

**D115** Induction of luteinized unruptured follicle by indomethacin in the gonadotropin-primed immature rat

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Luteinized unruptured follicle(LUF) has been considered as a typical cause of unexplained infertility in women and as another structure appeared in mammalian folliculogenesis. To clarify the mechanism leading to LUF, changes of steroid hormonal status, histological characterization, ovulation rate and integrity of ovarian cell DNA in induced LUF by indomethacin(prostaglandin synthesis inhibitor) administration were investigated in gonadotropin-primed immature rat system. Serum, oviducts and ovaries were collected from these animals at 1/2, 1, 2, 3, 4 days after hCG injection. It was revealed that the concentration of progesterone was decreased markedly in comparison with that of control at 12hr after treatment( $p < 0.05$ ), so it maintained lower level through the duration of the present experiment. Serum level of estradiol was temporarily decreased only at 12hr after treatment( $p < 0.05$ ), and was recovered soon up to the control level. Various types of unruptured follicles were found on day 1/2 in treated ovaries. All of large Graafian follicles in treated group were found to be atretic. And ovulation rate of treated group was less than 10% in all animals. The ladder patterns of fragmented DNA reveals that the size of oligonucleosomal-length DNA in treated animals were distributed on much more smaller fractions than that of controls. Therefore it is concluded that LUF may be occurred by inhibit the prostaglandin synthesis pathway and generated by abnormal changes in steroidogenesis.

**D116** Involvement of Fas-antigen expression in granulosa cell death during ovarian follicular atresia

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Granulosa cell death during ovarian follicular atresia is being speculated to occur by apoptosis, an active genetically governed process of selective cell deletion. In this connection, we initially confirmed DNA fragmentation, generalized feature of apoptotic cell death, in ovarian granulosa cells and investigated the expression of Fas-antigen, a transmembrane receptor which triggers apoptosis in a variety of tumor and hematopoietic cells, in the course of follicular atresia induced by 15IU PMSG-treatment to immature female rat during 5 days. The earliest morphological signs of atresia were detected 4 days after PMSG injection as evidenced by degeneration and detachment of granulosa cells from the basal lamina. Electrophoretic analysis of DNA in granulosa cell lysates revealed a definitive ladder pattern of oligonucleosomal-length DNA fragments on days 4 and 5 after PMSG injection. This pattern was not detectable on day 1 and 2 after treatment. RNA blot analysis and RT-PCR assay of Fas-antigen expression in granulosa cells during ovarian follicular atresia indicated that the signals were gradually intensified from day 1 to 5, respectively. We conclude that the product of the Fas-antigen gene is down-regulated by gonadotropin during first 2-3 days after injection and thereafter initiates its expression by the waning levels of tropic support caused by metabolism of the gonadotropin, and may be involved in promoting granulosa cell apoptosis during follicular atresia.