

which estrogens can regulate inflammation<sup>(27)</sup>.

Recently, a study showed an inappropriate immune response to sex hormones especially estrogen and progesterone in RPL women as compared with the control group due to hypersensitivity to sex hormones<sup>(28)</sup>.

On the contrary, a study compared the serum level of progesterone and estradiol between a group of non-pregnant women with history of RPL during the follicular phase, and nulligravid females with tubal or male-factor infertility without miscarriage, showed comparable results in both groups with very few cases showing higher estrogen and lower progesterone levels in the study group<sup>(29)</sup>. But our data come from the local expression of the hormone at the materno-fetal interface meaning that we try to study the actual hormonal environment during pregnancy. Also apart from systemic changes in the maternal immune system, local immunomodulation at the materno-fetal interface via wide array of hormones and cytokines and immune effector cells also play a very critical role in maintaining the balance of a desirable immune response<sup>(30, 31)</sup>.

In conclusion, increased expression of estrogen receptor in women with RPL could give a clue to its role as a pro-inflammatory stimulant augment the effect of Th1 cytokines participating in the pathology of RPL.

### **References**

1. NaPro Technology. Com. Recurrent spontaneous abortion (miscarriage). 2006.
2. Baird DD, Weinberg CR and Wilcox AJ. Hormonal profiles of natural conception cycles ending in early pregnancy loss. *J Clin Endocr and Metab.* 1999; 72: 793-800.
3. Hatasaka HH. Recurrent miscarriage: Epidemiologic factors, definitions and incidence. *Clin Obstet Gynaecol.* 1994; 37: 625-634.
4. Hill JA. Sporadic and recurrent spontaneous abortion. *Curr Probl Obstet Gynecol Fertil.* 1994; 4: 113-162.
5. Jurkovic D, Gruboeck K, Tailor A and Nicolaides KH. Ultrasound screening for congenital uterine anomalies. *Br J Obstet Gynaecol.* 1997; 104: 1320-1321.
6. Bermas BL and Hill JA. Proliferative responses to recall antigens are associated with pregnancy outcome in women with a history of RSA. *J Clin Invest.* 1997; 100: 6: 1330-1334.
7. Dixit VD, Yang H, Udhayakumar V and Sridaran R. Gonadotropin-releasing hormone alters the T helper cytokine balance in the pregnant rat. *Biol Reprod.* 2003; 68: 2215-2221.
8. Norwitz ER, Schust DJ and Fisher SJ. Implantation and the survival of early pregnancy. *N Engl J Med.* 2001; 345: 1400-1408.
9. Ansar Ahmed S, Hissong BD, Verthelyi D, Donner K, Becker K, Karpuzoglu- Sahin E. Gender and risk of autoimmune diseases: possible role of estrogenic compounds. *Environ Health Perspect.* 1999; 107(Suppl 5):681-686.
10. Cutolo M, Serio B, Villaggio B, Pizzorni C, Cravio C, Sulli A. Androgens and estrogens modulate the immune and inflammatory responses in rheumatoid arthritis. *Ann NY Acad Sci.* 2002; 966:131-142
11. Lahita RG. The role of sex hormones in systemic lupus erythematosus. *Curr Opin Rheumatol.* 1999; 11:352-356
12. Karpuzoglu-Sahin E, Hissong BD, Ansar Ahmed S. IFN- $\gamma$  levels are upregulated by 17 $\beta$ -estradiol and diethylstilbestrol. *J Reprod Immunol.* 2001; 52:113-127
13. Karpuzoglu-Sahin E, Zhi-Jun Y, Lengi A, Sriranganathan N, Ansar Ahmed S. Effects of long-term estrogen treatment on IFN- $\gamma$ , IL-2 and IL-4 gene expression and protein synthesis in spleen and thymus of normal C57BL/6 mice. *Cytokine.* 2001; 14:208-217
14. Karpuzoglu E, Fenaux JB, Phillips RA, Lengi AJ, Elvinger F and Ahmed SA. Estrogen Up-Regulates Inducible Nitric Oxide Synthase, Nitric Oxide, and Cyclooxygenase-2 in Splenocytes Activated with T Cell Stimulants: Role of Interferon- $\gamma$ . *Endocrinology.* 2006; 147(2):662-671.
15. Lydon JP, DeMayo FJ, Funk CR, Mani SK, Hughes AR et al. Mice lacking progesterone receptor exhibit pleiotropic reproductive abnormalities. *Genes Dev.* 1995; 9: 2266-2278.
16. Tibbetts TA, Conneely OM and O'Malley BW. Progesterone via its receptor antagonizes the pro-inflammatory activity of estrogen in the