

## Selección de Resúmenes de Menopausia

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### **Hormones and Aging: An Endocrine Society Scientific Statement**

Anne R Cappola 1, Richard J Auchus 2 3, Ghada El-Hajj Fuleihan 4, David J Handelsman, Rita R Kalyani, et al. Multiple changes occur across various endocrine systems as an individual ages. The understanding of the factors that cause age-related changes and how they should be managed clinically is evolving. This statement reviews the current state of research in the growth hormone, adrenal, ovarian, testicular, and thyroid axes, as well as in osteoporosis, vitamin D deficiency, type 2 diabetes, and water metabolism, with a specific focus on older individuals. Each section describes the natural history and observational data in older individuals, available therapies, clinical trial data on efficacy and safety in older individuals, key points, and scientific gaps. The goal of this statement is to inform future research that refines prevention and treatment strategies in age-associated endocrine conditions, with the goal of improving the health of older individuals.

**Eur J Neurol. 2023 Jun 16. doi: 10.1111/ene.15916. Online ahead of print.**

### **Sex steroid hormones and epilepsy: Effects of hormonal replacement therapy on the seizures' frequency of postmenopausal women with epilepsy - A systematic review**

Vanessa Carvalho # 1 2 3, Isabella Colonna # 4, Giulia Curia 5, Maria Teresa Ferretti 6, Gennarina Arabia 7, et al. Background: Hormonal replacement therapy (HRT) is used for symptomatic treatment of menopause. Some evidence suggests a proconvulsant effect of estrogen and an anti-convulsant role of progesterone. Thus, the use of exogenous sex steroid hormones might influence the course of epilepsy in peri- and postmenopausal women with epilepsy (WWE). We conducted a systematic review on the impact of HRT on the frequency of seizures of WWE. Methods: PubMed and Scopus were searched for articles published from inception until August 2022. Abstracts from the last five years from the European Academy of Neurology and European Epilepsy Congresses were also reviewed. Article reference lists were screened, and relevant articles were retrieved for consultation. Interventional and observational studies on WWE and animal models of estrogen deficiency were included. Critical appraisal was performed using the Revised Cochrane risk-of-bias tool for randomized trials and ROBINS-E tools. Results Of 497 manuscripts screened, thirteen studies were included, including three human studies. One cross-sectional study showed a decrease in seizures' frequency in WWE using combined HRT, a case-control study showed an increase in comparison with controls and a Randomized Clinical Trial found a dose-dependent increase in seizures' frequency in women with focal epilepsy taking combined HRT. Ten studies addressing the impact of HRT in rat models were also included, which showed conflicting results. Discussion and Conclusion There is scarce evidence of the impact of HRT in WWE. Further studies should evaluate the harmful potential and prospective registries are needed for monitoring in this population.

**J Gerontol A Biol Sci Med Sci. 2023 Jun 16;78(Supplement\_1):38-43. doi: 10.1093/gerona/glad022.**

### **Growth Hormone Secretagogues as Potential Therapeutic Agents to Restore Growth Hormone Secretion in Older Subjects to Those Observed in Young Adults**

Roy G Smith 1 2, Michael O Thorner 3 4

The discovery of the growth hormone secretagogues (GHS) and the reverse pharmacology leading to the discovery of GHS receptor which enabled the identification of ghrelin as the natural ligand for the receptor have opened a new horizon in growth hormone (GH) physiology, pathophysiology, and therapeutics. Major progress has been made and we now have orally active GHS which are able to restore optimal pulsatile GH secretion which cannot be overstimulated as insulin-like growth factor feedback regulates the peaks to the optimum level. This enables GH to be restored in the older to levels normally seen in 20- to 30-year-old people; this leads to an increase in fat-free mass and redistribution of fat to the limbs. As these agents are ultimately approved and investigated further, it is likely that they

will be shown to restore growth in children with moderate-to-mild GH deficiency; their benefits will be investigated in other indications such as nonalcoholic fatty liver disease, frailty, anemia, osteoporosis, and immune compromise in older subjects. The exquisite regulation of GH secretion reflects the importance of GH pulsatility in the regulation of somatotroph action of GH.

**J Gerontol A Biol Sci Med Sci. 2023 Jun 16;78(Supplement\_1):73-78. doi: 10.1093/gerona/glad073.**

## **The Effects of Vitamin D Supplementation on Musculoskeletal Health: The VITAL and DO-Health Trials**

Meryl S LeBoff 1 2, Heike A Bischoff-Ferrari 3

Previous clinical trials and systematic reviews on the effects of supplemental vitamin D on musculoskeletal outcomes are conflicting. In this paper, we review the literature and summarize the effects of a high daily dose of 2 000 IU vitamin D on musculoskeletal outcomes in generally healthy adults, in men ( $\geq 50$  years) and women ( $\geq 55$  years) in the 5.3-year US VITamin D and Omega-3 Trial (VITAL) trial ( $n = 25\ 871$ ) and women and men ( $\geq 70$  years) in the 3-year European DO-HEALTH trial ( $n = 2\ 157$ ). These studies found no benefit of 2 000 IU/d of supplemental vitamin D on nonvertebral fractures, falls, functional decline, or frailty. In VITAL, supplementation with 2 000 IU/d of vitamin D did not reduce the risk of total or hip fractures. In a subcohort of VITAL, supplemental vitamin D did not improve bone density or structure ( $n = 771$ ) or physical performance measures ( $n = 1\ 054$ ). In DO-HEALTH, which investigated additive benefits of vitamin D with omega-3 and a simple home exercise program, the 3 treatments combined showed a significant 39% decreased odds of becoming prefrail compared to the control. The mean baseline 25(OH)D levels were  $30.7 \pm 10$  ng/mL in VITAL and  $22.4 \pm 8.0$  ng/mL in DO-HEALTH and increased to 41.2 ng/mL and 37.6 ng/mL in the vitamin D treatment groups, respectively. In generally healthy and vitamin D-replete older adults not preselected for vitamin D deficiency or low bone mass or osteoporosis, 2 000 IU/d of vitamin D had no musculoskeletal health benefits. These findings may not apply to individuals with very low 25(OH)D levels, gastrointestinal disorders causing malabsorption, or those with osteoporosis.

**Menopause. 2023 Jun 13. doi: 10.1097/GME.0000000000002198. Online ahead of print.**

## **Association between vasomotor symptom frequency and weight gain in the Study of Women's Health Across the Nation**

Carolyn J Gibson 1, Aki Shiozawa 2, Andrew J Epstein 3, Wei Han 2, Shayna Mancuso 2

Objective: The menopause transition is associated with weight gain in women. We examined whether changes in vasomotor symptom (VMS) frequency precede weight changes. Methods: This longitudinal retrospective analysis included data from the multisite, multiethnic Study of Women's Health Across the Nation. Women in premenopause or perimenopause aged 42 to 52 years at baseline self-reported VMS frequency (hot flashes/night sweats) and sleep problems at up to 10 annual visits. Menopause status, weight, body mass index, and waist circumference were compared across visits. The primary objective was to measure the association between VMS frequency and weight gain using a lagged approach with first-difference regression models. Secondary objectives were to statistically quantify mediation by sleep problems and moderation by menopause status and explore the association between cumulative, 10-year VMS exposure and long-term weight gain. Results: The primary analysis sample included 2,361 participants (12,030 visits; 1995-2008). Increased VMS frequency across visits was associated with subsequently increased weight (0.24 kg), body mass index (0.08 kg/m<sup>2</sup>), and waist circumference (0.20 cm). Cumulative exposure to a high frequency of VMS ( $\geq 6$  d/2 wk) over 10 consecutive annual visits was associated with increases in weight measures, including a 3.0-cm increase in waist circumference. Contemporaneous sleep problems mediated no more than 27% of waist circumference increases. Menopause status was not a consistent moderator. Conclusions: This study demonstrates that increases in VMS, onset of a high frequency of VMS, and persistent VMS symptoms over time may precede weight gain in women.

**JAMA Netw Open. 2023 Jun 1;6(6):e2317145. doi: 10.1001/jamanetworkopen.2023.17145.**

## **Association of Early Hysterectomy with Risk of Cardiovascular Disease in Korean Women**

Jin-Sung Yuk 1, Byung Gyu Kim 2, Byoung Kwon Lee 3, Jongkwon Seo 2, Gwang Sil Kim 2, Kyongjin Min, et al.

**Importance:** Women who undergo surgical hysterectomy before natural menopause may have an earlier increase in hematocrit and storage iron levels than those who continue menstruation, thereby increasing the risk of cardiovascular disease (CVD) at ages younger than usually seen. Examining this issue may provide important implications for women's cardiovascular health to both physicians and patients. **Objective:** To evaluate the association of hysterectomy with the risk of incident CVD among women before age 50 years. **Design, setting, and participants:** In this Korean population-based cohort study, 135 575 women aged 40 to 49 years were evaluated from January 1, 2011, to December 31, 2014. After propensity score matching in covariates including age, socioeconomic status, region, Charlson Comorbidity Index, hypertension, diabetes, dyslipidemia, menopause, menopausal hormone therapy, and adnexal surgery before inclusion, 55 539 pairs were included in the hysterectomy and nonhysterectomy groups. Participants were followed up until December 31, 2020. Data analysis was conducted from December 20, 2021, to February 17, 2022. **Main outcomes and measures:** The primary outcome was an incidental CVD, a composite of myocardial infarction, coronary artery revascularization, and stroke. The individual components of the primary outcome were also evaluated. **Results:** A total of 55 539 pairs were included; median age in the combined groups was 45 (IQR, 42-47) years. During median follow-up periods in the hysterectomy group of 7.9 (IQR, 6.8-8.9) years and nonhysterectomy group of 7.9 (IQR, 6.8-8.8) years, the incidence of CVD was 115 per 100 000 person-years for the hysterectomy group and 96 per 100 000 person-years for the nonhysterectomy group. After adjusting for confounding factors, the hysterectomy group had an increased risk of CVD compared with the nonhysterectomy group (hazard ratio [HR], 1.25; 95% CI, 1.09-1.44). The incidences of myocardial infarction and coronary artery revascularization were comparable between the groups, whereas the risk of stroke was significantly higher in the hysterectomy group (HR, 1.31; 95% CI, 1.12-1.53). Even after excluding women who underwent oophorectomy, the hysterectomy group had higher risks of CVD (HR, 1.24; 95% CI, 1.06-1.44). **Conclusions and relevance:** The findings of this cohort study suggest early menopause owing to hysterectomy was associated with increased risks for a composite of CVD, particularly stroke.