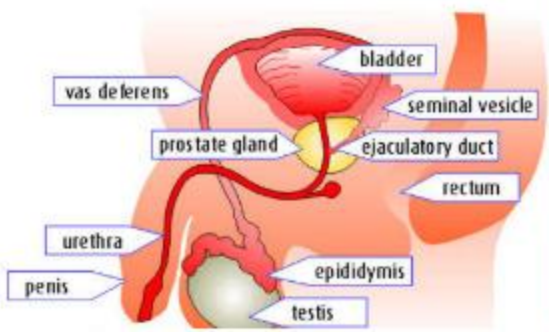
REPRODUCTIVE TECHNOLOGY (22ZOOME22)

ANATOMY OF MALE REPRODUCTIVE SYSTEM

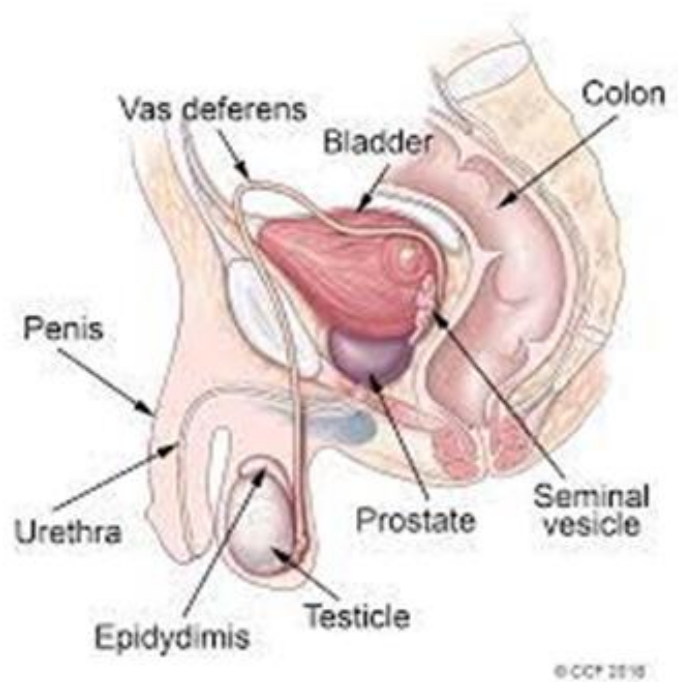
- **Andrology** - the branches of science and medicine dealing with male reproductive functions under physiological and pathological conditions
- Central topics of andrology are infertility, hypogonadism, and erectile dysfunction.



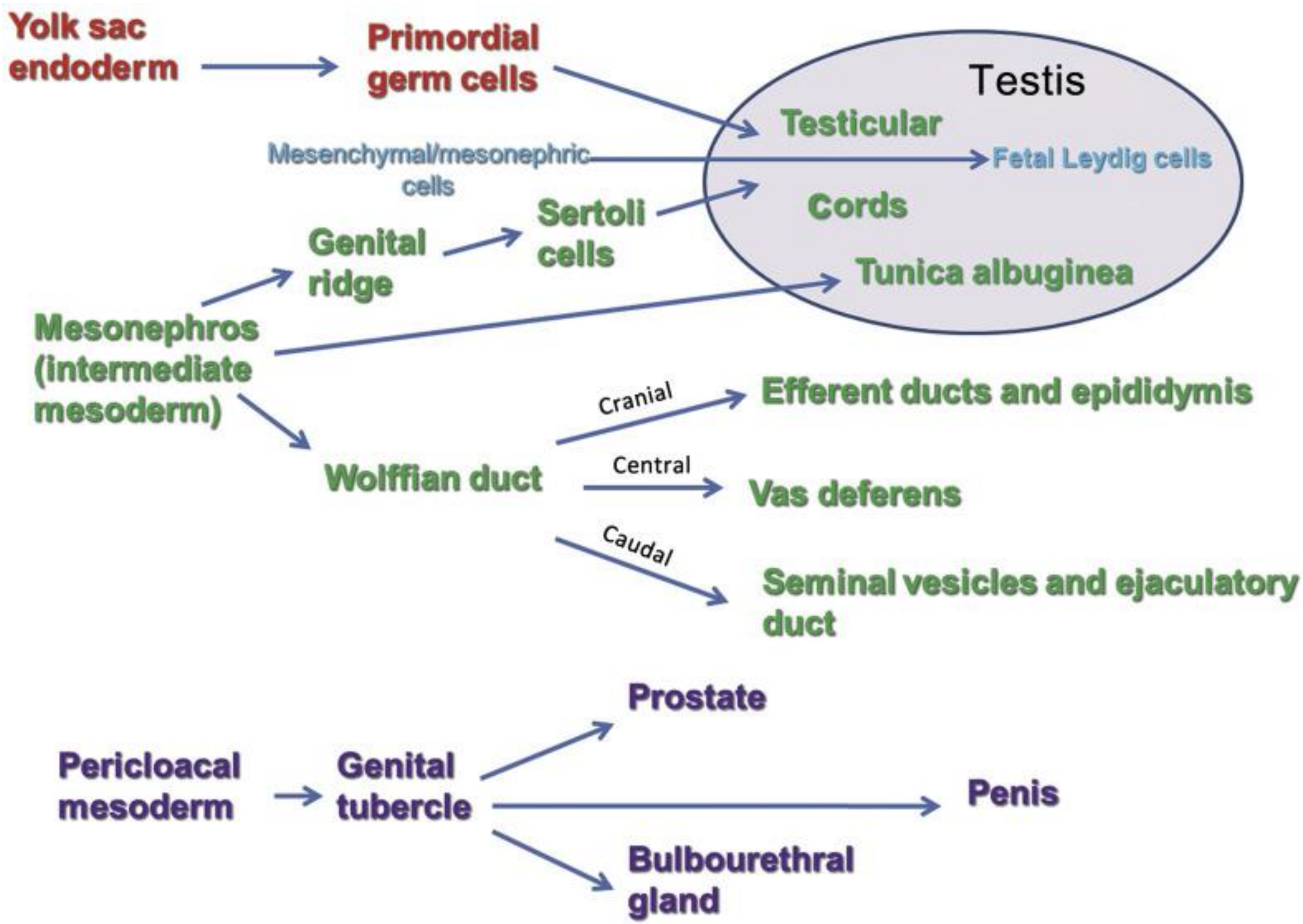
- The organs of the male reproductive system play a role in the **production, maintenance, and transportation of sperm and semen to the female reproductive tract during sexual intercourse as well as the production and secretion of male sex hormones** responsible for maintaining the male reproductive system

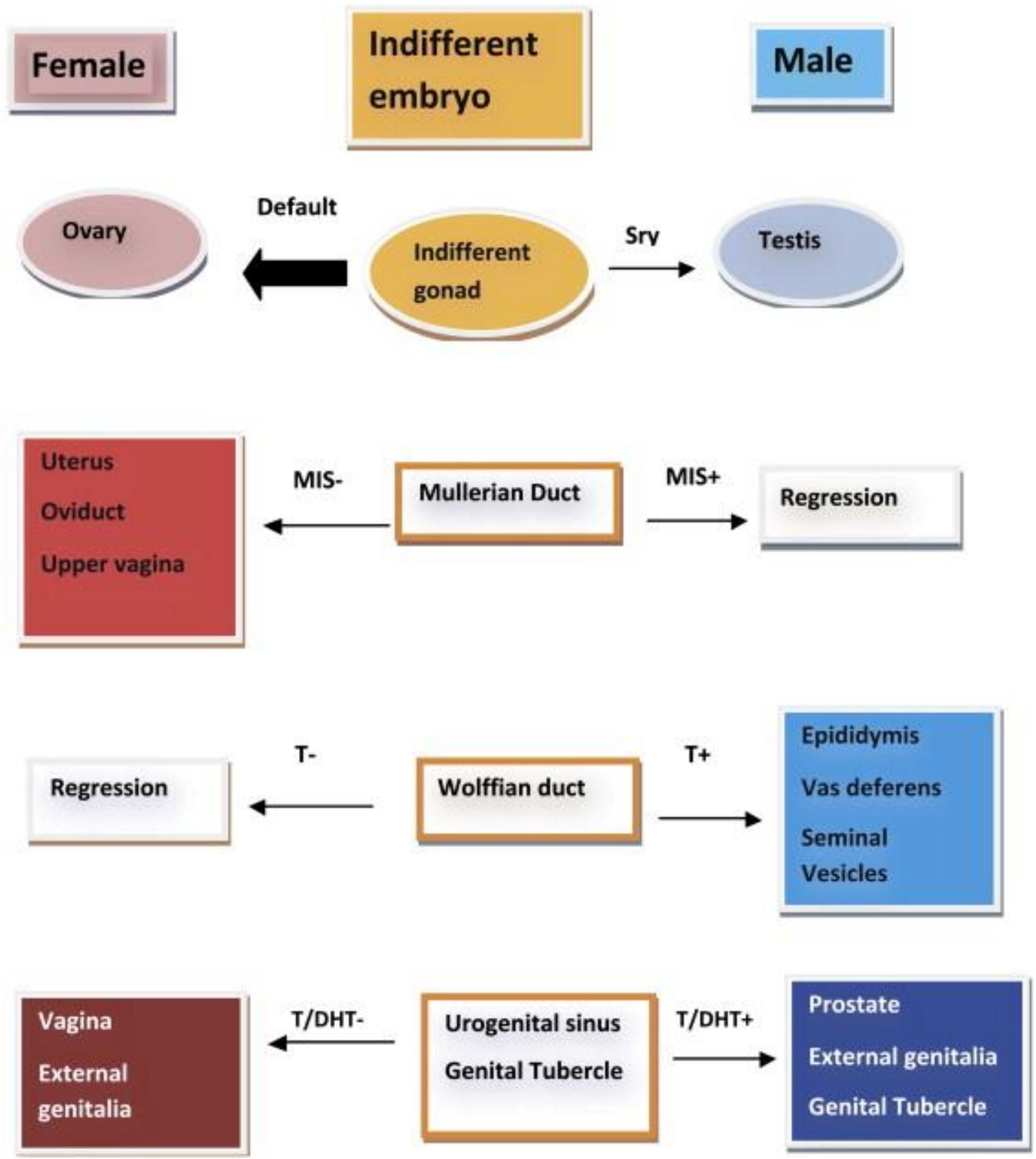
The male reproductive tract

- consists of a pair of testes, epididymis, vas deferens, ejaculatory duct, penis and accessory sex glands (seminal vesicles, prostate, and bulbourethral glands) and is under the control of hormones from hypothalamus, pituitary, and gonads.

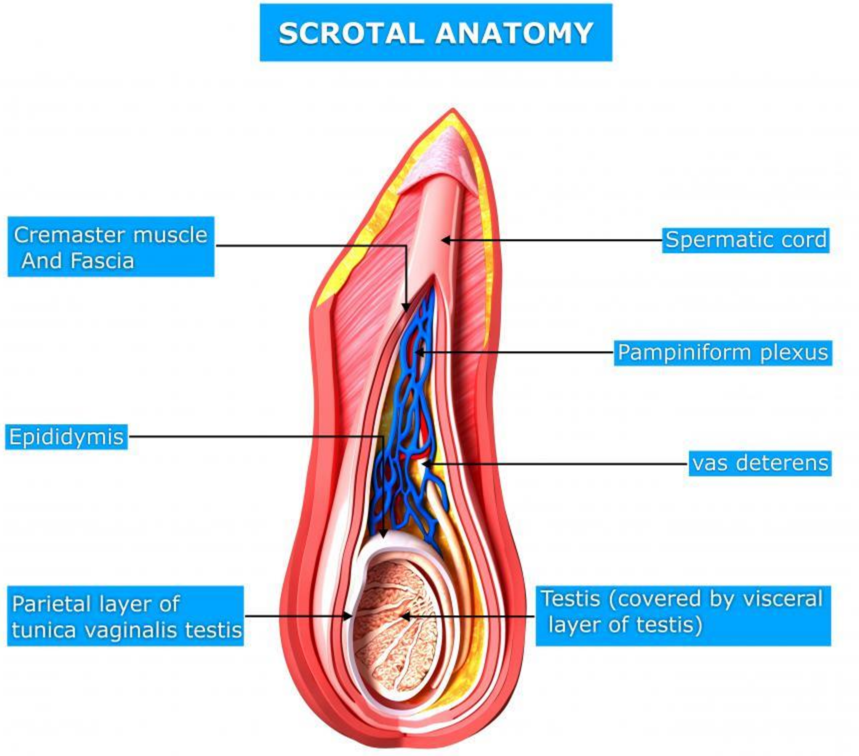


- All these organs are vulnerable to toxicants from the environment, drugs, hormonal disruptors, etc.
- These agents can affect the male reproductive system during embryonic stage and/or throughout the life cycle.
- Under their influence, the reproductive potential of adult male is compromised affecting his fertility capacity.
- It may also result in mutagenesis and other developmental issues in the progeny.
- male reproductive tract as the target site of many such factors, endocrine disruptors (EDs), and their potential mechanisms of action

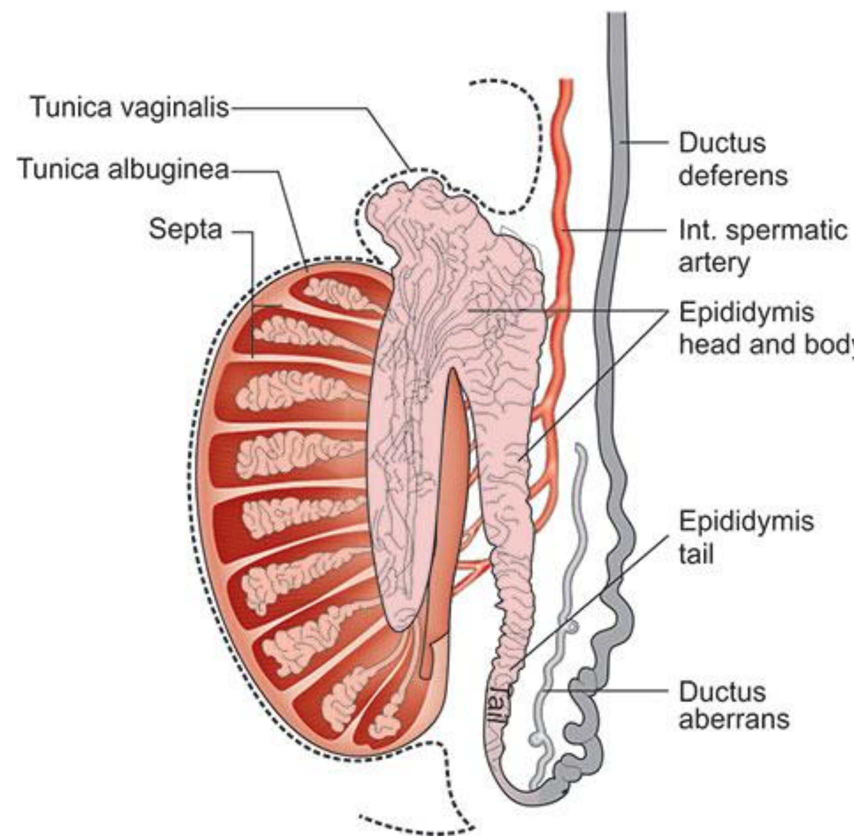

Yolk sac endoderm
Primordial germ cells
Testis
Testicular
Mesenchymal/mesonephric cells
Fetal Leydig cells
Cords
Sertoli cells
Genital ridge
Tunica albuginea
Mesonephros (intermediate mesoderm)
Cranial
Efferent ducts and epididymis
Wolffian duct
Central
Vas deferens
Caudal
Seminal vesicles and ejaculatory duct
Prostate
Pericloacal mesoderm
Genital tubercle
Penis
Bulbourethral gland


Female
Indifferent embryo
Male
Ovary
Default
Indifferent gonad
Sry
Testis
Uterus
Oviduct
Upper vagina
MIS-
Mullerian Duct
MIS+
Regression
T-
Regression
Wolffian duct
T+
Epididymis
Vas deferens
Seminal Vesicles
Vagina
External genitalia
T/DHT-
Urogenital sinus
Genital Tubercle
T/DHT+
Prostate
External genitalia
Genital Tubercle

- Each testis is oval, with a length of about 4.0 cm (1.5 in) and a width of 2.5 cm (1.0 in).
- On the outside of each testis is a shiny covering of serous membrane, the *tunica vaginalis*

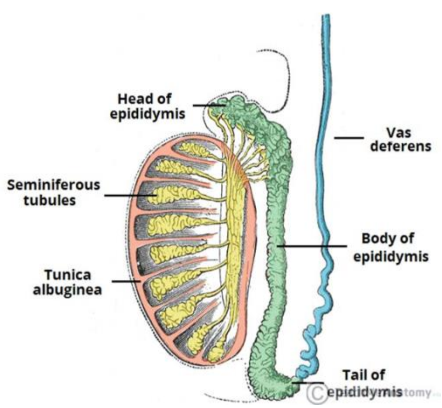


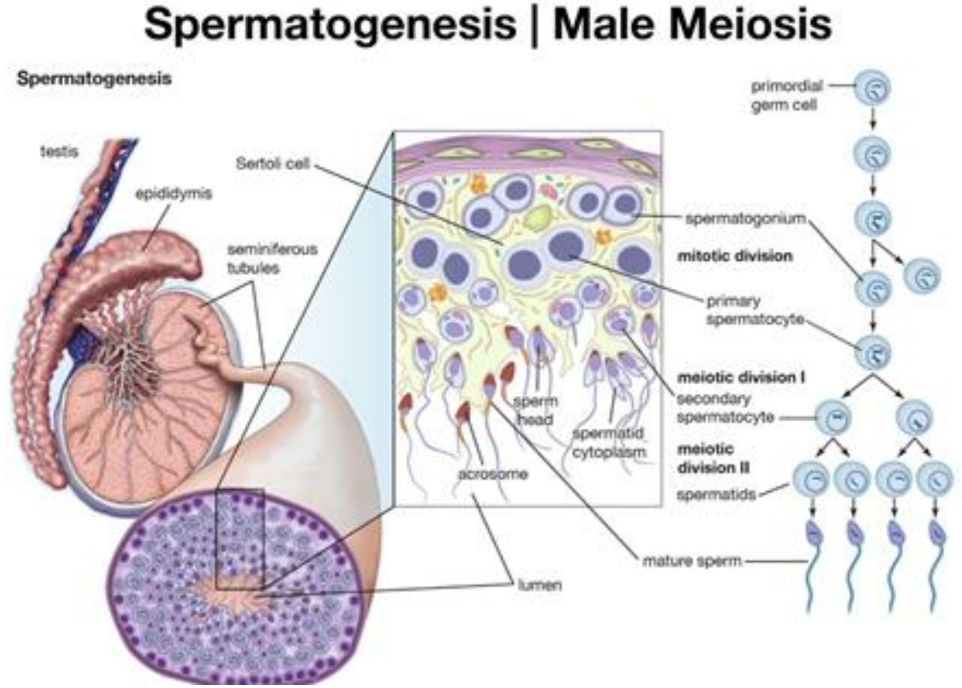
- Immediately under the **tunica vaginalis** is a thin, dense covering of the testis itself, the ***tunica albuginea.***
- Inside each testis are about 250 compartments, *testicular lobules*, which are separated from each other by septa (tissue barriers).



Seminiferous Tubules

- Each seminiferous tubule is lined on its inside by the ***seminiferous epithelium***, which contains two kinds of cells:
  - – male germ cells &
  - – Sertoli cells.

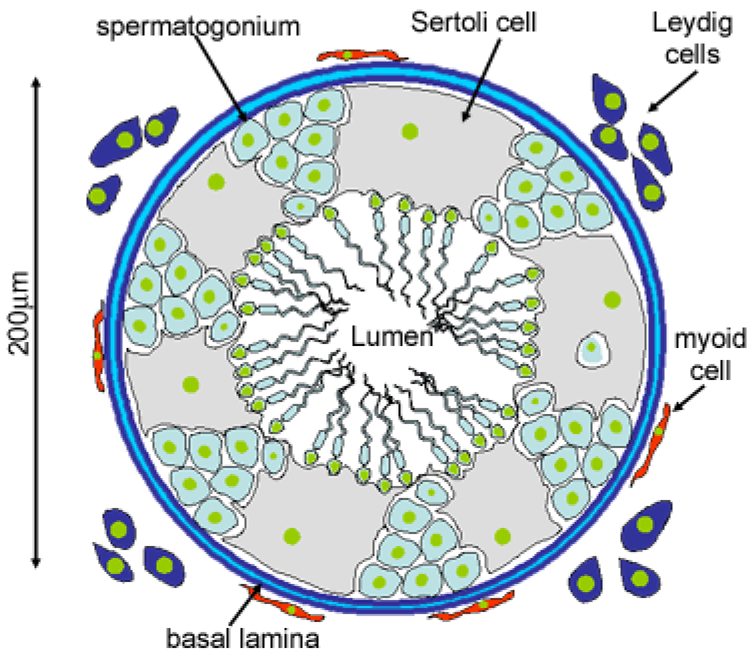




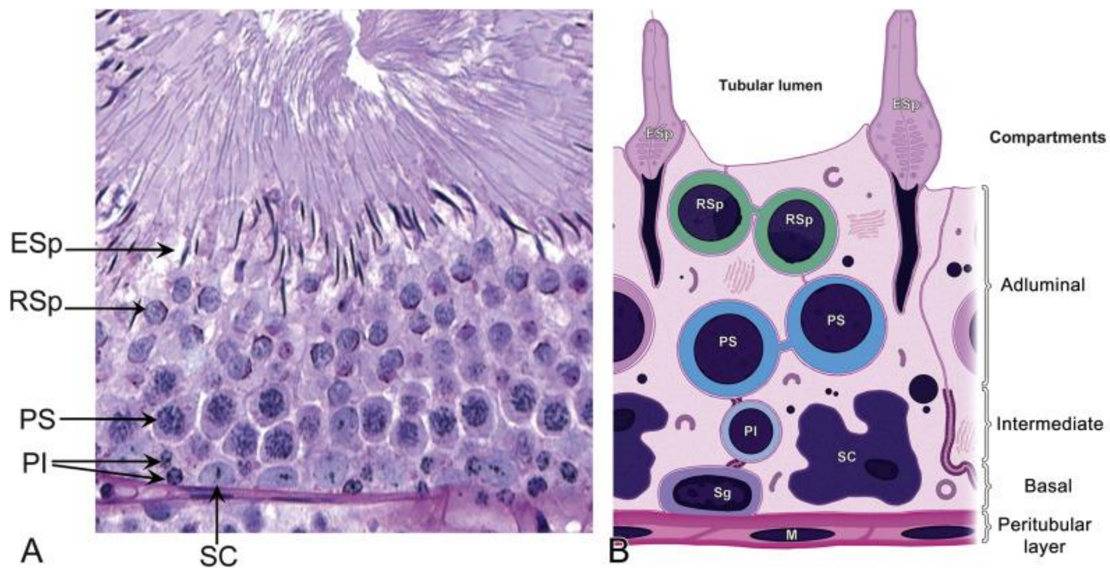
- Each lobule contains one to three highly coiled *seminiferous tubules*
- If a single seminiferous tubule were stretched to its maximal length, it would measure about 30–91 cm (1–3 ft), and the total length of all the tubules would be longer than a football field
- Sperm are produced in the seminiferous tubules, and each tubule contains male germ cells in various stages of differentiation.

Sertoli Cells

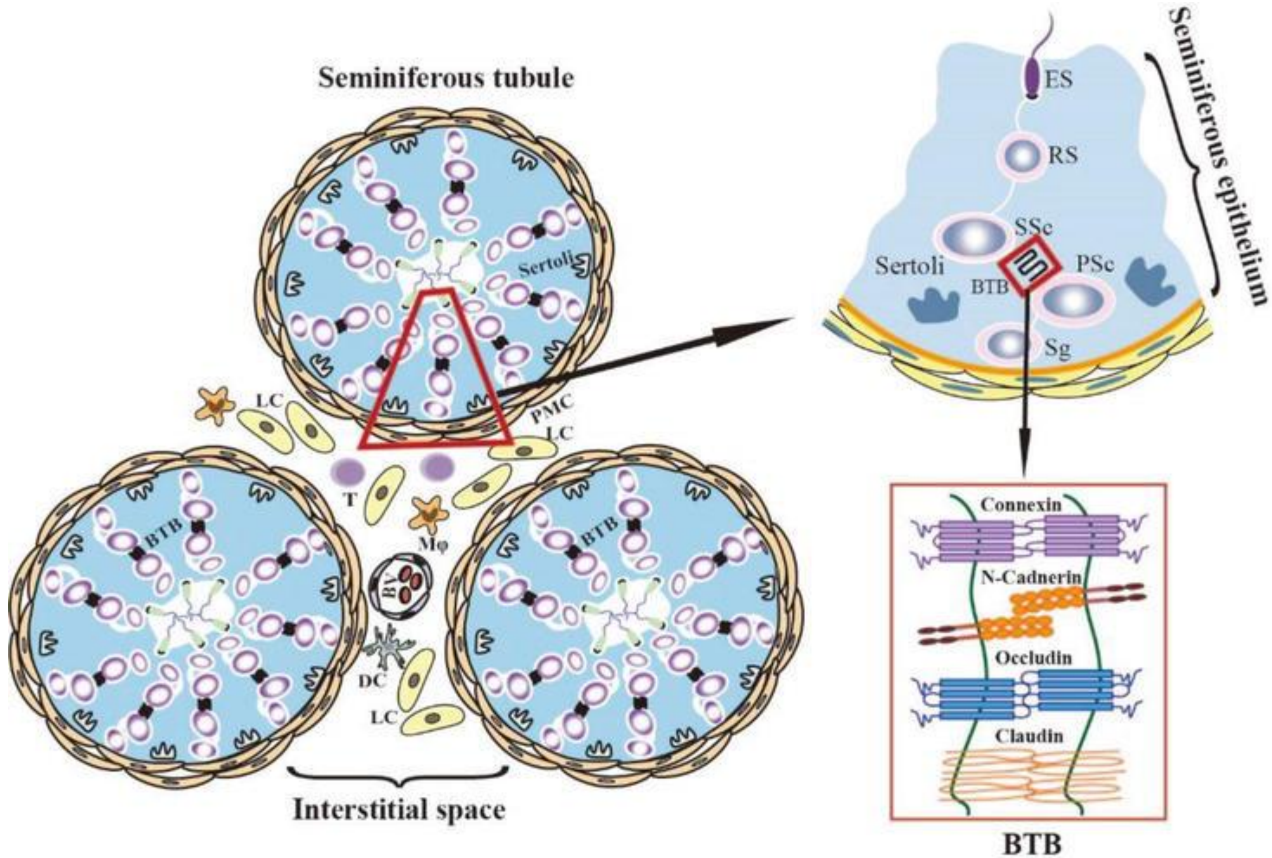
- *sustentacular cells*
- approximately pyramid-shaped cells lying within the seminiferous epithelium
- Their bases lie against the basement membrane of each tubule, and their tips point toward the cavity in the middle of each tubule.
- These "nurse cells" play an essential role in nurturing and providing structural support for the sperm cells during their development.
- About 30–50 spermatogenic cells are embedded in recesses of each Sertoli cell and migrate from the base toward the lumen of the seminiferous tubules as they mature.



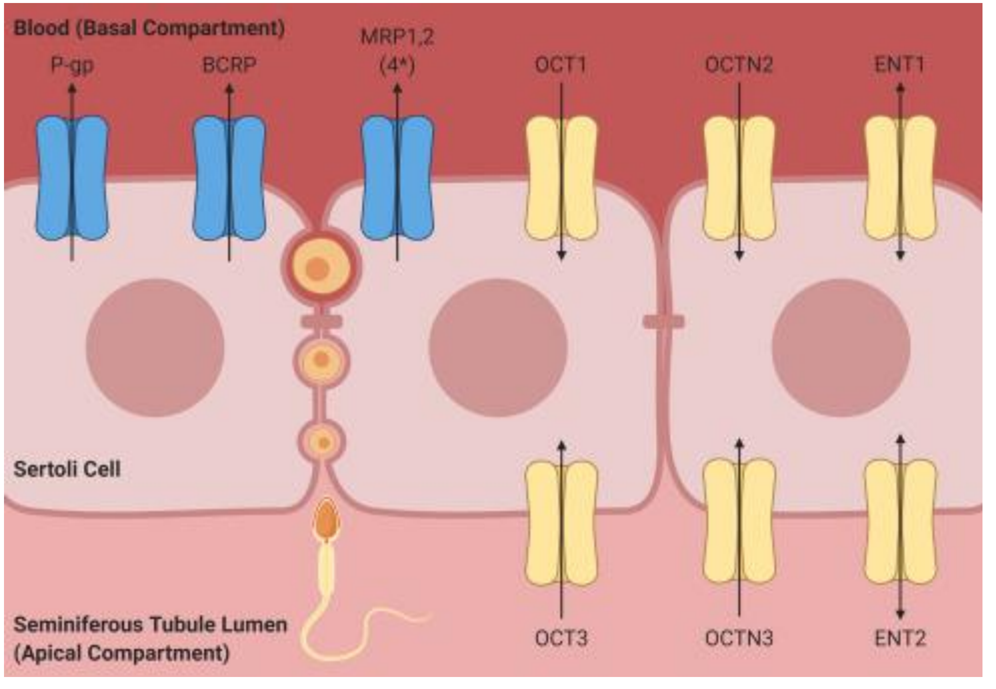
- The plasma membranes of Sertoli cells adjust to accommodate the gradual movement of the germ cells, and thus the complex shape of the Sertoli cell is constantly in flux.
- Sperm heads are released from the Sertoli cells at spermiation.



- functions of Sertoli cells are the secretion of testicular fluid into the tubular cavity and *phagocytosis* (engulfing) of the remains of degenerated germ cells



- Tight junctions between the basal portions of adjacent Sertoli cells provide for a *blood–testis barrier*.
- the blood–testis barrier protects spermatocytes and spermatids from immune attack, as these haploid cells are recognized as foreign by a man's immune system.

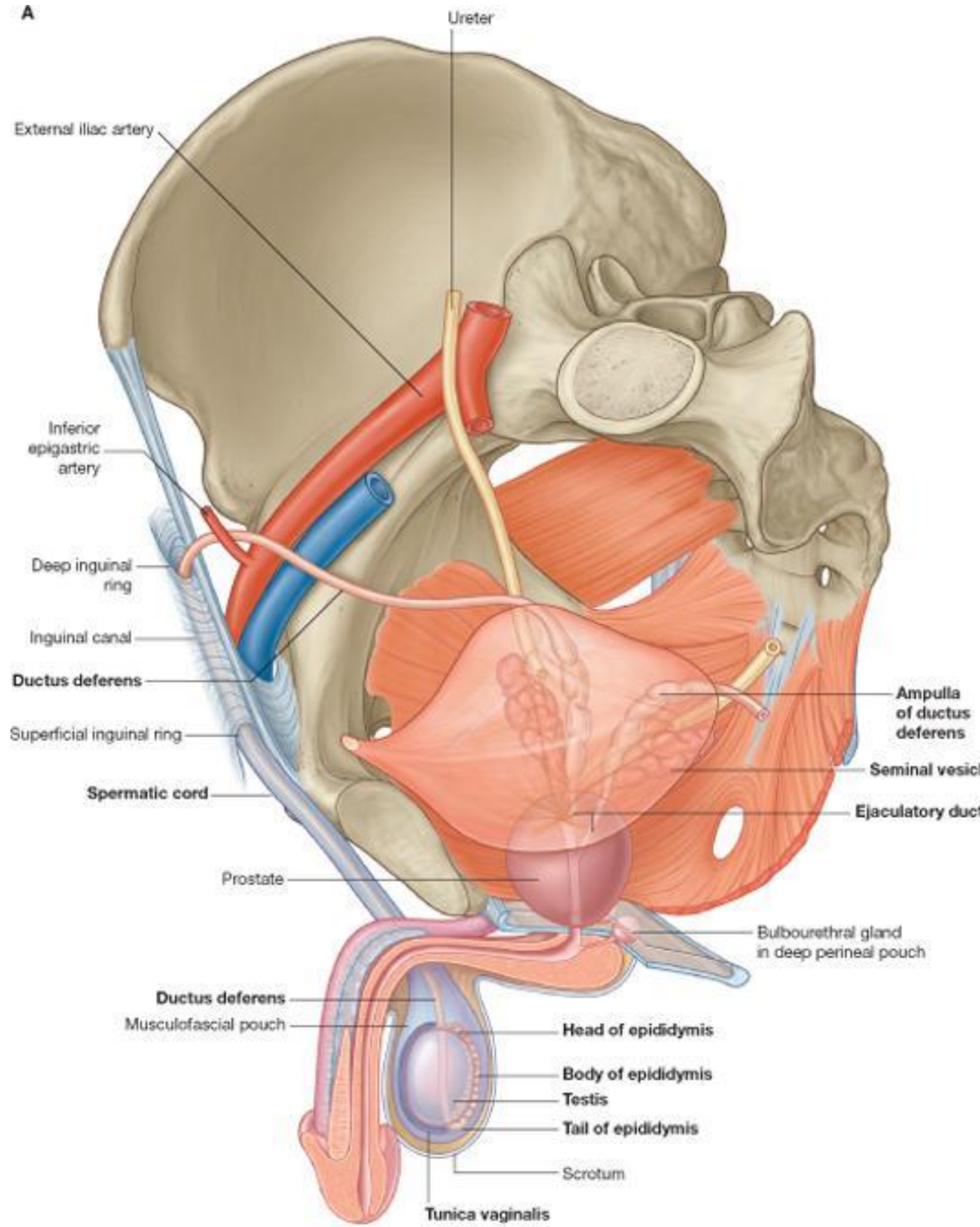


- This prevents the leakage of certain molecules between Sertoli cells and allows these cells to control the chemical composition of testicular fluid within the seminiferous tubules, resulting in a unique microenvironment in the tubules.

- Sertoli cells secrete various proteins, including androgen-binding protein, as well as hormones such as inhibin and anti-Müllerian hormone
- These cells produce enzymes that convert testosterone to estrogen and to 5α- dihydrotestosterone (DHT).
- Sertoli cells may also play an important role in the hormonal control of spermatogenesis.
- Because of the dependence of male germ cell development on Sertoli cells, the rate of a man's sperm production is related to the number of Sertoli cells in his testes.
- Sertoli cell number is determined at puberty; no new Sertoli cells are produced in adult men.

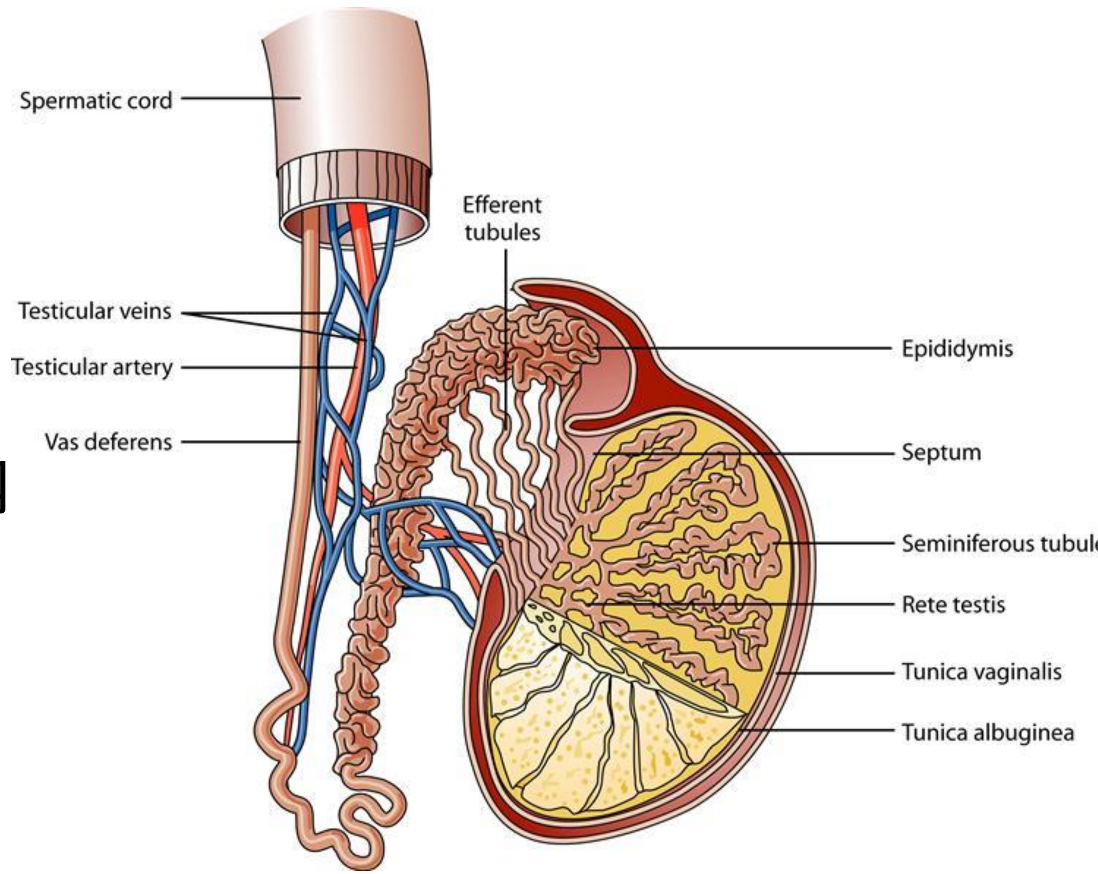
- The outer or basal surfaces of the seminiferous tubules are covered with a collagenous *basement membrane* in which scattered *myoid cells* are embedded.
- these muscle-like cells contract weakly to help move sperm cells and fluid through the seminiferous tubules.
- Like Sertoli cells, myoid cells are influenced by testicular hormones.

- Each testis is suspended from the body wall by a *spermatic cord*, which penetrates into the pelvic cavity through the *inguinal canal*, the route through which the testes originally descended into the scrotum from the pelvic cavity before birth

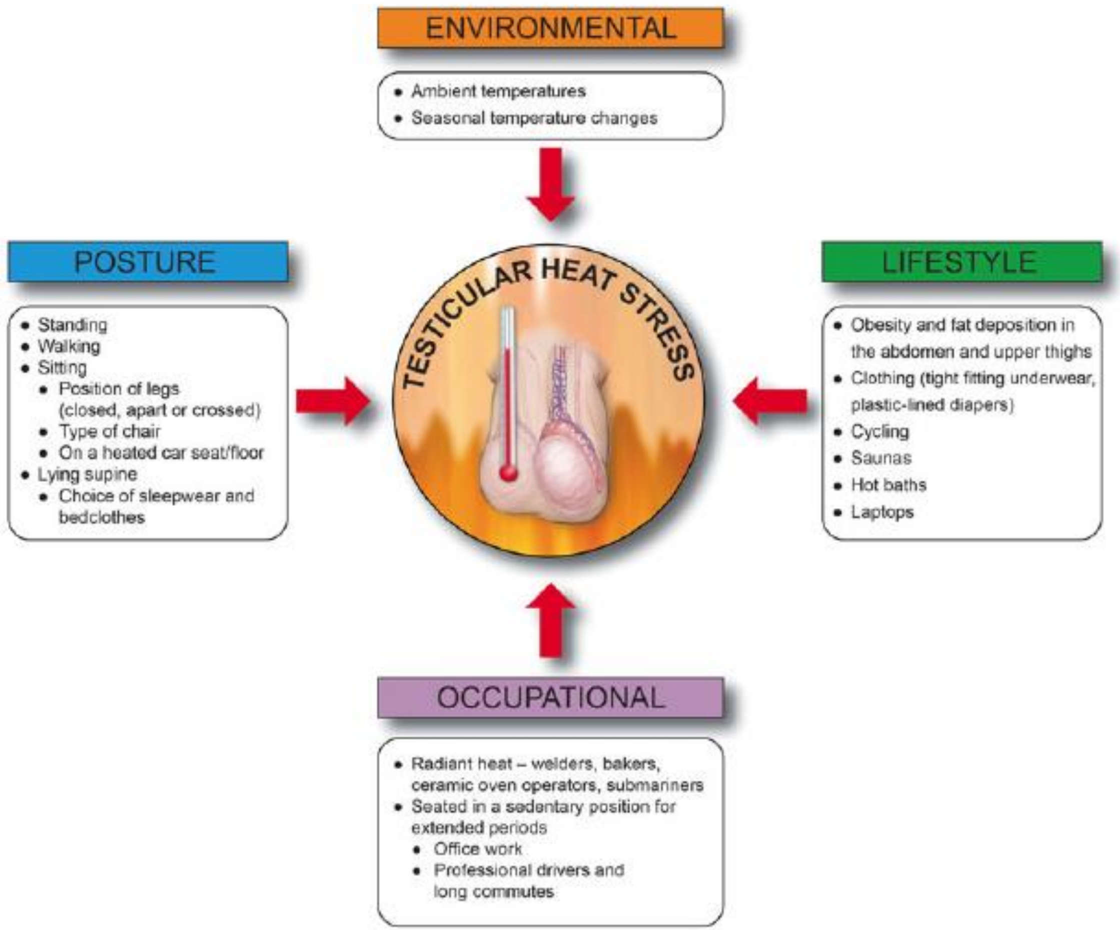


Drake: Gray's Anatomy for Students, 2nd Edition.

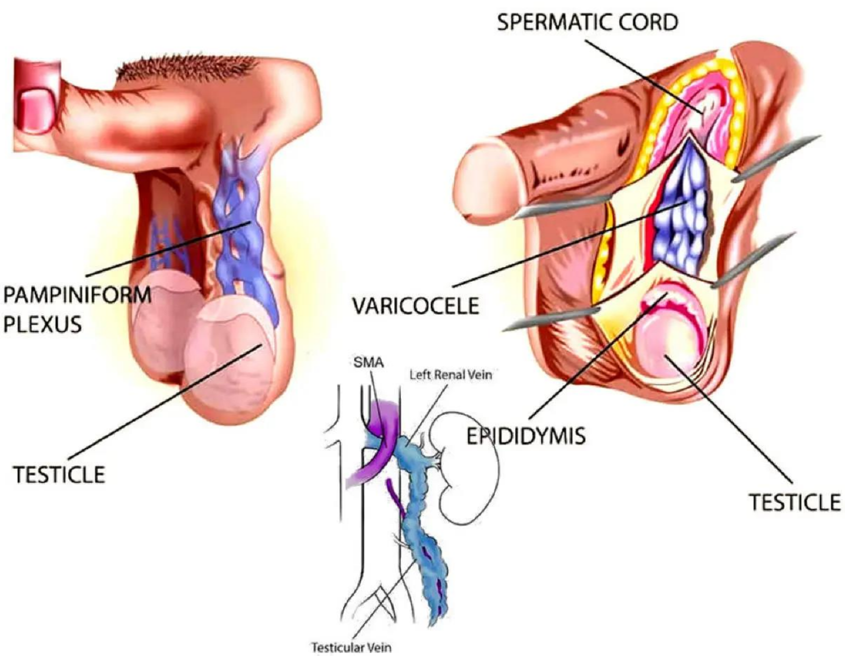
- Each spermatic cord contains one of the accessory ducts (the *vas deferens*), a testicular nerve, and three coiled blood vessels (the *testicular artery*, or spermatic artery, carrying blood to the testis and epididymis, and two *testicular veins*, or spermatic veins, carrying blood away from the testis).



- The vascular system serving the testes helps to maintain testicular temperature sufficiently below body core temperature to support spermatogenesis



- The spermatic veins returning cooled blood from the testes branch into an anastomosing network, the *pampiniform plexus*, which surrounds the testicular artery.
- This acts as a countercurrent heat exchange system, cooling incoming blood in the adjacent arteries.
- Abnormal dilation of the pampiniform plexus is a medical disorder called *varicocele*, which can cause pain, discomfort, and reduction in fertility.



Sex Accessory Ducts

- The male sex accessory ducts include the tubuli recti, rete testis, vasa efferentia, ductus epididymis, vas deferens, ejaculatory duct, and urethra
- These ducts serve to nurture and transport sperm.
- Mature sperm, suspended in testicular fluid, leave the highly coiled seminiferous tubules and enter the short, straight *tubuli recti*.
- These tubules empty into a network of tubules still within the testis, the *rete testis*.
- The sperm then enter ducts that eventually leave the testis, the *vasa efferentia*
- The vasa efferentia lead to an organ lying outside the testis, the epididymis.

Epididymis

- The *epididymis* is a comma-shaped structure, about 3.8 cm (1.5 in) long, that lies along the posterior surface of each testis
- As the vasa efferentia leave the testis, they enter the larger, upper portion (“head”) of the epididymis.
- The vasa efferentia then join to form a single, coiled *ductus epididymis* in the middle region (“body”) of the epididymis.
- This duct then enlarges to form the beginning of the vas deferens in the “tail” region of the epididymis.
- Tubules within the epididymis secrete important substances that help the sperm survive and mature.
- While in the body of the epididymis, sperm are nurtured by epididymal secretions and undergo further stages of their maturation.
- For example, human sperm taken from the head portion of the epididymis can swim, but only in a circle.
- In contrast, those taken from the body of the epididymis can move forward by swimming in a spiral path.

Vas Deferens

- The vas deferens (or *ductus deferens*) is a 45-cm (18-in) long tube that ascends on the posterior border of each testis, penetrates the body wall through the inguinal canal, and enters the pelvic cavity.
- Once inside, each vas deferens loops over the urinary bladder and extends down toward the region of the urethra
- The end of each vas deferens has an expanded portion, the ampulla, that serves as a reservoir for sperm.
- Each vas deferens enters an *ejaculatory duct*, which is 2 cm (1 in) long. These short ducts then lead into the urethra

Urethra

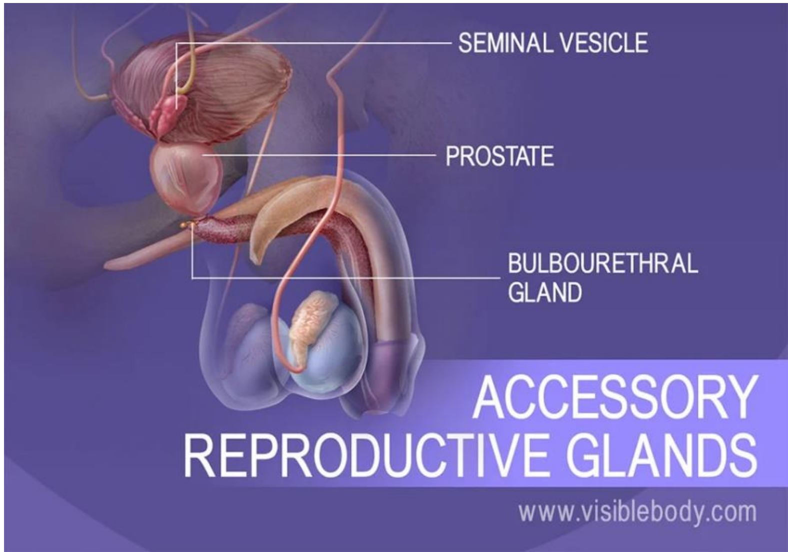
- The *urethra* is a tube extending from the urinary bladder, through the floor of the pelvic cavity ("urogenital diaphragm"), and then through the length of the penis to its external opening (the *urethral orifice*).
- Thus, the urethra serves as a passageway for urine.
- Since, however, the ejaculatory ducts enter the urethra, this tube also transports sperm to the outside.
- The prostate gland surrounds the point where the ejaculatory ducts enter the urethra; that is why this portion is called the *prostatic urethra*.
- The region of the urethra that passes through the urogenital diaphragm is the *membranous urethra*, and when in the penis this duct is the *spongy* (or *cavernous*) *urethra*

How do sperm move through these sex accessory ducts?

- Their journey through the seminiferous tubules, tubuli recti, rete testis, and vasa efferentia is passive, i.e. they do not swim.
- Instead, the cells lining these ducts have cilia, and the beating of these hair-like processes moves the fluid and its suspended sperm toward the ductus epididymis.
- Cilia also help the sperm move through the ductus epididymis and vas deferens.
- The walls of the latter two ducts contain smooth muscle, and this tissue contracts in waves to propel the sperm into the urethra during ejaculation

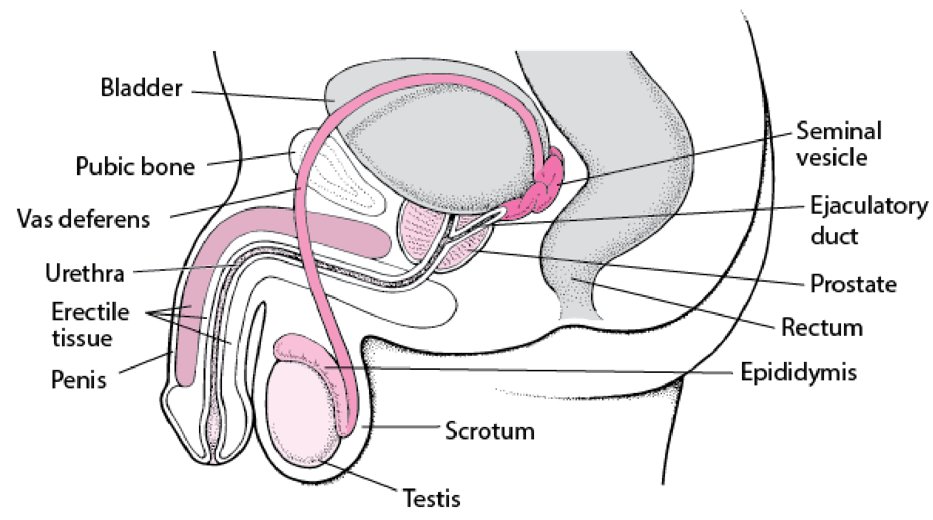
Sex Accessory Glands

- Male *sex accessory glands* include the seminal vesicles, prostate gland, and bulbourethral glands
- These glands secrete substances into ducts that join the sex accessory ducts.
- Thus, the secretion of these glands, *seminal plasma*, mixes with sperm and testicular fluid to form *semen* or *seminal fluid*.



Seminal Vesicles

- The *seminal vesicles* are paired pouch-like glands, about 5 cm (2 in) long, that lie at the base of the urinary bladder.
- Each seminal vesicle joins the ampulla of the vas deferens to form the ejaculatory duct.
- These glands secrete an alkaline, viscous fluid rich in the sugar fructose, an important nutrient for sperm
- A majority of the volume of seminal plasma is secreted by the seminal vesicles.

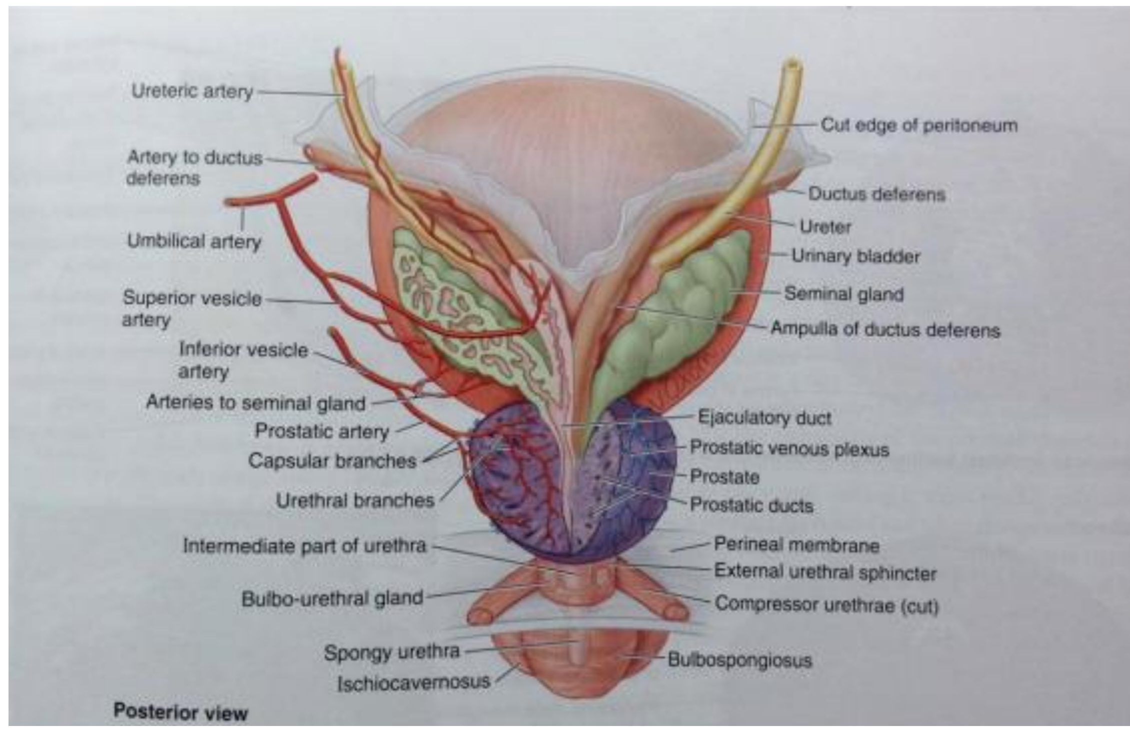


Prostate Gland

- The *prostate gland* is a single doughnut-shaped organ about the size of a golf ball.
- It lies below the urinary bladder and surrounds the prostatic urethra
- The alkaline secretion of this gland makes up about 13–33% of seminal plasma.
- The secretion enters the prostatic urethra through several (up to a dozen) tiny ducts.

Bulbourethral Glands

- The paired *bulbourethral glands* (or *Cowper's glands*), each about the size of a small pea, lie on either side of the membranous urethra
- Their ducts empty into the spongy urethra.
- These glands secrete mucus that lubricates the urethra during ejaculation.



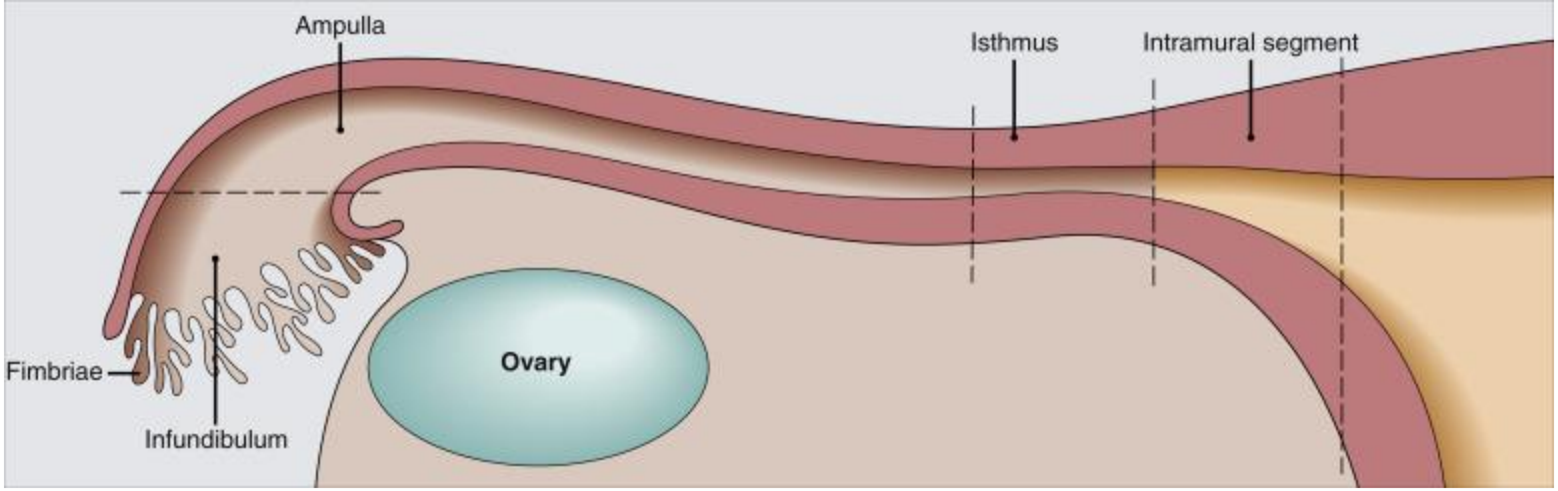
REPRODUCTIVE TECHNOLOGY (22ZOOME22)

ANATOMY OF FEMALE REPRODUCTIVE SYSTEM

Female Reproductive System

ANATOMY OF FEMALE REPRODUCTIVE SYSTEM

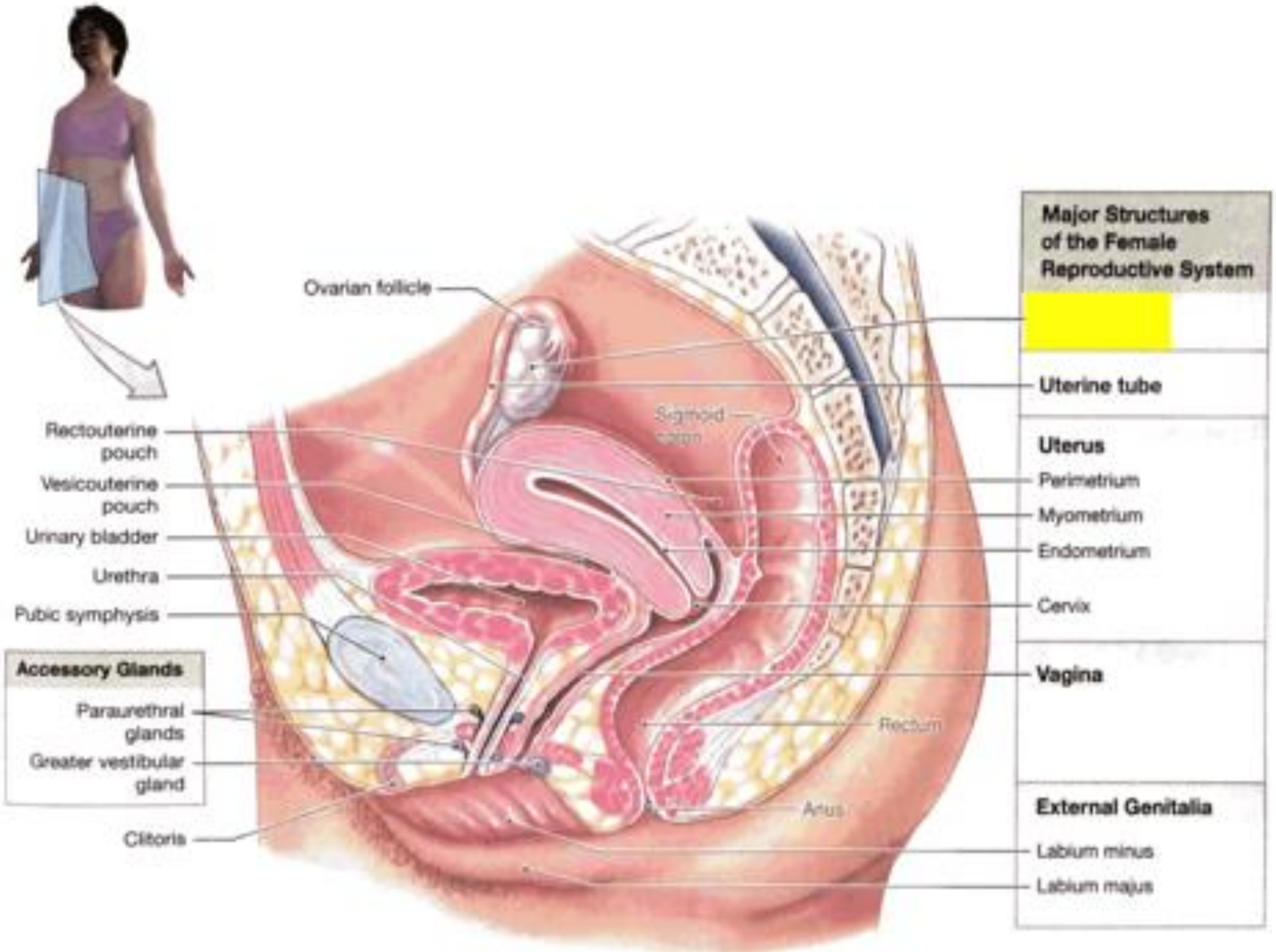
- FEMALE GONODS - ?
- RESIDING WITHIN THE PELVIC CAVITY
- NO TUBULES IN THE OVARY
- Instead, the gametes (primary oocytes) become invested with epithelial and stromal cells that make up an ovarian follicle.
- With growth, the follicle ultimately creates its own private fluid-filled lumen (called an antrum).
- At the time of gamete release, the gamete (now an egg arrested in meiotic metaphase II) and a thin covering of epithelial cells become free-floating within this lumen.
- Ovulation involves a complex set of events that essentially erode the follicular and ovarian walls at the point where the follicle is pushing against the ovarian surface, followed by the release of the egg.
- Unlike the male tract, the egg is released into the pelvic cavity and has to be captured by the proximal segment of the female tract called the oviduct



- The **oviduct** has an opening at its proximal, free end (the infundibulum), through which the captured egg is transported.
- There is usually only one egg ovulated, either from the right or left side, depending on which side had the largest follicle at the beginning of the menstrual cycle.
- The oviduct transports the egg toward the midline uterus and allows for the movement of sperm from the uterus laterally toward the egg.
- Fertilization and early development (5 to 6 days) normally occur in the oviduct.
- The early embryo (blastocyst) eventually moves into the uterine lumen and implants into the uterine mucosa.
- The growing fetus is supported in part by the elastic and fibrous inferior end of the uterus called the cervix.
- At term, the newborn is expelled from the uterus through the cervix and vagina.
- The vagina acts as both the copulatory organ and the birth canal.

- The female external genitalia surround the superficial opening of the vagina (called introitus).
- The labia majora are homologous to an unclosed scrotum.
- Vestibular bulbs (deep to the labia minora) and the clitoris represent structures homologous to the erectile tissue of the penis.
- However, unlike the penis, erection of these structures is not required for fertility.
- Sensory (pudendal) innervation of these structures and the vaginal wall may lead to orgasm during coitus, thereby providing reinforcement to libido.

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



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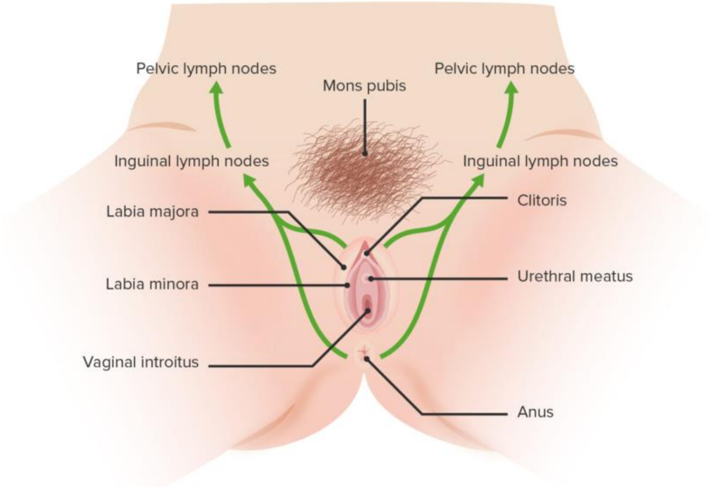

The female reproductive tract

- The female reproductive tract does not connect directly to the ovaries
- The internal portion of the tract consists of right and left oviducts and the following midline structures:
  - uterus,
  - cervix, and
  - vagina.
- The external opening of the vagina is surrounded by the external genitalia.

The Oviduct

- The oviducts (also called the uterine tubes or fallopian tubes) are muscular tubes that are opened at both ends.
- The end of the oviduct close to the surface of each ovary has finger-like projections, called fimbriae.
- The opposite end pierces the wall of the uterus and opens into the uterine lumen.
- The oviducts can de divided into four sections
- Going from ovary to uterus, these sections are named as follows:
  - 1. Infundibulum, which includes the fimbriae
  - 2. Ampulla, which has a relatively wide lumen and extensive folding of the mucosa
  - 3. Isthmus, which has a relatively narrow lumen and less mucosal folding
  - 4. Intramural or uterine segment, which extends through the uterine wall at the superior corners (horns) of the uterus
- The wall of the oviduct is composed of a mucosa called the endosalpinx, a two-layered muscularis called the myosalpinx, and outer-lying connective tissue,
- the perisalpinx, that contains numerous blood vessels
- The endosalpinx is lined by a simple epithelium made up of two cell types: ciliated cells

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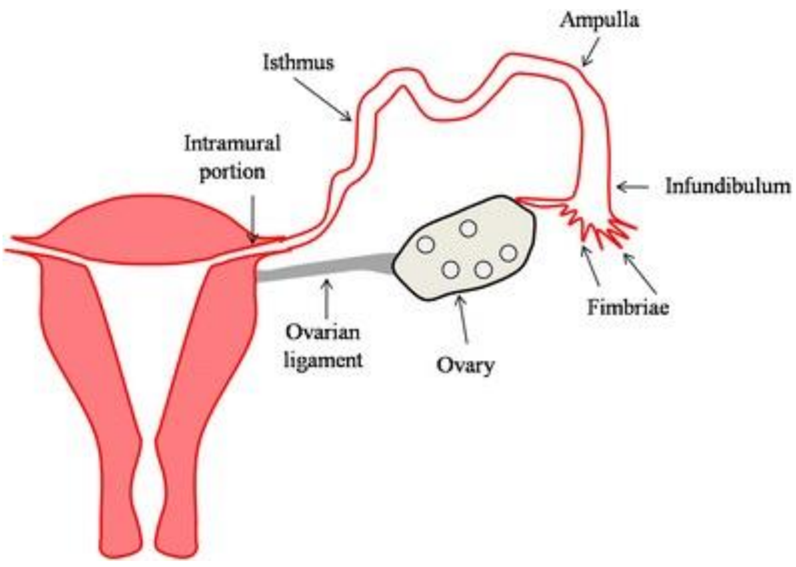
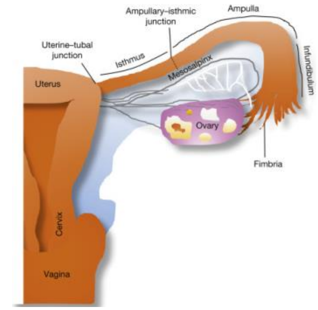
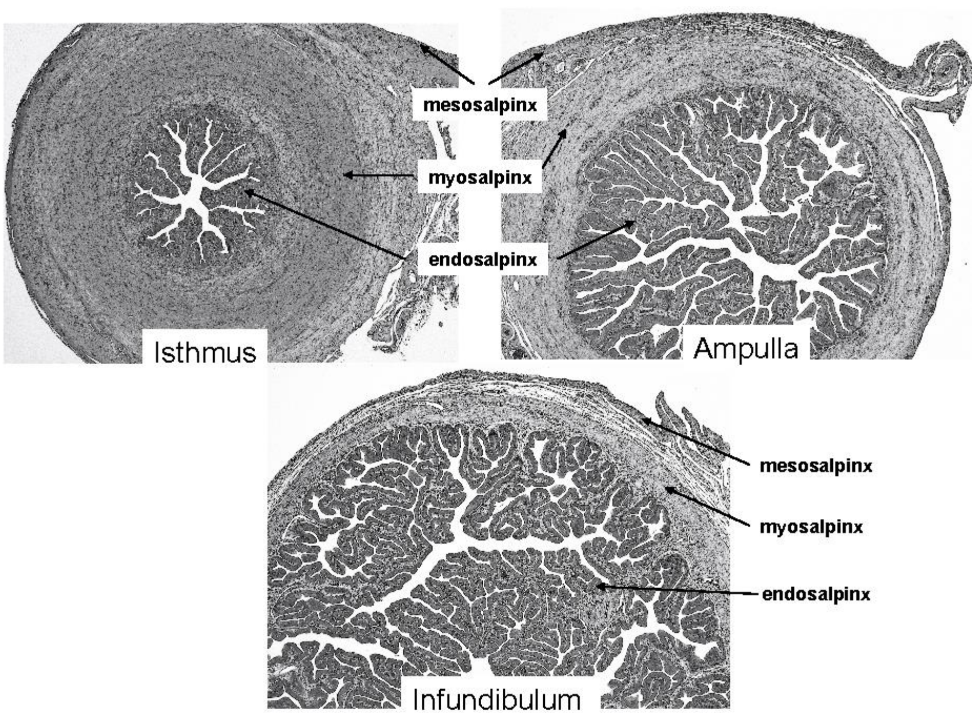
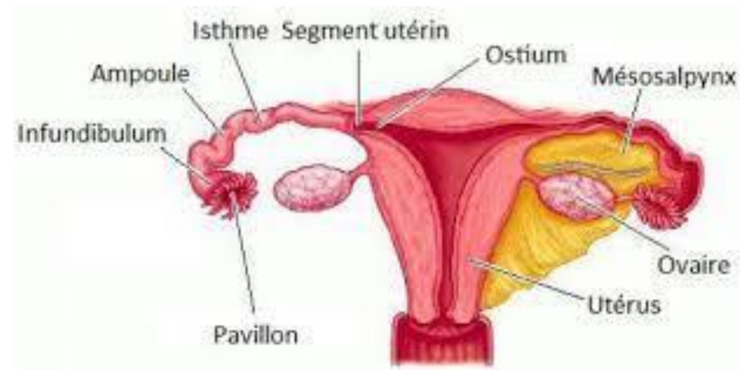


The Oviduct

- The wall of the oviduct is composed of a mucosa called the **endosalpinx,** a two-layered muscularis called the **myosalpinx**, and outer-lying connective tissue, the **perisalpinx**, that contains numerous blood vessels
- The endosalpinx is lined by a simple epithelium made up of two cell types: ciliated cells and secretory cells.







- The cilia are most numerous at the ovarian end (infundibulum and ampulla) and beat toward the uterus.
- The cilia on the fimbriae are the sole mechanism for transport of the ovulated cumulus oocyte complex into the oviduct.
- Once the complex passes through the ostium of the oviduct and enters the ampulla, it is moved by both cilia and peristaltic contractions of the myosalpinx.
- The ovarian end of the oviduct (infundibulum and ampulla) has a wide lumen partially filled with a highly folded myosalpinx.
- This allows the cumulus-oocyte complex to be transported while in intimate contact with ciliated mucosal cells.
- The uterine end of the oviduct (isthmus and intramural segment) has a narrow lumen and a relatively thicker muscularis.
- This allows for slow transport of an early embryo to the uterus primarily by peristaltic waves of the muscularis.

Main functions of the oviducts

- 1. Capture of the cumulus-oocyte complex at ovulation and transport of the cumulus-oocyte complex to a midway point (theampullary-isthmus junction), where fertilization takes place.
  - Oviductal secretions coat and infuse the cumulus-oocyte complex and may be required for viability and fertilizability.
- 2. Providing **a site for sperm storage.**
  - Women who ovulate up to 5 days after sexual intercourse can become pregnant.
  - Sperm remain viable by adhering to the epithelial cells lining the isthmus.
  - The secretions of the oviduct also induce capacitation and hyperactivity of sperm
- 3. Providing nutritional support to the preimplantation embryo by the oviductal secretions.
  - timing of the movement of the embryo into the uterus is critical because the human uterus has an implantation window of about 3 days.
  - The oviduct needs to harbor the early embryo until it reaches the blastocyst stage (5 days after fertilization); then it allows the embryo to move into the uterine cavity

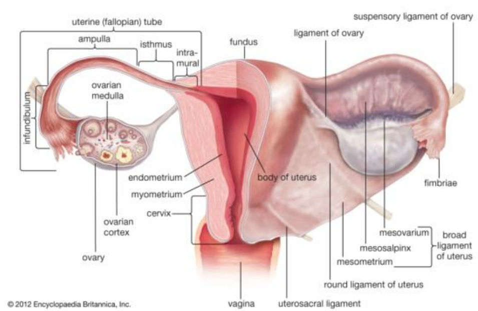
- The secretory cells produce a protein-rich mucus that is conveyed along the oviduct to the uterus by the cilia.
- This ciliary-mucus escalator maintains a healthy epithelium, moves the cumulus-oocyte complex toward the uterus, and may provide directional cues for swimming sperm.
- The movement of the cumulus-oocyte complex slows at the ampullaryisthmus junction, where fertilization normally takes place.
- This appears to be due in part to a thick mucus that is produced by the human isthmus and to an increased tone of the muscularis of the isthmus.
- The composition of oviductal secretions is complex and includes growth factors, enzymes, and oviduct-specific glycoproteins.
- IVF - the secretions of the oviduct are not absolutely necessary for fertility by in vitro techniques. However, normal oviductal function is absolutely required for both fertilization and implantation from in vivo insemination, and to minimize the risk for ectopic implantation (i.e., implantation outside of the uterus).
- The most common site of ectopic implantation is the oviduct.

Hormonal Regulation During the Menstrual Cycle

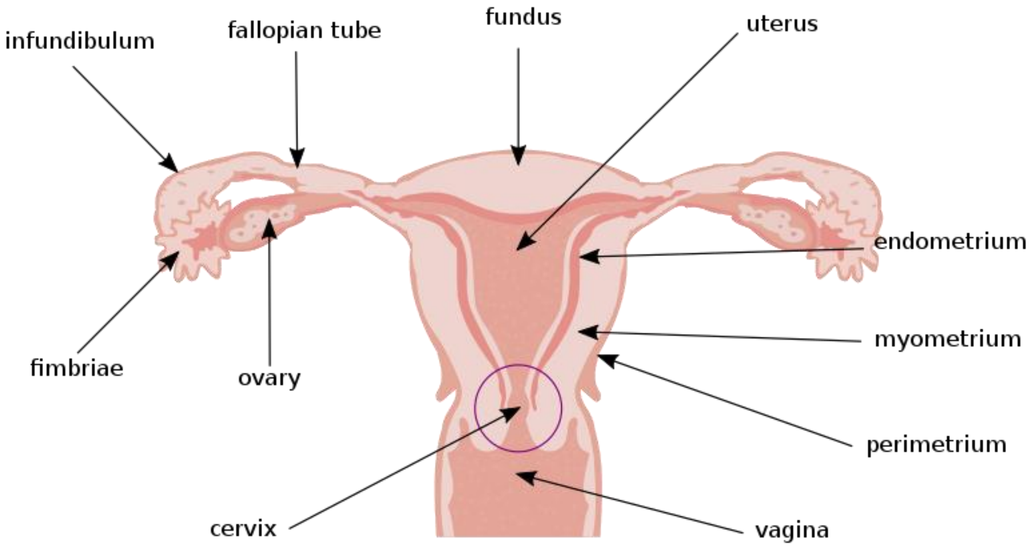
- In general, estrogen secreted during the follicular phase increases endosalpinx epithelial cell size and height.
- Estrogen increases blood flow to the lamina propria of the oviducts, increases the production of oviductspecific glycoproteins (whose functions are poorly understood), and increases ciliogenesis throughout the oviduct.
- Estrogen promotes the secretion of a thick mucus in the isthmus and increases tone of the muscularis of the isthmus, thereby keeping the cumulusoocyte complex at the ampullary-isthmus junction for fertilization.
- High progesterone, along with estrogen, during the early to midluteal phase decreases epithelial cell size and function.
- Progesterone promotes deciliation. Progesterone also decreases the secretion of thick mucus and relaxes the tone in the isthmus

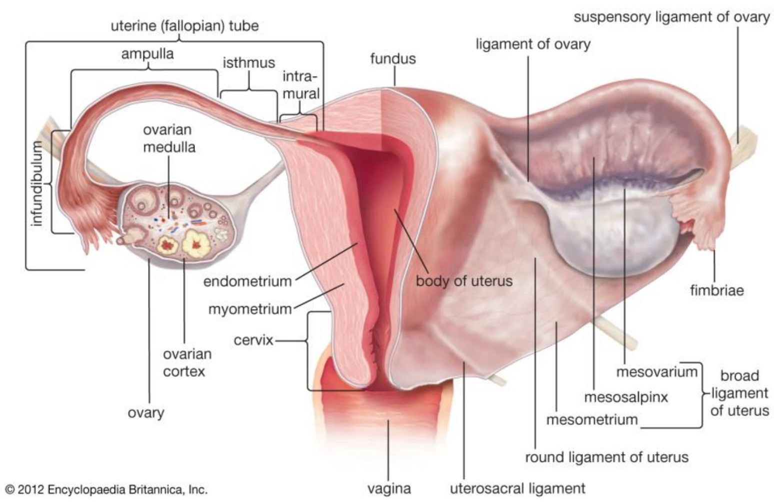
The Uterus

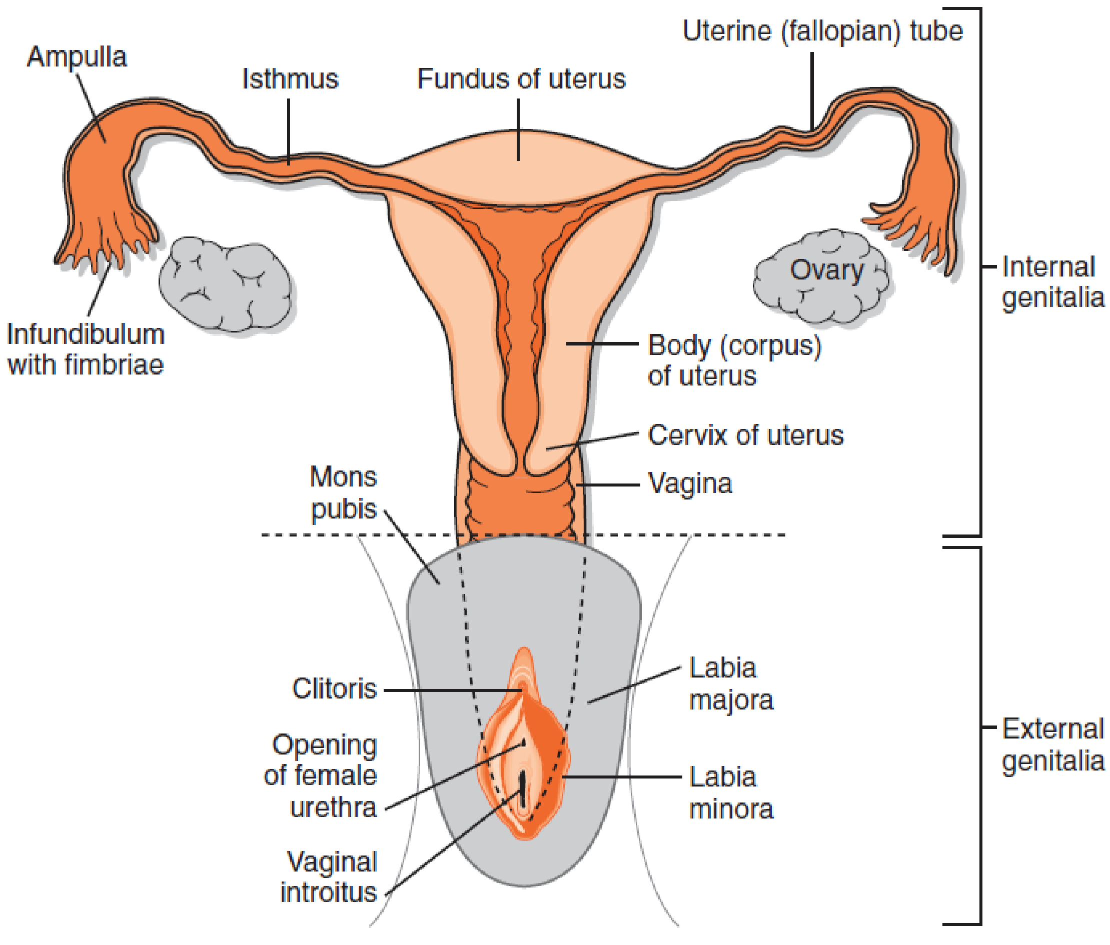
- Single organ that sits in the midline of the pelvic cavity between the bladder and the rectum.
- The mucosa of the uterus is called the **endometrium**, the three-layered, thick muscularis is called the **myometrium**, and the outer connective tissue and serosa are called the **perimetrium**.
- The parts of the uterus are the **fundus**, which is that portion that rises superiorly from the **entrance of the oviducts**; the body, which makes up most of the uterus; **the isthmus**, a short narrowed part of the body at its inferior end; and **the cervix**, which extends into the **vagina**.
- Because the cervical mucosa is distinct from the rest of the uterus and does not undergo the process of menstruation, it is discussed separately.
- The established functions of the uterus are related to supporting a pregnancy.



- 1. Provide a suitable site for attachment and implantation of the blastocyst, including a thick, nutrient rich stroma
- 2. Limit the invasiveness of the implanting embryo so that it stays in the endometriumand does not reach the myometrium
- 3. Provide a maternal side of the mature placental architecture. This includes the basal plate, to which the fetal side attaches, and large, intervillous spaces that become filled with maternal blood after the first trimester
- 4. Grow and expand with the growing fetus so that the fetus develops within an aqueous, largely non-adhesive environment
- 5. Provide strong muscular contractions to expel the fetus and placenta at term







The anatomy of the female reproductive tract.

(Adapted from Koeppen BM, Stanton BA: Berne andLevyPhysiology, 6th ed., updated edition, Philadelphia, 2010, Mosby.)

- An understanding of the function of the uterus and hormonally induced uterine changes during non-fertile menstrual cycles requires a basic knowledge of the fine structure of the endometrium and of the relationship of the uterine blood supply to the endometrium
- The luminal surface of the endometrium is covered by a simple **cuboidal-columnar epithelium**.
- The epithelium is continuous with **mucosal glands** (called uterine glands) that extend deep into the endometrium.
- The mucosa is **vascularized by spiral arter**ies, which are branches of the uterine artery that runs through the myometrium.

- The terminal arterioles of the spiral arteries project to a position just beneath the surface epithelium.
- These arterioles give rise to a subepithelial plexus of capillaries and venules, which have ballooned, thin-walled segments called venous lakes or lacunae.
- The lamina propria (i.e., the connective tissue and stroma of the mucosa supporting the epithelium) itself is densely cellular.
- The stromal cells of the lamina propria play important roles both during pregnancy and menstruation.
- About two thirds of the luminal side of the endometrium is lost during menstruation and is called the functional zone (also called the stratum functionalis)
- The basal one third of endometrium that remains after menstruation is called the basal zone (also called the stratum basale).
- The basal zone is fed by straight arteries that are separate from the spiral arteries and contains all of the cell types of the endometrium (i.e., epithelial cells from the remaining tips of glands, stromal cells, and endothelial cells).

Hormonal Regulation of the Uterine Endometrium

- During the Menstrual Cycle Phases the of uterine cycle are controlled by ovarian estrogen and progesterone
- Thus, phases of the endometrial cycle correspond to phases of the ovarian cycle

The Proliferative Phase

- At the end of menses (days 3 to 5), the functional layer of the uterine endometrium has been shed, and the basal layer is undergoing reepithelialization.
- In the ovary, the follicular phase is under way. By day 5 of the ovarian cycle, FSH has recruited a cohort of 2- to 5-mmlarge antral follicles that begin producing low but increasing levels of estradiol.
- Once the dominant follicle is selected at mid follicular phase, estradiol production increases dramatically.
- The estrogen produced by the **follicular phase of the ovary** drives the proliferative phase of the uterine endometrium.
- Estrogen induces all cell types in the basal layer to proliferate.
- Estrogen increases cell proliferation directly through estrogen receptor-a (ERa) and indirectly through the production of growth factors, such as insulin-like growth factor-1 (IGF-1).
- Estrogen also induces the expression of progesterone receptors, thereby priming the uterine endometrium so that it can respond to progesterone during the luteal phase of the ovary.
- During the proliferative phase, the functional layer of the endometrium is rebuilt, and the endometrium increases from about 0.5 to 5 mmin thickness.
- The uterine glands display a straight or coiled shape with narrow lumina.

- The Secretory Phase By ovulation, the thickness of stratum functionalis - reestablished under the proliferative actions of estradiol.
- After ovulation, the corpus luteum produces high levels of progesterone, along with estradiol.
- The luteal phase of the ovary switches the proliferative phase of the uterine endometrium to the secretory phase.
- Progesterone inhibits - endometrial growth and induces the differentiation of epithelial and stromal cells.
- Progesterone induces the uterine glands to secrete a nutrient-rich product, which will support implanting blastocyst viability.
- As the secretory phase proceeds, the mucosal uterine glands become corkscrewed and sacculated.
- Progesterone also induces changes in the adhesivity of the surface epithelium, thereby generating the window of receptivity for implantation.
- Progesterone also promotes the differentiation of the stromal cells into predecidual cells, which must be prepared to form the decidua of pregnancy, or to orchestratemenstruation in the absence of pregnancy.
- Progesterone opposes the proliferative actions of estradiol. Progesterone down regulates the estrogen receptor.
- Progesterone also induces inactivating isoforms of 17b-HSD, thereby converting the active estradiol into the inactive estrone.
- Progesterone also up regulates the expression of a steroid sulfotransferase that sulfates and inactivates estrogen.

The Menstrual Phase

- In a non-fertile cycle, death of the corpus luteum leads to a sudden withdrawal of progesterone and estrogen, which leads to changes in the uterine endometrium that result in the loss of the lamina functionalis.
- Menstruation normally lasts 3 to 5 days (called a period), and the volume of blood loss ranges from 25 to 35 mL.
- Menstruation coincides with the early follicular phase of the ovary.
- The breakdown of the stratum functionalis is due to the up regulation of hydrolytic enzymes, called matrix metalloproteases, which destroy the extracellular matrix and basal lamina of the endometrium.

- These enzymes are produced by the three resident cell types of the endometrium: the epithelial cell, the stromal cell, and the endothelial cell.
- Matrix metalloproteases also are produced by leukocytes, which infiltrate into the endometrium just before menstruation.
- The other major component that leads to menstruation is the production of prostaglandins.
- The inducible enzyme required for prostaglandin synthesis, cyclooxygenase-2 (COX-2), is increased in endothelial cells on progesterone withdrawal.
- This increases production of inflammatory prostaglandins, especially PGF2a, which, in turn, promotes contraction of the smooth muscle cells of the myometrium and the vascular smooth muscle cells of the spiral arteries.
- Intermittent spiral artery contraction and dilation cause hypoxic necrosis, followed by reperfusion injury of weakened tissue.
- The degree of tissue loss and the onset of tissue repair appear to be dependent on increasing estrogen levels during the early follicular phase.

Hormonal Regulation of the Myometrium

- The smooth muscle cells of the myometrium also are responsive to changes in steroid hormones.
- Peristaltic contractions of the myometrium favor movement of luminal contents from the cervix to the fundus at ovulation, and these contractions may play a role in rapid bulk transport of ejaculated sperm from the cervix to the oviducts.
- During menstruation, contractions propagate from the fundus to the cervix, thereby promoting expulsion of sloughed functional zone.
- The size and number of smooth muscle cells are determined by estrogen and progesterone.
- Healthy cycling women maintain a robust myometrium, whereas the myometrium progressively thins in postmenopausal women.

The Cervix

- The cervix represents the inferior extension of the uterus that projects into the vagina
- It has a mucosa that lines the endocervical canal, which has a highly elastic lamina propria, and a muscularis that is continuous with the myometrium.
- The cervix acts as a gateway to the upper female tract; at midcycle, the endocervical canal facilitates sperm viability and entry.
- During the luteal phase, changes in the endocervical canal serve to impede the passage of sperm and microbes, thereby minimizing the chance of superimplantation of a second embryo, as well as inhibiting ascending infections into the placenta, fetal membranes, and fetus.
- The cervix physically supports the weight of the growing fetus.
- At term, cervical softening and dilation allow passage of the newborn and placenta from the uterus into the vagina.

Hormonal Regulation of Cervical Mucus During the Menstrual Cycle

- The endocervical canal is lined by a simple columnar epithelial gland that secretes cervical mucus in a hormonally responsive manner.
- Estrogen stimulates production of a copious quantity of thin, watery, slightly alkaline mucus that is an ideal environment for sperm.
- The macromolecules within this mucus are thought to facilitate sperm movement.
- Progesterone stimulates production of a scant, viscous, slightly acidic mucus that is hostile to sperm and does not "fern."
- This thick mucus forms a barrier within the endocervical canal during the secretory phase of the endometrium and during pregnancy, when the placenta produces high amounts of progesterone

The Vagina

- The vagina represents one of the copulatory structures in women and acts as the birth canal
- Its mucosa is lined by a nonkeratinized, stratified squamous epithelium.
- The mucosa has a thick lamina propria enriched with elastic fibers and is well vascularized.
- There are no glands in the vagina, so lubrication during intercourse comes from the following:
  - Cervical mucus (especially during midcycle)
  - A transudate (i.e., ultrafiltrate) from the blood vessels of the lamina propria
- From the vestibular glands
- The mucosa is surrounded by a relatively thin (i.e., relative to the uterus and cervix) two-layeredmuscularis and an outer connective tissue.
- The vaginal wall is innervated by branches of the pudendal nerve which contribute to sexual pleasure and orgasm during intercourse.

Hormonal Regulation During the Menstrual Cycle

- The superficial cells of the vaginal epithelium are continually desquamating and the nature of these cells is influenced by the hormonal environment.
- Estrogen stimulates proliferation of the vaginal epithelium and increases their glycogen content.
- Estradiol also induces minimal keratinization of the apical layers.
- Progesterone increases the desquamation of the epithelial cells.
- The glycogen is metabolized to lactic acid by commensal lactobacilli, thereby maintaining an acidic environment.
- This relative acidity inhibits infections by non-commensal bacteria and fungi.

The External Genitalia

- The female external genitals are surrounded by the labia majora (homologs of the scrotum) laterally and the mons pubis anteriorly
- The vulva collectively refers to an area that includes the labia majora and the mons pubis, plus the labia minora, the clitoris, the vestibule of the vagina, the vestibular bulbs (glands), and the external urethral orifice
- The vulva also is referred to as the pudendum by clinicians.
- The structures of the vulva serve the functions of sexual arousal and orgasm, directing the flow of urine and providing a partial cover of the opening of the vagina, thereby inhibiting the entry of pathogens.

Hormonal Regulation During the Menstrual Cycle

- The structures of the vulva do not show marked changes during the menstrual cycle.
- The health and function of these structures, however, are dependent on hormonal support.
- The external genitalia and vagina appear to be responsive to androgens (testosterone and dihydrotestosterone), as well as estrogen.
- Androgens also act on the central nervous system (CNS) to increase libido in women

Similarities between male and female reproductive systems

- The reproductive systems of the male and female have some basic similarities and some specialized differences.
- They are the same in that most of the reproductive organs of both sexes develop from **similar embryonic tissue**, meaning they are homologous.
- Both systems have **gonads that produce (sperm and egg or ovum) and sex organs**.
- And both systems experience **maturation of their reproductive organs**, which become functional during puberty as a result of the gonads **secreting sex hormones**.
- In short, this is a known list of sex organs that **evolve from the same tissue in a human life.**

Differences between male and female reproductive systems

- The differences between the female and male reproductive systems are based on the functions of each individual's role in the reproduction cycle.
- A male who is healthy, and sexually mature, continuously produces sperm.
- The development of women's "eggs" are arrested during fetal development.
- This means she is born with a predetermined number of oocytes and cannot produce new ones.
- At about **5 months gestation**, the ovaries contain approximately six to seven million oogonia, which initiate meiosis.
- The oogonia produce primary oocytes that are arrested in prophase I of meiosis from the time of birth until puberty.
- After puberty, during each menstrual cycle, one or several oocytes resume meiosis and undergo their first meiotic division during ovulation.
- This results in the production of a secondary oocyte and one polar body.
- The meiotic division is arrested in metaphase II.
- Fertilization triggers completion of the second meiotic division and the result is one ovum and an additional polar body.

- The ovaries of a newborn baby girl contain about **one million oocytes**.
- This number declines to 400,000 to 500,000 by the time puberty is reached.
- On average, 500-1000 oocytes are ovulated during a woman's reproductive lifetime.
- When a young woman reaches puberty around age 10 to 13, a promary oocyte is discharged from one of the ovaries every 28 days.
- This continues until the woman reaches menopause, usually around the age of 50 years.
- Oocytes are present at birth, and age as a woman ages.
- Female Reproductive System
  - Produces eggs (ova)
  - Secretes sex hormones
  - Receives the male spermatazoa during
  - Protects and nourishes the fertilized egg until it is fully developed
  - Delivers fetus through birth canal
  - Provides nourishment to the baby through milk secreted by mammary glands in the breast

Undifferentiated	Male	Female
Gonad	Testis	Ovary
Mullerian duct	Appendix testis	Fallopian tubes
Mullerian duct	Prostatic utricle	Uterus, proximal
Wolffian duct	Rete testis	Rete ovarii
Mesonephric tubules	Efferent ducts	Epoophoron
Wolffian duct	Epididymis	Gartner's duct
Wolffian duct	Vas deferens	
Wolffian duct	Seminal vesicle	
Wolffian duct	Prostate	Skene's glands
Urogenital sinus	Bladder, urethra	Bladder, urethra, distal
Urogenital sinus	Bulbourethral gland	Bartholin's gland
Genital swelling	Scrotum	Labia majora
Urogenital folds	Distal urethra	Labia minora
Genital tubercle	Penis	Clitoris
Prepuce		Clitoral hood
	Bulb of penis	Vestibular bulbs
	Glans penis	Clitoral glans
	Crus of penis	Clitoral crura

Gonad

Mullerian duct

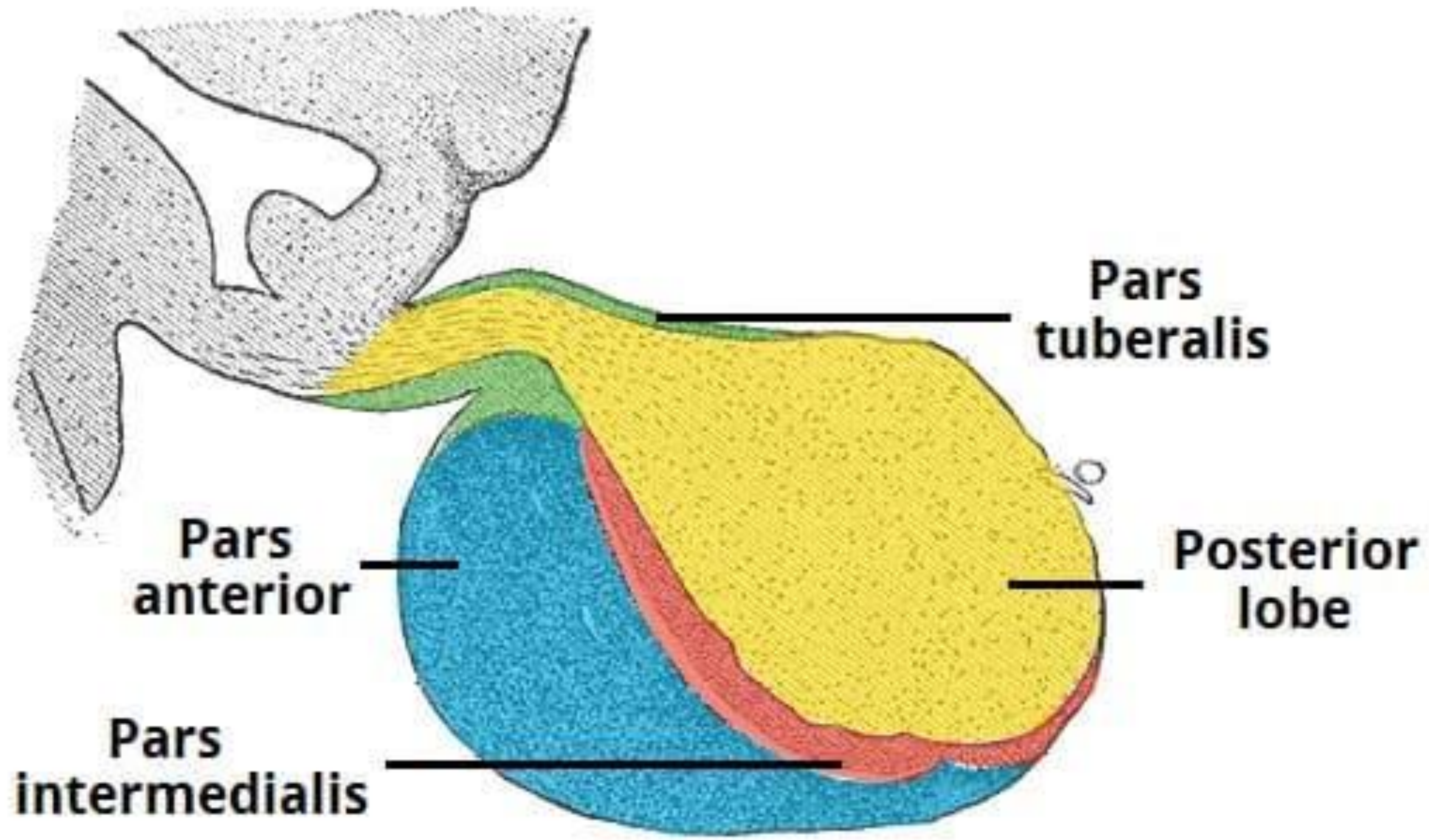
Wolffian duct

Urogenital sinus

Reproductive Technology (22ZOOME22)

Anatomy of endocrine glands and hormones

Structure and Function of Pituitary

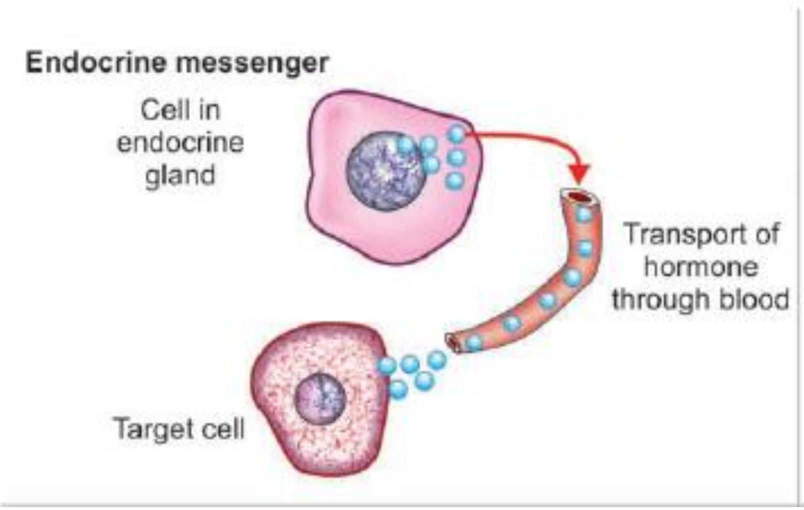


Introduction of Endocrine System

- All the physiological activities are regulated by two major systems:
- 1. Nervous system
- 2. Endocrine system.
- These two systems interact with one another and regulate the body functions.
- Endocrine system functions by secreting some chemical substances called hormones.
- **CELL-TO-CELL SIGNALING** Cell to cell signaling refers to the transfer of information from one cell to another. This is also called **cell signalling** or intercellular communication.
- The cells of the body communicate with each other through some chemical substances called chemical messengers.

- **CHEMICAL MESSENGERS**
- Chemical messengers - involved in cell signalling.
- These messengers secreted from endocrine glands.
- Some are secreted by nerve endings and the cells of several other tissues
- All these chemical messengers carry the message (signal) from the signalling cells (controlling cells) to the target cells.
- The messenger substances may be the hormones or hormone like substances.

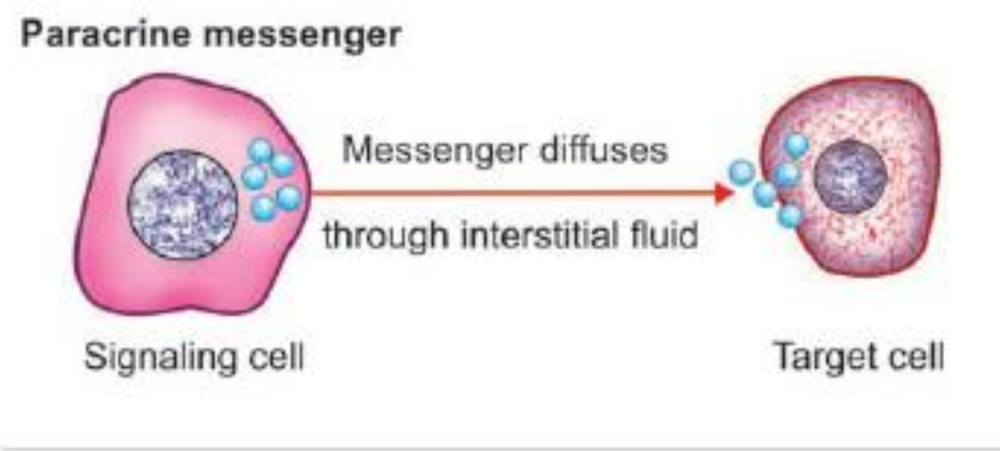
- ***Classification of Chemical Messengers***
  - 1. Classical hormones secreted by endocrine glands
  - 2. Local hormones secreted from other tissues.
- However, recently chemical messengers are classified into four types:
- 1. Endocrine messengers
- 2. Paracrine messengers
- 3. Autocrine messengers
- 4. Neurocrine messengers.

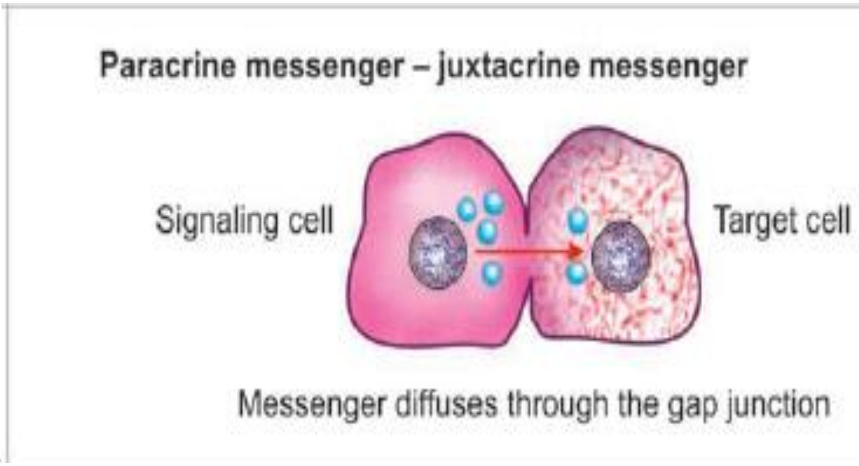


1. *Endocrine Messengers*

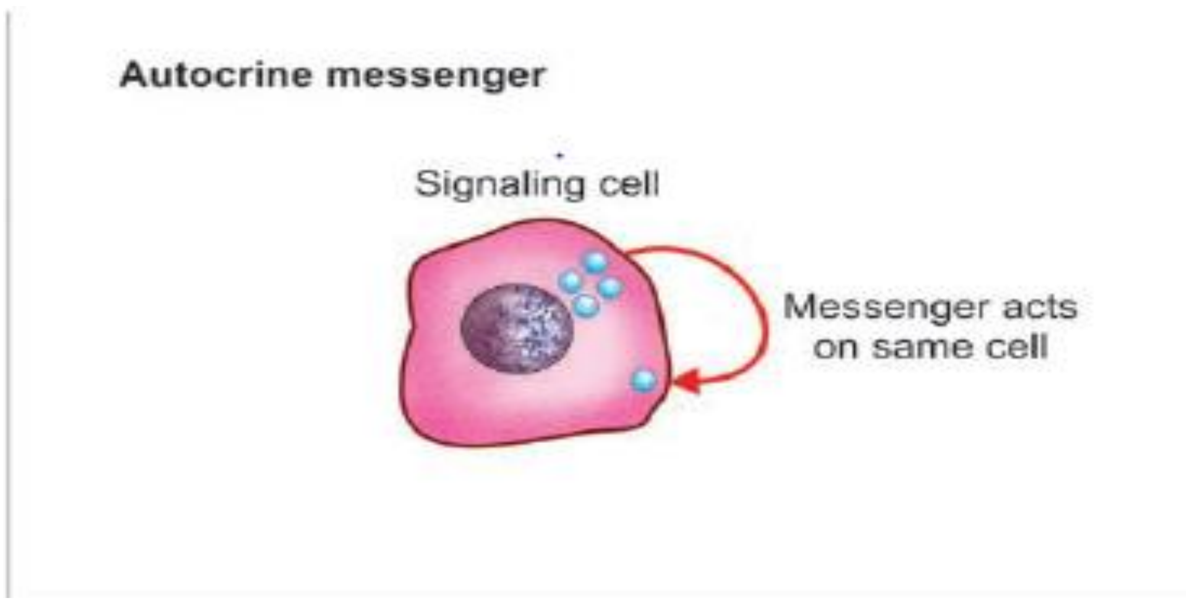
- Endocrine messengers are the classical hormones.
- A hormone is defined as a chemical messenger, synthesized by endocrine glands and transported by blood to the target organs or tissues (site of action). Examples are growth hormone and insulin.

- **2. *Paracrine Messengers***
- chemical messengers, which diffuse from the control cells to the target cells through the interstitial fluid.
- Some of these substances directly enter the neighboring target cells through gap junctions.
- Such substances are also called **juxtacrine messengers or local hormones.** Examples are prostaglandins and histamine.





- **3. *Autocrine Messengers***
- chemical messengers that control the source cells which secrete them.
- So,these messengers are also called **intracellular chemical mediators.**
- Examples are leukotrienes.



4. *Neurocrine or Neural Messenger*

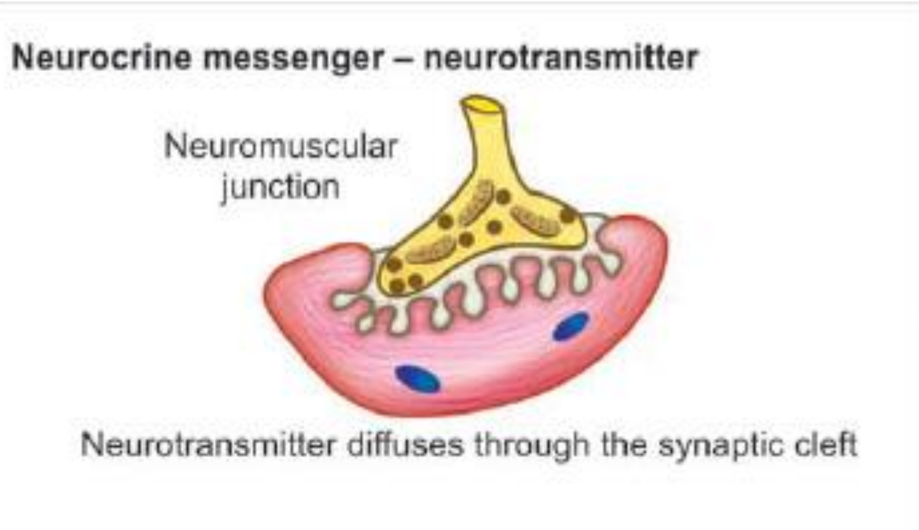
Neurotransmitter is an endogenous signaling molecule that carries information from one nerve cell to another nerve cell or muscle or another tissue.

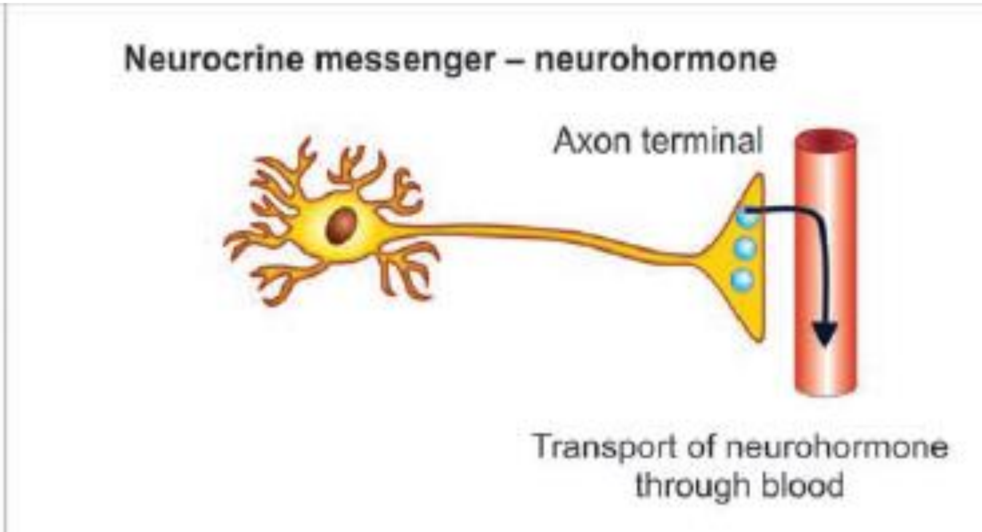
Ex- acetylcholine and dopamine

Neurohormone is a chemical substance that is released by the nerve cell directly into the blood and transported to the distant target cells.

Ex- oxytocin, antidiuretic hormone and hypothalamic releasing hormones.

Some of the chemical mediators act as more than one type of chemical messengers. For example, noradrenaline and dopamine function as classical hormones as well as neurotransmitters. Similarly, histamine acts as neurotransmitter and paracrine messenger.





- **ENDOCRINE GLANDS**
- Endocrine glands are the glands which synthesize and release the classical hormones into the blood.
- Endocrine glands are also called **ductless glands** **because the** Endocrine glands play an important role in homeostasis and control of various other activities in the body through their hormones.
- Hormones are transported by blood to target organs or tissues in different parts of the body, where the actions are executed.

TABLE 64.1: Hormones secreted by major endocrine glands

Anterior pituitary	1. Growth hormone (GH) 2. Thyroid-stimulating hormone (TSH) 3. Adrenocorticotropic hormone (ACTH) 4. Follicle stimulating hormone (FSH) 5. Luteinizing hormone (LH) 6. Prolactin	Adrenal cortex	*Mineralocorticoids* 1. Aldosterone 2. 11-deoxycorticosterone *Glucocorticoids* 1. Cortisol 2. Corticosterone
Posterior pituitary	1. Antidiuretic hormone (ADH) 2. Oxytocin		*Sex hormones* 1. Androgens 2. Estrogen 3. Progesterone
Thyroid gland	1. Thyroxine (T_4) 2. Triiodothyronine (T_3) 3. Calcitonin		
Parathyroid gland	Parathormone	Adrenal medulla	1. Catecholamines 2. Adrenaline (Epinephrine) 3. Noradrenaline (Norepinephrine) 4. Dopamine
Pancreas – Islets of Langerhans	1. Insulin 2. Glucagon 3. Somatostatin 4. Pancreatic polypeptide		

TABLE 64.2: Hormones secreted by gonads

Testis	1. Testosterone 2. Dihydrotestosterone 3. Androstenedion
Ovary	1. Estrogen 2. Progesterone

TABLE 64.3: Hormones secreted by other organs

Pineal gland	Melatonin
Thymus	1. Thymosin 2. Thymin
Kidney	1. Erythropoietin 2. Thrombopoietin 3. Renin 4. 1,25-dihydroxycholecalcifero (calcitriol) 5. Prostaglandins
Heart	1. Atrial natriuretic peptide 2. Brain natriuretic peptide 3. C-type natriuretic peptide
Placenta	1. Human chorionic gonadotropin (HCG) 2. Human chorionic somatomammotropin 3. Estrogen 4. Progesterone

TABLE 64.4: Local hormones

1. Prostaglandins 2. Thromboxanes 3. Prostacyclin 4. Leukotrienes 5. Lipoxins 6. Acetylcholine	7. Serotonin 8. Histamine 9. Substance P 10. Heparin 11. Bradykinin 12. Gastrointestinal hormones

Classification of hormones

- Hormones are **chemical messengers**, synthesized by endocrine glands.
- Based on chemical nature, hormones are classified into three types
- 1. Steroid hormones 2. Protein hormones
- 3. Derivatives of the amino acid called tyrosine.

STEROID HORMONES

- Steroid hormones are the hormones synthesized from cholesterol or its derivatives, cholesterol as a functional group.
- Fat-soluble; as a result can diffuse into target cells .
- Steroid hormones are secreted by adrenal cortex, gonads and placenta.

PROTEIN HORMONES

- Protein hormones are large or small peptides.
- fat insoluble; cannot diffuse across the membrane of target
- cells .
- Protein hormones are secreted by pituitary gland, parathyroid glands, pancreas and placenta ('P's).

TYROSINE DERIVATIVES

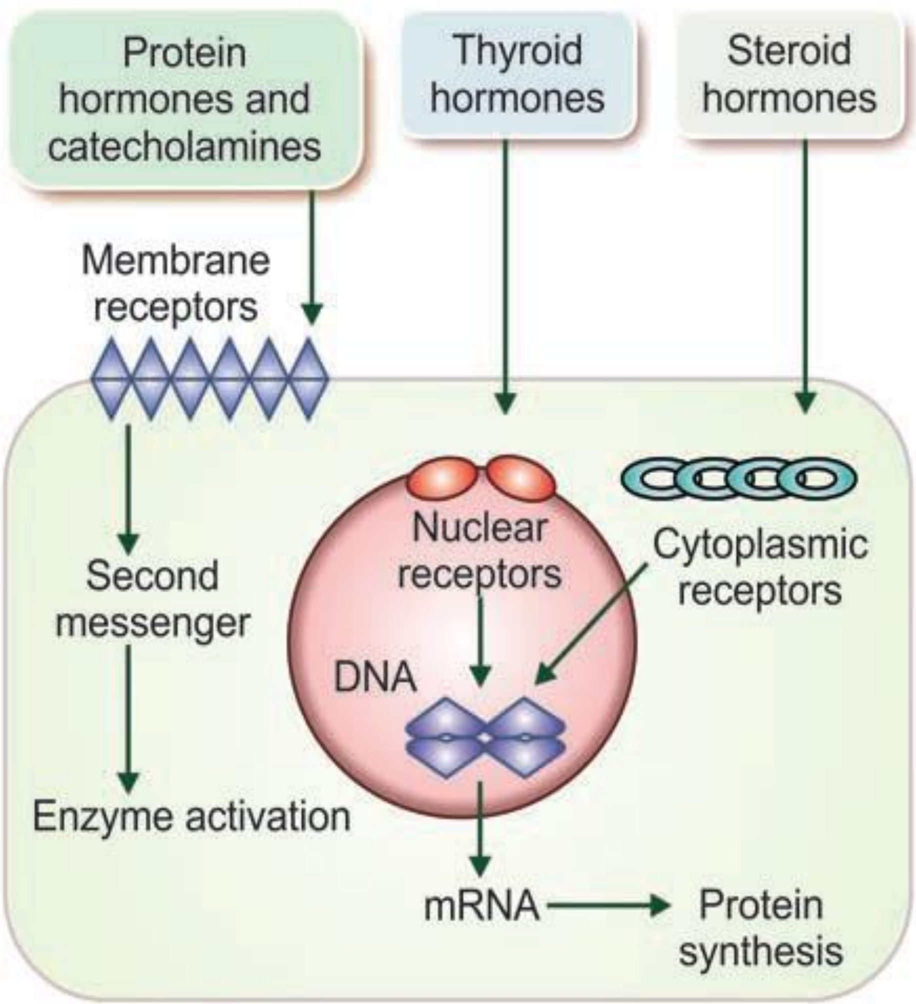
- Two types of hormones, namely thyroid hormones and
- adrenal medullary hormones are derived from the aminoacid tyrosine.

TABLE 65.1: Classification of hormones depending upon chemical nature

Steroids	Proteins	Derivatives of tyrosine
Aldosterone 11-deoxycorticosterone Cortisol Corticosterone Testosterone Dihydrotestosterone Dehydroepiandrosterone Androstenedione Estrogen Progesterone	Growth hormone (GH) Thyroid-stimulating hormone (TSH) Adrenocorticotropic hormone (ACTH) Follicle-stimulating hormone (FSH) Luteinizing hormone (LH) Prolactin Antidiuretic hormone (ADH) Oxytocin Parathormone Calcitonin Insulin Glucagon Somatostatin Pancreatic polypeptide Human chorionic gonadotropin (HCG) Human chorionic somatomammotropin.	Thyroxine (T_4) Triiodothyronine (T_3) Adrenaline (Epinephrine) Noradrenaline (Norepinephrine) Dopamine.

Hormone Action

- Hormone does not act directly on target cells.
- First it combines with receptor present on the target cells and forms a **hormone-receptor complex.**
- This hormone receptor complex induces various changes or reactions in the target cells.



- ***Regulation of Hormone Receptors***
- Receptor proteins are not static components of the cell.
- Their number increases or decreases in various conditions.
- Generally, when a hormone is secreted in excess, the number of receptors of that hormone decreases due to binding of hormone with receptors.
- This process is called **down regulation.**
- During the deficiency of the hormone, the number of receptor increases, which is called **upregulation.**
- Hormone in the form of hormone-receptor complex enters the target cell by means of endocytosis and executes the actions.
- The whole process is called **internalization.**
- After internalization, some receptors are recycled, whereas many of them are degraded and new receptors are formed.
- Formation of new receptors takes a long time. So, the number of receptors decreases when hormone level increases.

MECHANISM OF HORMONAL ACTION

- Hormone does not act on the target cell directly.
- It combines with receptor to form hormone-receptor
- complex.
- This complex executes the hormonal action by any one of the following mechanisms:
- 1. By altering permeability of cell membrane
- 2. By activating intracellular enzyme
- 3. By acting on genes.

BY ALTERING PERMEABILITY OF CELL MEMBRANE

- Neurotransmitters in synapse or neuromuscular junction act by changing the permeability of postsynaptic membrane.
- Ex. In neuromuscular junction, when an impulse (action potential) reaches the axon terminal of the motor nerve, acetylcholine is released from the vesicles.
- Acetylcholine increases the permeability of the postsynaptic membrane for sodium, by opening the ligand-gated sodium channels.
- So, sodium ions enter the neuromuscular junction from ECF through the channels and cause the development of endplate potential.

BY ACTIVATING INTRACELLULAR ENZYME

- Protein hormones and the catecholamines act by activating the intracellular enzymes.

First Messenger

- The hormone which acts on a target cell, is called first messenger or **chemical mediator.** It combines with the receptor and forms hormone-receptor complex.

Second Messenger

- Hormone-receptor complex activates the enzymes of the cell and causes the formation of another substance called the second messenger or **intracellular hormonal mediator.**
- Second messenger produces the effects of the hormone inside the cells. Protein hormones and the catecholamines act through second messenger.
- Most common second messenger is cyclic AMP.

Cyclic AMP or cAMP or cyclic adenosine 3′5′- monophosphate acts as a second messenger for protein hormones and catecholamines.

Formation of cAMP – Role of G proteins

- G proteins or **guanosine nucleotide-binding proteins** are the membrane proteins situated on the inner surface of cell membrane.
- These proteins play an important role in the formation of cAMP
- Each G protein molecule is made up of trimeric (three) subunits called α, β and γ subunits.
- The α-subunit is responsible for most of the biological actions.
- It is bound with **guanosine diphosphate** (GDP) and forms α-GDP unit.
- The α-subunit is also having the intrinsic enzyme activity called **GTPase** activity.
- The β and γ subunits always bind together to form the β-γ dimmer.
- It can also bring about some actions. In the inactivated G protein, both α-GDP unit and β-γ dimmer are united

Sequence of events in the formation of cAMP

i. forms the hormone-receptor complex

ii. It activates the G protein

iii. G protein releases GDP from α-GDP unit

iv. The α-subunit now binds with a new molecule of GTP, i.e. the GDP is exchanged for GTP

v. This exchange triggers the dissociation of α-GTP unit and β-γ dimmer from the receptor

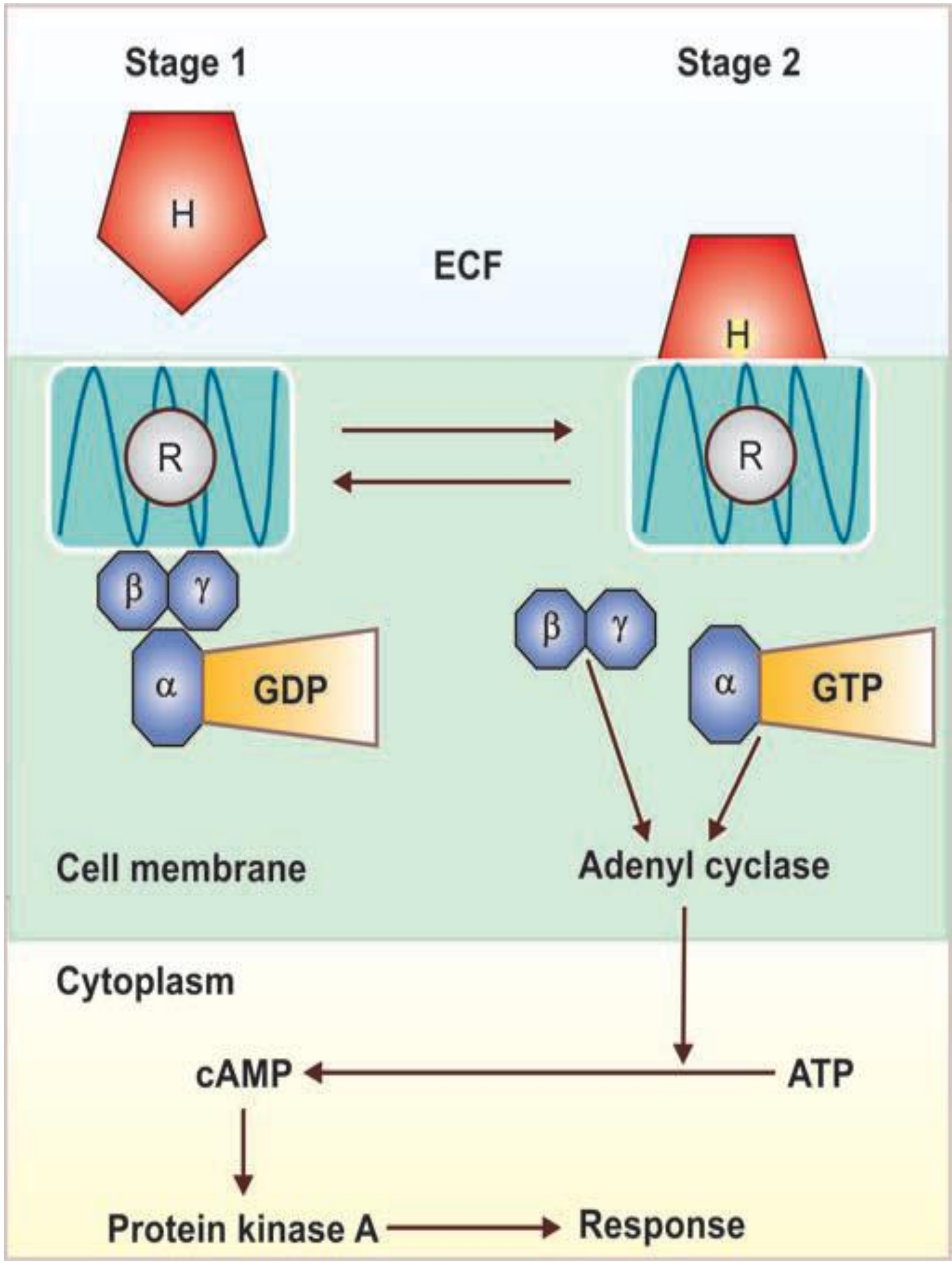
vi. Both α-GTP unit and β-γ dimmer now activate the second messenger pathways

vii. The α-GTP unit activates the enzyme adenyl cyclase, which is also present in the cell membrane.

viii. Activated adenyl cyclase converts the adenosine triphosphate of the cytoplasm into cyclic adenosine monophosphate (cAMP)

When the action is over, α-subunit hydrolyzes the attached GTP to GDP by its GTPase activity.

This allows the reunion of α-subunit with β-γ dimmer and commencing a new cycle



Other Secondary Messengers-

i. Calcium ions and calmodulin

Many hormones act by increasing the calcium ion, which functions as second messenger along with another protein called calmodulin or troponin C.

Calmodulin- smooth muscles and troponin C - skeletal muscles.

- ii. *Inositol triphosphate* - Inositol triphosphate (IP3) is formed from phosphatidylinositol biphosphate (PIP2).
- iii. *Diacylglycerol-* Diacylglycerol (DAG) is also produced from PIP2. It acts via protein kinase C.
- iv. *Cyclic guanosine monophosphate*

Sequence of Events during Activation of Genes

i. Hormone enters the interior of cell and binds with receptor in cytoplasm (steroid hormone) or in nucleus (thyroid hormone) and forms hormonereceptor complex

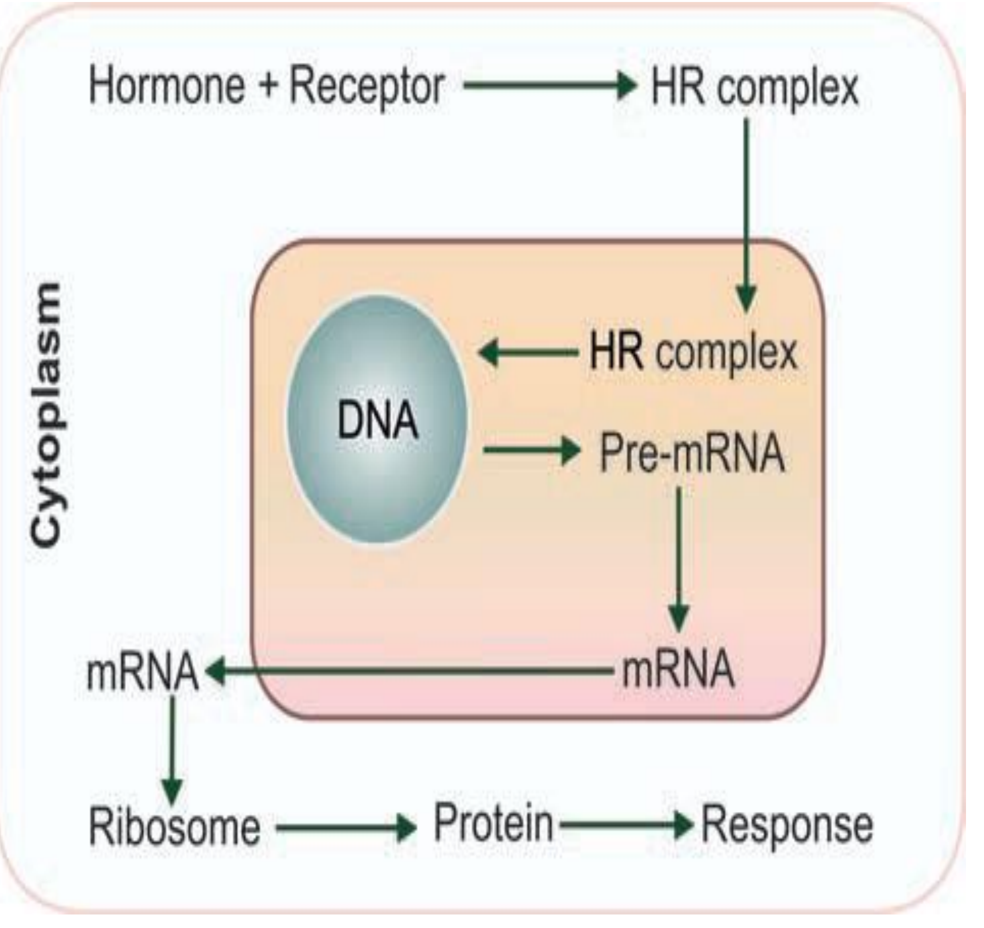
ii. Hormone-receptor complex moves towards the DNA and binds with DNA

iii. This increases transcription of mRNA

iv. The mRNA moves out of nucleus and reaches ribosomes and activates them

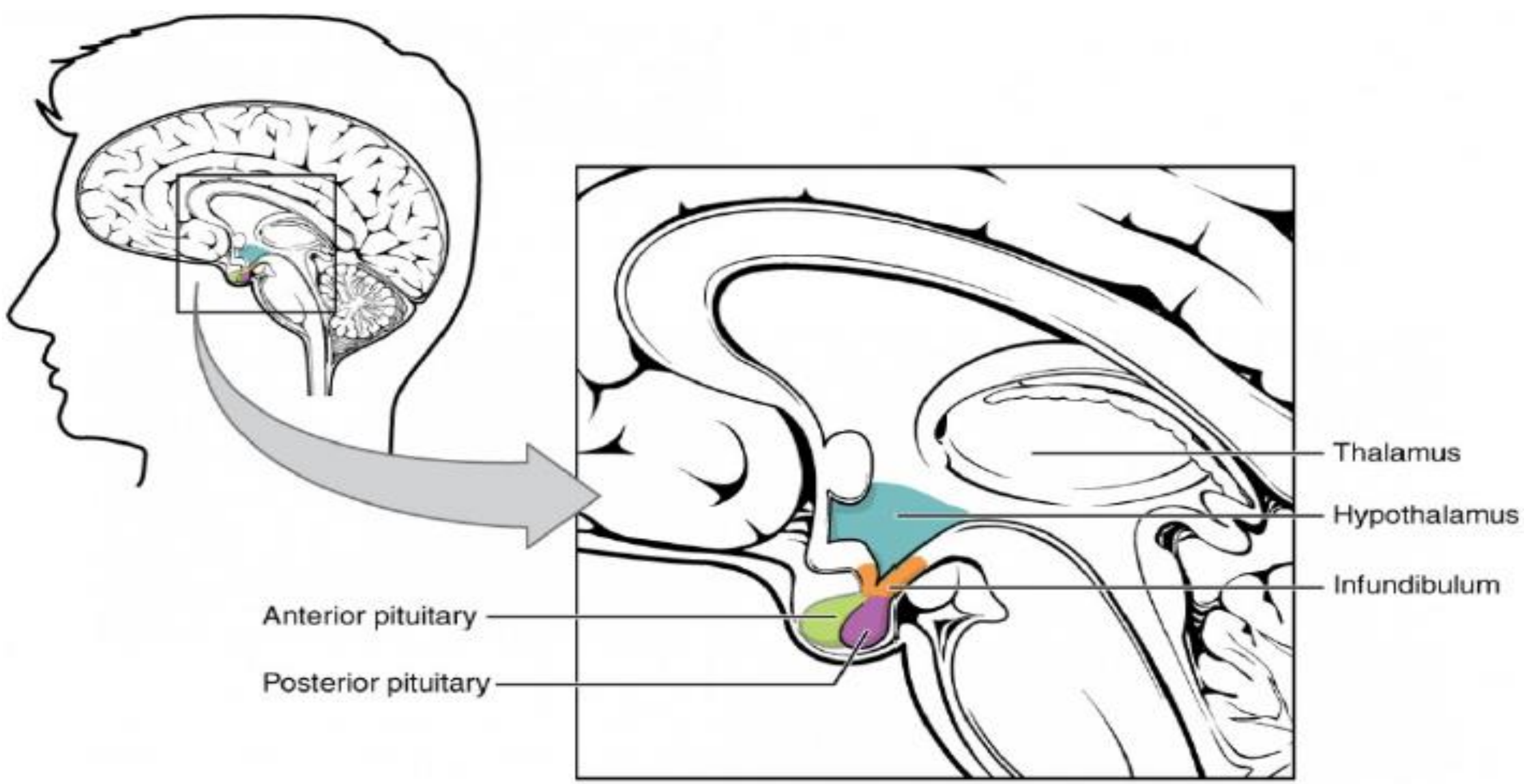
v. Activated ribosomes produce large quantities of proteins

vi. These proteins produce physiological responses in the target cells.

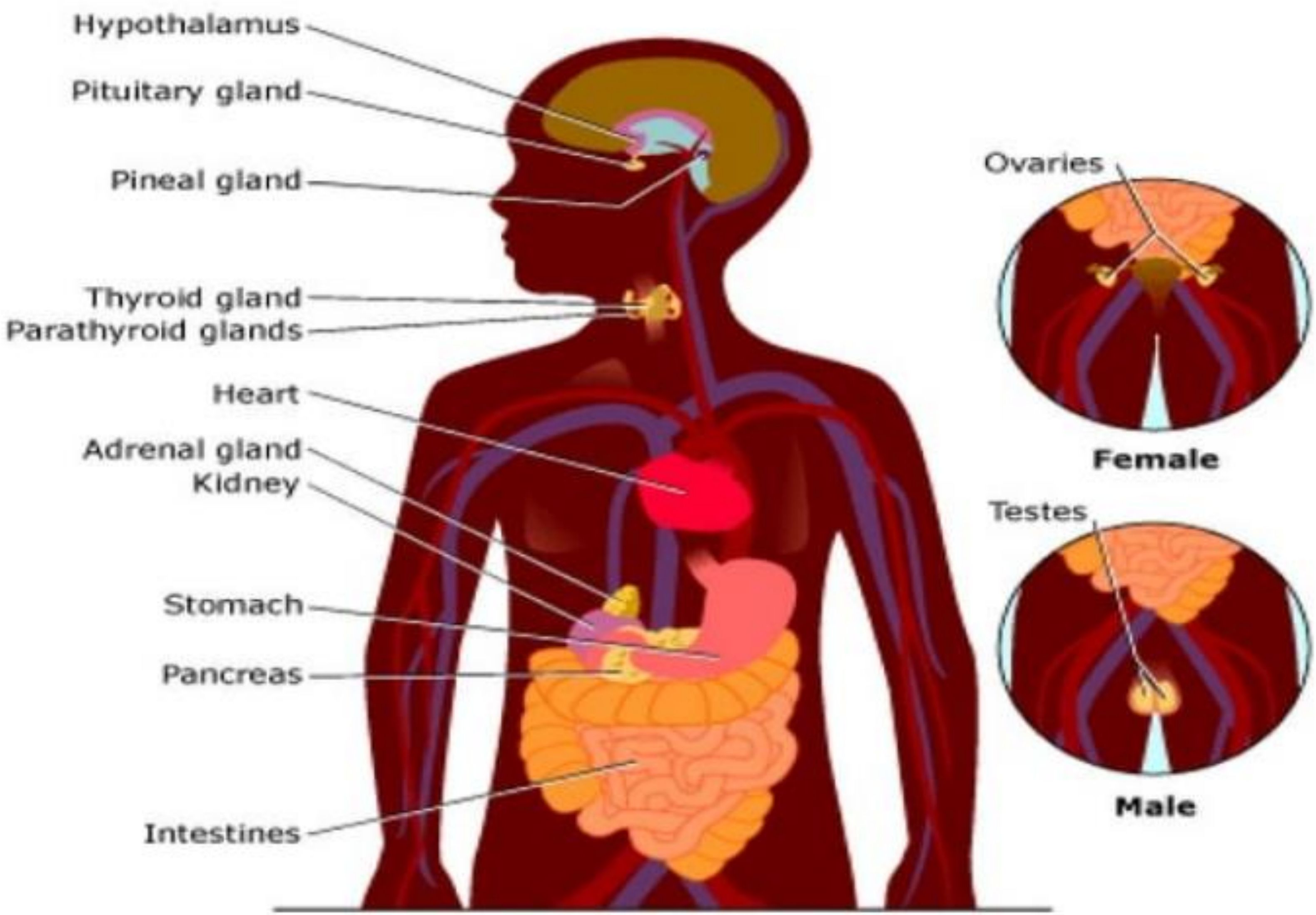


HYPOTHALAMUS

- It is located in the center of the brain.
- It makes increase or decrease the release of the hormones made in the pituitary gland it also makes hormones that help to control water balance, sleep, temperature, appetite and blood pressure.

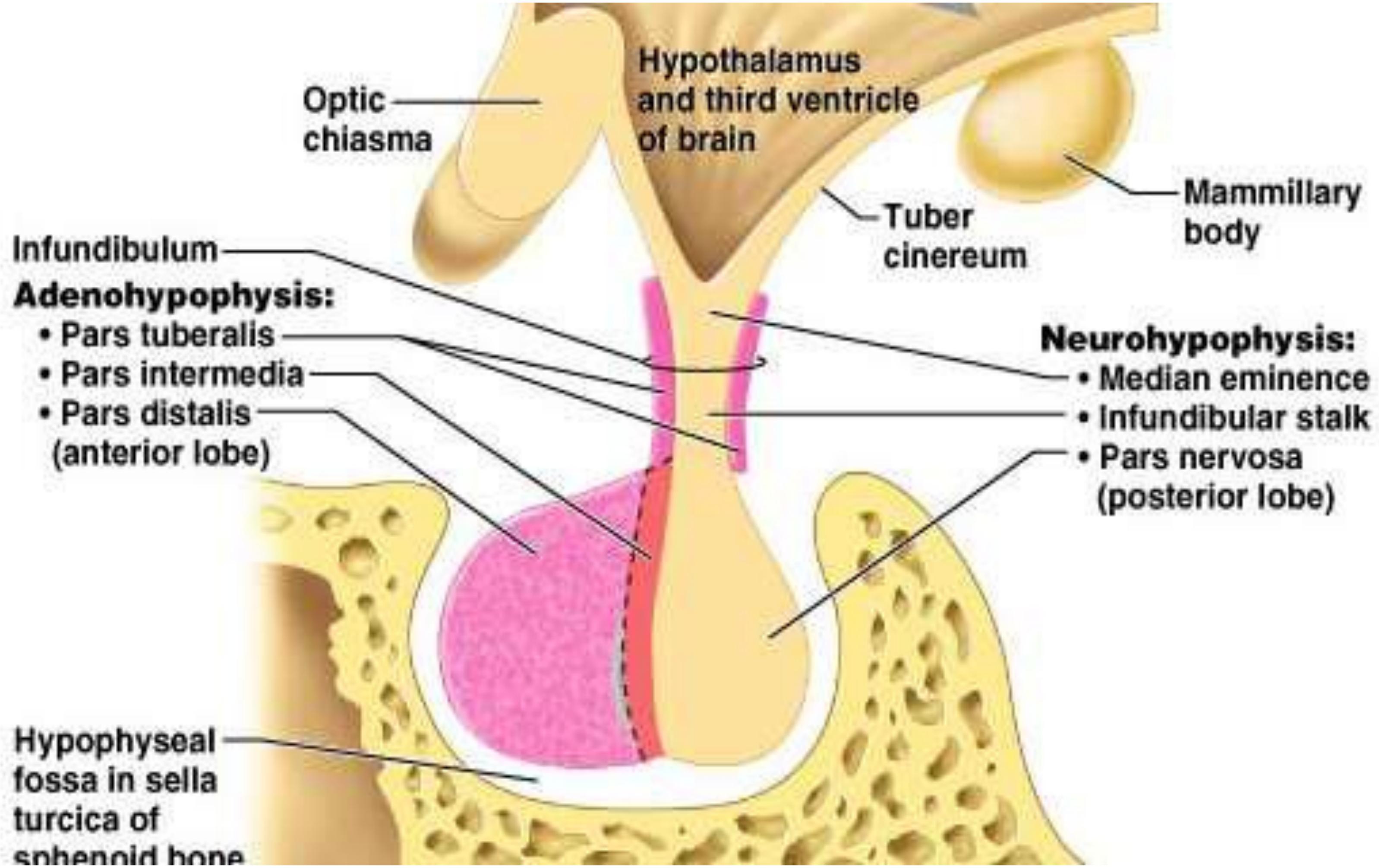


- The hypothalamus is a structure of the diencephalon of the brain located anterior and inferior to the thalamus.
- It has both neural and endocrine functions, producing and secreting many hormones.
- In addition, the hypothalamus is anatomically and functionally related to the pituitary gland (or hypophysis), a bean-sized organ suspended from it by a stem called the infundibulum (or pituitary stalk).
- The pituitary gland is cradled within the sella turcica of the sphenoid bone of the skull.



The Endocrine System

Structure of pituitary



- The pituitary gland is an endocrine gland that works to maintain cellular homeostasis in the body by the release of different hormones.
- The pituitary gland is also called the master gland as it regulates the working and secretion of other endocrine glands.
- The term 'pituitary' is derived from the Latin term 'pituita', meaning phlegm or slime.
- Structurally, the pituitary gland is divided into two distinct parts; anterior pituitary and posterior pituitary.

- The anterior pituitary is the glandular part called adenohypophysis, whereas the posterior pituitary is composed of neural tissue called neurohypophysis.
- In between the two lobes of the pituitary gland is a small avascular region called the pars intermedia
- The two lobes of the gland have different embryological origins;
- the anteriorpituitary originates from the Rathke's pouch present in the pharyngeal epithelium, whereas the posterior pituitary originates from the neural tissue outgrowth in the hypothalamus.

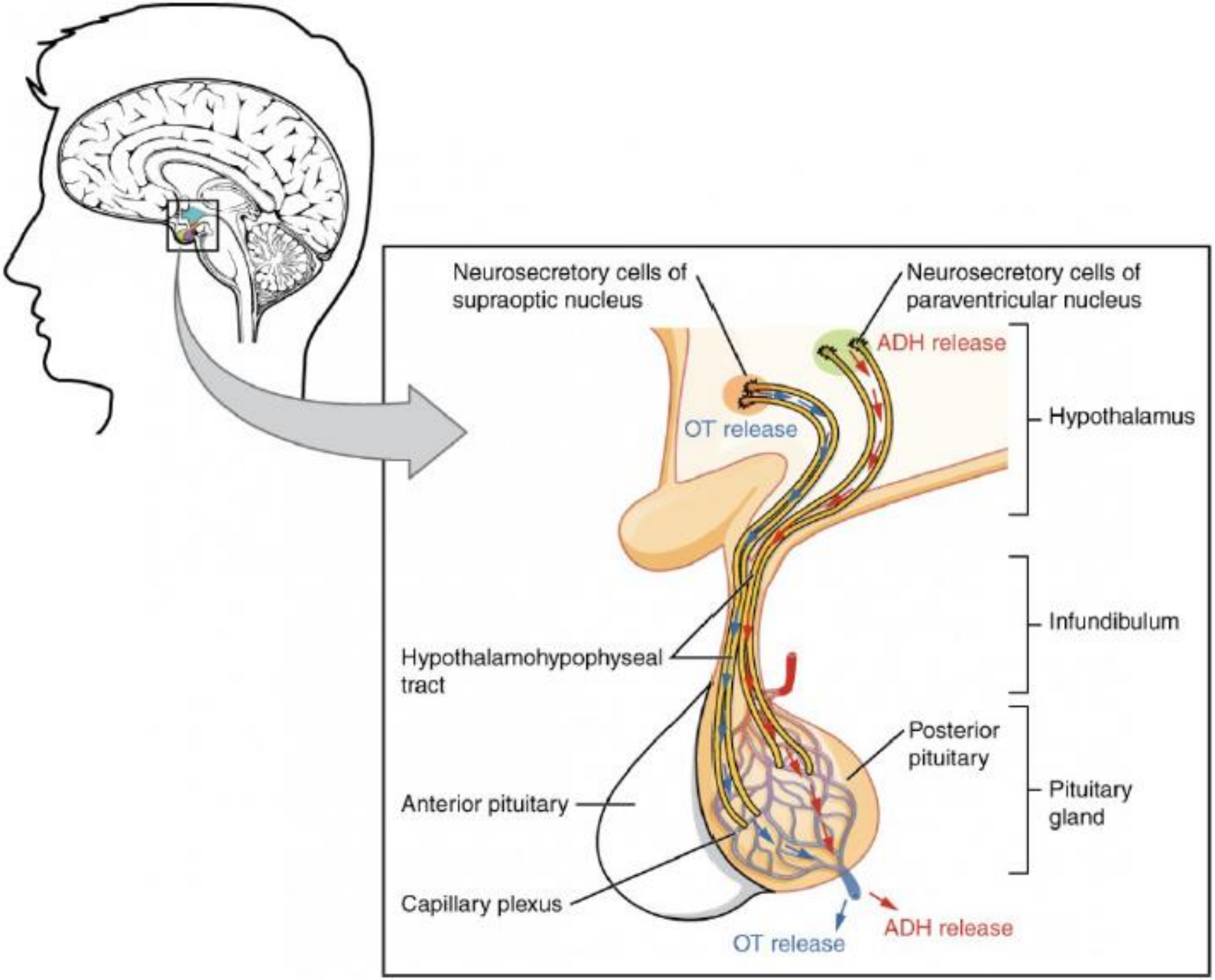
- The pituitary gland is a small pea-shaped gland that occurs at the base of the skull,
- The gland weighs about 0.5 to 1g depending on the age and physiological condition of the individual.
- Typically, the pituitary gland consists of three distinct lobes; anterior lobe, posterior lobe, and intermediate lobe.
- The anterior pituitary is composed of glandular epithelium with cells having secretary functions.
- The posterior pituitary is composed of neurons that do not secrete their own hormone but act as a region of hormone storage.

- **The anterior lobe has three regions:**

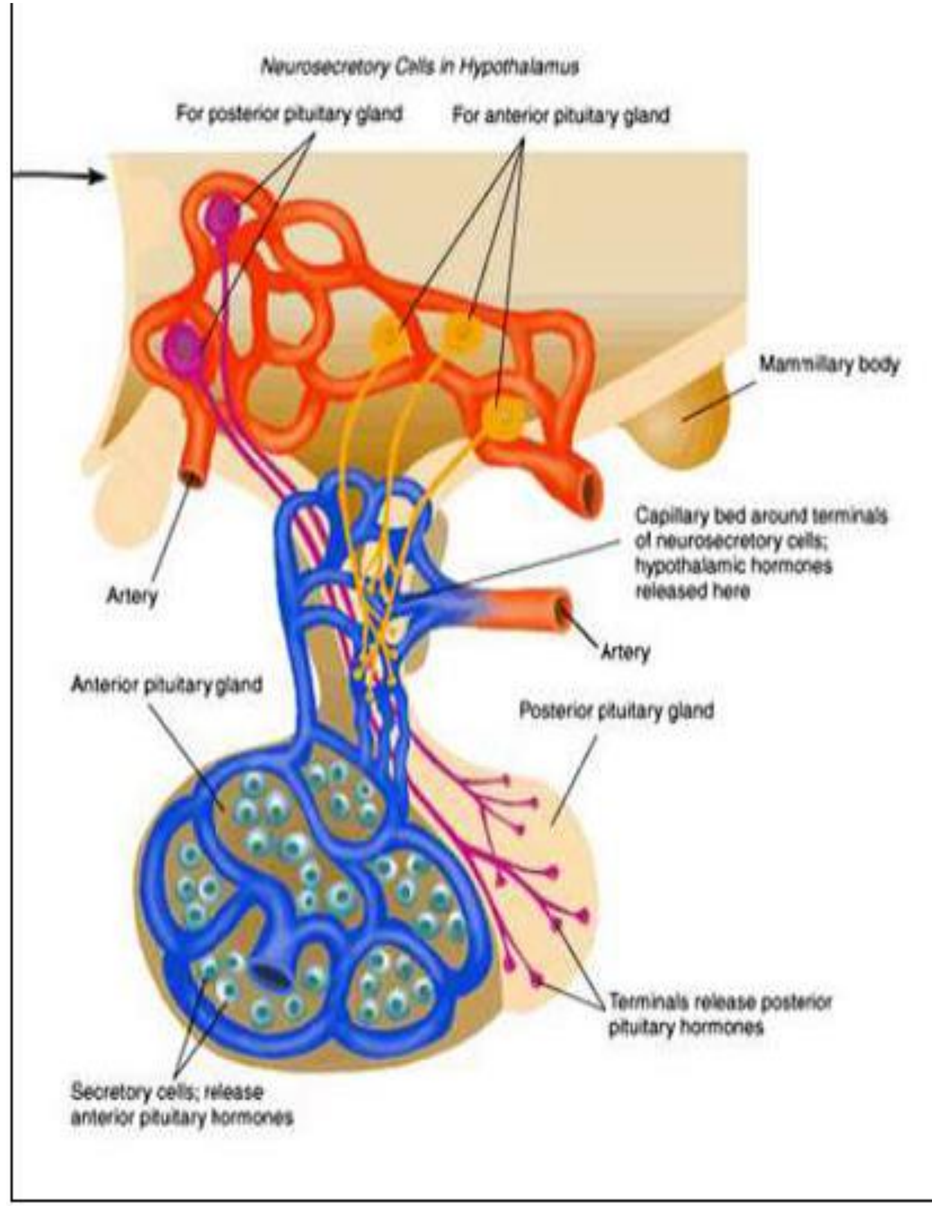
- Pars distalis: The largest, most anterior part of the pituitary gland.
- Pars tuberalis: The extension that wraps around the adjacent area of the infundibulum.
- Pars intermedia: The slender and narrow band that borders the posterior lobe of the pituitary gland; this section may secrete two types of melanocyte stimulating hormone, also known as melanotropin.
- It stimulates the melanocytes of the skin to increase production of melanin, and the release of melanocyte-stimulating hormone is inhibited by dopamine.

Hormones of Intermediate Lobe:

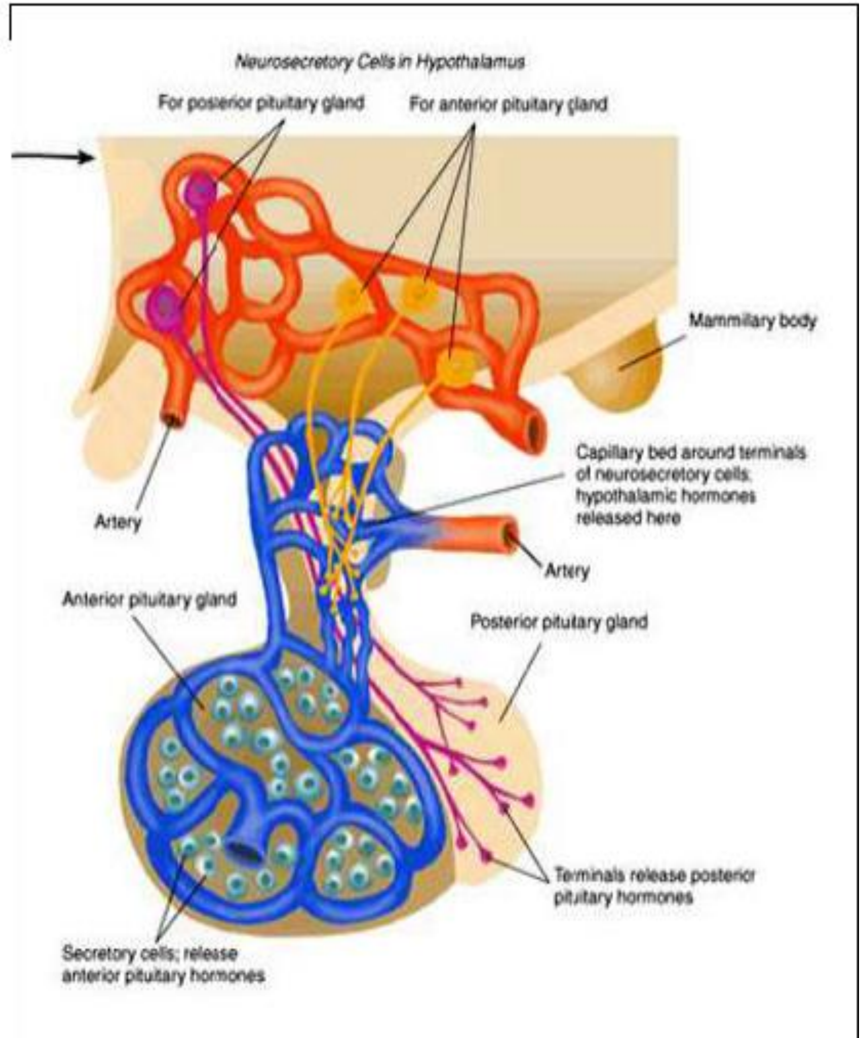
- The intermediate lobe produces intermedin which controls the expansion of black pigment melanophores in elasmobranchs, amphibians, and many reptiles so that the skin becomes darker due to spreading of pigment granules.
- In birds and mammals the intermediate lobe is much reduced though intermedin is secreted but it has no effect on their pigments.
- The secretion of intermedin is due to a response to visual stimuli of the eyes which stimulate the intermediate lobe to secrete.


Neurosecretory cells of supraoptic nucleus
Neurosecretory cells of paraventricular nucleus
ADH release
OT release
Hypothalamus
Infundibulum
Hypothalamohypophyseal tract
Posterior pituitary
Pituitary gland
Anterior pituitary
Capillary plexus
OT release
ADH release

- Hormone-releasing &
- inhibiting factors
- produced by hypothalamus
- Use Hypophyseal Portal
- System of vessels to
- reach the Anterior lobe of
- pituitary gland



- The neurohypophysis receives a
- nerve supply from some of the
- hypothalamic nuclei (supraoptic &
- paraventricular)
- The axons of these nuclei convey
- their neurosecretion to the
- Posterior lobe of pituitary gland
- through Hypothalamo-
- Hypophyseal tract from where it
- passes into the blood stream.



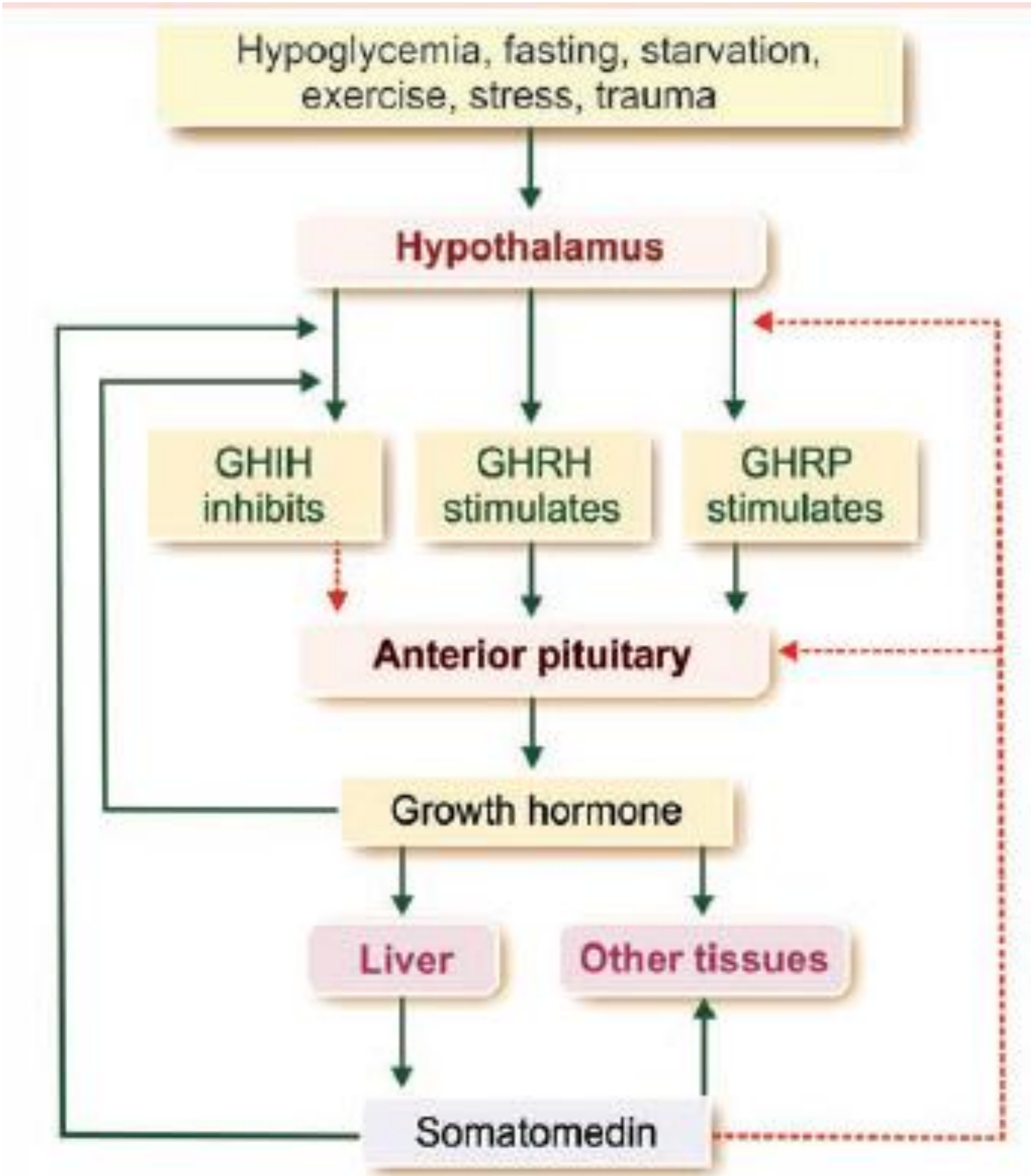
- **HORMONES SECRETED BY ANTERIOR PITUITARY**
- 1. Growth hormone (GH) or somatotropic hormone (STH)
- 2. Thyroid-stimulating hormone (TSH) or thyrotropic hormone
- 3. Adrenocorticotropic hormone (ACTH)
- 4. Follicle-stimulating hormone (FSH)
- 5. Luteinizing hormone (LH) in females or interstitialcell-stimulating hormone (ICSH) in males
- 6. Prolactin.
- Recently, the hormone β-lipotropin is found to be secreted by anterior pituitary.

Growth hormone (GH) or somatotropic hormone (STH)

- GH is protein in nature, having a single-chain polypeptide
- with 191 amino acids. Its molecular weight is 21,500.
- Basal level of GH concentration in blood of normal adult is up to 300 g/dL and in children, it is up to 500 ng/dL.
- Its daily output in adults is 0.5 to1.0 mg.
- Growth hormone is transported in blood by GH-binding
- proteins (GHBPs).
- Half-life of circulating growth hormone is about 20 minutes.
- It is degraded in liver and kidney.

- GH is responsible for the general growth of the body.
- Hypersecretion of GH causes enormous growth of the
- body, leading to **gigantism.**
- **Deficiency of GH in children**
- causes stunted growth, leading to **dwarfism.**
- ***Mode of Action of GH – Somatomedin***
- GH acts on bones, growth and protein metabolism through somatomedin secreted by liver.
- GH stimulates the liver to secrete somatomedin. Sometimes, in spite of normal secretion of GH, growth is arrested (dwarfism) due to the absence or deficiency of somatomedin.

- Somatomedin is defined as a substance through which growth hormone acts.
- It is a polypeptide with the molecular weight of about 7,500.
- Somatomedins are of two types:
- i. Insulin-like growth factor-I (IGF-I), which is also called somatomedin C
- acts on the bones and protein metabolism
- ii. Insulin-like growth factor-II. Somatomedin C (IGF-I- important role in the growth of fetus.

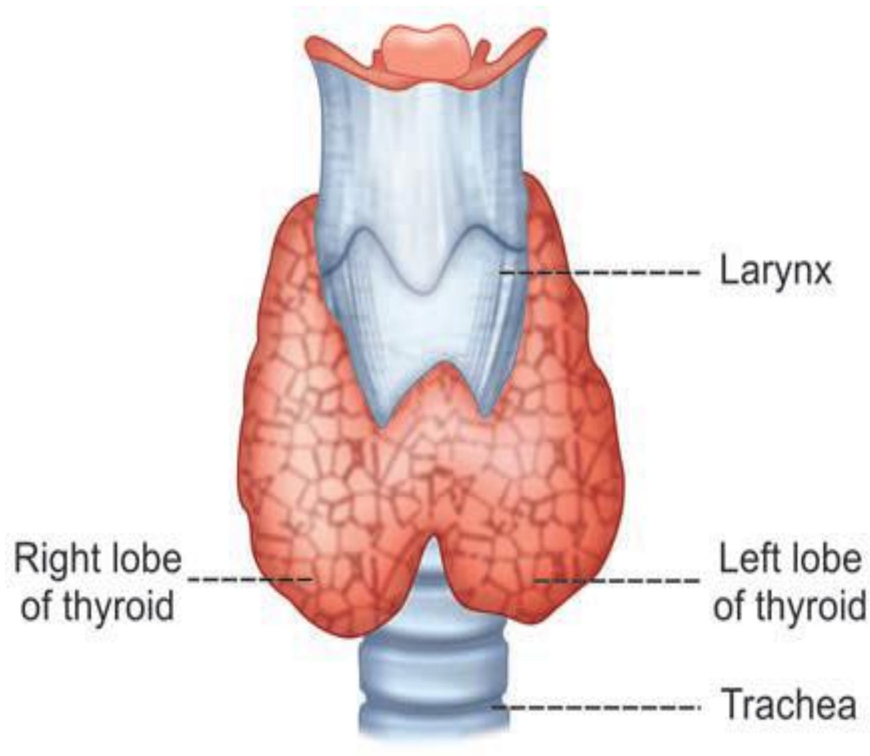

Hypoglycemia, fasting, starvation, exercise, stress, trauma
Hypothalamus
GHIH inhibits
GHRH stimulates
GHRP stimulates
Anterior pituitary
Growth hormone
Liver
Other tissues
Somatomedin

Thyroid gland

- Thyroid is an endocrine gland situated at the root of the neck on either side of the trachea.
- It has two **lobes,** which are connected in the middle by an **isthmus**
- It weighs about 20 to 40 g in adults.
- Thyroid is larger in females than in males.
- The structure and the function of the thyroid gland change in different stages of the sexual cycle in females.
- Its function increases slightly during pregnancy and lactation and decreases during menopause.

Thyroid gland secretes three hormones:

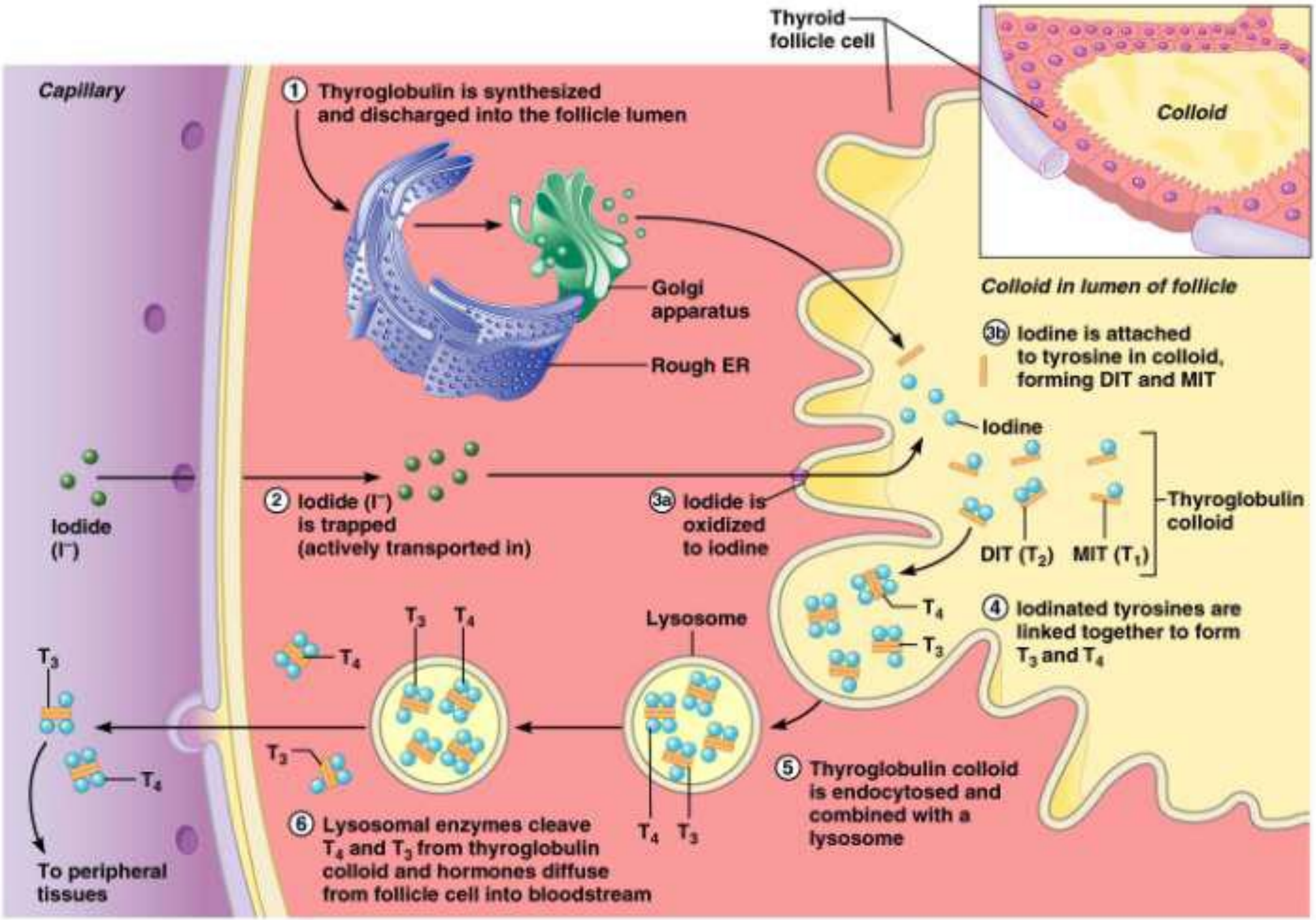
- 1. Tetraiodothyronine or T4 (thyroxine)
- 2. Tri-iodothyronine or T3
- 3. Calcitonin.
- T4 is otherwise known as **thyroxine and it forms**
- about 90% of the total secretion, whereas T3 is only 9% to 10%.



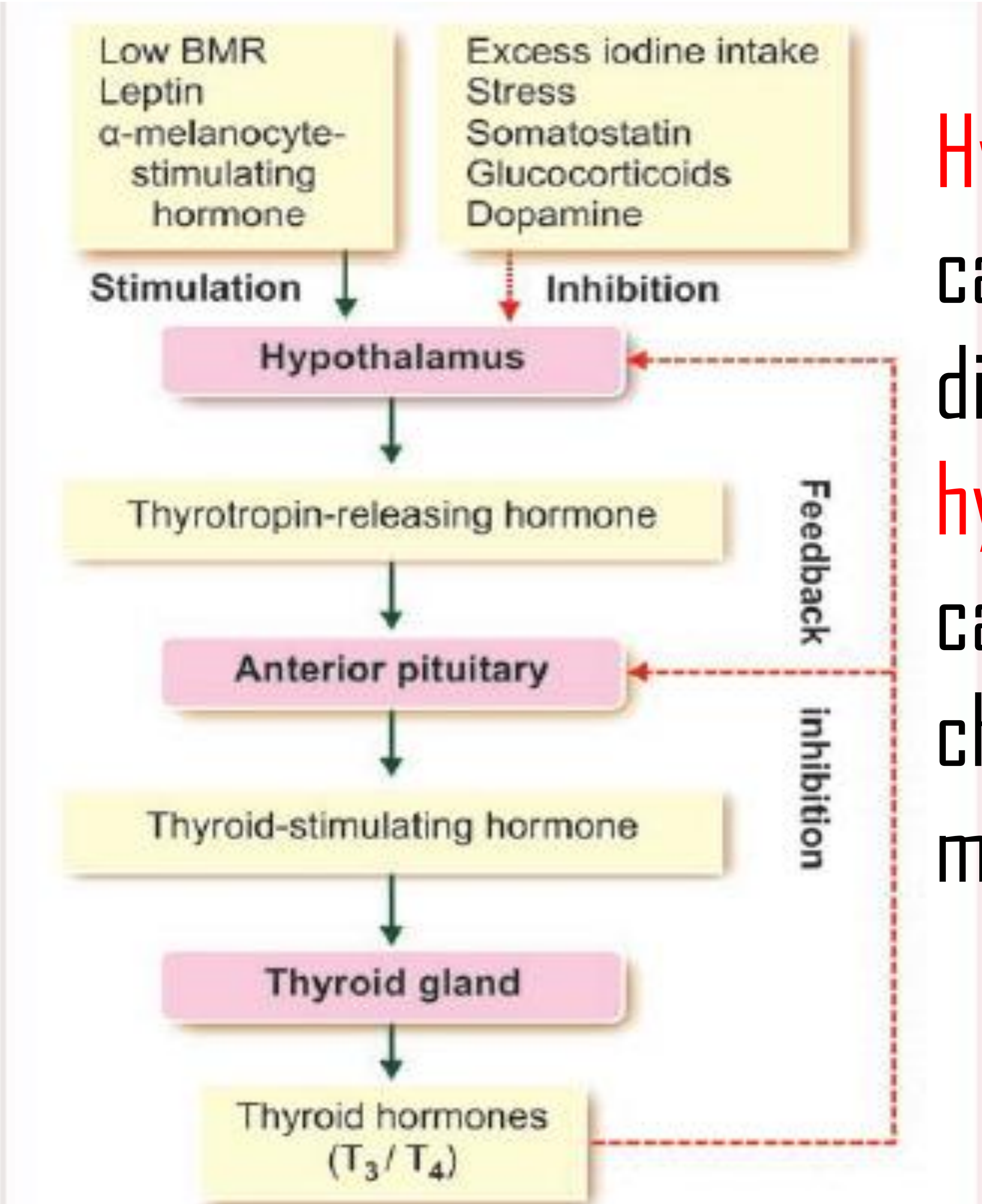
- Both T4 and T3 are iodine-containing derivatives of amino acid **tyrosine.**
- ***Potency and Duration of Action***
- The potency of T3 is four times more than that of T4. T4 acts for longer period than T3. Duration of T4 action is four times more than T3 action.
- This is because of the difference in the affinity of these hormones to plasma proteins.
- T3 has less affinity for plasma proteins and combines loosely with them, so that it is released quickly.
- T4 has more affinity and strongly binds with plasma proteins, so that it is released slowly.
- Therefore, T3 acts on the target cells immediately and T4 acts slowly.

- ***Half-life***
- Thyroid hormones have long half-life.
- T4 has a long halflife of 7 days.
- Half-life of T3 is varying between 10 and 24 hours).
- ***Rate of Secretion***
- Thyroxine = 80 to 90 μg/day
- Tri-iodothyronine = 4 to 5 μg/day
- Reverse T3 = 1 to 2 μg/day.
- ***Plasma Level***
- Total T3 = 0.12 μg/dL
- Total T4 = 8 μg/dL.

Synthesis of thyroid hormone



- Thyroid hormones are transported in the blood by three types of proteins:
- 1. Thyroxine-binding globulin (TBG)
- 2. Thyroxine-binding prealbumin (TBPA)
- 3. Albumin.
- **FUNCTIONS OF THYROID HORMONES**
- Thyroid hormones have two major effects on the body:
- I. To increase basal metabolic rate
- II. To stimulate growth in children.



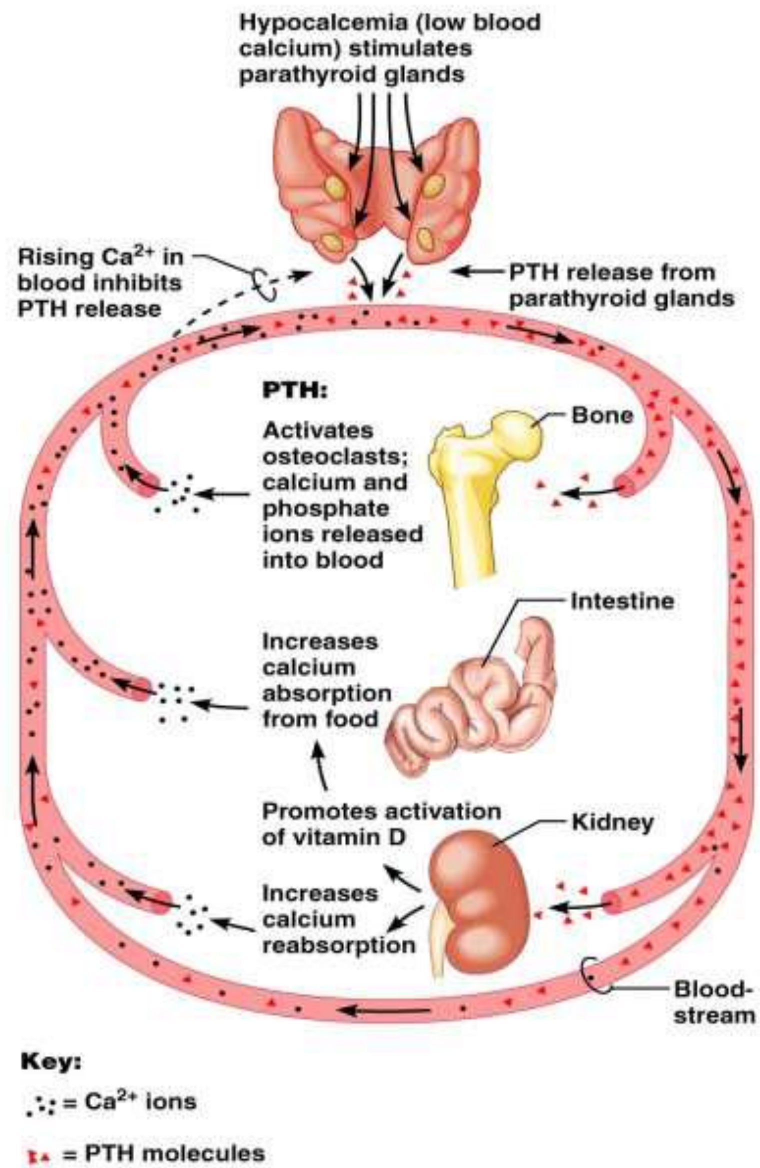
Hypersecretion causes Grave's disease, and hyposecretion causes cretinism in children and myxedema in adults

- **GOITER**
- Goiter means enlargement of the thyroid gland.
- It occurs both in hypothyroidism and hyperthyroidism.
- ***Goiter in Hyperthyroidism – Toxic Goiter***
- Toxic goiter is the enlargement of thyroid gland with increased secretion of thyroid hormones, caused by thyroid tumor.
- ***Goiter in Hypothyroidism – Non-toxic Goiter***
- Non-toxic goiter is the enlargement of thyroid gland
- without increase in hormone secretion. It is also called **hypothyroid goiter**

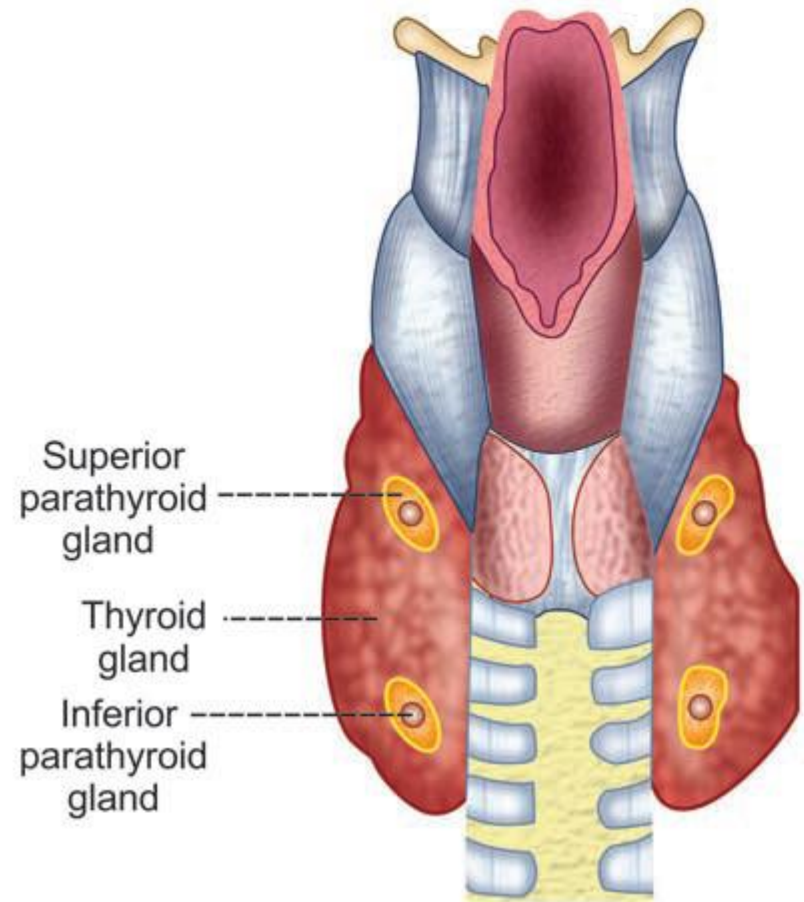

Parathyroid glands

 Four oval-shaped glands embedded in the posterior surface of the thyroid gland. Parathyroid glands are very small in size, measuring about 6 mm long, 3 mm wide and 2 mm thick, with dark brown color.

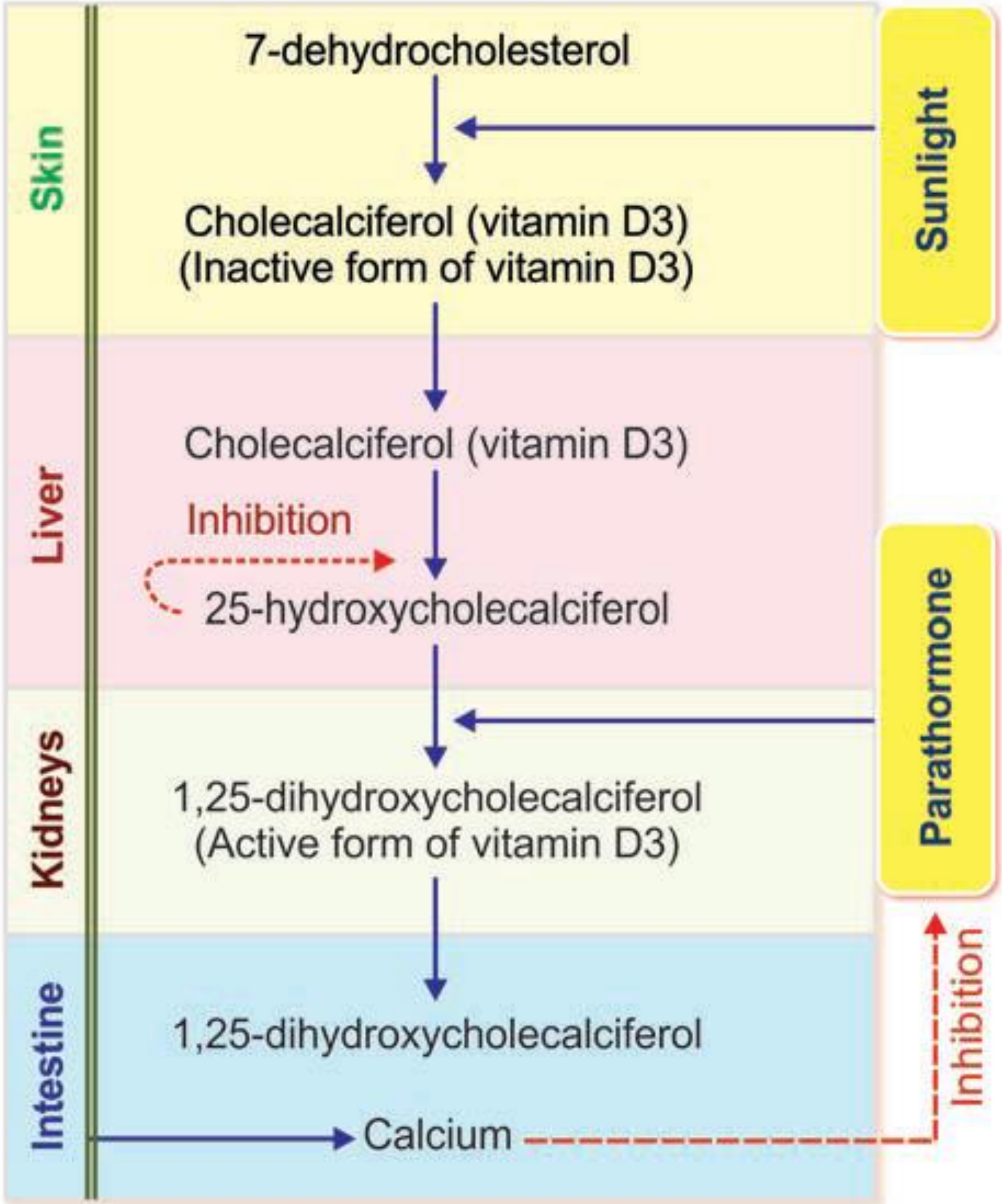
 Secrete only 1 protein hormone called parathyroid hormone (PTH) or parathormone to raise blood calcium level and lower blood phosphate level. [Hyposecretion causes tetany, and hypersecretion causes osteitis fibrosa cystica].



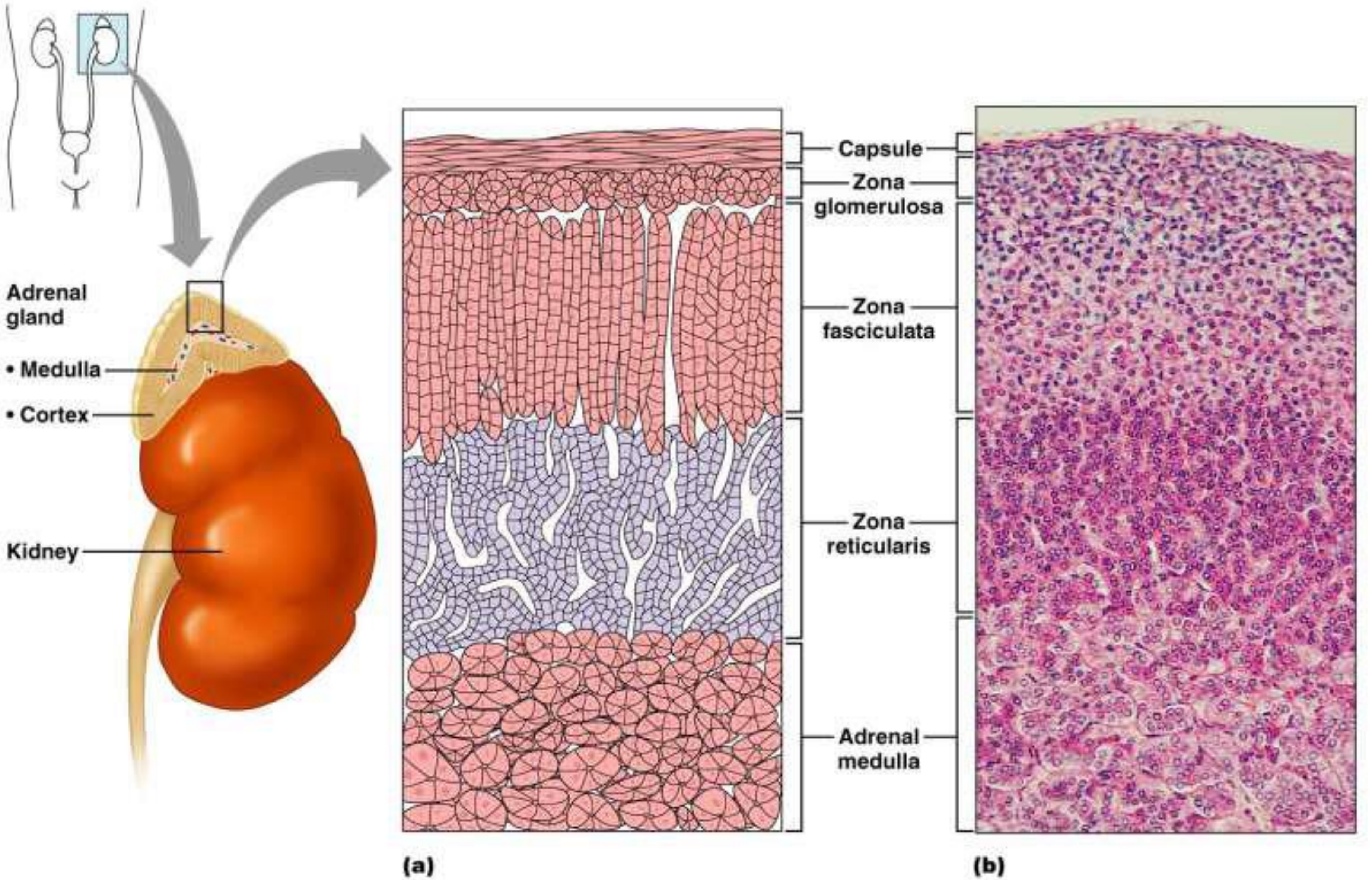
Parathormone secreted by parathyroid gland is essential
for the maintenance of blood calcium level within a very
narrow critical level. Maintenance of blood calcium level
is necessary because calcium is an important inorganic
ion for many physiological functions
Parathormone is protein in nature, having 84 amino
acids. Its molecular weight is 9,500.
Parathormone has a half-life of 10 minutes. Normal
plasma level of PTH is about 1.5 to 5.5 ng/dL.



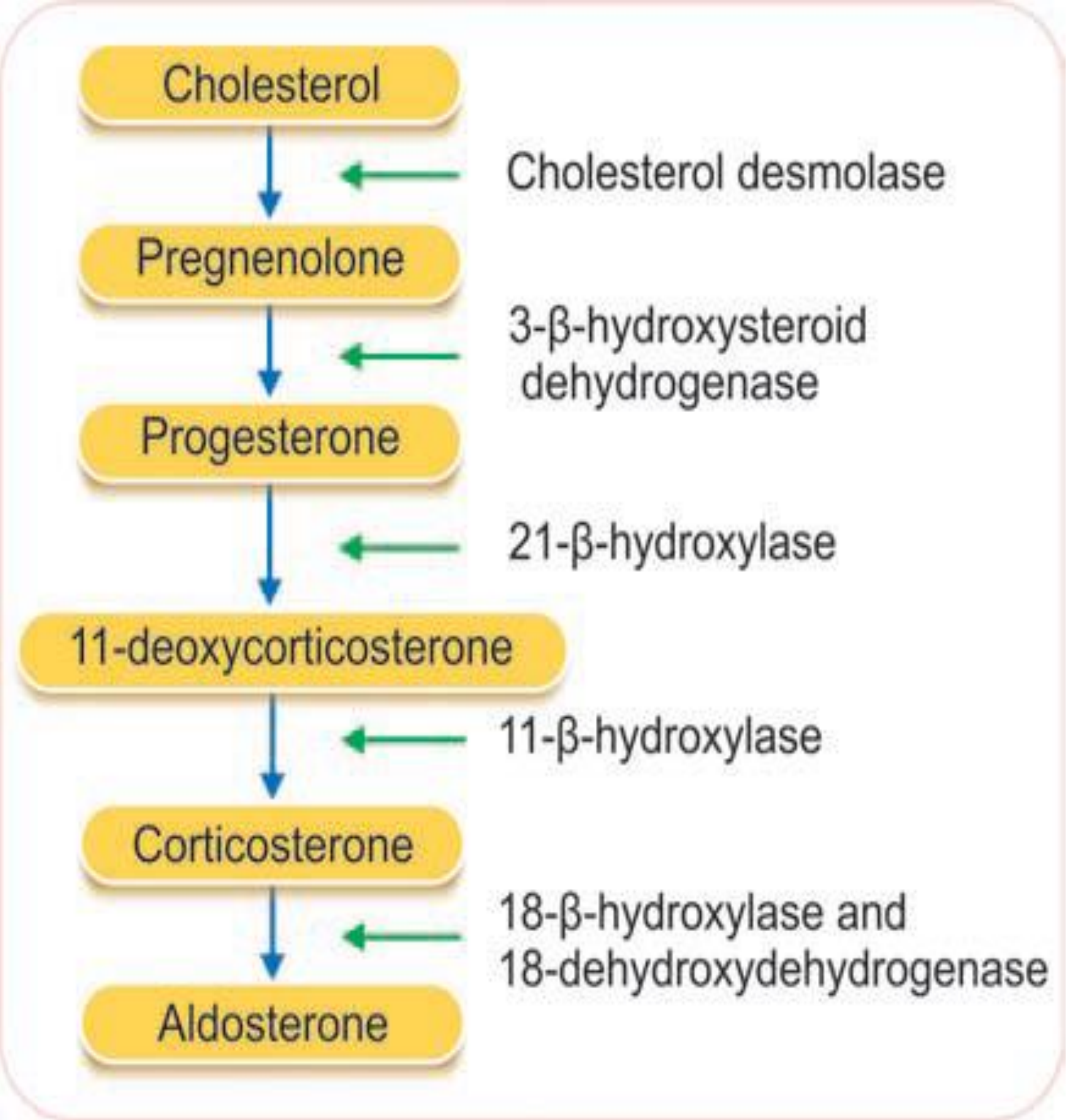
- ***Synthesis***
- Parathormone is synthesized from the precursor called **prepro-PTH containing 115 amino acids. First, the**
- prepro-PTH enters the endoplasmic reticulum of chief cells of parathyroid glands. There it is converted into a
- prohormone called **pro-PTH, which contains 96 amino** acids. Pro-PTH enters the Golgi apparatus, where it is
- converted into PTH.
- ***Metabolism***
- Sixty to seventy percent of PTH is degraded by **Kupffer cells of liver, by means of proteolysis. Degradation of**
- about 20% to 30% PTH occurs in kidneys and to a lesser extent in other organs.


Skin
Liver
Kidneys
Intestine
7-dehydrocholesterol
Sunlight
Cholecalciferol (vitamin D3)
(Inactive form of vitamin D3)
Cholecalciferol (vitamin D3)
Inhibition
25-hydroxycholecalciferol
Parathormone
1,25-dihydroxycholecalciferol
(Active form of vitamin D3)
1,25-dihydroxycholecalciferol
Calcium
Inhibition

Adrenal Gland



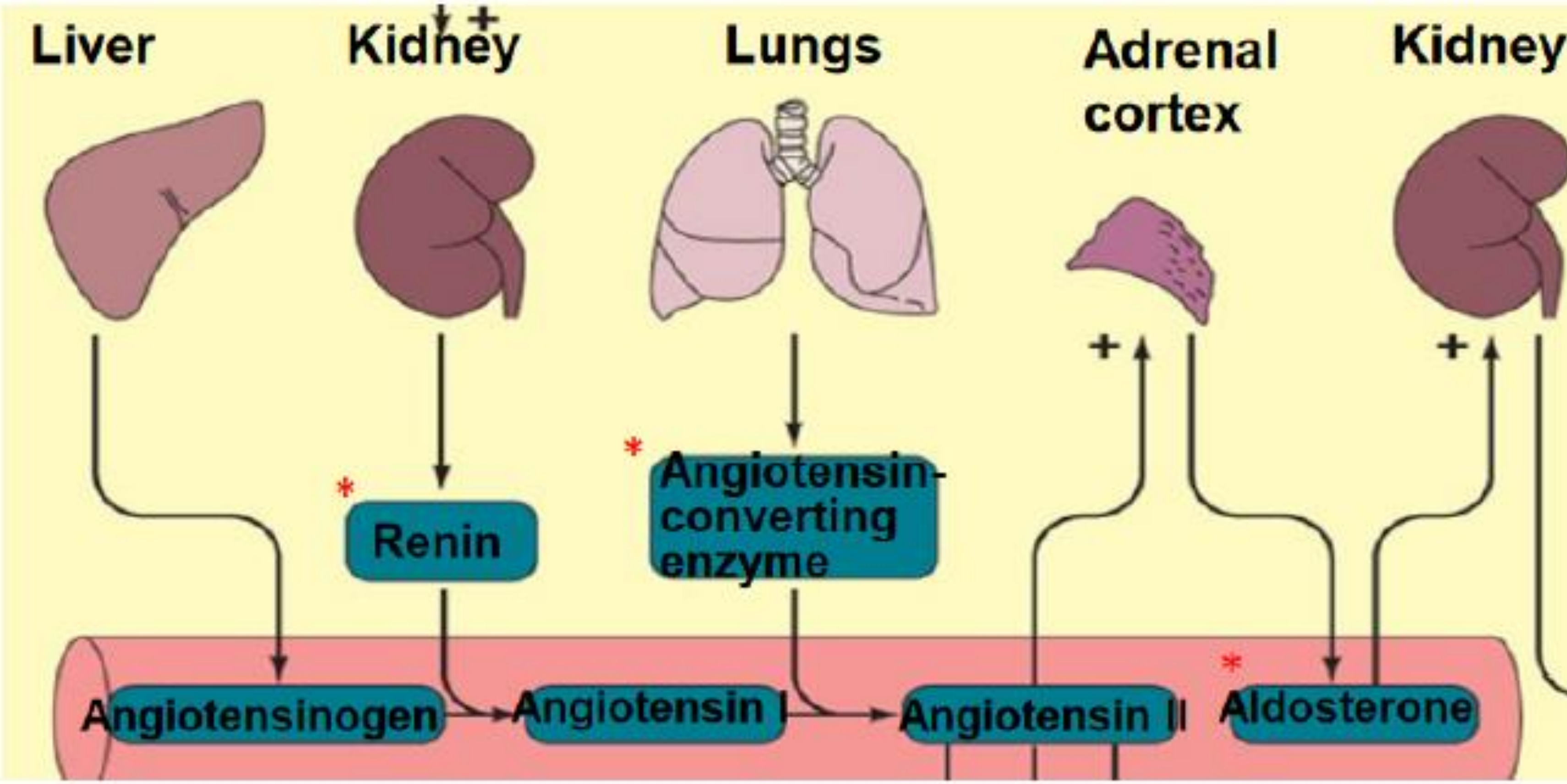
- **A. Adrenal Cortex:** outer portion of the adrenal gland which is attached to the superior surface of the kidney.
- Divided into 3 regions, from outside to inside : Zona glomerulosa, Zona fasciculate , and Zona reticularis.
- Secretes over 30 steroid-based substances and several steroid hormones, all crucial for normal homeostasis .
- Zona glomerulosa secretes mineralocorticoids which help regulate the levels of minerals such as sodium, potassium and magnesium.
- Aldosterone is the most important hormone in this group, where it raises blood levels of sodium and water, and lowers blood potassium level.

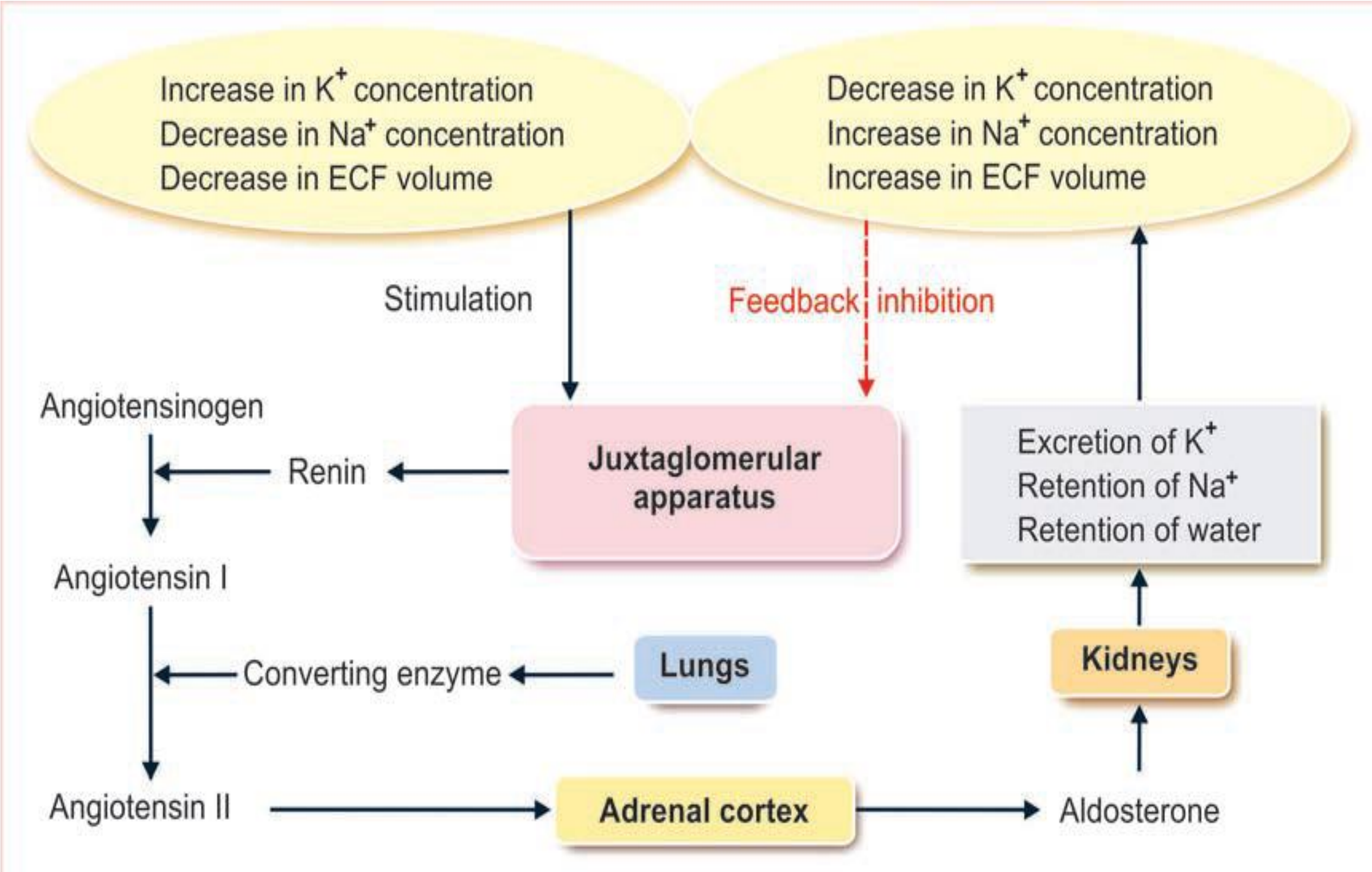

Cholesterol
Cholesterol desmolase
Pregnenolone
3-β-hydroxysteroid dehydrogenase
Progesterone
21-β-hydroxylase
11-deoxycorticosterone
11-β-hydroxylase
Corticosterone
18-β-hydroxylase and 18-dehydroxydehydrogenase
Aldosterone

Regulating aldosterone secretion

- This hormone stimulates the kidneys to reabsorb sodium and secrete potassium.
- Secondary effects is retention of water and the expansion of extracellular fluid volume.
- A decrease in sodium concentrations in the body and blood pressure activates the Renin-Angiotensin-Aldosterone System (i.e., RAAS).
- Similarly, a raise in the body's potassium levels act directly on the adrenal cortex to produce aldosterone:

Activation of RAAS

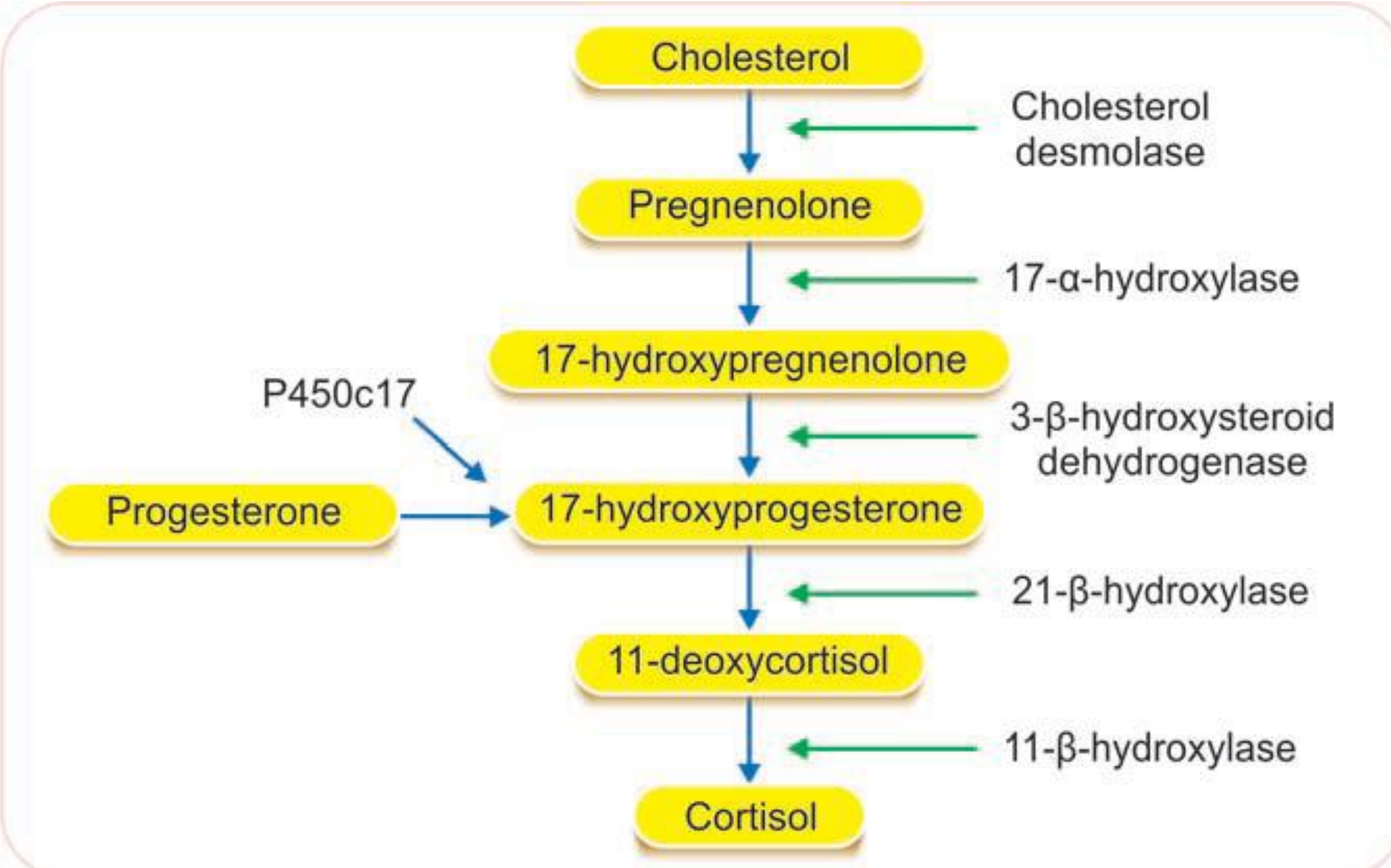




Increase in K+ concentration
Decrease in Na+ concentration
Decrease in ECF volume
Decrease in K+ concentration
Increase in Na+ concentration
Increase in ECF volume
Stimulation
Feedback inhibition
Angiotensinogen
Renin
Juxtaglomerular apparatus
Excretion of K+
Retention of Na+
Retention of water
Angiotensin I
Converting enzyme
Lungs
Kidneys
Angiotensin II
Adrenal cortex
Aldosterone

- Zona fasciculate secretes glucocorticoids which affect glucose or carbohydrate metabolism.
- Cortisol is involved in carbohydrate, lipid and protein metabolism and also helps fight stress and inflammation .
- [Hyposecretion-Addison's disease and hypersecretion - Cushing's syndrome].
- Functions of glucocorticoids
- Stimulation of gluconeogenesis
- Inhibting glucose uptake
- Reducing protein stores and encouraging proteolysis
- Lipolysis in the limbs and promoting fatty acid oxidation
- Lipogenesis in the face and in the torso.

Synthesis of cortisol



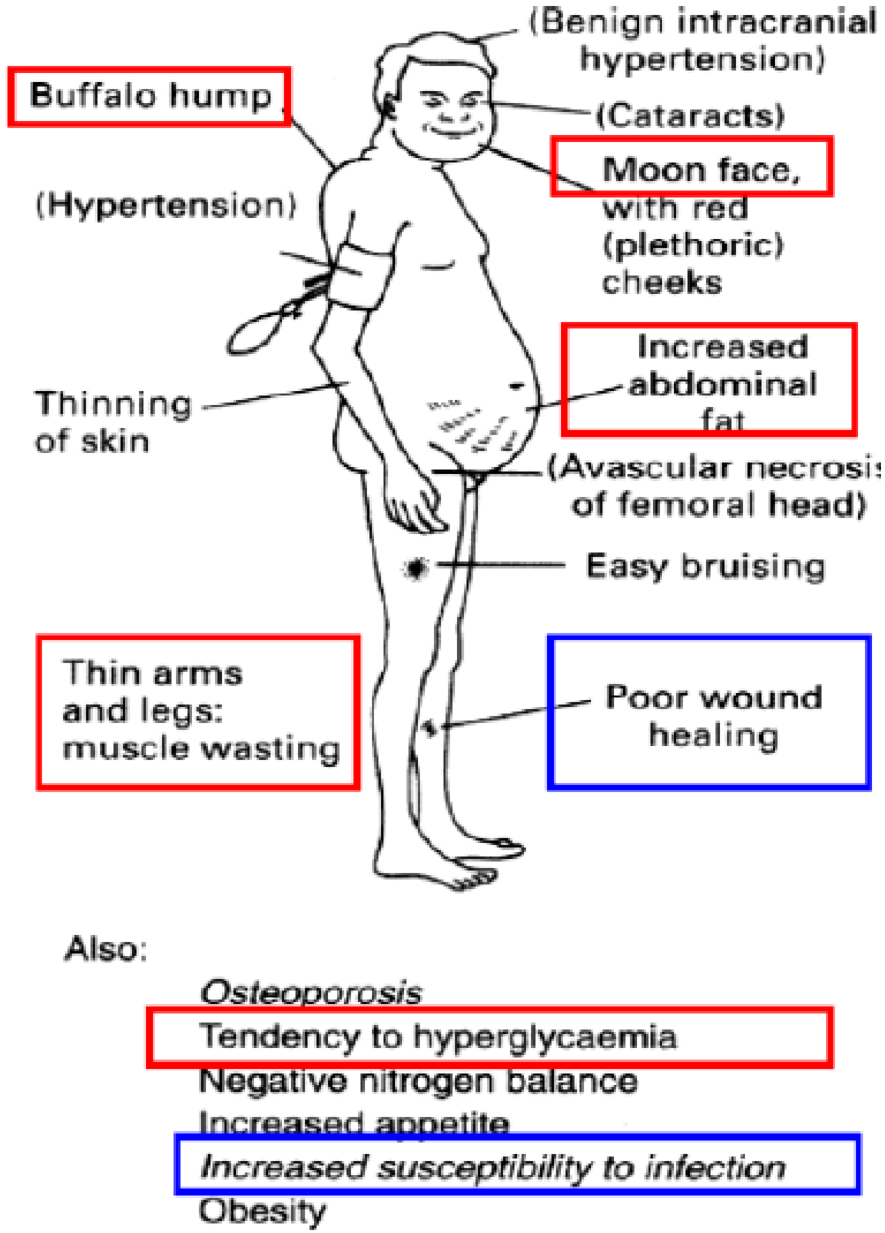
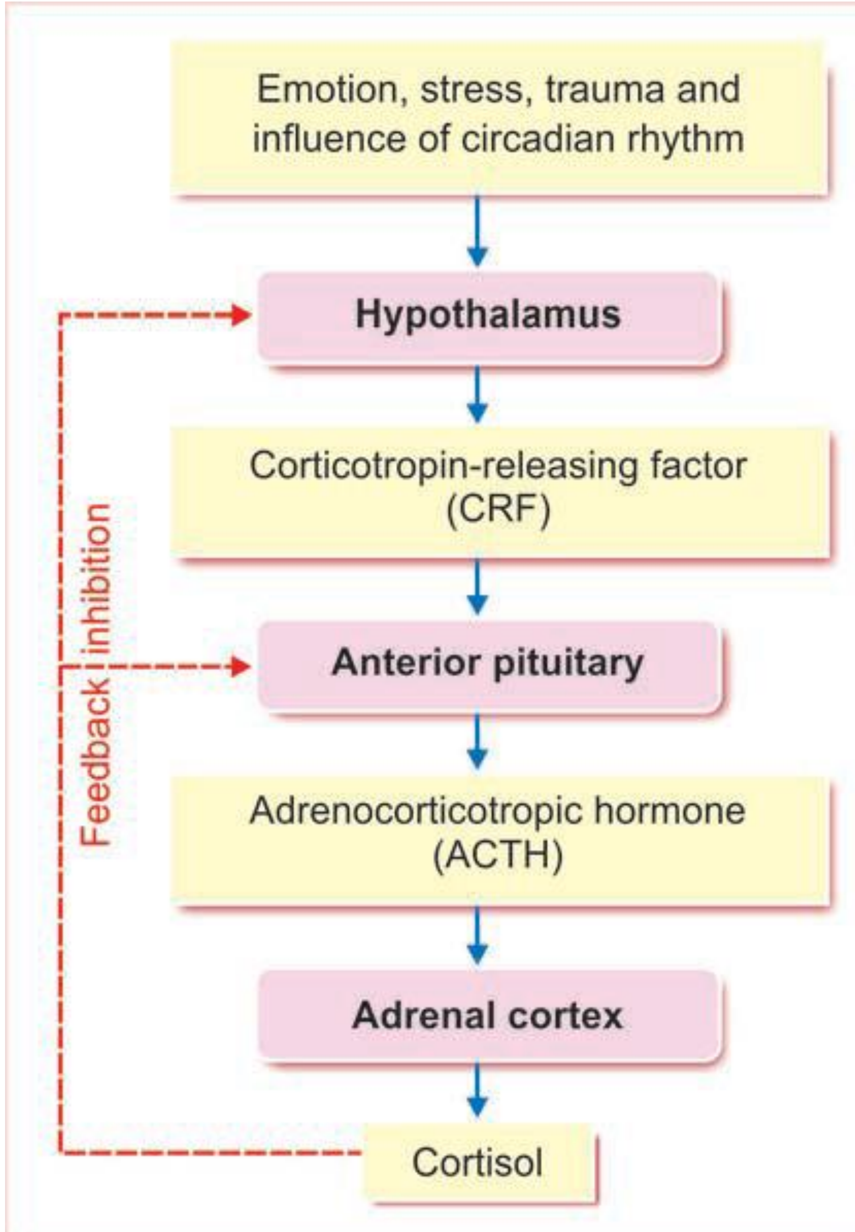


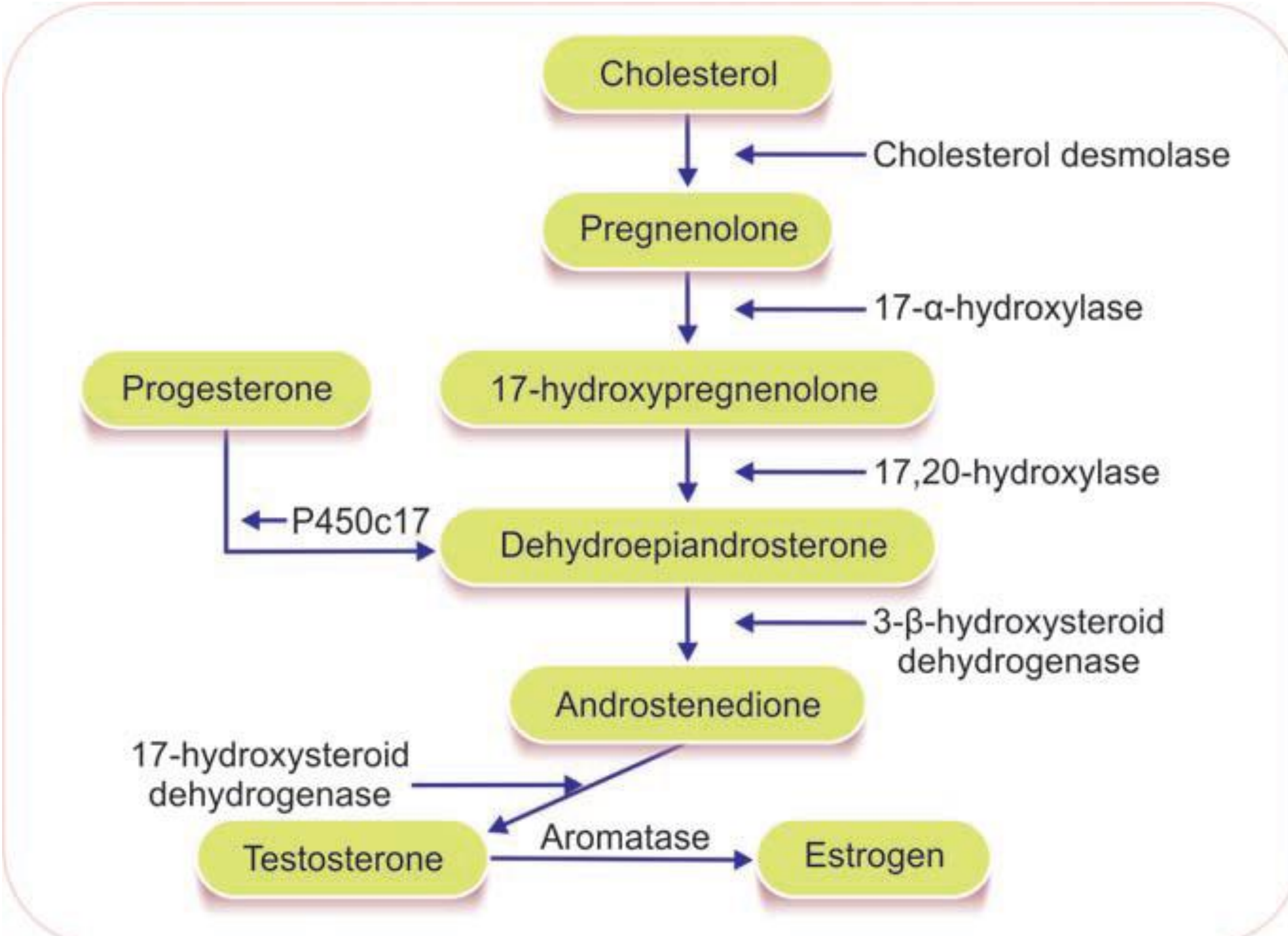
Figure 4.13: Cushing's Syndrome

Regulation of Cortisol



- Zona reticularis secretes gonadocorticoids which supplement sex hormones from the testes and ovaries and stimulate early development of reproductive organs.
- These hormones are male (adrenal androgens), namely testosterone , but can be converted into female types, such as estrogens, [Hyposecretion- congenital adrenal hyperplasia, and hypersecretion causes gynecomastia in male].

Synthesis of Adrenal Sex hormones



B. Adrenal Medulla: inner portion of the adrenal gland.

- Made of modified nerve tissue that is under direct regulation of
- sympathetic nerves of the autonomic nervous system.
- Contains glandular cells which secrete 2 closely related hormones - Epinephrine (or adrenaline) and Norepinephrine (or noradrenaline).
- Effects of these hormones resemble sympathetic stimulation, where body activities such as cardiac actions, blood pressure and breathing rate are increased,
- while digestive processes are decreased due to hyposecretion of these,
- but hypersecretion can caused hypertension, increased blood
- glucose level and high heart rate].

- The medulla produces 80% epinephrine and 20% norepinephrine (collectively known ascatecholamines).
- Norepinephrine is a neurotransmitter in post-ganglionic neurons;
- Epinephrine and norepinephrine receptors are *adrenergic, of which the and are the major classes:*
- Alpha 1-receptors activate the phospholipase C pathway.
- Alpha 2-receptors inhibit the adenylate cyclase pathway.
- Beta 1 & 2 receptors bind to G proteins.

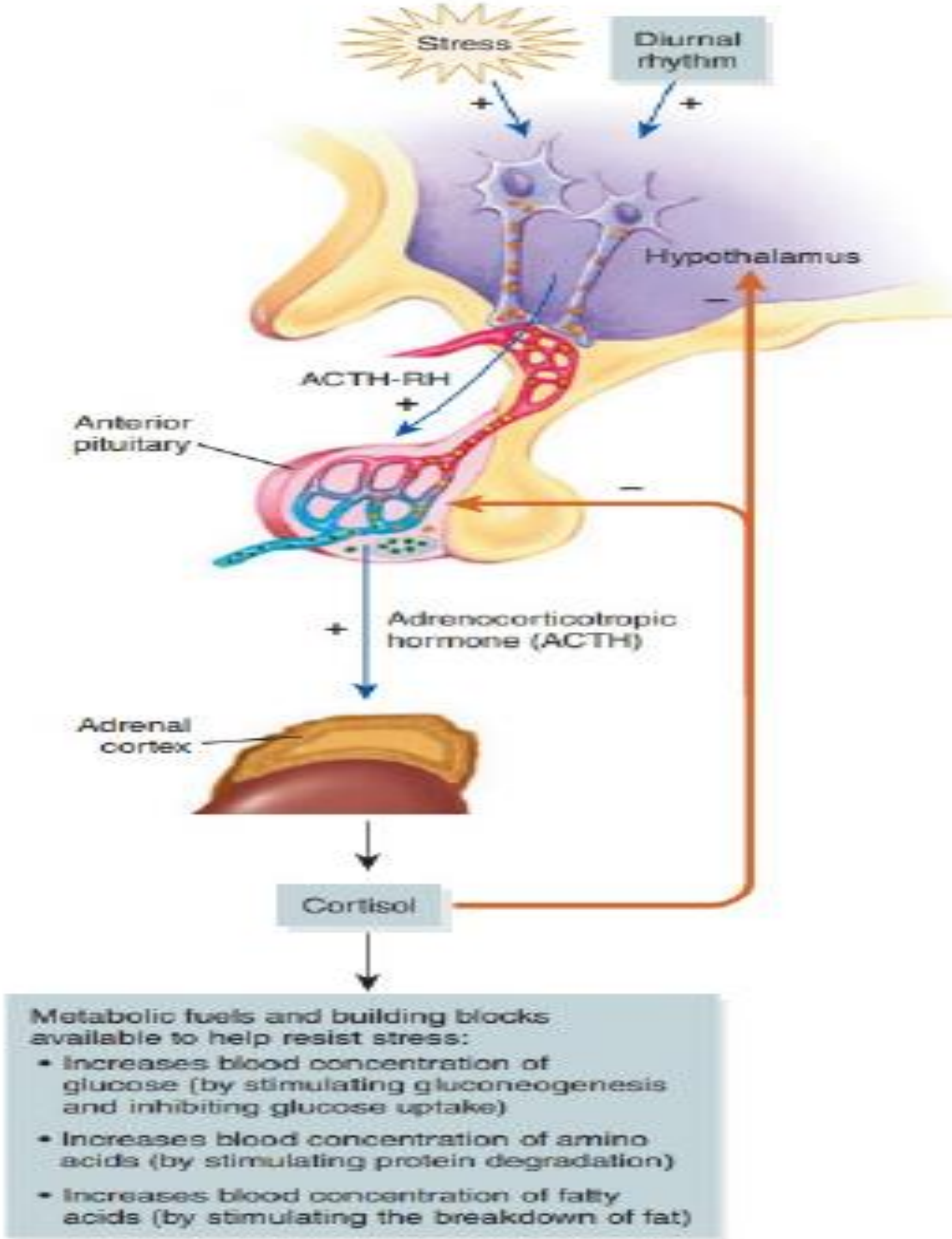
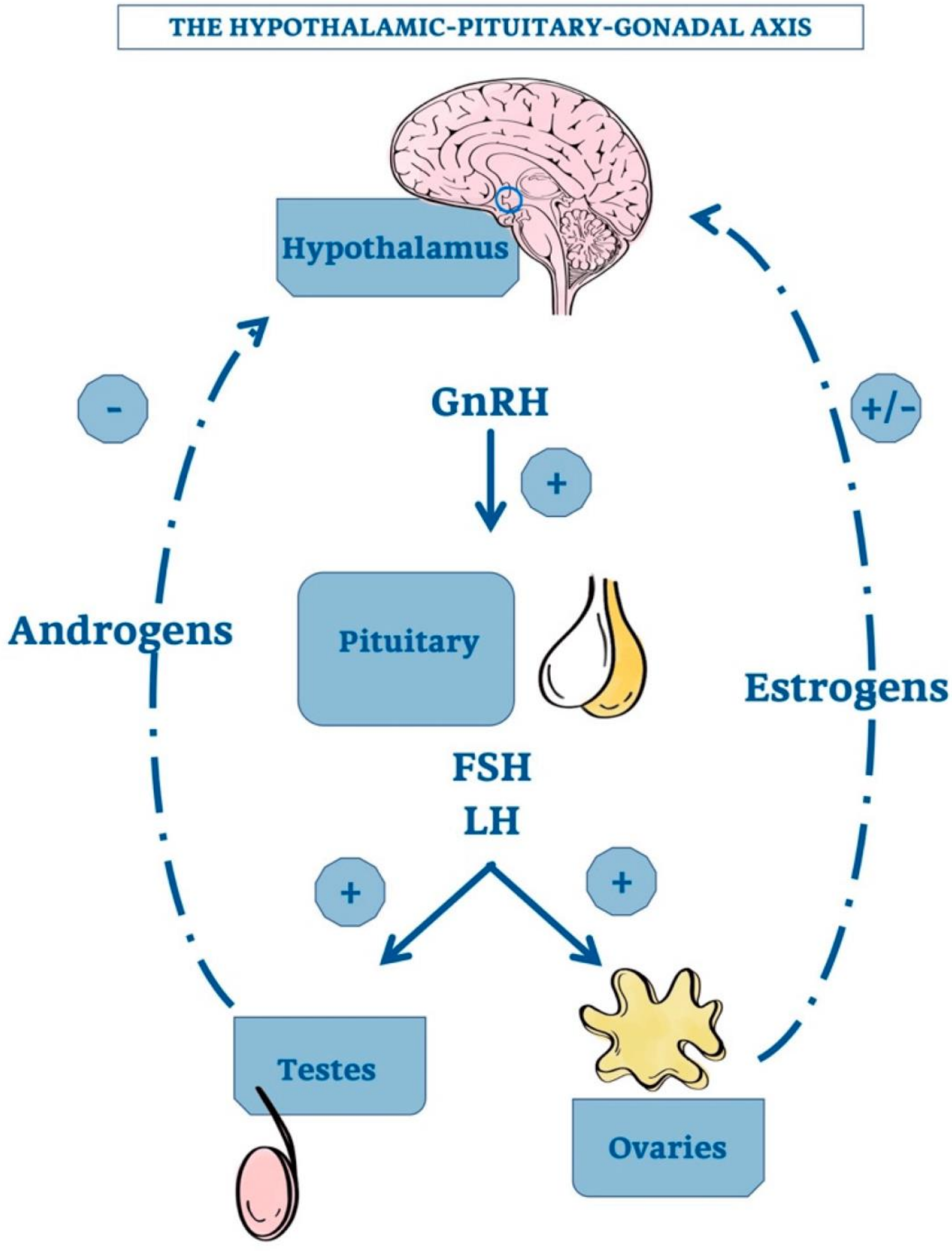


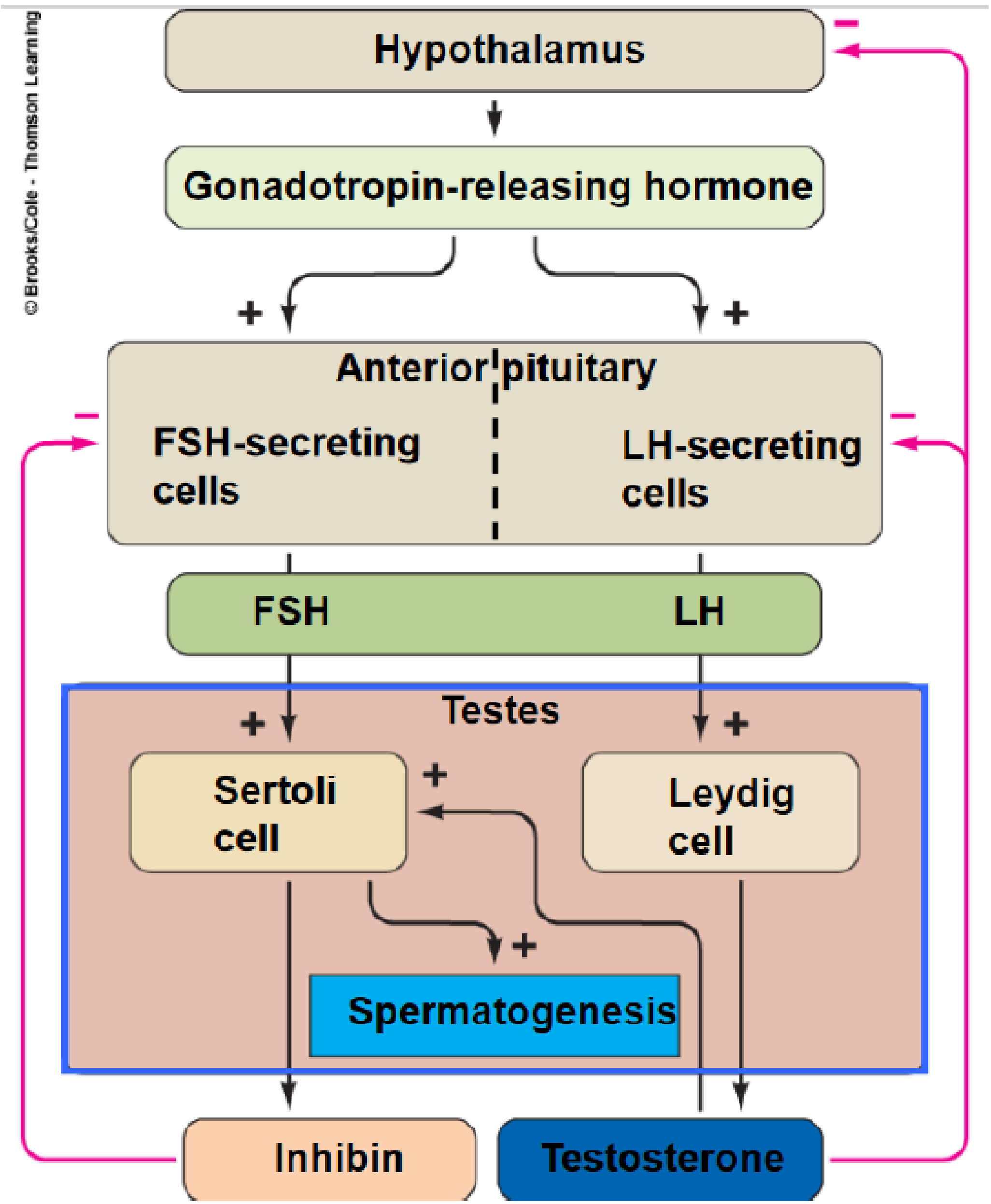
FIGURE 16-11 Feedback control of ACTH.

Gonadotropins

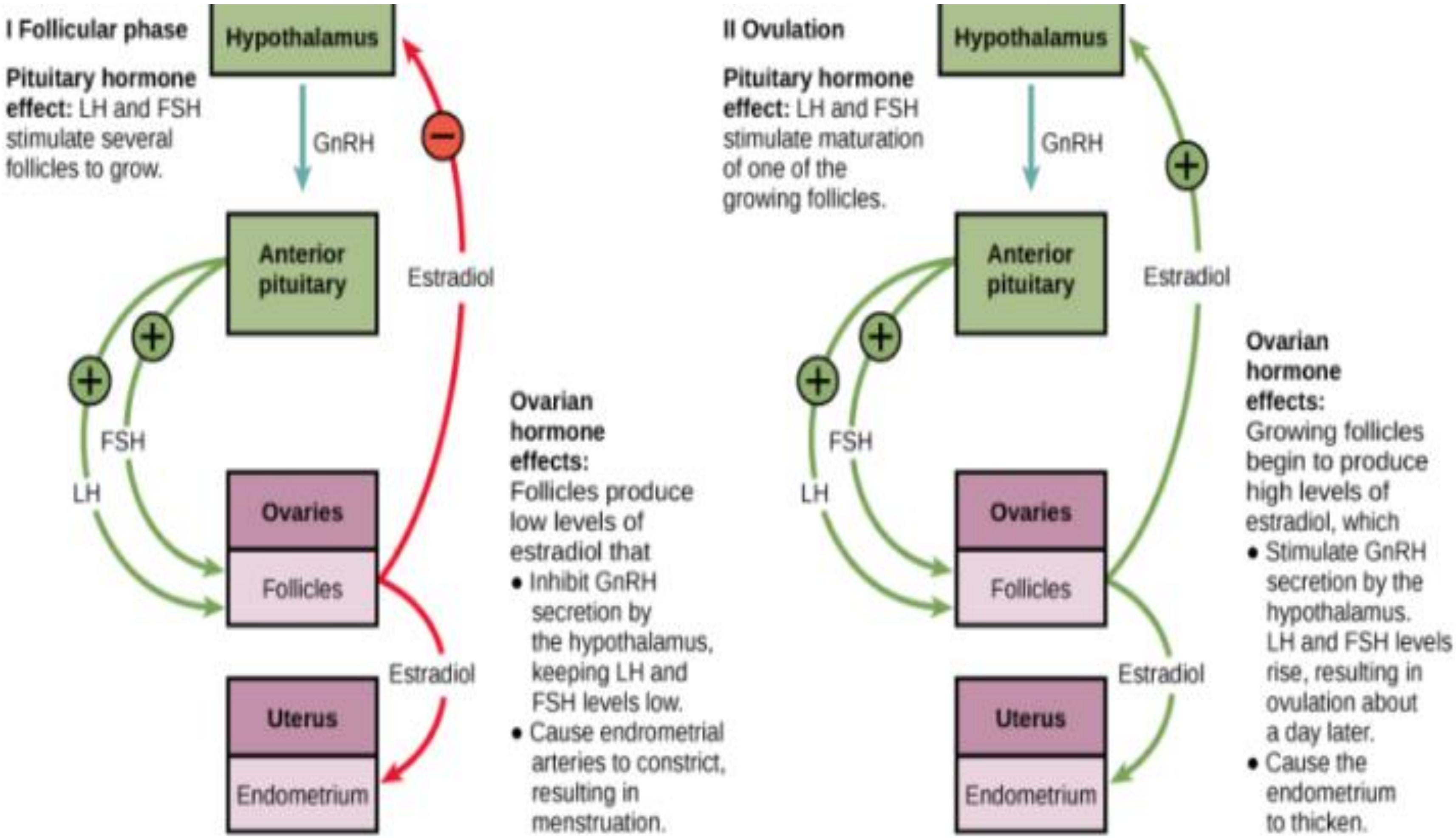
- FSH and LH are **gonadotropins** affecting the reproductive organs or *gonads*. In males, these are the *testes* and in females, the *ovaries*.
- In the testes, FSH stimulates the production of sperm, and in the eggs in the ovary.
- In males, LH stimulates the interstitial cells in the testes to produce testosterone, and in females, LH along with FSH causes the ovarian follicle to mature.
- LH then triggers ovulation and regulates ovarian hormone synthesis and release. Gonadotropins become more active during puberty, prompted by hypothalamic release of *gonadotropin-releasing hormone* (GRH).
- The hormone called *inhibin* decreases FSH levels in both males and females.


THE HYPOTHALAMIC-PITUITARY-GONADAL AXIS
Hypothalamus
GnRH
+
-
+/-
Androgens
Pituitary
Estrogens
FSH
LH
+
+
Testes
Ovaries

Regulation of Hormone in male Reproductive system

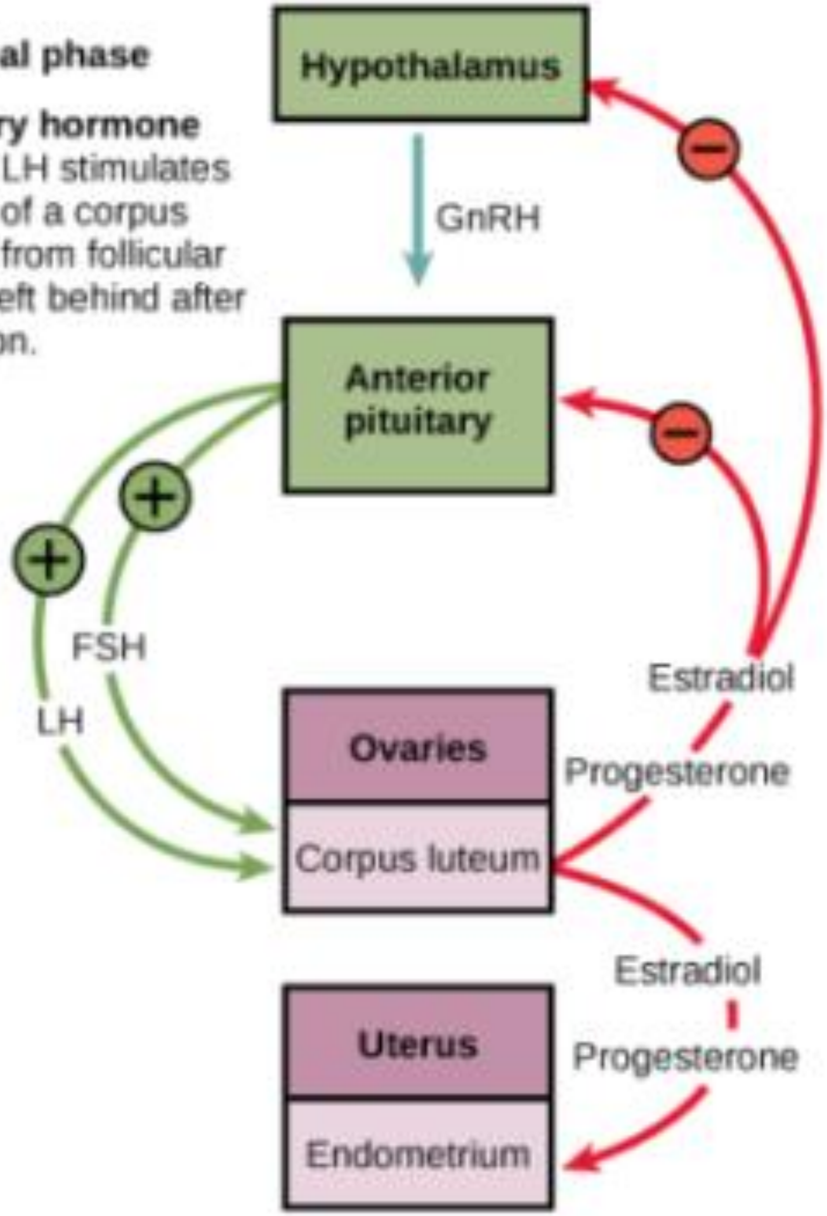


Regulation of Female Reproductive system



III Luteal phase

Pituitary hormone effect: LH stimulates growth of a corpus luteum from follicular tissue left behind after ovulation.



Ovarian hormone effects:
The corpus luteum secretes estradiol and progesterone that

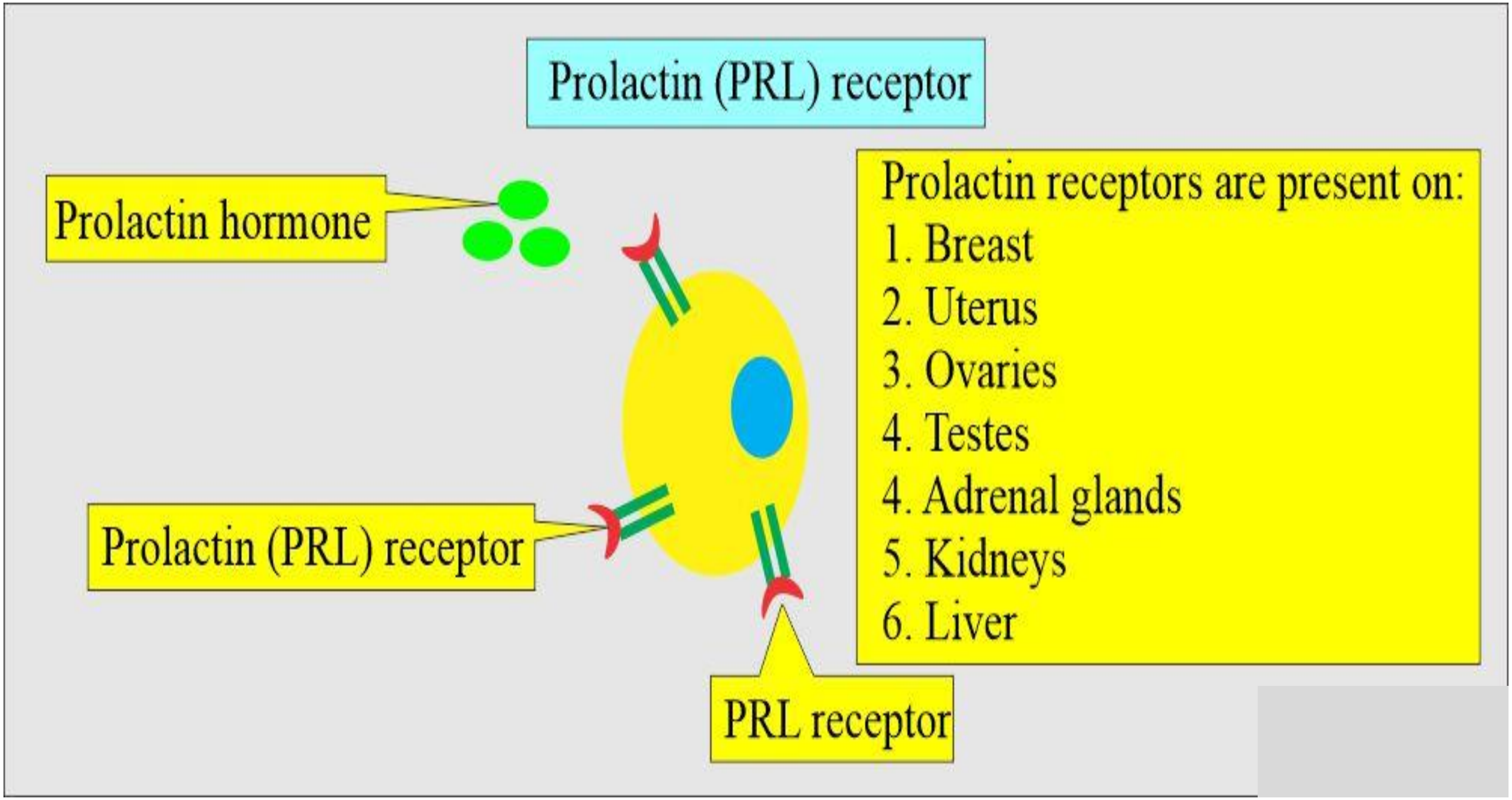
- Block GnRH production by the hypothalamus and LH and FSH production by the pituitary.
- Cause the endometrium to further develop.

- **Prolactin**
- PRL is a protein hormone that controls milk production in women after they give birth.
- In males, it may also help to maintain sperm production.
- Prolactin is also called Lactogen. Lactoropin. Luteotropin.
    - Galactopoietic hormone. Mammotropin.
- Elevated levels of PRL can interrupt sexual function in both females and males.
- The secretion of PRL is regulated by a *neuroendocrine reflex*, a reflex involving both the endocrine and nervous systems.
- During the breastfeeding process, sensory fibers in the breast are stimulated, sending nerve impulses to the hypothalamus.

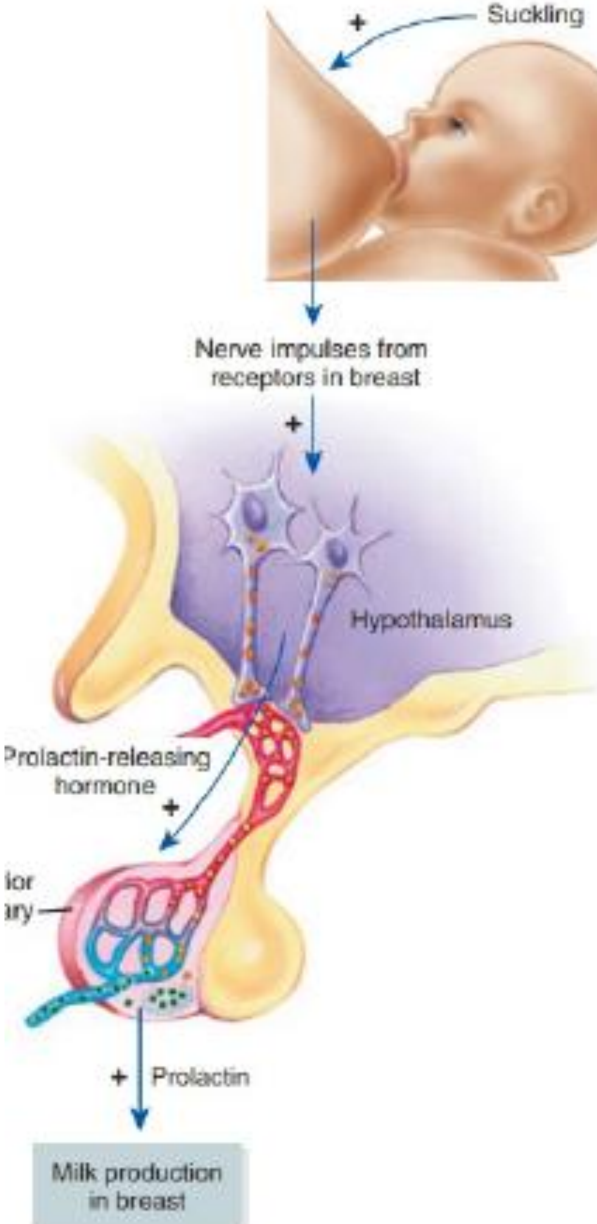
Prolactin (PRL) structure:

- It is 32 kD and is synthesized as preprolactin.
- It consists of 199 amino acids and has three intramolecular disulfide bridges.
- It is produced by the pituitary gland's lactotroph cells (acidophilic acids).
- It circulates in the blood as:
- Monomeric prolactin (PRL) = 23 kDa. This is also known as little prolactin.
- This is the most bioactive form than the other forms.
- It has the greatest response to TRH and hypothalamic-releasing factors that stimulate the pituitary glands.
- Dimeric prolactin (PRL) = 48 to 56 kDa. This is also known as big prolactin (PRL).
- Polymeric form prolactin (PRL) = >100 kDa. It is also known as big-big prolactin (PRL).
- There is an increase in lactotroph cells during pregnancy.

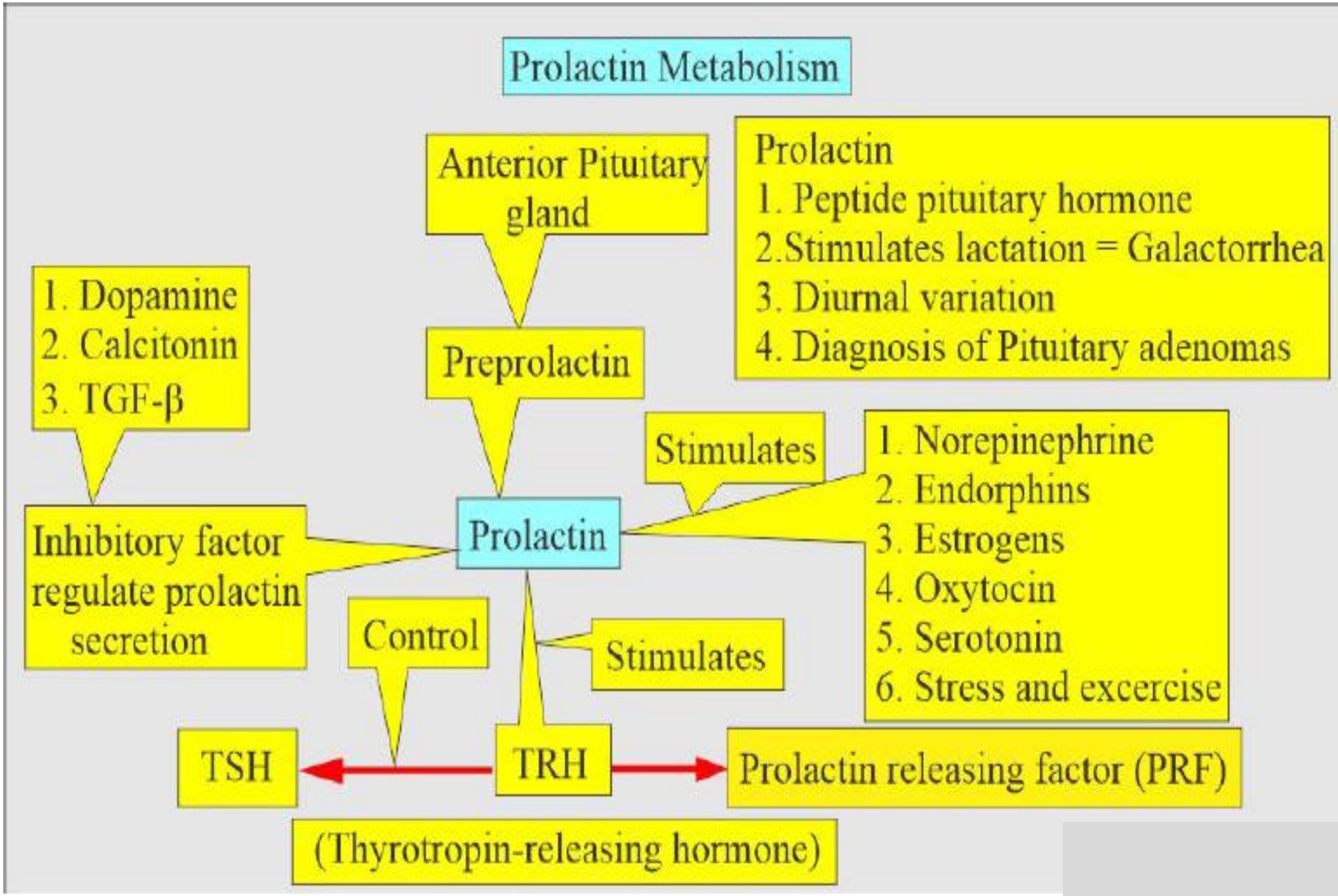
- The hypothalamus responds by secreting PRL-releasing hormone, causing PRL release.
- The PRL--inhibiting hormone is **dopamine**.
- Lower PRL-inhibiting hormone secretion causes increased PRL release.
- There are many PRL-releasing factors, one of which is thyroid-releasing hormone.
- In women, estrogen stimulates PRL release, which is part of the cause of breast tenderness before menstruation.



Prolactin (PRL) receptor
Prolactin hormone
Prolactin receptors are present on:
1. Breast
2. Uterus
3. Ovaries
4. Testes
4. Adrenal glands
5. Kidneys
6. Liver
Prolactin (PRL) receptor
PRL receptor



16-9 Neuroendocrine reflex and prolactin secretion.


Prolactin Metabolism
Anterior Pituitary gland
Preprolactin
Prolactin
1. Peptide pituitary hormone
2.Stimulates lactation = Galactorrhea
3. Diurnal variation
4. Diagnosis of Pituitary adenomas
1. Dopamine
2. Calcitonin
3. TGF-β
Inhibitory factor regulate prolactin secretion
Prolactin
Stimulates
1. Norepinephrine
2. Endorphins
3. Estrogens
4. Oxytocin
5. Serotonin
6. Stress and excercise
Control
Stimulates
TSH
TRH
Prolactin releasing factor (PRF)
(Thyrotropin-releasing hormone)

Prolactin

Functions

1. It helps in initiatation and maintinance of lactation
2. It induce ductal growth and lobular-alveolar system
3. It takes part in synthesis of milk protein like casein and lactoalbumin
4. It is important in control of osmolality
5. It helps in metabolism of subcutaneous fat, carbohydrate, calcium and vitamin D
6. It helps fetal lung development
7. It takes part in steriodogenesis (formation of steroids from the adrenal cortex, testes and ovaries)

- **Increased Prolactin Level Is Seen In :**
- Breast stimulation.
- Pregnancy.
- Nursing.
- Stress.
- Exercise.
- Pituitary tumors form acidophilic cells that produce prolactin.
- **The Moderate Level Increase Is Seen In:**
- Secondary amenorrhea.
- Galactorrhea.
- Primary hypothyroidism.
- Polycystic ovary syndrome.
- Anorexia

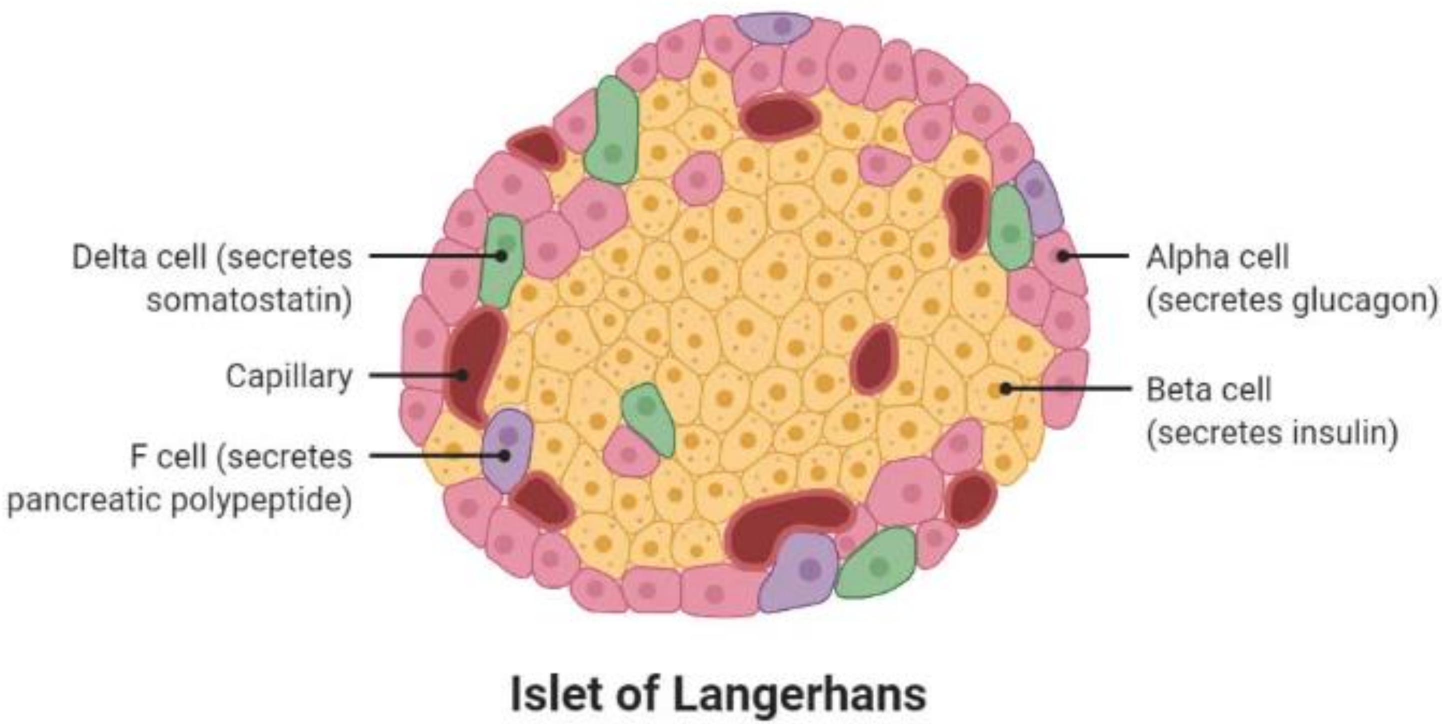
- Decreased Prolactin (PRL) level is seen in the following:
- Sheehan's syndrome (after delivery, may have hemorrhage or infarction of the pituitary gland).
- Pituitary destruction by the tumors, e.g., Craniopharyngioma.

Pancreas

- The only gland that is both exocrine and endocrine in physiology.
- In its exocrine aspect, 99% of its mass is composed of cells called acini which secrete digestive enzymes and fluids into the small intestine through the pancreatic ducts
- In its endocrine aspect, 1% of its mass is little groups of cells called
- islets of langerhans (or pancreatic islets) which secrete hormones to
- regulate blood glucose level.
- in each pancreatic islet , alpha cells (α cells) secrete glucagons to raise blood glucose level.
- beta cells (β cells) secrete insulin to lower blood glucose level.
- [Hyposecretion causes diabetes mellitus where excessive glucose is
- present in urine, and hypersecretion causes hyperinsulinism].

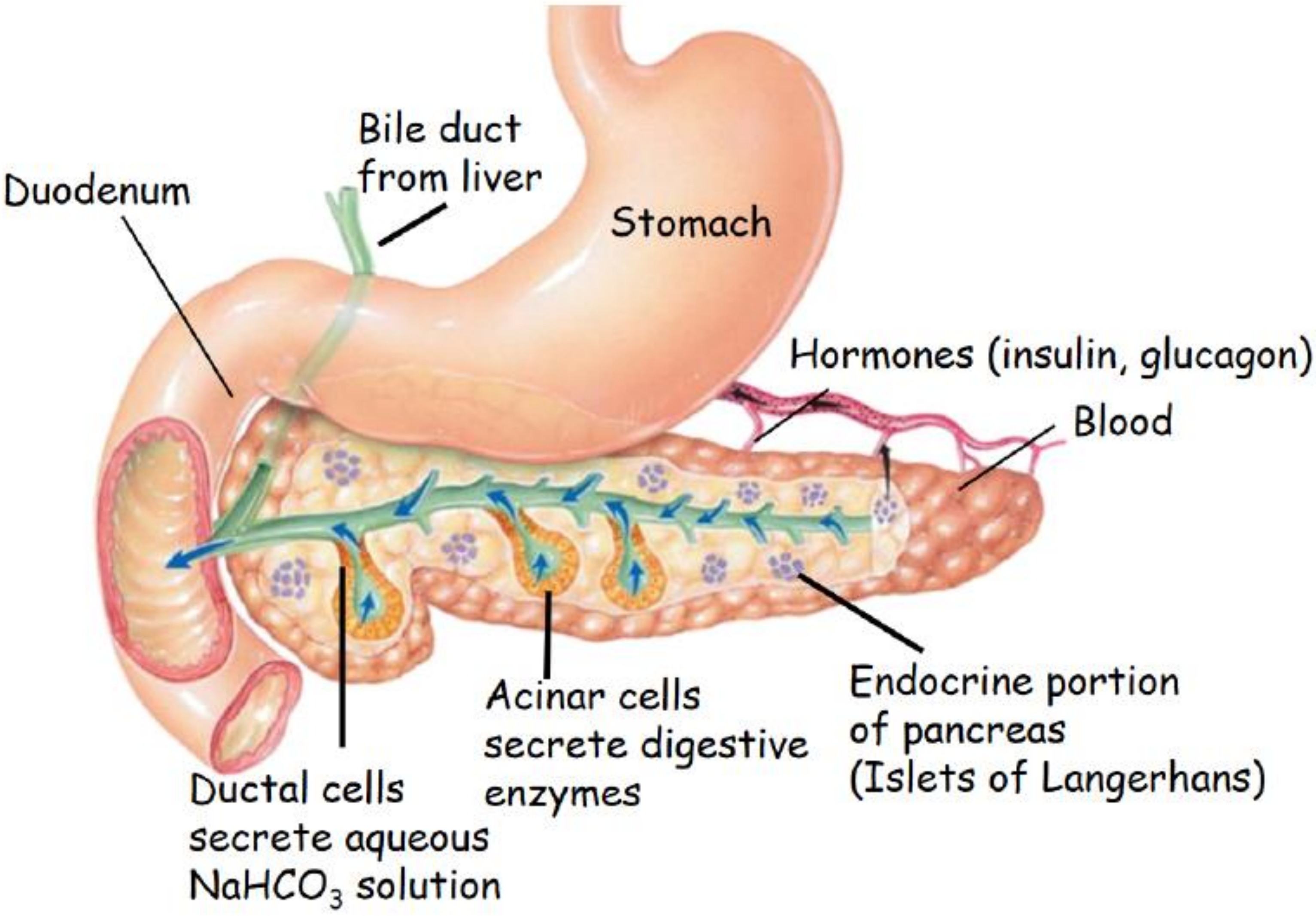
- the total number of islets in humans ranging between 3.2 to 14.8 million.
- The cellular composition of the islets differs in different species, and it has been studied that there are functional differences in islets of different species as well.
- The Islets of Langerhans in humans consist of four different types of cells; α cells, β cells, δ cells, and γ or PP (pancreatic polypeptide-producing) cells.

- The β cells of the pancreas account for about 60% of the total islet mass, followed by α cells that occupy 30% of the mass. The remaining 10% is covered by the δ and PP cells.
- The four different cells of the islets secrete four different hormones that influence the metabolism of the body.



- A pancreas is present in all vertebrates.
- In lampreys, some bony fishes, lungfishes and lower tetrapods, it is a diffuse organ embedded in the liver, mesenteries and intestinal wall.
- Hagfishes have a small pancreas.
- Elasmobranchs have a well defined bilobed pancreas.
- In higher tetrapoda it is generally a compact gland. One or two pancreatic ducts open into the duodenum.

Anatomy of Pancreas

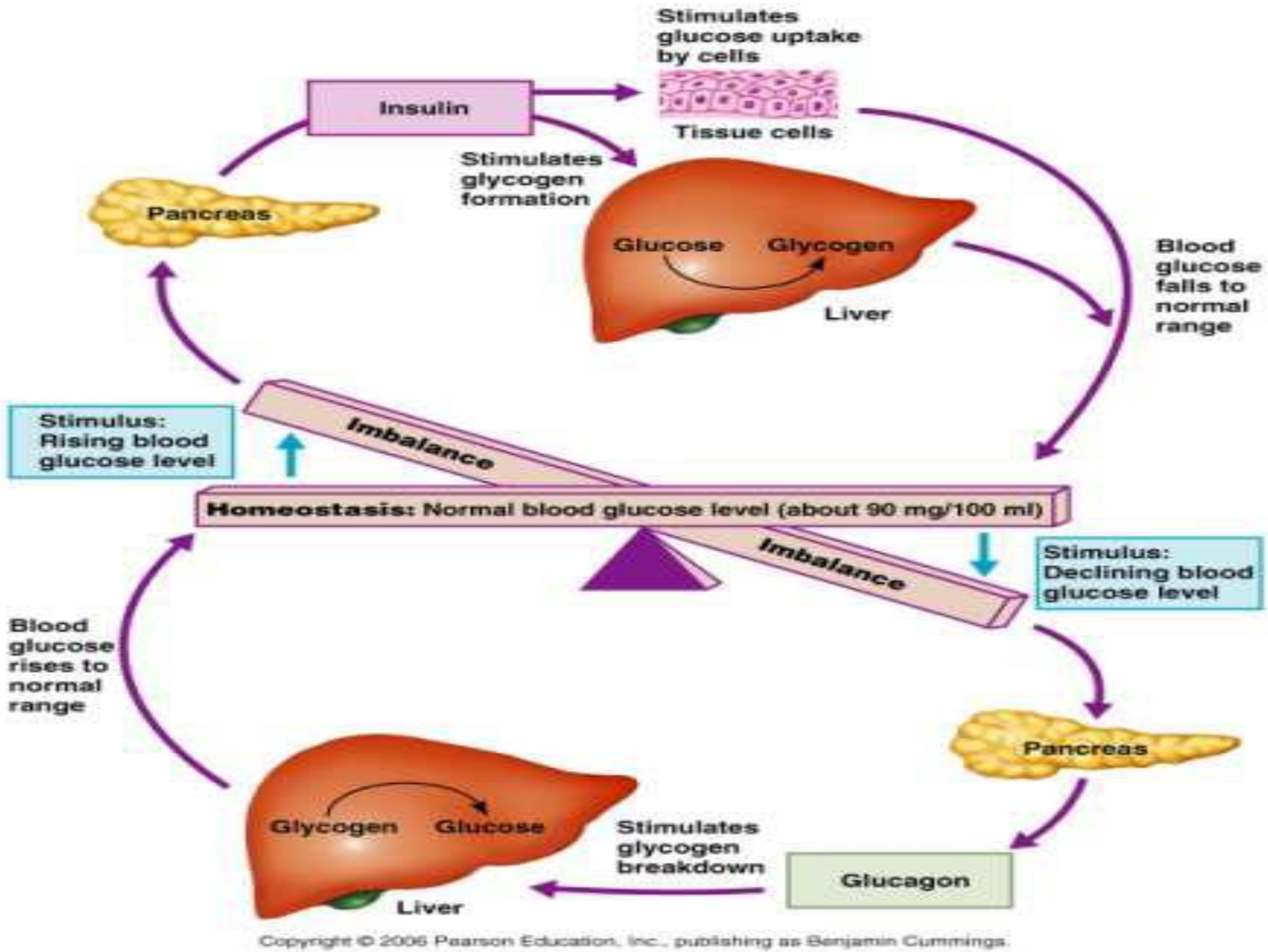


Hormones of Pancreas

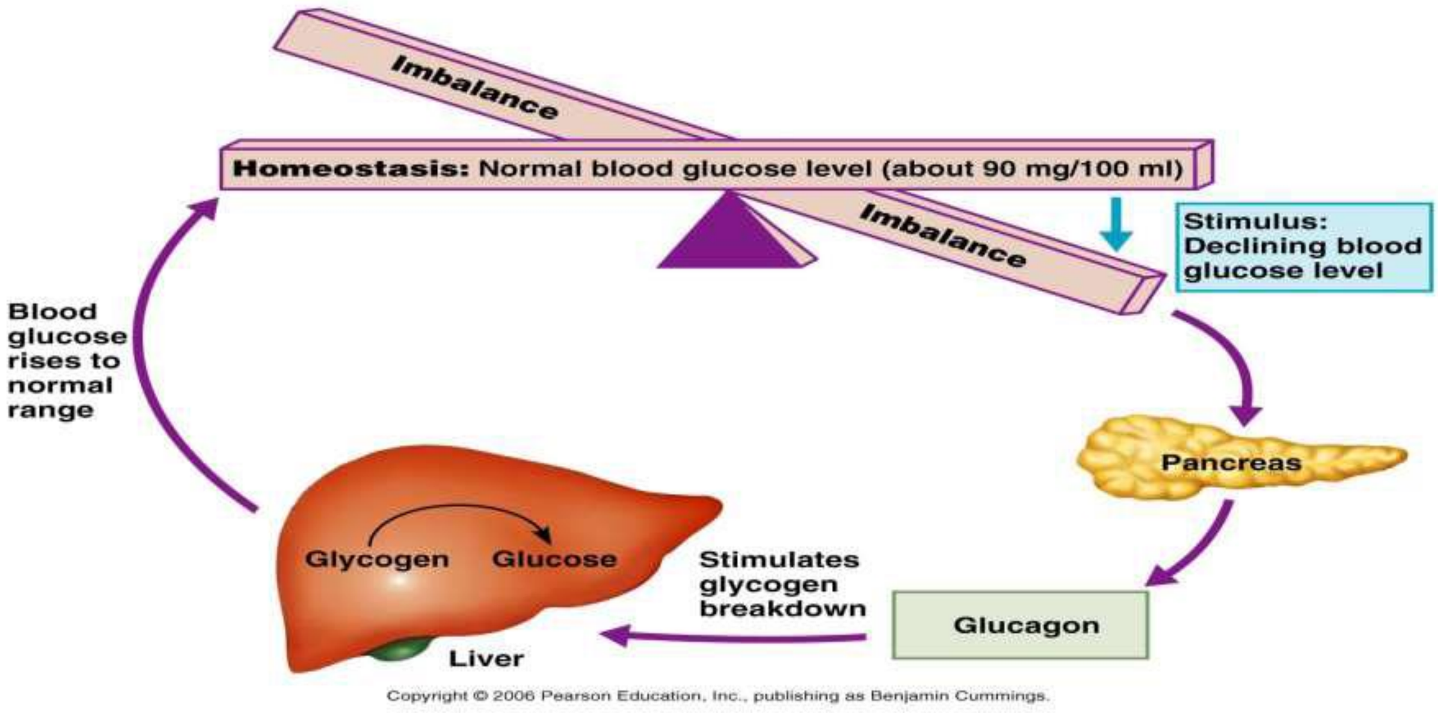
- **Insulin**
- Insulin is secreted by the β cells of the Islets of Langerhans as a polypeptide consisting of about 50 amino acids.
- Their function is to lower the blood nutrient level, mostly of glucose
- to facilitate the storage of nutrients in the body.
- Insulin is synthesized as a part of a larger polypeptide unit called proinsulin to release the insulin.
- Insulin works by enhances the transport of glucose into different cells of the body and also inhibits the breakdown of glycogen into glucose.

- **Glucagon**
- Secreted by the α cells of the pancreas, which works opposite to insulin.
- Glucagon is a polypeptide consisting of 29 amino acids linked together to form a longer polypeptide.
- Glucagon is an extremely potent hyperglycaemic agent that causes the release of glucose into the blood.
- The target organ of the glucagon hormone is the liver where it promotes the breakdown of glycogen into glucose so as it increases the blood glucose level.
- The increase in blood glucose level results decreased amino acid levels in the blood.
- The release of glucagon by the α cells is stimulated by falling blood glucose levels via sympathetic nervous system stimulation as well as rising amino acids levels

Regulation of blood glucose



- delta cells (δ cells) secrete somatostation or growth hormone inhibiting hormone (GHIH) which helps regulate
- carbohydrate metabolism by inhibiting the secretion of
- glucagons.

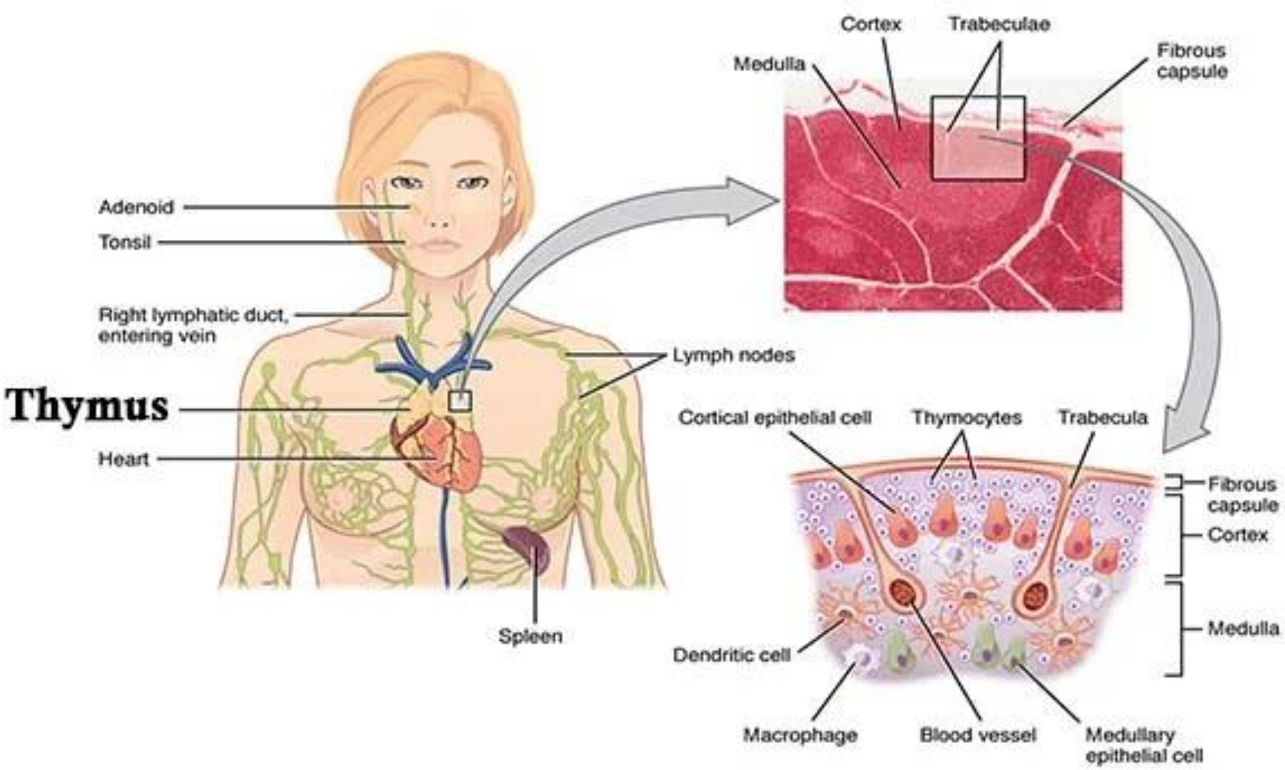


- **Functions of Pancreas**
- to maintain the blood nutrient level in the body.
- Insulin responsible for decreasing the blood glucose level
- Glucagon, which works to increase the blood glucose levels if the levels go down beyond normal.
- The δ cells release the somatostatin hormone, which inhibits the secretion of both insulin and glucagon while inhibiting the secretion of growth hormone by the pituitary.

Structure and Function of Thymus

- The thymus is a lymphocyte-rich, bilobed, encapsulated organ located behind the sternum, above and in front of the heart.
- The activity is maximal in the fetus and in early childhood and then undergoes atrophy at puberty but never totally disappearing.
- The thymus is derived from the third and fourth pharyngeal pouches during embryonic life and circulating T cell precursors derived from hemopoietic stem cells (HSC) in the bone marrow.

- It is essential for the maturation of T cells and the development of cell-mediated immunity thus referred to as primary lymphoid organ.
- In fact, the term 'T cell' means thymus-derived cell

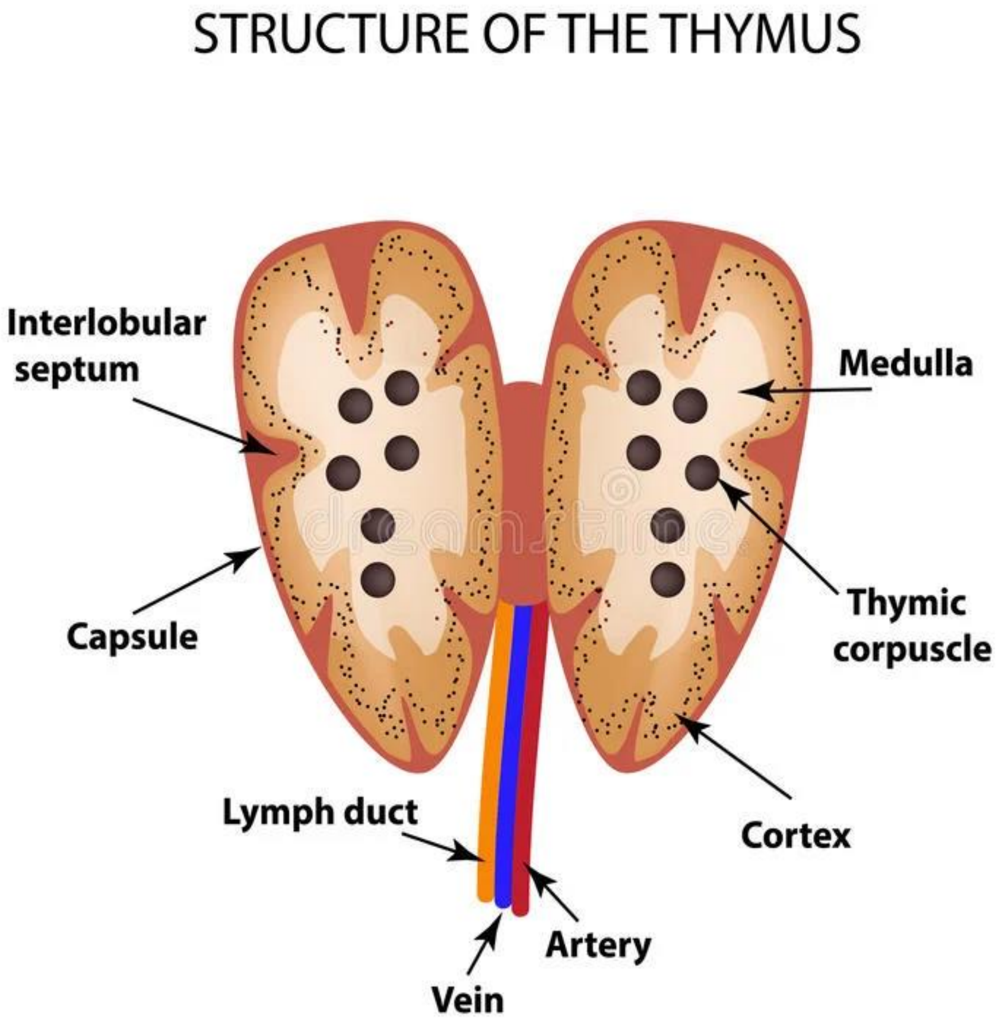


Structure of Thymus

- It is a pink, flattened, asymmetrical structure lying between sternum and pericardium in anterior mediastinum.
- It is large in infants weighing upto 70 g in adult to about 3g.
- The thymus consists of two lobes joined by aerolar tissues.
- The two thymic lobes are surrounded by a thin connective tissue capsule.
- Fibrous extensions of capsule around the thymus called trabeculae or septa divide thymus into lobules.

An Outer Cortex

- Dark-staining outer part packed with lymphocytes, compartmentalized by elongated epithelial cells.
- It consists of immature T -cells.
- The process of proliferation and selection occurs mainly here.

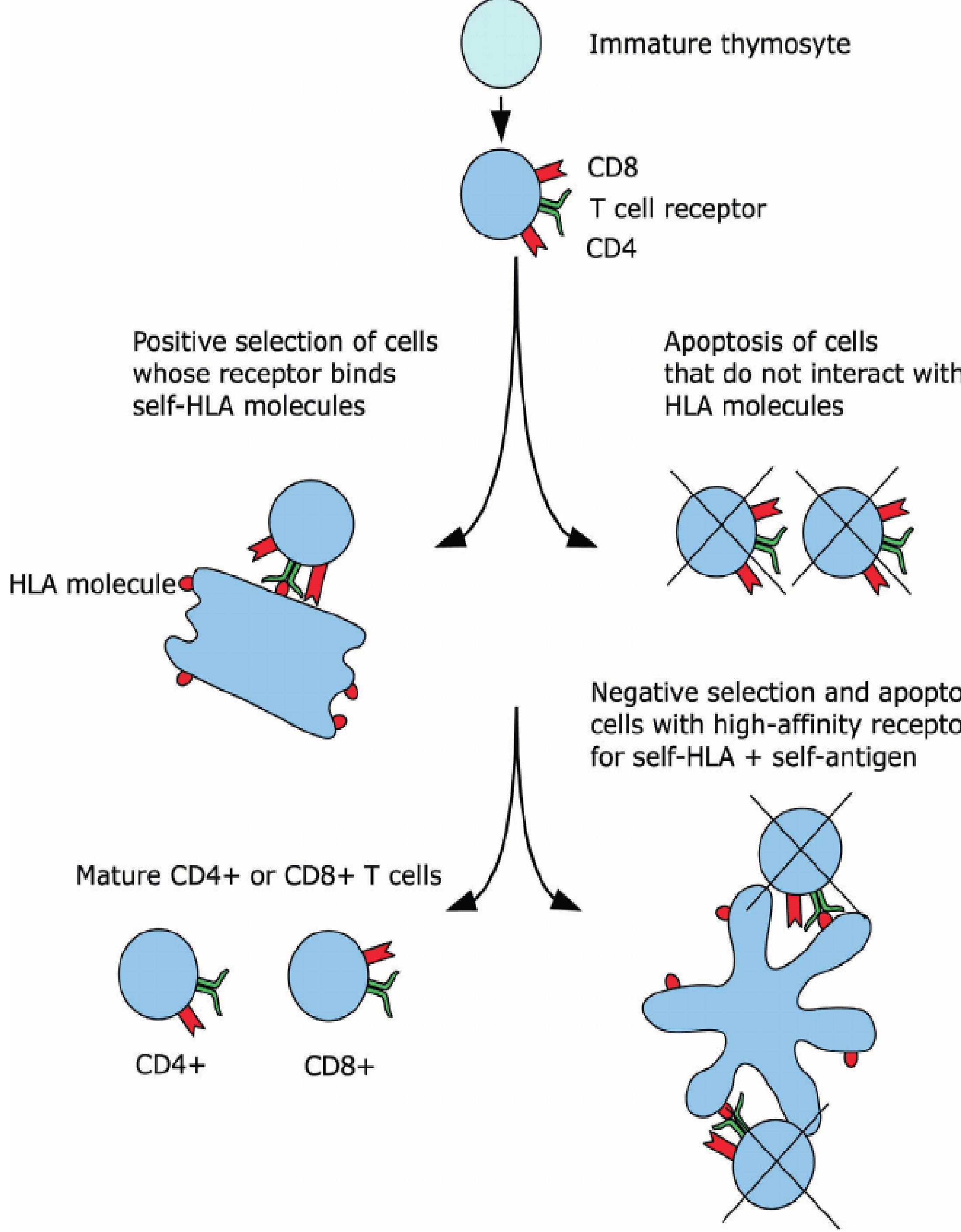


An Inner Medulla

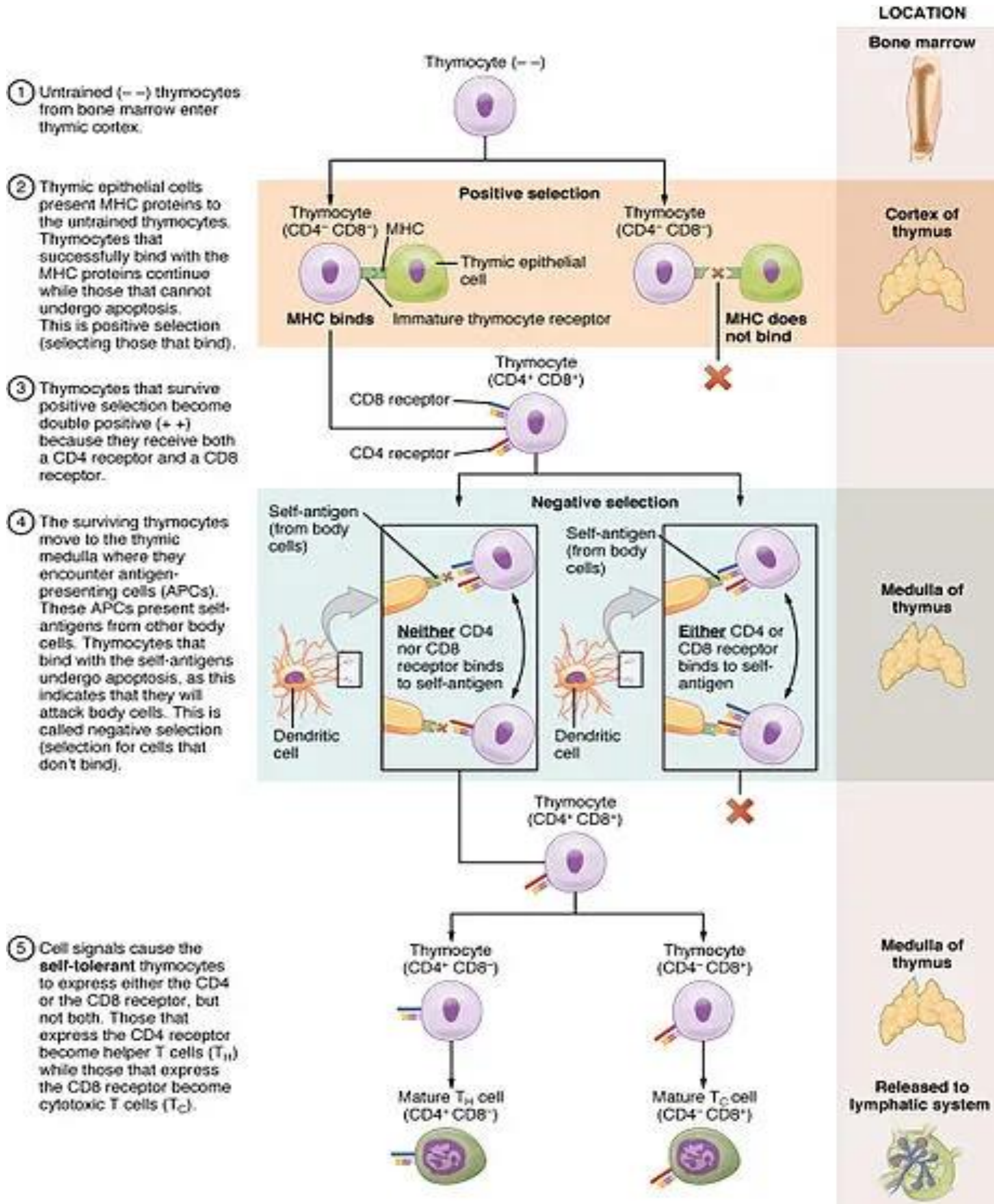
- Lighter central zone with fewer lymphocytes but more epithelial reticular cells.
- It consists of mature T-cells.
- It is predominantly the epithelial part, to which cortical lymphocytes migrate before export via venules and lymphatics.
- Also, the final stages of selection may occur at the cortico-medullary junction.
- Medulla also consists of thymic corpuscles alternatively called Hassall's corpuscles which are oval structures consisting of round whorls of flattened epithelial cells.

The thymus is the organ primarily responsible for the production and maturation of T cells, functioning as the initial site of T cell immune maturation through positive and negative selection processes.

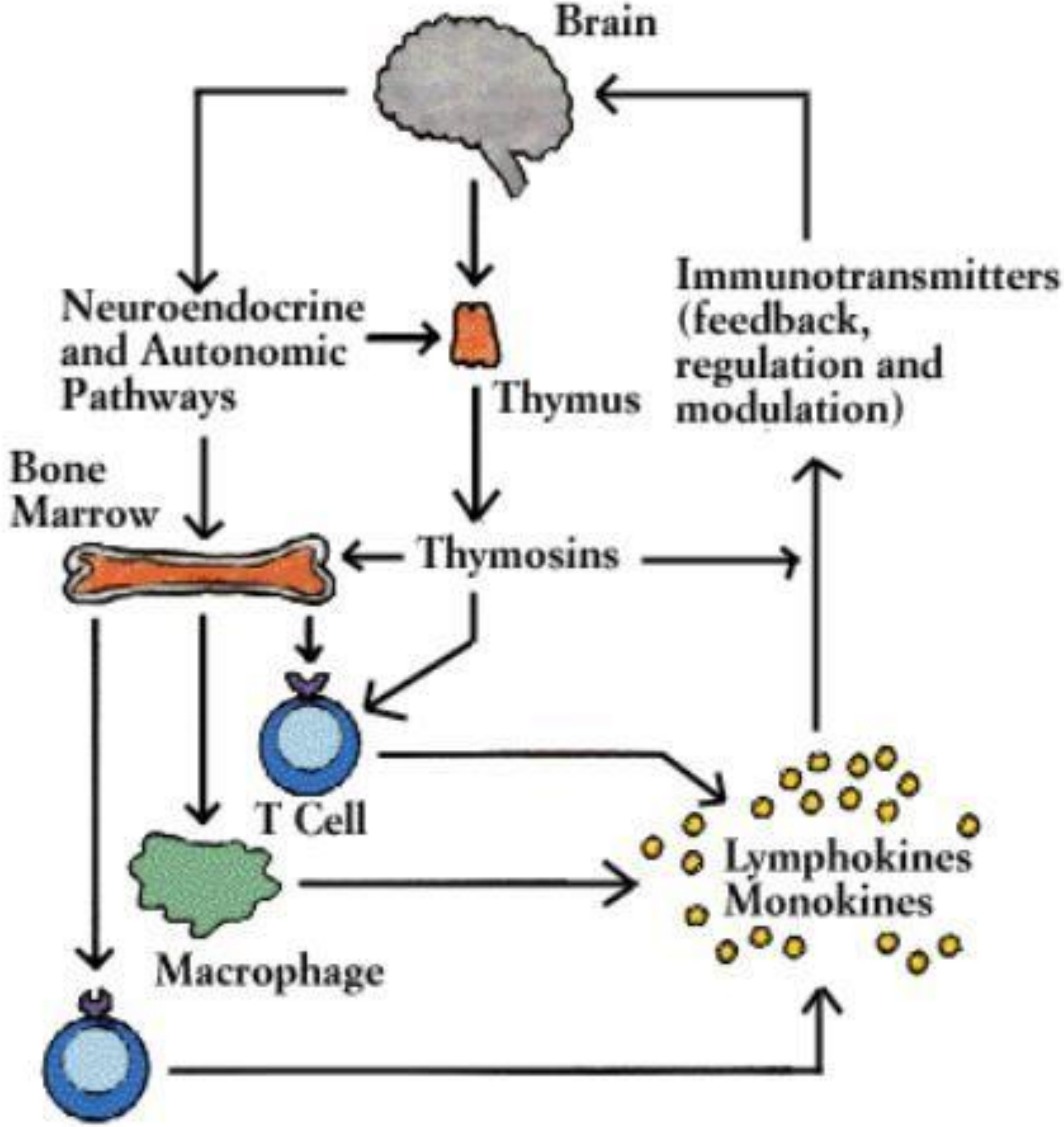
T cells are so named as they mature in the thymus and B cells are named thus as they mature in the bone marrow. Both are a type of leukocyte.



- T cells originate in the bone marrow and mature in the thymus.
- T cells, in the thymus, multiply and differentiate into helper, regulatory, or cytotoxic T cells or become memory T cells. They are next sent to peripheral tissues or circulate in the blood or lymphatic system.
- Upon stimulation by the appropriate antigen, helper T cells secrete cytokines, which stimulate the differentiation of B cells into plasma cells (antibody-producing cells).
- Regulatory T cells act to control immune reactions.
- Cytotoxic T cells, which are activated by various cytokines, bind to and kill infected cells and cancer cells.



LOCATION
Bone marrow
Thymocyte (– –)
1 Untrained (– –) thymocytes from bone marrow enter thymic cortex.
2 Thymic epithelial cells present MHC proteins to the untrained thymocytes. Thymocytes that successfully bind with the MHC proteins continue while those that cannot undergo apoptosis. This is positive selection (selecting those that bind).
Positive selection
Thymocyte (CD4⁻ CD8⁻)
MHC
Thymic epithelial cell
MHC binds
Immature thymocyte receptor
Thymocyte (CD4⁻ CD8⁻)
MHC does not bind
Cortex of thymus
3 Thymocytes that survive positive selection become double positive (+ +) because they receive both a CD4 receptor and a CD8 receptor.
Thymocyte (CD4⁺ CD8⁺)
CD8 receptor
CD4 receptor
4 The surviving thymocytes move to the thymic medulla where they encounter antigen-presenting cells (APCs). These APCs present self-antigens from other body cells. Thymocytes that bind with the self-antigens undergo apoptosis, as this indicates that they will attack body cells. This is called negative selection (selection for cells that don't bind).
Negative selection
Self-antigen (from body cells)
Neither CD4 nor CD8 receptor binds to self-antigen
Dendritic cell
Self-antigen (from body cells)
Either CD4 or CD8 receptor binds to self-antigen
Dendritic cell
Medulla of thymus
Thymocyte (CD4⁺ CD8⁺)
5 Cell signals cause the self-tolerant thymocytes to express either the CD4 or the CD8 receptor, but not both. Those that express the CD4 receptor become helper T cells (T_H) while those that express the CD8 receptor become cytotoxic T cells (T_C).
Thymocyte (CD4⁺ CD8⁻)
Thymocyte (CD4⁻ CD8⁺)
Medulla of thymus
Mature T_H cell (CD4⁺ CD8⁻)
Mature T_C cell (CD4⁻ CD8⁺)
Released to lymphatic system


Brain
Neuroendocrine
and Autonomic
Pathways
Thymus
Immunotransmitters
(feedback,
regulation and
modulation)
Bone
Marrow
Thymosins
T Cell
Lymphokines
Monokines
Macrophage

Functions of Thymus

1) T cell maturation and development

- Immature T cell precursors travel from the bone marrow to the thymus (to become thymocytes) and then migrate to the peripheral lymphoid tissues as mature T cells.
- (a) To produce sufficient numbers (millions) of different T cells each expressing unique T cell receptors.
- (b) To select T cells for survival in such a way that the chance for an auto-immune response is minimized.

2) Production of Hormones

- It secretes four hormones such **as thymulin, thymosin, thymopoietin and thymic humoral factor (THF).** The primary function of thymus is the production of immuno competent 'T' lymphocytes which provides cell mediated immunity.

POSTERIOR PITUITARY OR NEUROHYPOPHYSIS

PARTS

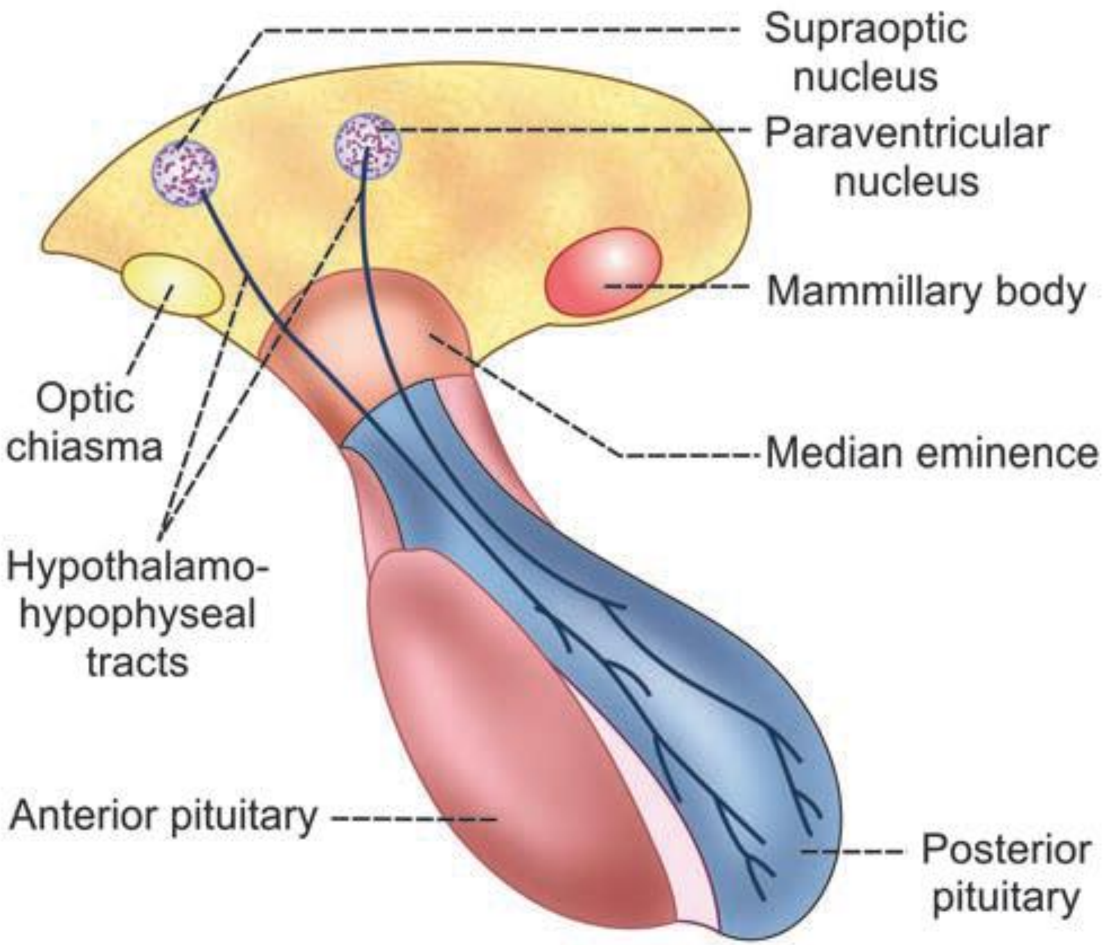
- Posterior pituitary consists of three parts:
- 1. Pars nervosa or infundibular process
- 2. Neural stalk or infundibular stem
- 3. Median eminence.
- Pars tuberalis of anterior pituitary and the neural
- stalk of posterior pituitary together form the **hypophyseal stalk.**

Posterior pituitary hormones are:

- 1. Antidiuretic hormone (ADH) or vasopressin
- 2. Oxytocin.
- Actually, the posterior pituitary does not secrete any hormone.
- ADH and oxytocin are synthesized in the hypothalamus.
- From hypothalamus, these two hormones are transported to the posterior pituitary through the axonic flow.
- Proteins involved in transport of these hormones are called neurophysins
- In the posterior pituitary, these hormones are stored at the nerve endings. Whenever, the impulses from hypothalamus reach the posterior pituitary, these
- hormones are released from the nerve endings into the circulation.
- Hence, these two hormones are called **neurohormones**

Neurophysins

- Neurophysins are the binding proteins which transport
- ADH and oxytocin from hypothalamus to posterior
- pituitary via hypothalamo-hypophyseal tract and storage
- of these hormones in posterior pituitary.
- Neurophysin I or oxytocin-neurophysin is the binding protein for oxytocin
- and neurophysin II or ADH-neurophysin is the binding protein for ADH.



Antidiuretic hormone (ADH) is secreted mainly by **supraoptic nucleus** of hypothalamus. It is also secreted by **paraventricular nucleus** in small quantity.

Antidiuretic hormone is a polypeptide containing 9 amino acids.

Its half-life is 18 to 20 minutes

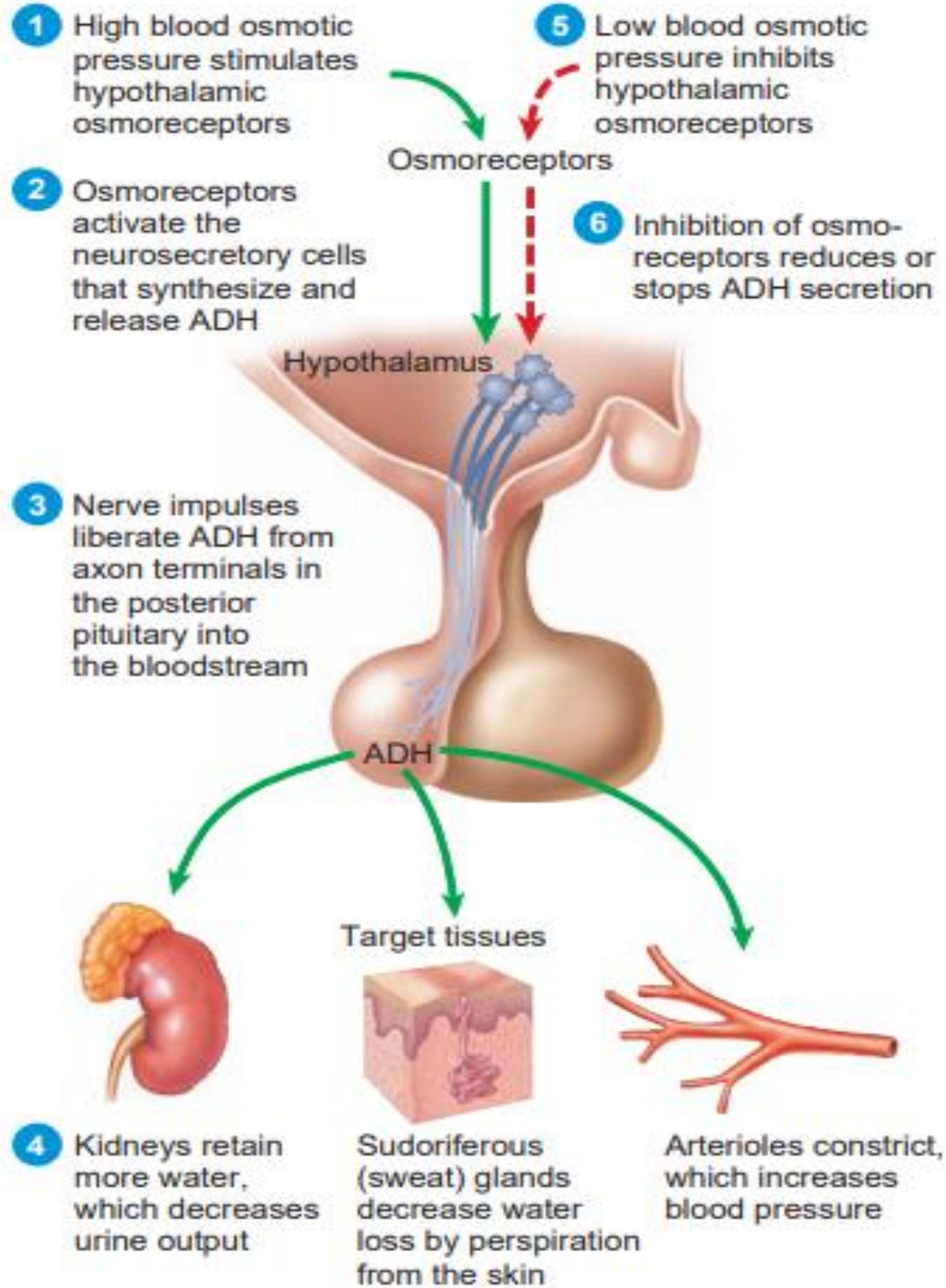
- Antidiuretic hormone has two actions:
- 1. Retention of water 2. Vasopressor action.
- 1. *Retention of water*
- Major function of ADH is retention of water by acting on kidneys. It increases the **facultative reabsorption** of water from distal convoluted tubule and collecting duct in the kidneys.
- In the absence of ADH, the distal convoluted tubule and collecting duct are totally impermeable to water.
- So, reabsorption of water does not occur in the renal tubules and dilute urine is excreted.
- This leads to loss of large amount of water through urine.
- This condition is called **diabetes insipidus** and the excretion of large amount of water is called diuresis.

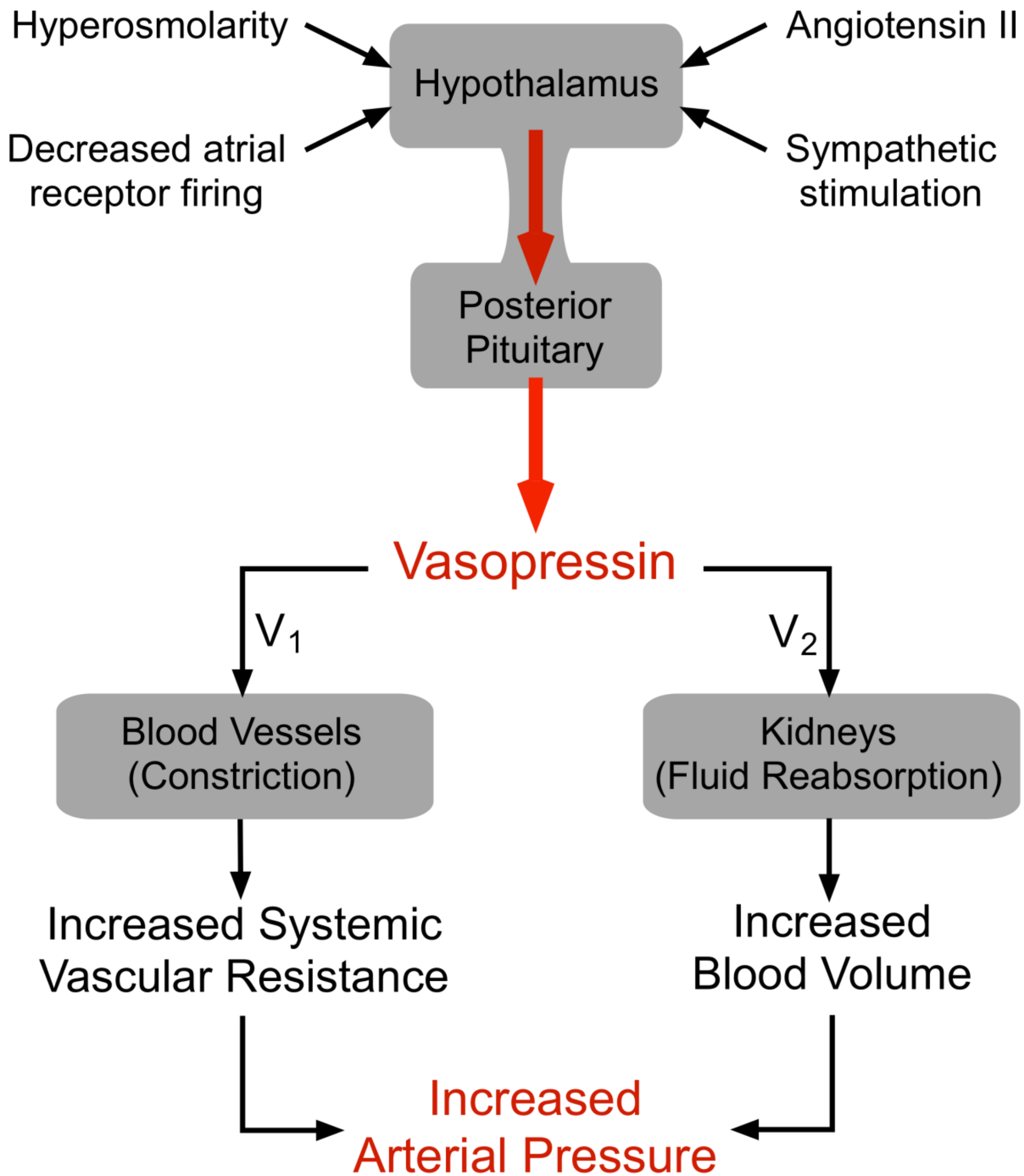
- ADH increases water reabsorption in tubular epithelial membrane by regulating the **water channel proteins** called **aquaporins** through **V2 receptors**

2. *Vasopressor action*

- In large amount, ADH shows vasoconstrictor action.
- Particularly, causes constriction of the arteries in all parts of the body. Due to vasoconstriction, the blood pressure increases.
- ADH acts on blood vessels through V_{1A} receptors.
- However, the amount of ADH required to cause the vasopressor effect is greater than the amount required to cause the **antidiuretic effect.**

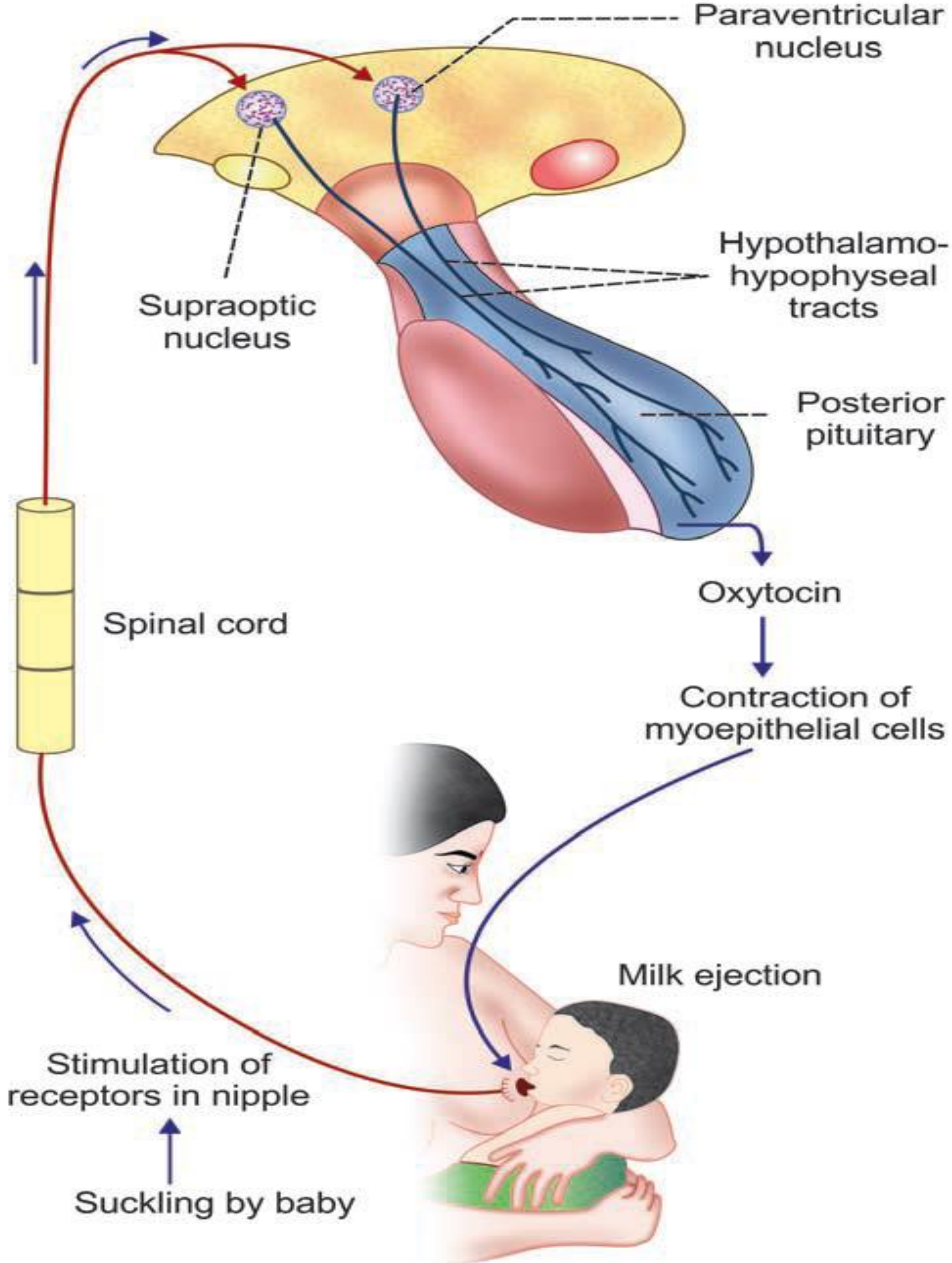
- ***Regulation of Secretion***
- ADH secretion depends upon the volume of body fluid and the osmolarity of the body fluids.
- *Role of osmoreceptors*
- Osmoreceptors are the receptors which give response to change in the osmolar concentration of the blood.
- These receptors are situated in the hypothalamus near supraoptic and paraventricular nuclei.
- When osmolar concentration of blood increases, the osmoreceptors are activated. In turn, the osmoreceptors stimulate the supraoptic and paraventricular nuclei which send motor impulses to posterior pituitary through the nerve fibers and cause release of ADH.
- ADH causes reabsorption of water from the renal tubules.
- This increases ECF volume and restores the normal osmolarity.


1 High blood osmotic pressure stimulates hypothalamic osmoreceptors
5 Low blood osmotic pressure inhibits hypothalamic osmoreceptors
Osmoreceptors
2 Osmoreceptors activate the neurosecretory cells that synthesize and release ADH
6 Inhibition of osmoreceptors reduces or stops ADH secretion
Hypothalamus
3 Nerve impulses liberate ADH from axon terminals in the posterior pituitary into the bloodstream
ADH
Target tissues
4 Kidneys retain more water, which decreases urine output
Sudoriferous (sweat) glands decrease water loss by perspiration from the skin
Arterioles constrict, which increases blood pressure

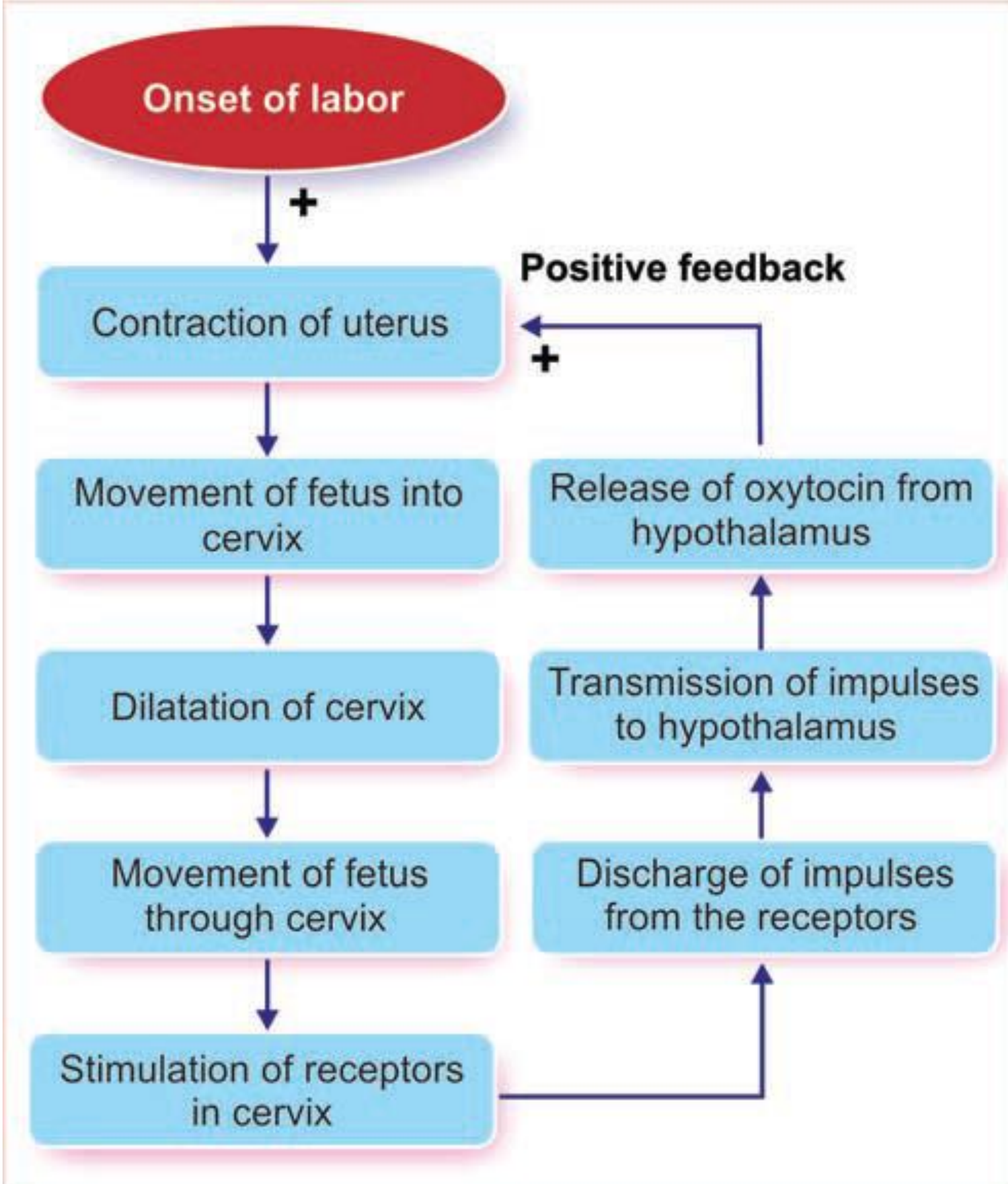

Hyperosmolarity
Angiotensin II
Hypothalamus
Decreased atrial receptor firing
Sympathetic stimulation
Posterior Pituitary
Vasopressin
V_1
V_2
Blood Vessels (Constriction)
Kidneys (Fluid Reabsorption)
Increased Systemic Vascular Resistance
Increased Blood Volume
Increased Arterial Pressure

OXYTOCIN

- Oxytocin is secreted mainly by **paraventricular nucleus** of hypothalamus.
- It is also secreted by **supraoptic nucleus** in small quantity
- In the posterior pituitary, the oxytocin is stored in the nerve endings of hypothalamo-hypophyseal tract.
- When suitable stimuli reach the posterior pituitary from hypothalamus, oxytocin is released into the blood.
- Oxytocin is secreted in both males and females.
- Oxytocin is a polypeptide having 9 amino acids. half-life 6 minutes.
- In females, oxytocin acts on mammary glands and uterus.


Paraventricular nucleus
Supraoptic nucleus
Hypothalamo-hypophyseal tracts
Posterior pituitary
Oxytocin
Spinal cord
Contraction of myoepithelial cells
Milk ejection
Stimulation of receptors in nipple
Suckling by baby

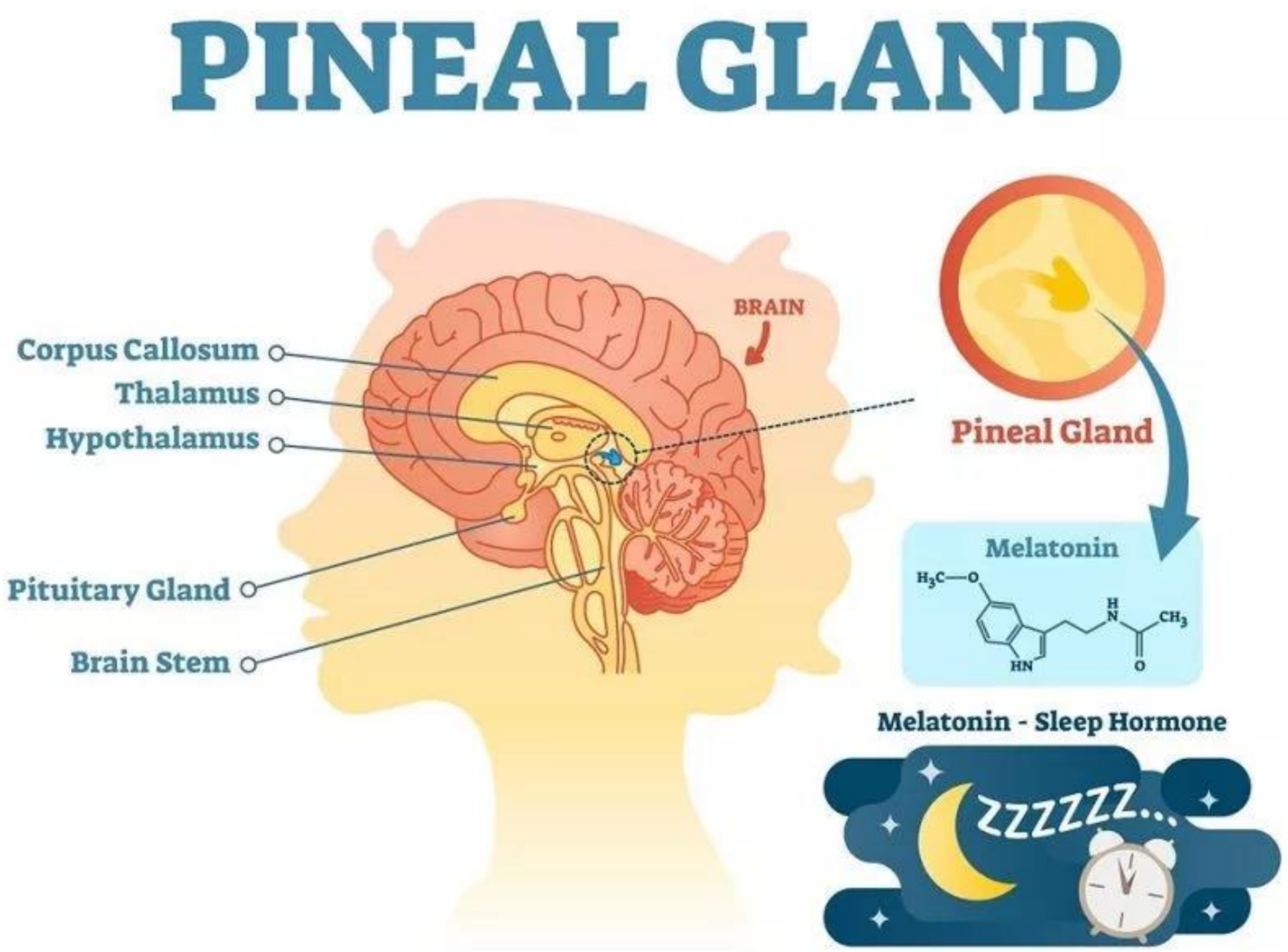
- Oxytocin acts on pregnant uterus and also non-pregnant
- uterus.
- Throughout the period of pregnancy, oxytocin secretion
- is inhibited by estrogen and progesterone.
- At the end of pregnancy, the secretion of these two hormones
- decreases suddenly and the secretion of oxytocin increases. Oxytocin causes contraction of uterus and helps in the expulsion of fetus.
- During the later stages of pregnancy, the number of
- receptors for oxytocin increases in the wall of the uterus.
- Because of this, the uterus becomes more sensitive to
- oxytocin. Oxytocin secretion increases during **labor.**


Onset of labor
+
Positive feedback
Contraction of uterus
+
Movement of fetus into cervix
Release of oxytocin from hypothalamus
Dilatation of cervix
Transmission of impulses to hypothalamus
Movement of fetus through cervix
Discharge of impulses from the receptors
Stimulation of receptors in cervix

On non-pregnant uterus

- The action of oxytocin on non-pregnant uterus is to facilitate the transport of sperms through female genital tract up to the fallopian tube, by producing the uterine contraction during sexual intercourse.
- In males, the release of oxytocin increases during ejaculation. It facilitates release of sperm into urethra by causing contraction of smooth muscle fibers in reproductive tract, particularly vas deferens.
- Oxytocin acts on mammary glands and uterus by activating **G-protein coupled oxytocin receptor.**

Pineal Gland



- The pineal gland is an endocrine gland present at the geometric center of the brain that is essential in the circadian cycle of sleep and wakefulness of the body.
- It occurs in all vertebrates, and it has been studied that pineal-like organs can also be found invertebrate - insects.
- It is a photo-neuro-endocrine gland that secretes hormones and other compounds like serotonin, melatonin, and N, N-dimethyltryptamine.
- The most important and notable function is the production of melatonin which is produced in a rhythmic pattern.

- The activity is influenced by the light received by the retina, which is then converted from the neural input into endocrine output by the pineal gland.
- The pineal gland has also been called 'The Third Eye' due to the histological similarities between the pineal gland and the lateral eyes of amniotic vertebrates.
- The pineal gland is a tiny pine cone-shaped gland that hangs from the roof of the third ventricle of the brain.
- The pineal gland is a secretory neuroendocrine organ that is highly vascularized and weighs about 0.1g.

- The secretory cells of the pineal gland are called pinealocytes that are arranged in the form of compact cords and clusters.
- In between the cells are calcerous bodies that are prone to calcification, the risk of which increases with age.
- The calcareous deposits are also called acervuli.
- The deposits are assumed to be formed by the combination of the polypeptide secreted by the pinealocytes and calcium accumulated interstitially.
- The pinealocytes in humans have a prominent nucleus and a granular cytoplasm.
- The cytoplasm also contains cytoplasmic processes that terminate into fenestrated capillaries.
- Besides, the extracellular space of the gland is occupied by neuroglia that surrounds pinealocytes and peripheral patches.

Hormone in Pineal Gland

- Melatonin is an amine-derived hormone formed from serotonin.
- The release of melatonin by the pineal gland occurs in a rhythmic pattern where the levels rise and fall depending on the diurnal cycle.
- The precursor of melatonin is tryptophan which is hydroxylated by the pinealocytes into 5-hydroxytryptophan in the presence of hydroxylase.
- The most important effect of melatonin is to coordinate with the diurnal rhythms in the body by stimulating the hypothalamus.

Functions of Pineal Gland

- The hormone produce by the gland is essential for the regulation of the circadian or diurnal cycle of the body.
- The gland functions as a mediator between the nervous system and the endocrine system as the ganglion on the gland help to convert the photo input from the eyes into neural output.
- In the case of other mammals like rodents, the pineal gland influences the action of different drugs like antidepressants and cocaine.

REPRODUCTIVE TECHNOLOGY (22ZOOME22)

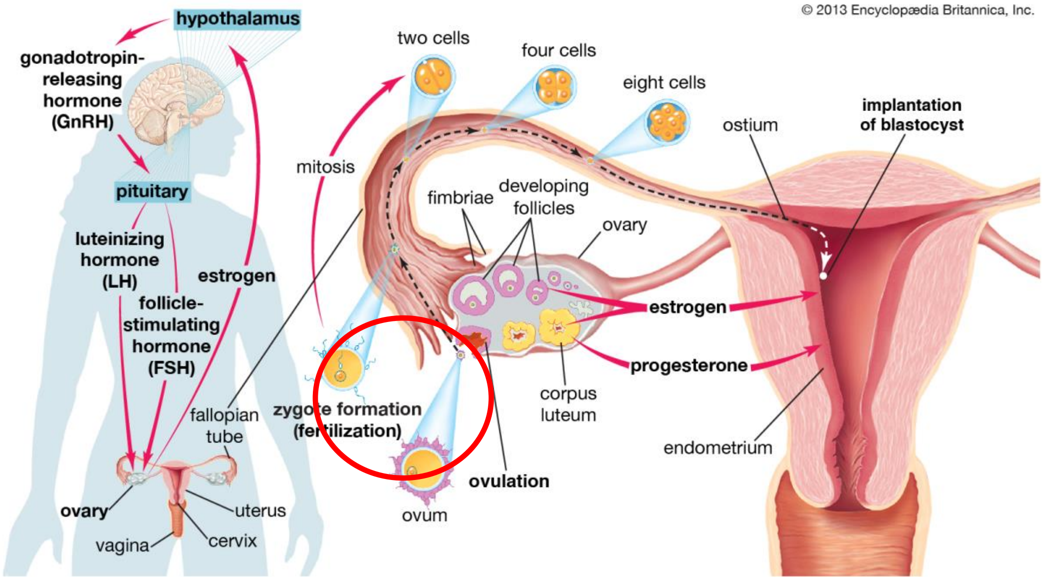
HORMONAL REGULATION IN PREGNANCY, PARTURITION & LACTATION

Hormones of pregnancy

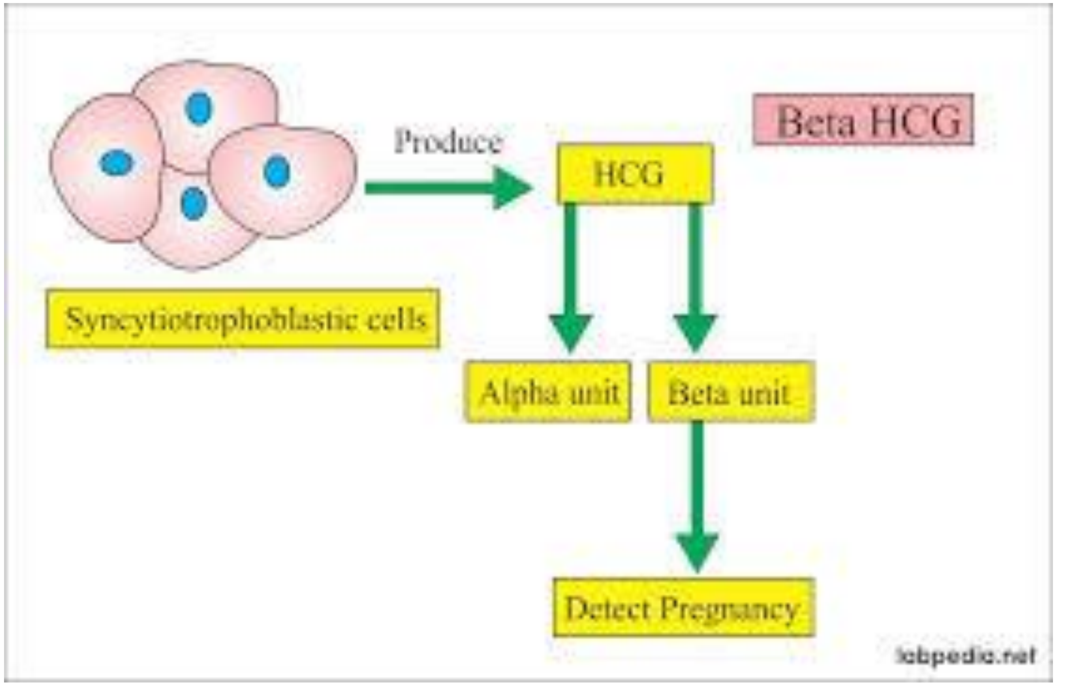
- Human chorionic gonadotrophin (hCG)
- Oestrogens
- Progestogens
- Relaxin
- Human placental lactogen (hPL)
- Human growth hormone placental variant (hGH-pV)

Human chorionic gonadotrophin (hCG)

- The ovarian steroid hormones, **oestrogens and progesterone**, are essential for the early process of endometrial preparation and for the process of implantation, and at this very early stage of pregnancy their source is the corpus luteum in the ovary.
- During the first 6 weeks of pregnancy, loss of the ovaries results in the termination of pregnancy, but there after ovariectomy has no effect on it.
- This is because of the crucial role of the ovaries, specifically the corpus luteum, during those first few weeks by providing the necessary quantities of oestrogens and progesterone.
- Subsequently, the fetoplacental unit takes over this role.



- There is an apparent paradox which requires resolution with regard to the continuing provision of steroid hormones by the ovaries during the first few weeks of pregnancy:
- Stimulates the luteal cells once the increasing circulating levels of both **17β-oestradiol and particularly progesterone** have inhibited the anterior pituitary production of luteinising hormone (LH) and follicle-stimulating hormone (FSH) by their direct and indirect negative feedback effects on the maternal hypothalamo-adenohypophysial axis?
- Another glycoprotein hormone very similar to LH, with the same α sub-unit, called human chorionic gonadotrophin (hCG), which is produced by the implanting **syncytiotrophoblast cells**.



- This molecule can be detected by the **10th day of pregnancy**, and indeed a standard pregnancy test depends on the measurement of a fragment of this hCG molecule.
- It binds to the **LH receptors on the luteal cells in the corpus luteum** and thereby stimulates these cells to continue synthesising 17β-oestradiol and progesterone, despite the now **diminished maternal LH**.
- Its concentration in the maternal blood increases to reach maximum levels around the **10th to 12th week of pregnancy** after which levels decline, although it is present (in varying small amounts) throughout the rest of pregnancy.

Estrogens

- From the **sixth week of pregnancy**, the placenta is the source of most of the oestrogens being produced, but both mother and fetus provide the necessary precursor molecules.
- The **largest quantity of oestrogen now produced is no longer 17β-oestradiol but the less potent oestriol**, with the metabolite oestrone also being produced in small amounts.
- One androgenic precursor provided by both mother and fetus is **dehydroepiandrosterone sulphate (DHEAS)** which is aromatised to oestrone and 17β-oestradiol by the placenta.
- The **oestriol is synthesised by the placenta** purely from the androgenic 16α-hydroxyDHEAS which is produced by the fetus
- By **late pregnancy, oestrogen levels are normally very high**.
- **Measurement of urinary oestrogen excretion levels** can be a useful indicator of fetal well-being.
- The oestriol concentration is likely to be more adversely affected than the other two oestrogens when the fetus is distressed, since its precursor is almost entirely provided by it.
- The ratio of oestriol to the sum of the other two oestrogens (17β-oestradiol and oestrone) would be decreased.

- **Estrogens are vital for the normal growth and development of the fetus throughout the pregnancy**, and are necessary for **preparing the mammary glands by stimulating their growth and development**.
- They are also necessary for the preparation of the smooth muscle of the myometrial lining of the uterus.
- They stimulate the synthesis of oxytocin receptors and promote the synthesis of prostaglandins.
- They stimulate the production of prolactin from the **maternal adenohypophysis.**
- The reason why some of these effects of oestrogens do not actually occur noticeably until the approach of parturition is at least partly due to the counteracting inhibitory effects of progesterone.

Progesterone

- During pregnancy, progesterone is also necessary for the normal growth and development of the fetus as well as other, maternal tissues such as the mammary glands.
- Its source is chiefly the placenta, once this tissue has taken over the synthesis role from the corpus luteum.
- Its concentration in the maternal blood increases steadily throughout pregnancy reaching concentrations of the order of 120–200 $ng.ml^{-1}$, a 10-fold increase compared with the peak during the luteal phase of the menstrual cycle.
- Progesterone counterbalances the generally stimulatory effects of the oestrogens, for instance on the synthesis of oxytocin receptors and prostaglandins. It also appears to stimulate maternal appetite.

Relaxin

- This polypeptide hormone is produced by **the corpus luteum and then the placenta throughout pregnancy**.
- In women, **plasma relaxin concentrations** are highest towards the **end of the first trimester** after which they fall to a steady lower level throughout the rest of pregnancy.
- It is a cytokine with a structure similar to that of insulin.
- It stimulates angiogenesis, so this effect on the vasculature may be particularly important during the establishment of the maternal-fetal interface (i.e. the placenta).
- At least in other mammals, when levels reach **their highest at term**, it seems mainly to have a role in the **induction of cervical 'softening', a pelvic and cervical expansion due to an effect on associated ligaments, to help passage of the fetus at delivery**.
- It may also have a **relaxing effect on uterine smooth muscle**

Human placental lactogen (hPL)

- Human placental lactogen, like hCG, has structural and other similarities with anterior pituitary hormones, in this case with growth hormone and prolactin.
- As hCG levels decline from about the 10th week of pregnancy, hPL levels begin to rise.
- It is synthesised in increasing quantities **from the fetoplacental unit from the end of the first trimester onwards**.
- It is a protein hormone of 119 amino acids, which has mainly growth hormone and some prolactin activity, increasing lipolysis from the progesterone-stimulated maternal fat deposits.
- It **increases insulin resistance as pregnancy develops, and in susceptible women the rising levels of glucose in the blood can lead to gestational diabetes mellitus**.

Human growth hormone placental variant (hGH-pV)

- This hormone is also produced by the fetoplacental unit and as with hPL its levels rise from the end of the first trimester onwards.
- Like GH it is a protein, with 217 amino acids.
- It seems to have such similarity to growth hormone itself that as its levels rise, maternal GH levels fall, indicating an effective **negative feedback on the mother's adenohypophysis**.
- By acting on GH receptors, it is likely to provide GH-like effects on the mother's metabolism, **increasing lipolysis and protein synthesis**.
- In the liver, a major role **is to stimulate the synthesis of insulin-like growth factor 1 (IGF1)**.

Other maternal hormones…

- As pregnancy progresses, many of the **maternal endocrine glands increase in size and consequently hormone production rises**.
- Thus there is an increased production of all the **anterior pituitary hormones** except for the gonadotrophins LH and FSH and GH.
- Likewise the thyroid increases its output of **iodothyronines**, and the adrenals increase their output of **glucocorticoids**.
- At least part of the latter effects is likely to be due to the **oestrogenstimulated hepatic production of the plasma-binding proteins, raising total hormone levels**

Pregnancy and embryonic development

- After implantation, finger-like projections appear on the trophoblast called chorionic villi which are surrounded by the uterine tissue and maternal blood.
- The chorionic villi and uterine tissue become inter digitated with each other and jointly form a structural and functional unit between developing embryo (foetus) and maternal body called placenta.

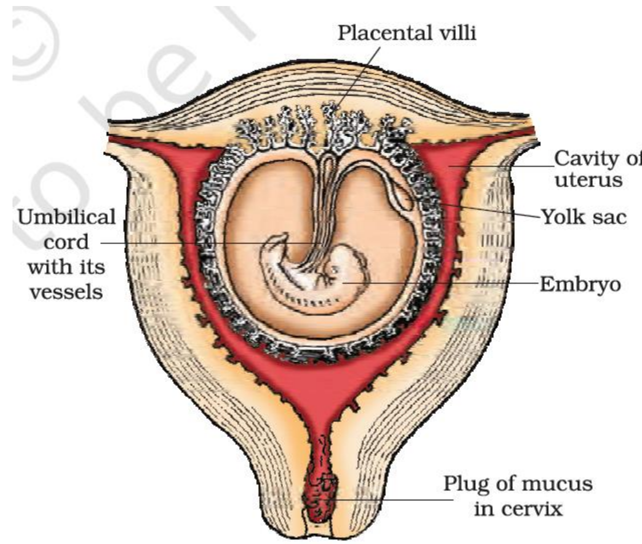


Figure 3.12 The human foetus within the uterus

The placenta facilitate the supply of oxygen and nutrients to the embryo and also removal of carbon dioxide and excretory/waste materials produced by the embryo.

The placenta is connected to the embryo through an umbilical cord which helps in the transport of substances to and from the embryo.

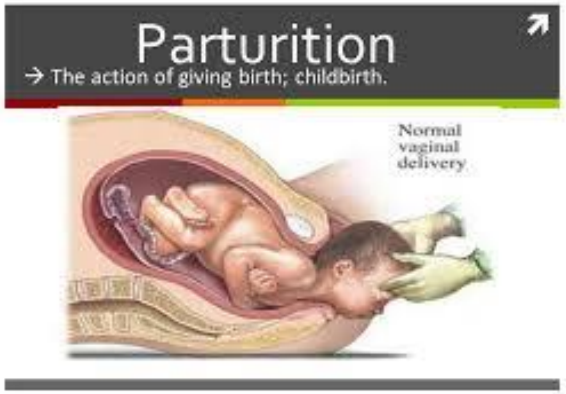
Placenta also acts as an endocrine tissue and produces several hormones like human chorionic gonadotropin (hCG), human placental lactogen (hPL), estrogens, progestogens, etc.

In the later phase of pregnancy, a hormone called relaxin is also secreted by the ovary.

- hCG, hPL and relaxin are produced in women only during pregnancy.
- during pregnancy the levels of other hormones like estrogens, progestogens, cortisol, prolactin, thyroxine, etc., are increased several folds in the maternal blood.
- Increased production of these hormones is essential for supporting the fetal growth, metabolic changes in the mother and maintenance of pregnancy.
- Immediately after implantation, the inner cell mass (embryo) differentiates into an outer layer called **ectoderm** and an inner layer called **endoderm**.
- A **mesoderm** soon appears between the ectoderm and the endoderm.
- These three layers give rise to all tissues (organs) in adults. It needs to be mentioned here that the inner cell mass contains certain cells called stem cells which have the potency to give rise to all the tissues and organs.

PARTURITION AND LACTATION

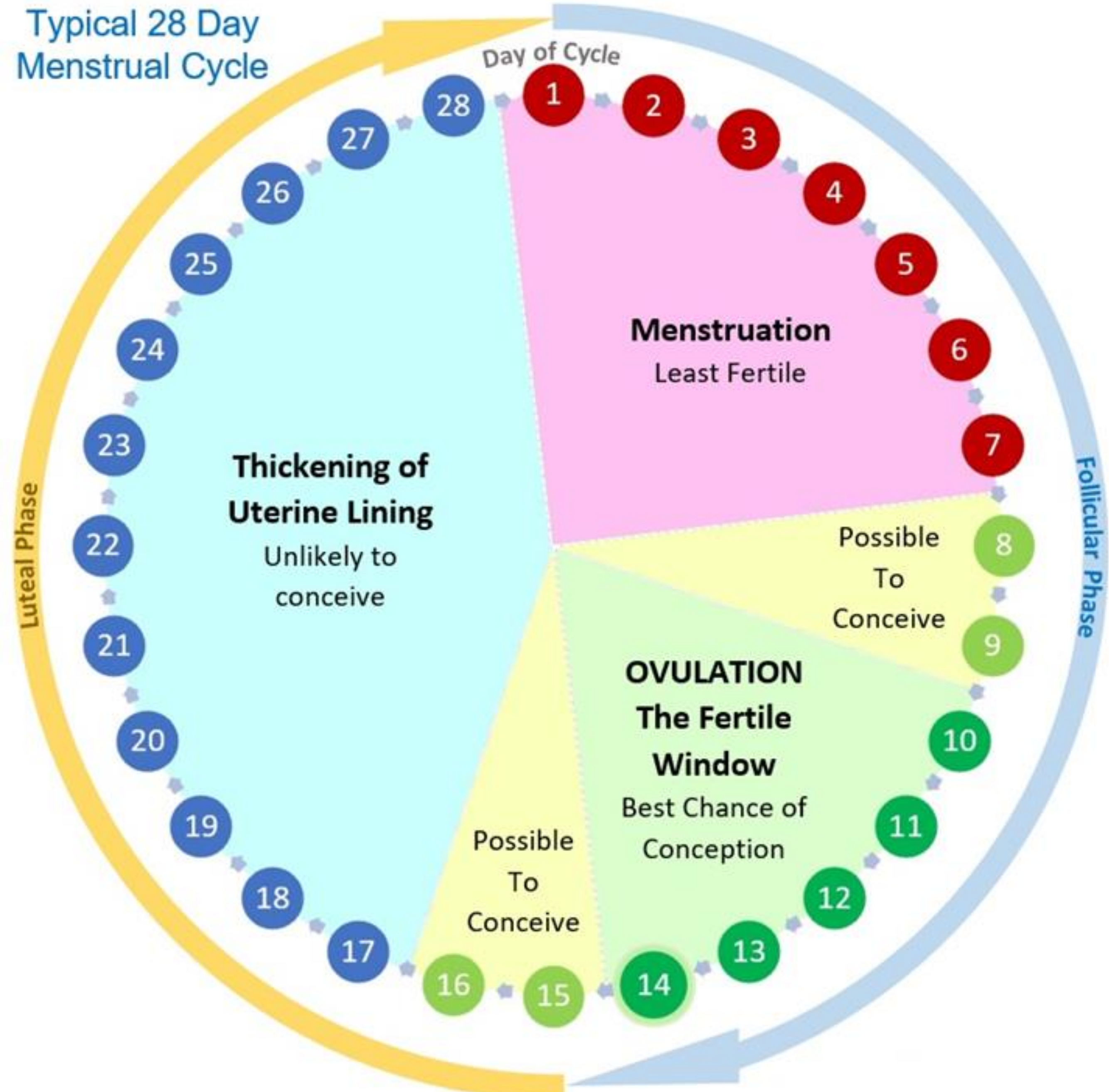
- Gestation period
  - The average duration of human pregnancy is about 9 months
- Vigorous contraction of the uterus at the end of pregnancy causes expulsion/delivery of the foetus
- This process of delivery of the foetus (childbirth) is called parturition.
- Parturition is induced by a complex neuroendocrine mechanism.
- The signals for parturition originate from the fully developed foetus and the placenta which induce mild uterine contractions called foetal ejection reflex.



- This triggers release of oxytocin from the maternal pituitary.
- Oxytocin acts on the uterine muscle and causes stronger uterine contractions, which in turn stimulates further secretion of oxytocin.
- The **stimulatory reflex** between the uterine contraction and oxytocin secretion continues resulting in stronger and stronger contractions.
- This leads to expulsion of the baby out of the uterus through the birth canal – parturition.
- Soon after the infant is delivered, the placenta is also expelled out of the uterus.
- **What do you think the doctors inject to induce delivery?**


Baby pushes against cervix, causing it to stretch
Stretching of cervix causes nerve impulses to be sent to brain
Brain stimulates posterior pituitary to release oxytocin
Oxytocin causes smooth muscle lining the uterus to contract

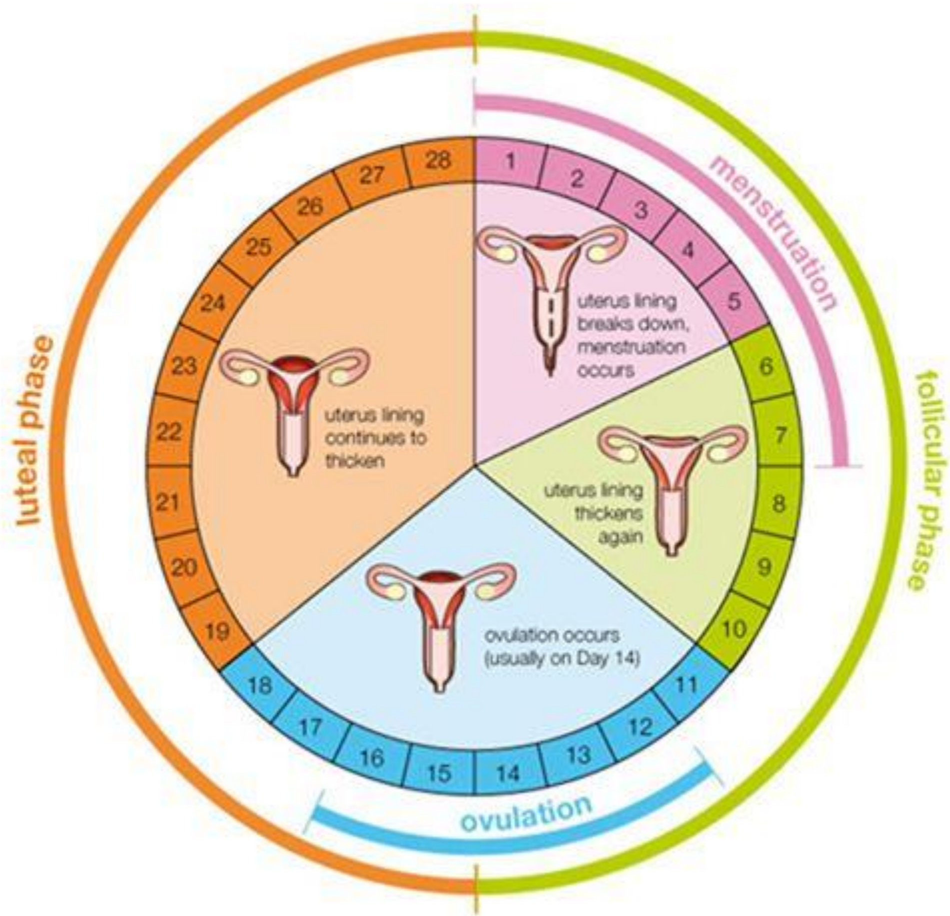
- The mammary glands of the female undergo differentiation during pregnancy and starts producing milk towards the end of pregnancy by the process called **lactation**.
- This helps the mother in feeding the new born.
- The milk produced during the initial few days of lactation is called **colostrum** which contains several antibodies absolutely essential to develop resistance for the new-born babies.
- Breast-feeding during the initial period of infant growth is recommended by doctors for bringing up a healthy baby.

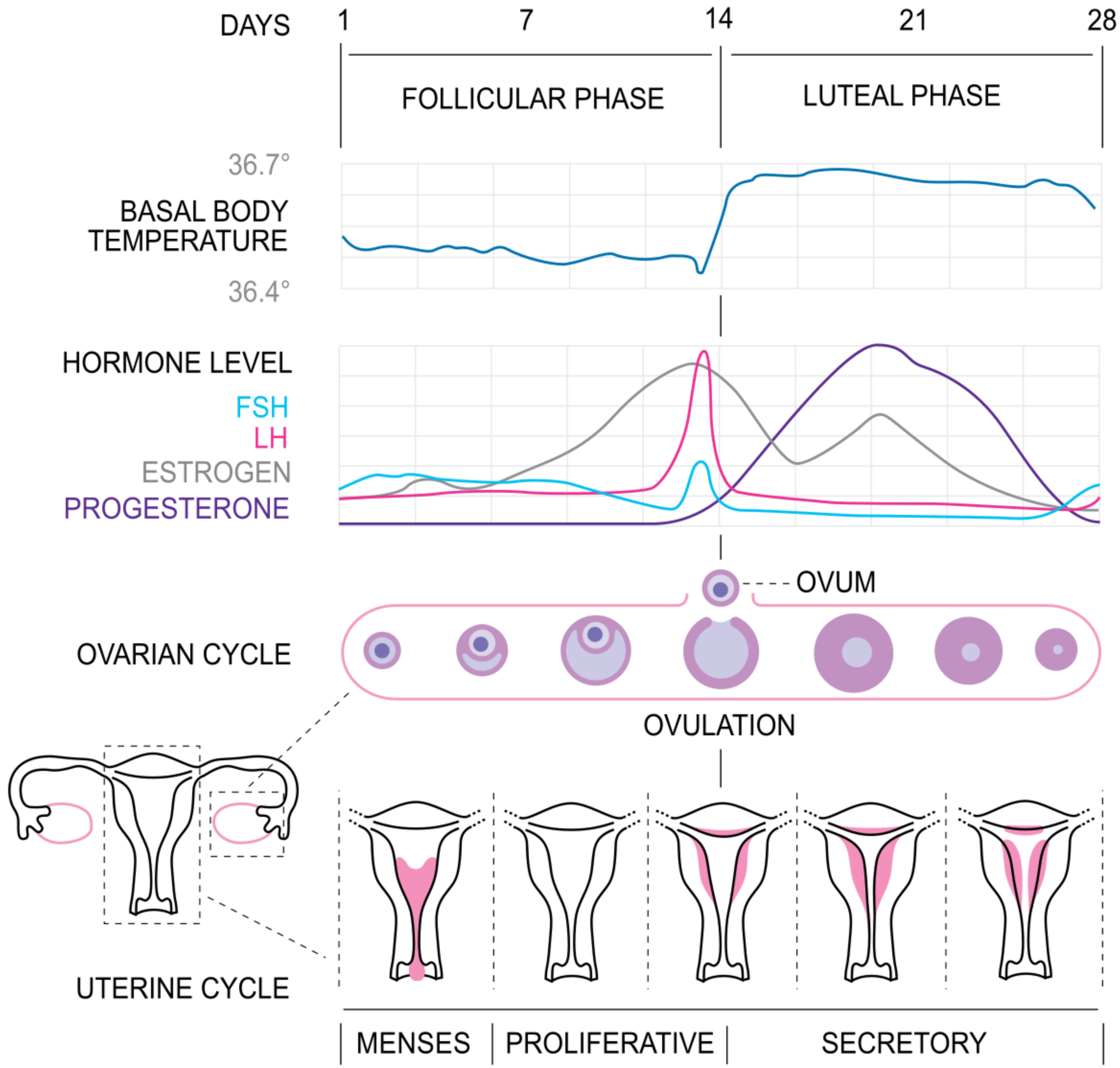


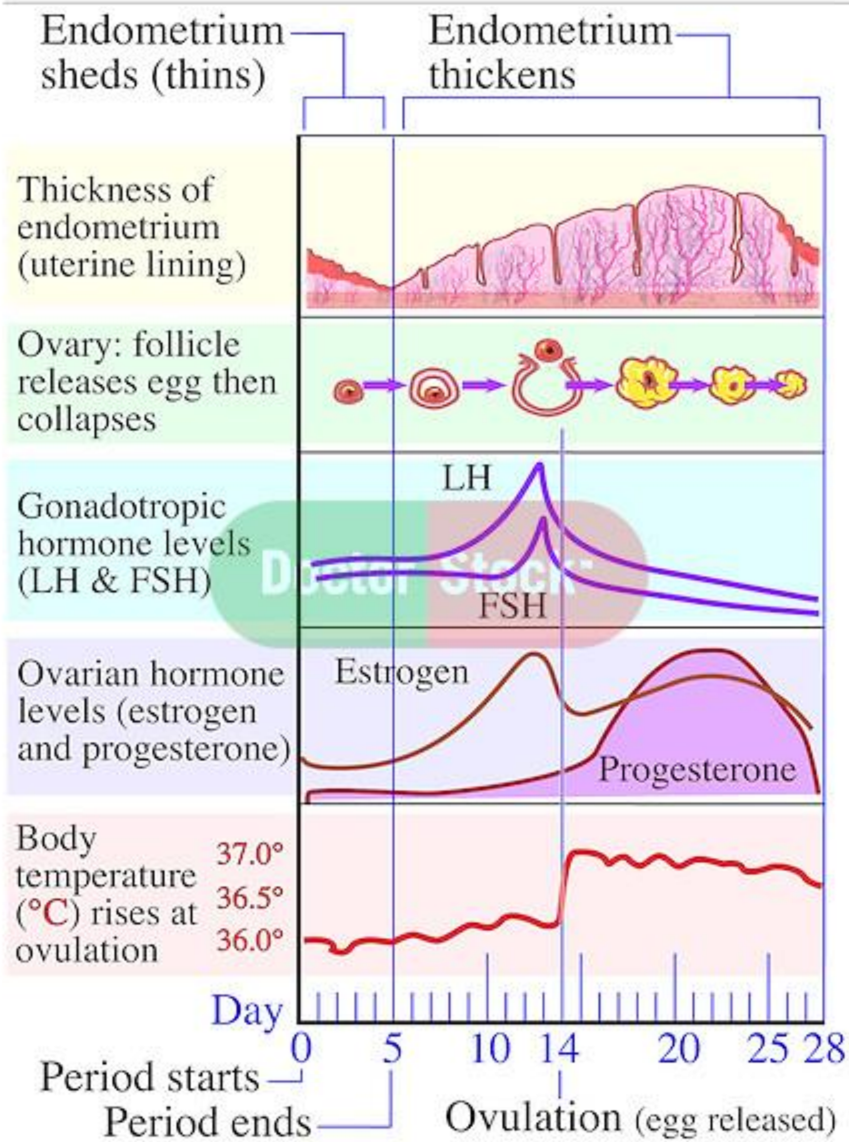
Typical 28 Day
Menstrual Cycle
Day of Cycle
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
Menstruation
Least Fertile
Possible
To
Conceive
OVULATION
The Fertile
Window
Best Chance of
Conception
Possible
To
Conceive
Thickening of
Uterine Lining
Unlikely to
conceive
Luteal Phase
Follicular Phase

Stages of Menstruation

- Stage 1 – Follicular Phase
- Stage 2 – Ovulation
- Stage 3 – Luteal Phase
- Stage 4 – Menstruation




DAYS
1
7
14
21
28
FOLLICULAR PHASE
LUTEAL PHASE
36.7°
BASAL BODY TEMPERATURE
36.4°
HORMONE LEVEL
FSH
LH
ESTROGEN
PROGESTERONE
OVUM
OVARIAN CYCLE
OVULATION
UTERINE CYCLE
MENSES
PROLIFERATIVE
SECRETORY



Endometrium sheds (thins)
Endometrium thickens
Thickness of endometrium (uterine lining)
Ovary: follicle releases egg then collapses
Gonadotropic hormone levels (LH & FSH)
LH
FSH
Ovarian hormone levels (estrogen and progesterone)
Estrogen
Progesterone
Body temperature (°C) rises at ovulation
37.0°
36.5°
36.0°
Day
0
5
10
14
20
25
28
Period starts
Period ends
Ovulation (egg released)

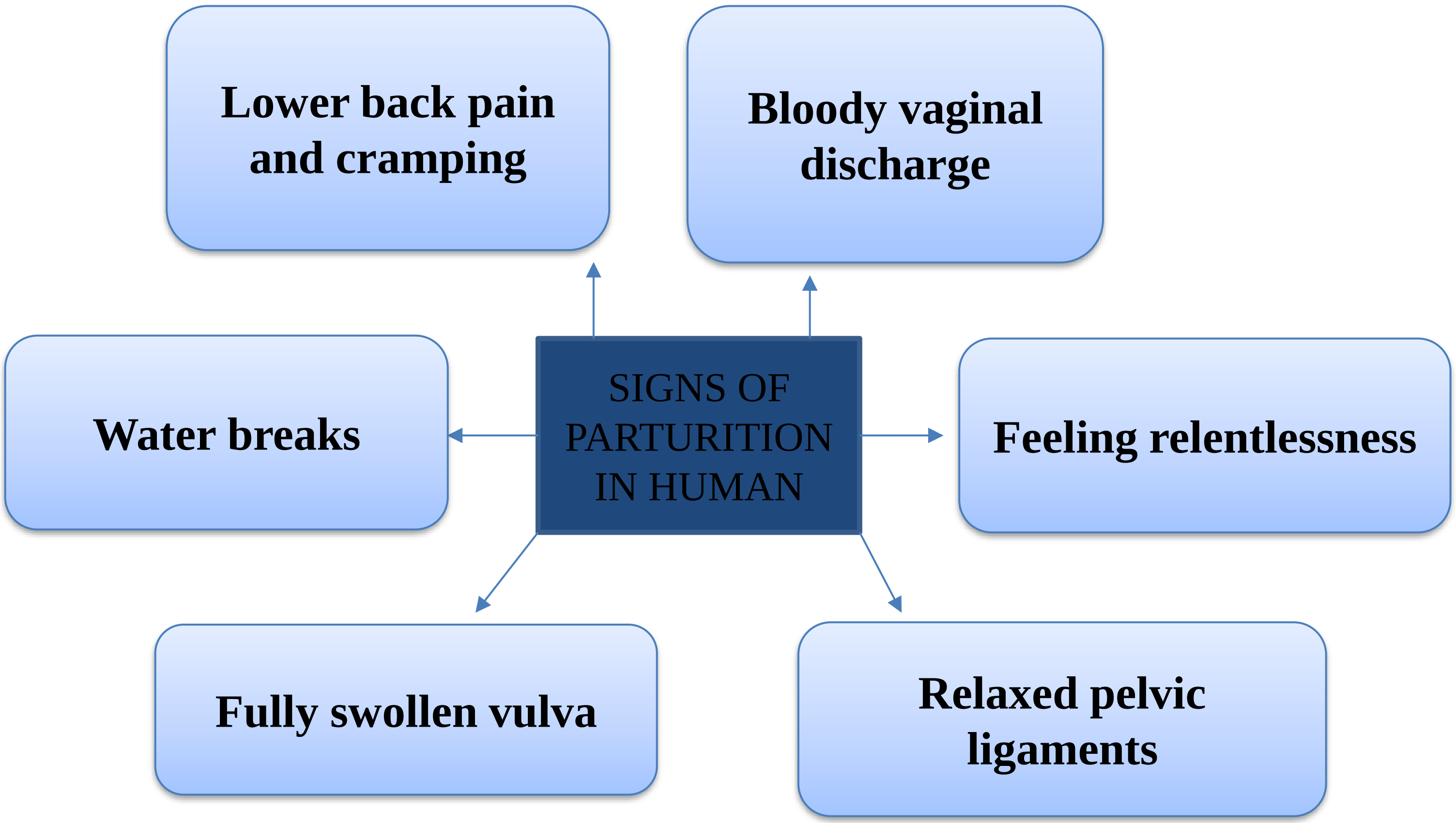
Parturition

Parturition comes from the latin word Parturire, "meaning to be in labor" or "to produce"

- Parturition or childbirth is the process of delivering the fully grown foetus on the completion of normal pregnancy period . Towards the end of pregnancy, the uterus becomes progressively more excitable , until it develops strong rhythmic contraction so that the baby is expelled.

ROLE OF PLACENTA

- The placenta is a temporary organ that connects the developing foetus via the umbilical cord to the uterine wall to allow nutrient uptake, thermo-regulation, waste elimination and gas exchange via the mothers blood supply ; to fight against internal infection ;and to produce hormone which support pregnancy.



SIGNS OF PARTURITION IN HUMAN
Lower back pain and cramping
Bloody vaginal discharge
Water breaks
Feeling relentlessness
Fully swollen vulva
Relaxed pelvic ligaments

What is labour pain?

- ✓ Labour is accompanied by localized sensation of discomfort or agony called Labour pain .
- ✓ Throughout pregnancy the uterus undergoes periodic episodes of weak and strong contraction .
- ✓ These contractions called Braxter-Hicks contractions lead to false labour.

- ✓ Parturition is a hormonal process; induced by a complex neuroendocrine mechanism.
- ✓ Signals for parturition originated from the fully developed fetus and placenta.
- ✓ This mild uterine contractions is called foetus ejection reflex / Ferguson reflex.
- ✓ It is accompanied by rise in estrogen ; progesterone ratio and increase in oxytocin receptor in uterine muscle.

OXYTOCIN=PARTURITION HORMONE

Foetal ejection reflex

(4)
Oxytocin causes smooth muscle lining of uterus to contract

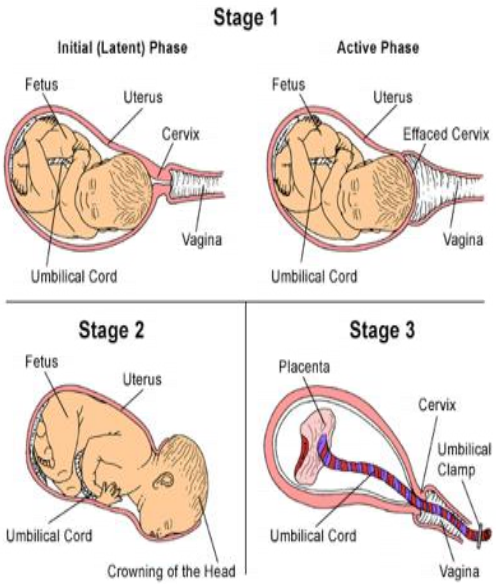
(1)
Baby pushes against cervix, causing it to stretch

(2)
Stretching of cervix cause nerve impulses to be sent to brain

(3)
Brain stimulates posterior pituitary to release oxytocin

The fully developed foetus gives signals for the uterine contractions by secreting Adrenocorticotropic hormone (ACTH) from pituitary and corticosteroids from adrenal gland.

- ✓ This triggers release of oxytocin from mothers pituitary gland ,which acts on uterine muscles of mother and causing vigorous uterine contraction.
- ✓ This leads to expulsion of the baby from the uterus.



Three stages of parturition:

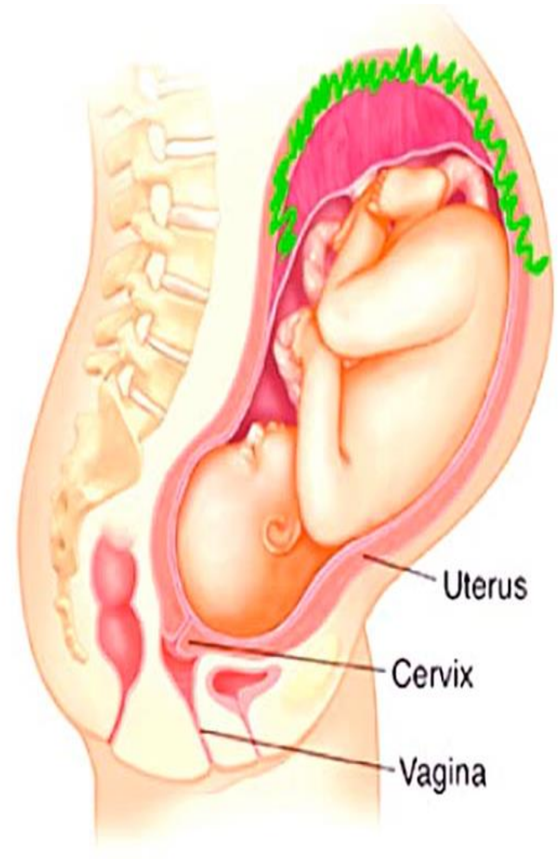
1.Dilation stage

2.Expulsion stage

3.After birth stage

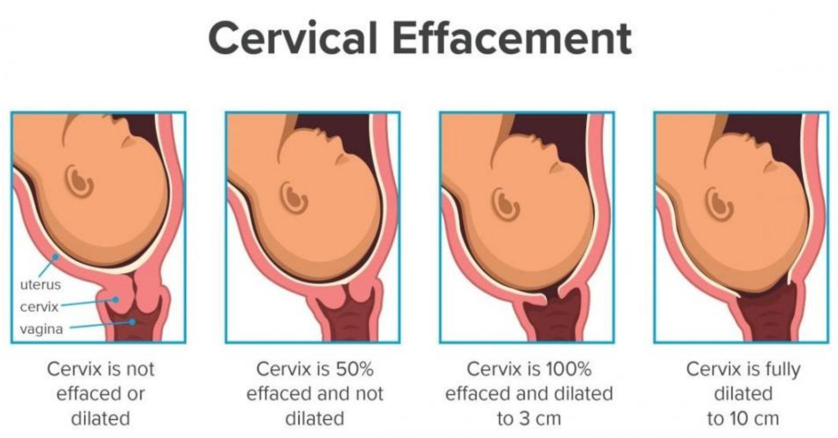
DILATION STAGE

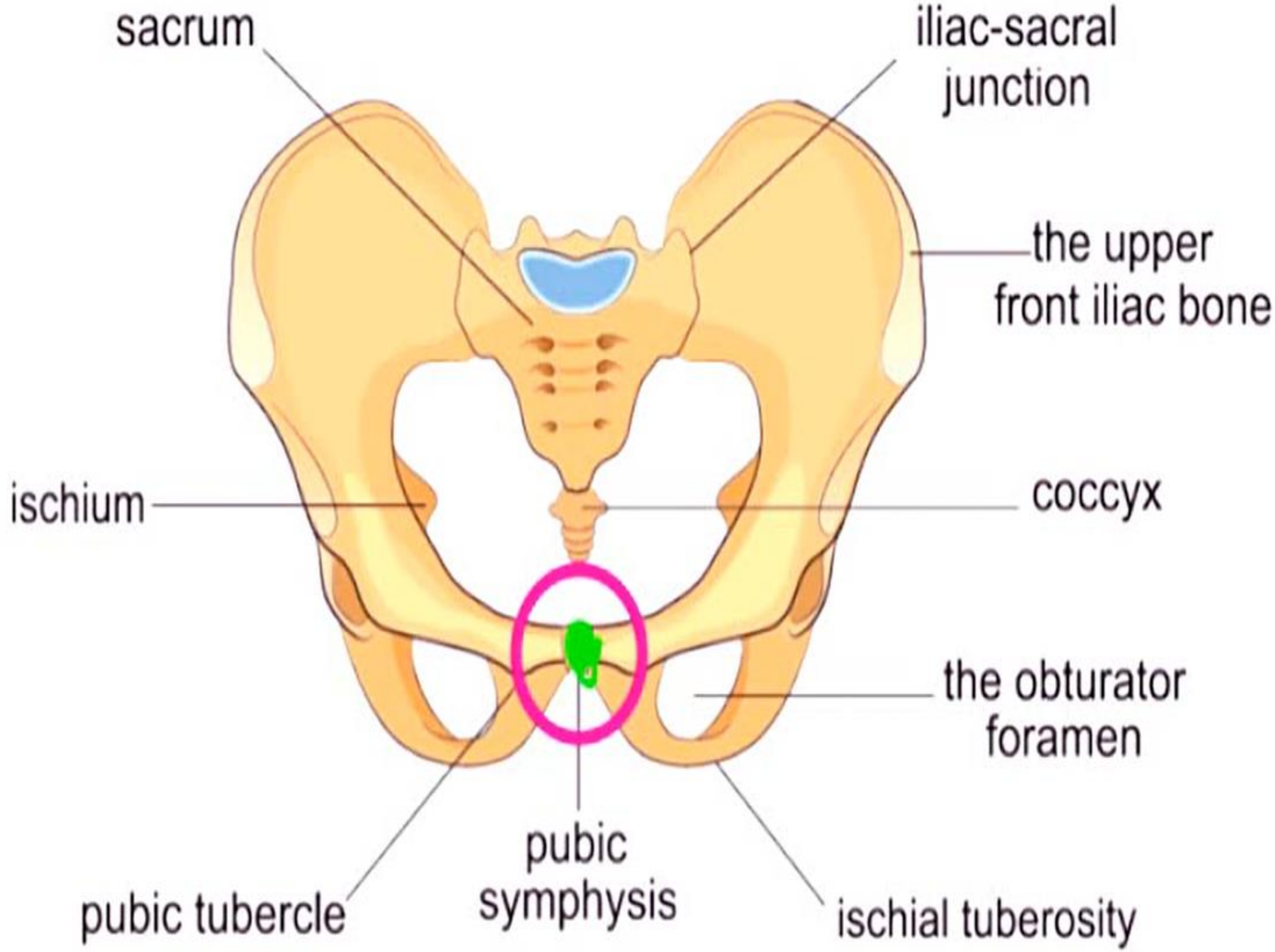
- ✓Uterine contractions begin from top , forcing the baby towards the cervix.
- ✓Concentrations are accompanied by pain cause by compression of blood vessels.
- ✓Oxytocin induced uterine contractions become stronger and stronger due to stimulatory reflex.



Dilation stages

- ✓ As the baby is pushed down in the uterus, its head comes to lie against cervix .
- ✓ Cervix gets dilated . The vagina also shows similar dilation.
- ✓ This stages last upto few hours .
- ✓ Relaxin hormone secreted by placenta and corpous luteum also promotes parturition by relaxing the pelvic joints (pubic symphysis) and by dilation of the cervix with continued powerful contractions.
- ✓ It ends in the rupturing of amniotic membrane of foetus.



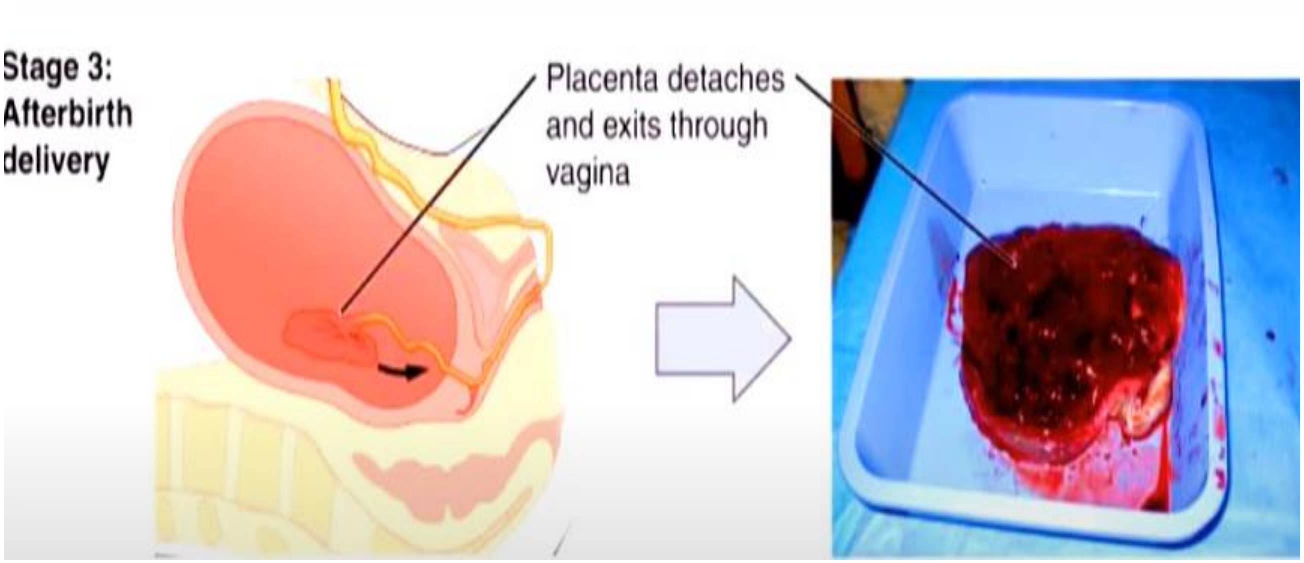

sacrum
iliac-sacral junction
the upper front iliac bone
ischium
coccyx
the obturator foramen
pubic symphysis
pubic tubercle
ischial tuberosity

2. Expulsion stages

- The uterine and abdominal contractions become stronger.
- In normal delivery ,the foetus passes out through cervix and vagina with head in forward direction (crowing of the head).
- It takes 20 to 60min.
- The umbilical cord is tied and cut off close to the baby's navel.

3.After birth

- ✓ After the delivery of the body the placenta separates from the uterus and is expelled out as “after birth” , due to severe contraction of the uterus .
- ✓ This process happens within 10 to 45 minutes of delivery.



HORMONES	FUNCTION	HYPOSECRETION	HYPERSECRETION
HUMAN CHRONIC GONODOTROPIN	• Prevents involution of corpus luteum. • Secrete large quantities of sex hormones. • Development of endometrium. • Early pregnancy discomforts	• Slow rate of rise or drop in HCG levels during 8-10 weeks-death of trophoblasts tissue. • Indicate ectotopic or non-viable intrauterine pregnancy.	• If the baseline level is higher than 5mIU/ml, doctors may order a repeat test a couple days to see if the number doubles.
ESTROGEN	Function on most reproductive & associaten organs of mother.	• Cause miscarriage in more than 50% of pregnant baboons. • Fetus die before miscarriage & fertility issues.	• Enlargement of mother uterus, mother breast. • Enlargement of female external external genitilia. • Relaxes pelvic ligament of mother.

HORMONES	FUNCTION	HYPOSECRETION	HYPERSECRETION
PROGESTERONE	• Cause decidual cells to develop in endometrium. • Decrease contractility of pregnant uterus. • Development conceptus. • To prepare mothers breasts for lactation.	• Result in miscarriage or fetal death, infertility. • May indicate ectopic pregnancy.	• Cause internal structure to increase in size such as ureters molar pregnancy. • Similar to pre-menstural syndrome such as anxiety, breast swelling, tenderness etc.
OXYTOCIN	• Stimulating the milk glands, milk ejection reflex. • Refer as cuddle hormone, can be released in response to pleasurable contact with baby, partner & during sex.	• Causing contraction to stop or slow & making labor take longer. • Resulting in excessive bleeding at the placenta site after birth. • Stop uterine contraction during the birthing process & prevent milk ejection after giving birth.	• Lead to increase in both the intensity and frequency of contraction.

HORMONES	FUNCTION	HYPOSECREATION	HYPERSECRETION
MELANOCYTE	• Melanin production. • Cell are dark, dendritic in shape.	• Lack of pigmentation	• Dark pigmentation.
RELAXIN	• Soften & lengthen ligaments. • Tissue to allow for easier passage of baby through the birth canal.	• Skin thickens& hardens. • Development of fibrosis & scarring on skin.	• Rupture of fetal membrane. • Opening of cervix.
ENDORPHINS	• Response in pains or stress. • Produced throughout the pregnancy, especially during child birth.	• Levels of endorphins will drop after delivering the baby.	
PROLACTIN	• Prevent in high concentration in amniotic fluid. • Cause breast to grow & make milk during pregnancy and after pregnancy	• Triggers the body to make milk for breastfeeding. • Who aren't pregnant, helps to regulate the menstrual cycle.	• Lacks of breast milk production after giving birth. • In these cases, hypopituitarism is often to cause.