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Progestin-only systemic hormone therapy for menopausal hot flashes

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Hot flash is one of the most common vasomotor symptoms related to hypoestrogenemia in postmenopausal women. Although estrogen replacement therapy is the best and direct treatment for hot flash, it is always concerned regarding its risk of increasing thromboembolic events, breast and endometrial cancers, and hepatobiliary function deterioration. Especially for women with pre-existing diseases as endometrial cancer, endometriosis, leiomyoma, gall bladder stone and liver diseases etc. that make estrogen containing hormone replacement contraindicated.

The field of menopausal medication is dominated by studies reporting the effectiveness of systemic estrogen or estrogen-progestin hormone therapy for hot flashes. The effectiveness of progestin-only systemic hormone therapy for the treatment of hot flashes is much less studied and seldom utilized in clinical practice. Recently, increasing evidences have revealed progestin-only therapy can also effectively treat hot flushes and is an option for women with a contraindication to estrogen therapy.

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Management of perimenopausal endometrioma

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Endometriosis affects up to 10 percent of women and is defined as the presence of endometrial glands and stroma outside the uterine cavity, predominantly, but not exclusively, in the pelvic compartment. It is an estrogen-dependent chronic inflammatory condition that affects women in their reproductive period, and is associated with pelvic pain and infertility. One of the most common manifestations of the disease is the presence of an ovarian mass arising from growth of ectopic endometrial tissue in the ovary, called ovarian endometrioma or chocolate cyst. Between 17% and 44% of patients with endometriosis have ovarian endometrioma. In addition, the association between endometriosis and specific epithelial ovarian cancer histotypes is assumed to be causal.

As defined by the STRAW criteria the terms perimenopause or menopausal transition cover the transition from the reproductive age through to menopause, i.e. early perimenopause stage -2, late perimenopause stage -1, the last menstrual period stage 0 and early postmenopause stage +1. Menstrual periods may be more frequent and heavier during the years leading up to full menopause, meaning women with endometriosis may find symptoms occur more often and are worse during this time. Endometriosis is estrogen-dependent, so when estrogen is gone, so is the disease. However, this does not mean every woman suddenly finds herself pain-free at menopause. Chronic pelvic pain may continue, and we’ ll tackle that very important condition in a future blog.

Whether symptoms abate or not, after menopause, conversations about endometriosis may need to include some additional concerns: Osteoporosis; women who have been controlling endometriosis symptoms by taking medications that reduce estrogen may be at higher risk of osteoporosis. Recommendation of women ask about osteoporosis medications like anti-resorptive drugs and be diligent about bone density testing, bone-healthy habits, and follow-up. Auto-immune disorders; endometriosis is not considered an autoimmune disease, but it does appear that women who have endo are at higher risk of such diseases, including lupus, MS, arthritis and coeliac disease, as well as allergies and asthma. Women should be vigilant about their health, and if they start to develop new symptoms should pay more attention. Cancer; women with endometriosis may face a slightly higher risk of ovarian cancer, and because the symptoms can mimic those of endometriosis, women should pay attention if symptoms worsen or return.

MHT may or may not bring symptoms back, as it is lower dose than menstrual hormones. Many women do just fine if they wait a year or so to start. Hormones that are applied topically may also have less chance of reviving endometriosis.

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Female hormones and Covid – how relevant are they?

病毒對人類的健康威脅，尤其是在新冠病毒肆虐之後顯得越來越嚴重。在美國的報告，新冠病毒所造成的人類死亡，已經位居十大死亡原因的首位。臺灣在今年，由於新冠病毒的變異，導致防疫越來越困難。從世界各國的經驗，接種新冠病毒疫苗是最有效的防疫方法。但是目前的新冠病毒疫苗，也常見有一些嚴重的副作用，其中最重要的就是血栓，尤其是在婦女族群，當使用避孕藥會加重血栓發生。因此，有關女性使用荷爾蒙，與新冠病毒疫苗接種，是否應列為警示，於是出現很多爭議。在今天演講，將會闡述婦女荷爾蒙與新冠病毒疫苗的相關性。

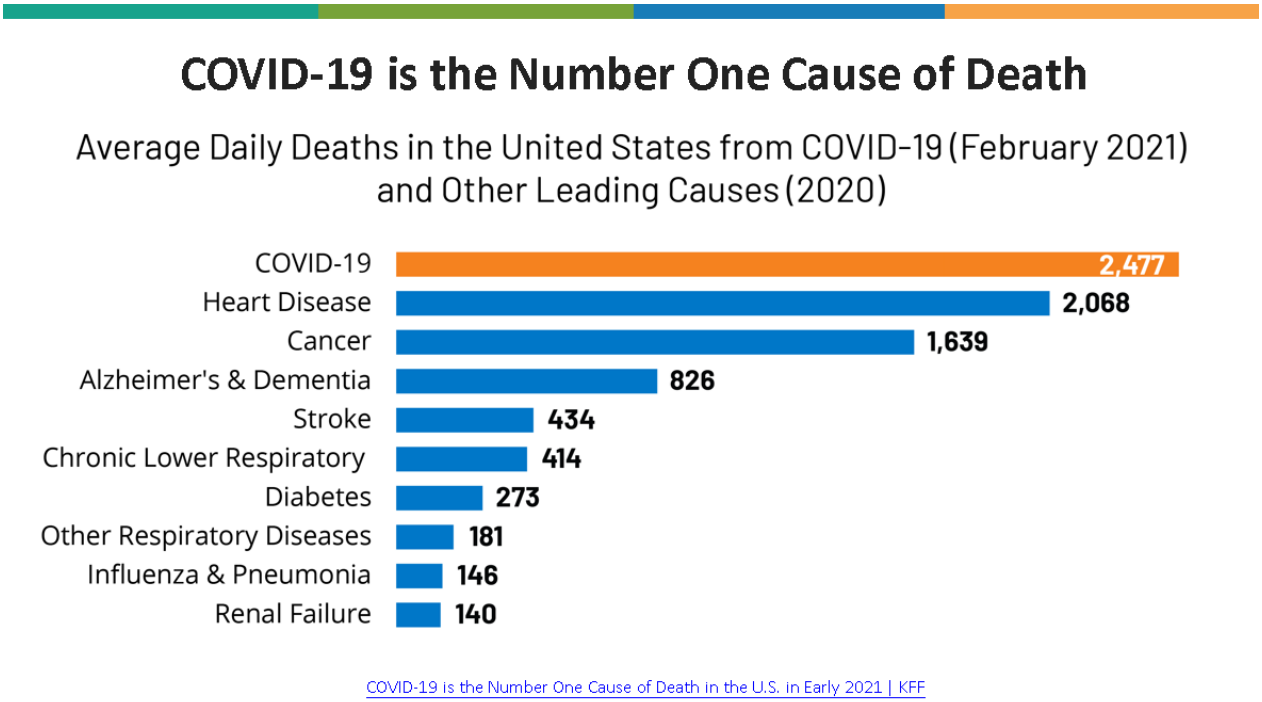
在去年世界各國接種新冠病毒苗後，統計數據發現有較高的血栓發生。因此，在去年的臨床指引，便有針對正在使用荷爾蒙藥物的女性，告知要務實且應謹慎使用新冠病毒疫苗。但是在後來的各國數據報告呈現，會產生血栓真正的原因，與荷爾蒙的關係仍有很多爭議。

首先，會導致血栓最主要的原因，並不是荷爾蒙，而是由新冠病毒所造成的血管發炎反應，帶有新冠病毒的人會造成血栓的發生率，是服用荷爾蒙製劑病患的 100 倍。尤其是使用荷爾蒙複方藥，也就是有黃體素合併動情素的荷爾蒙，確實會增加血栓的風險。可是從文獻的資料呈現，如果只是使用黃體素荷爾蒙製劑的婦女，並不會增加血栓的風險。也就是意謂著，會造成血栓風險的荷爾蒙，只限於有複方成份的荷爾蒙，而不是黃體素荷爾蒙。因此，當使用黃體素荷爾蒙的婦女，仍可安全接種新冠病毒疫苗。同時，全世界在經過 1 年多新冠病毒肆虐之後，意外發現女性罹患新冠病毒的感染率，與男性相同。但是，女性罹患新冠病毒的死亡率，卻只有男性的一半，也就是女性荷爾蒙對新冠病毒，有降低演變成為重症，以及減低死亡率的效益。

事實上，在以往流行性感冒的重症與死亡率，也有發現同樣的結果，也就是女性荷爾蒙，可以降低病毒感染的重症率與死亡率。因此。荷爾蒙對於新冠病毒，到底是正向還是負向的因素？反而引起醫學界更大的重視。

在今年，經過感染族群的大數據分析結果呈現，有荷爾蒙分泌的女性，罹患新冠病毒的重症率和死亡率遠低於男性，或是也低於更年期的婦女。因此，女性荷爾蒙對於新冠病毒來說，並不是一個負向的機轉。謹慎地使用荷爾蒙，反而對新冠病毒的重症率和死亡率，具有預防與保護的效果。因此在荷爾蒙的使用，對新冠病毒來說，除了有積極的預防成為重症與降低死亡率的效果之外，黃體素荷爾蒙也不會增加血栓的風險。所以當民眾接種新冠病毒疫苗時，並不需要禁止或限制使用黃體素荷爾蒙。此外，新冠病毒疫苗與血栓的關係，經過兩年來的世界大數據觀察發現，不管是哪一種疫苗，其發生血栓的風險一致，發生的機率是十萬分之 4 至 6，所以也不會有血栓風險的人，應該避免接種疫苗。

總結，當民眾接種新冠病毒疫苗時，可以告知婦女朋友們，應避免使用複方的避孕藥，可以轉換成為使用單方黃體素的避孕藥。除此之外，當民眾使用荷爾蒙製劑，用來預防子宮內膜異位的時候，使用黃體素單方的相關藥物是安全的。



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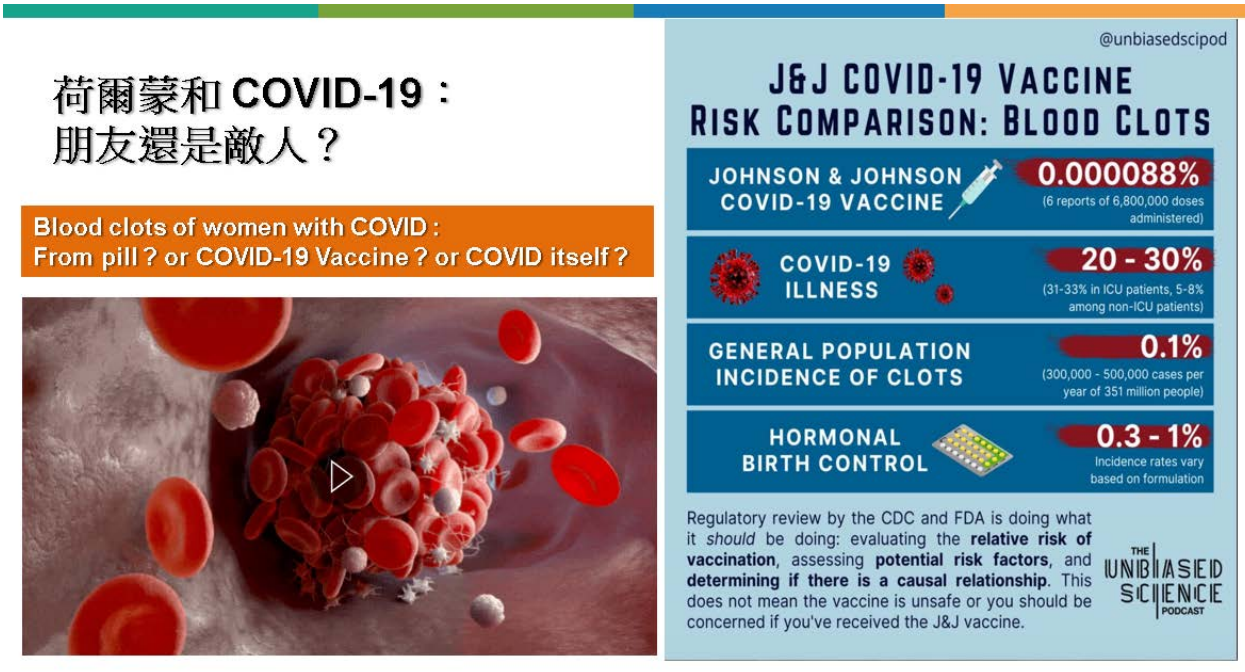

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Optimal Dosage of Estrogen for MHT

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Despite previous reports have suggested it might be some specific progestins in the regimen of MHT that increased the risk of breast cancer, long-term estrogen exposure alone might increase breast cancer risk has been reported in some studies. It is not known whether use of lower dosages of estrogen will be less likely to increase the risk of breast cancer but high dose of estrogen can increase the breast density as demonstrated in mammography.

Lower doses of estrogen appear to be as effective as the most commonly prescribed doses for relief of vasomotor symptom after menopause and may allow more patients to obtain the benefits of MHT. Although Recent studies have suggested transdermally administered estrogen has little or no effect in elevating prothrombotic substances, but the result is dose depended. The use of transdermal MHT containing low doses of oestrogen was proved safer and not associated with an increased risk of stroke.Garciia-Perez et al. reported similar efficacy of low and standard doses of transdermal estradiol in controlling bone turnover in postmenopausal women.Low dose estrogen and calcium have an additive effect on bone resorption in older women. Lower doses of CEE/MPA were also reported to be effective in relief patient from vaginal atrophy and protecting the endometrium.

Women taking low dosages of estrogens are less likely to have unacceptable side effects and potential harm caused by standard dosages of estrogen with progestin may be prevented by use of lower estrogen doses.Start MHT with lower doses, and titrate up to relieve symptoms if necessary. The intention, dose and regimen of HRT need to be individualized, based on the principle of choosing the lowest appropriate dose in relation to the severity of symptoms and the time and menopause age.

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