28

The Reproductive System

Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

28-1 List the basic **components of the human reproductive system**, and summarize the **functions** of each.

28-2 Describe the components of the **male reproductive system** and the roles played by the **reproductive tract and accessory glands** in producing **spermatozoa**; specify the **composition of semen**; and summarize the **hormonal mechanisms** that regulate male reproductive functions.

28-3 Describe the components of the **female reproductive system** and the **ovarian roles in oogenesis**; explain the complete **ovarian and uterine cycles**; outline the histology, anatomy, and functions of the **vagina**; and summarize all aspects of the **female reproductive cycle**.

28-4 Discuss the physiology of **sexual intercourse** in males and females.

28-5 Describe the **reproductive system changes** that occur with aging.

28-6 Give examples of **interactions between the reproductive system and** each of the **other organ systems**.

Clinical Notes

Spotlights

An Introduction to the Reproductive System

There are approximately 6.6 billion people currently living on the Earth. This is an astonishing number given that the reproductive system is the only system that is not essential to the life of the individual. Its activities do, however, affect other systems. This chapter discusses how the male and female reproductive organs produce and store specialized reproductive cells that combine to form new individuals, and how various reproductive organs also secrete hormones that play major roles in the maintenance of normal sexual function.

28-1 Basic reproductive system structures are gonads, ducts, accessory glands and organs, and external genitalia

In this chapter we examine the anatomy and physiology of the human **reproductive system.** This system ensures the continued existence of the human species—by producing, storing, nourishing, and transporting functional male and female reproductive cells called **gametes** (GAM-ēts).

The reproductive system includes the following basic components:

- **Gonads** (GŌ-nadz; *gone*, seed, generation), 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** (jen-i-TĀ-lē-uh).

In both males and females, the ducts are connected to chambers and passageways that open to the outside. The structures involved make up the *reproductive tract*. The male and female reproductive systems are functionally quite different, however. In adult males, the **testes** (TES-tēz; singular, *testis*), or male gonads, secrete sex hormones called *androgens*. The main androgen is *testosterone*, which was introduced in Chapter 18. ↩ p. 626 The testes also produce the male gametes, called **spermatozoa** (sper-ma-tō-ZŌ-uh; singular, *spermatozoon*), or *sperm*. The male produces about one-half billion sperm 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** (SĒ-men). During *ejaculation*, semen is expelled from the body.

In adult females, the **ovaries,** or female gonads, release only one immature gamete, called an **oocyte.** Normally only one oocyte is released each month. This oocyte travels along one of two short *uterine tubes*, which end in the muscular organ called the *uterus* (Ū-ter-us). If a sperm reaches the oocyte and starts the process of *fertilization*, the oocyte matures into an **ovum** (plural, *ova*). A short passageway, the *vagina* (va-JĪ-nuh), 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.

Next we examine the anatomy of the male and female reproductive systems further, and will consider the physiological and hormonal mechanisms responsible for the regulation of reproductive function. Earlier chapters introduced the anatomical reference points used in the discussions that follow. You may find it helpful to review the figures on the pelvic girdle (**Figures 8–7** and **Figure 8–8**, pp. 241, 242), perineal musculature (**Figure 11–12**, p. 346), pelvic innervation (**Figure 13–13**, p. 433), and regional blood supply (**Figures 21–26** and **21–30**, pp. 746, 751).

Checkpoint

1. **Define gamete.**
2. **List the basic components of the reproductive system.**
3. **Define gonads.**

See the blue Answers tab at the back of the book.

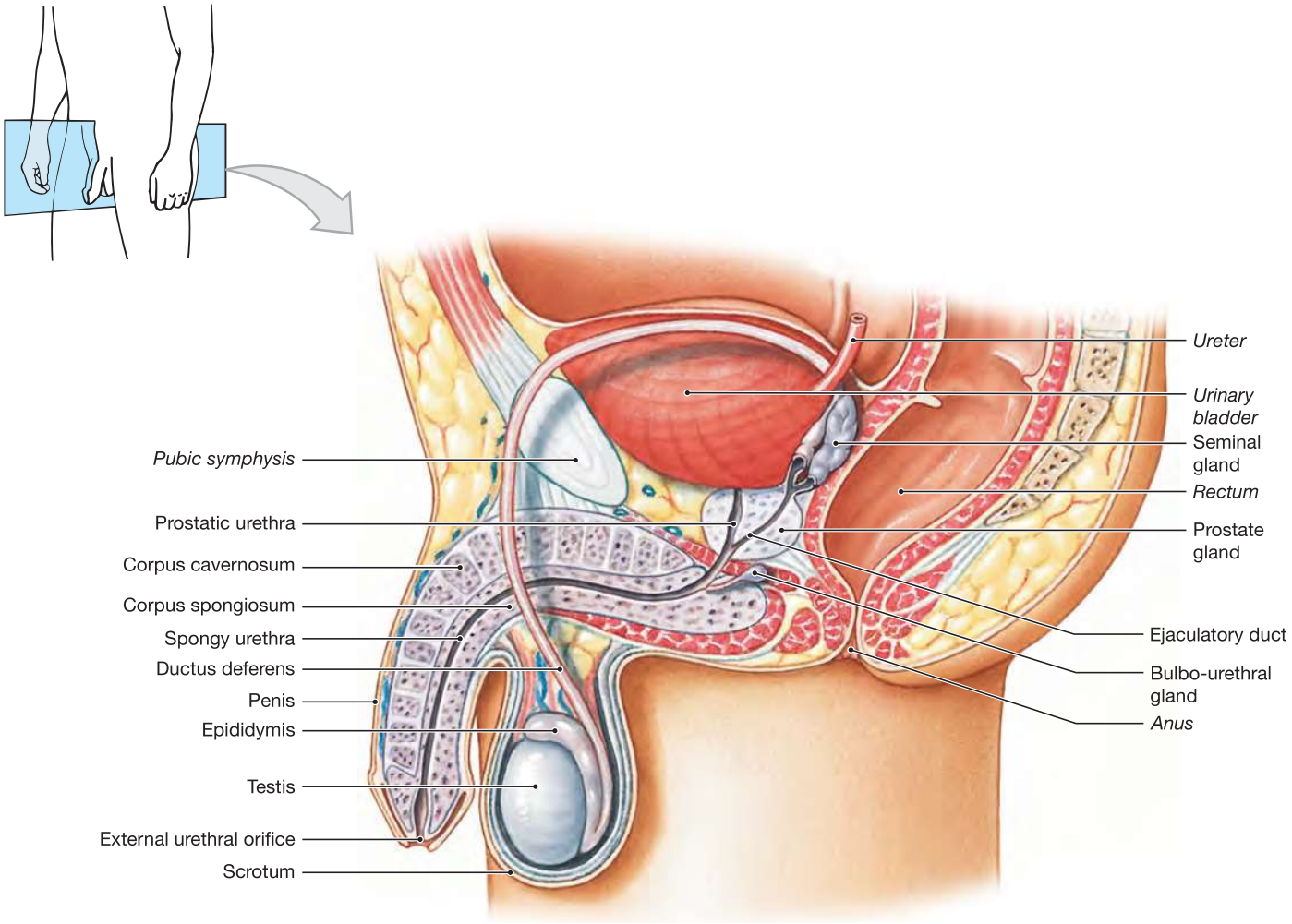
28-2 Spermatogenesis occurs in the testes, and hormones from the hypothalamus, anterior lobe of the pituitary gland, and testes control male reproductive functions

The main structures of the male reproductive system are shown in **Figure 28–1**. Proceeding from a testis, the spermatozoa travel within the *epididymis* (ep-i-DID-i-mus); the *ductus deferens* (DUK-tus DEF-e-renz), or *vas deferens*; the *ejaculatory duct*; and the *urethra* before leaving the body. Accessory organs—the *seminal* (SEM-i-nal) *glands* (seminal vesicles), the *prostate* (PROS-tāt) *gland*, and the *bulbo-urethral* (bul-bō-ū-RĒ-thral) *glands*—secrete various fluids into the ejaculatory ducts and urethra. The external genitalia consist of the *scrotum* (SKRŌ-tum), which encloses the testes, and the *penis* (PĒ-nis), an erectile organ. The distal portion of the urethra passes through the distal portion of the penis.

The Testes

Each testis is about 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).

Figure 28–1 The Male Reproductive System. A sagittal section of the male reproductive organs. ATLAS: Plate 64



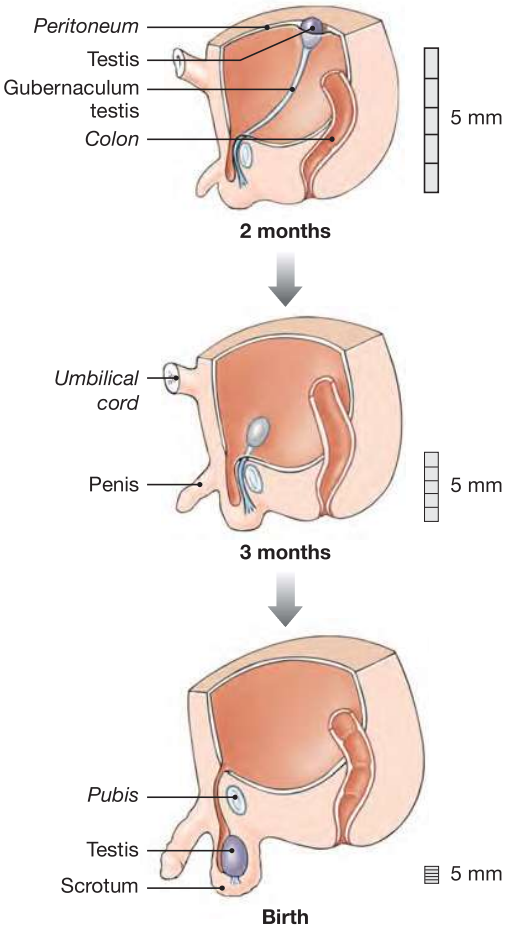
The testes hang within the **scrotum,** a fleshy pouch suspended inferior to the perineum. The scrotum is anterior to the anus, and posterior to the base of the penis (**Figure 28–1**). ATLAS: Embryology Summary 21: The Development of the Reproductive System

Descent of the Testes

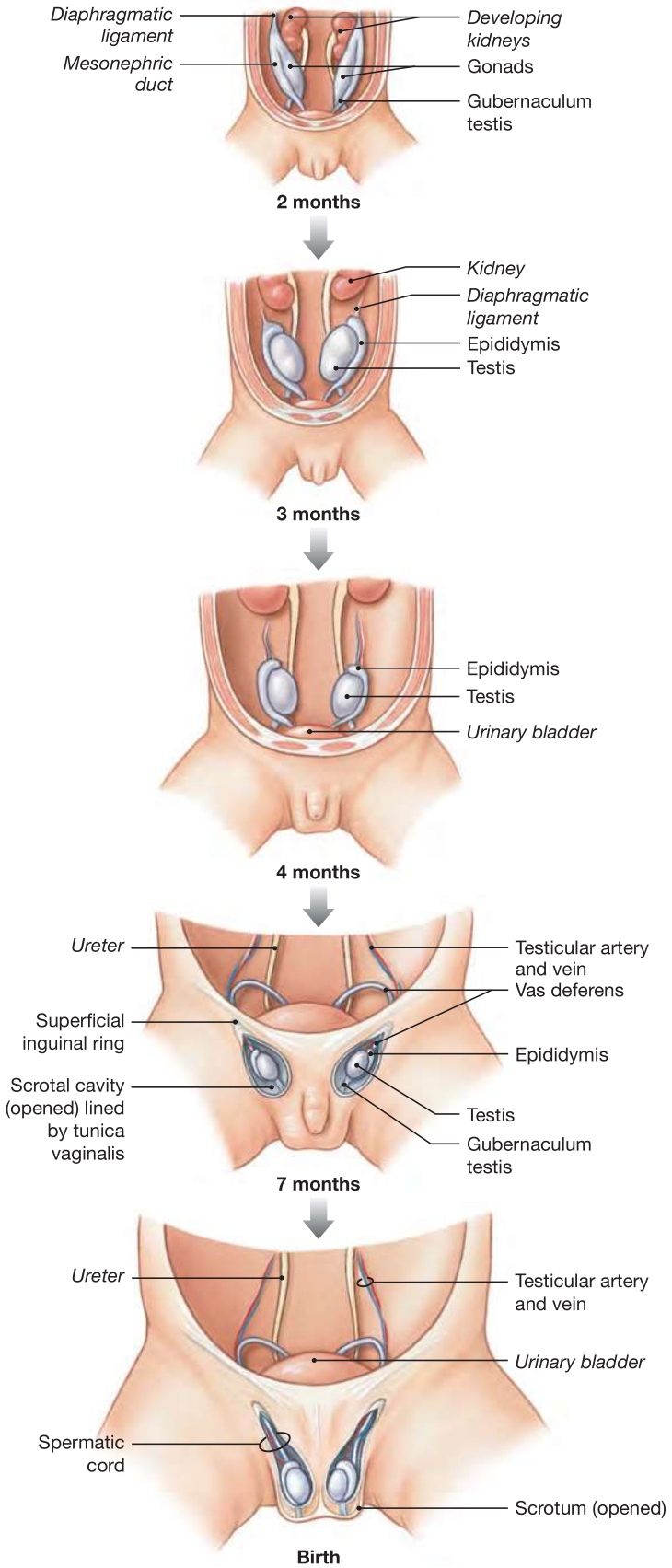
During fetal development, the testes form inside the body cavity adjacent to the kidneys. A bundle of connective tissue fibers—called the **gubernaculum testis** (goo-bur-NAK-ū-lum TES-tis)—extends from each testis to the posterior wall of a small anterior and inferior pocket of the peritoneum (**Figure 28–2a**). As the fetus grows, the gubernacula do not get any longer, so they lock the testes in position. As a result, the 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 rapidly, and circulating hormones stimulate a contraction of the gubernaculum testis. Over this period, each testis moves through the abdominal musculature, along with small pockets of the peritoneal cavity. This process is called the **descent of the testes** (**Figure 28–2**).

In *cryptorchidism* (krip-TOR-ki-dizm; *crypto,* hidden + *orchis,* testis), one or both of the testes have not descended into the scrotum by the time of birth. Typically, the cryptorchid (abdominal) testes are lodged in the abdominal cavity or within the inguinal canal. Cryptorchidism occurs in about 3 percent of full-term deliveries and in roughly 30 percent of premature births. In most instances, normal descent occurs a few weeks later, but the condition can be surgically corrected if it persists. Corrective measures should be taken before *puberty* (sexual maturation), because a cryptorchid testis will not produce spermatozoa. If both testes are cryptorchid, the individual will be *sterile (infertile)* and unable to father children. If the testes cannot be moved into the scrotum, they will usually be removed. This surgical procedure to remove the testes is called an

Figure 28–2 The Descent of the Testes.



a Sagittal sectional views of the positional changes involved in the descent of the right testis. Because the size of the gubernaculum testis remains constant (see the scale bar at the right) while the rest of the fetus grows, the relative position of the testis shifts.



b Frontal views showing the descent of the testes and the formation of the spermatic cords.

orchiectomy (or-kē-EK-tō-mē). About 10 percent of males with uncorrected cryptorchid testes eventually develop testicular cancer.

As each testis moves through the body wall, the ductus deferens and the testicular blood vessels, nerves, and lymphatic vessels accompany it. Together, these structures form the body of the spermatic cord, which we discuss next.

The Spermatic Cords

The **spermatic cords** are paired structures extending between the abdominopelvic cavity and the testes (**Figure 28–3**). 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** (pam-PIN-i-form; *pampinus*, tendril + *forma*, form) **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.

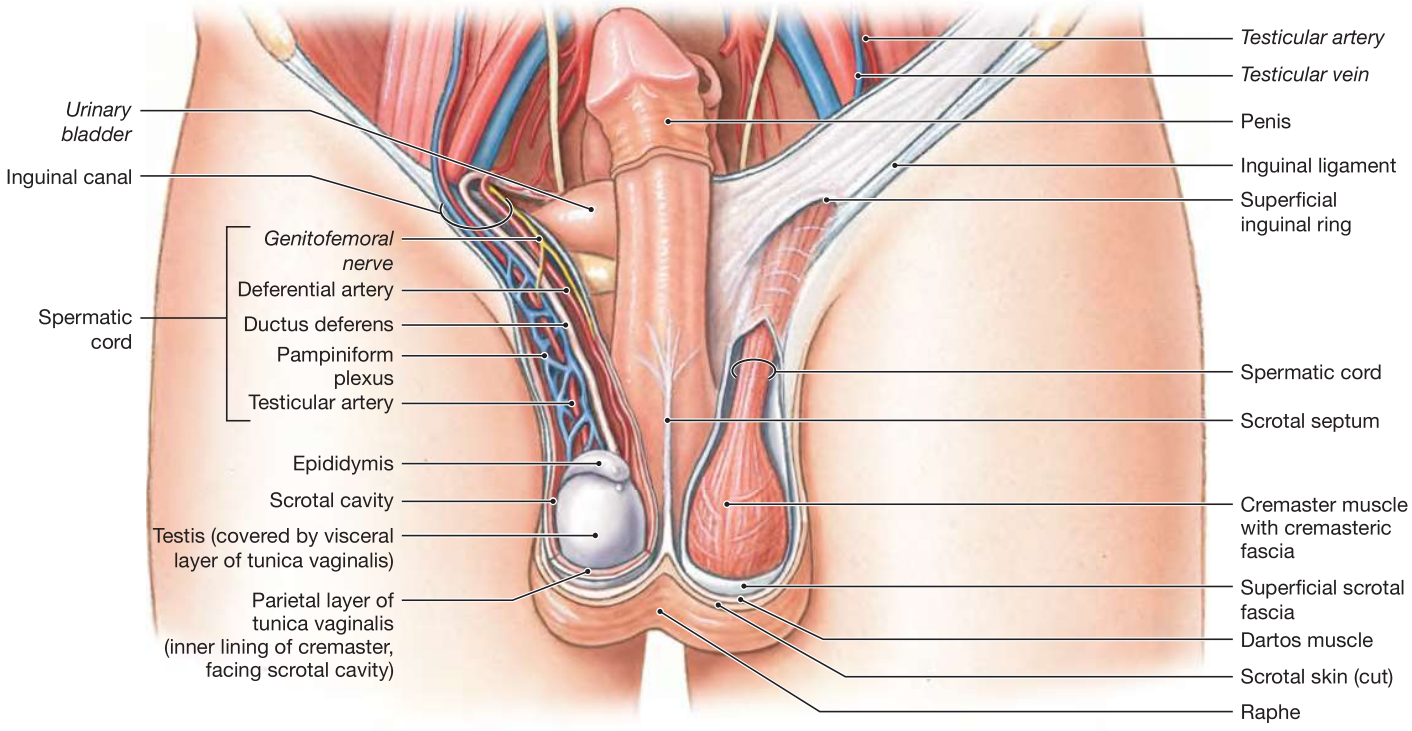
The inguinal canals form during development as the testes descend into the scrotum. At that time, these canals link the scrotal cavities with the peritoneal cavity. In normal adult males, the inguinal canals are closed, but the presence of the spermatic cords creates weak points in the abdominal wall that remain throughout life. As a result, *inguinal hernias*—protrusions of visceral tissues or organs into the inguinal canal—are fairly common in males. The inguinal canals in females are very small, containing only the *ilioinguinal 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. A raised thickening in the scrotal surface known as the **raphe** (RĀ-fē) divides it in two (**Figure 28–3**). 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 normally spread to the other. A narrow space separates the inner surface of the scrotum from the outer surface of the testis. The **tunica vaginalis** (TOO-ni-ka vaj-i-NAL-is), 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** (DAR-tōs) **muscle.** Resting muscle tone in the dartos muscle elevates the testes and causes the characteristic wrinkling of the scrotal surface. A layer of skeletal muscle, the **cremaster** (krē-MAS-ter) **muscle,** lies deep to the dermis. Contraction of the cremaster muscle during sexual arousal or in response to decreased temperature tenses the scrotum and pulls the testes closer to the body. The cremasteric reflex can be initiated by stroking the skin on the upper thigh, causing the scrotum to move 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. Sudden cooling of the scrotum, as occurs during entry into a cold swimming pool, results in contractions that pull the testes closer to the body and keep testicular temperatures from falling.

Figure 28–3 The Male Reproductive System in Anterior View.



Structure of the Testes

Deep to the tunica vaginalis covering the testis is the **tunica albuginea** (al-bū-JIN-ē-uh), a dense layer of connective tissue rich in collagen fibers (Figure 28–4a). These fibers are continuous with those surrounding the adjacent epididymis and extend into 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.

Histology of the Testes

The septa subdivide the testis into a series of **lobules** (Figure 28–4a). Distributed among the lobules are approximately 800 slender, tightly coiled **seminiferous** (sem-i-NIF-er-us) **tubules** (Figures 28–4 and 28–5). Each tubule averages about 80 cm (32 in.) in length. A typical testis contains nearly one-half mile of seminiferous tubules. Sperm production occurs within these tubules.

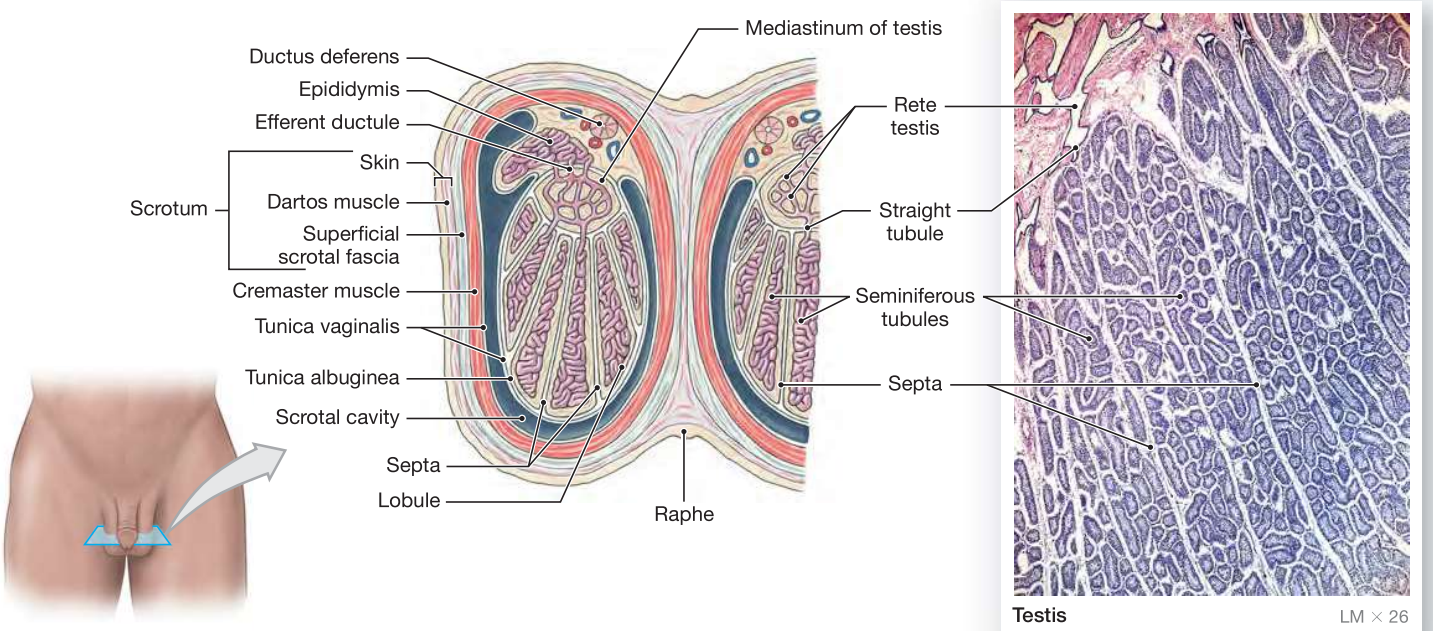
Each seminiferous tubule is U-shaped and connected to a single **straight tubule** that enters the mediastinum of the testis. Straight tubules are extensively interconnected, forming a maze of passageways known as the **rete** (RĒ-tē; *rete*, a net) **testis** (Figure 28–4). Fifteen to 20 large **efferent ductules** connect the rete testis to the epididymis.

Because the seminiferous tubules are tightly coiled, most tissue slides show them in transverse section (Figure 28–5a). A delicate connective tissue capsule surrounds each tubule, and areolar tissue fills the spaces between the tubules (Figure 28–5b). Within those spaces are numerous blood vessels and large **interstitial cells** (*Leydig cells*). Interstitial cells produce *androgens*, the dominant sex hormones in males. *Testosterone* is the most important androgen.

Spermatogenesis (sper-ma-tō-JEN-e-sis) is the process of spermatozoa formation. It begins at the outermost layer of cells in the seminiferous tubules and proceeds toward the lumen (Figure 28–5c,d). At each step in this process, the daughter cells move closer to the lumen. First, stem cells called **spermatogonia** (sper-ma-tō-GŌ-nē-uh) 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** (sper-MA-tō-sīts) 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 divide and differentiate into **spermatids** (SPER-ma-tidz)—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 **nurse cells.** Nurse cells are also known as *sustentacular* (sus-ten-TAK-ū-lar) cells or *Sertoli cells*. Nurse cells provide a microenvironment that supports spermatogenesis (Figure 28–5b,c).

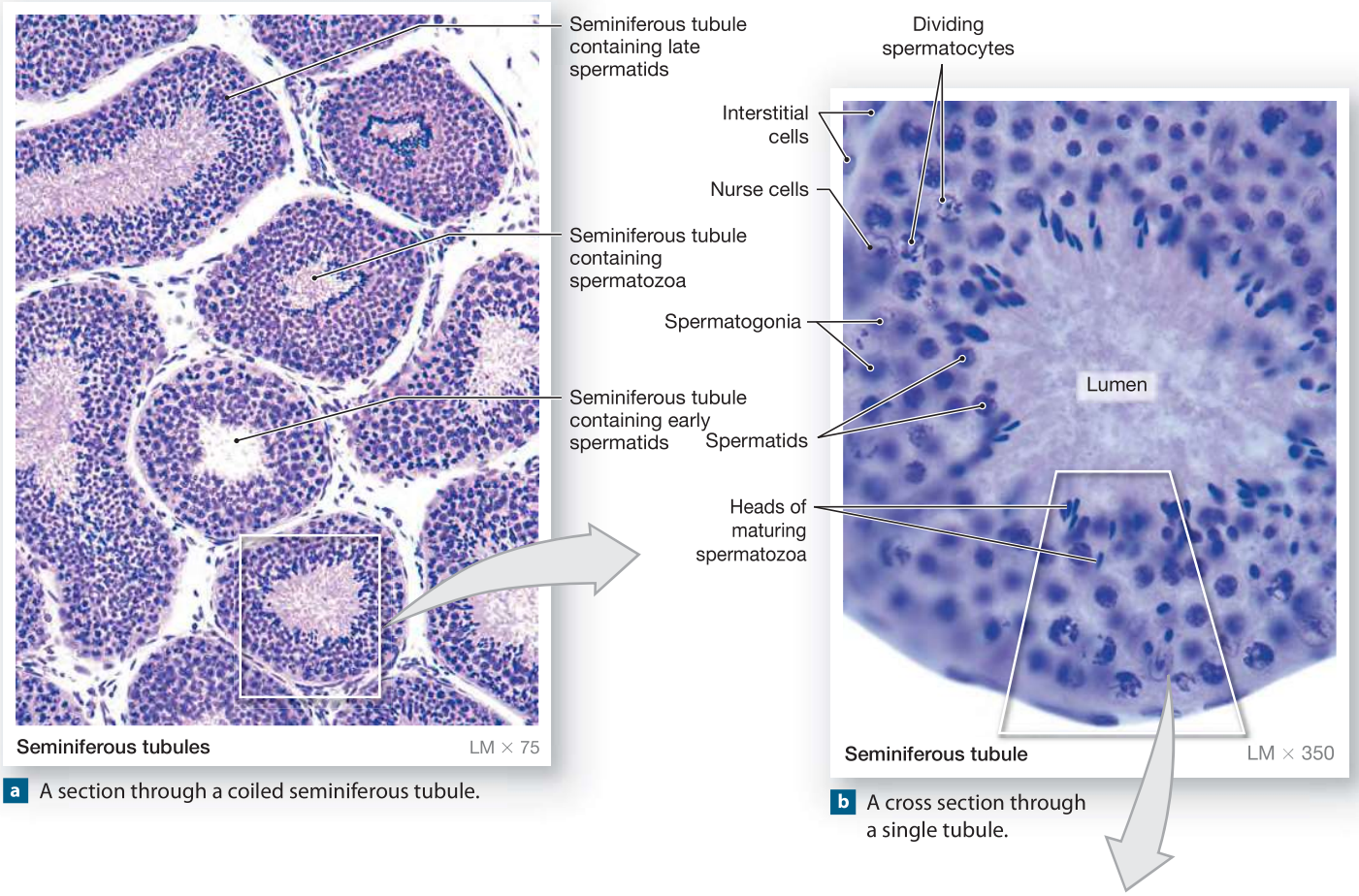
Figure 28–4 The Structure of the Testes.



a A transverse section of the scrotum and testes

b A section through a testis

Figure 28–5 The Seminiferous Tubules.



a A section through a coiled seminiferous tubule.

b A cross section through a single tubule.

c Nurse cells surround the stem cells of the tubule and support the developing spermatocytes and spermatids.

d Stages in spermatogenesis in the wall of a seminiferous tubule.

Spermatogenesis

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. Spermatogenesis involves three integrated processes:

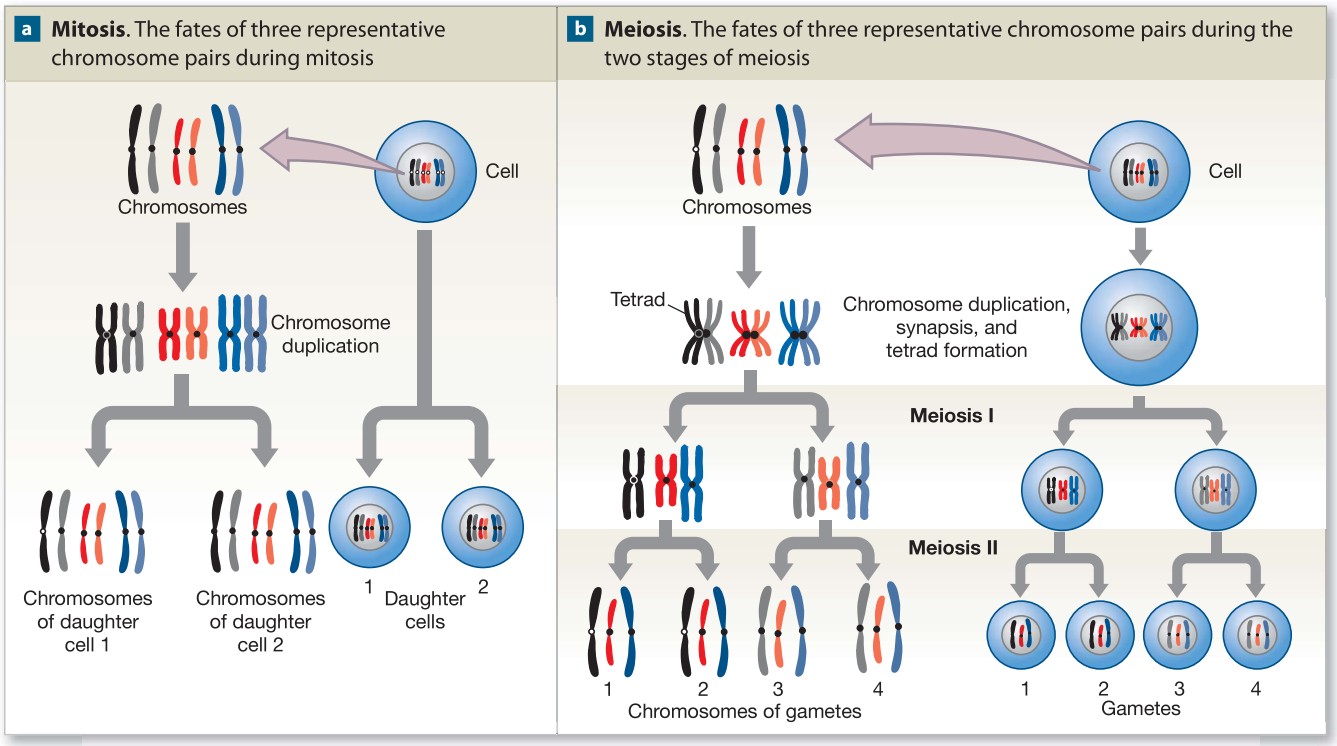
1. *Mitosis.* Spermatogonia undergo cell divisions throughout adult life. (You can review the description of mitosis and cell division in Chapter 3. ↩ pp. 98–99) One daughter cell from each division remains in place while the other is pushed toward the lumen (space) of the seminiferous tubule. The displaced cells differentiate into primary spermatocytes, which prepare to begin meiosis.
2. *Meiosis.* Meiosis (mī-Ō-sis) is a special form of cell division involved in gamete production. In humans, gametes contain 23 chromosomes, half the amount found in somatic cells. 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.
3. *Spermiogenesis.* Spermatids are small, 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. As you may recall from Chapter 3, 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. The pattern is illustrated in **Figure 28–6a**. Because daughter cells contain both members of each chromosome pair (for a total of 46 chromosomes), they are called **diploid** (DIP-loyd; *diplo*, double) cells. Meiosis (**Figure 28–6b**) 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** (HAP-loyd; *haplo*, single) cells. The events in the nucleus shown in **Figure 28–6b** are the same for the formation of spermatozoa or oocytes.

As a cell prepares to begin meiosis, DNA replication occurs within the nucleus just as it does in a cell preparing for 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*.

Figure 28–6 **Chromosomes in Mitosis and Meiosis.**



At this point, the close similarities between meiosis and mitosis end. In meiosis, the corresponding maternal (inherited from the mother) and paternal (inherited from the father) chromosomes now come together, an event known as **synapsis** (si-NAP-sis). 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** (TET-rad; *tetras*, four) (**Figure 28–6b**). 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. We discuss genetics in Chapter 29.

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. (Compare the two parts of **Figure 28–6**.)

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 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 relatively huge oocyte and three tiny, nonfunctional polar bodies. (If fertilization occurs, the oocyte completes meiosis II, yielding an ovum.) We examine the details of spermatogenesis here (**Figure 28–7**) and will consider oogenesis in a later section.

Spermiogenesis

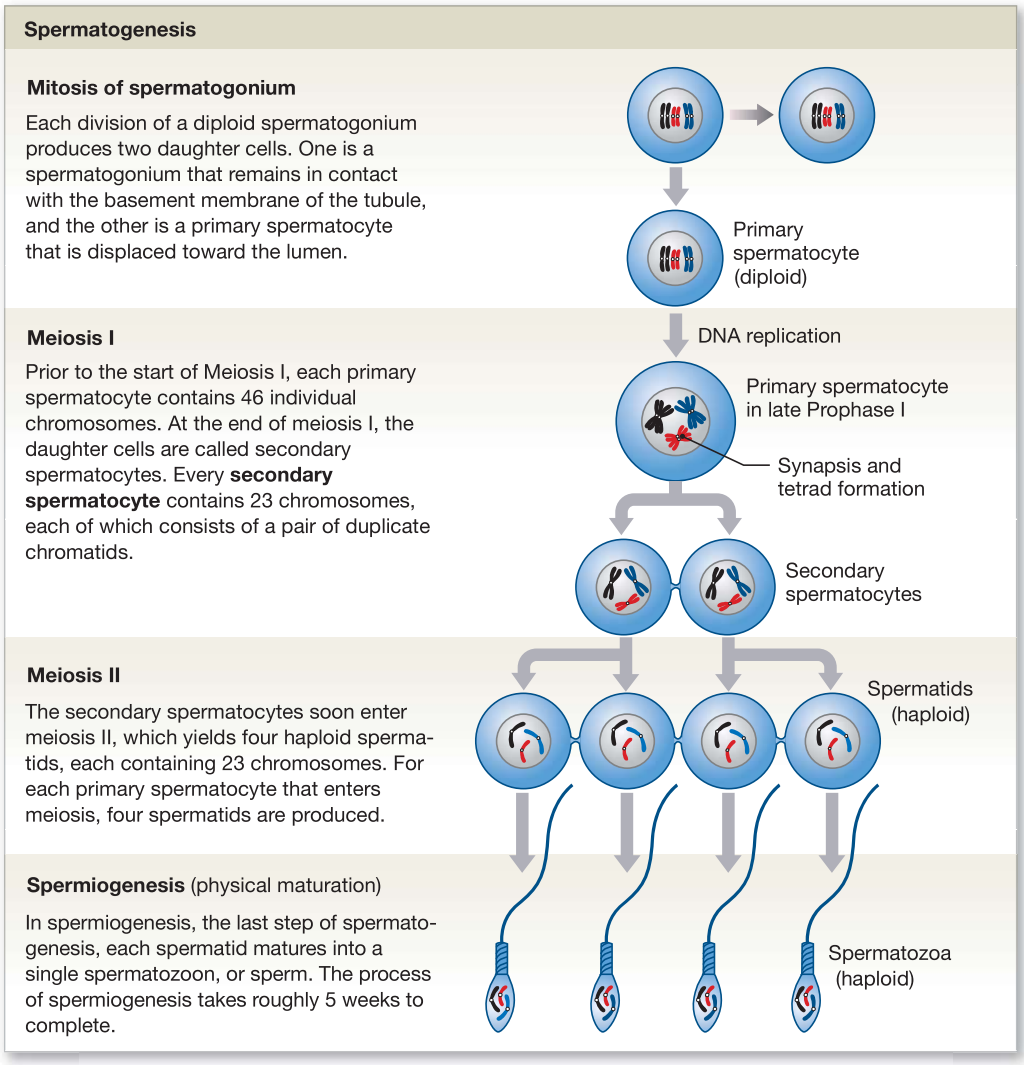
Because cytokinesis (cytoplasmic division) is not completed in meiosis I or meiosis II, the four spermatids initially remain interconnected by bridges of cytoplasm. These connections assist in the transfer of nutrients and hormones between the cells, helping ensure that the cells develop in synchrony. The bridges are not broken until the last stages of physical maturation.

In **spermiogenesis,** the last step of spermatogenesis, each spermatid matures into a single spermatozoon, or *sperm* (**Figure 28–7**). Developing spermatocytes undergoing meiosis, and spermatids undergoing spermiogenesis, are not free in the seminiferous tubules. Instead, they are surrounded by the cytoplasm of the nurse cells. As spermiogenesis proceeds, the spermatids gradually develop into mature spermatozoa. At *spermiation*, a spermatozoon loses its attachment to the nurse cell and enters the lumen of the seminiferous tubule. The entire process, from spermatogonial division to spermiation, takes about nine weeks.

Nurse Cells. Nurse 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:

1. *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. ↩ p. 455 Nurse cells are joined by tight junctions, forming a layer that divides the seminiferous tubule into an outer basal compartment and an inner luminal compartment. The *basal compartment* contains the spermatogonia, and meiosis and spermiogenesis occur in the *luminal compartment* (**Figure 28–5d**). Transport across the nurse cells is tightly regulated, so conditions in the luminal compartment remain very stable. The fluid in the lumen of a seminiferous tubule is produced by the nurse cells, which also regulate the fluid's composition. This fluid is very different from the surrounding interstitial fluid; it is high in androgens, estrogens, potassium, and amino acids. The blood–testis barrier is essential to preserving the differences between the tubular fluid and the interstitial fluid. In addition, this barrier prevents immune system cells from detecting and attacking the developing spermatozoa. The plasma membranes of spermatozoa contain sperm-specific antigens not found in somatic cell membranes, so they might be identified as "foreign."
2. *Support of Mitosis and Meiosis.* Circulating follicle-stimulating hormone (FSH) and testosterone stimulate nurse cells. These stimulated nurse cells then promote the division of spermatogonia and the meiotic divisions of spermatocytes.
3. *Support of Spermiogenesis.* Spermiogenesis requires the presence of nurse cells. These cells surround and enfold the spermatids, providing nutrients and chemical stimuli that promote their development. Nurse cells also phagocytize cytoplasm that is shed by spermatids as they develop into spermatozoa.

Figure 28–7 Spermatogenesis. The events depicted occur in the seminiferous tubules. The fates of three representative chromosome pairs are shown; for clarity, maternal and paternal chromatids are not identified.

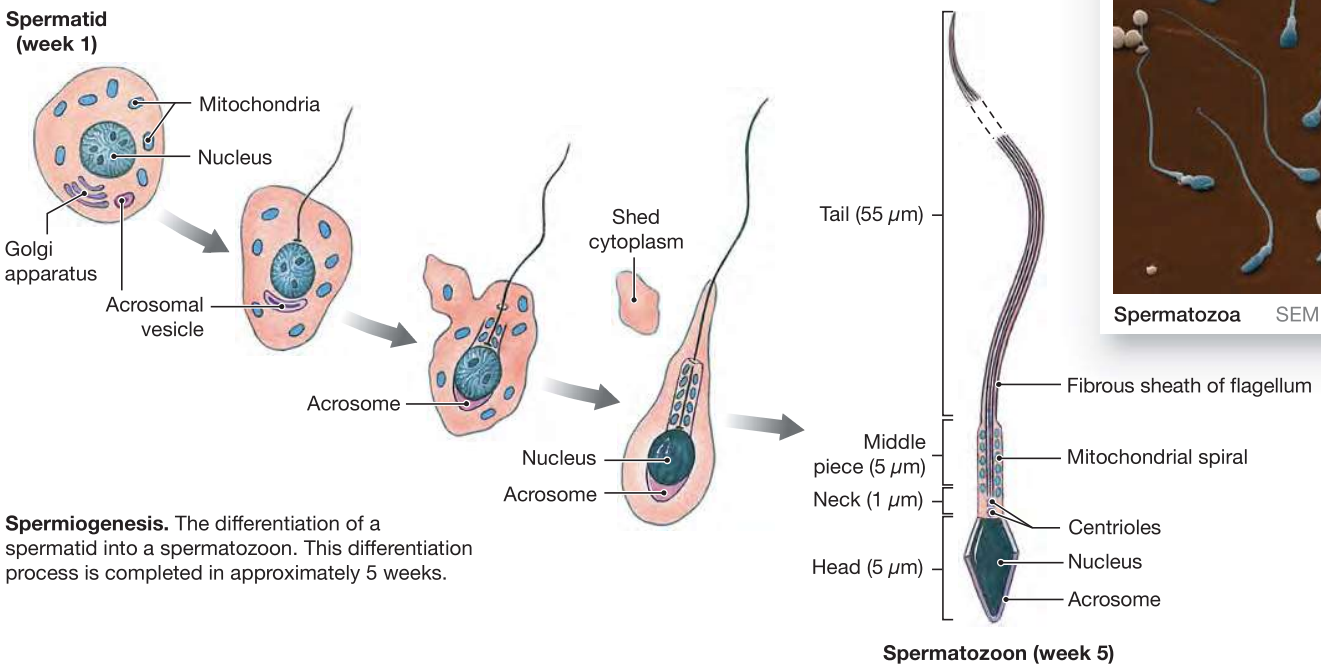


4. *Secretion of Inhibin.* Nurse cells secrete the peptide hormone *inhibin* (in-HIB-in) in response to factors released by developing spermatozoa. Inhibin depresses the pituitary production of FSH, and perhaps the hypothalamic secretion of gonadotropin-releasing hormone (GnRH). The faster the rate of sperm production, the more inhibin is secreted. By regulating FSH and GnRH secretion, nurse cells provide feedback control of spermatogenesis.
5. *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. FSH stimulates the production of ABP.
6. *Secretion of Müllerian-Inhibiting Factor.* In the developing testes, nurse cells secrete *Müllerian-inhibiting factor (MIF)*. This hormone causes regression of the fetal *Müllerian (paramesonephric) ducts*, passageways that form the uterine tubes and the uterus in females. In males, inadequate MIF production during fetal development causes retention of these ducts and the failure of the testes to descend into the scrotum.

The Anatomy of a Spermatozoon

Each spermatozoon has four distinct regions: head, neck, middle piece, and tail (**Figure 28–8**). The **head** is a flattened ellipse containing a nucleus with densely packed chromosomes. At the tip of the head is the **acrosome** (ak-rō-SŌM), a cap-like com-

Figure 28–8 Spermiogenesis and Spermatozoon Structure ATLAS: Plate 60a



Spermiogenesis. The differentiation of a spermatid into a spermatozoon. This differentiation process is completed in approximately 5 weeks.

partment 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 acrosome 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. Whereas cilia beat in a predictable, wavelike fashion, the flagellum of a spermatozoon has a whiplike, corkscrew motion.

Unlike other, less specialized cells, a mature spermatozoon lacks an endoplasmic reticulum, a Golgi apparatus, lysosomes, peroxisomes, inclusions, and many other organelles. 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 a spermatozoon lacks glycogen or other energy reserves, it must absorb nutrients (primarily fructose) from the surrounding fluid.

The Male Reproductive Tract

The testes produce physically mature spermatozoa that are not capable 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.

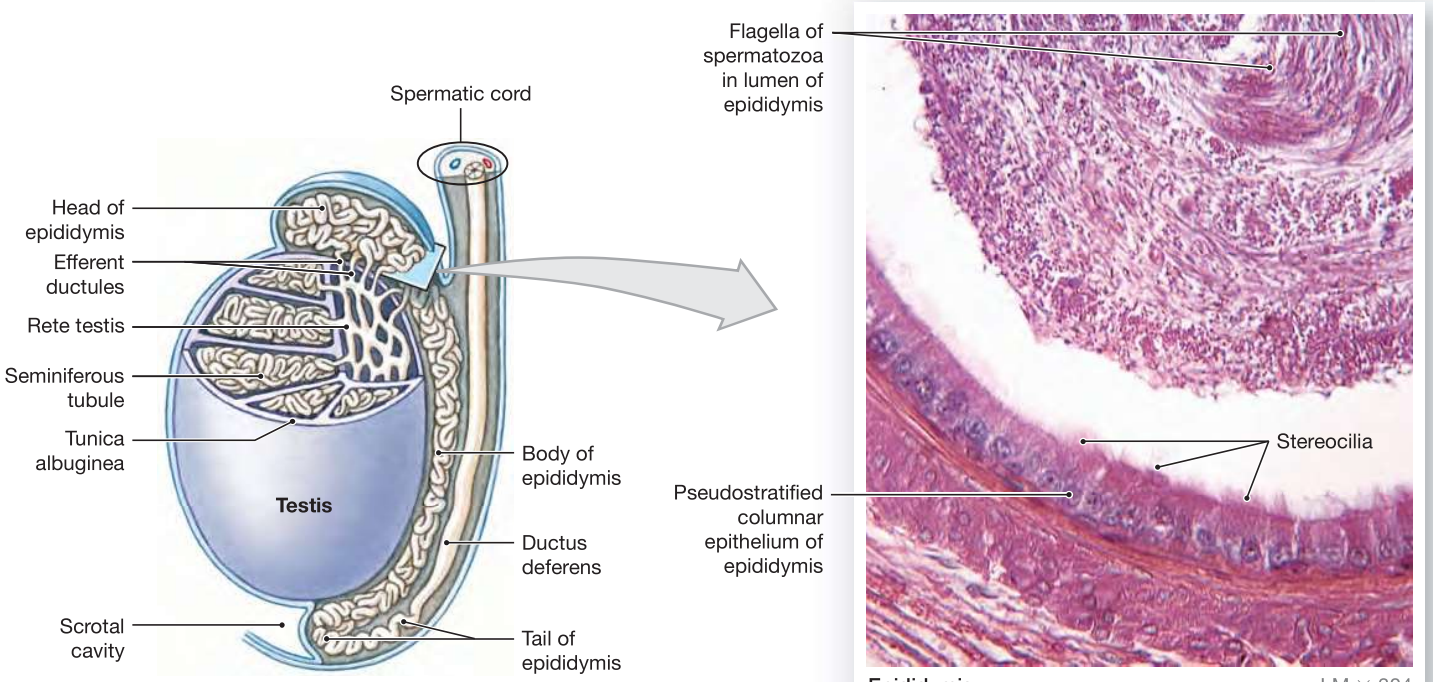
The Epididymis

Late in their development, spermatozoa detach from the nurse 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 (**Figure 28–4a**). The **epididymis** (ep-i-DID-i-mis; *epi*, on + *didymos*, twin), the start of the male reproductive tract, is a coiled tube bound to the posterior border of each testis.

The epididymides (ep-i-DID-i-mi-dēz) can be felt through the skin of the scrotum. A tubule almost 7 m (23 ft) long, the epididymis is coiled and twisted so it takes up very little space. It has a head, a body, and a tail (**Figure 28–9a**). 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 re-curves and ascends to its connection with the ductus deferens. Spermatozoa are stored primarily within the tail of the epididymis.

Figure 28–9 The Epididymis. ATLAS: Plate 60a



a A diagrammatic view of the head, body, and tail of an epididymis

b Epithelial features, especially the elongate stereocilia characteristic of the epididymis

The epididymis has three functions:

1. *It monitors and adjusts the composition of the fluid produced by the seminiferous tubules.* The pseudostratified columnar epithelial lining of the epididymis has distinctive stereocilia (**Figure 28–9b**). These stereocilia increase the surface area available for absorption from, and secretion into, the fluid in the tubule.
2. *It acts as a recycling center for damaged spermatozoa.* Cellular debris and damaged spermatozoa are absorbed in the epididymis. The products of enzymatic breakdown are released into the surrounding interstitial fluids for pickup by the epididymal blood vessels.
3. *It stores and protects spermatozoa and facilitates their functional maturation.* A spermatozoon passes through the epididymis in about two weeks and completes its functional maturation at that time. Over this time, spermatozoa exist in a sheltered environment that is precisely regulated by the surrounding epithelial cells. Spermatozoa leaving the epididymis are mature, but 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 glands, 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.

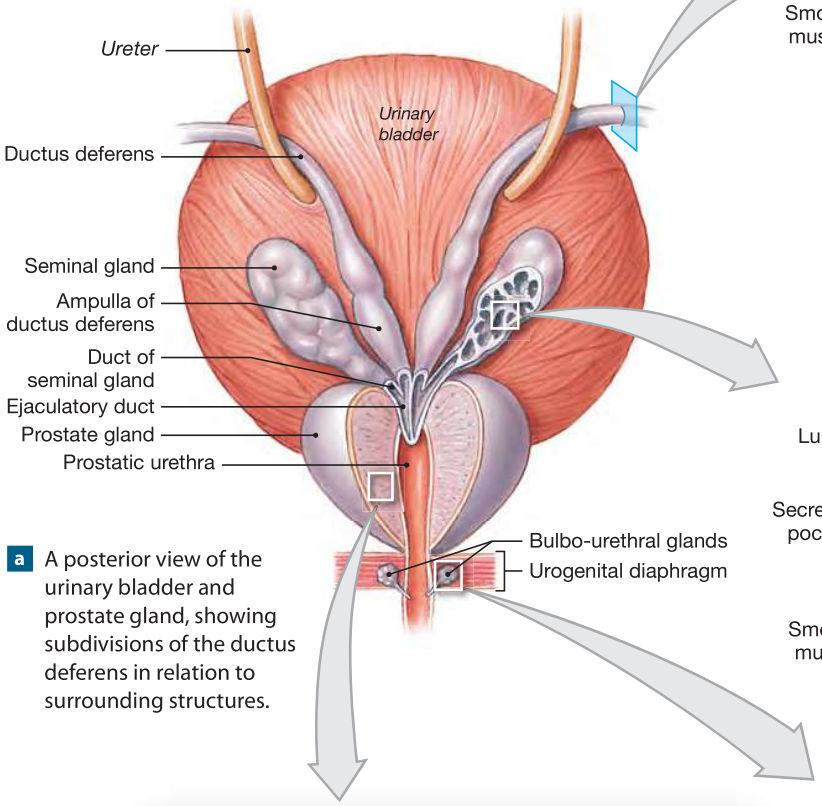
Transport along the epididymis involves a combination of fluid movement and peristaltic contractions of smooth muscle in the epididymis. After passing along the tail of the epididymis, the spermatozoa enter the ductus deferens.

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 (**Figure 28–9a**) and, as part of the spermatic cord, ascends through the inguinal canal (**Figure 28–3**). 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 (**Figure 28–1**). Just before the ductus deferens reaches the prostate gland and seminal glands, its lumen enlarges. This expanded portion is known as the **ampulla** (am-PUL-luh) of the ductus deferens (**Figure 28–10a**).

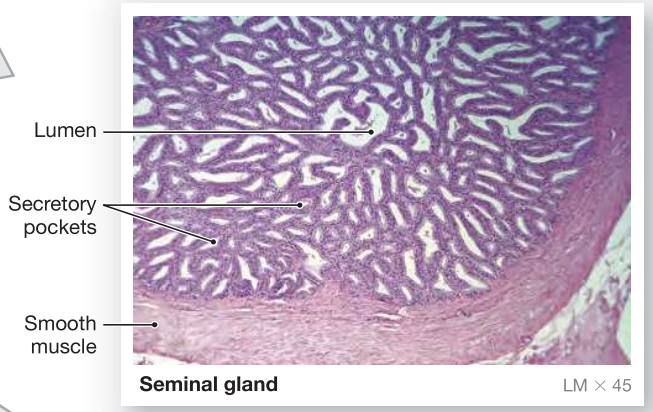
The wall of the ductus deferens contains a thick layer of smooth muscle (**Figure 28–10b**). Peristaltic contractions in this layer propel spermatozoa and fluid along the duct, which

Figure 28–10 The Ductus Deferens and Accessory Glands.



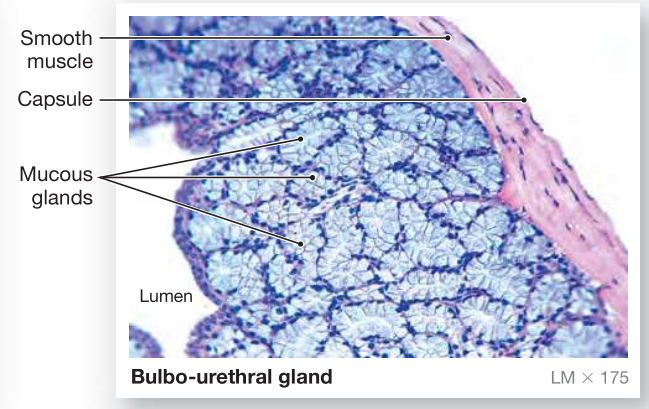
a A posterior view of the urinary bladder and prostate gland, showing subdivisions of the ductus deferens in relation to surrounding structures.

b Light micrograph showing the thick layers of smooth muscle in the wall of the ductus deferens.



c Histology of the seminal glands. These organs produce most of the volume of seminal fluid.

d Histological detail of the glands of the prostate. The tissue between the individual glandular units consists largely of smooth muscle. Contractions of this muscle tissue help move the secretions into the ejaculatory duct and urethra.



e Histology of the bulbo-urethral glands, which secrete a thick mucus into the spongy urethra.

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 temporary state of inactivity with low metabolic rates.

The junction of the ampulla with the duct of the seminal gland 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 (**Figures 28–1** and **28–10a**).

The Urethra

In males, the **urethra** extends 18–20 cm (7–8 in.) from the urinary bladder to the tip of the penis (**Figure 28–1**). It is divided into *prostatic*, *membranous*, and *spongy* regions. The male urethra is a passageway used by both the urinary and reproductive systems.

The Accessory Glands

The fluids secreted 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 glands*, the *prostate gland*, and the *bulbo-urethral 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 Glands (Seminal Vesicles)

The ductus deferens on each side ends at the junction between the ampulla and the duct that drains the seminal gland (**Figure 28–10a**). The **seminal glands,** also called 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 gland 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 glands are extremely active secretory glands with an epithelial lining that contains extensive folds (**Figure 28–10c**). The seminal glands secrete about 60 percent of the volume of semen. Although the glandular 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 glands 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 semen clot within the vagina. The secretions of the seminal glands 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 glands, previously inactive but functional spermatozoa undergo the first step in capacitation and begin beating their flagella, becoming highly motile.

The secretions of the seminal glands are discharged into the ejaculatory duct at *emission*, when peristaltic contractions are under way in the ductus deferens, seminal glands, 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 (**Figure 28–10a**). The glandular tissue of the prostate (**Figure 28–10d**) consists of a cluster of 30–50 compound tubuloalveolar glands. ↩ p. 120 These glands are surrounded by and wrapped in a thick blanket of smooth muscle fibers.

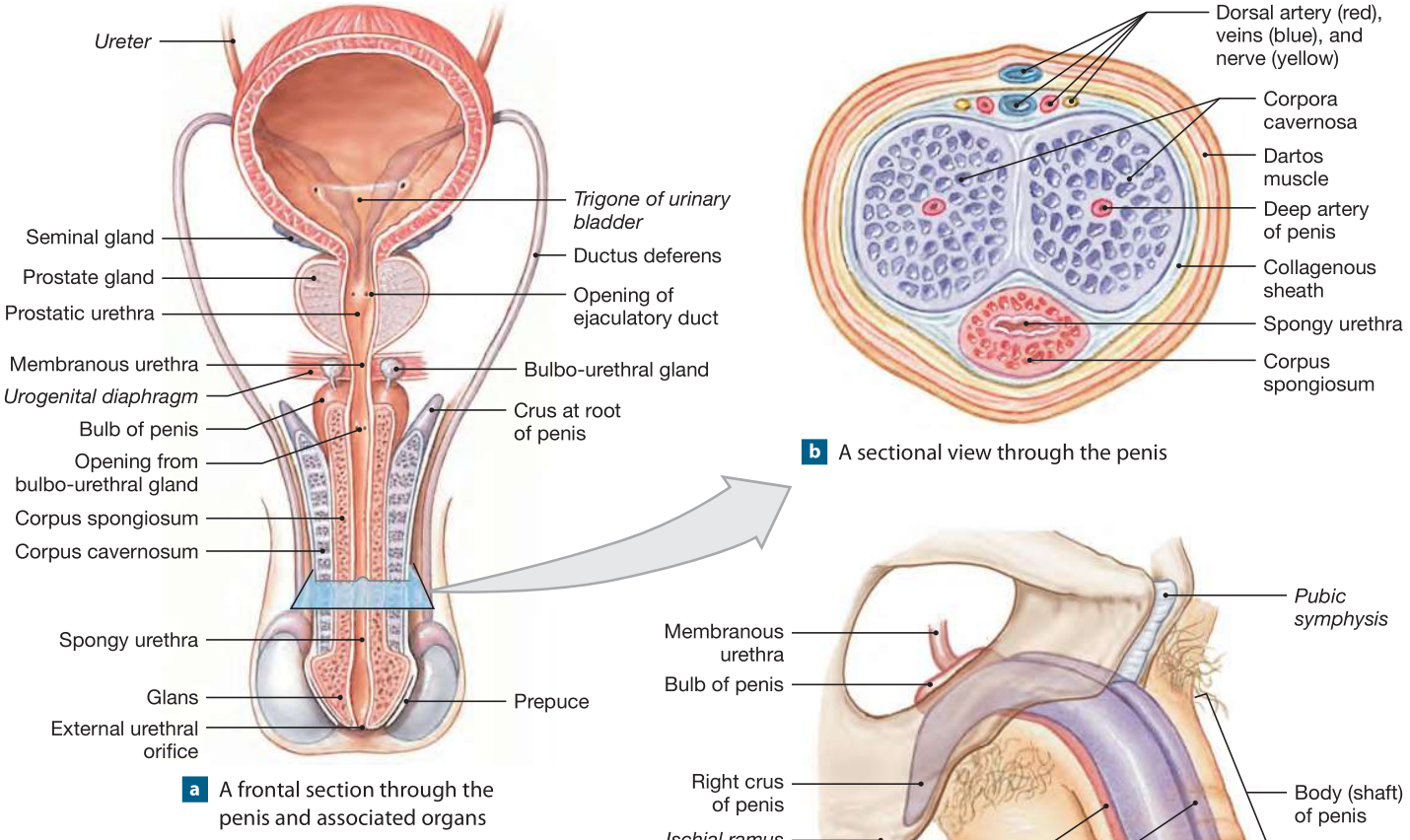
The prostate gland produces **prostatic fluid,** a slightly acidic solution that makes up 20–30 percent of the volume of semen. In addition to several other compounds of uncertain significance, prostatic secretions contain **seminalplasmin** (sem-i-nal-PLAZ-min), a protein with antibiotic properties 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** (pros-ta-TĪ-tis), 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. Symptoms can resemble those of prostate cancer. Individuals with prostatitis may complain of pain in the lower back, perineum, or rectum. In some cases, the symptoms are accompanied by painful urination and the discharge of mucus from the external urethral orifice. Antibiotic therapy is effective in treating most cases caused by bacterial infection.

The Bulbo-urethral Glands

The paired **bulbo-urethral glands,** or *Cowper's glands*, are located at the base of the penis, covered by the fascia of the urogenital diaphragm (**Figures 28–10a** and **28–11a**). The bulbo-urethral glands are round, with diameters nearly 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 bulbo-urethral glands are compound tubular mucous glands (**Figure 28–10e**) that secrete 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.

Figure 28–11 The Penis. ATLAS: Plate 60b



Semen

A typical ejaculation releases 2–5 mL of semen. An abnormally low volume may indicate problems with the prostate gland or seminal glands. 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:

- *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. Normal sperm will be actively swimming.
- *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 glands (60 percent), the prostate gland (30 percent), the nurse cells and epididymis (5 percent), and the bulbo-urethral glands (less than 5 percent).
- *Enzymes.* Several important enzymes are in seminal fluid, including (1) a protease that may help dissolve mucus in the vagina; (2) seminalplasmin, a 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.

A complete chemical analysis of semen appears in the Appendix.

The External Genitalia

The male external genitalia consist of the scrotum and penis. The structure of the scrotum has already been described (p. 1035). The **penis** is a tubular organ through which the distal portion of the urethra passes (**Figure 28–11a**). It conducts urine to the exterior and introduces semen into the female's vagina during sexual intercourse. The penis is divided into three main regions: the root, the body, and the glans (**Figure 28–11c**). 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** (PRĒ-poos), 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** (prē-PŪ-shē-al) **glands** in the skin of the neck and the inner surface of the prepuce secrete a waxy material known as **smegma** (SMEG-ma). Unfortunately, smegma can be an excellent nutrient source for bacteria. Mild inflammation and infections in this area are common, especially if the area is not washed thoroughly and frequently. One way to avoid such problems is **circumcision** (ser-kum-SIZH-un), the surgical removal of the prepuce. In Western societies (especially the United States), this procedure is generally performed shortly after birth. Circumcision lowers the risks of developing urinary tract infections, HIV infection, and penile cancer. Because it is a surgical procedure with risk of bleeding, infection, and other complications, the practice remains controversial.

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** (**Figure 28–11b**). 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 parasympathetic innervation of the penile arteries involves neurons that release nitric oxide at their synaptic terminals. The smooth muscles in the arterial walls relax when nitric oxide is released, at which time the vessels dilate, blood flow increases, the vascular channels become engorged with blood, and **erection** of the penis occurs. The flaccid (nonerect) penis hangs inferior to the pubic symphysis and anterior to the scrotum, but during erection the penis stiffens and elevates to an upright position.

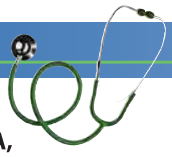
The anterior surface of the flaccid penis covers two cylindrical masses of erectile tissue: the **corpora cavernosa** (KOR-por-a ka-ver-NŌ-suh; singular, *corpus cavernosum*). The two are separated by a thin septum and encircled by a dense collagenous sheath (**Figure 28–11b**). The corpora cavernosa diverge at their bases, forming the **crura** (*crura*, legs; singular, *crus*) of the penis (**Figure 28–11a**). 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, or deep artery of the penis (**Figure 28–11b**).

The relatively slender **corpus spongiosum** (spon-jē-Ō-sum) surrounds the penile urethra (**Figure 28–11a,b**). 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

The hormonal interactions that regulate male reproductive function are diagrammed in **Spotlight Figure 28–12**. The major

Clinical Note

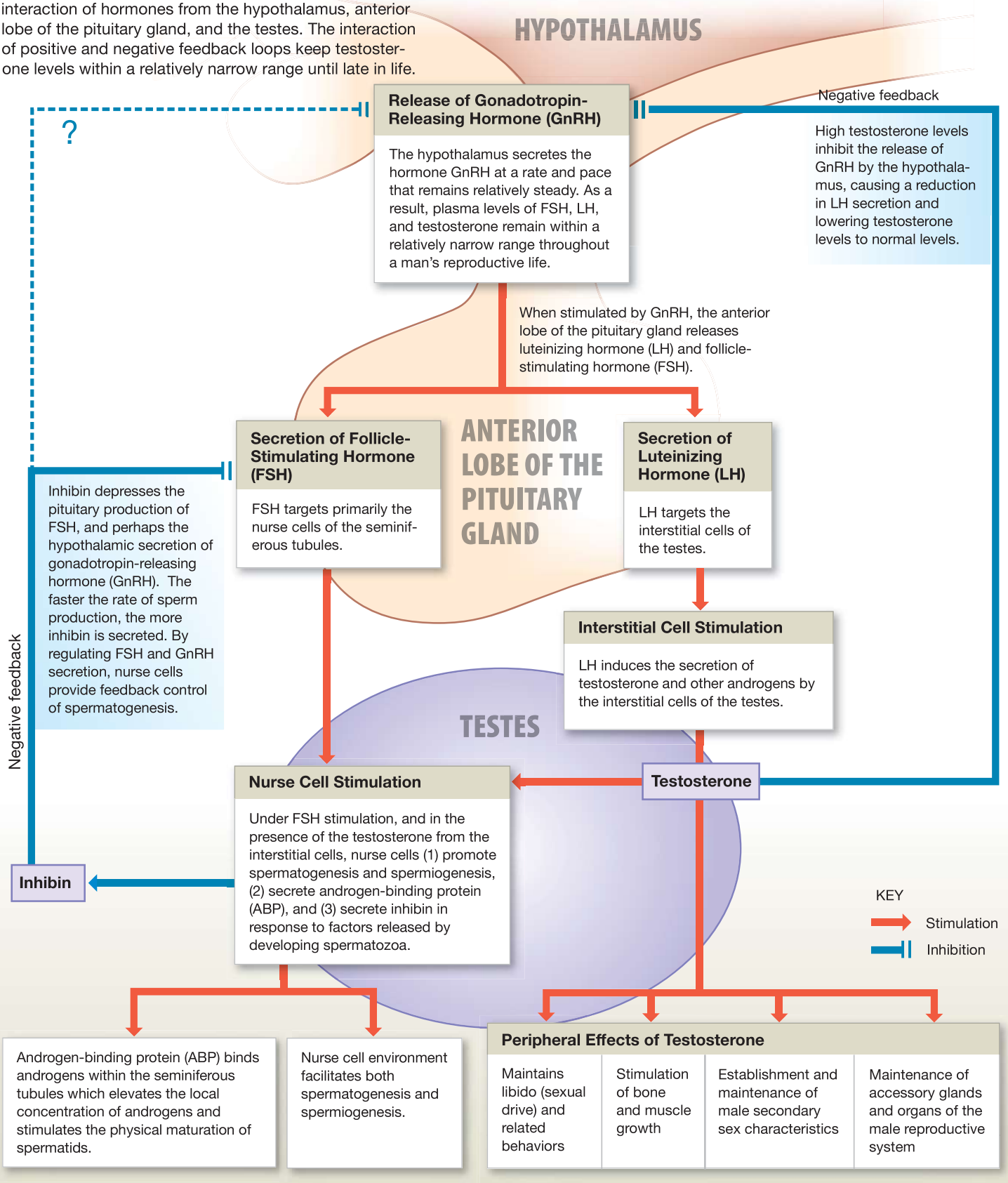


Dehydroepiandrosterone (DHEA) *Dehydroepiandrosterone*, or **DHEA,** is the primary androgen secreted by the zona reticularis of the adrenal cortex. ↩ p. 618 As noted in Chapter 18, these androgens, which are secreted in small amounts, are converted to testosterone (or estrogens) by other tissues. The significance of this small adrenal androgen secretion in both sexes remains unclear, but DHEA is being promoted as a wonder drug for increasing vitality, strength, and muscle mass. Food supplements prepared from wild Mexican yams are now being advertised as containing "DHEA precursors." These claims are false; the compounds contained in these supplements have no effect on circulating DHEA levels. The current recommendations are that DHEA use be restricted to controlled, supervised clinical trials, and that no one under age 40 use the drug. The effects of long-term high doses of DHEA remain largely unknown; however, recall from Chapter 18 that the long-term effects of androgen abuse can be quite serious. ↩ p. 629 High levels of DHEA in women have been linked to an increased risk of ovarian cancer as well as to masculinization, due to the conversion of DHEA to testosterone. The IOC (International Olympic Committee), NCAA, and NFL have banned the use of DHEA for muscle enhancement; and it is detected by urinalysis.

Spotlight

Figure 28–12
Regulation of Male Reproduction

Male reproductive function is regulated by the complex interaction of hormones from the hypothalamus, anterior lobe of the pituitary gland, and the testes. The interaction of positive and negative feedback loops keep testosterone levels within a relatively narrow range until late in life.



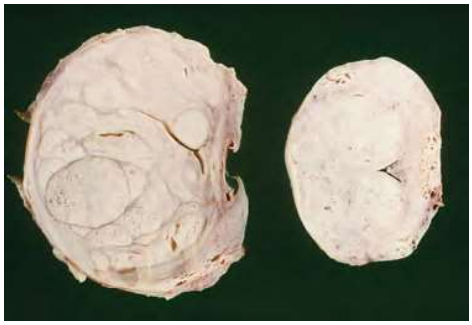
Clinical Note

Prostatic Hypertrophy and Prostate Cancer

Get early screening

Enlargement of the prostate gland, or **benign prostatic hypertrophy,** typically occurs spontaneously in men over age 50. The increase in size happens as testosterone production by the interstitial cells decreases. For unknown reasons, small masses called *prostatic concretions* may form within the glands. At the same time, the interstitial cells begin releasing small quantities of estrogens into the bloodstream. The combination of lower testosterone levels and the presence of estrogens probably stimulates prostatic growth. In severe cases, prostatic swelling constricts and blocks the urethra and constricts the rectum. If not corrected, the urinary obstruction can cause permanent kidney damage.[1] Partial surgical removal is the most effective treatment. In the procedure known as a **TURP** (*transurethral prostatectomy)* an instrument pushed along the urethra restores normal function by cutting away the swollen prostatic tissue. Most of the prostate gland remains in place, and no external scars result.

Prostate cancer, a malignancy of the prostate gland, is the second most common cancer and the second most common cause of cancer deaths in males. The American Cancer Society estimates that approximately 217,730 new prostate cancer cases in 2010 will result in about 32,050 deaths. Most patients are elderly. (The average age at diagnosis is 72.) For reasons that are poorly understood, prostate cancer rates for Asian American males are relatively low compared with those of either Caucasian Americans or African Americans. For all age and ethnic groups, the rates of prostate cancer are rising sharply. The reason for the increase is not known. Aggressive diagnosis and treatment of localized prostate cancer in elderly patients is controversial because many of these men have nonmetastatic tumors, and even if untreated are more likely to die of some other disease.



Prostate cancer normally originates in one of the secretory glands. As the cancer progresses, it produces a nodular lump or swelling on the surface of the prostate gland. Palpation of this gland through the rectal wall—a procedure known as a *digital rectal exam* (DRE)—is the easiest diagnostic screening procedure. *Transrectal prostatic ultrasound* (TRUS) is used to obtain more detailed information about the status of the prostate. Blood tests are also used for screening purposes. The most sensitive is a blood test for **prostate-specific antigen (PSA).** Elevated levels of this antigen, normally present in low concentrations, may indicate the presence of prostate cancer. Once prostrate cancer is detected, treatment decisions vary depending on how rapidly PSA levels are rising. Screening with periodic PSA tests is now being recommended for men over age 50.

If cancer is detected before it has spread to other organs, and the patient is elderly or has other serious health problems, "watchful waiting" is an option. In other cases, the usual treatment is localized radiation or surgical removal of the prostate gland. This operation, a **prostatectomy** (pros-ta-TEK-tō-mē), can be effective in controlling the condition. Both surgery and radiation can have undesirable side effects, including urinary incontinence and loss of sexual function. Modified treatment procedures along with medications such as Viagra can reduce the risks and maintain normal sexual function in perhaps three out of four patients.

The prognosis is much worse for prostate cancer diagnosed after metastasis has occurred, because metastasis rapidly involves the lymphatic system, lungs, bone marrow, liver, or adrenal glands. Survival rates at this stage are relatively low. Treatments for metastasized prostate cancer include widespread irradiation, hormonal manipulation, lymph node removal, and aggressive chemotherapy. Because the cancer cells are stimulated by testosterone, treatment may involve castration or administering hormones that depress GnRH or LH production. There are three treatment options: (1) an estrogen, typically diethylstilbestrol (DES); (2) drugs that mimic GnRH, which when given in high doses produce a surge in LH production followed by a sharp decline to very low levels (presumably as the endocrine cells adapt to the excessive stimulation); and (3) drugs that block the binding of androgens to the receptors on target cells (including the drugs flutamide and bicalutamide), which prevent the stimulation of cancer cells by testosterone. The death rate for prostate cancer may be falling in some countries, perhaps due to earlier detection and more effective treatment.

[1]Symptoms are improved by drug therapy with alpha-blockers that relax smooth muscle, or with *finasteride*, which inhibits production of DHT, an active derivative of testosterone.

reproductive hormones were introduced in Chapter 18. ↩ p. 626 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). Unlike the situation in women, which we will consider later in the chapter, the GnRH pulse frequency in adult males remains relatively steady from hour to hour, day to day, and year to year. As a result, plasma levels of FSH, LH, and testosterone remain within a relatively narrow range until relatively late in life (see p. 1069).

Testosterone plays a major role in maintaining male sexual function (**Spotlight Figure 28–12**). 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 about two-thirds of the circulating testosterone, and (2) the albumins, which bind the remaining one-third. Testosterone diffuses across the plasma 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 **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. Dihydrotestosterone can also enter peripheral cells and bind to the same hormone receptors targeted by testosterone. In addition, some tissues (notably those of the external genitalia) respond to DHT rather than to testosterone, and other tissues (including the prostate gland) are more sensitive to DHT than to testosterone.

Testosterone production begins around the seventh week of fetal development and reaches a prenatal peak after six months. Over this period, the secretion of Müllerian-inhibiting factor by developing nurse cells leads to the regression of the Müllerian 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 factors responsible for regulating the fetal production of testosterone are not known.

Testosterone levels are low at birth. Until puberty, background testosterone levels, although still relatively low, are higher in males than in females. Testosterone secretion accelerates markedly at puberty, initiating sexual maturation and the appearance of secondary sex characteristics. In adult males, negative feedback controls the level of testosterone production. Above-normal testosterone levels inhibit the release of GnRH by the hypothalamus, causing a reduction in LH secretion and lowering testosterone levels (**Spotlight Figure 28–12**).

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. Interstitial cells and nurse cells of the testes secrete the rest. An enzyme called aromatase converts testosterone to estradiol. For unknown reasons, estradiol production increases in older men.

Checkpoint

4. **Name the male reproductive structures.**
5. **On a warm day, would the cremaster muscle be contracted or relaxed? Why?**
6. **What happens when the arteries within the penis dilate?**
7. **What effect would low FSH levels have on sperm production?**
8. **Trace the pathway that a sperm travels from the site of its production to outside the body.**

See the blue Answers tab at the back of the book.

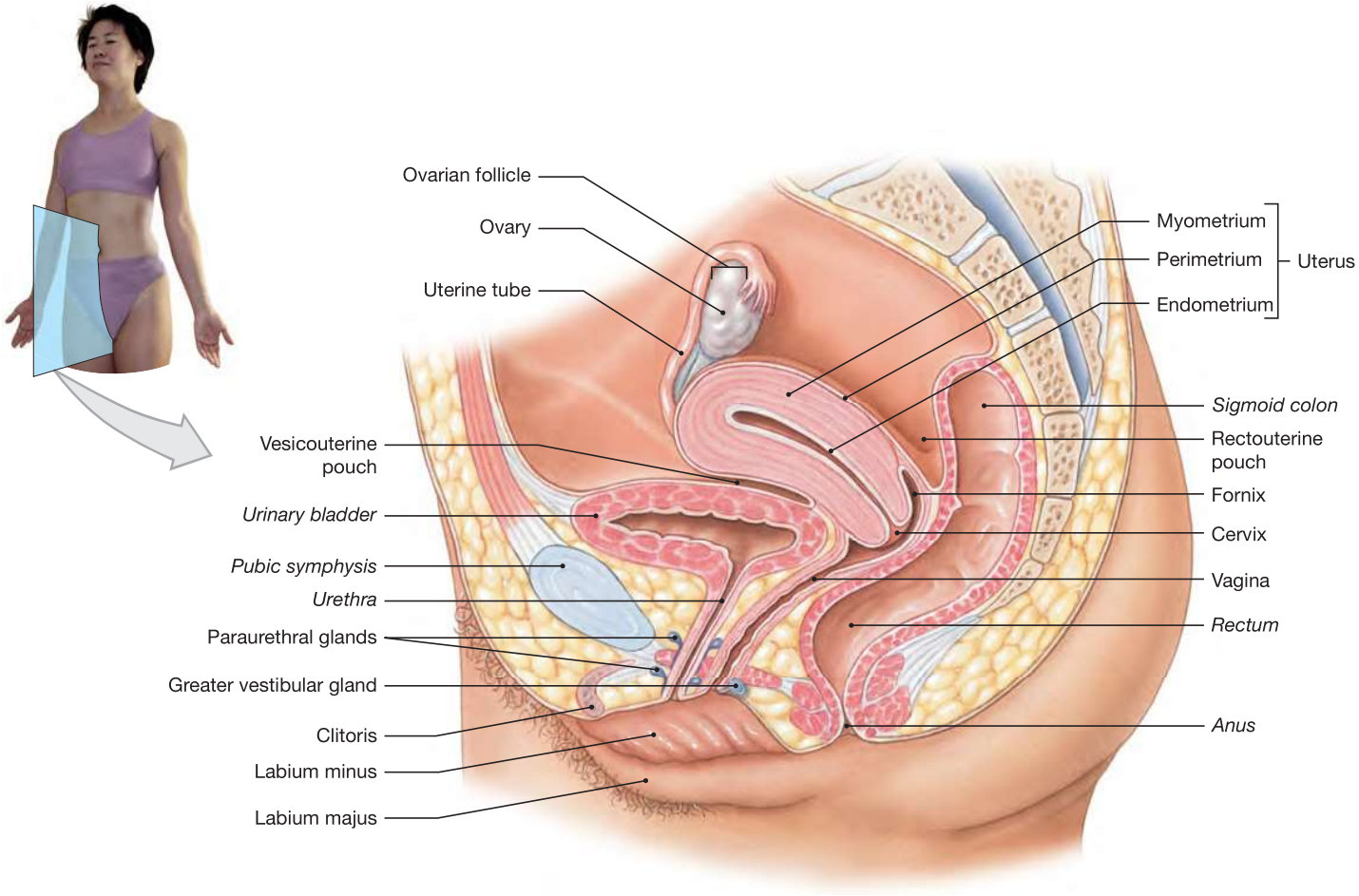
28-3 Oogenesis occurs in the ovaries, and hormones from the pituitary gland and gonads control female reproductive functions

A woman's reproductive system produces sex hormones and functional gametes. It must also be able to protect and support a developing embryo and nourish a newborn infant. The main organs of the female reproductive system are the *ovaries*, the *uterine tubes*, the *uterus*, the *vagina*, and the components of the external genitalia (**Figure 28–13**). 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** (mez-ō-VĀ-rē-um), a thickened fold of mesentery, supports and stabilizes the position of each ovary (**Figure 28–14a**). The broad ligament attaches to the sides and floor of the pelvic cavity, where it becomes continuous with the parietal peritoneum. The broad ligament 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** (rek-tō-Ū-ter-in) **pouch** (**Figure 28–13**). The pocket formed between the uterus and the posterior wall of the bladder is the **vesicouterine** (ves-i-kō-Ū-ter-in) **pouch.** These subdivisions are easily seen in sagittal section.

Several other ligaments assist the broad ligament in supporting and stabilizing 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

Figure 28–13 The Female Reproductive System. A sagittal section of the female reproductive organs. ATLAS: Plate 65



the other ligaments (described in our discussion of the ovaries and uterus) prevent superior–inferior movement.

The Ovaries

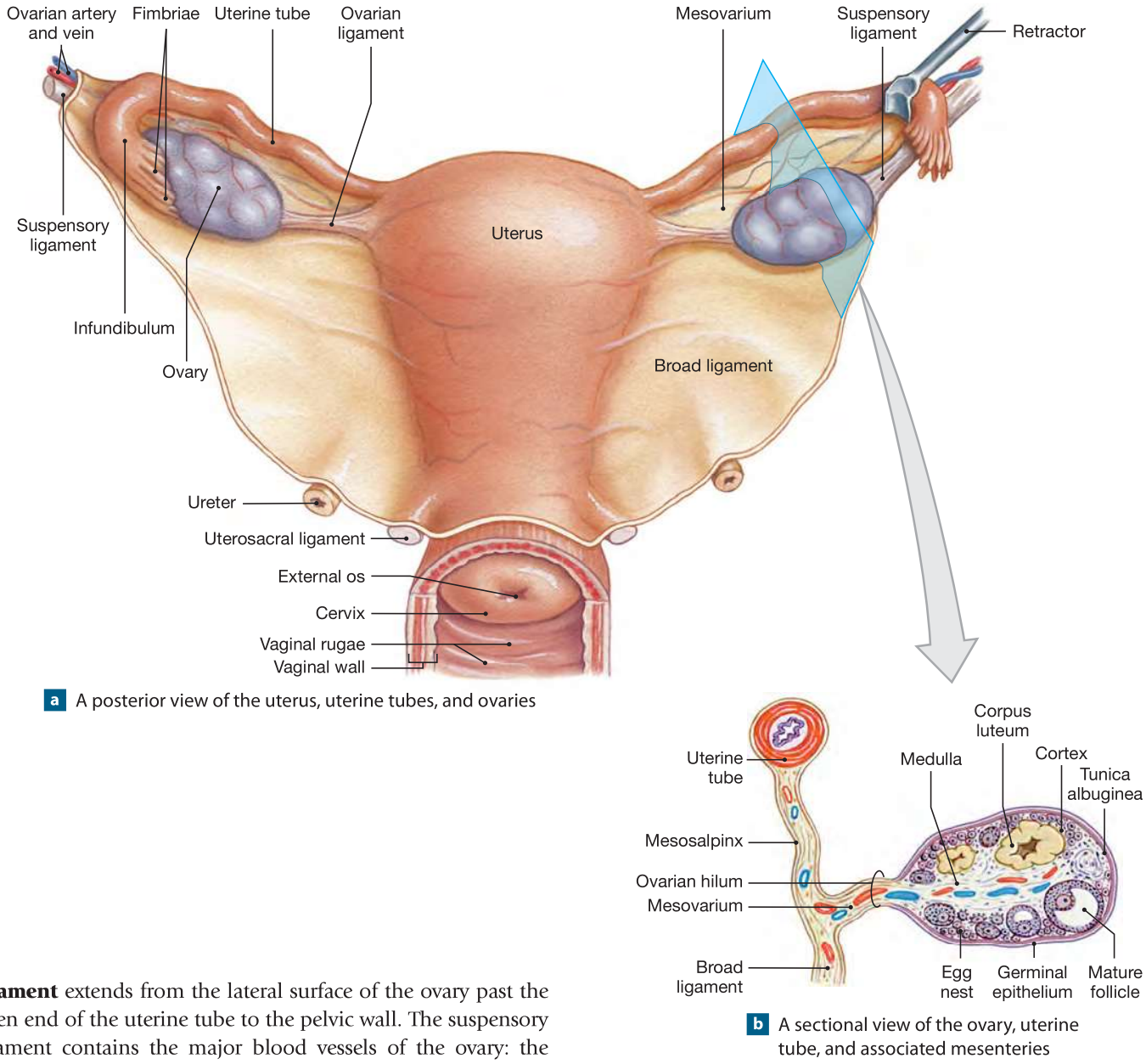
The paired ovaries are small, lumpy, almond-shaped organs near the lateral walls of the pelvic cavity (**Figure 28–14**). The ovaries perform three main functions: (1) production of immature female gametes, or oocytes; (2) secretion of female sex hormones, including estrogens and progestins; and (3) secretion of inhibin, involved in the feedback control of pituitary FSH production.

Each ovary is stabilized by the mesovarium and by a pair of supporting ligaments: the ovarian ligament and the suspensory (infundibulopelvic) ligament (**Figure 28–14a**). The **ovarian ligament** extends from the uterus, near the attachment of the uterine tube, to the medial surface of the ovary. The **suspensory**

Clinical Note

Ovarian Cancer A woman in the United States has a 1-in-72 chance of developing **ovarian cancer** in her lifetime. In 2010, an estimated 21,850 ovarian cancer cases will be diagnosed, and about 13,800 deaths will occur as a result of this condition. Although ovarian cancer is the third most common reproductive cancer among women, it is the most dangerous because it is seldom diagnosed in its early stages. The prognosis is relatively good for cancers that originate in the general ovarian tissues or from abnormal oocytes. These cancers respond well to some combination of chemotherapy, radiation, and surgery. However, 85 percent of ovarian cancers develop from epithelial cells, and sustained remission occurs in only about one-third of these cases.

Figure 28–14 **The Ovaries and Their Relationships to the Uterine Tube and Uterus.** ATLAS: Plate 67



a A posterior view of the uterus, uterine tubes, and ovaries

b A sectional view of the ovary, uterine tube, and associated mesenteries

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 (**Figure 28–14b**).

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** (**Figure 28–14b**). 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.

Oogenesis

Ovum production, or **oogenesis** (ō-ō-JEN-e-sis; *oon*, egg), 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*.

Oogenesis is summarized in **Figure 28–15**. Female reproductive stem cells complete the mitotic production of *primary oocytes* before birth. These cells proceed as far as prophase of meiosis I, and remain in that state until the individual reaches puberty.

Not all primary oocytes produced during fetal development survive until puberty. The ovaries have approximately 2 million *primordial follicles* at birth, each containing a primary oocyte. By puberty, the number has dropped to about 400,000. The rest of the primordial follicles degenerate in a process called **atresia** (a-TRĒ-zē-uh).

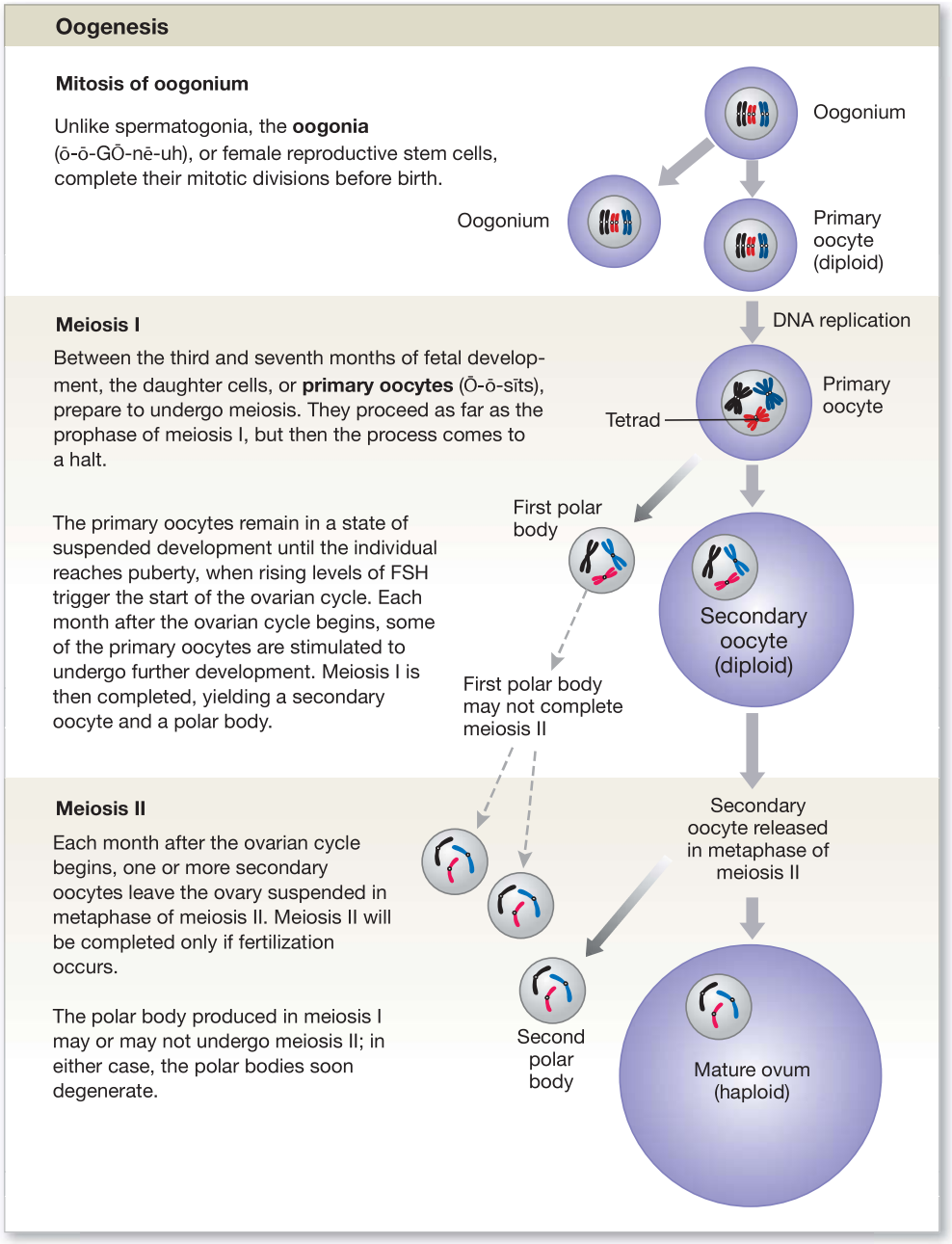
Although the nuclear events in the ovaries during meiosis are the same as those in the testes, the process differs in two important details:

1. The cytoplasm of the primary oocyte is unevenly distributed during the two meiotic divisions. Oogenesis produces one secondary oocyte, which contains most of the original cytoplasm, and two or three **polar bodies,** nonfunctional cells that later disintegrate.
2. 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.

The Ovarian Cycle

Ovarian follicles are specialized structures in the cortex of the ovaries where both oocyte growth and meiosis I occur. 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 are summarized in **Figure 28–16**.

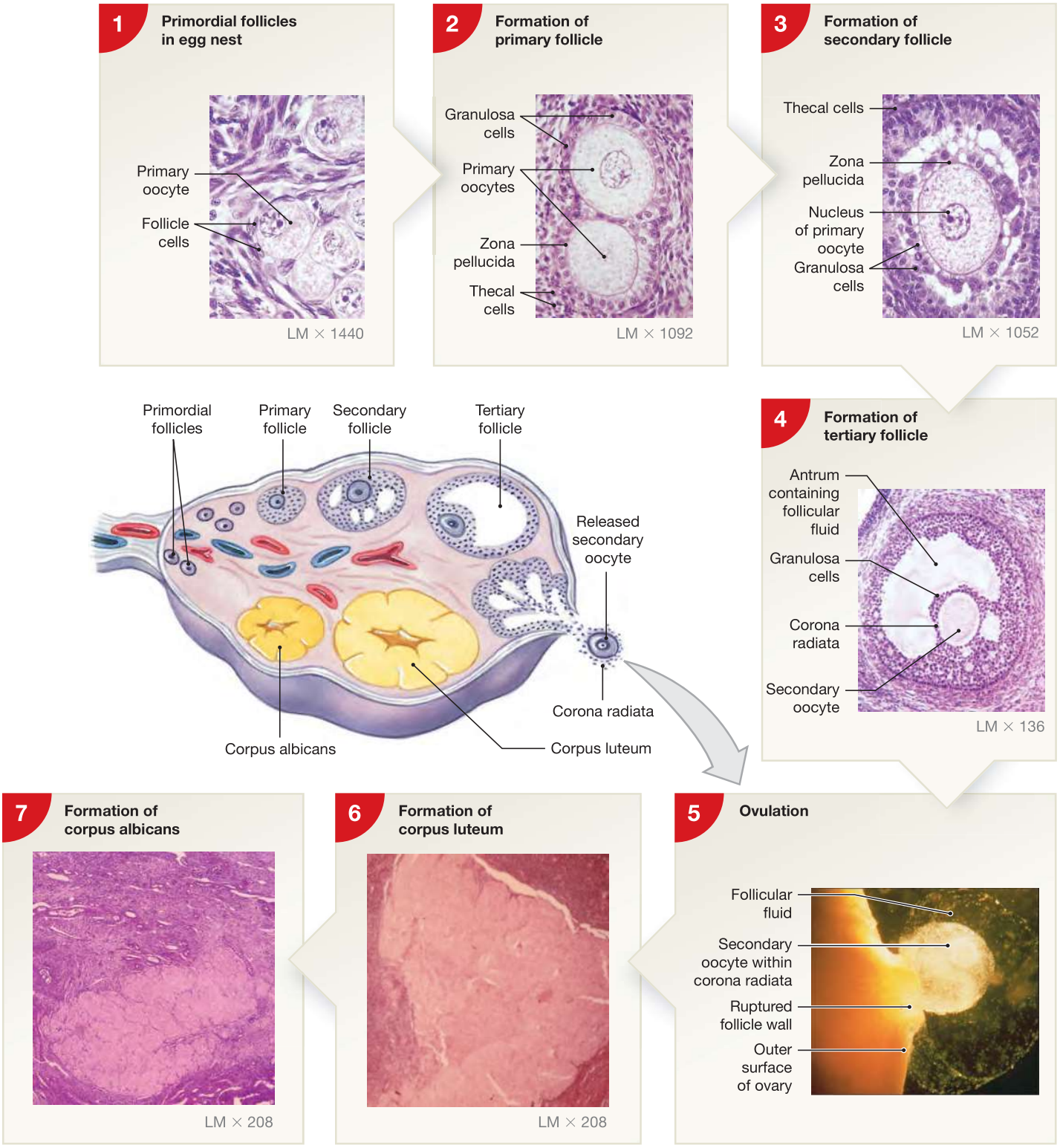
Figure 28–15 Oogenesis. For clarity, maternal and paternal chromatids are not identified.



1 ***Primordial Follicles in Egg Nest.*** Primary oocytes are located in the outer portion of the ovarian cortex, near the tunica albuginea, in clusters called *egg nests*. A single squamous layer of *follicle cells* surrounds each primary oocyte within an egg nest. The primary oocyte and its follicle cells form a **primordial follicle.** Beginning at puberty, primordial follicles are continuously activated to join other follicles already in development. Although the activating mechanism is unknown, local hormones or growth factors within the ovary may be involved. The activated primordial follicle will either mature and be released as a secondary oocyte or degenerate (atresia). This monthly process is known as the **ovarian cycle.**

2 ***The Formation of Primary Follicles.*** The preliminary steps in follicle development are of variable length but may take almost a year to complete. Follicle development begins with the activation of primordial follicles into **primary follicles.** The follicular cells enlarge, divide, and form several layers of

Figure 28–16 The Ovarian Cycle.



cells around the growing primary oocyte. These follicle cells, which become rounded in appearance, are now called **granulosa cells.** Microvilli from the surrounding follicular cells intermingle with microvilli originating at the surface of the oocyte. This glycoprotein-rich region is called the **zona pellucida** (ZŌ-na pe-LOO-sid-uh; *pellucidus,* translucent).

The microvilli increase the surface area available for the transfer of materials from the follicular cells to the growing oocyte. As the granulosa cells enlarge and multiply, adjacent cells in the ovarian stroma form a layer of **thecal cells** (*theca*, a box) around the follicle. Thecal cells and granulosa cells work together to produce sex hormones called *estrogens*.

3 ***The Formation of Secondary Follicles.*** Although many primordial follicles develop into primary follicles, only a few of the primary follicles mature further. This process is apparently under the control of a growth factor produced by the oocyte. The transformation begins as the wall of the follicle thickens and the deeper follicular 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 slowly, the follicle as a whole enlarges rapidly because follicular fluid accumulates.

4 ***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* (GRAF-ē-an) *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** (AN-trum), 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** (kō-RŌ-nuh rā-dē-AH-tuh).

5 ***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 (and the oocyte) attached to the surface of the ovary. The oocyte is then moved into the uterine tube by contact with the fimbriae (**Figure 28–14a**) that extend from its funnel-like opening, or by fluid currents produced by the cilia that line it. Ovulation marks the end of the follicular phase of the ovarian cycle and the start of the luteal phase.

6 ***The Formation 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** (LOO-tē-um; *lutea*, yellow), named for its yellow color. LH stimulates this process.

The cholesterol contained in the corpus luteum is used to manufacture steroid hormones known as **progestins** (prō-JES-tinz), primarily the steroid **progesterone** (prō-JES-ter-ōn). Although the corpus luteum also secretes moderate amounts of estrogens, levels are not as high as they were at ovulation, and progesterone is the main 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.

Tips & Tricks:

Progesterone literally means a steroid (-***one***) that favors (***pro***-) gestation (-***gest***).

7 ***Formation of the Corpus Albicans.*** Degeneration of the corpus luteum begins about 12 days after ovulation (unless fertilization occurs). Progesterone and estrogen levels then fall markedly. Fibroblasts invade the nonfunctional corpus luteum, producing a knot of pale scar tissue called a **corpus albicans** (AL-bi-kanz). 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 secondary oocytes will have been ovulated.

Tips & Tricks

The maturation of an ovum takes several cycles to complete. That is why at any given time, oocytes are in various stages of development within the ovary.

The Uterine Tubes

Each **uterine tube** (*Fallopian tube* or *oviduct*) is a hollow, muscular cylinder measuring roughly 13 cm (5.2 in.) in length (**Figures 28–13** and **28–14**). Each uterine tube is divided into three segments (**Figure 28–17a**):

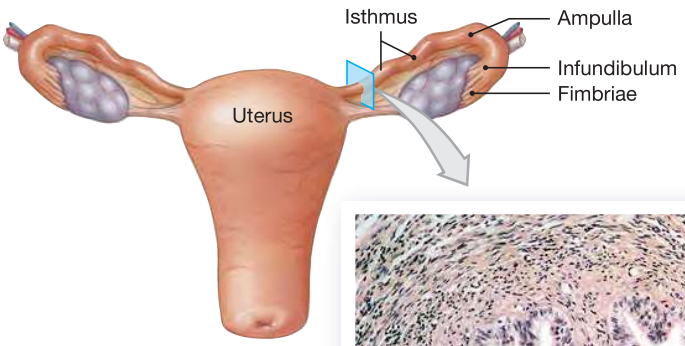
1. *The Infundibulum.* The end closest to the ovary forms an expanded funnel, or **infundibulum**, with numerous finger-like projections that extend into the pelvic cavity. The projections are called **fimbriae** (FIM-brē-ē). Fimbriae drape over the surface of the ovary, but there is no physical connection between the two structures. The inner surfaces of the infundibulum are lined with cilia that beat toward the middle segment of the uterine tube, called the *ampulla*.
2. *The Ampulla.* The **ampulla** is the middle region between the infundibulum and the isthmus. The thickness of its smooth muscle layers gradually increases as the tube approaches the uterus.
3. *The Isthmus.* The ampulla leads to the **isthmus** (IS-mus), a short segment connected to the uterine wall.

Histology of the Uterine Tube

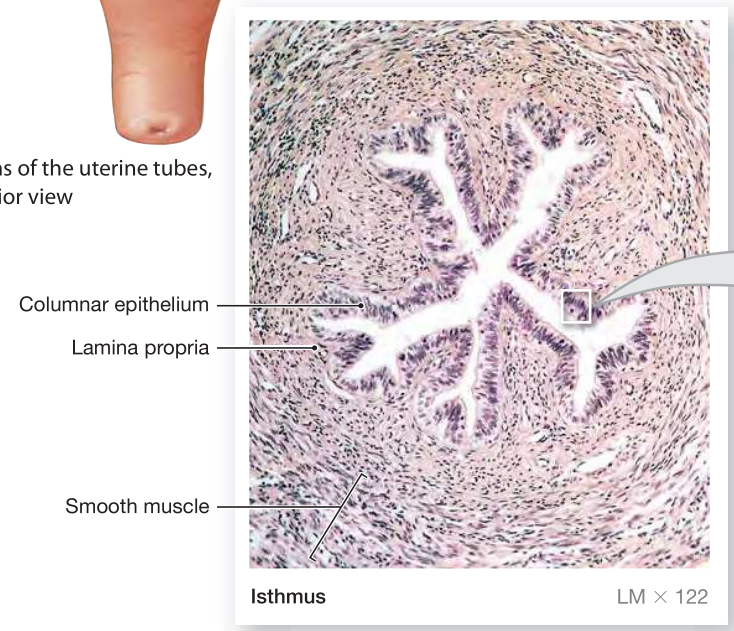
The epithelium lining the uterine tube is composed of ciliated columnar epithelial cells with scattered mucin-secreting cells (**Figure 28–17c**). Concentric layers of smooth muscle surround the mucosa (**Figure 28–17b**). Oocytes are transported by a combination of ciliary movement and peristaltic contractions 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 nourishes both spermatozoa and a developing *pre-embryo* (the cell cluster produced by the initial mitotic divisions following fertilization). Unfertilized oocytes

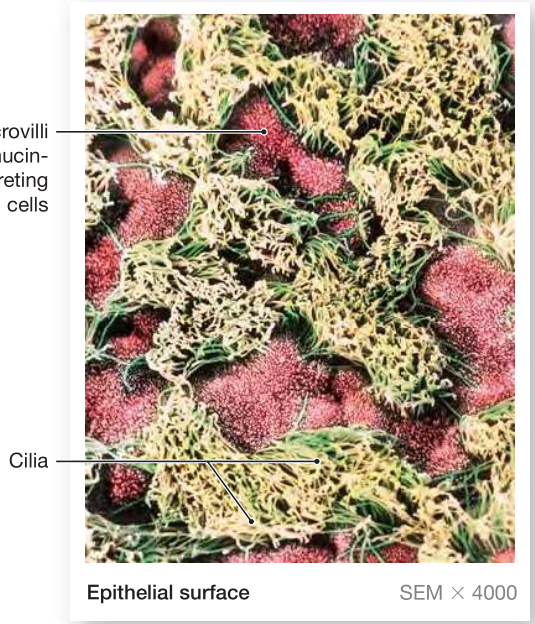
Figure 28–17 The Uterine Tubes.



a Regions of the uterine tubes, posterior view



b A sectional view of the isthmus



c A colorized SEM of the ciliated lining of the uterine tube

degenerate in the terminal portions of the uterine tubes or within the uterus without completing meiosis.

In addition to ciliated cells, the epithelium lining the uterine tubes contains *peg cells* and scattered mucin-secreting cells. The peg cells project into the lumen of the uterine tube, and they secrete a fluid that both completes the capacitation of spermatozoa and supplies nutrients to spermatozoa and the developing pre-embryo.

The Uterus

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 of the muscular uterus are important in ejecting the fetus at birth.

The uterus is a small, pear-shaped organ (**Figure 28–18a**) about 7.5 cm (3 in.) long with a maximum diameter of 5 cm (2 in.). It weighs 50–100 g (1.75–3.5 oz). In its normal position, the uterus bends anteriorly near its base (**Figure 28–13**), a condition known as *anteflexion* (an-tē-FLEK-shun). 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* (re-trō-FLEK-shun). 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 uterus and limit its range of movement (**Figure 28–18b**). The **uterosacral** (ū-te-rō-SĀ-krul) **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 posterior movement of the uterus. The **cardinal** (*lateral*) **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. The muscles and fascia of the pelvic floor provide additional mechanical support.

Internal Anatomy of the Uterus

We can divide the uterus into anatomical regions (**Figure 28–18a**). The uterine **body** 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** (SER-viks) 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 **external os** (*os*, an opening or mouth) of the uterus. The external os leads into the **cervical canal,** a constricted passageway that opens into the **uterine cavity** of the body at the **internal os.**

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 S_3 and S_4 (parasympathetic). Sensory information reaches the central nervous system within the dorsal roots of spinal nerves T_{11} and T_{12}. The most delicate anesthetic procedures used during labor and delivery, known as *segmental blocks*, target only spinal nerves T_{10}–L_1.

The Uterine Wall

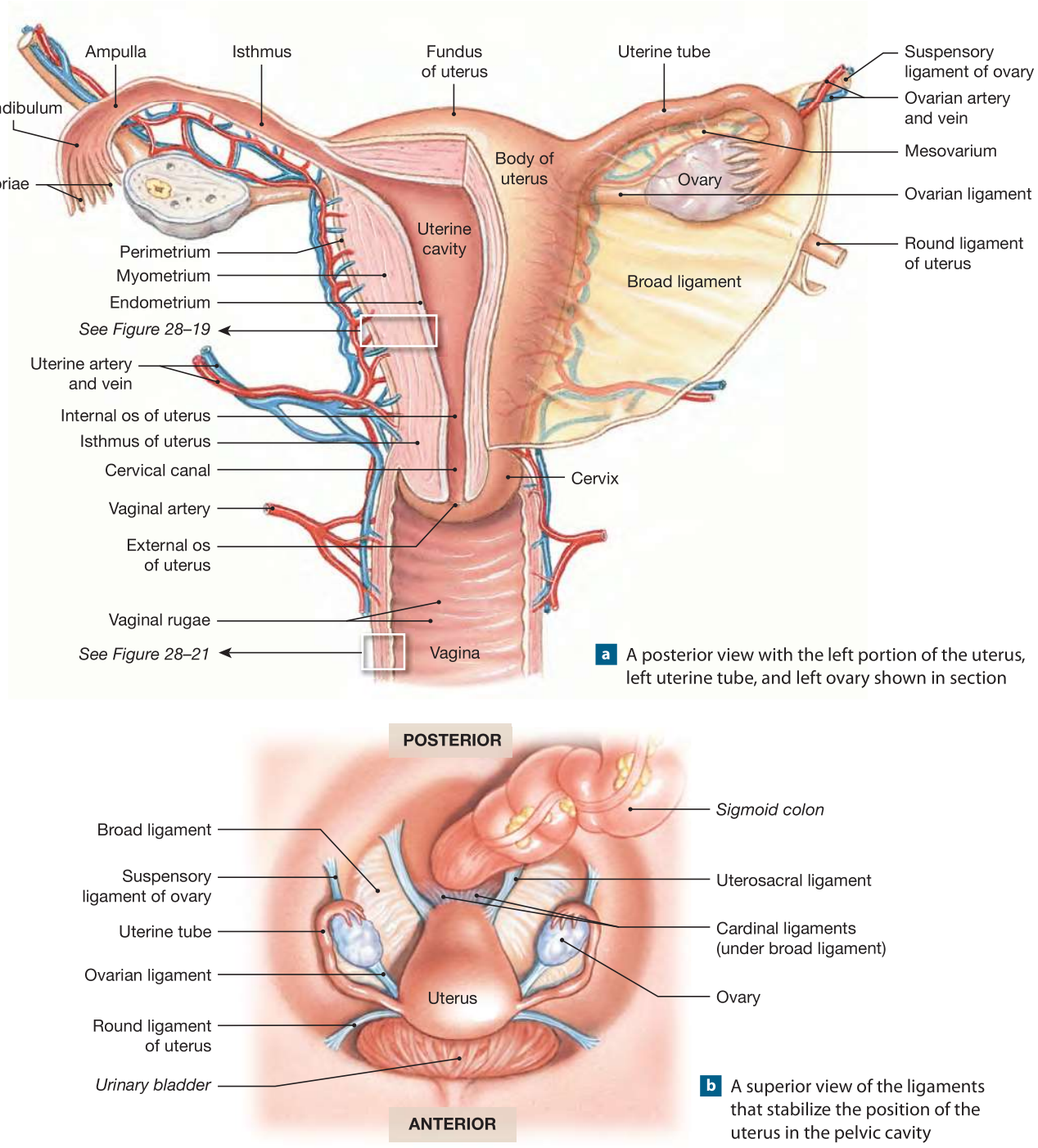
The dimensions of the uterus are highly variable. In women of reproductive age who have not given birth, the uterine wall is about 1.5 cm (0.6 in.) thick. The wall has a thick, outer, muscular **myometrium** (mī-ō-MĒ-trē-um; *myo-*, muscle + *metra*, uterus) and a thin, inner, glandular **endometrium** (en-dō-MĒ-trē-um) (**Figure 28–19**). 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 makes up about 10 percent of 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

Clinical Note

Cervical cancer is the most common cancer of the reproductive system in women ages 15–34. Each year roughly 13,000 U.S. women are diagnosed with invasive cervical cancer, and approximately one-third of them eventually die from the condition. Another 35,000 women are diagnosed with a less aggressive form of cervical cancer. *Gardisil* is a new vaccine against two types of human papillomavirus (HPV) that cause most cervical cancers.

Figure 28–18 The Uterus. ATLAS: Plates 66; 67

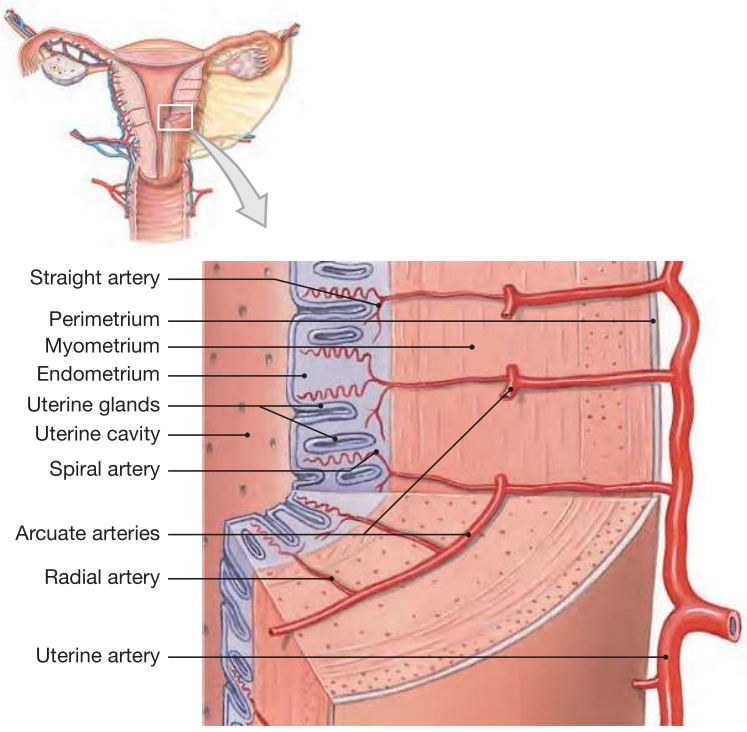


glands, blood vessels, and epithelium change with the phases of the monthly *uterine cycle*.

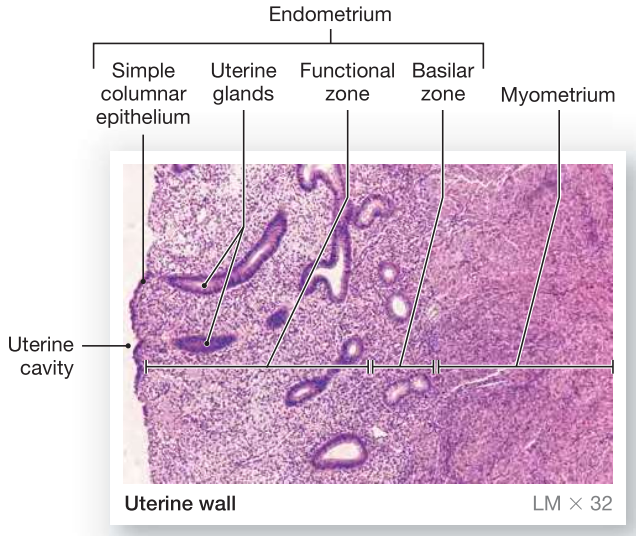
The myometrium, the thickest portion of the uterine wall, makes up almost 90 percent of the mass of the uterus. Smooth muscle in the myometrium is arranged into longitudinal, circular, and oblique layers. The smooth muscle tissue of the myometrium provides much of the force needed to move a fetus out 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 (**Figure 28–19b**). The

Figure 28–19 The Uterine Wall.



a A diagrammatic sectional view of the uterine wall, showing the endometrial regions and the circulatory supply to the endometrium



b The basic histological structure of the uterine wall

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 uterine glands.

Within the myometrium, branches of the uterine arteries form **arcuate arteries,** which encircle the endometrium (Figure 28–19a). **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 fairly constant over time, but that of the functional zone undergoes cyclical changes in response to sex hormone levels. These cyclical changes produce the characteristic histological features of the uterine cycle.

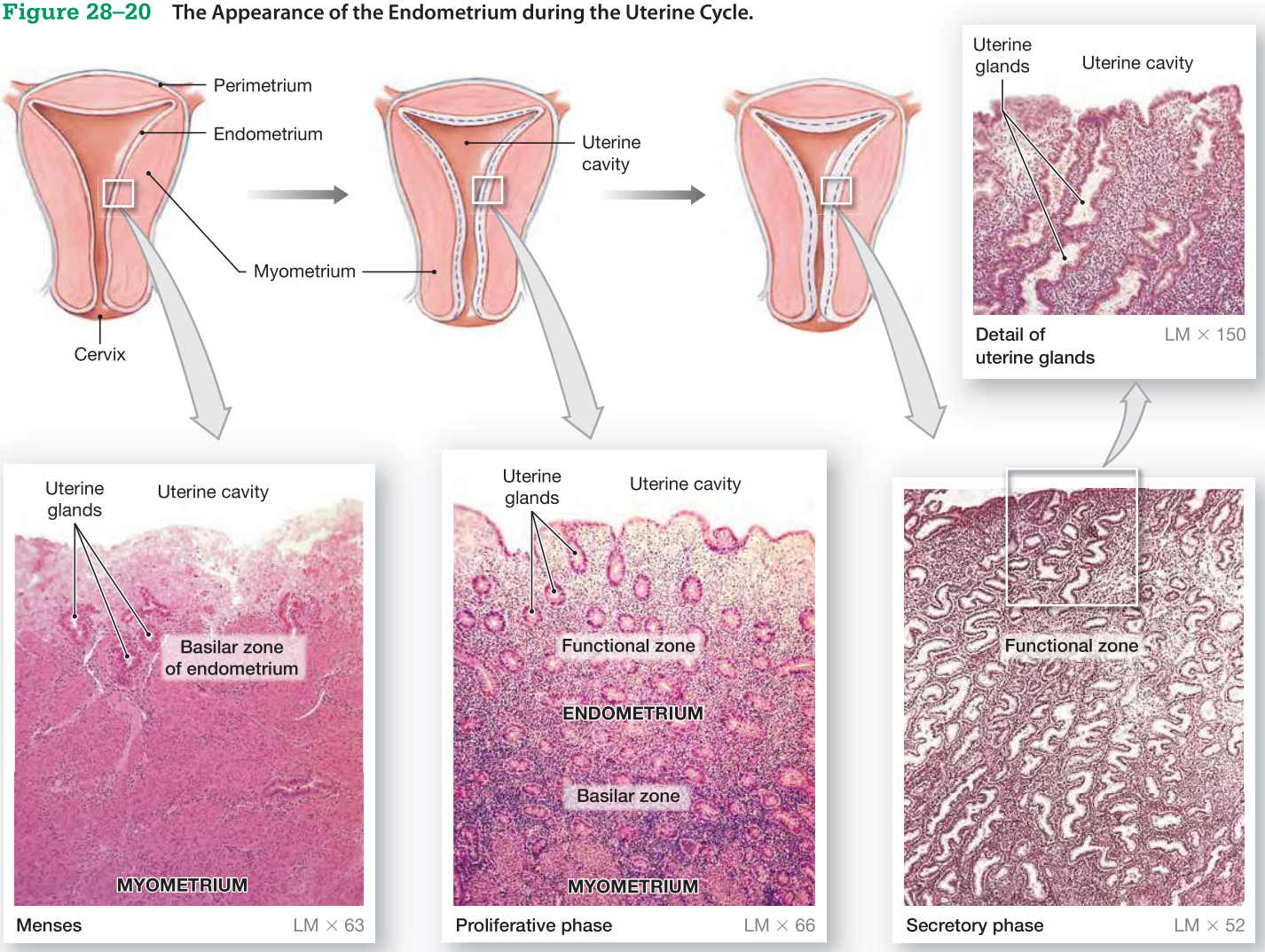
The Uterine Cycle

The **uterine cycle**, or *menstrual* (MEN-stroo-ul) *cycle*, is a repeating series of changes in the structure of the endometrium (Figure 28–20). 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 ovarian cycle. We consider the regulatory mechanism involved in a later section.

Menses. The uterine cycle begins with the onset of **menses** (MEN-sēz), an interval marked by the degeneration of the functional zone of the endometrium (Figure 28–20a). 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 cavity, to be lost by passage through the external os and into the vagina. Only the functional zone is affected, because the deeper, basilar layer is provided with blood from the straight arteries, which remain unconstricted.

The sloughing off (shedding) 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** (men-stroo-Ā-shun), generally lasts from one to seven days.

Figure 28–20 The Appearance of the Endometrium during the Uterine Cycle.



a The appearance of the endometrium at menses

b The appearance of the endometrium during the proliferative phase

c The appearance of the endometrium during the secretory phase of the uterine cycle

During this time about 35 to 50 mL (1.2–1.7 oz) of blood are lost. The process can be relatively painless. Painful menstruation, or **dysmenorrhea,** can result from uterine inflammation, myometrial contractions ("cramps"), or from conditions involving adjacent pelvic structures.

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 uterine epithelium (**Figure 28–20b**). 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 uterine glands are manufacturing a mucus rich in glycogen. This specialized mucus appears to be essential for the survival of the fertilized ovum through its earliest developmental stages. (These stages will be considered in Chapter 29.) The entire functional zone is highly vascularized, with small arteries spiraling toward the endometrial surface from larger arteries in the myometrium.

The Secretory Phase. During the **secretory phase** of the uterine cycle, the uterine 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

(Figure 28–20c). 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** (me-NAR-kē; *men*, month + *arche*, beginning), typically occurs at age 11–12. The cycles continue until **menopause** (MEN-ō-pawz), 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** (ā-men-ō-RĒ-uh) exists. *Primary amenorrhea* is the failure to initiate menses. This condition may indicate developmental abnormalities, such as nonfunctional ovaries, the absence of a uterus, or an endocrine or genetic disorder. It can also result from malnutrition: Puberty is delayed if leptin levels are too low. p. 628 Transient *secondary amenorrhea* can be caused by severe physical or emotional stresses. In effect, the reproductive system gets "switched off." Factors associated with amenorrhea include drastic weight loss, anorexia nervosa, and severe depression or grief. Amenorrhea has also been observed in marathon runners and other women engaged in training programs that require sustained high levels of exertion, which severely reduce body lipid reserves.

The Vagina

The **vagina** is an elastic, muscular tube extending between the cervix and the exterior. It opens into the *vestibule*, a space bounded by the female external genitalia (Figure 28–13). 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** (FOR-niks). 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 by the **vaginal branches** of the internal iliac (or uterine) arteries and veins. Innervation is from the hypogastric plexus, sacral nerves S_2–S_4, and branches of the pudendal nerve. pp. 432, 746, 753

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

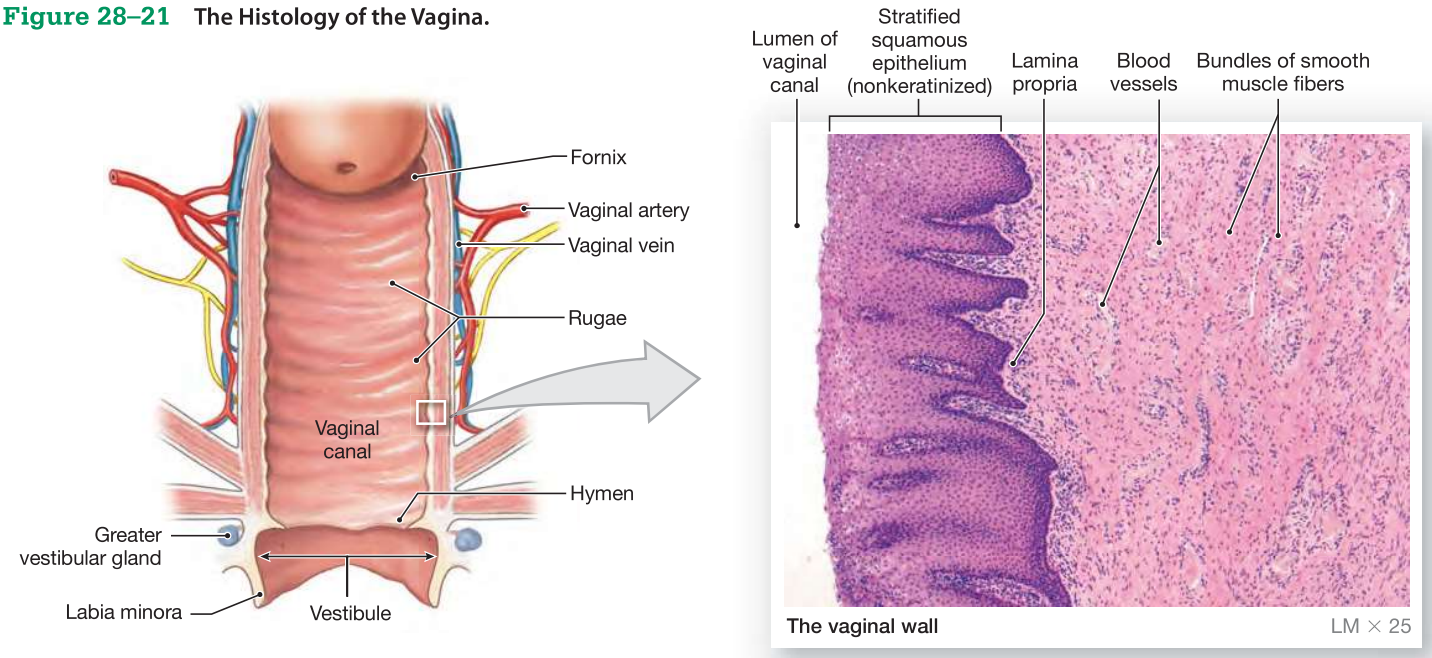
In sectional view, the lumen of the vagina appears constricted, forming a rough H-shape. The vaginal walls contain a network of blood vessels and layers of smooth muscle (Figure 28–21). The lining is moistened by secretions of the cervical glands and by the movement of water across the permeable epithelium. The **hymen** (HĪ-men) is an elastic epithelial fold of variable size that partially blocks the entrance to the vagina. An intact hymen is typically stretched or torn during first sexual intercourse, tampon use, pelvic examination, or physical activity. The two *bulbospongiosus muscles* extend along either side of the vaginal entrance. Contractions of the bulbospongiosus muscles constrict the vagina. p. 346 These muscles cover the **vestibular bulbs,** masses of erectile tissue on either side of the vaginal entrance (Figure 28–22). 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 (Figure 28–21). 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. Fungi, bacteria, or parasites can cause **vaginitis** (vaj-i-NĪ-tis), an inflammation of the vaginal canal. In addition to any discomfort that may result, the condition may affect the survival of spermatozoa and thereby reduce fertility. An acidic environment also inhibits the motility of sperm. For this reason, the buffers in semen are important to successful fertilization.

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 stages in the ovarian and uterine cycles. This diagnostic procedure is an example of *exfoliative cytology*. p. 115

Figure 28–21 The Histology of the Vagina.



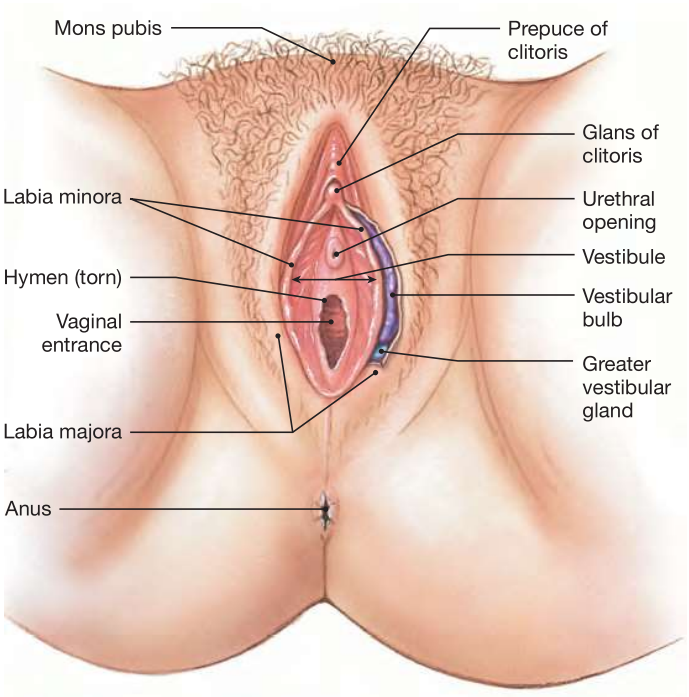
The External Genitalia

The area containing the female external genitalia is the **vulva** (VUL-vuh), or *pudendum* (pū-DEN-dum; **Figure 28–22**). The vagina opens into the **vestibule,** a central space surrounded by small folds known as the **labia minora** (LĀ-bē-uh mi-NOR-uh; singular, *labium minus*). The labia minora are covered with a smooth, hairless 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** (KLIT-ō-ris) 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; a small erectile *glans* sits atop it. The vestibular bulbs along the sides of the vestibule are comparable to the corpus spongiosum. These erectile tissues engorge with blood during sexual arousal. Extensions of the labia minora encircle the body of the clitoris, forming its **prepuce,** or *hood*. ATLAS: Embryology Summary 21: The Development of the Reproductive System

A variable number of small **lesser vestibular glands** discharge their secretions onto the exposed surface of the vestibule between the orifices of the vagina and urethra. During sexual arousal, the **greater vestibular glands** *(Bartholin's glands)*, located on either side of the distal portion of the vagina, secrete into the vestibule. These mucous glands keep the area moist and lubricated. The vestibular glands have the same embryological origins as the bulbo-urethral glands in males.

The outer margins of the vulva are formed by the mons pubis and the labia majora. The **mons pubis** is a pad of adipose tissue covering the symphysis pubis. Adipose tissue also accumulates within the **labia majora** (singular, *labium majus*), 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 hairless. Sebaceous glands

Figure 28–22 The Female External Genitalia.



and scattered apocrine sweat glands secrete onto the inner surface of the labia majora, moistening and lubricating them.

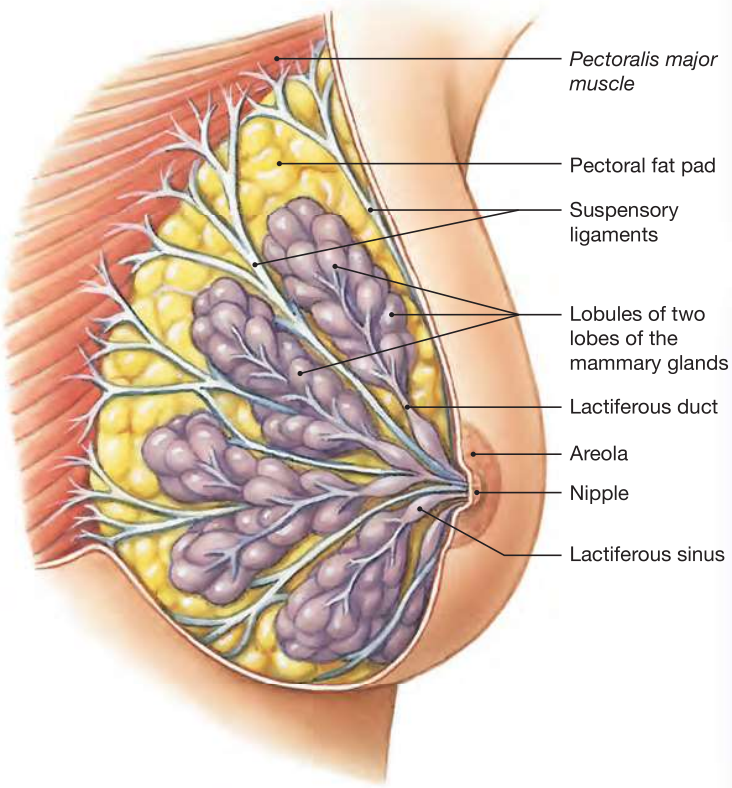
The Mammary Glands

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 is nourished from the milk secreted by the maternal **mammary glands.** Milk production, or **lactation** (lak-TĀ-shun), 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.

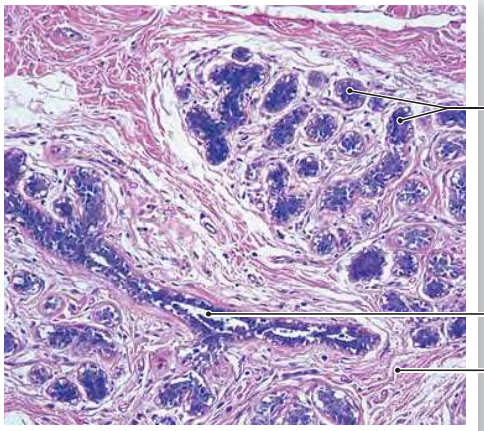
On each side, a mammary gland lies in the subcutaneous tissue of the **pectoral fat pad** deep to the skin of the chest (**Figure 28–23a**). Each breast has a **nipple,** a small conical projection where the ducts of the underlying mammary gland open onto the body surface. The reddish-brown skin around each nipple is the **areola** (a-RĒ-ō-luh). 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** (lak-TIF-er-us) **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

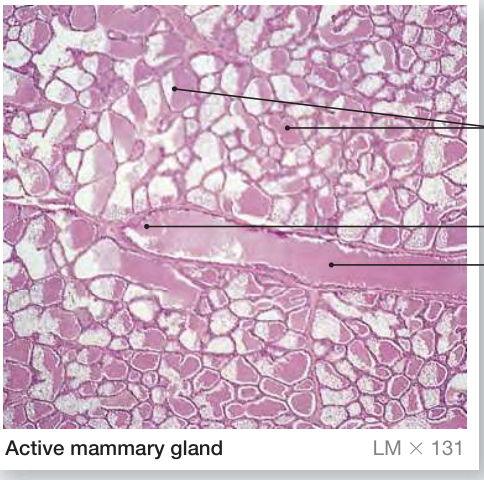
Figure 28–23 The Mammary Glands. ATLAS: Plate 28



a The mammary glands of the left breast



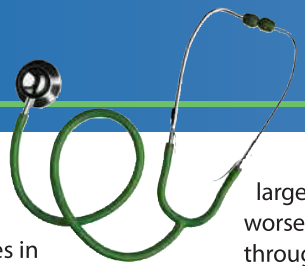
b An inactive mammary gland of a nonpregnant woman



c An active mammary gland of a nursing woman

Clinical Note

Breast Cancer



A fight for the cure

The uterine cycle also influences cyclical changes in the mammary glands. The effects usually go unnoticed, but occasional discomfort or even inflammation of mammary gland tissues can occur late in the cycle. If inflamed lobules become walled off by scar tissue, **cysts** are created. Clusters of cysts can be felt in the breast as discrete masses, a condition known as **fibrocystic disease.** Because its symptoms are similar to those of breast cancer, biopsies may be needed to distinguish between this benign condition and breast cancer.

Breast cancer is a malignant, metastasizing tumor of the mammary gland. It is the leading cause of death in women between ages 35 and 45, but it is most common in women over age 50. Approximately 40,170 female deaths and 440 male deaths will occur in the United States from breast cancer in 2010, and approximately 209,060 new cases will be reported for both sexes. Of the newly reported cases, about 1900 will occur in males. An estimated 12 percent of U.S. women will develop breast cancer at some point in their lifetime. The incidence is highest among Caucasian Americans, somewhat lower in African Americans, and lowest in Asian Americans and American Indians. Notable risk factors include (1) a family history of breast cancer, (2) a first pregnancy after age 30, and (3) early menarche or late menopause.

Despite repeated studies, no links have been proven between breast cancer and oral contraceptive use, fat consumption, or alcohol use. It appears likely that multiple factors are involved. In some families an inherited genetic variation has been linked to higher-than-normal risk of developing the disease. However, most women never develop breast cancer—even women in families with a history of the disease. Mothers who breast-fed (nursed) their babies have a 20 percent lower incidence of breast cancer after menopause than do mothers who did not breast-feed. The reason is not known. Adding to the mystery, nursing does not appear to affect the incidence of premenopausal breast cancer.

Early detection of breast cancer is the key to saving lives, and thus the use of clinical screening techniques has increased in recent years. **Mammography** involves the use of x-rays to examine breast tissues. The radiation dosage can be low, because only soft tissues must be penetrated. This procedure gives the clearest picture of conditions in the breast tissues. Ultrasound can provide some information, but the resulting images lack the detail of standard mammograms.

Treatment is more successful if breast cancer is identified while it is still a relatively small, localized tumor. Once it has grown larger than 2 cm (0.78 in.), the chances of long-term survival worsen. A poor prognosis also follows if cancer cells have spread through the lymphatic system to the axillary lymph nodes. If the nodes are not yet involved, the chances of five-year survival are about 92 percent, but if four or more nodes are involved, the survival rate drops to 25 percent. More than 90 percent of breast cancers are now diagnosed at the local or regional stage.

Treatment of breast cancer begins with the removal of the tumor. Because in many cases cancer cells begin to spread before the condition is diagnosed, part or all of the affected mammary gland is surgically removed and usually the axillary lymph nodes on that side are biopsied.

- In a *lumpectomy*, only a portion of the breast is removed.
- In a *total mastectomy*, the entire breast is removed.
- In *axillary lymph node dissection,* one or more of the axillary lymph nodes (called sentinel nodes) are removed to check for metastatic cells. If there are no cancer cells in the nodes checked, the other lymph nodes may be left in place.

A combination of chemotherapy, radiation treatments, and hormone treatments may be used to supplement the surgical procedures. Tamoxifen is an antiestrogen drug that is used to treat some cases of breast cancer. It is more effective than conventional chemotherapy for treating breast cancer in women over 50, and it has fewer unpleasant side effects. It can also be used in addition to regular chemotherapy in the treatment of advanced-stage disease. As an added bonus, tamoxifen prevents and even reverses age-related osteoporosis. This drug has risks, however: When given to premenopausal women, tamoxifen can cause amenorrhea and hot flashes similar to those of menopause. Tamoxifen has also been linked to an increased risk of endometrial cancer, and potentially to liver cancer as well. However, tamoxifen has been approved for use to prevent breast cancer in women at risk for the disease. Alternatively, aromatase inhibitors, such as anastrozole or letrozole, are given after surgery because they have been found superior to tamoxifen in preventing recurrence.

mammary gland complex from the underlying pectoralis muscles. Branches of the *internal thoracic artery* (see **Figure 21–22**, p. 741) supply blood to each mammary gland.

Figure 28–23b,c compares the histological organizations of inactive and active mammary glands. 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. We will discuss the hormonal mechanisms involved in lactation in Chapter 29.

Hormones and the Female Reproductive Cycle

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 doesn't 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. If the hypothalamus were a radio station, the pulse frequency would correspond to the radio frequency it's transmitting on, and the amplitude would be the volume. We will consider changes in pulse frequency, as their effects are both dramatic and reasonably well understood. Circulating levels of estrogens and progestins primarily control changes in GnRH pulse frequency. 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. For example, consider the *gonadotropes*, the cells responsible for FSH and LH production. At one pulse frequency, the gonadotropes respond preferentially and secrete FSH, whereas at another frequency, LH is the primary hormone released. FSH and LH production also occurs in pulses that follow the rhythm of GnRH pulses. If GnRH is absent or is supplied at a constant rate (without pulses), FSH and LH secretion will stop in a matter of hours.

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, interstitial cells scattered throughout the ovarian stroma secrete small quantities of estrogens. 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** (es-tra-DĪ-ol). It is the dominant hormone prior to ovulation. In estradiol synthesis (**Figure 28–24**), androstenedione is first converted to testosterone, which the enzyme aromatase converts to estradiol. The synthesis of both *estrone* and *estriol* proceeds directly from androstenedione.

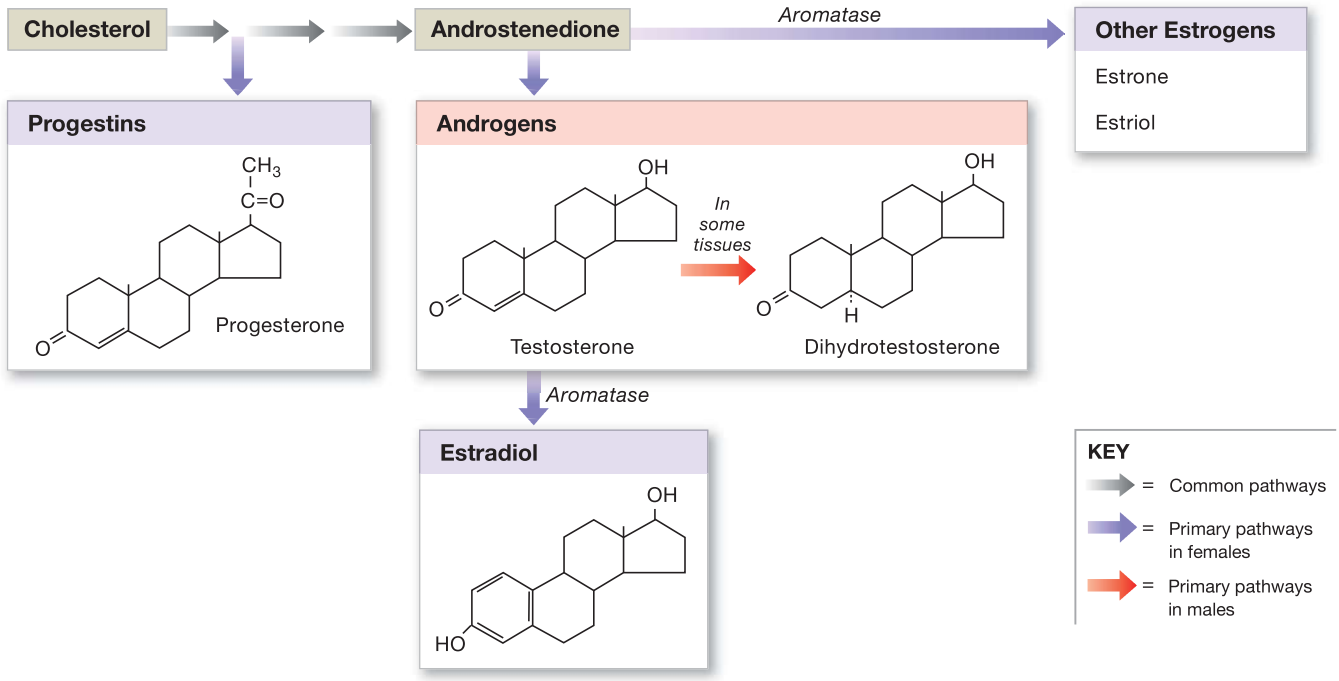
Estrogens have multiple functions that affect the activities of many tissues and organs throughout the body. Among the important general functions of estrogens are (1) stimulating bone and muscle growth; (2) maintaining female secondary sex characteristics, such as body hair distribution and the location of adipose tissue deposits; (3) affecting central nervous system 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. **Spotlight Figure 28–25** diagrams the hormonal regulation of ovarian activity.

Summary: Hormonal Regulation of the Female Reproductive Cycle

Spotlight Figure 28–25 shows the changes in circulating hormone levels that accompany the ovarian and uterine cycles. Early in the follicular phase of the ovarian cycle and prior to day 10, 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 lobe of the 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, around 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

Figure 28–24 Pathways of Steroid Hormone Synthesis in Males and Females. All gonadal steroids are derived from cholesterol. In men, the pathway ends with the synthesis of testosterone, which may subsequently be converted to dihydrotestosterone. In women, an additional step past testosterone leads to estradiol synthesis. The synthesis of progesterone and estrogens other than estradiol involves alternative pathways.



result is a massive release of LH from the anterior lobe of the pituitary gland. This sudden surge in LH concentration triggers (1) the completion of meiosis I by the primary oocyte, (2) the forceful 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 uterine glands. Progesterone levels remain high for the next week, but unless pregnancy occurs, the corpus luteum begins to degenerate. Approximately 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

Spotlight Figure 28–25 also shows the changes in the endometrium during a single 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 uterine glands and an increase in their secretions.

Hormones and Body Temperature

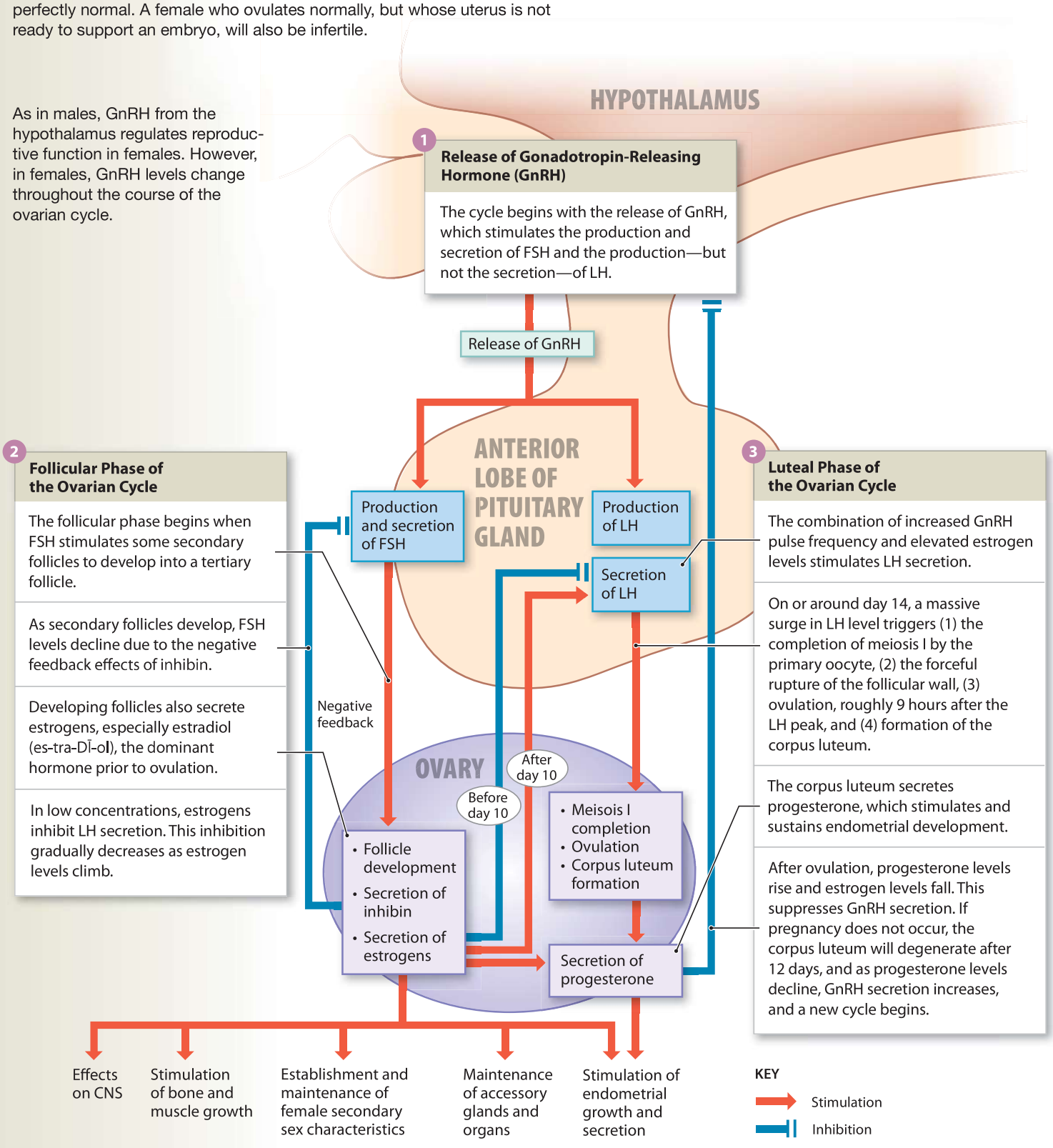
At the time of ovulation, the basal body temperature (BBT) declines noticeably, making the rise in temperature over the next day even more noticeable (**Spotlight Figure 28–25**). Urine

Spotlight

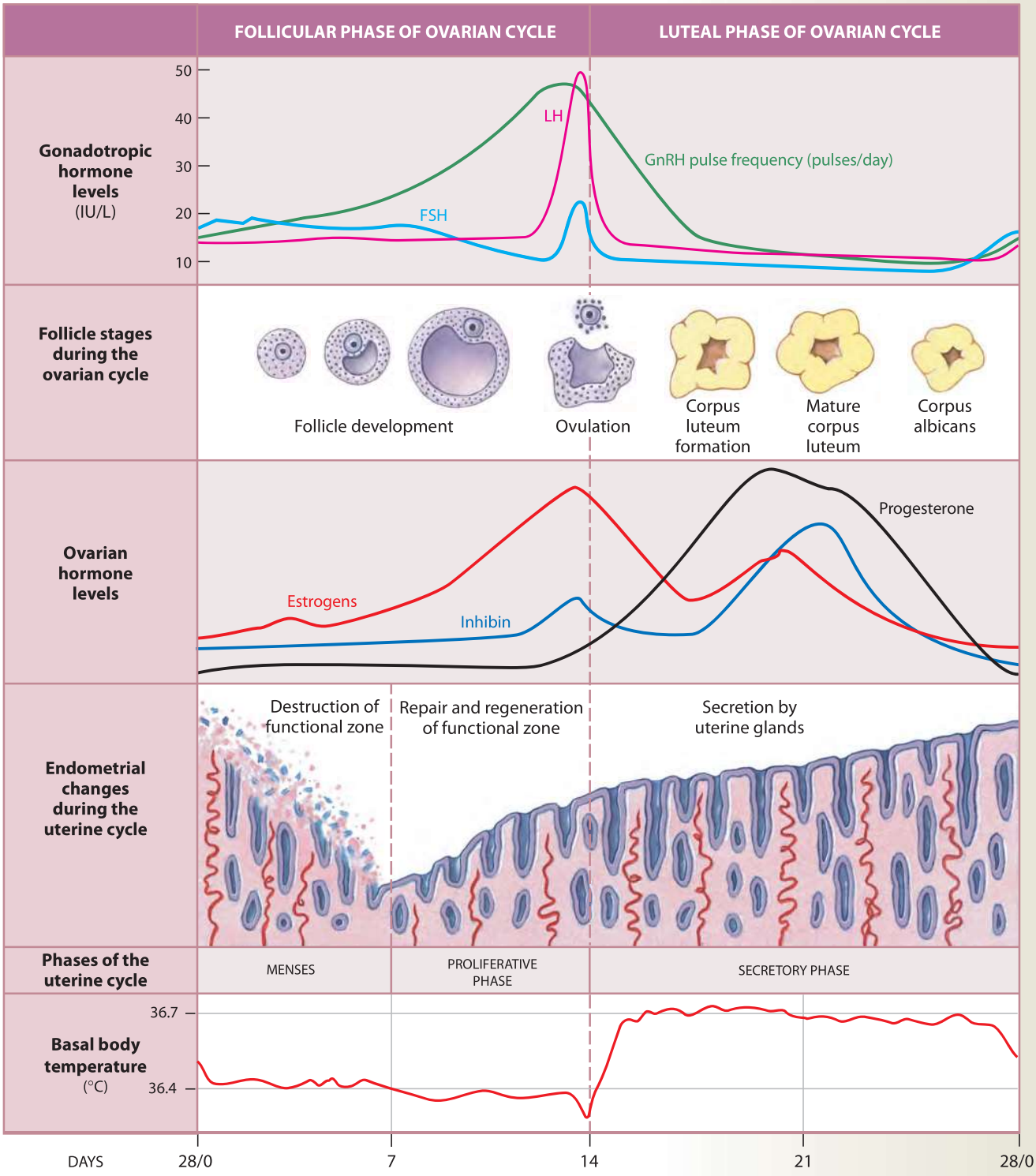
Figure 28–25
Regulation of Female Reproduction

The ovarian and uterine cycles must operate in synchrony to ensure proper reproductive function. If the two cycles are not properly coordinated, infertility results. A female who doesn't ovulate cannot conceive, even if her uterus is perfectly normal. A female who ovulates normally, but whose uterus is not ready to support an embryo, will also be infertile.

As in males, GnRH from the hypothalamus regulates reproductive function in females. However, in females, GnRH levels change throughout the course of the ovarian cycle.



This illustration can aid your understanding of female reproductive physiology by integrating the key events in the ovarian and uterine cycles. The monthly hormonal fluctuations cause physiological changes that affect core body temperature. During the follicular phase—when estrogens are the dominant hormones—the **basal body temperature**, or the resting body temperature measured upon awakening in the morning, is about 0.3°C (0.5°F) lower than it is during the luteal phase, when progesterone dominates.



tests that detect LH are available, and testing daily for several days before expected ovulation can detect the LH surge more reliably than the BBT changes. This information can be important for individuals who wish to avoid or promote a pregnancy, because fertilization typically occurs within a day of ovulation. Thereafter, oocyte viability and the likelihood of successful fertilization decrease markedly.

Checkpoint

9. Name structures of the female reproductive system.
10. What effect would blockage of both uterine tubes by scar tissue (resulting from an infection such as gonorrhea) have on a woman's ability to conceive?
11. What benefit does the acidic pH of the vagina provide?
12. Which layer of the uterus is sloughed off, or shed, during menstruation?
13. Would the blockage of a single lactiferous sinus interfere with the delivery of milk to the nipple? Explain.
14. What changes would you expect to observe in the ovarian cycle if the LH surge did not occur?
15. What effect would a blockage of progesterone receptors in the uterus have on the endometrium?
16. What event in the uterine cycle occurs when the levels of estrogens and progesterone decline?

See the blue Answers tab at the back of the book.

28-4 The autonomic nervous system influences male and female sexual function

Sexual intercourse, also known as *coitus* (KŌ-i-tus) or *copulation*, introduces semen into the female reproductive tract. We now consider the process as it affects the male and female reproductive systems.

Male Sexual Function

Complex neural reflexes coordinate sexual function in males. 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 (discussed on p. 1046). The skin covering the glans of the penis contains numerous sensory receptors, and erection tenses the skin and increases sensitivity. Subsequent stimulation can initiate the secretion of the bulbourethral glands, providing **lubrication** for 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 glands 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 prevent 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. The contractions of both muscles are controlled by somatic motor neurons in the inferior lumbar and superior sacral segments of the spinal cord. (The positions of these muscles are shown in Figure 11–12b, p. 346.) Contraction of the smooth muscle within the prostate acts to pinch off the urethra, preventing the passage of urine through the erect penis.

Ejaculation is associated with intensely pleasurable sensations, an experience known as male **orgasm** (OR-gazm). Several other noteworthy physiological changes occur at this time, including pronounced but temporary increases in heart rate and blood pressure. After ejaculation, blood begins to leave the erectile tissue, and the erection begins to subside. This subsidence, called **detumescence** (dē-tū-MES-ens), is mediated by the sympathetic nervous system.

In sum, 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 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. Various physical causes may be responsible for impotence, because erection involves vascular changes as well as neural commands. For example, low blood pressure in the arteries supplying the penis, due to a circulatory blockage such as a plaque, will reduce the ability to attain an erection. Drugs, alcohol, trauma, or illnesses that affect the autonomic

nervous system or the central nervous system can have the same effect. But male sexual performance can also be strongly affected by the psychological state of the individual. Temporary periods of impotence are fairly common in healthy individuals who are experiencing severe stresses or emotional problems. Depression, anxiety, and fear of impotence are examples of emotional factors that can result in sexual dysfunction. The prescription drugs Viagra, Levitra, and Cialis, which enhance and prolong the effects of nitric oxide on the erectile tissue of the penis, have proven useful in treating many cases of impotence.

Female Sexual Function

The events in female sexual function are largely 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, through impulses traveling over the pudendal nerves, rhythmic contractions of the bulbospongiosus and ischiocavernosus muscles. The latter contractions give rise to the intensely pleasurable sensations of orgasm.

Sexual activity carries with it the risk of infection with a variety of microorganisms. The consequences of such an infection may range from merely inconvenient to potentially lethal. **Sexually transmitted diseases (STDs)** are transferred from individual to individual, primarily or exclusively by sexual intercourse. At least two dozen bacterial, viral, and fungal infections are currently recognized as STDs. The bacterium *Chlamydia* can cause **pelvic inflammatory disease (PID)** and infertility; AIDS, caused by a virus, is deadly. The incidence of STDs has been increasing in the United States since 1984; an estimated 19 million new cases occur each year, almost 50 percent in persons aged 19–24. Poverty, intravenous drug use, prostitution, and the appearance of drug-resistant pathogens all contribute to the problem.

Checkpoint

17. **List the physiological events of sexual intercourse in both sexes, and indicate those that occur in males but not in females.**
18. **An inability to contract the ischiocavernosus and bulbospongiosus muscles would interfere with which part of the male sex act?**
19. **What changes occur in females during sexual arousal as the result of increased parasympathetic stimulation?**

See the blue Answers tab at the back of the book.

28-5 With age, decreasing levels of reproductive hormones cause functional changes

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. The aging process affects all body systems, including the reproductive systems of men and women alike. As noted earlier in the chapter, these systems become fully functional at puberty. Thereafter, 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 primordial follicles responding each month begins to drop markedly. As their numbers decrease, 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. A variety of neural effects are reported as well, including "hot flashes," anxiety, and depression. Hot flashes typically begin while estrogen levels are declining, and cease when estrogen levels reach minimal values. These intervals of elevated body temperature are associated with surges in LH production. The hormonal mechanisms involved in other CNS effects of menopause are poorly understood. In addition, the risks of atherosclerosis and other forms of cardiovascular disease increase after menopause.

The majority of women experience only mild symptoms, but some individuals experience acutely unpleasant symptoms in perimenopause or during or after menopause. For most of those women, hormone replacement therapy (HRT) involving a combination of estrogens and progestins can control the unpleasant neural and vascular changes associated with menopause. The hormones are administered as pills, by injection, or by transdermal "estrogen patches." However, recent studies suggest that taking estrogen replacement therapy for more than five years increases the risk of heart disease, breast cancer, Alzheimer's disease, blood clots, and stroke. HRT should be used only after a full discussion and assessment of the potential risks and benefits, and taken for as short a time as possible.

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 80s can father children), older men experience a gradual reduction in sexual activity. This decrease may be linked to declining testosterone levels. Some clinicians suggest the use of testosterone replacement therapy to enhance the libido (sexual drive) of elderly men, but this may increase the risk of prostate disease.

Checkpoint

20. **Define menopause.**
21. **Why does the level of FSH rise and remain high during menopause?**
22. **What is the male climacteric?**

See the blue Answers tab at the back of the book.

28-6 The reproductive system secretes hormones affecting growth and metabolism of all body systems

Normal human reproduction is a complex process that requires the participation of multiple systems. The hormones discussed in this chapter play a major role in coordinating reproductive events (Table 28–1). Physical factors also play a role. The man's sperm

Table 28–1 Hormones of the Reproductive System

Hormone	Source	Regulation of Secretion	Primary Effects
Gonadotropin-releasing hormone (GnRH)	Hypothalamus	*Males*: inhibited by testosterone and possibly by inhibin *Females*: GnRH pulse frequency increased by estrogens, decreased by progestins	Stimulates FSH secretion and LH synthesis in males Stimulates FSH secretion and LH synthesis in females
Follicle-stimulating hormone (FSH)	Anterior lobe of the pituitary gland	*Males*: stimulated by GnRH, inhibited by inhibin *Females*: stimulated by GnRH, inhibited by inhibin	*Males*: stimulates spermatogenesis and spermiogenesis through effects on nurse cells *Females*: stimulates follicle development, estrogen production, and oocyte maturation
Luteinizing hormone (LH)	Anterior lobe of the pituitary gland	*Males*: stimulated by GnRH *Females*: production stimulated by GnRH, secretion by the combination of high GnRH pulse frequencies and high estrogen levels	*Males*: stimulates interstitial cells to secrete testosterone *Females*: stimulates ovulation, formation of corpus luteum, and progestin secretion
Androgens (primarily testosterone and dihydrotestosterone)	Interstitial cells of testes	Stimulated by LH	Establish and maintain male secondary sex characteristics and sexual behavior; promote maturation of spermatozoa; inhibit GnRH secretion
Estrogens (primarily estradiol)	Granulosa and thecal cells of developing follicles; corpus luteum	Stimulated by FSH	Stimulate LH secretion (at high levels); establish and maintain female secondary sex characteristics and sexual behavior; stimulate repair and growth of endometrium; increase frequency of GnRH pulses
Progestins (primarily progesterone)	Granulosa cells from midcycle through functional life of corpus luteum	Stimulated by LH	Stimulate endometrial growth and glandular secretion; reduce frequency of GnRH pulses
Inhibin	Nurse cells of testes and granulosa cells of ovaries	Stimulated by factors released by developing spermatozoa (male) and developing follicles (female)	Inhibits secretion of FSH (and possibly of GnRH)

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). In Chapter 29 we will consider the process of development, focusing on the mechanisms that determine both the structure of the body and the distinctive characteristics of each individual.

Even though the reproductive system's primary function—producing children—doesn't play a role in maintaining homeostasis, reproduction depends on a variety of physical, physiological, and psychological factors, many of which require intersystem cooperation. In addition, the hormones that control and coordinate sexual function have direct effects on the organs and tissues of other systems. For example, testosterone and estradiol affect both muscular development and bone density. **Figure 28–26** summarizes the relationships between the reproductive system and other physiological systems.

Checkpoint

23. **Describe the interaction between the reproductive system and the cardiovascular system.**
24. **Describe the interaction between the reproductive system and the skeletal system.**

See the blue Answers tab at the back of the book.

Related Clinical Terms

cervical dysplasia: The abnormal growth of noncancerous epithelial cells on the surface of the cervix; the condition might be a precursor to cancer.

endometriosis: The growth of endometrial tissue outside the uterus.

erectile dysfunction (ED): Condition in which the male is unable to achieve or maintain an erection until ejaculation.

genital herpes: A sexually transmitted disease caused by a herpes virus and characterized by painful blisters in the genital area.

gonorrhea: A sexually transmitted bacterial disease caused by *Neisseria gonorrhoeae*. Commonly called "the clap."

gynecology: The branch of medicine that deals with the functions and diseases specific to women and girls affecting the reproductive system.

hydrocele: The accumulation of serous fluid in any body sac, but especially in the tunica vaginalis of the testis or along the spermatic cord.

hysterectomy: The surgical removal of the uterus.

menorrhagia: The condition of experiencing extremely heavy bleeding at menstruation.

oophorectomy: The surgical removal of one or both ovaries.

orchitis: Inflammation of one or both testicles.

ovarian cyst: A common condition in which sacs containing fluid or semisolid material develop in or on the surface of an ovary. While these cysts are usually harmless, they may cause signs and symptoms similar to cancerous tumors.

polycystic ovary syndrome (PCOS): A condition in women that is characterized by irregular or no menstrual periods, acne, obesity, and excessive hair growth.

premature ejaculation: A common complaint of ejaculating semen sooner than the man desires while achieving orgasm during intercourse. An estimated 30 percent of men regularly experience the problem.

premenstrual dysphoric disorder (PMDD): A collection of physical and emotional symptoms that occur 5 to 11 days before a woman's period begins, and goes away once menstruation starts. Over 150 symptoms have been associated with the condition, with the most common being headache; swelling of ankles, feet, and hands; backache; abdominal cramps; heaviness or pain; bloating and/or gas; muscle spasms; breast tenderness; weight gain; recurrent cold sores; acne; nausea; constipation or diarrhea; food cravings; anxiety or panic; confusion; difficulty concentrating and forgetfulness; poor judgment; and depression.

premenstrual syndrome: A condition occurring in the last half of a woman's menstrual cycle after ovulation that is a combination of physical and mood disturbances which normally end with the onset of the menstrual flow. Physical features of this syndrome include breast tenderness and bloating, while mood or psychological changes include anger and depression.

salpingitis: Inflammation of a uterine tube.

uterine fibroids (leiomyomas): Benign tumors of the uterus composed of smooth muscle tissue that grows in the wall of the uterus of some women. While not usually dangerous they can cause problems such as very heavy menstrual periods and pain. They may in some cases cause infertility and the tendency to miscarry.

uterine prolapse: Condition that occurs when a woman's pelvic floor muscles and ligaments stretch and weaken and provide inadequate support for the uterus, which then descends into the vaginal canal.

vasectomy: The surgical removal of a segment of each ductus deferens, making it impossible for spermatozoa to reach the distal portions of the male reproductive tract.

vulvovaginal candidiasis: A common female vaginal infection caused by the yeast *Candida*, usually *Candida albicans*. Historically, this type of infection has not caused many problems, but with the overuse of antibiotics, some serious categories of candidiasis have become more common.

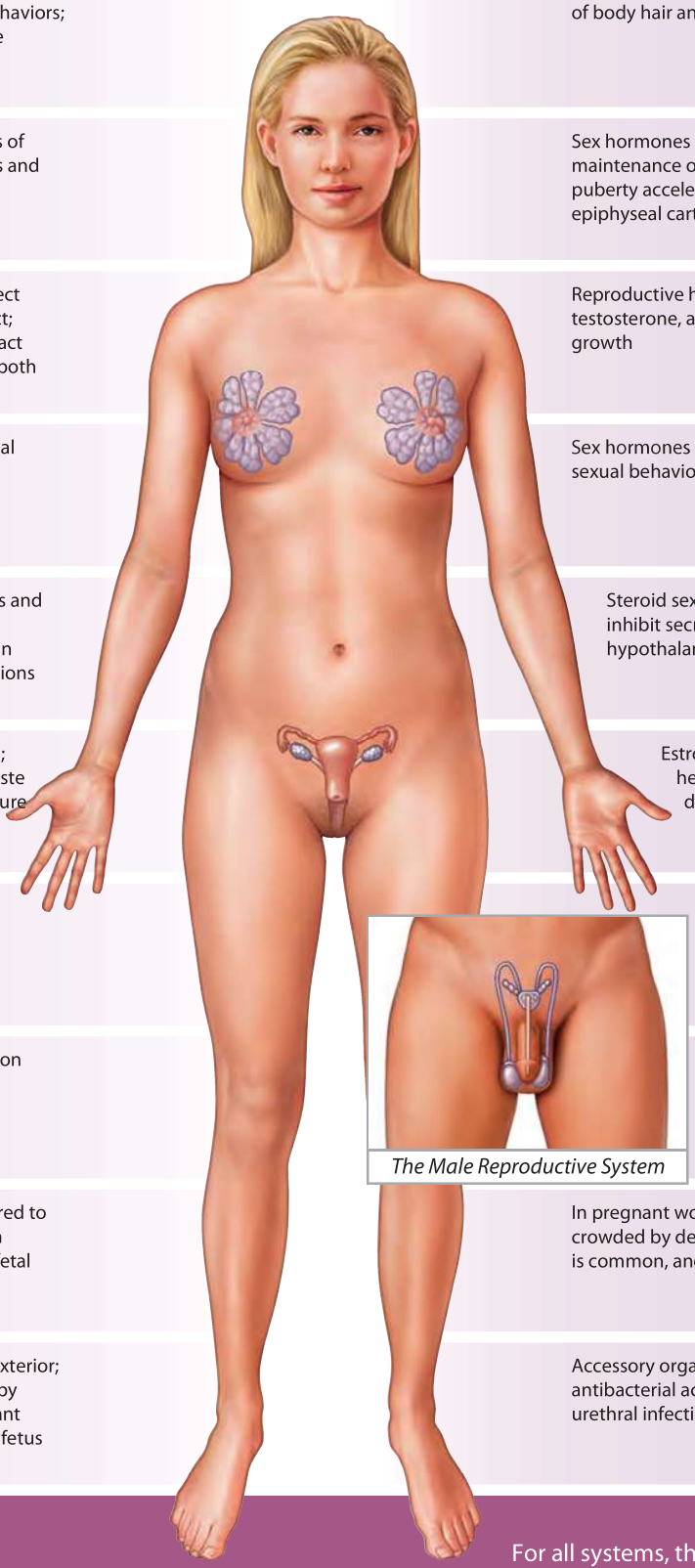
SYSTEM INTEGRATOR

Body System → Reproductive System

Integumentary	Covers external genitalia; provides sensations that stimulate sexual behaviors; mammary gland secretions provide nourishment for newborn
Skeletal	Pelvis protects reproductive organs of females, portion of ductus deferens and accessory glands in males
Muscular	Contractions of skeletal muscles eject semen from male reproductive tract; muscle contractions during sexual act produce pleasurable sensations in both sexes
Nervous	Controls sexual behaviors and sexual function
Endocrine	Hypothalamic regulatory hormones and pituitary hormones regulate sexual development and function; oxytocin stimulates smooth muscle contractions in uterus and mammary glands
Cardiovascular	Distributes reproductive hormones; provides nutrients, oxygen, and waste removal for fetus; local blood pressure changes responsible for physical changes during sexual arousal
Lymphatic	Provides IgA for secretions by epithelial glands; assists in repairs and defense against infection
Respiratory	Provides oxygen and removes carbon dioxide generated by tissues of reproductive system
Digestive	Provides additional nutrients required to support gamete production and (in pregnant women) embryonic and fetal development
Urinary	Urethra in males carries semen to exterior; kidneys remove wastes generated by reproductive tissues and (in pregnant women) by a growing embryo and fetus

Reproductive System → Body System

Integumentary Page 165	Reproductive hormones affect distribution of body hair and subcutaneous fat deposits
Skeletal Page 275	Sex hormones stimulate growth and maintenance of bones; sex hormones at puberty accelerate growth and closure of epiphyseal cartilages
Muscular Page 369	Reproductive hormones, especially testosterone, accelerate skeletal muscle growth
Nervous Page 543	Sex hormones affect CNS development and sexual behaviors
Endocrine Page 632	Steroid sex hormones and inhibin inhibit secretory activities of hypothalamus and pituitary gland
Cardiovascular Page 759	Estrogens may help maintain healthy vessels and slow development of atherosclerosis
Lymphatic Page 807	Lysozymes and bactericidal chemicals in secretions provide innate defense against reproductive tract infections
Respiratory Page 857	Changes in respiratory rate and depth occur during sexual arousal, under control of the nervous system
Digestive Page 910	In pregnant women, digestive organs are crowded by developing fetus, constipation is common, and appetite increases
Urinary Page 992	Accessory organ secretions may have antibacterial action that helps prevent urethral infections in males



The Male Reproductive System

The REPRODUCTIVE System

Figure 28–26 diagrams the functional relationships between the reproductive system and the other body systems.

For all systems, the reproductive system secretes hormones with effects on growth and metabolism.

Chapter Review

Study Outline

28-1 Basic reproductive system structures are gonads, ducts, accessory glands and organs, and external genitalia p. 1032

1. The human **reproductive system** produces, stores, nourishes, and transports functional **gametes** (reproductive cells). **Fertilization** is the fusion of male and female gametes.
2. The reproductive system includes **gonads (testes** or **ovaries),** ducts, accessory glands and organs, and the **external genitalia.**
3. In males, the testes produce **spermatozoa**, which are expelled from the body in **semen** during *ejaculation*. The ovaries of a sexually mature female produce **oocytes** (immature **ova**) that travel along *uterine tubes* toward the *uterus*. The *vagina* connects the uterus with the exterior of the body.

28-2 Spermatogenesis occurs in the testes, and hormones from the hypothalamus, anterior lobe of the pituitary gland, and testes control male reproductive functions p. 1032

4. Spermatozoa travel along the *epididymis*, the *ductus deferens*, the *ejaculatory duct*, and the *urethra* before leaving the body. Accessory organs (notably the *seminal glands*, *prostate gland*, and *bulbo-urethral glands*) secrete fluids into the ejaculatory ducts and the urethra. The *scrotum* encloses the testes, and the *penis* is an erectile organ. *(Figure 28–1)*
5. The **descent of the testes** through the *inguinal canals* occurs during fetal development. The testes remain connected to internal structures by the **spermatic cords.** The **raphe** marks the boundary between the two chambers in the **scrotum**. *(Figures 28–2, 28–3)*
6. The **dartos** muscle tightens the scrotum, giving it a wrinkled appearance as it elevates the testes. The **cremaster muscles** are more substantial muscles that pull the testes close to the body.
7. The **tunica albuginea** surrounds each testis. Septa extend from the tunica albuginea to the region of the testis closest to the entrance to the epididymis, creating a series of **lobules.** *(Figure 28–4)*
8. **Seminiferous tubules** within each lobule are the sites of sperm production. From there, spermatozoa pass through the **rete testis.** Seminiferous tubules connect to a **straight tubule. Efferent ductules** connect the rete testis to the epididymis. Between the seminiferous tubules are **interstitial cells**, which secrete sex hormones. *(Figures 28–4, 28–5)*
9. Seminiferous tubules contain **spermatogonia,** stem cells involved in **spermatogenesis** (the production of spermatozoa), and **nurse** (sustentacular or Sertoli) **cells,** which sustain and promote the development of spermatozoa. *(Figures 28–6, 28–7)*
10. Each **spermatozoon** has a **head** tipped by an **acrosome,** a **middle piece,** and a **tail**. *(Figure 28–8)*
11. From the testis, the spermatozoa enter the **epididymis,** an elongated tubule with **head, body,** and **tail** regions. The epididymis monitors and adjusts the composition of the fluid in the seminiferous tubules, serves as a recycling center for damaged spermatozoa, stores and protects spermatozoa, and facilitates their functional maturation. *(Figure 28–9)*
12. The **ductus deferens,** or *vas deferens*, begins at the epididymis and passes through the inguinal canal as part of the spermatic cord. Near the prostate gland, the ductus deferens enlarges to form the **ampulla.** The junction of the base of the seminal gland and the ampulla creates the **ejaculatory duct,** which empties into the urethra. *(Figures 28–9, 28–10)*
13. The **urethra** extends from the urinary bladder to the tip of the penis. The urethra can be divided into *prostatic*, *membranous*, and *spongy regions*.
14. Each **seminal gland (seminal vesicle)** is an active secretory gland that contributes about 60 percent of the volume of semen. Its secretions contain fructose (which is easily metabolized by spermatozoa), bicarbonate ions, prostaglandins, and fibrinogen. The **prostate gland** secretes slightly acidic **prostatic fluid.** Alkaline mucus secreted by the **bulbo-urethral glands** has lubricating properties. *(Figures 28–10, 28–11)*
15. A typical ejaculation releases 2–5 mL of semen **(ejaculate),** which contains 20–100 million spermatozoa per milliliter. The fluid component of semen is **seminal fluid.**
16. The skin overlying the **penis** resembles that of the scrotum. Most of the **body** of the penis consists of three masses of **erectile tissue.** Beneath the superficial fascia are two **corpora cavernosa** and a single **corpus spongiosum**, which surrounds the urethra. Dilation of the blood vessels within the erectile tissue produces an **erection.** *(Figure 28–11)*
17. Important regulatory hormones include **FSH** *(follicle-stimulating hormone)*, **LH** *(luteinizing hormone)*, and **GnRH** *(gonadotropin-releasing hormone)*. *Testosterone* is the most important androgen. *(Spotlight Figure 28–12)*

28-3 Oogenesis occurs in the ovaries, and hormones from the pituitary gland and gonads control female reproductive functions p. 1049

18. Principal organs of the female reproductive system include the *ovaries*, *uterine tubes*, *uterus*, *vagina*, and external genitalia. *(Figure 28–13)*
19. The ovaries, uterine tubes, and uterus are enclosed within the **broad ligament.** The **mesovarium** supports and stabilizes each ovary. *(Figure 28–14)*
20. The ovaries are held in position by the **ovarian ligament** and the **suspensory ligament.** Major blood vessels enter the ovary at the **ovarian hilum.** Each ovary is covered by a **tunica albuginea.** *(Figure 28–14)*
21. **Oogenesis** (ovum production) occurs monthly in **ovarian follicles** as part of the **ovarian cycle,** which is divided into a **follicular** *(preovulatory)* **phase** and a **luteal** *(postovulatory)* **phase.** *(Figures 28–15, 28–16)*
22. As follicle development proceeds, **primary, secondary,** and **tertiary follicles** are produced in turn. At **ovulation,** a **secondary oocyte** and the attached follicular cells of the **corona radiata** are released through the ruptured ovarian wall. The follicular cells remaining within the ovary form the **corpus luteum,** which later degenerates into scar tissue called a **corpus albicans.** *(Figure 28–16)*
23. Each **uterine tube** has an **infundibulum** with **fimbriae** (fingerlike projections), an **ampulla,** and an **isthmus.** Each uterine tube opens into the *uterine cavity*. For fertilization to occur, a secondary oocyte must encounter spermatozoa during

the first 12–24 hours of its passage from the infundibulum to the uterus. *(Figure 28–17)*

24. *Peg cells* lining the uterine tube secrete a fluid that completes the capacitation of spermatozoa.
25. The **uterus** provides mechanical protection, nutritional support, and waste removal for the developing embryo. Normally, the uterus bends anteriorly near its base *(anteflexion)*. The **broad ligament, uterosacral ligaments, round ligaments,** and **lateral ligaments** stabilize the uterus. *(Figure 28–18)*
26. Major anatomical landmarks of the uterus include the **body, isthmus**, **cervix, external os** *(external orifice)*, **uterine cavity, cervical canal,** and **internal os** *(internal orifice)*. The uterine wall consists of an inner **endometrium,** a muscular **myometrium,** and a superficial **perimetrium** (an incomplete serous layer). *(Figures 28–18, 28–19)*
27. A typical 28-day **uterine,** or *menstrual*, **cycle** begins with the onset of **menses** and the destruction of the **functional zone** of the endometrium. This process of **menstruation** continues from one to seven days. *(Figure 28–20)*
28. After menses, the **proliferative phase** begins, and the functional zone thickens and undergoes repair. The proliferative phase is followed by the **secretory phase,** during which uterine glands enlarge. Menstrual activity begins at **menarche** and continues until **menopause.** *(Figure 28–20)*
29. The **vagina** is a muscular tube extending between the uterus and the external genitalia; it is lined by a nonkeratinized stratified squamous epithelium. A thin epithelial fold, the **hymen**, partially blocks the entrance to the vagina until physical distortion ruptures the membrane. *(Figures 28–21, 28–22)*
30. The components of the **vulva** are the **vestibule, labia minora, paraurethral glands, clitoris**, **labia majora,** and **lesser** and **greater vestibular glands.** *(Figure 28–22)*
31. A newborn infant is nourished from milk secreted by maternal **mammary glands.** *(Figure 28–23)*
32. Hormonal regulation of the **female reproductive cycle** involves the coordination of the ovarian and uterine cycles.
33. **Estradiol,** the most important *estrogen*, is the dominant hormone of the follicular phase. Ovulation occurs in response to a midcycle surge in LH. *(Figure 28–24, Spotlight Figure 28–25)*
34. The hypothalamic secretion of GnRH occurs in pulses that trigger the pituitary secretion of FSH and LH. FSH initiates follicular development, and activated follicles and ovarian interstitial cells produce estrogens. High estrogen levels stimulate LH secretion, increase pituitary sensitivity to GnRH, and increase the GnRH pulse frequency. **Progesterone,** one of the **progestins,** is the principal hormone of the luteal phase. Changes in estrogen and progesterone levels are responsible for maintaining the uterine cycle. *(Spotlight Figure 28–25)*

28-4 The autonomic nervous system influences male and female sexual function p. 1068

35. During sexual **arousal** in males, erotic thoughts, sensory stimulation, or both lead to parasympathetic activity that produces erection. Stimuli accompanying **sexual intercourse** lead to **emission** and **ejaculation.** Contractions of the bulbospongiosus muscles are associated with **orgasm.**
36. The events of female sexual function resemble those of male sexual function, with parasympathetic arousal and skeletal muscle contractions associated with orgasm.

28-5 With age, decreasing levels of reproductive hormones cause functional changes p. 1069

37. Menopause (the time that ovulation and menstruation stop) typically occurs at ages 45–55. The production of GnRH, FSH, and LH rise, whereas circulating concentrations of estrogen and progesterone decline.
38. During the **male climacteric,** at ages 50–60, circulating testosterone levels fall, and FSH and LH levels rise.

28-6 The reproductive system secretes hormones affecting growth and metabolism of all body systems p. 1070

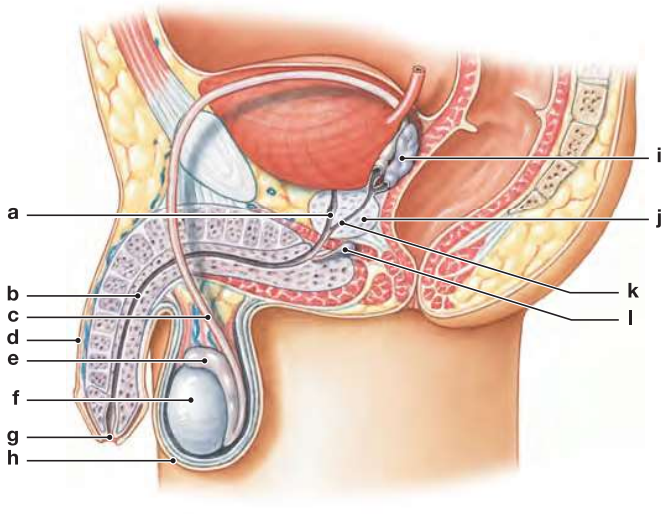
39. Normal human reproduction depends on a variety of physical, physiological, and psychological factors, many of which require intersystem cooperation. *(Figure 28–26)*

Review Questions

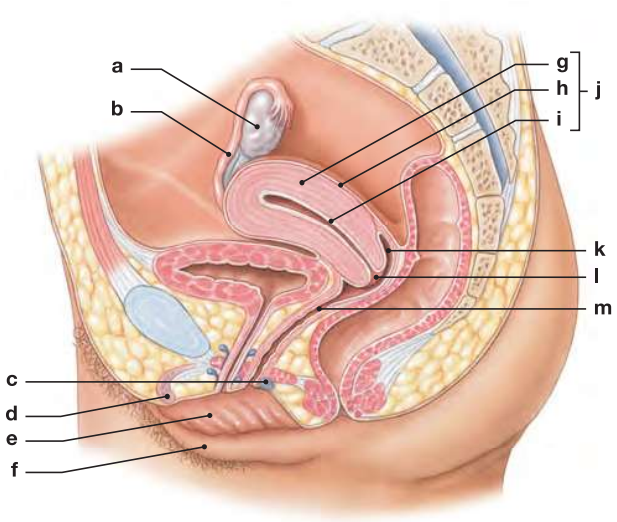
See the blue Answers tab at the back of the book.

LEVEL 1 Reviewing Facts and Terms

1. Identify the principal structures of the male reproductive system in the diagram at right.
   (a) _____
   (b) _____
   (c) _____
   (d) _____
   (e) _____
   (f) _____
   (g) _____
   (h) _____
   (i) _____
   (j) _____
   (k) _____
   (l) _____



2. Identify the principal structures of the female reproductive system in the following diagram.



(a) _____ (b) _____
(c) _____ (d) _____
(e) _____ (f) _____
(g) _____ (h) _____
(i) _____ (j) _____
(k) _____ (l) _____
(m) _____

3. Developing spermatozoa are nourished by
   (a) interstitial cells. (b) the seminal glands.
   (c) nurse cells. (d) Leydig cells.
   (e) the epididymis.
4. The ovaries are responsible for
   (a) the production of female gametes.
   (b) the secretion of female sex hormones.
   (c) the secretion of inhibin.
   (d) all of these.
5. In females, meiosis II is not completed until
   (a) birth.
   (b) puberty.
   (c) fertilization occurs.
   (d) uterine implantation occurs.
6. A sudden surge in LH secretion causes the
   (a) onset of menses.
   (b) rupture of the follicular wall and ovulation.
   (c) beginning of the proliferative phase.
   (d) end of the uterine cycle.
7. The principal hormone of the postovulatory phase is
   (a) progesterone. (b) estradiol.
   (c) estrogen. (d) luteinizing hormone.
8. Which accessory structures contribute to the composition of semen? What are the functions of each structure?
9. What types of cells in the testes are responsible for functions related to reproductive activity? What are the functions of each cell type?
10. Identify the three regions of the male urethra.
11. List the functions of testosterone in males.
12. List and summarize the important steps in the ovarian cycle.
13. Describe the histological composition of the uterine wall.
14. What is the role of the clitoris in the female reproductive system?
15. Trace the route of milk from its site of production to outside the female.

LEVEL 2 Reviewing Concepts

16. Which of the following is *not* true of pelvic inflammatory disease?
   (a) It is frequently caused by sexually transmitted pathogens.
   (b) It causes fever and abdominal pain.
   (c) It can lead to a ruptured urinary bladder.
   (d) It can possibly lead to peritonitis.
   (e) It can cause sterility.
17. In the follicular phase of the ovarian cycle, the ovary
   (a) undergoes atresia.
   (b) forms a corpus luteum.
   (c) releases a mature ovum.
   (d) secretes progesterone.
   (e) matures a follicle.
18. What are the main differences in gamete production between males and females?
19. Describe the erectile tissues of the penis. How does erection occur?
20. Describe each of the three phases of a typical 28-day uterine cycle.
21. Describe the hormonal events associated with the ovarian cycle.
22. Describe the hormonal events associated with the uterine cycle.
23. Summarize the events that occur in sexual arousal and orgasm. Do these processes differ in males and females?
24. How does the aging process affect the reproductive systems of men and women?

LEVEL 3 Critical Thinking and Clinical Applications

25. Diane has peritonitis (an inflammation of the peritoneum), which her physician says resulted from a urinary tract infection. Why might this condition occur more readily in females than in males?
26. In a condition known as endometriosis, endometrial cells are believed to migrate from the body of the uterus into the uterine tubes or by way of the uterine tubes into the peritoneal cavity, where they become established. A major symptom of endometriosis is periodic pain. Why does such pain occur?
27. Contraceptive pills contain estradiol and progesterone, or progesterone alone, administered at programmed doses during the ovarian cycle to prevent follicle maturation and ovulation. Explain how such pills are effective.
28. Female bodybuilders and women with eating disorders such as anorexia nervosa commonly experience amenorrhea. What does this fact suggest about the relation between body fat and menstruation? What might be the benefit of amenorrhea under such circumstances?