Selección de Resúmenes de Menopausia

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Membrane estrogen receptor α signaling modulates the sensitivity to estradiol treatment in a dose- and tissue- dependent manner

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Estradiol (E2) affects both reproductive and non-reproductive tissues, and the sensitivity to different doses of E2 varies between tissues. Membrane estrogen receptor α (mERα)-initiated signaling plays a tissue-specific role in mediating E2 effects, however, it is unclear if mERα signaling modulates E2 sensitivity. To determine this, we treated ovariectomized C451A females, lacking mERα signaling, and wildtype (WT) littermates with physiological (0.05 μg/mouse/day (low); 0.6 μg/mouse/day (medium)) or supraphysiological (6 μg/mouse/day (high)) doses of E2 (17β-estradiol-3-benzoate) for three weeks. Low-dose treatment increased uterus weight in WT, but not C451A mice, while non-reproductive tissues (gonadal fat, thymus, trabecular and cortical bone) were unaffected in both genotypes. Medium-dose treatment increased uterus weight and bone mass and decreased thymus and gonadal fat weights in WT mice. Uterus weight was also increased in C451A mice, but the response was significantly attenuated (- 85%) compared to WT mice, and no effects were triggered in non-reproductive tissues. High-dose treatment effects in thymus and trabecular bone were significantly blunted (- 34% and - 64%, respectively) in C451A compared to WT mice, and responses in cortical bone and gonadal fat were similar between genotypes. Interestingly, the high dose effect in uterus was enhanced (+ 26%) in C451A compared to WT mice. In conclusion, loss of mERα signaling reduces the sensitivity to physiological E2 treatment in both non-reproductive tissues and uterus. Furthermore, the E2 effect after high-dose treatment in uterus is enhanced in the absence of mERα, suggesting a protective effect of mERα signaling in this tissue against supraphysiological E2 levels.

Age but not menopausal status is linked to lower resting energy expenditure

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Context: It remains uncertain whether aging before late adulthood and menopause are associated with fat-free mass and fat mass-adjusted resting energy expenditure (REEadj). Objectives: We investigated whether REEadj differs between middle-aged and younger women and between middle-aged women with different menopausal statuses. We repeated the age group comparison between middle-aged mothers and their daughters to partially control for genotype. We also explored whether serum estradiol and follicle-stimulating hormone concentrations explain REEadj in midlife. Methods: We divided 120 women, including 16 mother-daughter pairs, into age groups; group I (n=26) consisted of participants aged 17-21, group II (n=35) of those aged 22-38 and group III (n=59) of those aged 41-58 years. The women in group III were further categorized as pre- or perimenopausal (n=19), postmenopausal (n=30) or postmenopausal hormone therapy users (n=10). REE was assessed using indirect calorimetry, body composition using dual-energy X-ray absorptiometry and hormones using immunoassays. Results: The REEadj of group I was 126 kcal/d (95% CI: 93-160) higher than that of group III, and the REEadj of group II was 88 kcal/d (95% CI: 49-127) higher. Furthermore, daughters had a 100 kcal/d (95% CI: 63-138 kcal/d) higher REEadj than their middle-aged mothers (all P<0.001). In group III, REEadj was not lower in postmenopausal women and did not vary by sex hormone concentrations. Conclusions: We demonstrated that REEadj declines with age in women before late adulthood, also when controlling partially for genetic background, and that menopause may not contribute to this decline.

Association between muscle strength and mass and bone mineral density in the US general population: data from NHANES 1999-2002

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Purpose: It is known that muscle strength and muscle mass play a crucial role in maintaining bone mineral density (BMD). Despite this, there are uncertainties about how muscle mass, lower extremity muscular strength, and BMD are

related. We examined the impact of lower extremity muscle strength and mass on BMD in the general American population using cross-sectional analysis. Methods: In the study, we extracted 2165 individuals from the National Health and Nutrition Examination Survey 1999-2002. Multivariate logistic regression models were used to examine the association between muscle strength, muscle mass, and BMD. Fitted smoothing curves and generalized additive models were also performed. To ensure data stability and avoid confounding factors, subgroup analysis was also conducted on gender and race/ethnicity. Results: After full adjustment for potential confounders, significant positive associations were detected between peak force (PF) [0.167 (0.084, 0.249) P < 0.001], appendicular skeletal muscle index (ASMI) [0.029 (0.022, 0.036) P < 0.001], and lumbar spine BMD. A positive correlation was also found between PF, ASMI, and pelvis and total BMD. Following stratification by gender and race/ethnicity, our analyses illustrated a significant correlation between PF and lumbar spine BMD in both men [0.232 (0.130, 0.333) P < 0.001] and women [0.281 (0.142, 0.420) P < 0.001]. This was also seen in non-Hispanic white [0.178 (0.068, 0.288) P = 0.002], but not in non-Hispanic black, Mexican American and other race-ethnicity. Additionally, there was a positive link between ASMI and BMD in both genders in non-Hispanic whites, and non-Hispanic blacks, but not in any other racial group. Conclusion: PF and ASMI were positively associated with BMD in American adults. In the future, the findings reported here may have profound implications for public health in terms of osteopenia and osteoporosis prevention, early diagnosis, and treatment.

Nonalcoholic fatty liver disease is associated with decreased bone mineral density in adults: A systematic review and meta-analysis

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This systematic review and meta-analysis aimed to investigate the effect of nonalcoholic fatty liver disease (NAFLD) on bone mineral density (BMD), and the risk of osteoporosis and osteoporotic fracture in adults. We searched PubMed, MEDLINE, Embase, CINAHL, Web of Science, Cochrane Library, and Scopus for observational studies published from inception to January 2023 that reported adjusted effect sizes of NAFLD on BMD, osteopenia/osteoporosis, and osteoporotic fracture. The data were synthesized using multilevel and random-effects models. A total of 19 studies were included; of these, nine (21,294 participants) evaluated the effect of NAFLD on BMD, six (133,319 participants) investigated the risk of osteoporosis, and five (227,901 participants) assessed the risk of osteoporotic fracture. This meta-analysis showed that NAFLD was associated with decreased BMD (mean difference: -0.019 g/cm2 , 95% confidence interval [CI]: -0.036 to -0.002, I2 : 93%) and increased risks of osteoporosis (adjusted risk ratio [RR]: 1.28, 95% CI: 1.08 to 1.52, I2 : 84%) and osteoporotic fractures (adjusted RR: 1.17, 95% CI: 1.00 to 1.37, I2 : 67%). Subgroup analyses revealed that NAFLD had a significantly detrimental effect on BMD in men and on the BMD of the femoral neck and total hip. Stratified analyses by ethnicity demonstrated that NAFLD was not associated with BMD, osteoporosis, or osteoporotic fracture in non-Asian populations. The publication bias of all included studies was low; however, there was considerable heterogeneity among the studies, warranting a careful interpretation of the findings. Overall, our results suggest that NAFLD is associated with decreased BMD and an increased risk of osteoporosis or osteoporotic fractures. Male sex and the BMD of the femoral neck and total hip may be potential risk factors for decreased BMD in adults with NAFLD. Additionally, ethnic disparities were observed between Asian and non-Asian populations regarding BMD and osteoporotic fractures.

Progesterone from ovulatory menstrual cycles is an important cause of breast cancer

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Many factors, including reproductive hormones, have been linked to a woman's risk of developing breast cancer (BC). We reviewed the literature regarding the relationship between ovulatory menstrual cycles (MCs) and BC risk. Physiological variations in the frequency of MCs and interference with MCs through genetic variations, pathological conditions and or pharmaceutical interventions revealed a strong link between BC risk and the lifetime number of MCs. A substantial reduction in BC risk is observed in situations without MCs. In genetic or transgender situations with normal female breasts and estrogens, but no progesterone (P4), the incidence of BC is very low, suggesting an essential role of P4. During the MC, P4 has a strong proliferative effect on normal breast epithelium, whereas estradiol (E2) has only a minimal effect. The origin of BC has been strongly linked to proliferation associated DNA replication

errors, and the repeated stimulation of the breast epithelium by P4 with each MC is likely to impact the epithelial mutational burden. Long-lived cells, such as stem cells, present in the breast epithelium, can carry mutations forward for an extended period of time, and studies show that breast tumors tend to take decades to develop before detection. We therefore postulate that P4 is an important factor in a woman's lifetime risk of developing BC, and that breast tumors arising during hormonal contraception or after menopause, with or without menopausal hormone therapy, are the consequence of the outgrowth of pre-existing neoplastic lesions, eventually stimulated by estrogens and some progestins.

The 2023 nonhormone therapy position statement of The North American Menopause Society

Objective: To update the evidence-based Nonhormonal Management of Menopause-Associated Vasomotor Symptoms: 2015 Position Statement of The North American Menopause Society. Methods: An advisory panel of clinicians and research experts in women's health were selected to review and evaluate the literature published since the Nonhormonal Management of Menopause-Associated Vasomotor Symptoms: 2015 Position Statement of The North American Menopause Society. Topics were divided into five sections for ease of review: lifestyle; mind-body techniques; prescription therapies; dietary supplements; and acupuncture, other treatments, and technologies. The panel assessed the most current and available literature to determine whether to recommend or not recommend use based on these levels of evidence: Level I, good and consistent scientific evidence; Level II, limited or inconsistent scientific evidence, and Level III, consensus and expert opinion. Results: Evidence-based review of the literature resulted in several nonhormone options for the treatment of vasomotor symptoms. Recommended: Cognitive-behavioral therapy, clinical hypnosis, selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors, gabapentin, fezolinetant (Level I); oxybutynin (Levels I-II); weight loss, stellate ganglion block (Levels II-III). Not recommended: Paced respiration (Level I); supplements/herbal remedies (Levels I-II); cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation, suvorexant, soy foods and soy extracts, soy metabolite equol, cannabinoids, acupuncture, calibration of neural oscillations (Level II); chiropractic interventions, clonidine; (Levels I-III); dietary modification and pregabalin (Level III). Conclusion: Hormone therapy remains the most effective treatment for vasomotor symptoms and should be considered in menopausal women within 10 years of their final menstrual periods. For women who are not good candidates for hormone therapy because of contraindications (eg, estrogen-dependent cancers or cardiovascular disease) or personal preference, it is important for healthcare professionals to be well informed about nonhormone treatment options for reducing vasomotor symptoms that are supported by the evidence.

Understanding the Impact of Obesity on Ageing in the Radiance of DNA Metabolism

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Ageing is a multi-factorial phenomenon which is considered as a major risk factor for the development of neurodegeneration, osteoporosis, cardiovascular disease, dementia, cancer, and other chronic diseases. Phenotypically, ageing is related with a combination of molecular, cellular, and physiological levels like genomic and epi-genomic alterations, loss of proteostasis, deregulation of cellular and subcellular function and mitochondrial dysfunction. Though, no single molecular mechanism accounts for the functional decline of different organ systems in older humans but accumulation of DNA damage or mutations is a dominant theory which contributes largely to the development of ageing and age-related diseases. However, mechanistic, and hierarchical order of these features of ageing has not been clarified yet. Scientific community now focus on the effect of obesity on accelerated ageing process. Obesity is a complex chronic disease that affects multiple organs and tissues. It can not only lead to various health conditions such as diabetes, cancer, and cardiovascular disease but also can decrease life expectancy which shows similar phenotype of ageing. Higher loads of DNA damage were also observed in the genome of obese people. Thus, inability of DNA damage repair may contribute to both ageing and obesity apart from cancer predisposition. The present review emphasizes on the involvement of molecular phenomenon of DNA metabolism in development of obesity and how it accelerates ageing in mammals.