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CLIMATERIO

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Climateric
Abstracs de Progesterona

1.-
The history of natural progesterone, the never-ending story.
Piette, P.
Vol. 21 Nr. 4 Página 308 - 314 Fecha de publicación 01082018
Resumen
The term progesterone should only be used for the natural hormone produced by the ovaries or included in a registered drug. The modern history of progesterone begins with the first book-length description of the female reproductive system including the corpus luteum and later with the Nobel Prize winner, Adolf Butenandt who took a crucial step when he succeeded in converting pregnanediol into a chemically pure form of progesterone, the corpus luteum hormone. The deficient production of progesterone was shown first to be the cause of the luteal-phase deficiency responsible for infertility and early pregnancy loss due to inadequate secretory transformation of the endometrium. Later, progesterone was confirmed to be the best and safest method of providing luteal-phase support in assisted reproductive technology. Progesterone provides adequate endometrial protection and is suggested to be the optimal progestagen in menopausal hormone therapy in terms of cardiovascular effects, venous thromboembolism, probably stroke and even breast cancer risk. Neuroprotective effects of progesterone have also been demonstrated in several of experimental models including cerebral ischemic stroke and Alzheimer's disease. Vaginal progesterone was shown to decrease the risk of preterm birth in women with a mid-trimester sonographic short cervix and to improve perinatal outcomes in singleton and twin gestations.

2.-
Non-clinical studies of progesterone.
Sitruk-Ware, R.
Vol. 21 Nr. 4 Página 315 - 320 Fecha de publicación 01082018
Resumen
Progesterone is a steroid hormone that is essential for the regulation of reproductive function. Progesterone has been approved for several indications including the treatment of anovulatory menstrual cycles, assisted reproductive technology, contraception during lactation and, when combined with estrogen, for the prevention of endometrial hyperplasia in postmenopausal hormonal therapy. In addition to its role in reproduction, progesterone regulates a number of biologically distinct processes in other tissues, particularly in the nervous system. This physiological hormone is poorly absorbed when administered in a crystalline form and is not active when given orally, unless in micronized form, or from different non-oral delivery systems that allow a more constant delivery rate. A limited number of preclinical studies have been conducted to document the toxicity, carcinogenicity and overall animal safety of progesterone delivered from different formulations, and these rather old studies showed no safety concern. More recently, it has been shown in animal experiments that progesterone, its metabolite allopregnanolone and structurally related progestins have positive effects on neuroregeneration and repair of brain damage, as well as myelin repair. These recent preclinical findings have the potential to accelerate therapeutic translation for multiple unmet neurological needs.

3.-
Progesterone, progestins and the endometrium in perimenopause and in menopausal hormone therapy.
Gompel, A.
Vol. 21 Nr. 4 Página 321 - 325 Fecha de publicación 01082018
Resumen
It is well established that unopposed estrogen for hormone therapy in postmenopausal women (MHT) induces a dose-related stimulation of the endometrium associated with an increased risk of hyperplasia and endometrial cancer. Progesterone acts physiologically to counteract the proliferative effects of estradiol during the menstrual cycle. In MHT, progestogens protect the endometrium against the proliferative effects of estrogens in women with a uterus. Recent data suggest that, whereas micronized progesterone is apparently safer for the breast, it could be less efficient than synthetic progestin on the endometrium. An update on progestogen and endometrial safety in MHT is the subject of this review.

4.-
Progesterone, progestins and the breast in menopause treatment.
Gompel, A.; Plu-Bureau, G.
Vol. 21 Nr. 4 Página 326 - 332 Fecha de publicación 01082018
Resumen
Breast cancer is the main risk associated with menopause hormone therapy (MHT). It is a hormone -dependent cancer. In postmenopausal women, about 80% of cases are estradiol receptor-positive. In cohort studies only estradiol receptor-positive breast cancers are promoted by MHT. Different levels of risk with estrogen-only treatment and combined treatment with estrogen + progestin are shown in randomized trials and observational studies. Several non-randomized studies show a lower risk with progesterone and retroprogesterone than with synthetic progestins. Progesterone and progestin are non-selective ligands for the progesterone receptor and bind also with other steroid receptors, with agonistic or antagonistic effects according to the structure of the molecule. Their half-life and metabolism are also different, progesterone being rapidly degraded with a short half-life. These aspects will be discussed in this review.

5.-
Progestogens and venous thromboembolism in menopausal women an updated oral versus transdermal estrogen meta-analysis.
Scarabin, P.Y.
Vol. 21 Nr. 4 Página 341 - 345 Fecha de publicación 01082018
Resumen
Postmenopausal hormone therapy (HT) is a modifiable risk factor for venous thromboembolism (VTE). While the route of estrogen administration is now well recognized as an important determinant of VTE risk, there is also increasing evidence that progestogens may modulate the estrogen-related VTE risk. This review updates previous meta-analyses of VTE risk in HT users, focusing on the route of estrogen administration, hormonal regimen and progestogen type. Among women using estrogen-only preparations, oral but not transdermal preparations increased VTE risk (relative risk (RR) 1.48, 95% confidence interval (CI) 1.39-1.58; RR 0.97, 95% CI 0.87-1.09, respectively). In women using opposed estrogen, results were highly heterogeneous due to important differences between the molecules of progestogen. In transdermal estrogen users, there was no change in VTE risk in women using micronized progesterone (RR 0.93, 95% CI 0.65-1.33), whereas norpregnane derivatives were associated with increased VTE risk (RR 2.42, 95% CI 1.84-3.18). Among women using opposed oral estrogen, there was higher VTE risk in women using medroxyprogesterone acetate (RR 2.77, 95% CI 2.33-3.30) than in those using other progestins. These clinical findings, together with consistent biological data, emphasize the safety advantage of transdermal estrogen combined with progesterone and support the current evidence-based recommendations on HT, especially in women at high VTE risk.

6.-
Evidence on the use of progesterone in menopausal hormone therapy.
Mirkin, S.
Vol. 21 Nr. 4 Página 346 - 354 Fecha de publicación 01082018
Resumen
A need exists for a regulatory agency-approved hormone therapy (HT) with naturally occurring hormones combining progesterone (P4) and estradiol (E2), since no single product contains both endogenous hormones. Many women choose HT with P4 and millions of women around the world are using unapproved, poorly regulated compounded HT. The use of natural P4 in HT results, for the most part, in favorable outcomes without deleterious effects, as shown in clinical studies of postmenopausal women. Importantly, P4 used in HT prevents endometrial hyperplasia from estrogens while helping relieve vasomotor symptoms and improving quality-of-life measures. Additionally, risk of venous thromboembolism and breast cancer does not appear to increase with use of P4 plus estrogens as shown with synthetic progestins plus estrogens in large observations studies, and no detrimental effects of P4 in HT have been found on outcomes related to cardiovascular disease or cognition. A regulatory agency-approved HT with naturally occurring E2P4 could be an option for the millions of women who desire a bioidentical product andor are exposed to potential risks of inadequately studied and under-regulated compounded HT.

7.-
Progesterone for treatment of symptomatic menopausal women.
Prior, J.C.
Vol. 21 Nr. 4 Página 358 - 365 Fecha de publicación 01082018
Resumen
This review's purpose is to highlight evidence that oral micronized progesterone (progesterone) is effective for hot flushes and night sweats (vasomotor symptoms, VMS), improves sleep and is likely safe in menopausal women (who are more than 1 year since last menstruation). Methods include randomized controlled clinical trials (RCT) supplemented with basic science, population and observational data as needed. The barrier to use of progesterone is lack of awareness that safety concerns with estrogen-including 'menopausal hormone therapy' (MHT) are not applicable to progesterone. In a single 3-month RCT, progesterone (300 mg at bedtime) was effective treatment of VMS in 133 healthy menopausal women. It caused an overall 55% VMS decrease, no withdrawal-related VMS rebound and a greater VMS decrease in 46 women with =50 moderate-intense VMSweek. Progesterone is equally or more effective than estradiol in improving cardiovascular endothelial function and caused no cardiovascular safety concerns in a 3-month RCT. An 8-year prospective cohort study (E3N) in more than 80 000 menopausal women showed progesterone prevented breast cancer in estrogen-treated women. Multiple RCTs confirm that progesterone (300 mg daily at bedtime) does not cause depression and improves deep sleep. In conclusion, progesterone effectively treats VMS, improves sleep and may be the only therapy that symptomatic women, who are menopausal at a normal age and without osteoporosis, need.

8.-
Vaginal progesterone and the vaginal first-pass effect.
Warren, M.P.
Vol. 21 Nr. 4 Página 355 - 357 Fecha de publicación 01082018
Resumen
Vaginal progesterone is an effective alternative to systemic administration by oral or intramuscular use. The first-pass effect is reviewed, as are the most common uses for this route of delivery. This includes use in hormone replacement therapy, luteal support particularly in assisted reproduction, and avoidance of side-effects of oral progestins and progesterone. Vaginal progesterone represents a unique therapeutic solution to a number of clinical problems.

9.-
Progesterone for the prevention and treatment of osteoporosis in women.
Prior, J.C.
Vol. 21 Nr. 4 Página 366 - 374 Fecha de publicación 01082018
Resumen
Estradiol (E2) is women's dominant 'bone hormone' since it is essential for development of adolescent peak bone mineral density (BMD) and physiological levels prevent the rapid (3-week) bone resorption that causes most adult BMD loss. However, deceasing E2 levels trigger bone resorption-loss. Progesterone (P4) is E2's physiological partner, collaborating with E2 in every celltissue; its bone 'job' is to increase P4-receptor-mediated, slow (3-4 months) osteoblastic new bone formation. When menstrual cycles are normal length and normally ovulatory, E2 and P4 are balanced and BMD is stable. However, clinically normal cycles commonly have ovulatory disturbances (anovulation, short luteal phases) and low P4 levels; these are more frequent in teen and perimenopausal women and increased by everyday stressors energy insufficiency, emotionalsocialeconomic threats and illness. Meta-analysis shows that almost 1%year spinal BMD loss occurs in those with greater than median (~31%) of ovulatory disturbed cycles. Prevention of osteoporosis and fragility fractures requires the reversal of stressors, detection and treatment of teen-to-perimenopausal recurrent cycleovulatory disturbances with cyclic oral micronized progesterone. Low 'Peak Perimenopausal BMD' is likely the primary risk for fragility fractures in later life. Progesterone plus estradiol or other antiresorptive therapies adds 0.68%year and may be a highly effective osteoporosis treatment. Randomized controlled trials are still needed to confirm progesterone's important role in women's bone formation.

10.-
Selective progesterone receptor modulators current applications and perspectives.
Chabbert-Buffet, N.; Kolanska, K.; Daraï, E.; Bouchard, P.
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Resumen
Selective progesterone receptor modulators (SPRMs) are steroid progesterone receptor ligands able to induce agonistic or antagonistic activities. Mifepristone, the class leader, was primarily used for pregnancy termination from the 1980s. Emergency contraception with extended activity was the second major development 30 years later, with mifepristone in some countries and ulipristal acetate world-wide. More recently, ulipristal acetate was released for the treatment of myoma-related uterine bleeding. In addition to a very rapid cessation of bleeding, SPRMs allow a decrease in myoma volume, as do gonadotropin releasing hormone analogs. However, estradiol secretion is not blunted by SPRMs. This offers new alternatives for myoma treatment, especially in women close to menopause. In conclusion, use of SPRMs has allowed significant progress in emergency contraception and treatment of myoma-related symptoms. Numerous future perspectives in women's health care are currently under evaluation.

11.-
Progestogens and pregnancy loss.
Carp, H.J.A
Vol. 21 Nr. 4 Página 380 - 384 Fecha de publicación 01082018
Resumen
Progestational agents are often prescribed to prevent pregnancy loss. Progestogens affect implantation, cytokine balance, natural killer cell activity, arachidonic acid release and myometrial contractility. Progestogens have therefore been used at all stages of pregnancy including luteal-phase support prior to pregnancy, threatened miscarriage, recurrent miscarriage, and to prevent preterm labor. In luteal support, a Cochrane review reported that progestogens were associated with a higher rate of live births or ongoing pregnancy in the progesterone group (odds ratio 1.77, 95% confidence interval (CI) 1.09-2.86). Evidence suggests that progestogens are also effective for treating threatened miscarriage. Again, in a Cochrane Database review, progestogens were associated with a reduced odds ratio of 0.53 (95% CI 0.35-0.79) when progestogens were used. In recurrent miscarriage, progestogens also seem to have a beneficial effect. A meta-analysis of progestational agents showed a 28% increase in the live birth rate (relative risk 0.72, 95% CI 0.53-0.97). For the last 30 years, progestogens have been used to prevent preterm labor. Recent meta-analyses also report beneficial effects. This review summarizes the literature and the author's experience using progestogens to prevent pregnancy loss.

12.-
Surgical challenges in the treatment of perimenopausal and postmenopausal endometriosis.
Ozyurek, E.S.; Yoldemir, T.; Kalkan, U.
Vol. 21 Nr. 4 Página 385 - 390 Fecha de publicación 01082018
Resumen
Endometriosis is classically defined as a chronic, recurrent and progressive disease. It is known to be estrogen-dependent, but can still be observed during the peri- and postmenopausal periods. Medical management of endometriosis is palliative symptomatic relief. Surgery when properly and timely performed for the right person may treat endometriosis. However, there is always a risk of possible major or minor surgical complications, as well as loss of some functions due to nerve damage. Management of endometriosis in the woman approaching the end of her reproductive life may require special attention both due to the potential for recurrence and transformation into various endometriosis-associated malignancies.