Sex and the Brain

Introduction

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.

Sex differentiation

Males possess one X and one Y chromosome; whereas females have two X chromosomes. During fetal development the SRY gene on the Y chromosome induces the development of the testes (about week 7). 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 of Wolffian ducts and Mullerian ducts. In the male the testes secrete testosterone from the interstitial cells and Mullerian inhibiting substance (MIS) from the sertoli cells. The SRY protein induces the expression of the gene for MIS, which in turn 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 MIS allows the Mullerian ducts to develop into the uterine tubes and uterus. 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 22.1. 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 require a temperature about 1.1C lower that core body temperature. For every primary spermatocyte, four sperm are produced.

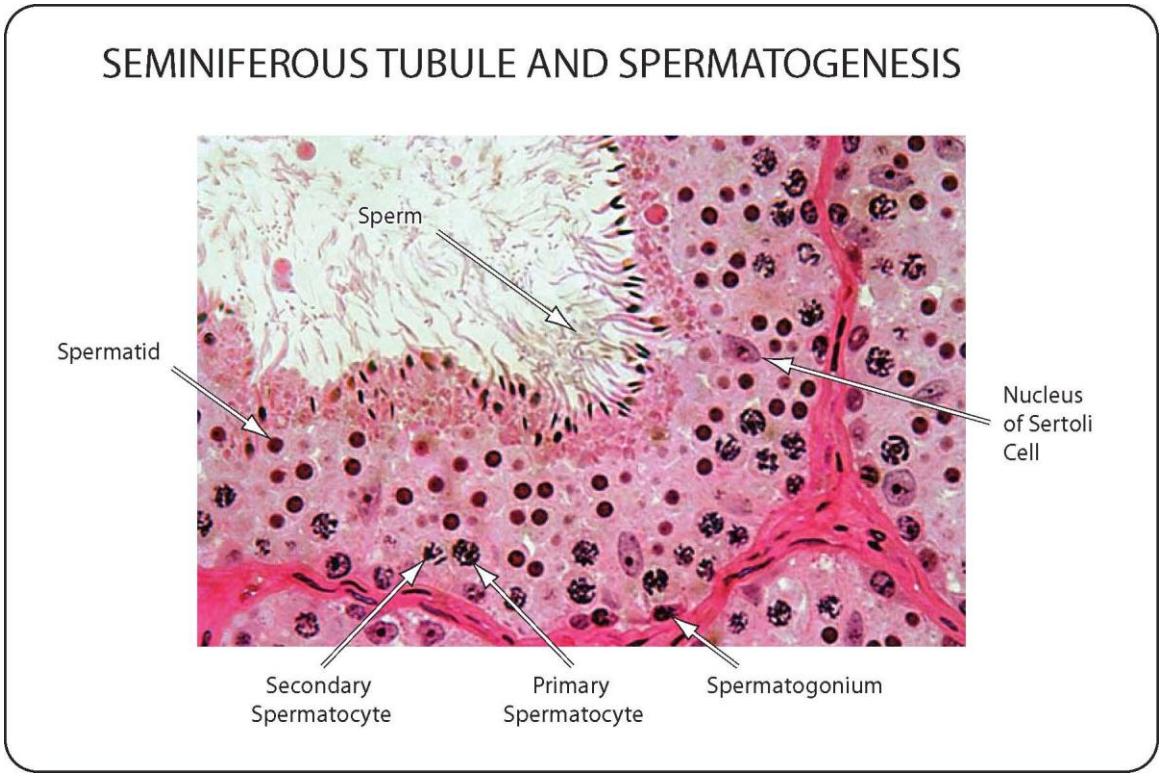

Figure 22.1 © 2007 David G. Ward, Ph.D.

Transport of Sperm, Erection and Ejaculation

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.

Erection

Erection usually precedes ejaculation, and depends on filling the penis with blood. The neural control of erection is shown in Figure 22.2. 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 corpus 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 lead to the release of nitric oxide which dilates arterioles of the erectile tissues. Veins from the erectile tissues constrict and the vascular compartments engorge with blood.

Nitric oxide stimulates guanylyl cyclase which converts GMP to cyclic GMP leading to decreased intracellular calcium and relaxation of smooth muscle. These actions are terminated by the breakdown of cyclic GMP by phosphodiesterase type 5 (PDE5). Sildenafil (Viagra), vardenafil (Levitra), and tadalafil (Cilais) are PDE5 inhibitors that permit a higher concentration of cyclic GMP.

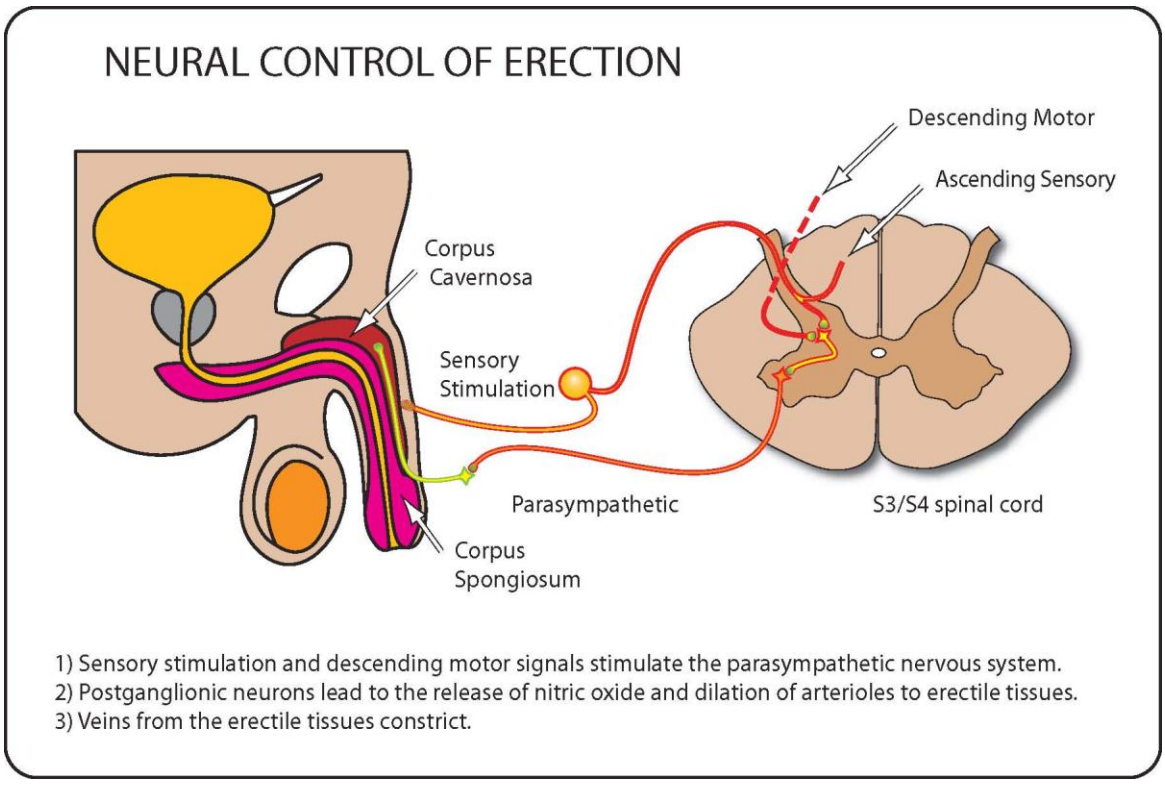

Figure 22.2 © 2007 David G. Ward, Ph.D.

Ejaculation

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.

Hormonal control of male reproductive function

The reproductive anterior pituitary hormones control the testes and together with the hypothalamus form the hypothalamic-pituitary-gonadal axis in the male, as shown in Figure 22.3.

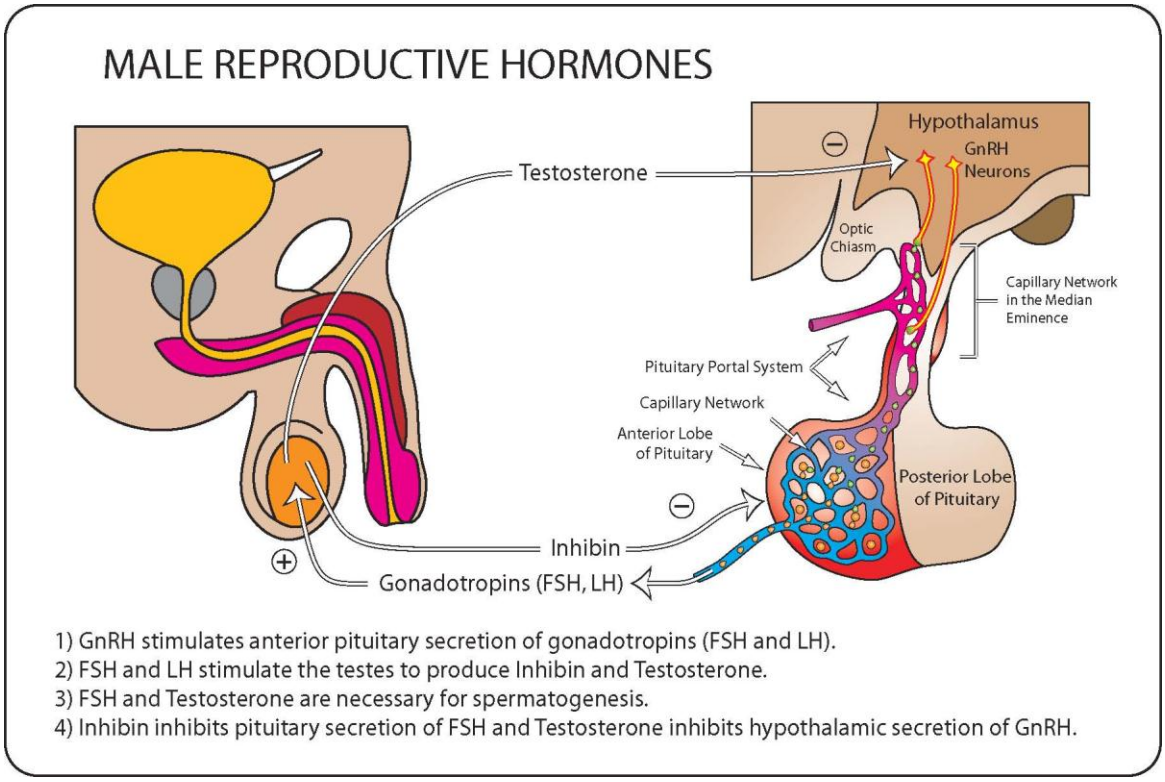

Figure 22.3 © 2007 David G. Ward, Ph.D.

- 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 to produce inhibin and androgen binding globulin.
- LH stimulates the interstitial cells (Leydig cells) between the seminiferous tubules to synthesize and release testosterone.
- Inhibin acts on pituitary gonadotrophs to inhibit the secretion of FSH.
- Androgen binding globulin permits a high local concentration of testosterone which enables spermatogenesis in the seminiferous tubules and sperm maturation in the epididymis.
- 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 negative feedback regulation of spermatogenesis and testosterone 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 22.4. For every primary oocyte only one ovum is produced and only if the secondary oocyte is penetrated by a sperm.

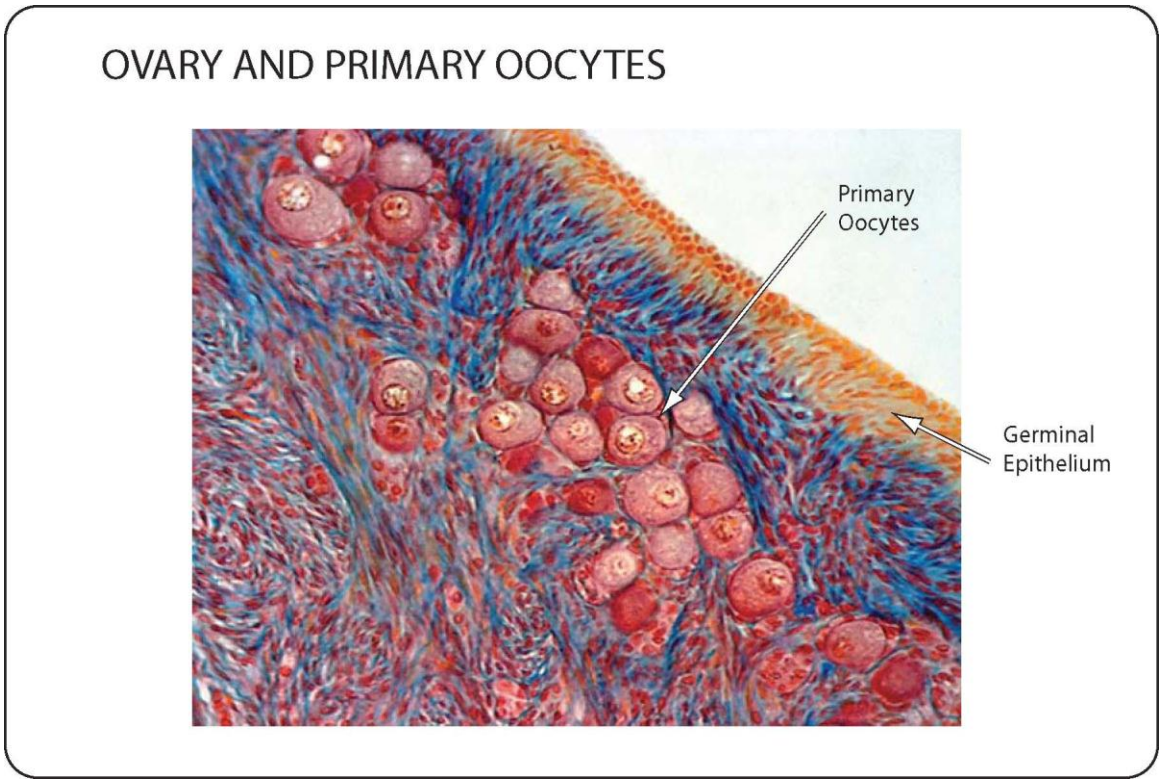

Figure 22.4 © 2007 David G. Ward, Ph.D.

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 22.5

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.

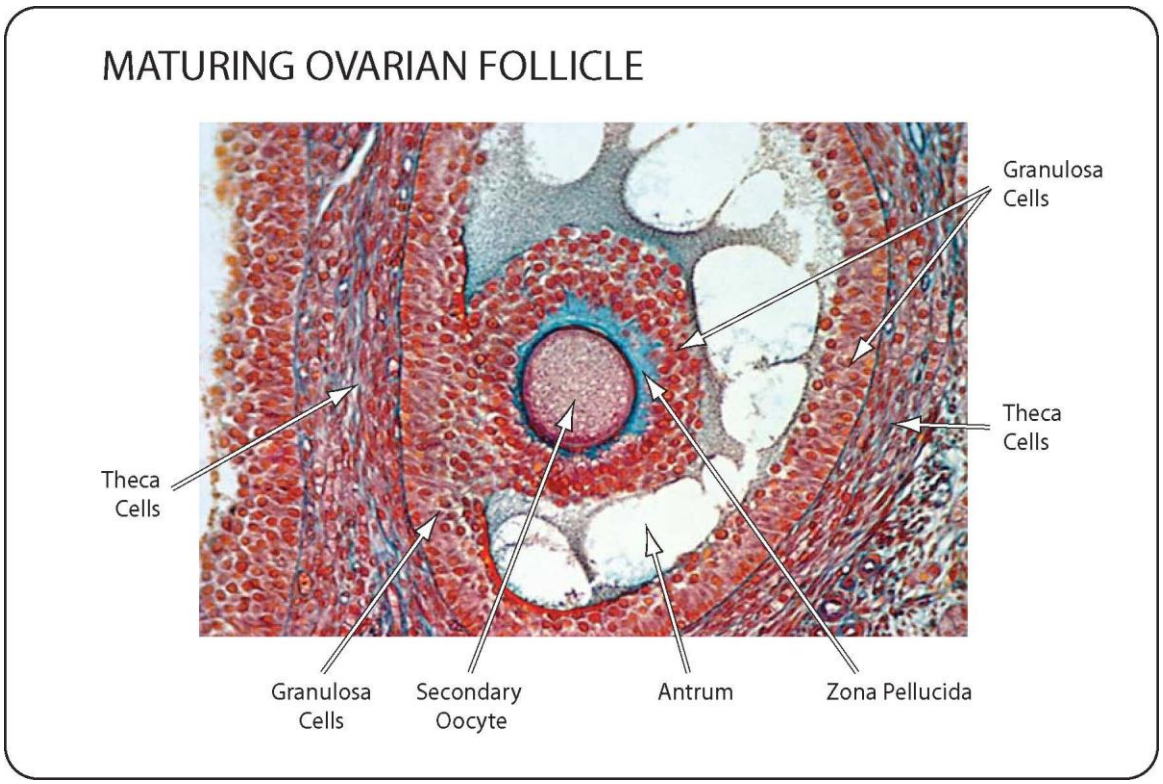

Figure 22.5 © 2007 David G. Ward, Ph.D.

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 22.6. 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 penetrate 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.

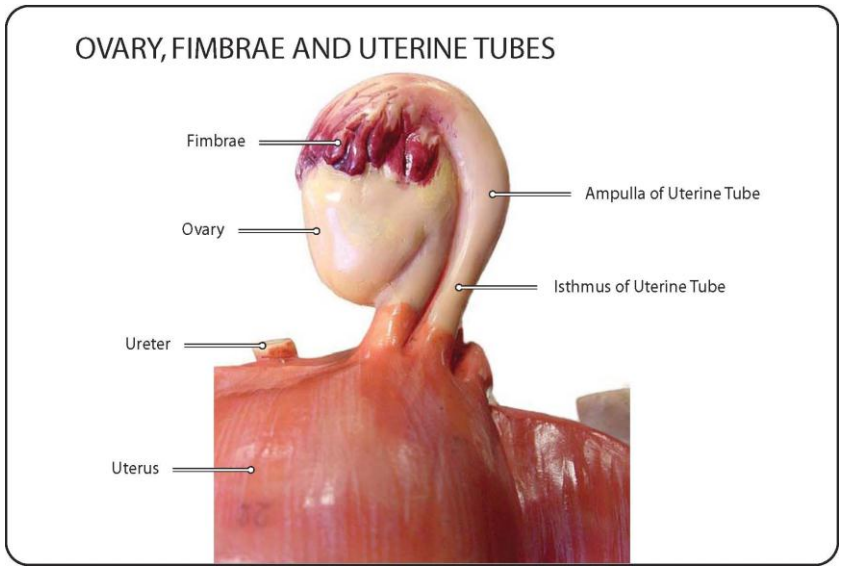

Figure 22.6 © 2007 David G. Ward, Ph.D.

Hormonal control of female reproductive function

The reproductive anterior pituitary hormones 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 22.7.

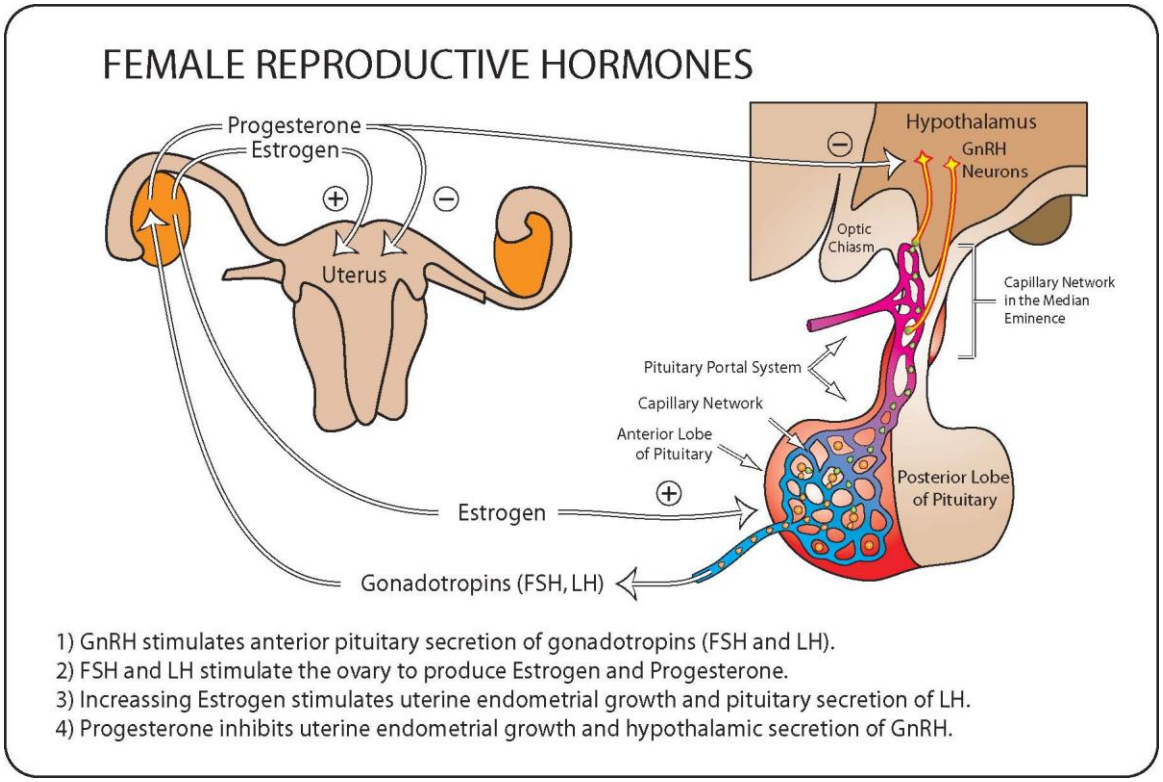

Figure 22.7 © 2007 David G. Ward, Ph.D.

- Gonadotropin releasing hormone (GnRH) secreted from hypothalamic neurons stimulates the anterior pituitary to secrete follicle stimulating hormone (FSH) and some luteinizing hormone (LH).
- FSH stimulates the ovary to produce estrogen, and later LH stimulates the ovary to produce progesterone.
- Increasing estrogen stimulates uterine endometrial growth and enhances secretion of LH by pituitary gonadotrophs.
- 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.

Early Follicular Phase

Pacemaker cells in the hypothalamus set the baseline stimulation of GnRH neurons. GnRH stimulates the anterior pituitary to secrete FSH and some LH that in turn stimulate the ovary to synthesize androgens and the conversion of androgens to estrogen. Accordingly, estrogen starts to rise.

Late Follicular Phase

The secretion of LH by the anterior pituitary increases markedly in response to estrogen. 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 an LH surge that stimulates ovulation and transforms the ovarian follicle into the corpus luteum.

Luteal Phase

LH stimulates the corpus luteum to produce progesterone. Progesterone inhibits GnRH neurons and restores the hypothalamic-pituitary-gonadal axis to the point it was at the beginning of the menstrual cycle – low secretion of FSH and LH.

Without adequate stimulation of the corpus luteum by LH, the corpus luteum disintegrates and progesterone production basically stops. Without progesterone the blood vessels of the functional zone of the endometrium constrict and cause the sloughing off of the endometrium and the uterine bleeding that 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, maintains the integrity of the endometrium of the uterus and provides a negative feedback inhibition to the hypothalamus that prevents menstrual cycling.