Selección de Resúmenes de Menopausia

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Oxidative stress as a possible pathogenic cofactor of post-menopausal osteoporosis: Existing evidence in support of the axis oestrogen deficiency-redox imbalance-bone loss.

Bonaccorsi G, Piva I, Greco P, Cervellati C.

Post-menopausal osteoporosis (PO) is one of the major health issues associated with menopause-related oestrogen withdrawal. Despite the intense research and the relevant progress achieved in the last two decades, the pathogenic mechanism underlying PO is still poorly understood. As a consequence of this gap in the knowledge, such disorder and the related complications are still difficult to be effectively prevented. A wealth of experimental and epidemiological/clinical evidence suggests that the endocrine change associated to menopausal transition might lead to a derangement of redox homeostasis, that is, the prelude to the health-threaten condition of oxidative stress (OxS). In turn, this (bio)chemical stress has been widely hypothesized to contribute, most likely in synergy with inflammation, to the development of menopause-related diseases, including PO. The main aim of this review is to discuss the current literature evidence on the association between post-menopausal oestrogen withdrawal, OxS and PO. It is also aimed to provide a critical overview of the most significant epidemiological studies on the effects of dietary antioxidants on bone health and to devise a strategy to overcome the limitations emerged and controversial results.

Cell Rep. 2018 Jul 10;24(2):271-277. doi: 10.1016/j.celrep.2018.06.037.

A Neural Circuit Underlying the Generation of Hot Flushes.

Padilla SL, Johnson CW, Barker FD, Patterson MA, Palmiter RD.

Hot flushes are a sudden feeling of warmth commonly associated with the decline of gonadal hormones at menopause. Neurons in the arcuate nucleus of the hypothalamus that express kisspeptin and neurokinin B (Kiss1ARH neurons) are candidates for mediating hot flushes because they are negatively regulated by sex hormones. We used a combination of genetic and viral technologies in mice to demonstrate that artificial activation of Kiss1ARH neurons evokes a heat-dissipation response resulting in vasodilation (flushing) and a corresponding reduction of core-body temperature in both females and males. This response is sensitized by ovariectomy. Brief activation of Kiss1ARH axon terminals in the preoptic area of the hypothalamus recapitulates this response, while pharmacological blockade of neurokinin B (NkB) receptors in the same brain region abolishes it. We conclude that transient activation of Kiss1ARH neurons following sex-hormone withdrawal contributes to the occurrence of hot flushes via NkB release in the rostral preoptic area.

Obstet Gynecol. 2018 Jul 10. doi: 10.1097/AOG.0000000000002733. [Epub ahead of print]

Female Sexual Dysfunction and the Placebo Effect: A Meta-analysis.

Weinberger JM, Houman J, Caron AT, Patel DN, Baskin AS, Ackerman AL, Eilber KS, Anger JT.

OBJECTIVE: To quantify the placebo effect of various pharmacologic modalities including neuromodulators, hormonal agents, and onabotulinum toxin A for female sexual dysfunction. DATA SOURCES: Using Meta-analyses Of Observational Studies in Epidemiology guidelines, we conducted a systematic review of PubMed, EMBASE, ClinicalTrials.gov, and the Cochrane Review databases. METHODS OF STUDY SELECTION: Eleven search terms, "female sexual dysfunction" "treatment" in combination with "hypoactive sexual desire," "arousal disorder," "sexual pain disorder," "genitourinary syndrome of menopause," "orgasmic disorder," "vulvovaginal atrophy," "vaginismus," "vaginal atrophy," "vulvodynia," and "vestibulitis," were used. Studies were included if their design was randomized, included a placebo arm, and used the Female Sexual Function Index as an outcome measure. TABULATION, INTEGRATION, AND RESULTS: The placebo effect on the Female Sexual Function Index was compared with each respective study's treatment effect using inverse-variance weighting in a random-effects analysis model. Six hundred five relevant articles were retrieved. Twenty-four randomized controlled trials included a

placebo arm. Of these, eight studies used the Female Sexual Function Index. Across these studies, 1,723 women with clinical pretreatment female sexual dysfunction received placebo. Two thousand two hundred thirty-six women were in the treatment arm of the respective studies and received various pharmacologic interventions including flibanserin, bupropion, onabotulinum toxin A, intravaginal prasterone, intranasal oxytocin, ospemifene, and bremelanotide. Women receiving placebo improved 3.62 (95% CI 3.29-3.94) on the Female Sexual Function Index. The treatment arm had a corresponding increase of 5.35 (95% CI 4.13-6.57). CONCLUSION: This meta-analysis of Level I evidence demonstrates that 67.7% of the treatment effect for female sexual dysfunction is accounted for by placebo. Our findings suggest that the current treatments for female sexual dysfunction are, overall, minimally superior to placebo, which emphasizes the ongoing need for more efficacious treatment for female sexual dysfunction.

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Ovariectomy and obesity have equal impact in causing mitochondrial dysfunction and impaired skeletal muscle contraction in rats.

Sutham W, Sripetchwandee J, Minta W, Mantor D, Pattanakuhar S, Palee S, Pratchayasakul W, et al.

OBJECTIVE: Previous studies have demonstrated that either an obese-insulin resistance condition or a condition involving loss of estrogen impaired skeletal muscle function as indicated by a decrease in muscle contraction. The differing effects of combined estrogen deficiency over obese-insulin resistance on skeletal muscle function have, however, not yet been determined. Our hypothesis was that estrogen deficiency aggravates skeletal muscle dysfunction in obese-insulin resistant rats, via increased muscle oxidative stress and mitochondrial dysfunction. METHODS: Twenty-four female Wistar rats were divided into 2 groups and animals in each group were fed either a normal diet (ND) or a high-fat diet (HFD) for 24 weeks. At week 13, rats in each group were subdivided into 2 subgroups: sham-operated or ovariectomized (n=6/subgroup). At the end of the experimental period the contraction of the gastrocnemius muscles was tested before the rats were sacrificed. Skeletal muscle was removed to assess oxidative stress and mitochondrial function. RESULTS: We found that an obese-insulin resistant condition was observed in sham-operated HFD-fed rats, ovariectomized ND-fed rats, and ovariectomized HFD-fed rats. Skeletal muscle contractile function (peak-force ratio [g/g]; 25.40±2.03 [ovariectomized ND-fed rats], 22.44±0.85 [sham-operated HFD-fed rats] and 25.06±0.61 [ovariectomized HFD-fed rats]), skeletal muscle mitochondrial function, and oxidative stress were equally significantly impaired in all 3 groups, when compared with those of sham-operated ND-fed rats (31.12±1.88 g/g [NDS]; $P<0.05$). Surprisingly, loss of estrogen did not aggravate these dysfunctions of skeletal muscles in HFD-fed rats. CONCLUSIONS: These findings suggest that skeletal muscle dysfunction may occur due to increased muscle oxidative stress and mitochondrial dysfunction as a result of ovariectomy and obese-insulin resistance. Loss of estrogen, however, did not aggravate these impairments in the muscle of rats with obese-insulin resistant condition.

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Physical activity and weight gain after smoking cessation in postmenopausal women.

Luo J, Manson JE, Hendryx M, Shadyab AH, Johnson KC, Dinh PC Jr, Going SB, Chlebowski R, ET AL.

OBJECTIVE: Weight gain frequently occurs after smoking cessation. The objective of this study was to examine whether weight gain after smoking cessation was attenuated by physical activity (PA) in postmenopausal women. METHODS: A total of 4,717 baseline smokers from the Women's Health Initiative were followed for 3 years. One thousand two hundred eighty-two women quit smoking, and 3,435 continued smoking. Weight was measured at baseline and at the year 3 visit. PA was assessed at both times by self-report, summarized as metabolic equivalent task-hours per week. Multiple linear regression models were used to assess the association between PA and postcessation weight gain, adjusting for potential confounding factors. RESULTS: Compared with continuing smokers, quitters gained an average of 3.5 kg (SD=5.6) between the baseline and year 3 visit. Quitters with decreased PA had the highest amount of weight gain (3.88 kg, 95% CI: 3.22-4.54); quitters with increased PA (≥15 metabolic equivalent task-hours /week) had the lowest weight gain (2.55 kg, 95% CI: 1.59-3.52). Increased PA had a stronger beneficial association for postcessation weight gain for women with obesity compared to normal weight women. Quitters who had low PA at baseline and high PA at year 3 and were also enrolled in a dietary modification intervention had nonsignificant weight gain (1.88 kg, 95% CI: -0.21-3.96) compared with continuing smokers. CONCLUSIONS: Our data demonstrate that even a modest increase in PA (equivalent to current recommendations)

can attenuate weight gain after quitting smoking among postmenopausal women, especially in combination with improved diet.

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Serum androgen profiles in women with premature ovarian insufficiency: a systematic review and meta-analysis.

Soman M, Huang LC, Cai WH, Xu JB, Chen JY, He RK, Ruan HC, Xu XR, Qian ZD, Zhu XM.

OBJECTIVE: This meta-analysis aims to investigate serum androgen profiles (testosterone, dehydroepiandrosterone sulfate, androstenedione, and sex hormone-binding globulin) in women with premature ovarian failure and to establish if there is evidence of diminished androgen levels in these women. METHODS: Various Internet sources of PubMed, Cochrane library, and Medline were searched systematically until February, 2018. Out of a pool of 2,461 studies, after applying the inclusion/exclusion criterion, 14, 8, 10, and 9 studies were chosen for testosterone, dehydroepiandrosterone sulfate, androstenedione, and sex hormone-binding globulin, respectively, for this meta-analysis. The effect measure was the standardized mean difference with 95% confidence interval (95% CI) in a random-effects model. RESULTS: The testosterone concentrations in premature ovarian insufficiency were compared with fertile controls: stamdard mean difference (IV, random, 95% CI) -0.73 [-0.99, -0.46], P value<0.05. The dehydroepiandrosterone sulfate concentrations in premature ovarian insufficiency compared to fertile controls: standard mean difference (IV, random, 95% CI) -0.65 [-0.92, -0.37], P value<0.05. Androstenedione in premature ovarian insufficiency were compared with fertile controls: standard mean difference (IV, random, 95% CI) -1.09 [-1.71, -0.48], P value<0.05. Sex hormone-binding globulin levels did not show statistical significance. The dehydroepiandrosterone sulfate levels were reduced in premature ovarian insufficiency cases, but still showed a higher level than in postmenopausal women. CONCLUSIONS: Women with premature ovarian insufficiency are at risk for decreased concentrations of testosterone, dehydroepiandrosterone sulfate, and androstenedione. Dehydroepiandrosterone sulfate levels were more reduced in postmenopausal controls when compared with premature ovarian insufficiency cases.

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Sexual well-being after menopause: An International Menopause Society White Paper.

Simon JA, Davis SR, Althof SE, Chedraui P, Clayton AH, Kingsberg SA, Nappi RE, Parish SJ, Wolfman W.

Sexual well-being frequently declines following the menopause transition and can be associated with significant personal and relationship distress. This distress is the hallmark of female sexual dysfunction (FSD). FSD is highly prevalent in postmenopausal women. The prevalence of sexual problems increases with age, but conversely this is associated with decreasing distress with advancing age. This pattern has been seen across multiple international populations with varied cultural norms. While the etiology of FSD is multifactorial, the physiological changes of sex hormone insufficiency and postmenopausal symptoms, such as dyspareunia, are primary factors contributing to FSD at midlife. The International Menopause Society is working to increase awareness of FSD and to provide a framework for practitioners to address sexual medicine concerns. This White Paper aims to review the process of care for female sexual well-being following menopause, from initially approaching the discussion of FSD, to identifying clinical signs and symptoms, and ultimately determining the best available biopsychosocial therapies. As with most processes of care, the first step is often the most difficult. Health-care practitioners need to broach the topic of sexuality in the clinical setting. Lack of information on, comfort with, and biases about the topic of sexuality after menopause are significant hurdles that the International Menopause Society addresses in this document. Each member of the Writing Group remains committed to continued advocacy for the validity of FSD as a diagnosis, the need for therapies for women to be both available and included in health insurance coverage, and continued therapeutic research to provide evidence-based solutions.

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Menopausal hormone therapy and cardiovascular risk. Where are we now?

Anagnostis P, Paschou SA, Katsiki N, Krikidis D, Lambrinoudaki I, Goulis DG.

Transition to menopause is associated with an increase in cardiovascular disease (CVD) risk, mainly attributed to lipid and glucose metabolism dysregulation, as well as to body fat redistribution, leading to abdominal obesity.

Indeed, epidemiological evidence suggests that both early menopause (EM, defined as age at menopause <45 years) and premature ovarian insufficiency (POI, defined as age at menopause <40 years) are associated with 1.5-2-fold increase in CVD risk. Menopausal hormone therapy (MHT) exerts a favorable effect on CVD risk factors (with subtle differences regarding estrogen dose, route of administration, monotherapy or combination with progestogen and type of progestogen). Concerning CVD morbidity and mortality, most studies have shown a beneficial effect of MHT in women at early menopausal age [<10 years since the final menstrual period (FMP)] or younger than 60 years. MHT is strongly recommended in women with EM and POI, as these women, if left untreated, are at risk of CVD, osteoporosis, dementia, depression and premature death. MHT has also a favourable benefit/risk profile in perimenopausal and early postmenopausal women, provided that the patient is not at a high CVD risk (as assessed by 10-year calculation tools). Transdermal estrogens have a lower risk of thrombosis compared with oral regimens. Concerning progestogens, natural progesterone and dydrogesterone has a neutral effect on CVD risk factors. In any case, the decision for MHT should be individualized, tailored according to the symptoms, patient preference and the risk of CVD, thrombotic episodes and breast cancer.

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Systematic review with meta-analysis: the prevalence of coeliac disease in patients with osteoporosis.

Laszkowska M, Mahadev S, Sundström J, Lebwohl B, Green PHR, Michaelsson K, Ludvigsson JF.

BACKGROUND: Earlier studies have produced highly varying risk estimates for the prevalence of coeliac disease (CD) in osteoporosis. AIMS: To investigate the prevalence of CD among individuals with osteoporosis. METHODS: We conducted a systematic review of articles published in PubMed, Medline or EMBASE through May 2017 to identify studies looking at prevalence of CD in patients with osteoporosis. Search terms included "coeliac disease" combined with "fractures", "bone disease", "bone density", "densitometry", "osteoporos*", "osteomal*", "osteodys" or "dexa" or "dxa" or "skelet". Non-English papers with English-language abstracts were included. We used fixed-effects inverse variance-weighted models, and tested heterogeneity through subgroup analysis as well as through meta-regression. RESULTS: We identified eight relevant studies, comprising data from 3188 individuals with osteoporosis. Of these, 59 individuals (1.9%) had CD. A weighted pooled analysis demonstrated biopsy-confirmed CD in 1.6% (95% CI = 1.1%-2.0%) of individuals with osteoporosis. The heterogeneity was moderate (I2 = 40.1%), and influenced by the underlying CD prevalence in the general population. After adding four studies (n = 814) with CD defined as positive tissue transglutaminase or endomysial antibodies, the pooled prevalence was comparable (1.6%; 95% CI = 1.2%-2.0%). CONCLUSIONS: About 1 in 62 individuals with osteoporosis, or 1.6%, have biopsy-verified CD. This prevalence is comparable to that in the general population. These findings argue against routinely screening patients with osteoporosis for CD, which is contrary to current guideline recommendations. Additional studies are needed to determine the true utility of such screening programs.