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L1

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Endometriosis and Long-term Management Strategy

Endometriosis now has been redefined as a systemic inflammatory disease beyond pelvic cavity which require effective and lifelong management. It is characterized by the presence of endometrial tissue outside the uterine cavity, which leads to inflammatory reactions and infiltration of anatomic structures. The disease-associated symptoms such as pain, cramps and fatigue are debilitating and can profoundly affect women' s quality of life in all aspects including sexual life, work life, and social relationships. No permanent cure is available, and the disease often recurs after discontinuation of medications or conservative therapies. The aim of endometriosis treatments is to alleviate disease-related symptoms and to improve the overall quality of life in affected individuals, ideally by maximizing the use of medical treatment and avoiding repeated surgical procedures, especially in those women who wish to preserve fertility. Adequate treatment often requires a dynamic multidisciplinary approach of surgical, hormonal and pain management strategies and may depend on the presented symptoms, endometriosis type and severity, as well as on the women's personal choice. The complexity of the disease with its multiple manifestations and many unexplored aspects is reflected also in an uneven treatment and diagnostic landscape among physicians, medical centers and countries although best-practice guidelines are increasingly attempting to close this gap and to standardize endometriosisrelated procedures.

Even though endometriosis is a chronic disease, some medications have a limited duration of use due to their side effects; gonadotropin-releasing hormone analogues (GnRH-a) have a negative effect on bone mineral density and are normally prescribed for 3–6 months and users of Danazol, a testosterone analog which can cause androgenization, are advised not to take the medication on a continuous, long-term basis without an intake break. Combined oral contraceptives (COCs) are widely used in clinical practice to treat the symptoms of endometriosis but are not approved for this indication and their efficacy is still debated. Thus, there is an outstanding need for an effective and well-tolerated long-term medication. And Dienogest (DNG) 2 mg is a 19-nortestosterone derivative progestin which was launched in Europe for endometriosis treatment in 2010 and was shown to cause a reduction in endometriosis-related pain, while suppressing estrogen levels only moderately. In more and more international guidelines and expert consensus, dienogest is strongly recommended as the first line treatment and be used as long-term therapy for endometriosis. In this talk, I will share more evidence and discuss these strategies for long-term endometriosis management.

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L2

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維生素B6於情緒調控之臨床新知

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Mood disorders including major depression and anxiety are major health problems that undermine quality of life, health care costs and increase disability, medical morbidity and mortality. The affected population is estimated about more than 350 million in 2020 with significant growing trand, reported by World Health Organization. Malnutrition plays a major contributor to the eiotlogy of mood disorders. Associations of vitamin B6 deficiency and major derpessive symptoms are consistently reported across age, gender and regions. Vitamin B6, a collective term for 6 chemical compounds, is most active in the form of pyridozal 5' phosphate (PLP). They participate as enzymatic cofactors in more than hundes of biochemical pahtyways that are essential in the production of amino acids, neurotransmitters, heme and the metabolisms of fatty acids and glycogen. Many of these compounds play critical roles in the development of psychiatric disorders and are promising therapeutic targets in managing mood disorders. In this session, an updated knowledge of vitamin B6 in current research will be discussed with the following highlights.

- Positive correlation between vitamin B6 and depressions is reported in young adults, postpartum women, geriatric population and those with particular lifestyles, such as contraceptive and alcohol use. Findings are consistent in both cross-sectional observations and longitudinal follow ups.
- An insight of the underlying pathophysiological mechanisms involving serotonin, tryotophan and gamma-aminobutyric acid (GABA) in the nervous system and immune system is examined.
- Evidence of the therapeutic benefits of vitamin B6 in depression is analyzed in both clinical data and animal studies.

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L3

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Genome-wide NIPT: 國外及台灣單一實驗室經驗

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NIPT uses cell-free DNA (cfDNA) in maternal plasma derived from the placenta to screen for fetal aneuploidies. Although many NIPT technologies are based on low pass whole-genome sequencing and allow detection of rare autosomal trisomies (RAT) and copy number variants (CNVs), offering genome-wide NIPT (GW-NIPT) to pregnant women has been the subject of scientific debate. To date, the performance of cfDNA screening for CNVs has been less than ideal. Several studies have documented a significantly lower positive predictive value (PPV) for CNVs compared with common aneuploidies. Similarly, the sensitivity of cfDNA screening for CNVs appears suboptimal. There is little consensus regarding these estimates, with values for both PPV and sensitivity varying dramatically across studies. Most reports include information only about positivity rates, and therefore PPVs have been calculated from those cohorts. The cohorts in these studies are heterogeneous and any contain fetuses with ultrasound anomalies, suggesting that estimates are likely to be impacted by ascertainment bias. The reported PPVs ranging from 0% to 80.56%. (Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genetics in Medicine 2023)

RATs are any trisomy other than those involving chromosomes 13, 18, 21, X, or Y. The positive predictive value of cell-free DNA in diagnosing RAT is approximately 11% according to a meta-analysis published in 2023. (Melissa L. Acreman et al, The predictive value of prenatal cell-free DNA testing for rare autosomal trisomies: a systematic review and meta-analysis American Journal of Obstetircs & Gynecology 2023).

From 2014 to 2023, Taiwan Gene Health provided GW-NIPT for the pregnant women. The PPV is 22% for all CNVs, 33% for trisomy 9, 0% for trisomy 16, 14% for trisomy 22, and 2% for other RATs. An accurate determination of birth prevalence, sensitivity, and negative predictive value (NPV) was extremely difficult and not performed. Clinical validation of NIPT for rare disorders is challenging. Small CNV-driven syndromes or low-grade mosaicism often escape detection even at birth, making an accurate determination of birth prevalence, PPV and negative predictive value (NPV) difficult. Additional studies that include follow-up genomic testing of newborns are needed to correctly define the sensitivity, PPV and NPV.

許世典 L4

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【子宮頸癌-台灣現況與展望】如何加速消弭子宮頸癌

人類乳突病毒(HPV)是一種常見的性傳播病毒,也是許多癌症的主要原因之一。根據統計數據,在全球範圍內,HPV 感染與子宮頸癌、肛門癌、口腔咽喉癌等多種癌症有關。我們從 HPV 疫苗預防效果及其安全性數據顯示,HPV 疫苗可以預防感染 HPV 病毒,並減少相關癌症的風險。根據研究顯示,接種 HPV 疫苗能有效預防導致子宮頸癌和其他 HPV 相關癌症的高風險型別。此外,疫苗也被證明對於預防 HPV 感染的其他常見型別有一定的保護效果。關於疫苗的安全性,多項研究表明,HPV 疫苗是安全有效的。雖然 HPV 疫苗通常在青少年接種,但熟女施打 HPV 疫苗仍然具有重要性和保護效益。根據研究,即使在成年女性施打疫苗,也能減少 HPV 感染及相關癌症的風險。此外,施打 HPV 疫苗可以提高熟女健康保護的綜效,預防性器官癌症和其他相關疾病。積極配合世界衛生組織(WHO)制定 2030 年消滅子宮頸癌的全球策略,我們應提供完整的子宮頸癌預防措施,包括廣泛推廣 HPV 疫苗接種和增加篩查和治療服務的可及性,以實現在全球範圍內消滅子宮頸癌的目標。

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How to optimize the management of preterm labor

Preterm birth is a significant global health issue affecting 11% of pregnancies globally every year. The consequences of prematurity are significant with an increased incidence of conditions such as cerebral palsy, neurodevelopmental delay, bronchopulmonary dysplasia and necrotizing enterocolitis. The risks of these complications occurring are inversely proportional to the gestation of delivery.

Current strategies to minimize the effects of preterm delivery focus on three aspects: prediction prevention and preparation/optimization. Prediction entails ensuring that women who have risk factors for a preterm delivery are reviewed early and by appropriately experienced clinicians to evaluate the likelihood of a preterm delivery. This can encompass taking a thorough history and assessing features such as an ultrasound derived cervical length assessment and considering biomarkers for prediction of preterm labour such as quantitative fetal fibronectin. These components can be combined by using predictive algorithms such as the QuIPP app to individualise risk prediction for high risk women.

Preventative strategies can then be deployed. These include giving women with existing risk factors such as a previous preterm delivery progesterone or women who have a short cervix identified on transvaginal ultrasound (less than 25mm). High risk women who are identified to have a short cervix can either be offered cervical cerclage (RCOG Greentop Guidelines on Cervical Cerclage).

When despite these interventions women still present in preterm labour additional treatments can be given to mitigate the effects of prematurity. These include steroids to promote lung maturity (although they have a therapeutic window of optimal effect which is up to 7 days) commonly administered from viability to 34 weeks gestation and considered 34-35+6 (NICE), Magnesium sulphate can also be administered as a neuroprotective agent reducing the incidence of subsequent cerebral palsy. Tocolytics can be beneficial in certain situations. All tocolytics have been shown to reduce the chance of delivery within 48 hours or 7 days. This facilities time for steroids and magnesium to have their maximum benefit improving neonatal outcomes and allows transfer to other hospitals where appropriate. Tocolytics can have significant adverse maternal effects causing cessation of treatment which needs to be considered when choosing an agent. Betamimetics can cause significant adverse side effects such as maternal hypotension. Currently NICE guidelines advocate the use of Nifedipine as a first line agent although atosiban is licenced in the UK as a tocolytic and has an excellent side effect profile. The WHO also advocates the use of calcium channel blockers/atosiban or nitric oxide donors. In certain situations atosiban may be an appropriate first line agent, for example women with cardiac disease or multiple pregnancies. This talk will outline the evidence regarding tocolytics at present and how WHO, NICE and ACOG guidance currently differs. After the session clinicians will be able to understand rationale for tocolytic choice in women who present in early preterm labour.

Keywords: preterm birth, tocolysis

Highlights

- Tocolytics can be associated with a reduction in neonatal morbidity as they facilitate time for steroids and Magnesium to have their maximal effect as well as allowing for transfer to other units were appropriate
- Risk benefit analysis needs to be undertaken when deciding which tocolytic agent is most appropriate.

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各階段女性的體重管理策略 Women's Weight Management Over Generations

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肥胖會對人體帶來諸多不良影響,像是心血管健康、患病罹癌風險、骨骼關節負擔等等;但女性肥胖造成的不良影響會是男性兩倍。肥胖者發生糖尿病、代謝症候群及血脂異常的風險超過3倍,發生高血壓、心血管疾病、膝關節炎及痛風也有2倍風險。研究證實,當肥胖者減少5%以上體重(如成人90公斤,減少5公斤),就可以為健康帶來許多益處,高血壓、糖尿病等與肥胖相關疾病將可改善。

Liraglutide 是一種與人體陽道荷爾蒙 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。