

## Selección de Resúmenes de Menopausia

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### **Advances in the cellular immunological pathogenesis and related treatment of primary ovarian insufficiency**

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Premature ovarian insufficiency (POI) is a significant cause of female infertility and impact physical and psychological health of women. Symptoms of patients with POI are similar to that of menopause, such as amenorrhea, anovulation, early depletion of the ovarian reserve, decreased estrogen, and elevated follicle-stimulating hormone (FSH) levels. The cause of POI remains unresolved and evidences support that the role of autoimmunity may be one potential cause of disease etiopathogenesis. Therefore, most previous research has focused on finding ovary-related antibodies. In recent years, advances in the field of cellular immunity have increased our understanding of the etiopathogenesis of POI, which includes changed levels of cytokines and immunological cells especially Th1/Th2 ratio, Tregs cells and Th17 cells. To describe the immunological mechanism in the pathogenesis of POI, we summarize the alternations in humoral immunity and cellular immunity in patients with POI. Based on these advances in cellular immunity of POI, many associated treatment methods including DHEA supplementation, Traditional Chinese Medicine, adoptive transfer of Treg cells and stem cell transplantation have become research hotspots, which hold promise for effective treatment of POI in the clinical practice.

**J Bone Miner Res. 2022 Aug 10. doi: 10.1002/jbmr.4674. Online ahead of print.**

### **Decreased Mortality and Subsequent Fracture Risk in Patients With a Major and Hip Fracture After the Introduction of a Fracture Liaison Service: A 3-Year Follow-Up Survey**

Lisanne Vranken 1 2, Irma J A de Bruin 1, Annemarië H M Driessen 3, Piet P M Geusens 4 5, John A Eisman , et al. Fracture liaison services (FLS) are considered to be the most effective organizational approach for secondary fracture prevention. In this study, we evaluated whether FLS care was associated with reduced subsequent fracture and mortality risk over 3 years of follow-up. In total, 8682 consecutive patients aged 50-90 years with a recent fracture were included. Before FLS introduction, regular fracture treatment procedures were followed (pre-FLS). After FLS introduction, patients were invited to the FLS and FLS attenders were assessed for osteoporosis, prevalent vertebral fractures, metabolic bone disorders, medication use, and fall risk, and treatment for fracture prevention was initiated according to Dutch guidelines. All fractures were radiographically confirmed and categorized into major/hip (pelvis, proximal humerus or tibia, vertebral, multiple rib, distal femur) and non-major/non-hip (all other fractures). Mortality risk was examined using age and sex adjusted Cox proportional hazard models. For subsequent fracture risk, Cox proportional hazard models were adjusted for age, sex, and competing mortality risk (subdistribution hazard [SHR] approach). The pre-FLS group consisted of 2530 patients (72% women), of whom 1188 (46.9%) had major/hip index fractures, the post-FLS group consisted of 6152 patients (69% women), of whom 2973 (48.3%) had major/hip index fractures. In patients with a non-major/non-hip fracture there was no difference in subsequent non-major/non-hip fracture risk or mortality between pre-FLS and post-FLS. In patients with a major/hip index fracture, mortality risk was lower post-FLS (hazard ratio [HR] 0.84; 95% confidence interval [CI], 0.73-0.96) and subsequent major/hip fracture risk was lower in the first 360 days after index fracture post-FLS compared to pre-FLS (SHR 0.67; 95% CI, 0.52-0.87). In conclusion, FLS care was associated with a lower mortality risk in the first 3 years and a lower subsequent major/hip fracture risk in the first year in patients with a major/hip index fracture but not in patients with a non-major/non-hip fracture.

**Medicine (Baltimore). 2022 Sep 9;101(36):e30352. doi: 10.1097/MD.00000000000030352.**

### **Ten-year atherosclerotic cardiovascular disease risk prediction for postmenopausal women: Impacts of isolated postchallenge hyperglycemia**

Tsung-Hui Wu 1, Yi-Chun Lin 2 3, Chii-Min Hwu 1 2

Isolated postchallenge hyperglycemia (IPH) is a type of diabetes mellitus defined as 2-h glucose  $\geq 200$  mg/dL but fasting glucose  $< 126$  mg/dL. The purpose of the study was to assess impacts of IPH on 10-year atherosclerotic cardiovascular disease (ASCVD) risk scores in postmenopausal women. This study analyzed data from 428 postmenopausal women who underwent oral glucose tolerance test at a medical center. Ten-year ASCVD risk was evaluated by using Pooled Cohort Equations. Logistic regression analysis was performed to estimate odds ratios for having high 10-year ASCVD risk scores ( $\geq 5\%$ ) among these women. The subjects with IPH had higher systolic blood pressure and worse lipid profile than those without IPH. Ten-year ASCVD risk scores for postmenopausal women with IPH were calculated under 2 scenarios: the IPH women were considered non-diabetic, they were designated as patients with DM. The median ASCVD risk score of the participants with IPH increased significantly from 3.7% under scenario 1 to 7.1% under scenario 2. Approximately 20% women with IPH were re-categorized from risk category of  $< 5\%$  to  $\geq 7.5\%$  once they were identified as patients with DM (scenario 2). The results of logistic regression analyses showed that IPH was independently positively associated with 10-year ASCVD risk scores  $\geq 5\%$  under both scenarios. Postmenopausal women with IPH were characterized by unfavorable cardiovascular risk profile and high predicted 10-year ASCVD risk. Knowing the women's hidden DM status would significantly alter their risk categorization.

**Maturitas. 2022 Aug 30;166:65-85. doi: 10.1016/j.maturitas.2022.08.008. Online ahead of print. Texto adjunto**  
**Eligibility criteria for Menopausal Hormone Therapy (MHT): a position statement from a consortium of scientific societies for the use of MHT in women with medical conditions. MHT Eligibility Criteria Group**

Nicolás Mendoza 1, Isabel Ramírez 2, Esther de la Viuda 2, Pluvio Coronado 2, Laura Baquedano 2, et al.  
 This project aims to develop eligibility criteria for menopausal hormone therapy (MHT). The tool should be similar to those already established for contraception. A consortium of scientific societies coordinated by the Spanish Menopause Society met to formulate recommendations for the use of MHT by women with medical conditions based on the best available evidence. The project was developed in two phases. As a first step, we conducted 14 systematic reviews and 32 meta-analyses on the safety of MHT (in nine areas: age, time of menopause onset, treatment duration, women with thrombotic risk, women with a personal history of cardiovascular disease, women with metabolic syndrome, women with gastrointestinal diseases, survivors of breast cancer or of other cancers, and women who smoke) and on the most relevant pharmacological interactions with MHT. These systematic reviews and meta-analyses helped inform a structured process in which a panel of experts defined the eligibility criteria according to a specific framework, which facilitated the discussion and development process. To unify the proposal, the following eligibility criteria have been defined in accordance with the WHO international nomenclature for the different alternatives for MHT (category 1, no restriction on the use of MHT; category 2, the benefits outweigh the risks; category 3, the risks generally outweigh the benefits; category 4, MHT should not be used). Quality was classified as high, moderate, low or very low, based on several factors (including risk of bias, inaccuracy, inconsistency, lack of directionality and publication bias). When no direct evidence was identified, but plausibility, clinical experience or indirect evidence were available, "Expert opinion" was categorized. For the first time, a set of eligibility criteria, based on clinical evidence and developed according to the most rigorous methodological tools, has been defined. This will provide health professionals with a powerful decision-making tool that can be used to manage menopausal symptoms.

**Gynecol Endocrinol. 2022 Sep 8;1-20. doi: 10.1080/09513590.2022.2118254. Online ahead of print.**  
**Review of menopausal hormone therapy with estradiol and progesterone versus other estrogens and progestins**

Shelli Graham 1, David F Archer 2, James A Simon 3, Kathleen M Ohlert 4, Brian Bernick 1  
 Objective: The objective of the present document was to review/summarize reported outcomes compared between menopausal hormone therapy (MHT) containing estradiol (E2) versus other estrogens and MHT with progesterone (P4) versus progestins (defined as synthetic progestogens). Methods: PubMed and EMBASE were systematically searched through February 2021 for studies comparing oral E2 versus oral conjugated equine estrogens (CEE) or P4 versus progestins for endometrial outcomes, venous thromboembolism (VTE), cardiovascular outcomes, breast outcomes, cognition, and bone outcomes in postmenopausal women. Results: A total of 74 comparative publications were identified/summarized. Randomized studies suggested that P4 and progestins are likely equally effective in preventing endometrial hyperplasia/cancer when used at adequate doses. E2- versus CEE-based MHT had a similar or possibly better risk profile for VTE and cardiovascular outcomes, and P4- versus progestin-based MHT had a similar or possibly

better profile for breast cancer and cardiovascular outcomes. E2 may potentially protect better against age-related cognitive decline and bone fractures versus CEE; P4 was similar or possibly better versus progestins for these outcomes. Limitations are that many studies were observational and some were not adequately powered for the reported outcomes. Conclusions: Evidence suggests a differential effect of MHT containing E2 or P4 and those containing CEE or progestins, with some evidence trending to a potentially better safety profile with E2 and/or P4.

**J Drugs Dermatol. 2022 Sep 1;21(9):954-960. doi: 10.36849/JDD.6232.**

## **The Role of Hormone Therapy in Female Aesthetic Rejuvenation**

Keira Barr, Alana Kurtti, Jared Jagdeo

Hormones are intricately involved in age-related aesthetic changes. Declining levels of several hormones in the postmenopausal period are associated with unwanted changes in appearance, including weight gain, fat redistribution, aged skin, and hair thinning. Hormone therapies may prevent or reverse these changes. In this article, we explore the role of estrogen, progesterone, testosterone, dehydroepiandrosterone, and melatonin in female aesthetics. Based on our current understanding of the literature, dermatologists may safely and efficaciously incorporate several hormone formulations in their repertoire of treatments for female aesthetic rejuvenation.

**Maturitas. 2022 Aug 11;166:58-64. doi: 10.1016/j.maturitas.2022.08.003. Online ahead of print.**

## **Persistent gap in menopause care 20 years after the WHI: a population-based study of menopause-related symptoms and their management**

Florence A Trémollières 1, Gabriel André 2, Brigitte Letombe 3, Luc Barthélemy 4, Amélie Pichard 4, et al.

**Objectives:** To assess the current management of menopause in France with regard to menopause-related and genitourinary symptoms, with a focus on use of menopause hormone therapy (MHT). **Design, setting, and participants:** The ELISA Study is a population-based survey of 5004 French representative women aged 50 to 65 years. From July to August 2020, the participating women answered an online computer-assisted web interview on menopause-related and genitourinary symptoms and their management, including use of MHT. **Main outcomes and measures:** Prevalence of menopause-related and genitourinary symptoms in postmenopausal women. Management of these symptoms, including the reasons for not doing so, management by health care providers, and use of MHT. **Results:** Among the 5004 selected women, 4041 whose postmenopausal status was confirmed were included in the final analyses. Of the untreated 3685 women, 87 % reported at least 1 menopausal symptom, with a significantly higher percentage of symptomatic women in the 50-54 age group (92 %,  $p < 0.05$ ) than in the other two age groups (55-59 years: 89 % and 60-64 years: 82 %). 68 % of the surveyed women experienced on average 2.5 symptoms of the genitourinary syndrome of menopause (GSM). Using a visual analogue scale (VAS) from 0 (no impact) to 10 (high impact) to evaluate the impact of menopausal/GSM symptoms on their quality of life, mean VAS score was 5.9 (SD: 2.2), with 25 % of the women aged 55-59 years rating their quality of life between 8 and 10. 61 % of the surveyed women reported being regularly followed by a health care professional. 44 % of women reported never having discussed their menopausal/GSM symptoms with a health care provider. The main reasons were because menopause is "a normal part of women's lives", because it was not "necessary to do so", or their symptoms were "not serious enough". Only 242 women (6 %) were current MHT users, of whom 49 % were using estrogen-alone therapy and 71 % were using transdermal estrogens. Fear of hormones (35 %) and MHT side-effects (25 %) were the main reasons given for not using MHT. 62 % of the women reported that the decision not to take MHT was supported by their physician. **Conclusions and relevance:** This large population-based survey confirmed not only the high prevalence of menopause-related and GSM symptoms in postmenopausal women within the first 10-15 years after menopause, but also the very low percentage of MHT users in France. Twenty years after the publication of the initial Women's Health Initiative (WHI) results, management of postmenopausal women is still characterized by unmet needs in menopausal care. Therefore, there is a strong need to educate the public and health care providers about menopause-related problems and possible solutions, including MHT, through dedicated educational programs.