Chapter 24 – Reproduction and Reproductive Cycles

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To explain the general process of gametogenesis.
B. To explain the basic processes in sex differentiation.
C. To explain spermatogenesis in the male.
D. To explain the transport of sperm through the male reproductive system, and the mechanisms for causing an erection.
E. To explain the hypothalamic-pituitary-gonad control of male reproductive function.
F. To explain oogenesis in the female.
G. To explain the development of the ovarian follicle and the transport of the oocyte.
H. To explain the hypothalamic-pituitary-gonad control of female reproductive function.
I. To compare and contrast the early follicular, late follicular, and luteal phases of the menstrual cycle.
J. To explain how pregnancy prevents the sloughing off of the endometrium of the uterus.

Although males and females are different in many respects, they have much in common. Both have gonads that function in gametogenesis and in the production of steroid reproductive hormones. Both have systems of ducts for the passage of sperm and eggs. The female is unique however, in having structures for the housing, support, and nourishment of the fetus.

Gametogenesis

The general process for gametogenesis, shown in Figure 24.1, starts with a primordial germ cell. Each primordial germ cell contains 46 chromosomes (23 pairs of homologous chromosomes). The two chromosomes of each pair are said to be homologous to each other. One of the chromosomes of each pair is of maternal origin (from mother), the other chromosome of each pair is of paternal origin (from father). Throughout most of interphase each chromosome has just one chromatid.

Mitosis – In late interphase, in preparation for mitosis, the chromatids of each chromosome are duplicated and each chromosome now has two chromatids (sister chromatids).

During mitosis the sister chromatids of each primordial cell separate and move into two cells, a mother cell and a daughter. Both the mother cell and the daughter cell have 46 chromosomes (23 pairs of homologous chromosomes) and each chromosome now has one chromatid.

Meiosis part I (1) – In preparation for meiosis part I, the chromatids of each chromosome are duplicated and each of the 46 chromosomes now has two chromatids (sister chromatids).

As meiosis part I begins, homologous chromosomes line up next to each other, forming what are sometimes called tetrads. Overlapping portions of the homologous chromosomes often break off and exchange with each (crossing-over). The orientation of each set of homologous chromosomes (tetrads) is random with 2^{23} different combinations of maternal and paternal chromosomes possible.

The pairs of homologous chromosomes (tetrads) separate and move into two new daughter cells. Each of the daughter cells now has 23 single chromosomes and each chromosome has two chromatids (sister chromatids).

Meiosis part II (2) – The new daughter cells continue into meiosis part II. The sister chromatids of each single chromosome separate and move into two new daughter cells. Each of the new daughter cells now has 23 single chromosomes and each chromosome now has just one chromatid. These new daughter cells are often called gametes.

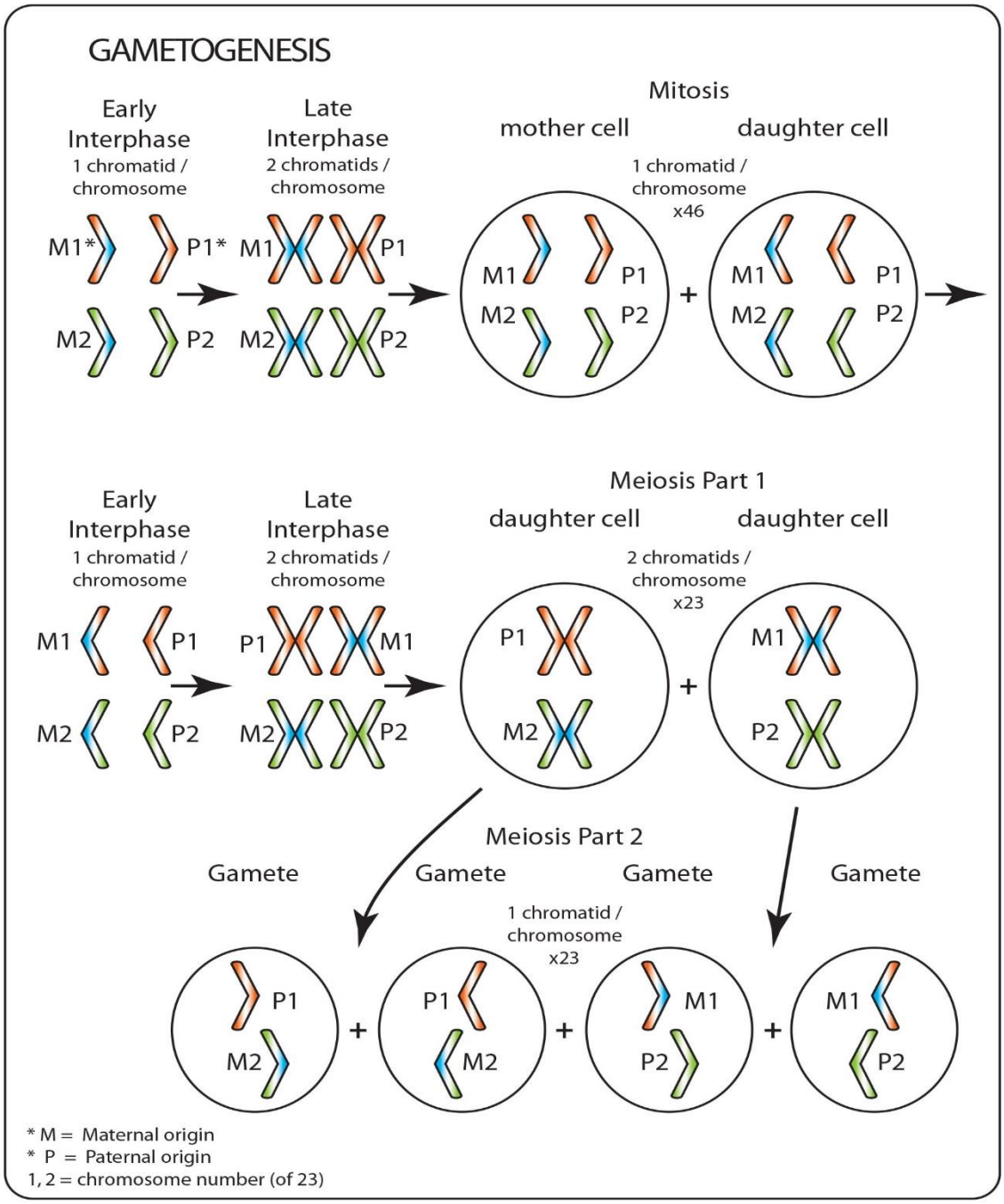

Figure 24.1 © 2014 David G. Ward, Ph.D.

Sex differentiation

Males possess one X and one Y chromosome; whereas females have two X chromosomes. During fetal development expression of the SRY gene on the Y chromosome in the male stimulates the development of the testes (at about week 7). In the absence of the Y chromosome in the female testes do not develop. Most of the sex differences are determined by substances produced by the gonads, especially the testes.

Before the fetal gonads are functional the primitive reproductive tract consists both of Wolffian ducts and of Mullerian ducts.

In the male, the Sertoli cells of the testes secrete Mullerian inhibiting substance (MIS) and the interstitial cells of the testes secrete testosterone. MIS causes the degeneration of the Mullerian ducts. Testosterone stimulates the differentiation of the Wolffian ducts into the epididymis, vas deferens, ejaculatory duct and seminal vesicles. The external genitalia develop from other structures.

In the female, the absence of testes, and thus the absence of MIS allows the Mullerian ducts to develop into the uterine tubes and uterus. The absence of testes, and thus the absence of testosterone causes the Wolffian ducts to degenerate and the vagina and external genitalia to develop from structures at the body surface.

Male Reproduction

The male reproductive system includes the testes, epididymis, vas deferens, ejaculatory duct, urethra, seminal vesicle, prostate and penis. The primary purpose of the male reproductive system is to produce sperm that contain random permutations of the male's paternal and maternal DNA, and transfer it to a receptive female. Sperm is produced by the testes, matured in the epididymis, transported through the vas deferens and ejaculatory duct, mixed with fluids from the seminal vesicle and prostate, and transported through the urethra in the penis.

Spermatogenesis

A photomicrograph of the seminiferous tubules with ongoing spermatogenesis is shown in Figure 24.2. In the male the primordial germ cells are called spermatogonia (singular is spermatogonium) and they undergo mitosis throughout adult life. Normal development of the sperm requires a temperature about 1.1C lower that core body temperature. The process of spermatogenesis is outlined below (please refer to Figure 24.1). For every primary spermatocyte, four sperm are produced.

1) Spermatogonium (1)
    - contains 23 pairs of homologous chromosomes with 1 or 2 chromatids each
    - undergoes mitosis in the seminiferous tubules through adulthood
    - produces a primary spermatocyte and a daughter spermatogonium
2) Primary Spermatocyte (1)
    - contain 23 pairs of homologous chromosomes with 1 or 2 chromatids each
    - undergoes meiosis I in the seminiferous tubules
    - produces two secondary spermatocytes
3) Secondary Spermatocytes (2)
    - contain 23 single chromosomes with 2 chromatids each
    - undergoes meiosis II in the seminiferous tubules
    - each secondary spermatocyte produces two spermatids
4) Spermatids (4)
    - contain 23 chromosomes with one chromatid each
    - mature into sperm
5) Sperm (Spermatozoa) (4)
    - contain 23 chromosomes with one chromatid each

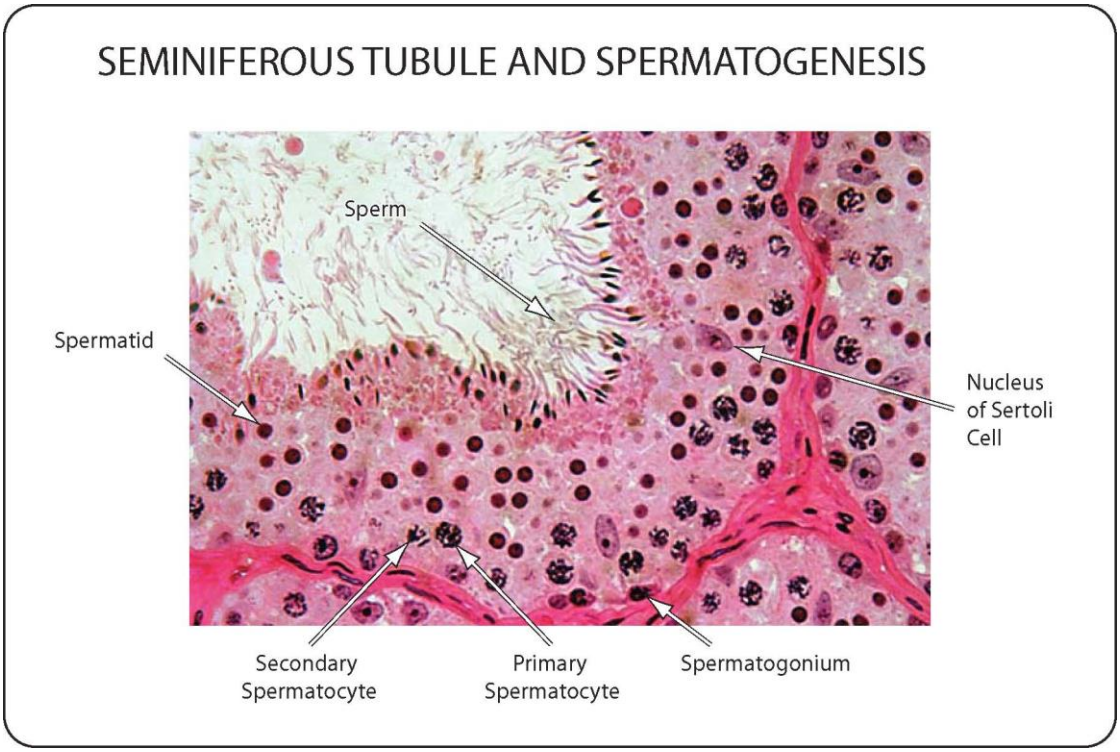

Figure 24.2 © 2007 David G. Ward, Ph.D.

Transport of sperm

The sperm are pushed from the seminiferous tubules into the rete testis where the sperm from many tubules are mixed together. The sperm move through the efferent ducts to the epididymis where the sperm are concentrated dramatically by fluid absorption and mature. From the epididymis the sperm move by peristaltic contraction of the smooth muscle of the epididymis and vas deferens. Ejaculation involves two phases. First, sperm are moved to the ejaculatory ducts where they are mixed with glucose rich fluid from the seminal vesicles. The sperm is pushed through the prostate where additional fluid and enzymes are added before the semen empties into the urethra. The semen is expelled from the urethra by a series of rapid contractions of the urethral smooth muscle and by contraction of skeletal muscle at the base of the penis.

Erection usually precedes ejaculation, and depends on filling the penis with blood. The neural control of erection is shown in Figure 24.3.

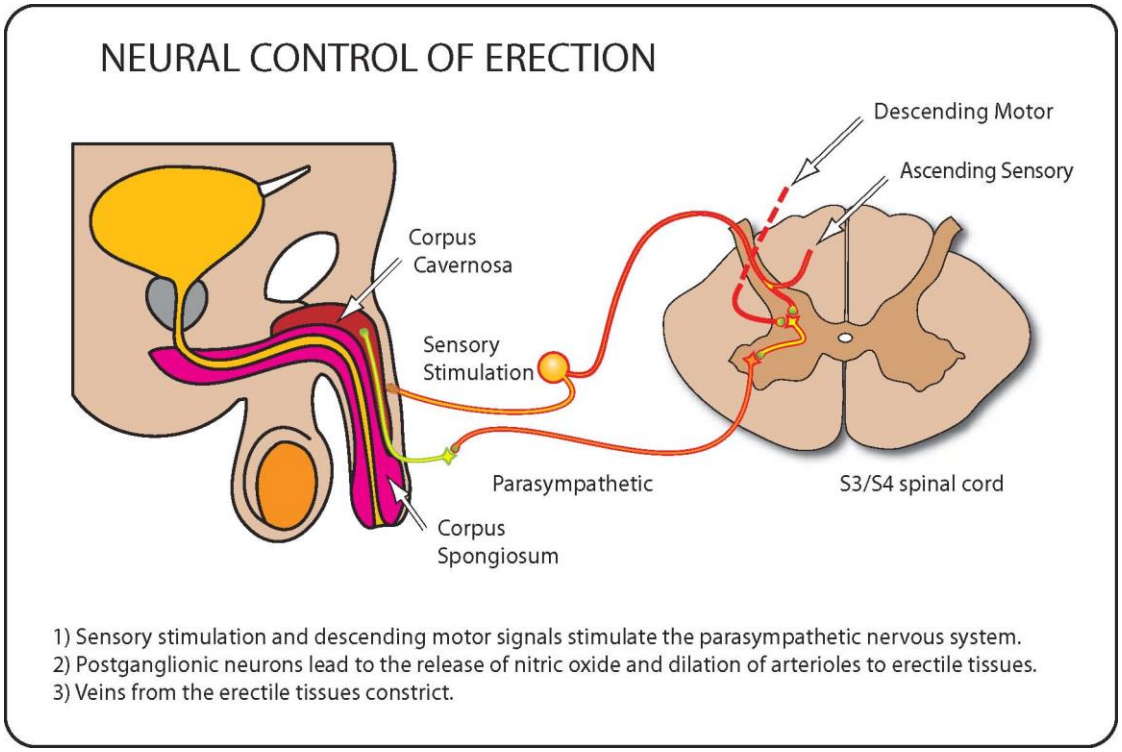

Figure 24.3 © 2007 David G. Ward, Ph.D.

The penis is composed mainly of three vascular compartments, often called erectile tissue. One compartment, the corpus spongiosum, encircles the entire length of the urethra. Two other compartments, the two corpora cavernosa, are located bilaterally above and anterior to the corpus spongiosum. Signals from sensory stimulation of the penis or from descending motor pathways stimulate the parasympathetic nervous system. Postganglionic neurons secrete acetylcholine which binds to M-3 receptors of endothelial cells causing them to the release nitric oxide which diffuses to the smooth muscle and dilates the arterioles of the erectile tissues. Veins from the erectile tissues constrict and the vascular compartments engorge with blood. In the smooth muscle of the arterioles nitric oxide stimulates guanylyl cyclase which converts GMP to cyclic GMP leading to decreased intracellular calcium and relaxation of the smooth muscle.

These actions are terminated by the breakdown of cyclic GMP by phosphodiesterase type 5 (PDE5). Sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cialis) are PDE5 inhibitors that permit a higher concentration of cyclic GMP.

Hormonal control of male reproductive function

The reproductive anterior pituitary hormones described in chapter 15 control the testes and together with the hypothalamus form the hypothalamic-pituitary-gonad axis in the male, as shown in Figure 24.4.

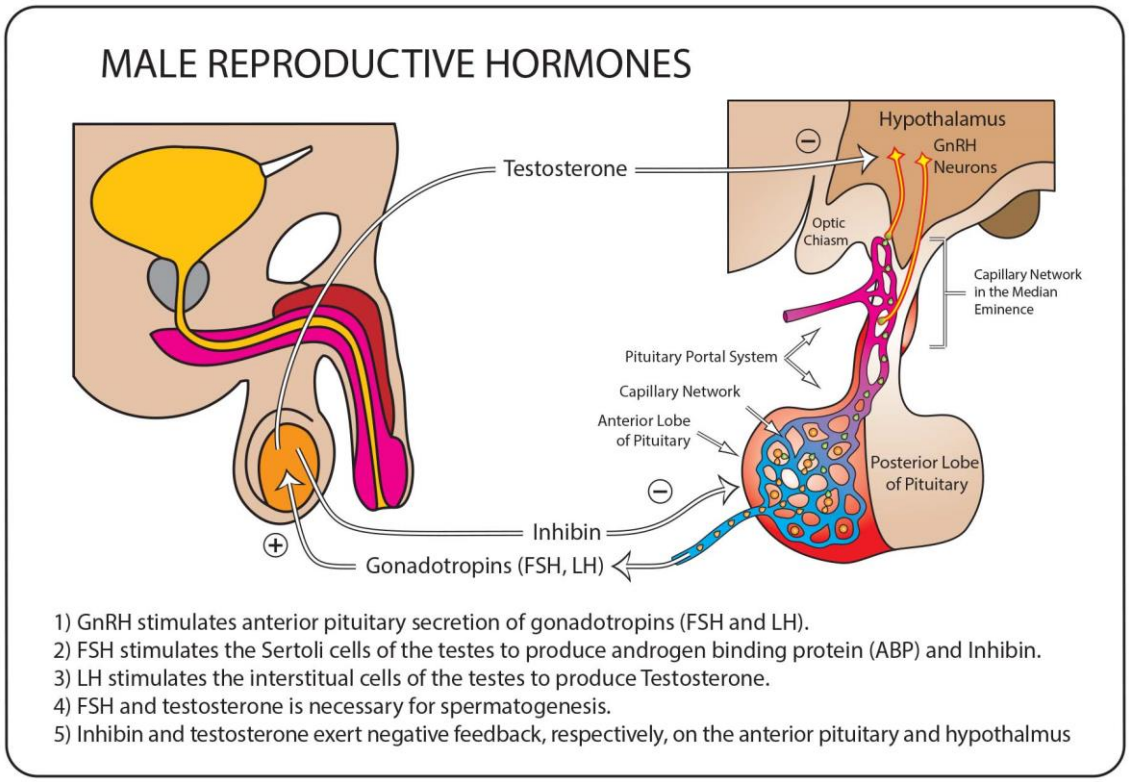

Figure 24.4 © 2020 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) secreted from hypothalamic neurons stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- FSH stimulates the Sertoli cells of the testes to produce inhibin and androgen binding protein.
- LH stimulates the interstitial cells (between the seminiferous tubules) of the testes to synthesize and release testosterone.
- Inhibin acts on pituitary gonadotrophs to inhibit the secretion of FSH.
- Androgen binding protein binds to testosterone, keeps the concentration of testosterone high in the seminiferous tubules, and thus enables spermatogenesis and sperm maturation.
- Testosterone inhibits secretion of GnRH by hypothalamic neurons.

Testosterone has other actions which include

- maintains accessory organs of male reproductive tract
- determines secondary male sexual characteristics
- stimulates protein synthesis and muscle growth
- influences sexual behavior by increasing libido

The inhibition of the pituitary gonadotrophs by inhibin and the inhibition of GnRH neurons by testosterone provide a check and balance of testosterone and sperm production.

Female Reproduction

The female reproductive system includes the ovaries, fimbrae, uterine tubes, uterus, vagina, and supporting ligaments. The primary purpose of the female reproductive system is to produce oocytes that contain random permutations of the female's paternal and maternal DNA, to receive sperm from a male, and to support and nourish the embryo and fetus. Oocytes are produced by the ovaries, captured by the fimbrae and transported into the uterine tube and uterus.

Oogenesis

In the female, the primordial germ cells are called oogonia (singular oogonium) and they undergo mitosis only during fetal development. The ovaries of the female infant do not contain oogonia, rather they contain primary oocytes. A photomicrograph of an ovary with primary oocytes is shown in Figure 24.5. The process of oogenesis is outlined below (please refer to Figure 24.1). For every primary oocyte only one ovum is produced and only if the secondary oocyte is penetrated by a sperm.

1) Oogonium (1)
   - contains 23 pairs of homologous chromosomes
   - undergoes mitosis only during fetal development
   - produces primary oocytes
2) Primary Oocyte (1)
   - contains 23 pairs of homologous chromosomes with 1 or 2 chromatids each
   - undergoes meiosis I in the maturing ovary, in the maturing ovarian follicle
   - produces one secondary oocyte and one polar body
3) Secondary Oocyte (1)
   - contains 23 single chromosomes with 2 chromatids each
   - undergoes meiosis II(2) after penetration by the sperm
   - produces one ovum and one polar body
4) Ovum (1)
   - contains 23 chromosomes with one chromatid each

Development of the ovarian follicle and transport of the oocyte

The handling of the primary oocyte in the ovary is much different than the handling of the spermatocyte in the testes. In the ovary the primary oocytes are surrounded by a layer of simple squamous epithelium that is responsive to follicle stimulating hormone (FSH). Stimulation of these epithelial cells by FSH leads to the development of a follicle around the primary oocyte. A maturing ovarian follicle is shown in Figure 24.6

1) First, granulosa cells surround and attach to the primary oocyte by glycoproteins forming what is called the zona pellucida.
2) The granulosa cells proliferate and soon separate forming a fluid filled space in the follicle called the antrum.
3) Subsequently, theca cells develop around the outside granulosa cells of the follicle.
4) At about the time the theca cells develop, the primary oocyte undergoes meiosis I and produces a secondary oocyte and a polar body.

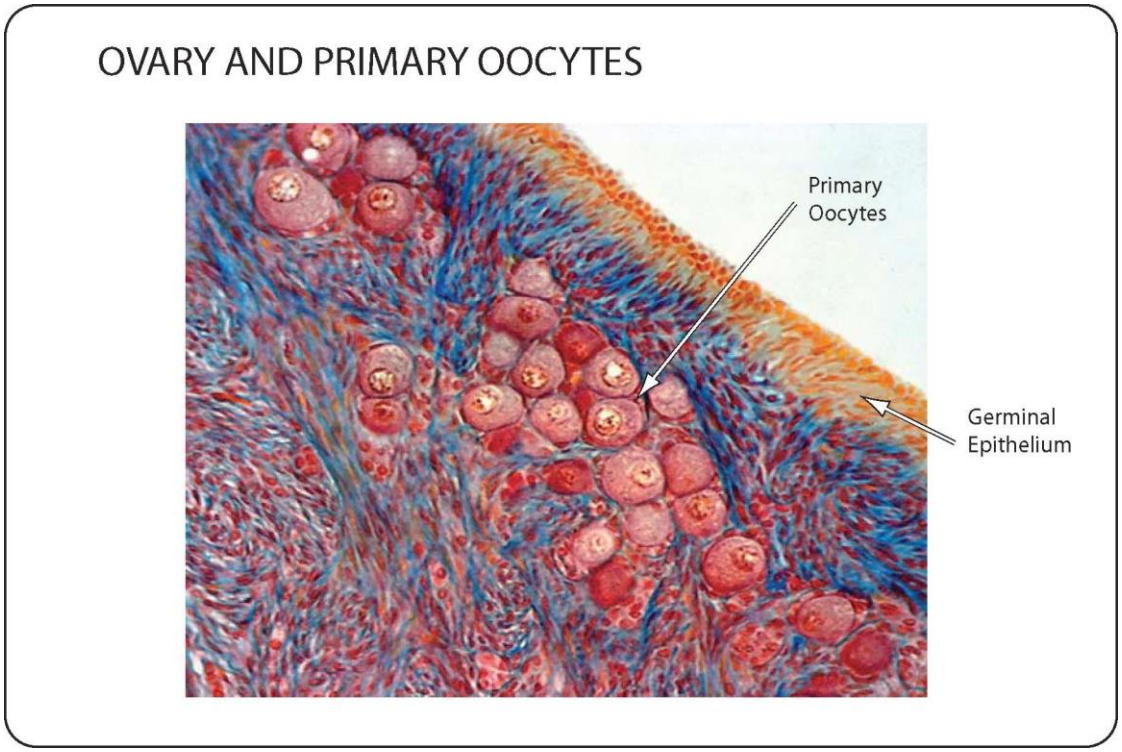

Figure 24.5 © 2007 David G. Ward, Ph.D.

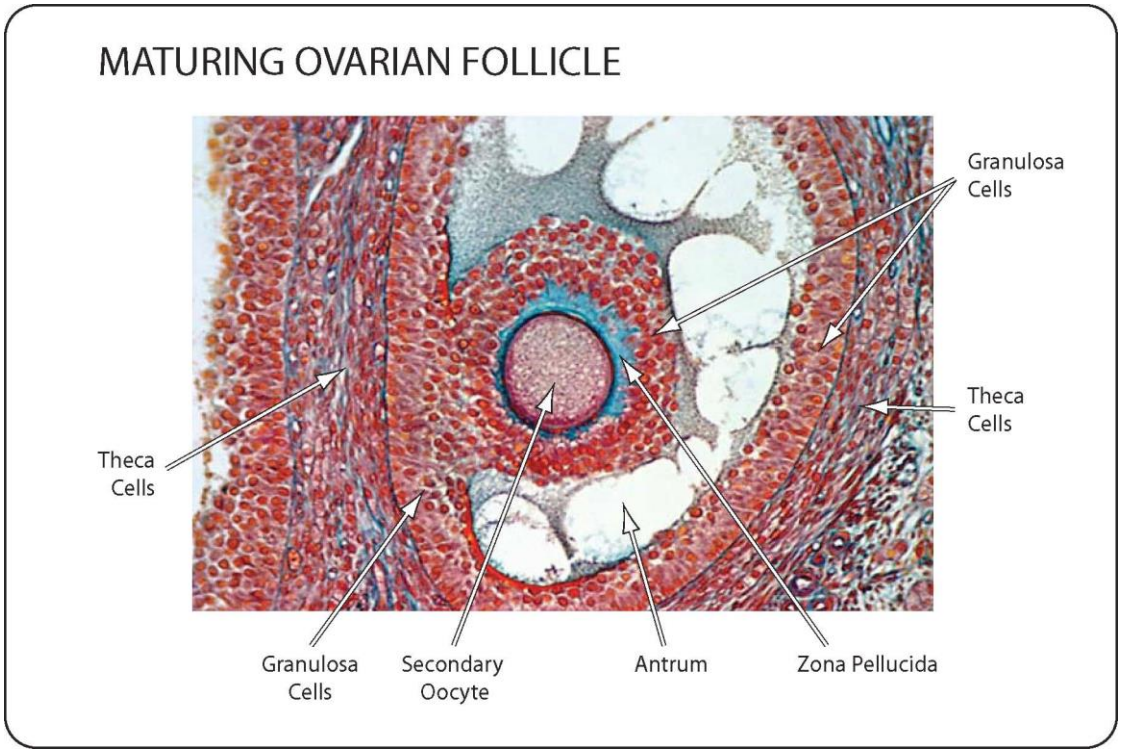

Figure 24.6 © 2007 David G. Ward, Ph.D.

Luteinizing hormone (LH) stimulates the rupture of the mature ovarian follicle and the release of the secondary oocyte. The secondary oocyte floats on the surface of the ovary until captured by the fimbrae and taken up into the uterine tube. The ovary and its relation to the fimbrae and uterine tube are shown in Figure 24.7. The uterine tube narrows at the isthmus before it enters the uterus. As a result the secondary oocyte may remain in the ampulla of the uterine tube for several days before moving into the uterus. A sperm most commonly penetrates the secondary oocyte in the uterine tube rather than in the uterus. Penetration stimulates meiosis II and the production of the ovum and a polar body. If the sperm is located in the ovum rather than in the polar body the ovum is fertilized. The separate nuclear membranes of the ovum and the sperm disintegrate and reform around both the paternal and maternal chromosomes, forming the zygote.

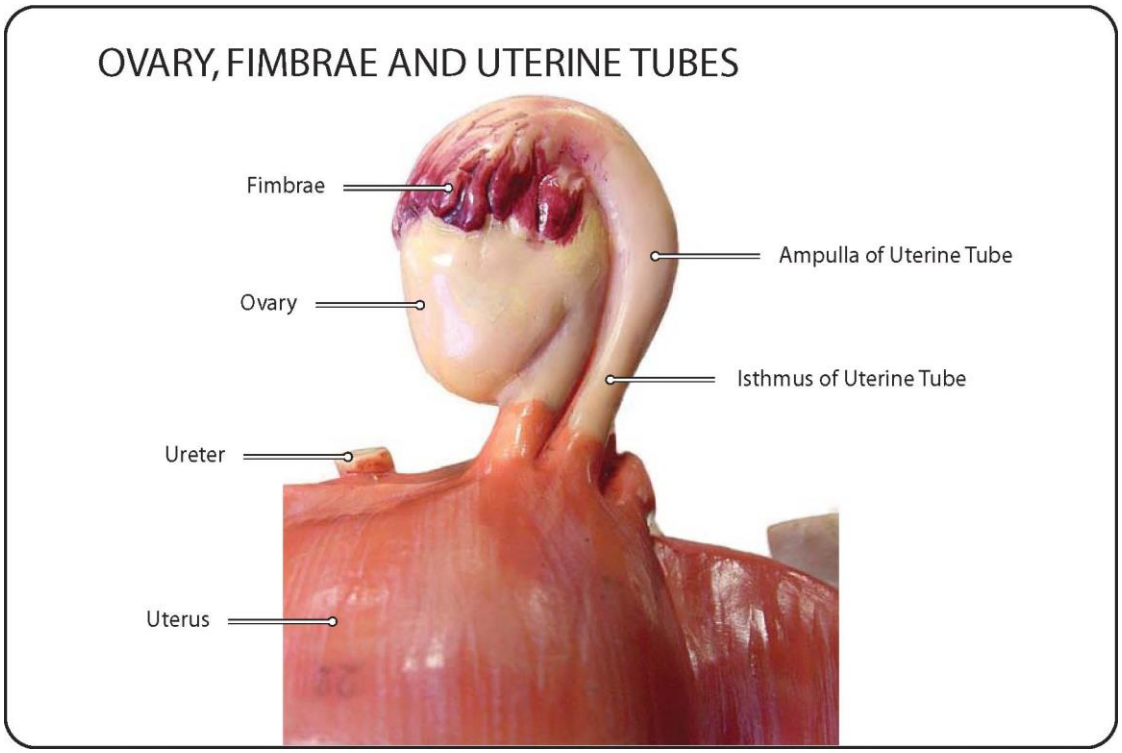

Figure 24.7 © 2007 David G. Ward, Ph.D.

Hormonal control of female reproductive function

The reproductive anterior pituitary hormones described in chapter 15 control the ovaries and together with the hypothalamus form the hypothalamic-pituitary-gonad axis in the female. An overview of female reproductive hormones is shown in Figure 24.8.

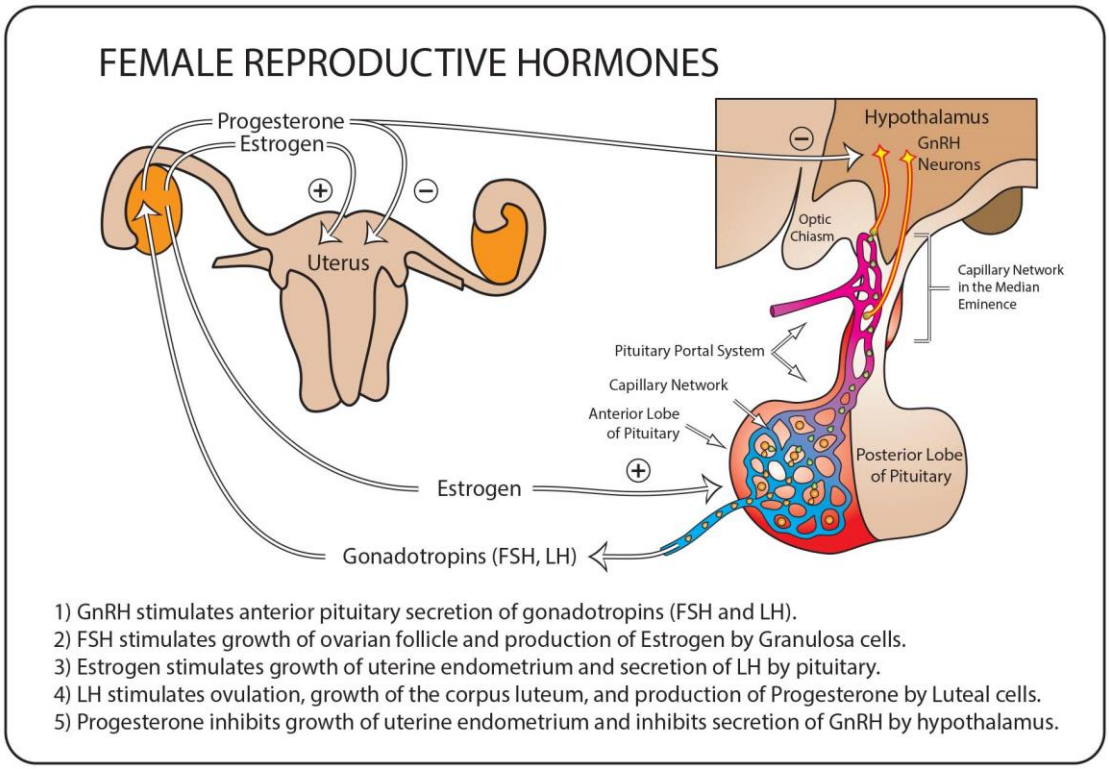

Figure 24.8 © 2020 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) from the hypothalamus stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- FSH stimulates the ovary to produce estrogen.
- Estrogen stimulates growth of the endometrium of the uterus
- Estrogen stimulates secretion of LH by pituitary gonadotrophs.
- LH stimulates the ovary to produce progesterone.
- Progesterone inhibits uterine endometrial growth and hypothalamic secretion of GnRH.

Menstrual cycle

The menstrual cycle is readily divided into two parts. The follicular phase starts with uterine bleeding and ends with ovulation and lasts for about 14 days. The luteal phase starts with ovulation and ends with the start of uterine bleeding and lasts for another 14 days. The menstrual cycle is the result of negative and positive feedback amongst the components of the hypothalamic-pituitary-gonad axis.

During the menstrual cycle the concentration of FSH, LH, estrogen, and progesterone in the blood vary considerably as shown in Figure 24.9. In the early part of the follicular phase FSH shows an early increase, estrogen shows a later increase, whereas LH and progesterone are relatively flat. In the late part of the follicular phase estrogen increases substantially, followed by a moderate increase in FSH and a dramatic increase in LH, sometimes called the LH surge. In the luteal phase FSH and LH decline, estrogen fluctuates, and progesterone increases substantially before falling.

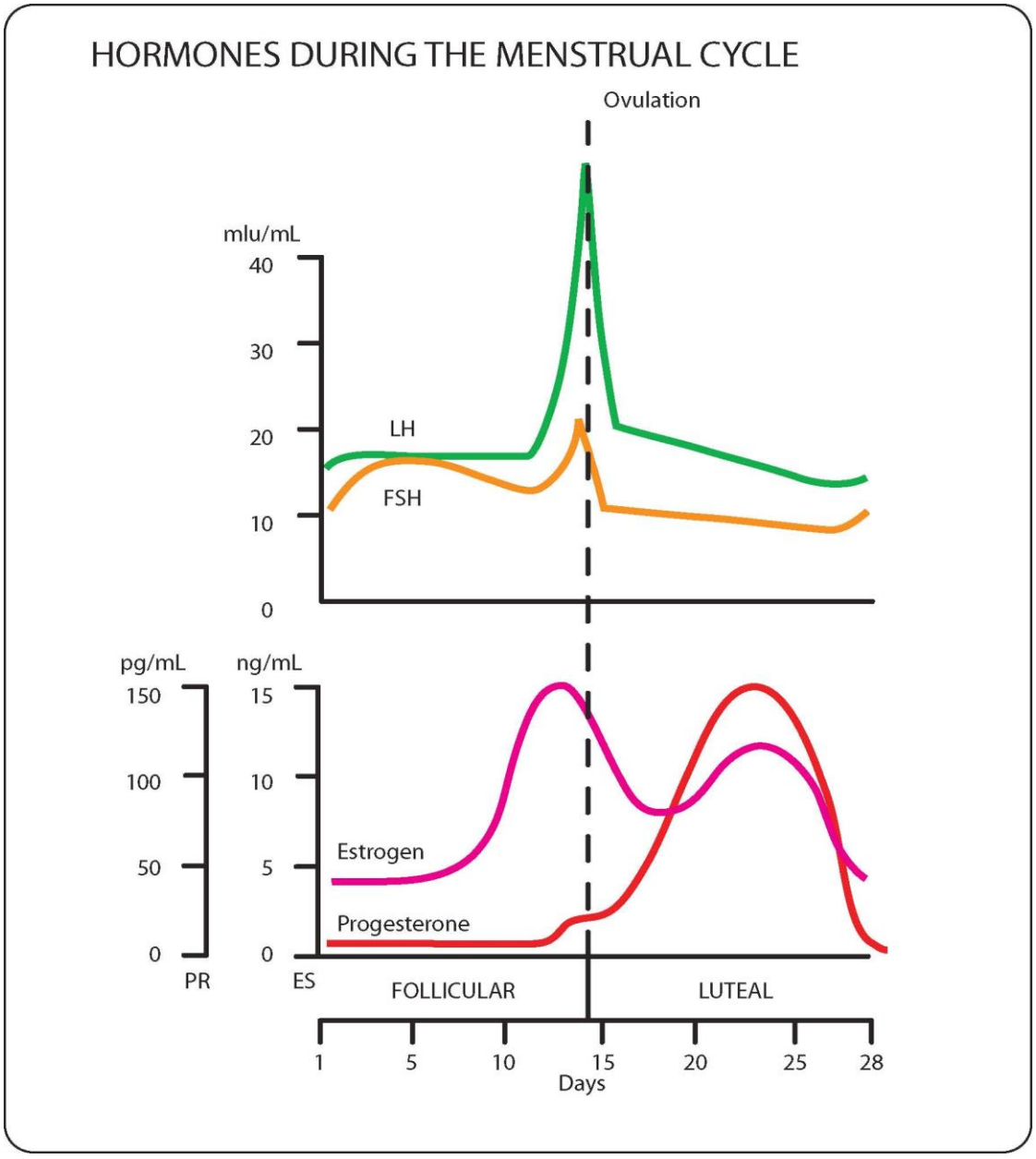

Figure 24.9 © 2007 David G. Ward, Ph.D.

The regulation of the reproductive hormones is rather complex and is considered during three time periods; the early follicular phase, the late follicular phase, and the luteal phase. It will be helpful to refer to the Figure 24.9 as we continue.

The regulation of the reproductive hormones during the early follicular phase is illustrated in Figure 24.10. Pacemaker cells in the hypothalamus set the baseline stimulation of GnRH neurons. Negative feedback from inhibin and estrogen keep FSH and LH levels relatively constant. The conversion of androgens to estrogen by granulosa cells and the synthesis of androgens by theca cells are stimulated by relatively small increases in FSH and LH. Accordingly, estrogen starts to rise.

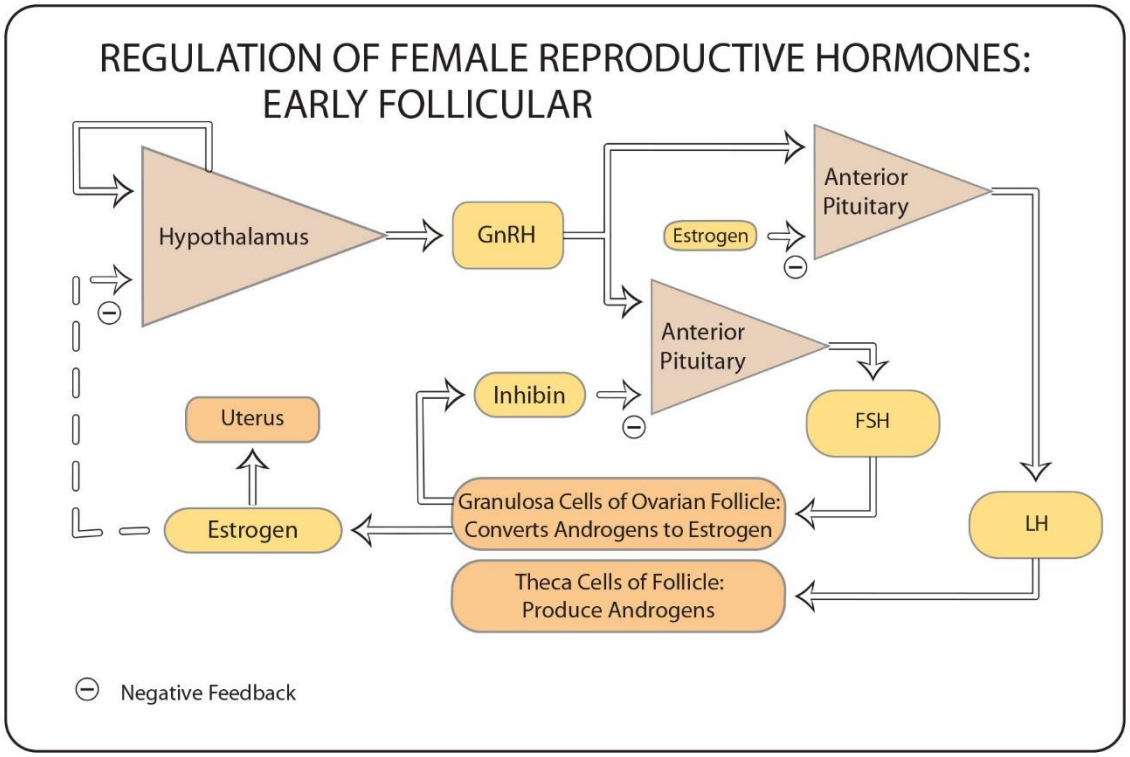

Figure 24.10 © 2014 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) secreted from hypothalamic neurons stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- FSH stimulates the granulosa cells of the ovarian follicles to increase secretion of inhibin and increase conversion of androgens to estrogen.
- LH stimulates the theca cells around the ovarian follicles to increase synthesis of androgens.
- Inhibin inhibits the secretion of FSH by the pituitary.
- Estrogen stimulate the growth of the functional zone of the endometrium of the uterus.
- Estrogen inhibits secretion of GnRH by hypothalamus and inhibits LH by the pituitary.

The regulation of the reproductive hormones during the late follicular phase is illustrated in Figure 24.11. The secretion of LH by pituitary gonadotrophs is markedly increased by estrogen and GnRH. Furthermore, ovarian granulosa cells are relatively insensitive to LH at low concentrations, and markedly responsive at elevated concentrations. Accordingly, there is a positive feedback stimulation of LH that results in a marked increase in LH (the LH surge) that stimulates ovulation and the transformation of the empty follicle into the corpus luteum.

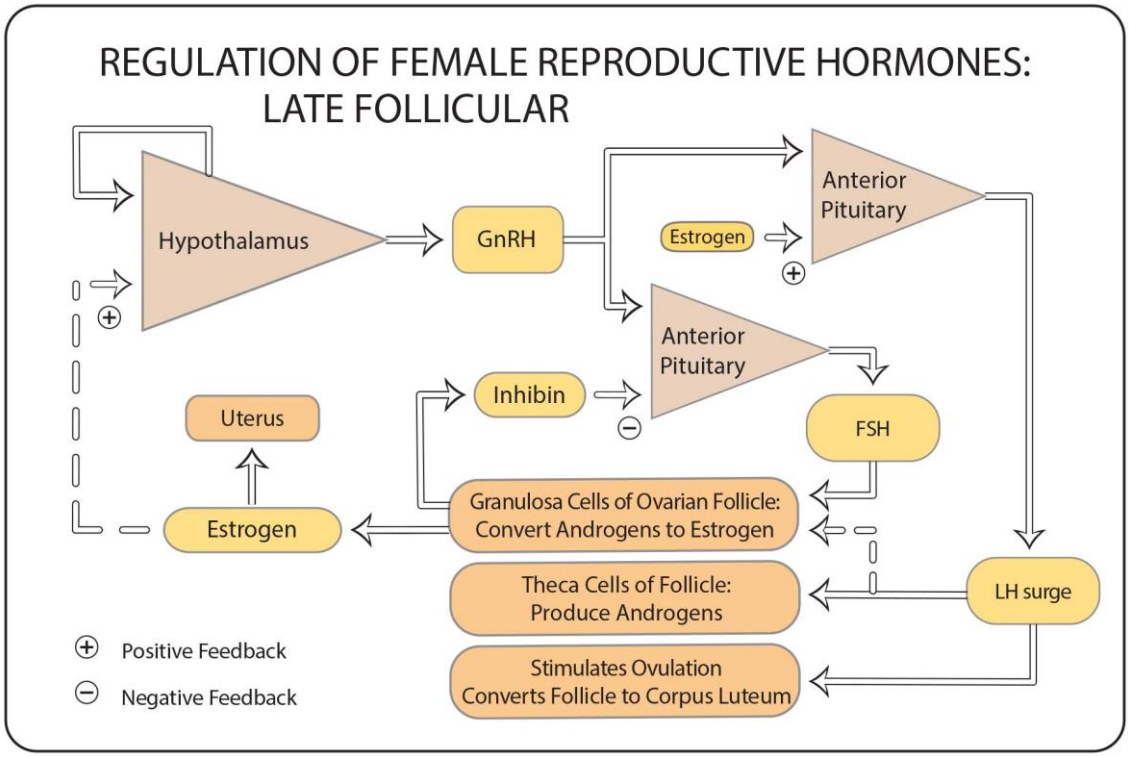

Figure 24.11 © 2020 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) secreted from hypothalamic neurons stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- FSH stimulates the granulosa cells of the ovarian follicles to increase secretion of inhibin and to increase conversion of androgens to estrogen.
- LH stimulates the theca cells around the ovarian follicles to increase synthesis of androgens (to be used by granulosa cells for conversion to estrogen).
- Inhibin inhibits secretion of FSH by the pituitary.
- Estrogen stimulates secretion of GnRH by the hypothalamus and stimulates secretion of LH by the pituitary.
- The resulting surge of LH stimulates ovulation and the transformation of the empty follicle into the corpus luteum.

The regulation of the reproductive hormones during the luteal phase is illustrated in Figure 24.12. Both the granulosa cells and the theca cells of the corpus luteum produce progesterone. In addition, the granulosa cells produce some estrogen. The large quantity of progesterone, together with estrogen, provides a powerful negative feedback signal that inhibits the GnRH neurons of hypothalamus and restores the hypothalamus and pituitary back to the point they were, at the beginning of the menstrual cycle.

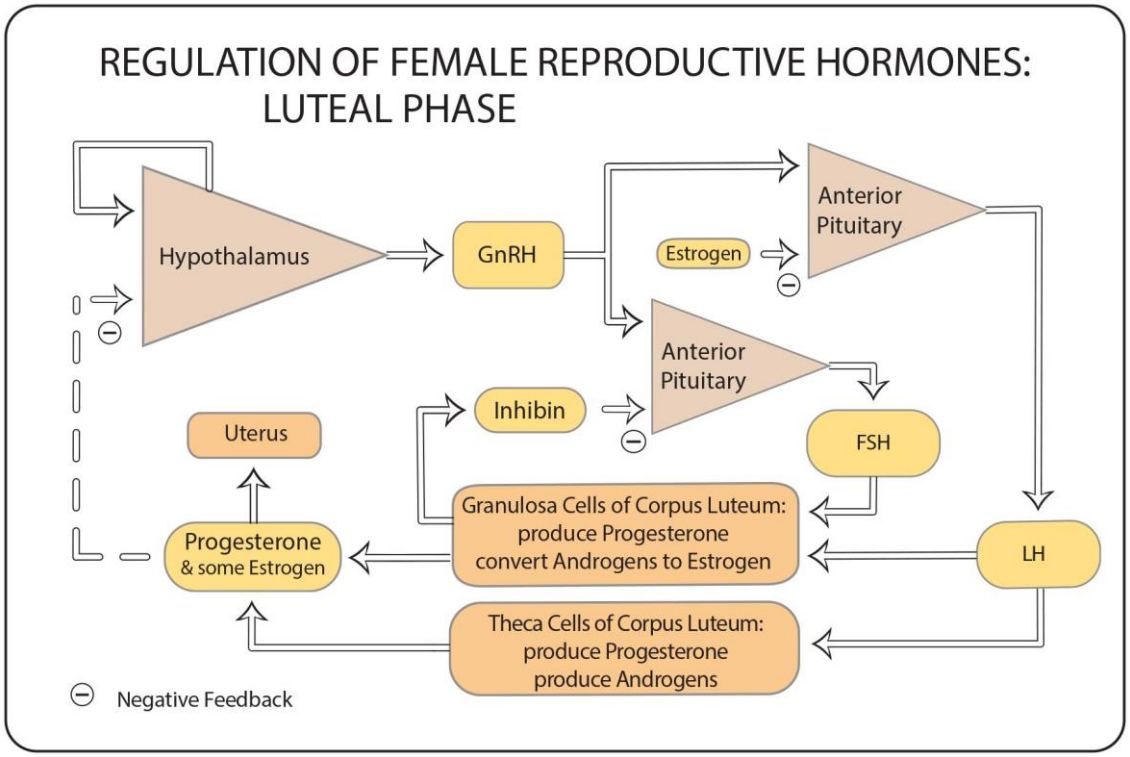

Figure 24.12 © 2018 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) secreted from hypothalamic neurons stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and luteinizing hormone (LH).
- FSH acts on the granulosa cells of the corpus luteum to increase secretion of inhibin, to increase production of progesterone, and to increase conversion of androgens to estrogen.
- LH acts on the theca cells of the corpus luteum to increase production of progesterone and androgens.
- Inhibin inhibits secretion of FSH by the pituitary.
- Estrogen inhibits secretion of LH by the pituitary.
- Progesterone inhibits the growth of the functional zone of the endometrium and stimulates growth of blood vessels in the uterus.
- Progesterone inhibits secretion of GnRH by the hypothalamus.

Without adequate stimulation of the corpus luteum by LH and FSH, the corpus luteum disintegrates and progesterone production stops. The corpus luteum is replaced by fibrous connective tissue, which can lead to scarring (fibrosis) of the ovaries if it accumulates. Without adequate stimulation of the functional zone of the endometrium by progesterone, the blood vessels constrict and strangulate the endometrium causing the endometrium to slough off and bleed (menses). This marks the beginning of the follicular phase.

During pregnancy the chorion surrounding the embryo secretes a peptide that acts very much like LH. This peptide, human chorionic gonadotropin (hCG), stimulates the corpus luteum and maintains production of progesterone. The progesterone, in turn, inhibits further growth of the endometrium of the uterus and maintains the growth of the blood vessels of the endometrium. In addition, progesterone inhibits the GnRH neurons of the hypothalamus and thus prevents the menstrual cycle.

Quiz Yourself

1-5. Matching (dominant actions)

A)	FSH	increase spermatogenesis	1) _____
B)	LH	stimulates sertoli cells to produce inhibin	2) _____
C)	A and B	stimulates granulosa cells to produce estradiol	3) _____
		stimulates interstitial cells to produce testosterone	4) _____
		stimulates sertoli cells to produce testosterone binding protein	5) _____

6-10. Matching (dominant actions)

A)	inhibin	increases production of LH by gonadotrophs in pituitary	6) _____
B)	estradiol	stimulates growth of endometrium of uterus	7) _____
C)	testosterone	inhibits growth of endometrium of uterus	8) _____
D)	progesterone	inhibits GnRH neurons in hypothalamus	9) _____
E)	C and D	inhibits gonadotrophs in pituitary	10) _____

11-15. Matching (dominant actions)

A)	FSH	stimulates ovulation	11) _____
B)	LH	stimulates growth of ovarian follicle	12) _____
		stimulates production of androgens by theca cells	13) _____
		stimulates production of estradiol by granulosa cells	14) _____
		stimulates conversion of the empty follicle into the corpus luteum	15) _____

16-20. Matching (dominant actions)

A)	Progesterone	is produced by the chorion of the embryo	16) _____
B)	LH	inhibits GnRH neurons of the hypothalamus	17) _____
C)	hCG	absence causes the death of the corpus luteum	18) _____
D)	B and C	absence causes the loss of the functional endometrium	19) _____
E)	all of the above	stimulates the corpus luteum to produce progesterone	20) _____

Fill in

21. Spermatogenesis occurs in the _____ _____ of the testes.

22. Oogenesis begins in the _____ and often continues in the _____ _____.

23. Production of testosterone is moderated by feedback inhibition of the _____ neurons of the hypothalamus.

24. Vascular dilation of the erectile tissues depend on the release of _____ _____.

25. Production of _____ by the chorion maintains the corpus luteum.

Study Questions

1. Explain the general process of gametogenesis.
2. Explain the control of spermatogenesis by the hypothalamus, pituitary, and testes.
3. Explain the processes involved in sperm transport.
4. Explain the control of the menstrual cycle by the hypothalamus, pituitary, and ovaries.
5. Explain the role of ovarian hormones in the growth and death of the functional zone of the endometrium.