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高尿酸血症與婦女健康之精準醫療

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血中尿酸濃度高會引發“痛風”[Gout, Podagra]，是一個非常古老的疾病，為公元前 2640 年埃及人首先發現稱“podagra”好發在第一蹠趾關節的急性痛風；西元前四百六十多年，醫學始祖醫學之父 Hippocrates[西波克拉底] 對這個”腳痛且不良於行的現象稱 “無法行走的疾病” 並有五個經典性描述 1.太監不禿頭不痛風 2.女人不痛風，除非她的月經停止了 3. 青少年在性交前不會患痛風 4. 痛風發作、炎症要 40 天 5. 痛風在春秋兩季活躍。 縱觀歷史，痛風與豐富的食物和過量飲酒有關。因為痛風在過去，顯然與富人才能負擔得起的生活方式有關，所以痛風被稱為“國王病”。在 2000 多年前古希臘有證據當時人們能從秋番紅花（秋水仙）中提取秋水仙素，此種生物鹼被用作強效瀉藥，秋水仙素首次作為選擇性和特異性治療痛風的方法是歸功於拜占庭公元六世紀，Tralles 的基督教醫師亞歷山大。在現代 20 世紀，非副腎皮質體類抗炎藥（NSAID)則是治療急性痛風的首選藥物。治療高尿酸血症最重要的歷史進展 ，實屬黃嘌呤氧化酶抑製劑(Xanthineboxidase inhibitors)的開發，該抑製劑可有效降低血漿尿酸濃度，排尿酸劑於 19 世紀末首次使用。可以逆轉痛風石沉積物的形成。

尿酸是瞟呤的代謝產物在高等哺乳類動物生理系統如人類或者是人猿才有在生理的情況：尿酸形成 分泌和排泄系統是要維持血尿酸平衡，當系統出問題，發生高尿酸血症，檢驗報告 後面加註的正常範圍，是根據多年來流行病學的調查：男性的尿酸超過 7mg/dL,女性高過 6 可稱之高尿酸血症，然近年來對心臟血管更深入研究發現尿酸濃度女性高過 4.7 ， 男性的尿酸超過 5.6，都會增加整體死亡率和心臟血管疾病的死亡率; 由於不健康的生活形態越來越多 ,不止三高愈多，高尿酸血症的情況也日益增加，2019 中國大陸就報告境內高尿酸的有 170 百萬人口而同時美國有 32.5 百萬人口；1980 開始 Framingham 心血管疾病研究顯示高尿酸與心血管疾病風險相關，帶起專家學者之重視，對高血壓，糖尿病，血管粥狀硬化，慢性腎臟病疾病，和心房顫動影響不容忽視，尤其分生病理研究尿得知高尿酸血症之酸結晶分子會導致發炎反應，胰島素阻抗，內皮細胞功能失調，和胞內內質網破壞的病理分生變化，至今高尿酸與健康的關係是不亞於高膽固醇心血管疾病 ，高血糖新陳代謝，高血壓 等慢性三高後的第四高！實證臨床使用降尿酸藥物 allopurinol 經驗顯示降尿酸藥物可以改善心血管疾病 的預後（all course of morality， MI，congestive HF ）CHD 有 hyperuricemia 患者）。降低尿酸的藥(ULT)實分二大類一、降低尿酸合成（如 allopurinol, febuxostate)二, 增加尿酸排出(如 benzbromarone, probenecid, dapagliflozin… etc)。近期研究重點是 ULT 不止對慢性疾病的改善預後，更期盼對慢性疾病的預防，例如在年輕高血壓病患，allopurinol 有不錯的預防效果。

■專題演講——一般婦科

21 世紀近年來 分生技術進步，尿酸的代謝研究，進入生理病理分子機轉和並進一步了解其調控蛋白質與基因背景分析調查,多個跟腎臟廓清尿酸蛋白：SLA2A9, ABCG2, SLC17A1, SLC22A11, PDZK1,SLC16A9,SLC11A122 的基因多形性與高尿酸血症明顯相關，公衛的調查顯示：一般 女性血中尿酸濃度較同齡男性較低，與雌激素明顯相關，因爲雌激素對腎臟近端調控尿酸再回收轉運蛋白質功能有重要之調控角色！

２１世紀重個人化醫療 強調超前部署已是時勢所趨， 高尿酸血症不只影響男性 也影響女性心血管健康；高尿酸血症不只是男人的痛風病，其對婦女健康有明顯不良影響，故高尿酸血症體質，若在合併 相關慢性病必需精準管理尿酸濃度減少對心血管，腎臟之傷害 :諸如減重至理想體之體脂， 膳食成分要質與量的調整，即時添加膳食優化補充劑，例如櫻桃；儘量減少酒精之攝入；在可能、適當和安全的情況下，不用”減少尿酸鹽排泄或增加尿酸鹽產生的藥物和膳食添加劑” ，賀爾蒙失調女性，尤其建議善用精準醫療。

Hyperuricemia is due to high levels of uric acid in the blood and is the main cause of gout. A manifestation of gout is podagra, which is a painful condition of the big toe and was first identified by the Egyptians in 2640 BC. In 460 BC, Hippocrates, the father of medicine, referred to podagra as “the unwalkable disease.” In the distant past, gout was most common in wealthy people with excessive food and alcohol intake; therefore, it was also called “the disease of kings.”

Uric acid is a metabolite of xanthine, which is a purine, by the action of xanthine oxidase. Normally, uric acid is converted to allantoin by uricase and later to urea, which are excreted in the urine. Normal uric acid levels are 2.4-6.0 mg/dL for women and 3.4-7.0 mg/dL for men. However, it was recently found that females with a level > 4.7 mg/dl and males with a level >5.6 mg/dl have increased mortality rates and higher risk of cardiovascular diseases.

Colchicine is an alkaloid derived from *Colchicum autumnale.* It was originally used as a laxative in ancient Greece about 2000 years ago and was first used to treat gout by the Byzantine Christian physician Alexander of Tralles at about 600 Anno Domini (AD). *Colchicine* has anti-inflammatory effect and can quickly reduce the swelling and buildup of uric acid crystals in affected joints. Although colchicine is generally well tolerated at prescribed doses, it has a narrow therapeutic window and has caused fatalities with single doses as low as 7 mg. The most common side effects are diarrhea, vomiting, and nausea, which may occur in > 20% of colchicine users.

In recent years, non-steroid anti-inflammatory drugs (NSAID) are the first line medicines for gout. The most important historical advance in the treatment of gout was the development of xanthine oxidase inhibitors, which reduce the production of uric acid. Currently, there are two different ways to treat hyperuricemia. The first one is to reduce the production of uric acid using drugs such as allopurinol and febuxostat. The second method is to increase the excretion of uric acid with drugs such as benzbromarone, probenecid, and dapagliflozin.

Similar to hypertension, hyperlipidemia, and hyperglycemia, the prevalence of hyperuricemia has significantly increased in recent years because of unhealthy lifestyles. In a

recent study, 170 million in China and 32.5 million in the US were found to have hyperuricemia. High serum uric acid levels have been shown to be a prognostic predictor of survival in heart failure. Furthermore, hyperuricemia associated with uric acid deposit has been identified as a risk factor for ischemic heart disease, stroke, peripheral arteriopathy, and renal failure. The risk of developing hyperuricemia in men is 5 times higher than women. However, postmenopausal women have a risk almost as high as that of men, mainly because of decreased levels of estrogen, as it can enhance the activity of proteins involved in the reabsorption of uric acid.

With the advance in molecular medicine, several proteins such as SLA2A9, ABCG2, SLC17A1, SLC22A11, PDZK1, SLC16A9, and SLC11A122 have been associated with the production, transport, metabolism, or excretion of uric acid. As uric acid has adverse effects on the cardiovascular system, women are as susceptible as men to complications of hyperuricemia. Adequate physical exercise and appropriate diets are beneficial. Reduced consumption of alcohol and intake of medicines that may increase the production or decrease the excretion of uric acid are also critical in the maintenance of health, especially in women with hormone imbalance.

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超音波卵巢癌評估系統 (O-RADS and ADNEX model)

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To date, ultrasound represents the first-line imaging tool for the evaluation of adnexal lesions. Ovarian cancer (OC) has a low prevalence but is highly lethal. The overall five-year survival rate of OC is less than half. Accurately diagnosing adnexal lesions plays a vital role in patient management.

In recent years, several ultrasound structured reporting systems have been developed to assess the risk of OC. In 2000, the International Ovarian Tumor Analysis (IOTA) group presented the terminology and definitions to describe sonographic features of adnexal tumors, and it subsequently developed the "Logistic Regression Model" in 2005, "Simple-Rules" in 2008, "ADNEX Model" in 2014, and "Simple-Rules-Risk model (SR-Risk) in 2016. A large multicenter study included 4905 patients with adnexal lesions undergoing surgery and it concluded that the ADNEX model had more practical advantages than other 5 models. In 2018, the American College of Radiology (ACR) published a white paper lexicon for descriptions of adnexal lesions. In 2020, the ACR developed Ovarian-Adnexal Reporting and Data System (O-RADS) ultrasound risk classification into six categories. O-RADS 0 represents incomplete evaluation. O-RADS 1 Indicates a normal ovary with physiologic cyst. O-RADS 2 indicates an almost certainly benign lesion with <1% of malignant risk. O-RADS 3 indicates lesions with a low risk of malignancy (1% to <10%). O-RADS 4 indicates intermediate malignant risk (10% to <50%). Furthermore, O-RADS 5 indicates high risk malignancy (≥50%).

The goals of this lecture were to compare the O-RADS with the ADNEX model.

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子宮頸癌篩檢結果異常與子宮頸癌前驅病變之處理

本次報告的內容，包含子宮頸篩檢工具的操作要點、陰道鏡檢查要點、子宮頸癌前驅病變手術治療之操作要點，以及美國 2019 ASCCP 臨床指引之台灣應用。25 歲以上女性的子宮頸篩檢，宜以 HPV 為主，輔以細胞學檢查。子宮頸若有肉眼可見的可疑病灶，則不管子宮頸細胞學或 HPV 檢查結果如何，皆應進行切片檢查。CIN1 以追蹤為主;持續 CIN1 至少兩年以上者，通常還是繼續追蹤，但若想治療也可以。HPV 16 或 18 呈陽性者，即使子宮頸細胞學檢查正常，仍應進行陰道鏡檢查。細胞學檢查為 HSIL 及以上或 HPV 檢查為 16 或 18 型者，應充分進行陰道鏡與切片(至少 2-4 切)。然而，有些狀況之下，可以不經過陰鏡切片，而直接進行治療。除了考量減少後續早產風險的個案, HSIL 的切除性 (excisional) 治療比燒蝕性 (ablative)治療受到青睞; 如果沒切乾淨，可以先追蹤或繼續再切。另一方面，24 歲或以下的 CIN2 患者，也可考慮不治療，而改以每半年進行追蹤。懷孕期間，不可做子宮內頸搔刮或子宮內膜切片，也不進行 HSIL 的治療，但若高度懷疑有癌症，而子宮頸切片無法確認診斷，就只好考慮進行診斷性子宮頸圓錐狀切除手術。細胞學檢查呈良性子宮內膜細胞者，若已停經，則進行子宮內膜切片。細胞學檢查呈 AGC 的患者，除了陰道鏡，還需考慮子宮內頸搔刮與子宮內膜切片之需要。如果細胞學檢查是 AGC favor neoplasm 或是 AIS，但是陰道鏡和諸切片皆找不到病灶，則要進行診斷性子宮頸圓錐狀切除手術。AIS 患者需進行子宮頸錐狀切除手術，且要切到手術切緣已無病灶為止，而若無生育考量，則建議切除子宮。子宮頸癌前驅病變的追蹤，宜以 HPV 為主，輔以細胞學檢查。HSIL 或 AIS 治療之後，即使子宮已切除，至少要追蹤 25 年。