

Reproductive Physiology

GAMETOGENESIS

- Reproduction control in males and females
- General principles of Gametogenesis
- Sex determination
- Sex differentiation

Reproduction Control in males and females

FEATURE (and functions)	MALE	FEMALE
GONAD	Testes/testis	Ovaries/ ovary
1 st function Production of gametes	Spermatozoa/ spermatazoan	Ova/ ovum
2 nd function Secretion of sex hormones/ gonadal steroids	Testosterone	1) Estradiol 2) progesterone

Testosterone

- It belongs to a group of steroid hormones called '**androgens**'.
- it is synthesized in the testes.
- Other androgens are produced by the adrenal cortex.
- E.g DHEA (dehydroepiandrosterone)

Estradiol and Progesterone

- One of three major ‘**estrogens**’.
- It is the predominant estrogen in the plasma.

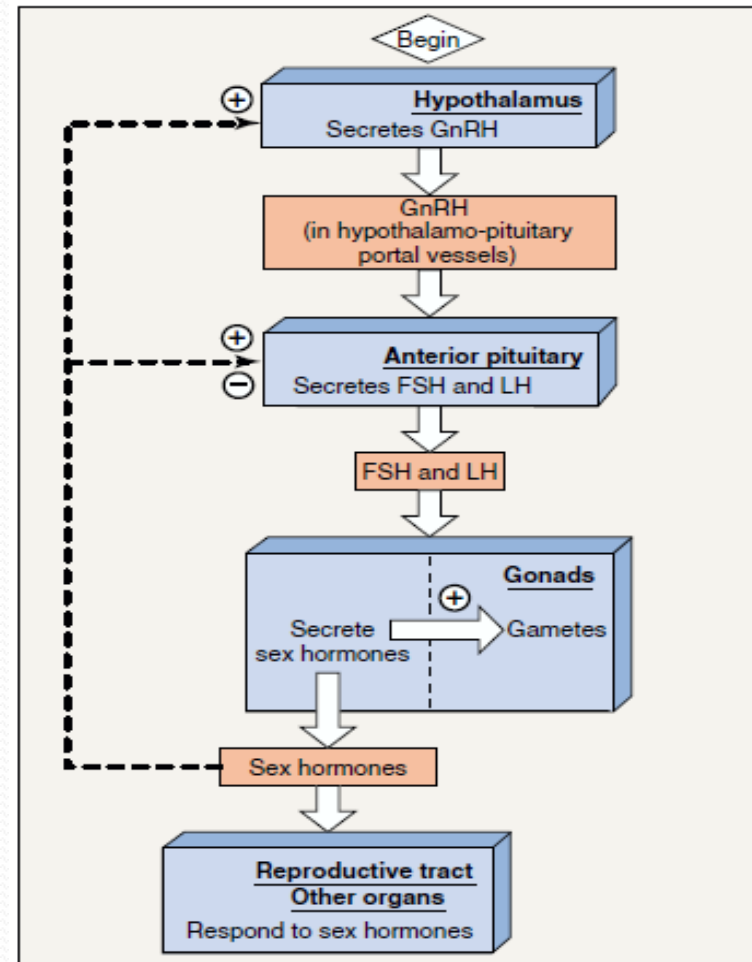
The two other major estrogens are

- Estrone
- Estriol
- Progesterone is a major secretory product of the ovary in specific times of the menstrual cycle as well as from the placenta during pregnancy.

Control Of Reproductive Functions

- For both male and female reproduction, the reproductive function is controlled by a chain of hormones. the first hormone in the chain is **gonadotropin-releasing hormone (GnRH)**, released by the hypothalamus to stimulate the release of pituitary gonadotropins - follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland. In both males and females these two hormones act to promote gametogenesis and androgen/estrogen secretion.

- In addition the gonadal steroids exert feed back effects on the secretion of GnRH, FSH and LH.



General Principles Of Gametogenesis

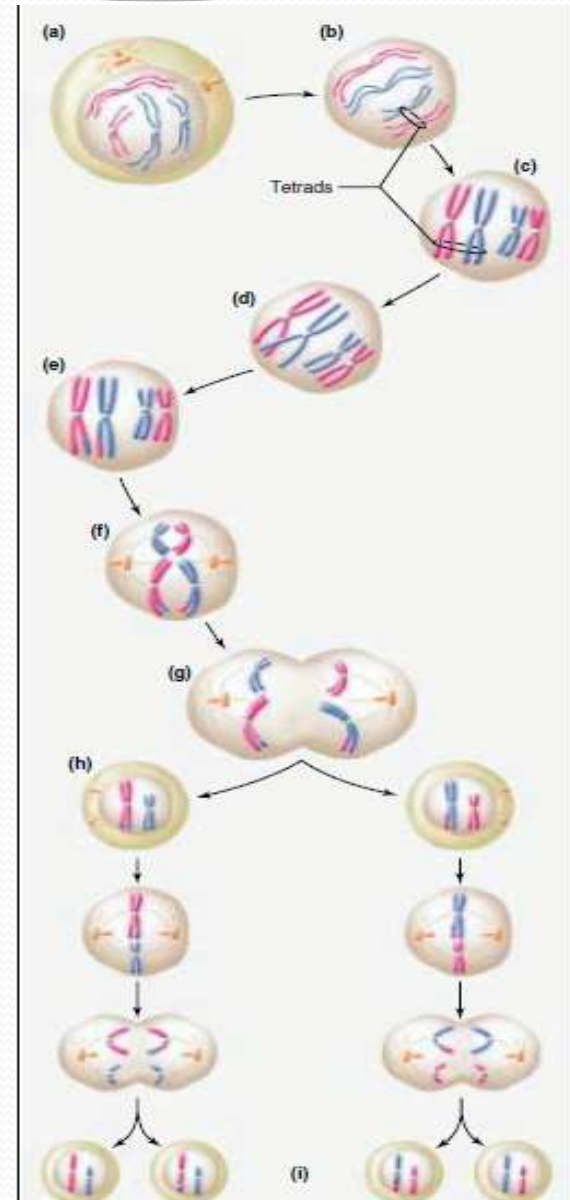
Gametogenesis is the process of formation of gametes from the germ cells in the testes and ovaries.

- *The first stage* is the division of the primordial (immature) germ cells by mitosis.
- The DNA of each nucleated cell with the exception of gametes, contains 46 chromosomes.
- In this first stage, (mitosis) the 46 chromosomes of the dividing cell are replicated.
- The end result are two daughter cells containing the full 46 chromosomes identical to those of the original cell.

- In this manner mitosis of primordial germ cells, each containing 46 chromosomes provides a supply of identical germ cells for the next stages.
- **NB:** in females the timing of mitosis of germ cells occurs during fetal development in the ovary.
in males mitosis occurs in the testes at puberty and usually continues throughout life.

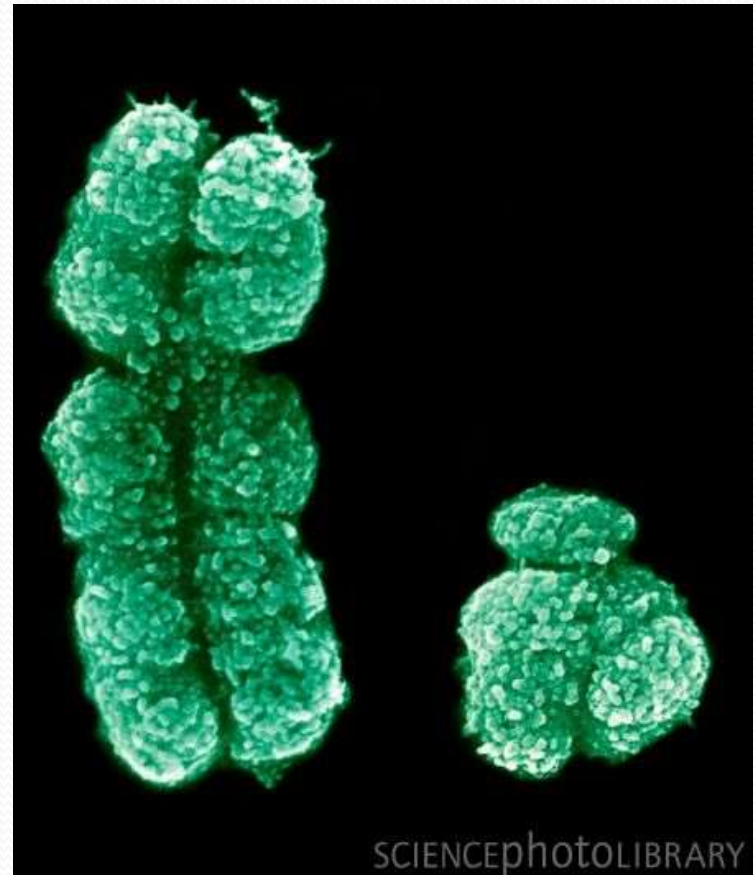
In the second stage (meiosis), each resulting gamete receives only 23 chromosomes from a 46-chromosome germ cell.

Because a sperm and ovulated egg has only 23 chromosomes, their union at fertilization results in a full 46 chromosomes in the cell.



Sex Determination

- Gender is determined by the genetic inheritance of two chromosomes called the **sex chromosomes, X and Y**.
- Males possess one X (larger chromosome) and one Y chromosome.
(heterogametic)
- Females possess two X chromosomes.
(homogametic)



Sex Determination cont'd

- The ovum can contribute only an X chromosome , where as half of the sperm produced during meiosis are X and half are Y. When the sperm and egg join, 50% should have XX and 50% should have XY.
- However sex ratios at birth are not exactly 1:1 there tends to be a slight predominance of male births due to the functional differences in sperm carrying the X vs Y chromosome.

Method for Determining Sex

- The female pattern;
- When two X chromosomes are present, only one functions and the non functional X chromosome condenses to form a nuclear mass termed sex chromatin (Barr Body).
- Scrapings from the cheek mucosa or white blood cells are convenient cells to be examined.

Sex Differentiation

- Even though gender is determined at conception, the fetus doesn't develop its external sexual organs until the fourth month of pregnancy.
- Sex differentiation may be defined as the multiple processes involved in the development of the reproductive system in the fetus.
- In some cases, individuals with atypical chromosomal combinations manifest atypical sexual development.

Sex Differentiation cont'd

- In other cases, individuals were found to have normal chromosomal combinations but abnormal appearance and function(phenotype).
- In these people sex differentiation has been atypical- their phenotype may not correspond with their genotype.

Differentiation of the Gonads

The male and female gonads derive embryologically from the same site- **the urogenetial ridge.**

- In the genetic male, testes begin to develop during the seventh week.
- A gene on the Y chromosome (the SRY gene) is expressed at this time on the urogenital ridge cells and triggers this development.
- In the absence of a Y chromosome, testes do not develop. Instead ovaries begin to develop in the same area at about 11 weeks.

Differentiation of External and Internal Genitalia

- Before the functioning of the fetal gonads, the primitive reproductive tract includes a double genital duct system—**Wolffian ducts and Müllerian ducts**—and a common opening for the genital duct and urinary system to the outside.

- If the embryo is female (XX), then no testosterone is made. The Wolffian duct will degrade, and the Mullerian duct will develop into female sex organs. The female clitoris is the remnants of the Wolffian duct.
- If the embryo is a male (XY chromosomes), then testosterone will stimulate the Wolffian duct to develop male sex organs, and the Mullerian duct will degrade.

Reproductive Physiology

Male reproductive physiology

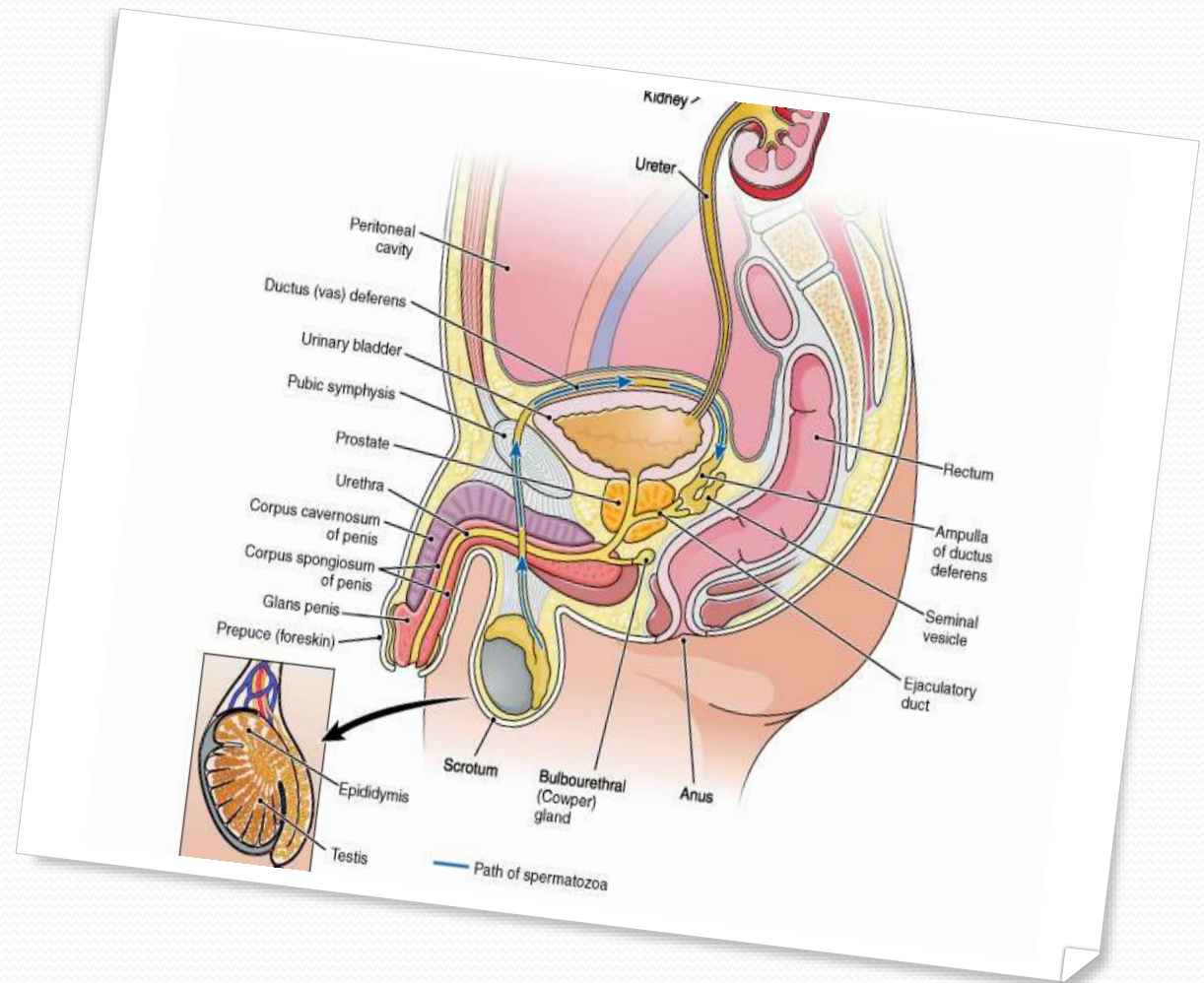
Female reproductive physiology

Testes

The functions of testes are spermatogenesis and secretion of testosterone.

It occupies the scrotum and lies outside the body cavity.

This is essential as it maintains a 1 degree to 2 degree for normal spermatogenesis.



Male reproductive system

- Divided into two groups
 - Primary Organs
 - **Gonads** or sex glands
 - Produce the germ cells and manufacture hormones
 - Male gonad is the Testis
 - Accessory Organs
 - Series of ducts that transport the germ cells as well as various exocrine glands



Seminiferous Tubules

- 80% of adult testis are composed of seminiferous tubules which are convoluted loops, 120 to 300 μ m in diameter this is surrounded by connective tissue.
- Epithelium lining of seminiferous tubules consist of three types of cells
- Spermatogonia; stem cells
- Spermatocytes; these are cells that are in the process to become sperm
- Sertoli cells: support development of sperm

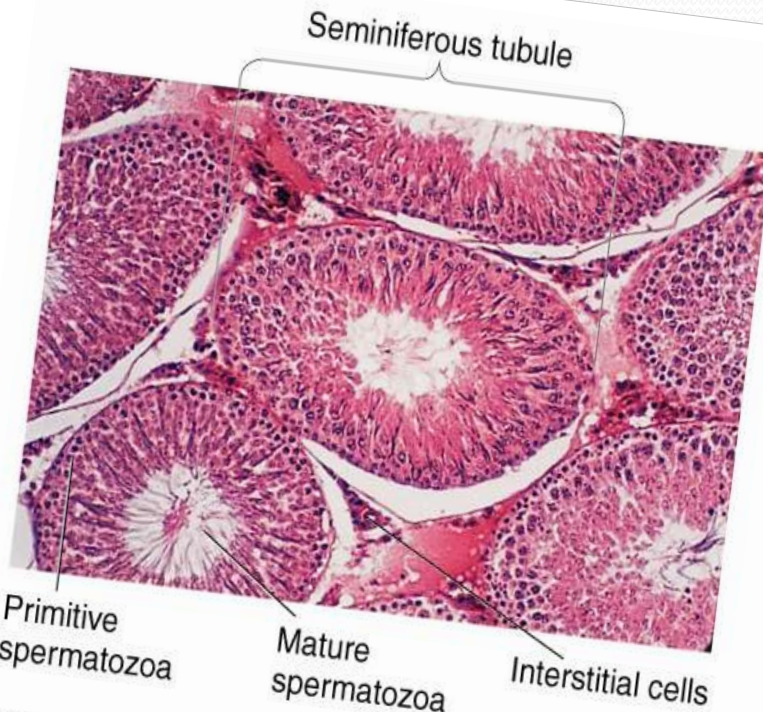


Figure 20-3 Microscopic view of the testis. (Courtesy of Dana Morse Bittus and BJ Cohen.)

Copyright © 2005 Lippincott Williams & Wilkins

Functions of sertoli cells

- Sertoli cells provide nutrients to differentiating sperm (which are isolated from the blood stream)
- Sertoli cells form tight junctions with each other creating a barrier between the testes and the blood stream.
- This is selectively permeable admitting passage of some substances such as testosterone, but prohibits noxious substances that may harm the sperm such as bacteria
- Sertoli cells secrete aqueous fluid in the lumen of seminiferous tubules which helps to transport sperm through the tubules of the epididymis.

Leydig Cells

- Leydig cells is a connective tissues that in the next 20%
- Leydig cells synthesises and secrete testosterone the male sex hormone.
- Testosterone has paracrine effects that support spermatogenesis in the testicular sertoli cells and endocrine effects on other target organs

Testosterone

- After its secretion, testosterone is absorbed directly into the blood stream
- Hormone has 3 functions:
 - Development and maintenance of the reproductive structures
 - Development of spermatozoa
 - Development of secondary sex characteristics (traits that characterize male and females but not directly concerned with reproduction). Deepened voice, broad shoulders, narrow hips, muscle tissue and body hair

Development of spermatozoon

Phase 1

- Mitotic division
- Spermatogonia generate spermatocytes which become mature sperm

Phase 2

- Meiotic Division
- Meiotic division of spermatocytes which decreases chromosome number and produce haploid spermatids.

Phase 3

- Spermiation
- Spermatids are transformed into mature sperm through loss of cytoplasm and development of flagella

Spermatozoa(haploid 1n)

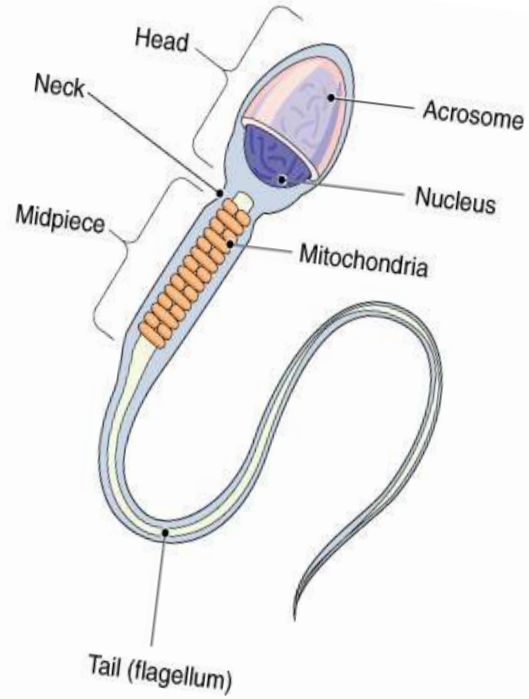



Figure 20-4 Diagram of a human spermatozoon. Major structural features are shown.

Copyright © 2005 Lippincott Williams & Wilkins

- 
- One full cycle of spermatogenesis requires about 64days.
 - Spermatogenic wave organises successful production of sperm in the spermatogenic cycle

Spermatozoa

- Tiny individual male sex cells
- 200 million contained in average ejaculation (release of semen)
- After puberty, sperm cells are manufactured continuously in the seminiferous tubules of the testes
- Has an oval head
 - Largely nucleus containing chromosomes
- The **acrosome** covers the head like a cap
- Contains enzymes that help sperm penetrate the ovum
- Tail propels the sperm, with whip like movements, through the female reproductive system
- Mid-piece of sperm contains many mitochondria to provide energy for movement

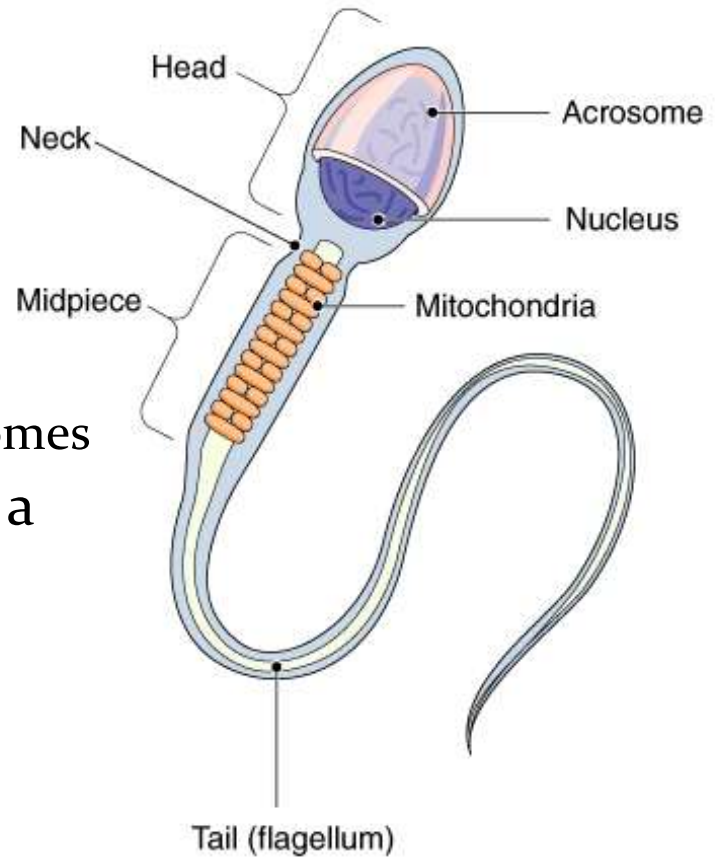
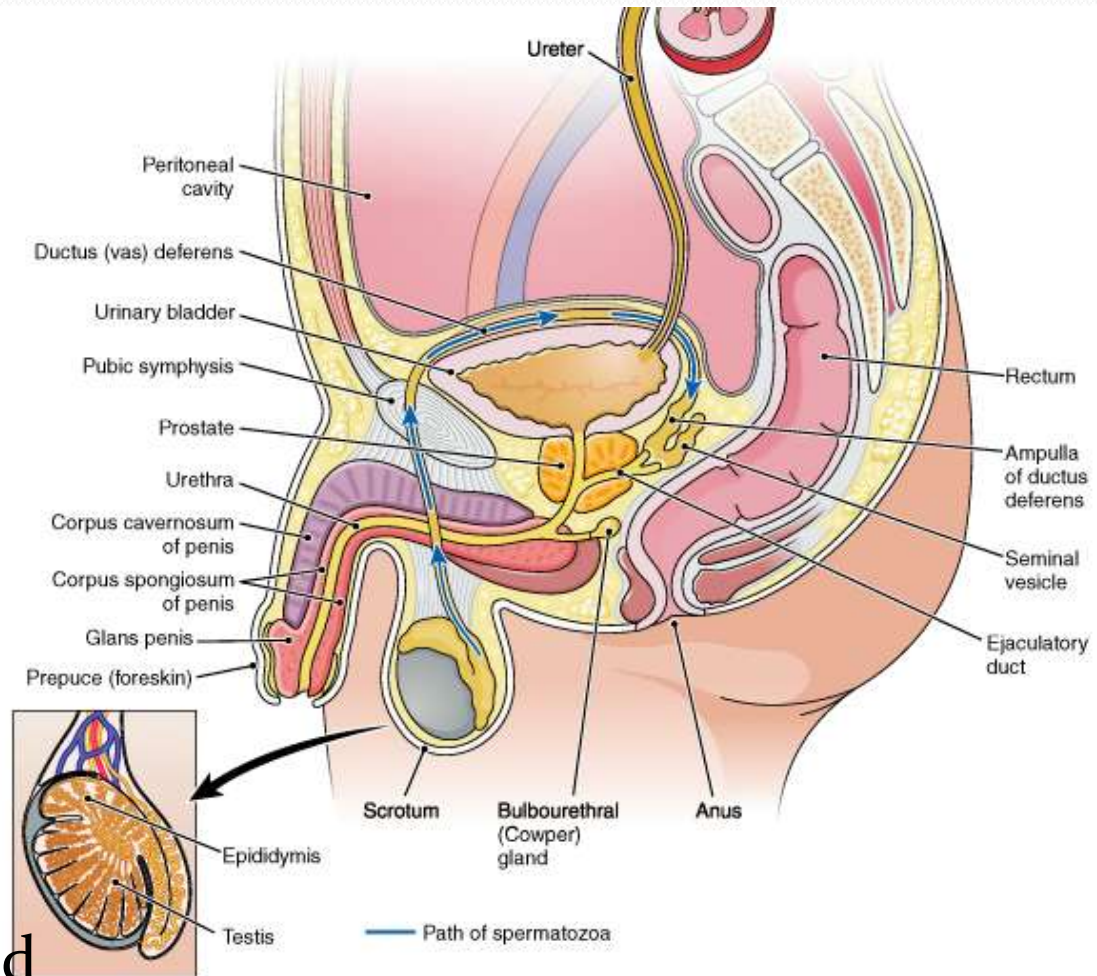


Diagram of a human spermatozoon. Major structural features are s

ippincott Williams & Wilkins

Accessory Organs

- The ductus deferens separates from the remainder of the spermatic cord and curves behind the urinary bladder
- It joins with the duct of the seminal vesicle on the same side to form the ejaculatory duct
- Left and right ejaculatory ducts travel to the prostate gland and empty into the urethra



Accessory Organs

- System of ducts that transport sperm beginning with tubules inside the testis
- From these tubules the cells collect in a greatly coiled tube called the **epididymis** (located on the surface of the testis inside the scrotal sac)
- Sperm cells mature in epididymis and are able to move by themselves
- Epididymis extends upward as the **ductus deferens** (vas deferens)
- Vas deferens is contained in the spermatic cord and continues into the abdominal cavity

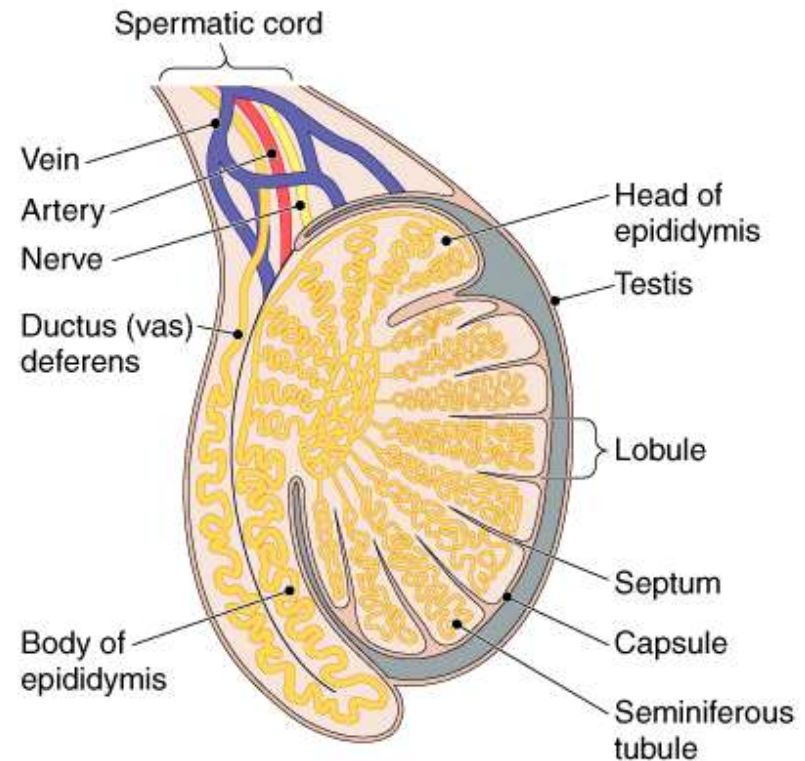
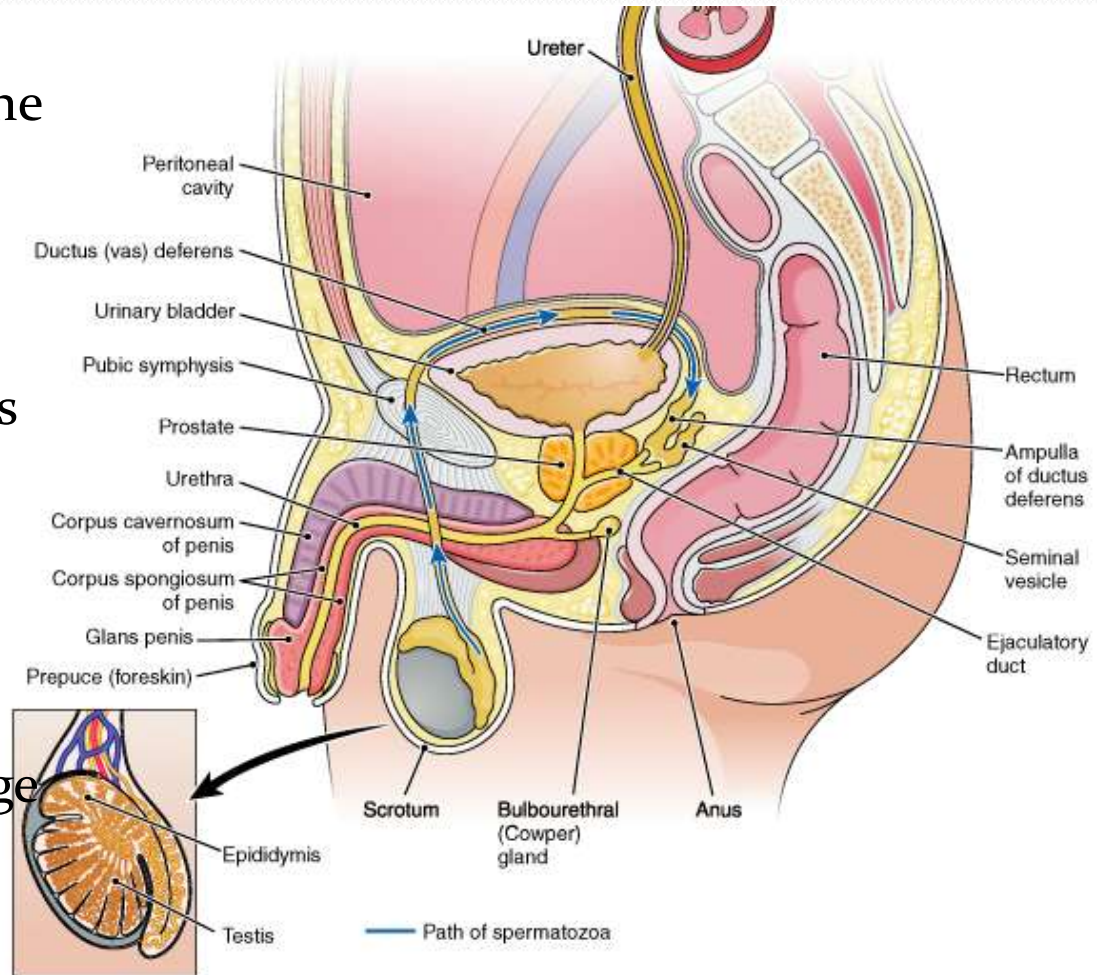


Figure 20-2 Structure of the testis. The epididymis and spermatic cord are also shown.

Copyright © 2005 Lippincott Williams & Wilkins

Seminal Vesicles

- Twisted muscular tubes with many small out pouchings
- About 3 inches long and are attached at the posterior of the urinary bladder
- Produces a thick, yellow, alkaline secretion composed of fructose, citrate, prostaglandins and fibrinogen.
- Contains large quantities of simple sugars and other substances that provide nourishment for the sperm
- Seminal fluid makes up a large part of the semen's volume.



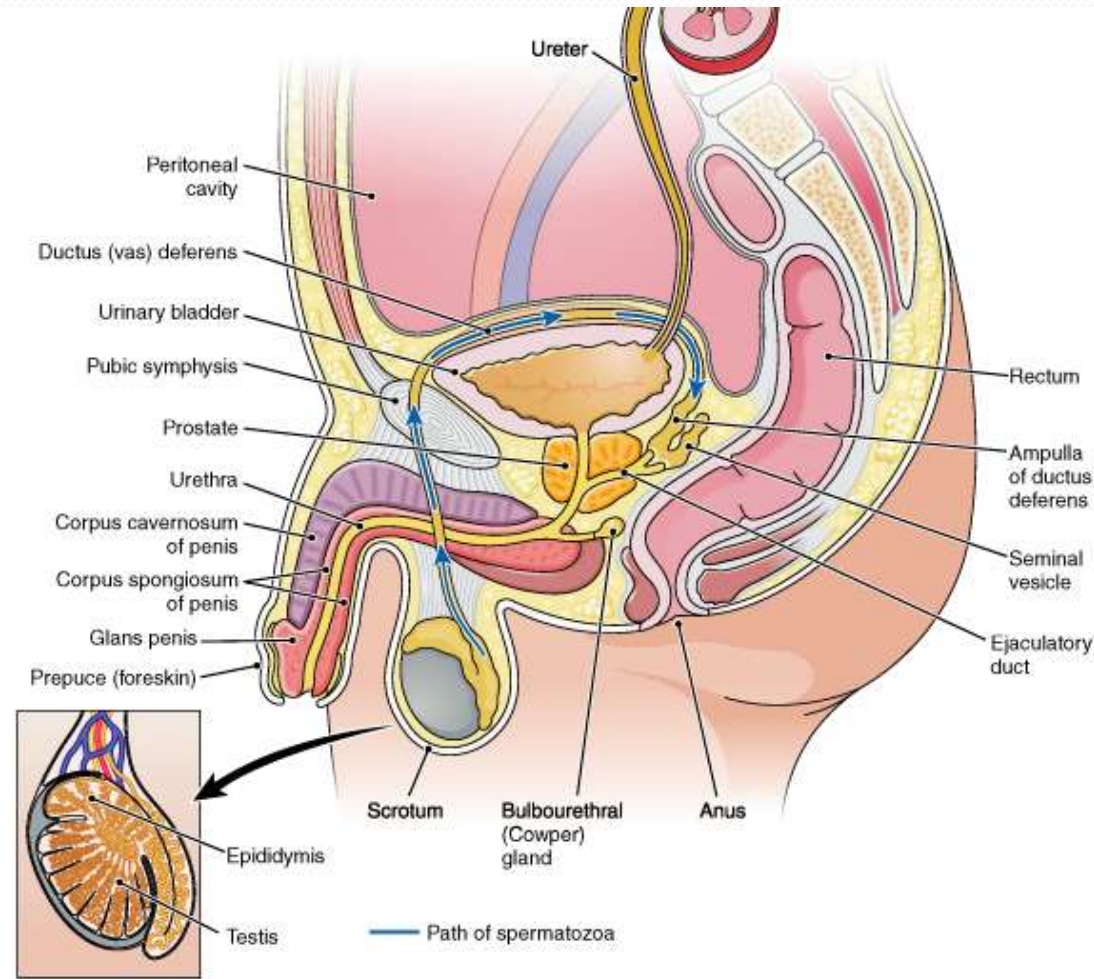


- Functions of Prostaglandins

1. Prostaglandins react with cervical mucus to make it more penetrable to sperm
2. Prostaglandins induce peristaltic contractions in female reproductive tract(i.e uterus and fallopian tubes).this helps in sperm being propelled up the tract.

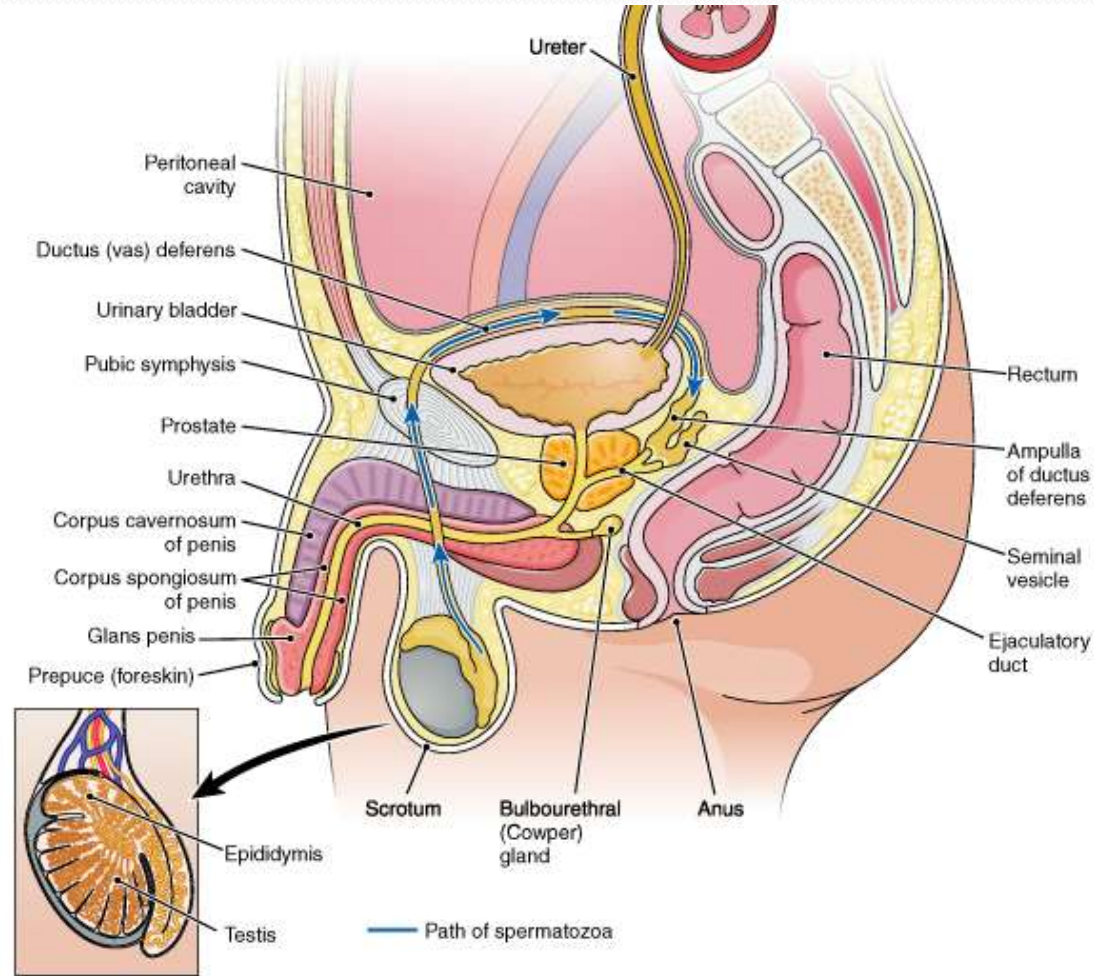
Prostate Gland

- Lies immediately inferior to the urinary bladder
- Surrounds first part of urethra
- Ducts from the prostate carry its secretions into the urethra.
- Thin alkaline prostatic secretion helps neutralize the acidity of the vaginal tract and enhance the motility of the spermatozoa
- Supplied with muscular tissue
- Upon signals from the nervous system, muscles contract to aid in the expulsion of the semen from the body



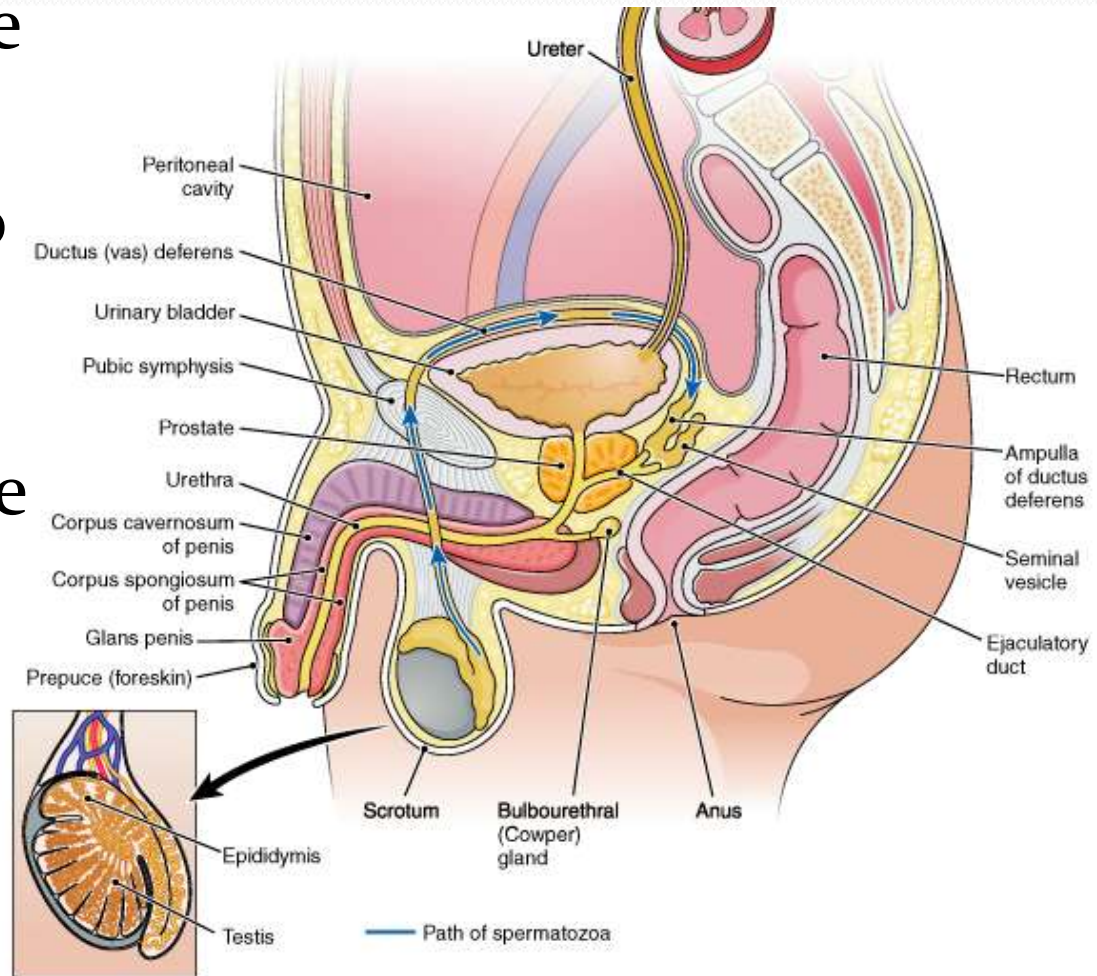
Bulbourethral glands

- Also called the Cowper glands
- Pair of pea-sized organs located in the pelvic floor, inferior to prostate gland
- Secrete mucus to lubricate the urethra and tip of the penis during sexual stimulation
- Ducts of these glands empty into the urethra before it extends into the penis



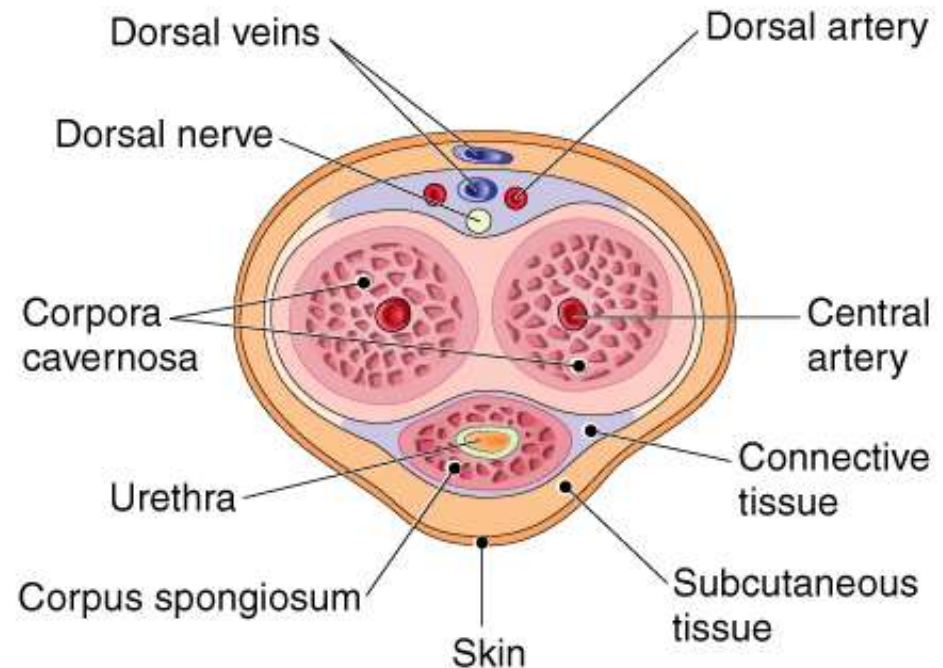
Urethra & Penis

- Male urethra conveys urine and reproductive cells to the outside
- Ejection of semen into the receiving canal (vagina) of the female is made possible by the erection (stiffening and enlargement) of the penis



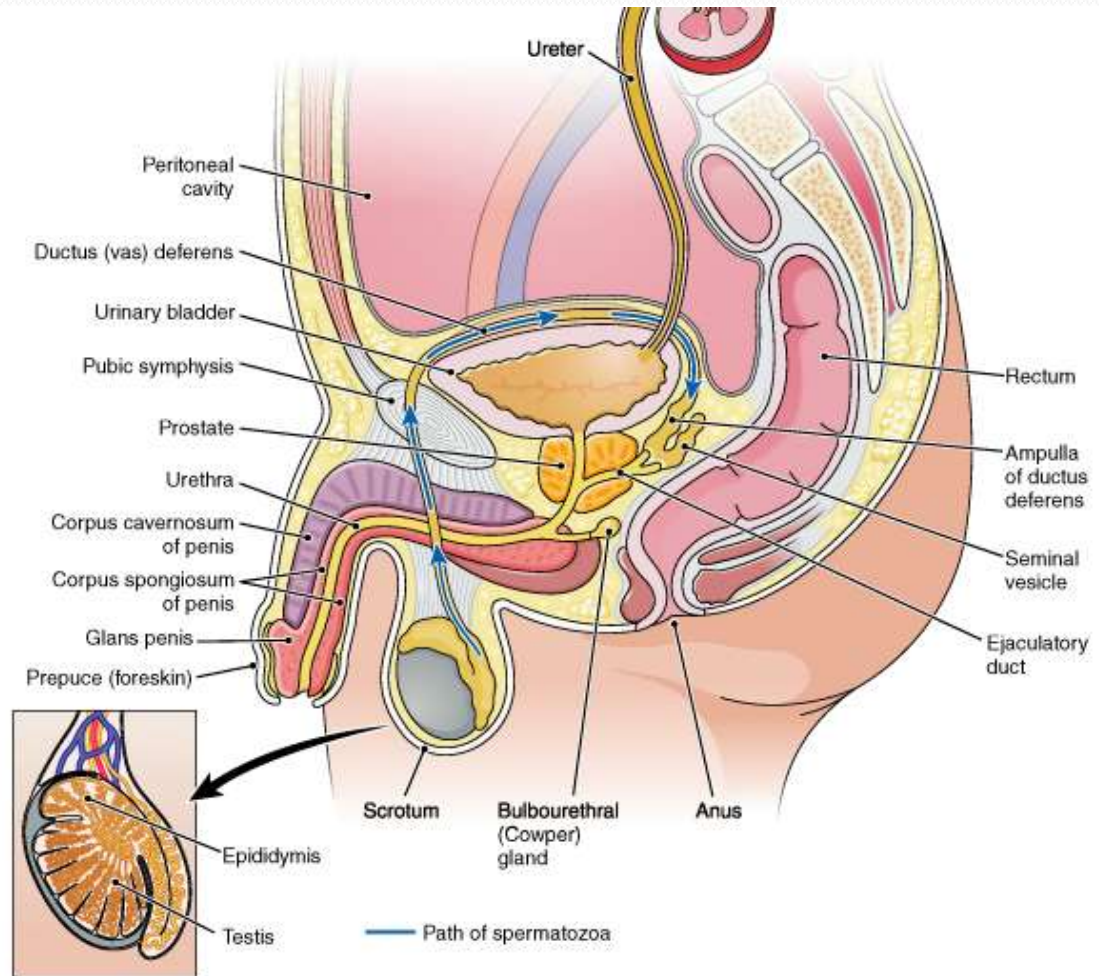
Urethra & Penis

- Penis made of spongy tissue containing many blood spaces that are relatively empty when the organ is flaccid
- Fill with blood and distend when the penis is erect
- The penis and the scrotum make up the external genitalia of the male



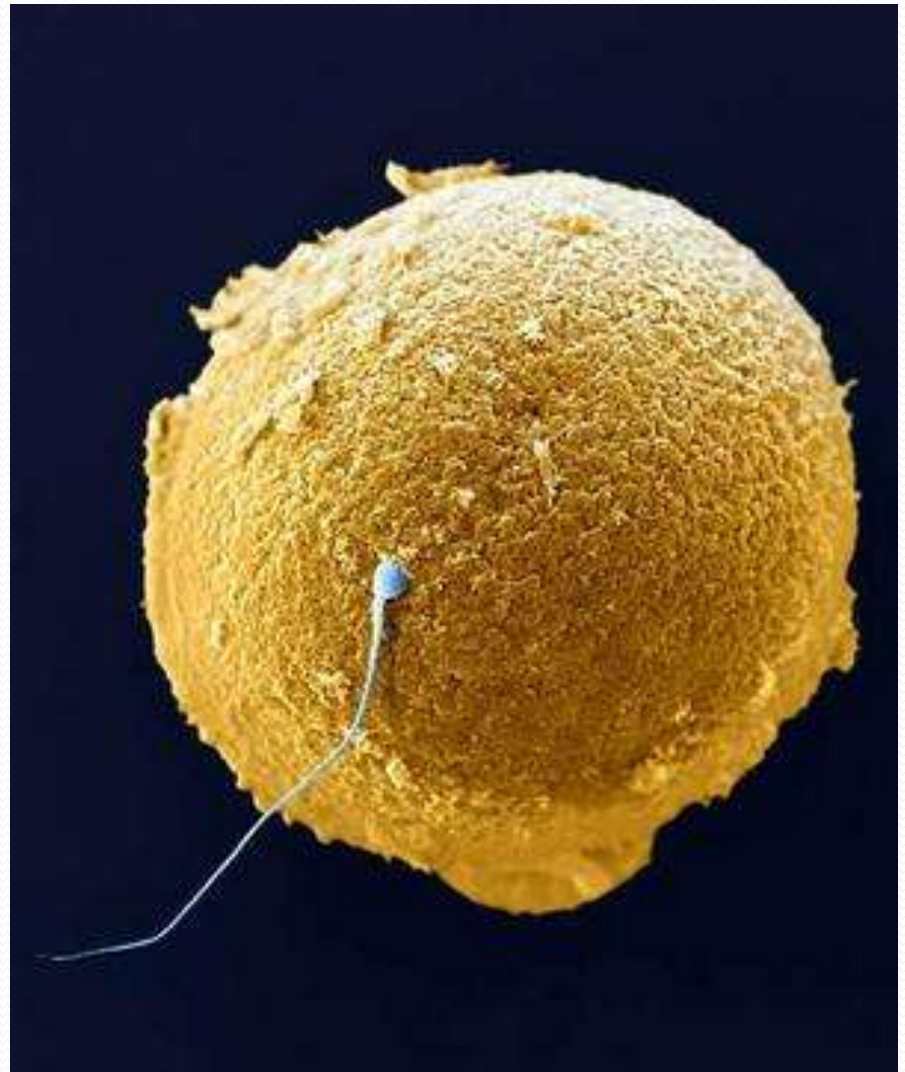
Ejaculation

- The forceful expulsion of semen through the urethra to the outside
- Process initiated by reflex centers in the spinal cord that stimulates smooth muscle contraction in the prostate
- This is followed by contraction of skeletal muscle in the pelvic floor which provides the force needed for expulsion
- During ejaculation, the involuntary sphincter at the base of the bladder closes to prevent the release of urine



Ejaculation

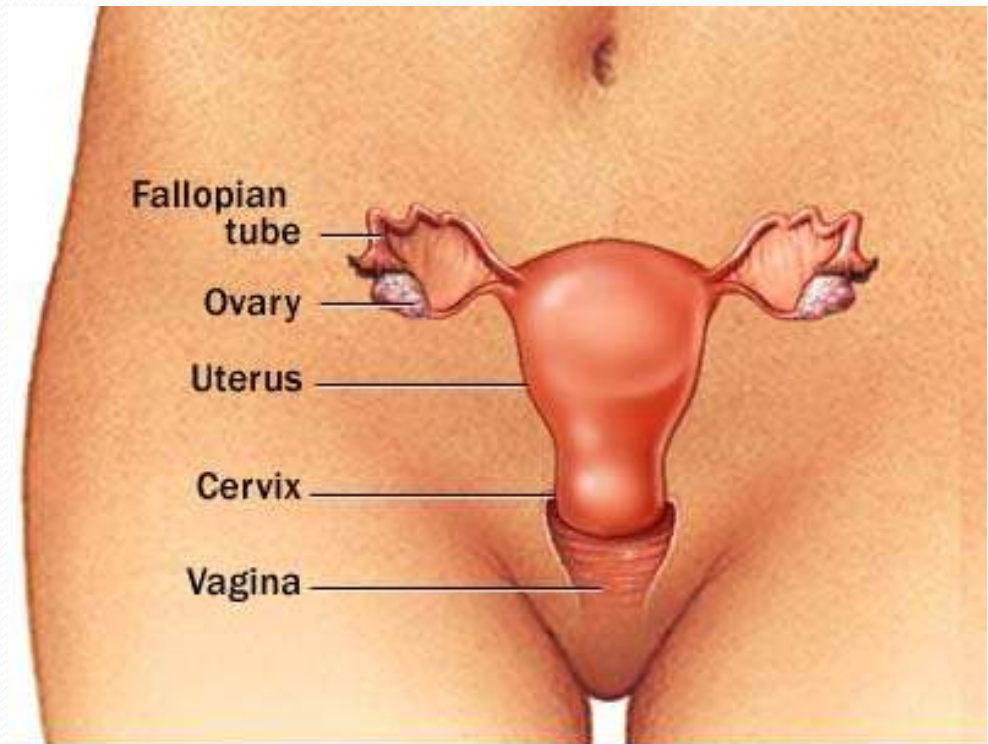
- Male can ejaculate 2-5ml of semen containing 50 million-150 million sperm cells per ml
- Only one spermatozoa can fertilize an ovum
- Remainder of cells live from only a few hours maximum of 3 days



Female Reproductive Physiology

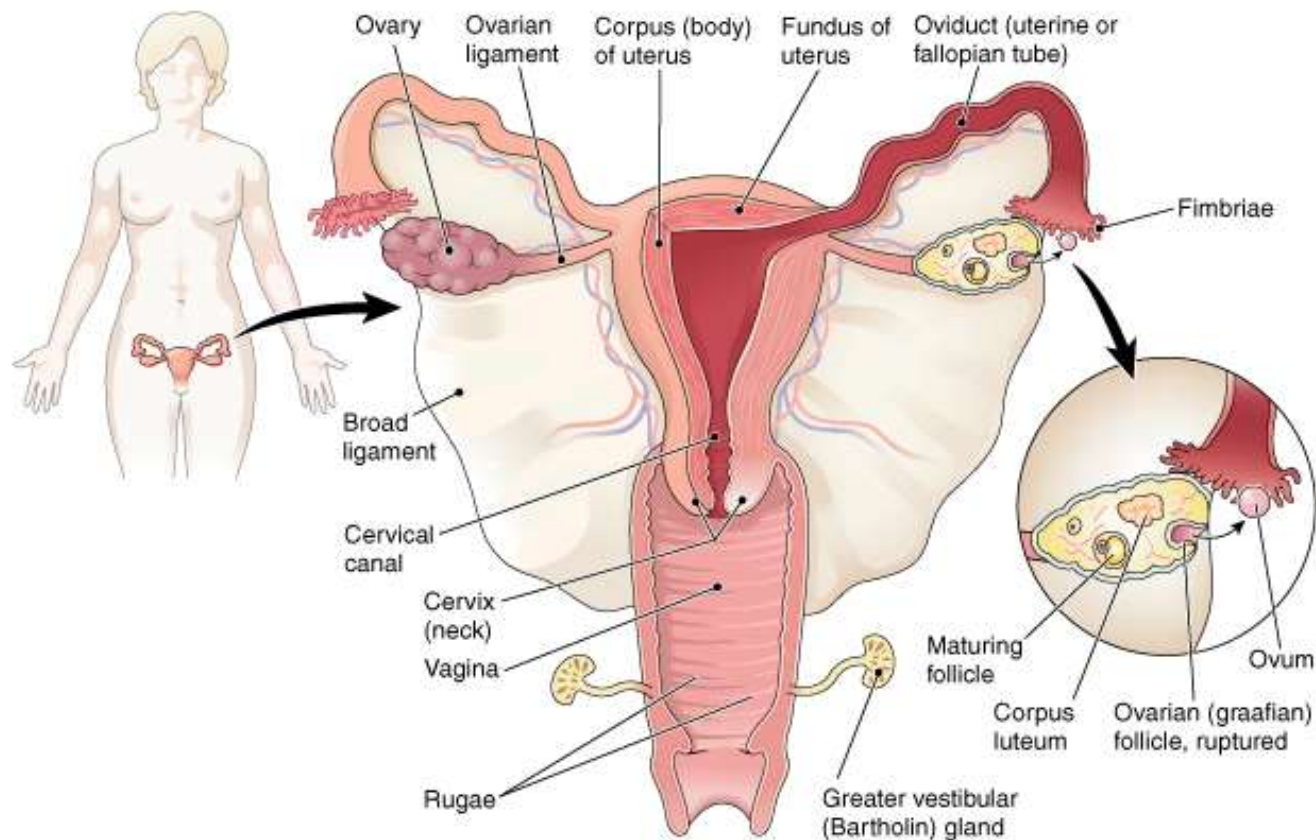
Female Reproductive System

- Female gonads are the ovaries where the female sex cells or ova are formed
- Remainder of female reproductive tract consists of:
 - an organ (uterus) to hold and nourish a developing infant
 - various passageways
 - External genital organs



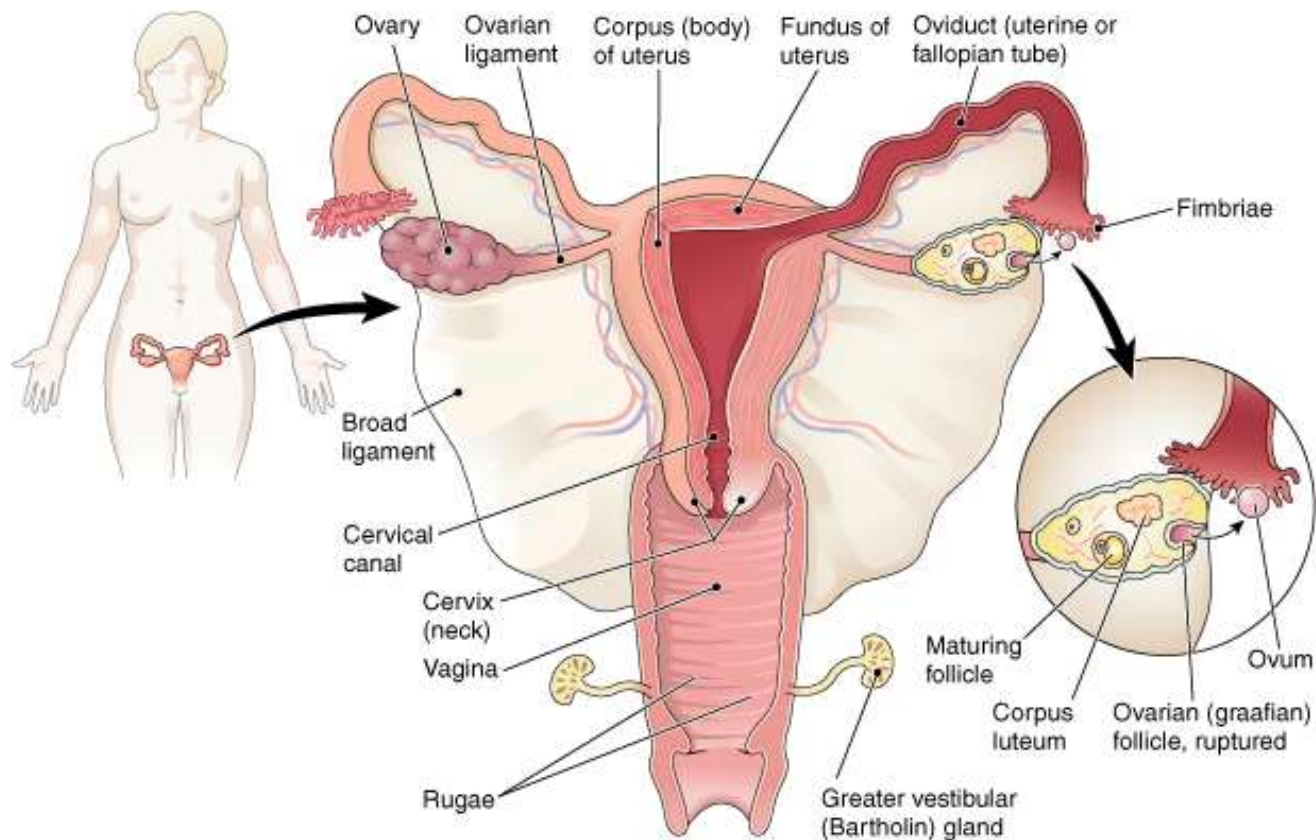
Ovaries

- Small, somewhat flattened oval body
- Like the testes, ovaries descend but only as far as the pelvic portion of the abdomen
- Held in place by ligaments that attach them to the uterus and body wall



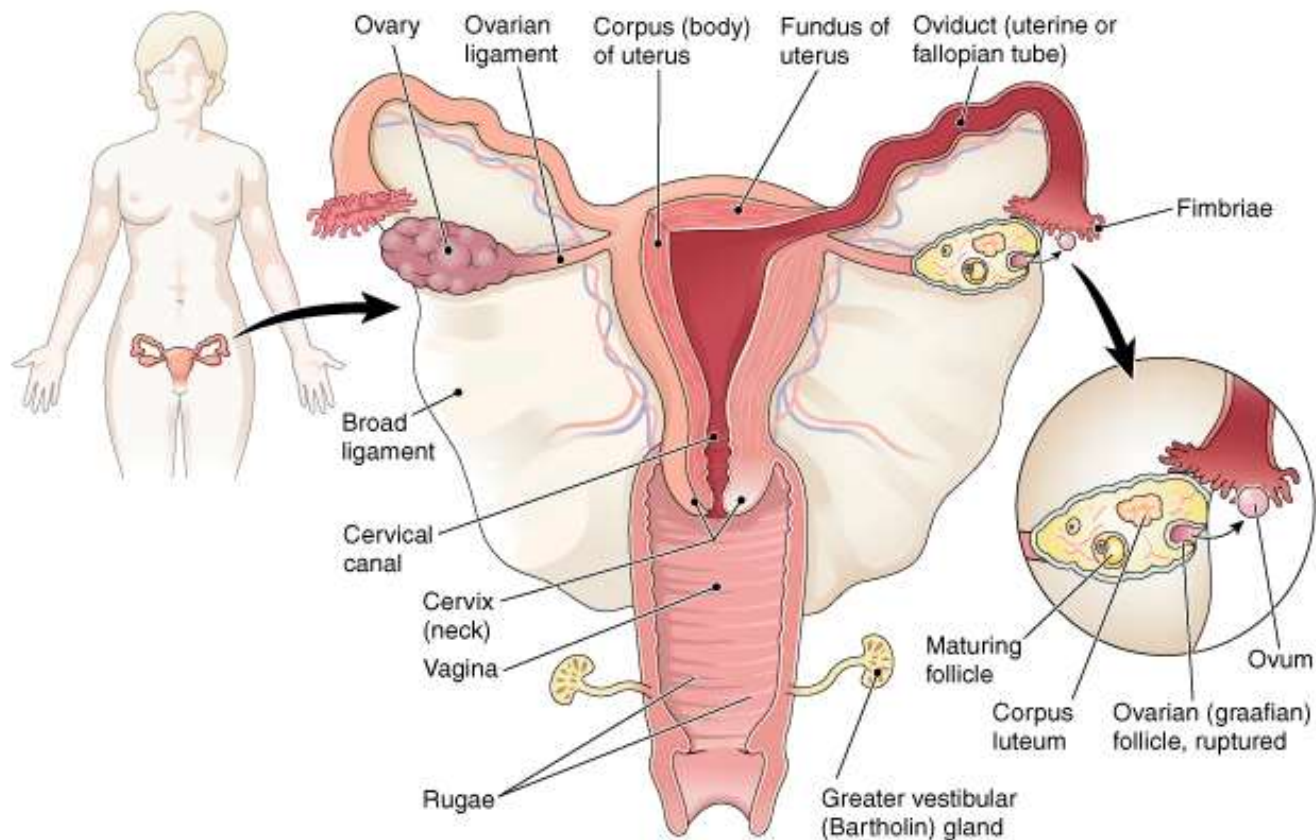
Ova and Ovulation

- Ovaries of a newborn female contain a large number of potential ova
- Each month during the reproductive years, several ripen but only one is released

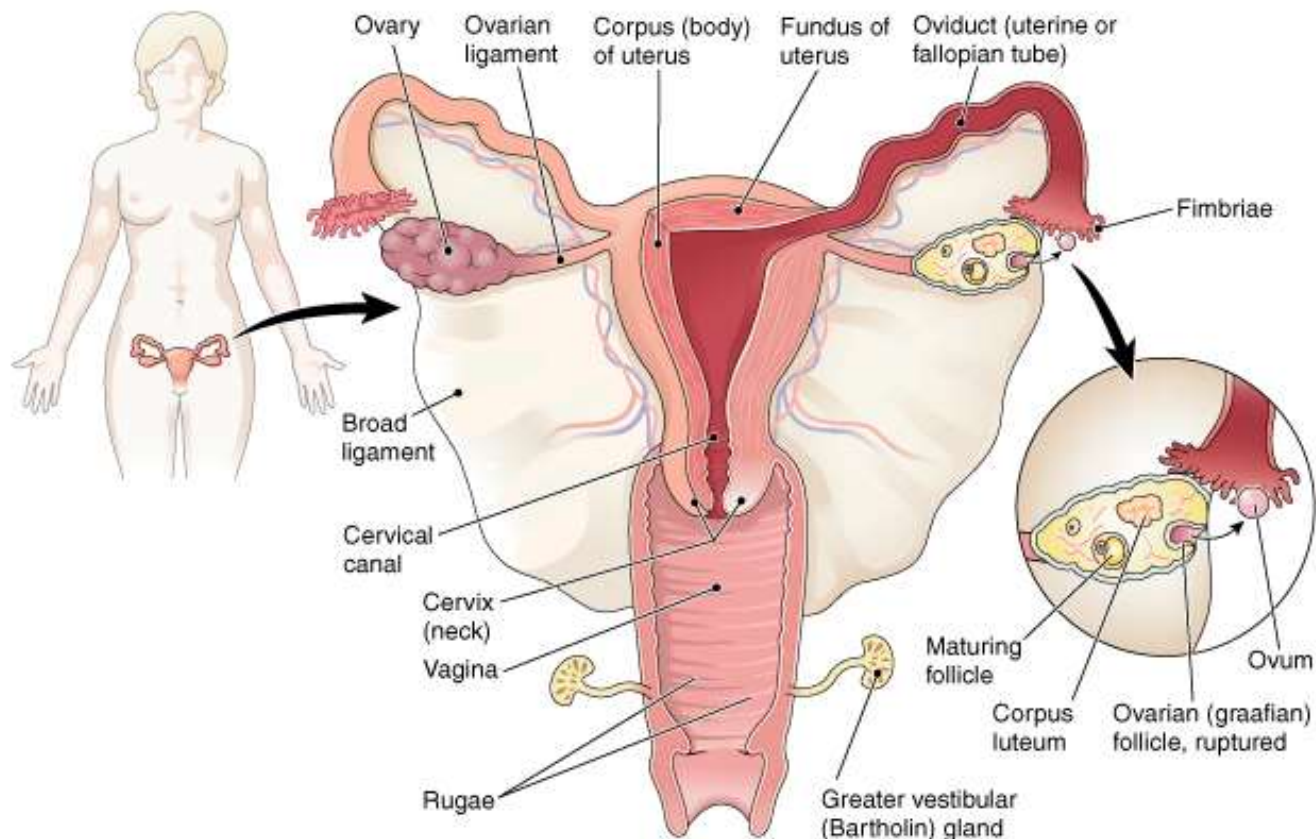


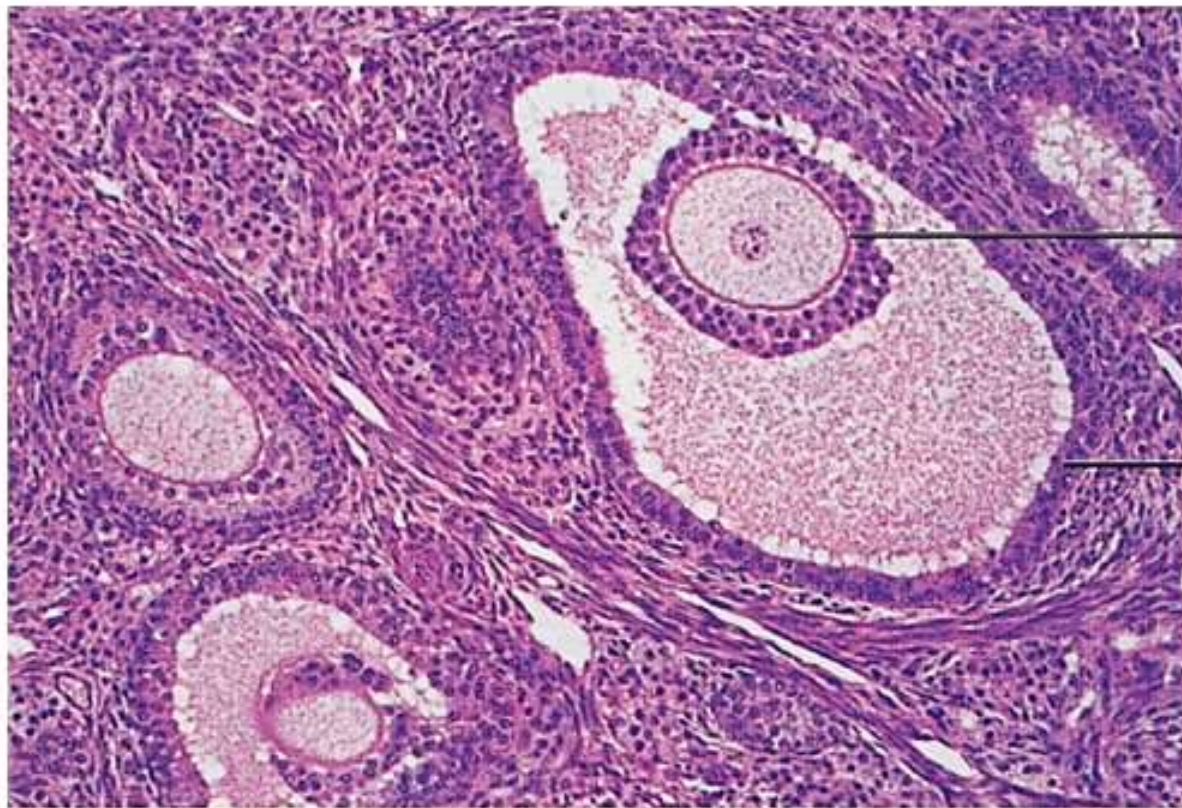
Ova and Ovulation

- Maturation of the ovum takes place in a small fluid-filled cluster of cells called the ovarian follicle (graafian follicle)
- As the follicle develops, cells in its wall secrete estrogen which stimulates growth of the uterine lining



- When an ovum has ripened, the ovarian follicle may rupture and discharge the egg cell from the ovary's surface
- The rupture of a follicle allowing the escape of an ovum is called ovulation.
- Any ova that are not released degenerate
- Released egg cell makes its way to the nearest oviduct
 - A tube that arches over the ovary and leads to the uterus





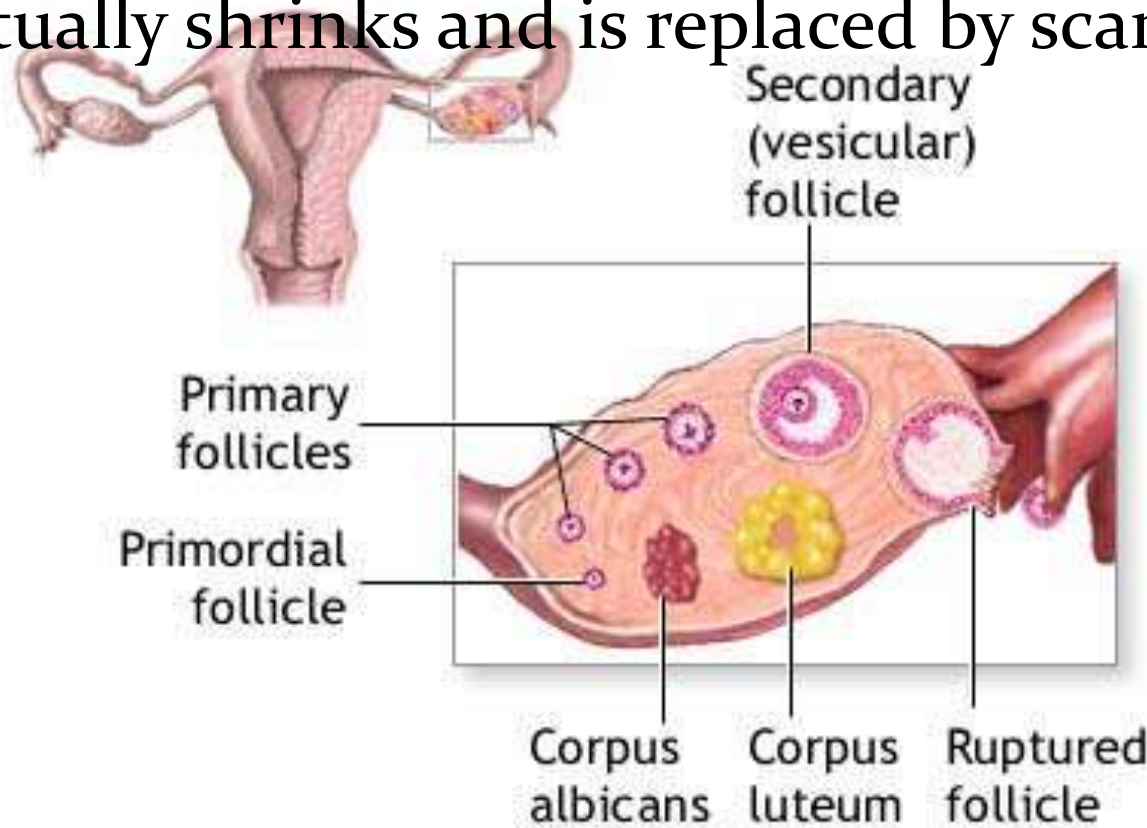
Ovum

Ovarian
(graafian)
follicle

Figure 20-7 **Microscopic view of the ovary.** The photomicrograph shows egg cells (ova) developing within ovarian (graafian) follicles. (Courtesy of Dana Morse Bittus and BJ Cohen.)

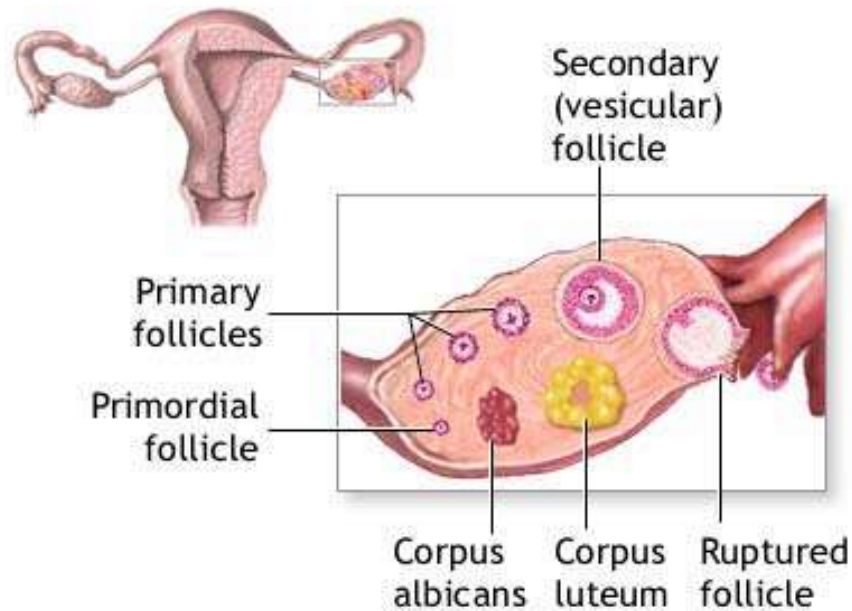
Corpus Luteum

- After the ovum is expelled, the remaining follicle is transformed into a solid mass called the corpus luteum
- Secretes estrogen and progesterone
- Eventually shrinks and is replaced by scar tissue



Corpus Luteum

- When a pregnancy occurs, however, the structure remains active
- Sometimes during a normal ovulation, the corpus luteum persists and forms a small ovarian cyst (fluid filled sac)
- Resolves without treatment

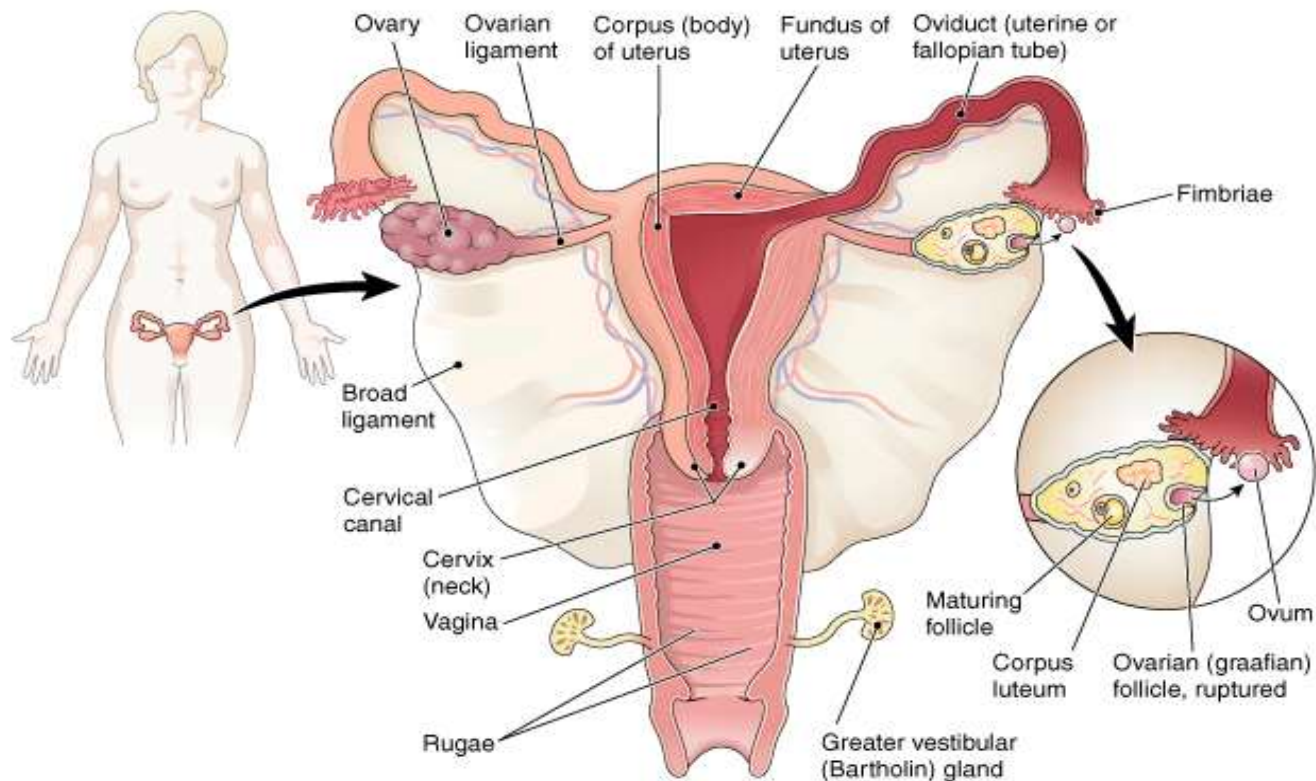


Accessory Organs

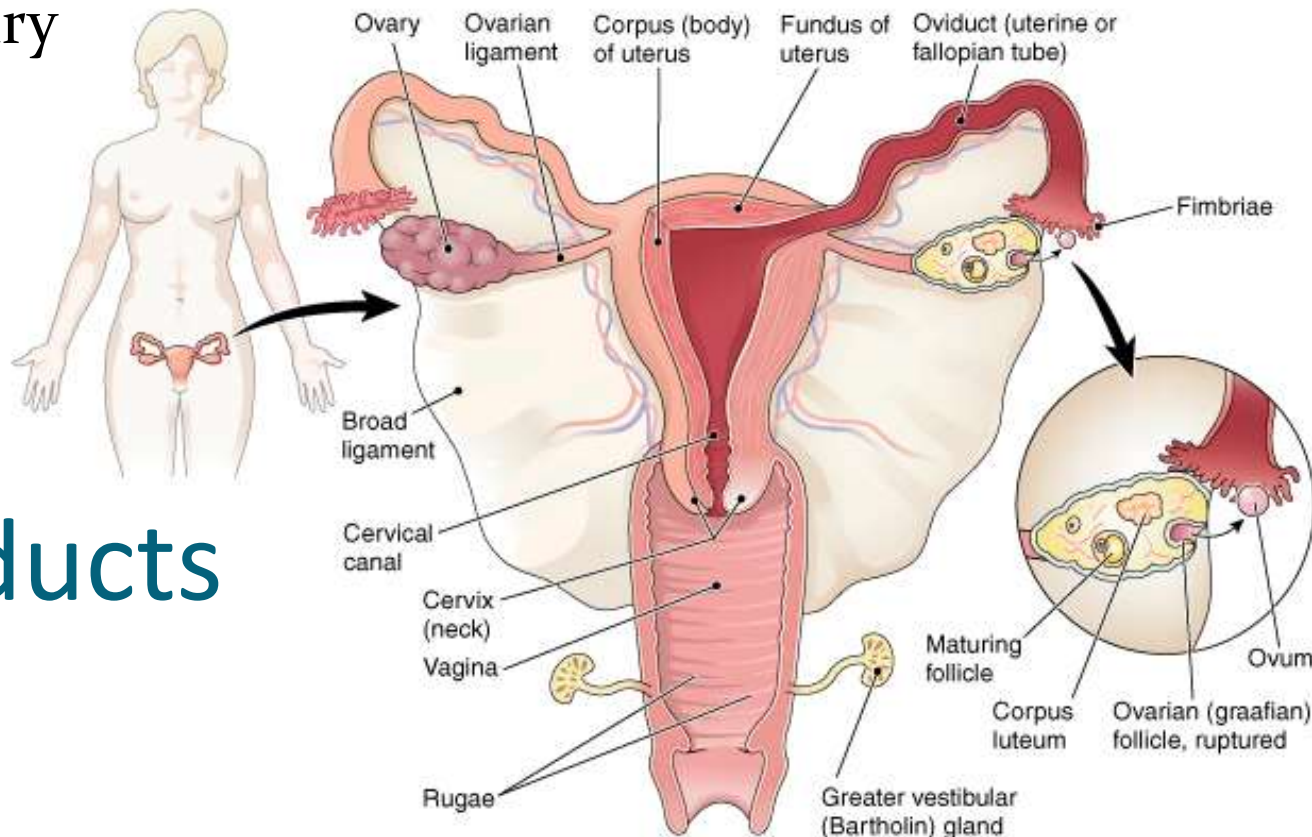
- Include :
 - oviducts
 - the uterus
 - vagina
 - greater vestibular glands
 - vulva
 - perineum

Oviducts

- Tubes that transport the ova in the female reproductive system
- Also known as the uterine tubes or fallopian tubes
- No direct connection between ovary and this tube
- Ovum is swept into oviduct by a current in the peritoneal fluid



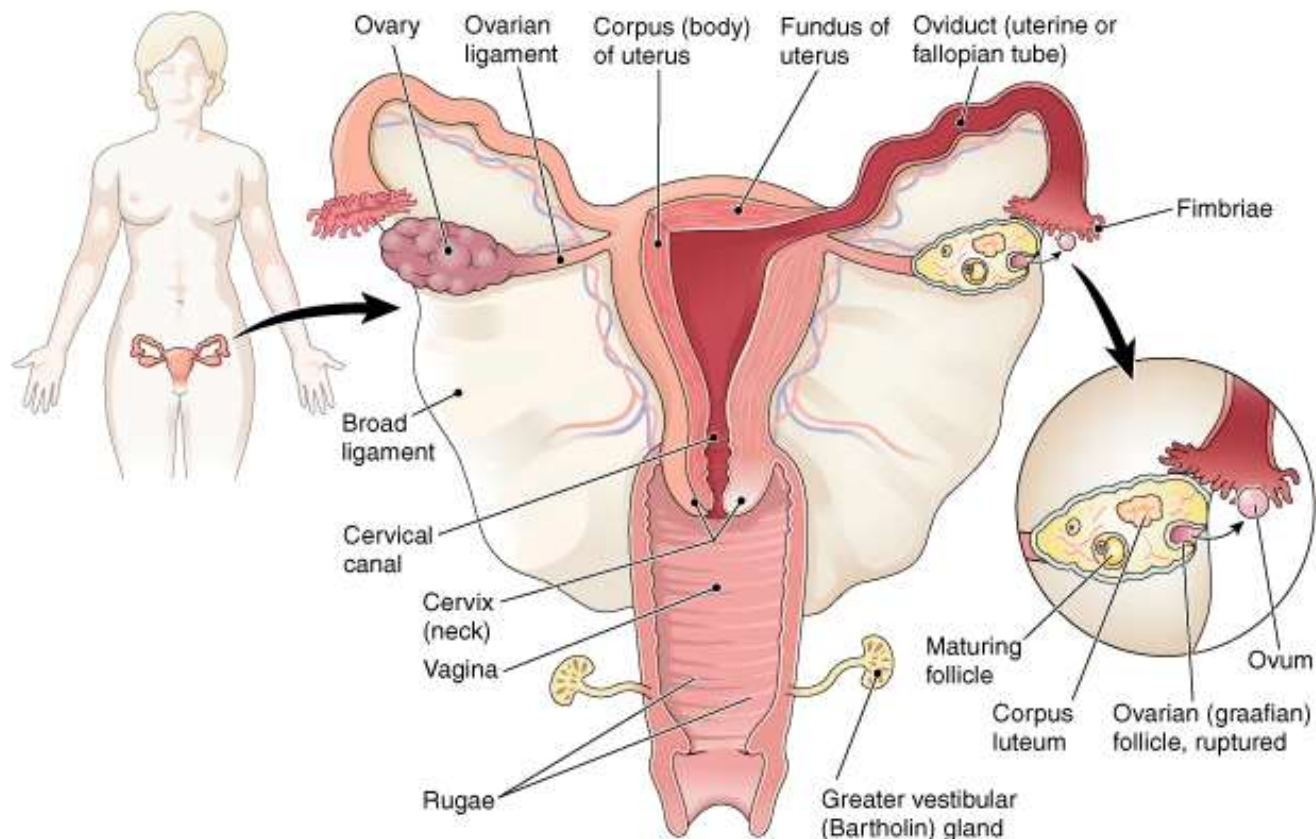
- Peritoneal fluid produced by fimbriae (small, fringelike extensions located at the edge of the tube's opening into the abdomen)
- Ova can not move on own
- Movement depends on sweeping action of cilia in the oviduct's lining and on peristalsis of the tube
- Takes 5 days for an ovum to reach the uterus form the ovary



Oviducts

Uterus

- Organ in which a fetus can develop to maturity
- Oviducts lead to the uterus
- Superior portion rests on upper surface of the urinary bladder
- Inferior portion embedded in the pelvic floor between the bladder and the rectum



Uterus

- The walls of the uterus include:
- a muscular layer (myometrium)
- an inner lining called the endometrium
- The inner layer changes during menstrual cycle

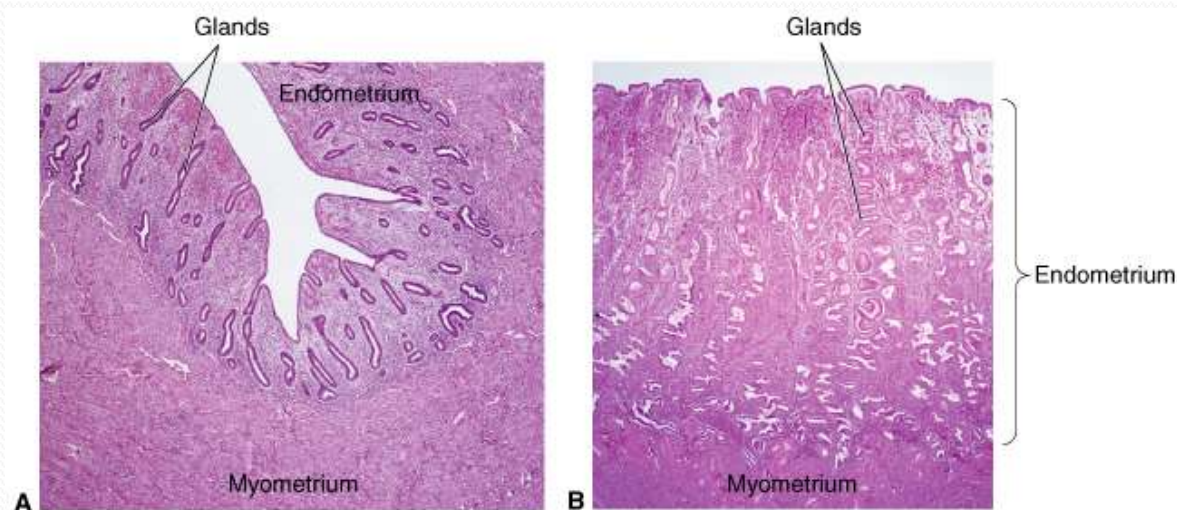


Figure 20-8 **The uterus as seen under the microscope.** The photomicrographs show the myometrium and endometrium and illustrate the changes that occur in the endometrium during the menstrual cycle. (A) Proliferative phase (first part of cycle). (B) Secretory phase (second part of cycle). (Reprinted with permission from Cormack DH. *Essential Histology*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2001.)

Vagina

- Distal part of the birth canal which opens to the outside of the body
- Cervix (opening of the uterus) leads to the vagina
- Muscular tube connecting the uterine cavity with outside
- Lining of the vagina is a wrinkled mucous membrane similar to that found in the stomach
- Rugae (folds) permit enlargement so that childbirth usually does not tear the lining
- Vagina is an organ for child birth and also receives the penis during sexual intercourse
- a fold of membrane, called the hymen, may sometimes be found near the vaginal canal opening

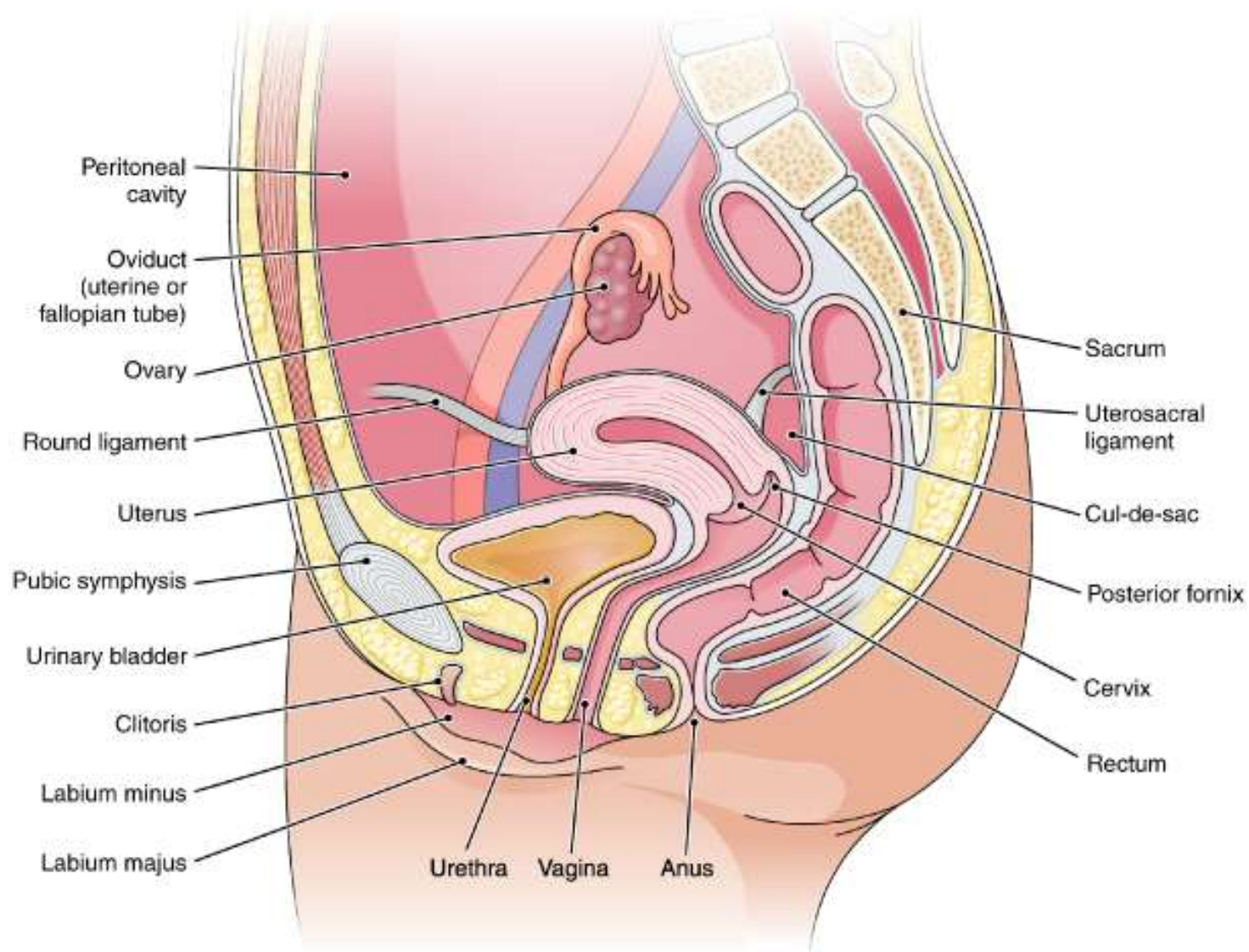


Figure 20-9 Female reproductive system (sagittal section). This view shows the relationship of the reproductive organs to each other and to other structures in the pelvic cavity.

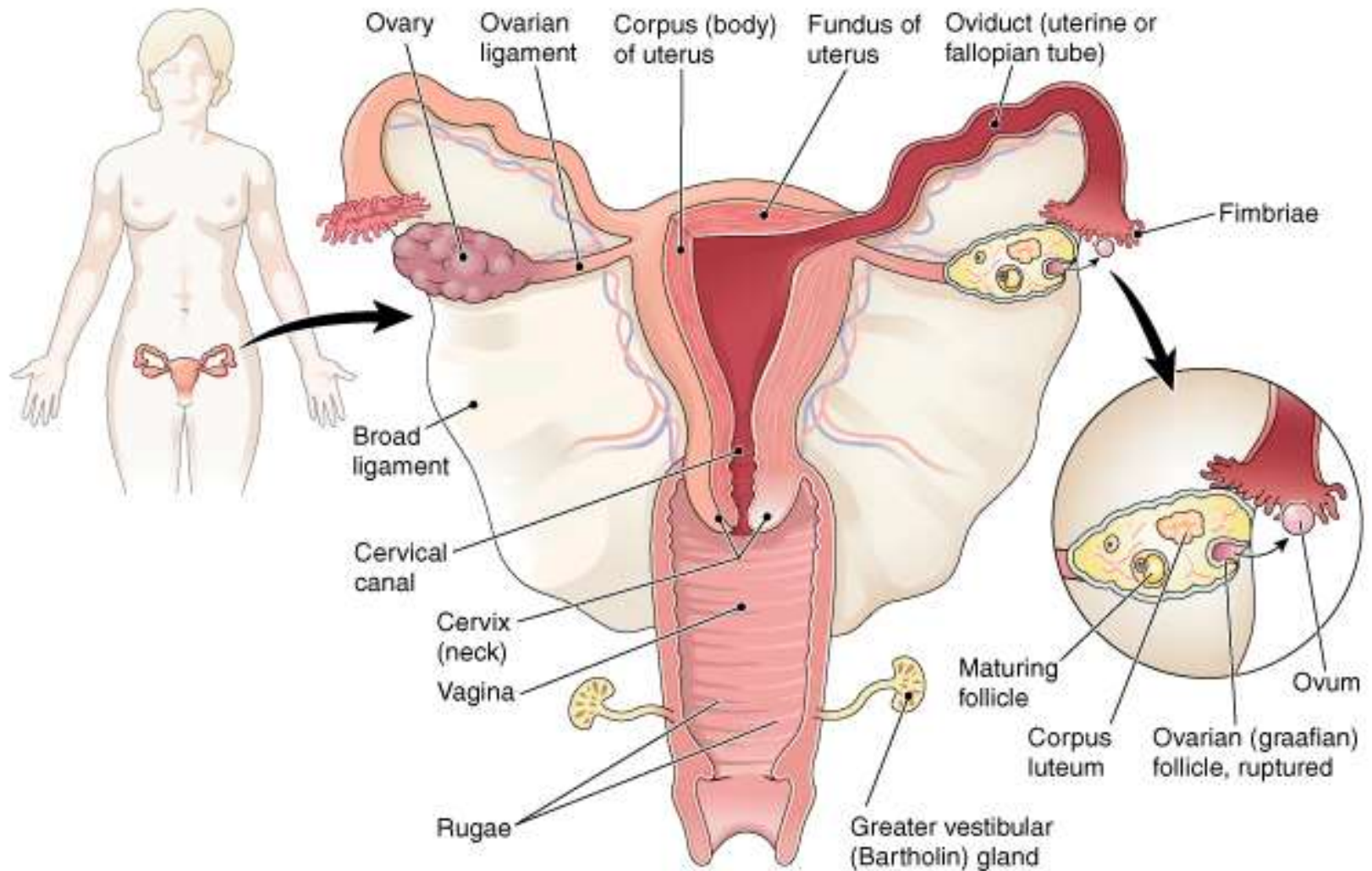


Figure 20-6 **Female reproductive system.** The enlargement (right) shows ovulation.

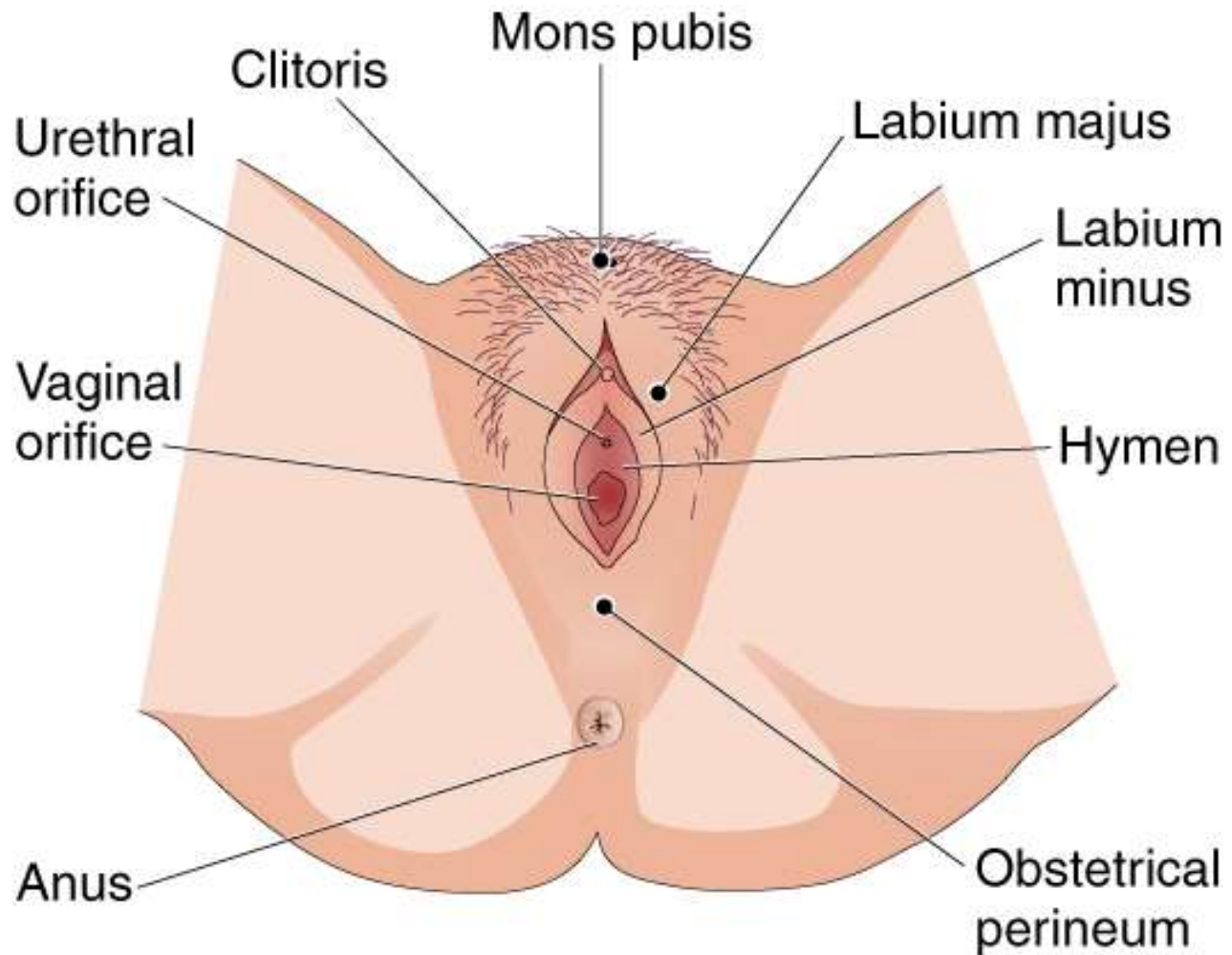
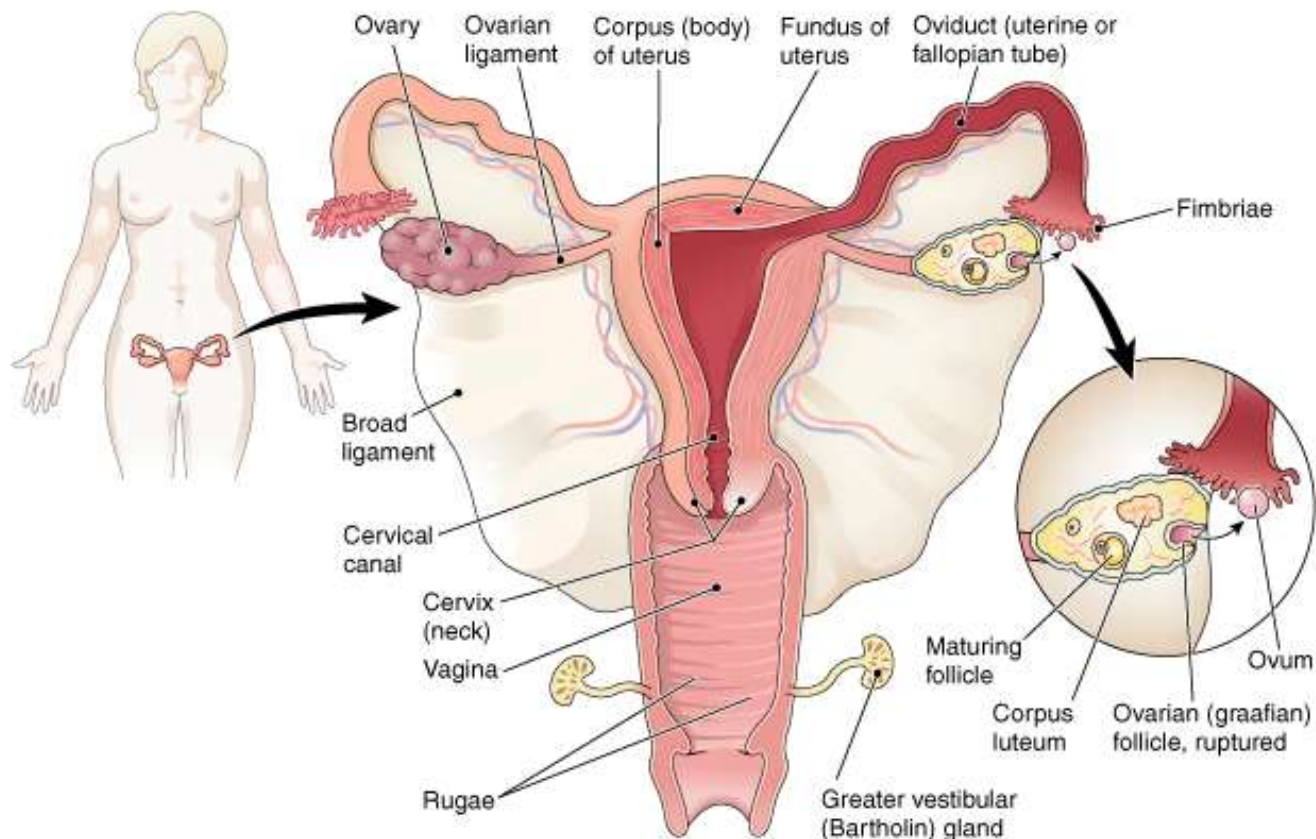


Figure 20-10 **External parts of the female reproductive system.** Related structures are also shown.

Greater Vestibular Glands

- Just superior and lateral to the vaginal opening are the two mucus-producing greater vestibular glands
- These glands secrete into an area near the vaginal opening known as the vestibule
- These glands provide lubrication during intercourse



- External parts of the female reproductive system comprise the vulva
- Includes:
 - two pairs of lips (labia)
 - Clitoris (small organ of great sensitivity)
- Entire pelvic floor in male and female referred to as perineum
 - However, in pregnant women, the area between the vaginal opening and the anus is referred to as the obstetrical perineum

Vulva & Perineum

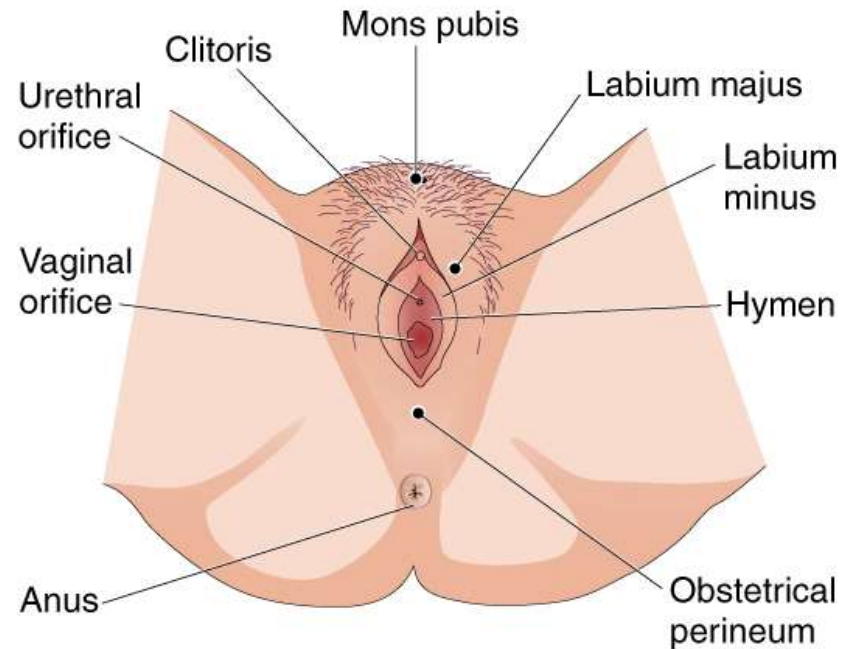
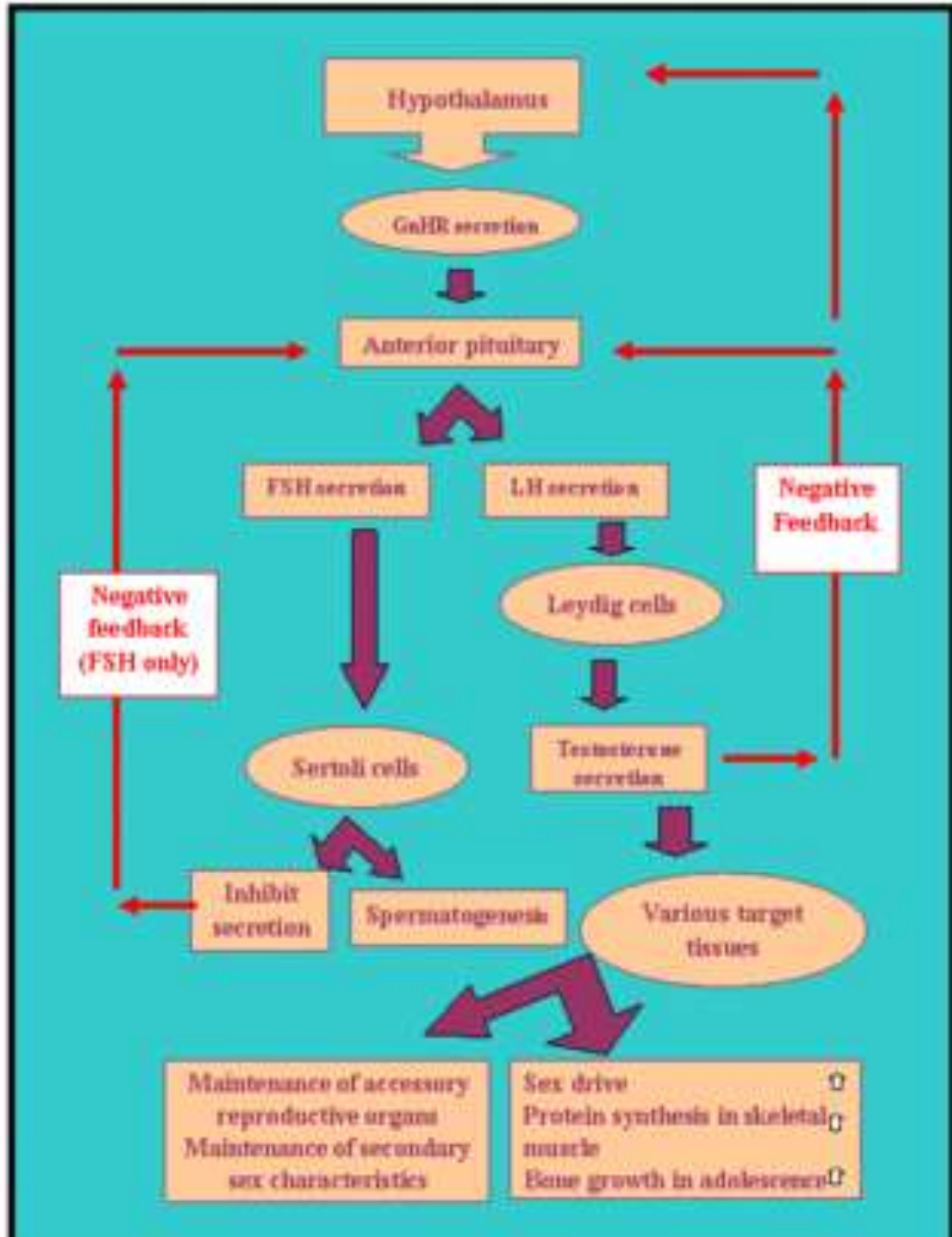


Figure 20-10 External parts of the female reproductive system. Related structures are also shown.



Control of the testes

- GnRH secreting neuroendocrine cells in the hypothalamus fire a brief burst of action potentials approx. every 90min, secreting GnRH at these times.
- The GnRH reaching the anterior pituitary gland via the hypothalamo-pituitary portal vessels during each periodic pulse triggers the release of both LH and FSH from the same cell type but not necessarily in equal amounts.
- FSH acts primarily on the Sertoli cells to stimulate the secretion of paracrine agents required for spermatogenesis.
- LH acts primarily on the Leydig cells to stimulate testosterone secretion.
- The testosterone secreted by the Leydig cells also acts locally, in a paracrine manner by diffusing from the interstitial spaces into the seminiferous tubules. It enters the Sertoli cells, where it facilitates spermatogenesis.

Control of the testes

- Despite the absence of a direct effect on cells in the seminiferous tubules, LH exerts an essential indirect effect because the testosterone secretion stimulated by LH is required for spermatogenesis.
- Even though FSH and LH are produced by the same cell type, their secretion rates can be altered to different degrees by negative feedback inputs.
- Testosterone inhibits LH secretion in two ways:
 1. It acts on the hypothalamus to decrease amplitude of GnRH bursts, which result in a decrease in gonadotropins
 2. It acts directly on the anterior pituitary gland to decrease the LH response to any given amount of GnRH.
- FSH stimulates Sertoli cells to increase both spermatogenesis and inhibin production, and inhibin decreases FSH release, this is a logical completion of a negative feedback loop.
- Despite all these complexities the total amounts of GnRH, LH, FSH, testosterone and inhibin secreted and sperm produced do not change dramatically from day to day.

testosterone

Effects of Testosterone in the Male

1. Required for initiation and maintenance of spermatogenesis (acts via Sertoli cells)
2. Decreases GnRH secretion via an action on the hypothalamus
3. Inhibits LH secretion via a direct action on the anterior pituitary gland
4. Induces differentiation of male accessory reproductive organs and maintain their function
5. Induces male secondary sex characteristics; opposes action of estrogen on breast growth
6. Stimulates protein anabolism, bone growth and cessation of bone growth
7. Required for sex drive and may enhance aggressive behaviour
8. Stimulates erythropoietin secretion by the kidneys

testosterone

- Testosterone needs to undergo transformation in many(not all) of its target cells in order to be effective.
- Depending on the target cells testosterone act as testosterone, dihydrotestosterone(D estradiol).
- Therapy for prostate cancer makes use of these facts because prostate cancer cells are stimulated by dihydrotestosterone, so the cancer can be treated with inhibitors of 5^{α} - reductase.
- Male pattern baldness may also be treated with 5^{α} - reductase inhibitors because DHT tends promote hair loss from the scalp.

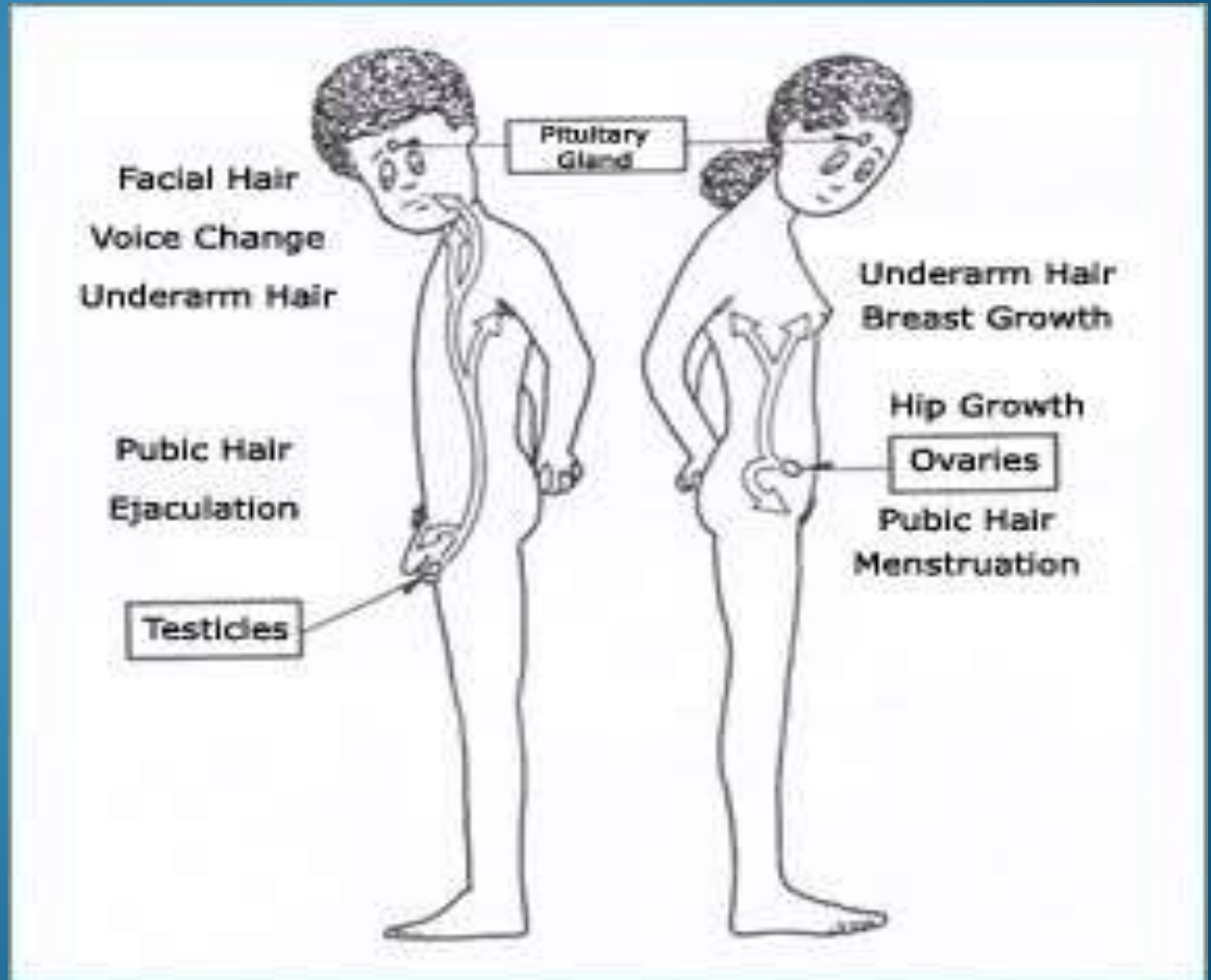


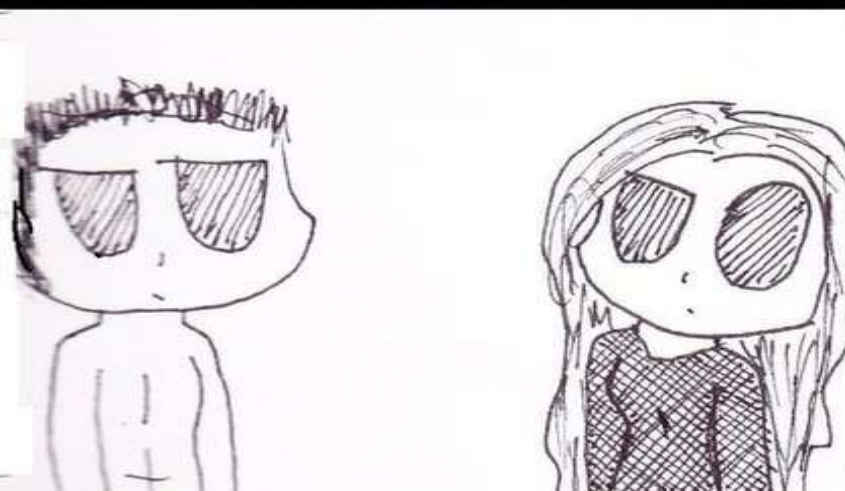
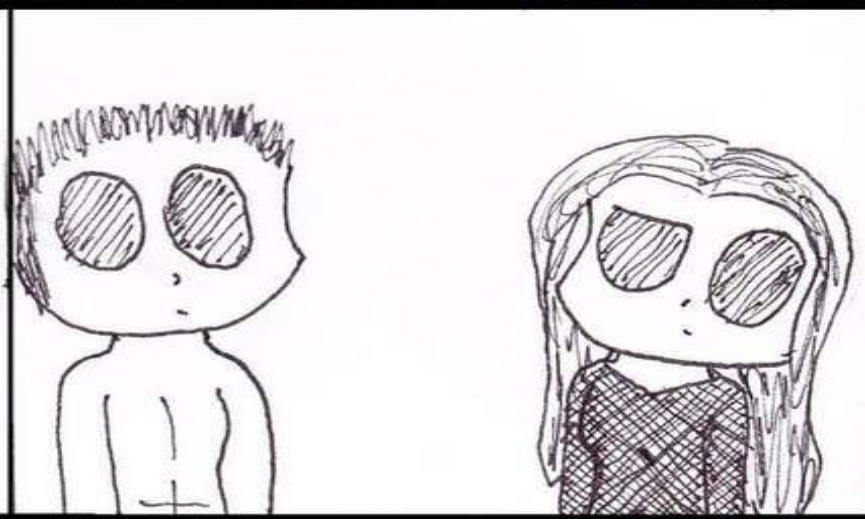
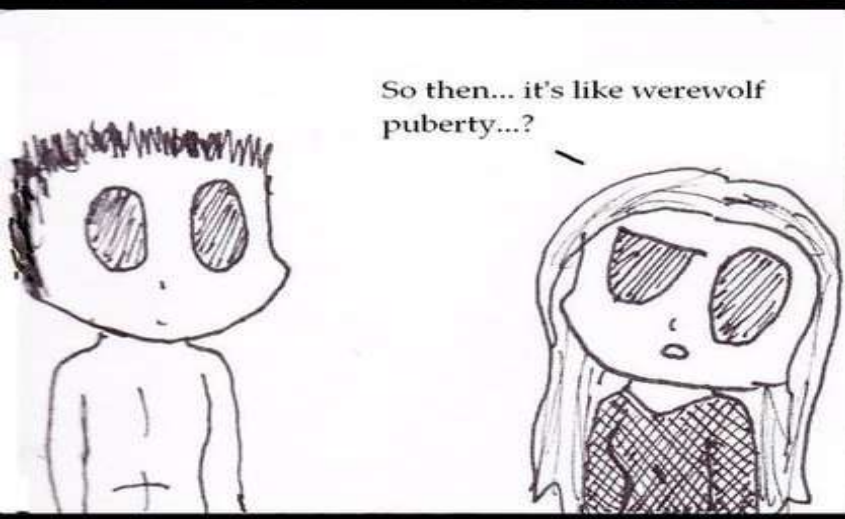
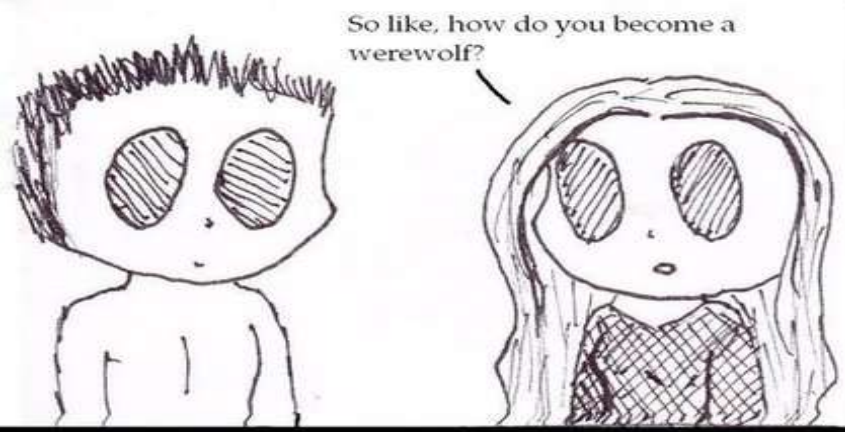
• Accessory reproductive organs

- The fetal differentiation and later growth and function of the entire male duct system, glands, and penis all depend upon testosterone.
- When testicular function is lost, the accessory reproductive organs decrease in size, the glands markedly reduce their secretion rates and the smooth muscle activity of the ducts is diminished. Sex drive(libido) and ejaculation are usually impaired.
- These defects lessen with the administration of testosterone. This would also occur with castration(removal of gonads) which might be done to treat testicular cancer.



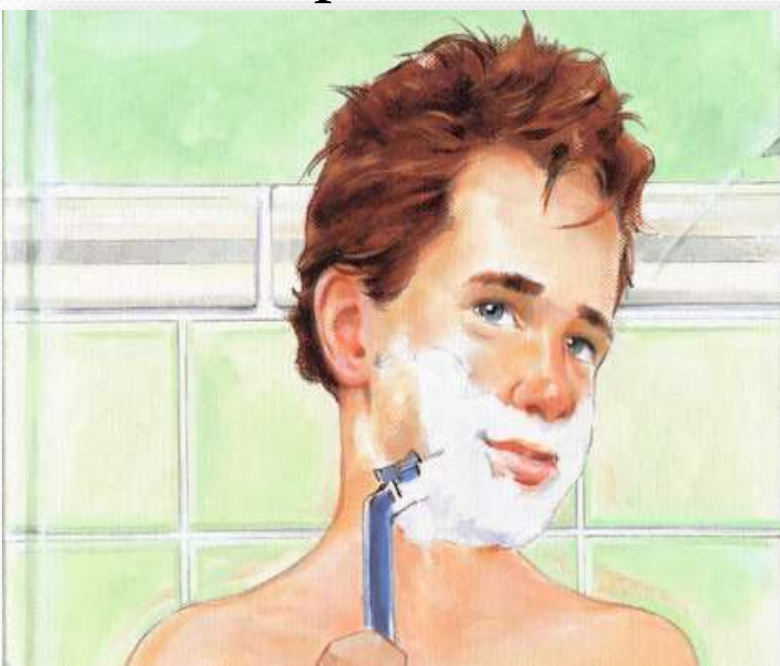
Puberty



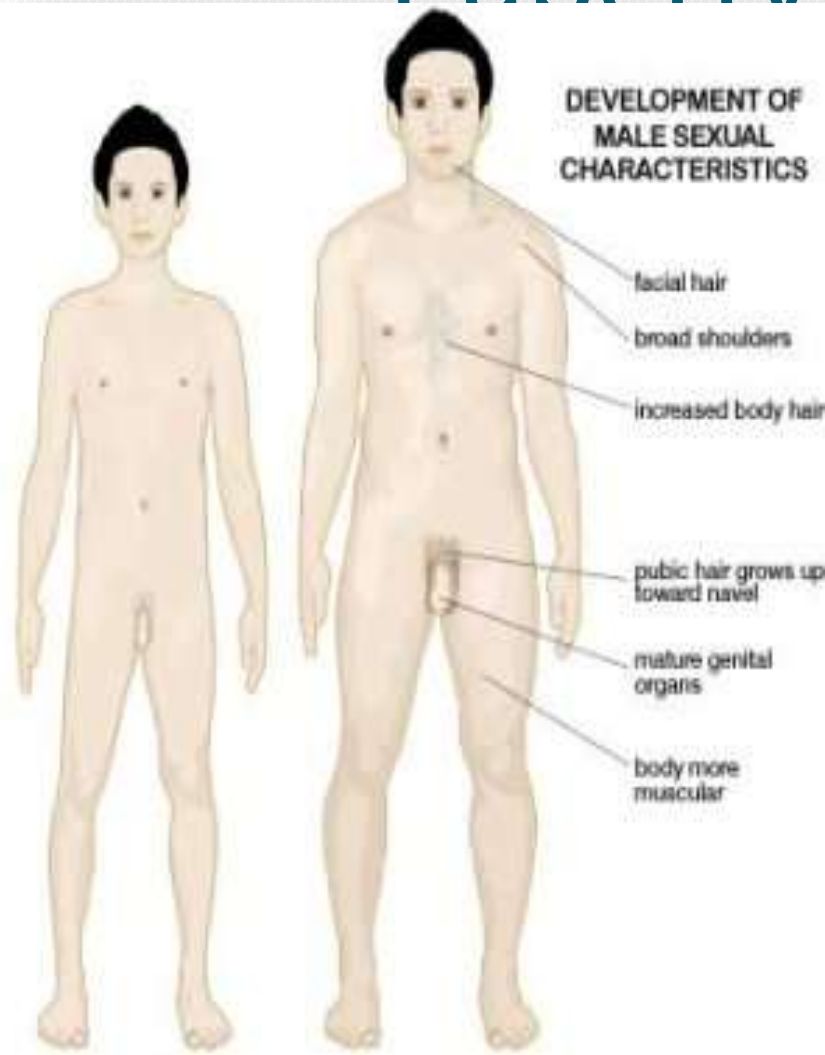


What is puberty?

- Puberty is the period during which the reproductive organs mature and reproduction becomes possible.



Puberty in males



- Occurs between 12 and 16yrs of age.
- The first signs of puberty are due to the increased secretion of adrenal androgens, under the stimulation of adrenocorticotrophic hormone (ACTH)

Puberty in males

These androgens cause the very early development of pubic and axillary (armpit) hair as well as the early stages of puberal growth spurt in concert with growth hormone and insulin-like growth factor I. However, all other developments in puberty are reflections of increased activity of the hypothalamic-anterior pituitary gland-gonadal axis.

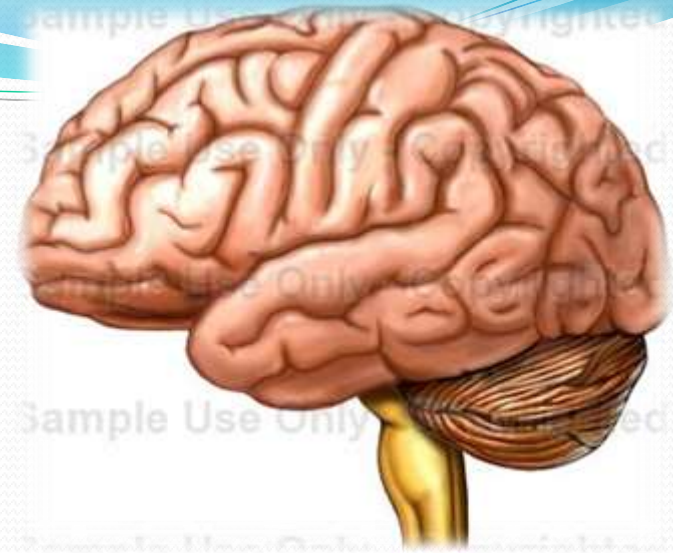
Increased GnRH secretion at puberty causes increased secretion of pituitary gonadotropins, which stimulate the seminiferous tubules and testosterone secretion.



Puberty in males

- Testosterone induces the puberal changes that occur in the accessory reproductive organs, secondary sex characteristics, and sex drive.
- The mechanism of brain change that results in increased GnRH secretion is unknown.

- However, the brain becomes less sensitive to the negative feedback effects of gonadal hormones at the time of puberty.



Puberty in males

Secondary Sex Characteristics and Growth

- All male secondary sex characteristics are dependent on testosterone and its metabolite, DHT*.
- Other androgen-dependent secondary sexual characteristics are:
 1. Deepening of the voice-from the growth of the larynx
 2. Thick secretion of the skin oil glands-often causing acne
 3. The masculine pattern of fat distribution.



Androgens also stimulate bone growth, through the stimulation of growth hormone secretion.

However,

they terminate bone growth by causing closure of epiphyseal plates.



Bone

Puberty in males

Secondary Sex Characteristics and Growth

- Androgens are “anabolic steroids” in that they exert a direct stimulatory effect on protein synthesis in muscle.
- They also stimulate the secretion of erythropoietin by the kidneys- this is a major reason why men have higher hematocrit* than women.

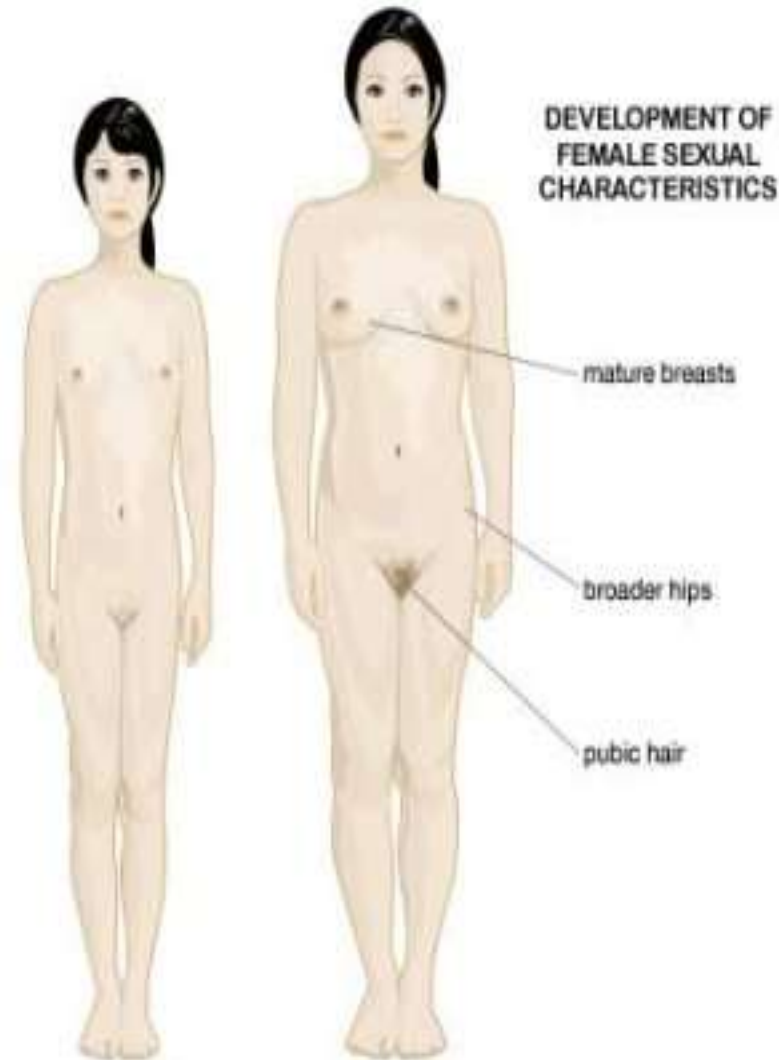
Behaviour

- Androgens are essential for the development of sex drive at puberty, and play an important role in maintaining sex drive(libido) in adulthood.



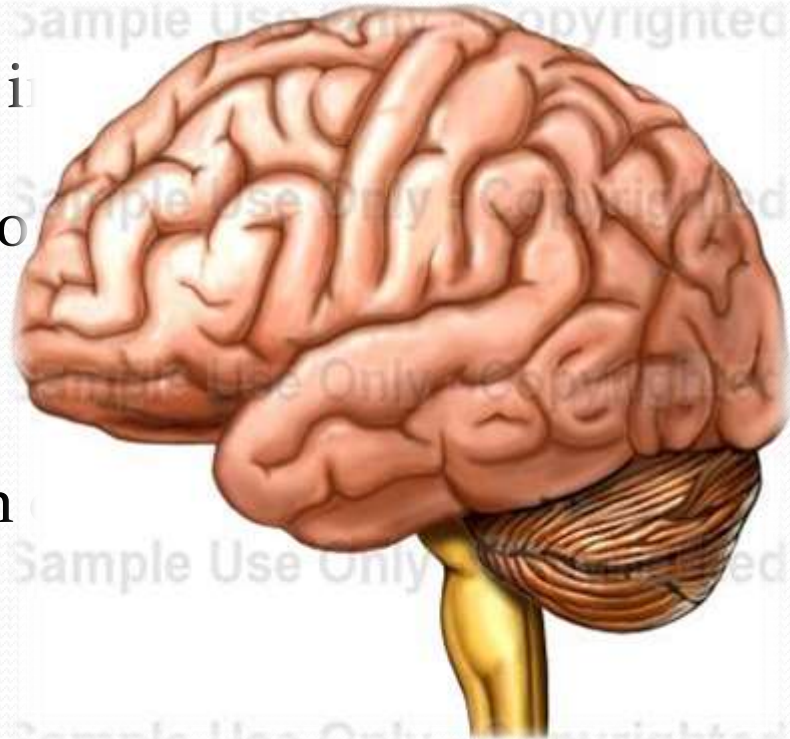
Puberty in females

- Begins usually around ages 10 to 12 yrs.
- GnRH, the pituitary gland gonadotropins, and estrogen are all secreted at very low levels during childhood. Therefore, follicle maturation occurs beyond the early antral stage and menstrual cycles do not occur.
- The female accessory sex organs remain small and non-functional, and there are minimal secondary sex characteristics.



Puberty in females

- The onset of puberty is caused by an alteration in brain function that increases the secretion of GnRH. This hypothalamic* hormone in turn stimulates the secretion of the pituitary gland gonadotropins, which stimulate follicle development and estrogen secretion.



Puberty in females

- Estrogen, in addition to its critical role in follicle development, induces the changes in accessory sex organs and secondary sex characteristics associated with puberty. **Menarche**, the first menstruation, is a late event of puberty.
- The mechanism of brain change that results in increased GnRH secretion in girls at puberty remains unknown.
- The brain may become less sensitive to the negative feedback effects of gonadal hormones at the time of puberty. (averaging age 12.3)



Puberty in females

- The adipose-tissue hormone leptin is known to stimulate the secretion of GnRH and may play a role in puberty. This may explain why the onset of puberty tends to correlate with the attainment of a certain level of energy stores(fat) in the girl's body.
- The failure to have a normal menstrual cycle is called **amenorrhea**. Primary amenorrhea is the failure to initial normal menstrual cycles at puberty(menarche), whereas secondary amenorrhea is defined as the loss of previously normal menstrual cycles(common causes pregnancy and menopause).
- Excessive exercise and anorexia nervosa can cause both primary and secondary amenorrhea.

Precocious puberty

- The age of normal onset of puberty is controversial. However, pubertal onset before the age of 6-7 in girls and 8-9 in boys warrants clinical investigation.
- Precocious puberty is defined as the premature appearance of secondary sex characteristics and is usually caused by an early increase in gonadal steroid production. This leads to an early onset of the puberty growth spurt, maturation of the skeleton, breast development (in girls) and enlargement of genitalia in boys. True precocious is caused by the premature activation of GnRH and LH and FSH secretion. Often caused by tumors or infections in the area of the central nervous system that control GnRH release. Treatments that decrease LH and FSH release are important to allow normal development.



To illustrate Dr. HARRY CAMPBELL'S Case of Premature Puberty. From photographs taken when the patient was six years old.

Danielson & Co., Sc.

Control of Ovarian Functions & the effects of Estrogen and Progesterone

Control of Ovarian Functions

The ovaries have several functions

- Oogenesis-the production of gametes during the fetal period
- Maturation of the oocyte
- Expulsion of the mature oocyte(ovulation)
- Secretion of the female sex steroid hormones (estrogen and progesterone). It also secretes the peptide hormone inhibin.

Control of Ovarian Functions

The major factors controlling the ovaries are

GnRH – Gonadotropin-releasing hormone

FSH- Follicle stimulating hormone

LH- luteinizing hormone

Estrogen

Progesterone

Control of Ovarian Functions

Gonadotropin-releasing hormone is secreted from the hypothalamus and it stimulates the anterior pituitary gland to secrete LH and FSH.

LH is released from the pituitary gland. Its main function is to cause ovulation and it causes the formation of the corpus luteum.

FSH is primarily responsible for stimulating the growth of the ovarian follicle.

Estrogen is secreted from the ovary and it is involved in the thickening of the endometrium of the uterus and the growth of the uterus

Progesterone is cause the endometrium to secrete special proteins during the second half of the menstrual cycle, preparing it to receive and nourish an implanted fertilized egg.

Control of Ovarian Functions

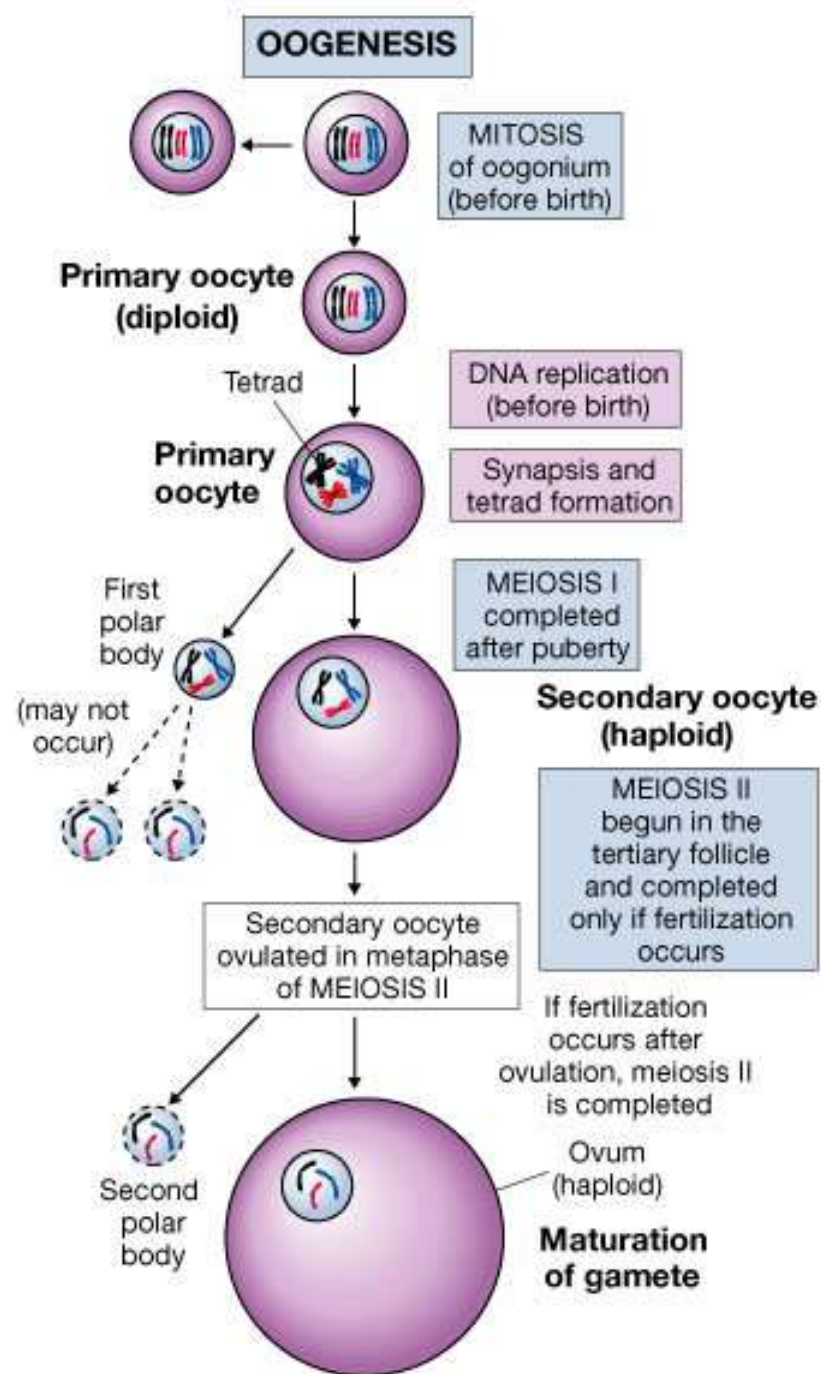
During early *in utero* development, the primitive germ cells, or oogonia, undergo numerous mitotic divisions. Around the seventh month after conception, the fetal oogonia cease dividing. During fetal life, all the oogonia develop into primary oocytes, which then begin a first meiotic division by replicating their DNA. They do not complete division in the fetus. The cells are said to be in a state of meiotic arrest. This state continues until puberty and the onset of renewed activity in the ovaries.

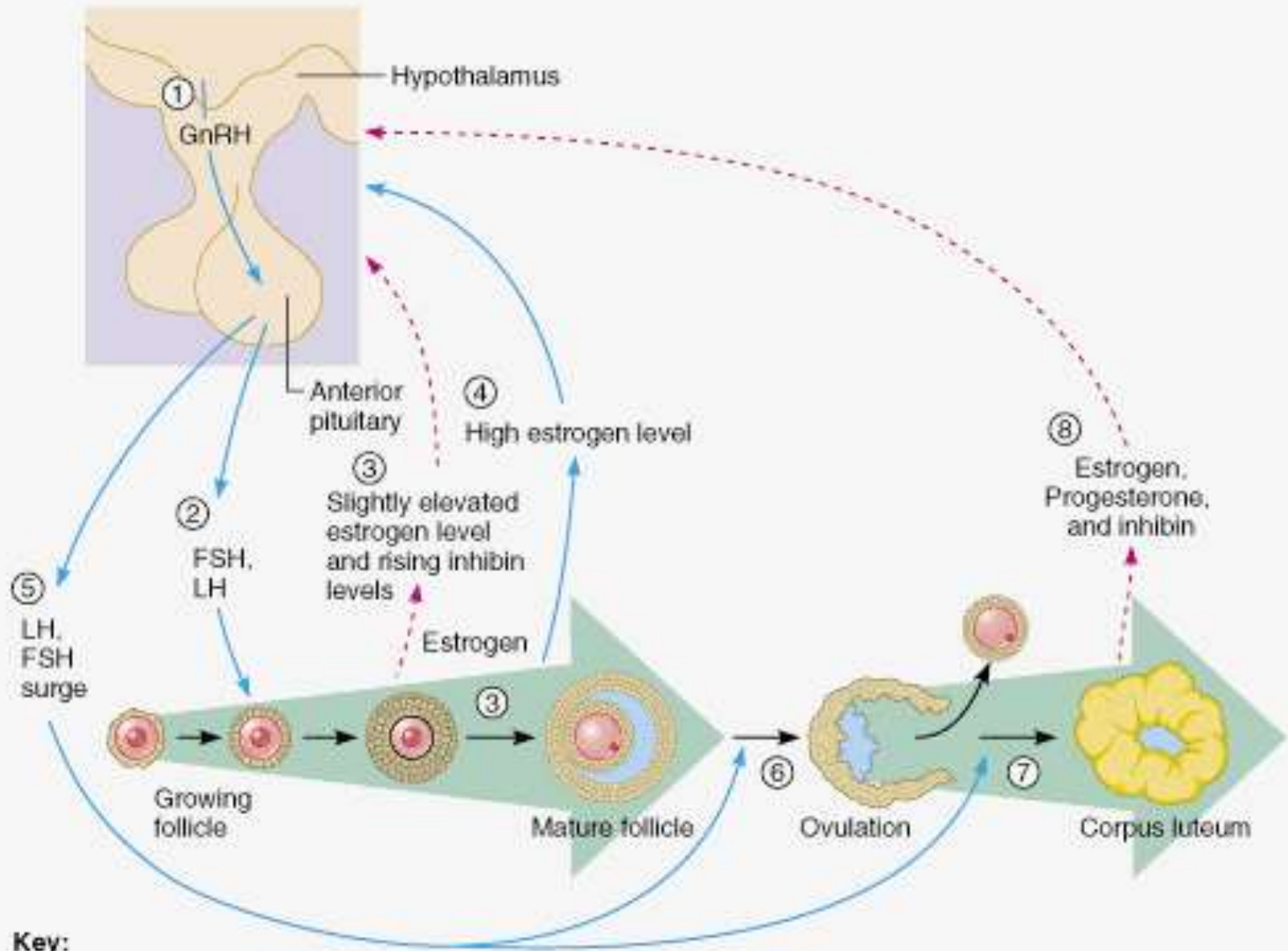
Control of Ovarian Functions

Only those primary oocytes destined for ovulation will ever complete the first meiotic division, for it occurs just before the egg is ovulated. Each daughter cell receives 23 chromosomes, each with two chromatid. In this division, one of the two daughter cells, the secondary oocyte, retains virtually all the cytoplasm. The other called the first polar body is small and non-functional. Thus, the primary oocyte, which is already as large as the egg will be, passes on to the secondary oocyte just half of its chromosomes but almost all of its nutrient-rich cytoplasm.

Control of Ovarian Functions

The second meiotic division occurs in the fallopian tube after ovulation, but only if the secondary oocyte is fertilized. As a result of this second meiotic division, the daughter cells receive 23 chromosomes, each with a single chromatid. Once again, the daughter cell, now called an ovum, retains nearly all the cytoplasm. The other daughter cell, the second polar body is very small and non-functional. The net result of oogenesis is that each primary oocyte can produce only one ovum.

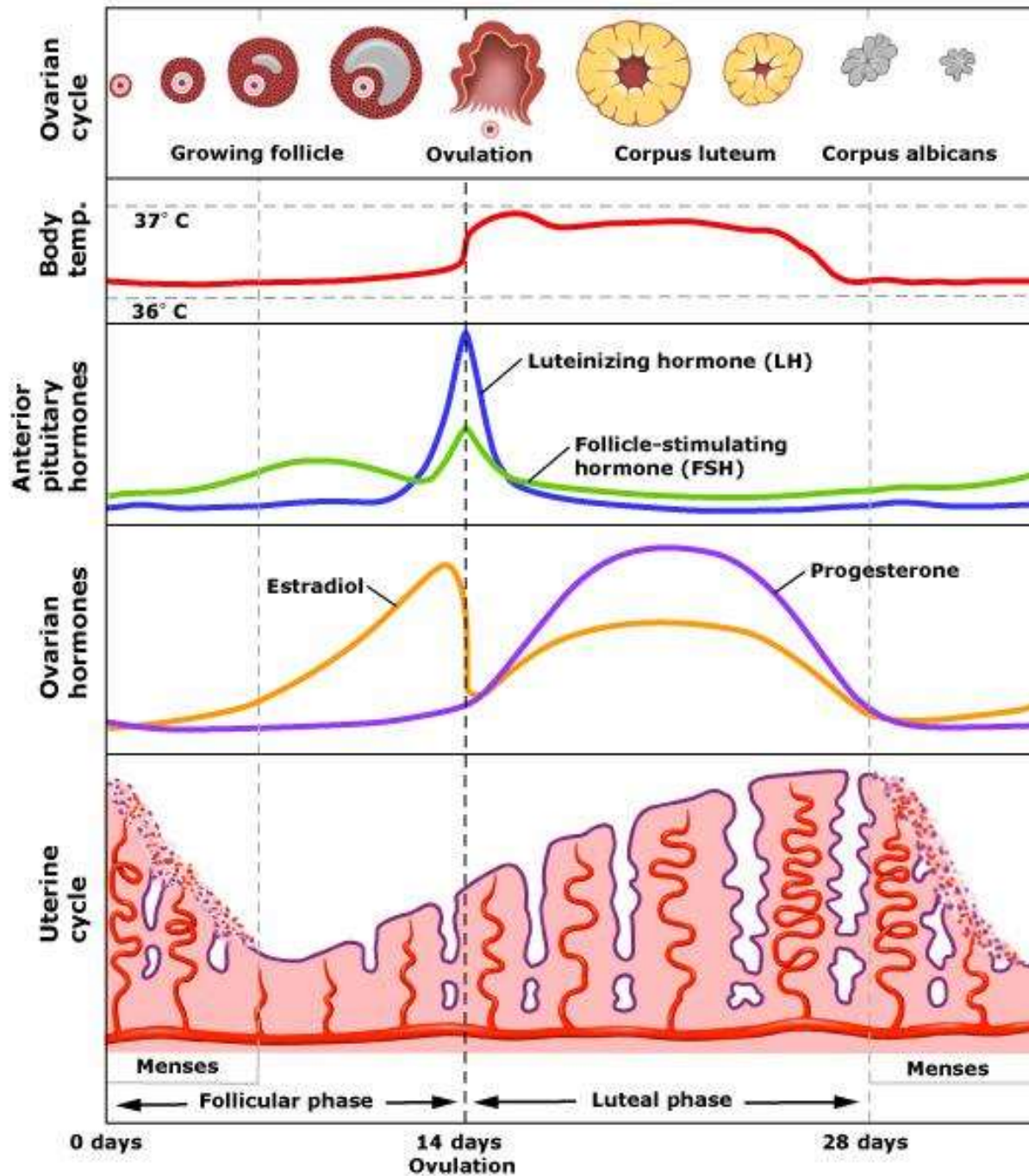


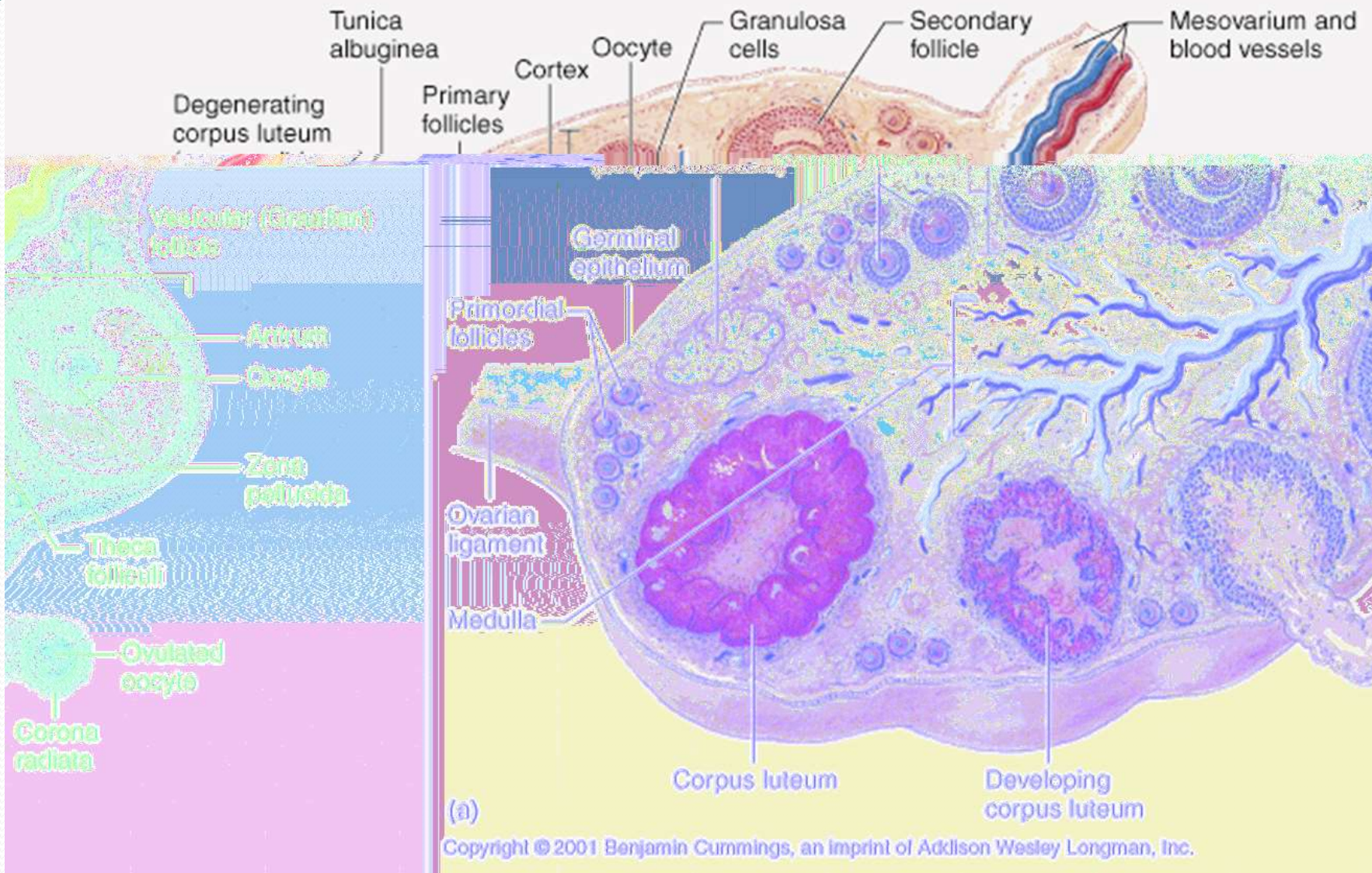


Key:

→ = Stimulates

- - - → = Inhibits





(a)

Control of Ovarian Functions

- GnRH is secreted from the hypothalamus. This causes the secretion of LH and FSH from the anterior pituitary gland.
- LH and FSH levels increase (slightly elevated levels of estrogen and inhibin exhibit little negative feedback)
- Multiple antral follicles begin to enlarge and secrete estrogen. Estrogen concentration increase markedly.
- FSH secretion and FSH plasma concentration decrease.
- The increasing plasma estrogen concentration exerts a “positive” feedback on gonadotropin secretion
- An LH and FSH surge is triggered

Control of Ovarian Functions

- Ovulation occurs
- The corpus luteum forms and begins to secrete large amounts of both estrogen and progesterone.
- Plasma concentrations of estrogen and progesterone increase
- FSH and LH concentrations secretion are inhibited and their plasma concentrations decrease
- The corpus luteum begins to degenerate and decrease its hormone secretion
- Plasma estrogen and progesterone concentrations decrease
- FSH and LH concentrations begin to increase and a new cycle begins

Effects of Estrogen & Progesterone

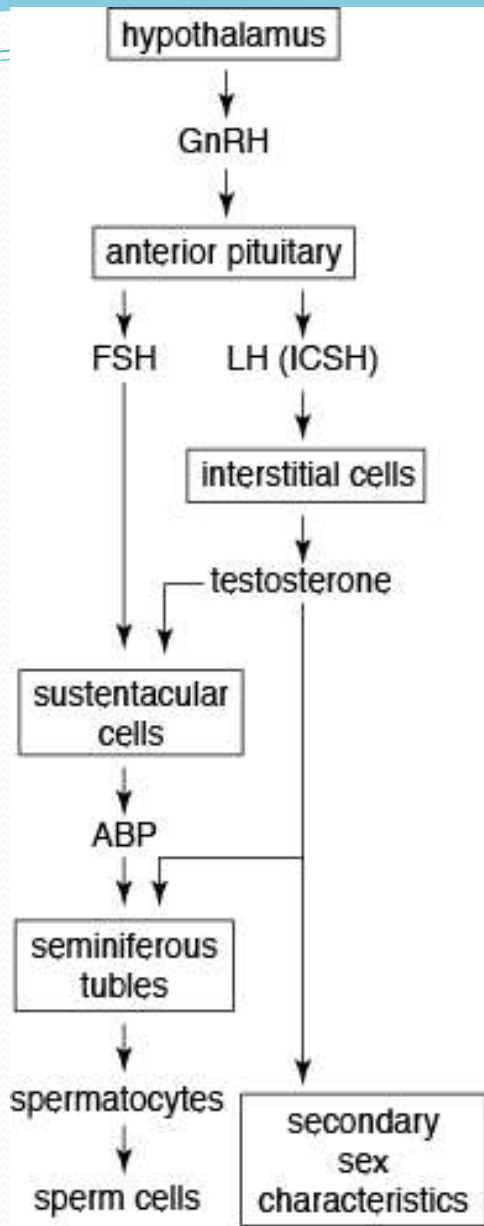
Estrogen

- Stimulates the growth of the ovary and follicles
- Stimulates external genitalia
- Stimulates breast growth, particularly ducts and fat deposition in puberty
- Stimulates female body configuration development during puberty: narrow shoulders, broad hips, female fat distribution (deposition on hips and breasts)
- Vascular effects (deficiency produces hot flashes)
- Stimulates prolactin secretion but inhibits prolactin's milk-inducing action on the breasts

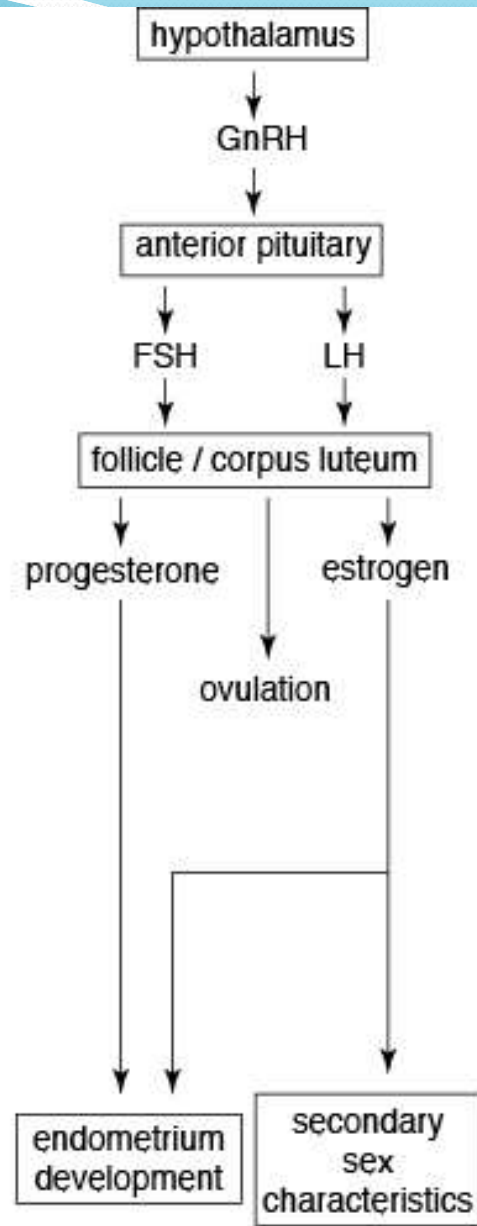
Effects of Estrogen & Progesterone

Progesterone

- Converts the estrogen primed endometrium to an actively secreting tissue suitable for implantation of the embryo
- Decreases contraction of the fallopian tubes and myometrium
- Increases body temperature
- Decreases proliferation of vaginal epithelial cells
- Induces thick, sticky cervical mucus
- Inhibits milk producing effects of prolactin
- Stimulates breast growth, particularly glandular tissue



(a) Hormone Regulation In the Male Reproductive System



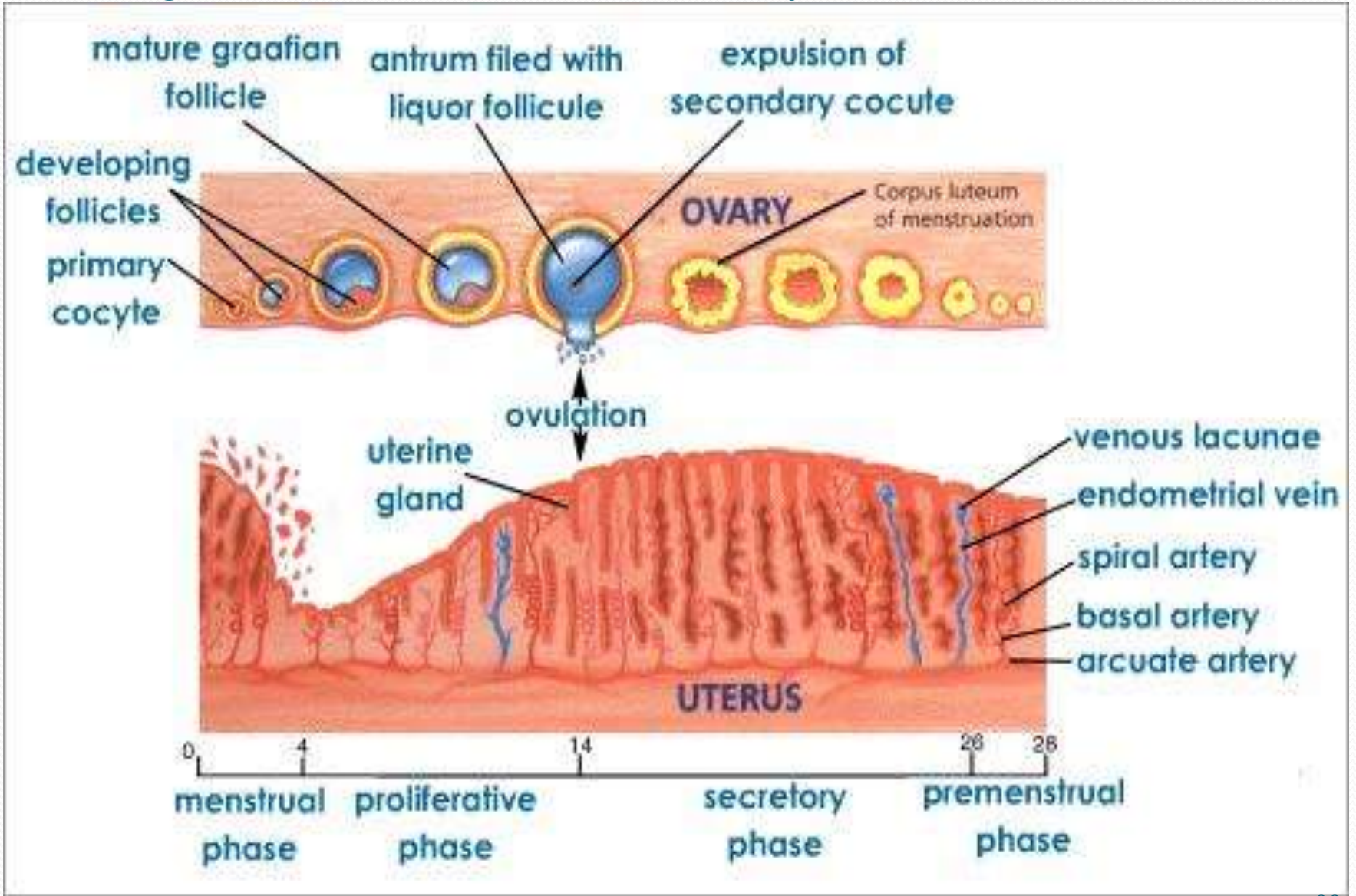
(b) Hormone Regulation In the Female Reproductive System

Uterine Changes in the menstrual cycle

There are mainly 4 phases in the menstrual cycle:

- Menstrual phase
- Proliferative phase
- Secretory phase
- Menstrual or Premenstrual phase

A diagram of the Menstrual cycle



Uterine changes are caused by changes in the plasma concentrations of estrogen and progesterone.

Menstrual phase

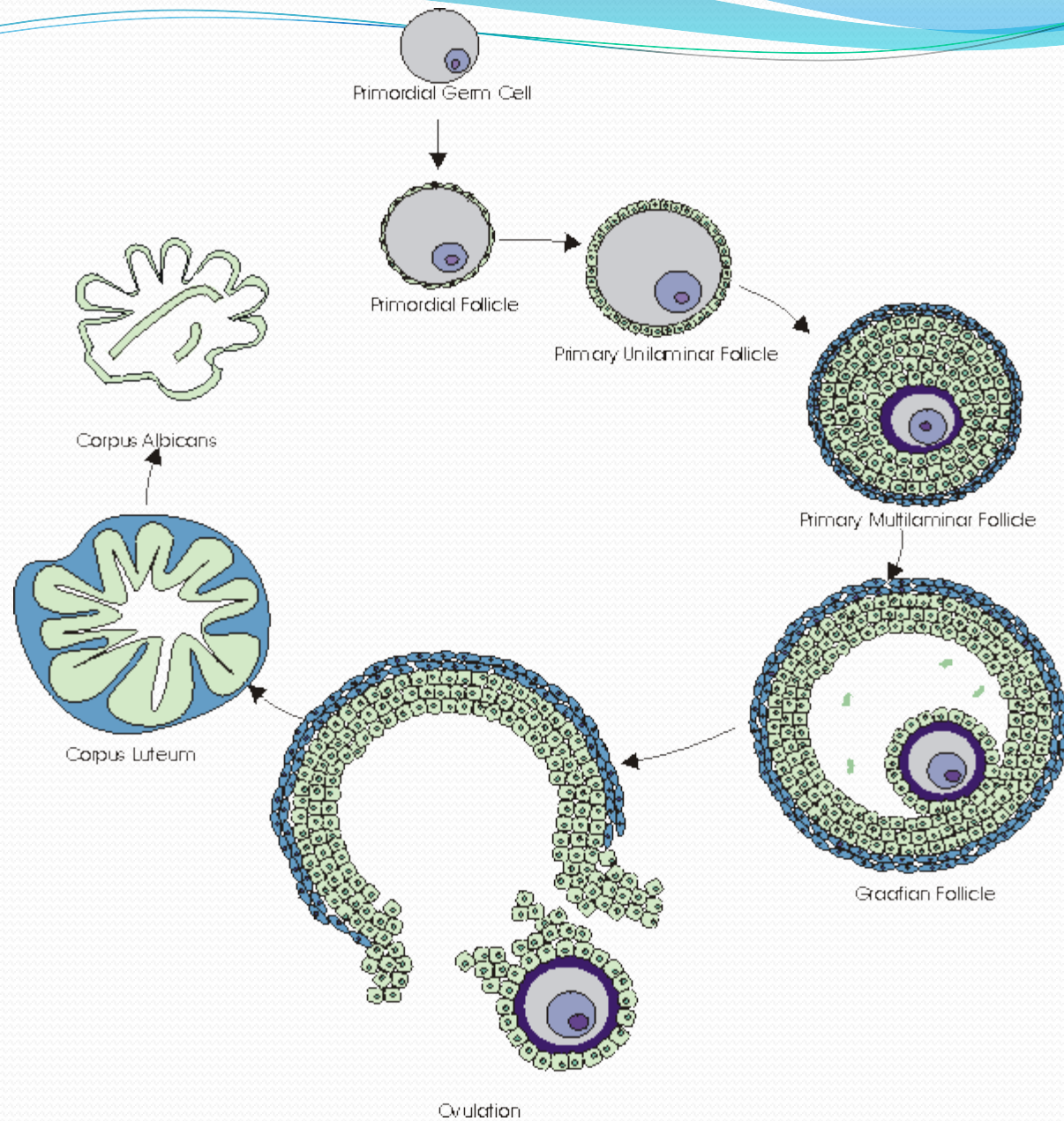
- Lasts an average of 3-5days.
- Endometrium degenerates resulting in the menstrual flow.
- After the menstrual flow the endometrium begins to thicken due to the influence of estrogen.

Proliferative phase

- Lasts approximately 10 days.
- Occurs between the end of the menstrual phase, during ovulation.
- When flow ceases, the endometrium begins to thicken influenced by estrogen.
- Estrogen stimulates growth of the endometrium and the uterine smooth muscle (myometrium) also inducing the synthesis of progesterone receptors on endometrial cells.

Secretory Phase

- After ovulation the endometrium increases secretory activity under the influence of progesterone and estrogen, the formation of the corpus luteum, progesterone acts upon the endometrium to convert it to an actively secreting tissue.
- The endometrial glands become coiled and filled with glycogen, the blood vessels become more numerous and enzymes accumulate in the glands and connective tissue. These changes are necessary for implantation and nourishment of a developing embryo.



Ovulation

Table 1 summary of menstrual cycle

Day(s)	Major event
1-5	<p>Estrogen and progesterone are low because the previous corpus luteum is regressing.</p> <p>Therefore: (a) Endometrial lining sloughs. (b) Secretion of FSH and LH is released from inhibition, and their plasma concentrations increase. Several follicles are stimulated to mature.</p>
7	<p>A single follicle (usually) becomes dominant.</p>
7-12	<p>Plasma estrogen increases because of secretion by the dominant follicle.</p> <p>Therefore: Endometrium is stimulated to proliferate.</p>

7-12	LH and FSH decrease due to estrogen and inhibin negative feedback. Therefore: Degradation of nondominant follicle occurs.
12-13	LH surge is induced by increasing plasma estrogen. Therefore: (a) Oocyte is induced to complete its first meiotic division and undergo cytoplasmic maturation. (b) Follicle is stimulated to secrete digestive enzymes and prostaglandins
14	Ovulation is mediated by follicular enzymes and prostaglandins.

15-25

Corpus luteum degenerates and, under the influence of low but adequate levels of LH, secretes estrogen and progesterone, increasing plasma concentrations of these hormones.

Therefore: (a) Secretory endometrium develops

(b) Secretion of FSH and LH is inhibited, lowering their plasma concentrations. No new follicles develop.

25-28

Corpus luteum degenerates (if implantation of the conceptus does not occur).

Therefore: Plasma estrogen and progesterone concentrations decrease. Endometrium begins to slough at conclusion of the 28th day and a new cycle begins.

Prostaglandins

- Prostaglandins, are like hormones in that they act as chemical messengers, but do not move to other sites, but work right within the cells where they are synthesized.
- Prostaglandins produced by the endometrium resulting in vasoconstriction and uterine contractions in response in a decrease in plasma estrogen and progesterone.

Table 2 shows some effects of female sex steroids.

Estrogen

1. Stimulates growth of ovary and follicles.
2. Stimulates growth of smooth muscle and proliferation of epithelial linings of reproductive tract. In addition
 - a. Fallopian tubes –increase in contractions and ciliary activity.
 - b. Uterus-Increases myometrial contractions and responsiveness to oxytocin. Stimulates secretion of abundant watery cervical mucus. Prepares endometrium for progesterone’s action by inducing progesterone receptors.
 - c. Vagina-Increases layering of epithelial cells
3. Stimulates external genitalia growth, particularly during puberty.
4. Stimulates breast growth, particularly ducts and fat deposition during puberty.

5. Stimulates female body configuration development during puberty :narrow shoulders, broad hips, female fat distribution (deposition on hips and breast).

6. Stimulates fluid secretion from lipid (sebum) producing skin glands (sebaceous glands)

7. Stimulates bone growth and ultimate cessation of bone growth, protects against osteoporosis; does not have an anabolic effect on skeletal muscles.

8. Vascular effects (deficiencies produce 'hot flashes')

9. Has feedback effects on hypothalamas and anterior pituitary.

10. Stimulates prolactin secretion but inhibits prolactin's milk-inducing action on the breasts.

11. Protects against atherosclerosis by effects on plasma cholesterol, blood vessels and blood clotting.

Progesterone

1. Converts the estrogen-primed endometrium to an actively secreting tissue suitable for implantation of an embryo.

2. Induces thick, sticky cervical mucus.

3. Decreases contractions of fallopian tubes and myometrium.

4. Decreases proliferation of vaginal epithelial cells.

5. Stimulates breast growth, particularly glandular tissue.

6. Inhibits milk inducing effects of prolactin.

7. Has feedback effects on hypothalamus and anterior pituitary.

8. Increase body temperature approximately 0.5°C .

phase)

In the brain(the hypothalamus secretes GnRH)



GnRH triggers pituitary gland to release (FSH)



FSH travels to ovaries in bloodstream & initiates growth of the follicle.



A developed follicle generates estrogen.



Estrogen levels peak approximately 1 day before ovulation (typically day13).



There is a surge of LH from the pituitary gland. This acts on the ovarian follicle. A mature egg is released into fallopian tubes leaving behind the corpus luteum.

Menopause

- Occurs around the age of 50.
- It is where menstrual cycles become less regular and will eventually cease.
- Perimenopause– The beginning of menstrual irregularities, involving emotional and physical changes.
- Menopause is due to ovarian failure. Ovaries lose their ability to respond to gonadotropins because most ovarian follicles and eggs have disappeared.

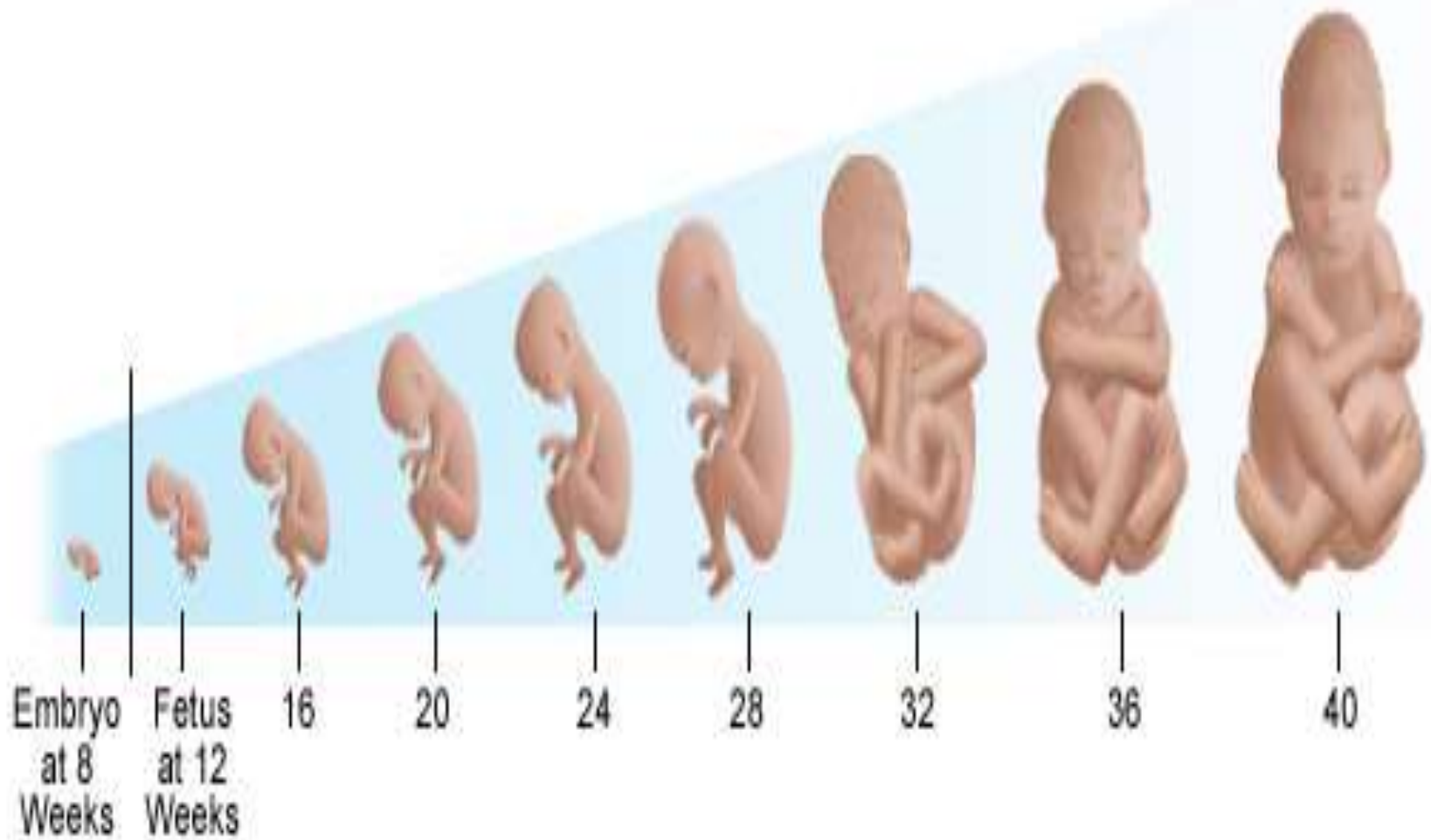
- After menopause there is usually a small amount of estrogen in the plasma.
- The breasts and genital organs gradually atrophy to a large degree.
- Estrogen is needed for bone growth, with little estrogen bone mass decreases (osteoporosis).
- Women experience hot flashes.
- There is the increase in incidence of Cardiovascular disease and coronary artery disease.

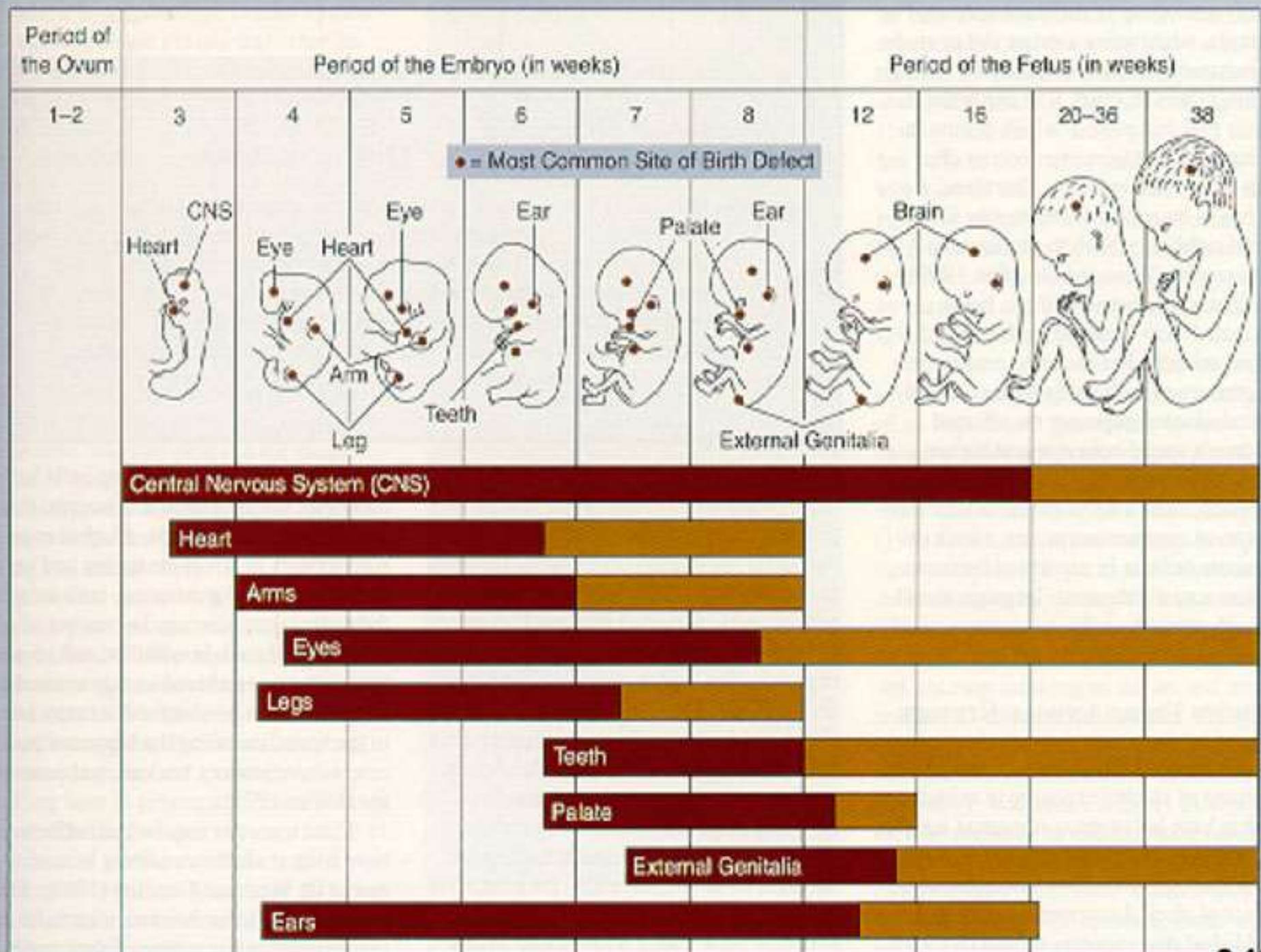
- Administering estrogen increases the risk of developing uterine endometrial cancer and breast cancer.
- Endometrial cancer can be treated with progesterone ,not breast cancer.
- Drugs called selective estrogen receptor modulators (SERMs) are being used as hormone replacers. They activate estrogen receptor in certain tissues.
- SERMs act as estrogen antagonists, therefore it could be used to treat osteoporosis, heart attacks and Alzheimer's disease.

Pregnancy



Fetal Growth From 8 to 40 Weeks





PREGNANCY

- If ovum is fertilized by a sperm the fertilized ovum begins to divide and becomes a fetus.
- This period of the fetus is called pregnancy or gestation.
- Lasts approx 40 weeks
- Levels of estrogen and progesterone increase steadily

Their function are to:


- ❑ Maintain the endometrium
- ❑ Development of breasts for lactation
- ❑ Suppression of development of new ovarian follicles.

EVENTS OF EARLY PREGNANCY

- Fertilization
- Takes place 24 hours after ovulation.
- In a distal portion of the oviduct(ampulla).
- 4 days after ovulation, the fertilized ovum (blastocyst) arrives in the uterine cavity

Implantation

- The blastocyst floats in the cavity for 1 day.
- Then implants in the endometrium 5 days after ovulation.
- A low estrogen/progesterone ratio is needed for the endometrium to be receptive to the fertilized ovum.
- At implantation the blastocyst consists of an inner mass of cells. This is the fetus.
- Outer rim of cells is called the trophoblast.
- Trophoblast contributes the fetal portion of the placenta.

- 
- Trophoblastic cells proliferate and form the syncytiotrophoblast.
 - Its function is to allow the blastocyst to penetrate deep into the endometrium

Secretion of HCG

- Trophoblast becomes the placenta.
- Begins secreting HCG, 8 days after ovulation.
- HCG “informs” the corpus luteum that fertilization has occurred.
- Corpus luteum synthesizes progesterone and estrogen to maintain the endometrium for implantation.
- High levels of estrogen and progesterone suppress the development of the next cohort of ovarian follicles.
- The pregnancy test is based on the excretion of HCG in the urine.

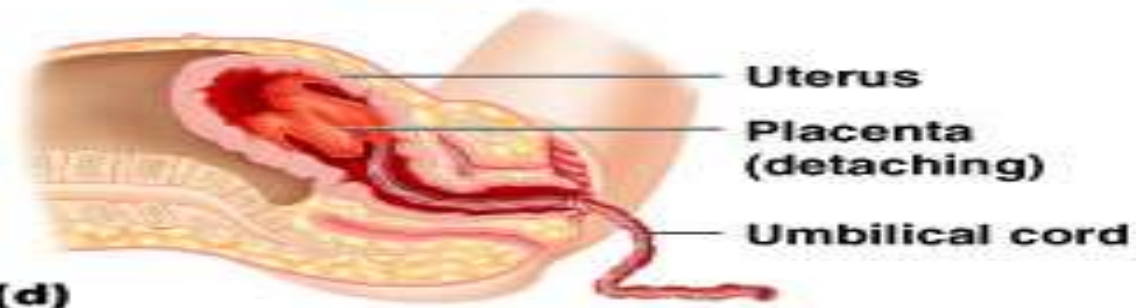
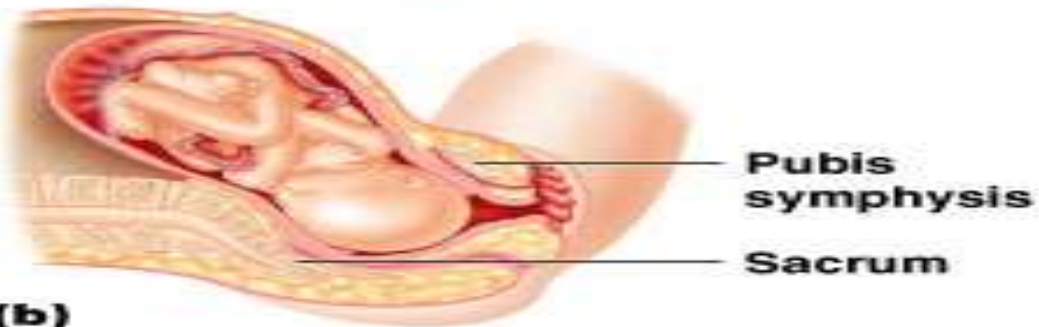
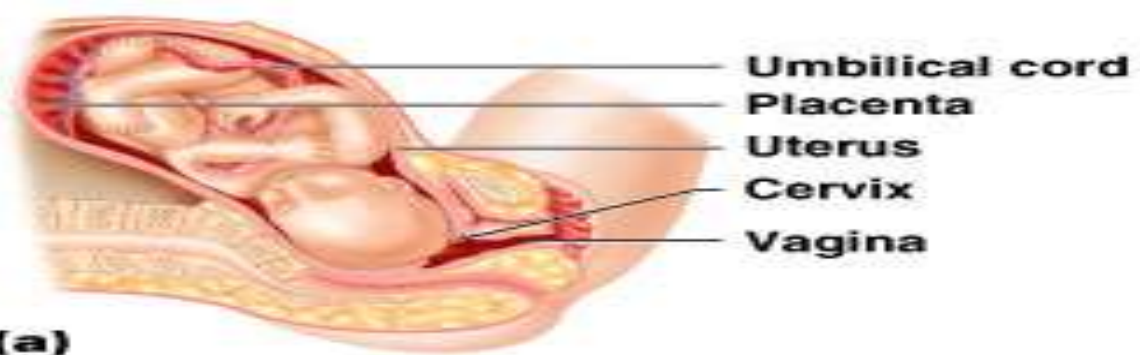
Hormones of pregnancy

The First Tri-mester

- HCG is produced by the trophoblast.
- HCG also stimulates corpus luteal production of progesterone and estrogen.

Second and Third Tri-mesters

- Progesterone is produced by the placenta.
- Estriol (a major form of estrogen) is also produced.



PARTURITION

- Delivery of the fetus.
- The following events may contribute to parturition:
- Fetus reaches a critical size.
- Thus distention of uterus increases its contractility.
- Braxton Hicks contractions begin approximately one month before parturition.
- Cortisol increases estrogen/progesterone ratio.
- This increases the sensitivity of the uterus to contractile stimuli.

- Estrogen stimulates production of the prostaglandins.
- Prostaglandins increase the intra-cellular calcium concentration of uterine smooth muscle.
- This thereby increases contractility.
- Oxytocin is used to induce labour.
- The dilation of the cervix stimulates oxytocin secretion.

LACTATION

- Estrogen and progesterone stimulate the growth and development of breasts.
- Hence preparing them for lactation.
- Estrogen stimulates prolactin secretion.
- Prolactin is very high during pregnancy but lactation does not occur.
- This is due because progesterone and estrogen block the action of prolactin.
- After parturition, estrogen and progesterone levels fall therefore they no longer block the prolactin.

- Hence lactation can now proceed.
- Lactation is maintained by suckling.
- This stimulates the secretion of oxytocin and prolactin.
- During lactation there is a suppression of ovulation.
- Prolactin inhibits GnRH secretion by the hypothalamus.
- FSH and LH secretion by the anterior pituitary



Structure of the Breast

MENOPAUSE

- Occurs at approximately at 50 years
- Several years preceding menopause anovulatory becomes common
- The number of ovarian follicles also decreases
- Estrogen secretion decreases and eventually declines
- Due to the decreased levels there is a negative feedback on anterior pituitary

Symptoms of menopause are caused by:

- Loss of ovarian source of estrogens
- Thinning of the vaginal epithelium
- Decreased vaginal secretions
- Decreased breast mass
- Accelerated bone loss
- Vascular instability (*hot flashes*)
- Emotional liability

NB//

estrogen can be produced from androgenic precursors in adipose tissue. Obese woman tend to be less symptomatic than non obese women.


ESTROGEN REPLACEMENT THERAPY


Aims at replacing the ovarian source of estrogen, thus minimizing or preventing the symptoms of menopause.

ANDROPAUSE

Andropause or male menopause

sometimes colloquially called
"man-opause"

- 
- This relates to the slow but steady reduction of the production of the hormones testosterone and dehydroepiandrosterone in middle-aged men
 - Unlike women, middle-aged men do not experience a complete and permanent physiological shutting down of the reproductive system

- 
- This drop in testosterone levels is considered to lead in some cases to loss of energy and concentration, depression, and mood swings.
 - Many experience bouts of impotence
 - Premature andropause can occur in males who experience excessive female hormone stimulation through workplace exposure to estrogen



The following treatments have been found to be effective. These include:

- Hormone replacement therapy
- Exercise, dietary changes, stress reduction
- Selective androgen receptor modulators have also been proposed.