Chapter 28: The Reproductive System

Introduction to the Reproductive System, p. 1030

Objective

1. Specify the principal components of the human reproductive system and summarize their functions.
   - The reproductive system includes the following components:
     - Gonads, or reproductive organs that produce gametes and hormones.
     - Ducts that receive and transport the gametes.
     - Accessory glands and organs that secrete fluids into the ducts of the reproductive system or into other excretory ducts.
     - Perineal structures that are collectively known as the external genitalia.
   - In both males and females, the ducts are connected to chambers and passageways that open to the exterior of the body. The structures involved constitute the reproductive tract.
   - The male and female reproductive systems are functionally quite different.
     - In adult males, the testes, or male gonads, secrete sex hormones called androgens. The testes also produce the male gametes, called spermatozoa, or sperm—one-half billion each day.
     - During emission, mature spermatozoa travel along a lengthy duct system, where they are mixed with the secretions of accessory glands. The mixture created is known as semen.
     - During ejaculation, semen is expelled from the body.
     - In adult females, the ovaries, or female gonads, typically release only one immature gamete, an oocyte, per month. This immature gamete travels along one of two short uterine tubes, which end in the muscular organ called the uterus. If a sperm reaches the oocyte and initiates the process of fertilization, the oocyte matures into an ovum.
     - A short passageway, the vagina, connects the uterus with the exterior. Ejaculation introduces semen into the vagina during sexual intercourse, and the spermatozoa then ascend the female reproductive tract.
     - If fertilization occurs, the uterus will enclose and support a developing embryo as it grows into a fetus and prepares for birth.

The Reproductive System of the Male, p. 1030

Objectives

1. Describe the components of the male reproductive system.
2. Outline the processes of meiosis and spermatogenesis in the testes.
3. Explain the roles played by the male reproductive tract and accessory glands in the functional maturation, nourishment, storage, and transport of spermatozoa.
4. Specify the normal composition of semen.
5. Summarize the hormonal mechanisms that regulate male reproductive functions.

Figure 28-1

- Proceeding from a testis, the spermatozoa travel within the epididymis; the ductus deferens, or vas deferens; the ejaculatory duct; and the urethra before leaving the body.
- Accessory organs—the seminal vesicles, the prostate gland, and the bulbourethral glands—secrete various fluids into the ejaculatory ducts and urethra.
- The external genitalia consist of the scrotum, which encloses the testes, and the penis, an erectile organ through which the distal portion of the urethra passes.

The Testes
• Each testis has the shape of a flattened egg that is roughly 5 cm (2 in.) long, 3 cm (1.2 in.) wide, and 2.5 cm (1 in.) thick. Each has a weight of 10–15 g (0.35–0.53 oz). The testes hang within the scrotum, a fleshy pouch suspended inferior to the perineum, anterior to the anus and posterior to the base of the penis.

**Figure 28-2**

• Descent of the Testes During development of the fetus, the testes form inside the body cavity adjacent to the kidneys. A bundle of connective tissue fibers—called the gubernaculum testis—extends from each testis to the posterior wall of a small anterior and inferior pocket of the peritoneum. As the fetus grows, the gubernacula do not get any longer, so they lock the testes in position.
  
  • The relative position of each testis changes as the body enlarges: The testis gradually moves inferiorly and anteriorly toward the anterior abdominal wall. During the seventh developmental month, fetal growth continues at a rapid pace, and circulating hormones stimulate a contraction of the gubernaculum testis. Over this period, each testis moves through the abdominal musculature, accompanied by small pockets of the peritoneal cavity. This process is called the descent of the testes.
  
  • In cryptorchidism, one or both of the testes have not descended into the scrotum by the time of birth.

• As each testis moves through the body wall, it is accompanied by the ductus deferens and the testicular blood vessels, nerves, and lymphatic vessels. Together, these structures form the body of the spermatic cord.

**Figure 28-3**

• The Spermatic Cords The spermatic cords are paired structures extending between the abdominopelvic cavity and the testes. Each spermatic cord consists of layers of fascia and muscle enclosing the ductus deferens and the blood vessels, nerves, and lymphatic vessels that supply the testes. The blood vessels include the deferential artery, a testicular artery, and the pampiniform plexus of a testicular vein.

• Branches of the genitofemoral nerve from the lumbar plexus provide innervation. Each spermatic cord begins at the entrance to the inguinal canal (a passageway through the abdominal musculature). After passing through the inguinal canal, the spermatic cord descends into the scrotum. The inguinal canals form during development as the testes descend into the scrotum; at that time, these canals link the scrotal cavities with the peritoneal cavity.

• In normal adult males, the inguinal canals are closed, but the presence of the spermatic cords creates weak points in the abdominal wall that remain throughout life. As a result, inguinal hernias—protrusions of visceral tissues or organs into the inguinal canal—are relatively common in males.

• The inguinal canals in females are very small, containing only the iliouinguinal nerves and the round ligaments of the uterus; the abdominal wall is nearly intact, so inguinal hernias in women are very rare.

• The Scrotum and the Position of the Testes The scrotum is divided internally into two chambers. The partition between the two is marked by a raised thickening in the scrotal surface known as the raphe.
  
  • Each testis lies in a separate chamber, or scrotal cavity. Because the scrotal cavities are separated by a partition, infection or inflammation of one testis does not ordinarily spread to the other. A narrow space separates the inner surface of the scrotum from the outer surface of the testis.

  • The tunica vaginalis, a serous membrane, lines the scrotal cavity and reduces friction between the opposing parietal (scrotal) and visceral (testicular) surfaces. The tunica vaginalis is an isolated portion of the peritoneum that lost its connection with the peritoneal cavity after the testes descended, when the inguinal canal closed.
The scrotum consists of a thin layer of skin and the underlying superficial fascia. The dermis contains a layer of smooth muscle, the dartos muscle. Resting muscle tone in the dartos muscle causes the characteristic wrinkling of the scrotal surface.

- A layer of skeletal muscle, the cremaster muscle, lies deep to the dermis. Contraction of the cremaster muscle during sexual arousal or in response to decreased testicular temperature tenses the scrotum and pulls the testes closer to the body.
- Normal development of spermatozoa in the testes requires temperatures about 1.1°C (2°F) lower than those elsewhere in the body. The cremaster and dartos muscles relax or contract to move the testes away from or toward the body as needed to maintain acceptable testicular temperatures. When air or body temperature rises, these muscles relax and the testes move away from the body.

Figure 28-4
- Structure of the Testes Deep to the tunica vaginalis covering the testis is the tunica albuginea, a dense layer of connective tissue rich in collagen fibers. These fibers are continuous with those surrounding the adjacent epididymis and extend into the substance of the testis. There they form fibrous partitions, or septa, that converge toward the region nearest the entrance to the epididymis.
- The connective tissues in this region support the blood vessels and lymphatic vessels that supply and drain the testis, and the efferent ductules, which transport spermatozoa to the epididymis.

Figure 28-5
- Histology of the Testes The septa subdivide the testis into a series of lobules. Distributed among the lobules are roughly 800 slender, tightly coiled seminiferous tubules. Each tubule averages about 80 cm (32 in.) in length, and a typical testis contains nearly one-half mile of seminiferous tubules. Sperm production occurs within these tubules.
- Each seminiferous tubule forms a loop that is connected to a maze of passageways known as the rete testis. Fifteen to 20 large efferent ductules connect the rete testis to the epididymis. Because the seminiferous tubules are tightly coiled, most histological preparations show them in transverse section.
- Each tubule is surrounded by a delicate connective tissue capsule, and areolar tissue fills the spaces between the tubules. Within those spaces are numerous blood vessels and large interstitial cells (cells of Leydig). Interstitial cells are responsible for the production of androgens, the dominant sex hormones in males. Testosterone is the most important androgen.
- Spermatozoa are produced by the process of spermatogenesis. Spermatogenesis begins at the outermost layer of cells in the seminiferous tubules and proceeds toward the lumen. At each step in this process, the daughter cells move closer to the lumen.
  - First, stem cells called spermatogonia divide by mitosis to produce two daughter cells, one of which remains at that location as a spermatogonium while the other differentiates into a primary spermatocyte.
  - Primary spermatocytes are the cells that begin meiosis, a specialized form of cell division involved only in the production of gametes (spermatozoa in males, ova in females). Primary spermatocytes give rise to secondary spermatocytes that differentiate into spermatids—immature gametes that subsequently differentiate into spermatozoa.
  - The spermatozoa lose contact with the wall of the seminiferous tubule and enter the fluid in the lumen. Each seminiferous tubule contains spermatogonia, spermatocytes at various stages of meiosis, spermatids, spermatozoa, and large sustentacular cells (or Sertoli cells). Sustentacular cells are attached to the tubular capsule and extend to the lumen between the other types of cells.

Spermatogenesis
Figure 28-6

- Spermatogenesis involves three integrated processes:
  - **Mitosis.** Spermatogonia undergo cell divisions throughout adult life. One daughter cell from each division remains in place while the other is pushed toward the lumen of the seminiferous tubule. The displaced cells differentiate into primary spermatocytes, which prepare to begin meiosis.
  - **Meiosis.** Meiosis is a special form of cell division involved in gamete production. In humans, gametes contain 23 chromosomes, half the normal set. As a result, the fusion of the nuclei of a male gamete and a female gamete produces a cell that has the normal number of chromosomes (46), rather than twice that number. In the seminiferous tubules, meiotic divisions that begin with primary spermatocytes produce spermatids, the undifferentiated male gametes.
  - **Spermiogenesis.** Spermatids are small, relatively unspecialized cells. In spermiogenesis, spermatids differentiate into physically mature spermatozoa, which are among the most highly specialized cells in the body. Spermiogenesis involves major changes in a spermatid’s internal and external structures.

- **Mitosis and Meiosis.** In both males and females, mitosis and meiosis differ significantly in terms of the events occurring in the nucleus. Somatic cells contain 23 pairs of chromosomes. Each pair consists of one chromosome provided by the father, and another provided by the mother, at the time of fertilization.
  - Mitosis is part of the process of somatic cell division, producing two daughter cells each containing identical pairs of chromosomes. Because daughter cells contain both members of each chromosome pair (for a total of 46 chromosomes), they are called diploid cells.
  - Meiosis involves two cycles of cell division (meiosis I and meiosis II) and produces four cells, each of which contains 23 individual chromosomes. Because these cells contain only one member of each pair of chromosomes, they are called haploid cells. The events in the nucleus are the same for the formation of spermatozoa or ova. As a cell prepares to begin meiosis, DNA replication occurs within the nucleus just as it does in a cell preparing to undergo mitosis.
  - This similarity continues as prophase I arrives; the chromosomes condense and become visible with a light microscope. As in mitosis, each chromosome consists of two duplicate chromatids. At this point, the close similarities between meiosis and mitosis end.
  - In meiosis, the corresponding maternal and paternal chromosomes now come together, an event known as synopsis. Synapsis involves 23 pairs of chromosomes; each member of each pair consists of two chromatids. A matched set of four chromatids is called a tetrad.
  - Some exchange of genetic material can occur between the chromatids of a chromosome pair at this stage of meiosis. Such an exchange, called crossing over, increases genetic variation among offspring.
  - Meiosis includes two division cycles, referred to as meiosis I and meiosis II. The stages within each phase are identified as prophase I, metaphase II, and so on. The nuclear envelope disappears at the end of prophase I. As metaphase I begins, the tetrads line up along the metaphase plate. As anaphase I begins, the tetrads break up—the maternal and paternal chromosomes separate. This is a major difference between mitosis and meiosis: In mitosis, each daughter cell receives one of the two copies of every chromosome, maternal and paternal; in meiosis I, each daughter cell receives both copies of either the maternal chromosome or the paternal chromosome from each tetrad.
  - As anaphase proceeds, the maternal and paternal components are randomly and independently distributed. That is, as each tetrad splits, one cannot predict which
daughter cell will receive copies of the maternal chromosome, and which will receive copies of the paternal chromosome.

- As a result, telophase I ends with the formation of two daughter cells containing unique combinations of maternal and paternal chromosomes. Both cells contain 23 chromosomes. Because the first meiotic division reduces the number of chromosomes from 46 to 23, it is called a reductional division. Each of these chromosomes still consists of two duplicate chromatids.
- The duplicates will separate during meiosis II. The interphase separating meiosis I and meiosis II is very brief, and no DNA is replicated during that period. Each cell proceeds through prophase II, metaphase II, and anaphase II.
- During anaphase II, the duplicate chromatids separate. Telophase II thus yields four cells, each containing 23 chromosomes. Because the number of chromosomes has not changed, meiosis II is an equational division. Although chromosomes are evenly distributed among these four cells, the cytoplasm may not be.
- In males, meiosis produces four immature gametes that are identical in size; each will develop into a functional sperm. In females, meiosis produces one huge ovum and three tiny, nonfunctional polar bodies.

**Figure 28-7**

- In spermatogenesis, the mitotic division of each diploid spermatogonium produces two daughter cells. One is a spermatogonium that remains in contact with the basal lamina, and the other is a primary spermatocyte that is displaced toward the lumen.
- As meiosis begins, each primary spermatocyte contains 46 individual chromosomes. At the end of meiosis I, the daughter cells are called secondary spermatocytes. Every secondary spermatocyte contains 23 chromosomes, each of which consists of a pair of duplicate chromatids.
- The secondary spermatocytes soon enter prophase II. The completion of metaphase II, anaphase II, and telophase II yields four haploid spermatids, each containing 23 chromosomes.
- For each primary spermatocyte that enters meiosis, four spermatids are produced. Because cytokinesis (cytoplasmic division) is not completed in meiosis I or meiosis II, the four spermatids initially remain interconnected by bridges of cytoplasm. These connections assist in the transfer of nutrients and hormones between the cells, helping ensure that the cells develop in synchrony. The bridges are not broken until the last stages of physical maturation.

**Keys**

- Meiosis produces gametes that contain half the number of chromosomes found in somatic cells.
- For each cell entering meiosis, the testes produce four spermatozoa, whereas the ovaries produce a single ovum.

- **Spermiogenesis** In spermiogenesis, the last step of spermatogenesis, each spermatid matures into a single spermatozoon, or sperm.
  - Developing spermatocytes undergoing meiosis, and spermatids undergoing spermiogenesis, are not free in the seminiferous tubules. Instead, they are surrounded by the cytoplasm of the sustentacular cells.
  - As spermiogenesis proceeds, the spermatids gradually develop the appearance of mature spermatozoa. At **spermiation**, a spermatozoon loses its attachment to the sustentacular cell and enters the lumen of the seminiferous tubule.
  - The entire process, from spermatogonial division to spermiation, takes approximately nine weeks.

- **Sustentacular Cells** Sustentacular cells, also called **Sertoli cells**, play a key role in spermatogenesis. These cells have six important functions that directly or indirectly affect mitosis, meiosis, and spermiogenesis within the seminiferous tubules:
- **Maintenance of the Blood–Testis Barrier.** The seminiferous tubules are isolated from the general circulation by a blood–testis barrier, comparable in function to the blood–brain barrier. Sustentacular cells are joined by tight junctions, forming a layer that divides the seminiferous tubule into an outer basal compartment, which contains the spermatogonia, and an inner lumenal compartment (or adlumenal compartment), where meiosis and spermiogenesis occur.

- **Support of Mitosis and Meiosis.** Spermatogenesis depends on the stimulation of sustentacular cells by circulating follicle-stimulating hormone (FSH) and testosterone. Stimulated sustentacular cells then promote the division of spermatogonia and the meiotic divisions of spermatocytes.

- **Support of Spermiogenesis.** Spermiogenesis requires the presence of sustentacular cells. These cells surround and enfold the spermatids, providing nutrients and chemical stimuli that promote their development. Sustentacular cells also phagocytize cytoplasm that is shed by spermatids as they develop into spermatozoa.

- **Secretion of Inhibin.** Sustentacular cells secrete the peptide hormone inhibin in response to factors released by developing spermatozoa. Inhibit depresses the pituitary production of FSH, and perhaps the hypothalamic secretion of gonadotropin-releasing hormone (GnRH). The faster the rate of sperm production, the more inhibin is secreted. By regulating FSH and GnRH secretion, sustentacular cells provide feedback control of spermatogenesis.

- **Secretion of Androgen-Binding Protein.** Androgen-binding protein (ABP) binds androgens (primarily testosterone) in the fluid contents of the seminiferous tubules. This protein is thought to be important in both elevating the concentration of androgens within the seminiferous tubules and stimulating spermiogenesis. The production of ABP is stimulated by FSH.

- **Secretion of Müllerian-Inhibiting Factor.** Müllerian-inhibiting factor (MIF) is secreted by sustentacular cells in the developing testes. This hormone causes regression of the fetal Müllerian ducts, passageways that participate in the formation of the uterine tubes and the uterus in females. In males, inadequate MIF production during fetal development leads to the retention of these ducts and the failure of the testes to descend into the scrotum.

### The Anatomy of a Spermatozoon

**Figure 28-8**

- Each spermatozoon has three distinct regions: the head, the middle piece, and the tail.
- In humans, the head is a flattened ellipse containing a nucleus with densely packed chromosomes. At the tip of the head is the acrosomal cap, a membranous compartment containing enzymes essential to fertilization. During spermiogenesis, saccules of the spermatid’s Golgi apparatus fuse and flatten into an acrosomal vesicle, which ultimately forms the acrosomal cap of the spermatozoon.
- A short neck attaches the head to the middle piece. The neck contains both centrioles of the original spermatid. The microtubules of the distal centriole are continuous with those of the middle piece and tail. Mitochondria in the middle piece are arranged in a spiral around the microtubules. Mitochondrial activity provides the ATP required to move the tail.
- The tail is the only flagellum in the human body. A flagellum, a whiplike organelle, moves a cell from one place to another. The flagellum of a spermatozoon has a complex, corkscrew motion.
- A mature spermatozoon lacks an endoplasmic reticulum, a Golgi apparatus, lysosomes, peroxisomes, inclusions, and many other intracellular structures. The loss of these organelles reduces the cell’s size and mass; it is essentially a mobile carrier for the enclosed chromosomes, and extra weight would slow it down. Because the cell lacks glycogen or other energy reserves, it must absorb nutrients (primarily fructose) from the surrounding fluid.

### Keys
• Spermatogenesis begins at puberty and continues until relatively late in life (past age 70). It is a continuous process, and all stages of meiosis can be observed within the seminiferous tubules.

The Male Reproductive Tract

Figure 28-9

• The testes produce physically mature spermatozoa that are incapable of successfully fertilizing an oocyte. The other portions of the male reproductive system are responsible for the functional maturation, nourishment, storage, and transport of spermatozoa.

• The Epididymis Late in their development, spermatozoa detach from the sustentacular cells and lie within the lumen of the seminiferous tubule. They have most of the physical characteristics of mature spermatozoa, but are functionally immature and incapable of coordinated locomotion or fertilization. Fluid currents, created by cilia lining the efferent ductules, transport the immobile gametes into the epididymis.

• The epididymis, the start of the male reproductive tract, is a coiled tube bound to the posterior border of the testis. The epididymis can be felt through the skin of the scrotum. A tube almost 7 m (23 ft) long, the epididymis is coiled and twisted so as to take up very little space. It has a head, a body, and a tail. The superior head is the portion of the epididymis proximal to the testis. The head receives spermatozoa from the efferent ductules. The body begins distal to the last efferent ductule and extends inferiorly along the posterior margin of the testis. Near the inferior border of the testis, the number of coils decreases, marking the start of the tail. The tail recurves and ascends to its connection with the ductus deferens. Spermatozoa are stored primarily within the tail of the epididymis.

• The epididymis has three functions:
  o It Monitors and Adjusts the Composition of the Fluid Produced by the Seminiferous Tubules.
  o It Acts as a Recycling Center for Damaged Spermatozoa
  o It Stores and Protects Spermatozoa and Facilitates Their Functional Maturation.

• Although spermatozoa leaving the epididymis are mature, they remain immobile. To become motile (actively swimming) and fully functional, spermatozoa must undergo a process called capacitation. Capacitation normally occurs in two steps: (1) Spermatozoa become motile when they are mixed with secretions of the seminal vesicles, and (2) they become capable of successful fertilization when exposed to conditions in the female reproductive tract. The epididymis secretes a substance (as yet unidentified) that prevents premature capacitation.

Figure 28-10

• The Ductus Deferens Each ductus deferens, or vas deferens, is 40–45 cm (16–18 in.) long. It begins at the tail of the epididymis and, as part of the spermatic cord, ascends through the inguinal canal. Inside the abdominal cavity, the ductus deferens passes posteriorly, curving inferiorly along the lateral surface of the urinary bladder toward the superior and posterior margin of the prostate gland.

• Just before the ductus deferens reaches the prostate gland and seminal vesicles, its lumen enlarges. This expanded portion is known as the ampulla of the ductus deferens. The wall of the ductus deferens contains a thick layer of smooth muscle.

• Peristaltic contractions in this layer propel spermatozoa and fluid along the duct, which is lined by a pseudostratified ciliated columnar epithelium. In addition to transporting spermatozoa, the ductus deferens can store spermatozoa for several months. During this time, the spermatozoa remain in a state of suspended animation and have low metabolic rates.

• The junction of the ampulla with the duct of the seminal vesicle marks the start of the ejaculatory duct. This short passageway (2 cm, or less than 1 in.) penetrates the muscular wall of the prostate gland and empties into the urethra near the opening of the ejaculatory duct from the opposite side.
The Accessory Glands

The fluids contributed by the seminiferous tubules and the epididymis account for only about 5 percent of the volume of semen. The fluid component of semen is a mixture of secretions—each with distinctive biochemical characteristics—from many glands. Important glands include the seminal vesicles, the prostate gland, and the bulbourethral glands, all of which occur only in males.

Among the major functions of these glands are (1) activating spermatozoa; (2) providing the nutrients spermatozoa need for motility; (3) propelling spermatozoa and fluids along the reproductive tract, mainly by peristaltic contractions; and (4) producing buffers that counteract the acidity of the urethral and vaginal environments.

The Seminal Vesicles The ductus deferens on each side ends at the junction between the ampulla and the duct that drains the seminal vesicle. The seminal vesicles are glands embedded in connective tissue on either side of the midline, sandwiched between the posterior wall of the urinary bladder and the rectum.

Each seminal vesicle is a tubular gland with a total length of about 15 cm (6 in.). The body of the gland has many short side branches. The entire assemblage is coiled and folded into a compact, tapered mass roughly 5 cm 2.5 cm (2 in. 1 in.). Seminal vesicles are extremely active secretory glands with an epithelial lining that contains extensive folds. The seminal vesicles contribute about 60 percent of the volume of semen.

Although the vesicular fluid generally has the same osmotic concentration as that of blood plasma, the compositions of the two fluids are quite different. In particular, the secretion of the seminal vesicles contains (1) higher concentrations of fructose, which is easily metabolized by spermatozoa; (2) prostaglandins, which can stimulate smooth muscle contractions along the male and female reproductive tracts; and (3) fibrinogen, which after ejaculation forms a temporary clot within the vagina.

The secretions of the seminal vesicles are slightly alkaline, helping to neutralize acids in the secretions of the prostate gland and within the vagina. When mixed with the secretions of the seminal vesicles, previously inactive but functional spermatozoa undergo the first step in capacitation and begin beating their flagella, becoming highly motile.

The secretions of the seminal vesicles are discharged into the ejaculatory duct at emission, when peristaltic contractions are under way in the ductus deferens, seminal vesicles, and prostate gland. These contractions are under the control of the sympathetic nervous system.

The Prostate Gland The prostate gland is a small, muscular, rounded organ about 4 cm (1.6 in.) in diameter. The prostate gland encircles the proximal portion of the urethra as it leaves the urinary bladder. The glandular tissue of the prostate consists of a cluster of 30–50 compound tubuloalveolar glands. These glands are surrounded by and wrapped in a thick blanket of smooth muscle fibers.

The prostate gland produces prostatic fluid, a slightly acidic solution that contributes 20–30 percent of the volume of semen. In addition to several other compounds of uncertain significance, prostatic secretions contain seminalplasmin, an antibiotic that may help prevent urinary tract infections in males. These secretions are ejected into the prostatic urethra by peristaltic contractions of the muscular prostate wall.

Prostatic inflammation, or prostatitis, can occur in males at any age, but it most commonly afflicts older men. Prostatitis can result from bacterial infections but also occurs in the apparent absence of pathogens.

Figure 28-11

The Bulbourethral Glands The paired bulbourethral glands, or Cowper’s glands, are situated at the base of the penis, covered by the fascia of the urogenital diaphragm. The bulbourethral glands are round, with diameters approaching 10 mm (less than 0.5 in.).
• The duct of each gland travels alongside the penile urethra for 3–4 cm (1.2–1.6 in.) before emptying into the urethral lumen. The bulbourethral glands are compound, tubuloalveolar mucous glands that secrete a thick, alkaline mucus. The secretion helps neutralize any urinary acids that may remain in the urethra, and it lubricates the glans, or tip of the penis.

**Semen**

• A typical ejaculation releases 2–5 ml of semen; an abnormally low volume may indicate problems with the prostate gland or seminal vesicles. When sampled for analysis, semen is collected after a 36-hour period of sexual abstinence. The volume of fluid produced by an ejaculation, called the ejaculate, typically contains the following:
  o Spermatozoa. The normal sperm count ranges from 20 million to 100 million spermatozoa per milliliter of semen. Most individuals with lower sperm counts are infertile, because too few spermatozoa survive the ascent of the female reproductive tract to perform fertilization. A low sperm count may reflect inflammation of the epididymis, ductus deferens, or prostate gland. In a fertile male, at least 60 percent of the spermatozoa in the sample are normal in appearance; common abnormalities are malformed heads and “twin” spermatozoa that did not separate at the time of spermiation. The normal sperm will be swimming actively.
  o Seminal Fluid. Seminal fluid, the fluid component of semen, is a mixture of glandular secretions with a distinct ionic and nutrient composition. A typical sample of seminal fluid contains the combined secretions of the seminal vesicles (60 percent), the prostate gland (30 percent), the sustentacular cells and epididymis (5 percent), and the bulbourethral glands (less than 5 percent).
  o Enzymes. Several important enzymes are present in seminal fluid, including (1) a protease that may help dissolve mucous secretions in the vagina; (2) seminalplasmin, an antibiotic prostatic enzyme that kills a variety of bacteria, including *Escherichia coli*; (3) a prostatic enzyme that coagulates the semen within a few minutes after ejaculation by converting fibrinogen to fibrin; and (4) fibrinolysin, which liquefies the clotted semen after 15–30 minutes.

**The External Genitalia**

• The male external genitalia consist of the scrotum and penis. The penis is a tubular organ through which the distal portion of the urethra passes. It conducts urine to the exterior and introduces semen into the female’s vagina during sexual intercourse.
• The penis is divided into three regions: the root, the body, and the glans. The root of the penis is the fixed portion that attaches the penis to the body wall. This connection occurs within the urogenital triangle immediately inferior to the pubic symphysis. The body (shaft) of the penis is the tubular, movable portion of the organ. The glans of the penis is the expanded distal end that surrounds the external urethral orifice. The neck is the narrow portion of the penis between the shaft and the glans. The skin overlying the penis resembles that of the scrotum.
• The dermis contains a layer of smooth muscle that is a continuation of the dartos muscle of the scrotum, and the underlying areolar tissue allows the thin skin to move without distorting underlying structures. The subcutaneous layer also contains superficial arteries, veins, and lymphatic vessels.
• A fold of skin called the prepuce, or foreskin, surrounds the tip of the penis. The prepuce attaches to the relatively narrow neck of the penis and continues over the glans. Preputial glands in the skin of the neck and the inner surface of the prepuce secrete a waxy material known as smegma. Unfortunately, smegma can be an excellent nutrient source for bacteria.
• Deep to the areolar tissue, a dense network of elastic fibers encircles the internal structures of the penis. Most of the body of the penis consists of three cylindrical columns of erectile tissue. Erectile tissue consists of a three-dimensional maze of vascular channels incompletely separated by partitions of elastic connective tissue and smooth muscle fibers. In the resting state, the arterial branches are constricted and the muscular partitions are tense. This combination restricts blood flow into the erectile tissue.
The flaccid (nonerect) penis hangs inferior to the pubic symphysis and anterior to the scrotum, but during erection the penis stiffens and assumes a more upright position. The anterior surface of the flaccid penis covers two cylindrical masses of erectile tissue: the corpora cavernosa. The two are separated by a thin septum and encircled by a dense collagenous sheath. The corpora cavernosa diverge at their bases, forming the crura of the penis. Each crus is bound to the ramus of the ischium and pubis by tough connective-tissue ligaments.

The corpora cavernosa extend along the length of the penis as far as its neck. The erectile tissue within each corpus cavernosum surrounds a central artery. The relatively slender corpus spongiosum surrounds the penile urethra. This erectile body extends from the superficial fascia of the urogenital diaphragm to the tip of the penis, where it expands to form the glans. The sheath surrounding the corpus spongiosum contains more elastic fibers than does that of the corpora cavernosa, and the erectile tissue contains a pair of small arteries.

**Hormones and Male Reproductive Function**

**Figure 28-12**

- The anterior lobe of the pituitary gland releases follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The pituitary release of these hormones occurs in response to gonadotropin-releasing hormone (GnRH), a peptide synthesized in the hypothalamus and carried to the anterior lobe by the hypophyseal portal system. The hormone GnRH is secreted in pulses rather than continuously.
- In adult males, small pulses occur at 60–90-minute intervals. As levels of GnRH change, so do the rates of secretion of FSH and LH (and testosterone, which is released in response to LH).
- FSH and Spermatogenesis In males, FSH targets primarily the sustentacular cells of the seminiferous tubules. Under FSH stimulation, and in the presence of testosterone from the interstitial cells, sustentacular cells (1) promote spermatogenesis and spermio genesis and (2) secrete androgen-binding protein (ABP).
- The rate of spermatogenesis is regulated by a negative feedback mechanism involving GnRH, FSH, and inhibin. Under GnRH stimulation, FSH promotes spermatogenesis along the seminiferous tubules. As spermatogenesis accelerates, however, so does the rate of inhibin secretion by the sustentacular cells of the testes.
- Inhibin inhibits FSH production in the anterior lobe of the pituitary gland and may also suppress the secretion of GnRH at the hypothalamus. The net effect is that when FSH levels become elevated, inhibin production increases until FSH levels return to normal. If FSH levels decline, inhibin production falls, so the rate of FSH production accelerates.
- LH and Androgen Production In males, LH induces the secretion of testosterone and other androgens by the interstitial cells of the testes. Testosterone, the most important androgen, has numerous functions: (1) stimulating spermatogenesis and promoting the functional maturation of spermatozoa, through its effects on sustentacular cells; (2) affecting central nervous system (CNS) function, including the libido (sexual drive) and related behaviors; (3) stimulating metabolism throughout the body, especially pathways concerned with protein synthesis, blood cell formation, and muscle growth; (4) establishing and maintaining male secondary sex characteristics, such as the distribution of facial hair, increased muscle mass and body size, and the quantity and location of characteristic adipose tissue deposits; and (5) maintaining the accessory glands and organs of the male reproductive tract.
- Testosterone functions like other steroid hormones, circulating in the bloodstream while bound to one of two types of transport proteins: (1) gonadal steroid-binding globulin (GBG), which carries roughly two-thirds of the circulating testosterone, and (2) the albumins, which bind the remaining one-third. Testosterone diffuses across the cell membrane of target cells and binds to an intracellular receptor. The hormone–receptor complex then binds to the DNA in the nucleus. In many target tissues, some of the arriving testosterone is converted to
The Ovaries

**Figure 28-13**

- The paired ovaries are small, lumpy, almond-shaped organs near the lateral walls of the pelvic cavity.

**The Reproductive System of the Female, p. 1048**

**Objectives**

1. Describe the components of the female reproductive system.
2. Outline the processes of meiosis and oogenesis in the ovaries.
3. Identify the phases and events of the ovarian and uterine cycles.
4. Describe the structure, histology, and functions of the vagina.
5. Summarize the anatomical, physiological, and hormonal aspects of the female reproductive cycle.

**Figure 28-13**

- A woman’s reproductive system produces sex hormones and functional gametes, and it must also be able to protect and support a developing embryo and nourish a newborn infant. The principal organs of the female reproductive system are the ovaries, the uterine tubes, the uterus, the vagina, and the components of the external genitalia. As in males, a variety of accessory glands release secretions into the female reproductive tract.

- The ovaries, uterine tubes, and uterus are enclosed within an extensive mesentery known as the broad ligament. The uterine tubes run along the superior border of the broad ligament and open into the pelvic cavity lateral to the ovaries. The mesovarium, a thickened fold of mesentery, supports and stabilizes the position of each ovary. The broad ligament attaches to the sides and floor of the pelvic cavity, where it becomes continuous with the parietal peritoneum.

- The broad ligament thus subdivides this part of the peritoneal cavity. The pocket formed between the posterior wall of the uterus and the anterior surface of the colon is the rectouterine pouch; the pocket formed between the uterus and the posterior wall of the bladder is the vesicouterine pouch.

- Several other ligaments assist the broad ligament in supporting and stabilizing the position of the uterus and associated reproductive organs. These ligaments lie within the mesentery sheet of the broad ligament and are connected to the ovaries or uterus. The broad ligament limits side-to-side movement and rotation, and the other ligaments prevent superior–inferior movement.

**The Ovaries**

**Figure 28-14**

- The paired ovaries are small, lumpy, almond-shaped organs near the lateral walls of the pelvic cavity.

Dihydrotestosterone (DHT). A small amount of DHT diffuses back out of the cell and into the bloodstream, and DHT levels are usually about 10 percent of circulating testosterone levels.

- Testosterone production begins around the seventh week of fetal development and reaches a prenatal peak after roughly six months. Over this period, the secretion of Müllarian inhibiting factor by developing sustentacular cells leads to the regression of the Müllarian ducts. The early surge in testosterone levels stimulates the differentiation of the male duct system and accessory organs and affects CNS development.

- The best-known CNS effects occur in the developing hypothalamus. There, testosterone apparently programs the hypothalamic centers that are involved with (1) GnRH production and the regulation of pituitary FSH and LH secretion, (2) sexual behaviors, and (3) sexual drive. As a result of this prenatal exposure to testosterone, the hypothalamic centers will respond appropriately when the individual becomes sexually mature.

- The plasma of adult males also contains relatively small amounts of estradiol (2 ng/dl, versus 525 ng/dl of testosterone). Seventy percent of the estradiol is formed from circulating testosterone; the rest is secreted, primarily by the interstitial and sustentacular cells of the testes. The conversion of testosterone to estradiol is performed by an enzyme called aromatase.
The ovaries perform three main functions: (1) production of immature female gametes, or oocytes, (2) secretion of female sex hormones, including estrogens and progesterins, and (3) secretion of inhibin, involved in the feedback control of pituitary FSH production.

The position of each ovary is stabilized by the mesovarium and by a pair of supporting ligaments: the ovarian ligament and the suspensory ligament. The ovarian ligament extends from the uterus, near the attachment of the uterine tube, to the medial surface of the ovary. The suspensory ligament extends from the lateral surface of the ovary past the open end of the uterine tube to the pelvic wall.

The suspensory ligament contains the major blood vessels of the ovary: the ovarian artery and ovarian vein. These vessels are connected to the ovary at the ovarian hilum, where the ovary attaches to the mesovarium.

A typical ovary is about 5 cm long, 2.5 cm wide, and 8 mm thick (2 in. 1 in. 0.33 in.) and weighs 6–8 g (roughly 0.25 oz). An ovary is pink or yellowish and has a nodular consistency.

The visceral peritoneum, or germinal epithelium, covering the surface of each ovary consists of a layer of columnar epithelial cells that overlies a dense connective-tissue layer called the tunica albuginea.

We can divide the interior tissues, or stroma, of the ovary into a superficial cortex and a deeper medulla. Gametes are produced in the cortex.

**Figure 28-15**

- Oogenesis Ovum production, or oogenesis, begins before a woman’s birth, accelerates at puberty, and ends at menopause.
- Between puberty and menopause, oogenesis occurs on a monthly basis as part of the ovarian cycle.
- Unlike spermatogonia, the oogonia, or stem cells of females, complete their mitotic divisions before birth. Between the third and seventh months of fetal development, the daughter cells, or primary oocytes, prepare to undergo meiosis. They proceed as far as the prophase of meiosis I, but then the process comes to a halt.
- The primary oocytes remain in a state of suspended development until the individual reaches puberty, when rising levels of FSH trigger the start of the ovarian cycle. Each month thereafter, some of the primary oocytes are stimulated to undergo further development. Not all primary oocytes produced during development survive until puberty.
- The ovaries have roughly 2 million primordial follicles at birth, each containing a primary oocyte. By the time of puberty, the number has dropped to about 400,000. The rest of the primordial follicles degenerate in a process called atresia.
- Although the nuclear events in the ovaries during meiosis are the same as those in the testes, the process differs in two important details:
  - The cytoplasm of the primary oocyte is unevenly distributed during the two meiotic divisions. Oogenesis produces one functional ovum, which contains most of the original cytoplasm, and two or three polar bodies, nonfunctional cells that later disintegrate.
  - The ovary releases a secondary oocyte rather than a mature ovum. The secondary oocyte is suspended in metaphase of meiosis II; meiosis will not be completed unless and until fertilization occurs.

**Figure 28-16**

- The Ovarian Cycle Ovarian follicles are specialized structures in the cortex of the ovaries where both oocyte growth and meiosis I occur. Primary oocytes are located in the outer portion of the ovarian cortex, near the tunica albuginea, in clusters called egg nests.
- Each primary oocyte within an egg nest is surrounded by a single squamous layer of follicle cells. The primary oocyte and its follicle cells form a primordial follicle.
- After sexual maturation, a different group of primordial follicles is activated each month. This monthly process is known as the ovarian cycle. The ovarian cycle can be divided into a follicular phase, or preovulatory phase, and a luteal phase, or postovulatory phase.
• Important steps in the ovarian cycle can be summarized as follows:
  o Step 1 The Formation of Primary Follicles. The ovarian cycle begins as activated primordial follicles develop into primary follicles. In a primary follicle, the follicle cells enlarge and undergo repeated divisions that create several layers of follicle cells around the oocyte. These follicle cells, which become rounded in appearance, are now called granulosa cells. As layers of granulosa cells develop around the primary oocyte, microvilli from the surrounding granulosa cells intermingle with those of the primary oocyte. The microvilli are surrounded by a layer of glycoproteins; the entire region is called the zona pellucida. The microvilli increase the surface area available for the transfer of materials from the granulosa cells to the rapidly enlarging primary oocyte. The conversion from primordial to primary follicles and subsequent follicular development occurs under stimulation of FSH from the anterior lobe of the pituitary gland. As the granulosa cells enlarge and multiply, adjacent cells in the ovarian stroma form a layer of thecal cells around the follicle. Thecal cells and granulosa cells work together to produce sex hormones called estrogens.
  o Step 2 The Formation of Secondary Follicles. Although many primordial follicles develop into primary follicles, only a few will proceed to this step. The transformation begins as the wall of the follicle thickens and the granulosa cells begin secreting small amounts of fluid. This follicular fluid, or liquor folliculi, accumulates in small pockets that gradually expand and separate the inner and outer layers of the follicle. At this stage, the complex is known as a secondary follicle. Although the primary oocyte continues to grow at a steady pace, the follicle as a whole now enlarges rapidly because follicular fluid accumulates.
  o Step 3 The Formation of a Tertiary Follicle. Eight to 10 days after the start of the ovarian cycle, the ovaries generally contain only a single secondary follicle destined for further development. By the 10th to the 14th day of the cycle, that follicle has become a tertiary follicle, or mature Graafian follicle, roughly 15 mm in diameter. This complex spans the entire width of the ovarian cortex and distorts the ovarian capsule, creating a prominent bulge in the surface of the ovary. The oocyte projects into the antrum, or expanded central chamber of the follicle. The antrum is surrounded by a mass of granulosa cells. Until this time, the primary oocyte has been suspended in prophase of meiosis I. As the development of the tertiary follicle ends, LH levels begin rising, prompting the primary oocyte to complete meiosis I. Instead of producing two secondary oocytes, the first meiotic division yields a secondary oocyte and a small, nonfunctional polar body. The secondary oocyte then enters meiosis II, but stops once again upon reaching metaphase. Meiosis II will not be completed unless fertilization occurs. Generally, on day 14 of a 28-day cycle, the secondary oocyte and the attached granulosa cells lose their connections with the follicular wall and drift free within the antrum. The granulosa cells still associated with the secondary oocyte form a protective layer known as the corona radiata.
  o Step 4 Ovulation. At ovulation, the tertiary follicle releases the secondary oocyte. The distended follicular wall suddenly ruptures, ejecting the follicular contents, including the secondary oocyte and corona radiata, into the pelvic cavity. The sticky follicular fluid keeps the corona radiata attached to the surface of the ovary, where direct contact with projections surrounding the entrance to the uterine tube or with fluid currents established by the ciliated epithelium lining the uterus can transfer the secondary oocyte to the uterine tube. Ovulation marks the end of the follicular phase of the ovarian cycle and the start of the luteal phase.
  o Step 5 The Formation and Degeneration of the Corpus Luteum. The empty tertiary follicle initially collapses, and ruptured vessels bleed into the antrum. The remaining granulosa cells then invade the area, proliferating to create an endocrine
structure known as the corpus luteum, named for its yellow color. This process occurs under LH stimulation. The cholesterol contained in the corpus luteum is used to manufacture steroid hormones known as progestins, principally the steroid progesterone. Although the corpus luteum also secretes moderate amounts of estrogens, levels are not as high as they were at ovulation, and progesterone is the principal hormone in the luteal phase. Progesterone’s primary function is to prepare the uterus for pregnancy by stimulating the maturation of the uterine lining and the secretions of uterine glands.

- Step 6 Unless Fertilization Occurs, the Corpus Luteum Begins to Degenerate Roughly 12 Days after Ovulation. Progesterone and estrogen levels then fall markedly. Fibroblasts invade the nonfunctional corpus luteum, producing a knot of pale scar tissue called a corpus albicans. The disintegration, or involution, of the corpus luteum marks the end of the ovarian cycle. A new ovarian cycle then begins with the activation of another group of primordial follicles.

- Age and Oogenesis Although many primordial follicles may have developed into primary follicles, and several primary follicles may have been converted to secondary follicles, generally only a single oocyte is released into the pelvic cavity at ovulation. The rest undergo atresia. At puberty, each ovary contains about 200,000 primordial follicles. Forty years later, few if any follicles remain, although only about 500 will have been ovulated in the interim.

**Keys**

- Oogenesis begins during embryonic development, and primary oocyte production is completed before birth.
- Each month after puberty, the ovarian cycle produces one or more secondary oocytes from the pre-existing population of primary oocytes.
- The number of viable and responsive primary oocytes declines markedly over time, until ovarian cycles end at age 45–55.

**The Uterine Tubes**

**Figure 28-17**

- Each uterine tube (Fallopian tube or oviduct) is a hollow, muscular tube measuring roughly 13 cm (5.2 in.) in length. Each uterine tube is divided into three segments:
  - The Infundibulum. The end closest to the ovary forms an expanded funnel, or infundibulum, with numerous fingerlike projections that extend into the pelvic cavity. The projections are called fimbriae. The inner surfaces of the infundibulum are lined with cilia that beat toward the middle segment of the uterine tube, called the ampulla.
  - The Ampulla. The thickness of the smooth muscle layers in the wall of the ampulla, the middle segment of the uterine tube, gradually increases as the tube approaches the uterus.
  - The Isthmus. The ampulla leads to the isthmus, a short segment connected to the uterine wall.

- Histology of the Uterine Tube The epithelium lining the uterine tube is composed of ciliated columnar epithelial cells with scattered mucin secreting cells. The mucosa is surrounded by concentric layers of smooth muscle.
- Oocyte transport involves a combination of ciliary movement and peristaltic contractions in the walls of the uterine tube. A few hours before ovulation, sympathetic and parasympathetic nerves from the hypogastric plexus “turn on” this beating pattern and initiate peristalsis.
- It normally takes three to four days for an oocyte to travel from the infundibulum to the uterine cavity. If fertilization is to occur, the secondary oocyte must encounter spermatozoa during the first 12–24 hours of its passage. Fertilization typically occurs near the boundary between the ampulla and isthmus of the uterine tube.
- In addition to its transport function, the uterine tube provides a nutrient-rich environment that contains lipids and glycogen. This mixture supplies nutrients to both spermatozoa and a
developing pre-embryo (the cell cluster produced by the initial divisions following fertilization). Unfertilized oocytes degenerate in the terminal portions of the uterine tubes or within the uterus.

**The Uterus**

**Figure 28-18**

- The uterus provides mechanical protection, nutritional support, and waste removal for the developing embryo (weeks 1–8) and fetus (week 9 through delivery). In addition, contractions in the muscular wall of the uterus are important in ejecting the fetus at birth.
- The uterus is a small, pear-shaped organ about 7.5 cm (3 in.) long and with a maximum diameter of 5 cm (2 in.). It weighs 30–40 g (1–1.4 oz). In its normal position, the uterus bends anteriorly near its base, a condition known as anteflexion.
- In this position, the uterus covers the superior and posterior surfaces of the urinary bladder. If the uterus bends backward toward the sacrum, the condition is termed retroflexion. Retroflexion, which occurs in about 20 percent of adult women, has no clinical significance. (A retroflexed uterus generally becomes anteflexed spontaneously during the third month of pregnancy.)
- **Suspensory Ligaments of the Uterus** In addition to the broad ligament, three pairs of suspensory ligaments stabilize the position of the uterus and limit its range of movement.
  - The uterosacral ligaments extend from the lateral surfaces of the uterus to the anterior face of the sacrum, keeping the body of the uterus from moving inferiorly and anteriorly. The round ligaments arise on the lateral margins of the uterus just posterior and inferior to the attachments of the uterine tubes. These ligaments extend through the inguinal canal and end in the connective tissues of the external genitalia. The round ligaments restrict primarily posterior movement of the uterus. The lateral (cardinal) ligaments extend from the base of the uterus and vagina to the lateral walls of the pelvis. These ligaments tend to prevent inferior movement of the uterus. Additional mechanical support is provided by the muscles and fascia of the pelvic floor.
  - **Internal Anatomy of the Uterus** We can divide the uterus into two anatomical regions: the body and the cervix.
  - The uterine body, or corpus, is the largest portion of the uterus. The fundus is the rounded portion of the body superior to the attachment of the uterine tubes. The body ends at a constriction known as the **isthmus** of the uterus.
  - The cervix is the inferior portion of the uterus that extends from the isthmus to the **vagina**. The tubular cervix projects about 1.25 cm (0.5 in.) into the vagina. Within the vagina, the distal end of the cervix forms a curving surface that surrounds the **cervical os**, or external orifice of the uterus. The cervical os leads into the **cervical canal**, a constricted passageway that opens into the uterine cavity of the body at the **internal os**, or internal orifice.
  - The uterus receives blood from branches of the uterine arteries, which arise from branches of the **internal iliac arteries**, and from the **ovarian arteries**, which arise from the abdominal aorta inferior to the renal arteries. The arteries to the uterus are extensively interconnected, ensuring a reliable flow of blood to the organ despite changes in its position and shape during pregnancy.
  - Numerous veins and lymphatic vessels also drain each portion of the uterus. The organ is innervated by autonomic fibers from the hypogastric plexus (sympathetic) and from sacral segments and (parasympathetic). The most delicate anesthetic procedures used during labor and delivery, known as **segmental blocks**, target only spinal nerves T10–L1.

**Figure 28-19**

- **The Uterine Wall** The dimensions of the uterus are highly variable. In women of reproductive age who have not given birth, the uterine wall is about 1.5 cm (0.6 in.) thick.
  - The wall has a thick, outer, muscular **myometrium** and a thin, inner, glandular **endometrium**, or **mucosa**. The fundus and the posterior surface of the uterine body and isthmus are covered by a serous membrane that is continuous with the peritoneal lining. This incomplete serosa is
called the *perimetrium*. The *endometrium* contributes about 10 percent to the mass of the uterus. The glandular and vascular tissues of the endometrium support the physiological demands of the growing fetus.

- Vast numbers of uterine glands open onto the endometrial surface and extend deep into the lamina propria, almost to the myometrium. Under the influence of estrogen, the uterine glands, blood vessels, and epithelium change with the phases of the monthly *uterine cycle*.
- The myometrium, the thickest portion of the uterine wall, constitutes almost 90 percent of the mass of the uterus. Smooth muscle in the myometrium is arranged into longitudinal, circular, and oblique layers. The smooth muscle tissue of the myometrium provides much of the force needed to move a fetus out of the uterus and into the vagina.
- **Histology of the Uterus** We can divide the endometrium into a **functional zone**—the layer closest to the uterine cavity—and a *basilar zone*, adjacent to the myometrium.
- The functional zone contains most of the uterine glands and contributes most of the endometrial thickness. It is this zone that undergoes the dramatic changes in thickness and structure during the menstrual cycle.
- The basilar zone attaches the endometrium to the myometrium and contains the terminal branches of the tubular endometrial glands.
- Within the myometrium, branches of the uterine arteries form arcuate arteries, which encircle the endometrium. *Radial arteries* supply *straight arteries*, which deliver blood to the basilar zone of the endometrium, and *spiral arteries*, which supply the functional zone.
- The structure of the basilar zone remains relatively constant over time, but that of the functional zone undergoes cyclic changes in response to sex hormone levels. These cyclical changes produce the characteristic histological features of the uterine cycle.

**Figure 28-20**

- **The Uterine Cycle** The *uterine cycle*, or *menstrual cycle*, is a repeating series of changes in the structure of the endometrium. The uterine cycle averages 28 days in length, but it can range from 21 to 35 days in healthy women of reproductive age.
- We can divide the uterine cycle into three phases: (1) *menses*, (2) the *proliferative phase*, and (3) the *secretory phase*. The phases occur in response to hormones associated with the regulation of the ovarian cycle. Menses and the proliferative phase occur during the follicular phase of the ovarian cycle; the secretory phase corresponds to the luteal phase of the cycle.
- **Menses** The uterine cycle begins with the onset of menses, an interval marked by the degeneration of the functional zone of the endometrium. This degeneration occurs in patches and is caused by constriction of the spiral arteries, which reduces blood flow to areas of endometrium. Deprived of oxygen and nutrients, the secretory glands and other tissues in the functional zone begin to deteriorate. Eventually, the weakened arterial walls rupture, and blood pours into the connective tissues of the functional zone.
- Blood cells and degenerating tissues then break away and enter the uterine lumen, to be lost by passage through the cervical os and into the vagina. Only the functional zone is affected, because the deeper, basilar zone is provided with blood from the straight arteries, which remain unconstriicted.
- The sloughing off of tissue is gradual, and at each site repairs begin almost at once. Nevertheless, before menses has ended, the entire functional zone has been lost. The process of endometrial sloughing, called *menstruation*, generally lasts from one to seven days. Over this period roughly 35 to 50 ml of blood are lost. The process can be relatively painless.
- **The Proliferative Phase** The basilar zone, including the basal parts of the uterine glands, survives menses intact. In the days after menses, the epithelial cells of the uterine glands multiply and spread across the endometrial surface, restoring the integrity of the uterine epithelium. Further growth and vascularization result in the complete restoration of the functional zone.
- As this reorganization proceeds, the endometrium is in the proliferative phase. *Restoration* occurs at the same time as the enlargement of primary and secondary follicles in the ovary.
The proliferative phase is stimulated and sustained by estrogens secreted by the developing ovarian follicles.

- By the time ovulation occurs, the functional zone is several millimeters thick, and prominent mucous glands extend to the border with the basilar zone. At this time, the endometrial glands are manufacturing a mucus rich in glycogen. This specialized mucus appears to be essential for the survival of the fertilized egg through its earliest developmental stages. The entire functional zone is highly vascularized, with small arteries spiralizing toward the inner surface from larger arteries in the myometrium.

- **The Secretory Phase** During the secretory phase of the uterine cycle, the endometrial glands enlarge, accelerating their rates of secretion, and the arteries that supply the uterine wall elongate and spiral through the tissues of the functional zone. This activity occurs under the combined stimulatory effects of progestins and estrogens from the corpus luteum. The secretory phase begins at the time of ovulation and persists as long as the corpus luteum remains intact. Secretory activities peak about 12 days after ovulation. Over the next day or two, glandular activity declines, and the uterine cycle ends as the corpus luteum stops producing stimulatory hormones.

- A new cycle then begins with the onset of menses and the disintegration of the functional zone. The secretory phase generally lasts 14 days. As a result, you can identify the date of ovulation by counting backward 14 days from the first day of menses.

- **Menarche and Menopause** The uterine cycle begins at puberty. The first cycle, known as menarche, typically occurs at age 11–12. The cycles continue until menopause, the termination of the uterine cycle, at age 45–55.

- Over the interim, the regular appearance of uterine cycles is interrupted only by circumstances such as illness, stress, starvation, or pregnancy. If menarche does not appear by age 16, or if the normal uterine cycle of an adult woman becomes interrupted for six months or more, the condition of amenorrhea exists. Primary amenorrhea is the failure to initiate menses. Transient secondary amenorrhea can be caused by severe physical or emotional stresses.

**The Vagina**

**Figure 28-21**

- The vagina is an elastic, muscular tube extending between the **cervix** and the **vestibule**, a space bounded by the female external genitalia. The vagina is typically 7.5–9 cm (3–3.6 in.) long, but its diameter varies because it is highly distensible.

- At the proximal end of the vagina, the cervix projects into the **vaginal canal**. The shallow recess surrounding the cervical protrusion is known as the **fornix**.

- The vagina lies parallel to the rectum, and the two are in close contact posteriorly. Anteriorly, the urethra extends along the superior wall of the vagina from the urinary bladder to the external urethral orifice, which opens into the vestibule.

- The primary blood supply of the vagina is via the vaginal branches of the internal iliac (or uterine) arteries and veins. Innervation is from the hypogastric plexus, sacral nerves and branches of the pudendal nerve.

- The vagina has three major functions: It (1) serves as a passageway for the elimination of menstrual fluids, (2) receives the penis during sexual intercourse, and holds spermatozoa prior to their passage into the uterus, and (3) forms the inferior portion of the birth canal, through which the fetus passes during delivery.

- **Anatomy and Histology of the Vagina** In sectional view, the lumen of the vagina appears constricted, forming a rough H. The vaginal walls contain a network of blood vessels and layers of smooth muscle. The lining is moistened by secretions of the cervical glands and by the movement of water across the permeable epithelium. Throughout childhood the vagina and vestibule are usually separated by the **hymen**, an elastic epithelial fold that partially or completely blocks the entrance to the vagina; an intact hymen is typically ruptured during sexual intercourse or tampon usage.
The two bulbospongious muscles extend along either side of the vaginal entrance, which is constricted by their contractions. These muscles cover the vestibular bulbs, masses of erectile tissue on either side of the vaginal entrance. The vestibular bulbs have the same embryological origins as the corpus spongiosum of the penis in males.

The vaginal lumen is lined by a nonkeratinized stratified squamous epithelium. In the relaxed state, this epithelium forms folds called rugae. The underlying lamina propria is thick and elastic, and it contains small blood vessels, nerves, and lymph nodes.

The vaginal mucosa is surrounded by an elastic muscularis layer consisting of layers of smooth muscle fibers arranged in circular and longitudinal bundles continuous with the uterine myometrium. The portion of the vagina adjacent to the uterus has a serosal covering that is continuous with the pelvic peritoneum. Along the rest of the vagina, the muscularis layer is surrounded by an adventitia of fibrous connective tissue.

The vagina contains a population of resident bacteria, usually harmless, supported by nutrients in the cervical mucus. The metabolic activity of these bacteria creates an acidic environment, which restricts the growth of many pathogens. Vaginitis, an inflammation of the vaginal canal, is caused by fungi, bacteria, or parasites.

The hormonal changes associated with the ovarian cycle also affect the vaginal epithelium. By examining a vaginal smear—a sample of epithelial cells shed at the surface of the vagina—a clinician can estimate the corresponding stage in the ovarian and uterine cycles.

**The External Genitalia**

**Figure 28-22**

- The area containing the female external genitalia is the vulva, or pudendum. The vagina opens into the vestibule, a central space bounded by small folds known as the labia minora. The labia minora are covered with a hairless, smooth skin. The urethra opens into the vestibule just anterior to the vaginal entrance.
- The paraurethral glands, or Skene’s glands, discharge into the urethra near the external urethral opening. Anterior to this opening, the clitoris projects into the vestibule. A small, rounded tissue projection, the clitoris is derived from the same embryonic structures as the penis in males. Internally, it contains erectile tissue comparable to the corpora cavernosa of the penis. The clitoris engorges with blood during sexual arousal.
- A small erectile glans sits atop it; extensions of the labia minora encircle the body of the clitoris, forming its prepuce, or hood.
- A variable number of small lesser vestibular glands discharge their secretions onto the exposed surface of the vestibule, keeping it moist. During sexual arousal, a pair of ducts discharges the secretions of the greater vestibular glands (Bartholin’s glands) into the vestibule near the posterolateral margins of the vaginal entrance. These mucous glands have the same embryological origins as the bulbourethral glands of males.
- The outer limits of the vulva are established by the mons pubis and the labia majora. The bulge of the mons pubis is created by adipose tissue deep to the skin superficial to the pubic symphysis.
- Adipose tissue also accumulates within the labia majora, prominent folds of skin that encircle and partially conceal the labia minora and adjacent structures. The outer margins of the labia majora and the mons pubis are covered with coarse hair, but the inner surfaces of the labia majora are relatively hairless. Sebaceous glands and scattered apocrine sweat glands release their secretions onto the inner surface of the labia majora, moistening and lubricating them.

**The Mammary Glands**

**Figure 28-23**

- A newborn infant cannot fend for itself, and several of its key systems have yet to complete development. Over the initial period of adjustment to an independent existence, the infant can gain nourishment from the milk secreted by the maternal mammary glands.
- Milk production, or lactation, occurs in these glands. In females, mammary glands are specialized organs of the integumentary system that are controlled mainly by hormones of the
reproductive system and by the **placenta**, a temporary structure that provides the embryo and fetus with nutrients.

- On each side, a mammary gland lies in the subcutaneous tissue of the pectoral fat pad deep to the skin of the chest. Each breast bears a **nipple**, a small conical projection where the ducts of the underlying mammary gland open onto the body surface. The reddish-brown skin around each nipple is the **areola**.
- Large sebaceous glands deep to the areolar surface give it a grainy texture. The glandular tissue of a mammary gland consists of separate lobes, each containing several secretory lobules. Ducts leaving the lobules converge, giving rise to a single **lactiferous duct** in each lobe. Near the nipple, that lactiferous duct enlarges, forming an expanded chamber called a **lactiferous sinus**.
- Typically, 15–20 lactiferous sinuses open onto the surface of each nipple. Dense connective tissue surrounds the duct system and forms partitions that extend between the lobes and the lobules. These bands of connective tissue, the **suspensory ligaments of the breast**, originate in the dermis of the overlying skin. A layer of areolar tissue separates the mammary gland complex from the underlying pectoralis muscles.
- Branches of the **internal thoracic artery** supply blood to each mammary gland.
- An inactive, or **resting**, mammary gland is dominated by a duct system rather than by active glandular cells. The size of the mammary glands in a nonpregnant woman reflects primarily the amount of adipose tissue present, not the amount of glandular tissue.
- The secretory apparatus normally does not complete its development unless pregnancy occurs. An active mammary gland is a tubuloalveolar gland, consisting of multiple glandular tubes that end in secretory alveoli.

**Hormones and the Female Reproductive Cycle**

- The activity of the female reproductive tract is under hormonal control that involves an interplay between secretions of both the pituitary gland and the gonads. But the regulatory pattern in females is much more complicated than in males, because it must coordinate the ovarian and uterine cycles.
- Circulating hormones control the female reproductive cycle, coordinating the ovarian and uterine cycles to ensure proper reproductive function. If the two cycles are not properly coordinated, infertility results. A woman who fails to ovulate cannot conceive, even if her uterus is perfectly normal. A woman who ovulates normally, but whose uterus is not ready to support an embryo, will also be infertile.
- Because the processes are complex and difficult to study, many of the biochemical details of the female reproductive cycle still elude us, but the general patterns are reasonably clear. As in males, GnRH from the hypothalamus regulates reproductive function in females. However, in females, the GnRH pulse frequency and amplitude (amount secreted per pulse) change throughout the course of the ovarian cycle. Changes in GnRH pulse frequency are controlled primarily by circulating levels of estrogens and progestins. Estrogens increase the GnRH pulse frequency, and progestins decrease it.
- The endocrine cells of the anterior lobe of the pituitary gland respond as if each group of endocrine cells is monitoring different frequencies. As a result, each group of cells is sensitive to some GnRH pulse frequencies and insensitive to others.

**Figure 28-24**

- **Hormones and the Follicular Phase** Follicular development begins under FSH stimulation; each month some of the primordial follicles begin to develop into primary follicles. As the follicles enlarge, thecal cells start producing **androstenedione**, a steroid hormone that is a key intermediate in the synthesis of estrogens and androgens. Androstenedione is absorbed by the granulosa cells and converted to estrogens.
- In addition, small quantities of estrogens are secreted by interstitial cells scattered throughout the ovarian stroma. Circulating estrogens are bound primarily to albumins, with lesser amounts carried by **gonadal steroid binding globulin (GBG)**.
• Of the three estrogens circulating in the bloodstream—estradiol, estrone, and estriol—the one that is most abundant and has the most pronounced effects on target tissues is estradiol. It is the dominant hormone prior to ovulation.

• In estradiol synthesis, androstenedione is first converted to testosterone, which the enzyme aromatase converts to estradiol. The synthesis of both estrone and estriol proceeds directly from androstenedione. Estrogens have multiple functions that affect the activities of many tissues and organs throughout the body.

Figure 28-25

• Among the important general functions of estrogens are (1) stimulating bone and muscle growth, (2) maintaining female secondary sex characteristics, such as body hair distribution and the location of adipose tissue deposits, (3) affecting central nervous system (CNS) activity (especially in the hypothalamus, where estrogens increase the sexual drive), (4) maintaining functional accessory reproductive glands and organs, and (5) initiating the repair and growth of the endometrium.

Summary: Hormonal Regulation of the Female Reproductive Cycle

Figure 28-26

• Early in the follicular phase, estrogen levels are low and the GnRH pulse frequency is 16–24 per day (one pulse every 60–90 minutes). At this frequency, FSH is the dominant hormone released by the anterior pituitary gland; the estrogens released by developing follicles inhibit LH secretion.

• As secondary follicles develop, FSH levels decline due to the negative feedback effects of inhibin. Follicular development and maturation continue, however, supported by the combination of estrogens, FSH, and LH.

• As one or more tertiary follicles begin forming, the concentration of circulating estrogens rises steeply. As a result, the GnRH pulse frequency increases to about 36 per day (one pulse every 30–60 minutes). The increased pulse frequency stimulates LH secretion. In addition, at roughly day 10 of the cycle, the effect of estrogen on LH secretion changes from inhibition to stimulation.

• The switchover occurs only after rising estrogen levels have exceeded a specific threshold value for about 36 hours. (The threshold value and the time required vary among individuals.) High estrogen levels also increase gonadotrope sensitivity to GnRH. At about day 14, the estrogen level has peaked, the gonadotropes are at maximum sensitivity, and the GnRH pulses are arriving about every 30 minutes.

• The result is a massive release of LH from the anterior pituitary gland. This sudden surge in LH concentration triggers (1) the completion of meiosis I by the primary oocyte, (2) the rupture of the follicular wall, and (3) ovulation. Typically, ovulation occurs 34–38 hours after the LH surge begins, roughly 9 hours after the LH peak.

• Hormones and the Luteal Phase The high LH levels that trigger ovulation also promote progesterone secretion and the formation of the corpus luteum. As progesterone levels rise and estrogen levels fall, the GnRH pulse frequency declines sharply, soon reaching 1–4 pulses per day.

• This frequency of GnRH pulses stimulates LH secretion more than it does FSH secretion, and the LH maintains the structure and secretory function of the corpus luteum. Although moderate amounts of estrogens are secreted by the corpus luteum, progesterone is the main hormone of the luteal phase. Its primary function is to continue the preparation of the uterus for pregnancy by enhancing the blood supply to the functional zone and stimulating the secretion of endometrial glands.

• Progesterone levels remain high for the next week, but unless pregnancy occurs, the corpus luteum begins to degenerate. Roughly 12 days after ovulation, the corpus luteum becomes nonfunctional, and progesterone and estrogen levels fall markedly. The blood supply to the functional zone is restricted, and the endometrial tissues begin to deteriorate.
• As progesterone and estrogen levels drop, the GnRH pulse frequency increases, stimulating FSH secretion by the anterior lobe of the pituitary gland, and the ovarian cycle begins again. The hormonal changes involved with the ovarian cycle in turn affect the activities of other reproductive tissues and organs. At the uterus, the hormonal changes maintain the uterine cycle.

• **Hormones and the Uterine Cycle** The declines in progesterone and estrogen levels that accompany the degeneration of the corpus luteum result in menses. The shedding of endometrial tissue continues for several days, until rising estrogen levels stimulate the repair and regeneration of the functional zone of the endometrium.

• The proliferative phase continues until rising progesterone levels mark the arrival of the secretory phase. The combination of estrogen and progesterone then causes the enlargement of the endometrial glands and an increase in their secretory activities.

• **Hormones and Body Temperature** The monthly hormonal fluctuations cause physiological changes that affect core body temperature. During the follicular phase, when estrogen is the dominant hormone, the basal body temperature, or the resting body temperature measured upon awakening in the morning, is about 0.3°C lower than it is during the luteal phase, when progesterone dominates.

• At the time of ovulation, the basal body temperature declines noticeably, making the rise in temperature over the next day even more noticeable. As a result, by keeping records of body temperature over a few uterine cycles, a woman can often determine the precise day of ovulation.

**Keys**

• Cyclic changes in FSH and LH levels are responsible for the maintenance of the ovarian cycle; the hormones produced by the ovaries in turn regulate the uterine cycle.

• Inadequate hormone levels, inappropriate or inadequate responses to circulating hormones, or poor coordination and timing of hormone production or secondary oocyte release will reduce or eliminate the chances of pregnancy.

**The Physiology of Sexual Intercourse, p. 1065**

**Objective**

1. Discuss the physiology of sexual intercourse as it affects the reproductive systems of males and females.

2. Sexual intercourse, also known as coitus or copulation, introduces semen into the female reproductive tract.

**Male Sexual Function**

• Sexual function in males is coordinated by complex neural reflexes that we do not yet understand completely. The reflex pathways utilize the sympathetic and parasympathetic divisions of the autonomic nervous system.

• During sexual arousal, erotic thoughts, the stimulation of sensory nerves in the genital region, or both lead to an increase in parasympathetic outflow over the pelvic nerves. This outflow in turn leads to erection of the penis. The integument covering the glans of the penis contains numerous sensory receptors, and erection tenses the skin and increases their sensitivity.

• Subsequent stimulation can initiate the secretion of the bulbourethral glands, lubricating the penile urethra and the surface of the glans. During intercourse, the sensory receptors of the penis are rhythmically stimulated. This stimulation eventually results in the coordinated processes of emission and ejaculation. Emission occurs under sympathetic stimulation.

• The process begins when the peristaltic contractions of the ampulla push fluid and spermatozoa into the prostatic urethra. The seminal vesicles then begin contracting, and the contractions increase in force and duration over the next few seconds. Peristaltic contractions also appear in the walls of the prostate gland. The combination moves the seminal mixture into the membranous and penile portions of the urethra.
• While the contractions are proceeding, sympathetic commands also cause the contraction of the urinary bladder and the internal urethral sphincter. The combination of elevated pressure inside the bladder and the contraction of the sphincter effectively prevents the passage of semen into the bladder. Ejaculation occurs as powerful, rhythmic contractions appear in the ischiocavernosus and bulbospongiosus muscles, two superficial skeletal muscles of the pelvic floor. The ischiocavernosus muscles insert along the sides of the penis; their contractions serve primarily to stiffen that organ. The bulbospongiosus muscle wraps around the base of the penis; the contraction of this muscle pushes semen toward the external urethral opening.
• Ejaculation is associated with intensely pleasurable sensations, an experience known as male orgasm.
• Arousal, erection, emission, and ejaculation are controlled by a complex interplay between the sympathetic and parasympathetic divisions of the autonomic nervous system. Higher centers, including the cerebral cortex, can facilitate or inhibit many of the important reflexes, thereby modifying the patterns of sexual function. Any physical or psychological factor that affects a single component of the system can result in male sexual dysfunction, also called impotence. Impotence is defined as an inability to achieve or maintain an erection.

Female Sexual Function
• The phases of female sexual function are comparable to those of male sexual function. During sexual arousal, parasympathetic activation leads to engorgement of the erectile tissues of the clitoris and increased secretion of cervical mucous glands and the greater vestibular glands.
• Clitoral erection increases the receptors’ sensitivity to stimulation, and the cervical and vestibular glands lubricate the vaginal walls. A network of blood vessels in the vaginal walls becomes filled with blood at this time, and the vaginal surfaces are also moistened by fluid that moves across the epithelium from underlying connective tissues. (This process accelerates during intercourse as the result of mechanical stimulation.) Parasympathetic stimulation also causes contraction of subcutaneous smooth muscle of the nipples, making them more sensitive to touch and pressure.
• During sexual intercourse, rhythmic contact of the penis with the clitoris and vaginal walls—reinforced by touch sensations from the breasts and other stimuli (visual, olfactory, and auditory)—provides stimulation that leads to orgasm. Female orgasm is accompanied by peristaltic contractions of the uterine and vaginal walls and, by means of impulses traveling over the pudendal nerves, rhythmic contractions of the bulbospongious and ischiocavernous muscles. The latter contractions give rise to the intensely pleasurable sensations of orgasm.

Aging and the Reproductive System, p. 1066

Objective
1. Describe the changes in the reproductive system that occur with aging.
• The aging process affects all body systems, including the reproductive systems of men and women alike. The most striking age-related changes in the female reproductive system occur at menopause. Comparable age-related changes in the male reproductive system occur more gradually and over a longer period of time.

Menopause
• Menopause is usually defined as the time that ovulation and menstruation cease. Menopause typically occurs at age 45–55, but in the years immediately preceding it, the ovarian and uterine cycles become irregular. This interval is called perimenopause. A shortage of primordial follicles is the underlying cause of the irregular cycles. It has been estimated that almost 7 million potential oocytes are in fetal ovaries after five months of development, but the number drops to about 2 million at birth, and to a few hundred thousand at puberty.
• With the arrival of perimenopause, the number of follicles responding each month begins to drop markedly. As the number of available follicles decreases, estrogen levels decline and
may not rise enough to trigger ovulation. By age 50, there are often no primordial follicles left to respond to FSH. In premature menopause, this depletion occurs before age 40.

- Menopause is accompanied by a decline in circulating concentrations of estrogens and progesterone, and a sharp and sustained rise in the production of GnRH, FSH, and LH. The decline in estrogen levels leads to reductions in the size of the uterus and breasts, accompanied by a thinning of the urethral and vaginal epithelia. The reduced estrogen concentrations have also been linked to the development of osteoporosis, presumably because bone deposition proceeds at a slower rate.

**The Male Climacteric**

- Changes in the male reproductive system occur more gradually than do those in the female reproductive system. The period of declining reproductive function, which corresponds to perimenopause in women, is known as the male climacteric or andropause.
- Levels of circulating testosterone begin to decline between the ages of 50 and 60, and levels of circulating FSH and LH increase. Although sperm production continues (men well into their eighties can father children), older men experience a gradual reduction in sexual activity. This decrease may be linked to declining testosterone levels.

**Keys**

- Sex hormones have widespread effects on the body. They affect brain development and behavioral drives, muscle mass, bone mass and density, body proportions, and the patterns of hair and body fat distribution.
- As aging occurs, reductions in sex hormone levels affect appearance, strength, and a variety of physiological functions.

**Integration with Other Systems**

**Figure 28-27**

**Table 28-I**

- Normal human reproduction is a complex process that requires the participation of multiple systems. Physical factors also play a role. The man’s sperm count must be adequate, the semen must have the correct pH and nutrients, and erection and ejaculation must occur in the proper sequence; the woman’s ovarian and uterine cycles must be properly coordinated, ovulation and oocyte transport must occur normally, and her reproductive tract must provide a hospitable environment for the survival and movement of sperm, and for the subsequent fertilization of the oocyte.
- For these steps to occur, the reproductive, digestive, endocrine, nervous, cardiovascular, and urinary systems must all be functioning normally. Even when all else is normal and fertilization occurs at the proper time and place, a healthy infant will not be produced unless the zygote—a single cell the size of a pinhead—manages to develop into a full-term fetus that typically weighs about 3 kg (6.6 lb).