

Lesson

**Hormonal Regulation of the
Estrous Cycle**

Hormones of female reproduction

- Estrogens
- Progesterone
- Gonadotropins

Estrogens

- The important estrogens in mammals are steroids, produced by the ovary (granulosa cells of follicles), placenta, and adrenal cortex.
- Estradiol-17 β and estrone are estrogens that predominate in domestic nonpregnant and pregnant animals, respectively.

Generally, the principal function of the estrogens is to cause cellular proliferation and growth of the tissues related to reproduction. Tissue responses caused by estrogens include:

- 1. stimulation of endometrial gland growth;
- 2. stimulation of duct growth in the mammary gland;
- 3. increase in secretory activity of uterine ducts;
- 4. initiation of sexual receptivity;

- 5. regulation of secretion of luteinizing hormone (LH) by the anterior pituitary gland;
- 6. possible regulation of $\text{PGF2}\alpha$ release from the nongravid and gravid uterus;
- 7. early union of the epiphysis with the shafts of long bones, whereby growth of long bones ceases;
- 8. protein anabolism;
- 9. epitheliotropic activity.

Progesterone

- Progesterone, like the estrogens, is a steroid sex hormone produced by the corpus luteum (CL) of the ovary, placenta, and adrenal cortex.
- It is the principal progestational hormone. Certain synthetic and natural progestational agents are called progestins.

The activities associated with progesterone are often performed in concert with estrogens, and usually require previous estrogen priming. The functions of progesterone include:

- 1. promotion of endometrial gland growth,
- 2. stimulation of secretory activity of the oviduct and endometrial glands to provide nutrients for the developing embryo before implantation

- 3. promotion of lobuloalveolar growth in the mammary gland
- 4. prevention of contractility of the uterus during pregnancy
- 5. regulation of secretion of gonadotropins.

Gonadotropins

- Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are collectively referred to as the gonadotropins because of their role in stimulating cells within the ovary and testis (the gonads).
- FSH and LH are hormones secreted by cells within the anterior pituitary. Both are classified chemically as glycoproteins

- The main function of FSH in the female is promotion of the growth of follicles.
- LH is important for the ovulatory process and the luteinization of the granulosa, an essential aspect of CL formation.

- FSH and LH concentrations exist in the plasma at a tonic or basal level.
- These levels are controlled by negative feedback from the gonads. Tonic levels are increased by estrogen and decreased by progesterone.

- The release of FSH and LH from the anterior pituitary is controlled by a gonadotropin releasing hormone (GnRH) from the hypothalamus.
- GnRH is secreted in response to low levels of LH or FSH and is then followed by secretion of LH or FSH.

- The concentrations of estrogens and progesterone also influence the amount of LH or FSH secretion.
- Generally, an increasing concentration of estrogen causes an increase in sensitivity of the anterior pituitary to GnRH, and results in an increased release of gonadotropins.

- Progesterone decreases sensitivity of the anterior pituitary to GnRH, and LH and FSH concentrations decrease.
- These influences, particularly those of estrogen, depend on gradually increasing concentrations of estrogen over a period of time, which results in the preovulatory surge of LH release.
- Conversely, when estrogen concentration is basal and of short duration, LH and FSH secretions are suppressed.

Prostaglandins

- The prostaglandins were first isolated from accessory sex gland fluids and were termed prostaglandins because of their association with the prostate gland. It is now recognized that they are secreted by almost all body tissues and, indeed, the prostate gland association is too narrow a definition.

- The prostaglandins are derived from arachidonic acid. The prostaglandins are usually short-acting. Some forms never appear in the blood (so some have not been classified as hormones) and others are degraded after they circulate throughout the liver and lungs.

- Prostaglandin F₂α (PGF₂α) is the natural luteolytic agent that terminates the luteal phase of the estrous cycle and allows for the initiation of a new estrous cycle in the absence of fertilization. PGF₂α is also particularly potent in terminating early pregnancy.

- *The prostaglandins promote inflammation. The anti-inflammatory activity of aspirin (and of other drugs) is a result of its ability to inhibit the synthesis of prostaglandin G₂ (PGG₂) from arachidonic acid.*

Summary of Ovarian Cycle Events

- 1. After regression of the CL (luteolysis caused by $\text{PGF2}\alpha$), FSH and LH secretion increases (because of a decrease in the concentration of progesterone).
- 2. LH stimulates secretion of androgens by the theca interna cells, which diffuse into the granulosa cells.

- 3. FSH stimulates conversion of androgen to estrogen by the granulosa cells, and the estrogen concentration gradually increases.
- 4. FSH stimulates the formation of LH receptors on the granulosa cells.
- 5. Estrogen-rich fluid formed by the granulosa cells separates the granulosa cells and forms a pocket known as an antrum

- 6. The gradually increasing estrogen concentration causes a preovulatory surge of LH release.
- 7. The LH surge promotes the maturation of oocytes by resuming meiosis through the first polar body stage.
- 8. The LH surge promotes the intrafollicular production of prostaglandins A and E (PGA and PGE), associated with rupture of the follicle.

- 9. Concomitant with PGA and PGE production is the formation of multivesicular bodies (MVB), which form as out-pockets of the exposed theca externa.
- 10. MVBs seem to secrete proteolytic enzymes that digest ground substance cementing the theca externa fibroblasts, allowing escape of the oocyte (ovulation).

- 11. The LH surge causes reduction in the number of FSH receptors on the granulosa cells, so the rate of conversion of androgen to estrogen diminishes.
- 12. LH attaches to granulosa cell LH receptors and begins the conversion of the granulosa from estrogen secretion in the follicular phase to progesterone secretion in the luteal phase.

- 13. At some point in the latter stages of these events, ovulation occurs and the cavity previously occupied by the mature follicle becomes a corpus luteum.
- 14. The corpus luteum secretes progesterone, which causes a decrease in the output of FSH and LH by the anterior pituitary.

- 15. The corpus luteum regresses and the output of progesterone begins to decrease.
- 16. A decrease in the level of progesterone causes FSH and LH secretion to increase, and the cycle is repeated.