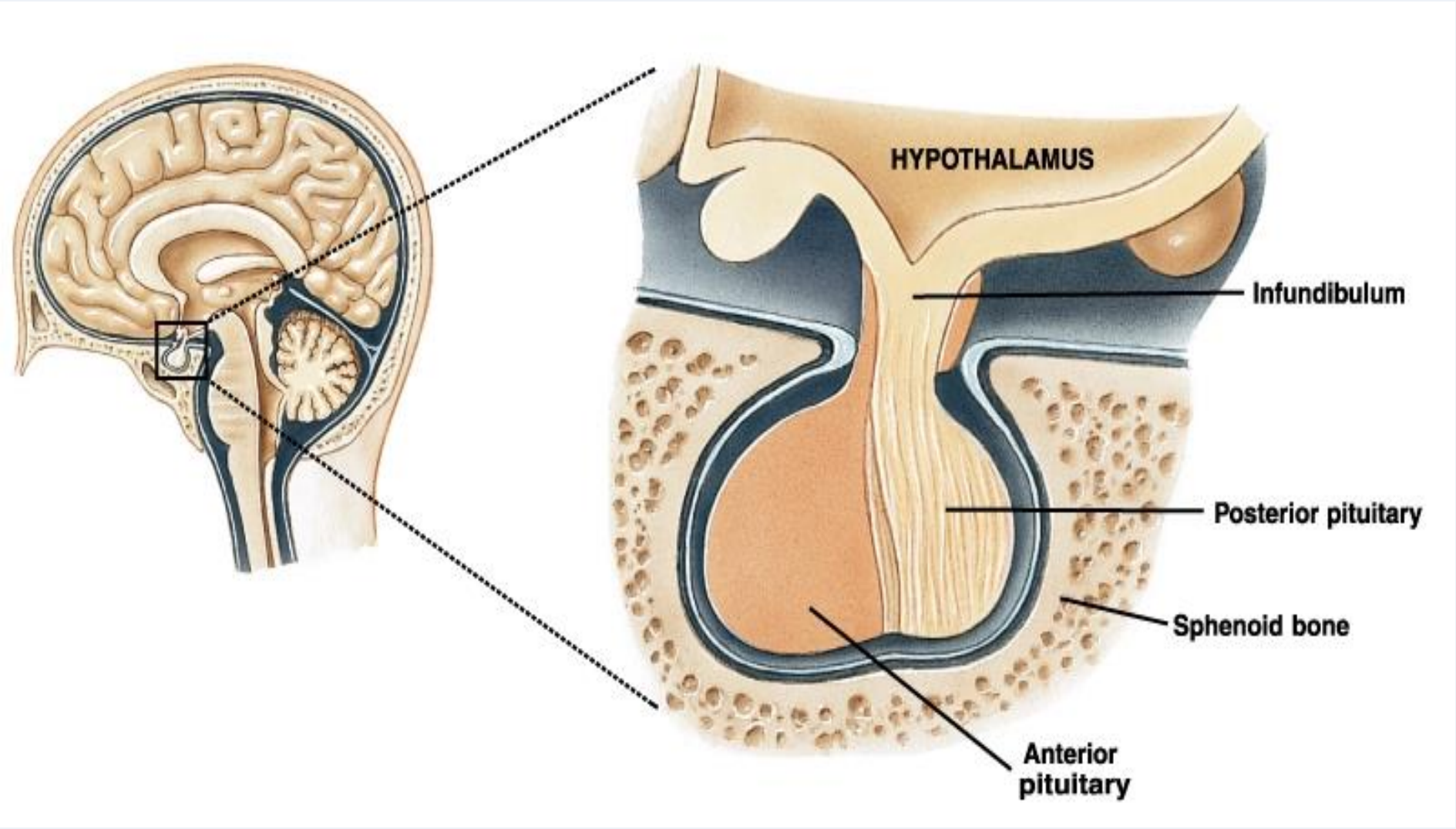
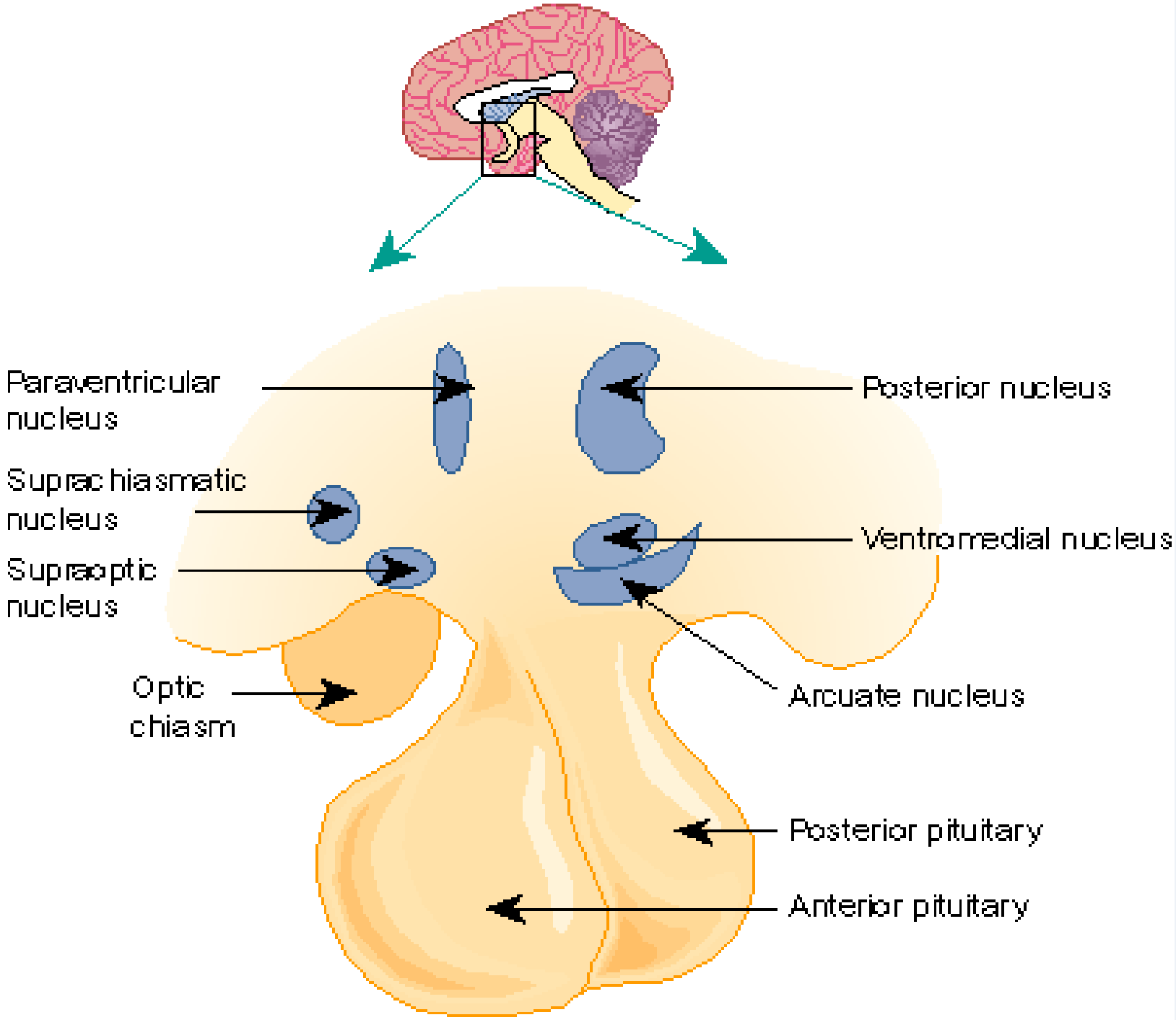
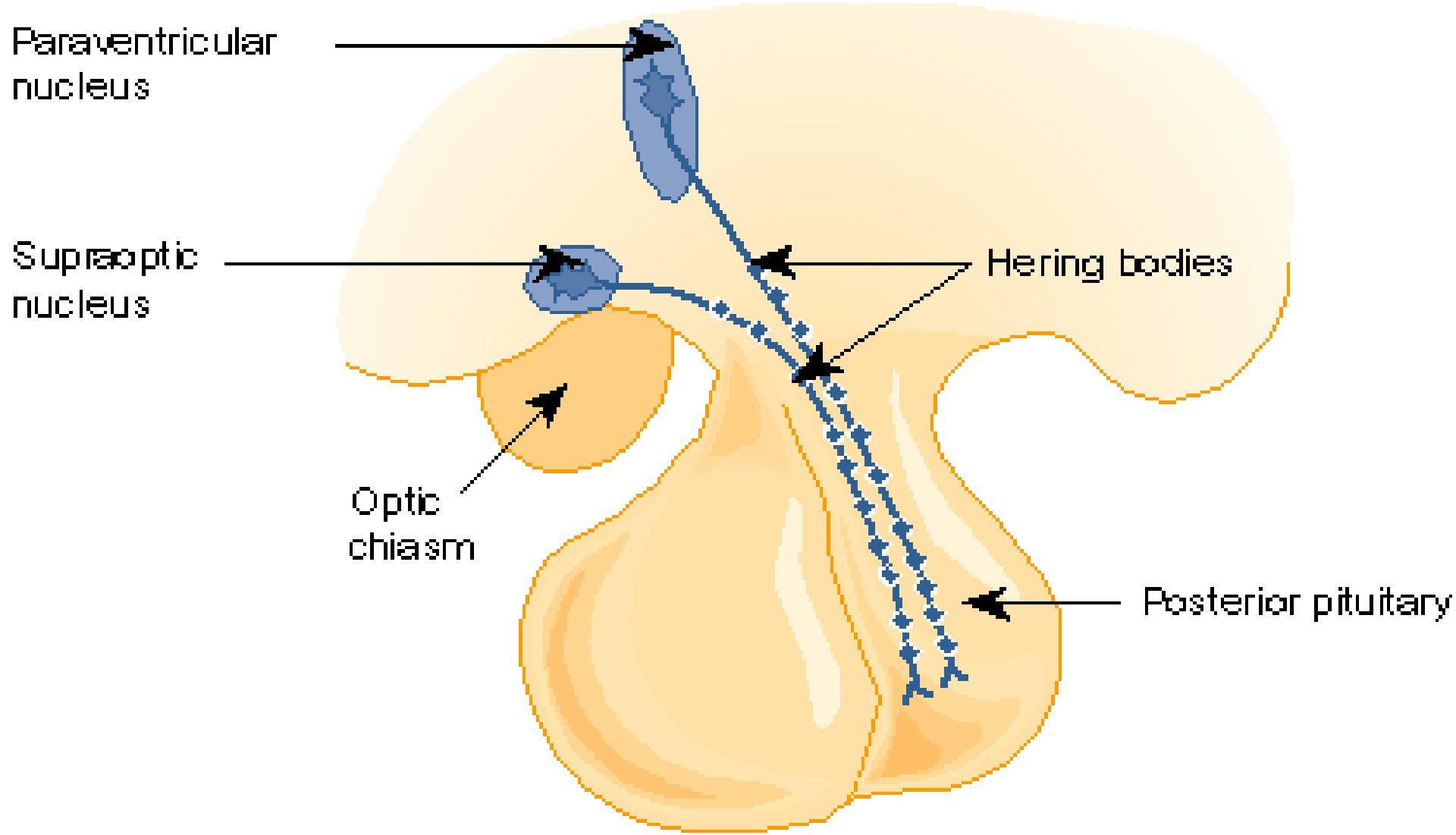
THE PITUITARY GLAND

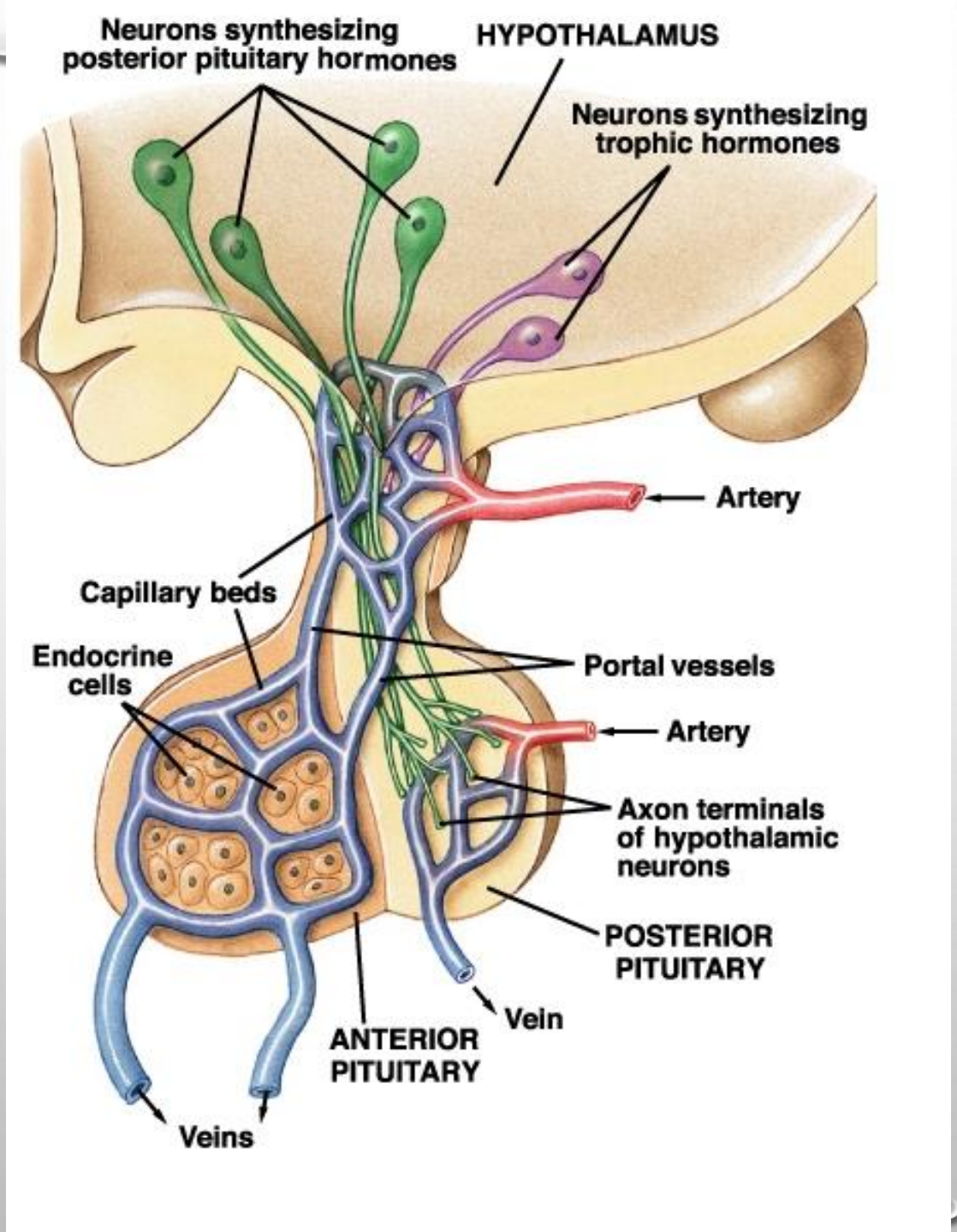
Pituitary Gland

- Size of a grape
- Hangs by a stalk from the hypothalamus
- Protected by the sphenoid bone
- Has two functional lobes
  - Anterior pituitary – glandular tissue
  - Posterior pituitary – nervous tissue


HYPOTHALAMUS
Infundibulum
Posterior pituitary
Sphenoid bone
Anterior pituitary

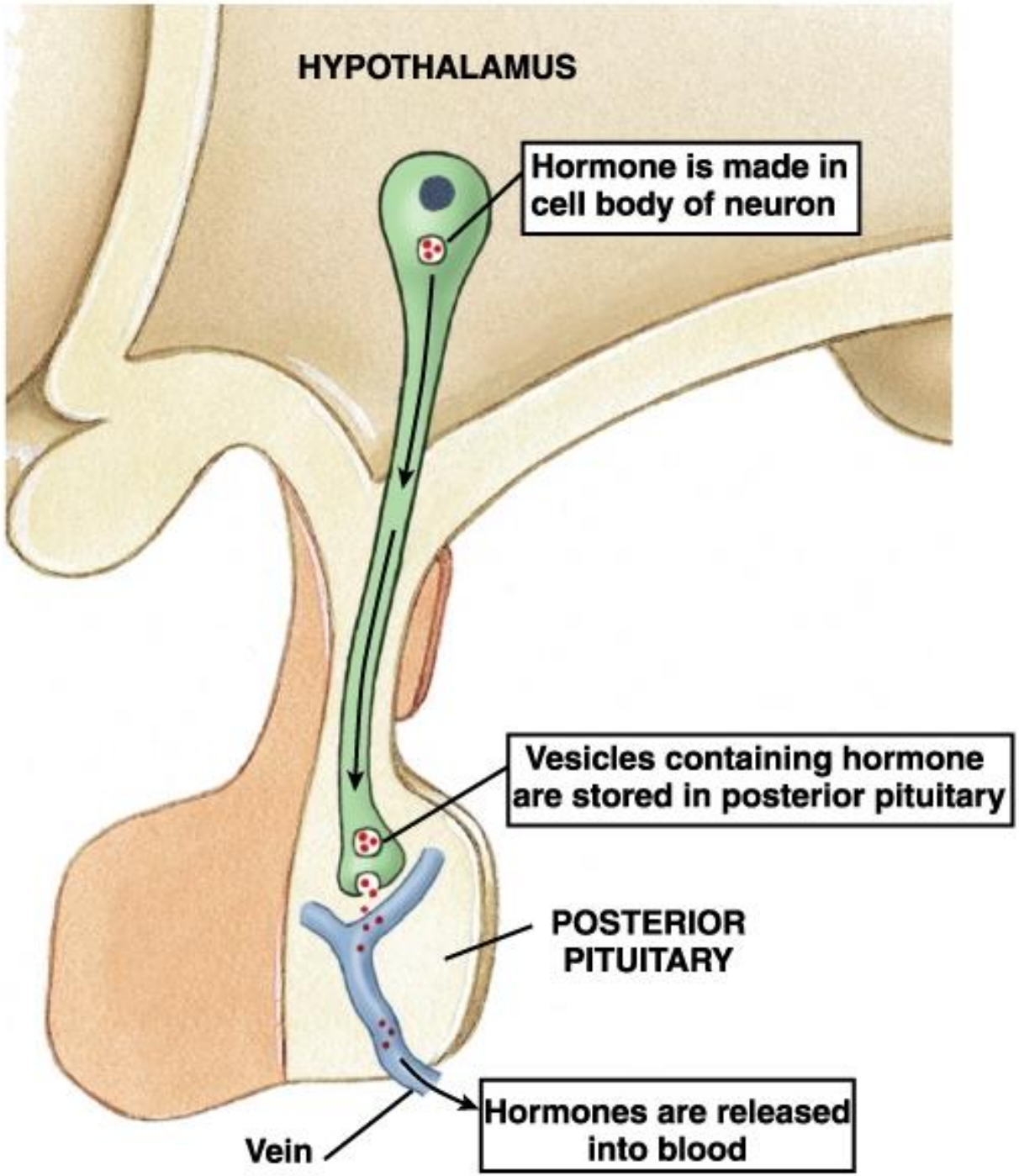

Paraventricular nucleus
Posterior nucleus
Suprachiasmatic nucleus
Ventromedial nucleus
Supraoptic nucleus
Optic chiasm
Arcuate nucleus
Posterior pituitary
Anterior pituitary

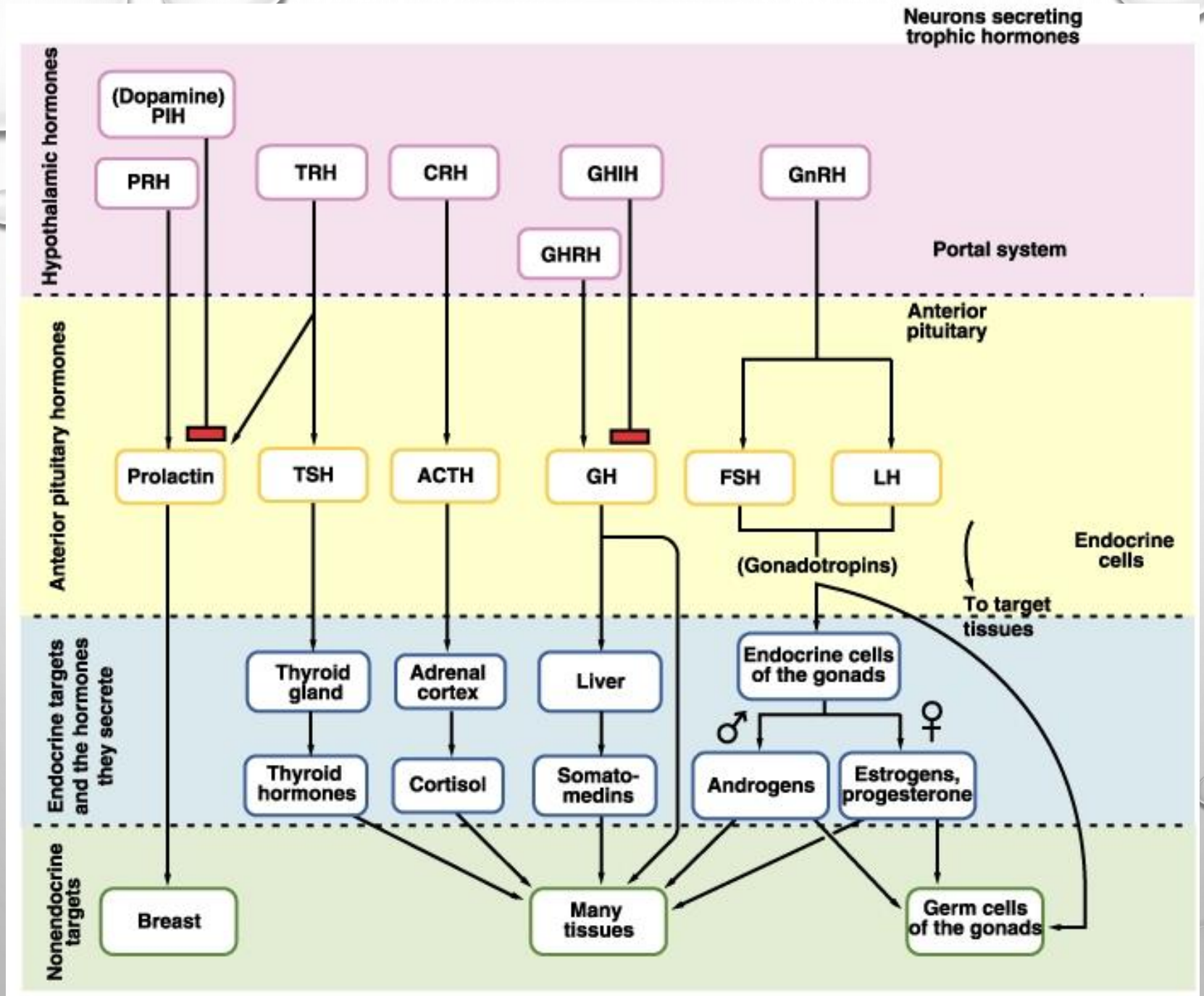

Paraventricular nucleus
Supraoptic nucleus
Hering bodies
Optic chiasm
Posterior pituitary


Neurons synthesizing posterior pituitary hormones
HYPOTHALAMUS
Neurons synthesizing trophic hormones
Artery
Capillary beds
Endocrine cells
Portal vessels
Artery
Axon terminals of hypothalamic neurons
POSTERIOR PITUITARY
Vein
ANTERIOR PITUITARY
Veins

HYPOTHALAMIC-HYPOPHYSEAL PORTAL SYSTEM

- Vessels pass through stalk of pituitary from hypothalamus to anterior pituitary
- Carry hypothalamic regulatory hormones


HYPOTHALAMUS
Hormone is made in cell body of neuron
Vesicles containing hormone are stored in posterior pituitary
POSTERIOR PITUITARY
Hormones are released into blood
Vein


Neurons secreting trophic hormones
Hypothalamic hormones
(Dopamine) PIH
PRH
TRH
CRH
GHIH
GHRH
GnRH
Portal system
Anterior pituitary
Anterior pituitary hormones
Prolactin
TSH
ACTH
GH
FSH
LH
(Gonadotropins)
Endocrine cells
To target tissues
Endocrine targets and the hormones they secrete
Thyroid gland
Adrenal cortex
Liver
Endocrine cells of the gonads
♂
♀
Thyroid hormones
Cortisol
Somato-medins
Androgens
Estrogens, progesterone
Nonendocrine targets
Breast
Many tissues
Germ cells of the gonads

Hormones of the Posterior Pituitary

- Oxytocin
  - Stimulates contractions of the uterus during labor
  - Causes milk ejection
- Antidiuretic hormone (ADH)
  - Can inhibit urine production
  - In large amounts, causes vasoconstriction leading to increased blood pressure (vasopressin)

VASOPRESSIN (ADH)

Action

- Antidiuretic effect
- Vasoconstrictor effect (in high conc.)

The antidiuretic action is caused by the synthesis of many protein water channels in the lumenal membrane of DT and CT leading to conc. Urine ,decrease urine volume and decrease osmotic pressure of all body fluids .

REGULATION OF ADH SECRETION

1.Osmotic stimuli (285 mosm\liter)

2.Volume effect :

A- low pressure recep.

Great veins and atria

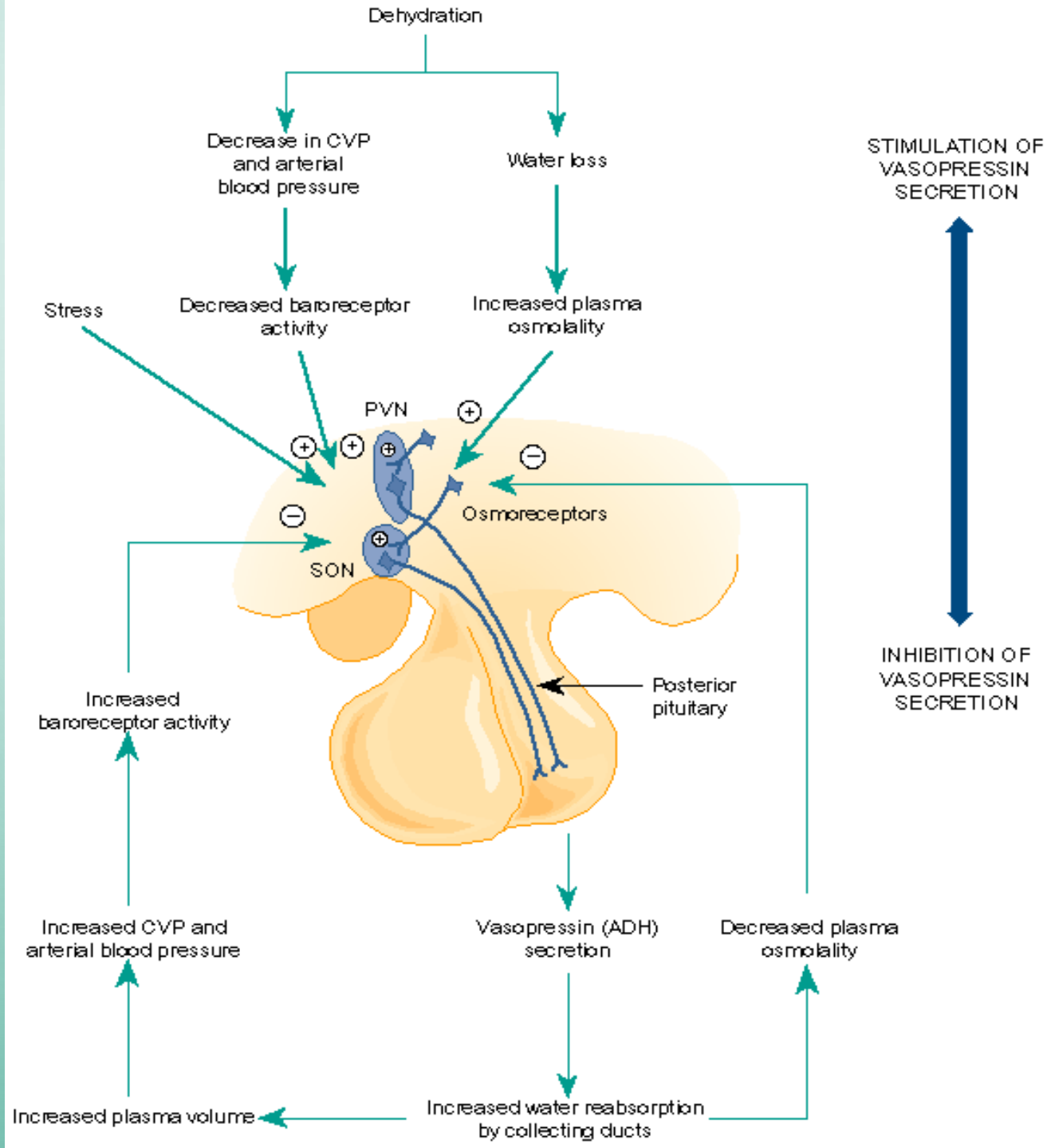
B-high pressure recep.

Carotid sinus & aortic arch

3-other stimuli :

Pain ,nausea ,stress ↑

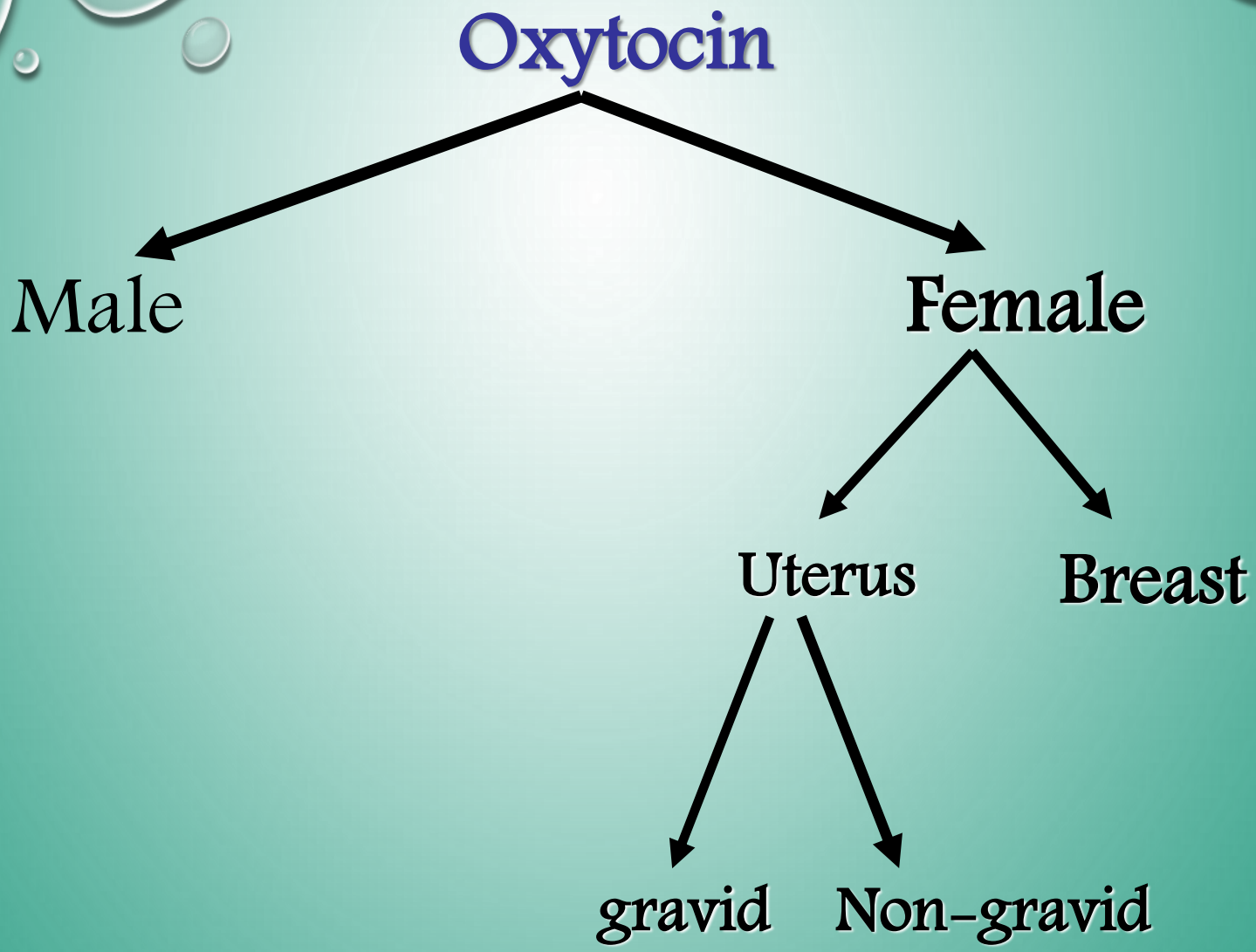
Alcohol ↓



DIABETES INSIPIDUS (PITUITARY DIABETES)

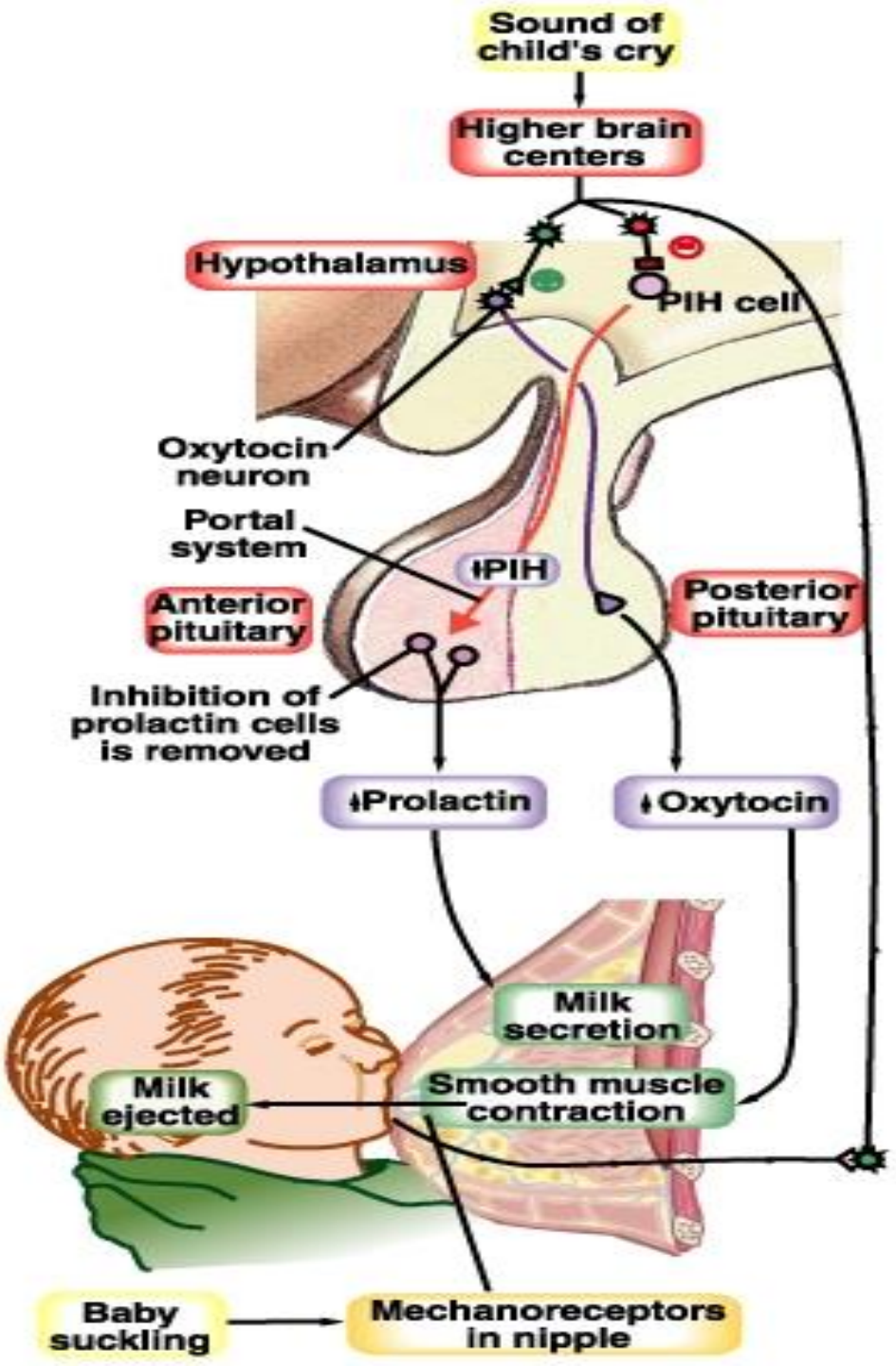
- DECREASED ANTIDIURETIC HORMONE (ADH)
- SIGNS/SYMPTOMS
  - POLYURIA
  - EXTREME THIRST
  - DEHYDRATION
- DX: OSMOLALITY

Test	DI	Normal
Serum Sodium	>145 meq/L	135-145 meql/L
Plasma Osmolality	>295 mOsm	278-209 mOsm
Urine Osmolality	<300 mOsm	50-1200 mOsm
U/P osmol ratio	<1	3-4
Urine output	> 2.5 L/d	~2.5 L/d

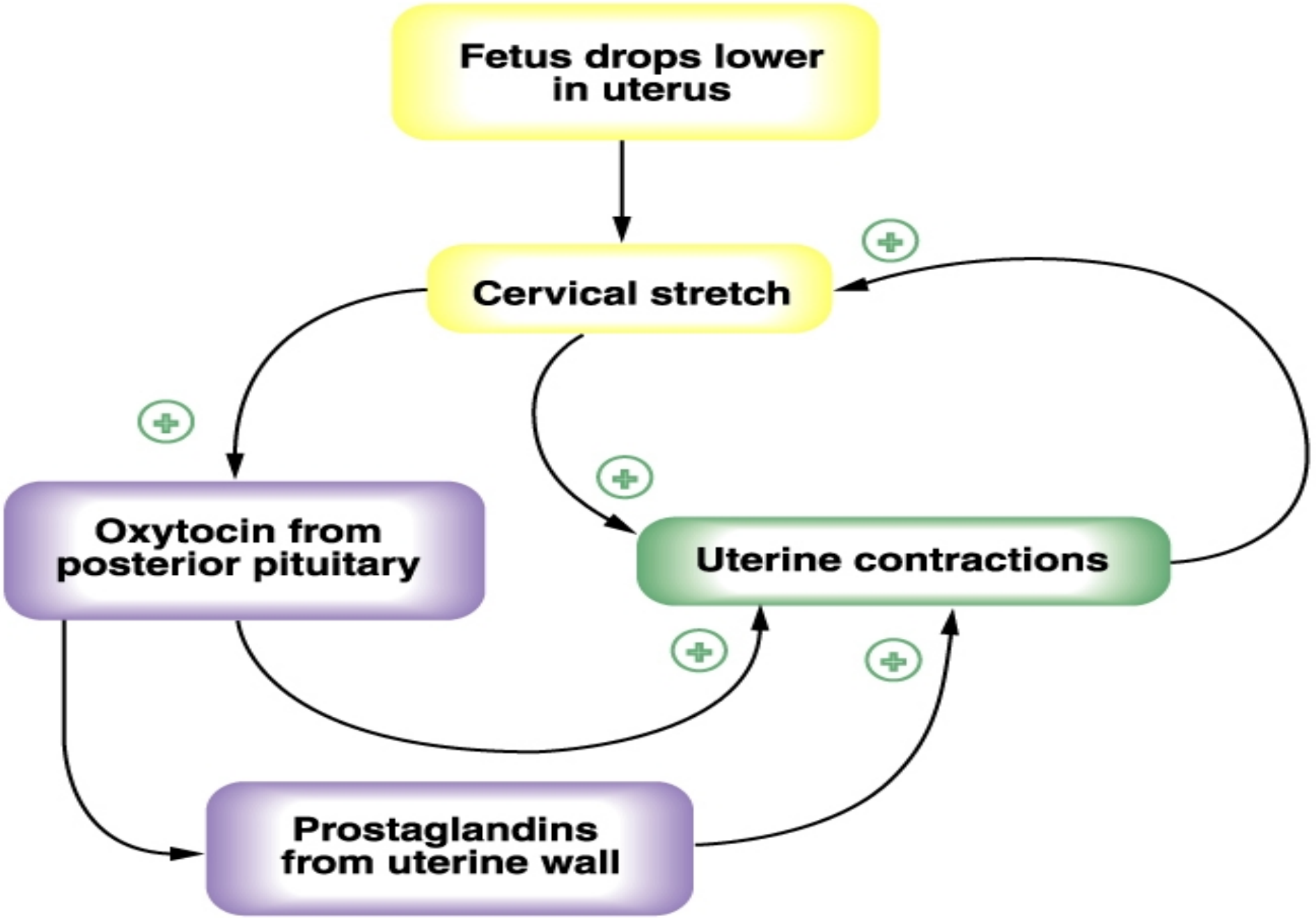

Oxytocin
Male
Female
Uterus
Breast
gravid
Non-gravid

Oxytocin

(milk ejection reflex)

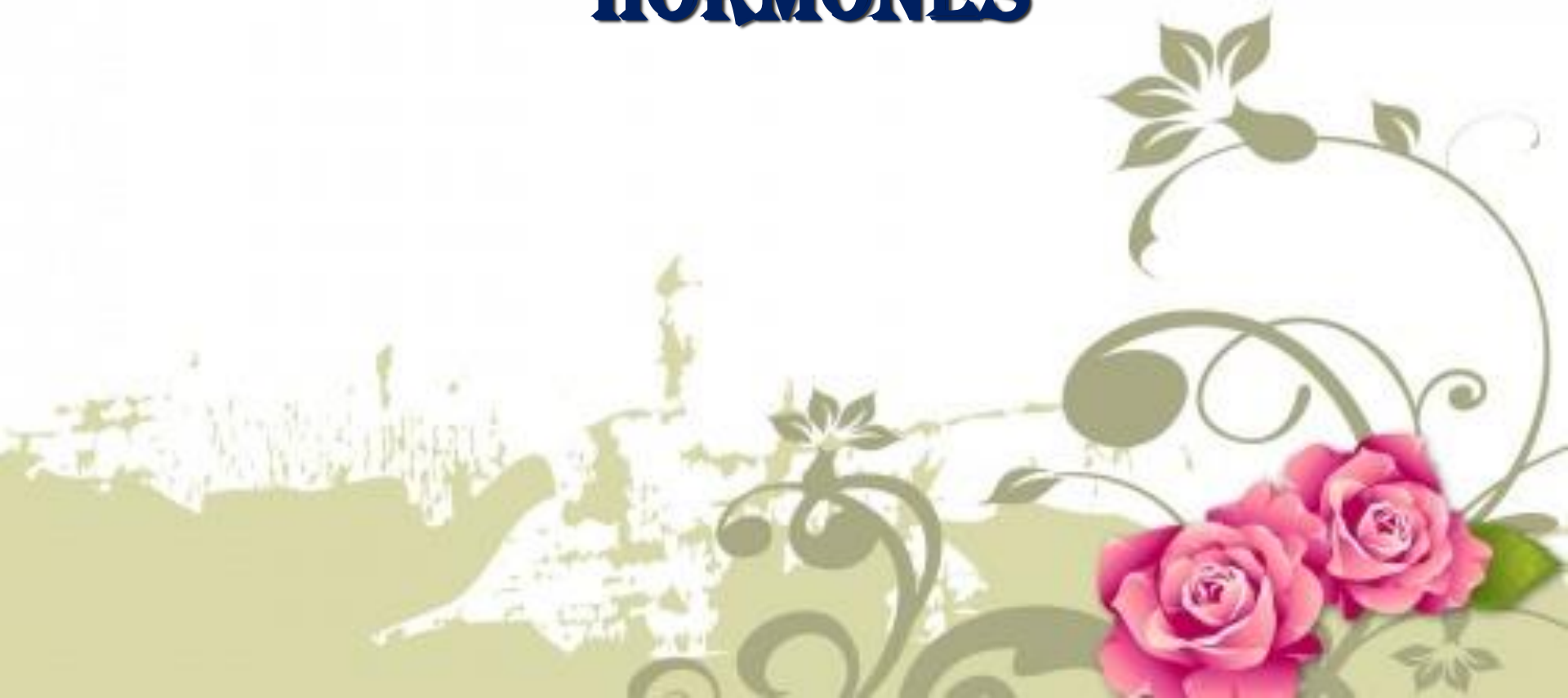


Oxytocin On gravid uterus



MSH

MELANINE STIMULATING HORMONES



MSH

- The melanocyte-stimulating hormone (MSH), melanin is synthesized from Tyrosin via Dopa and Dopaquinon.
- MSH stimulates melanocytes for the synthesis of black pigment, melanin, which is responsible for the dark colour of the skin.
- Because of the similarity of the chemical structure, ACTH has considerable MSH activity.

MSH

- MSH is produced from the intermediate lobe (rudimentary in human).
- Treatment with MSH accelerates melanin synthesis and causes detectable darkening of the skin of humans in 24 hours.

PIGMENT ABNORMALITIES IN HUMANS

- **Abnormal pallor :** is a hallmark for hypopituitarism. Hyperpigmentation occurs due to adrenal insufficiency due to primary adrenal disease and not secondary to pituitary disease as the pituitary must be intact for pigmentation to occur.
- **Albinism :** is congenital inability to synthesize melanin.

ALBINISM

ALBINISM

VITIIIGO

- Patchy loss of melanin which is progressive and develops after birth, occur due to genetic defect in the migration of pigment cells precursor from neural crest to the skin.

VITIIIGO

ANTERIOR PITUITARY LOBE

- **Anterior pituitary**: connected to the hypothalamus by hypothalmoanterior pituitary portal vessels.

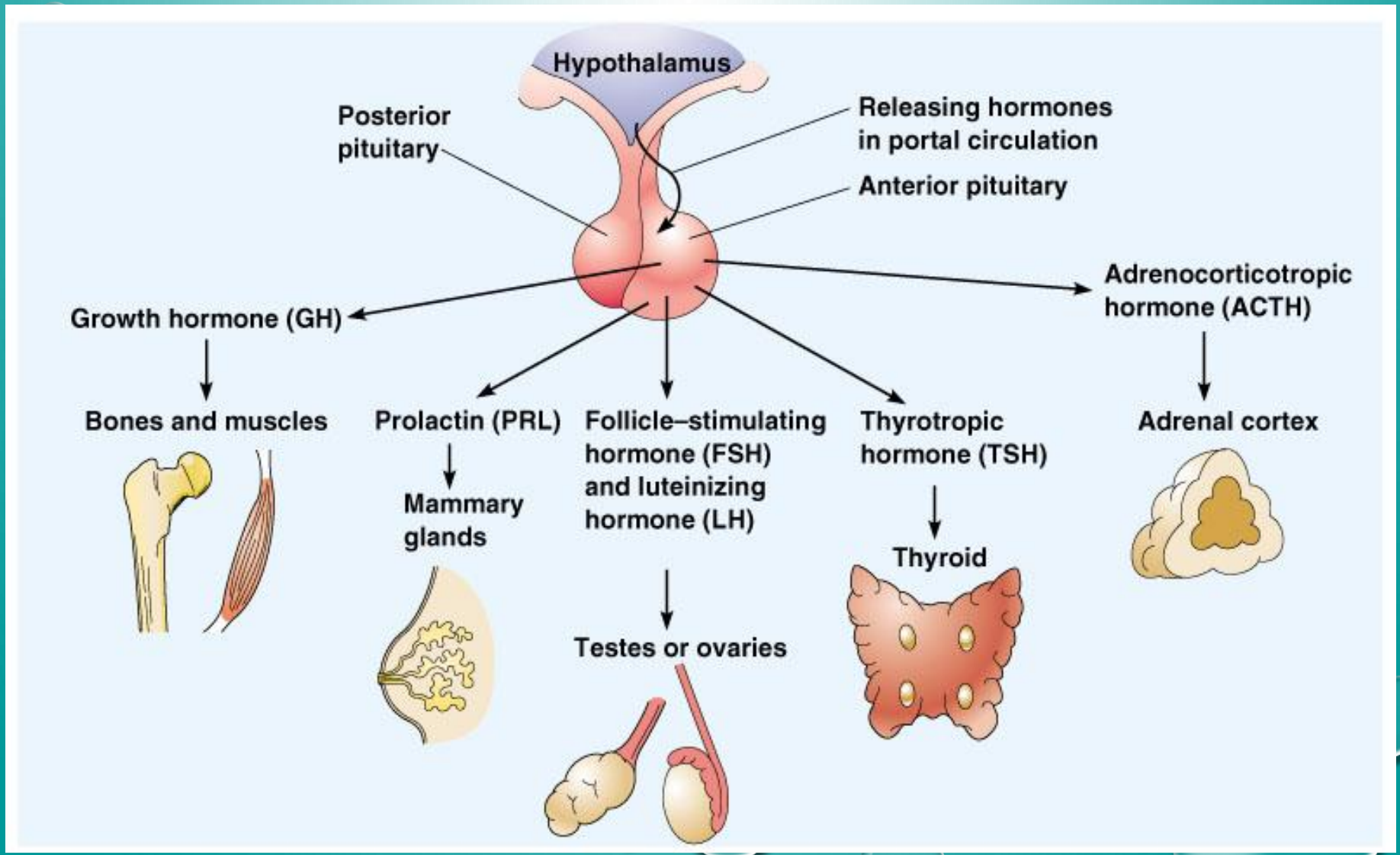
The anterior pituitary produces six peptide hormones:

- Adrenocorticotropic hormone (ACTH) from agranular chromophobe
- Prolactin from acidophils granular chromophobe cells,
- Growth hormone (GH) from acidophils granular chromophobe cells,
- Thyroid stimulating hormone (TSH) from basophil granular chromophobe cells,
- Follicle-stimulating hormone (FSH) from basophil granular chromophobe cells,
- Luteinizing hormone (LH) from basophil granular chromophobe cells.

Hormones of the Anterior Pituitary

- **Six anterior pituitary hormones**
  - Two affect non-endocrine targets
  - Four stimulate other endocrine glands (tropic hormones)
- **Characteristics of all anterior pituitary hormones**
  - Proteins (or peptides)
  - Act through second-messenger systems
  - Regulated by hormonal stimuli, mostly negative feedback

HORMONES OF THE ANTERIOR PITUITARY



Functions of other anterior pituitary hormones

- **Prolactin (PRL)**
  - Stimulates and maintains milk production following childbirth
  - Function in males is unknown
- **Adrenocorticotropic hormone (ACTH)**

  Regulates endocrine activity of the adrenal cortex
- **Thyroid-stimulating hormone (TSH)**

  Influences growth and activity of the thyroid

Functions of Other Anterior Pituitary Hormones

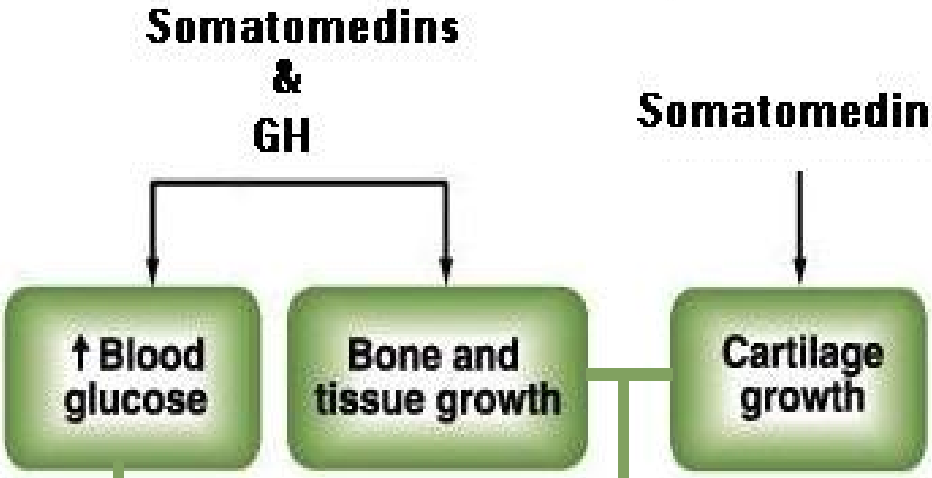
- Gonadotropic hormones
  - Regulate hormonal activity of the gonads
    - Follicle-stimulating hormone (FSH)
      - Stimulates follicle development in ovaries
      - Stimulates sperm development in testes

GROWTH HORMONE (GH)

GROWTH HORMONE (GH)

- General metabolic hormone
- Major effects are directed to growth of skeletal muscles and long bones
- Causes amino acids to be built into proteins
- Causes fats to be broken down for a source of energy

ACTION OF GH



By increases the size and mitotic activity of the cells of most of tissues,
anabolic effect on protein,
increases the length of long bones by: Increases deposition of protein by chondroeytes and osteogenic cells, Increases osteoblasts activity and inhibits osteoclastic activity.

By enhances glycogen deposition in the cells,
diminishes glucose uptake by cells,
increases hepatic glucose output &
decreases the number and affinity of insulin receptors (Pituitary Diabetes).

- **EFFECTS ON FAT :**

Increase FFA and ketone bodies

Decreases cholesterol

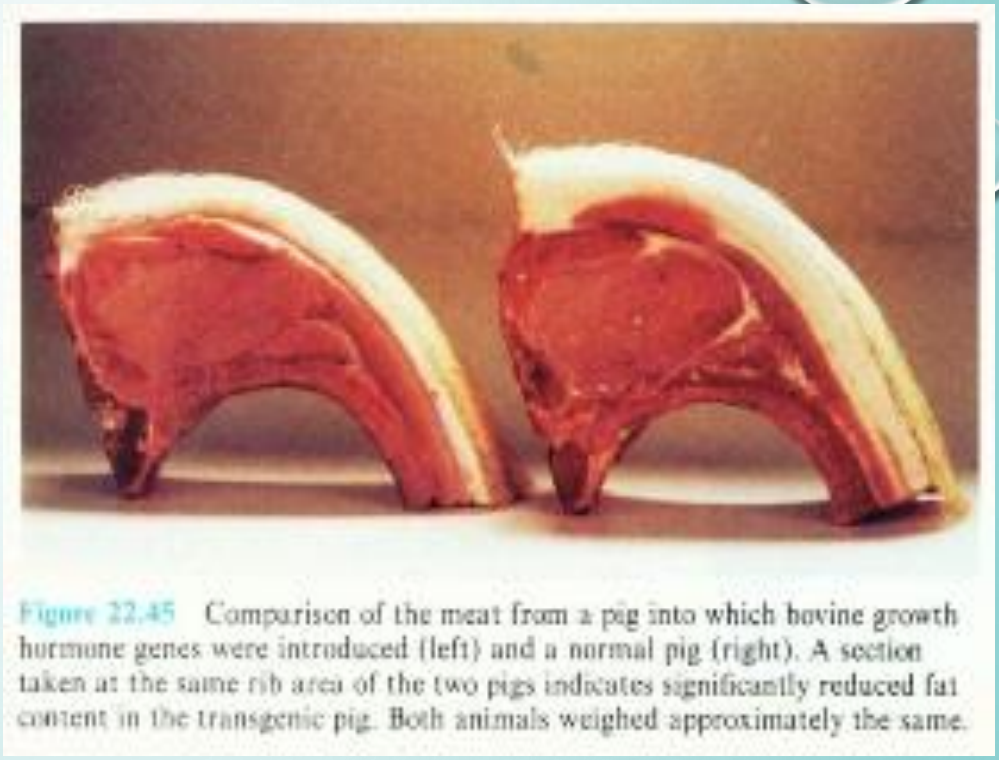


Figure 22.45 Comparison of the meat from a pig into which bovine growth hormone genes were introduced (left) and a normal pig (right). A section taken at the same rib area of the two pigs indicates significantly reduced fat content in the transgenic pig. Both animals weighed approximately the same.

- **EFFECT ON ELECTROLYTES**

Increase GIT absorption of Ca and P

Decrease execration of Na and K

- **GROWTH HORMONE AFFECTS THE LIVER TO PRODUCE SOMATOMEDINS WHICH ARE :-**

1. IGF-I AND IGF-II .
2. RELAXINS

Control of GH secretion :

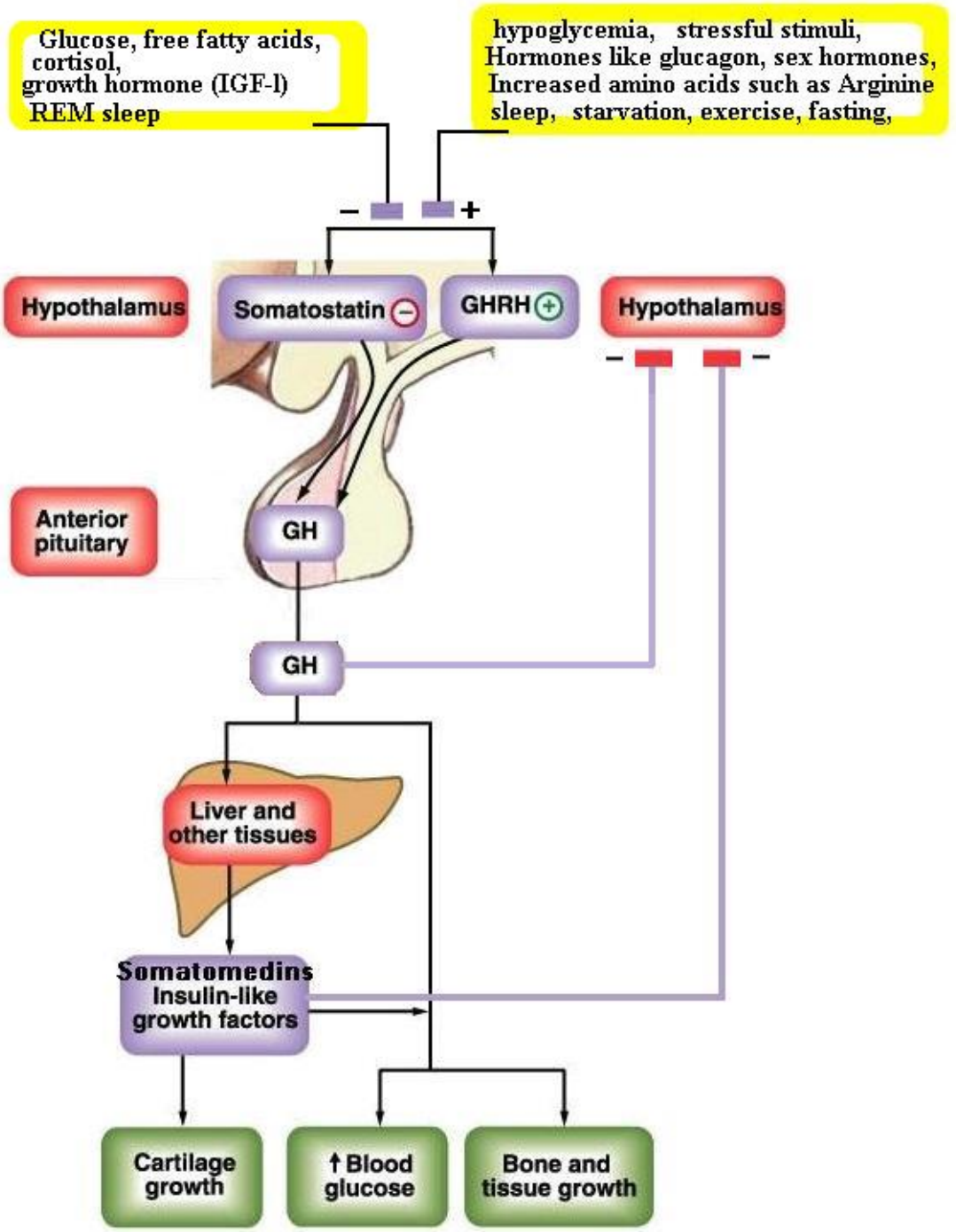
1- GHRH & GHIH

2- IGF1 (FEEDBACK CONTROL)

↑ HYPOGLYCEMIA , STRESSFULL STIMLI , GLUCAGON, SEX HORMONE , ARGININE , GOING TO SLEEP

↓ GLUCOSE ,FATTY ACIDS, CORTISOL, IGF1 AND REM SLEEP

FEEDBACK CONTROL OF GROWTH HORMONE



PHYSIOLOGY OF GROWTH

Affected by:

- Genetic factors
- Nutrition
- Hormonal effect

❖ GH

❖ Sex hormones (through anabolic effect, through increase GH & IGF-1 secretion and sensitivity)

❖ Thyroid hormones (through permissive effect)

❖ Adrenocortical hormones (through permissive effect)

❖ Insulin

7.43 Pituitary dwarfism with growth hormone deficiency. This 10-year-old girl was 1.02 m tall, far below the 5th percentile for her age.

7.44, 7.45 Turner's syndrome is a genetic disorder with the chromosome configuration 45XO. This produces a phenotypic female with gonadal dysgenesis and primary amenorrhoea, retarded growth and short stature, webbed neck, absent breast development, an increased carrying angle at the elbow (cubitus valgus), congenital heart disease (especially coarctation of the aorta) and bilateral 'streak' gonads. These patients have a normal IQ. Noonan's syndrome has broadly similar appearances, but occurs in phenotypic males.

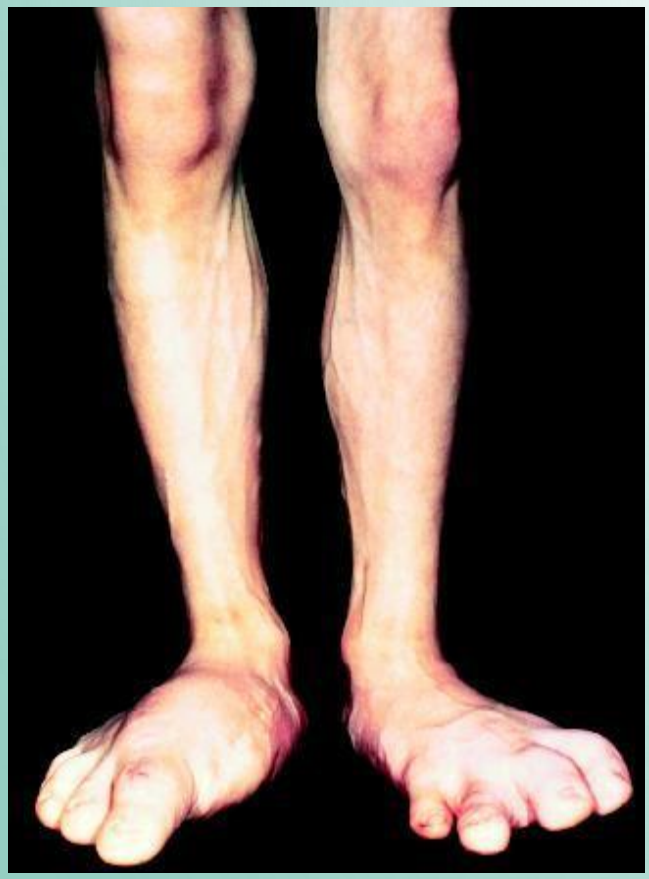
7.46, 7.47 Achondroplasia in infancy and adult life. Note the short stature, large head, prominent forehead and disproportion between the size of the body and limbs. Seventy to eighty per cent of cases of achondroplasia represent new mutations.

Marfan's syndrome is an autosomal dominant condition, in which there is tall stature, and reduced upper segment to lower segment ratio, long fingers and toes, and often a high arched palate. It is commonly associated with laxity of the joints, dislocation of the lens in the eye, dissecting aneurysm of the aorta, aortic regurgitation and a floppy mitral valve. The length of the fingers can be demonstrated by the 'wrist sign', in which the patient can encircle his wrist with the opposite thumb and fifth finger. The ability to do this is strongly suggestive of Marfan's syndrome.

GIGANTISM

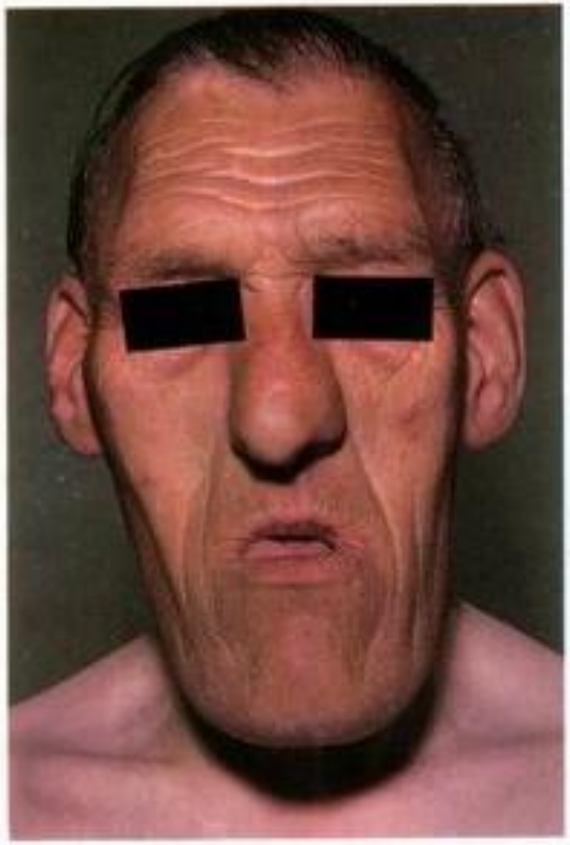
- Hyper secretion of HGH during an individual's growing years.

ACROMEGALY

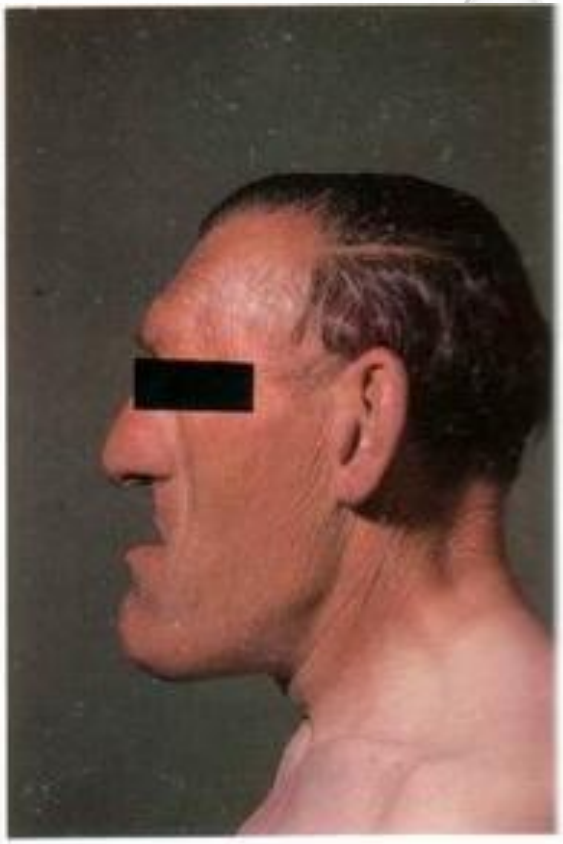


- Hypersecretion of HGH during adulthood
- Disfiguring by overgrowth of bones & soft tissues

7.12 Mild gigantism resulting from the presence of increased growth hormone levels before epiphyseal fusion. The patient was 15 when this photograph was taken, and he reached a final height of 2.02 m.



7.13 The characteristic facial features of acromegaly include thickening of the soft tissues and skin, enlargement of the nose and the supraorbital ridges, acne, thickening of the lips and prognathism.



7.14 Acromegaly. Profile of the patient shown in **7.13,** showing prognathism, thickening of the soft tissues and skin, and increased prominence of the supraorbital ridge and nose.

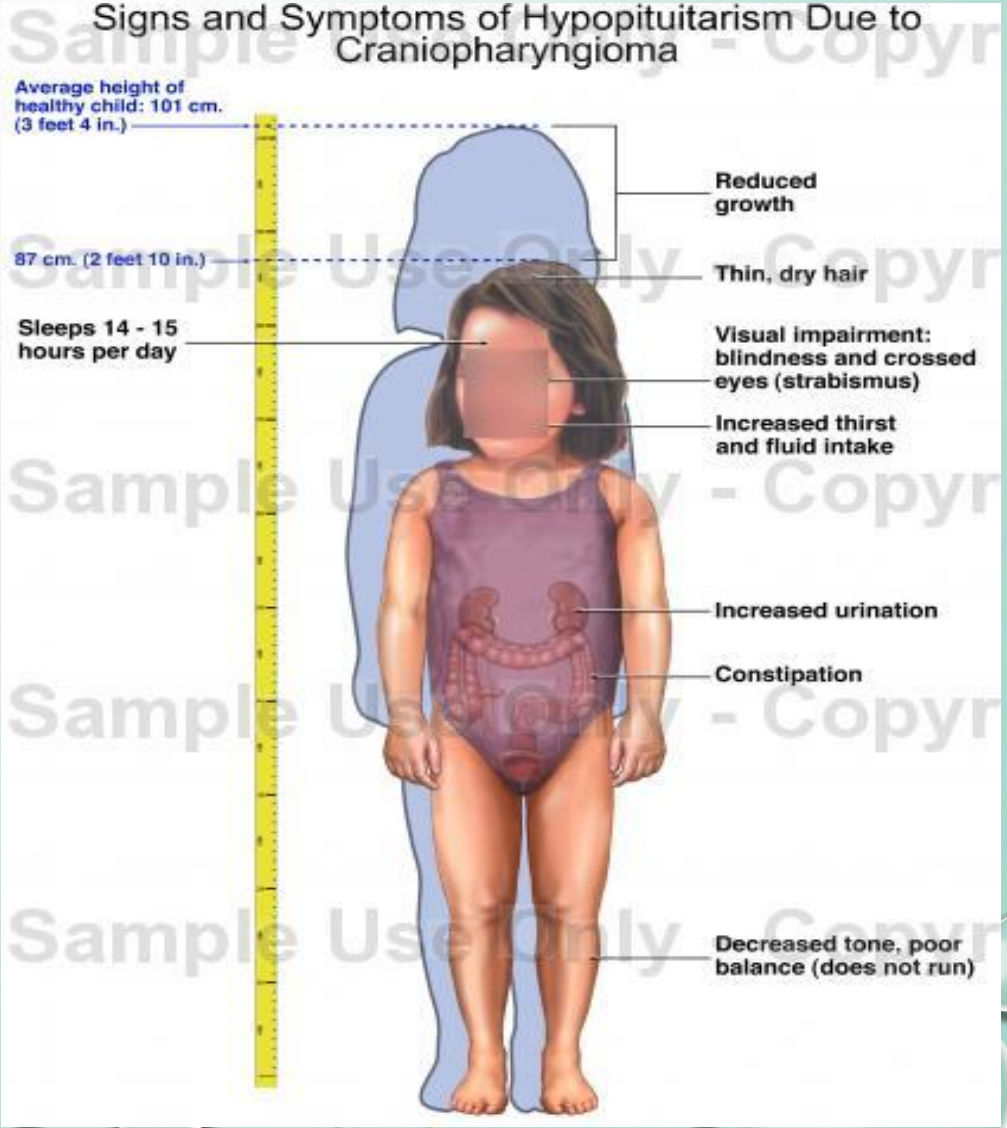
7.15 Malocclusion and separation of the teeth are commonly associated with the development of prognathism in acromegaly.

7.16 Spade-like hands are often an obvious abnormality in acromegaly. Compare the acromegalic hands on the right with the normal hand on the left. Overgrowth of the soft tissues may also cause compression of the median nerve at the wrist (carpal tunnel syndrome —*see* p. 515).

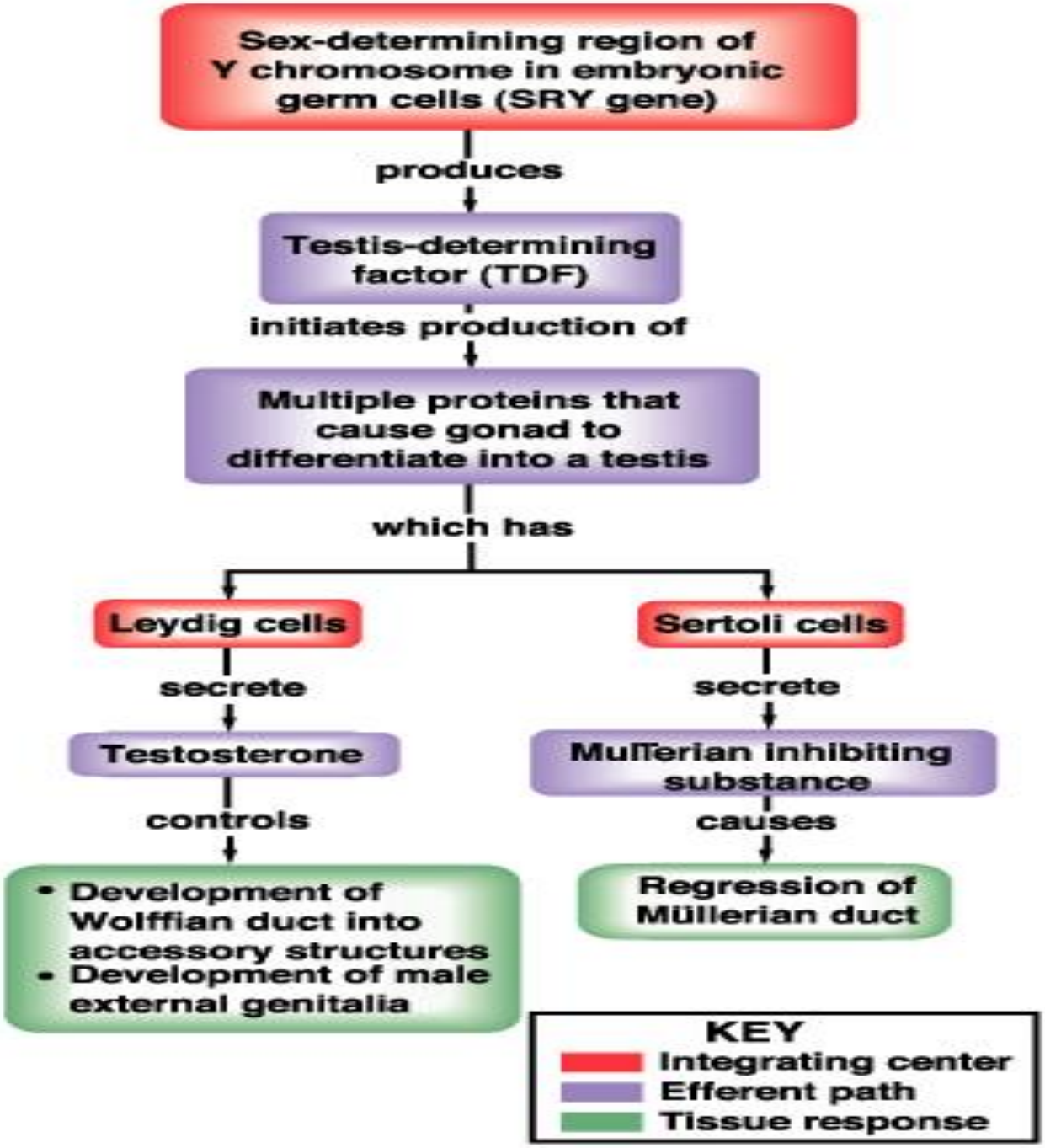
7.18 Enlargement of the tongue in acromegaly is obvious in this patient, who also shows other facial signs, and has classic changes in her hands.

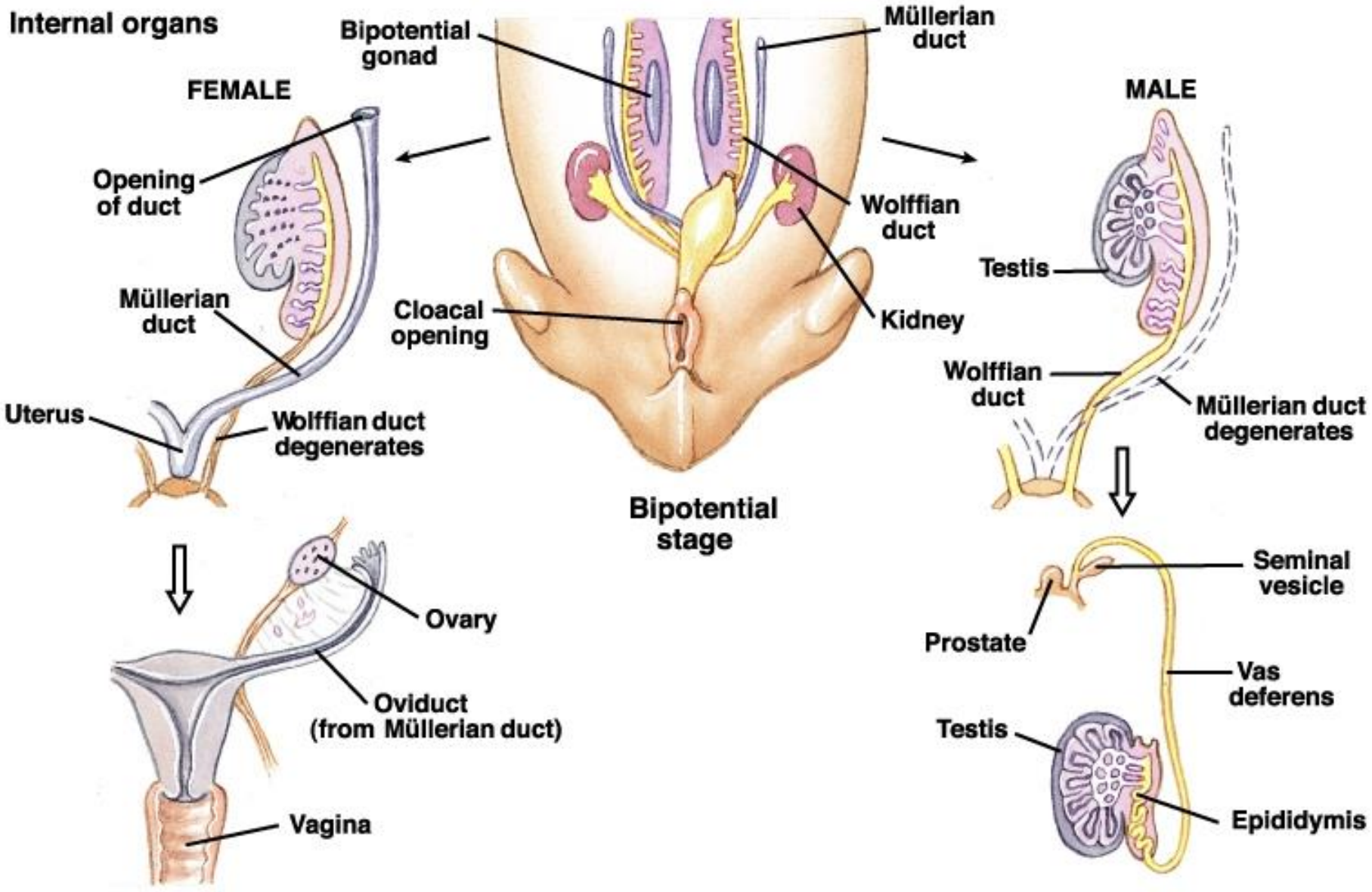
HYPOPITUITARISM

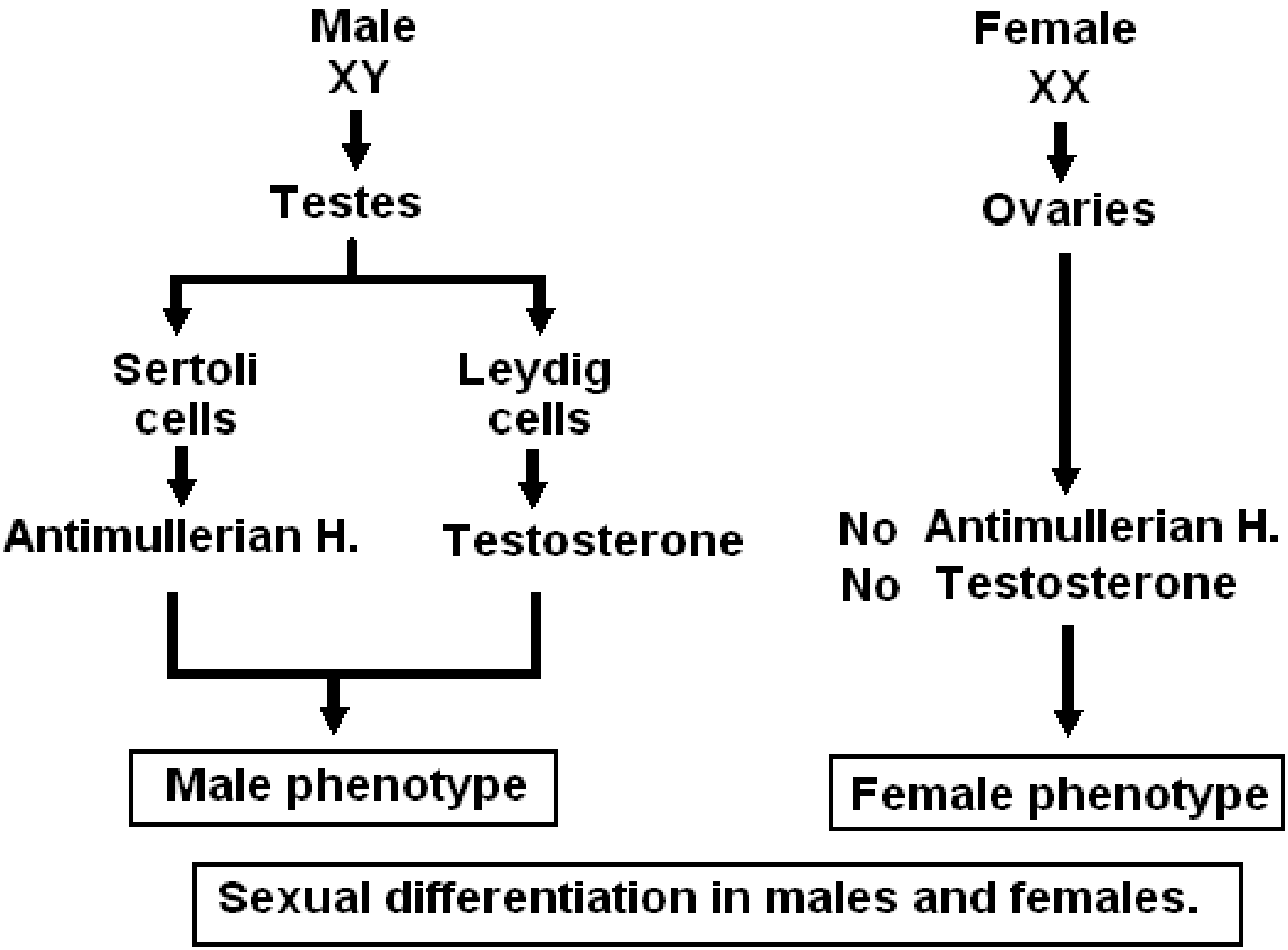
- Deficiency of hormones
  - Gonadotropin
  - HGH
- Signs/symptoms
  - Dwarfism
  - Emergence of secondary sexual characteristics
  - Amenorrhea
  - Decreased libido
  - Loss of facial/body hair



THE REPRODUCTIVE SYSTEM

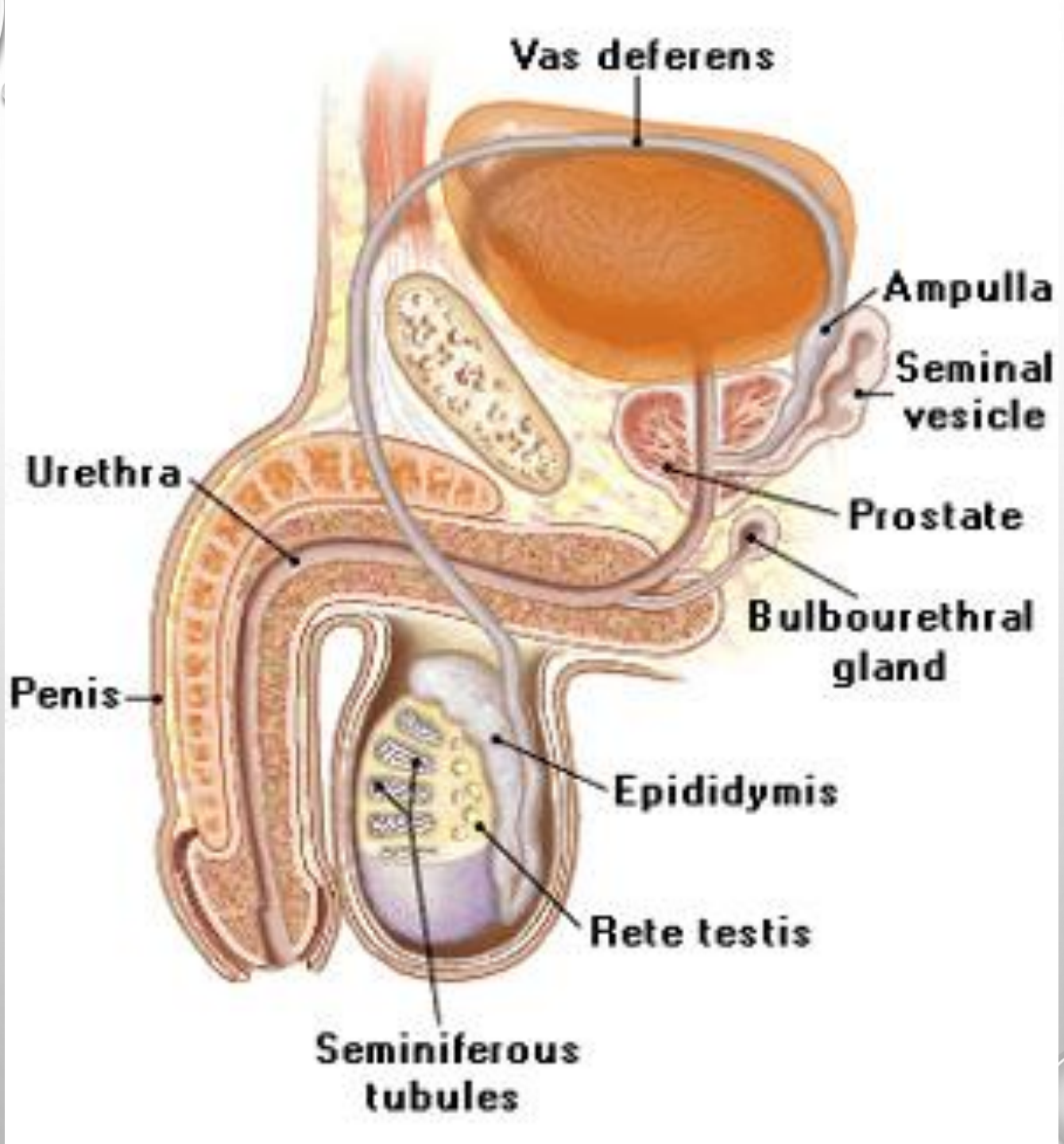

Sex-determining region of Y chromosome in embryonic germ cells (SRY gene)
produces
Testis-determining factor (TDF)
initiates production of
Multiple proteins that cause gonad to differentiate into a testis
which has
Leydig cells
Sertoli cells
secrete
secrete
Testosterone
Mullerian inhibiting substance
controls
causes
• Development of Wolffian duct into accessory structures
• Development of male external genitalia
Regression of Müllerian duct
KEY
Integrating center
Efferent path
Tissue response

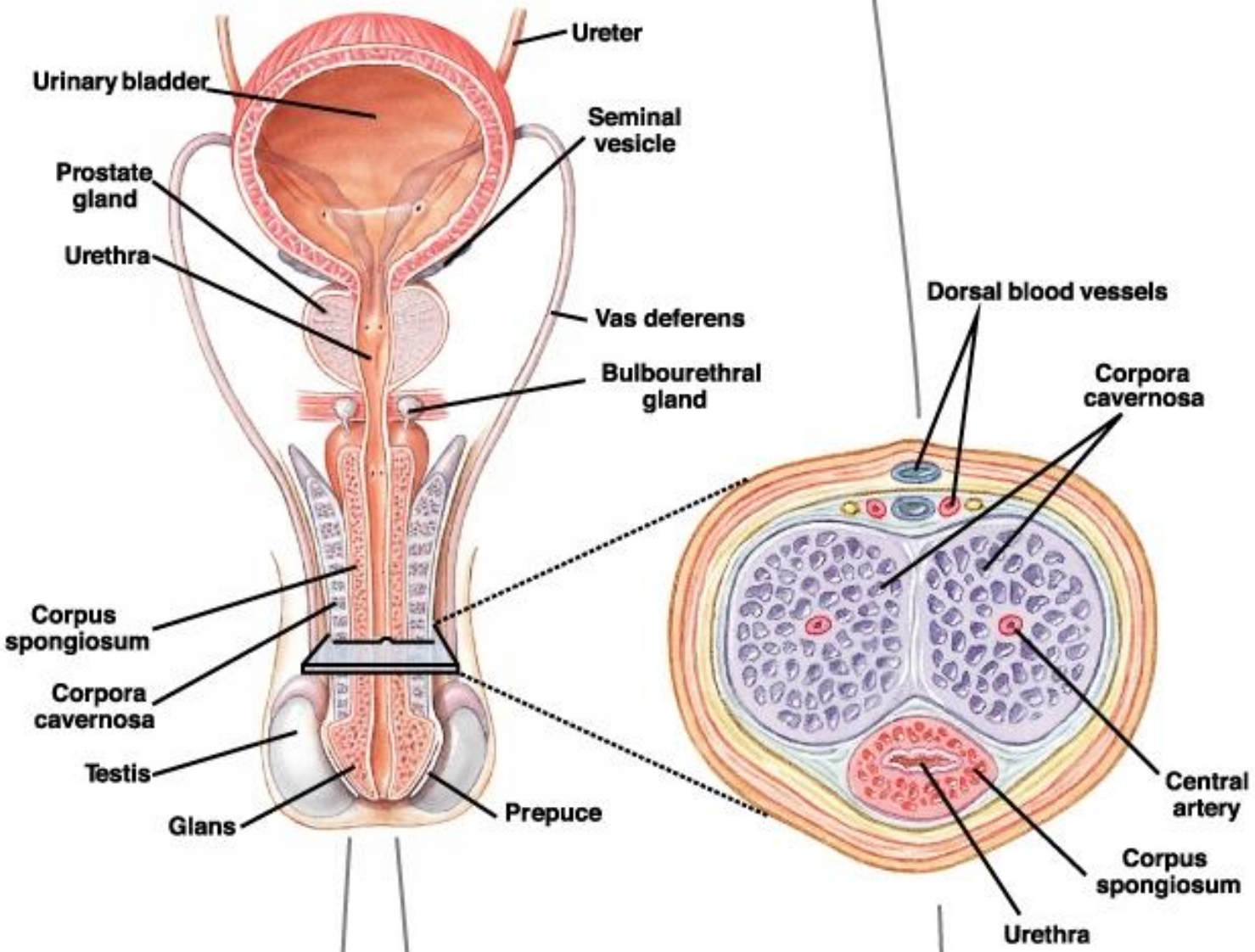

Internal organs
Bipotential gonad
Müllerian duct
FEMALE
MALE
Opening of duct
Wolffian duct
Testis
Müllerian duct
Cloacal opening
Kidney
Wolffian duct
Müllerian duct degenerates
Uterus
Wolffian duct degenerates
Bipotential stage
Seminal vesicle
Ovary
Prostate
Vas deferens
Oviduct (from Müllerian duct)
Testis
Vagina
Epididymis

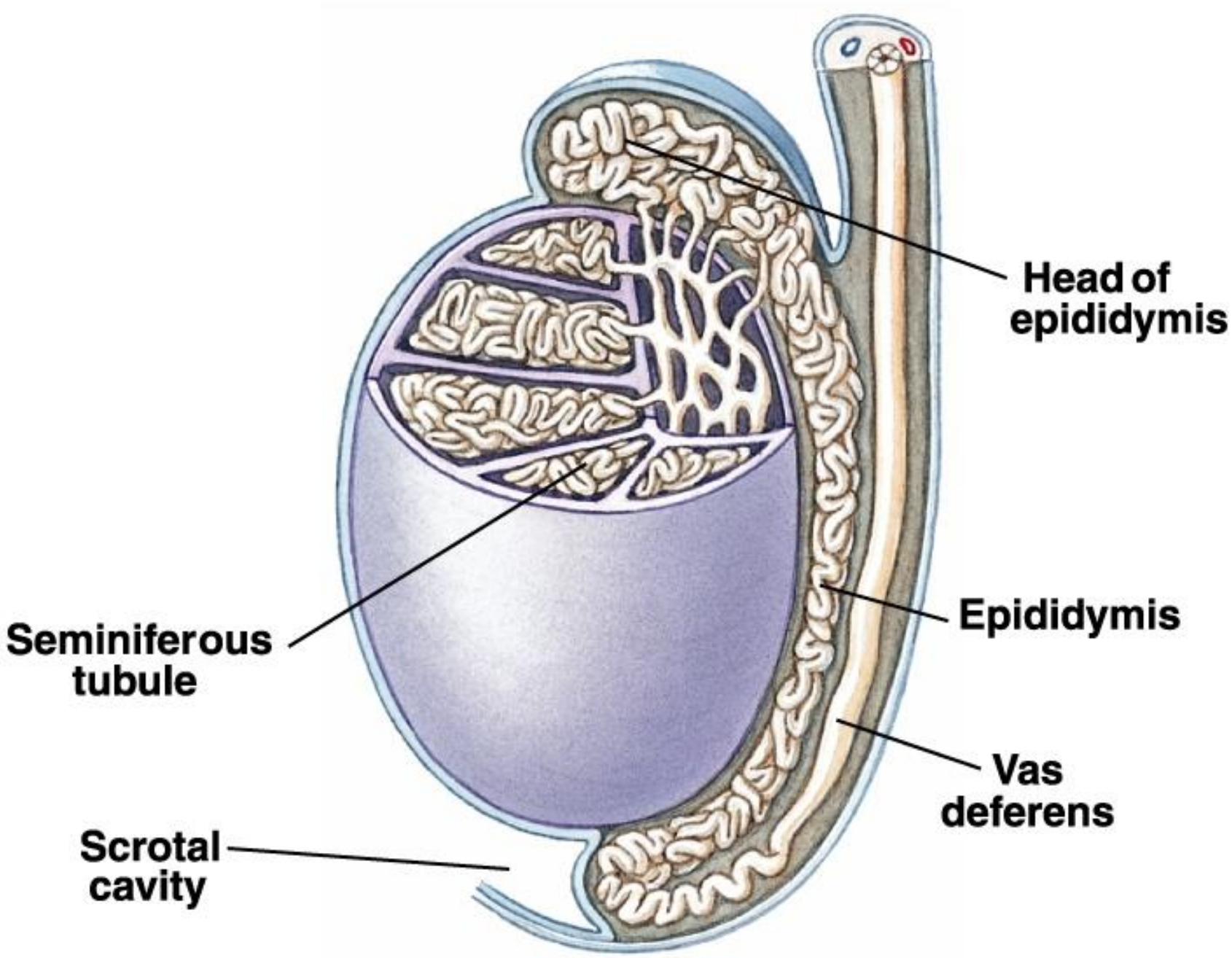


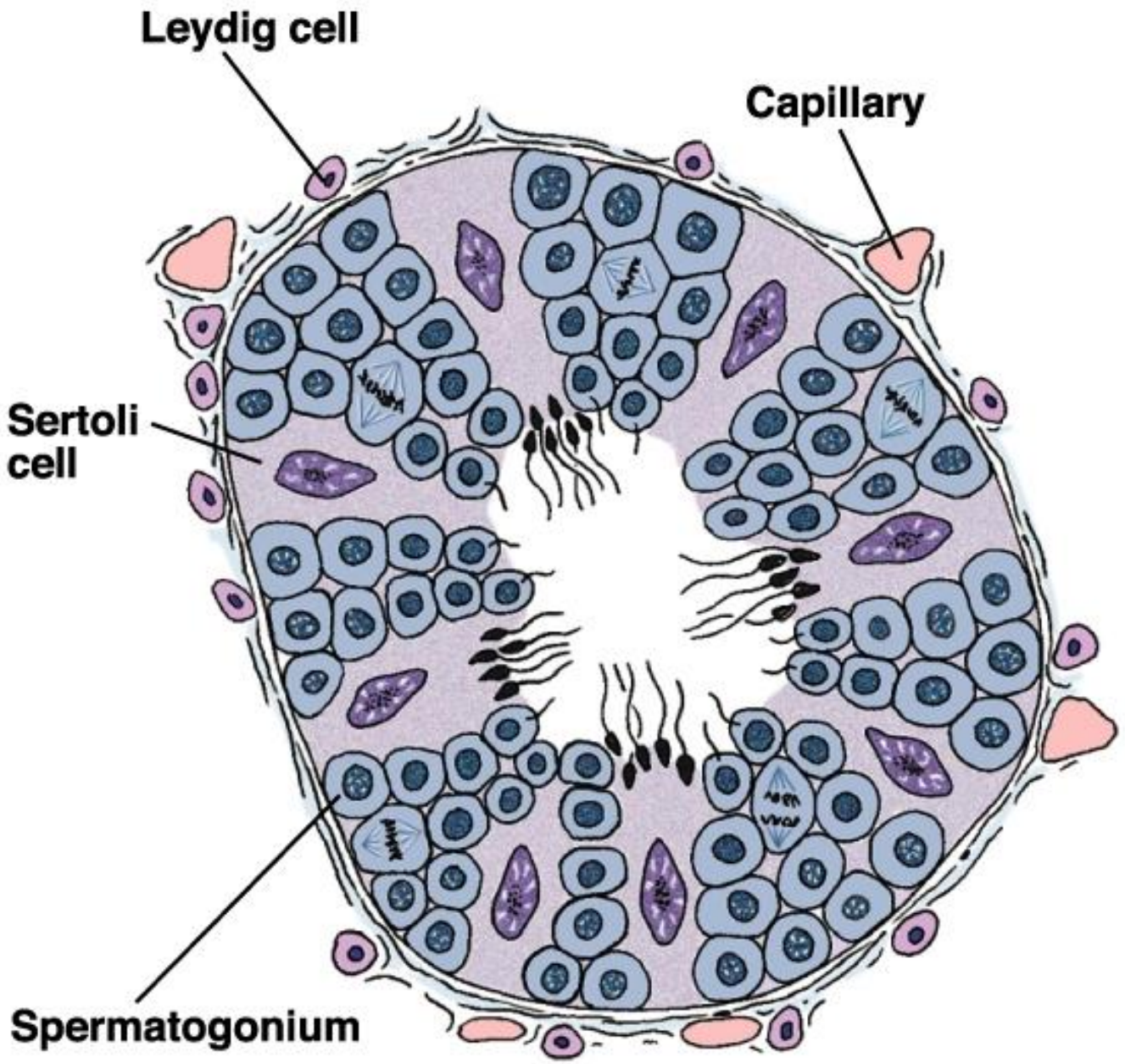
Sexual differentiation in males and females.

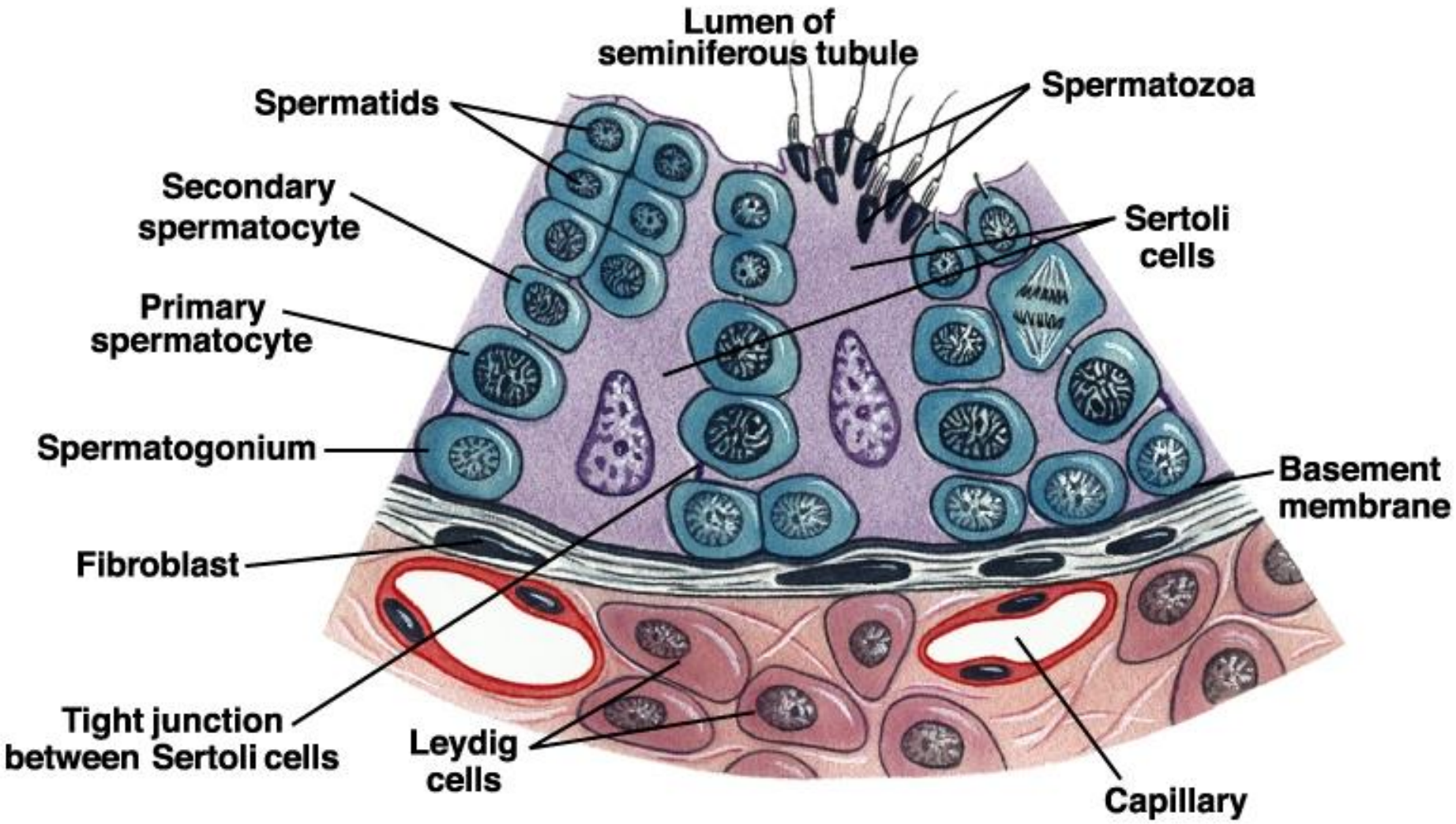
THE MALE REPRODUCTIVE SYSTEM


Vas deferens
Ampulla
Seminal vesicle
Urethra
Prostate
Bulbourethral gland
Penis
Epididymis
Rete testis
Seminiferous tubules


Ureter
Urinary bladder
Seminal vesicle
Prostate gland
Urethra
Vas deferens
Bulbourethral gland
Corpus spongiosum
Corpora cavernosa
Testis
Glans
Prepuce
Dorsal blood vessels
Corpora cavernosa
Central artery
Corpus spongiosum
Urethra


Head of epididymis
Epididymis
Vas deferens
Seminiferous tubule
Scrotal cavity


Leydig cell
Capillary
Sertoli cell
Spermatogonium


Lumen of seminiferous tubule
Spermatids
Spermatozoa
Secondary spermatocyte
Sertoli cells
Primary spermatocyte
Spermatogonium
Basement membrane
Fibroblast
Tight junction between Sertoli cells
Leydig cells
Capillary

FUNCTIONS OF BLOOD TESTES BARRIER

- Prevents large molecules from passing to lumen of tubules (allow germ cells to pass)
- Maintains the composition of fluids in the lumen (rich in androgen ,estrogen,k,inositol,glutamic acid and aspartic acid)
- Protects the germ cells from blood borne noxious agents
- Prevents antigenic product of germ cell division and maturation from entering to circulation
- Helps to establish an osmotic gradient that facilitates the movement of fluid into tubular lumen

THE SERTOLI CELLS SECRETES :

- Mullerian inhibiting substance (MIS)
- Inhibin that inhibits FSH secretion
- Androgen binding substance (ABP)
- Estrogen as sertoli cells contain aromatase enzyme responsible of conversion of androgen to estrogen

THE HORMONES THAT ARE ESSENTIAL IN SPERMATOGENESIS

- **TESTOSTERONE :**

  FOR MATURATION OF SPERMATIDS TO SPERMATOZOA

- **FSH :** 1.ON SERTOLI CELLS TO FACILITATE THE LAST STEP OF SPERMATID MATURATION

  2.STIMULATES ABP PRODUCTION

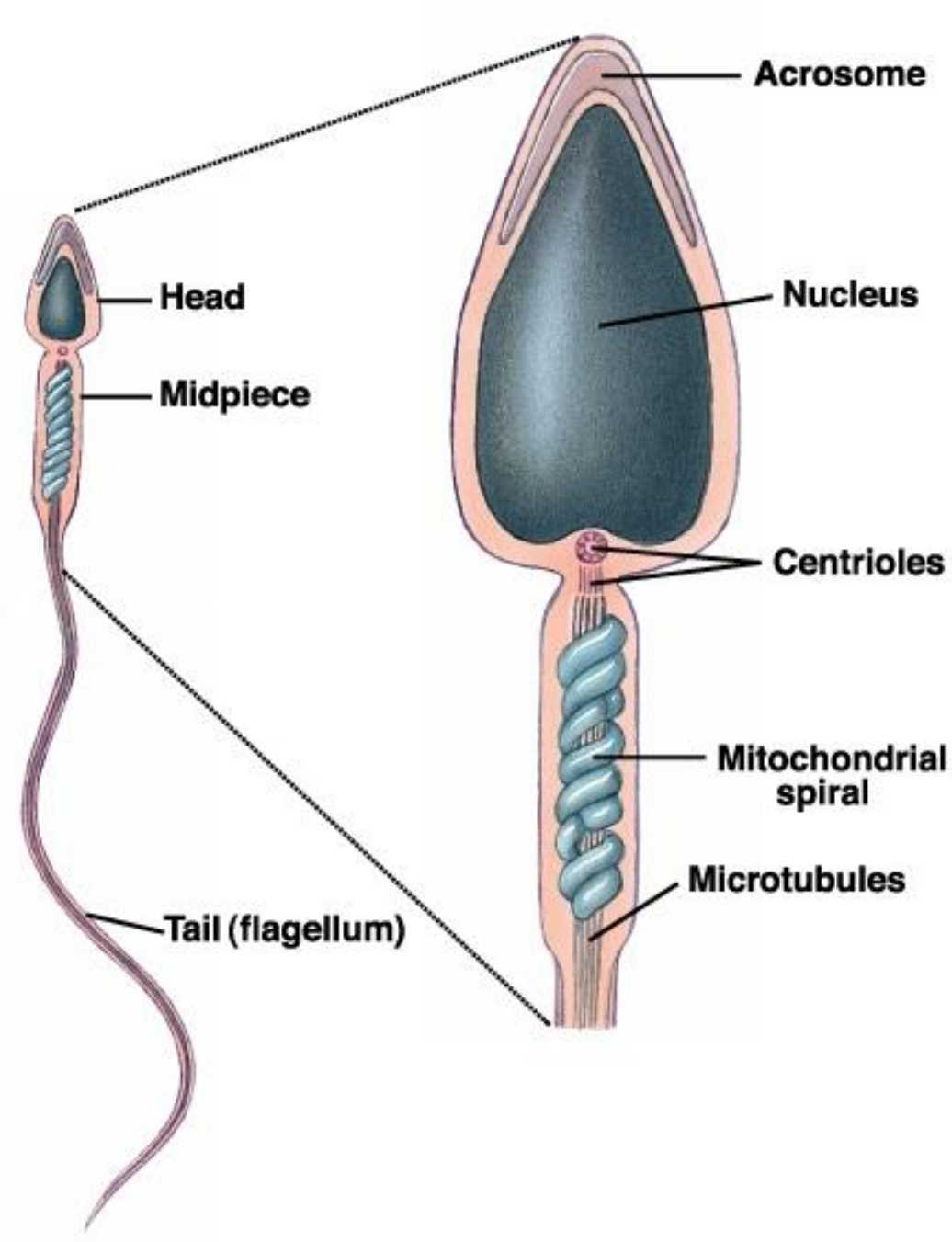
- **LH :**

  PRODUCTION OF ANDROGEN FROM LEYDIG CELLS

- **ESTROGEN**

- **GROWTH HORMONE:**

  1. NECESSARY FOR METABOLIC FUNCTION OF TESTES
  2. PROMOTES EARLY MATURATION OF SPERMATOGONIA


Acrosome
Head
Nucleus
Midpiece
Centrioles
Mitochondrial spiral
Microtubules
Tail (flagellum)

Semen

- It is the fluid that is ejaculated at the time of orgasm. The average volume is 2.5 – 3.5 ml after 4 – 5 days of abstinence.
- It is composed of the fluids from the vas deferens, from the seminal vesicles, from the prostate gland, and from the mucous gland, especially bulbo-urethral glands.

Its composition includes:

- colour : white opalescent.
- Specific gravity : 1 .028
- PH : 7.35 – 7.50.
- Sperm : about 100 million/ml (not more than20% of them are of abnormal forms).

Seminal vesicle fluid forms 60% of total volume and contains

- Fructose (1.5–6.5 mg/ml)
- Fibrinogen
- Ascorbic acid
- Prostaglandins
- Phosphorylcholine
- Ergothionine

It is the last to be ejaculated and serves to wash the sperm out of the ejaculatory duct and urethra. The seminal vesicle fluid and the mucous glands give the semen a mucoid consistency.

Prostatic fluid forms 30% of total volume. it gives the semen a milky appearance. It contains

- Spermine
- Citric acid
- Cholesterol
- phospholipids
- Fibrinolysin
- Fibrinogenase
- Zinc and acid phosphatase

The clotting enzyme of the prostatic fluid causes the finbrinogen of the seminal vesiclue fluid to form a weak coagulum, which then dissolutes during the next 15-20 minutes because of lysis by fibrinolysin formed from the prostatic profibrinolysin.

•**Buffer** : phosphate and bicarbonate.

Men become non-fertile if:

1. Sperm count below 20 million/mI : oligospermia.
2. Large number of non motile sperms.
3. Large number of abnormal shaped sperms.

- Human sperms move at a speed of 3 mm/min. through the female genital tract reaching the uterine tubes 30 – 60 minutes after copulation and can live 1-2 days in female genitalia.
- The clotting enzyme of prostate forms a weak coagulum that held the sperm in the deeper region of the vagina where the uterine cervix is present. The coagulum then dissolves during next 15 – 30 minutes by the Lysis action of fibrinolysin.

- The sperm in the epididymis become motile and mature (capable of fertilization due to the effect of estrogen and testosterone secreted by the epithelium of epididymis although it secretes several inhibitory proteins that prevent actual motility, but sperms take several days to pass the 6 meter long of epididymis.

In vas deference sperms can be stored up to one month. The seminal glands secrete fructose, (which is essential for sperm nutrition) citric acid, fibrinogen and PG which help the cervical mucus becoming more receptive to sperm movement and reverse the peristaltic contraction in uterus and fallopian tubes to move the sperms towards the ovaries.

The prostatic gland secretion is alkaline which is necessary to neutralize the fluid of vas deference (citric acid) and to neutralize the vaginal secretions which is a acidic pH (3.5 – 4.0) as the sperm needs alkaline media to be completely motile

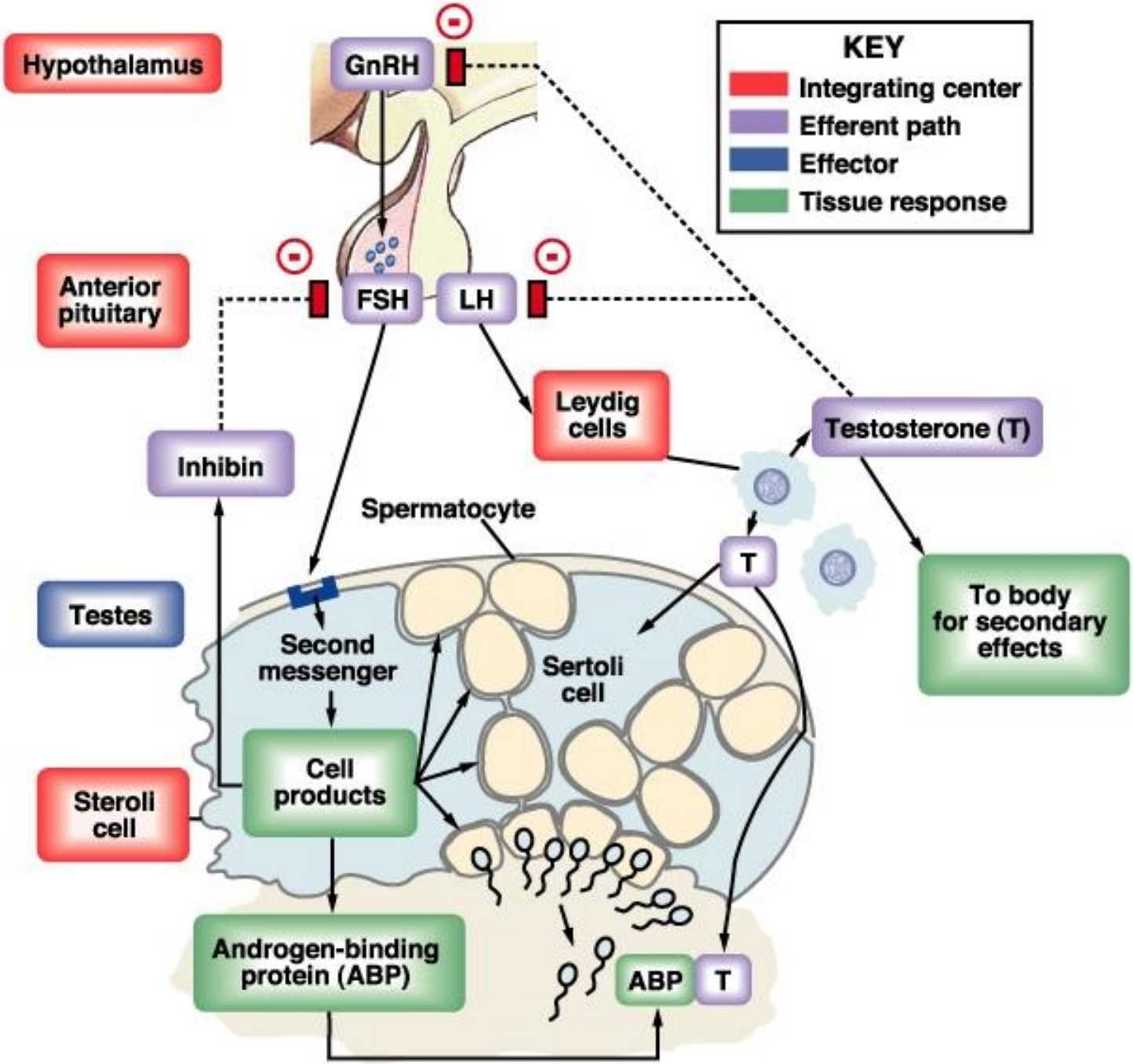
MOTILITY OF SPERMATOZOA IS INCREASED BY :

- Relaxin from prostate
- In female genital tract :

1. Removal of inhibitory factors that suppress sperm activity
2. Removal of cholestrol cover of acrosome that prevents proteolytic in male genitalia
3. Head of sperm becomes more permable to Ca so increasing the flagellated movement of the sperm

- Temp. Effect on spermatogenesis .
- Control of descend of testes .
- MIS :

1. Responsible for testicular descend to inguinal region
2. Testesterone responsible for testicular descend to the scrotum


KEY
Integrating center
Efferent path
Effector
Tissue response
Hypothalamus
GnRH
Anterior pituitary
FSH
LH
Leydig cells
Testosterone (T)
Inhibin
Spermatocyte
T
To body for secondary effects
Testes
Second messenger
Sertoli cell
Cell products
Steroli cell
Androgen-binding protein (ABP)
ABP
T

ENDOCRINE FUNCTION OF TESTES

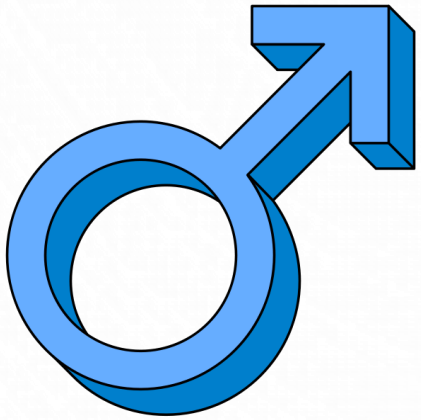
- Testosterone, the principal hormone of the testes. It is synthesized from cholesterol in the Leydig cells and also formed from androsterone secreted by adrenal cortex.
- Secretion of Testosterone is under the control of LH as LH stimulates Leydig cells by increase formation of camp. Camp increases the formation of cholesterol from cholesterol esters and conversion of cholesterol to pregnolone.

SECRETION

- Secretion rate of testosterone is high in normal adult male, but small amounts in female are secreted by adrenals.
- 98% of testosterone is bound to plasma proteins (65% to ß-globulin and 33% to albumin) and only 2% is freely present.
- The plasma level is (18.2 nmol/L) in male and (1.0 nmol/L) in female.

ACTIONS OF TESTOSTERONE

- During development it is responsible for development of male internal and external sex organs and also help in testes descending.



ACTIONS OF TESTOSTERONE

1. DEVELOPMENT OF SECONDARY SEXUAL CHARACTERS OF MALES AT PUBERTY.

- Mental: more aggressive, active attitude, interest in opposite sex develops.
- External genitalia: penis increase in size and width, scrotum becomes pigmented and rugges .
- Internal genitalia: seminal vesicles enlarges and secretes and begins to form fructose.
- Prostate: with bulbourethral glands enlarge and secretes.

ACTIONS OF TESTOSTERONE

1. DEVELOPMENT OF SECONDARY SEXUAL CHARACTERS OF MALES AT PUBERTY.

- Voice: larynx enlarge, vocal cords increase in length and thickness, voice becomes deeper.
- Hair growth: beard appears, male pattern hair of scalp and pubic and axilla, general body hair increase and may result in androgenic allopecia.
- Body conformation: shoulder broaden, muscle enlargement.
- Skin: acne formation.

ACTIONS OF TESTOSTERONE

- 2. Anabolic effects:
- In general increase synthesis and decrease breakdown of protein,
- Secondary effects of increased protein anabolism are: increase musculature and bone growth after puberty, increase of BMR by 5 – 10%, increase number of RBCs by 15 – 20%. It has a feedback mechanism to inhibit pituitary LH secretion and GnRH secretion from hypothalamus.

Leydig Cells

Sertoli Cells

Cholesterol

Pregnenolone

17α-Hydroxy-pregnenolone

Progesterone

Dehydroepi-androsterone

17α-Hydroxy-progesterone

11-Deoxy-corticosterone

Androstenedione

11-Deoxycortisol

Corticosterone

Testosterone

Cortisol

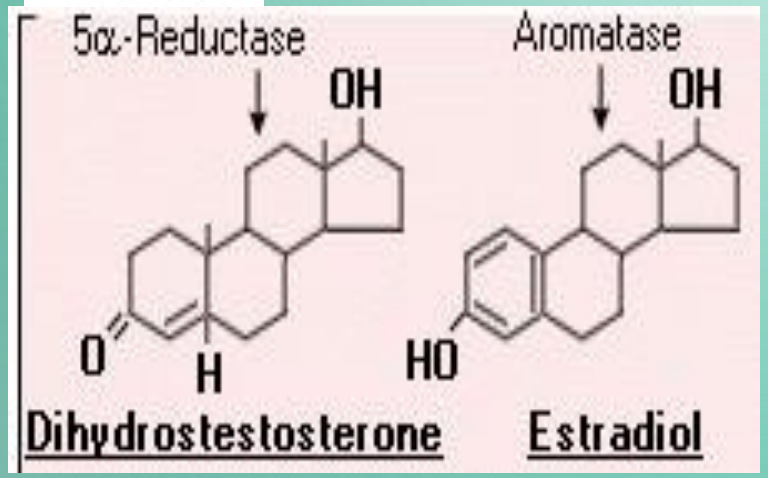
18-Hydroxy corticosterone

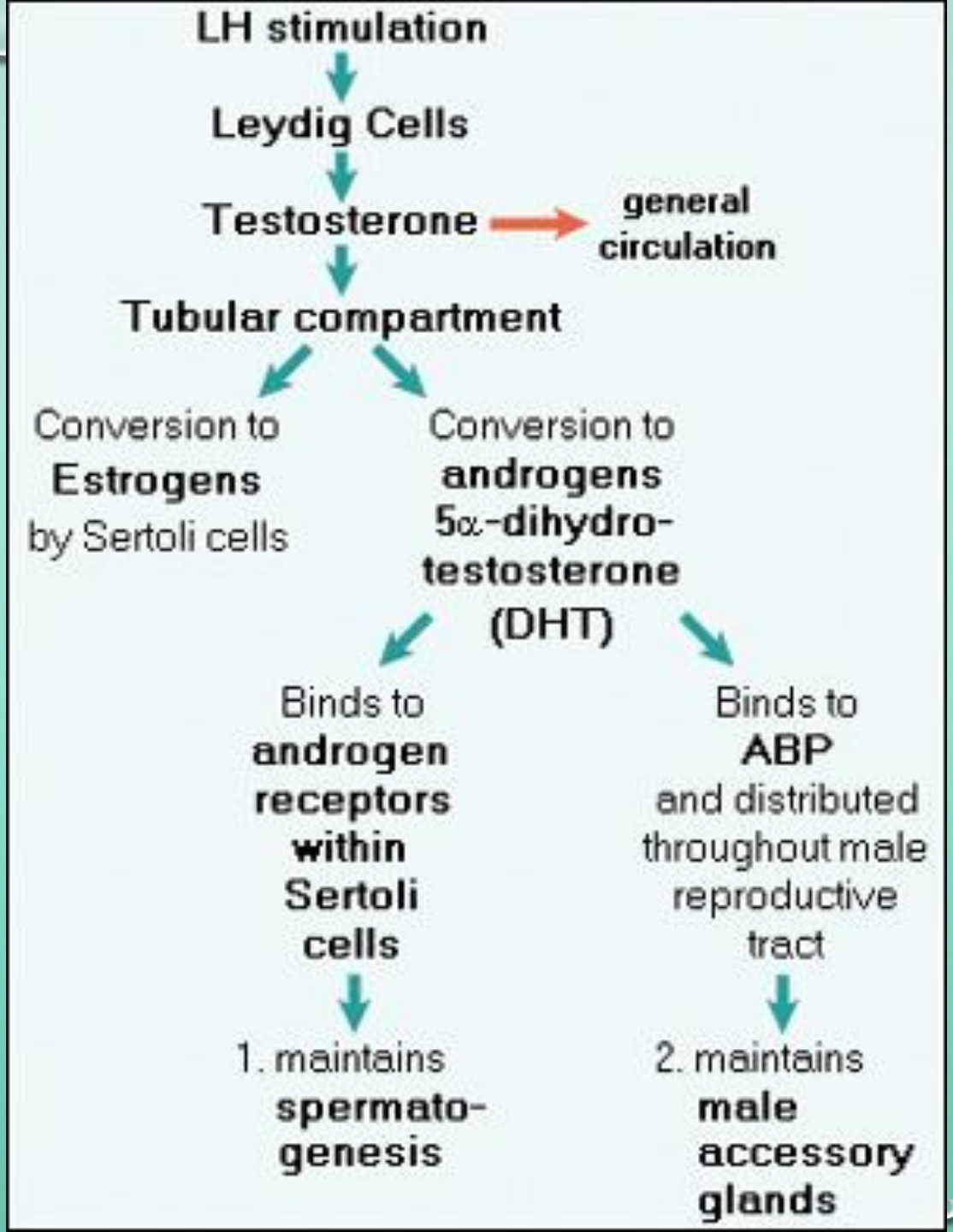
Mineralocorticoid Pathway

Glucocorticoid Pathway

Androgen Pathway

Aldosterone




LH stimulation
Leydig Cells
Testosterone
general circulation
Tubular compartment
Conversion to Estrogens by Sertoli cells
Conversion to androgens 5α-dihydro-testosterone (DHT)
Binds to androgen receptors within Sertoli cells
1. maintains spermato-genesis
Binds to ABP and distributed throughout male reproductive tract
2. maintains male accessory glands

Composition of Semen of Man

	Volume (ml)	Approximate Concentration	Principle source	Function
Spermatozoa (no.\ml)	2-6	50-150	Testis	.....
Fructose (mg\ml)		1.5+	Ampulla	Anaerobic fructolysis
Inositol (mg\ml)		0.4	Testis & Epididymis	Preserves seminal osmolarity
Citric acid (mg\ml)		0.1-0.3	Prostate	Ca^{2+} chelator (prevents seminal "stones")
Acid phosphatase(U/ml)		2,470	Prostate	Phospholipid metabolism
Glycerophos-phorylcholine (mg\ml)			Epididymis	Substrate for lipid metabolism
Prostaglandins			Seminal vesicles	Myometrial contractility
Bicarbonate	50-60%		Seminal vesicles	Buffering capacity

MALE SEX ACT

- **Errection** : parasympathetic reflex and ejaculation (sympathetic)

1. The errection reflex :

- Afferent impulses :from glans penis and high centres (erotic psychic stimuli)
- Errection center in the lumbar segment in spinal cord
- Efferent fibers are in the pelvic splanchnic nerve (nervi irigentis –ach)

2.The ejaculation reflex :

it is 2 parts spinal reflex

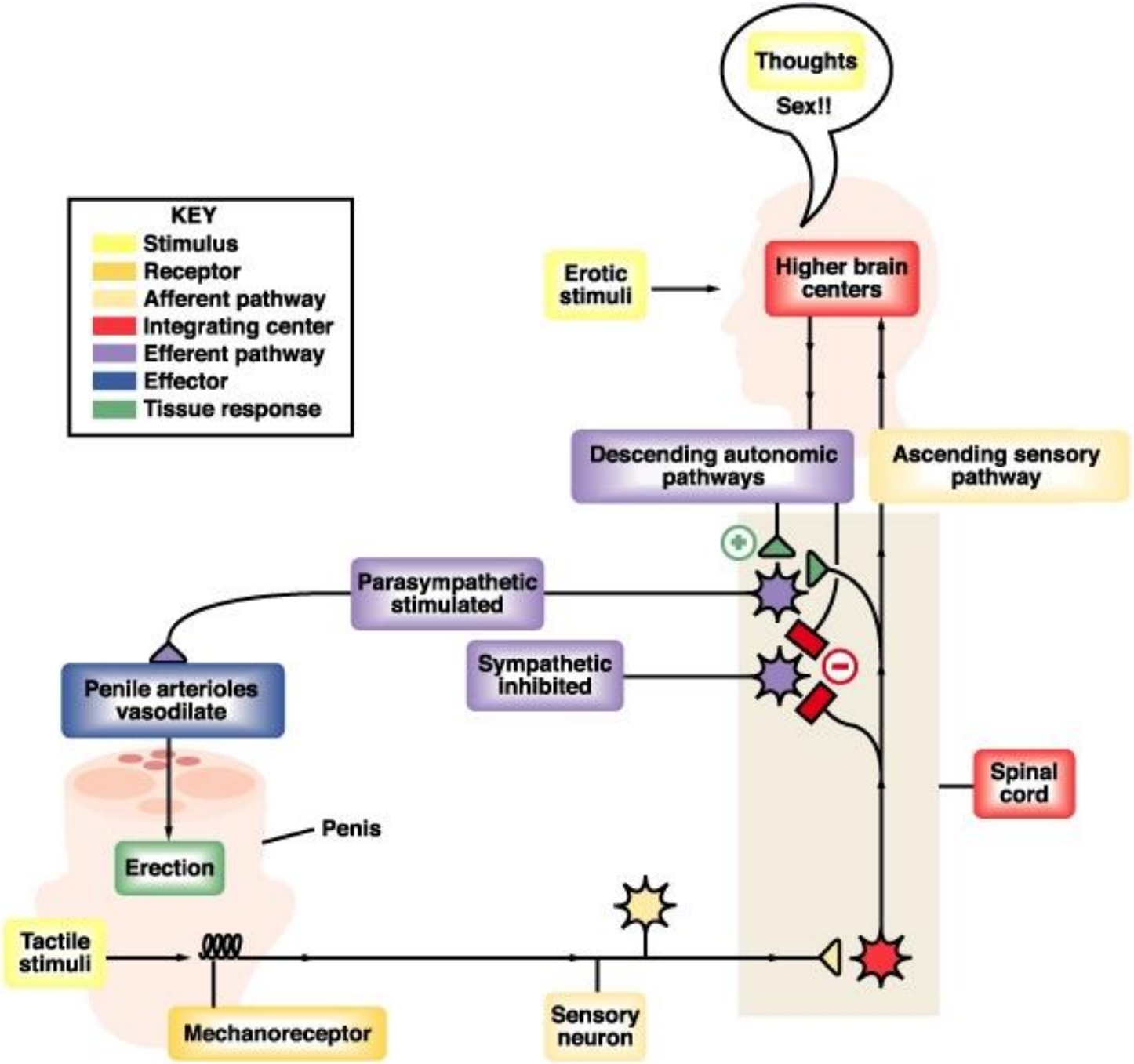
A- emission (movement of semen to the urethra)

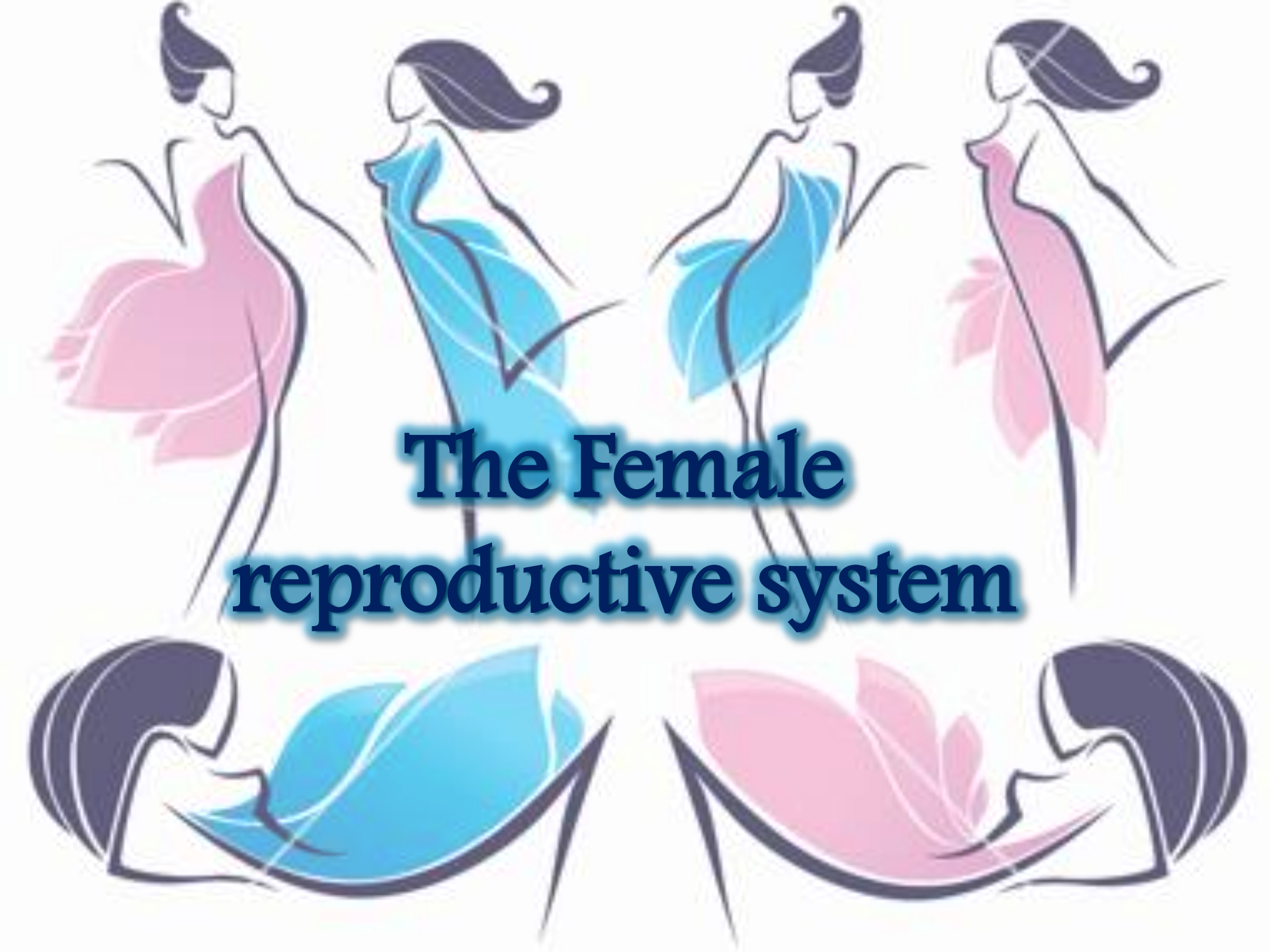
B- ejaculation (propultion of semen out of urethra at the time of orgasm)

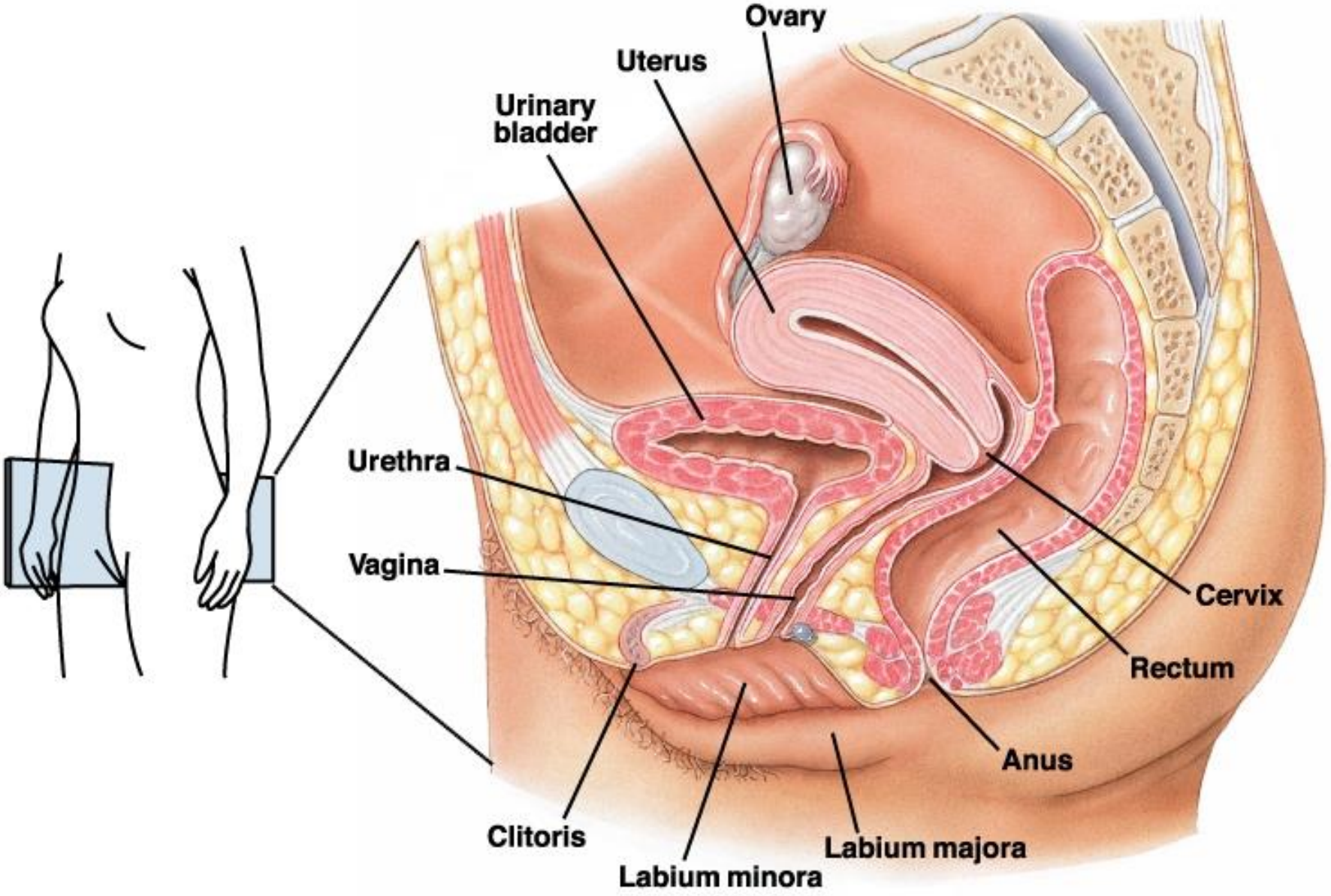
Afferent fibers from hypogastric nerve .

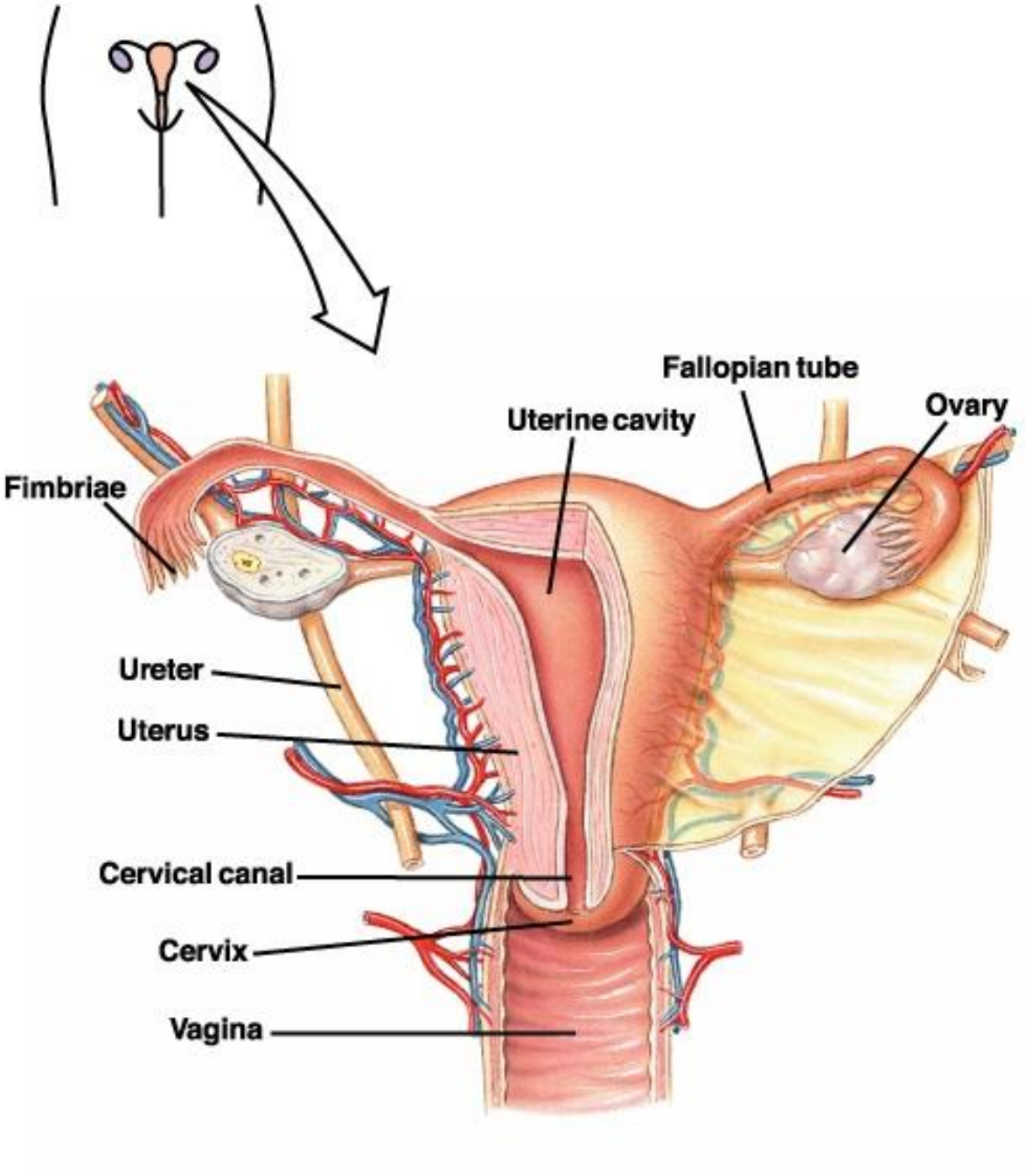
Centre is in lower lumbar and upper sacral segment

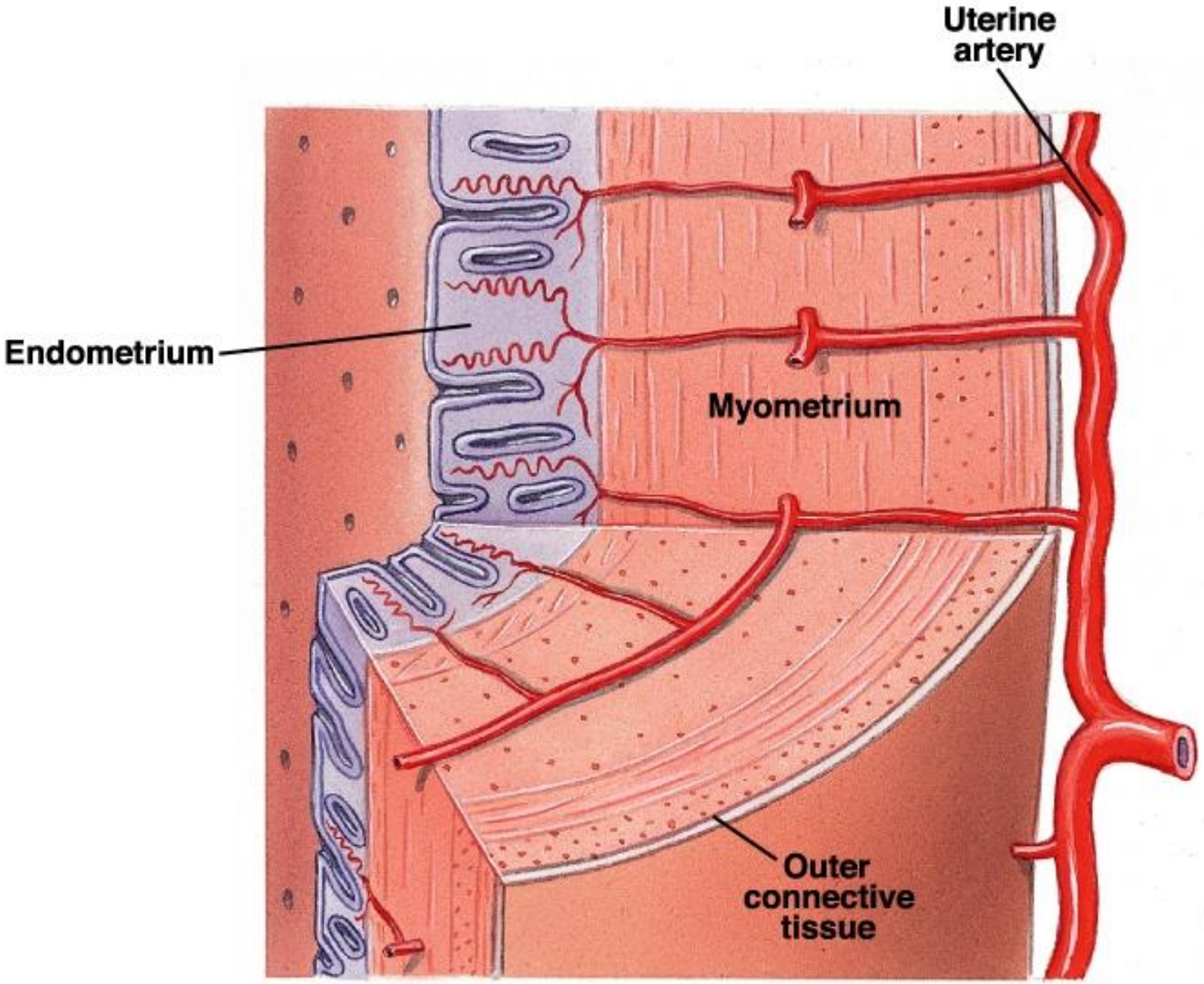
The efferent pathway is S1.2.3 roots (pudendal nerve)

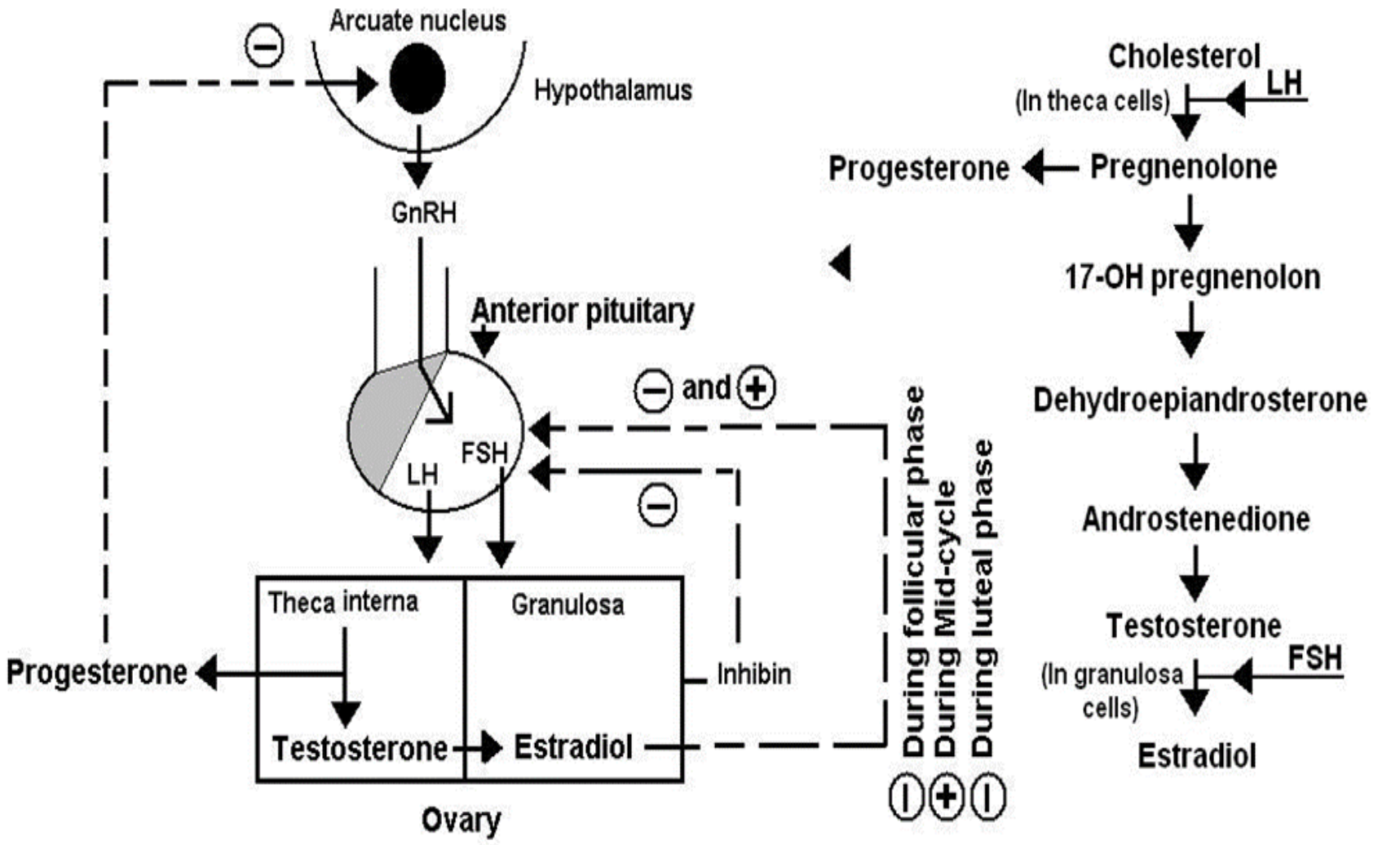

Thoughts
Sex!!
KEY
Stimulus
Receptor
Afferent pathway
Integrating center
Efferent pathway
Effector
Tissue response
Erotic stimuli
Higher brain centers
Descending autonomic pathways
Ascending sensory pathway
Parasympathetic stimulated
Sympathetic inhibited
Penile arterioles vasodilate
Spinal cord
Penis
Erection
Tactile stimuli
Mechanoreceptor
Sensory neuron


The Female
reproductive system


Ovary
Uterus
Urinary bladder
Urethra
Vagina
Cervix
Rectum
Anus
Clitoris
Labium minora
Labium majora


Fallopian tube
Ovary
Uterine cavity
Fimbriae
Ureter
Uterus
Cervical canal
Cervix
Vagina


Uterine artery
Endometrium
Myometrium
Outer connective tissue



Feedback regulation of ovarian function. + indicates stimulatory effects. – indicates inhibitory effects.

Synthesis of estrogen and progesterone

CONTROL OF OVARIAN FUNCTIONS

[1] Hypothalamus control:

- Hypothalamus secretes gonadotrophin-releasing hormone (GnRH) into portal hypophysial vessel to the pituitary gland. GnRH stimulates FSH and LH secretion. GnRH is secreted in pulses every 1-3 hours, each pulse lasting several minutes. This pulsatile release of GnRH causes pulsatile output of LH and FSH (lasting many hours).
- Continuous GnRH infusion experimentally causes inhibition of LH and FSH secretion and down regulation of it's receptors.

- Frequency of GnRH secretion is increased by estrogen and decreased by progesterone and testosterone.
- Arcuate nucleus in hypothalamus is responsible for release of GnRH, so it is regarded as nuclei of female sexual activity.
- There are multiple neurons connect arcuate nuclei to limbic system that is why psychic factors modify sexual function.

[2] Pituitary control:

- FSH from pituitary is responsible for maturation of ovarian follicles.
- The ovarian follicles, under the effect of FSH, secrete estrogen. Then at the end of follicular phase, a burst of LH secretion occurs (LH surge) which is responsible for ovulation and initial formation of corpus luteum .
- LH stimulates the secretion of estrogen and progesterone from the corpus luteum.

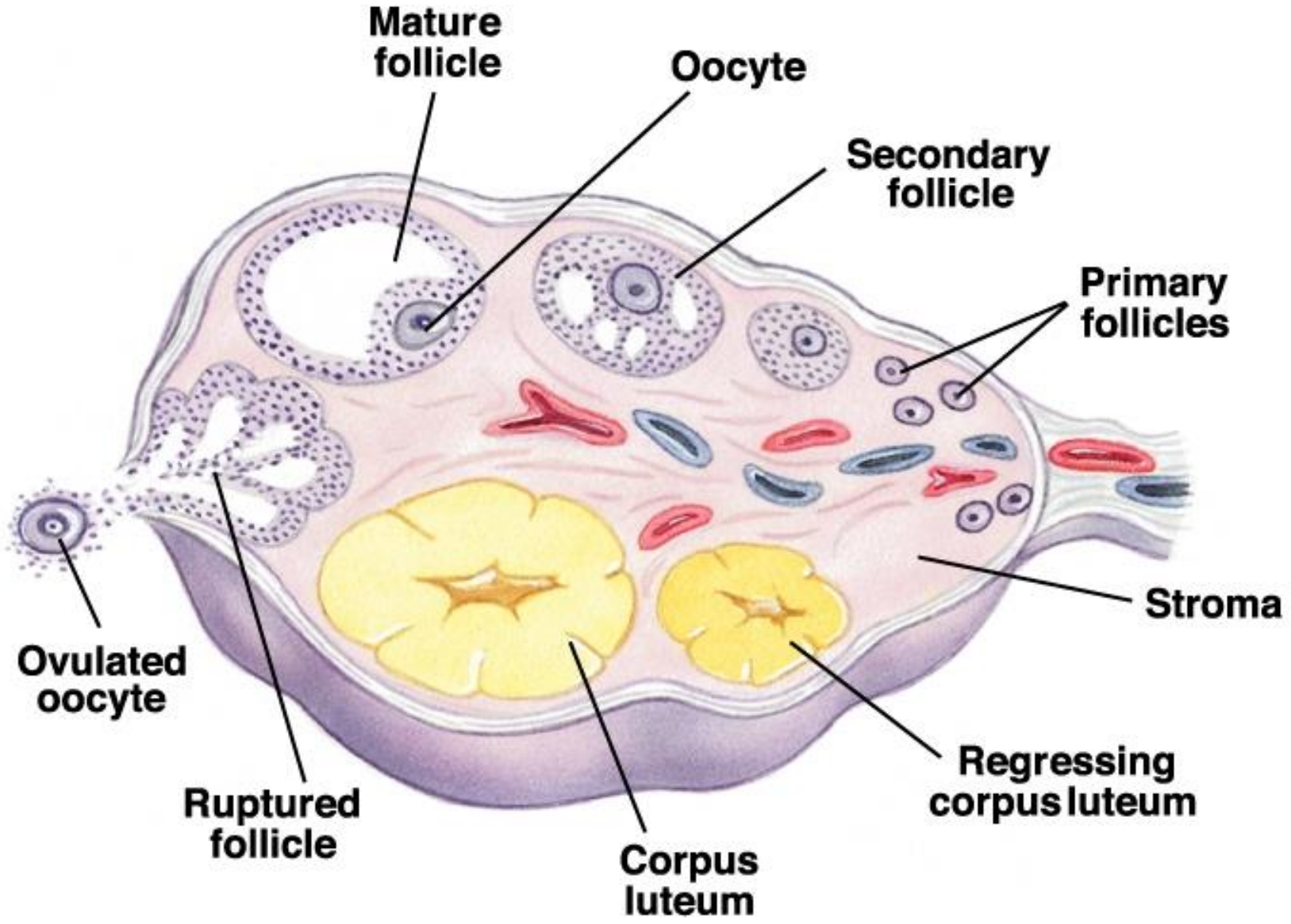
[3] Cyclic control:

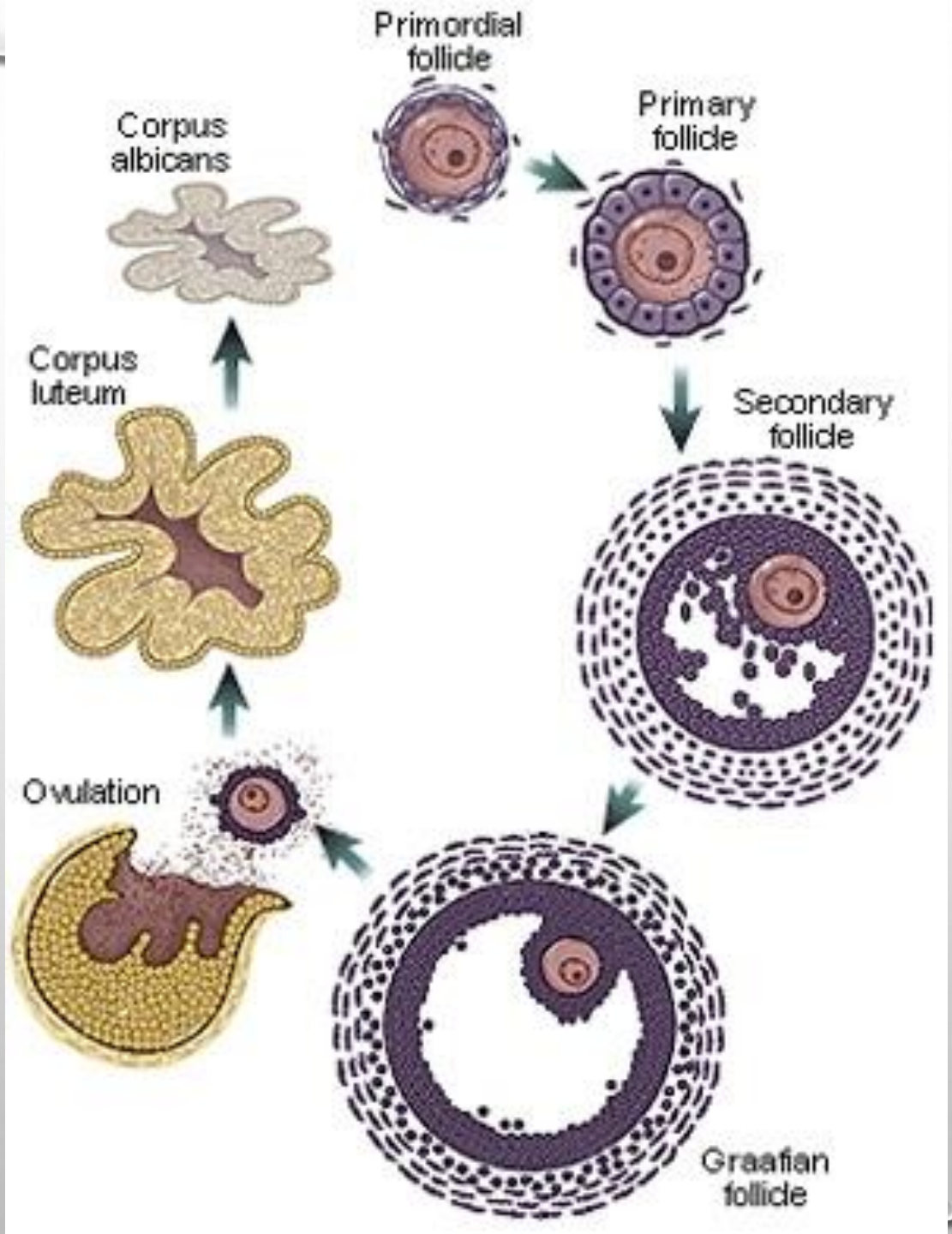
- Small amounts of estrogen had – ve Feedback on FSH, LH and GnRH, while large amounts of estrogen had + ve Feedback on the FSH, LH and GnRH.
- Progesterone and inhibin had – ve feedback effect on FSH, LH, and GnRH.
- Estrogen had two peaks during menstrual cycle; first one is two days before ovulation and the second peak during luteal phase while progesterone had only one peak in luteal phase. FSH and LH had one peak 36-48 hours before ovulation and this peak could be explained by feedback effects.

OVARIAN (MENSTRUAL) CYCLE

[A] The first phase: The Follicular phase:

- The first day of bleeding is regarded as first day of the cycle.
- The follicular phase extends from the 5th day of the cycle to the 14th day during which FSH will induce maturation of the primordial follicles vesicular follicles mature follicles (called Graffian follicles). Many follicles start to mature but only one follicle reaches maturation per cycle.

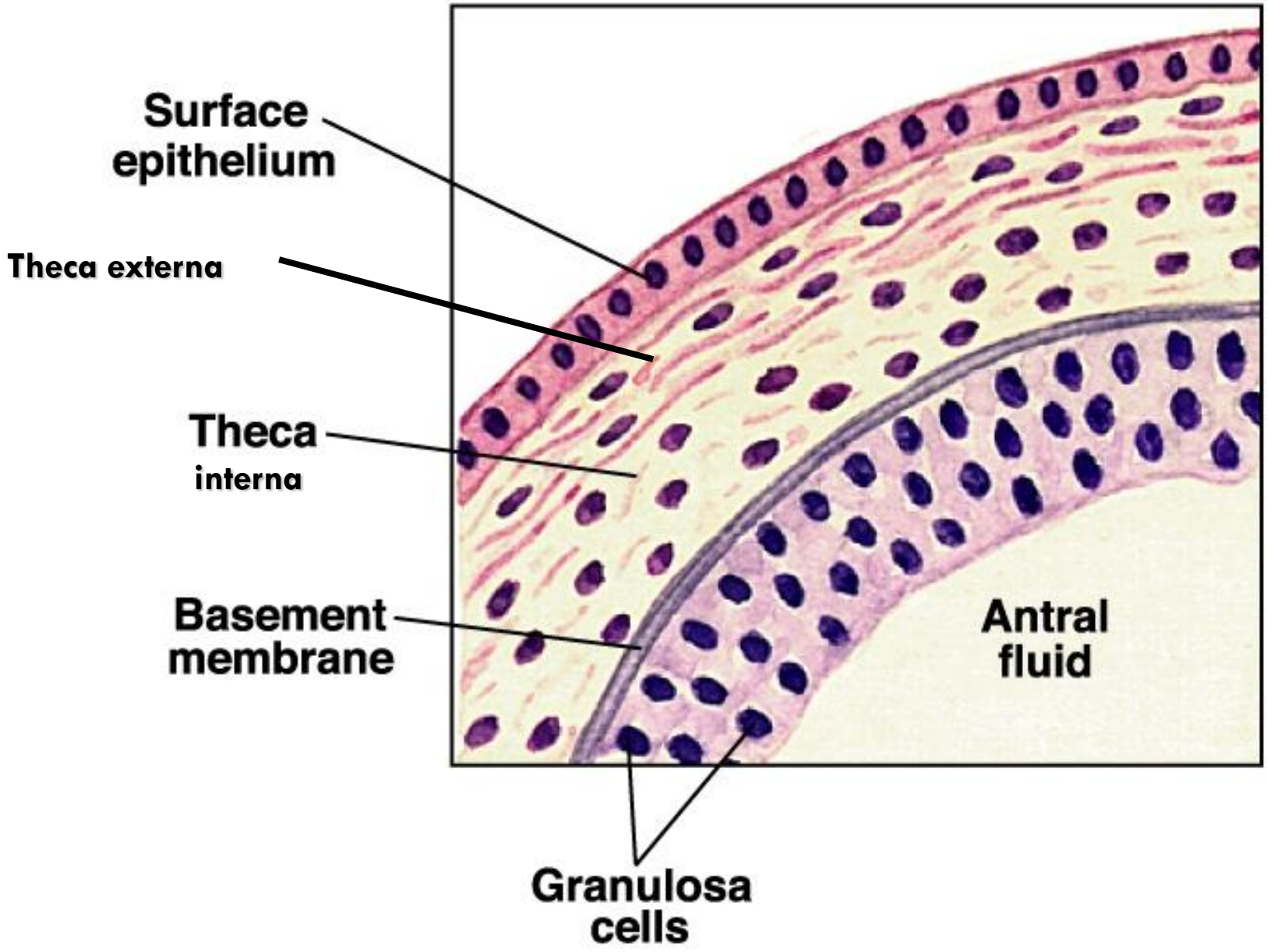

Mature follicle
Oocyte
Secondary follicle
Primary follicles
Stroma
Ovulated oocyte
Ruptured follicle
Corpus luteum
Regressing corpus luteum

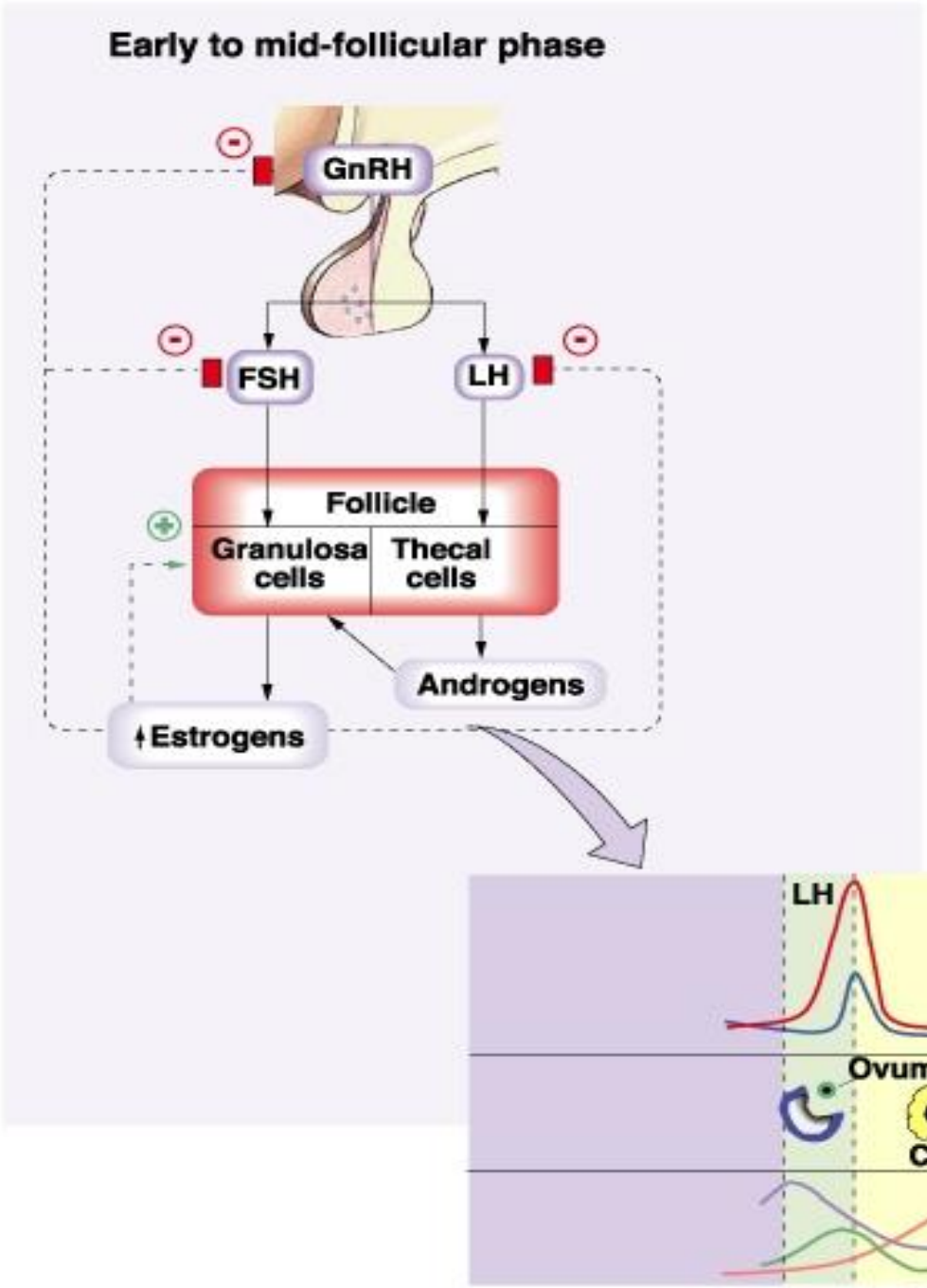

Primordial follicle
Primary follicle
Secondary follicle
Graafian follicle
Ovulation
Corpus luteum
Corpus albicans

The **Graffian follicle** contains 3 layers:

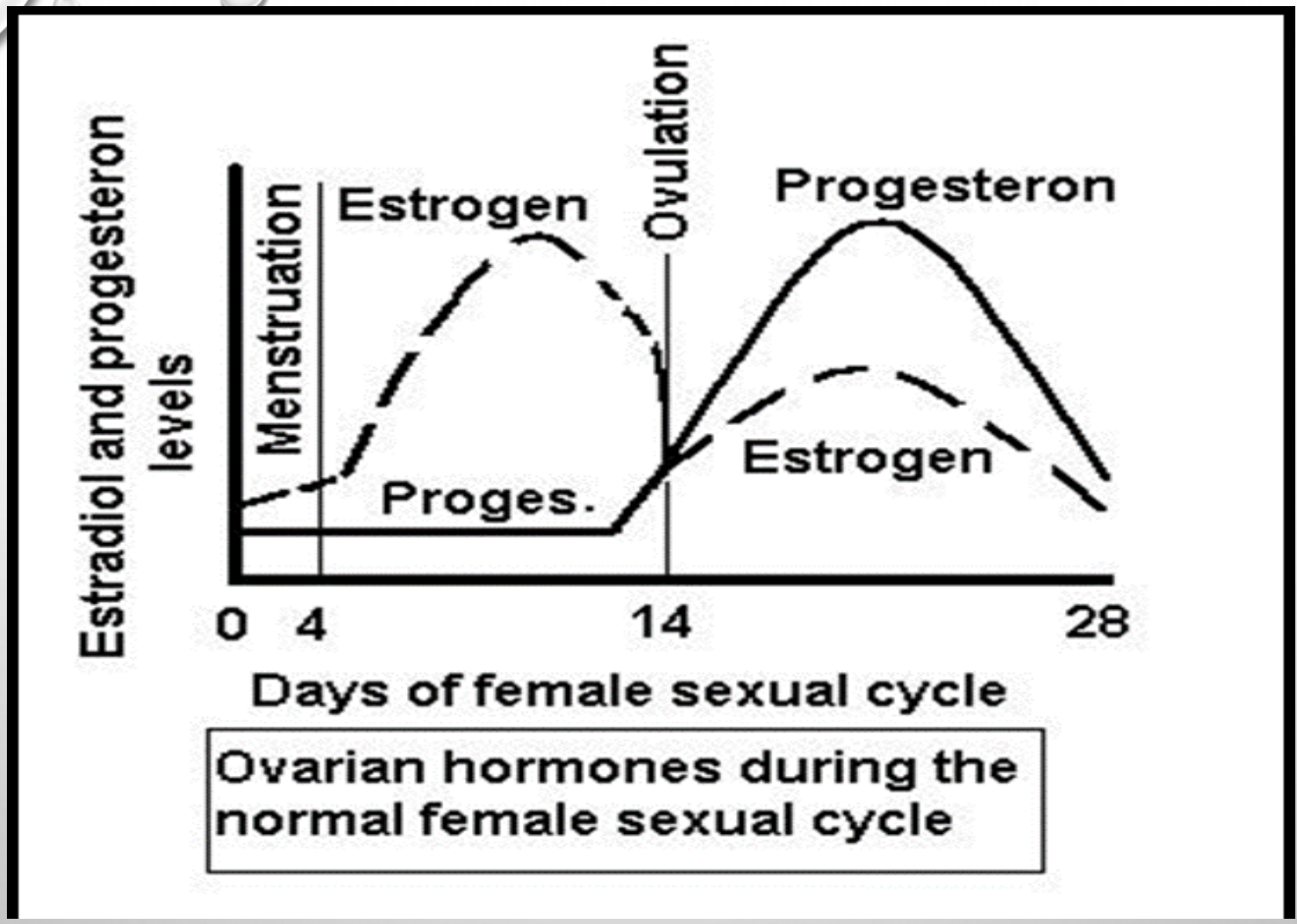
- Theca externa
- Theca interna
- Granulosa layer

The follicular fluid inside the antrum which contains the estrogen secreted by theca interna and granulosa under the influence of FSH.
The main source of circulating estrogen is the theca interna while the granulosa cells mainly form the estrogen in the antral fluid.


Surface epithelium
Theca externa
Theca interna
Basement membrane
Antral fluid
Granulosa cells



In early part of this phase, inhibin is low and FSH is modestly elevated fostering the follicular growth. LH secretion is held in check by the negative feedback of the rising plasma estrogen level.



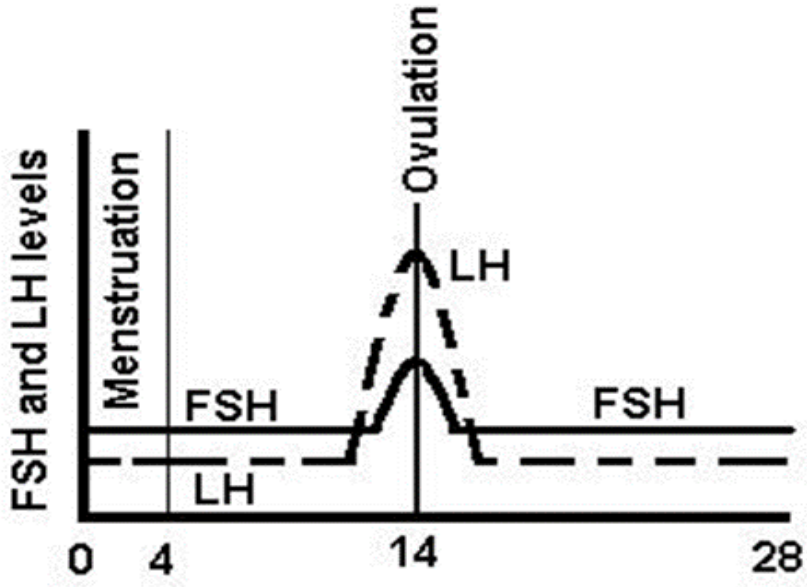
Ovarian hormones during the normal female sexual cycle

[B] The second phase (Ovulation):

Occurs 14 days before menses, regardless of the cycle length. Thus, in a 28-day cycle, ovulation occurs on day 15; in 35-day cycle, ovulation occurs on day 22. In ovulation, rupture of Graafian follicle occurs,

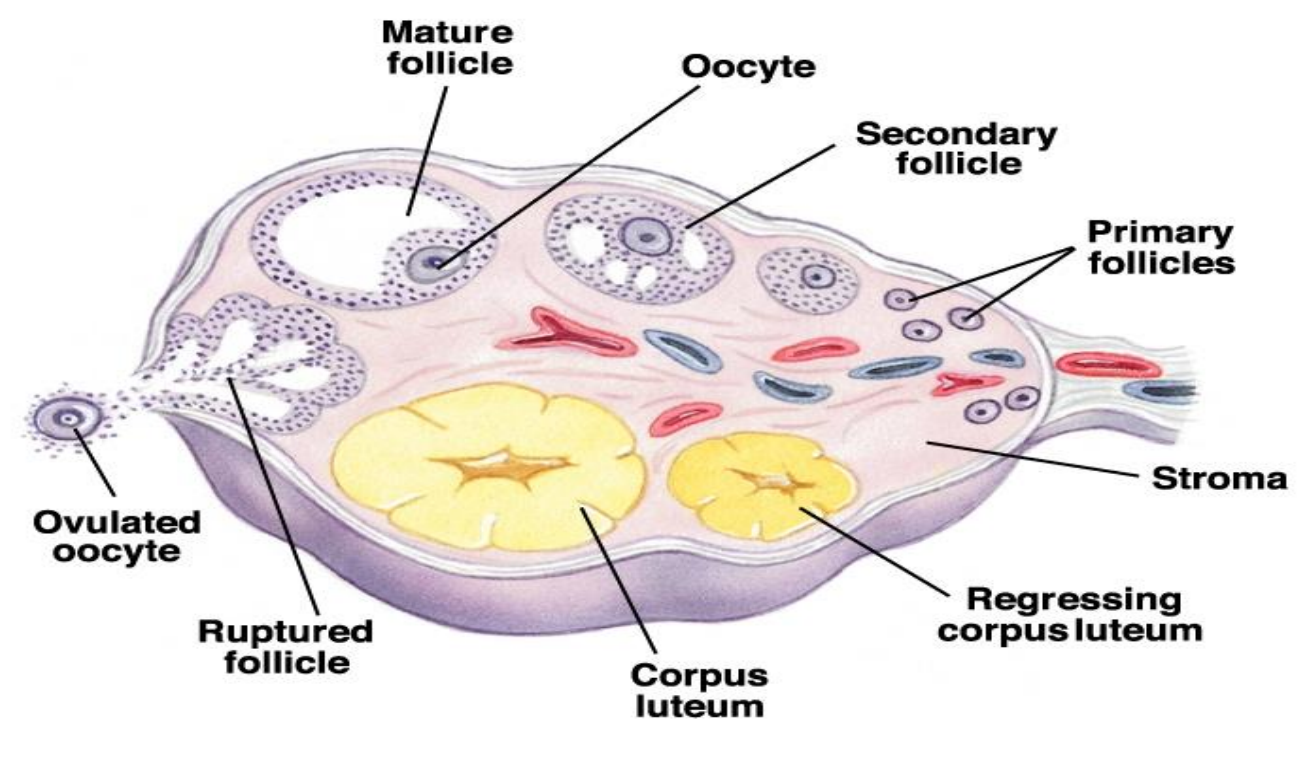
this process consists of two events,
occur under the effect of LH.

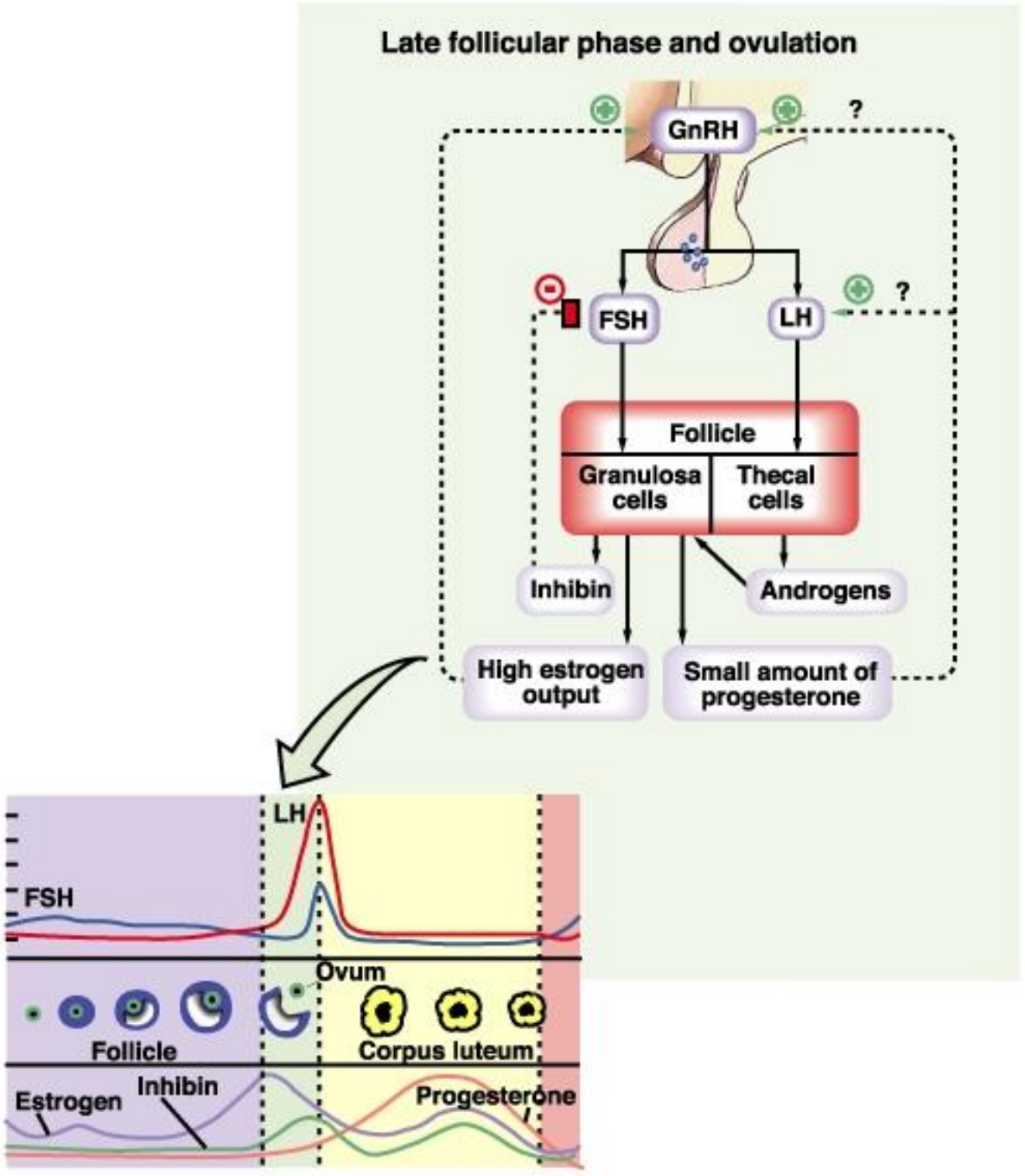
1-Theca externa release proteolytic enzymes leading to dissolution of the wall.



Pituitary hormones during the normal female sexual cycle

2- Rapid growth of new blood vessels into the follicle wall and at the same time prostaglandins are secreted (local hormones that cause vasodilatation) into the follicular fluid leading to plasma transudation into the follicle and follicular swelling, then rupture, and discharges the ovum to the abdominal cavity

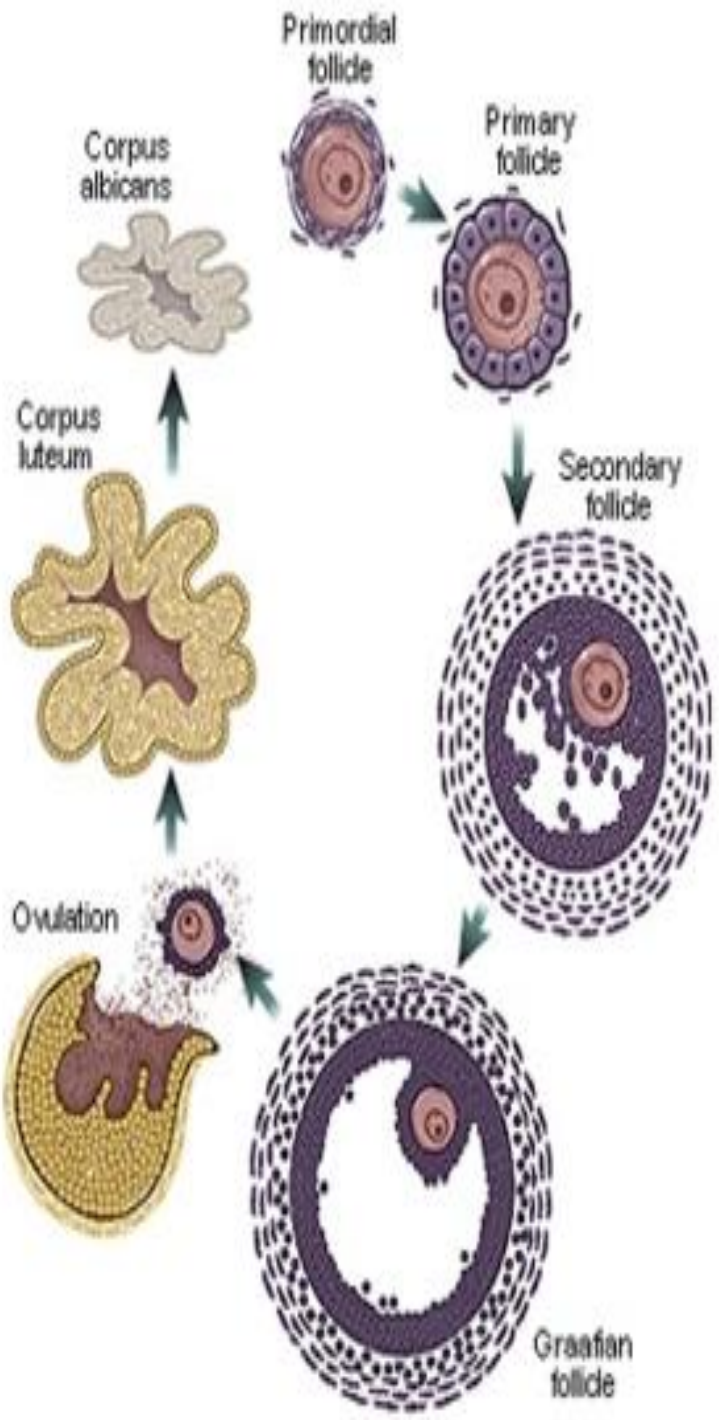


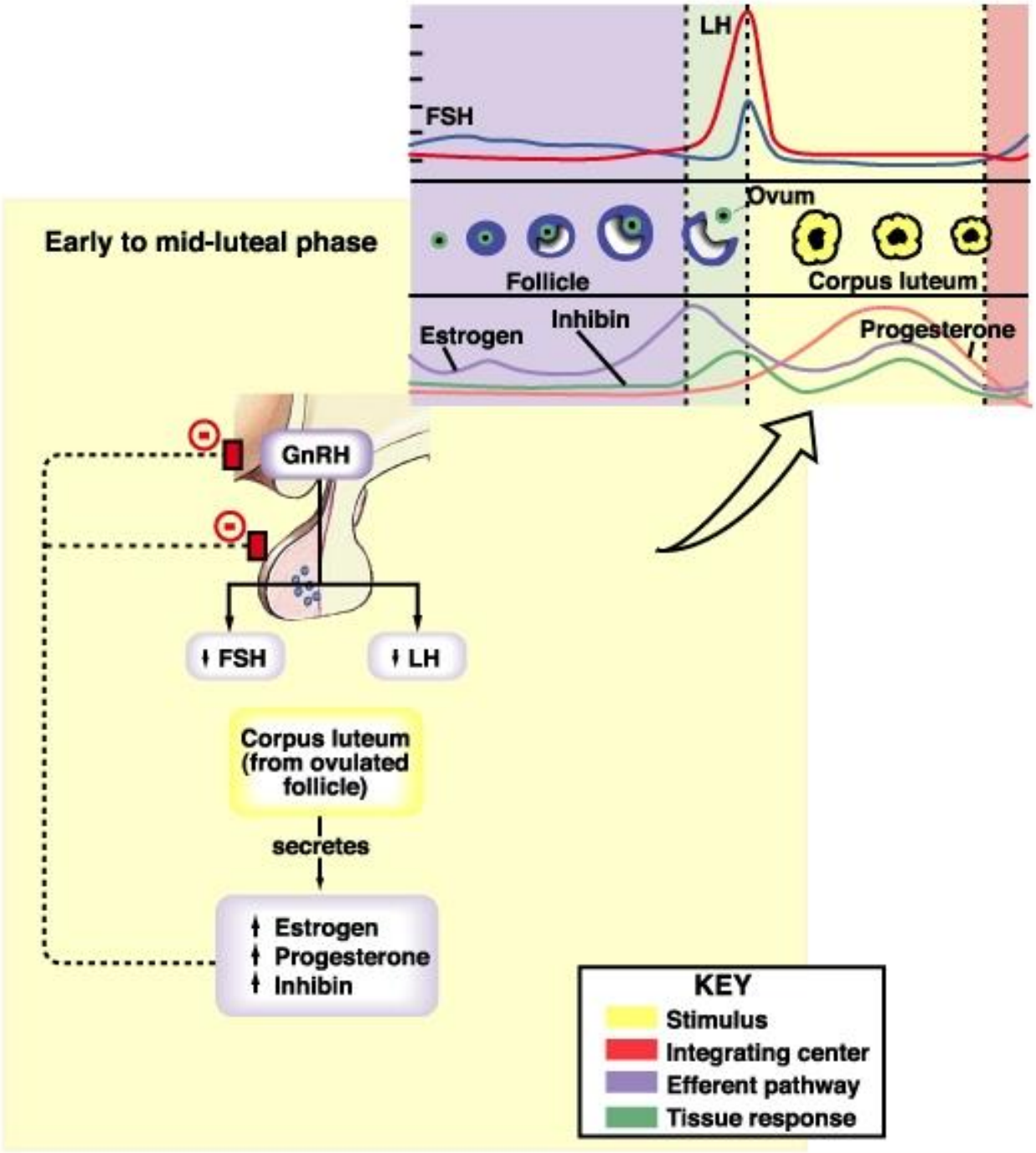

Late follicular phase and ovulation
GnRH
?
FSH
LH
?
Follicle
Granulosa cells
Thecal cells
Inhibin
Androgens
High estrogen output
Small amount of progesterone
LH
FSH
Ovum
Follicle
Corpus luteum
Inhibin
Estrogen
Progesterone

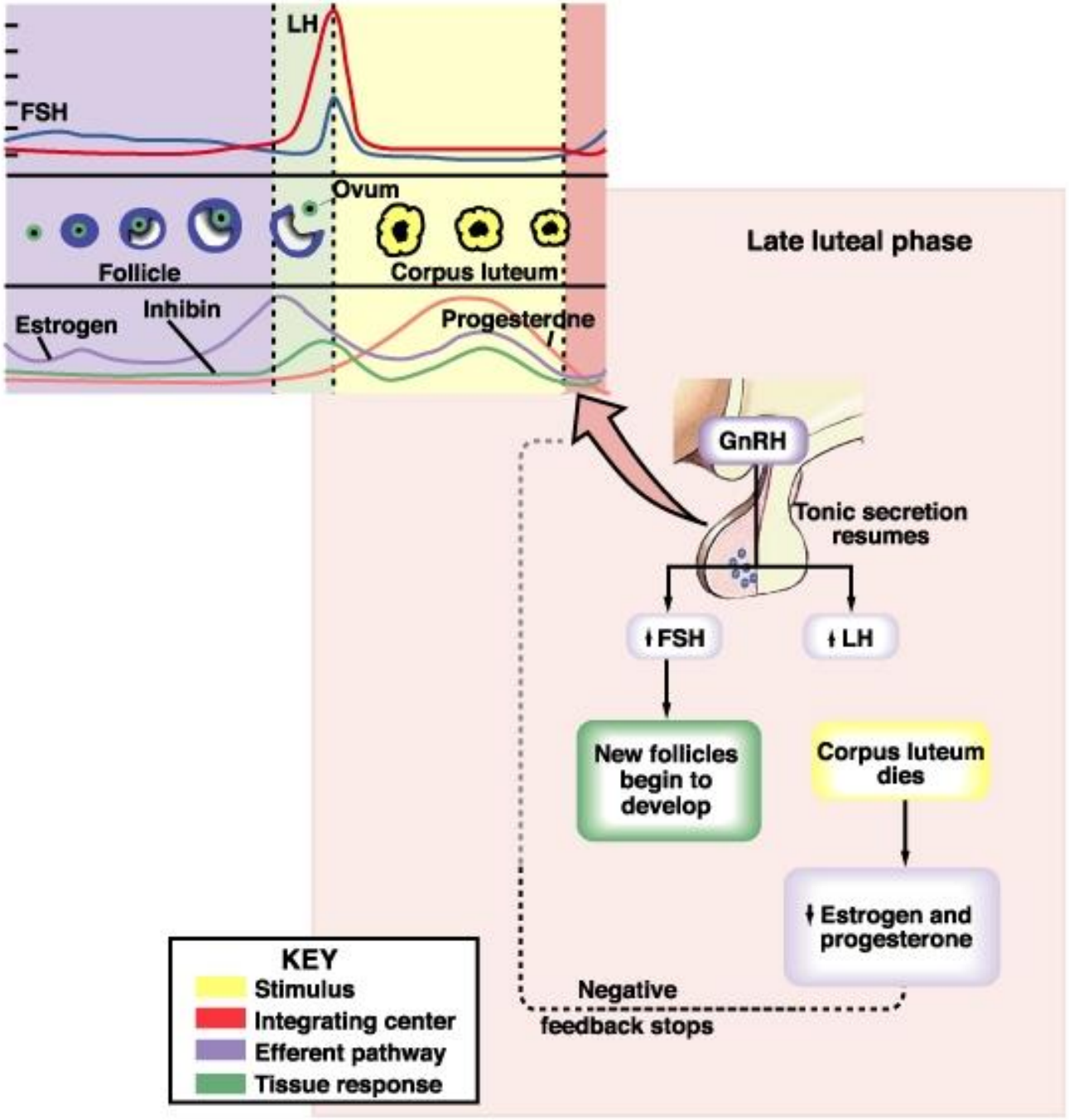
[C] The third phase(Luteal phase) :

- Begins from the 14th –28th day of the cycle, under the control of LH. The high levels of estrogen, progesterone and inhibin lead to – ve feedback so result in low FSH and LH.
- The ruptured follicle is filled with blood forming corpus haemorrhagicum. Minor bleeding from the rupture follicle in to the abdominal cavity causes lower abdominal pain due to peritoneal irritation which may be severe and misdiagnosed as acute appendicitis.

The theca cells and granulosa cells start to proliferate and blood inside the corpus haemorrhagicum is replaced by luteal cells forming mature corpus luteum. Luteal cells secrete estrogen and progesterone.
If pregnancy occur, corpus luteum will persist and no menstruation occur till pregnancy is over. If pregnancy does not occur, corpus luteum will degenerate in the 24th day of the cycle forming regressed corpus luteum and then replaced by scar forming corpus albicans



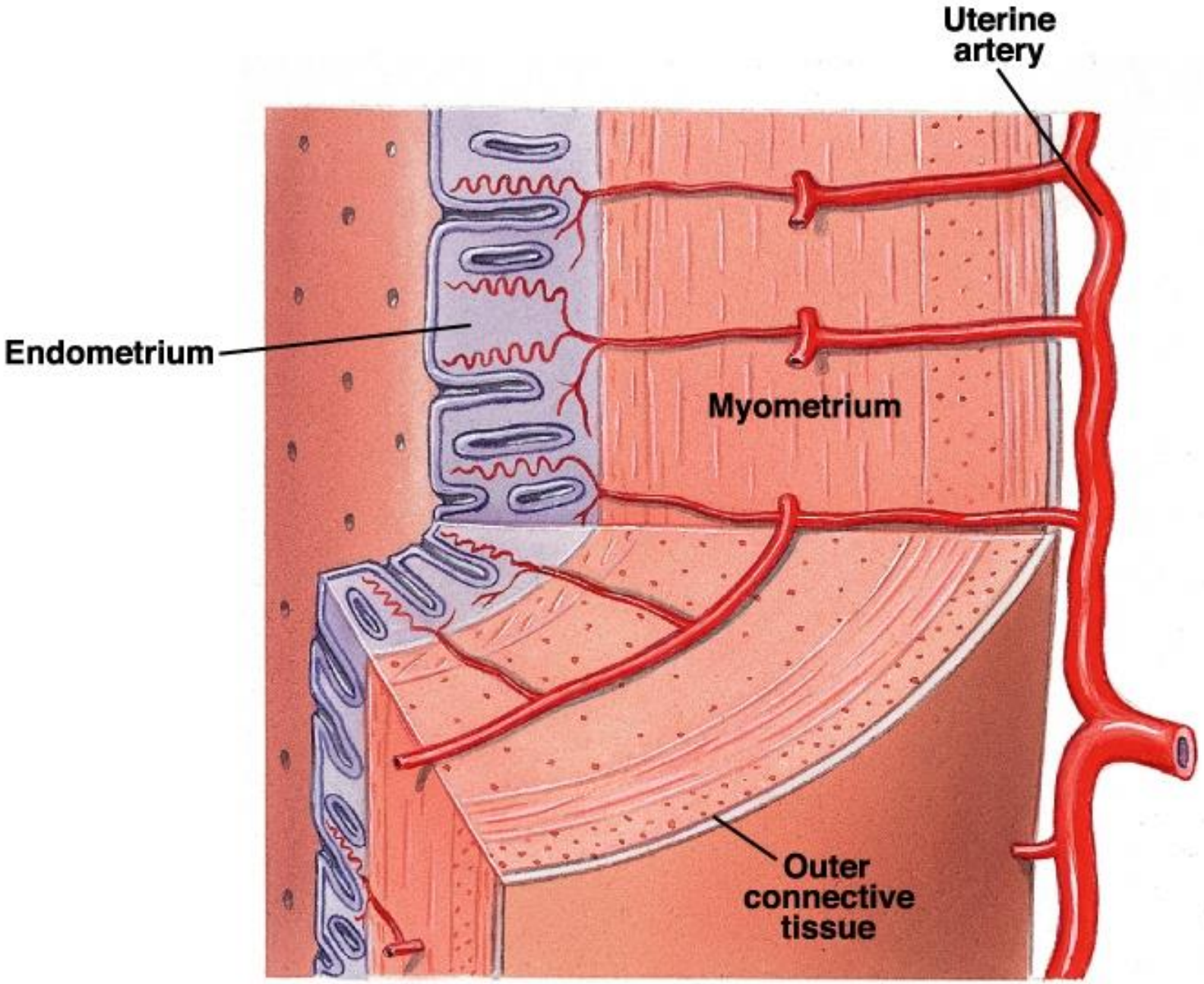

LH
FSH
Ovum
Early to mid-luteal phase
Follicle
Corpus luteum
Estrogen
Inhibin
Progesterone
GnRH
FSH
LH
Corpus luteum (from ovulated follicle)
secretes
Estrogen
Progesterone
Inhibin
KEY
Stimulus
Integrating center
Efferent pathway
Tissue response


LH
FSH
Ovum
Follicle
Corpus luteum
Estrogen
Inhibin
Progesterone
Late luteal phase
GnRH
Tonic secretion resumes
FSH
LH
New follicles begin to develop
Corpus luteum dies
Estrogen and progesterone
Negative feedback stops
KEY
Stimulus
Integrating center
Efferent pathway
Tissue response

Uterine cycle

[A] Proliferative phase (estrogen phase):

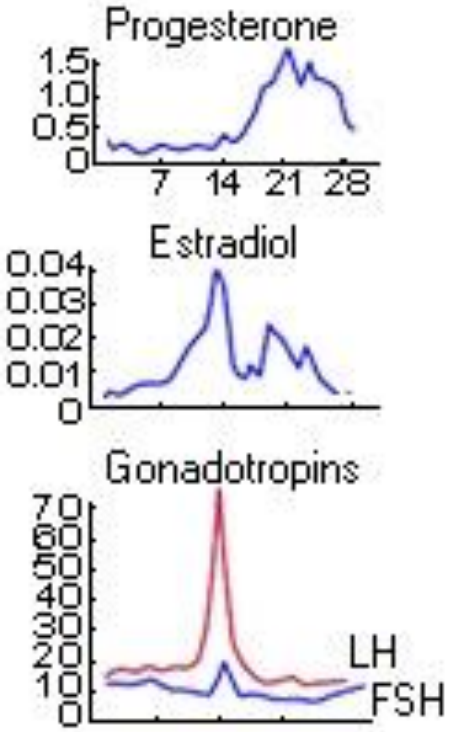
- Under the influence of estrogen from the developing follicle
- The endometrium increases rapidly in thickness and uterine glands increases in length from the 5th to the 14th days of menstrual cycle.

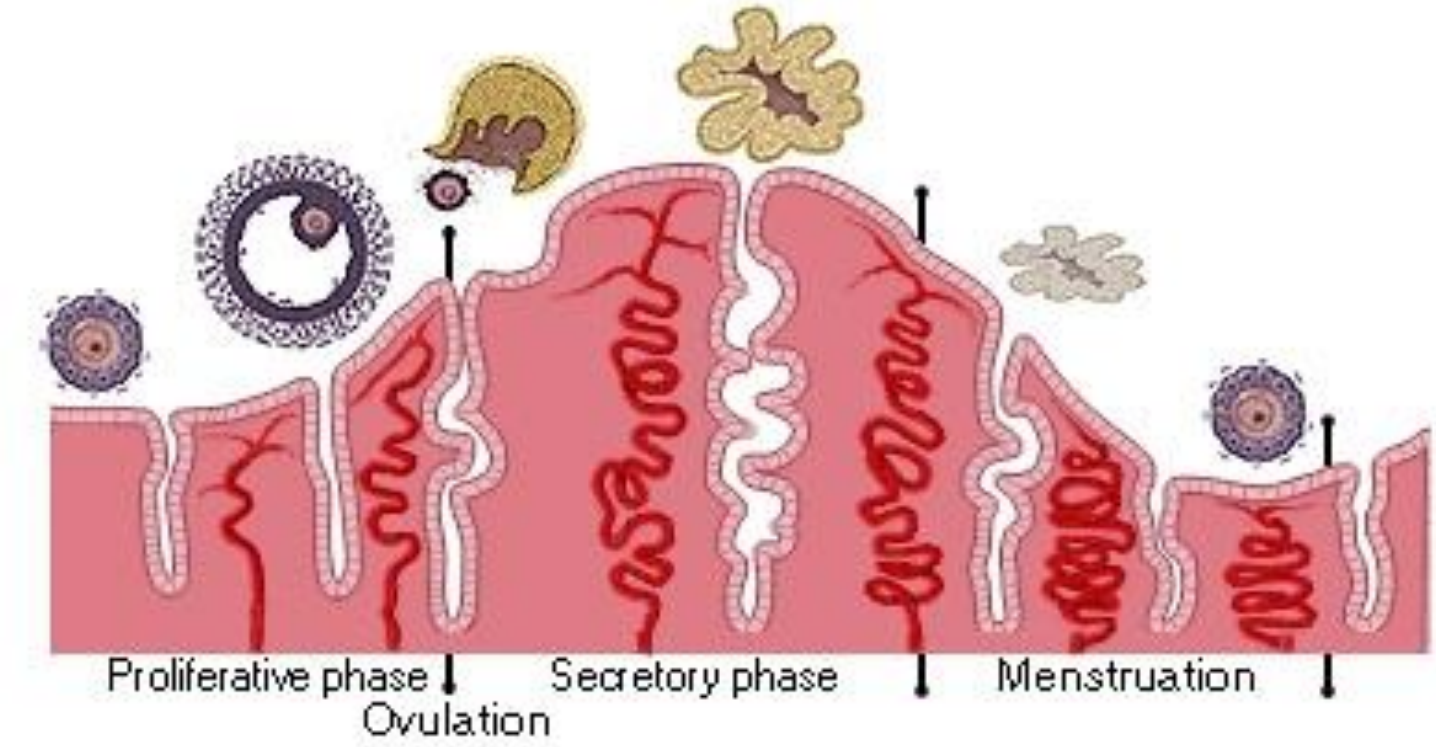

Uterine artery
Endometrium
Myometrium
Outer connective tissue

[B] Secretory or luteal phase(progestational phase):

- After ovulation the endometrium becomes more vascular and slightly edematous and the glands start to secrete clear fluid this occurs under the influence of estrogen and progesterone from corpus Luteum during the 14th to 28th days of menstrual cycle.
- So this phase is regarded as preparation of uterus for implantation of fertilized ovum.

Changes in the ovary and endometrium during the menstral cycle





[C] Desequamation of endometrium (menstruation)

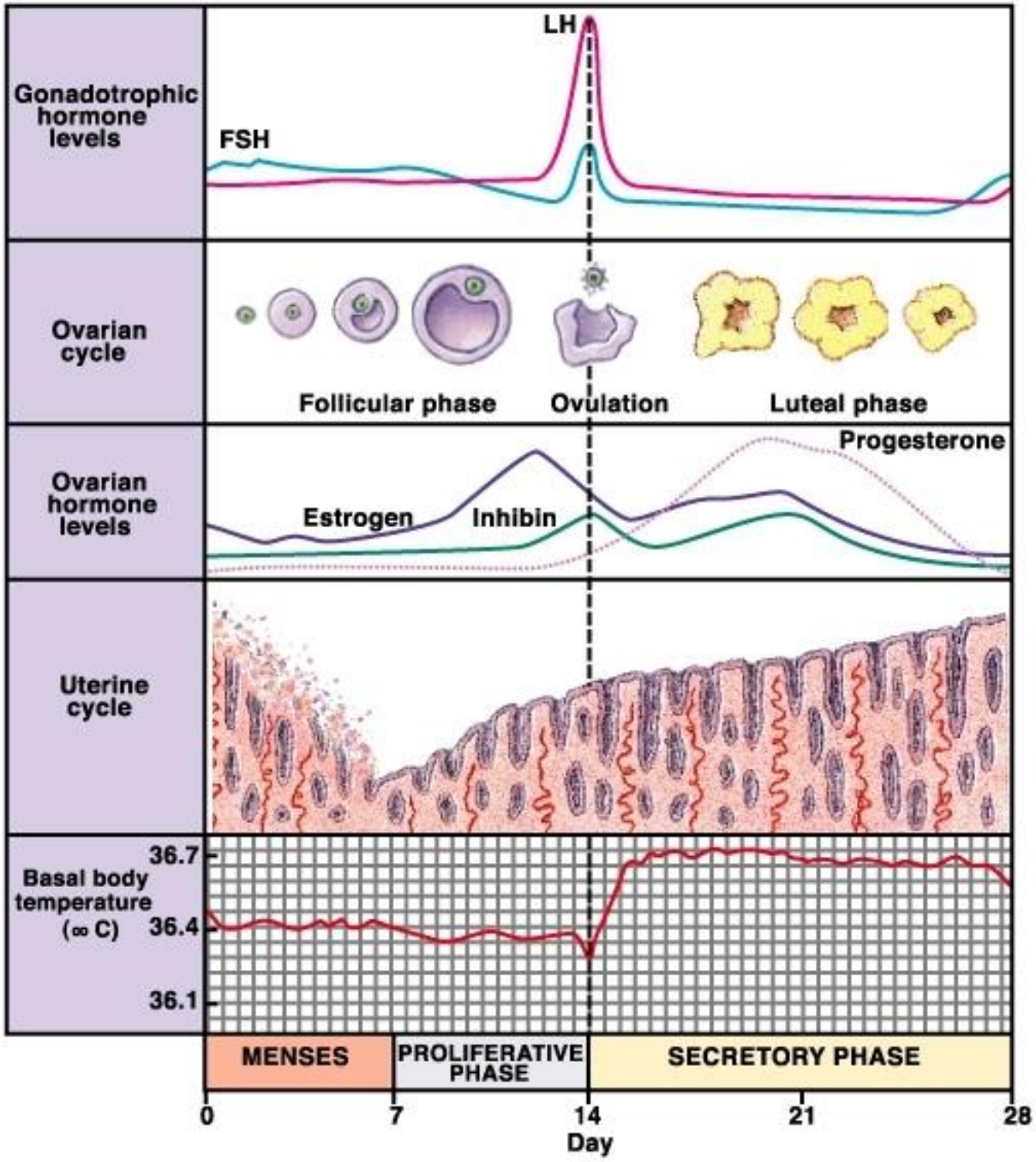
Regression of corpus Luteum ➔ Sharp withdrawal of estrogen and progesterone ➔ Shedding of endometrial tissue ➔ Spotting of blood ➔ confluent and menstrual flow (30 ml)

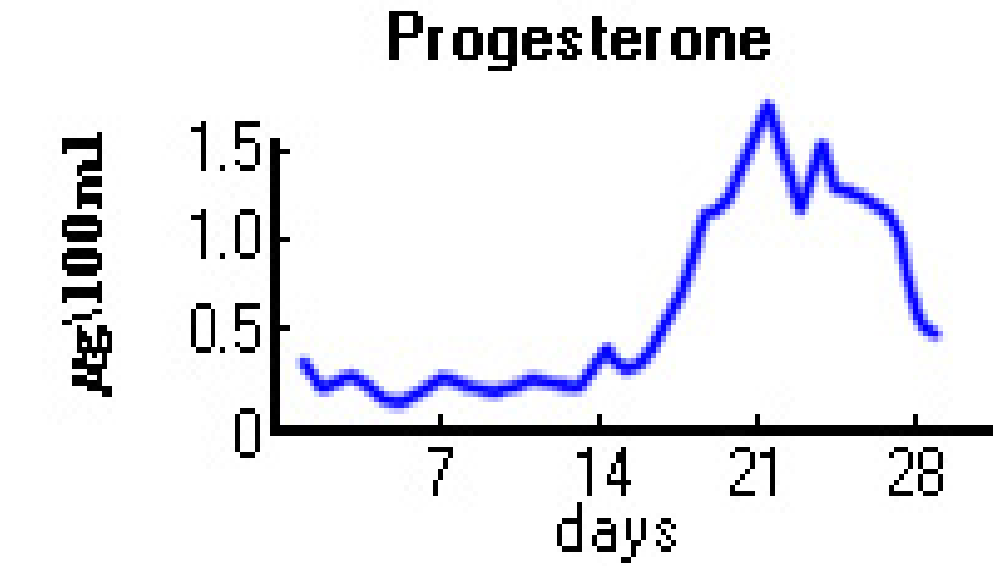
Contents:

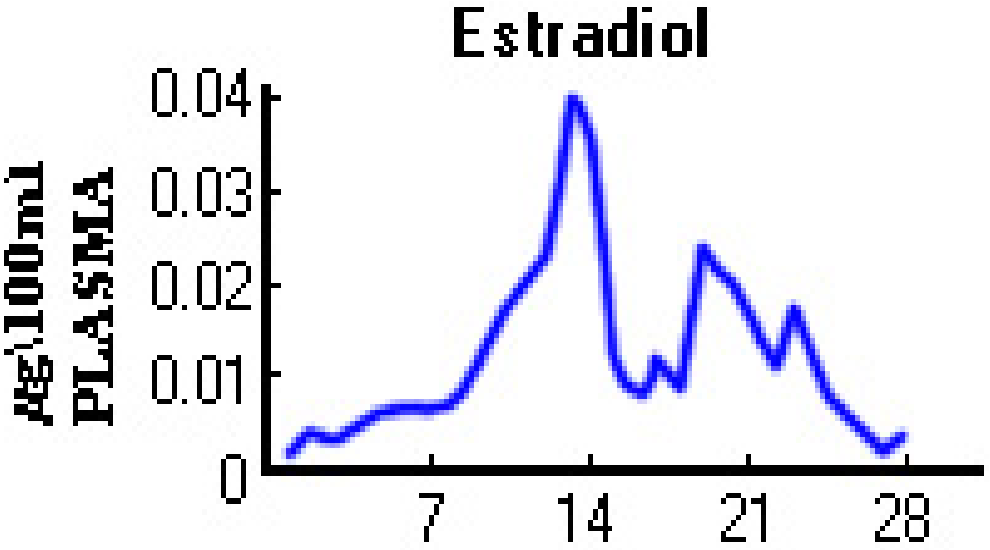
- Tissue derbies
- PGs
- Fibrinolysin
- Leukocytes (leukorrhea)

Onset

- Release of PGs from cellular phospholipids ➔ spasm of spiral artery
- Release of Lysosomal enzymes (from necrotic cells)


Gonadotrophic hormone levels
LH
FSH
Ovarian cycle
Follicular phase
Ovulation
Luteal phase
Ovarian hormone levels
Progesterone
Estrogen
Inhibin
Uterine cycle
Basal body temperature (∞ C)
36.7
36.4
36.1
MENSES
PROLIFERATIVE PHASE
SECRETORY PHASE
0
7
14
21
28
Day


Progesterone
µg\100ml
1.5
1.0
0.5
0
7
14
21
28
days


Estradiol
µg\100ml
PLASMA
0.04
0.03
0.02
0.01
0
7
14
21
28

CYCLIC CHANGES IN UTERINE CERVIX

- Estrogen in proliferative phase → Thin mucus + alkalin medium (promot survival and transport of sperm.
- Progesterone in secretory phase → thick tenacious and cellular mucus (fern like pattern)

CYCLIC CHANGES IN VAGINA

- Estrogen influences vaginal epithelium → becomes cornified epithelium.
- Progesterone influences vaginal epithelium → becomes proliferative epithelium and its secretion becomes thick and rich in leukocytes.

INDICATIONS OF OVULATION:

Endometrial biopsy ➔ secretory pattern (functioning corpus luteum)

Cervical mucus ➔ thick, cellular, fern like pattern (functioning corpus luteum)

Basal body temperature

Progesterone level

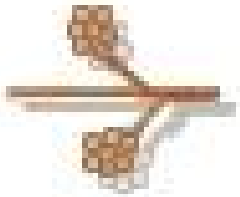
Immature Ducts 1

Estrogen

2

Duct Proliferation

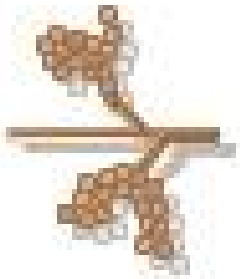
Progesterone 3



Lobulo-Alveolar Proliferation

Prolactin

4



Lactation

Estrogens (relative potency)	Physiologic Actions
17 β Estradiol (100%) **Estrone** (~ 1%)	1. Stimulate secondary sex characters of female 2. Prepare uterus for spermatozoal transport 3. Increase vascular permeability and tissue edema 4. Stimulate growth and activity of mammary gonad and endometrium 5. Prepare endometrium for progestagen action 6. Mildly anabolic 7. Present during pregnancy 8. Regulate secretion of gonadotrophins

ESTROGENS

- The naturally occurring estrogens are estradiol, estrone and estriol.
- Estradiol is the most potent and estriol is the least. They are secreted by theca interna and granulosa cells of ovarian follicle, the corpus luteum and placenta.
- 2% of the circulating estradiol is free.
- The secreted estrogen during menstrual cycle is of ovarian origin with two peaks of secretion: one just before ovulation and the other in the mid–luteal phase.

EFFECTS ON FEMALE GENITILIA

[A] estrogens facilitate growth of ovarian follicle.

[B] increase motility of fallopian tubes

[c] cyclic changes of endometrium, cervix and vagina as mentioned previously.

[D] increases uterine blood flow.

EFFECTS ON FEMALE GENITILIA

[E] increases the amount of uterine muscle and it's content of contractile proteins.

The muscle becomes active and more excitable.

[F] estrogen makes uterus more sensitive to oxytocin.

[G] vaginal epithelium is changed from cuboidal to stratified columnar epith.

EFFECT ON DEVELOPMENT OF SECONDARY SEXUAL CHARACTERS

[A] female body configuration: narrow shoulder, broad hip, converged thigh, diverged arm. Fat distribution in buttocks and breast .

[B] larynx: voice becomes high pitched.

[C] skin: soft, smooth, but thicker than childhood, more vascular, therefore, the skin is warm and bleed more than male, less body hair, more scalp hair, pubic hair is flat topped pattern (axillary and pubic hair is due to effect of adrenal androgen).

EFFECT ON DEVELOPMENT OF SECONDARY SEXUAL CHARACTERS

[D] sebaceous glands secretions become more fluid so reduced acne formation.

[E] breasts become enlarged due to growth of stromal tissue, ductal system deposition of fat, pigmentation of areola and appearance of mature female breast.

BEHAVIORAL EFFECTS

Estrogens are responsible for estrous behavior in animals and they increase libido in human due to effects on special neurons in hypothalaumus.

EFFECT ON SKELETON

- Estrogen had osteoblastic activity so it causes increase in bone length but later causes early closure of epiphyseal plate so low estrogen levels lead to ostroporosis, decrease bone matrix and decrease bone Ca^{+} and $PO4^{-}$.

MATABOLIC EFFECTS

- On proteins it causes protein anabolic effect on specific target organs like breast, skeleton, uterus and certain fatty areas.
- On fat it causes increase in BMR, increases deposition of fat in subcutaneous tissues and has significant plasma cholesterol lowering action (less atherosclerosis).

OTHER EFFECTS

- Mild Na and H_2O retention (significant in pregnancy only).
- Has positive and negative feedback effect on LH and FSH secretion.
- Increase size of pituitary.
- Increase secretion of angiotensinogen and thyroid binding protein.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PROGESTERONE

- It is secreted mainly from corpus luteum, placenta and less by the follicle.
- Small amounts enter circulation from testes and adrenal cortex.
- About 2% of circulating progesterone is free, 80% is bound to albumin and 18 % to corticosteroid binding protein.
- Plasma progesterone level in men is 1 nmol/L whereas in female is 3 nmol/L during follicular phase and 60 nmo/L in luteal phase

EFFECTS OF PROGESTERONE

UTERUS

[A] Cyclic changes on vagina and cervix.

[B] Progestational changes on endometrium.

[C] Antiestrogenic effect on myometrium including decreasing excitability of myometrium cells and their spontaneous electrical activity by increasing their membrane potential, also decrease number of estrogen receptors in endometrium and increase conversion of estradiol to less active estrogen.

EFFECTS OF PROGESTERONE

FALLOPIAN TUBES

Promotes secretory changes in mucosal membrane which are necessary for nutrition of fertilized ovum.

EFFECTS OF PROGESTERONE BREAST

- Stimulate the development of lobules and alveoli and increase fluid in subcutaneous tissue leading to breast swelling.
- It induces differentiation of Estrogen-prepared ductal tissues and support the secretory function of breast during lactation.

EFFECTS OF PROGESTERONE HYPOTHALAMUS & PITUITARY

High does of progesterone causes feedback effect and inhibit LH secretion and potentiate the inhibitory effect of estrogen preventing ovulation (the action of contraceptive pills).

OTHER EFFECTS OF PROGESTERONE

Large doses produce natriuresis by blocking the action of aldosterone on the kidney.

It has thermogenic effect causing rise in basal body temperature at time of ovulation. Progesterone causes stimulation of respiration and therefore, alveolar $Paco_2$ falls as progesterone secretion rises. The hormone does not have a significant anabolic effect.

RELAXIN

Polypeptide hormone produced by corpus luteum, uterus, placenta and mammary glands in women and from prostate in man. During pregnancy it relaxes pubic symphysis and other pelvic joints and softens and dilates uterine cervix to facilitate delivery. It also inhibits uterine contractions and may play a role in the development of mammary glands.

RELAXIN

- In non – pregnant woman it's function is unknown.
- In men Relaxin is found in semen and it may help to maintain sperm motility and aid sperm penetration to the ovum.

INHIBIN

A polypeptide produced by the granulosa cells and inhibits FSH secretion.

Progestagens (relative potency)	Physiologic Actions
Progesterone (100%)	1. Prepare uterus to receive embryo
	2. Maintain uterus during pregnancy
17a-Hydroxy-progesterone (~ 40-70%)	3. Stimulate growth of mammary glands, but suppress secretion of milk
20a-Hydroxy-progesterone (~ 5%)	4. Mild effect on Na^+ loss via distal convoluted tubule of kidney
	5. General mild catabolic effect
	6. Regulate secretion of gonadotrophins

CONTRACEPTION

Woman undergoing long term therapy with large dose of estrogen do not ovulate because of depressed levels of FSH, and multiple irregular bursts of LH secretion rather than single mid-cycle peak.

CONTRACEPTION

- Contraceptive pills of combined estrogen and progesterone also leads to failure of ovulation because both FSH and LH are suppressed in addition progesterone makes the cervical mucus thick and unfavorable to sperm migration and may interfere with implantation.
- The pills are given for 21 days then withdrawn for 5–7 days to allow menstrual flow started again.

PUBERTY

- Thelarche
- Pubarche
- Menarche
- Adenarche

PUBERTY

- In childhood, hormone levels are **lowest** and **FSH is more than LH**.
- At puberty and during the reproductive years, hormone level **increase** and **LH is more than FSH**.
- In senescence, hormone levels are **highest** and **FSH is more than LH**.

MENOPAUSE

- Cessation of menstrual cycles at age of 45 – 55 years is called menopause. The physiological changes include:-
- Unresponsiveness of ovaries to FSH and LH due to decline in number of primordial cells.
- Ovaries do not secrete estrogen and progesterone.

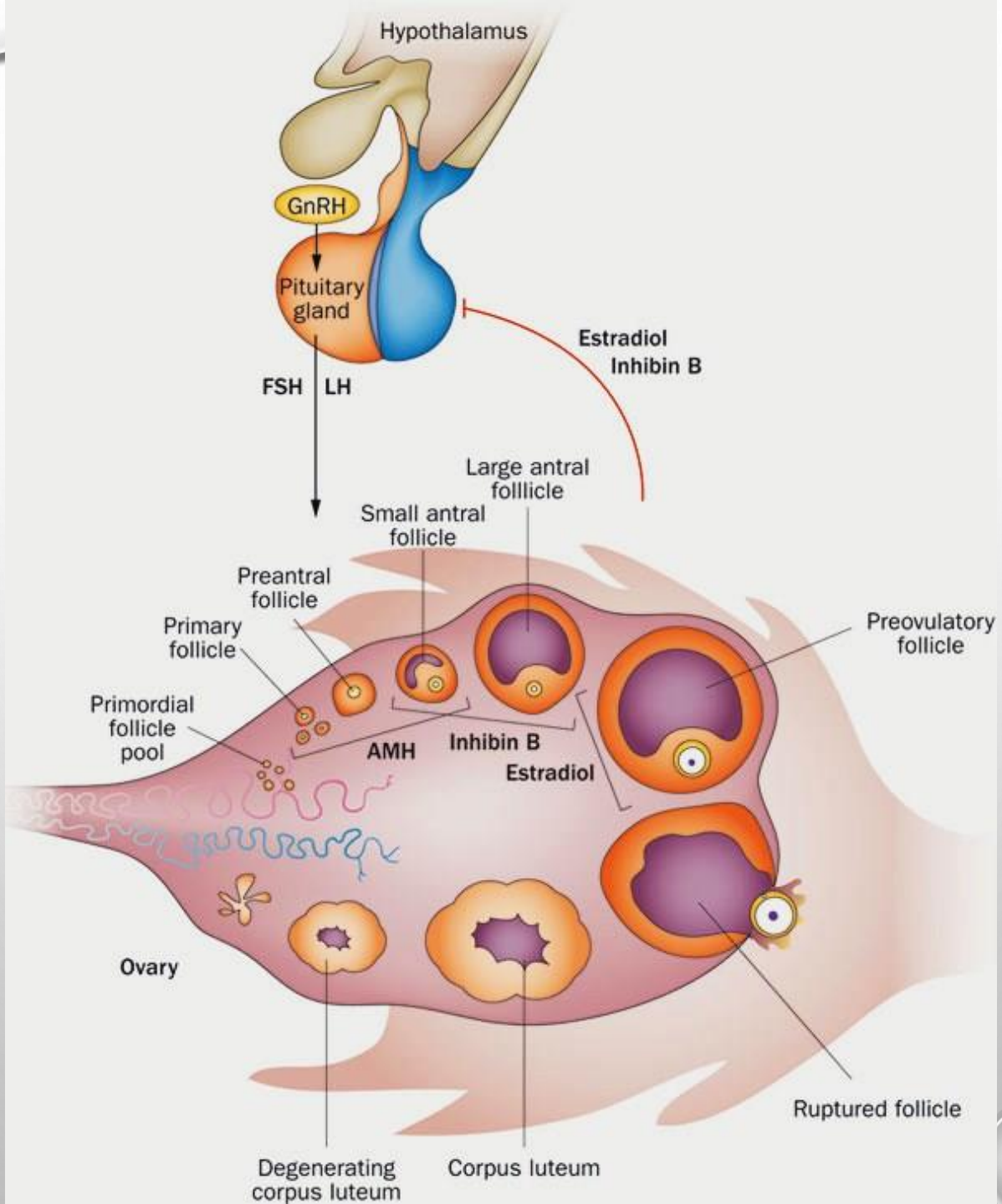
MENOPAUSE

- FSH and LH secretion and plasma levels are increased due to cessation of the – ve feedback.
- Clinical symptoms of low estrogen levels are experienced.

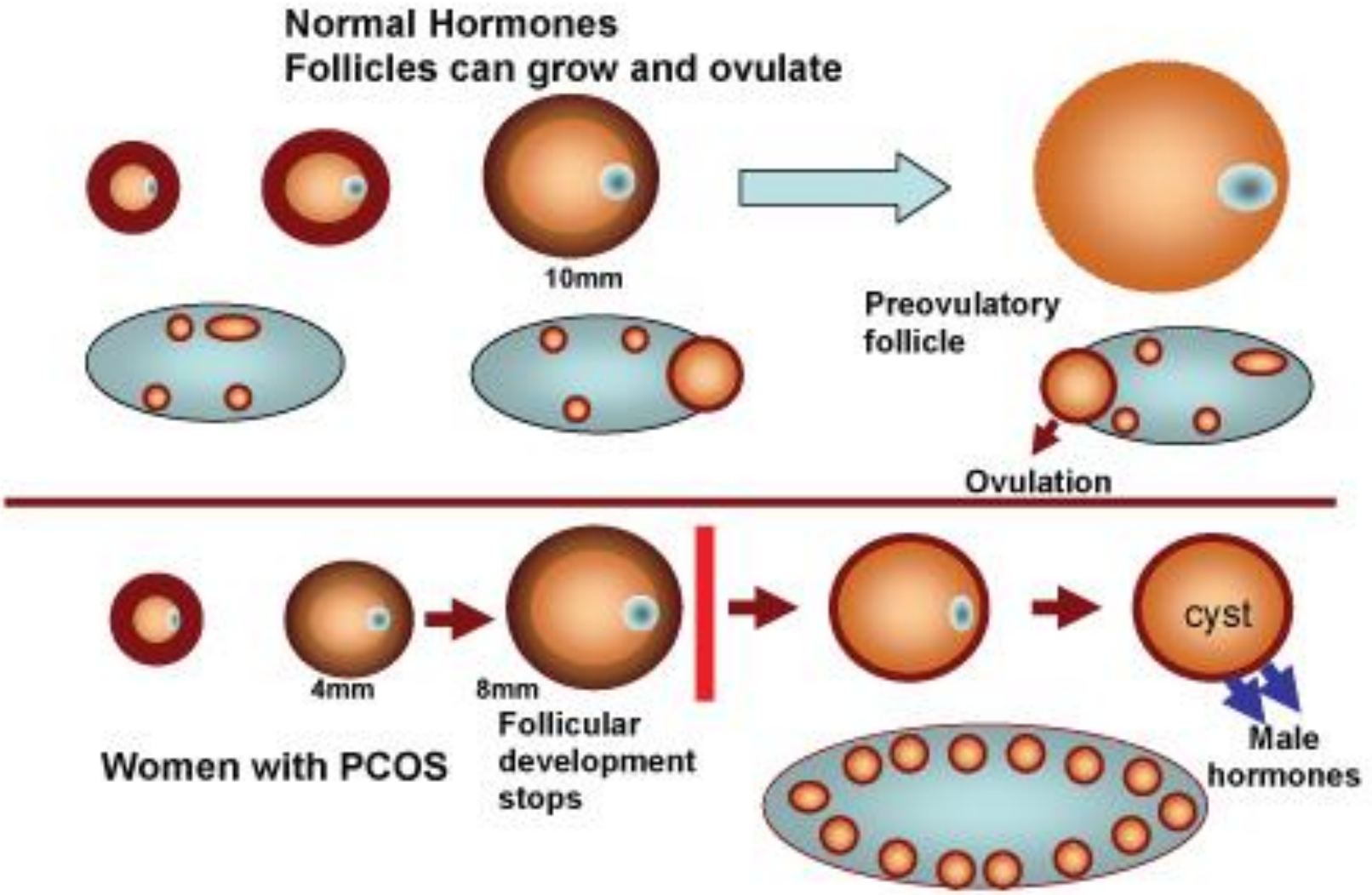
MENSTRUAL ABNORMALITIES

- Anovulatory cycles
- Amenorrhoea
- Dysmenorrhoea
- Premenstrual syndrome
- Menorrhagia
- Metrorrhagia
- Oligomenonhoea

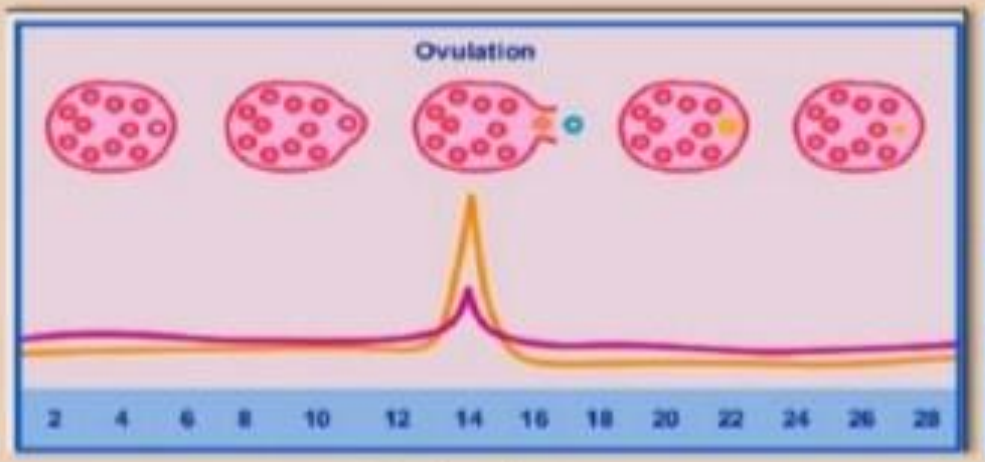
Normal ovarian function



Comparison between normal ovulation and PCOS

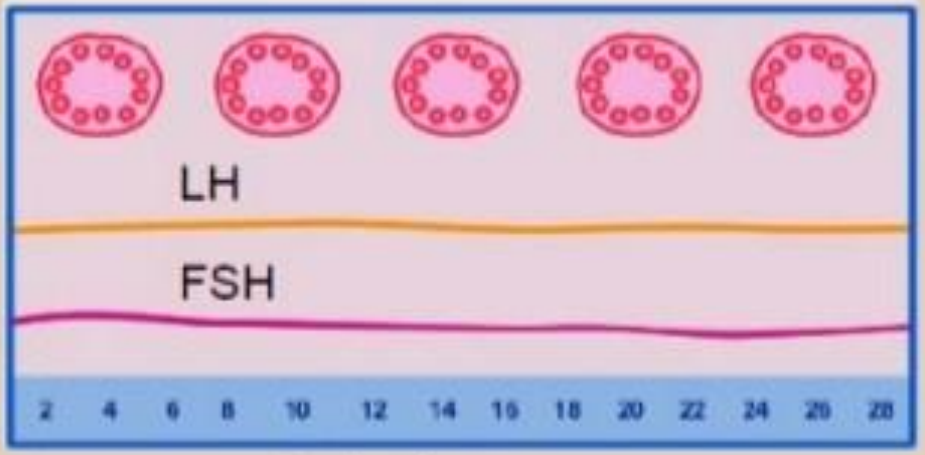


Normal Menstrual Cycle



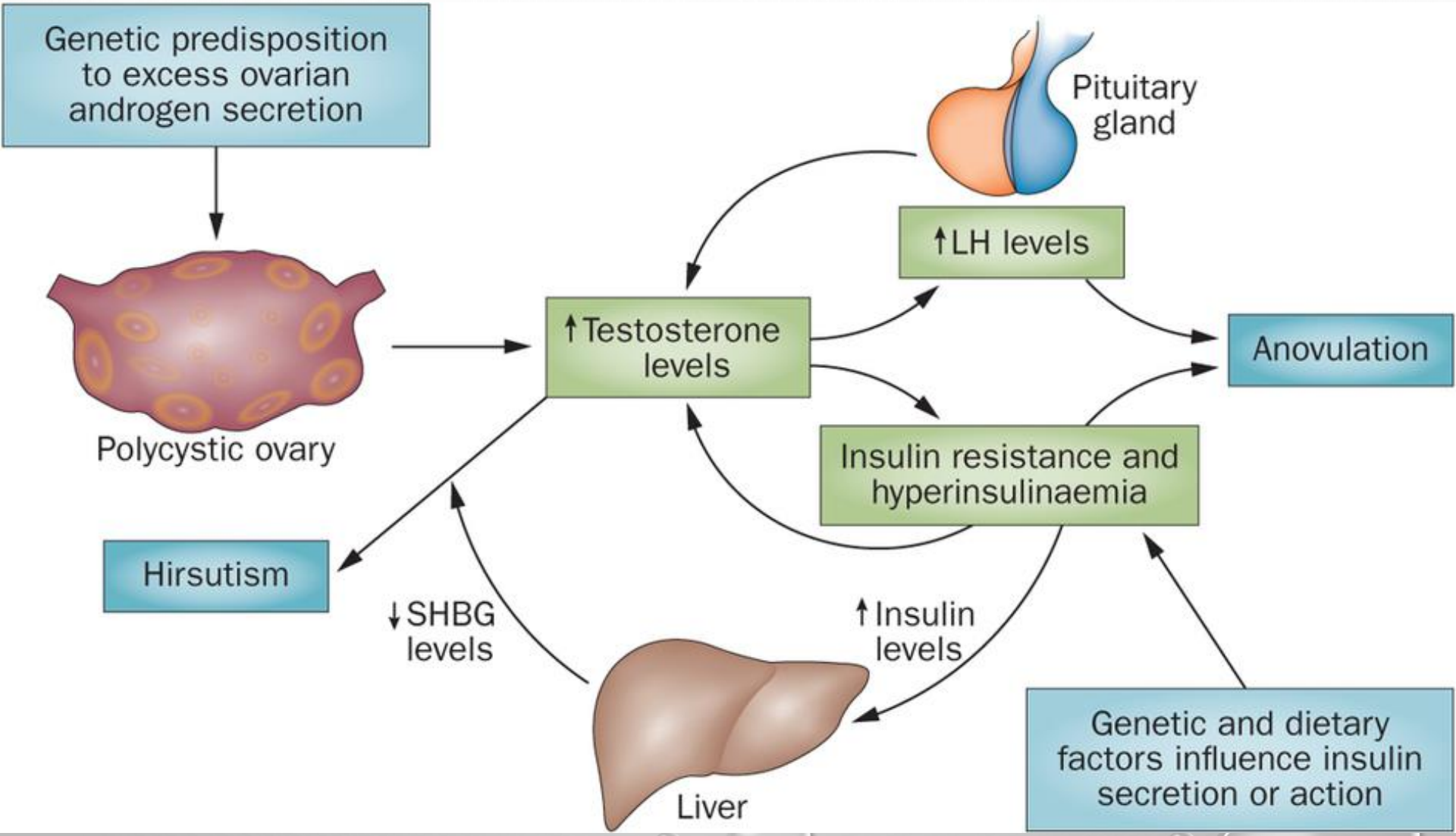
Cycle day

PCOS



Cycle day

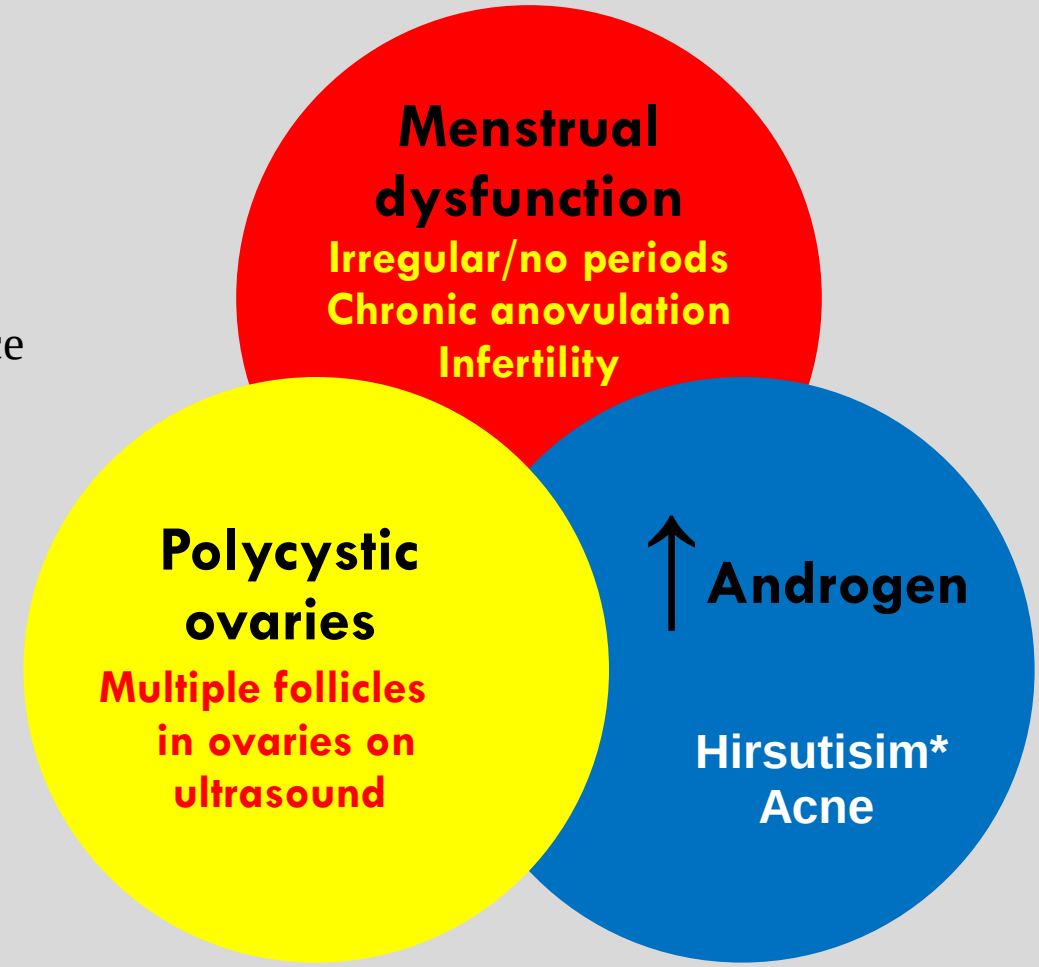
Pathophysiology of PCOS



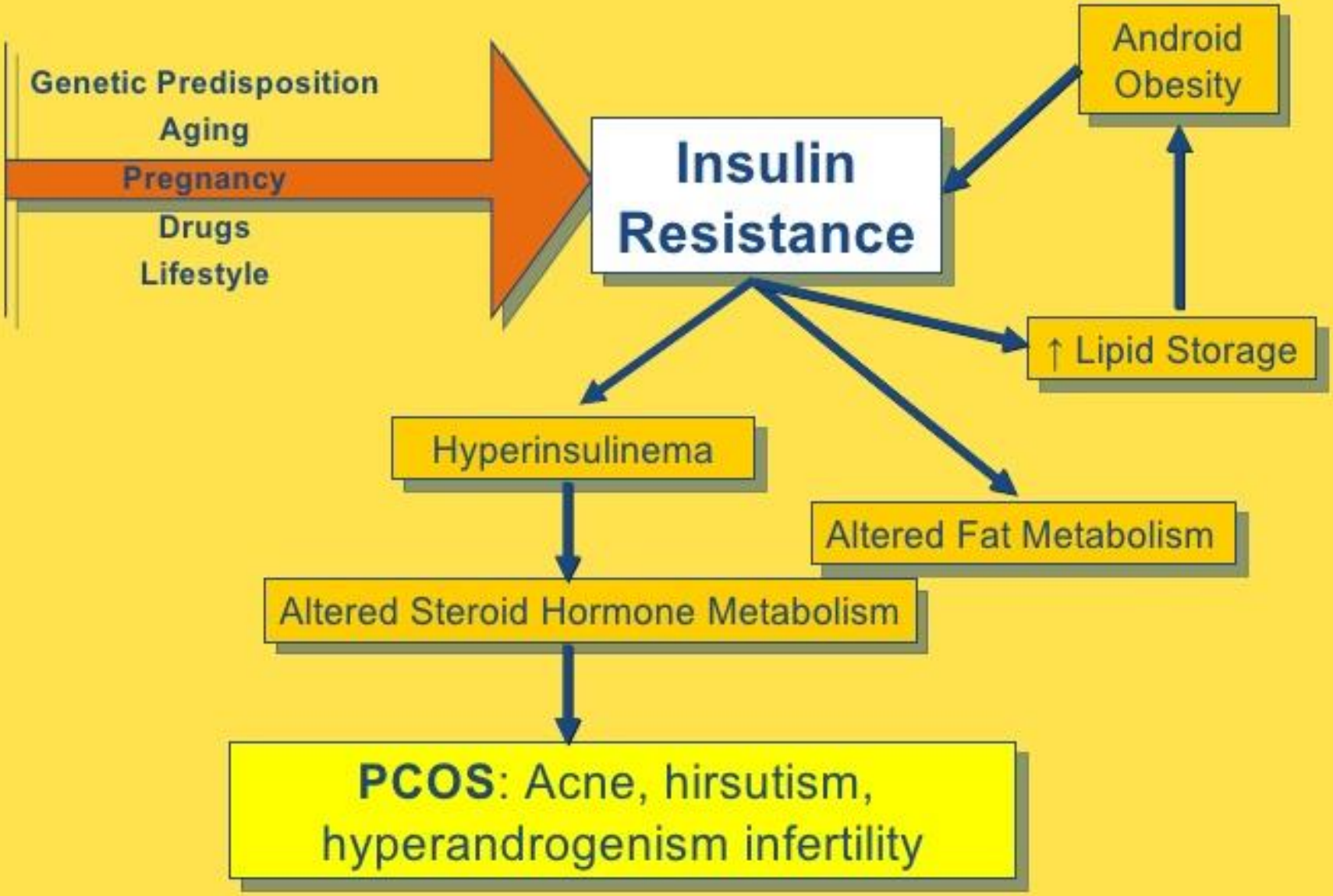
Classic PCOS Features

Common associations:

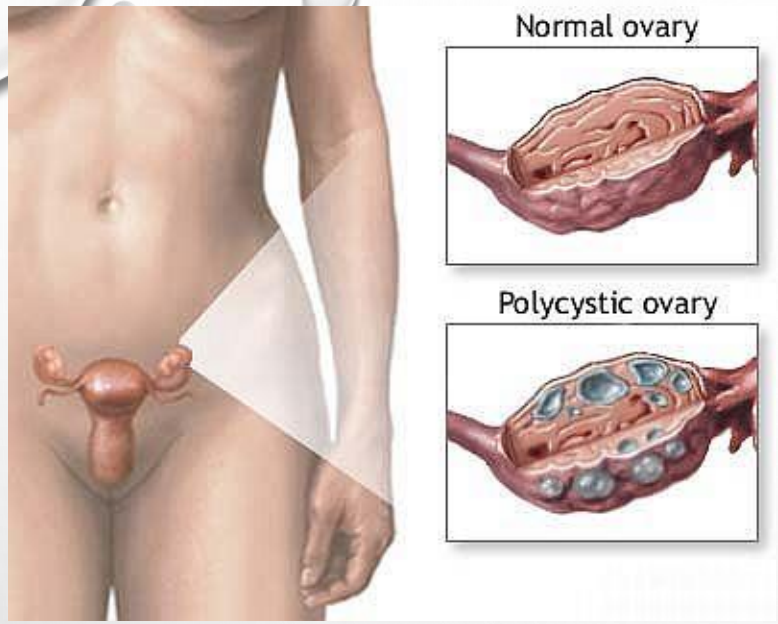
- ♦ Overweight
- ♦ Insulin resistance

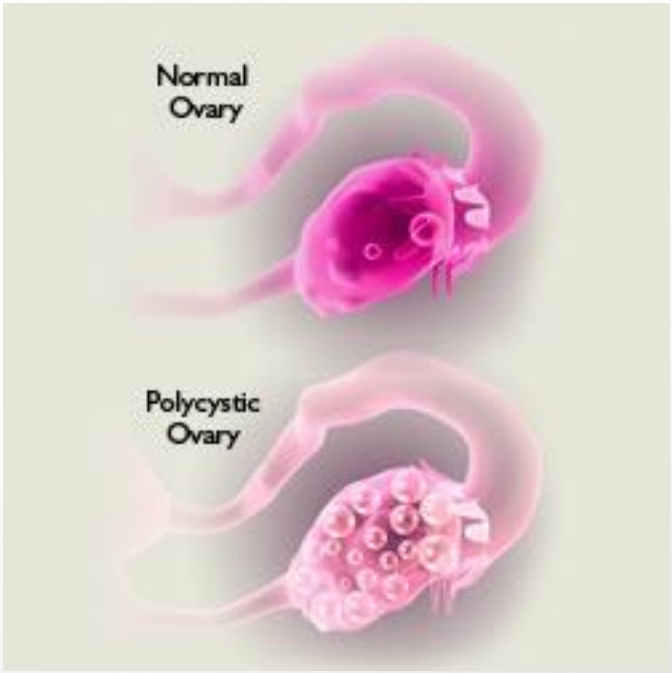


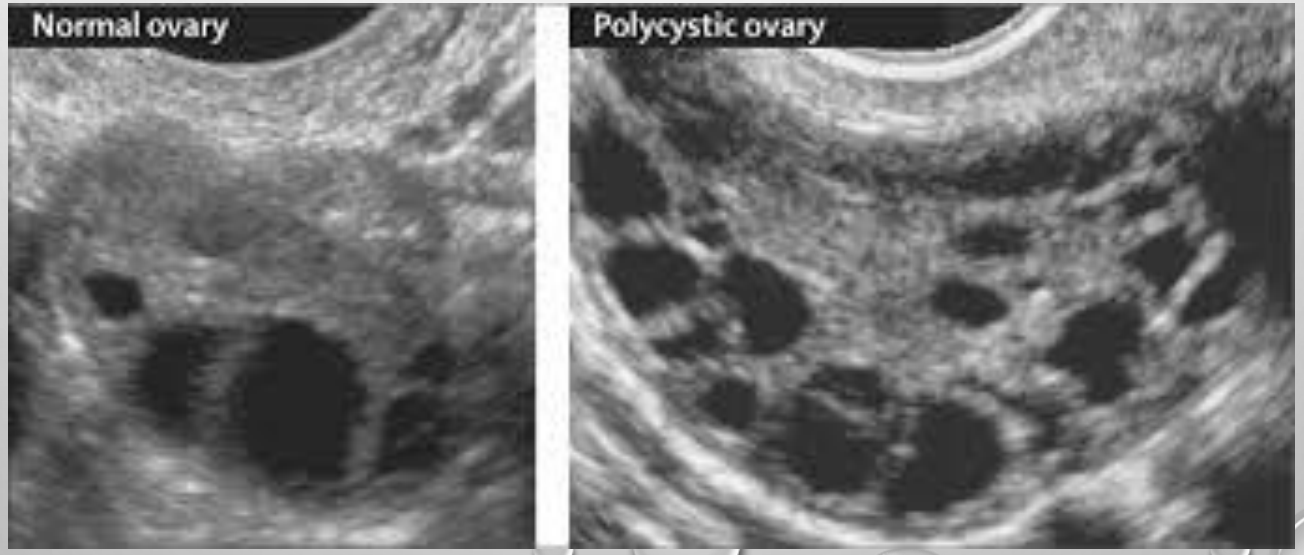
*** Increased facial and body hair growth**



Adapted from Cristello *et al*. Gynec Endocrin 21:340; 2005

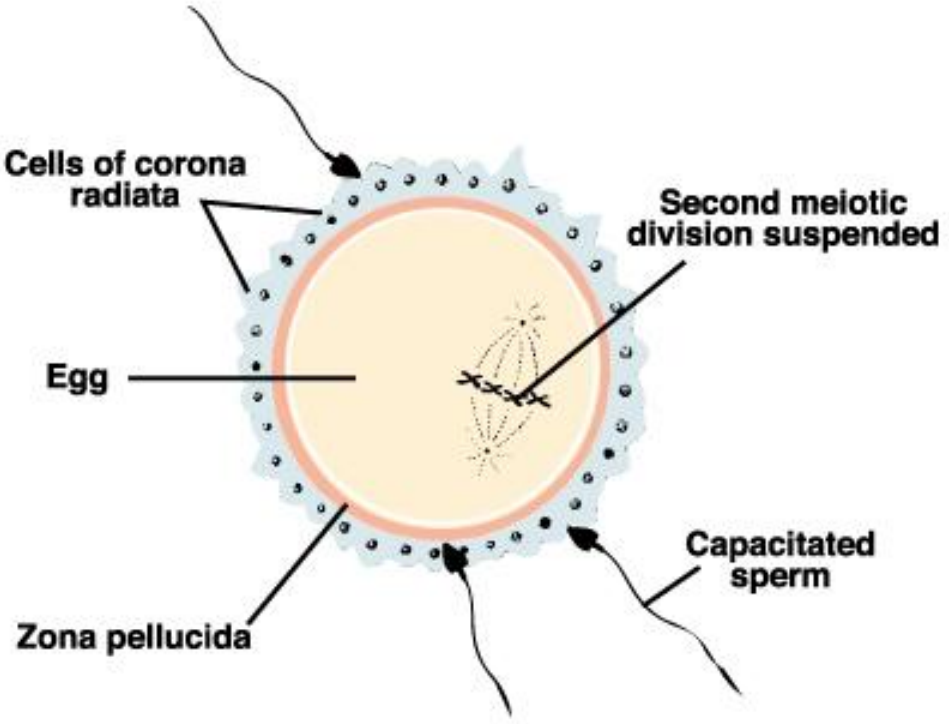

Normal ovary
Polycystic ovary

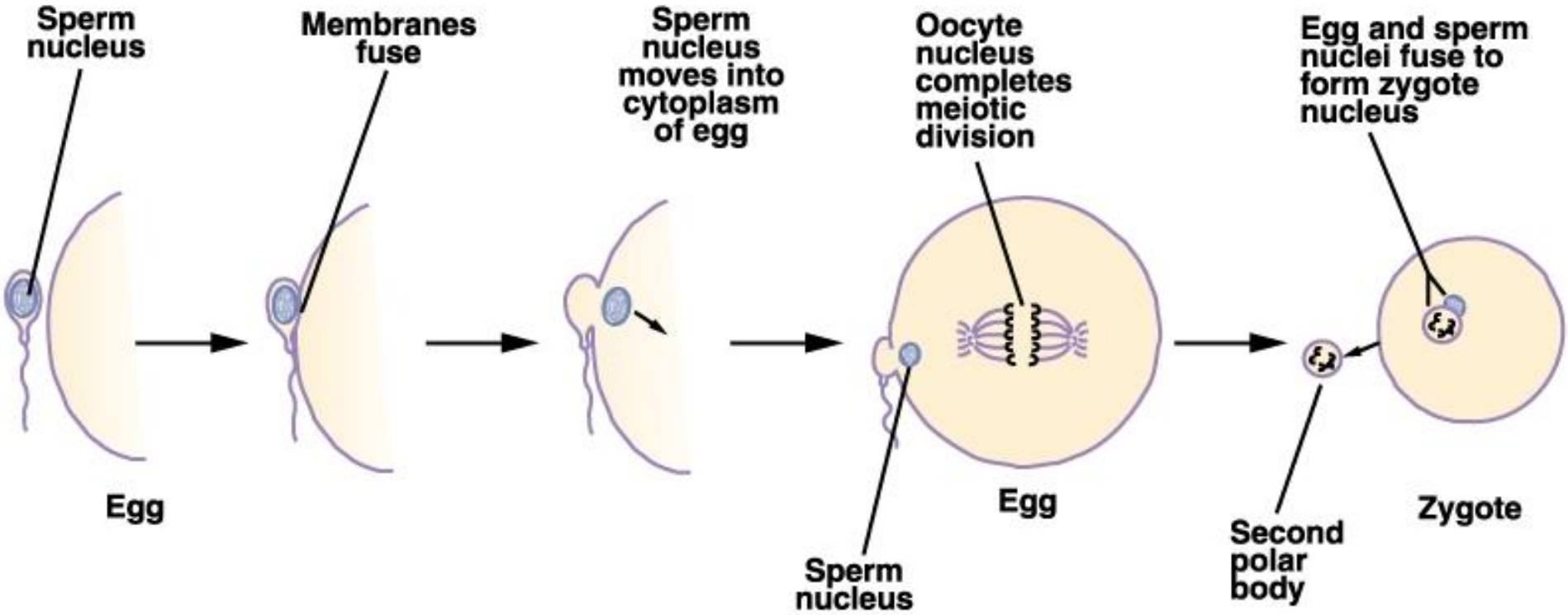

Normal
Ovary
Polycystic
Ovary


Normal ovary
Polycystic ovary

Mechanisms*	Manifestations
Pituitary dysfunction	High serum LH High serum prolactin
Anovulatory menstrual cycles	Oligomenorrhoea Secondary amenorrhoea Cystic ovaries Infertility
Androgen excess	Hirsutism Acne
Obesity	Hyperglycaemia Elevated oestrogens
Insulin resistance	Dyslipidaemia Hypertension

Fertilization




Sperm nucleus
Membranes fuse
Sperm nucleus moves into cytoplasm of egg
Oocyte nucleus completes meiotic division
Egg and sperm nuclei fuse to form zygote nucleus
Egg
Sperm nucleus
Egg
Second polar body
Zygote

FERTILIZATION AND IMPLANTATION

- The fusion is mediated by **fertilin** which is a protein found in the head of the sperm.

1. The signal that initiate development.
2. Reduction in membrane potential of the ovum that prevent polyspermy.

FERTILIZATION AND IMPLANTATION

- Fertilization occurs in the mid portion of uterine tube.
- Humans ovum secretes an attractant or chemotatic factor
- 50–100 sperms reach the ovum and contacts to zona pellucida.
- Sperms bind to a sperm receptor called zp3 in the zona.

FERTILIZATION AND IMPLANTATION

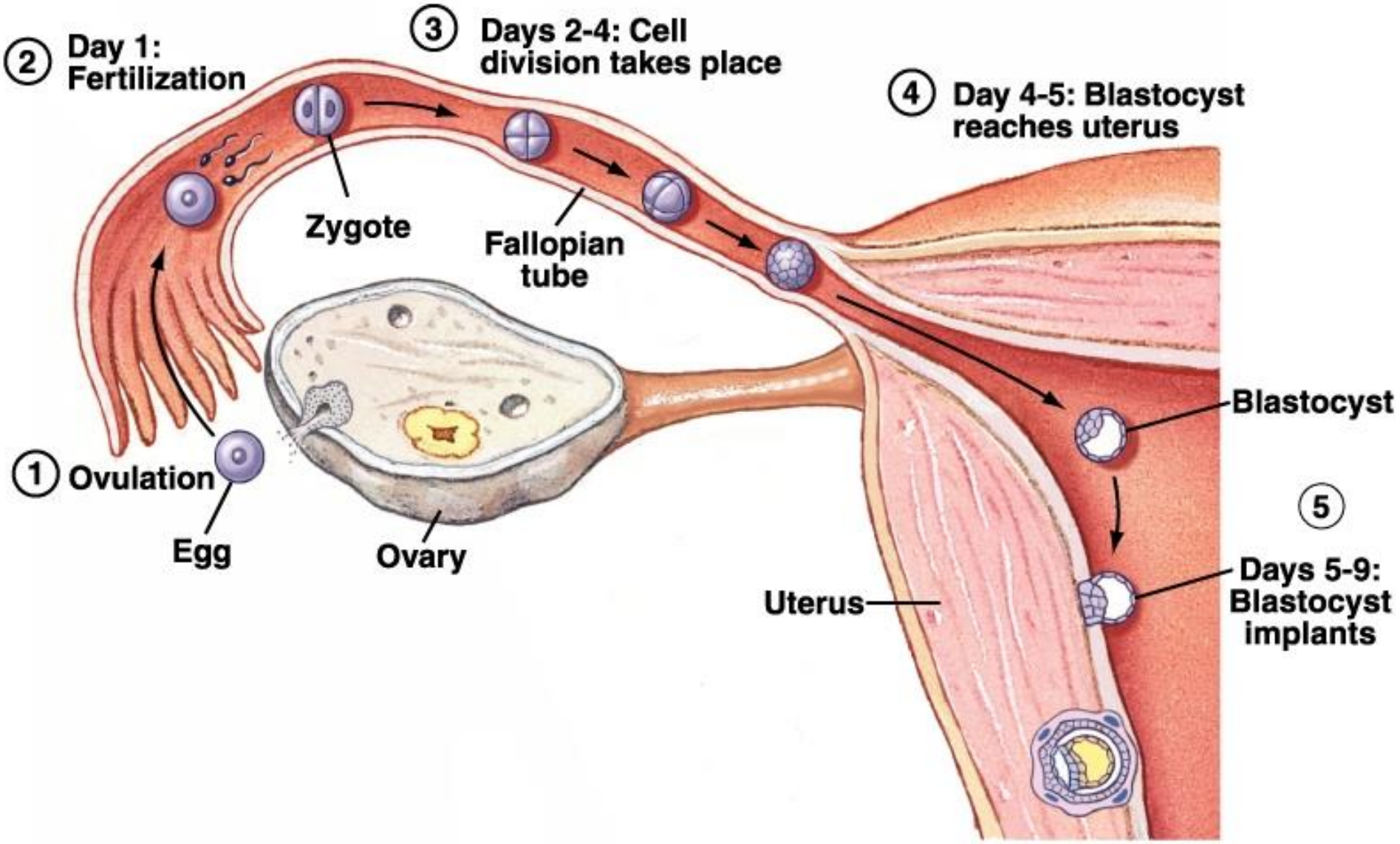
- Followed by acrosomal reaction during which the acrosome breakdown and release of acrosin which aids the penetration of sperm through zona pellucida.

FERTILIZATION AND IMPLANTATION

- The developing embryo is called blastocyst which moves down to the uterus (3 days duration) and reaches the 8 or 16-cells stage.
- Once reaching endometrium the blastocyst becomes surrounded by an outer layer of syncytiotrophoblast and inner layer called cytotrophoblast.

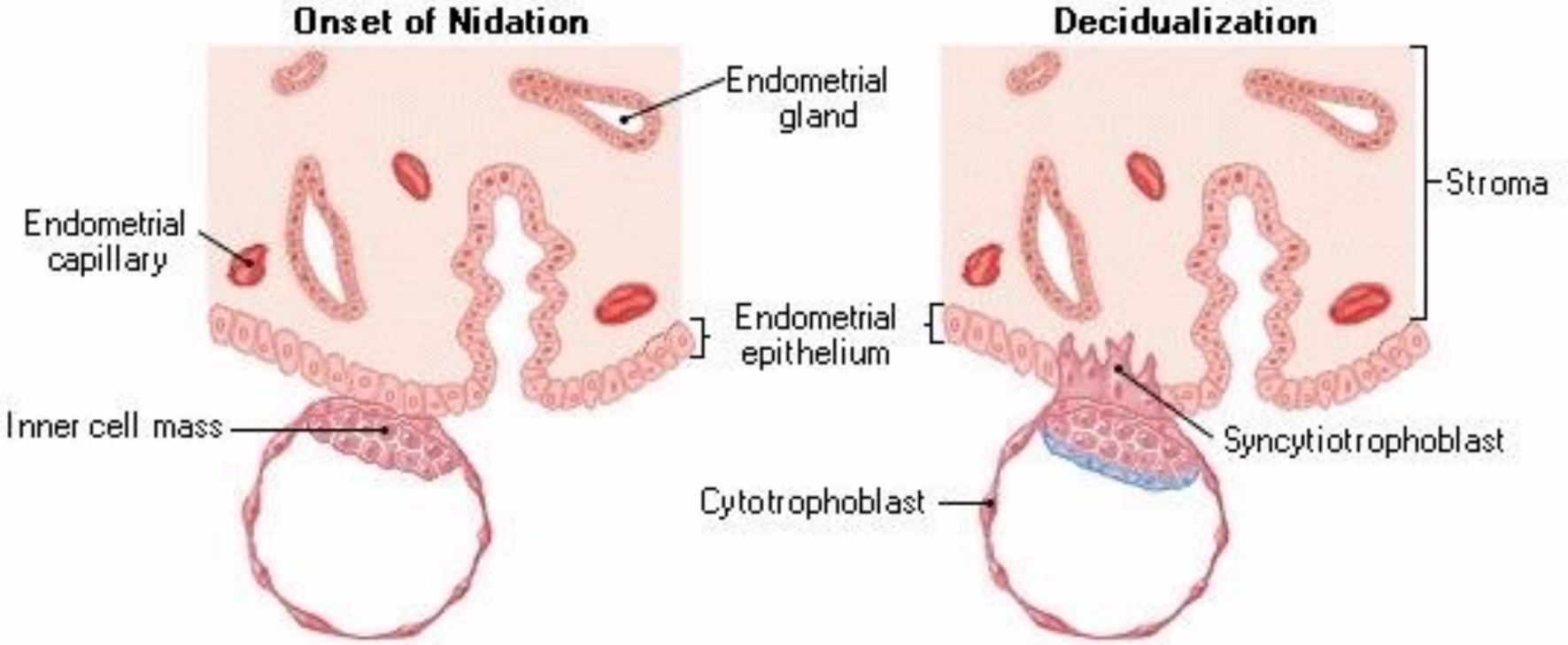
FERTILIZATION AND IMPLANTATION

- The syncytiotrophoblest erodes the endometrium and the blastocyst burrow into it (implantation), placenta then develops.
- Rejection does not occur because the placental trophoblast does not express the MHC I and II responsible for rejection and instead it express HLA –G which is a nonpolymorphic gene.


2 Day 1: Fertilization
3 Days 2-4: Cell division takes place
4 Day 4-5: Blastocyst reaches uterus
Zygote
Fallopian tube
Blastocyst
1 Ovulation
Egg
Ovary
5
Uterus
Days 5-9: Blastocyst implants

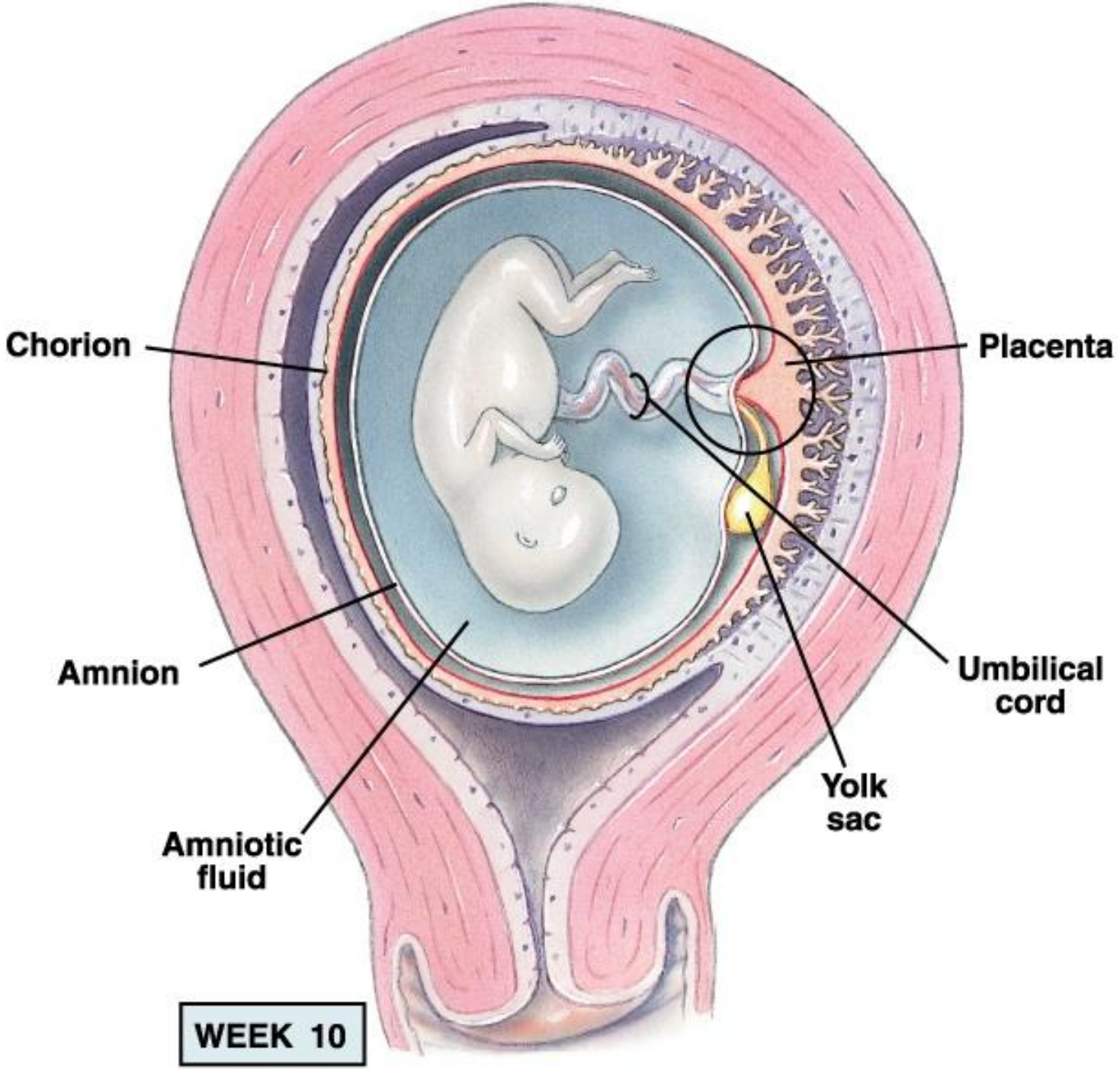
PREGNANCY

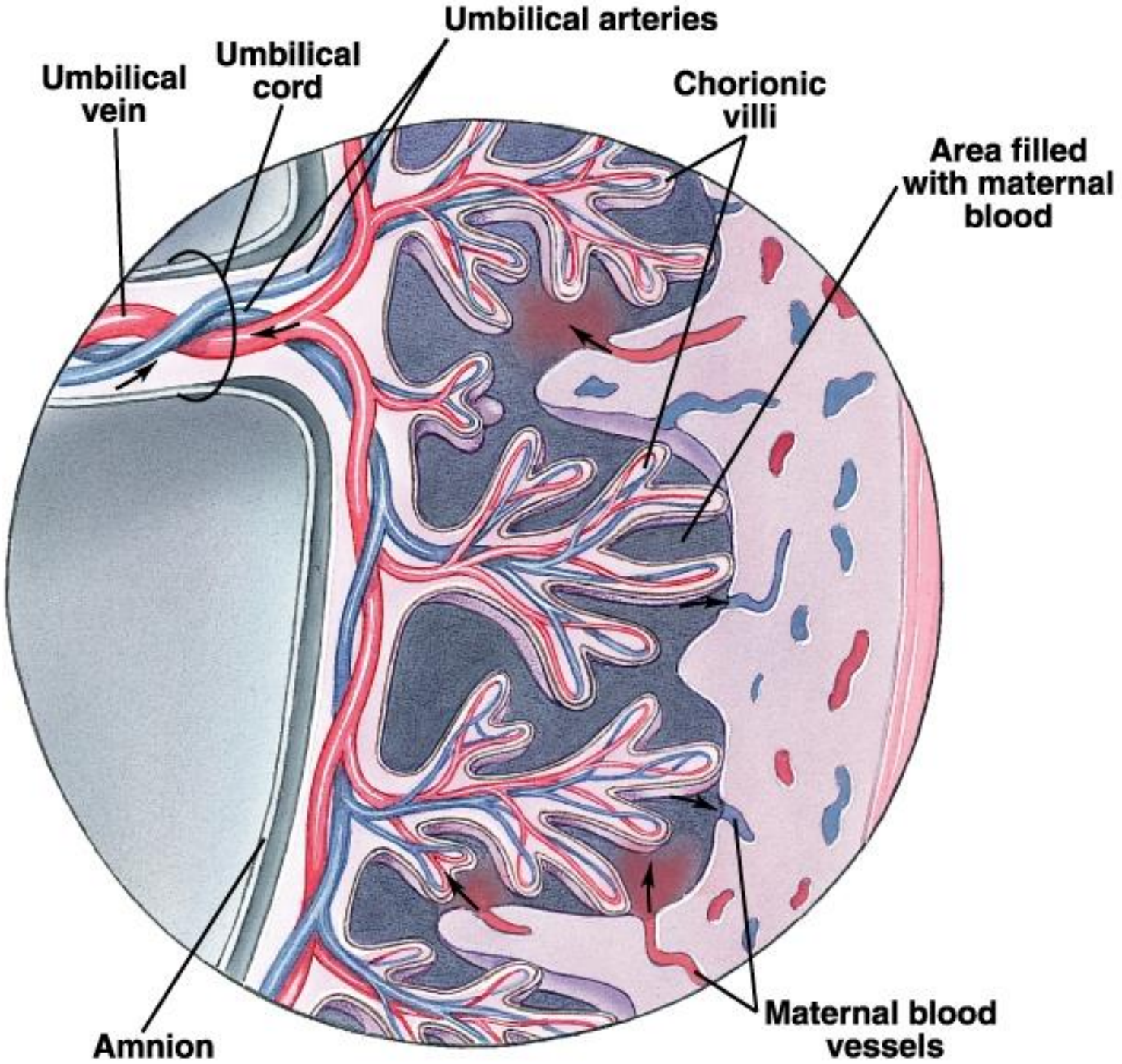
- It is characterized by steadily increasing levels of estrogen and progesterone, which maintain the endometrium for the fetus, suppress ovarian follicular function (by inhibiting FSH and LH secretion), and stimulate development of the breast.


Onset of Nidation
Endometrial gland
Endometrial capillary
Endometrial epithelium
Inner cell mass
Decidualization
Stroma
Syncytiotrophoblast
Cytotrophoblast

FERTILIZATION AND IMPLANTATION

Therefore antibodies against fetal proteins do not develop in addition there is a decrease in maternal antibody production during pregnancy.


Chorion
Placenta
Amnion
Umbilical cord
Yolk sac
Amniotic fluid
WEEK 10


Umbilical arteries
Umbilical vein
Umbilical cord
Chorionic villi
Area filled with maternal blood
Amnion
Maternal blood vessels

HORMONES SECRETED BY THE PLACENTA:

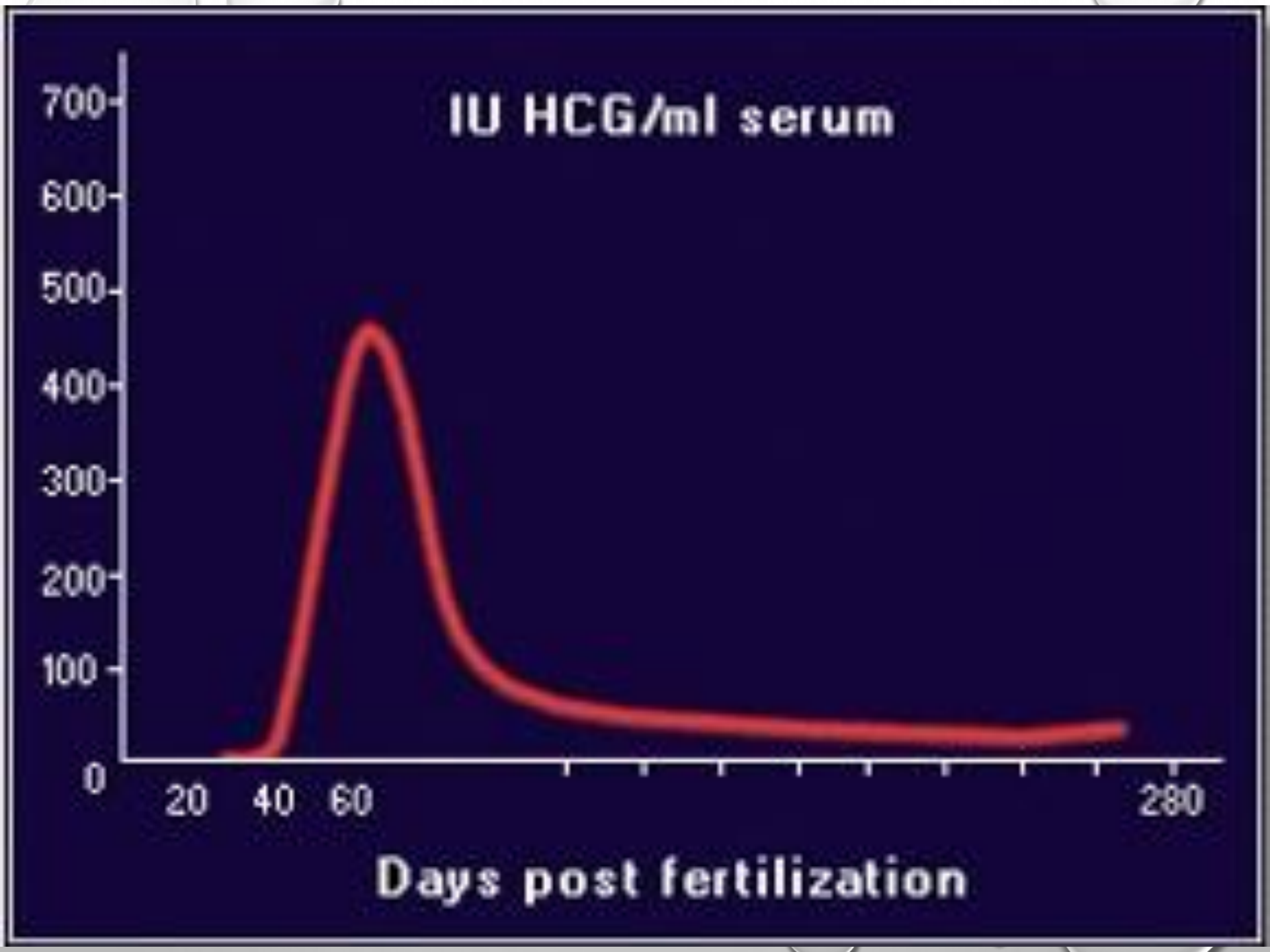
1. Human chorionic gonadotropin (HCG)
2. Human chorionic somatomamotropin (HCS, HPL)
3. Estrogen
4. Progesterone
5. Others

HCG

- Glycoprotein, alpha and beta subunits, the alpha subunit is similar to that of FSH, LH, and TSH.
- Appears in blood 6 days after conception and after14 days in urine (used as pregnanct test). Reached maximum level 10–12 weeks after gestation and least value 16–20 weeks of gestation till the end of pregnancy.

FUNCTIONS OF HCG

1. Stimulates corpus luteum to continue secrete estrogen and progestrone untill the 16^{th} week of gestation after that placenta will take over.
2. Exerts an interstitial cell–stimulating effect on the testes to produce testesterone in males till time of birth.


IU HCG/ml serum
700
600
500
400
300
200
100
0
20
40
60
280
Days post fertilization

HCS\HPL

Secreted by syncytiotrophoblast, the amount of HCS secreted is proportional to the size of placenta (normally the placenta`s weight is 1/6 of fetal weight, so it is an indicator of placental insufficiency).

Functions:

1. Has lactogenic effect with slight increase in breast size.
2. It has most action of GH (due to similar structure) but less potent.
3. It causes retention of N2, K, and Ca
4. Negative feedback mechanism on the GH of the mother.
5. It has anti-insulin effect, decrease the utilization of glucose in maternal tissue (diabetogenic effect).


15
10
5
hPL (µg/ml serum)
0
10
20
30
40
Weeks of pregnancy

PLACENTAL ESTROGEN

It differs from the estrogen secreted by the ovary by

1. Most of this estrogen is estriol (very week)
2. Its importance is in the interaction between the placenta and fetal adrenal cortex (fetoplacental unit)

Functions

1. Same function of ovarian estrogen.
2. Affects general aspect of fetal development (rate of cell reproduction of early embryo).

PLACENTAL PROGESTERONE

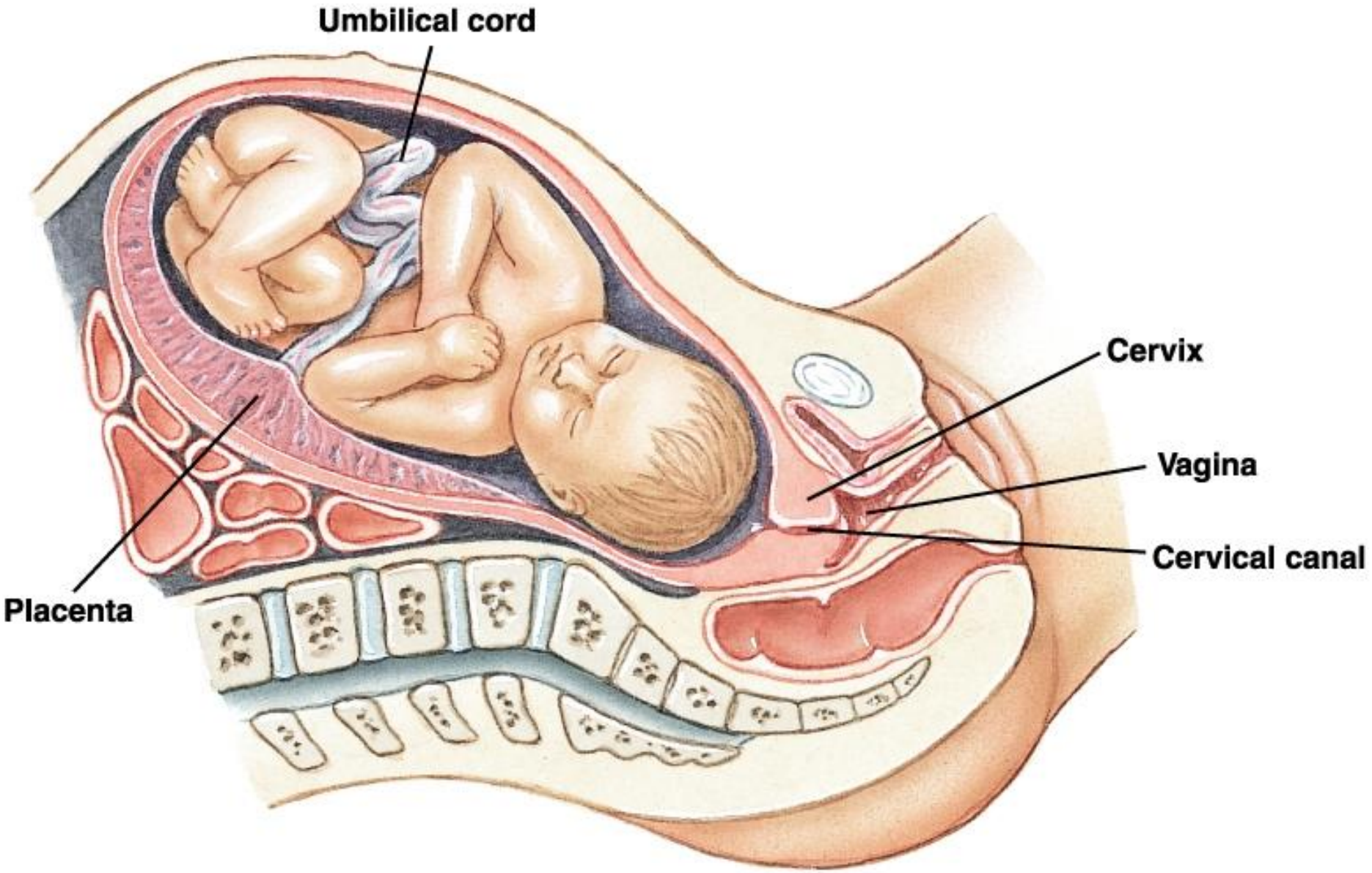
Its function during pregnancy are

1. Development of decidual cell in the endometrium which is very important for the nutrition of embryo in early pregnancy.
2. Decreases the contractility of the gravid uterus (prevent abortion)
3. Increases the secretion of fallopian tube and uterus to provide nutritive material for the developing of morula and blastocyte.

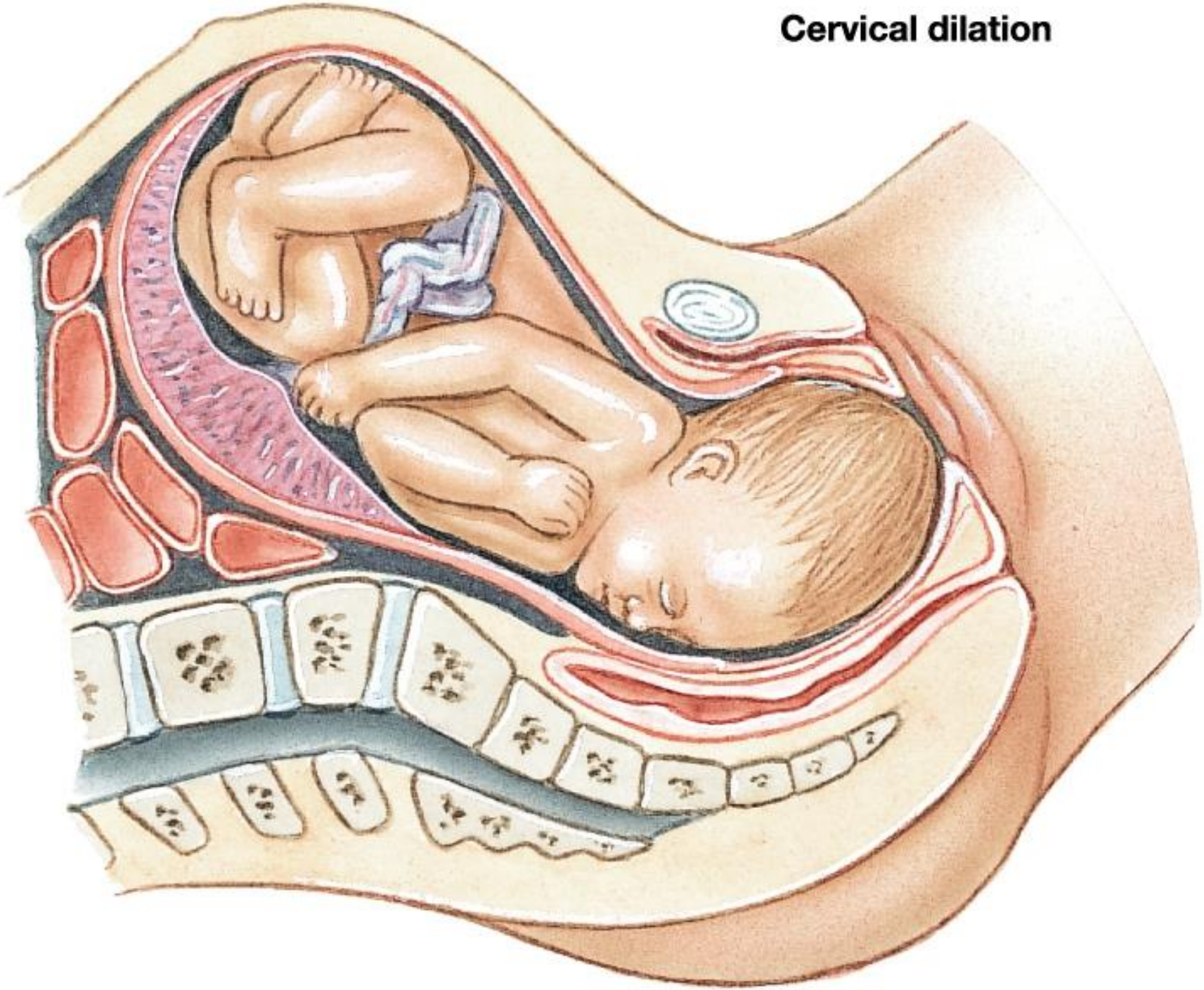
ENDOCRINAL CHANGES DURING PREGNANCY

1. **Pituitary gland:** Increase size. Increase secretion of ACTH, TSH, and prolactine, with decrease secretion of FSH and LH.
2. **Thyroid gland:** Increase size. Increase T4 due to Thyrotropic effect of HCG and human chorionic Thyrotropin from the placenta.
3. **Parathyroid gland:** Increase size. Increase PTH during pregnancy and lactation to meet the increase Ca demand.
4. **Adrenal gland:** Increase secretion of glucocorticoids and aldosterone causing water and sodium retention.
5. **Relaxin:** Helps to relax the pelvic joint.

Fully developed fetus



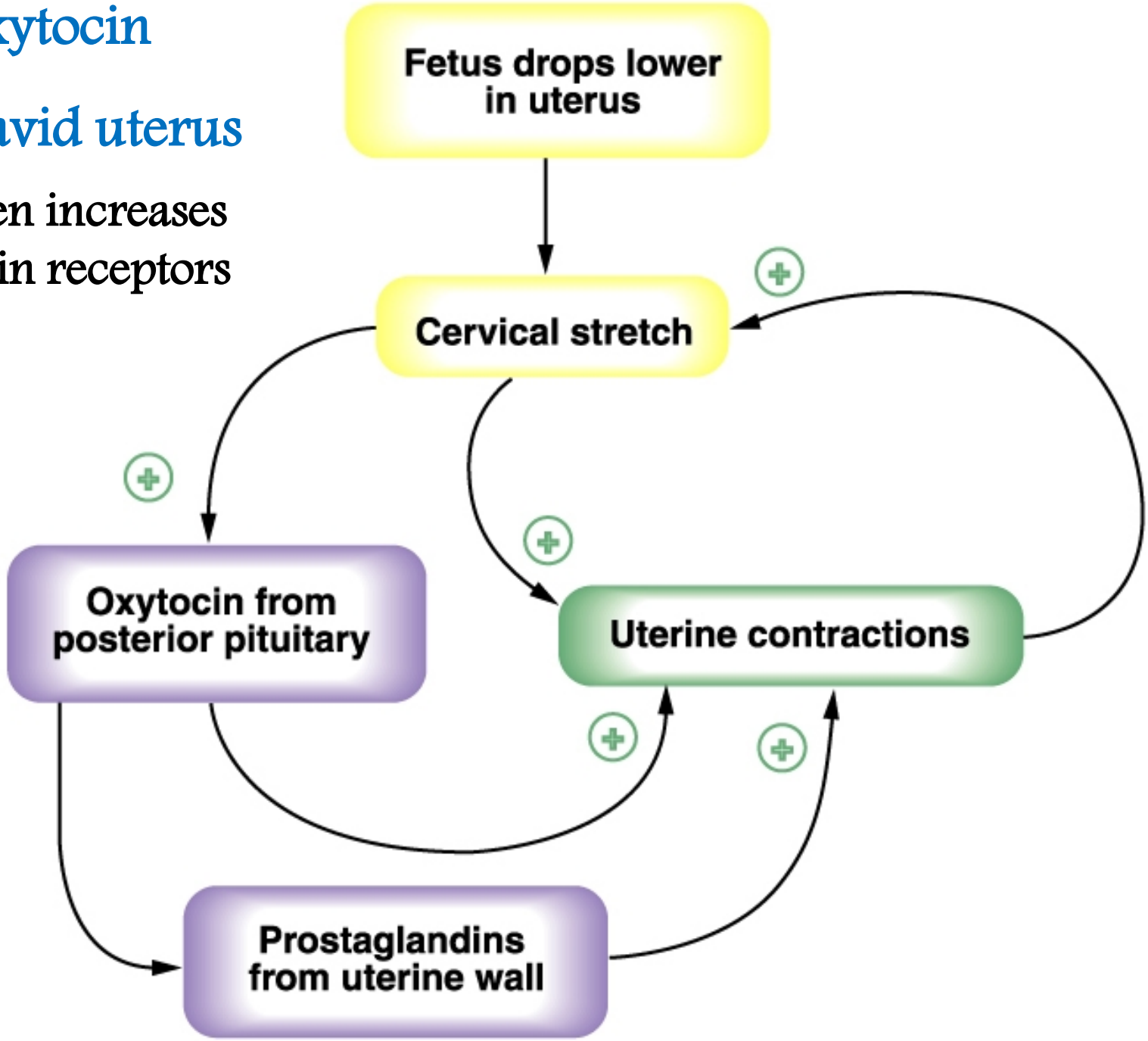
Cervical dilation



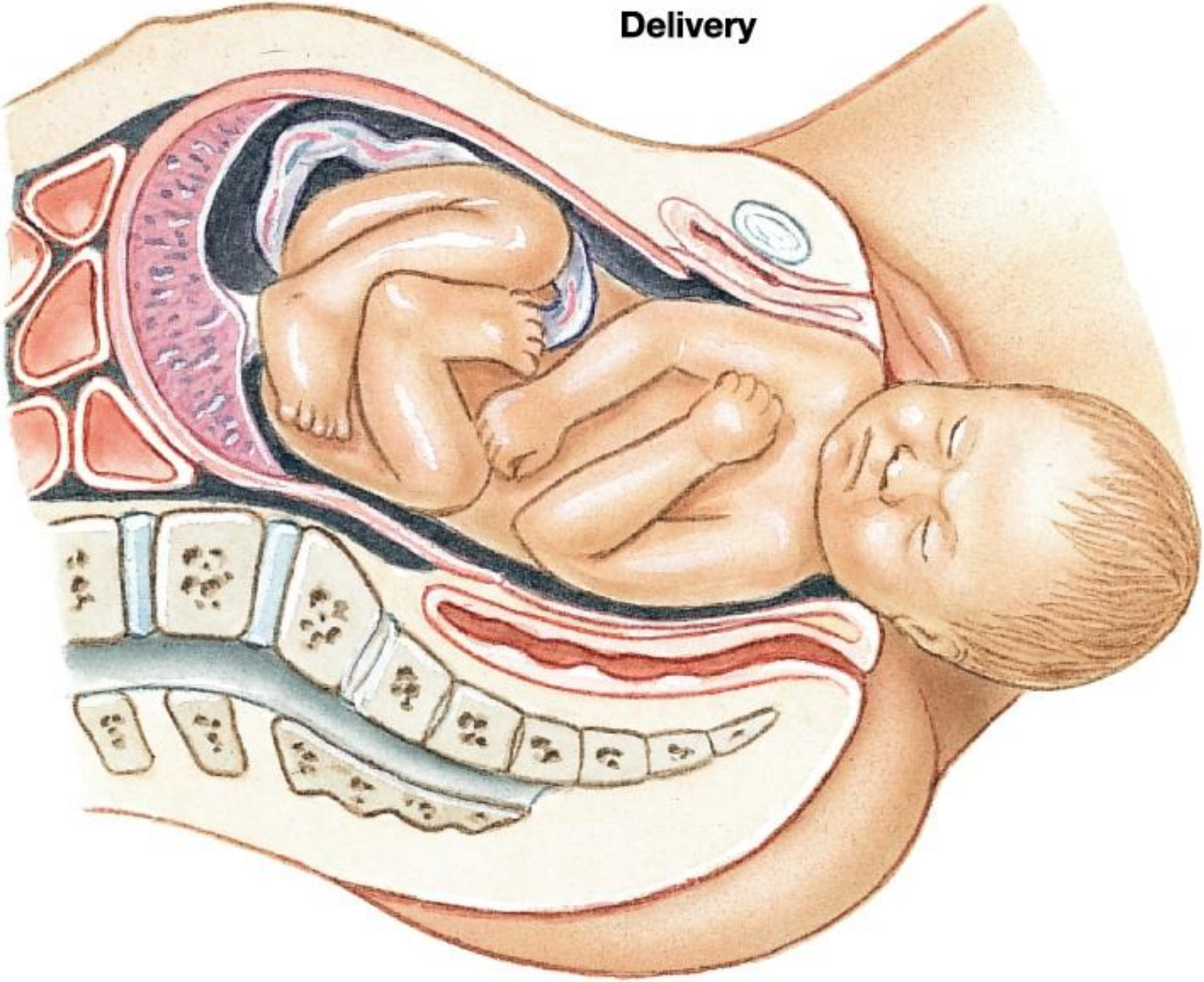
Oxytocin

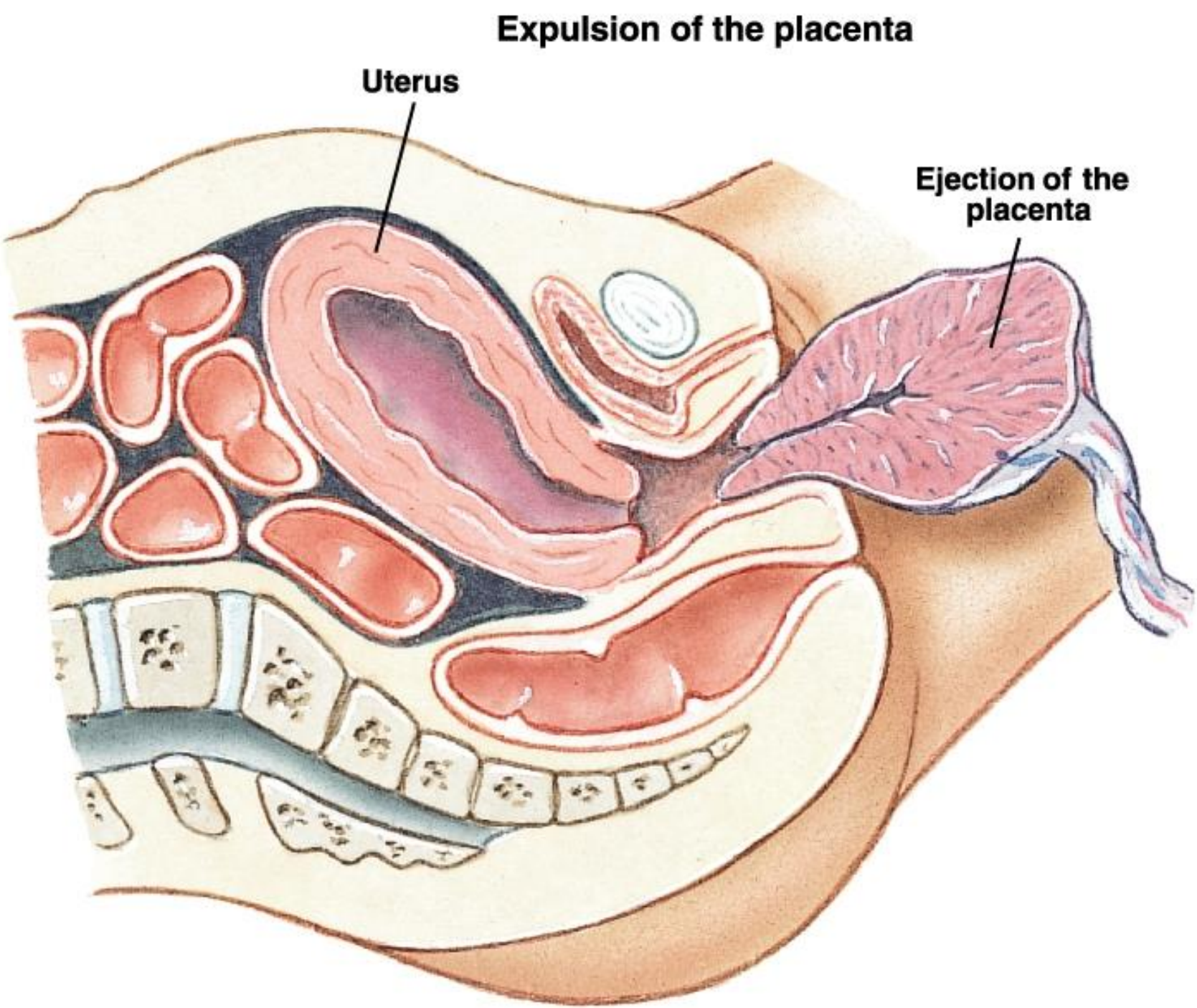
On gravid uterus

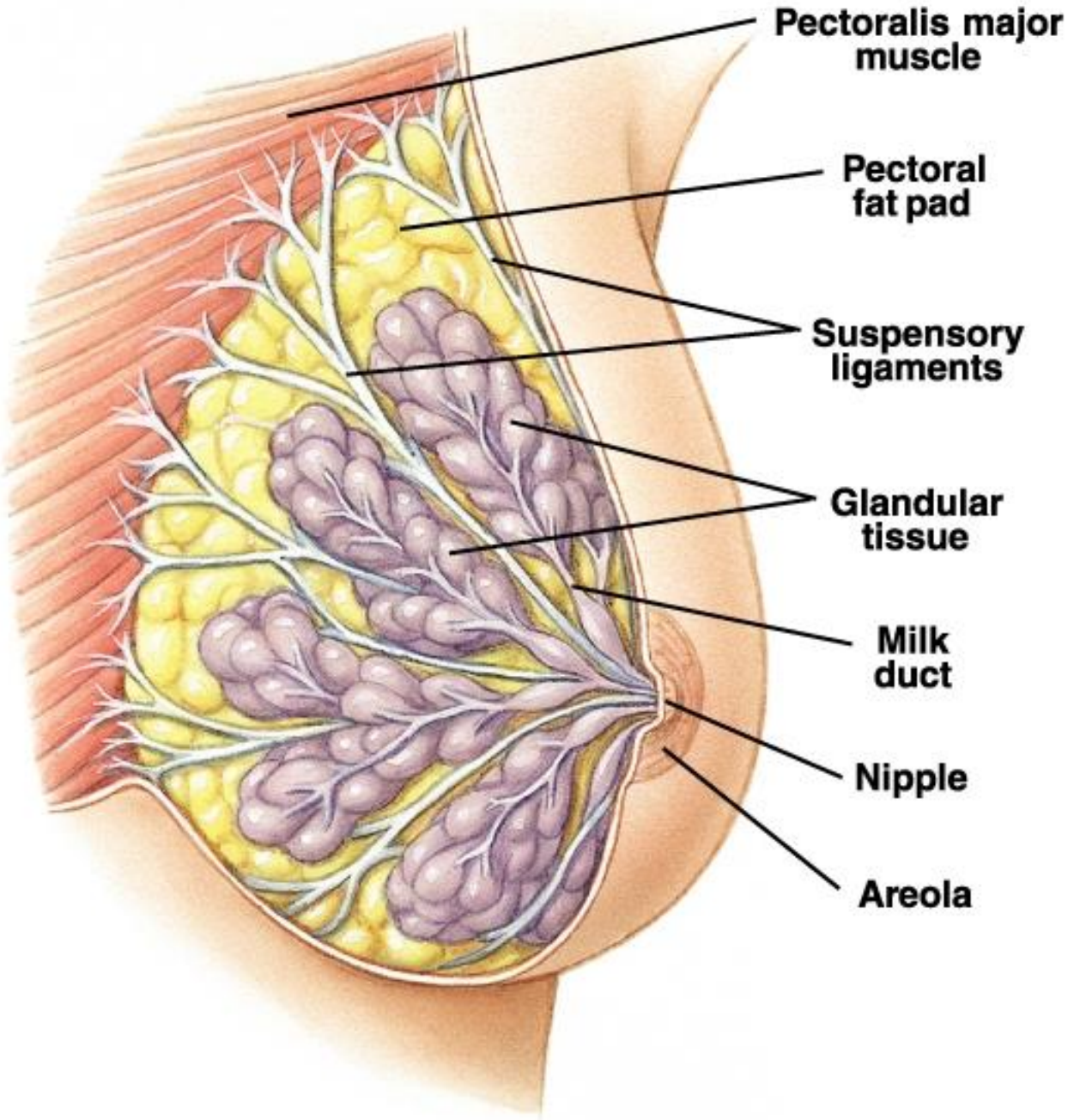
Estrogen increases oxytocin receptors

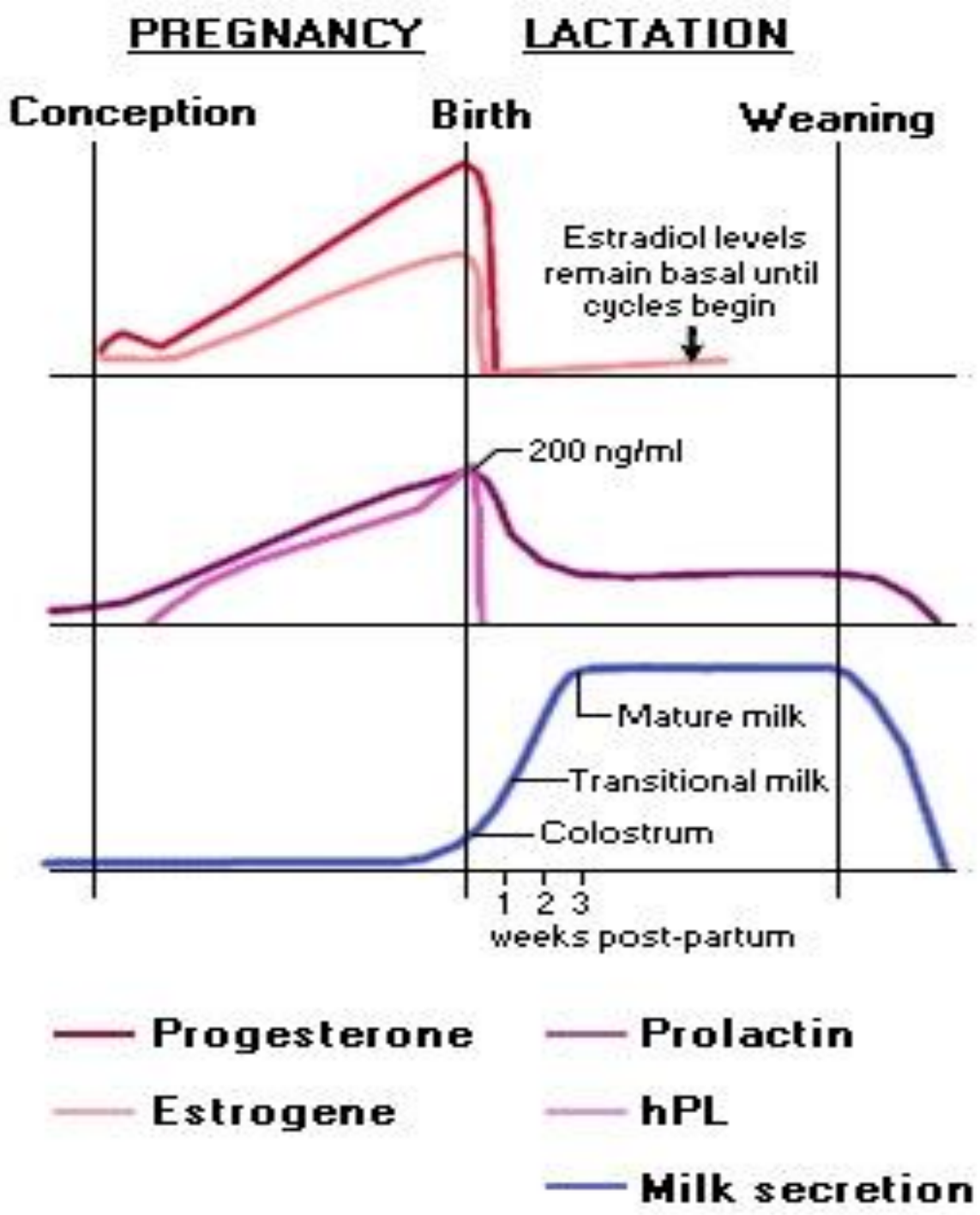


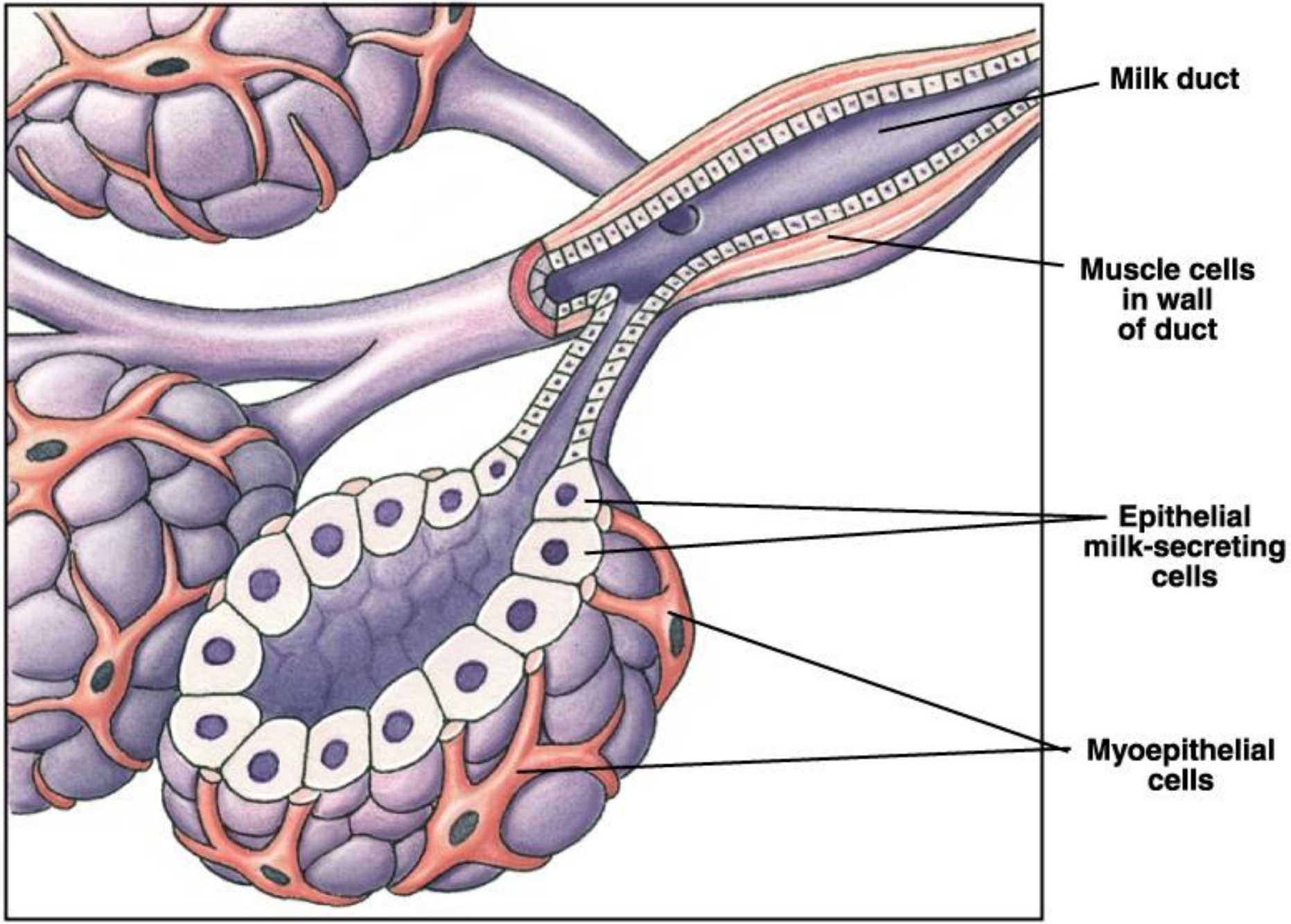
Delivery




Expulsion of the placenta
Uterus
Ejection of the placenta


Pectoralis major muscle
Pectoral fat pad
Suspensory ligaments
Glandular tissue
Milk duct
Nipple
Areola


PREGNANCY
LACTATION
Conception
Birth
Weaning
Estradiol levels remain basal until cycles begin
200 ng/ml
Mature milk
Transitional milk
Colostrum
1 2 3
weeks post-partum
Progesterone
Estrogene
Prolactin
hPL
Milk secretion

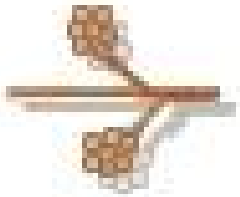

Milk duct
Muscle cells in wall of duct
Epithelial milk-secreting cells
Myoepithelial cells

Immature Ducts 1

Estrogen 2

Duct Proliferation

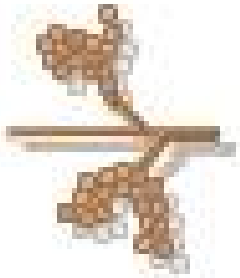
Progesterone 3



Lobulo-Alveolar Proliferation

Prolactin

4



Lactation

EFFECTS OF LACTATION ON MENSTRUAL CYCLE

Women who do not nurse their infants usually have their first cycle 6 weeks after delivery. But women who regularly nursing their babies have their first cycle 25-30 weeks after delivery.

- Prolactine stimuated by nursing inhibits GNRH secretion of hypothalamus ➔ Inhibition of piuitary FSH and LH ➔ Antagonize the action of FSH and LH on ovary ➔ Ovulation is inhibited leading to inactive ovaries ➔ Low estrogen and progesterone.
- 5-10% of breast-feeding mothers become pregnant during suckling period.
- 50% of the cycles in the first 6 moths after return of the cycle are unovulatory cycle.


Thank You