Selección de Resúmenes de Menopausia

Semana del 7 al 13 de febrero de 2018

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

J Clin Endocrinol Metab. 2018 Feb 7. doi: 10.1210/jc.2017-02694. [Epub ahead of print]

Inhibiting Cellular Senescence: A New Therapeutic Paradigm for Age-Related Osteoporosis.

Khosla S, Farr JN, Kirkland JL.

With the aging of the population and projected increase in osteoporotic fractures, coupled with the declining use of osteoporosis medications, there is a compelling need for new approaches to treat osteoporosis. Given that age-related osteoporosis generally co-exists with multiple other co-morbidities (e.g., atherosclerosis, diabetes, frailty), all sharing aging itself as the leading risk factor, there is growing interest in the "Geroscience Hypothesis", which posits that manipulation of fundamental aging mechanisms will delay the appearance or severity of multiple chronic diseases because these diseases share the same underlying risk factor - age. In this context, one fundamental aging mechanism that has received considerable attention recently as contributing to multiple age-related morbidities is cellular senescence. This mini-review provides an overview on cellular senescence with a particular focus on its role in mediating age-related bone loss. Methods: This summary is based on the authors' knowledge of the field supplemented by a PubMed search using the terms "senescence", "aging", and "bone". Results: There is now compelling evidence from pre-clinical models and supportive human data demonstrating an increase in senescent cells in the bone microenvironment with aging. These cells produce a pro-inflammatory secretome that leads to increased bone resorption and decreased bone formation, and approaches that either eliminate senescent cells or impair the production of their pro-inflammatory secretome have been shown to prevent age-related bone loss in mice. Conclusions: Targeting cellular senescence represents a novel therapeutic strategy to prevent not only bone loss but potentially multiple age-related diseases simultaneously.

Eur Rev Med Pharmacol Sci. 2018 Jan;22(2):567-574. doi: 10.26355/eurrev_201801_14211.

Menopause: new frontiers in the treatment of urogenital atrophy.

Casarotti GA, Chiodera P, Tremolada C.

OBJECTIVE: Urogenital atrophy is a degenerative process that may occur during menopause causing debilitating disorders and painful symptomatology. Estrogen therapy slows the onset of atrophy, but it requires ongoing therapy to maintain its effectiveness. To mitigate the degenerative evolutions associated with menopause, patients may benefit from new therapeutic approaches, such as the use of mesenchymal stem cells. Among the many sources, the adipose tissue is considered one of the smartest, due to its abundance and easy access. This study investigated the feasibility and potential benefits of using an autologous adipose tissue to treat the symptoms of urogenital atrophy. PATIENTS AND METHODS: In 2014, the first three women affected by post-menopausal urogenital atrophy were treated with injections of autologous and micro-fragmented adipose tissue (Lipogems®). Clinical outcomes were determined at 3, 6, 9, 12, 18, 24, and 36 months by evaluating vaginal dryness, burning, itching, stranguria, sensitivity, and dyspareunia. Pre- and 36 months post-op biopsies and vaginal discharge were also collected. RESULTS: The three women reported a significant improvement of the symptoms at 6 months with complete resolution at 9 months. This benefit, subjectively reported and confirmed by clinical evaluation, remained constant without recurrence at least until 36 months. Immunohistochemical analysis revealed a total recovery of vaginal vitality with production of glycogen, vasculature hyperplasia and regeneration of the epithelium and subcutaneous tissue at 36 months. The analysis of vaginal discharge showed a restoration of an acid pH with the colonization of lactobacilli. No postoperative complications nor adverse events were recorded. CONCLUSIONS: The results of these first three cases pointed to autologous and micro-fragmented adipose tissue as a safe, feasible and effective therapeutic approach for the treatment of post-menopausal urogenital atrophy.

J Clin Endocrinol Metab. 2018 Feb 1. doi: 10.1210/jc.2017-02421. [Epub ahead of print]

High androgens in postmenopausal women and the risk for atherosclerosis and cardiovascular disease: the Rotterdam Study.

Meun C, Franco OH, Dhana K, Jaspers L, Muka T, Louwers Y, Ikram MA, Fauser BCJM, Kavousi M, Laven JSE.

Context: Polycystic ovary syndrome (PCOS) is closely linked to hyperandrogenism. In PCOS, hyperandrogenism has been associated with metabolic disturbances which increase the risk for cardiovascular disease (CVD). Objective: To assess the association of high serum androgen levels, as a postmenopausal remnant of PCOS, with the prevalence of atherosclerosis and incidence of CVD in postmenopausal women. Design: The Rotterdam Study, a prospective population-based cohort study. Median follow up was 11.36 years. Setting: General community. Participants: 2578 women aged over 55. Exclusion criteria were missing informed consent or follow-up data, perimenopausal status, menopause by surgical intervention or at an unnatural age (age <40 or >62). Intervention: None. Main outcomes and measures: Linear, logistic, and cox regression models assessed the association of top quartiles (P75) of serum testosterone, free androgen index (FAI), dehydroepiandrosterone, and androstenedione and SHBG with coronary artery calcium, carotid intima media thickness (IMT), pulse wave velocity, peripheral artery disease and incidence of coronary heart disease, stroke, and CVD. Results: Mean age (standard deviation) was 70.19 (8.71) years and average time since menopause 19.85 (9.94) years. Highest quartile FAI was associated with higher pulse wave velocity [β (95%CI): 0.009 (0.000;0.018)]. Highest quartile dehydroepiandrosterone [β (95%CI): -0.008 (-0.015;-0.001)] and androstenedione [β (95%CI): -0.010 (-0.017;-0.003)] levels were associated with a lower IMT. We found no association between high androgen levels and incident stroke, coronary heart disease, or cardiovascular disease. Conclusion: Postmenopausal high androgen levels were not associated with an increased risk for CVD. Cardiovascular health in women with PCOS might be better than was anticipated.

Menopause. 2018 Feb 5. doi: 10.1097/GME.0000000000001064. [Epub ahead of print]

History of vasomotor symptoms, extent of coronary artery disease, and clinical outcomes after acute coronary syndrome in postmenopausal women.

Ferri LA, Morici N, Bassanelli G, Franco N, Misuraca L, Lenatti L, et al; LADIES ACS Investigators.

OBJECTIVE: Vasomotor symptoms (VMS) during menopausal transition have been linked to a higher burden of cardiovascular risk factors, subclinical vascular disease, and subsequent vascular events. We aim to investigate the association of VMS with the extent of coronary disease and their prognostic role after an acute coronary syndrome. METHODS: The Ladies Acute Coronary Syndrome study enrolled consecutive women with an acute coronary syndrome undergoing coronary angiography. A menopause questionnaire was administered during admission. Angiographic data underwent corelab analysis. Six out of 10 enrolling centers participated in 1-year follow-up. Outcome data included the composite endpoint of all-cause mortality, recurrent myocardial infarction, stroke, and rehospitalization for cardiovascular causes within 1 year. RESULTS: Of the 415 women with available angiographic corelab analysis, 373 (90%) had complete 1-year follow-up. Among them, 202 women had had VMS during menopausal transition. These women had the same mean age at menopause as those without VMS (50 years in both groups), but were younger at presentation (median age 71 vs 76 years; P<0.001), despite a more favorable cardiovascular risk profile (chronic kidney dysfunction 4.5% vs 15.9%; P=0.001; prior cerebrovascular disease 4.5 vs 12.2%; P=0.018). Extent of coronary disease at angiography was similar between groups (mean Gensini score 49 vs 51; P=0.6; mean SYNTAX score 14 vs 16; P=0.3). Overall cardiovascular events at 1 year did not differ between groups (19% vs 22%; P=0.5). CONCLUSIONS: In postmenopausal women with an acute coronary syndrome, a history of VMS was associated with younger age at presentation, despite a lower vascular disease burden and similar angiographically defined coronary disease as compared with women without VMS. No difference could be found in terms of overall clinical outcomes. These results should be interpreted cautiously as all analyses were unadjusted and did not account for risk factor differences between women with and without a history of VMS.

BMC Med. 2018 Feb 6;16(1):17. doi: 10.1186/s12916-018-1008-8.

Metabolic characterization of menopause: cross-sectional and longitudinal evidence.

Wang Q, Ferreira DLS, Nelson SM, Sattar N, Ala-Korpela M, Lawlor DA.

BACKGROUND: Women who experience menopause are at higher cardiometabolic risk and often display adverse changes in metabolic biomarkers compared with pre-menopausal women. It remains elusive whether the changes in cardiometabolic biomarkers during the menopausal transition are due to ovarian aging or chronological aging. Well-conducted longitudinal studies are required to determine this. The aim of this study was to explore the cross-sectional and longitudinal associations of reproductive status, defined according to the 2012 Stages of Reproductive Aging Workshop criteria, with 74 metabolic biomarkers, and establish whether any associations are independent of age-related changes. METHODS: We determined cross-sectional associations of reproductive status with metabolic

profiling in 3,312 UK midlife women. In a subgroup of 1,492 women who had repeat assessments after 2.5 years, we assessed how the change in reproductive status was associated with the changes in metabolic biomarkers. Metabolic profiles were measured by high-throughput quantitative nuclear magnetic resonance metabolomics. In longitudinal analyses, we compared the change in metabolic biomarkers for each reproductive-status category change to that of the reference of being pre-menopausal at both time points. As all women aged by a similar amount during follow-up, these analyses contribute to distinguishing age-related changes from those related to change in reproductive status. RESULTS: Consistent cross-sectional and longitudinal associations of menopause with a wide range of metabolic biomarkers were observed, suggesting the transition to menopause induces multiple metabolic changes independent of chronological aging. The metabolic changes included increased concentrations of very small very low-density lipoproteins, intermediate-density lipoproteins, low-density lipoproteins (LDLs), remnant, and LDL cholesterol, and reduced LDL particle size, all toward an atherogenic lipoprotein profile. Increased inflammation was suggested via an inflammatory biomarker, glycoprotein acetyls, but not via C-reactive protein. Also, levels of glutamine and albumin increased during the transition. Most of these metabolic changes seen at the time of becoming post-menopausal remained or became slightly stronger during the post-menopausal years. CONCLUSIONS: The transition to post-menopause has effects on multiple circulating metabolic biomarkers, over and above the underlying age trajectory. The adverse changes in multiple apolipoprotein-B-containing lipoprotein subclasses and increased inflammation may underlie women's increased cardiometabolic risk in their post-menopausal years.

Clin Colorectal Cancer. 2018 Jan 12. pii: S1533-0028(17)30284-0. doi: 10.1016/j.clcc.2018.01.003. [Epub ahead of print]

Hormone Replacement Therapy and Colorectal Cancer Incidence and Mortality in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

Symer MM, Wong NZ, Abelson JS, Milsom JW, Yeo HL.

INTRODUCTION: Hormone replacement therapy has been shown to reduce colorectal cancer incidence, but its effect on colorectal cancer mortality is controversial. The objective of this study was to determine the effect of hormone replacement therapy on survival from colorectal cancer. PATIENTS AND METHODS: We performed a secondary analysis of data from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, a large multicenter randomized trial run from 1993 to 2001, with follow-up data recently becoming mature. Participants were women aged 55 to 74 years, without recent colonoscopy. Data from the trial were analyzed to evaluate colorectal cancer incidence, disease-specific mortality, and all-cause mortality based on subjects' use of hormone replacement therapy at the time of randomization: never, current, or former users. RESULTS: A total of 75,587 women with 912 (1.21%) incident colorectal cancers and 239 associated deaths were analyzed, with median follow-up of 11.9 years. Overall, 88.6% were non-Hispanic white, and < 10% had not completed high school. The never-user group was slightly older than the current or former user groups (average, 63.8 vs. 61.4 vs. 63.3 years; P < .001). Almost one-half (47.1%) of the current users had undergone hysterectomy, compared with 21.6% of never-users and 34.0% of former users (P < .001). Adjusted colorectal cancer incidence in current users compared to never-users was lower (hazard ratio [HR], 0.81; 95% confidence interval [CI], 0.69-0.94; P = .005), as was death from colorectal cancer (HR, 0.63; 95% CI, 0.47-0.85; P = .002) and all-cause mortality (HR, 0.76; 95% CI, 0.72-0.80; P < .001). CONCLUSIONS: Hormone replacement therapy is associated with a reduced risk of colorectal cancer incidence and improved colorectal cancer-specific survival, as well as all-cause mortality.