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## E4/DRSP——口服避孕藥的新紀元

### E4/DRSP – a new era in oral contraception

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Combined oral contraceptives (COCs) contain a progestin to inhibit ovulation and an estrogen. The estrogen component contributes to the contraceptive activity and balances the progestin effect to provide an acceptable bleeding pattern and to counteract any potential estrogen deficiency symptoms. Estetrol (E4) is a natural human estrogen produced during human pregnancy in the fetal liver with a unique mechanism of action that displays tissue-selective activity, and behaves as a natural selective estrogen receptor modulator. It has a moderate affinity for both human estrogen receptor alpha (ER $\alpha$ ) and beta (ER $\beta$ ), with a preference for ER $\alpha$ . In preclinical models, estetrol has lower binding affinity for the estrogen receptor- $\alpha$  (ER- $\alpha$ ) in contrast to estradiol and has antagonistic properties against membrane ER- $\alpha$  in several tissues, including the breast, while retaining agonistic activity on receptors located in the nucleus. The low estrogenicity of estetrol may potentially contribute to reduced thrombotic risk.

Clinical studies have demonstrated possible use as an estrogen in combined oral contraceptives (COCs). COCs containing E4 and drospirenone (DRSP) showed a high acceptability, tolerability, and user satisfaction also when compared to COCs containing ethinyl estradiol (EE). E4/DRSP effectively inhibits ovulation, with a similar effect on endometrium thickness than that of EE-containing COCs. Low doses (15 mg) of E4 with DRSP (3 mg) showed promising results in term of bleeding pattern and cycle control, also when compared to other COCs containing synthetic estrogens. Moreover, the association has limited effects on serum lipids, liver, SHBG levels, and carbohydrate metabolism. This combination also could drive a lower risk of venous thromboembolism than EE-containing COCs. E4/DRSP is an effective and generally well-tolerated COC, with a potentially reduced risk of thrombosis.

*Prakash Trivedi*  
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  - 2023, 2016: Scientific Program Chair of AAGL International MIS CONGRESS in Mumbai, India
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  - 2015: President of FOGSI (Federation of ObGyn societies of India)
  - 2013-2015: President of IAGE All India Gyn endoscopy
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## When why & how to use a novel Progesterone for Endometriosis Infertility & bleeding during pregnancy

Dr. Trivedi's Total Health Care Hospital and Aakar IVF Centre, Mumbai is a University recognized centre for Post - Doctoral training, further it is a major referral centre for Endometriosis and Fibroids for more than 2 decades. By this talk, he will highlight the use of dydrogesterone in endometriosis which was publish as an original article as a part of meta-analysis from 1978 to 19<sup>th</sup> September 2019. Also, he will share experiences of endometriosis treated with dydrogesterone.

**Endometriosis:** The unique affinity of dydrogeseterone for ectopic endometrium i.e. endometriosis which decidualizes it and hence treat. The most important aspect of dydrogesterone is that it can be used from day 5 of period onwards without affecting ovulation and period.

● **Mild endometriosis:** In diagnosed mild endometriosis we start dydrogesterone from day 5- day 25 along with stimulation with ovulation induction tablets and injections for 3-6 months.

● **Moderate endometriosis or endometrioma:** If laparoscopic surgery is done, then after a surgery dydrogesterone is started from day 5 along with ovulation induction tablets and injections. Once patient misses the period dydrogesterone is still continued till 10-12 weeks.

● **Severe endometriosis:** In such cases depending on the EAPP (Endometriosis associated pelvic pain) after doing the AMH a good laparoscopic surgery is preferred. Then on stimulation dydrogesterone is added from day 5 till results.

**Endometriosis in ART:** In patients wherein there is a need of ART due to Endometriosis or any other factor we prefer to start dydrogesterone 10 mg thrice a day from day 5 onwards. The use of vaginal micronize progesterone is limited to 200 mg at night which continues till 14 weeks. If pregnancy results then dydrogesterone is continued till 24 weeks as it has the best immune modulatory effect to prevent abortion, pregnancy loss and mid trimester pregnancy loss. Use beyond 24 weeks doesn't have scientific support to reduce preterm labour or PROM.

*Please check more details in Dr. Trivedi's speech for the other indications and clinical practices because this is just an abstract.*

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### Challenge in endometriosis diagnosis

Endometriosis is an estrogen-dependent, progesterone-resistant gynecologic condition characterized by the presence of ectopic endometrial-like tissue outside the uterine cavity; endometriosis is strongly affected by cyclic changes in response to steroid hormones and is associated with an inflammatory response in the peritoneal cavity. Endometriosis is characterized by chronic pelvic pain, with common clinical presentations of dysmenorrhea, dyspareunia, dyschezia, dysuria, and infertility. Accordingly, it is an important cause of morbidity that can detrimentally affect the quality of life (QoL) in women of reproductive age. Delay in diagnosis of endometriosis is commonly reported, some as long as 11 years. Studies of diagnostic delays in Asia are less common, but it is possible that diagnosis in Asia may occur earlier including because of cultural and socioeconomic barriers limiting access to care. These delays can result in ongoing symptoms that detrimentally affect QoL and fertility. Limitations in current approaches for diagnosis of endometriosis may be contributing to these delays.

## 吳孟興

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### APAC Expert Opinion: Closing endometriosis diagnostics gaps in Taiwan

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 2022, clinicians with expertise in the diagnosis and treatment of endometriosis within APAC region met to critically addressing the diagnostic delays in endometriosis (APAC Endometriosis Expert (APEX) Panel Meeting) is to present the consensus from a group of Obstetrics and Gynecology experts across Asia Pacific on the followings:

- To address the diagnostic delays in endometriosis within APAC
- To discuss current practices and challenges in the diagnosis of endometriosis
- To identify barriers to diagnosis and causes of diagnostic delays in endometriosis
- To propose actionable measures to address these diagnostic delays

Learning from APEX panel meeting, today's lecture will be focused on how we can close the diagnostics gaps in Taiwan.

## 陳芳萍

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### Estriol review: Clinical Application of Esvatin

There are three major endogenous estrogens that have estrogenic hormonal activity: estrone (E1), estradiol(E2), and estriol (E3). Estriol is a dominant estrogen during pregnancy, and is secreted mainly by the placenta. Estriol possesses the weakest estrogenic effects of the three and has preferential affinity for estrogen receptors (ER)  $\beta$ . Thus, estriol is described as a relatively weak estrogen and has mixed agonist-antagonist activity at the ER.

Although estriol has weaker estrogenic effects, many studies demonstrate that estriol helps not only relieve menopausal symptoms, but also benefit bone, genitourinary tract health, and markers of cardiovascular risk. In addition, estriol acting as an antagonist of G protein-coupled estrogen receptor 1 (GPER) may reduce pro-carcinogenic effects of more powerful estrogens like estradiol. Thus, estriol is marketed widely in Europe and elsewhere throughout the world. However, for enhanced safety, topical estriol is generally recommended, especially for symptomatic genitourinary syndrome (GSM), to alleviate symptoms and to restore atrophic anatomic changes.

Several treatment options are recommended by “The 2022 genitourinary syndrome of menopause position statement of The North American Menopause Society”. Why choose Esvatinas low-dose vaginal ET for women suffering GSM? Esvatin vaginal tablets contain estriol and are safe and effective for GSM, since compared to estradiol, estriol possesses the weaker estrogenic effects and has preferential affinity for ER  $\beta$ . ER  $\beta$  is predominantly expressed at the non-squamous transitional epithelium of the lower urinary tract. In addition, as aforementioned, estriol has mixed agonist-antagonist activity at the ER and acts as an antagonist of G protein-coupled estrogen receptor 1 (GPER). Thus, the potential risk for endometrium and breast is very low. Furthermore, since estriol is not converted to estrone or to estradiol, systemic side-effects are limited.

In the presentation, the clinical effects and safety of estriol will be discussed. Especially, it will be demonstrated why Esvatin (estriol) vaginal therapy should be considered for clinical use in GSM.

## 黃玉成

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### 產前及產後孕婦及新生兒疫苗-百日咳疫苗最新臍帶血研究及小兒腦膜炎疫苗介紹

Pertussis, also known as whooping cough, is a highly contagious disease caused by the bacterium *Bordetella pertussis*. The disease is primarily spread through airborne droplets. Vaccination against pertussis during pregnancy has been widely recommended in several countries to reduce the incidence of pertussis-related morbidity and mortality in newborns. However, the ideal timing of vaccination during pregnancy to achieve maximum protection for infants remains unclear. The newest study conducted a multi-country analysis to determine the impact of vaccination timing during pregnancy on infant antibody levels at birth.

Meningococcal disease in infants is a serious condition caused by a type of bacteria called *Neisseria meningitidis*. It can result in meningitis and sepsis, which can be fatal or lead to long-term complications. Fortunately, there are vaccines available that can help protect against this disease. It is important for parents and healthcare providers to be aware of the risks and prevention strategies associated with meningococcal disease in infants, and to consider vaccination as a way to reduce the likelihood of infection.

After the session, clinicians would better understand the newest vaccine study for Pertussis and Meningococcal disease.

Keywords: Pertussis, Meningococcal disease, vaccine

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## Women's weight management over generations

劉安潔

禾馨民權婦幼診所婦產科

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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## HIFU (high intensity focused ultrasound) surgery in gynecology: State of Art 2023

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Uterine fibroids and adenomyosis are common benign pathology condition of the female, especially in childbearing age. The incidence ranges from 20 to 40% in reproductive aged women. For this reason, they may gravely affect the fertility of women and cause cyclic menstruation symptoms such as dysmenorrhea and hypermenorrhea.

Surgical interventions such as myomectomy or hysterectomy, performed conventionally or laparoscopically, are the most common treatments for uterine fibroids and adenomyosis.

However, surgical intervention usually let women hesitate to treat their diseases. Hysterectomy is even a nightmare for many women. High-intensity focused ultrasound (HIFU) has been shown to be a successful non-surgical treatment for fibroids in many studies over the last 15 years.

HIFU ablation presents an attractive option to conventional and surgical medicine, as it is non-invasive, requires minimal hospitalization, has no surgical wound, and has good relief and outcome in many patients. Social and economic cost in days lost of work and production are minimized compared to open surgery. Other growing applications of HIFU ablation include liver cancer, osteosarcoma and solid tumors such as the kidney, breast, thyroid and prostate.

In our hospitals, we successfully used ultrasound-guided focused (USgFUS) to treat nearly 2000 cases of uterine fibroids and adenomyosis so far. The majority of patients improved their quality of life and were satisfied with the treatment results.

HIFU is safe and effective in treating uterine fibroids and adenomyosis. It is a reasonable treatment alternative with the advantages of symptom-relieving, non-invasiveness, minimal adverse reactions, rapid recovery and readiness for pregnancy.



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## The emerging trend of HPV gender neutral vaccination

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.

## 蔡慶璋

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### 孕產期呼吸道疾病預防新思維

Pregnancy is a time of excitement, anticipation, and preparation for the arrival of a new life. However, it can also be a time of increased vulnerability to infections and illnesses, which can have serious consequences for both the mother and her developing baby. The COVID-19 pandemic has added a new layer of concern for pregnant women, as the virus can cause severe illness, hospitalization, and even death.

Fortunately, vaccines have been developed to protect against COVID-19, as well as other infectious diseases that can affect pregnant women and their newborns. Several studies found that vaccinating against these diseases during pregnancy not only protects the pregnant woman but also provides protection to their newborns. For example, vaccinating against COVID-19 can reduce the risk of severe illness and hospitalization for pregnant women. It can also provide passive immunity to the baby through the transfer of antibodies in breast milk and the placenta. Similarly, the pertussis vaccine can protect newborns from contracting pertussis, a potentially fatal respiratory illness. Finally, the flu vaccine can reduce the risk of flu-related complications during pregnancy, such as pneumonia and premature labor. It can also provide passive immunity to the baby, protecting them from the flu during the critical first few months of life.

As a frontier healthcare provider, we shall educate pregnant women about the benefits of vaccinating against COVID-19, pertussis, and flu proactively. By taking this step, they can protect themselves and their babies and ensure a healthy start to their new lives together.