

**229** Nocturnal LH pulsatile secretion in adolescent patients with hypothalamic amenorrhea. D.Okuyama, M.Nagatsuka, S.Ooishi, H.Chiba, K.Kawai T.Yanaiharu, Dept.Obst. and Gynec., Showa Univ. Sch. Med., Tokyo

Pulsatile secretion of LH (LH pulse) which is closely related to GnRH secretion appears to be essential for the normal ovarian function in female after puberty. In the present study, blood sample was collected every 20 min from 8 p.m. to 6 a.m. and nocturnal secretion of LH was examined in 14 patients aged 16-21 y.o. with hypothalamic amenorrhea. Patients were divided into two groups, group I; withdrawal bleeding (grade I Am), group II; no withdrawal bleeding (grade II Am), by gestagen test. Nocturnal LH secretion was evaluated by basal LH level (Ba), frequency (Fr), amplitude (A) and basal estradiol level ( $E_2$ ), and were compared with normal women. No significant difference in Ba was noticed between normal and Am. However, significantly lower Fr and  $E_2$ , but higher tendency of A were observed in group II to compare with those in normal and group I. In group I, similar tendency was observed, though the difference was not significant to compare with normal. The appearance of LH pulsatile secretion especially frequency in puberty suggested to play an important role to establish menstrual cycle.

**230** Growth inhibition of MCF-7 human breast cancer cells by aromatase inhibitors. M.Fukuoka, J.Kitawaki, T.Yamamoto, M.Yoshihama\*, H.Okada, Dept.Obst. and Gynec., Kyoto Pref. Univ. of Med., Kyoto, \*Snow Brand Milk Products, Co. Ltd., Research Institute of Life Science, Tohigi.

MCF-7 cell line is a model for estrogen-dependent tumors that have both aromatase activity and estrogen receptor. We have previously reported that estrogens which are biosynthesized from androgens by the intracellular aromatase have significant role in growth stimulation of MCF-7 cells and that aromatase inhibitors block this pathway. Then we have compared the inhibitory effects of aromatase competitive inhibitor aminoglutethimide (AG) and suicide inhibitor 14 $\alpha$ -hydroxy-4-androstene-3,6,17-trione (14 $\alpha$ -OHAT). MCF-7 cells were cultured in phenol red-free medium containing 10% charcoal-treated fetal bovine serum and aromatase activity was measured by [<sup>3</sup>H]water method using [<sup>3</sup>H]androstenedione as the substrate. DNA synthesis was measured by [<sup>3</sup>H]thymidine incorporation method. Preincubation of MCF-7 cells with 14 $\alpha$ -OHAT resulted in a reduction of aromatase activity and thymidine incorporation. In contrast, preincubation with AG resulted in a stimulation of aromatase activity and thymidine incorporation. These contrasted effects enhanced by higher concentrations and longer preincubation period of inhibitors. The results suggest that 14 $\alpha$ -OHAT may be more effective than AG. Our model would be a useful technique for studying the regulation of estrogen-dependent tumors and for direct assessment of the potency of aromatase inhibitors.

**231** A study of endothelin-1 release from human decidual cells in early pregnancy. K.Sumori, T.Kubota, S.Kamada, M.Taguchi, Y.Hirata\*, F.Marumo\*, T.Aso. Dept.Obst. and Gynec., \*Dept.2nd Int. Medicine, Tokyo Medical and Dental Univ. Fac. Med., Tokyo.

It was reported that endothelin-1 (ET-1), a novel vasoconstrictive peptide, may play an important role in the human reproductive environment. The present study was undertaken to investigate the effect of ET-1 on the function of human decidua. The decidua in early pregnancy was enzymatically dispersed into a monocellular suspension, and were cultured for 48 hours. ET-1 concentrations in the media were measured by a specific RIA. High concentrations of ET-1 were detected in the condition medium from cultured decidual cells. The total ET-1 level in the control ( $550.3 \pm 24.2$  fmol/ml/48h, Mean  $\pm$  SD) was significantly greater ( $p < 0.05$ ) than that in  $10^{-8}$  M  $Ca^{2+}$  ionophore (INP,  $Ca^{2+}$  mobilizer) ( $488.7 \pm 40.1$ ). The ET-1 levels in  $10^{-7}$  M PMA, C-kinase activator, ( $360.5 \pm 17.2$  fmol/ml/24h) was significantly greater ( $p < 0.05$ ) than that in the control ( $314.4 \pm 27.3$ ). These effects of  $Ca^{2+}$  INP and PMA were in the dose dependent manner. However,  $10^{-7}$  M ET-1 had no significant effect on  $[Ca^{2+}]_i$  in decidual cells.

These results indicated that human decidual cells had releasing ability of ET-1. This releasing mechanism has tight connection with  $[Ca^{2+}]_i$  change through  $Ca^{2+}$  channel and with C-kinase activation, but ET-1 did not activate the function of the cells through the modulation of  $[Ca^{2+}]_i$ .