

## Selección de Resúmenes de Menopausia

Semana del 30 de noviembre al 6 de Diciembre de 2016 Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

## Gynecol Endocrinol. 2016 Dec 2:1-4. [Epub ahead of print] Standard hormone therapy is inadequate for bone density in premature ovarian insufficiency.

#### Giraldo H, Benetti-Pinto C, Ferreira V, Garmes H, Yela D, Giraldo P.

To assess standard dose hormone therapy (HT) and bone mass in premature ovarian insufficiency (POI), 239 women with POI, 132 using standard estrogen dose HT and 107 women without HT, were evaluated. All underwent bone mineral density (BMD) evaluation in the lumbar spine (LS) and total femur (TF). Mean age, age at last period and body mass index (BMI) for the untreated and for the HT groups were  $38.1 \pm 6.1$  and  $36.8 \pm 7.3$  years;  $31.4 \pm 7.3$  and  $30.7 \pm 7.2$  years;  $26.6 \pm 7.1$  and  $25.8 \pm 4.6$  kg/m2, respectively, (p=NS). The women taking standard dose HT started treatment at the age of  $33.8 \pm 6.3$  years and had been on hormone treatment for 3 years at the time of the bone densitometry examination. The BMD in LS was  $1.06 \pm 0.15$  and  $1.00 \pm 0.17$  g/cm2 (p=0.003); the BMD in TF was  $0.92 \pm 0.19$  and  $0.91 \pm 0.13$  g/cm2 (p=0.039), respectively, for the untreated and HT groups. A 45% altered BMD (osteopenia/osteoporosis) in LS was verified in women without treatment and 60.1% in those using the standard dose TH (p=0.01). The BMD in TF was altered in 32.3% in those without HT and 36.4% in the HT users (p=0.34). In conclusion, standard dose HT was not adequate to reduce impaired bone mass in the spine and femur of women with POI.

#### Recent Results Cancer Res. 2016;208:199-217.

# **Obesity Biomarkers, Metabolism and Risk of Cancer: An Epidemiological Perspective.**

#### Nimptsch K, Pischon T.

Obesity is associated with metabolic alterations that may pose a biological link between body fatness and risk of cancer. Elucidating the role of obesity-related biomarkers in cancer development is essential for developing targeted strategies aiming at obesity-associated cancer prevention. Molecular epidemiological studies of the past decades have provided evidence that major hormonal pathways linking obesity and cancer risk include the insulin and insulin-like growth factor-1 (IGF-1) axis, sex-steroid hormones, adipokines and chronic low-grade inflammation. These pathways are interrelated with each other, and their importance varies by obesity-related cancer type. The insulin/IGF-1 axis has been implicated to play an important mediating role in the association between obesity and risk of pancreatic, colorectal and prostate cancer. Endogenous sex-steroid hormone concentrations, in particular obesity-associated pre-diagnostic elevations of estrogens and androgens, play an important role in postmenopausal breast cancer and endometrial cancer development. The adipokines adiponectin and leptin and adipocyte-mediated chronic low-grade inflammation represented by the acute-phase C-reactive protein may explain a substantial part of the association between obesity and risk of colorectal cancer. In this chapter, the molecular epidemiologic evidence from prospective studies relating circulating obesity-related biomarkers to cancer risk is summarized, taking into account available evidence from Mendelian Randomization investigations aiming at improving causal inference.

#### Stroke. 2016 Dec 1. pii: STROKEAHA.116.014743. [Epub ahead of print]

## Lipid Changes Around the Final Menstrual Period Predict Carotid Subclinical Disease in Postmenopausal Women.

Matthews KA, El Khoudary SR, Brooks MM, Derby CA, Harlow SD, Barinas-Mitchell EJ, Thurston RC.

BACKGROUND AND PURPOSE: Atherogenic changes in lipids occur among women around the time of the natural menopause, that is, within 1 year of the final menstrual period (FMP). We investigated whether lipid changes around the FMP are related to carotid intima-media thickness, interadventitial diameter, and plaque in postmenopausal women. METHODS: A total of 863 natural postmenopausal women with no history of heart attack or stroke underwent carotid ultrasound scans at follow-up year 12 or 13 of the Study of Women's Health Across the Nation. Estimates of their annual

change in lipids were segmented into the year before and after the FMP, before the year before FMP, and 1 year after FMP. Multivariate analyses were adjusted for sociodemographic characteristics, time from FMP to scan, baseline body mass index and systolic blood pressure, and use of medications for hypertension and diabetes mellitus at the scan. RESULTS: Smaller increases in high-density lipoprotein cholesterol and apolipoprotein A1 within 1 year of the FMP were related to greater interadventitial diameter,  $\beta$  (SE)=-0.036 (0.015), P=0.02, and  $\beta$  (SE)=-0.035 (0.013), P=0.006, respectively. Greater increases in low-density lipoprotein cholesterol within 1 year of FMP were related to greater likelihood of plaque scores  $\geq 2$ , odds ratio, 1.071; 95% confidence interval, 1.018-1.127; P=0.009. Magnitude of associations was reduced but remained significant with further adjustment for premenopausal lipid levels. The difference in probability of elevated plaque scores was 50% between those in the highest and lowest low-density lipoprotein cholesterol change tertiles. CONCLUSIONS:Changes in lipids as women approach the FMP provide useful clinical information for understanding postmenopausal carotid indices.

### Am J Respir Crit Care Med. 2016 Dec 1. [Epub ahead of print] Menopause is Associated with Accelerated Lung Function Decline.

Triebner K. Matulonga B, Johannessen A, Suske S, Benediktsdóttir B, Demoly P, Dharmage SC, et al. RATIONALE: Menopause is associated with changes in sex hormones, which affect immunity, inflammation, and osteoporosis and may impair lung function. Lung function decline has not previously been investigated in relation to menopause. OBJECTIVES: To study whether lung function decline, assessed by forced vital capacity and forced expiratory volume in one second, is accelerated in women who undergo menopause. METHODS: The population-based longitudinal European Community Respiratory Health Survey provided serum samples, spirometry and questionnaire data about respiratory and reproductive health from three study waves (N=1438). We measured follicle stimulating hormone and luteinizing hormone and added information on menstrual patterns, to determine menopausal status using latent class analysis. Associations with lung function decline were investigated using linear mixed effects models, adjusting for age, height, weight, packyears, current smoking, age at completed full-time education, spirometer and including study center as random effect. MEASUREMENTS AND MAIN RESULTS: Menopausal status was associated with accelerated lung function decline. The adjusted mean forced vital capacity decline was increased by -10.2 ml/yr (95% Confidence interval -13.1 to -7.2) in transitional women and -12.5 ml/yr (-16.2 to -8.9) in postmenopausal women, compared to women menstruating regularly. The adjusted mean forced expiratory volume in one second decline increased by -3.8 ml/yr (-6.3 to -2.9) in transitional women and -5.2 ml/yr (-8.3 to -2.0) in postmenopausal women. CONCLUSIONS: Lung function declined more rapidly among transitional and postmenopausal women, in particular for forced vital capacity, beyond the expected age change. Clinicians should be aware that respiratory health often deteriorates during reproductive aging.

#### J Clin Endocrinol Metab. 2016 Dec 1:jc20163590. [Epub ahead of print]

## Lower Death Risk for Vascular Dementia than for Alzheimer's Disease with Postmenopausal Hormone Therapy Users.

Mikkola TS, Savolainen-Peltonen H, Tuomikoski P, Hoti F, Vattulainen P, Gissler M, Ylikorkala O.

CONTEXT: There are conflicting data on postmenopausal hormone therapy (HT) and the risk of vascular dementia (VD) and Alzheimer's disease (AD). OBJECTIVE: We analyzed the mortality risk attributable to VD or AD in women with a history of HT use. Design, Patients, Interventions and Main Outcome Measures: A total of 489,105 Finnish women using systemic HT in 1994-2009 were identified from the nationwide drug reimbursement register. Of these women, 581 died of VD and 1057 of AD in 1998-2009. The observed deaths in HT users with <5 or  $\geq 5$  years of exposure were compared with those having occurred in the age-standardized female population. Furthermore, we compared the VD or AD death risk of women who had started the use of HT at <60 versus  $\geq 60$  years of age. RESULTS: The risk of death caused by VD was reduced by 37-39% (<5 or  $\geq 5$  years of exposure) with the use of any systemic HT, and this reduction was not associated with the duration or type (estradiol-only or estradiol-progestin combination) of HT. The risk of death caused by AD was not reduced with systemic HT <5 years of use, but was slightly reduced (15%) if the HT exposure had exceeded 5 years. The age at systemic HT initiation of <60 versus  $\geq 60$  years did not affect the death risk reductions. CONCLUSION: Estradiol-based HT use is associated with a reduced risk of death both from VD and AD, but the risk reduction is larger and appears sooner in VD than AD.

J Res Med Sci. 2016 Sep 1;21:76. eCollection 2016.

## The association between Vitamin D and health outcomes in women: A review on the related evidence.

#### Jolfaie NR, Rouhani MH, Onvani S, Azadbakht L.

BACKGROUND: Vitamin D has a wide range of physiological functions in skeletal and nonskeletal tissues which may play a role in many diseases. The aim of this study was to evaluate the recent evidence regarding the effects of Vitamin D on several health outcomes in women including breast cancer, ovarian and endometrial cancers, hypertension, and osteoporosis. MATERIALS AND METHODS: We searched PubMed and Google Scholar databases through March 2016. We included the most current systematic reviews and meta-analyses assessing the associations of Vitamin D intake and/or serum 25-hydroxyvitamin D (25(OH)D) levels with the risk of incidence of breast cancer, ovarian and endometrial cancers, hypertension, and osteoporosis. RESULTS: Many studies have represented that Vitamin D supplementation and high 25(OH)D levels can decrease the risk of breast cancer occurrence or mortality. However, there is no strong evidence to support the existence of a relationship between Vitamin D and ovarian or endometrial cancers. Furthermore, the results regarding the effects of Vitamin D on hypertension were inconsistent. Although observational studies have shown an association between Vitamin D and hypertension, there is no evidence regarding effectiveness of Vitamin D in lowering blood pressure in several clinical trials. On the other hand, the findings associating the impact of Vitamin D on osteoporosis were more definitive and most studies have represented that Vitamin D may have beneficial effects on osteoporosis. CONCLUSION: Although the adequate Vitamin D level can play a protective role in the incidence and development of breast cancer, hypertension, and osteoporosis, there is limited evidence regarding ovarian and endometrial cancers.

#### Menopause. 2016 Nov 28. [Epub ahead of print]

## Prevalence and correlates of vaginal estrogenization in postmenopausal women in the United States.

Lindau ST, Dude A, Gavrilova N, Hoffmann JN, Schumm LP, McClintock MK.

OBJECTIVE: This work aims to establish current population-based vaginal estrogenization norms for postmenopausal US women. METHODS: Using a US national probability sample of 868 postmenopausal women ages 57 to 85 years (mean age  $67.6\pm0.3$  y,  $21.6\pm0.5$  y since menopause), we calculated the epithelial maturation value (MV) generated from self-collected vaginal specimens and compared findings with historical clinical data. Linear and logistic regressions were used to describe the relationship between vaginal estrogenization and sociodemographic, physical, gynecologic, and sexual characteristics. RESULTS: Among postmenopausal women, mean MV was 46.6±0.8 (SD 17.4, range 2.5-100) and stable across age groups. In every age group, vaginal estrogenization was higher among postmenopausal nonusers of hormone therapy (HT) in the 2005-2006 US cohort than reported for the 1960s Canadian clinical cohort. MV was also higher among women who used postmenopausal HT in the prior 12 months compared with those who did not  $(55.1\pm1.2 \text{ vs } 44.4\pm0.9, P<0.001)$ . In multivariate analyses, HT use, obesity and African American race were each independently associated with higher MV. Overall, MV was not associated with sexual activity, but low MV was associated with vaginal dryness during intercourse among sexually active women. CONCLUSIONS: Compared to 1960s clinical data, current population estimates revealed higher vaginal estrogenization across all age groups and no decline with age. The strongest independent correlates of vaginal estrogenization in postmenopausal US women were current HT use, obesity, and African American race. Postmenopause, half of all women exhibit low vaginal estrogenization.

## Gynecol Endocrinol. 2016 Nov 29:1-6. [Epub ahead of print] Estradiol therapy and breast cancer risk in perimenopausal and postmenopausal women: a systematic review and meta-analysis.

#### Yang Z, Hu Y, Zhang J, Xu L, Zeng R, Kang D.

OBJECTIVE: To investigate the association between estradiol therapy and incidence of breast cancer, taking into consideration of different types of combined progestogen, the duration of exposure and the type of regimen. METHOD: A systematic review and meta-analysis. RESULT: A total of 14 studies were included in our study. In estradiol-only therapy analysis, meta-analysis resulted a pooled OR =0.90, 95% CI (0.40, 2.02) from the RCTs and pooled OR = 1.11, 95% CI (0.98, 1.27) from observational studies. However, in the analysis of estradiol-progestogen therapy, the risk of breast cancer varies according to the type of progestogen and the duration with more than five years (OR = 2.43, 95% CI (1.79, 3.29)) presented a higher risk than using less than five years (OR = 1.49, 95% CI (1.03, 2.15)). CONCLUSIONS:

Estradiol-only therapy carries no risk for breast cancer, while the breast cancer risk varies according to the type of progestogen. Estradiol therapy combined with medroxyprogesterone, norethisterone and levonorgestrel related to an increased risk of breast cancer, estradiol therapy combined with dydrogesterone and progesterone carries no risk. The breast cancer risk rise progressively by prolonged use, furthermore, comparing to sequential therapy, continuous therapy carries a higher risk.