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Question one

Cyclic changes in the following

VAGINA.

Hitschmann and Adler showed that the human uterine mucosa undergoes cyclic morphologic changes, which depend on the ovarian function. Stockard and Papanicolaou, Long, Evans and Allen proved that in rodents not only the uterine mucosa but also the vaginal mucosa and vaginal secretion show cyclic morphologic changes determined by the ovarian function. Hence it is probable to assume that the human vagina is also under the influence of the ovarian hormones. Dierks1 in 1927 showed that during the menstrual cycle definite proliferative and destructive changes occur in the human vaginal epithelium. In the first days after the beginning of the last menstrual period a division of the vaginal epithelium into three layers is noticeable. This is more strikingly marked during the premenstrual period. Through the early appearance of an intra-epithelial zone of cornification. the human vaginal epithelium may be divided into a functionalis, the layer of regeneration and change

Vaginal cytology was evaluated weekly over 12 months in 20 adult female Cynomolgus monkeys (Macaca fascicularis). After sacrifice of the animals the histology of the ovaries, uterus and vagina were studied in different phases of the menstrual cycle. The cytological examination of the vaginal smears showed that the superficial cells increased in number towards the middle of the cycle and the number of intermediate cells declined gradually. Parabasal cells were observed mainly at the beginning of the cycle; they disappeared towards the middle of the menstrual cycle. During the early follicular phase, the cells were moderately separated from each other, and during the second half of the proliferative or follicular phase,

the superficial cells appeared clumped together. Leucocytes were usually absent except for at the beginning of the cycle and in the last few days of the late secretory or luteal phase. The maturation index of the vaginal smears can be considered as a tool for distinguishing the different phases of the menstrual cycle. The microscopic examination of the genital organs showed that during the proliferative or follicular phase of the cycle, which corresponds to the development of the ovarian follicles, the uterus showed growth of endometrial glands, stroma and endothelial cell proliferation with capillary sprouts. Shortly after ovulation and parallel to the formation of the corpora lutea, the endometrium enters the secretory or luteal phase, which is characterized by coiling of endometrial glands, glandular secretion and the differentiation of the spiral artery. The most striking changes in the vagina, is the marked basal cell proliferation and thickening of the stratum granulosum during the follicular phase of the menstrual cycle. The histological changes observed in the vagina demonstrated a good correlation with the observation on cytological examination of the smears. The present study demonstrated that the process of angiogenesis in the uterus during the different phases of the menstrual cycle is a multiple phenomenon involving proliferation, maturation and differentiation.

CERVIX.

Cervical mucus at midcycle is increased in amount, acellularity, water content, and fluidity. Furthermore, cervical mucus at this time is well supplied with carbohydrate and presumably amino acids. From a teleologic standpoint, we may conclude that because of these characteristics the sperm, on deposition in the vagina, find an environment propitious for their nutrition and migration through the cervical canal. During the ovulation phase the cervical mucus is thin and contains a high percentage of water; its dry content is low. (The dry content before and after the ovulation phase is higher.)

Assessment of the dry content of the cervical mucus is a practical and simple method for evaluating estrogenic stimulation, since estrogenic stimu- lation leads to the production of a watery cervical mucus with low dry content. Inadequate estrogenic stimulation results in scantiness of the cervi- cal mucus, which is thick and of relatively high dry content. Because progesterone inhibits the production of cervical mucus, the ad- ministration of progesterone to a woman in whom estrogenic stimulation is adequate depresses secretion and changes the character of the mucus. In a woman in whom estrogenic secretion is inadequate, the mucus becomes gelatinous and its dry content is increased.

Earlier studies in vitro2 have shown that in specimens with a mucus dry content of less than 5.0 per cent conditions for spermigration were optimal; in mucus with a dry content of 5.0 to 7.0 per cent conditions were relatively good; but in specimens with a dry content of more than 7.0 per cent, condi- tions were poor.

Only in that phase of the menstrual cycle during which the dry content of the cervical mucus was less than 5.0 per cent more were conditions for spermigration found to be optimal in vitro. Durillg this phase the cervical mucus and sperm are iso-osmotic, which may be a factor favoring optimal spermigration.4

In a gynecologic series in which each of 15 women were examined in the course of a single cycle, a dry content of less than 5 per cent for a period of 1-5 days was recorded in 13 (mean duration: 2.8 days); but in the other 2 no such decrease was observed. The period during which the mucus showed the characteristics of the water phase, and thereby of optimal conditions for spermigration, immediately preceded and coincided with the thermal shift.

QUESTION 2.

HORMONAL REGULATION OF THE MENSTRUAL CYCLE.

The menstrual cycle is regulated by a complex hormonal system with positive and negative feedback mechanisms and changes in sensitivity of peripheral tissues. Four concepts appear to be fundamental:

- Regular, pulsatile secretion of LHR is necessary to the functioning of the system
- Regulation is to a great extent effected by the pituitary gland in response to changes in ovarian steroid levels
- Changes in ovarian steroid levels are due to regulatory changes in receptivity to pituitary hormones, as well as to variations in enzyme activities
- At the periphery, changes in hormonal impacts are accompanied by modifications of receptivity to steroid hormones.

The menstrual cycle is regulated by the coordinated functions of the hypothalamus, pituitary, ovaries, and endometrium. The pulsatile secretion of gonadotrophin-releasing

hormone from the hypothalamus stimulates the anterior pituitary to secrete follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which in turn stimulates the development of ovarian follicles and the production of ovarian steroids. A negative feedback mechanism is crucial for its control and regulation. During the follicular phase, the recruited follicle prepares for ovulation. After the LH surge and ovulation, the luteal phase begins. The follicular and luteal phases correspond to the proliferative and secretory phases of the endometrium, which develops during the proliferative phase and is maintained during the secretory phase to prepare for implantation of the fertilized embryo. The endometrium is shed during menses in the early follicular/proliferative phase, and the cycle continues.