



## Selección de Resúmenes de Menopausia

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### **Parity, infertility, oral contraceptives, and hormone replacement therapy and the risk of ovarian serous borderline tumors: A nationwide case-control study.**

Rasmussen EL, Hannibal CG, Dehlendorff C, Baandrup L, Junge J, Vang R, Kurman RJ, Kjaer SK.

**OBJECTIVE:** Few studies have examined the risk of an ovarian serous borderline tumor (SBT) associated with parity, infertility, oral contraceptives (OCs), or hormone replacement therapy (HRT), which was the study aim. **METHODS:** This nationwide case-control study included all women with an SBT diagnosis in Denmark, 1978-2002. SBTs were confirmed by centralized expert pathology review. For each case, 15 age-matched female controls were randomly selected using risk-set sampling. Cases and controls with previous cancer (except for non-melanoma skin cancer) and controls with bilateral oophorectomy or salpingo-oophorectomy were excluded. Conditional logistic regression was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs). **RESULTS:** We found a strongly decreased risk of SBTs among parous women which decreased with increasing number of children ( $p < 0.01$ ). Older age at first birth also decreased the SBT risk ( $p = 0.03$ ). An increased SBT risk was associated with infertility (OR=3.31; 95% CI: 2.44-4.49), which was present both among parous and nulliparous women. HRT use increased the SBT risk (OR=1.32; 95% CI: 1.02-1.72), whereas OC use decreased the risk (OR=0.40; 95% CI: 0.26-0.62). **CONCLUSIONS:** Our nationwide study with expert histopathologic review of all SBTs showed that parity, infertility, use of HRT, and use of OCs, respectively, were strongly associated with the risk of SBTs. This is the first study to report a strong and significantly decreased SBT risk associated with OC use and a significantly increased risk with infertility, and HRT use. This supports that SBTs and serous ovarian cancer share similar risk factors.

**Br J Haematol. 2017 Jan 20. doi: 10.1111/bjh.14516. [Epub ahead of print]**

### **Recurrence risk of venous thromboembolism and hormone use in women from England: a cohort study using clinical practice research datalink.**

Kiconco S, Abdul Sultan A, Grainge MJ.

It is vital to identify people with low recurrence risk of venous thromboembolism (VTE) so as to protect them from dangers of prolonged anticoagulation therapy. Among women who develop VTE following hormone use, the evidence as to whether their risk of recurrence is low if they cease this therapy is conflicting. We investigated whether women whose initial VTE event was hormone-related have a lower risk of VTE recurrence than women whose initial event had no obvious cause (unprovoked). A cohort study utilising the Clinical Practice Research Datalink linked to Hospital Episode Statistics data from England was conducted. We selected 4170 women aged between 15 and 64 years who were diagnosed with a first VTE event between 1997 and 2011. Cox regression models were used to obtain hazard ratios (HR). Hormone users had 29% lower recurrence risk than non-users (adjusted HR = 0.71; 95% confidence interval 0.58-0.88), a relationship which existed both in women aged 15-44 years (predominantly oral contraceptive users) and those aged 45-64 years (predominantly hormone replacement therapy users). In conclusion, having a hormone-associated VTE is associated with a lower recurrence risk than one that is unprovoked after discontinuation of the hormone-containing preparation. Prolonged anticoagulation may therefore be unjustified in such women.

**Cell Transplant. 2017 Jan 20. doi: 10.3727/096368917X694651. [Epub ahead of print]**

### **Age related changes in bone marrow mesenchymal stromal cells: a potential impact on osteoporosis and osteoarthritis development.**

Ganguly P, J J, V P, N A, Ponchel F, A E.

Ageing at the cellular level is a complex process resulting from accumulation of various damages leading to functional impairment and a reduced quality of life at the level of the organism. With a rise in the elderly population, the worldwide incidence of osteoporosis (OP) and osteoarthritis (OA) has increased in the past few decades. A decline in the number and fitness of osteoblast progenitors, the mesenchymal stromal cells (MSCs) in the bone marrow (BM) niche has been suggested as one of the factors contributing to bone abnormalities in OP and OA. It is well-recognised

that MSCs acquire culture-induced ageing features such as gradual telomere shortening, increased numbers of senescent cells and reduced resistance to oxidative stress, as a result of serial population doublings. In contrast, there is only limited evidence that human BM MSCs similarly in vivo. This review compares the various aspects of in vitro and in vivo MSC ageing and suggests how our current knowledge on rejuvenating cultured MSCs could be applied to develop future strategies to target altered bone formation processes in OP and OA.

**Menopause. 2017 Jan 16. doi: 10.1097/GME.0000000000000808. [Epub ahead of print]**

### **Science of intracrinology in postmenopausal women.**

Labrie F, Bélanger A, Pelletier G, Martel C, Archer DF, Utian WH.

**OBJECTIVE:** To illustrate the marked differences between classical endocrinology that distributes hormones to all tissues of the body through the bloodstream and the science of intracrinology, whereby each cell of each peripheral tissue makes a small and appropriate amount of estrogens and androgens from the inactive precursor dehydroepiandrosterone (DHEA), DHEA being mainly of adrenal origin. Because only the inactivated sex steroids are released in the blood, influence in the other tissues is avoided. **METHODS:** Molecular biology has been used for the identification/characterization of the steroid-forming and steroid-inactivating enzymes, whereas steroids have been measured by mass spectrometry-based assays validated according to the US Food and Drug Administration guidelines. **RESULTS:** Evolution over 500 million years has engineered the expression of about 30 steroid-forming enzymes specific for each peripheral tissue. These tissue-specific enzymes transform DHEA into the appropriate small amounts of estrogens and androgens for a strictly intracellular and local action. Humans, contrary to species below primates, also possess intracellular steroid-inactivating enzymes, especially glucuronyl transferases and sulfotransferases, which inactivate the estrogens and androgens at their local site of formation, thus preventing the release of a biologically significant amount of estradiol (E2) and testosterone in the circulation. Since DHEA becomes the unique source of sex steroids after menopause, serum E2 and testosterone are thus maintained at low biologically inactive concentrations with no activity outside the cells of origin. DHEA secretion, unfortunately, starts decreasing at about the age of 30 at various rates in different women. Moreover, there is no feedback mechanism to increase DHEA secretion when the concentration of serum DHEA decreases. Considering this mechanism is unique to the human, it seems logical to replace DHEA locally in women suffering from vulvovaginal atrophy (genitourinary syndrome of menopause). The clinical data obtained using a small dose of intravaginal DHEA (prasterone) confirm the mechanisms of intracrinology mentioned above which avoid biologically significant changes in serum E2 and testosterone. **CONCLUSIONS:** The symptoms and signs of vulvovaginal atrophy (genitourinary syndrome of menopause) can be successfully treated by the intravaginal administration of DHEA without safety concerns. This strategy exclusively replaces in the vagina the missing cell-specific intracellular estrogens and androgens. This approach avoids systemic exposure and the potential risks of estrogen exposure for the tissues other than the vagina.

**J Midlife Health. 2016 Oct-Dec;7(4):163-168. doi: 10.4103/0976-7800.195694.**

### **Association between serum 25-hydroxyvitamin D levels and bone mineral density in normal postmenopausal women.**

Kamineni V, Latha AP, Ramathulasi K.

**AIM:** This study was conducted with the objective of assessing serum 25-hydroxyvitamin D (25(OH)D) in postmenopausal women (PMW), to detect osteopenia or osteoporosis in PMW and to establish a correlation between serum 25(OH)D levels and bone mineral density (BMD). **MATERIALS AND METHODS:** A total of 100 healthy PMW were selected, and a prospective observational study was conducted to correlate the BMD with serum 25(OH)D levels. Their laboratory investigations along with serum 25(OH)D levels were done. Their BMD was assessed with dual-energy X-ray absorptiometry at lumbar spine and neck of femur; T-scores were derived. Correlation analysis was done to investigate the relationship between serum 25(OH)D levels and BMD. **RESULTS:** The proportion of osteoporosis at the hip was 31.9% in deficient group, 16.1% in insufficient, and 18.2% in sufficient group and at lumbar spine, it was 27.7%, 16.1%, and 22.7%, respectively. Forty-seven percent of PMW had deficient (<20 ng/ml) serum 25(OH)D levels and 31% had insufficiency. T-score at hip in deficient group was  $-2.05 \pm 0.25$ , and in an insufficient group, it was  $-1.79 \pm 0.13$ ; T-score at lumbar spine was  $-1.92 \pm 0.12$  and  $-1.79 \pm 0.12$ , respectively, but both were not statistically significant. Osteoporosis was seen in 24%, osteopenia in 55% at hip level and 23% and 59% respectively at lumbar spine. There was no association between serum 25(OH)D levels and BMD neither at hip nor at lumbar spine ( $P = 0.51$  and  $P = 0.79$  respectively). **CONCLUSION:** In this study, among our cohort of patients there was no correlation between serum 25(OH)D levels and BMD. However, Vitamin D deficiency coexists with low BMD.

Vitamin D insufficiency is a common risk factor for osteoporosis associated with increased bone remodeling and low bone mass.

**Fertil Steril. 2017 Jan 12. pii: S0015-0282(16)63089-3. doi: 10.1016/j. [Epub ahead of print]**

**Normo- and hyperandrogenic women with polycystic ovary syndrome exhibit an adverse metabolic profile through life.**

Pinola P, Puukka K, Piltonen TT, Puurunen J, Vanky E, Sundström-Poromaa I, Stener-Victorin E, et al.

**OBJECTIVE:** To compare the metabolic profiles of normo- and hyperandrogenic women with polycystic ovary syndrome (PCOS) with those of control women at different ages during reproductive life. **DESIGN:** Case-control study. **SETTING:** Not applicable. **PATIENT(S):** In all, 1,550 women with normoandrogenic (n = 686) or hyperandrogenic (n = 842) PCOS and 447 control women were divided into three age groups: <30, 30-39, and >39 years). **INTERVENTIONS(S):** None. **MAIN OUTCOME MEASURE(S):** Body mass index (BMI), waist circumference, blood pressure, glucose, insulin, cholesterol, lipoproteins, triglycerides and high-sensitivity C-reactive protein. **RESULT(S):** Both normo- and hyperandrogenic women with PCOS were more obese, especially abdominally. They had increased serum levels of insulin (fasting and in oral glucose tolerance tests), triglycerides, low-density lipoprotein, and total cholesterol, higher blood pressure, and lower high-density lipoprotein levels independently from BMI compared with the control population as early as from young adulthood until menopause. The prevalence of metabolic syndrome was two- to fivefold higher in women with PCOS compared with control women, depending on age and phenotype, and the highest prevalence was observed in hyperandrogenic women with PCOS at late reproductive age. **CONCLUSION(S):** When evaluating metabolic risks in women with PCOS, androgenic status, especially abdominal obesity and age, should be taken into account, which would allow tailored management of the syndrome from early adulthood on.