

### Selección de Resúmenes de Menopausia

Semana del 24 al 30 de Mayo de 2017 Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

Maturitas. 2017 May 13. pii: S0378-5122(17)30493-0. doi: 10.1016/j.maturitas.2017.05.008. [Epub ahead of print] The effects of yoga and self-esteem on menopausal symptoms and quality of life in breast cancer survivors-A secondary analysis of a randomized controlled trial.

Koch AK, Rabsilber S, Lauche R, Kümmel S, Dobos G, Langhorst J, Cramer H.

OBJECTIVES: Previous research has found that yoga can enhance quality of life and ease menopausal symptoms of breast cancer survivors. The study examined whether self-esteem mediated the effects of yoga on quality of life, fatigue and menopausal symptoms, utilizing validated outcome measures. STUDY DESIGN: This is a secondary analysis of a randomized controlled trial comparing the effects of yoga with those of usual care in 40 breast cancer survivors who suffered from menopausal symptoms. All participants completed all 3 assessments (week 0, week 12, and week 24) and provided full data. MAIN OUTCOME MEASURES: Outcomes were measured using self-rating instruments. Mediation analyses were performed using SPSS. RESULTS: Self-esteem mediated the effect of yoga on total menopausal symptoms (B=-2.11, 95% BCI [-5.40 to -0.37]), psychological menopausal symptoms (B=-0.94, 95% BCI [-2.30 to -0.01]), and urogenital menopausal symptoms (B=-0.66, 95% BCI [-1.65 to -0.15]), quality of life (B=8.04, 95% BCI [3.15-17.03]), social well-being (B=1.80, 95% BCI [0.54-4.21]), emotional well-being (B=1.62, 95% BCI [0.70-3.34]), functional well-being (B=1.84, 95% BCI [0.59-4.13]), and fatigue (B=4.34, 95% BCI [1.28-9.55]). Self-esteem had no effect on somatovegetative menopausal symptoms (B=-0.50, 95% BCI n.s.) or on physical well-being (B=0.79, 95% BCI n.s.). CONCLUSIONS: Findings support the assumption that self-esteem plays a vital role in the beneficial effect of yoga and that yoga can have long-term benefits for women diagnosed with breast cancer and undergoing menopausal transition.

### Exp Gerontol. 2017 May 23. pii: S0531-5565(17)30248-6. doi: 10.1016/j.exger.2017.05.017. [Epub ahead of print] Vitamin B12 deficiency might be related to sarcopenia in older adults.

Bulut EA, Soysal P, Aydin AE, Dokuzlar O, Kocyigit SE, Isik AT.

Sarcopenia and dynapenia are related to repeated falls, mobility restriction, depression, frailty, increased mortality and morbidity. The aim of this study is to evaluate the relationship between vitamin B12 deficiency and sarcopenia in older adults. 403 patients, who attended to outpatient clinic and underwent comprehensive geriatric assessment, were included study. All cases' skeletal muscle mass (SMM), walking speed and hand grip strength were recorded by bioimpedance, 4meter walking test and hand dynamometer respectively. The diagnosis of sarcopenia was defined according to the criteria of the European Working Group on Sarcopenia in Older People. Sarcopenia was accepted low SMM with low handgrip strength or low physical performance. Dynapenia was defined as handgrip strength <30kg (men) and <20kg (women). The prevalence of sarcopenia and dynapenia was 24.8% and 32.0%, respectively. In the patients with sarcopenia, mean age, osteoporosis and frailty were higher, and MMSE, and instrumental ADL scores were lower than the patients without sarcopenia (p<0.05). The frequency of sarcopenia and dynapenia were 31.6% and 35.4%, respectively, in patients with vitamin B12 levels <400pg/mL. In addition lean body mass, total skeletal mass and skeletal muscle mass index were lower in the patients with vitamin B12 levels <400pg/mL compared to higher than 400pg/mL (p<0.05). Sarcopenia, which results in lots of negative clinical outcomes in older adults, might be related to vitamin B12 deficiency. Therefore, these patients should be periodically examined for vitamin B12 deficiency due to the potential negative clinical outcomes such as sarcopenia in older adults.

#### Obesity (Silver Spring). 2017 May 26. doi: 10.1002/oby.21877. [Epub ahead of print]

Exercise with weight loss improves adipose tissue and skeletal muscle markers of fatty acid metabolism in postmenopausal women.

Ortmeyer HK, Goldberg AP, Ryan AS.

OBJECTIVE: The effects of 6-month weight loss (WL) versus aerobic exercise training (AEX)+WL on fat and skeletal muscle markers of fatty acid metabolism were determined in normal (NGT) and impaired (IGT) glucose tolerant African-American and Caucasian postmenopausal women with overweight/obesity. METHODS: Fat (gluteal and

abdominal) lipoprotein lipase (LPL), skeletal muscle LPL, acyl-CoA synthase (ACS), ß-hydroxacyl-CoA dehydrogenase, carnitine palmitoyltransferase (CPT-1), and citrate synthase (CS) activities were measured at baseline (n=104) and before and after WL (n=34) and AEX+WL (n=37). RESULTS: After controlling for age and race, muscle LPL and CPT-1 were lower in IGT, and the ratios of fat/muscle LPL activity were higher in IGT compared to NGT. Muscle LPL was related to insulin sensitivity (M value) and inversely related to G120, fasting insulin, and homeostatic model assessment of insulin resistance. AEX+WL decreased abdominal fat LPL and increased muscle LPL, ACS, and CS. The ratios of fat/muscle LPL decreased after AEX+WL. The change in VO2 max was related to the changes in LPL, ACS, and CS and inversely related to the changes in fat/muscle LPL activity ratios. CONCLUSIONS: Six-month AEX+WL, and not WL alone, is capable of enhancing skeletal muscle fatty acid metabolism in postmenopausal African-American and Caucasian women with NGT, IGT, and overweight/obesity.

#### J Family Reprod Health. 2016 Dec;10(4):191-197.

# Investigating the Relationship Between Sexual Function and Quality of Life in Menopausal Women.

Ghazanfarpour M, Khadivzadeh T, Babakhanian M.

Objective: To evaluate the symptoms of menopausal women and the link between sexual function, menopausal symptoms and demographic variables. Materials and methods: This is a cross-sectional study in which 202 postmenopausal women admitted to the health care centers were selected. The Female Sexual Function Index (FSFI) questionnaire and Menopause-Specific Quality of Life (MENQOL) were the main means of data gathering. Results: The results of our study suggested that suggested that women experienced a number of menopausal symptoms such hot flash, headache and neck pains, reduced physical strength weight gain, pain or leg cramps, intensified sexual problem than women who lack such symptoms. The FSFI scores were lower in women who were more than 60 years old, had low educational level (illiterate and elementary), and smoked cigarette. The most common symptoms were hot flashes (45%), Sleeplessness (37%), and pain in joints and muscles (36%). Moreover, the highest mean score belonged to symptoms associated with hot flashes (1.49  $\pm$  1.38), sleeplessness (1.48  $\pm$  1.71), and headache and neck pains (1.14  $\pm$  1.59) table 2. Conclusion: Women with a history of sexual problem experienced more intense menopausal symptoms. This study sheds more light on the link between sexual problems and menopausal symptoms, which can helps healthcare professionals to offer a desirable package to their patients.

# Prz Menopauzalny. 2017 Mar;16(1):12-18. doi: 10.5114/pm.2017.66178. Epub 2017 Apr 26. Immunohistochemical evaluation of oestrogen receptors $\alpha$ and $\beta$ in epithelium of the vaginal mucous membrane in women after oestrogen therapy.

Sawczuk B, Gołebiewska M, Mazurek A, Chyczewski L.

Oestrogens act on target cells through  $\alpha$  and  $\beta$  receptors (ER $\alpha$  and ER $\beta$ ). Expression of oestrogen receptors is associated with the age and menopausal condition of women. The aim of the study was an immunohistochemical evaluation of ER $\alpha$  and ER $\beta$  receptors in epithelium of the vaginal mucous membrane of women subjected to different forms of hormonal therapy (HTM). Oestrogen receptors ER $\alpha$  and ER $\beta$  were identified using immunohistochemical methods and evaluated in smears of vaginal mucous membranes collected from 60 patients subjected to HTM (including 20 patients after oral therapy, 20 patients after transdermal therapy, and 20 patients after vaginal therapy). The results showed a significant change in immunoreactivity of both studied receptors after three months of hormone therapy. The biggest differences in the changes of intensity of ER $\alpha$  and ER $\beta$  reactions were observed in patients subjected to vaginal therapy. Immunostaining for  $\alpha$  receptor showed differences between three types of hormone therapy. The highest increase in the overall intensity occurred after three months of topical therapy. Immunostaining for Er $\beta$  also varied for different types of hormone therapy. The results indicate that hormone therapy administered vaginally is the most effective in the treatment of urogenital ailments during menopause. In addition, topical therapy eliminates adverse effects of systemic oestrogen.

Postgrad Med. 2017 May 31:1-5. doi: 10.1080/00325481.2017.1334507. [Epub ahead of print]
Transdermal estrogens in the changing landscape of hormone replacement therapy.

Beck KL, Anderson MC, Kirk JK.

Views and clinical practice on hormone replacement therapy (HRT) for postmenopausal women have varied widely over the last several decades. The 1990s showed a dramatic decline in prescribing and only recently are prescription rates increasing again. Use of HRT is first line for women suffering from the symptoms of menopause. For a certain population of postmenopausal women, HRT is recommended for prevention of fracture. More consideration is being given to patient risk factors, side effects, and formulations available. Transdermal patch estrogen formulations have been on the market for many years and are becoming more common although many physicians are less familiar with the various options. Transdermal preparations are worth consideration with regard to less adverse effects as there is the avoidance of liver metabolism and accumulation of metabolites with antiestrogenic activity. Data suggests that transdermal patch estrogen preparations are both safer and potentially more efficacious than oral estrogen therapy. Guidelines recommend the addition of progesterone for women who have not had a hysterectomy. Transdermal patch estrogen has a role for women as a choice for individualized therapy and providers need to be familiar with the formulations as well as unique challenges and advantages.

#### Maturitas. 2017 Jul;101:23-30. doi: 10.1016/j.maturitas.2017.04.008. Epub 2017 Apr 15.

## Drug holidays from bisphosphonates and denosumab in postmenopausal osteoporosis: EMAS position statement.

Anagnostis P, Paschou SA, Mintziori G, Ceausu I, Depypere H, Lambrinoudaki I, Mueck A, Pérez-López FR, et al. BACKGROUND: Bisphosphonates and denosumab are used extensively in the treatment of postmenopausal osteoporosis. Despite their proven efficacy in the reduction of vertebral and non-vertebral fractures, their optimal duration of use has not been determined. The occurrence of adverse effects, such as osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF), has raised the issue of bisphosphonate or denosumab discontinuation ("drug holiday") after a certain treatment period. AIM: To assess the effect of bisphosphonate and denosumab discontinuation on fracture risk, as well as its possible benefits in reducing the risk of adverse effects. METHODS: Systematic review and consensus of expert opinion. RESULTS AND CONCLUSIONS: Discontinuation of bisphosphonates should be considered in all patients who have beentreated for more than five years with alendronate, risedronate or zoledronic acid. In view of the limited evidence, no robust recommendations can be made for ibandronate and denosumab. If the patient has not experienced fractures before or during therapy and the fracture risk is low, a "drug holiday" canbe recommended. Although there is no solid evidence, 1-2 years for risedronate, 3-5 years for alendronate and 3-6 years for zoledronic acid are suggested. After this time, the patient should be reassessed. If a new fracture is experienced, or fracture risk has increased or BMD remains low (femoral neck T-score <-2.5), anti-osteoporotic treatment should be resumed. In the case of denosumab discontinuation, close monitoring is suggested, due to the possibility of rebound fractures.

### $Nature.\ 2017\ Jun\ 1; 546 (7656): 107\text{-}112.\ doi:\ 10.1038/nature 22342.\ Epub\ 2017\ May\ 24.$

### Blocking FSH induces thermogenic adipose tissue and reduces body fat.

Liu P, Ji Y1,, Yuen T, Rendina-Ruedy E, DeMambro VE, Dhawan S, Abu-Amer W, Izadmehr S, et al.

Menopause is associated with bone loss and enhanced visceral adiposity. A polyclonal antibody that targets the  $\beta$ -subunit of the pituitary hormone follicle-stimulating hormone (Fsh) increases bone mass in mice. Here, we report that this antibody sharply reduces adipose tissue in wild-type mice, phenocopying genetic haploinsufficiency for the Fsh receptor gene Fshr. The antibody also causes profound beiging, increases cellular mitochondrial density, activates brown adipose tissue and enhances thermogenesis. These actions result from the specific binding of the antibody to the  $\beta$ -subunit of Fsh to block its action. Our studies uncover opportunities for simultaneously treating obesity and osteoporosis.

#### Menopause. 2017 May 22. doi: 10.1097/GME.000000000000872. [Epub ahead of print]

# A systematic review of the exercise effect on bone health: the importance of assessing mechanical loading in perimenopausal and postmenopausal women.

Sañudo B, de Hoyo M, Del Pozo-Cruz J, Carrasco L, Del Pozo-Cruz B, Tejero S, Firth E.

OBJECTIVE: The aims of this systematic review were to determine the general effects of exercise on areal bone mineral density (BMD) in perimenopausal and postmenopausal women, and to provide information on the most suitable bone-loading exercise regimens that may improve bone health in this population group. METHODS: A computerized,

systematic literature search was performed in the electronic databases PubMed, Web of Science, CINAHL, SPORTDiscus, and The Cochrane Library, from January 2005 to November 2015, to identify all randomized controlled trials related to exercise in perimenopausal and postmenopausal women. The initial search identified 915 studies, with a final yield of 10 studies. Only randomized controlled trials that examined the effects of exercise programs longer than 24 weeks in women aged 35 to 70 years were included. The 10 studies quantified at least BMD and described training variables adequately (training period, frequency, volume, intensity). RESULTS: Ten studies with moderate quality evidence (6.4±1.8 points, range 4-9) were included. Significant changes in lumbar and femoral neck BMD were found mainly with high-impact exercise and whole body vibration interventions. CONCLUSIONS: While training effects must be interpreted with caution because of the heterogeneity of the protocols and exercises performed, this systematic review confirmed the effectiveness of impact exercises combined with other forms of training (vibration or strength training) to preserve BMD in perimenopausal and postmenopausal women. Despite the results possibly not representing a general dose-response relationship, we highlight the importance of quantifying loading intensity and frequency by means of accelerometry as these parameters are determinants for bone adaptation

### Cell Mol Biol Lett. 2016 Aug 12;21:12. doi: 10.1186/s11658-016-0013-1. eCollection 2016. Osteoporosis: the current status of mesenchymal stem cell-based therapy.

Phetfong J, Sanvoranart T, Nartprayut K, Nimsanor N, Seenprachawong K, Prachayasittikul V, Supokawej A. Osteoporosis, or bone loss, is a progressive, systemic skeletal disease that affects millions of people worldwide. Osteoporosis is generally age related, and it is underdiagnosed because it remains asymptomatic for several years until the development of fractures that confine daily life activities, particularly in elderly people. Most patients with osteoporotic fractures become bedridden and are in a life-threatening state. The consequences of fracture can be devastating, leading to substantial morbidity and mortality of the patients. The normal physiologic process of bone remodeling involves a balance between bone resorption and bone formation during early adulthood. In osteoporosis, this process becomes imbalanced, resulting in gradual losses of bone mass and density due to enhanced bone resorption and/or inadequate bone formation. Several growth factors underlying age-related osteoporosis and their signaling pathways have been identified, such as osteoprotegerin (OPG)/receptor activator of nuclear factor B (RANK)/RANK ligand (RANKL), bone morphogenetic protein (BMP), wingless-type MMTV integration site family (Wnt) proteins and signaling through parathyroid hormone receptors. In addition, the pathogenesis of osteoporosis has been connected to genetics. The current treatment of osteoporosis predominantly consists of antiresorptive and anabolic agents; however, the serious adverse effects of using these drugs are of concern. Cell-based replacement therapy via the use of mesenchymal stem cells (MSCs) may become one of the strategies for osteoporosis treatment in the future.

# Ann Pharmacother. 2017 May 1:1060028017710482. doi: 10.1177/1060028017710482. [Epub ahead of print] Adherence with Bisphosphonates and Long-Term Risk of Hip Fractures: A Nested Case-Control Study Using Real-World Data.

Shalev V, Sharman Moser S, Goldshtein I, Yu J, Weil C, Ish-Shalom S, Rouach V, Chodick G.

BACKGROUND: Hip fracture is a major complication of osteoporosis. Bisphosphonate medication is the mainstay of treatment for osteoporosis. However, concerns have been raised regarding the effectiveness of bisphosphonates in reducing hip fracture risk after long-term use, particularly among patients with suboptimal adherence. OBJECTIVE: To examine the association between adherence with bisphosphonate therapy and long-term risk of hip fracture. METHODS: Included in the present nested case-control study were osteoporotic women (n = 14 357) who initiated bisphosphonate therapy in 2000-2010 and were retrospectively followed for incident hip fracture through November 2014. Within this cohort, each case of primary hip fractures was individually matched to 3 controls without a primary hip fracture. Proportion of follow-up days covered (PDC) with bisphosphonates was calculated from bisphosphonate purchases. Adherence was categorized into the following groups: purchase of 1 or 2 months' supply (reference group), at least 3 months' supply to PDC  $\leq$ 20%, PDC >20% to  $\leq$ 80%, PDC >80% to  $\leq$ 100%. RESULTS: Included in the analysis were 426 case-control groups with a mean age (SD) of 73.7 years (7.9). Compared with the reference group, PDC of 80% to 100% with bisphosphonates was associated with a significant reduction in hip fracture risk for patients with 8 to 15 years of follow-up (OR = 0.39; 95% CI = 0.18-0.87). Among patients with a follow-up of up to 3 years, OR was 0.58 (95% CI = 0.31-1.06). CONCLUSIONS: Adherence with bisphosphonates among osteoporotic patients is associated with lower risk of hip fracture, with no indication of diminished effectiveness with long-term use.

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