健費用,甚至可能導致營養不均、體重減輕,影響孕婦及胎兒的健康。一旦孕婦出現噁心、嘔吐的情況,控制症狀就會變得更加困難,因此早期治療甚至預防性投藥可避免更嚴重的併發症發生。

維生素 B6 是每天都需要攝取的水溶性維生素,在人體的許多代謝過程中皆扮演至關重要的角色。維生素 B6 參與胺基酸合成與正常代謝、有助於紅血球的合成、幫助神經系統的發育,以及維持健全的免疫系統。若妊娠婦女缺乏維生素 B6,可能會造成孕婦疲倦、憂鬱、焦慮,增加噁心、嘔吐及妊娠劇吐的風險,以及影響胎兒神經系統的發育。

對早期妊娠婦女而言,維生素 B6 緩解孕吐的功效已被廣泛研究,許多文獻皆證實其可有效減輕孕婦噁心嘔吐症狀,美國婦產科學會(ACOG)將維生素 B6 列為第一線治療用藥。補充維生素 B6 能有效縮短孕吐病程及改善症狀嚴重程度,且為孕婦用藥 A級安全,因此,早期妊娠孕吐婦女可建議補充維生素 B6 以緩解孕吐。

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The Chamber of Secrets- Endometrial Preparation and Embryo Transfer

Shari Mackens (8/7/1987) graduated as a medical doctor from the Vrije Universiteit Brussel (VUB), Belgium, in 2012. Immediately afterwards, she started working at the Centre for Reproductive Medicine at the University Hospital Brussels, Belgium, as a PhD student and as a specialist in training in obstetrics and gynecology. From 2012 until 2017, she performed basic science research on endometrial receptivity and human embryo implantation. Her research was presented in her PhD thesis entitled 'Hypes and hopes for endometrial receptivity in ART' (2020). At present, she is a medical director at the Centre for Reproductive Medicine at the University Hospital Brussels and a professor at the VUB with a specific interest in translational research focusing on the role of the endometrium in ART.

In her presentation, Prof. Shari will elaborate on the role of the endometrium in human embryo implantation in fresh and frozen transfers following ART. The impact of ovarian stimulation on the endometrium will be discussed, as well as the different possibilities to prepare for frozen embryo transfer. Novel diagnostics and therapeutics will be critically evaluated and a roadmap for future research in this field will be put forward.

Keywords: ART, Endometrium, Embryo Transfer

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Shining a Light: Gene Therapies for Genetic Disorders

Prof. Chien Yin-Hsiu

Gene therapy can provide the opportunity to correct the underlying genetic defect by replacing a functional gene and offers therapeutic benefits to millions of people. The introduction of gene therapy makes neurodegenerative diseases that were once considered incurable now increasingly manageable.

Take the historically leading inherited cause of infant mortality, spinal muscular atrophy (SMA), as an example. SMA is an autosomal recessive disease characterized by degeneration of spinal cord motor neurons, leading to atrophy of skeletal muscle and overall weakness. Recently, novel therapies have ultimately change the disease course and showed significant clinical improvement compared with the historical cohort. Moreover, emerging evidence from clinical trials showed that most patients can achieve motor milestones within normal range by treating them before symptom develops, right after newborn screening.

郭佩雯 L11

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Genetic Screening and Family-centric Genetic Counseling

Kuo Pei-Wen

Gene therapy is changing the treatment landscape of spinal muscular atrophy. Moreover, Taiwan has a world-renowned newborn screening system, which saved numerous babies from tragic consequences before damage occurs. Accurate genetic counseling and an appropriate screening approach are imperatives to optimize the management of patients with SMA. Knowing the caveats, especially the false negatives of genetic testing and carefully interpreting the results are phenomenal for the professional interaction between a healthcare provider and the caregivers.

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Gender Equity in HPV Disease Prevention: What can we do more

The human papillomavirus is a DNA tumor virus that causes epithelial proliferation at cutaneous and mucosal surfaces. More than 100 different types of the virus exist, including approximately 30 to 40 strains that infect the human genital tract. Of these, there are oncogenic or high-risk that are associated with cervical, vulvar, vaginal, and anal cancers, and non-oncogenic or low-risk types that are associated with genital warts.

In recent years, a clear role for this virus in other malignancies is also emerging. Indeed, HPV plays a pathogenic role in a subset of head and neck cancers—mostly cancers of the oropharynx—with distinct epidemiological, clinical and molecular characteristics compared with head and neck cancers not caused by HPV. A rise in oropharyngeal squamous cell carcinoma are being found in a much younger population. Young men and women without the traditional risk factors, like smoking and drinking, are part of a growing trend of patients thought to have contracted the disease from exposure to the HPV.

HPV can also cause genital warts in men, just as in women and increase a man's risk of getting genital cancers, although these cancers are not common. For vaccination programs aiming solely at girls, the protection of men is dependent on the vaccination status of their female partners, and they leave men who have sex with men unprotected. Current girls-only vaccination programs vary by country. In more developed countries, 34% of the females aged 10– 20 years received all three doses of HPV vaccine, compared with only 3% of the females in the less developed regions. Such low vaccination coverage will not provide adequate cancer control or HPV-disease elimination. Gender-neutral vaccination approach can provide benefits to both males and females to help accelerating the elimination HPV related disease.