CHAPTER 12: REPRODUCTIVE SYSTEM

At the end of this chapter, student will be able to:

a) Describe the location, structure, and functions of the organs of the male reproductive system.
b) Discuss the process of spermatogenesis in the testes.
c) Describe the location, structure, and functions of the organs of the female reproductive system.
d) Discuss the process of oogenesis in the ovaries.
e) Compare the major events of the ovarian and uterine cycles.

12.1 INTRODUCTION

The male and female reproductive organs work together to produce offspring. In addition, the female reproductive organs contribute to sustaining the growth of embryos and foetuses.

Sexual reproduction is the process by which organisms produce offspring by making germ cells called **gametes**. After the male gamete unites with the female gamete an event called **fertilization**, the resulting cell contains one set of chromosomes from each parent. Males and females have anatomically distinct reproductive organs that are adapted for producing gametes, facilitating fertilization, and, in females, sustaining the growth of the embryo and fetus.

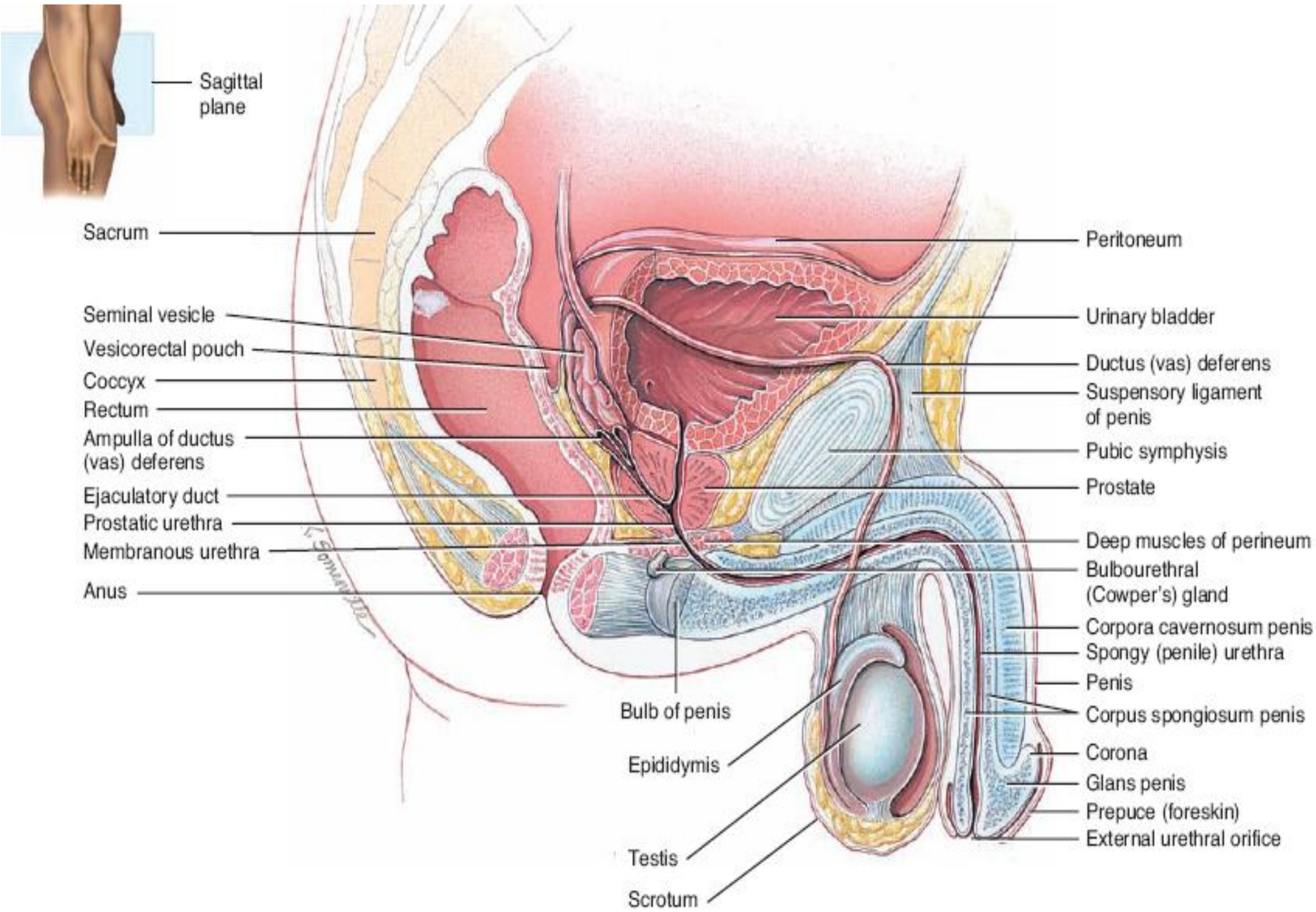
The male and female reproductive organs can be grouped by function. The **gonads**, testes in males and ovaries in females produce gametes and secrete sex hormones. Various **ducts** then store and transport the gametes, and **accessory sex glands** produce substances that protect the gametes and facilitate their movement. Finally, **supporting structures,** such as the penis in males and the uterus in females, assist the delivery of gametes, and the uterus is also the site for the growth of the embryo and fetus during pregnancy.

12.2 MALE REPRODUCTIVE SYSTEM

The organs of the **male reproductive system** include the **testes**, a **system of ducts** (including the epididymis, ductus deferens, ejaculatory ducts, and urethra), **accessory sex glands** (seminal vesicles, prostate, and bulbourethral glands), and **several supporting structures**, including the scrotum and the penis.

The testes (male gonads) produce sperm and secrete hormones.

The duct system transports and stores sperm, assists in their maturation, and conveys them to the exterior. Semen contains sperm plus the secretions provided by the accessory sex glands. The supporting structures have various functions. The penis delivers sperm into the female reproductive tract and the scrotum supports the testes.



SCROTUM

The **scrotum** (tum−bag), is the supporting structure for the testes, consists of movable skin and underlying subcutaneous layer that hangs from the root of the penis.

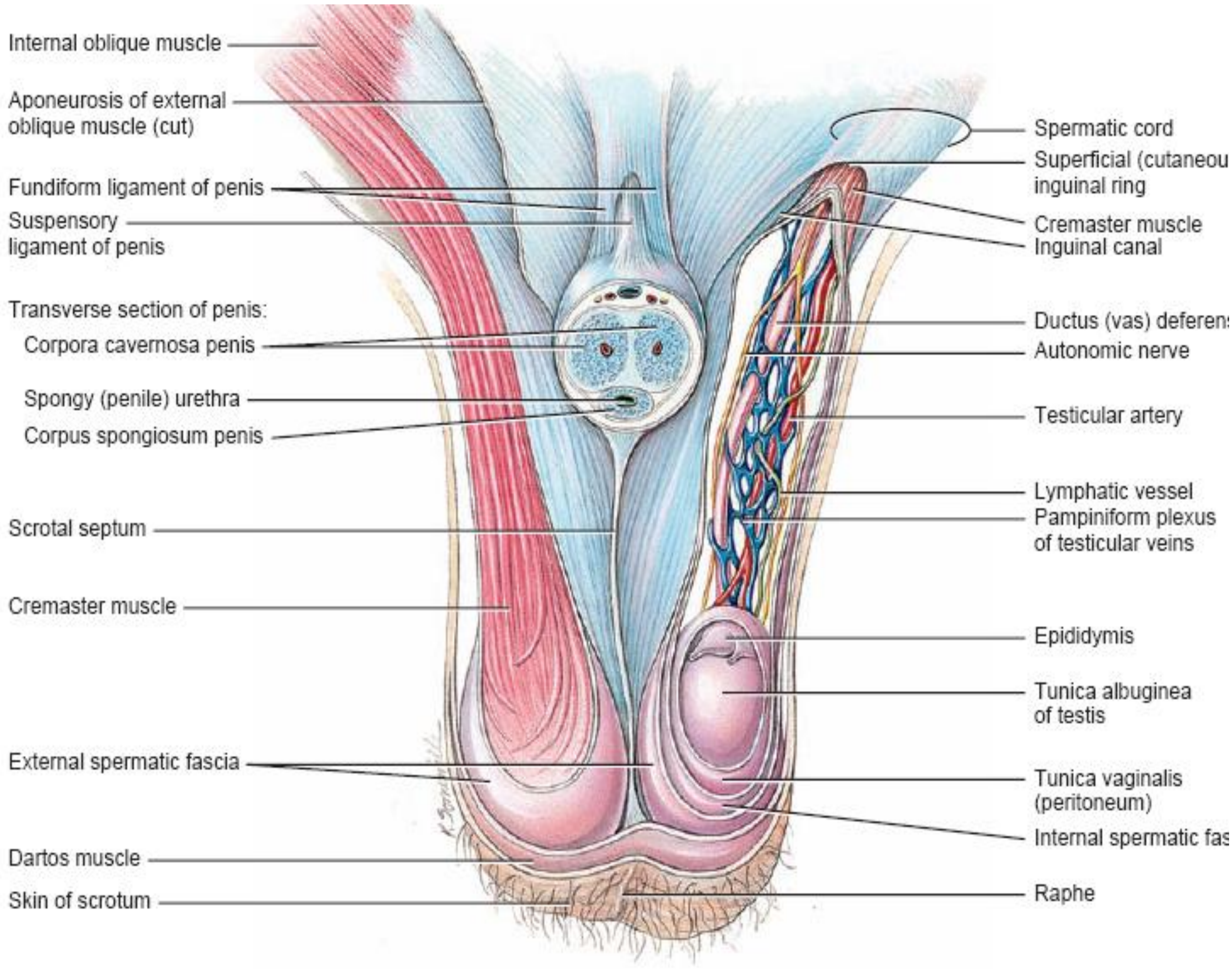
Externally, the scrotum looks like a single pouch of skin separated into lateral portions by a median ridge called the **raphe**.

Internally, the **scrotal septum** divides the scrotum into two sacs, each containing a single testi. **The septum** is made up of a subcutaneous layer and muscle tissue called the **dartos**

muscle (skinned), which is composed of bundles of smooth muscle fibers. The dartos muscle is also found in the subcutaneous layer of the scrotum.

Associated with each testis in the scrotum is the **cremaster muscle** (suspender), which is skeletal muscle.

The location of the scrotum and the contraction of its muscle fibers regulate the temperature of the testes. Normal sperm production requires a temperature about 2–3 ^{0}C below core body temperature. This lowered temperature is maintained within the scrotum because it is outside the pelvic cavity. In response to cold temperatures, the cremaster and dartos muscles contract. **Contraction of the cremaster muscles** moves the testes closer to the body, where they can absorb body heat. **Contraction of the dartos** muscle causes the scrotum to become tight, which reduces heat loss. Exposure to warmth reverses these actions.



Anterior view of scrotum and testes and transverse section of penis

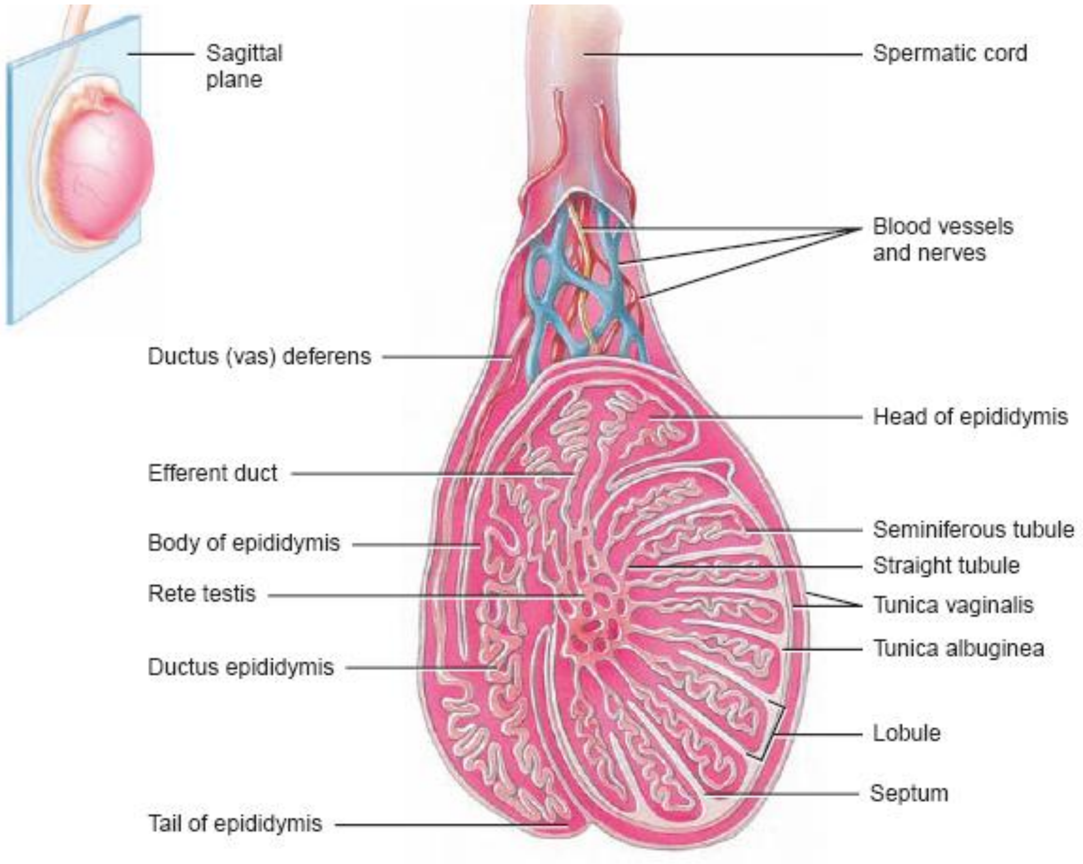
TESTES

The **testes**, or **testicles,** are paired oval glands in the scrotum measuring about 5 cm long and 2.5 cm in diameter. Each testis has a mass of 10–15 grams. The testes develop near the kidneys, in the posterior portion of the abdomen, and they usually begin their descent into the scrotum through the inguinal canals during the latter half of the seventh month of fetal development.

A serous membrane called the **tunica vaginalis** which is derived from the peritoneum and forms during the descent of the testes, partially covers the testes.).

Internal to the tunica vaginalis is a white fibrous capsule composed of dense irregular connective tissue, the **tunica albuginea** (white); it extends inward, forming septa that divide the testis into a series of internal compartments called **lobules.** Each of the 200–300 lobules contains one to three tightly coiled tubules, the **seminiferous tubules** where sperm are produced.

The process by which the seminiferous tubules of the testes produce sperm is called spermatogenesis.



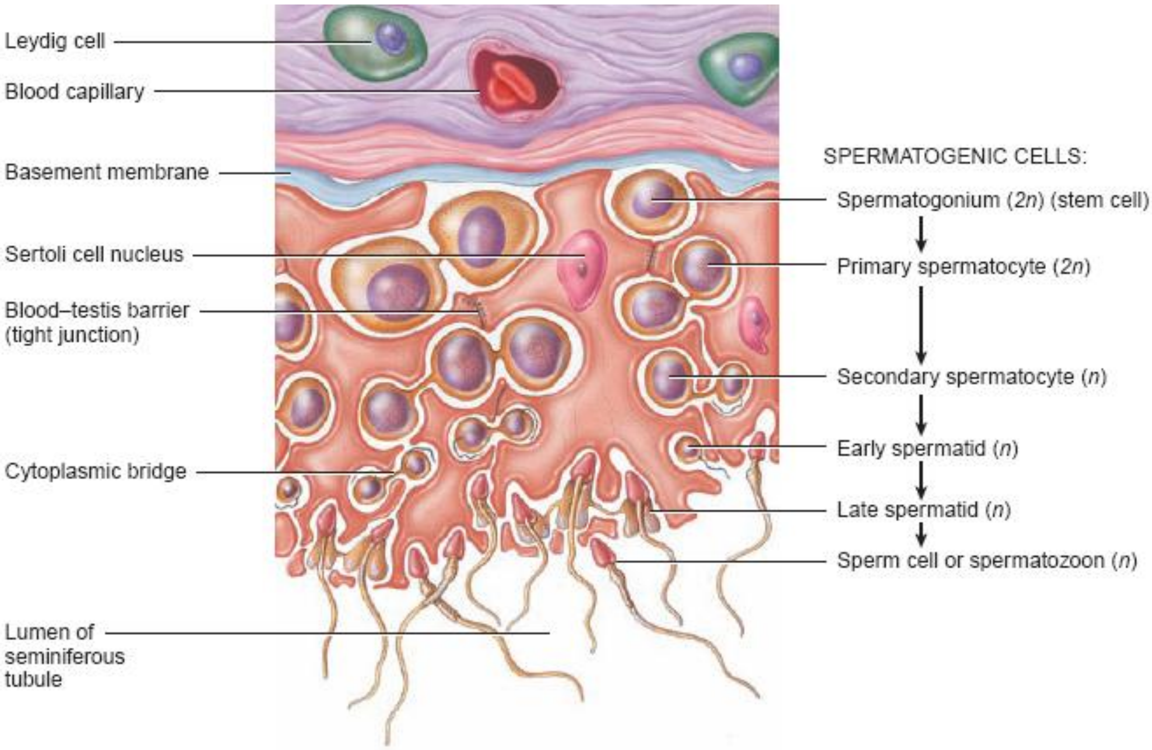
(a) Sagittal section of a testis showing seminiferous tubules

The seminiferous tubules contain **two types** of cells: **spermatogenic cells,** the sperm-forming cells, and **Sertoli cells,** which have several functions in supporting spermatogenesis

Stem cells called **spermatogonia** develop from **primordial germ cells** that arise from the yolk sac and enter the testes during the fifth week of development. In the embryonic testes, the primordial germ cells differentiate into spermatogonia, which remain dormant during childhood and actively begin producing sperm at puberty.

Toward the lumen of the seminiferous tubule are layers of progressively more mature cells. In order of advancing maturity, these are **primary spermatocytes, secondary spermatocytes, spermatids, and sperm cells**. After a **sperm cell,** or **spermatozoon** has formed, it is released into the lumen of the seminiferous tubule.

Embedded among the spermatogenic cells in the seminiferous tubules are large **Sertoli cells** which extend from the basement membrane to the lumen of the tubule. Internal to the basement membrane and spermatogonia, tight junctions join neighboring Sertoli cells to one another. These junctions form an obstruction known as the **blood–testis barrier** because substances must first pass through the Sertoli cells before they can reach the developing sperm. By isolating the developing gametes from the blood, the blood–testis barrier prevents an immune response against the spermatogenic cell's surface antigens, which are recognized as foreign by the immune system.



(b) Transverse section of a portion of a seminiferous tubule

Sertoli cells support and protect developing spermatogenic cells in several ways. They nourish spermatocytes, spermatids, and sperm; phagocytize excess spermatid cytoplasm as development proceeds; and control movements of spermatogenic cells and the release of sperm into the lumen of the seminiferous tubule. They also produce fluid for sperm transport, secrete the hormone inhibin, and regulate the effects of testosterone and FSH (follicle-stimulating hormone).

In the spaces between adjacent seminiferous tubules are clusters of cells called **Leydig (interstitial) cells.** These cells secrete **testosterone,** the most **prevalent androgen**. An **androgen** is a hormone that promotes the development of masculine characteristics. Testosterone also promotes a man's libido.

Spermatogenesis

In humans, spermatogenesis takes 65–75 days. It begins with the spermatogonia, which contain the diploid (2*n*) number of chromosomes. Spermatogonia are types of stem cells*;* when they undergo mitosis, some spermatogonia remain near the basement membrane of the seminiferous tubule in an undifferentiated state to serve as a reservoir of cells for future cell division and subsequent sperm production. The rest of the spermatogonia lose contact with the basement membrane, squeeze through the tight junctions of the blood–testis barrier, undergo developmental changes, and differentiate into **primary spermatocytes**. Primary spermatocytes, like spermatogonia, are diploid (2*n*); that is, they have 46 chromosomes.

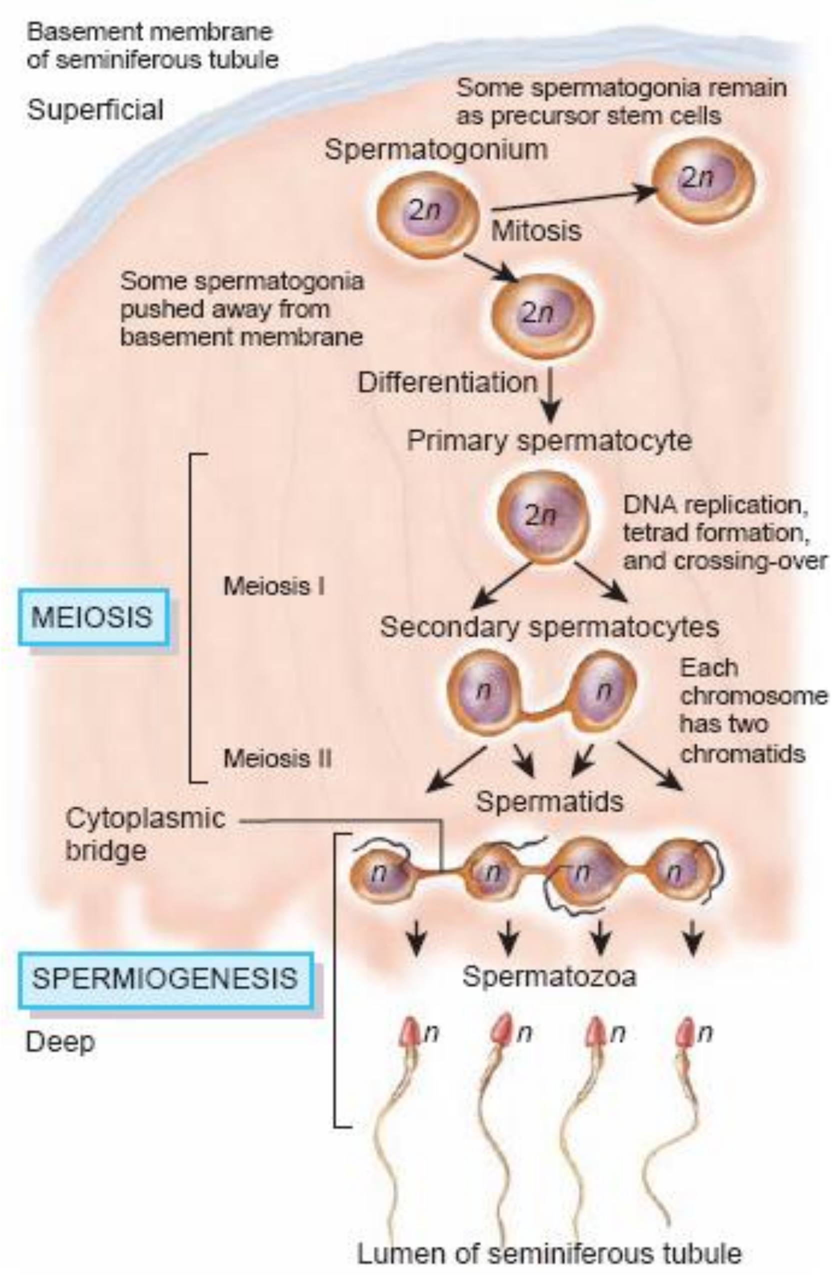
Shortly after it forms, each primary spermatocyte replicates its DNA and then meiosis begins.

In meiosis I, homologous pairs of chromosomes line up at the metaphase plate, and crossing-over occurs. Then, the meiotic spindle pulls one (duplicated) chromosome of each pair to an opposite pole of the dividing cell. The two cells formed by meiosis I are called **secondary spermatocytes.** Each secondary spermatocyte has 23 chromosomes, the haploid number (*n*). Each chromosome within a secondary spermatocyte, however, is made up of two chromatids (two copies of the DNA) still attached by a centromere.

In meiosis II, the chromosomes line up in single file along the metaphase plate, and the two chromatids of each chromosome separate. The four haploid cells resulting from meiosis II are called **spermatids.** A single primary spermatocyte therefore produces four **spermatids** via two rounds of cell division (meiosis I and meiosis II).

The final stage of spermatogenesis, **spermiogenesis** is the development of haploid spermatids into sperm. No cell division occurs in spermiogenesis; each spermatid becomes a single

sperm cell. During this process, spherical spermatids transform into elongated, slender sperm. An acrosome forms atop the nucleus, which condenses and elongates, a flagellum develops, and mitochondria multiply. Sertoli cells dispose of the excess cytoplasm that sloughs off. Finally, sperm are released from their connections to Sertoli cells, an event known as **spermiation.** Sperm then enter the lumen of the seminiferous tubule. Fluid secreted by Sertoli cells pushes sperm along their way, toward the ducts of the testes.

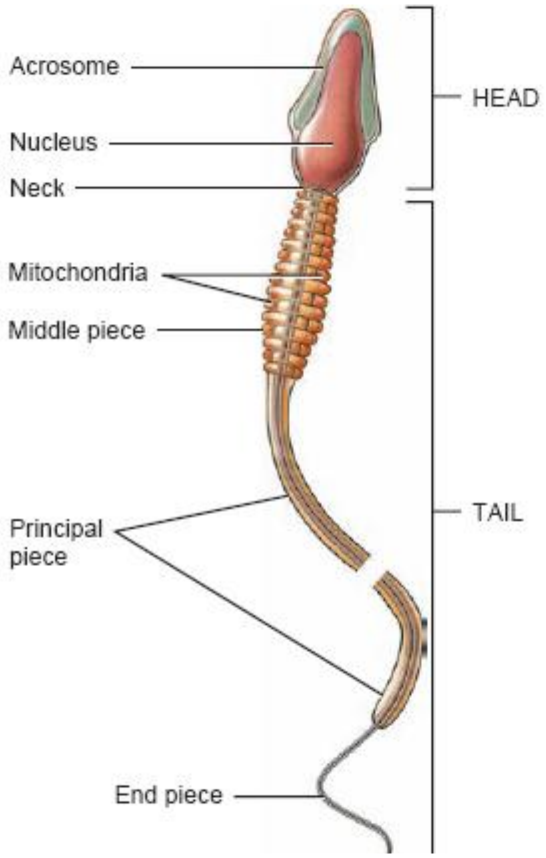


Sperm

Each day about 300 million sperm complete the process of spermatogenesis.

A sperm is about 60 micrometer long and contains several structures that are highly adapted for reaching and penetrating a secondary oocyte.

The major parts of a sperm are the **head and the tail**. The **head** of the sperm contains a **nucleus** with 23 highly condensed chromosomes. Covering the anterior two-thirds of the nucleus is the **acrosome**, a vesicle filled with enzymes that help a sperm to penetrate a secondary oocyte to bring about fertilization. Among the enzymes are **hyaluronidase** and **proteases**. The **tail** of a sperm is subdivided into **four parts**: **neck, middle piece, principal piece, and end piece.** The **neck** is the constricted region just behind the head that contains centrioles. The centrioles form the microtubules that comprise the remainder of the tail. The **middle piece** contains mitochondria arranged in a spiral, which provide the energy (ATP) for locomotion of sperm to the site of fertilization, and for sperm metabolism. The **principal piece** is the longest portion of the tail, and the **end piece** is the terminal, tapering portion of the tail. Once ejaculated, most sperm do not survive more than 48 hours within the female reproductive tract.



Hormonal Control of the Testes

Although the initiating factors are unknown, at puberty certain hypothalamic neurosecretory cells increase their secretion of **gonadotropin-releasing hormone (GnRH).** This hormone in turn stimulates gonadotrophs in the anterior pituitary to increase their secretion of the two gonadotropins, **luteinizing hormone (LH)** and **follicle-stimulating hormone (FSH).**

LH stimulates **Leydig cells**, which are located between seminiferous tubules, to secrete the hormone **testosterone.**

This steroid hormone is synthesized from cholesterol in the testes and is the principal androgen. It is lipid-soluble and readily diffuses out of Leydig cells into the interstitial fluid and then into blood. Via negative feedback, testosterone suppresses secretion of LH by anterior pituitary gonadotrophs and suppresses secretion of GnRH by hypothalamic neurosecretory cells. In some target cells, such as those in the external genitals and prostate, the enzyme 5 alpha-reductase converts testosterone to another androgen called **dihydrotestosterone (DHT).**

FSH acts indirectly to stimulate spermatogenesis FSH and testosterone act synergistically on the Sertoli cells to stimulate secretion of **androgen-binding protein (ABP)** into the lumen of the seminiferous tubules and into the interstitial fluid around the spermatogenic cells. ABP binds to testosterone, keeping its concentration high. Testosterone stimulates the final steps of spermatogenesis in the seminiferous tubules.

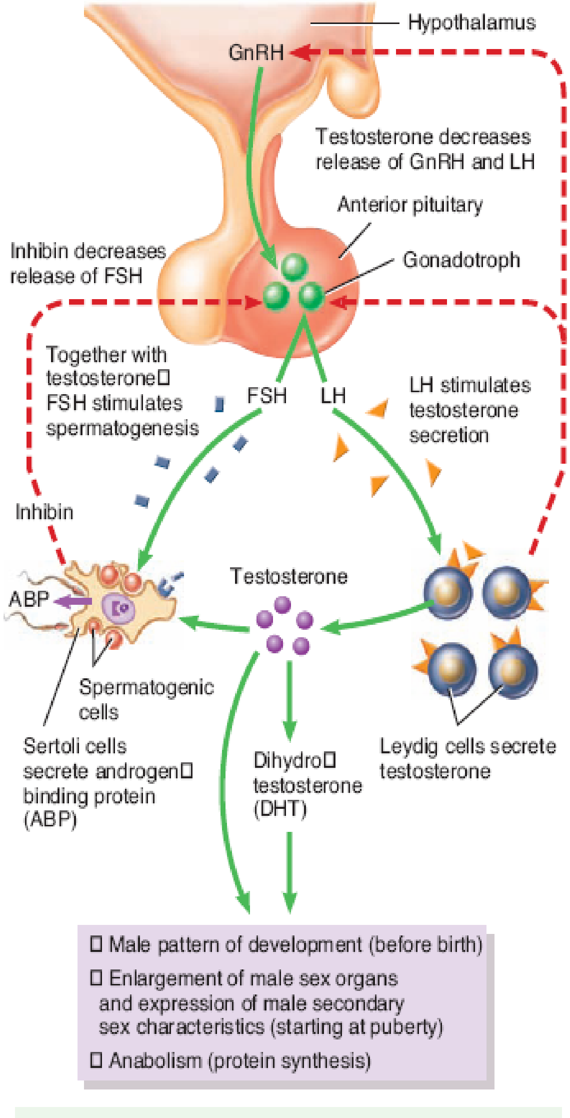
Once the degree of spermatogenesis required for male reproductive functions has been achieved, Sertoli cells release **inhibin,** a protein hormone named for its role in inhibiting FSH secretion by the anterior pituitary. If spermatogenesis is proceeding too slowly, less inhibin is released, which permits more FSH secretion and an increased rate of spermatogenesis.

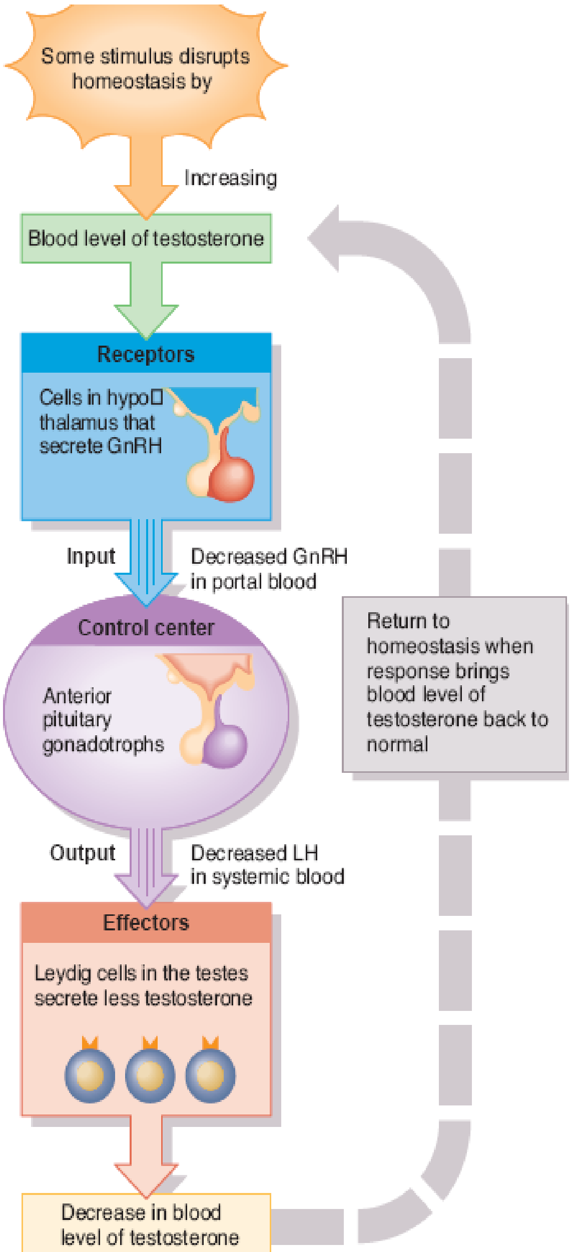
Testosterone and dihydrotestosterone both bind to the same androgen receptors, which are found within the nuclei of target cells. The hormone–receptor complex regulates gene expression, turning some genes on and others off. Because of these changes, the androgens produce several effects:

- **Prenatal development.** Before birth, testosterone stimulates the male pattern of development of reproductive system ducts and the descent of the testes. Dihydrotestosterone stimulates development of the external genitals.

  Testosterone also is converted in the brain to estrogens (feminizing hormones), which may play a role in the development of certain regions of the brain in males.

Release of FSH is stimulated by GnRH and inhibited by inhibin; release of LH is stimulated by GnRH and inhibited by testosterone.





- **Development of male sexual characteristics.** At puberty, testosterone and dihydrotestosterone bring about development and enlargement of the male sex organs and the development of masculine secondary sexual characteristics.

  Secondary sex characteristics are traits that distinguish males and females but do not have a direct role in reproduction.

  These include muscular and skeletal growth that results in wide shoulders and narrow hips; facial and chest hair and more hair on other parts of the body; thickening of the skin; increased sebaceous (oil) gland secretion; and enlargement of the larynx and consequent deepening of the voice.

- **Development of sexual function.** Androgens contribute to male sexual behavior and spermatogenesis and to sex drive (libido) in both males and females. The adrenal cortex is the main source of androgens in females.
- **Stimulation of anabolism.** Androgens are anabolic hormones; that is, they stimulate protein synthesis.

A negative feedback system regulates testosterone production. When testosterone concentration in the blood increases to a certain level, it inhibits the release of GnRH by cells in the hypothalamus. As a result, there is less GnRH in the portal blood that flows from the hypothalamus to the anterior pituitary.

Gonadotrophs in the anterior pituitary then release less LH, so the concentration of LH in systemic blood falls. With less stimulation by LH, the Leydig cells in the testes secrete less testosterone, and there is a return to homeostasis. If the testosterone concentration in the blood falls too low, however, GnRH is again released by the hypothalamus and stimulates secretion of LH by the anterior pituitary. LH in turn stimulates testosterone production by the testes.

REPRODUCTIVE SYSTEM DUCTS IN MALE

Ducts of the Testis

Pressure generated by the fluid secreted by Sertoli cells pushes sperm and fluid along the lumen of seminiferous tubules and then into a series of very short ducts called **straight tubules**. The straight tubules lead to a network of ducts in the testis called the **rete testis**. From the rete testis, sperm move into a series of coiled **efferent ducts** in the epididymis that empty into a single tube called the **ductus epididymis.**

Epididymis

The **epididymis** (epi- above or over; -didymis− testis) is a comma-shaped organ about 4 cm long that lies along the posterior border of each testis.

Each epididymis consists mostly of the tightly coiled **ductus epididymis.**

The efferent ducts from the testis join the ductus epididymis at the larger, superior portion of the epididymis called the **head.**

The **body** is the narrow midportion of the epididymis, and the **tail** is the smaller, inferior portion. At its distal end, the tail of the epididymis continues as the ductus (vas) deferens.

The ductus epididymis would measure about 6 m in length if it were uncoiled. Its lining surface contain **stereocilia,** which increase the surface area for the reabsorption of degenerated sperm.

Functionally, the epididymis is the site of **sperm maturation,** the process by which sperm acquire motility and the ability to fertilize an ovum. This occurs over a period of about 14 days.

The epididymis also helps **propel sperm** into the ductus (vas) deferens during sexual arousal by peristaltic contraction of its smooth muscle. In addition, the epididymis **stores sperm**, which remain viable here for up to several months. Any stored sperm that are not ejaculated by that time are eventually reabsorbed.

Ductus Deferens

Within the tail of the epididymis, the ductus epididymis becomes less convoluted, and its diameter increases. Beyond this point, the duct is known as the **ductus deferens** or **vas deferens.**

The ductus deferens, which is about 45 cm long, ascends along the posterior border of the epididymis through the spermatic cord and then enters the pelvic cavity. There it loops over the ureter and passes over the side and down the posterior surface of the urinary bladder.

The dilated terminal portion of the ductus deferens is the **ampulla.**

Functionally, the ductus deferens conveys sperm during sexual arousal from the epididymis toward the urethra by peristaltic contractions of its muscular coat. Like the epididymis, the ductus deferens also can store sperm for several months. Any stored sperm that are not ejaculated by that time are eventually reabsorbed.

Spermatic Cord

The **spermatic cord** is a supporting structure of the male reproductive system that ascends out of the scrotum. It consists of the ductus (vas) deferens as it ascends through the scrotum, the testicular artery, veins that drain the testes and carry testosterone into circulation (the pampiniform plexus), autonomic nerves, lymphatic vessels, and the cremaster muscle.

Ejaculatory Ducts

Each **ejaculatory duct** (ejacul- to expel) is about 2 cm long and is formed by the union of the duct from the seminal vesicle and the ampulla of the ductus (vas) deferens. The ejaculatory ducts form just superior to the base (superior portion) of the prostate and pass inferiorly and anteriorly through the prostate. They terminate in the prostatic urethra, where they eject sperm and seminal vesicle secretions just before the release of semen from the urethra to the exterior.

Urethra

In males, the **urethra** is the shared terminal duct of the reproductive and urinary systems; it serves as a passageway for both semen and urine. About 20 cm long, it passes through the prostate, the deep muscles of the perineum, and the penis, and is subdivided into three parts:
The **prostatic urethra** is 2–3 cm long and passes through the prostate.
As this duct continues inferiorly, it passes through the deep muscles of the perineum, where it is known as the **membranous urethra.** The membranous urethra is about 1 cm in length.
As this duct passes through the corpus spongiosum of the penis, it is known as the **spongy (penile) urethra,** which is about 15–20 cm long. The spongy urethra ends at the **external urethral orifice.**

ACCESSORY SEX GLANDS

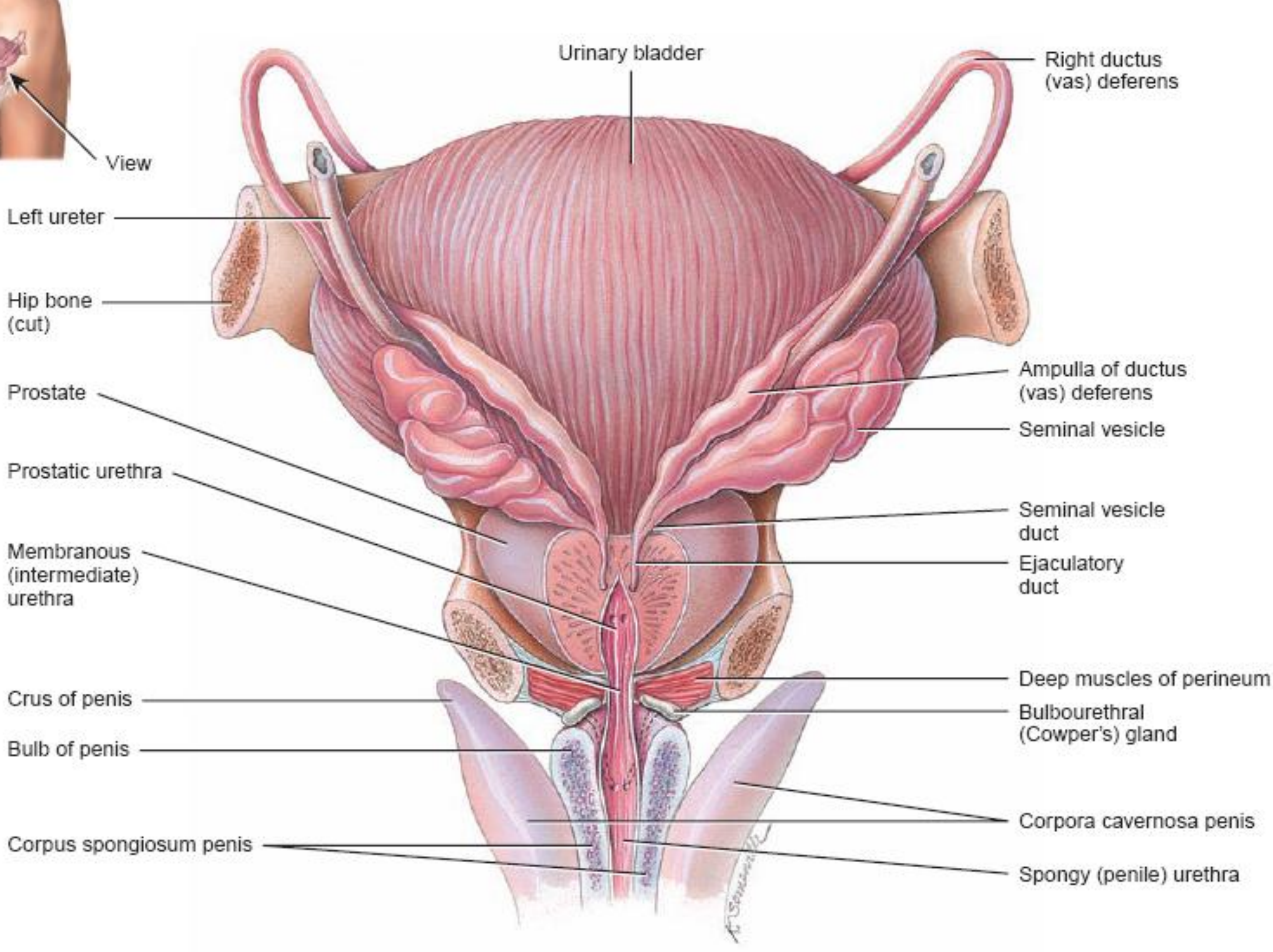
The ducts of the male reproductive system store and transport sperm cells, but the **accessory sex glands** secrete most of the liquid portion of semen. The accessory sex glands include the **seminal vesicles, the prostate, and the bulbourethral glands**.

Seminal Vesicles

The paired **seminal vesicles** or **seminal glands** are convoluted pouchlike structures, about 5 cm in length, lying posterior to the base of the urinary bladder and anterior to the rectum. Through the seminal vesicle ducts they secrete **an alkaline, viscous fluid** that contains fructose, prostaglandins, and clotting proteins that are different from those in blood. The **alkaline nature** of the seminal fluid helps to **neutralize the acidic** environment of the male urethra and female reproductive tract that otherwise would inactivate and kill sperm. The **fructose** is used for ATP production by sperm. **Prostaglandins** contribute to sperm motility and viability and may stimulate smooth muscle contractions within the female reproductive tract. The **clotting proteins** help semen coagulate after ejaculation. Fluid secreted by the seminal vesicles normally constitutes **about 60% of the volume of semen**.

Functions of Accessory Sex Gland Secretions

1. The seminal vesicles secrete alkaline, viscous fluid that helps neutralize acid in the female reproductive tract, provides fructose for ATP production by sperm, contributes to sperm motility and viability, and helps semen coagulate after ejaculation.
2. The prostate secretes a milky, slightly acidic fluid that helps semen coagulate after ejaculation and subsequently breaks down the clot.
3. The bulbourethral (Cowper's) glands secrete alkaline fluid that neutralizes the acidic environment of the urethra and mucus that lubricates the lining of the urethra and the tip of the penis during sexual intercourse.



(a) Posterior view of male accessory organs of reproduction

Prostate

The **prostate** is a single gland about the size of a golf ball. It measures about 4 cm from side to side, about 3 cm from top to bottom, and about 2 cm from front to back. It is inferior to the urinary bladder and surrounds the prostatic urethra.

The prostate secretes a milky, slightly **acidic fluid** (pH about 6.5) that contains **several substances.** (1) **Citric acid** in prostatic fluid is used by sperm for ATP production via the Krebs cycle.

(2) Several **proteolytic enzymes**, such as prostate-specific antigen *(PSA)*, pepsinogen, lysozyme, amylase, and hyaluronidase, eventually break down the clotting proteins from the seminal vesicles. (3) The function of the **acid phosphatase** secreted by the prostate is unknown. (4) **Seminalplasmin** in prostatic fluid is an antibiotic that can destroy bacteria. Seminalplasmin may help decrease the number of naturally occurring bacteria in semen and in the lower female reproductive tract.

Secretions of the prostate enter the prostatic urethra through **many prostatic ducts**. Prostatic secretions make up about 25% of the volume of semen and contribute to sperm motility and viability.

Bulbourethral Glands

The paired **bulbourethral glands** or **Cowper's glands,** are about the size of peas. They are located inferior to the prostate on either side of the membranous urethra within the deep muscles of the perineum, and their ducts open into the spongy urethra. During sexual arousal, the bulbourethral glands secrete an alkaline fluid into the urethra that protects the passing sperm by neutralizing acids from urine in the urethra. They also secrete mucus that lubricates the end of the penis and the lining of the urethra, decreasing the number of sperm damaged during ejaculation.

SEMEN

Semen is a mixture of **sperm** and **seminal fluid,** a liquid that consists of the secretions of the seminiferous tubules, seminal vesicles, prostate, and bulbourethral glands. The volume of semen in a typical ejaculation is 2.5–5 milliliter (mL), with 50–150 million sperm per mL. When the number falls below 20 million/mL, the male is likely to be infertile. A very large number of sperm is required for successful fertilization because only a tiny fraction ever reaches the secondary oocyte.

Despite the slight acidity of prostatic fluid, semen has a slightly alkaline pH of 7.2–7.7 due to the higher pH and larger volume of fluid from the seminal vesicles. The prostatic secretion gives semen a milky appearance, and fluids from the seminal vesicles and bulbourethral glands give it a sticky consistency.

Seminal fluid provides sperm with a transportation medium, nutrients, and protection from the hostile acidic environment of the male's urethra and the female's vagina.

Once ejaculated, liquid semen coagulates within 5 minutes due to the presence of clotting proteins from the seminal vesicles.

After about 10 to 20 minutes, semen reliquefies because prostate-specific antigen (PSA) and other proteolytic enzymes produced by the prostate break down the clot. Abnormal or delayed liquefaction of clotted semen may cause complete or partial immobilization of sperm, thereby inhibiting their movement through the cervix of the uterus.

PENIS

The **penis** contains the urethra and is a passageway for the ejaculation of semen and the excretion of urine. It is cylindrical in shape and consists of a **body, glans penis, and a root.**

The **body of the penis** is composed of **three cylindrical masses** of tissue, each surrounded by fibrous tissue called the **tunica albuginea.**

The **two dorsolateral** masses are called the **corpora cavernosa penis.**

The **smaller midventral** mass, the **corpus spongiosum penis,** contains the spongy urethra and keeps it open during ejaculation.

Skin and a subcutaneous layer enclose all three masses, which consist of **erectile tissue**. Erectile tissue is composed of numerous blood sinuses (vascular spaces) lined by endothelial cells and surrounded by smooth muscle and elastic connective tissue.

The distal end of the corpus spongiosum penis is a slightly enlarged region called the **glans penis;** its margin is the **corona.** The distal urethra enlarges within the glans penis and forms a terminal opening, the **external urethral orifice.**

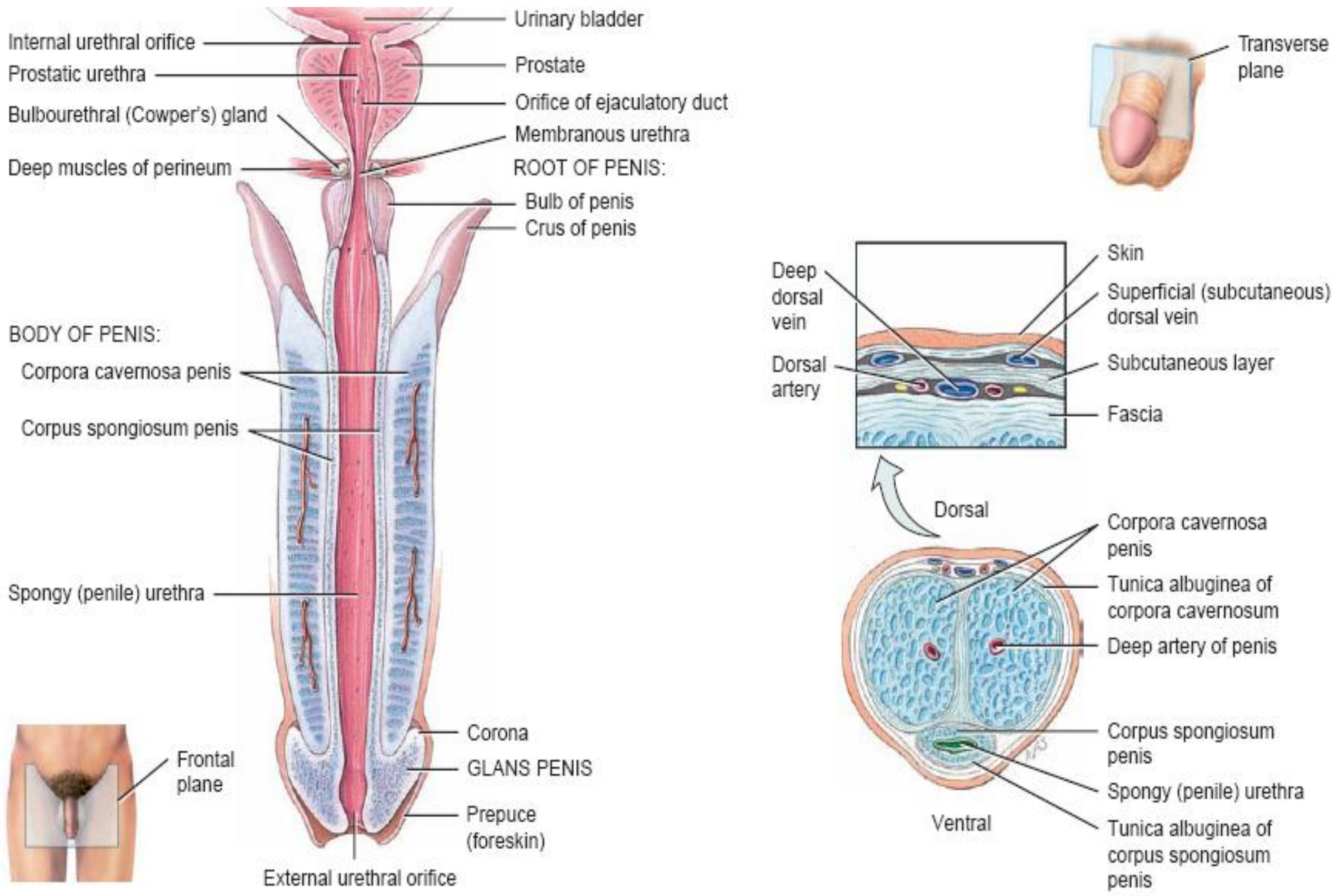
Covering the glans in an uncircumcised penis is the loosely fitting **prepuce** or **foreskin.**

The **root of the penis** is the attached portion (proximal portion).

It consists of the **bulb of the penis,** the expanded portion of the base of the corpus spongiosum penis, and the **crura of the penis** the two separated

and tapered portions of the corpora cavernosa penis.

The weight of the penis is supported by two ligaments that are continuous with the fascia of the penis. The **fundiform ligament** and the **suspensory ligament of the penis.**



(a) Frontal section (b) Transverse section

Upon **sexual stimulation** (visual, tactile, auditory, olfactory, or imagined), **parasympathetic fibers** from the sacral portion of the spinal cord initiate and maintain an **erection,** the enlargement and stiffening of the penis. The parasympathetic fibers release and cause local production of **nitric oxide (NO).** The NO causes smooth muscle in the walls of arterioles supplying erectile tissue to relax, which allows these blood vessels to dilate.

This in turn causes large amounts of blood to enter the erectile tissue of the penis. NO also causes the smooth muscle within the erectile tissue to relax, resulting in widening of the blood sinuses. The combination of **increased blood flow and widening** of the blood sinuses results in an erection. Expansion of the blood sinuses also compresses the veins that drain the penis; the slowing of blood outflow helps to maintain the erection.

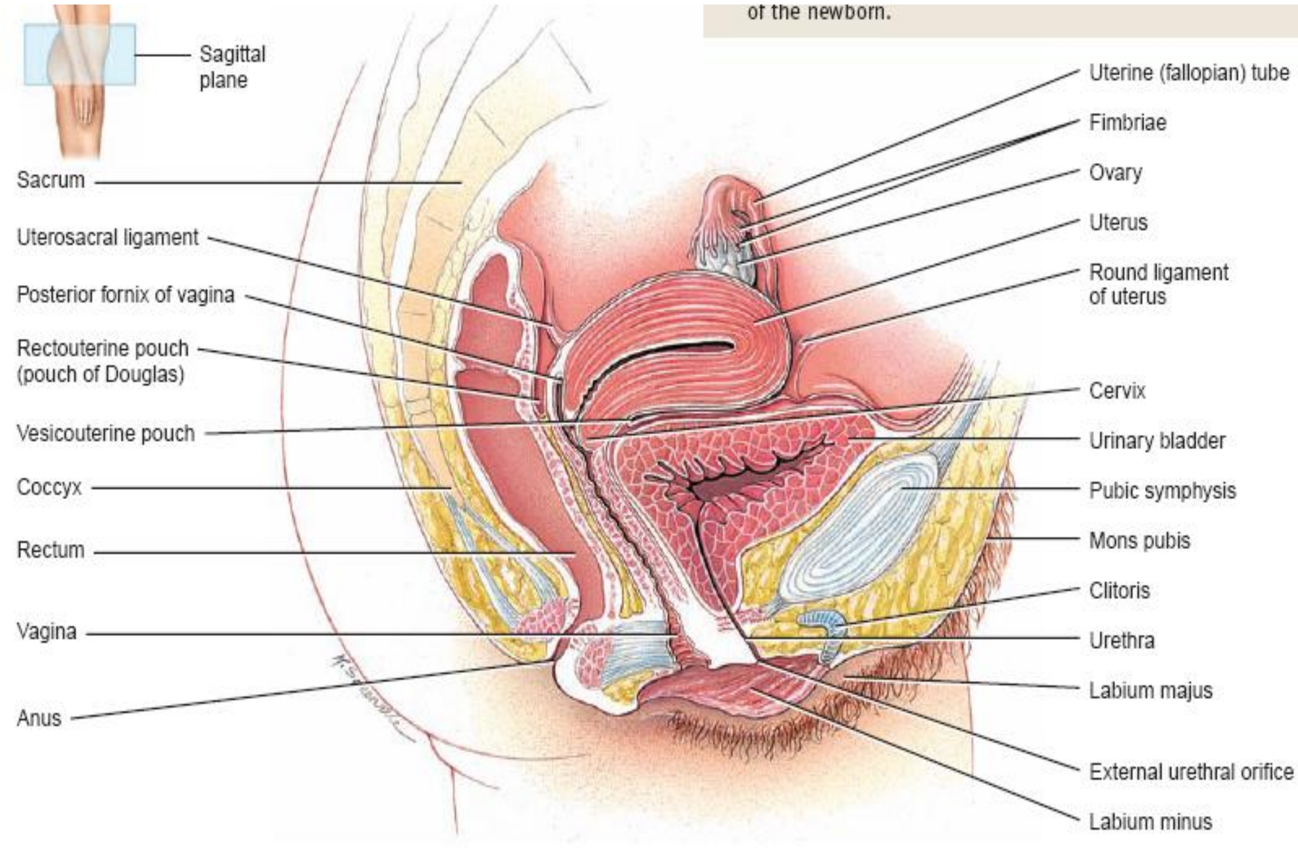
Once sexual stimulation of the penis has ended, the arterioles supplying the erectile tissue of the penis constrict and the smooth muscle within erectile tissue contracts, making the blood sinuses smaller. This relieves pressure on the veins supplying the penis and allows the blood to drain through them. Consequently, the penis returns to its flaccid (relaxed) state.

12.3 FEMALE REPRODUCTIVE SYSTEM

The organs of the **female reproductive system** include the **ovaries** (female gonads); the **uterine** (fallopian) tubes, or oviducts; **the uterus**; the **vagina**; and **external organs** which are collectively called the vulva, or pudendum. **The mammary glands** are considered part of both the integumentary system and the female reproductive system.

Functions of the Female Reproductive System

1. The ovaries produce secondary oocytes and hormones, including progesterone and estrogens (female sex hormones), inhibin, and relaxin.
2. The uterine tubes transport a secondary oocyte to the uterus and normally are the sites where fertilization occurs.
3. The uterus is the site of implantation of a fertilized ovum, development of the fetus during pregnancy, and labor.
4. The vagina receives the penis during sexual intercourse and is a passageway for childbirth.
5. The mammary glands synthesize, secrete, and eject milk for nourishment of the newborn.



(a) Sagittal section

OVARIES

The **ovaries** which are the female gonads, are paired glands.

The ovaries produce (1) **gametes**, secondary oocytes that develop into mature ova (eggs) after fertilization, and (2) **hormones**, including progesterone and estrogens (the female sex hormones), inhibin, and relaxin.

The ovaries, one on either side of the uterus, descend to the brim of the superior portion of the pelvic cavity during the third month of development.

A series of ligaments holds them in position:

The **broad ligament** of the uterus which is itself part of the parietal peritoneum, attaches to the ovaries by a double-layered fold of peritoneum called the **mesovarium.**

The **ovarian ligament** anchors the ovaries to the uterus, and

The **suspensory ligament** attaches them to the pelvic wall.

Each ovary contains a **hilum,** the point of entrance and exit for blood vessels and nerves along which the mesovarium is attached.

Histology of the Ovary

Each ovary consists of the following parts:

The **germinal epithelium** is a layer of simple epithelium that covers the surface of the ovary.

The **tunica albuginea** is a whitish capsule located immediately deep to the germinal epithelium.

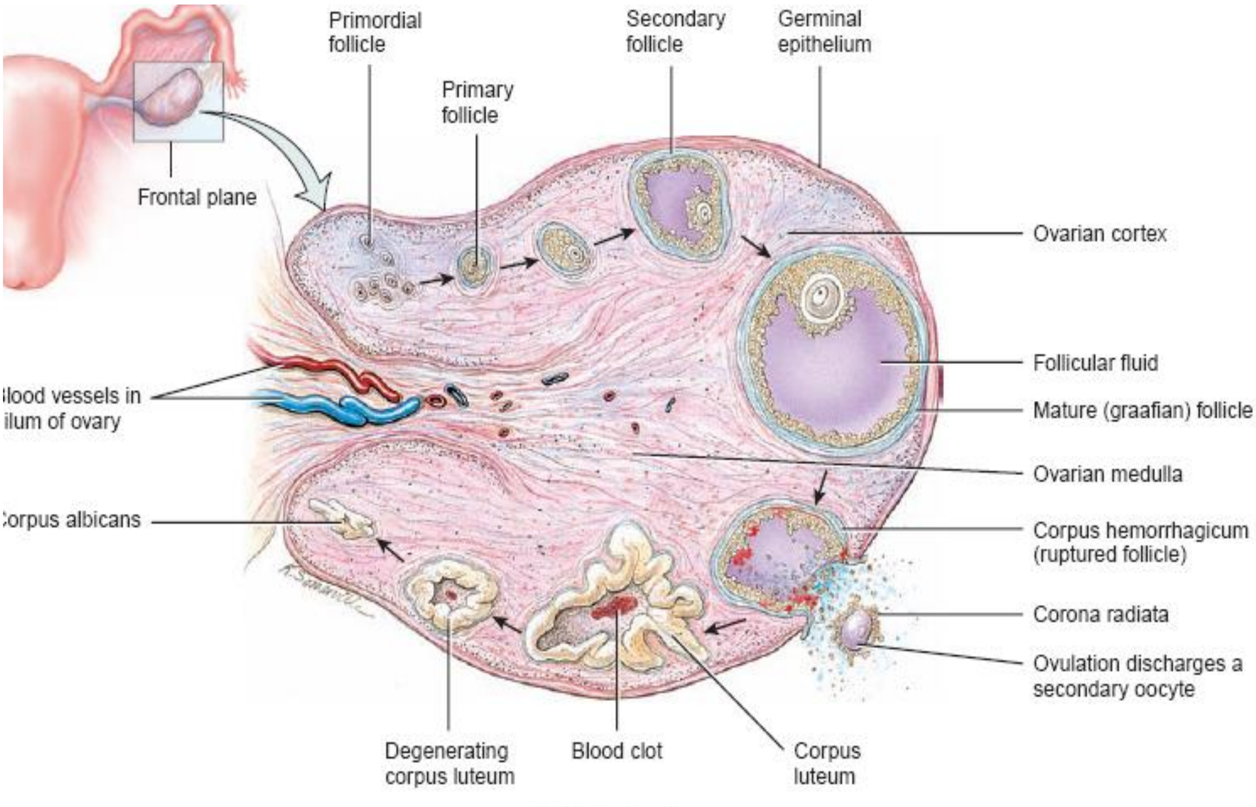
The **ovarian cortex** is a region just deep to the tunica albuginea. It consists of ovarian follicles surrounded by dense irregular connective tissue that contains collagen fibers and fibroblast-like cells called **stromal cells**.

The **ovarian medulla** is deep to the ovarian cortex. It consists of more loosely arranged connective tissue and contains **blood vessels, lymphatic vessels, and nerves.**

Ovarian follicles are in the cortex and consist of **oocytes** in various stages of development, plus the cells surrounding them. When the surrounding cells form a single layer, they are called **follicular cells;** later in development, when they form several layers, they are referred to as **granulosa cells.** The surrounding cells nourish the developing oocyte and begin to secrete estrogens as the follicle grows larger.

A **mature (graafian) follicle** is a large, fluid-filled follicle that is ready to rupture and expel its secondary oocyte, a process known as **ovulation.**

A **corpus luteum** (yellow body) contains the remnants of a mature follicle after ovulation. The corpus luteum produces progesterone, estrogens, relaxin, and inhibin until it degenerates into fibrous scar tissue called the **corpus albicans** (white body).



(a) Frontal section

Oogenesis and Follicular Development

The formation of gametes in the ovaries is termed **oogenesis**). In contrast to spermatogenesis, which begins in males at puberty, oogenesis begins in females before they are even born. Oogenesis occurs in essentially the same manner as spermatogenesis; meiosis takes place and the resulting germ cells undergo maturation. During early fetal development, primordial (primitive) germ cells migrate from the **yolk sac** to the ovaries. There, germ cells differentiate within the ovaries into **oogonia.**

Oogonia are diploid (2*n*) stem cells that divide mitotically to produce millions of germ cells. Even before birth, most of these germ cells degenerate in a process known as **atresia.** A few, however, develop into larger cells called **primary oocytes** that enter prophase of meiosis

I during fetal development but do not complete that phase until after puberty. During this arrested stage of development, each primary oocyte is surrounded by a single layer of **flat follicular cell**s, and the entire structure is called a **primordial follicle**

The ovarian cortex surrounding the primordial follicles consists of collagen fibers and fibroblast-like **stromal cells.**

At birth, approximately 200,000 to 2,000,000 primary oocytes remain in each ovary. Of these, about 40,000 are still present at puberty, and around 400 will mature and ovulate during a woman's reproductive lifetime. The remainder of the primary oocytes undergo atresia.

Each month after puberty until menopause, gonadotropins (FSH and LH) secreted by the anterior pituitary further stimulate the development of several primordial follicles, although only one will typically reach the maturity needed for ovulation.

A few primordial follicles start to grow, developing into **primary follicles.**

Each primary follicle consists of a primary oocyte that is surrounded in a later stage of development by several layers of cuboidal and low-columnar cells called **granulose cells.** The outermost granulosa cells rest on a basement membrane.

As the primary follicle grows, it forms a clear glycoprotein layer called the **zona pellucida** between the primary oocyte and the granulosa cells. In addition, stromal cells surrounding the basement membrane begin to form an organized layer called the **theca folliculi.**

With continuing maturation, a primary follicle develops into a secondary follicle.

In a **secondary follicle,** the theca differentiates into two layers: (1) the **theca interna,** a highly vascularized internal layer of cuboidal secretory cells that secrete **estrogens** and (2) the **theca externa,** an outer layer of stromal cells and collagen fibers.

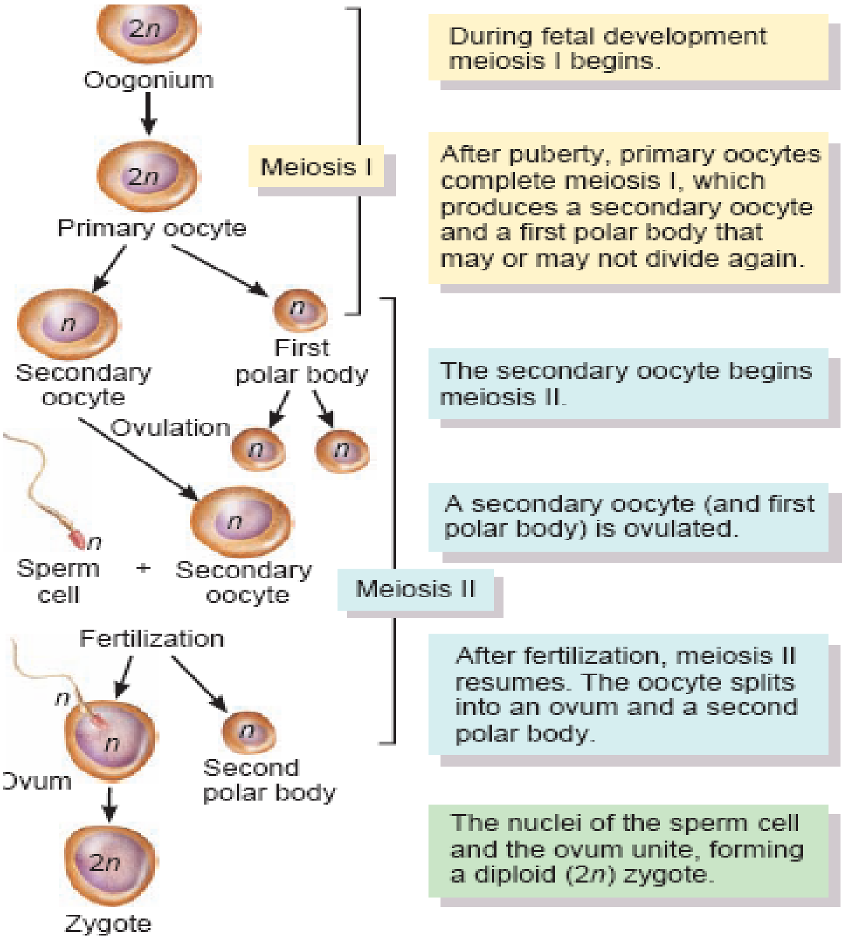
In addition, the granulosa cells begin to secrete follicular fluid, which builds up in a cavity called the **antrum** in the center of the secondary follicle. The innermost layer of granulosa cells becomes firmly attached to the zona pellucida and is now called the **corona radiata**

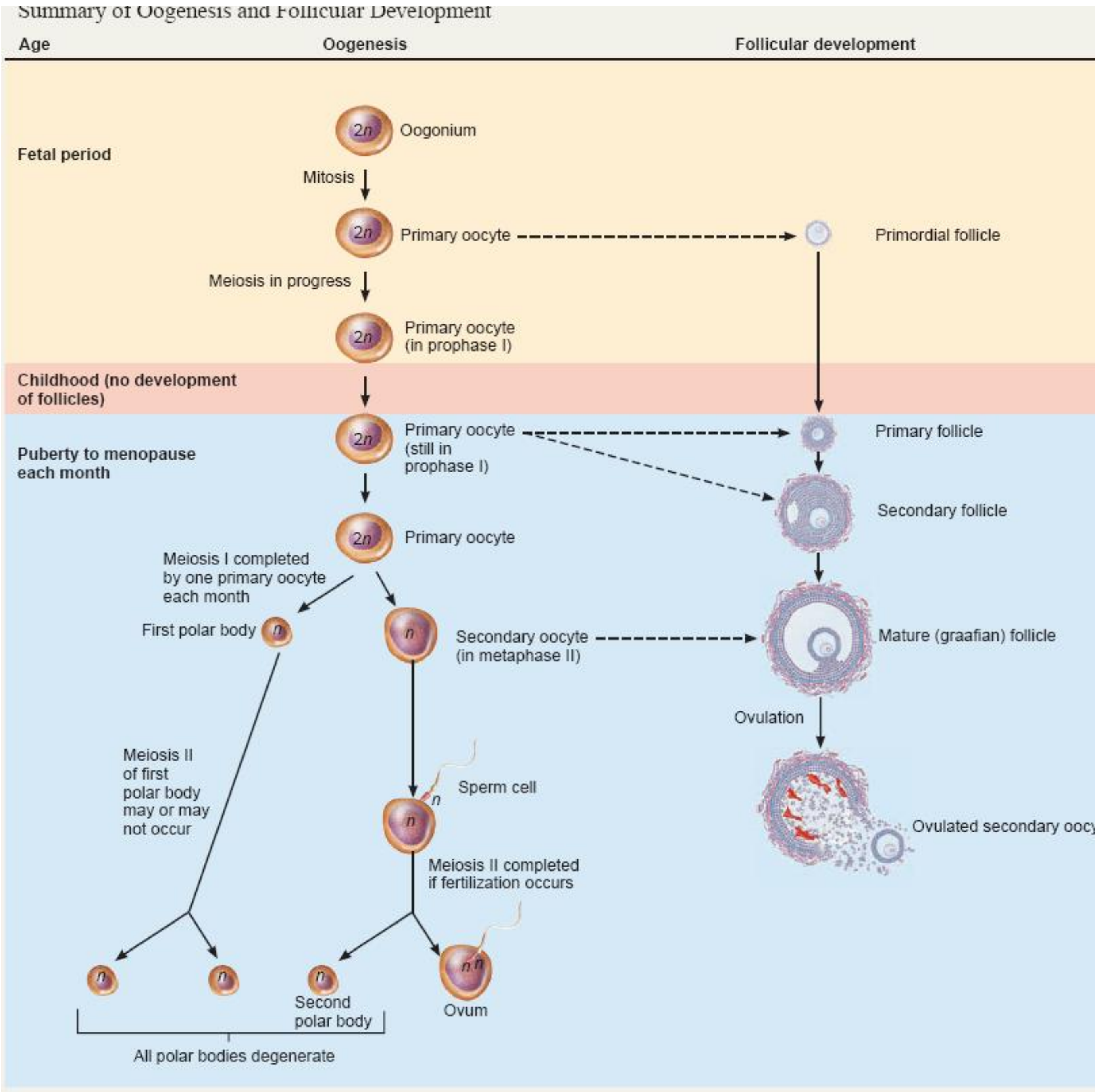
The secondary follicle eventually becomes larger, turning into a **mature (graafian) follicle**. While in this follicle, and just before ovulation, the diploid primary oocyte completes meiosis I, producing two haploid (*n*) cells **of unequal size** each with **23 chromosomes**. The **smaller cell** produced by meiosis I, called the **first polar body,** is essentially a packet of discarded nuclear material. The **larger cell**, known as the **secondary oocyte,** receives most of the cytoplasm.

Once a secondary oocyte is formed, it begins meiosis II but then stops in metaphase. The mature (graafian) follicle soon ruptures and releases its secondary oocyte, a process known as **ovulation.**

At ovulation, the secondary oocyte is expelled into the pelvic cavity together with the first polar body and corona radiata.

Normally these cells are swept into the uterine tube. If fertilization does not occur, the cells degenerate. If sperm are present in the uterine tube and one penetrates the secondary oocyte, however, meiosis II resumes. The secondary oocyte splits into two haploid cells, again of unequal size. The larger cell is the **ovum,** or mature egg; the smaller one is the **second polar body.** The nuclei of the sperm cell and the ovum then unite, forming a diploid **zygote.** If the first polar body undergoes another division to produce two polar bodies, then the primary oocyte ultimately gives rise to three haploid polar bodies, which all degenerate, and a single haploid ovum. Thus, one primary oocyte gives rise to a single gamete (an ovum). By contrast, recall that in males one primary spermatocyte produces four gametes (sperm).





UTERINE TUBES

Females have two **uterine (fallopian) tubes,** or **oviducts,** that extend laterally from the uterus. The tubes, which measure about 10 cm long, lie between the folds of the broad ligaments of the uterus. They provide a route for sperm to reach an ovum and transport secondary oocytes and fertilized ova from the ovaries to the uterus.

The funnel-shaped portion of each tube, called the **infundibulum,** is close to the ovary but is open to the pelvic cavity. It ends in a fringe (border) of fingerlike projections called **fimbriae**, one of which is attached to the lateral end of the ovary.

The **ampulla** of the uterine tube is the widest, longest portion, making up about the lateral two-thirds of its length.

The **isthmus** of the uterine tube is the more medial, short, narrow, thick-walled portion that joins the uterus.

Histologically, the uterine tubes are composed of three layers: **mucosa, muscularis, and serosa.**

The **mucosa** consists of epithelium and lamina propria (areolar connective tissue). The epithelium contains ciliated simple columnar cells, which help move a fertilized ovum (or secondary oocyte) within the uterine tube toward the uterus, and nonciliated cells called **peg cells**, which have microvilli and secrete a fluid that provides nutrition for the ovum.

The **muscularis**, is composed of smooth. Peristaltic contractions of the muscularis and the ciliary action of the mucosa help move the oocyte or fertilized ovum toward the uterus.

The **outer layer** of the uterine tubes is a serous membrane, the **serosa.**

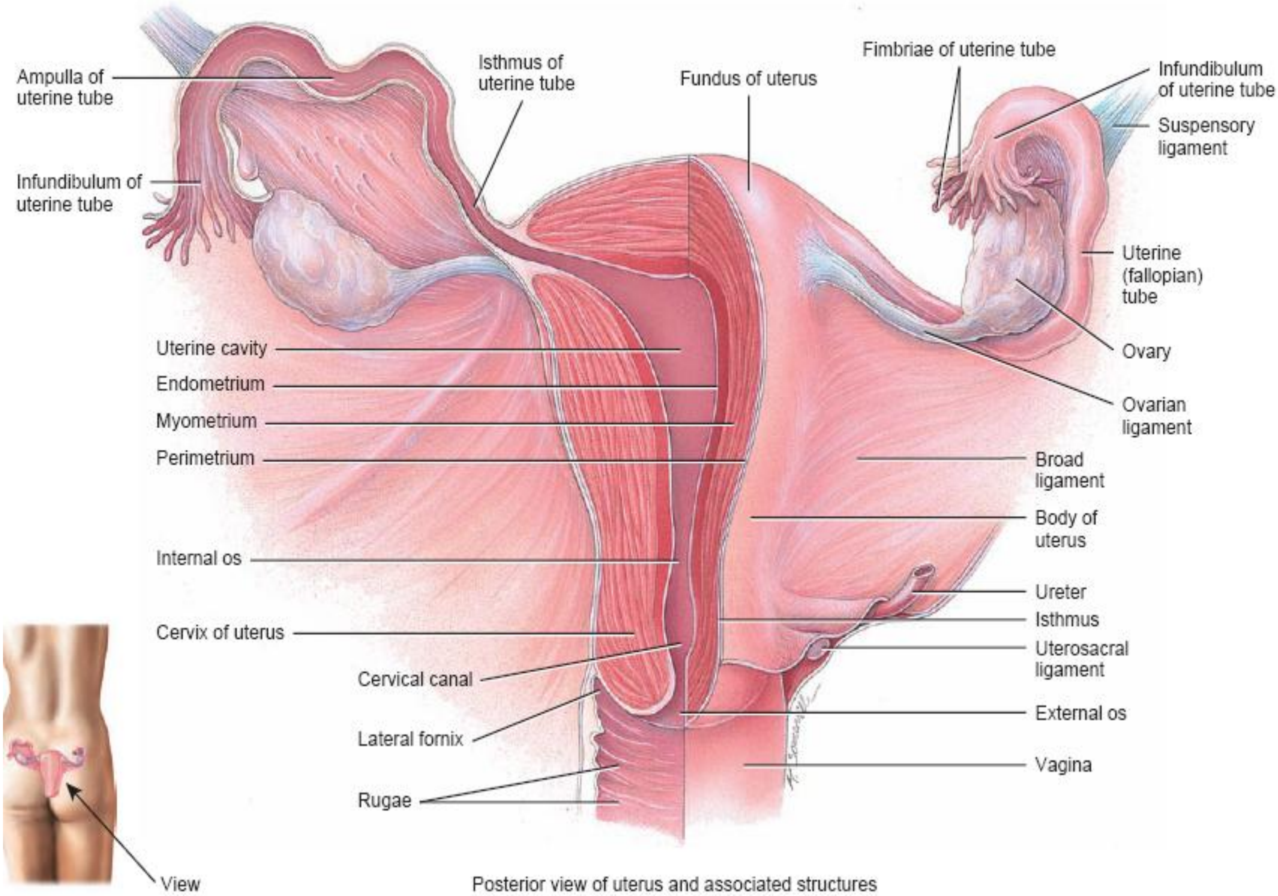
Local currents produced by movements of the fimbriae, which surround the ovary during ovulation, sweep the ovulated secondary oocyte from the pelvic cavity into the uterine tube. A sperm cell usually encounters and fertilizes a secondary oocyte in the ampulla of the uterine tube, although fertilization in the pelvic cavity is not uncommon. Fertilization can occur at any time up to about 24 hours after ovulation. Some hours after fertilization, the nuclear materials of the haploid ovum and sperm unite. The diploid fertilized ovum is now called a **zygote** and begins to undergo cell divisions while moving toward the uterus. It arrives at the uterus **6 to 7 days** after ovulation.

UTERUS

The **uterus** serves as part of the **pathway** for sperm deposited in the vagina to reach the uterine tubes. It is also the site of **implantation** of a fertilized ovum, **developmen**t of the fetus during pregnancy, and labor. During reproductive cycles when implantation does not occur, the uterus is the source of **menstrual flow.**

Anatomy of the Uterus

Situated between the urinary bladder and the rectum, the uterus is the size and shape of an inverted pear.



Posterior view of uterus and associated structures

In females who have never been pregnant, it is about 7.5 cm long, 5 cm wide, and 2.5 cm thick. The uterus is larger in females who have recently been pregnant, and smaller (atrophied) when sex hormone levels are low, as occurs after menopause.

Anatomical subdivisions of the uterus include: (1) a domeshaped portion superior to the uterine tubes called the **fundus,** (2) a tapering central portion called the **body,** and (3) an inferior narrow portion called the **cervix** that opens into the vagina.

Between the body of the uterus and the cervix is the **isthmus**, a constricted region about 1 cm long. The interior of the body of the uterus is called the **uterine cavity,** and the interior of the cervix is called the **cervical canal.** The cervical canal opens into the uterine cavity at the **internal os** (os-mouthlike opening) and into the vagina at the **external os.**

Several ligaments that are either extensions of the parietal peritoneum or fibromuscular cords maintain the position of the uterus:

The paired **broad ligaments** are double folds of peritoneum attaching the uterus to either side of the pelvic cavity.

The paired **uterosacral ligaments,** also peritoneal extensions, lie on either side of the rectum and connect the uterus to the sacrum.

The **cardinal (lateral cervical) ligaments** are located inferior to the bases of the broad ligaments and extend from the pelvic wall to the cervix and vagina.

The **round ligaments** are bands of fibrous connective tissue between the layers of the broad ligament; they extend from a point on the uterus just inferior to the uterine tubes to a portion of the labia majora of the external genitalia.

Although the ligaments normally maintain the anteflexed position of the uterus, they also allow the uterine body enough movement such that the uterus may become malpositioned.

Histology of the Uterus

Histologically, the uterus consists of three layers of tissue: **perimetrium, myometrium, and endometrium**.

The **outer layer**, the **perimetrium** or serosa is part of the visceral peritoneum; it is composed of simple squamous epithelium and areolar connective tissue.

Laterally, it becomes the broad ligament. Anteriorly, it covers the urinary bladder and forms a shallow pouch, the **vesicouterine pouch**.

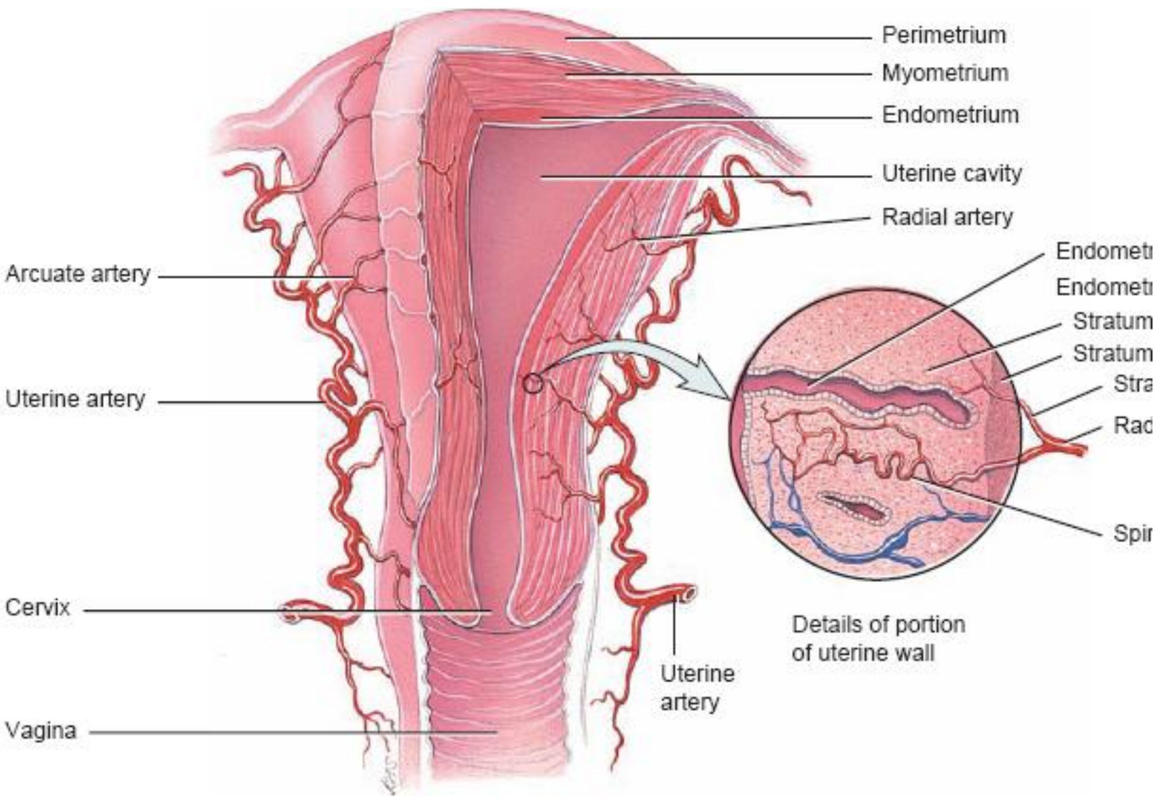
Posteriorly, it covers the rectum and forms a deep pouch between the uterus and urinary bladder, the **rectouterine pouch** or **pouch of Douglas** the most inferior point in the pelvic cavity.

The **middle layer** of the uterus, the **myometrium**, consists of **three layers** of smooth muscle fibers that are thickest in the fundus and thinnest in the cervix. During labor and childbirth, coordinated contractions of the myometrium in response to oxytocin from the posterior pituitary help expel the fetus from the uterus.

The **inner layer** of the uterus, the **endometrium**, is highly vascularized and has **three components**: (1) An **innermost layer** composed of simple columnar epithelium (ciliated and secretory cells) lines the lumen. (2) An underlying **endometrial stroma** is a very thick region of lamina propria (areolar connective tissue). (3) **Endometrial glands** develop as invaginations of the luminal epithelium and extend almost to the myometrium.

The endometrium is divided into **two layers**:

The **stratum functionalis** *(*functional layer*)* lines the uterine cavity and sloughs off during menstruation. The deeper layer, the **stratum basalis** (basal layer*)*, is permanent and gives rise to a new stratum functionalis after each menstruation.



Anterior view with left side of uterus partially sectioned

Branches of the internal iliac artery called **uterine arteries** supply blood to the uterus. Uterine arteries give off branches called **arcuate arteries** that are arranged in a circular fashion in the myometrium. These arteries branch into **radial arteries** that penetrate deeply into the myometrium. Just before the branches enter the endometrium, they divide into two kinds of arterioles: **Straight arterioles** supply the stratum basalis with the materials needed to regenerate the stratum functionalis; **spiral arterioles** supply the stratum functionalis and change markedly during the menstrual cycle.

Blood leaving the uterus is drained by the **uterine veins** into the internal iliac veins. The extensive blood supply of the uterus is essential to support regrowth of a new stratum functionalis after menstruation, implantation of a fertilized ovum, and development of the placenta.

Cervical Mucus

The secretory cells of the mucosa of the cervix produce a secretion called **cervical mucus,** a mixture of water, glycoproteins, lipids, enzymes, and inorganic salts. During their reproductive years, females secrete 20–60 mL of cervical mucus per day.

Cervical mucus is more hospitable to sperm at or near the time of ovulation because it is then less viscous and more alkaline (pH 8.5). At other times, a more viscous mucus forms a cervical plug that physically impedes sperm penetration. Cervical mucus supplements the energy needs of sperm, and both the cervix and cervical mucus protect sperm from phagocytes and the hostile environment of the vagina and uterus. Cervical mucus may also play a role in **capacitation** a series of functional changes that sperm undergo in the female reproductive tract before they are able to fertilize a secondary oocyte. Capacitation causes a sperm cell's tail to beat even more vigorously, and it prepares the sperm cell's plasma membrane to fuse with the oocyte's plasma membrane.

VAGINA

The **vagina** is a tubular, 10cm long fibromuscular canal lined with mucous membrane that extends from the exterior of the body to the uterine cervix. It is the **receptacle for the penis during sexual intercourse, the outlet for menstrual flow, and the passageway for childbirth.** Situated between the urinary bladder and the rectum, the vagina is directed superiorly and posteriorly, where it attaches to the uterus.

A recess called the **fornix** surrounds the vaginal attachment to the cervix.

The **mucosa** of the vagina is continuous with that of the uterus.

Histologically, it consists of nonkeratinized stratified squamous epithelium and areolar connective tissue that lies in a series of transverse folds called **rugae**.

Dendritic cells in the mucosa are **antigen-presenting cells**. Unfortunately, they also participate in the transmission of viruses, for example, HIV to a female during intercourse with an infected male. The mucosa of the vagina contains large stores of **glycogen**, the decomposition of which produces **organic acids**. The resulting acidic environment retards microbial growth, but it also is harmful to sperm.

Alkaline components of semen, mainly from the seminal vesicles, raise the pH of fluid in the vagina and increase viability of the sperm.

The **muscularis** is composed of an outer circular layer and an inner longitudinal layer of smooth muscle that can stretch considerably to accommodate the penis during sexual intercourse and a child during birth.

The **adventitia,** the superficial layer of the vagina, consists of areolar connective tissue. It anchors the vagina to adjacent organs such as the urethra and urinary bladder anteriorly and the rectum and anal canal posteriorly.

A thin fold of vascularized mucous membrane, called the **hymen** (membrane), forms a border around and partially closes the inferior end of the vaginal opening to the exterior, the **vaginal orifice**. Sometimes the hymen completely covers the orifice, a condition called **imperforate hymen.**

VULVA

The term **vulva** refers to the external genitals of the female. The following components comprise the vulva:

Anterior to the vaginal and urethral openings is the **mons pubis**, an elevation of adipose tissue covered by skin and coarse pubic hair that cushions the pubic symphysis.

From the mons pubis, two longitudinal folds of skin, the **labia majora (** labia - lips; majora-larger), extend inferiorly and posteriorly.

The labia majora are covered by pubic hair and contain an abundance of adipose tissue, sebaceous (oil) glands, and apocrine sudoriferous (sweat) glands.

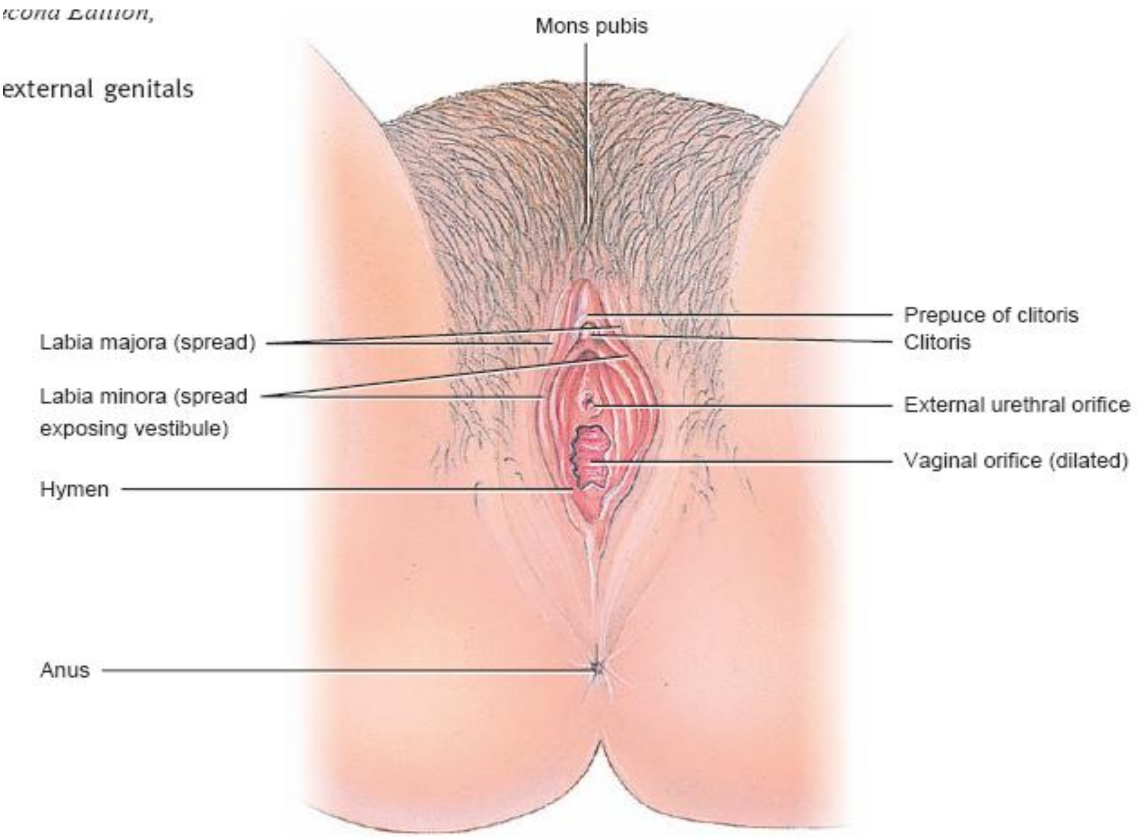
Medial to the labia majora are two smaller folds of skin called the **labia minora (**minora-smaller).Unlike the labia majora, the labia minora are devoid of pubic hair and fat and have few sudoriferous glands, but they do contain many sebaceous glands.

The **clitoris** (KLI-to-ris) is a small cylindrical mass composed of **two small erectile bodies**, the corpora cavernosa, and **numerous nerves and blood vessels**. The clitoris is located at the anterior junction of the labia minora. A layer of skin called the **prepuce of the clitoris** is formed at the point where the labia minora unite and covers the body of the clitoris. The exposed portion of the clitoris is the **glans clitoris.** Like the male structure, the clitoris is capable of enlargement upon tactile stimulation and has a role in sexual excitement in the female.

The region between the labia minora is the **vestibule.** Within the vestibule are the hymen (if still present), the vaginal orifice, the external urethral orifice, and the openings of the ducts of several glands. The **vaginal orifice** occupies the greater portion of the vestibule and is bordered by the hymen. Anterior to the vaginal orifice and posterior to the clitoris is the **external urethral orifice.**

On either side of the external urethral orifice are the openings of the ducts of the **paraurethral (Skene's) glands.** These mucus-secreting glands are embedded in the wall of the urethra.

On either side of the vaginal orifice itself are the **greater vestibular (Bartholin's) glands** which open by ducts into a groove between the hymen and labia minora. They produce a



(a) Inferior view

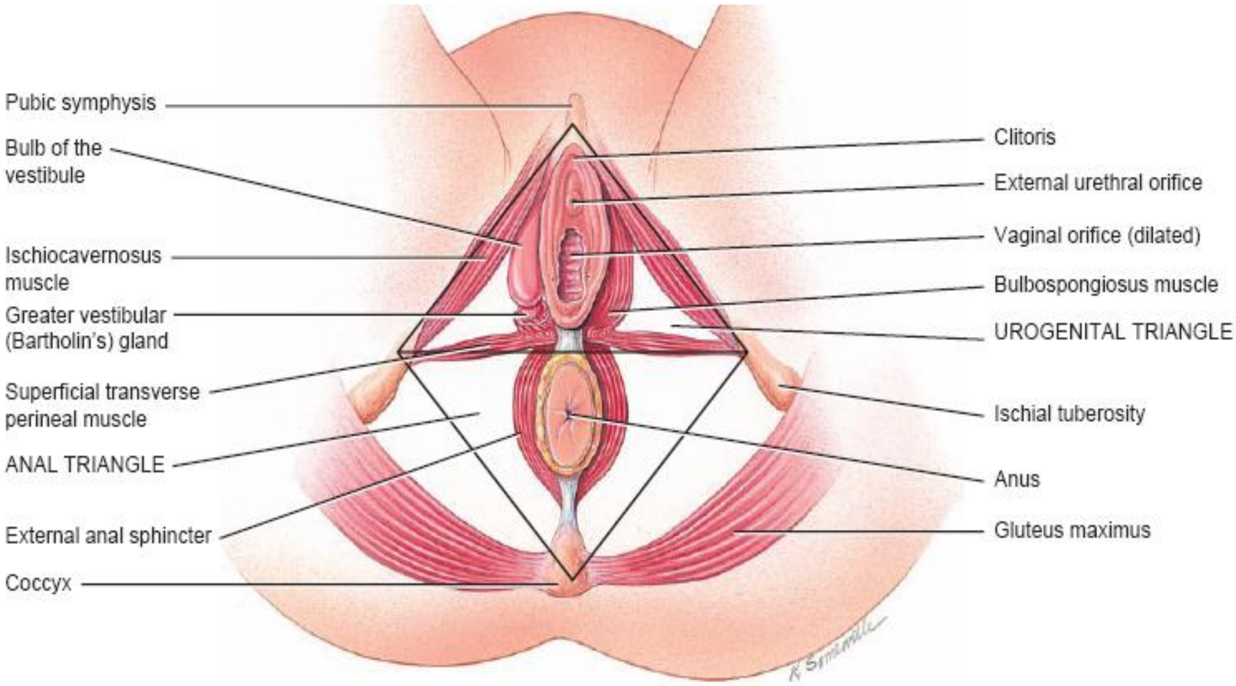
small quantity of mucus during sexual arousal and intercourse that adds to cervical mucus and provides lubrication.

Several **lesser vestibular glands** also open into the vestibule.

The **bulb of the vestibule** consists of two elongated masses of erectile tissue just deep to the labia on either side of the vaginal orifice. The bulb of the vestibule becomes engorged with blood during sexual arousal, narrowing the vaginal orifice and placing pressure on the penis during intercourse. The bulb of the vestibule is homologous to the corpus spongiosum and bulb of the penis in males.

PERINEUM

The **perineum** is the diamond-shaped area medial to the thighs and buttocks of both males and females. It contains the external genitals and anus. The perineum is bounded anteriorly by the pubic symphysis, laterally by the ischial tuberosities, and posteriorly by the coccyx. A transverse line drawn between the ischial tuberosities divides the perineum into an anterior **urogenital triangle** that contains the external genitals and a posterior **anal triangle** that contains the anus.



Inferior view

MAMMARY GLANDS

Each **breast** is a hemispheric projection of variable size anterior to the pectoralis major and serratus anterior muscles and attached to them by a layer of fascia composed of dense irregular connective tissue.

Each breast has one pigmented projection, the **nipple,** that has a series of closely spaced openings of ducts called **lactiferous ducts,** where milk emerges. The circular pigmented area of skin surrounding the nipple is called the **areola.**

The **suspensory ligaments of the breast (Cooper's ligaments)** run between the skin and fascia and support the breast.

Within each breast is a **mammary gland** that produces milk.

A mammary gland consists of **15 to 20 lobes, or compartments**. In each lobe are several smaller compartments called **lobules,** composed of grapelike clusters of milk-secreting glands termed **alveoli**. Contraction of **myoepithelial cells** surrounding the alveoli helps propel milk toward the nipples.

When milk is being produced, it passes from the alveoli into a series of **secondary tubules** and then into the **mammary ducts.** Near the nipple, the mammary ducts expand

to form sinuses called **lactiferous sinuses** where some milk may be stored before draining into a **lactiferous duct.** Each lactiferous duct typically carries milk from one of the lobes to the exterior.

The **functions** of the mammary glands are the synthesis, secretion, and ejection of milk; these functions, called **lactation.**

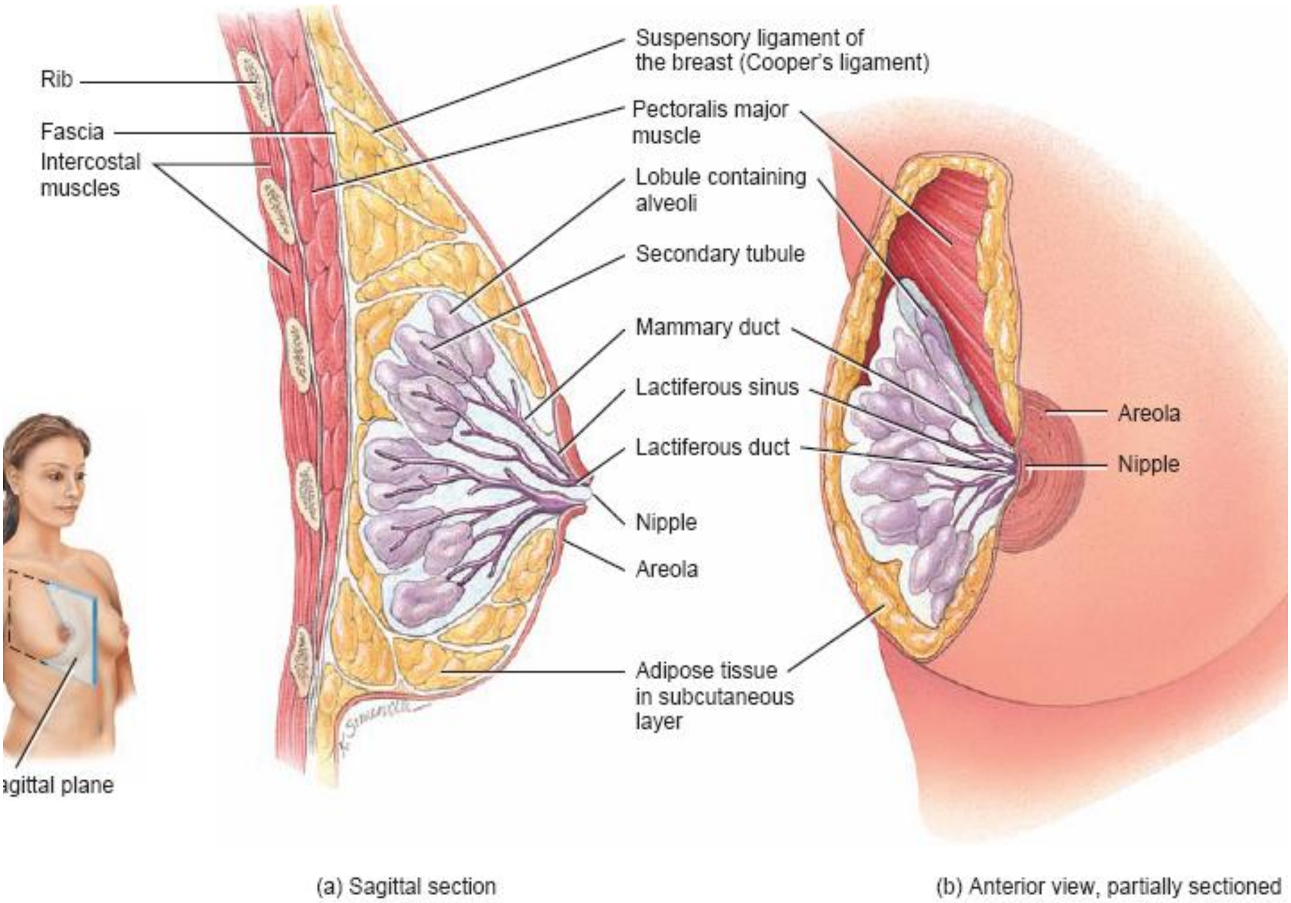


Figure: Mammary glands within the breasts

Milk production is stimulated largely by the hormone **prolactin** from the anterior pituitary, with contributions from **progesterone and estrogens**. The ejection of milk is stimulated by **oxytocin**, which is released from the posterior pituitary in response to the sucking of an infant on the mother’s nipple.

THE FEMALE REPRODUCTIVE CYCLE

During their reproductive years, non pregnant females normally show cyclical changes in the ovaries and uterus. Each cycle takes about a month and involves both oogenesis and preparation of the uterus to receive a fertilized ovum. Hormones secreted by the hypothalamus, anterior pituitary, and ovaries control the main events. The **ovarian cycle** is a series of events in the ovaries that occur during and after the maturation of an oocyte.

The **uterine (menstrual) cycle** is a concurrent series of changes in the endometrium of the uterus to prepare it for the arrival of a fertilized ovum that will develop there until birth. If fertilization does not occur, ovarian hormones diminish, which causes the stratum functionalis of the endometrium to slough off. The general term **female reproductive cycle** encompasses the ovarian and **uterine cycles, the hormonal changes that regulate them, and the related cyclical changes in the breasts and cervix.**

Hormonal regulation of the female reproductive cycle

Gonadotropin-releasing hormone (GnRH) secreted by the hypothalamus controls the ovarian and uterine cycles.

GnRH stimulates the release of **follicle-stimulating hormone (FSH)** and **luteinizing hormone (LH)** from the anterior pituitary. FSH initiates follicular growth, while LH stimulates further development of the ovarian follicles. In addition, both FSH and LH stimulate the ovarian follicles to secrete estrogens.

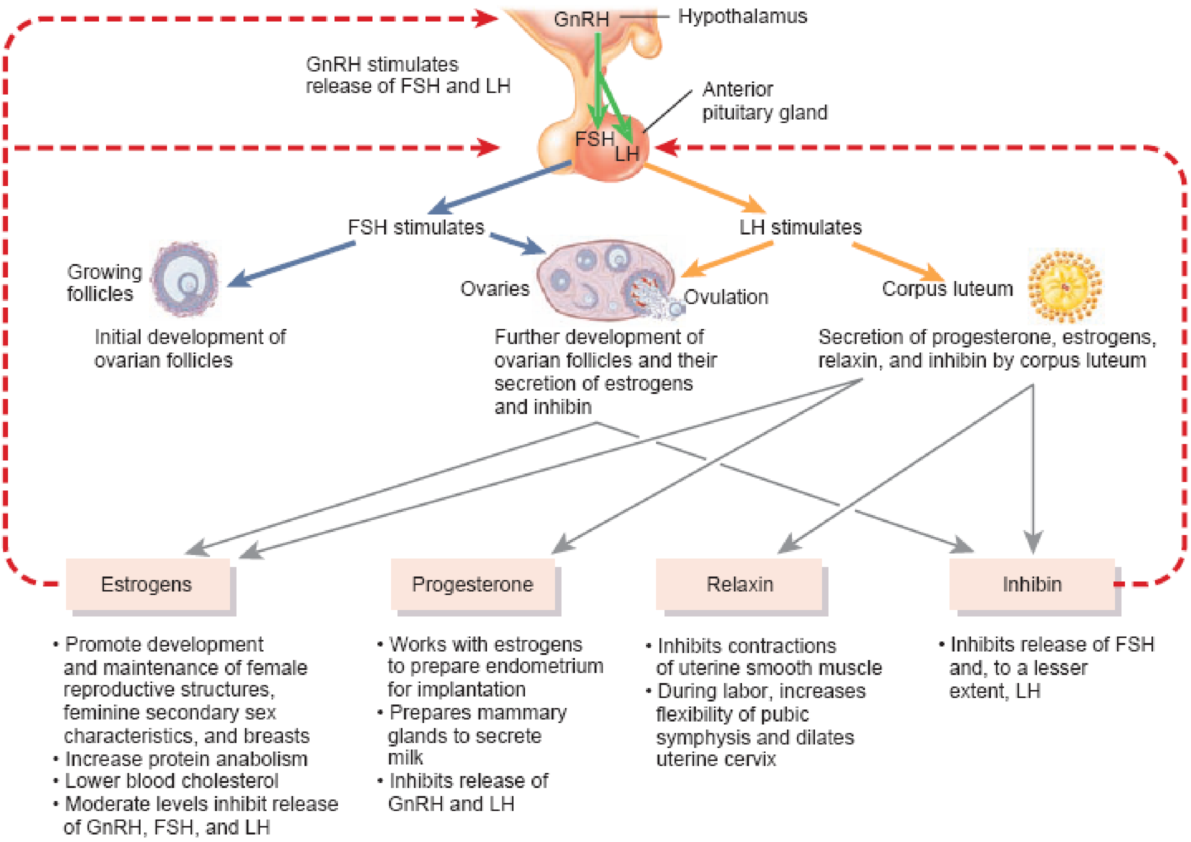
LH stimulates the theca cells of a developing follicle to produce androgens. Under the influence of FSH, the androgens are taken up by the granulosa cells of the follicle and then converted into estrogens. At midcycle, LH triggers ovulation and then promotes formation of the corpus luteum, the reason for the name luteinizing hormone. Stimulated by LH, the corpus luteum produces and secretes estrogens, progesterone, relaxin, and inhibin.

At least six different estrogens have been isolated from the plasma of human females, but only three are present in significant quantities: ***beta-estradiol, estrone,* and *estriol***. In a nonpregnant woman, the most abundant estrogen is ***beta*-estradiol**, which is synthesized from cholesterol in the ovaries.

Estrogens secreted by ovarian follicles have several important functions.

• Estrogens promote the development and maintenance of female reproductive structures, secondary sex characteristics, and the breasts. The secondary sex characteristics include distribution of adipose tissue in the breasts, abdomen, mons pubis, and hips; voice pitch; a broad pelvis; and pattern of hair growth on the head and body.

• Estrogens increase protein anabolism, including the building of strong bones. In this regard, estrogens are synergistic with human growth hormone (hGH).



• Estrogens lower blood cholesterol level, which is probably the reason that women under age 50 have a much lower risk of coronary artery disease than do men of comparable age.

• Moderate levels of estrogens in the blood inhibit both the release of GnRH by the hypothalamus and secretion of LH and FSH by the anterior pituitary.

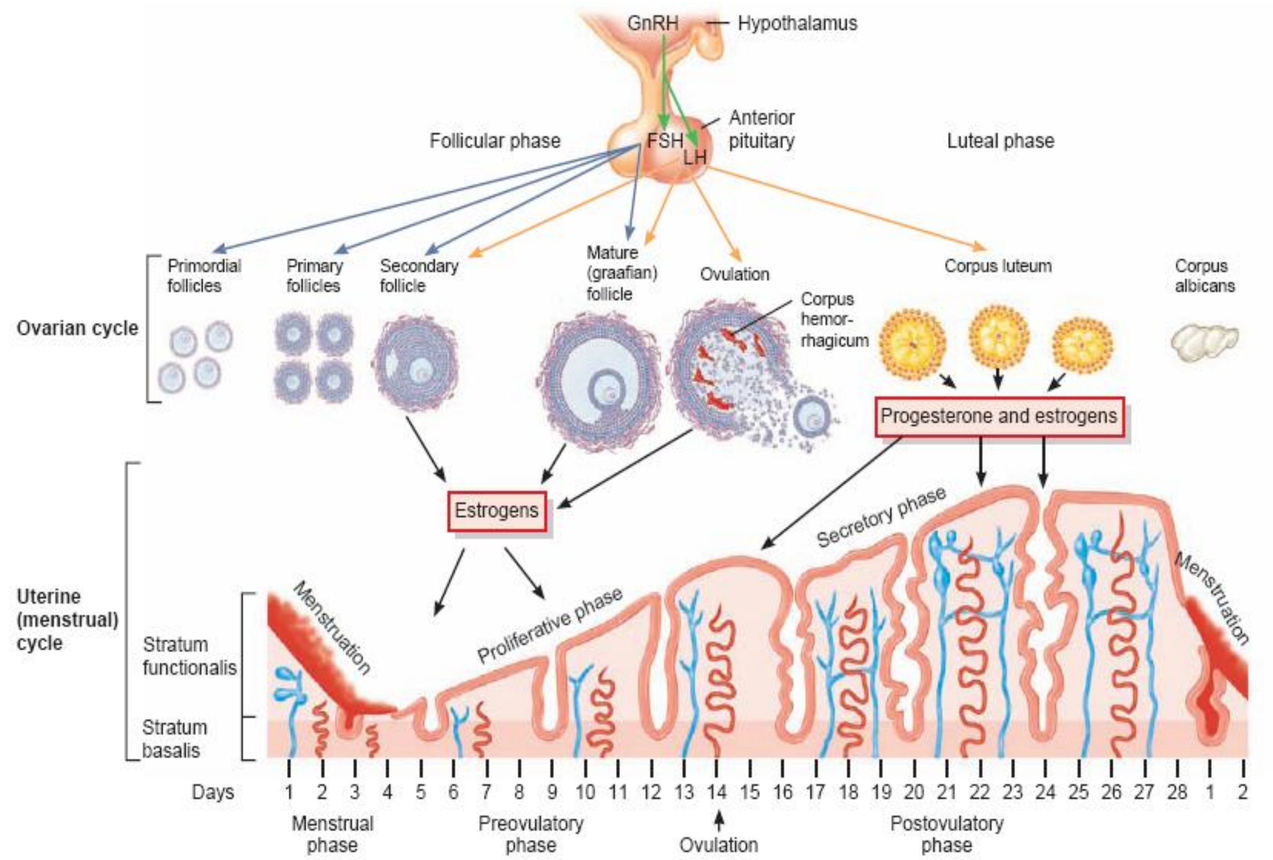
Progesterone, secreted mainly by cells of the corpus luteum, cooperates with estrogens to prepare and maintain the endometrium for implantation of a fertilized ovum and to prepare the mammary glands for milk secretion. High levels of progesterone also inhibit secretion of GnRH and LH.

The small quantity of **relaxin** produced by the corpus luteum during each monthly cycle relaxes the uterus by inhibiting contractions of the myometrium. Presumably, implantation of a fertilized ovum occurs more readily in a quiet uterus. During pregnancy, the placenta produces much more relaxin, and it continues to relax uterine smooth muscle. At the end of pregnancy, relaxin also increases the flexibility of the pubic symphysis and may help dilate the uterine cervix, both of which ease delivery of the baby.

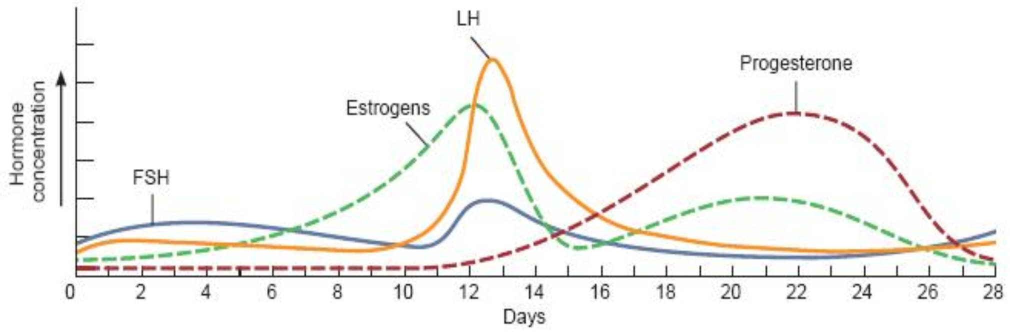
Inhibin is secreted by granulosa cells of growing follicles and by the corpus luteum after ovulation. It inhibits secretion of FSH and, to a lesser extent, LH.

Phases of the female reproductive cycle

The duration of the female reproductive cycle typically ranges from 24 to 35 days. For this discussion, we assume a duration of 28 days and divide it into four phases: **the menstrual phase, the preovulatory phase, ovulation, and the postovulatory phase.**



(a) Hormonal regulation of changes in the ovary and uterus



(b) Changes in concentration of anterior pituitary and ovarian hormones

THE MENSTRUAL PHASE

The **menstrual phase** also called **menstruation** or **menses** (month), lasts for roughly the first 5 days of the cycle. (By convention, the first day of menstruation is day one of a new cycle.)

EVENTS IN THE OVARIES

Under the influence of FSH, several primordial follicles develop into primary follicles and then into secondary follicles. This developmental process may take several months to occur. Therefore, a follicle that begins to develop
at the beginning of a particular menstrual cycle may not reach maturity and ovulate until several menstrual cycles later.

EVENTS IN THE UTERUS

Menstrual flow from the uterus consists of 50–150 mL of blood, tissue fluid, mucus, and epithelial cells shed from the endometrium. This discharge occurs because the declining levels of progesterone and estrogens stimulate release of prostaglandins that cause the uterine spiral arterioles to constrict. As a result, the cells they supply become oxygen-deprived and start to die. Eventually, the entire stratum functionalis sloughs off. At this time the endometrium is very thin, about2–5 mm, because only the stratum basalis remains. The menstrual flow passes from the uterine cavity through the cervix and vagina to the exterior.

Preovulatory Phase

The **preovulatory phase** is the time between the end of menstruation and ovulation. The preovulatory phase of the cycle is more variable in length than the other phases and accounts for most of the differences in length of the cycle. It lasts from days 6 to 13 in a 28-day cycle.

EVENTS IN THE OVARIES

Some of the secondary follicles in the ovaries begin to secrete estrogens and inhibin. By about day 6, a single secondary follicle in one of the two ovaries has outgrown all the others to become the **dominant follicle.** Estrogens and inhibin secreted by the dominant follicle decrease the secretion of FSH, which causes other, less well-developed follicles to stop growing and undergo atresia.

Normally, the one dominant secondary follicle becomes the **mature (graafian) follicle.**

With reference to the ovarian cycle, the menstrual and preovulatory phases together are termed the **follicular phase** because ovarian follicles are growing and developing.

EVENTS IN THE UTERUS

Estrogens liberated into the blood by growing ovarian follicles stimulate the repair of the endometrium; cells of the stratum basalis undergo mitosis and produce a new stratum functionalis. As the endometrium thickens, the short, straight endometrial glands develop, and the arterioles coil and lengthen as they penetrate the stratum functionalis. With reference to the uterine cycle, the preovulatory phase is also termed the **proliferative phase** because the endometrium is proliferating.

Ovulation

Ovulation, the rupture of the mature (graafian) follicle and the release of the secondary oocyte into the pelvic cavity, usually occurs on day 14 in a 28-day cycle. During ovulation, the secondary oocyte remains surrounded by its zona pellucida and corona radiata.

The **high levels of estrogens** during the last part of the preovulatory phase exert a **positive feedback** effect on the cells that secrete LH and gonadotropin-releasing hormone (GnRH) and cause ovulation, as follows:

- A high concentration of estrogens stimulates more frequent release of GnRH from the hypothalamus. It also directly stimulates gonadotrophs in the anterior pituitary to secrete LH.
- GnRH promotes the release of FSH and additional LH by the anterior pituitary.
- LH causes rupture of the mature (graafian) follicle and expulsion of a secondary oocyte about 9 hours after the peak of the LH surge. The ovulated oocyte and its corona radiate cells are usually swept into the uterine tube.

From time to time, an oocyte is lost into the pelvic cavity, where it later disintegrates. The small amount of blood that sometimes leaks into the pelvic cavity from the ruptured follicle can cause pain, known as **mittelschmerz** (pain in the middle), at the time of ovulation.

Postovulatory Phase

The **postovulatory phase** of the female reproductive cycle is the time between ovulation and onset of the next menses. In duration, it is the most constant part of the female reproductive cycle. It lasts for 14 days in a 28-day cycle, from day 15 to day 28.

EVENTS IN ONE OVARY

After ovulation, the mature follicle collapses, and the basement membrane between the granulose cells and theca interna breaks down. Once a blood clot forms from minor bleeding of the ruptured follicle, the follicle becomes the **corpus hemorrhagicum**. Theca interna cells mix with the granulosa cells as they all become transformed into **corpus luteum cells** under the influence of LH. Stimulated by LH, the corpus luteum secretes progesterone, estrogen, relaxin, and inhibin.

The luteal cells also absorb the blood clot. With reference to the ovarian cycle, this phase is also called the **luteal phase.**

Later events in an ovary that has ovulated an oocyte depend on whether the oocyte is fertilized. If the oocyte **is not fertilized**, the corpus luteum has a lifespan of only 2 weeks. Then, its secretory activity declines, and it degenerates into a **corpus albicans**. As the levels of progesterone, estrogens, and inhibin decrease, release of GnRH, FSH, and LH rises due to loss of negative feedback suppression by the ovarian hormones. Follicular growth resumes and a new ovarian cycle begins.

If the secondary oocyte **is fertilized** and begins to divide, the corpus luteum persists past its normal 2-week lifespan. It is rescued from degeneration by **human chorionic gonadotropin (hCG).** This hormone is produced by the chorion of the embryo beginning about 8 days after fertilization. Like LH, hCG stimulates the secretory activity of the corpus luteum.

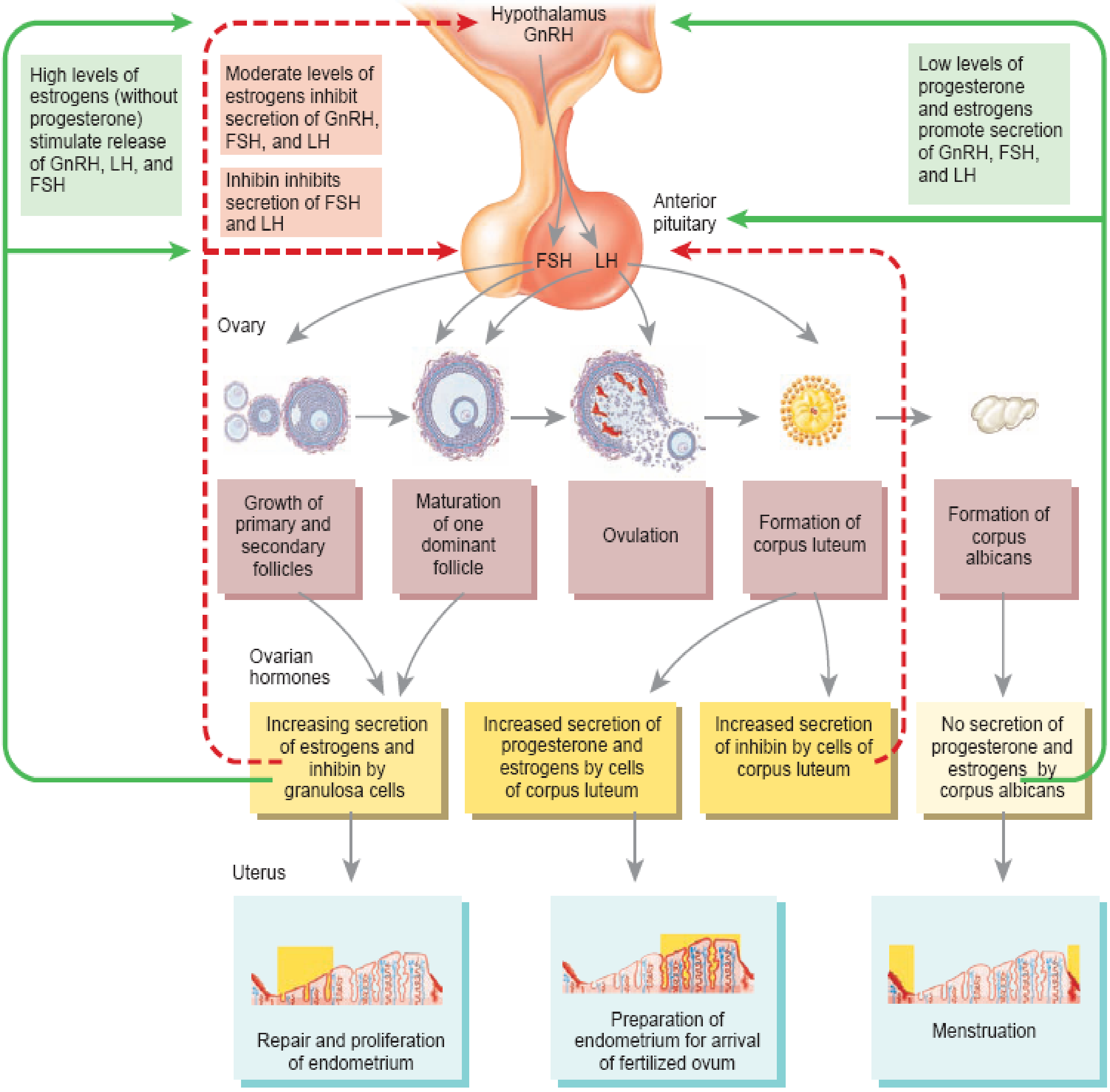
The presence of hCG in maternal blood or urine is an indicator of pregnancy and is the hormone detected by home pregnancy tests.

EVENTS IN THE UTERUS

Progesterone and estrogens produced by the corpus luteum promote growth and coiling of the endometrial glands, vascularization of the superficial endometrium, and thickening of the endometrium.

Because of the secretory activity of the endometrial glands, which begin to secrete glycogen, this period is called the **secretory phase** of the uterine cycle. These preparatory changes peak about one week after ovulation, at the time a fertilized ovum might arrive in the uterus. If fertilization does not occur, the levels of progesterone and estrogens decline due to degeneration of the corpus luteum. Withdrawal of progesterone and estrogens causes menstruation.

Summary of hormonal interactions in the ovarian and uterine cycles.



AGING AND THE REPRODUCTIVE SYSTEMS

For women there is a definite end to reproductive capability; this is called the menopause and usually occurs between the ages of 45 and 55. Estrogen secretion decreases; ovulation and menstrual cycles become irregular and finally cease. The decrease in estrogen has other effects as well. Loss of bone matrix may lead to osteoporosis and fractures; an increase in blood cholesterol makes women more likely to develop coronary artery disease; drying of the vaginal mucosa increases susceptibility to vaginal infections. Estrogen replacement therapy may delay some of these consequences of menopause, but there are risks involved, and women should be fully informed of them before starting such therapy. The likelihood of breast cancer also increases with age, and women over age 50 should consider having a mammogram to serve as a baseline, then one at least every other year. For most men, testosterone secretion continues throughout life, as does sperm production, though both diminish with advancing age. Perhaps the most common reproductive problem for older men is prostatic hypertrophy, enlargement of the prostate gland. As the urethra is compressed by the growing prostate gland, urination becomes difficult, and residual urine in the bladder increases the chance of urinary tract infection. Prostate hypertrophy is usually benign, but cancer of the prostate is one of the more common cancers in elderly men.

- **Applications to the nursing care**

1. *TRISOMY AND DOWN SYNDROME*

Trisomy means the presence of three (rather than the normal two) of a particular chromosome in the cells of an individual. This may occur because of non-disjunction (nonseparation) of a chromosome pair during the second meiotic division, usually in an egg cell.

The egg cell has two of a particular chromosome, and if fertilized by a sperm, will then contain three of that chromosome, and a total of 47 chromosomes. Most trisomies are probably lethal; that is, the affected embryo will quickly die, even before the woman realizes she is pregnant. When an embryofetus survives and a child is born with a trisomy, developmental defects are always present. The severity of trisomies may be seen in two of the more rarely occurring ones: Trisomy 13 and Trisomy 18, each of which occurs about once for every 5000 live births. Both of these trisomies are characterized by severe mental and physical retardation, heart defects, deafness, and bone abnormalities. Affected infants usually die within their first year.

Down syndrome (Trisomy 21) is the most common trisomy, with a frequency of about one per 750 live births. Children with Down syndrome are mentally retarded, but there is a great range of mental ability in this group. Physical characteristics include a skin fold above each eye, short stature, poor muscle tone, and heart defects.

Again, the degree of severity is highly variable. Women over the age of 35 are believed to be at greater risk of having a child with Down syndrome.

The reason may be that as egg cells age the process of meiosis is more likely to proceed incorrectly.

2. CONTRACEPTION

There are several methods of contraception, or birth control; some are more effective than others.

Sterilization: Sterilization in men involves a relatively simple procedure called a **vasectomy**. The ductus (vas) deferens is accessible in the scrotum, in which a small incision is made on eitherside. The ductus is then sutured and cut. Although sperm are still produced in the testes, they cannot pass the break in the ductus, and they simply die and are reabsorbed. Sterilization in women is usually accomplished by **tubal ligation**, the suturing and severing of the fallopian tubes. Usually this can be done by way of a small incision in the abdominal wall. Ova cannot pass the break in the tube, nor can sperm pass from the uterine side to fertilize an ovum. When done properly, these forms of surgical sterilization are virtually 100% effective.

Oral contraceptives ("**the pill**"): Birth control pills contain progesterone and estrogen in varying proportions. They prevent ovulation by inhibiting the secretion of FSH and LH from the anterior pituitary gland. When taken according to schedule, birth control pills are about 98% effective. Some women report side effects such as headaches, weight gain, and nausea. Women who use this method of contraception should not smoke, because smoking seems to be associated with abnormal clotting and a greater risk of heart attack or stroke.

Barrier methods: These include the condom, diaphragm, and cervical cap, which prevent sperm from reaching the uterus and fallopian tubes. The use of a spermicide (sperm-killing chemical) increases the effectiveness of these methods. A condom is a latex or rubber sheath that covers the penis and collects and contains ejaculated semen. Leakage is possible, however, and the condom is considered 80% to 90% effective. This is the only contraceptive method that decreases the spread of sexually transmitted diseases.

The diaphragm and cervical cap are plastic structures that are inserted into the vagina to cover the cervix. They are about 80% effective. These methods should not be used, however, by women with vaginal infections or abnormal Pap smears or by those who have had toxic shock syndrome.

3. *PROSTATIC HYPERTROPHY*

Prostatic hypertrophy is enlargement of the prostate gland. Benign prostatic hypertrophy is a common occurrence in men over the age of 60 years. The enlarged prostate compresses the urethra within it and may make urination difficult or result in urinary retention. A prostatectomy is the surgical removal of part or the entire prostate. A possible consequence is that ejaculation may be impaired.

Newer surgical procedures may preserve sexual function, however, and medications are available to shrink enlarged prostate tissue. Cancer of the prostate is the second most common cancer among men (lung cancer is first). Most cases occur in men over the age of 50 years. Treatment may include surgery to remove the prostate, radiation therapy, or hormone therapy to reduce the patient’s level of testosterone.

4. *IN VITRO* FERTILIZATION

***In vitro* fertilization** (IVF) is fertilization outside the body, usually in a glass dish. A woman who wishes to conceive by this method is given FSH to stimulate the simultaneous development of several ovarian follicles. LH may then be given to stimulate simultaneous ovulation. The ova are removed by way of a small incision in the abdominal wall and are placed in a solution containing the sperm of the woman’s partner (or an anonymous donor).

After fertilization and the first mitotic divisions of cleavage, the very early embryo is placed in the woman’s uterus. It is also possible to mix the removed ova with sperm and return them almost immediately to the woman’s fallopian tube. Development then proceeds as if the ova had been fertilized naturally.

Since the birth of the first "test tube baby" in 1978, many thousands of babies have been born following *in vitro* fertilization. The techniques are not always successful, and repeated attempts can be very expensive. As an adjunct to IVF, pre-implantation genetic diagnosis may be done, to test for genetic diseases and chromosome abnormalities. This may be especially useful for older women trying to conceive and for couples with a family history of a genetic disease such as sickle-cell anemia or cystic fibrosis.

5. SEXUALLY TRANSMITTED INFECTIONS

Sexually transmitted infections (**STIs**) are those in which the pathogen is acquired during sexual activity. Most are caused by bacteria or viruses.

a) Gonorrhea: caused by the bacterium *Neisseria gonorrhoeae*. Infected men have urethritis with painful and frequent urination and pus in the urine. Women are often asymptomatic, and the bacteria may spread from the cervix to other reproductive organs (pelvic inflammatory disease [PID]). The use of antibiotics in the eyes of all newborns has virtually eliminated neonatal conjunctivitis acquired from an infected mother. Gonorrhea can be treated with antibiotics, but resistant strains of the bacteria complicate treatment. Despite this, the number of reported cases of gonorrhea has been decreasing in recent years.

b) Syphilis: caused by the bacterium *Treponema pallidum*. Although syphilis can be cured with penicillin, it is a disease that may be ignored by the person who has it because the symptoms may seem minor and often do not last long. If untreated, however, syphilis may cause severe or even fatal damage to the nervous system and heart. In the last few years the number of reported cases of syphilis has been decreasing.

c) Genital herpes: caused by the virus herpes simplex (usually type 2). Painful lesions in the genital area are the primary symptom. Although the lesions heal within 5 to 9 days, recurrences are possible, perhaps triggered by physiological stresses such as illness. Although herpes is not curable at present, medications have proved useful in suppressing recurrences. It is estimated that 2 million new cases of genital herpes occur every year. **Neonatal herpes** is infection of a newborn during passage through the birth canal. The infant's immune system is too immature to control the herpes virus, and this infection may be fatal or cause brain damage. A pregnant woman with a history of genital herpes may choose to have the baby delivered by cesarean section to avoid this possible outcome.

d) Chlamydial infection: caused by the very simple bacterium *Chlamydia trachomatis*. This is one of the most prevalent STDs in the United States, with estimates of 4 million new cases yearly. Infected men may have urethritis or epididymitis.

Women often have no symptoms at first but may develop PID, which increases the risk of ectopic pregnancy.

Infants born to infected women may develop conjunctivitis or pneumonia. Chlamydial infection can be treated successfully with antibiotics such as erythromycin or azithromycin.

6. MAMMOGRAPHY

Mammography is an x-ray technique that is used to evaluate breast tissue for abnormalities. By far the most frequent usage is to detect breast cancer, which is one of the most common malignancies in women. If detected early, breast cancer may be cured through a combination of surgery, radiation, and chemotherapy. Women should practice breast self-examination monthly, but mammography can detect lumps that are too small to be felt manually. Women in their 30s may have a mammogram done to serve as a comparison for mammograms later in life.