ESTROGENS

Three ovarian estrogens (estradiol, estrone, and estriol) are secreted in significant amounts. Estradiol is the major estrogen because it exerts more estrogenic activity than the other two estrogens combined. The main function of the estrogens is to promote growth in tissues related to reproduction and sexual characteristics in women. More specific effects of estrogens on body tissues are described in Box 28–1.

In nonpregnant women, between puberty and menopause, estrogens are secreted in a monthly cycle called the menstrual cycle. During the first half of the cycle, before ovulation, estrogens are secreted in progressively larger amounts. During the second half of the cycle, estrogens and progesterone are secreted in increasing amounts until 2 to 3 days before the onset of menstruation. At that time, secretion of both hormones decreases abruptly. When the endometrial lining of the uterus loses its hormonal stimulation, it is discharged vaginally as menstrual flow.

During pregnancy, the placenta produces large amounts of estrogen, mainly estriol. The increased estrogen causes enlargement of the uterus and breasts, growth of glandular tissue in the breasts, and relaxation of ligaments and joints in the pelvis. All these changes are necessary for the growth and birth of the fetus.

Finally, estrogens are deactivated in the liver, partly or mainly by cytochrome P450 3A4 enzymes. The estrogens are then conjugated with glucuronic acid or sulfuric acid, which makes them water soluble and readily excreted through the kidneys. Metabolites are also formed in the gastrointestinal tract, brain, skin, and other steroid target tissues. Most of the conjugates are excreted in urine; some are excreted in bile and recirculated to the liver or excreted in feces.

PROGESTERONE

Progesterone is a progestin concerned almost entirely with reproduction. In the nonpregnant woman, progesterone is secreted by the corpus luteum during the last half of the menstrual cycle, which occurs after ovulation. This hormone continues the changes in the endometrial lining of the uterus begun by estrogens during the first half of the menstrual cycle. These changes provide for implantation and nourishment of a fertilized ovum. When fertilization does not take place, the estrogen and progesterone levels decrease and menstruation occurs.

If the ovum is fertilized, progesterone acts to maintain the pregnancy. The corpus luteum produces progesterone during the first few weeks of gestation. Then, the placenta produces the progesterone needed to maintain the endometrial lining of the uterus. In addition to its effects on the uterus, progesterone prepares the breasts for lactation by promoting development of milk-producing cells. Milk is not secreted, however, until the cells are further stimulated by prolactin from the

BOX 28–1 EFFECTS OF ENDOGENOUS ESTROGENS

Breasts
- Stimulate growth at puberty by causing deposition of fat, formation of connective tissue, and construction of ducts. These ducts become part of the milk-producing apparatus after additional stimulation by progesterone.

Sexual Organs
- Enlarge the fallopian tubes, uterus, vagina, and external genitalia at puberty, when estrogen secretion increases greatly.
- Cause the endometrial lining of the uterus to proliferate and develop glands that later nourish the implanted ovum when pregnancy occurs.
- Increase resistance of the epithelial lining of the vagina to trauma and infection.

Skeleton
- Stimulate skeletal growth so that, beginning at puberty, height increases rapidly for several years. Estrogen then causes the epiphyses to unite with the shafts of the long bones, and linear growth is halted. This effect of estrogen is stronger than the similar effect of testosterone in the male. Consequently, women stop growing in height several years earlier than men and on the average are shorter than men.
- Conserve calcium and phosphorus for healthy bones and teeth. This action promotes bone formation and decreases bone loss.
- Broaden the pelvis in preparation for childbirth.

Skin and Subcutaneous Tissue
- Increase vascularity in the skin. This leads to greater skin warmth and likelihood of bleeding in women.
- Cause deposition of fat in subcutaneous tissue, especially in the breasts, thighs, and buttocks, which produces the characteristic female figure.

Anterior Pituitary Gland
- Decrease pituitary secretion of follicle-stimulating hormone and increase secretion of luteinizing hormone when blood levels are sufficiently high (negative feedback mechanism).

Metabolism
- Affect metabolism of both reproductive and nonreproductive tissues. Estrogen receptors are found in female reproductive organs, breast tissue, bone, the brain, liver, heart, and blood vessels. They are also found in various tissues in men.
- Increase protein anabolism, bone growth, and epiphyseal closure in young girls.
- Decrease bone resorption.
- Increase sodium and water retention, serum triglycerides, and high-density lipoproteins (HDL or “good” cholesterol).
- Decrease low-density lipoproteins (LDL or “bad” cholesterol).
- Increase the amount of cholesterol in bile and thereby increase gallstone formation.

Blood Coagulation
- Enhance coagulation by increasing blood levels of several clotting factors, including prothrombin and factors VII, IX, and X, and probably increase platelet aggregation.