



Selección de Resúmenes de Menopausia

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Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

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In Defense of Progesterone: A Review of the Literature.

Lieberman A, Curtis L.

Context • The medical literature on the use of progesterone in postmenopausal women is often confusing and contradictory. Some physicians implicate natural progesterone in an increase in the risk of breast cancer. The chemical structure of natural progesterone (P4) is quite different from chemically altered, synthetic chemicals called progestins, which results in different actions at the cell level. **Objective** • The research team intended to review the literature to examine the benefits and safety of natural progesterone and determine whether it can cause an increase or decrease in breast cancer risk. **Design** • A review of the medical literature to examine the benefits and safety of natural progesterone as compared with synthetic progestins. **Intervention** • Studies examined compared controls not receiving hormone therapy with women receiving estrogen alone and in combination with natural progesterone and with various synthetic progestins, such as medroxyprogesterone acetate-the most commonly used synthetic progestin. **Outcome Measures** • Outcome measures included factors such as progression and survival of breast and other cancers and other epidemiological and laboratory data. **Results** • A meta-analysis of 3 studies involving 86 881 postmenopausal women reported that the use of natural progesterone was associated with a significantly lower risk of breast cancer compared with synthetic progestins. Anovulation and low levels of serum progesterone have been associated with a significantly higher risk of breast cancer in premenopausal women. Use of progesterone has been linked to lower rates of uterine and colon cancers and may also be useful in treating other cancers such as ovarian, melanoma, mesothelioma, and prostate. Progesterone may also be helpful in preventing cardiovascular disease and preventing and treating neurodegenerative conditions such as stroke and traumatic brain injury. **Conclusions** • Physicians should have no hesitation prescribing natural progesterone. The evidence is clear that progesterone does not cause breast cancer. Indeed, progesterone is protective and preventative of breast cancer.

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Cycle control with an extended-regimen oral contraceptive combining levonorgestrel and ethinyl estradiol that includes continuous low-dose ethinyl estradiol instead of the traditional hormone-free interval.

Nappi RE, Lobo Abascal P, Hsieh J, Micheletti MC.

PURPOSE: To evaluate scheduled and unscheduled bleeding and spotting over 1 year of treatment with 91-day extended-regimen combined oral contraception (COC) providing continuous low-dose ethinyl estradiol (EE) in place of the traditional 7-day hormone-free interval (HFI). **PATIENTS AND METHODS:** This post hoc analysis of a multicenter, open-label, 1-year, Phase 3 study of extended-regimen COC with 30 µg EE/150 µg levonorgestrel (LNG) for 84 days and EE 10 µg for 7 days included 799 sexually active, adult women who completed at least one 91-day cycle of therapy. Subjects recorded bleeding and spotting episodes daily using electronic diaries. Logistic regression analyses are reported as ORs with 95% CIs. **RESULTS:** There was a 10% increase (OR =1.102; 95% CI: 1.006-1.206) in the likelihood of reporting no scheduled bleeding for each additional 91-day cycle completed. From the third 91-day cycle, more than one fifth of women reported no scheduled bleeding (third cycle =23% [121/533]; fourth cycle =22% [97/446]). Among women who reported no scheduled bleeding at Cycle 1 (136/758 [18%]), ≥45% showed sustained lack of scheduled bleeding in later cycles. There were increases of 53% (OR =1.531; 95% CI: 1.393-1.683) and 31% (OR =1.307; 95% CI: 1.205-1.418) in the likelihood of reporting 0 to ≤6 days vs >6 days of unscheduled bleeding and spotting, respectively, for each additional 91-day cycle. By Cycle 2, more than 80% of women reported no unscheduled bleeding or ≤6 days of unscheduled bleeding during each 91-day cycle. **CONCLUSION:** Improved cycle control with decreased bleeding over time was shown during extended-regimen COC with 30 µg EE/150 µg LNG for 84 days and continuous low-dose EE instead of the traditional 7-day HFI. Women considering this regimen should be informed that those who complete at least one 91-day COC cycle will likely experience less bleeding/spotting in future cycles.

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Long-term Effects of Weight Loss & Exercise on Biomarkers Associated with Angiogenesis.

Duggan C, Tapsoba JD, Wang CY, Foster-Schubert KE, McTiernan A.

BACKGROUND: We tested the effect of weight-loss on circulating levels of the angiogenic factors vascular endothelial growth factor (VEGF), and pigment epithelium-derived factor (PEDF) in postmenopausal overweight/obese women, 18 months after completing a year-long 4-arm randomized controlled trial of behavioral weight-loss and/or exercise vs. control (i.e., 30-months post-randomization). **METHODS:** 439 overweight/obese, postmenopausal women, 50-75 years, were randomized to: diet (goal: 10% weight-loss, N=118), exercise (225 min/week moderate-to-vigorous activity, N=117), diet+exercise (N=117), or control (N=87). At 12-months, 399 women gave a blood sample; 156 returned at 30-months. Biomarkers were measured by immunoassay. Changes were compared using generalized estimating equations, adjusting for baseline BMI, age, and race/ethnicity. **RESULTS:** Participants randomized to diet, exercise and diet+exercise arms had greater reductions in VEGF at 30-months (-14.1% P=0.02; -19.7% P=0.003; -14.5% P=0.002, respectively), vs. controls (-4.5%). There were no statistically significant changes in PEDF in any intervention arm. Participants maintaining >10% of baseline weight-loss at 30-months had greater reductions in VEGF vs. those who gained weight/had no weight change (-22.3% vs. -10.2% respectively, P=0.002). Participants maintaining any weight-loss had significantly lower levels of PEDF at 30-months vs. those who gained weight/no weight change. **CONCLUSION:** Sustained weight-loss via diet and/or exercise results in reductions in angiogenic factors, and can be maintained up to 30-month follow-up. Limitations include relatively small numbers, and possible bias towards more successful weight-loss among women who returned at 30-months. **IMPACT:** Maintaining weight-loss can achieve long-term reductions in biomarkers of angiogenesis that can persist up to 18-months after completion of a weight-loss intervention.

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Effect of 2 years of endurance and high-impact training on preventing osteoporosis in postmenopausal women: randomized clinical trial.

García-Gomález C, Blasco JM, Macián-Romero C, Guillem-Hernández E, Iguál-Camacho C.

OBJECTIVE: The aim of the study was to analyze the effects of endurance and high-impact training oriented toward preventing osteoporosis in postmenopausal women with calcium and vitamin D supplementation. **METHODS:** This study was a randomized clinical trial. Thirty-six postmenopausal women were randomized to the control and experimental groups. Thirty-four women completed the 2-year interventions. The control group training involved walking at an intense pace. The experimental group conducted high-impact training specifically oriented to prevent osteoporosis. Dual-energy x-ray absorptiometry was used to estimate the T-scores of the lumbar spine and femoral neck. **RESULTS:** The fast-walking group showed constant T-scores in the femoral neck and improved T-scores in the lumbar spine. High-impact exercises produced improvements in both anatomical levels. Significant differences were found in the femoral neck ($\Delta_{\text{Control}}=-0.04$, $\Delta_{\text{Experimental}}=0.28$). The differences were not significant in the lumbar spine ($\Delta_{\text{Control}}=0.27$, $\Delta_{\text{Experimental}}=0.47$). Cohen's effect size ($d=0.52$) suggested a medium practical significance of the trial. The power was 51%. **CONCLUSIONS:** Calcium plus vitamin D supplementation combined with specifically oriented exercises had a higher impact in the femoral neck than walking at an intense pace. As there were no differences at the lumbar spine level, the results were, however, inconclusive concerning which type of exercise was the most convenient. Importantly, the fact that the T-scores did not decrease after 2 years supports the belief that both proposed interventions can be conveniently used to prevent osteoporosis in postmenopausal women. A trial with a larger sample size would provide consistency to the findings and is warranted given the possible effects and benefits.

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Bone Mineral Density after Weight Gain in 160 Patients with Anorexia Nervosa.

Achamrah N, Coëffier M, Jésus P, Charles J, Rimbert A, Déchelotte P, Grigioni S.

Low bone mineral density (BMD) is a frequent complication in anorexia nervosa (AN). There are controversial points of views regarding the restoration of bone mineralization after recovery in AN. We aimed to assess changes of

BMD at 3 years in patients with AN and to explore the relationships between body composition, physical activity, and BMD. Patients with AN were included from 2009 to 2011 in a first visit (T0) with evaluation of weight, height, body mass index (BMI), body composition [fat mass (FM) and fat-free mass], and BMD. Those who had low BMD, either osteoporosis or osteopenia, were admitted in a second visit (T1) to carry out a new bone densitometry examination and body composition; they were also asked for their physical activity. At T0, our study involved 160 patients. Low BMD was observed in 53.6% of them and significant factors associated with demineralization were lower BMIs (16.5 ± 2.1 vs 17.3 ± 2.3 kg/m², $p=0.01$) and higher duration of AN (11.4 ± 10.5 vs 6.4 ± 6.5 years, $p=0.001$). At 3 years follow-up (T1), 42 patients were involved and no significant changes in BMD were observed despite body weight increase (3.8 ± 6.1 kg). Interestingly, FM gain was a significant factor associated with BMD improvement at follow-up (8.0 ± 9.1 vs 3.0 ± 3.5 kg, $p=0.02$). Our findings suggest that the restoration of normal bone values is not related to the increase of body weight, at least after 3 years. FM seems to play an important role in the pathophysiological mechanism of osteoporosis and osteopenia in AN.

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Estrogen Metabolism in Abdominal Subcutaneous and Visceral Adipose Tissue in Postmenopausal Women.

Hetemäki N, Savolainen-Peltonen H, Tikkanen MJ, Wang F, Paatela H, Hämäläinen E, Turpeinen U, et al.

CONTEXT: In postmenopausal women, adipose tissue (AT) levels of estrogens exceed circulating concentrations. While increased visceral AT after menopause is related to metabolic diseases, little is known about differences in estrogen metabolism between different AT depots. **OBJECTIVE:** We compared concentrations of and metabolic pathways producing estrone and estradiol in abdominal subcutaneous and visceral AT in postmenopausal women. **DESIGN, SETTING, PATIENTS, AND INTERVENTIONS:** AT and serum samples were obtained from 37 postmenopausal women undergoing surgery for non-malignant gynecological reasons. Serum and AT estrone, estradiol, and serum estrone sulfate (E1S) concentrations were quantitated using liquid chromatography-tandem mass spectrometry. Activity of steroid sulfatase and reductive 17 β -hydroxysteroid dehydrogenase enzymes were measured using radiolabeled precursors. mRNA expression of estrogen-converting enzymes was analyzed by RT-qPCR. **RESULTS:** Estrone concentration was higher in visceral than subcutaneous AT (median 928 vs 706 pmol/kg, $P=0.002$) and correlated positively with BMI ($r=0.46$, $P=0.011$). Both AT depots hydrolyzed E1S to estrone, and visceral AT estrone and estradiol concentrations correlated positively with serum E1S. Compared to visceral AT, subcutaneous AT produced more estradiol from estrone (median rate of estradiol production, 1.02 vs 0.57 nmol/kg AT/h, $P=0.004$). In visceral AT, the conversion of estrone to estradiol increased with waist circumference ($r=0.65$, $P=0.022$), and estradiol concentration correlated positively with mRNA expression of HSD17B7 ($r=0.76$, $P=0.005$). **CONCLUSIONS:** Both estrone and estradiol production in visceral AT increased with adiposity, but estradiol was produced more effectively in subcutaneous fat. Both AT depots produced estrone from E1S. Increasing visceral adiposity could increase overall estrogen exposure in postmenopausal women.

J Gerontol A Biol Sci Med Sci. 2017 Sep 19. doi: 10.1093/gerona/glx175. [Epub ahead of print]

Negative Affect is Associated with Higher Risk of Incident Cognitive Impairment in Nondepressed Postmenopausal Women.

Korthauer LE, Goveas J, Espeland MA, Shumaker SA, Garcia KR, Tindle H, Salmoirago-Blotcher E, et al.

BACKGROUND: Positive affect (PA) and negative affect (NA) reflect subjective emotional experiences. Although related to depression and anxiety, these dimensions are distinct constructs representing affective states and patterns. Prior studies suggest that elevated depressive symptoms are associated with risk of mild cognitive impairment (MCI) and probable dementia, but whether affective states are associated with cognitive impairment is still unknown. The present study examined relationships between baseline affective states and cognitive impairment (MCI, probable dementia) in non-depressed women. **METHOD:** Baseline PA and NA were assessed in postmenopausal women ($N = 2137$; mean age = 73.8 years) from the Women's Health Initiative Study of Cognitive Aging (WHISCA) using the Positive and Negative Affect Schedule (PANAS). Women were followed annually for an average of 11.3 years; those with elevated depressive symptoms at baseline were excluded. **RESULTS:** Higher NA was associated with a higher risk of MCI and probable dementia, even after adjusting for important covariates including age, education, sociodemographic, lifestyle, and cardiovascular risk factors, global cognition, and hormone therapy assignment at baseline. PA was not significantly associated with either outcome. **CONCLUSIONS:** We present the first evidence to

date that greater NA, even in the absence of elevated depressive symptoms, is associated with higher risk of MCI and dementia. This suggests that NA may be an important, measureable and potentially modifiable risk factor for age-related cognitive decline.

Nutr Rev. 2017 Oct 1;75(10):858-870. doi: 10.1093/nutrit/nux046.

Influence of adipose tissue mass on bone mass in an overweight or obese population: systematic review and meta-analysis.

Dolan E, Swinton PA, Sale C, Healy A, O'Reilly J.

Context: The scientific literature shows conflicting evidence about the relationship between adiposity and bone mass in overweight and obese populations. The aim of this review was to quantify the correlation between adipose mass (absolute and relative) and bone mineral density (BMD) in overweight and obese populations. Three databases were searched electronically. In addition, reference lists of relevant articles were screened. A total of 16 studies, comprising 2587 participants and 75 correlation coefficients were selected for inclusion in the review. Data were extracted from each study using a standardized form. Multilevel modeling indicated opposing relationships between BMD and adiposity: absolute adiposity correlated positively, and relative adiposity negatively, with BMD. Sex and age were the primary moderators of these relationships. Strong evidence supported a negative relationship between relative adipose mass and BMD in men ($R = -0.37$; 95%CI, -0.57 to -0.12) and in those aged less than 25 years ($R = -0.28$; 95%CI, -0.45 to -0.08). To prevent bone loss in overweight and obese populations, nutrition- and exercise-based interventions that focus on a controlled reduction of adipose mass with concomitant preservation of lean mass are recommended.

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Global dietary calcium intake among adults: a systematic review.

Balk EM, Adam GP, Langberg VN, et al; International Osteoporosis Foundation Calcium Steering Committee.

Low calcium intake may adversely affect bone health in adults. Recognizing the presence of low calcium intake is necessary to develop national strategies to optimize intake. To highlight regions where calcium intake should be improved, we systematically searched for the most representative national dietary calcium intake data in adults from the general population in all countries. We searched 13 electronic databases and requested data from domain experts. Studies were double-screened for eligibility. Data were extracted into a standard form. We developed an interactive global map, categorizing countries based on average calcium intake and summarized differences in intake based on sex, age, and socioeconomic status. Searches yielded 9780 abstracts. Across the 74 countries with data, average national dietary calcium intake ranges from 175 to 1233 mg/day. Many countries in Asia have average dietary calcium intake less than 500 mg/day. Countries in Africa and South America mostly have low calcium intake between about 400 and 700 mg/day. Only Northern European countries have national calcium intake greater than 1000 mg/day. Survey data for three quarters of available countries were not nationally representative. Average calcium intake is generally lower in women than men, but there are no clear patterns across countries regarding relative calcium intake by age, sex, or socioeconomic status. The global calcium map reveals that many countries have low average calcium intake. But recent, nationally representative data are mostly lacking. This review draws attention to regions where measures to increase calcium intake are likely to have skeletal benefits.