Editorial

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Preface to Special Issue: Role of progestogens in women's health: an update

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At the occasion of the 18th World Congress of Gynecological Endocrinology in Florence, from the 7th to the 10th of March 2018 and the 16th World Congress of Menopause in Vancouver, from the 6th to the 9th of June 2018 the European Progestogen Club (EPC) has organized two scientific sessions under the heading "Role of Progestogens in Women's Health: An Update".

The topic was chosen as progestogens play an important role in premenopausal and postmenopausal women. The highlights are presented to further improve the practical clinical values so far achieved.

Part A. Severe adenomyosis is a difficult event, in particular, if a future pregnancy is desired. Clinical problems with severe adenomyosis (pain, conception problems) can be handled by hysterectomy. However, if pregnancy is desired, hormone treatment in severe cases will be not sufficient, and most likely will not restore fertility. Therefore, conservative surgery seems to be effective using the operation procedure of Osada. Based on a long-term follow-up a proper operative approach seems to be effective not only in controlling the symptoms, but even uneventful pregnancies combined with a cesarean section have been accomplished. This should stimulate further studies.

The second article by P.A. Regidor is very relevant regarding hormonal contraception. Besides the common estrogen/progestogen-combination as an oral medication, vaginal applications, transdermals or injectables have also been developed.

The progestogen used is based on several modes of action:

1. Strong antgonadotropic action
2. Thickening of the cervical mucus
3. Desynchronization of the endometrial changes necessary for implantation
4. Progestogen-only application is not burdened with an increase of thrombotic events.

The different progestogens have, besides the common progestogenic effect, different potency regarding clinical events and side effects. The new upcoming progestogen-only pill, taken for 24 days with progestogen medication and for 4 days without, is associated with a satisfying contraceptive action, a better menstrual bleeding pattern than before and no thrombotic risk. When introduced into the market further clinical studies will need to be done.

Endogenous as well as exogenous progesterone are converted to alloprenanolone, which is no longer progestogenic, but plays a dominant role in fetal brain development and function. Allopregnanolone also affects the maternal brain during pregnancy regarding timely parturition, lactation and the expression of appropriate maternal behavior postpartum. The favorable effect on post-partum depression has been shown. Low allopregnanolone levels during pregnancy appear to predict postpartum depression. Synthetic progestogens as used in hormonal contraception lead to a decrease of allopregnanolone and are causing negative mood changes and depressive states as synthetic progestogens cannot be converted to allopregnanolone. Indeed, hormonal contraceptives, particularly among adolescents have been associated with the subsequent use of antidepressants.

Taking into account that the worldwide decrease of hormone therapy (HT) in menopausal women has been finally recognized by the scientific community and also by the authors of the Women's Health Initiative (WHI) trials, because of the side effects following cancelling HT in menopausal women. Regarding the choice of a progestogen for HT in menopausal women, the authorsof the WHI-publication point out, that progesterone and to some extent dydrogesterone are not increasing in proliferation in breast tissue. Future studies may show

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the possibility to provide screening for patients at risk and perhaps predicting the prognosis of possible breast cancer.

Part B. An explanation of the clinical development of adenomyosis over time at a higher age parallel to the gradual decrease of endogenous progesterone seems to fit very well with the demonstrated polymorphism findings of the study leading to increasing concentrations of biologically active estrogens and their metabolites to create a progression of adenomyosis and is in line with the effects playing a role in breast and endometrial cancer development.

Because of the clinical relevance, the impact of progestogens in pre- and postmenopausal women on combined oral hormonal contraceptives and progestogen-only-pills (POPs) is discussed by Sven O. Skouby and Johannes J. Sidelmann. The differential effects of these preparations are detailed. An overall outlook regarding all types of hormonal contraceptives is given, but particular attention is directed towards the POPs.

The choice of progestogens for endometrial protection in combination with transdermal estradiol in menopausal women is detailed by A.O. Mueck and Th. Roemer. In the presence of an intact uterus concurrent administration of a progestogen is required for endometrial protection. No commercial product is available at present to apply estrogen and progestogen together transdermally. Practical recommendations for the choice of the progestogen (type and dose) particularly regarding endometrial protection are provided by A.O. Mueck and Th. Roemer.

There is an ever increasing number of publications showing that endometriosis becomes clinically manifest or reappears at menopause as outlined by L.M. Scemana and coworkers. The possibility is discussed regarding the negative impact of HT to trigger a recurrence of endometriosis and even an increased risk of malignancy.