

these steroids with  $\Delta 1/\Delta 5$  during oral glucose administration.

#### 417. Effect of Aminoglutethimide on Androstenedione Aromatase Activity in Human Uterine Myoma

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The incidence of uterine myoma is highest among benign uterine tumors. The origin of uterine myoma is under debate but the growth of the tumor is dependent upon estrogen. The authors have reported that uterine myoma possesses androstenedione aromatase (estrogen synthetase) activity and its enzyme activity is significantly higher than that in uterine myometrium. Aminoglutethimide (AG) is well known to be an inhibitor for aromatase activity of human placenta or human breast cancer. AG is used as an endocrine therapy for patients with advanced breast cancer. This study was planned whether or not AG suppresses androstenedione aromatase activity in human uterine myoma.

Uterine myoma microsome (30 mg of protein) was incubated with [6,7- $^3\text{H}$ ]-androstenedione (100 pmol) and NADPH in the various concentration of AG (0, 10 nM, 1  $\mu\text{M}$ , 100  $\mu\text{M}$ ) at 37°C for 1 hr in air. After stopping the enzyme reaction by ethyl acetate, [4- $^{14}\text{C}$ ]-estrone and [4- $^{14}\text{C}$ ]-estradiol were added in the incubated sample. The ethyl acetate extract was subjected to Bio-Rad AG1-X2 column, thin layer chromatographies and co-crystallization.

Aromatase activity in uterine myoma microsome was suppressed significantly by the addition of AG (inhibitory rate; 12-75% and 26-75% for 10 nM-AG and 1  $\mu\text{M}$ -AG, respectively). These results may show that the growth of uterine myoma is suppressed by a placental aromatase inactivator.

#### 418. Localization and Periodic Change of 17 $\beta$ -Hydroxysteroid Dehydrogenase in Human Uterine Cervix

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17 $\beta$ -HSD (hydroxysteroid dehydrogenase) activity

was measured by incubating 25  $\mu\text{M}$  of  $^{14}\text{C}$ -estradiol-17 $\beta$  with an 800 $\times$ g supernatant of human uterine cervical tissues and excess NAD at 37°C for 60 min under ambient air. The cervix obtained by hysterectomy was divided into columnar cell component, squamous cell component and connective tissue. The 17 $\beta$ -HSD activity was found to have linear relation with incubation time up to 120 min and with protein concentration up to 0.25 mg/ml. The apparent  $K_m$  value was  $2.0 \times 10^{-6}$  M. The enzymatic activity, expressed as pmol of products formed per hour and per mg of protein, showed  $49.1 \pm 8.9$  pmol/mg protein/hour (mean  $\pm$  SE), in columnar cell component,  $16.5 \pm 2.3$  in squamous cell component, and  $9.0 \pm 1.0$  in connective tissue at proliferative phase ( $n=5$ ), and  $42.8 \pm 6.6$  in columnar cell component,  $12.2 \pm 2.3$  in squamous cell component, and  $10.6 \pm 1.6$  in connective tissue at secretory phase ( $n=6$ ). It showed a marked increase in the columnar cell component at both phases ( $p<0.01$ ). While no significant difference was found among the different phases of the menstrual cycle.

#### 419. Ultrastructural Study on the Development of the Cervical Epithelium in the Human Fetal Uterus

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Prenatal development of the cervical epithelium was studied morphologically in 12 uteri obtained from human fetuses between 14 and 40 weeks of gestation.

By 15 weeks, the cervical epithelium was lined by pseudostratified columnar epithelium. The epithelium began to fold from 16 weeks, and by 21 weeks several cleft-like glandular structures were formed. At 40 weeks the glandular structures lined by tall columnar cells with basally situated nuclei were observed.

Ultrastructurally, the columnar cells at 15 weeks had centrally located nuclei and subnuclear glycogen deposit. By 18 weeks cytoplasmic organelles were well developed, and glycogen deposit in the subnuclear region became conspicuous. From 21 weeks, the apical cytoplasm containing glycogen began to protrude toward the lumina, resembling apocrine secretion. At 26 weeks this secretory activity became maximal and decreased at 31 weeks. At 40 weeks, the cells showed typical features of mucin-producing cells.

Morphologically, fetal cervical epithelium was con-

sidered to differentiate into mucin-producing cells by 40 weeks, through the phases of subnuclear glycogen storage from 14 to 18 weeks and apocrine-like secretion from 21 to 31 weeks. These changes by 31 weeks resemble those of adult endometrium during menstrual cycle. This suggests that fetal endocervical epithelium is under the influence of sex steroids during pregnancy, and that mucinous differentiation is induced on the cells which have passed through the morphological changes resembling endometrium.

#### 420. Cytochemical and Morphological Studies on Secretory Mechanism of Secretory Cells in Human Oviduct Epithelium

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To elucidate secretory mechanism of secretory cells in human oviduct epithelium, cytochemical and morphological changes of secretory cells during the menstrual cycle and after the menopause were studied with light microscopy, scanning and transmission electron microscopy. The ampullary epithelia of oviducts were obtained from 27 women at four reproductive stages of 6 cases each and at postmenopause of 3 cases.

The results were as follows:

1) Secretory cells contained diastase-resistant PAS positive and Alcian-Blue negative materials, which showed cyclic changes. The mean amount of this material in one secretory cell per case, which was semiquantitatively assessed using LM (0:-, 1:+, 2:#, 3:##), was low in both early follicular ( $1.30 \pm 0.08$ ) and late luteal ( $1.14 \pm 0.07$ ) phases, and increased significantly higher in both late follicular ( $1.97 \pm 0.06$ ) and early luteal ( $1.94 \pm 0.07$ ) phases, and decreased significantly lower in a few years after the menopause ( $0.68 \pm 0.07$ ) ( $p < 0.01$ ).

2) SEM studies revealed prominent swelling of secretory cells, their shortened microvilli and secretory material-like structure at ovulatory and ovum-passing periods.

3) TEM studies revealed numerous free ribosomes, developed rough endoplasmic reticulum and Golgi apparatus in secretory cells in late follicular phase. Secretory granules, which showed deposits of silver with an improved periodic acid-silver methenamine technique, appeared abundantly in apical

part of secretory cells at ovulatory period, and also exocytosis was characteristically observed in early luteal phase.

#### 421. Measurements of Adrenergic Neurotransmitter at Egg Transport in the Rabbit Oviduct

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To study the correlation with noadrenaline (NA) and egg transport in to oviducts, the amount and localization of NA were observed at estrus and various periods of gestation (10, 12, 24, 72 and 96 hr after mating). The effects of exogenous estradiol ( $E_2$ ) or reserpine administration on the amount of NA and egg transport were examined thereafter.

NA was measured by high-performance liquid chromatography.

1) In the distal isthmus, NA level was significantly lower at 12 hr after mating than at estrus NA level at the other sites was only insignificantly lowered at any other time after mating, as compared with that at estrus.

2) NA level at the distal and proximal isthmus was significantly elevated at 72 hr after the administration of  $E_2$  (25 or 250  $\mu\text{g/day sc}$ ), as compared with that before administration.

3) The concentration of NA in the oviduct at 24 and 72 hr after injection of hCG was significantly decreased by reserpine (0.3 or 0.6 mg/kg/day sc) treatment as compared with that before treatment.

4) After  $E_2$  or reserpine administration, the egg failed to enter the uterus and remained in the ampulla or distal isthmus.

5) The abundance of adrenergic nerve terminals was a significant feature of the isthmus confirmed by the histochemical method.

These findings suggest that during normal egg transport through the oviduct there is a correlation with decreased level of NA in the distal isthmus and passage of eggs into the isthmus, and that elevated or depleted levels of NA is associated with abnormal egg transport through the isthmus.

#### 422. An Application of CA125 Measurement to a Parameter of Ovarian Function

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