

REPRODUCTIVE TRACT

Virtually all structures of the reproductive tract are sensitive to the action of ovarian steroid hormones. It is not surprising, therefore that alterations are seen in the various components under the influence of steroid contraceptive agents. Differences depend upon the type and quantity of the compound used, the mode of administration, and the duration of use.

Vaginal cytologic effects are not remarkable but there is a shift toward basophilia with a predominance of intermediate cells during treatment with progestational agents (181). A distinct change is noted in the bacterial flora, with marked reduction in Doderlein bacilli, a remarkable increase in fungi, and a greater number of coccoid bacteria and trichomonads. Such alterations may be related to the increased sexual activity thought by some to occur in certain women who elect to use oral contraceptives.

Progestational compounds induce characteristic physicochemical changes in the cervical mucus (21, 118), including decreased viscosity, poor Spinnbarkeit, absence of arborization, a continuous alkaline pH with no tendency toward an increase in pH at midcycle, and the secretion of a viscous and cellular mucus that is hostile to sperm, as shown by inhibition of penetration and migration of spermatozoa in most treated subjects. With medication there is no cyclic variation in the content of proteins and no trend toward a specific ratio of the major proteins. In the normal cycle, however, a marked decrease in the albumin level and an increase in the mucoid level is noted immediately before and concomitant with ovulation, with reversal of this ratio shortly after ovulation. Inhibition of motility and of penetration of cervical mucus by sperm is demonstrable at all dosage levels of these oral contraceptives but these effects are less pronounced when small doses of progestins alone are used (112).

Biochemical changes in cervical mucus have not been extensively explored. The alpha-amylase content is increased more markedly after combined than after sequential therapy (71), and the glycogen content of the ectocervix is unaffected by steroid contraceptives in women.

Remarkable morphologic changes induced by progestational hormones have been described (59, 109, 168). Hypersecretion and hyperplasia of the cervical glands, stromal edema, and increased vascularity are the most consistent responses. In Gall's (59) study of 103 randomly selected women receiving oral contraceptives for periods of 1 to 60 months, gross lesions that failed to stain with Schiller's solution were noted in 84 per cent of patients examined. Endocervical erosion or eversion, edema, and softening were the main features. Histological examination showed an inflammatory infiltrate consisting predominantly of plasma cells. Fibrin thrombi were observed in the capillaries and arterioles in about 50 per cent of the biopsy specimens. Atypical polypoid endocervical hyperplasia was found in three cases.

This latter lesion was first described by Taylor and associates (168) in 13 women (median age of 25 years) receiving low-dosage progestational agents. There had been no previous reports of such lesions in women on high-dosage birth control pills. All lesions were associated with an inflammation and they disappeared after discontinuation of the drug. Reversibility of the lesion in cases studied emphasizes the importance of recognition in order to avoid an erroneous diagnosis of adenocarcinoma.

The histologic appearance of the endometrium varies considerably with the type of steroid regimen employed, although prolonged administration tends to diminish these differences (45, 139, 142). Combined therapy is associated with a shortened period of proliferation followed by an early but brief and limited secretory activity in the epithelium of the endometrial glands. Thinning or regression of the endometrium takes place after a few cycles and may be so severe that withdrawal bleeding cannot occur. Prolonged periods of amenorrhea following cessation of treatment may result in part from this action of progestational agents. It is not yet clear whether this oversuppression affects primarily the endometrium, the ovary, the pituitary, or the hypothalamic cycle of gonadotropin-releasing-factors (53, 58, 153).

Endometrial effects during sequential treatment are less pronounced. The progestin induces a partial or early secretory pattern comparable to that of the 18th or 19th day of the cycle, but development of the spiral arterioles is suppressed (123).

Histochemical studies of endometrial tissues have provided some information