REPRODUCTIVE SYSTEM

- **Process by which an organism produces offspring of its own kind to continue its very existence and to transfer genetic material from generation to generation**

➢ **Asexual reproduction :- ameba, hydra**

➢ **Sexual reproduction:- by fusion of gametes eg→ mammals**

❖ **Primary sex organs :- gonads (organs involved in the production of gametes → ovum in females & sperm in males)**

In males → testes, in females→ ovaries

- **Functions are gametogenesis and production of hormones**

Testis → testosterone, androgen binding protein, inhibin, small amounts of estrogen

Ovary → estrogen, progesterone, relaxin, inhibin, small amounts of androgen

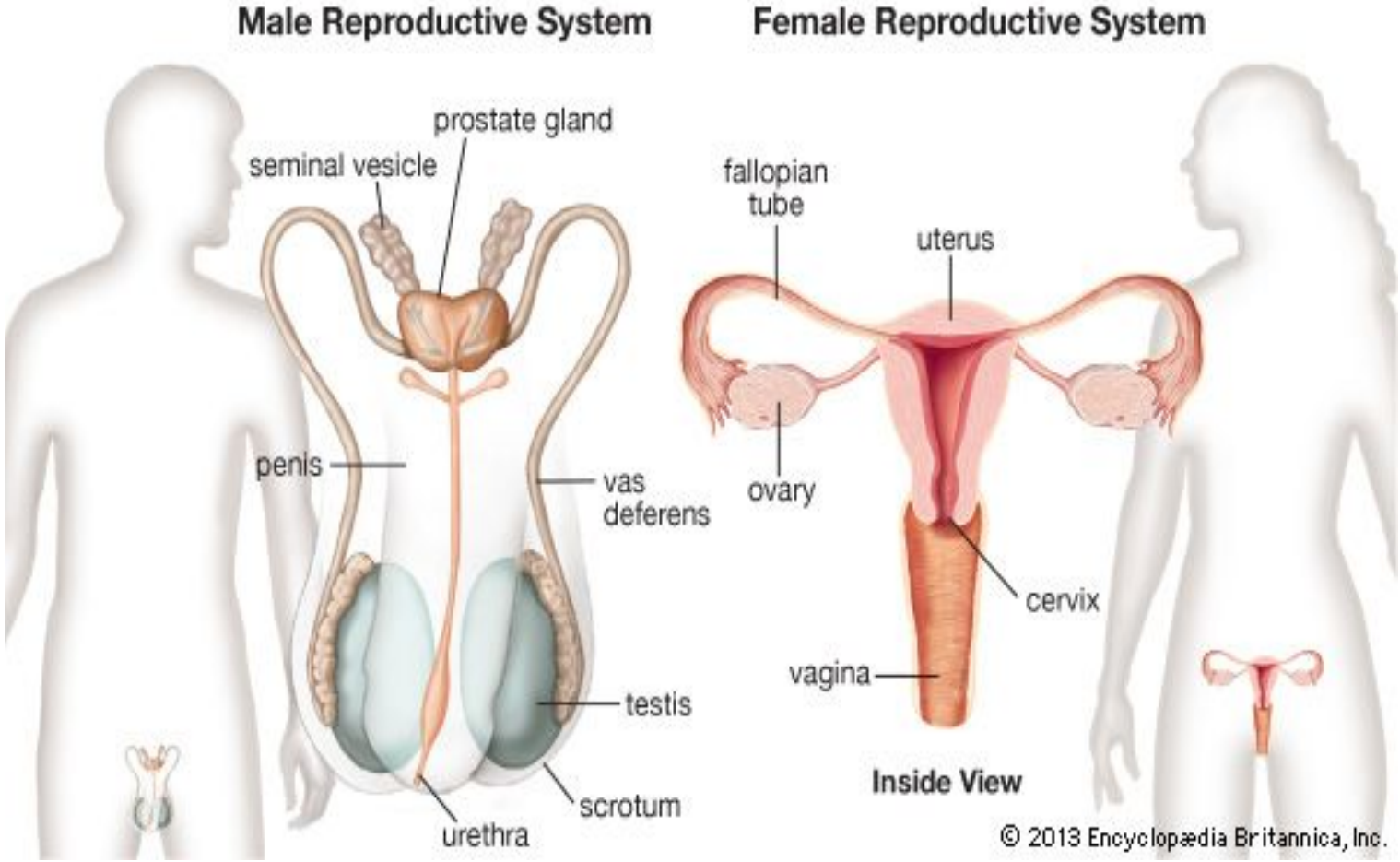
- **Accessory sex organs :- external and internal genitalia**
  - **In males → external genitalia (penis, urethra, scrotum) & internal genitalia (epididymis, vas deferens, seminal vesicle, prostate, Cowper's gland)**

In females → external genitalia (vulva) & internal genitalia (uterus, fallopian tube, vagina, Bartholin's gland)

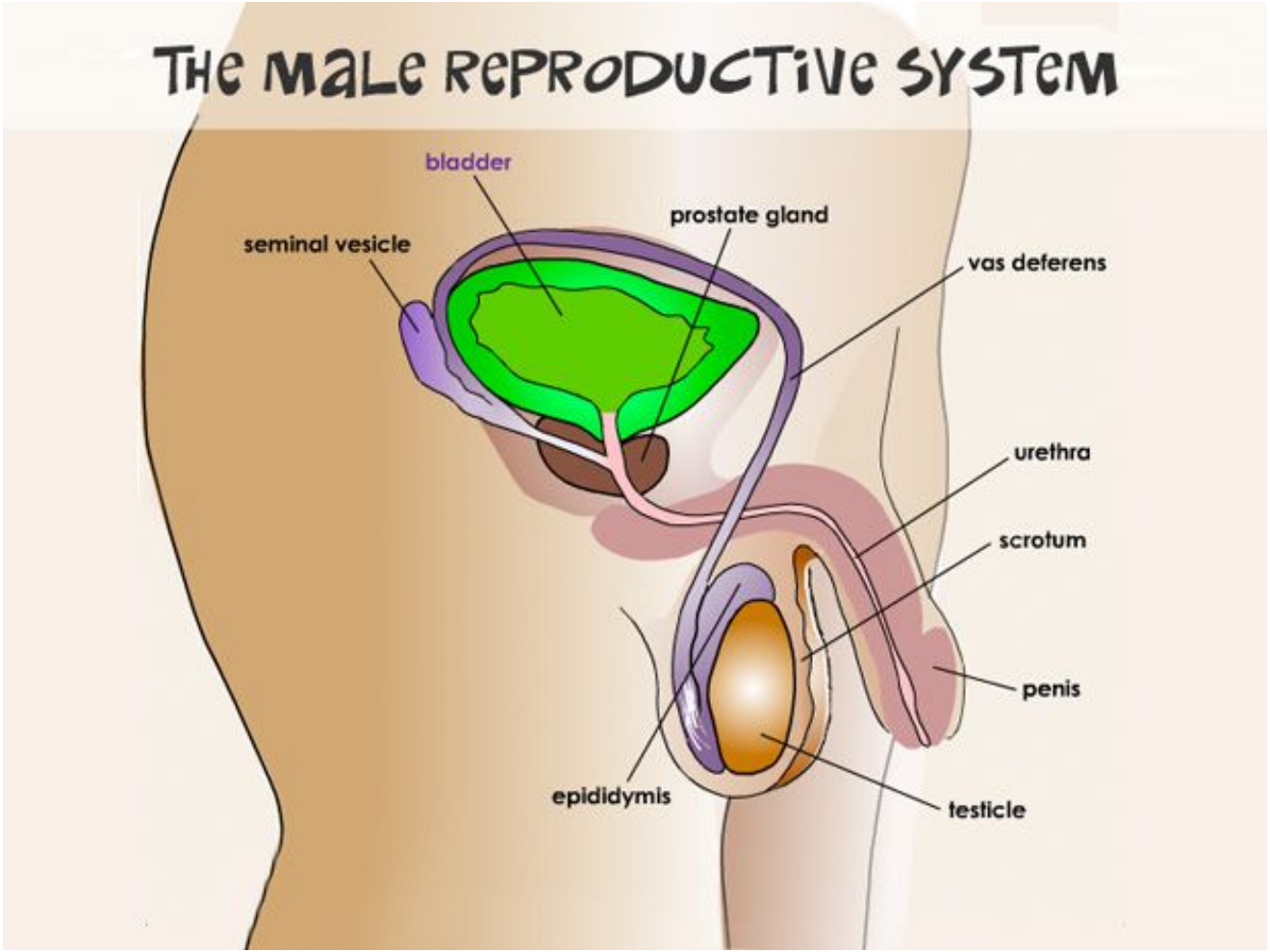
- **Secondary sex characters :- differentiate the sexes**

Hair on face, axilla, pubis & body

Muscular development, shape of pelvis, mammary gland, mental status


Male Reproductive System
prostate gland
seminal vesicle
penis
vas deferens
testis
scrotum
urethra
Female Reproductive System
fallopian tube
uterus
ovary
cervix
vagina
Inside View
© 2013 Encyclopædia Britannica, Inc.

The Male Reproductive System



SEXUAL GROWTH AND DEVELOPMENT

- Sex determination
- Sex differentiation

Sex determination - genetic differentiation/ chromosomal sex differentiation

➔ **Genetic sex determination of the embryo occurs during fertilization**

Ovum (22+ X), sperm (22+X/22+Y) ⇒ 44+XX (female genotype), 44+XY (male genotype)

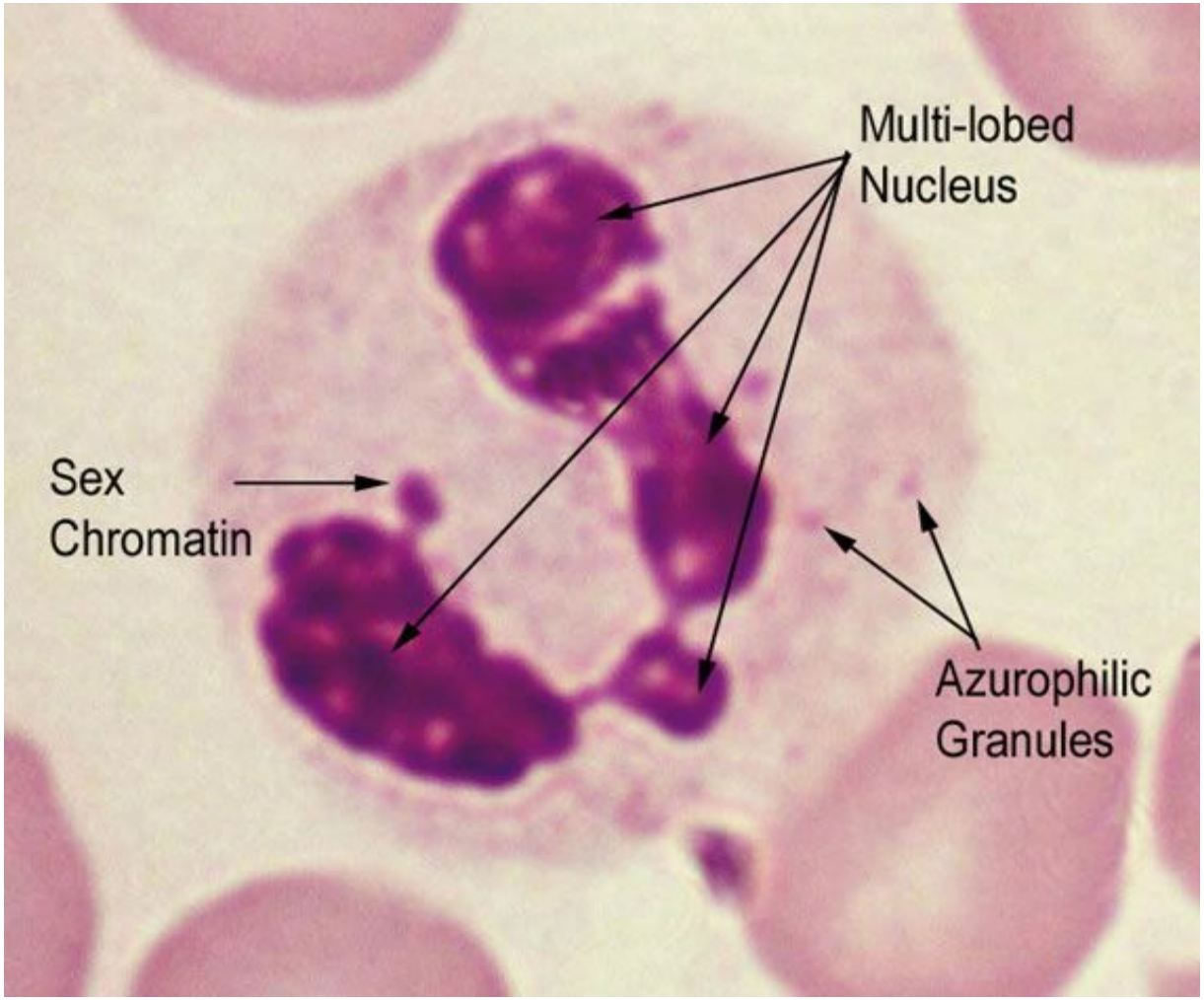
Sperms containing Y chromosomes are lighter and able to swim faster up in the female genital tract, reaching the ovum rapidly → no. of males born is slightly greater than no. of females

Sex chromatin / Barr body:- **condensation of functionally inactive X chromosome**

→ n-1 (n⇒ no. of X chromosomes)

Eg:- Klinefelter's syndrome (XXY) :- 1

Turner's syndrome (XO) :- 0


Multi-lobed
Nucleus
Sex
Chromatin
Azurophilic
Granules

- **Identification of sex genotype :- Barr bodies are present in somatic cells of females only**

➢ **Epithelial cells of epidermal spinous layer**

➢ **Buccal mucosal cells, vaginal mucosal cells**

➢ **Polymorphonuclear cells (15%) -drum stick appearance**

- **Identification of abnormal genotypes :-**

Sex differentiation

- **Gonadal differentiation**
- **Genital differentiation**
- **Psychological differentiation**

- **Gonadal differentiation:-** gonadogenesis (formation of gonads) → testes in male & ovaries in female

➔ From genital ridge (condensation of mesenchymal tissue on each side near adrenal glands) → bipotential gonads/ primitive gonads develops

➔ Primitive gonads consists of cortex, medulla & primordial germ cells

➔ Upto 6 wks of gestation, bipotential gonads are identical in both sexes

Testicular differentiation :- primitive gonads differentiate into testes at approx.6th wk. (from medulla)

Role of Y chromosomes :- one gene for formation of Mullerian duct inhibitory substance (MIS) and one gene for testicular differentiation (SRY gene) present in Y chromosome

SRY gene encodes the testis determining factor (TDF)

At about 35th wk of gestation→ descent of testes through inguinal canal into scrotum → final stage of testicular differentiation

Ovarian differentiation:- in a genetic female (44+XX) → 10th wk of gestation

It occurs in the absence of TDF

- Ovaries develop on each side from cortical region of bipotential gonad
- 11-12th wk of gestation → oocyte → end point of ovarian differentiation
- Embryonic ovary, like testis does not secrete any hormone
- Hormonal treatment of the mother has no effect on gonadal differentiation

- **Genital differentiation → phenotypic sex differentiation**
- **Development of internal genitalia:- Upto 7th wk of gestation, the embryo has both male and female primordial germinal ducts**

➔ **Male→ germinal duct is wolffian duct**

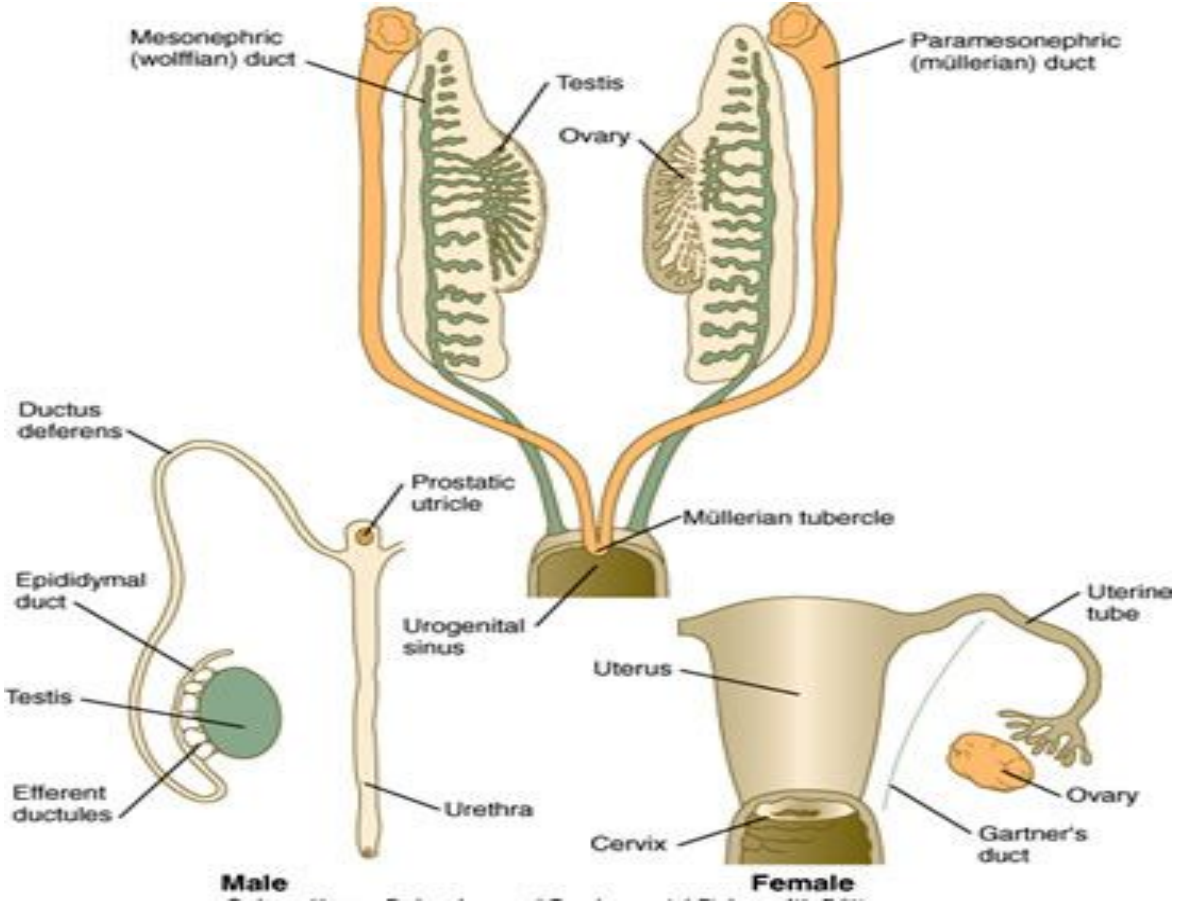
➔ **Female → mullerian duct**

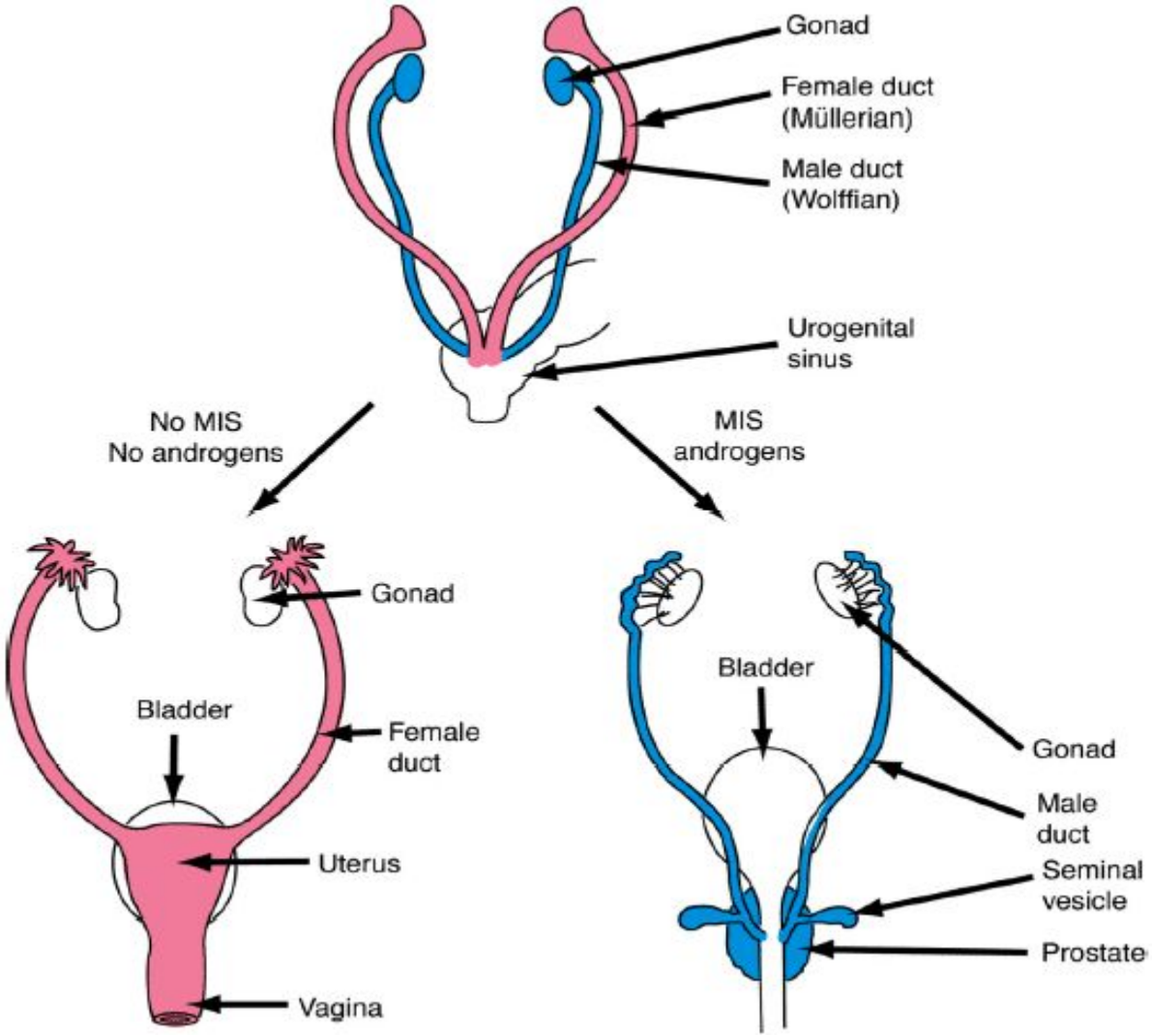
★ **Under the influence of testosterone, wolffian duct differentiates to epididymis, vas deferens and seminal vesicles**

★ **Mullerian duct degenerates by the action of MIS secreted by fetal testis**

- ★ In female fetus, due to absence of MIS, mullerian duct differentiates into uterus, fallopian tubes and upper two-third of vagina
- ★ In the absence of testosterone, Wolffian ducts degenerate

In a male genotype (XY), if the testis is removed around 7th wk of gestation, the newborn will have female genitalia


Mesonephric (wolffian) duct
Testis
Ovary
Paramesonephric (müllerian) duct
Ductus deferens
Prostatic utricle
Müllerian tubercle
Epididymal duct
Urogenital sinus
Uterine tube
Uterus
Testis
Efferent ductules
Urethra
Ovary
Cervix
Gartner's duct
Male
Female


Gonad
Female duct
(Müllerian)
Male duct
(Wolffian)
Urogenital
sinus
No MIS
No androgens
MIS
androgens
Gonad
Bladder
Female
duct
Uterus
Vagina
Bladder
Gonad
Male
duct
Seminal
vesicle
Prostate

Development of external genitalia

- Upto 8th wk of gestation, external genitalia are identical in both sexes
- In presence of testosterone, urogenital slit disappears→ develop.of male external genitalia
- Absence of testosterone→ urogenital slit remains open → develop.of female genitalia

Psychological differentiation

- The difference in male and female behaviour due to some anatomical and functional differences in certain areas of brain of two sexes
- Determined by the effect of androgens
- Exposure of fetal hypothalamus to androgens during early embryonic period→ male pattern of sexual behaviour
- Absence of exposure → female pattern

Hormonal control of development of genitalia

Abnormalities in sexual differentiation :-

- Defect in sex chromosomes leading to genetic abnormality
- Hormonal abnormalities leading to defect in gonadal and genital differentiation

❖ **Chromosomal abnormalities:-** nondisjunction of sex chromosomes

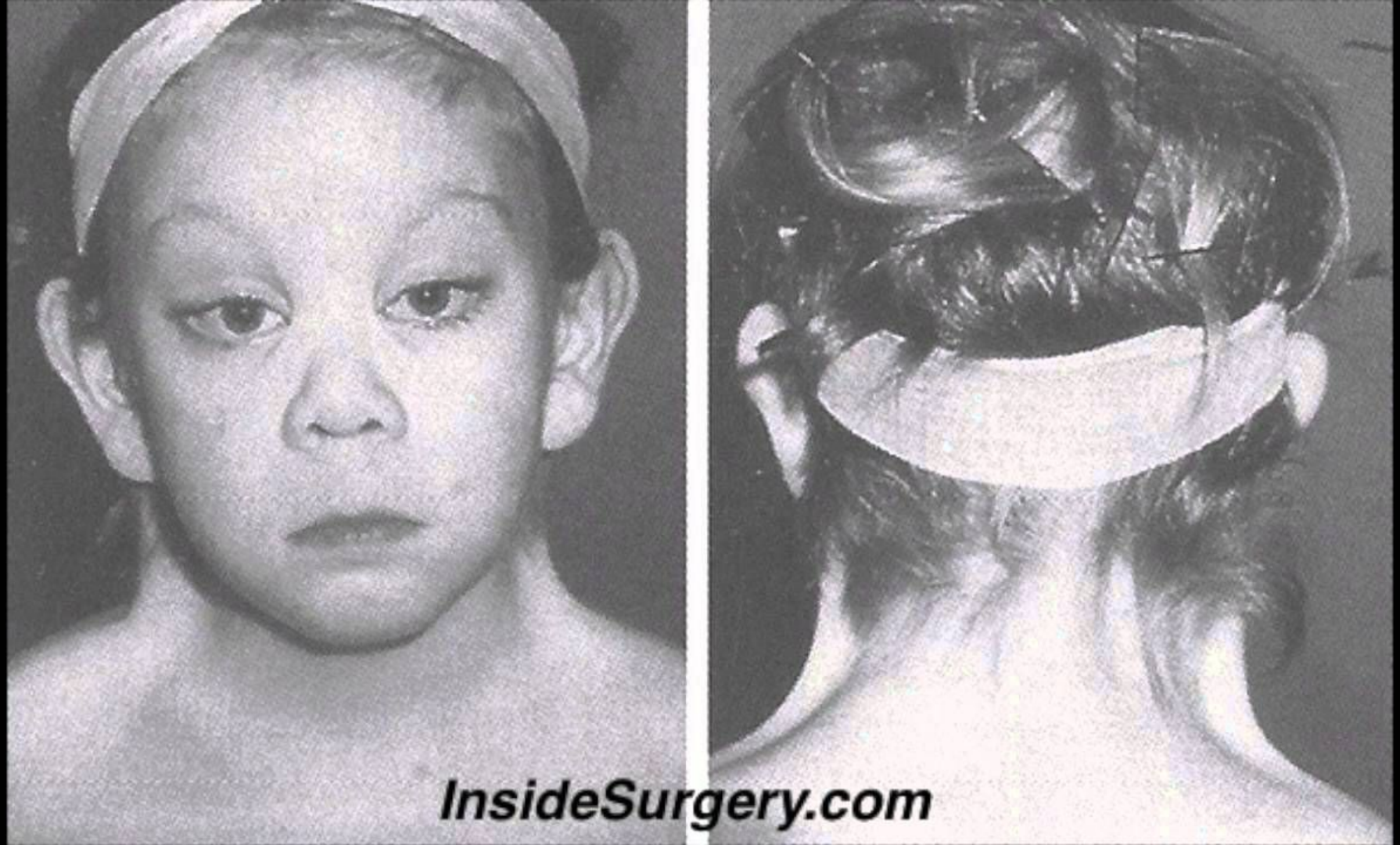
Eg:- trisomy → super female, Klinefelter's syndrome

Monosomy → Turner's syndrome

Turner's syndrome :- **gonadal dysgenesis/ ovarian agenesis**

- **44+XO**
- **Phenotype :- female**
- **Genetic sex :- sexless (XO)**
- **Gonadal sex :- nil (no testis or ovary)**
- **Sex chromatin test :- negative**
- **Female type of internal & external genitalia**

➢ **Primary amenorrhea, dwarfism, webbing of neck**


InsideSurgery.com

Klinefelter's syndrome :- most common

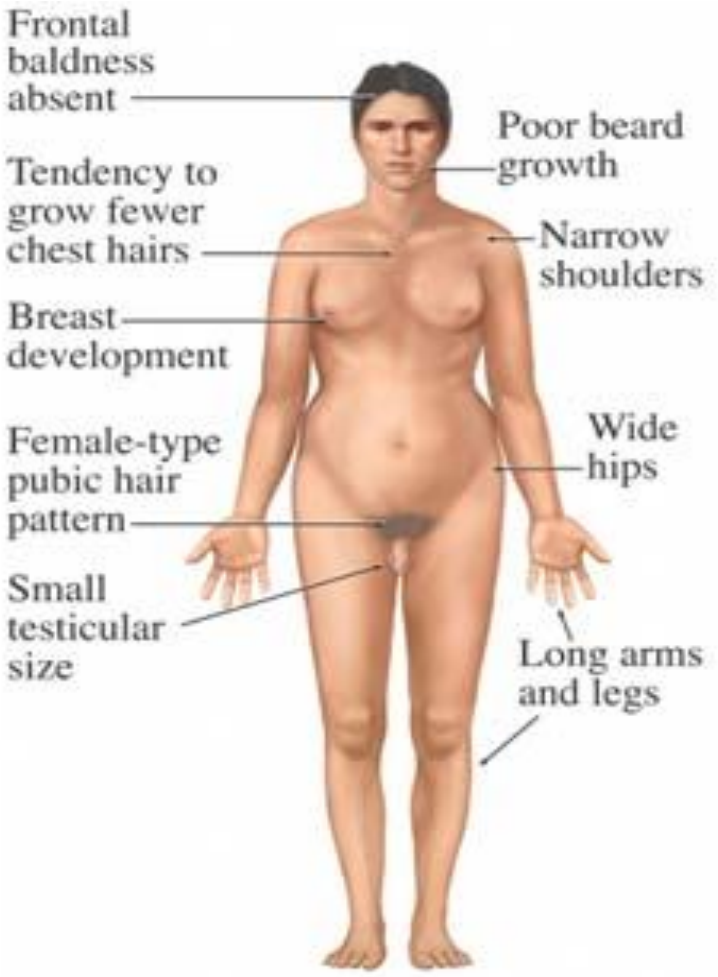
- 44+XXY
- Phenotype :- male
- Genetic sex:- female (XX)
- Gonadal sex :- male
- Sex chromatin test :- positive (1 barr body)
- Genitalia :- male type

➢ Patient is tall

➢ Gynecomastia

➢ Sterility, small penis & testis

➢ Sparse body &pubic hair


Frontal baldness absent
Poor beard growth
Tendency to grow fewer chest hairs
Narrow shoulders
Breast development
Wide hips
Female-type pubic hair pattern
Small testicular size
Long arms and legs

❖ **Hormonal abnormalities:- pseudohermaphroditism→ individual having genotype of one sex and genitalia of other sex**

- **Female pseudohermaphroditism**

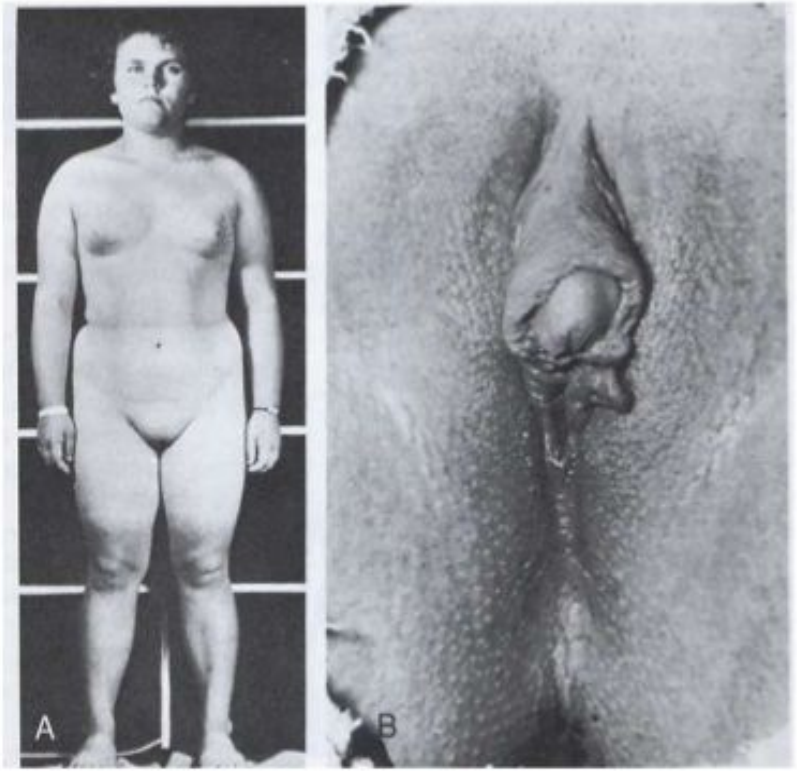
➔ **Exposure to increased level of androgens to genetic female fetus**

➔ **C/F:- genotypically female**

:- gonads and internal genitalia are feminine like (ovaries, oviduct, uterus present)

:- development of penis & diamond shaped pubic hair growth

Female pseudohermaphroditism (caused by congenital adrenal hyperplasia)



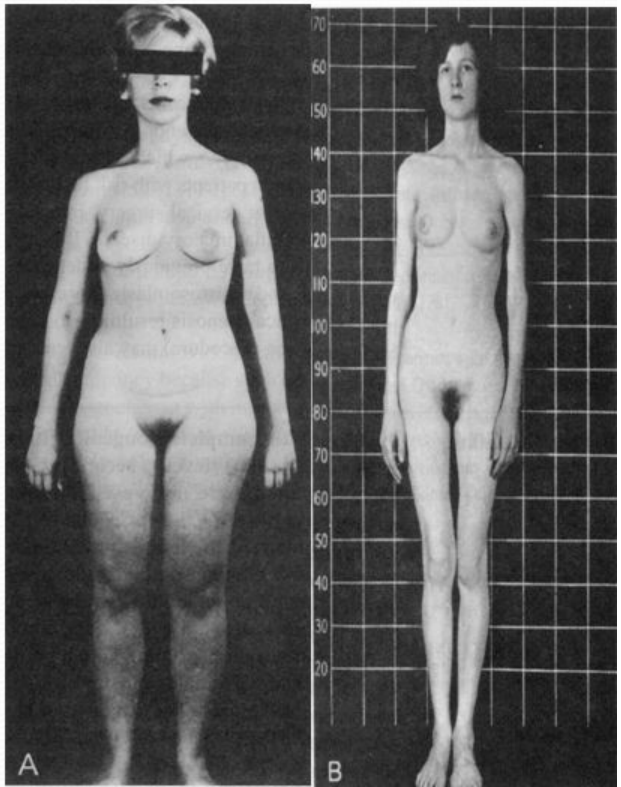
- ➔ Congenital virilizing adrenal hyperplasia, excess of maternal androgens
  - Male pseudohermaphroditism
- ➔ Person is genetically male but female internal & external genitalia
- ➔ In androgen resistance, defective testicular development etc
- ➔ Mild defect → infertility
- ➔ Severe → testicular feminising syndrome

External genitalia → female type, but vagina ends blindly

No female internal genitalia, primary amenorrhea

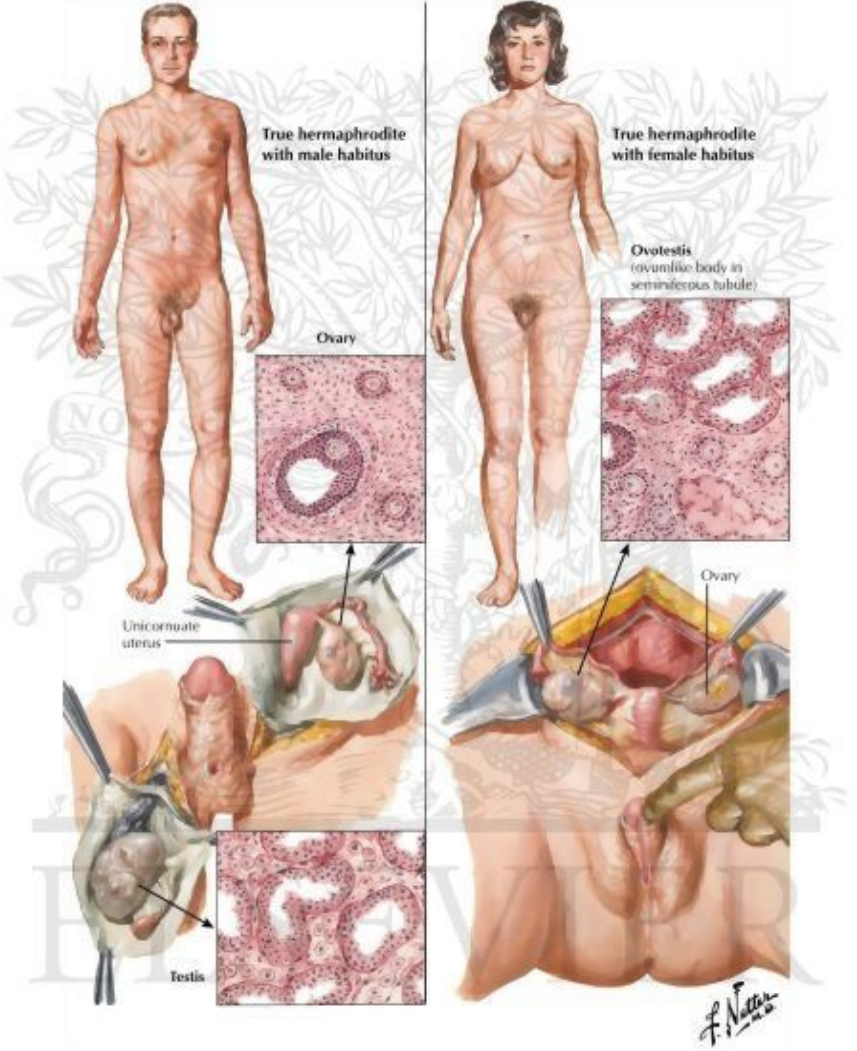
3. Androgen Insensitivity (Testicular Feminization)

- **Male Pseudohermaphrodite**
- **Gonadal Sex :46xy**
- **Phenotype Female**
  - Blind vaginal canal
  - Uterus absent
  - Absent or meager pubic and axillary hair
- **Malignancy,**
- **Hormone :**
  - **T or slightly**
  - **LH**



True hermaphroditism:- rare.

Gonads of both sexes are present (ovary on one side and testis on another side)



PUBERTY :-

- Stage of gonadal development and maturation to the point where reproduction is possible for the first time
- Average onset of puberty is 12 yrs in girls and 14 yrs in boys
- Principal components → sudden spurt of physical growth and appearance of secondary sex characters

Appearance of breast buds→ thelarche

Appearance of axillary and pubic hair→ pubarche

Starting of menstruation→ menarche

Hormonal changes during puberty

Besides ovaries and testes, other endocrine glands (adrenal, thyroid, anterior pituitary) also grow in size and their activity increases

- **Gonadotropins :- levels of follicular stimulating hormone (FSH) and luteinizing hormone (LH) secreted from anterior pituitary gland increases**
- **Adrenal androgens:- onset of stage of increase of secretion of adrenal androgens → adrenarche (girls→ 8-10yrs & boys→ 10-12yrs of age)**

➔ Growth of pubic and axillary hair

➔ Growth of muscle mass and its strength

- **Growth hormone :-** increase in frequency and amplitude of peaks of secretion
- **Thyroxine :-** secretion increases

➔ Necessary for normal growth and development

- **Gonadal hormones :-** rapid rise in estrogen secretion in girls and testosterone in boys

Control of onset of puberty

Role of hypothalamus

From birth to pre adolescent age:- slow release of Gonadotropin releasing hormone (GnRH) from hypothalamus (highly sensitive to feedback inhibition by circulating sex hormones→ adrenal cortex and prepubertal testes)

At the time of puberty:- pulsatile release of GnRH (hypothalamic cells become more mature and sensitivity decreases)

- **Hypothalamus positively stimulated by critical body mass, visual, external, olfactory and other sensory stimuli**
- **Role of leptin:- circulating protein, formed in fat cells**

➔ **Act on hypothalamus by feedback control mechanism leading to satiety and controls body weight**

➔ **Leptin acts as a link b/w critical body wt and onset of puberty**

Disorders of puberty

- Early onset of puberty → precocious puberty
- Late onset of puberty → delayed or absent puberty

Precocious puberty:-

- Onset of puberty in a child before 8 yrs of age
- Commonly seen in girls

★ True precocious puberty :- early development of secondary sex characters and gametogenesis

➔ Operates through normal hypothalamo-pituitary-gonadal axis without any other endocrinal disorder

Causes:- idiopathic

Disruption of neural pathway for feedback inhibition of GnRH release from hypothalamus eg: cerebral disorders, pineal gland tumours

→ gonadotropin dependent precocious puberty

Gonadotropin independent precocious puberty→ increased insensitivity of LH receptors to gonadotropins

★ Pseudoprecocious puberty

- **Early development of secondary sex characters without gametogenesis**
- **Due to abnormal exposure of sex hormones to immature child**
- **Causes:- androgen secreting tumours in males**

Estrogen secreting tumours in females

Delayed or absent puberty

- More common in boys
- If menarche doesn't occur by 17 yrs of age or testicular development and maturation fails to occur by 20yrs of age
- Conditions :-

➔ Failure of hypothalamus/pituitary to secrete gonadotropins

➔ Chromosomal abnormalities

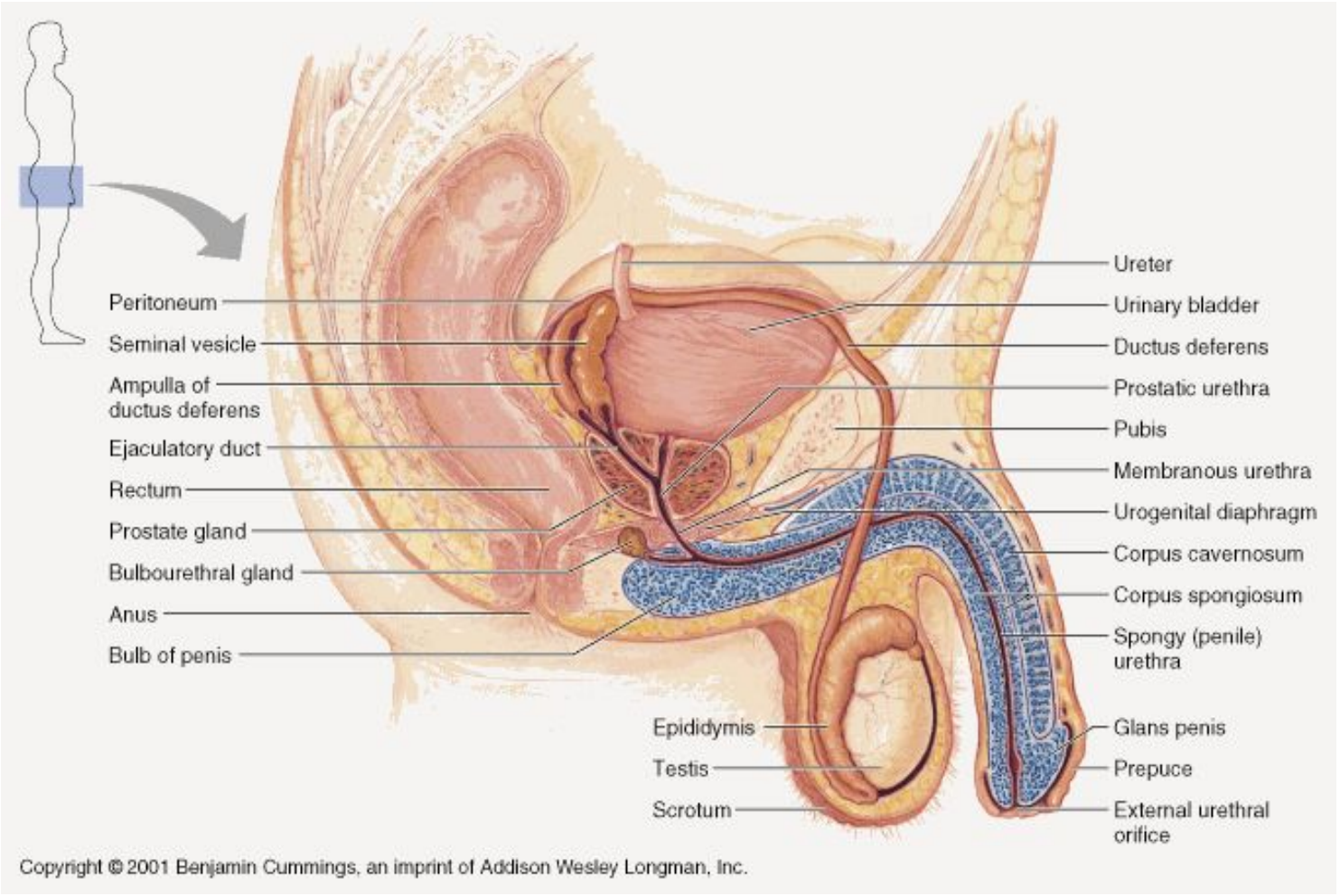
- Short stature (dwarf)

Puberty is absent even when gonads are present and other endocrines functioning normally

In male→ eunuchoidism

In female→ primary amenorrhoea

MALE REPRODUCTIVE PHYSIOLOGY



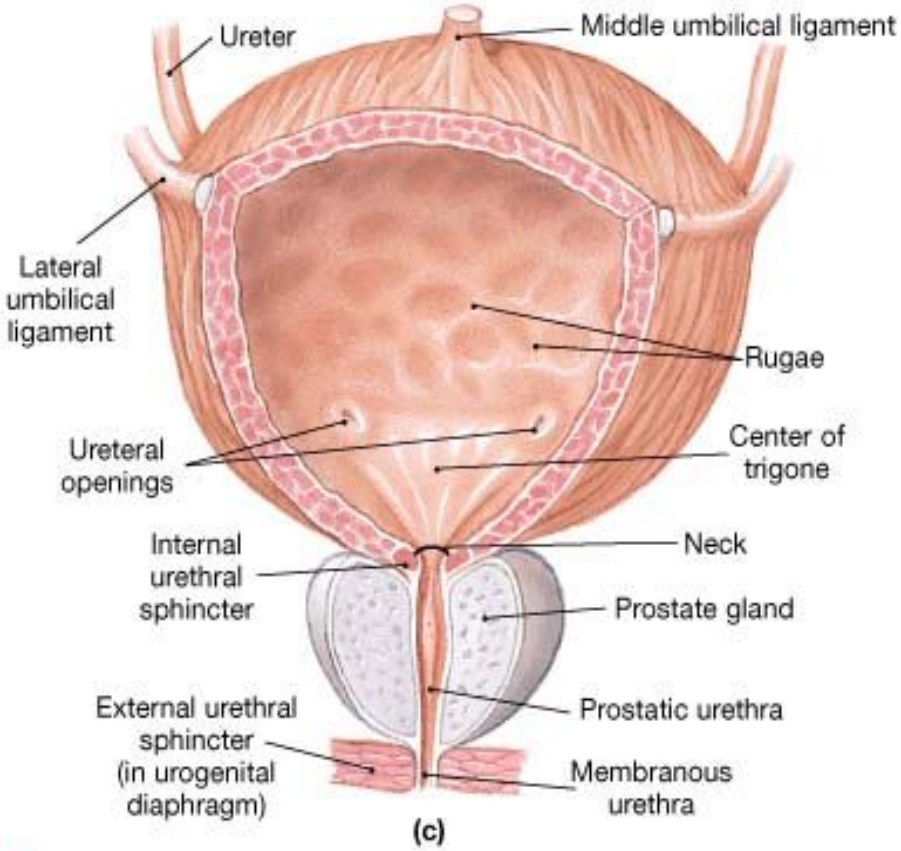
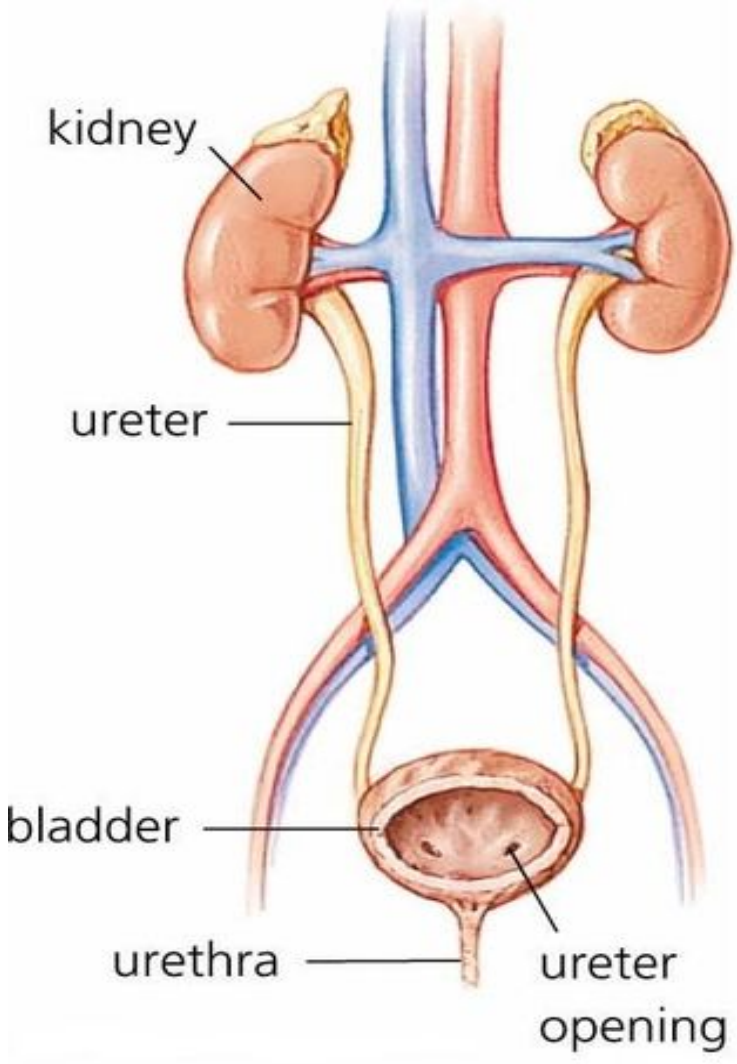


FIGURE 26-19 Organs for the Conduction and Storage of Urine. **(c)** The urinary bladder of a male.


kidney
ureter
bladder
urethra
ureter opening

Primary sex organ :- testes (production of sperms and secretion of testosterone)

Accessory sex glands:-

Seminal vesicles→ do not store sperms

- **Secrete a thick alkaline fluid that mixes with the sperms as they pass into ejaculatory ducts and urethra**
- **Its duct joins with ductus deferens forms ejaculatory duct**

Bulbourethral /Cowper's glands:-secretion enters the penile urethra during sexual arousal

Prostate gland:- largest accessory gland.Secretes a thin milky fluid, forms 30% of the volume of semen (a mixture of secretions produced by the testes, seminal vesicles, prostate and bulbourethral glands)

Ducts :-

Epididymis:- storage of sperms

- Sperms remain viable for a month in epididymis
- Its secretions provide nourishment to spermatozoa and help them to mature
- Non motile spermatozoa become motile after passing through it

Vas deferens or ductus deferens:- secondary storehouse for spermatozoa→ released at the time of ejaculation

In vasectomy (sterilization) → vas deferens is ligated and sectioned

Ejaculatory ducts:- union of ductus deferens with duct of seminal vesicle

Forms a part of prostatic urethra

Urethra:- provides an exit for semen (sperms and glandular secretions)

Supporting structures:-

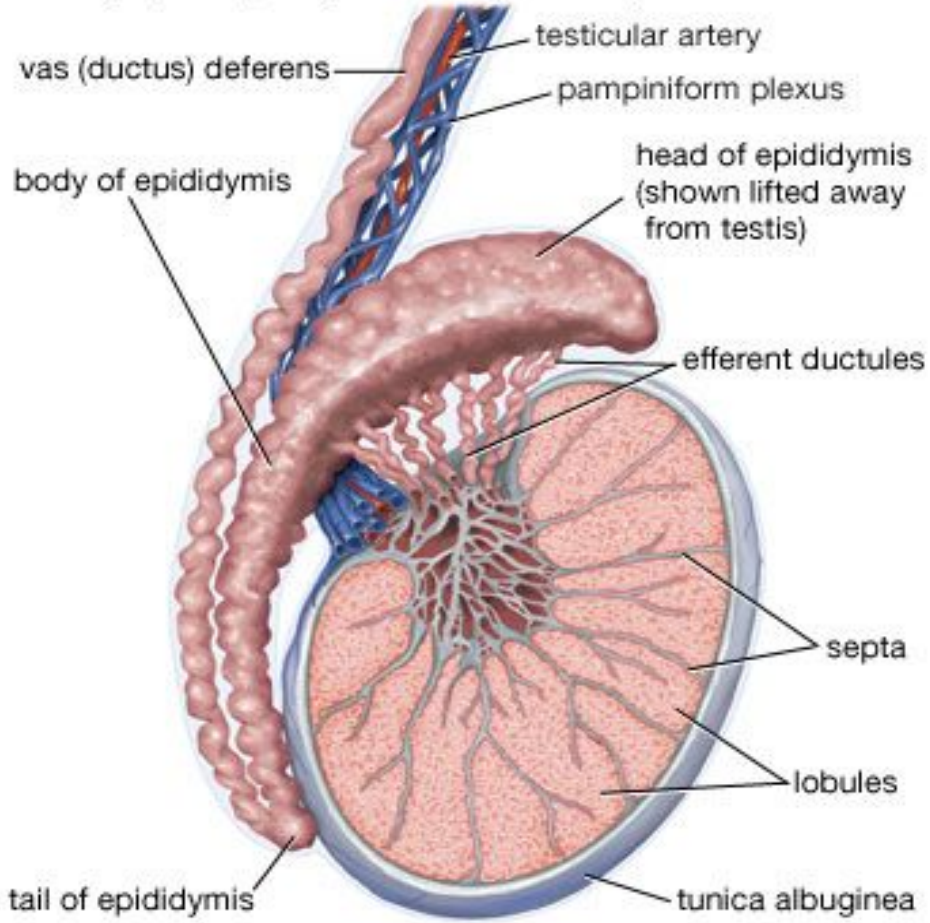
Spermatic cord→ suspends testes in the scrotum

- **Consists of vas deferens, testicular vessels (testicular artery, (testicular veins + veins of epididymis)→ pampiniform plexus) and nerves**

Scrotum:- maintains the temperature lower than normal body temperature (32^0C)--> necessary for normal spermatogenesis

- **Pampiniform plexus is a part of thermoregulatory mechanism→ countercurrent exchange of heat**

Testis, epididymis, and vas (ductus) deferens

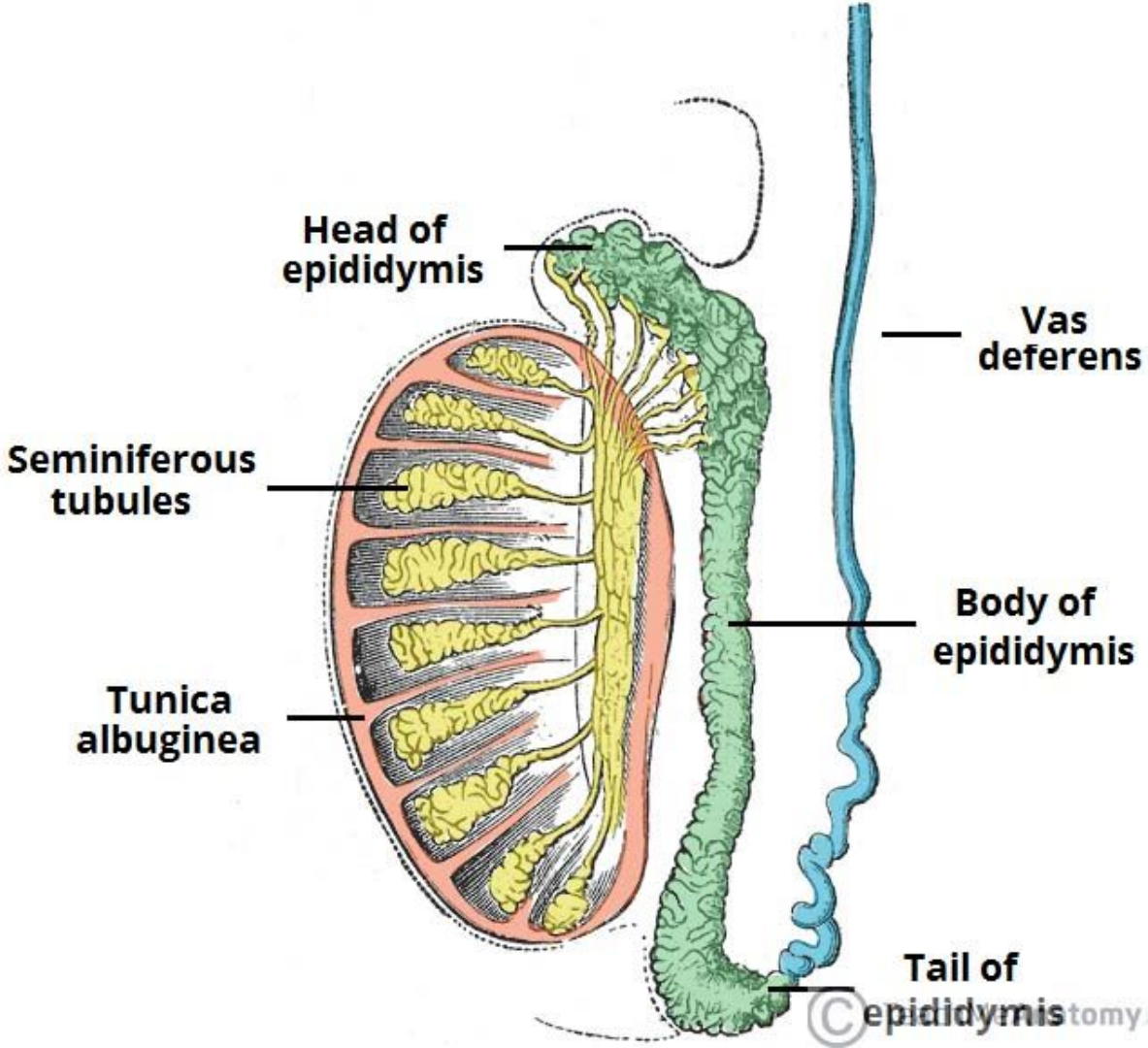


Exposure to cold also inhibits spermatogenesis→ contraction of dartos muscle keeps the testes warm

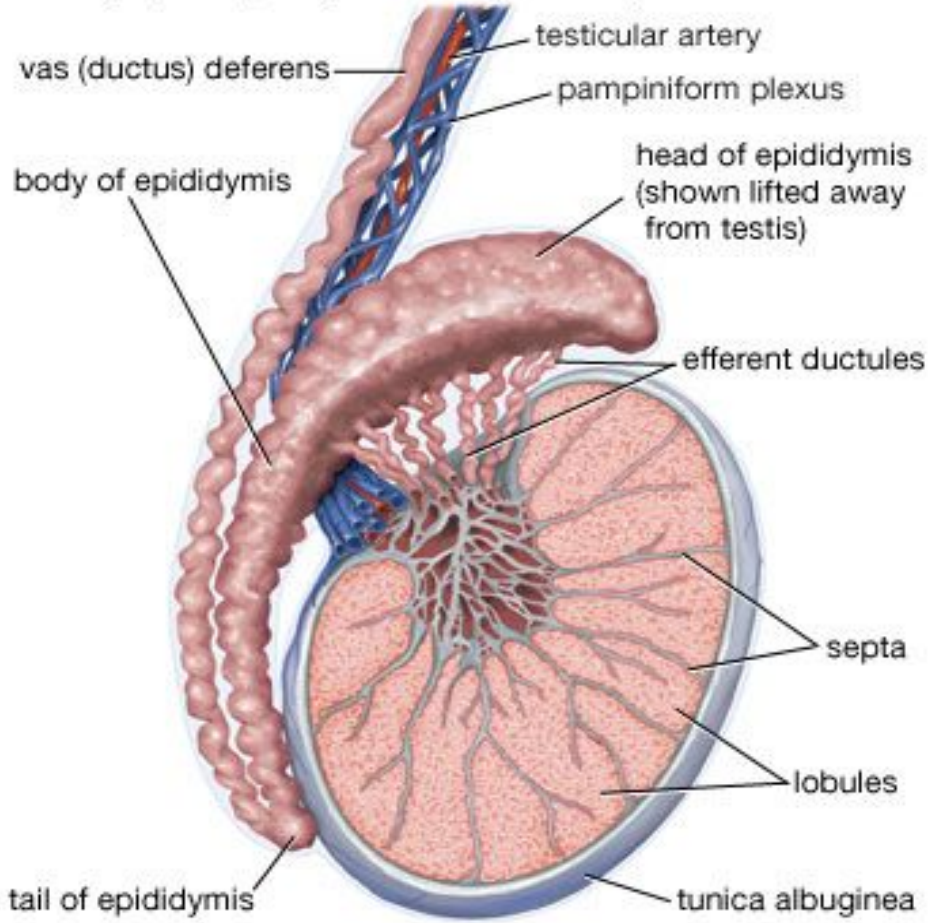
Penis:- male copulatory organ

Structure of testes

- Each testis is divided into 200-300 lobules and each lobule consists of seminiferous tubular compartment and interstitial compartment
- seminiferous tubular compartment :- each lobule consists of 1-3 seminiferous tubules.
- 90% volume of testis due to presence of seminiferous tubules.
- Epithelium of seminiferous tubule contains germ cells (spermatogenic cells) and supporting cells or sustentacular cells (sertoli cells)


Head of epididymis
Vas deferens
Seminiferous tubules
Body of epididymis
Tunica albuginea
Tail of epididymis

Testis, epididymis, and vas (ductus) deferens



- **Spermatogenic cells:- lies in b/w the sertoli cells**

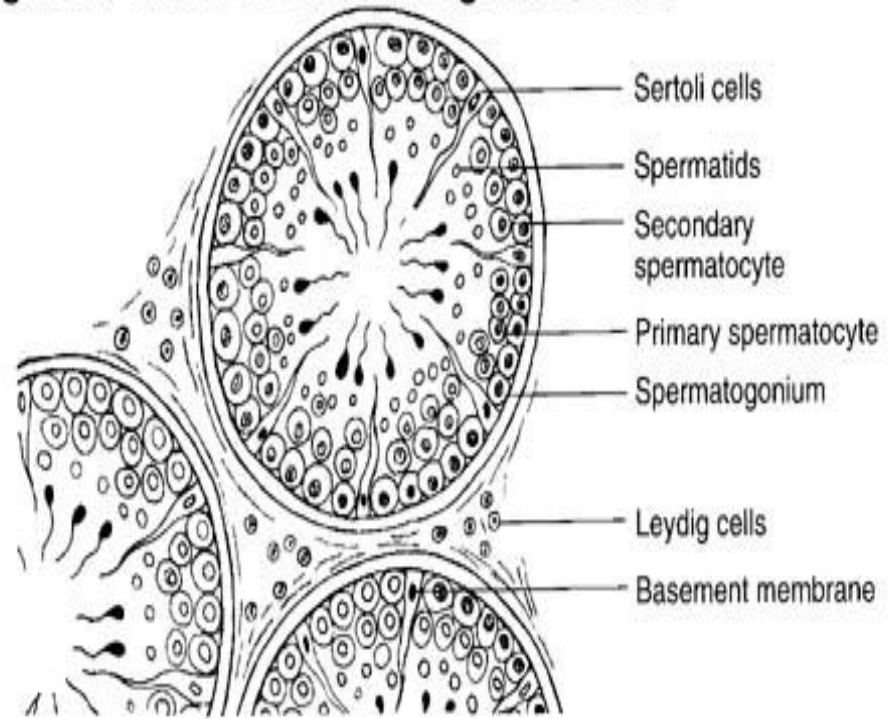
➢ **Arranged in layers (4-8 layers) extending from basal lamina to the lumen of seminiferous tubule**

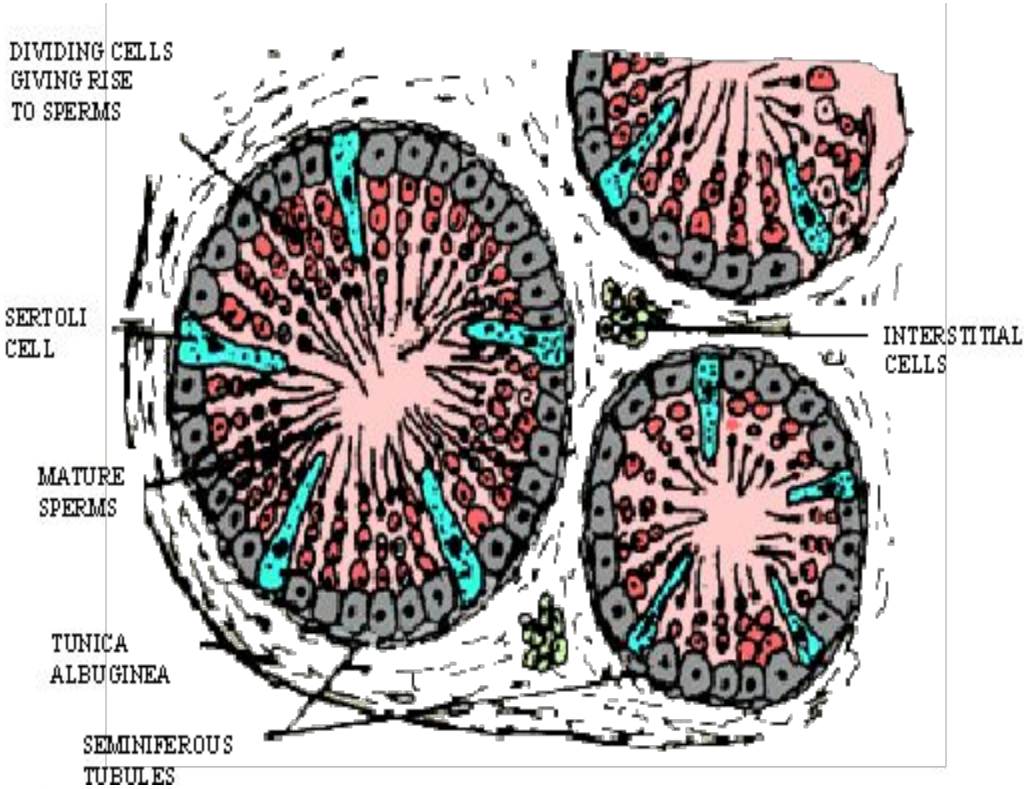
➢ **In sexually mature individuals, spermatogenic cells of all stages of differentiation are seen arranged in orderly manner**

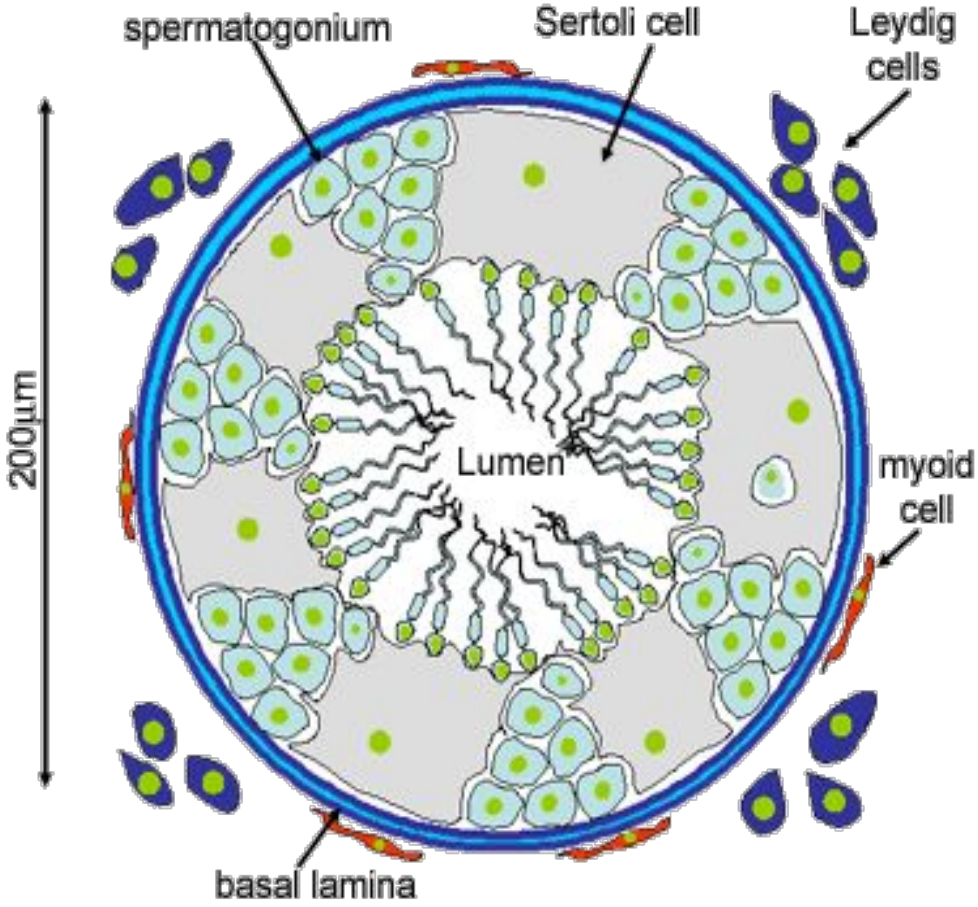
- **Sertoli cells:- extend from basal membrane to lumen of the tubule**

➢ **Plasma membranes of two adjoining cells are connected by tight junctions → blood-testis barrier**

igure 3. Cross section through the testis.






spermatogonium
Sertoli cell
Leydig cells
200µm
Lumen
myoid cell
basal lamina

Significance of blood-brain barrier

- Mature sperm cells are immunogenic when introduced into systemic circulation. BTB protects the cells of different stages of spermatogenesis from blood-borne toxic substances and from circulating antibodies
- Prevents entry of byproducts of gametogenesis into the blood
- Maintenance of luminal fluid composition (very low glucose and protein, high conc. of androgens and potassium ion)

- Steroids can easily cross through this barrier

➢ **Cytoplasm of sertoli cells contains abundant mitochondria, endoplasmic reticulum and other organelles**

Functions of sertoli cells

- Physical support and nutrition to maturing germ cells (being rich in glycogen contents) and also remove waste products from the germ cells
- Cytoplasmic byproducts or residues from spermatozoa during the conversion of spermatids to sperm are phagocytosed by sertoli cells

- Maintenance of blood-testis barrier
- Secretory functions

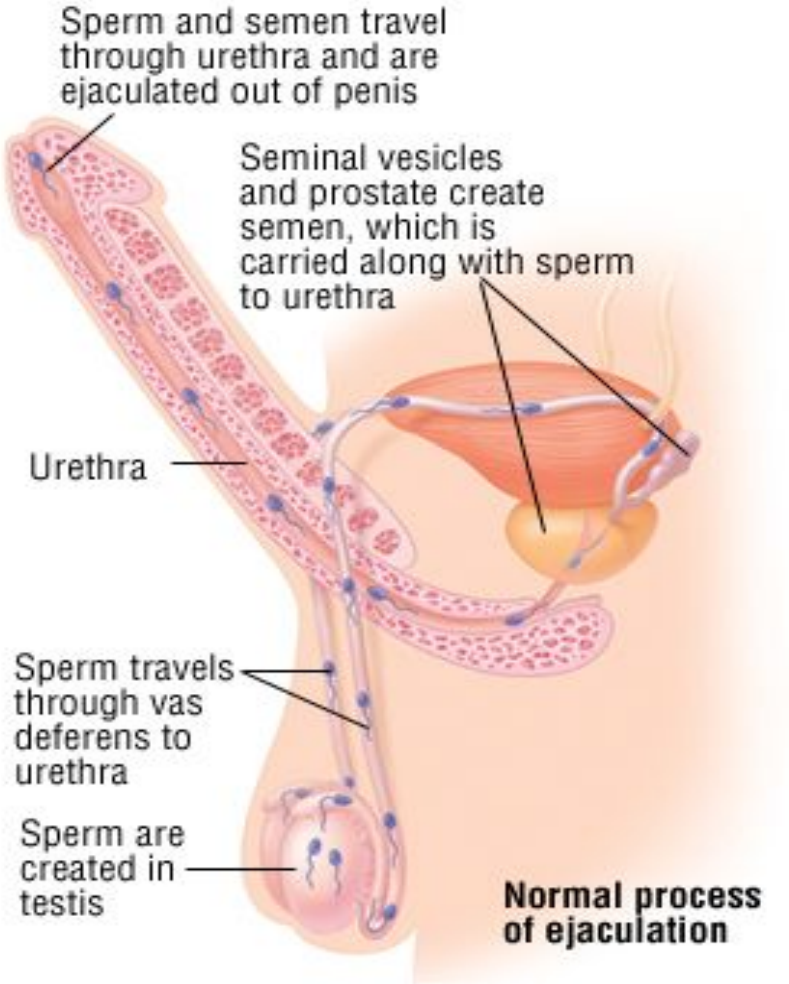
★ Mullerian duct inhibitory substance (MIS) → help in regression of mullerian duct in fetus and keep in male sexual development

★ Inhibin → inhibits spermatogenesis before onset of puberty by regulating FSH secretion by negative feedback at ant.pituitary level

★ Androgen Binding Protein (ABP) → has high affinity for testosterone --> maintaining high con.of androgens in the lumen of seminiferous tubules

★ Estrogen in small amount

- ★ **Transport proteins such as transferrin, ceruloplasmin**
- ★ **Plasminogen activator → required for proteolytic activity for the disruption of tight junctions during migration of maturing germ cells from basal to luminal compartment**
- ★ **Seminiferous tubular luminal fluid → sertoli cells secrete watery, K^+ and HCO_3^- rich fluid into lumen of seminiferous tubules--> provides a driving force for non motile spermatozoa**
- ❑ **Interstitial compartment:- Leydig cells (interstitial cells of Leydig) → secretion of testosterone**

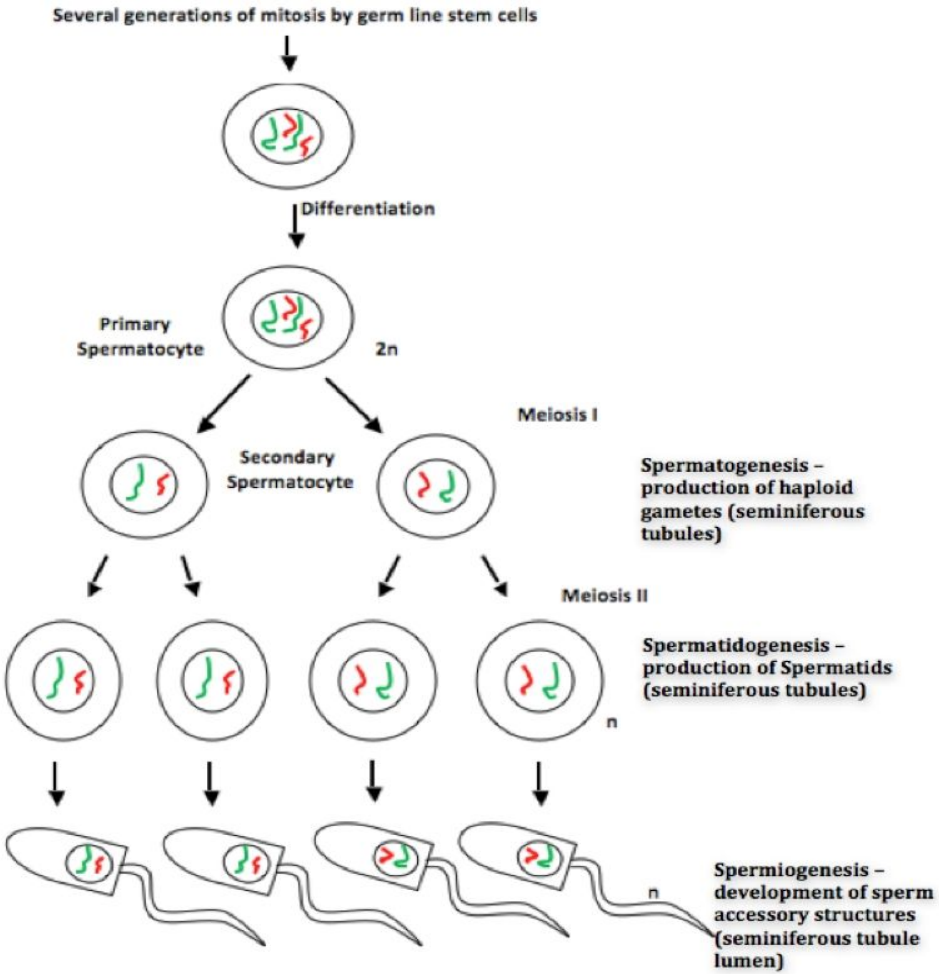

Sperm and semen travel through urethra and are ejaculated out of penis
Seminal vesicles and prostate create semen, which is carried along with sperm to urethra
Urethra
Sperm travels through vas deferens to urethra
Sperm are created in testis
Normal process of ejaculation

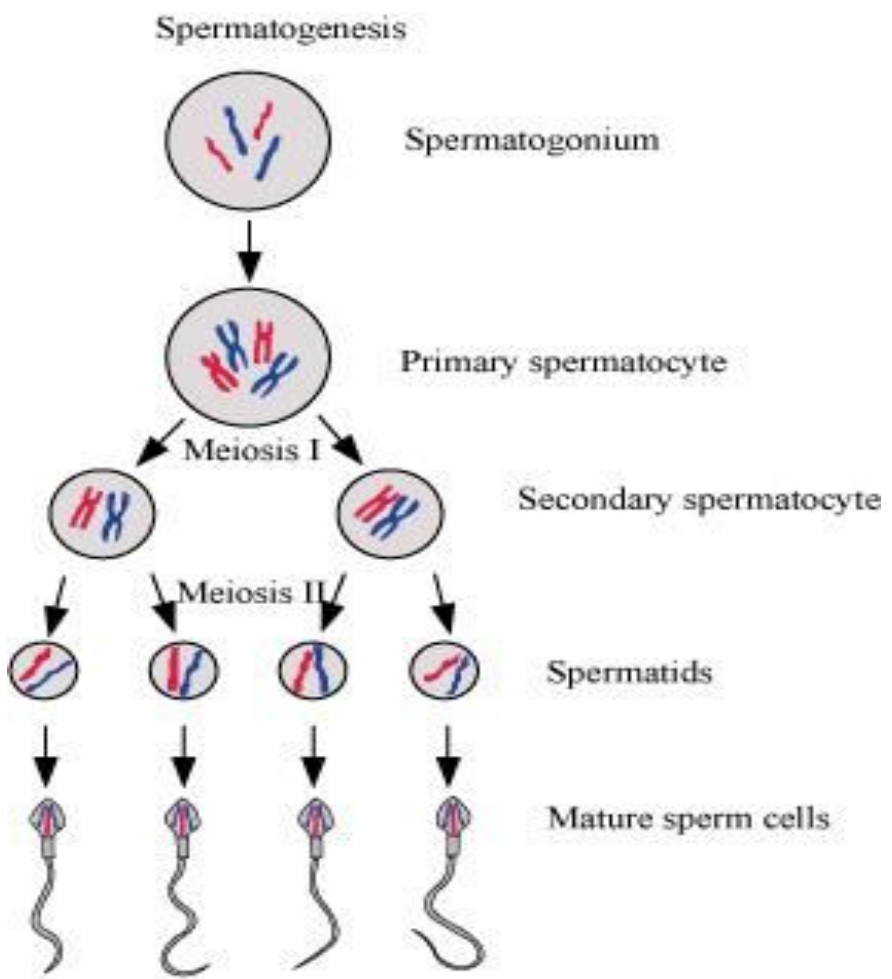
Function of testes

- ★ Gametogenic function (spermatogenesis)
- ★ Endocrine function

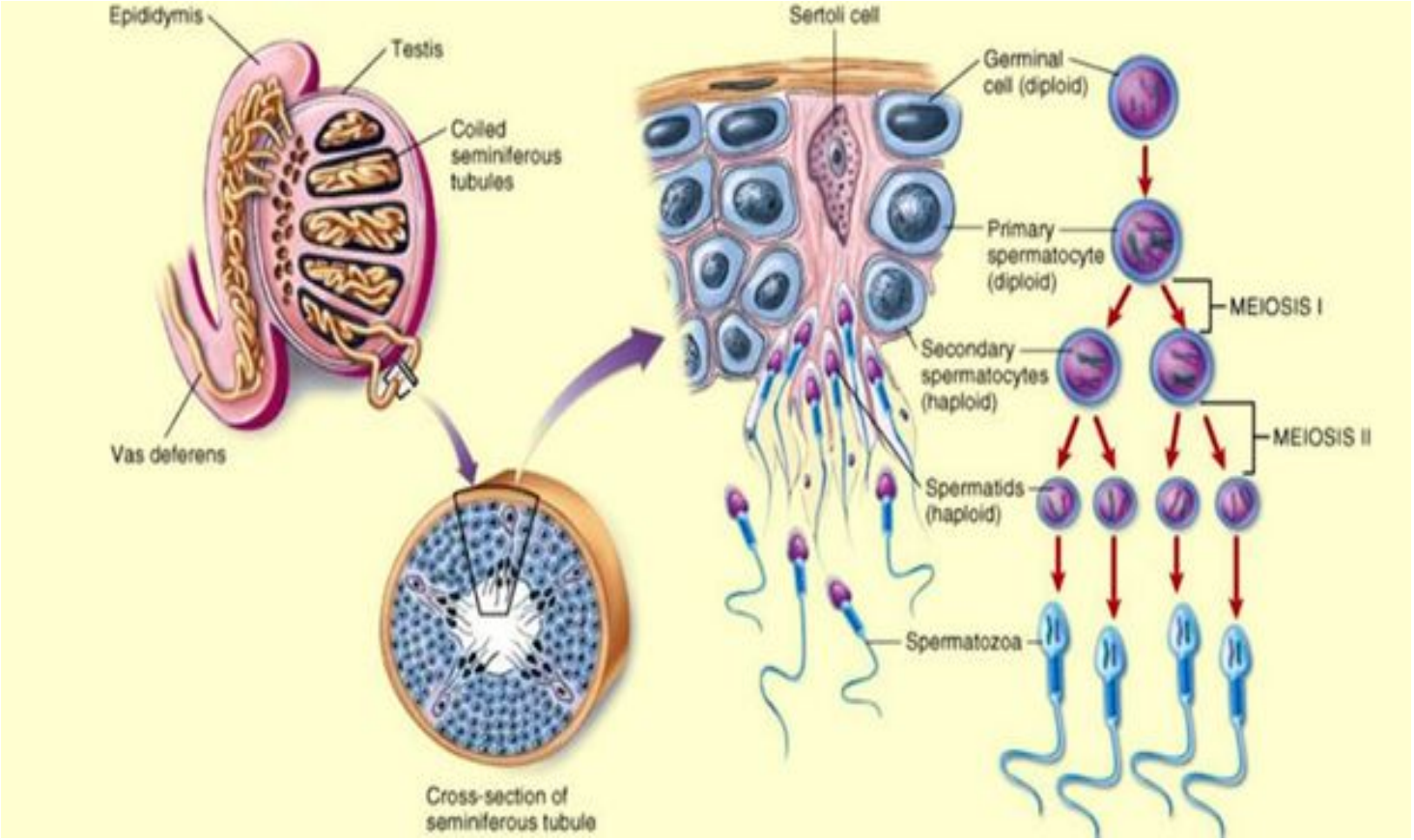
Spermatogenesis

- Process of formation of spermatozoa from the primitive germ cells (spermatogonia) occurs in seminiferous tubules
- Begins at puberty and continues throughout adult life to decline in old age
- Each differentiating spermatogonium develops into 512 spermatids
- Takes an average of 74 days to form a mature sperm from a primitive germ cell





Process of spermatogenesis


Epididymis
Testis
Coiled seminiferous tubules
Vas deferens
Cross-section of seminiferous tubule
Sertoli cell
Germinal cell (diploid)
Primary spermatocyte (diploid)
MEIOSIS I
Secondary spermatocytes (haploid)
MEIOSIS II
Spermatids (haploid)
Spermatozoa

Phases

- **Phase of mitotic division of spermatogonia**

Type A spermatogonia

Type B spermatogonia:- progenitor or precursor of sperms

➔ **Divides mitotically 5 times to form 32 type B spermatogonia (2n)**

- **Phase of formation of primary spermatocytes by mitotic division**

- ➔ **32 type B spermatogonia undergo mitosis to form 64 primary spermatocytes (2n)**
  - **Phase of formation of secondary spermatocytes by meiotic division**
- ➔ **In the prophase of meiotic division, each primary spermatocyte represented as 4n**
- ➔ **After first meiotic division, 64 primary spermatocytes (4n) are converted into 128 primary spermatocytes (2n)**
- ➔ **After second meiotic division, 128 primary spermatocytes converts to 256 secondary spermatocytes (n) either 22+X or 22+Y**

➔ 50% sperms will have X chromosomes and other 50% will have Y chromosomes

- **Phase of formation of spermatid**

Each secondary spermatocyte divides mitotically to give rise to 2 spermatids⇒ total of 512 from single spermatogonium

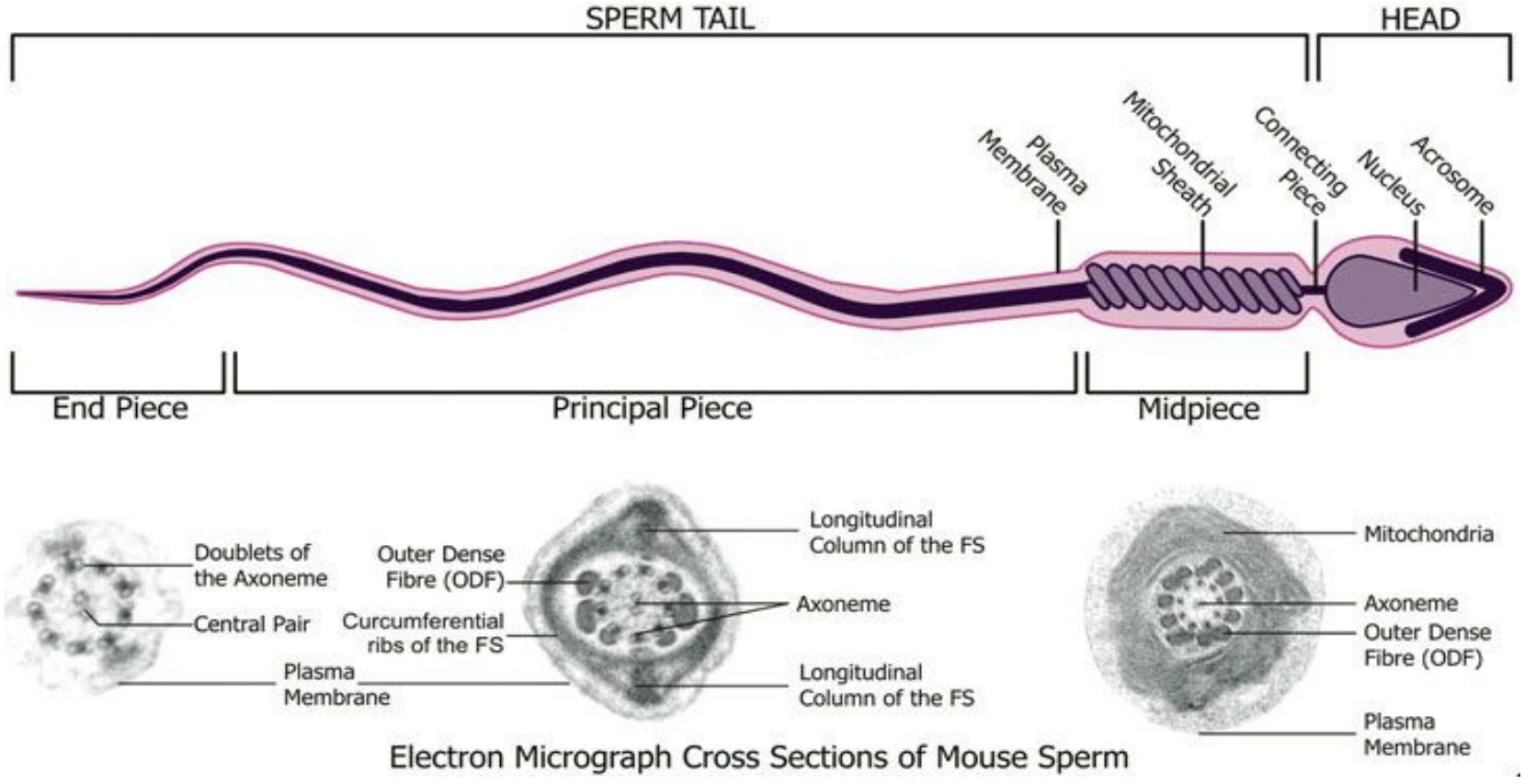
- **Spermiogenesis:-** formation of spermatozoa from spermatid

➔ Spermatids do not divide further

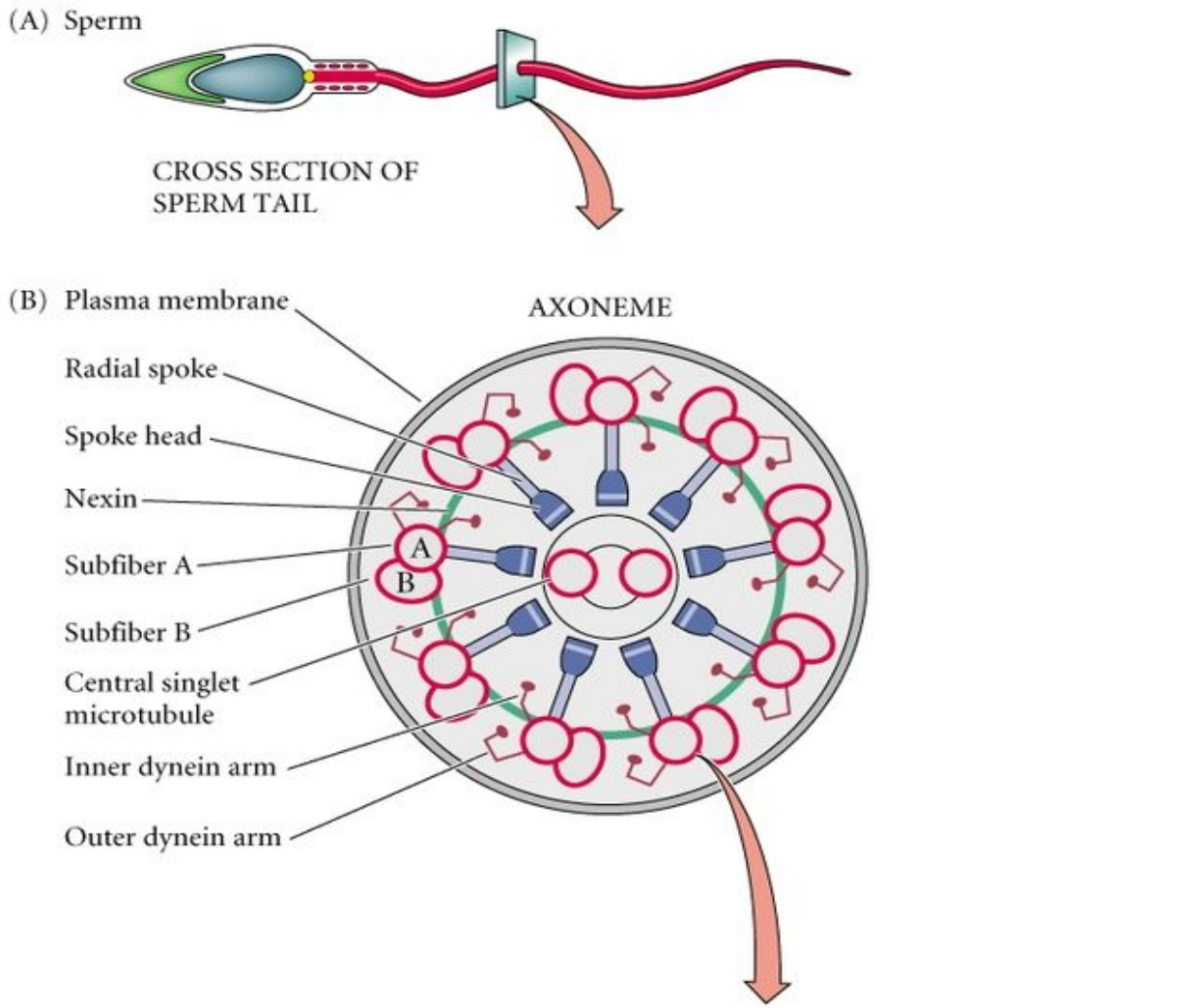
➔ Undergoes morphological changes to form sperm/spermatozoa

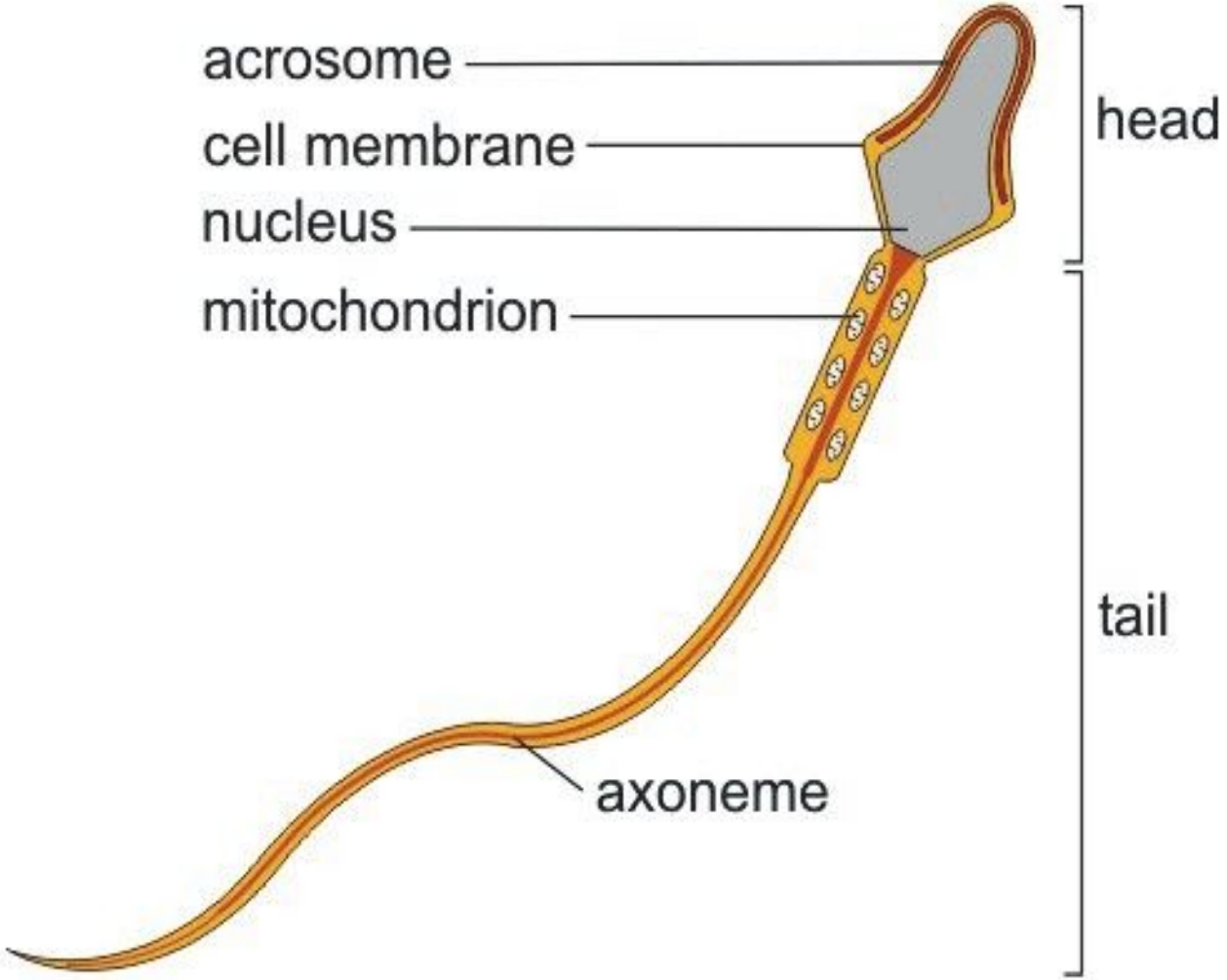
- ➔ Take place in cytoplasm of sertoli cells
- ★ Nucleus undergoes condensation and changes to head of the sperm
- ★ Golgi apparatus forms acrosome (cap-like structure covering anterior 2/3rd of the head. Contain hyaluronidase which help in the penetration of an ovum during fertilization
- ★ Mitochondria surrounds tail part of sperm wrapped in a sheath, provides energy for movements of sperm
- ★ Cell membrane persists as covering of sperm, contain germinal ACE (gACE)

★ **Cytoplasm and other organelles shed off as residual bodies, phagocytosed by sertoli cells**



Electron Micrograph Cross Sections of Mouse Sperm




acrosome
cell membrane
nucleus
mitochondrion
axoneme
head
tail

Factors affecting spermatogenesis

- **Hormonal factors:- controlled by hypothalamic-hypophyseal-testicular axis**

➔ **Role of hypothalamus:- it secretes GnRH which stimulates anterior pituitary to secretes LH and FSH**

➔ **Role of anterior pituitary:- it controls spermatogenesis through gonadotropic hormones (FSH,LH) and growth hormone**

★ **Role of FSH:- stimulates sertoli cells which plays a role in spermatogenesis**

Indirectly affects testosterone synthesis by increasing number of LH receptors on Leydig cells

★ Role of LH:- ICSH - stimulates Leydig cells to cause testosterone secretion, required for normal spermatogenesis

★ Role of growth hormone:- promotes early division of the spermatogonia

➔ Role of testicular hormones:- testosterone secreted by Leydig cells acts on both Sertoli cells and germ cells and thus maintains spermatogenesis

- Estrogen formed from testosterone also essential for spermatogenesis

- **Feedback inhibitory control**

- **Sertoli cells**

Nutritional support

Spermiogenesis

ABP

- **General factors**

➢ **Temperature:-**

➢ **Seasonal variation :- sperm count greater in winter season**

➢ **Infectious diseases:- mumps cause degeneration of seminiferous tubules → decreasing spermatogenesis (orchitis)**

➢ **Irradiation:- damages seminiferous tubules**

➢ **Age:- spermatogenesis decreases with advancing age**

➢ **Vasectomy:-**

- **Velocity of movement of sperm :- 1-4 mm/min**
- **About 120 million sperms are formed each day**
- **Stored in epididymis & vas deferens**
- **Epididymis is the site of extra testicular maturation of sperm and sperm acquire motility after passing through it**
- **Spermatozoa become fully motile only after ejaculation**
- **Sperm acquire ability to fertilize the ovum only after reaching in the female genital tract → capacitation**

Endocrine function of testes:-

Hormones secreted by testis are,

- **Testosterone**
- **Dihydrotestosterone**
- **Androstenedione**
- **Estrogen**
- **Inhibin**

Sources of hormones:-

- Leydig cells are the sources of androgens
- Sertoli cells secrete estrogen and inhibin

Testosterone :-

- Synthesized from cholesterol in the Leydig cells
- Also formed from androstenedione secreted by adrenal cortex
- Androstenedione is also formed from progesterone and it is then converted into testosterone
- LH stimulates Leydig cells to secrete testosterone

Androstenedione:-

Important steroid precursor for blood estrogens (oestradiol, oestrone) in men by aromatase enzyme

Dihydrotestosterone (DHT):-

- 20% of plasma DHT is formed in the testes by the action of 5 α reductase (from sertoli cells) on testosterone (by Leydig cells)
- 80% derived from peripheral conversion of testosterone (target tissues → skin, male reproductive tract {prostate, seminal vesicle, epididymis)by 5 α reductase

- DHT has more than twice the biologic activity of testosterone

➔ **98% of testosterone is transported in bound form**

- ❖ **65% → bound with globulin (GBG)**
- ❖ **33% → albumin**

Total plasma testosterone level → 300-1000 ng/dL

- ❑ **Metabolic degradation products are DHT, estradiol and estrone, androsterone and dehydroepindrosterone**

actions/functions of androgens

- **In fetal period:- testosterone secreted by fetal testis at about 2nd to 4th mnth of embryonic life**

➔ **Effect on sex differentiation**

★ **Gonadal sex differentiation**

★ **Genital differentiation→ differentiation of internal genitalia**

→ differentiation of external genitalia -DHT

➔ **Effect on descent of testes :- testosterone is necessary**

- **At puberty:-**

➔ **Effects on external genitalia:-** testosterone causes pubertal enlargement of penis

★ DHT increases size of scrotum, pigmentation and appearance of rugal folds

➔ **Effect on accessory sex organs:-** T causes enlargement of seminal vesicles

★ DHT promotes growth of prostate and stimulates prostatic secretions

➔ **Development of male secondary sexual characters:-**

★ Body hair:DHT stimulates hair follicles

★ T causes enlargement of larynx and thickness of

Vocal cords → low pitched voice

★ T causes enlargement of muscle mass

★ DHT increases the production of sebum→ acne

➔ **Effect on psyche:-**

★ Psychological differentiation

★ T initiates produces aggressive behaviour

★ T initiates sexual drive

➔ **Anabolic and general growth promoting effects**

★ T causes increased synthesis and decreased breakdown of tissue proteins → accelerated growth of body and skeletal muscles

★ **Bone growth:- T causes broadening of shoulders and early fusion of epiphysis in long bones**

★ **Increases basal metabolic rate**

★ **Causes renal retention of calcium, phosphate,sodium, potassium, water**

- **In adults:-**

★ **Hair growth**

★ **Behavioural attitudes are maintained**

★ **Prevention of osteoporosis and bone loss**

★ **Spermatogenesis is maintained along with FSH**

★ **Hematopoiesis:- T stimulates production of erythropoietin**

- T increases circulating levels of LDL cholesterol and decreases HDL cholesterol
- Regulation of gonadotropin secretion by negative feedback mechanism

SEMEN/ SEMINAL FLUID

- Fluid ejaculated during the orgasm at the time of male sexual act
- <u>Clinical features</u>

➔ Average volume of semen per ejaculation is 2.5-3.5 ml

➔ Milky appearance due to prostatic secretions

➔ Alkaline pH :- 7.5 (due to prostatic secretions)==> brings vaginal pH from 3.5-4 to 6-6.5, pH at which sperms show optimum motility

➔ When ejaculated, semen is liquid→ later it coagulates in the vagina (help to retain it in vagina)→ finally undergoes secondary liquefaction after 15-30 minutes (releases sperm for their free movement into uterine cavity for fertilization)

Mechanism of coagulation:-fibrinogen present in semen (contributed by seminal vesicles) is converted into weak coagulum by the clotting enzyme present in prostatic secretion

Mechanism of liquefaction:- by fibrinolysin, activated form of profibrinolysin in the prostatic secretion

- **Components and their characteristics**

❖ **Spermatozoa (10%):- normal sperm count → 35-200 million /ml of semen (average→ 100 million/ml of semen)**

➔ **Sperms move at a speed of 1-4 mm/ min through female genital tract**

➔ **Uterine contraction (reverse peristalsis) during sexual act facilitates movement of sperms**

➔ **Sperm remain capable of fertilizing ovum for 28-48 hrs after ejaculation in the female genital tract**

- **Secretions of seminal vesicles:- 60%**
- **Makes the fluid mucoid and viscous**
- **Neutral or slightly alkaline in nature**
- **Contains fructose, citric acid, fibrinogen, prostaglandins**
- **Functions :-**
  - **Nutrition to sperms after being ejaculated into female genital tract is provided by fructose**
  - **Clotting of semen soon after ejaculation due to fibrinogen**
  - **Fertilization of ovum is enhanced by prostaglandins by increasing the receptive capacity of cervical mucosa for sperms and inducing reverse peristalsis of uterus and fallopian tubes thereby increasing the rate of transport of sperms**

- ❖ **Secretion of prostate gland (about 30%)**
- ➔ **Contributes milky and alkaline fluid part of semen**
- ➔ **Contains calcium, citric acid, cholesterol, phosphate ion, profibrinolysin, a clotting enzyme, spermine**
- ➔ **Functions:-**
  - ➢ **Maintenance of optimum pH for fertilization**
  - ➢ **Clotting of semen**
  - ➢ **Lysis of coagulum**

Prostatic specific antigen (PSA) → protease secreted by prostate gland, increases sperm motility

Elevated level of PSA → diagnosis of prostate carcinoma

❖ **Secretion of bulbourethral gland:-**

➔ **Only a small amount of semen volume**

➔ **Provide mucoid consistency**

Sperm count less than 20 million/ ml of semen → sterility

(depends on activity and motility of sperm)

Erection:-

- Penile erection is the first effect of male sexual stimulation
- Initiated by dilatation of arterioles of penis
- Erectile tissues of penis (two corpora cavernosa and one corpus spongiosum) get filled with blood
- Compression of veins blocking outflow→ adds to turgor of penis
- Caused by parasympathetic impulses pass from sacral portion of spinal cord through pelvic nerves to penis → releases nitric oxide and/or vasoactive intestinal peptide in addition to Ach

→ NO activates guanylyl cyclase→ increased formation of cyclic guanosine monophosphate (cGMP) [potent vasodilator]→ relaxes arterioles and erectile tissues of penis→ blood flow to penis increases → release of NO from vascular endothelial cells and further vasodilation

Ejaculation:-

- Emission and ejaculation are the culmination of male sexual act
- Function of sympathetic nerves
- Spinal reflex

When the sexual stimulus becomes extremely intense, reflex centres of spinal cord begins to emit sympathetic impulses that leave the cord at T12 to L2 and pass to genital organs through hypogastric and pelvic sympathetic nerve plexuses to initiate emission

Emission begins with contraction of vas deferens to cause expulsion of sperm into internal urethra→ contraction of prostate followed by seminal vesicles expel prostatic and seminal fluid into urethra → forward movement of sperm → all these fluids mix in internal urethra with mucus by bulbourethral gland

Filling of internal urethra with semen elicits sensory signals pudental N sacral regions of cord => sudden fullness of internal genital organs

Sensory signals→ excite rhythmical contraction of internal genital organs cause contraction of ischiocavernosus and bulbocavernosus muscles that compress base of penile erectile tissue

⇒ rhythmical wave like increase in pressure in both erectile tissue of penis and urethra → ejaculation

Cryptorchidism:-

- Condition in which descent of testis may fail to occur or may be incomplete
- Normally by 35th wk of gestation→ descend of testis to scrotum
- Undescended testis may be in the abdominal cavity or inguinal canal
- High temperature causes irreversible damage to seminiferous tubules → sterility
- Treatment → gonadotropic treatment or surgery before puberty

Male hypogonadism:-

- **Results from absent or deficient testicular functions**
- **<u>Primary</u> :- defect in testis → circulating gonadotropin levels are elevated**
- **<u>Secondary</u>:- defect in hypothalamus or pituitary → circulating gonadotropin levels are depressed**

Hypogonadism before puberty:- eunuchoidism

Hypogonadism after puberty:-

Male precocious pseudopuberty:-androgen secreting Leydig cell tumors in prepubertal boys. Very rare

Extirpation / Castration

- Removal of testes
- Castration before puberty :- enuchoidism

➔ Permanent sterility

➔ Underdevelopment of external genitalia and accessory sex organs

➔ Underdevelopment of secondary sexual characters

❑ Hair growth on face, trunk, axilla scanty

❑ High pitched voice

❑ Muscle mass and shoulder girdle development is poor

❑ Female like body configuration

❑ Abnormal bone growth → tall

Male infertility:-

- Inability of sperm to fertilize the ovum
- Causes:-
- Androgen dysfunction with normal sperm count
- Isolated dysfunction of sperm cell production with normal androgen levels
- Combined androgen and sperm cell production defects
- Failure of deposition of sperms in female genital tract

Impotence:- lack of power in male to copulate

FEMALE REPRODUCTIVE SYSTEM

Primary sex organ :- a pair of ovaries

Secondary sex organs:-

Female internal genitalia:- uterus, fallopian tubes and vagina

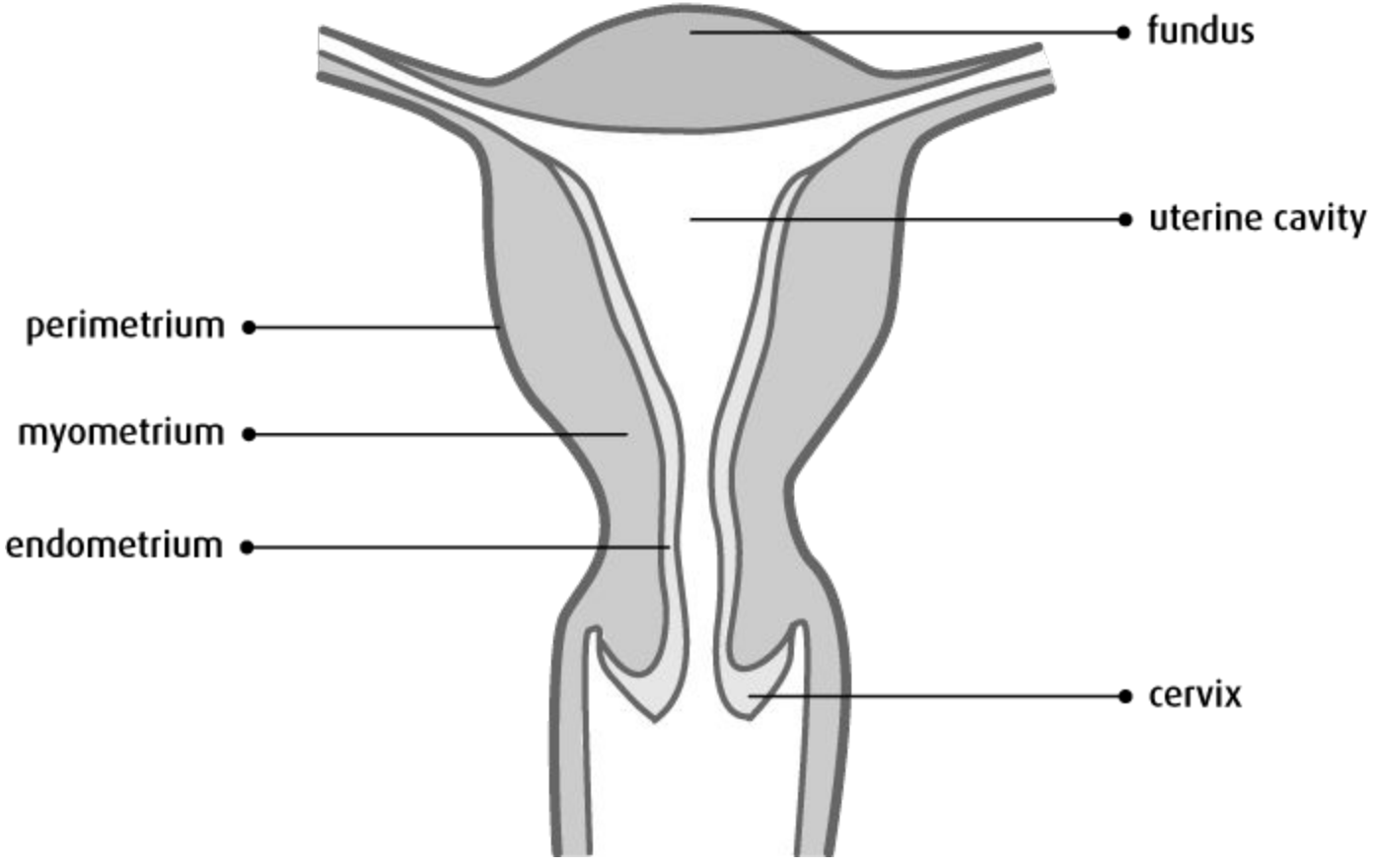
UTERUS:- body and cervix

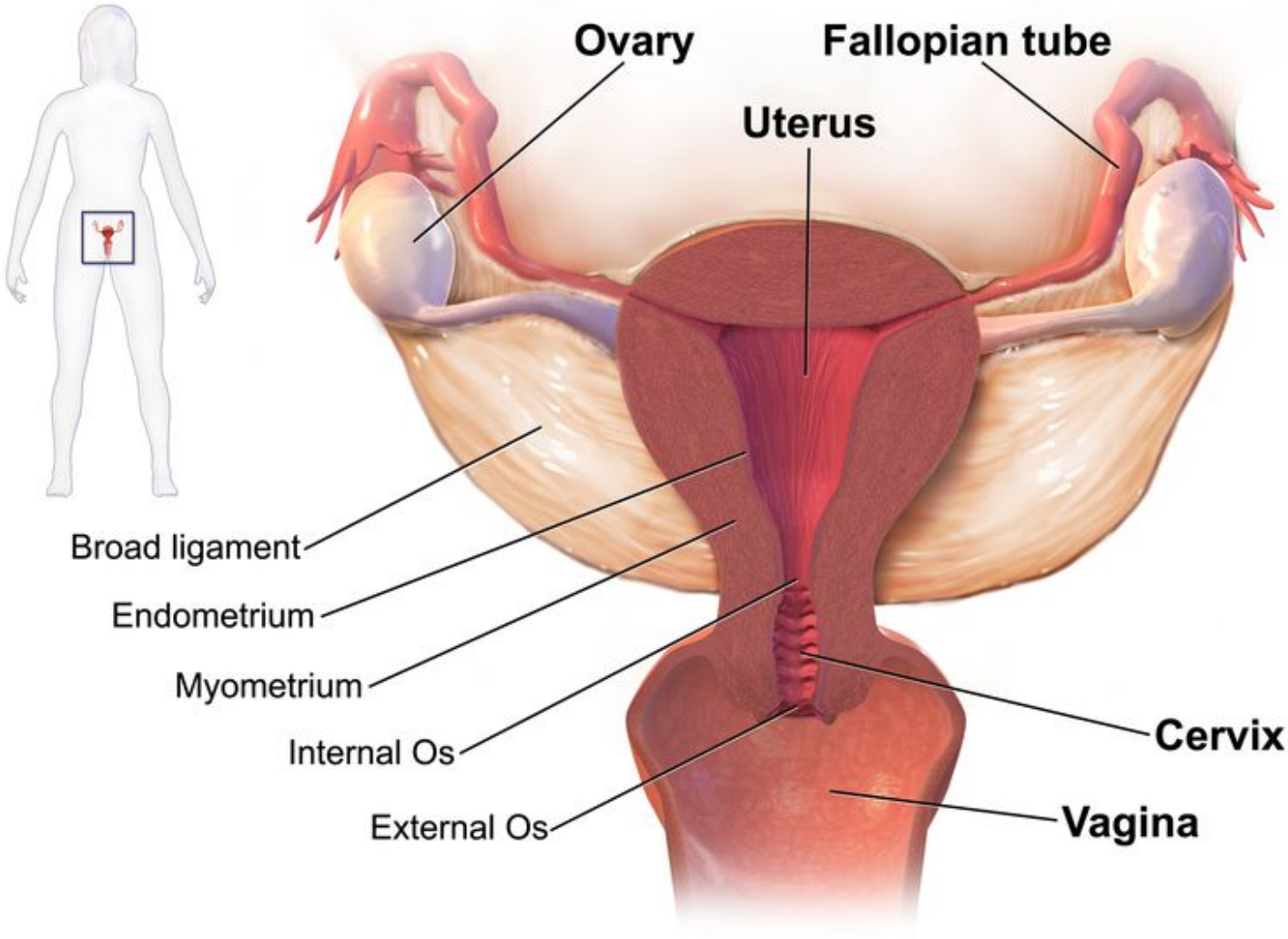
Body :- upper two third of uterus

Lower limit is at internal os

Fundus :- lies superior to opening of fallopian tubes

Structure of the Uterus




Ovary
Fallopian tube
Uterus
Broad ligament
Endometrium
Myometrium
Internal Os
External Os
Cervix
Vagina

Cervix :- lower part protrudes into uppermost vagina

Cavity extends from internal os to external os

Wall of uterus :-

Perimetrium:- external serosal layer

Myometrium :- middle muscular layer

Capable of undergoing great elongation in association with great enlargement of uterus in pregnancy

Contractions of myometrium are responsible for expulsion of fetus at the time of child birth

Endometrium :- epithelial lining and stroma

Epithelial lining :- made of columnar cells

Before menarche, → ciliated

Stroma :- highly cellular, contains numerous blood vessels and simple tubular uterine glands

Functional division of endometrium:-

Stratum functionale :- superficial two third

Undergoes monthly cyclic changes in preparation for implantation of fertilized ovum and is shed during menstruation

Supplied by long and spiral arteries

Stratum basale :- deeper one-third

Doesn’t participate in cyclic changes

Regenerative layer

Supplied by short and straight basal arteries

CERVIX :- perimetrium, myometrium, endocervix

FALLOPIAN TUBES:- uterine tube

Medial or uterine end and lateral end opens into peritoneal cavity near ovary

Four parts :-

Uterine or interstitial part :- passes through thick uterine wall

Isthmus :- narrow and thick walled , lies next to uterine part

Ampulla :- thin walled and dilated part . Fertilization takes place here

Infundibulum :- funnel shaped lateral end

Has finger like processes - fimbria

One fimbriae longer and attached to outer pole of ovary

Perimetrium, myometrium, endometrium

Functions :-

- **Conveys ova, shed by the ovaries. Ova enter the tube at its fimbriated end**
- **Sperms enter the tube after traversing vagina and uterine cavity**
- **Secretions present in it provides nutrition, oxygen, and other requirements for ova and spermatozoa**
- **Fertilization takes place in ampulla**
- **Fertilized ovum travels towards uterus with the help of ciliated epithelial cells lining the tube**

VAGINA:- musculomembranous tube

Upper end surrounds lower part of cervix and lower end (vaginal orifice) opens into vestibule of vagina (cleft b/w labia minora)

No glands opens into vagina

- **Small amount of secretion present (derived partly from mucous discharge from cervix and partly from transudation of fluid from vaginal epithelium, contains glycogen)**

- **Action of bacteria on glycogen produces lactic acid , maintains vaginal pH around 4.5**
- **Acidic environment prevents the growth of pathogenic organisms**

Structure :-

Mucous membrane :- epithelial cells are rich in glycogen, estrogen dependent

Muscle coat, adventitial coat

<u>Functions</u> :- serves as excretory duct for menstrual fluid

Forms inferior part of pelvic (birth) canal

Receives the penis and ejaculate during sexual intercourse

Female external genitalia:-

Mons pubis

Labia majora

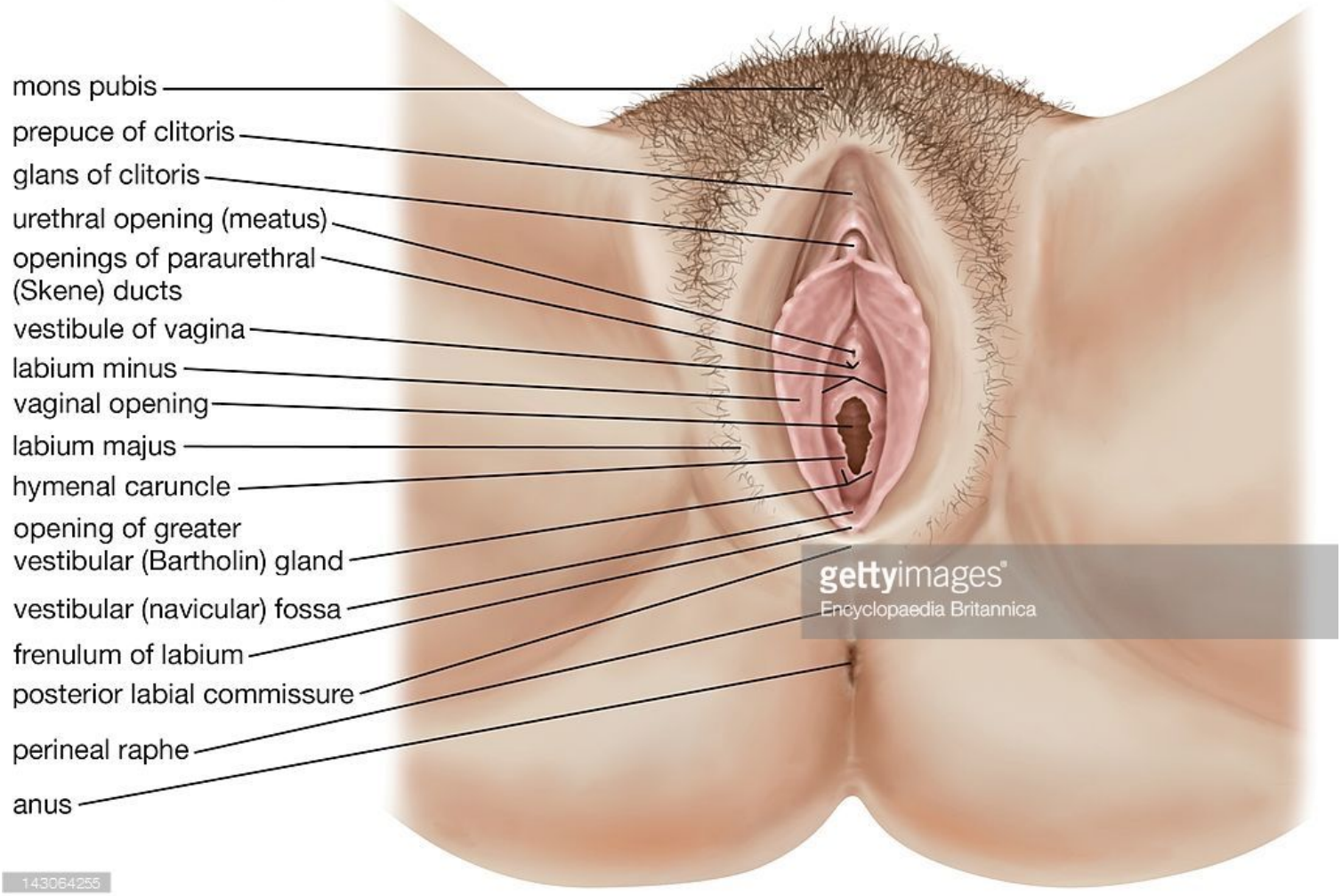
Labia minora

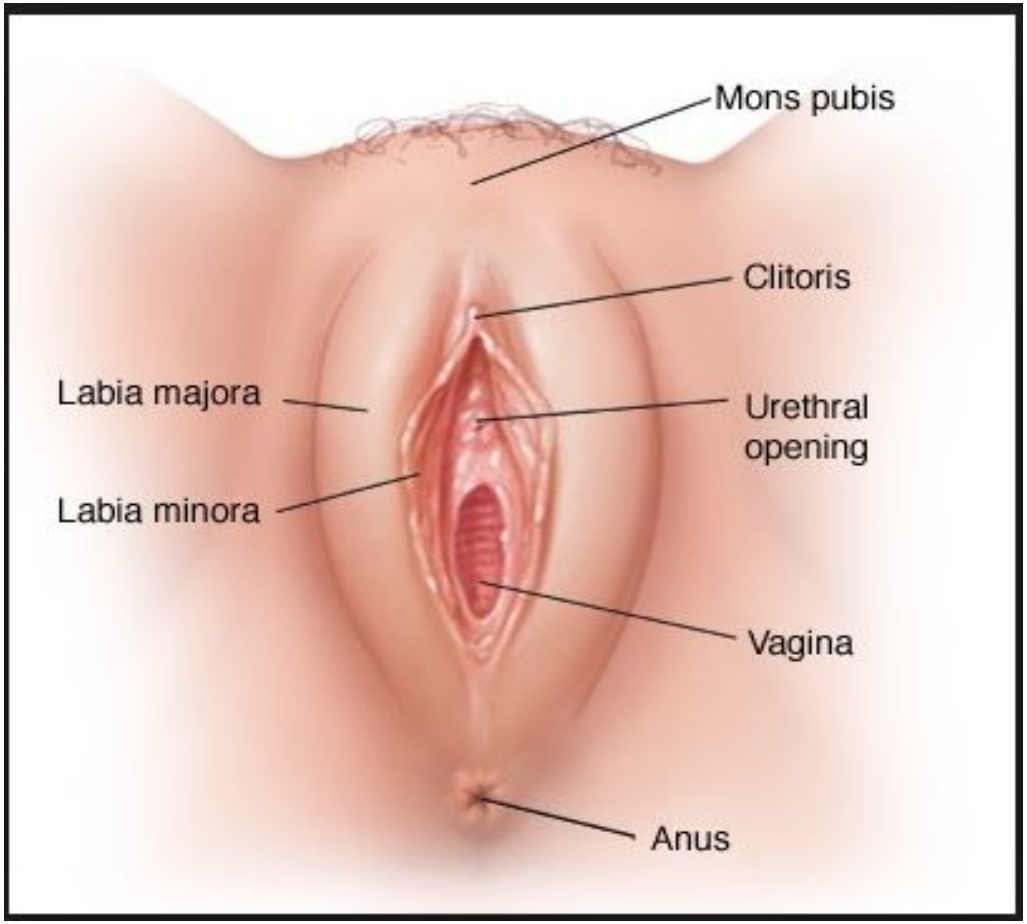
Clitoris

Vestibule

Vestibular glands

Female external genitalia




Mons pubis
Clitoris
Labia majora
Urethral opening
Labia minora
Vagina
Anus

OVARIES :-

- Combined wt :- 10-20g
- Attached to uterus by broad ligament and round ligament of ovary

Histology :-

Germinal epithelium :- epithelium lining outer surface of ovary ,single layer of cuboidal cells

- Cells of epithelium bear microvilli and contain numerous mitochondria→ larger in pregnancy

Cortex :- outer thick main part

Tunica albuginea:-

Stroma:- ovarian follicles at various stages of development are scattered

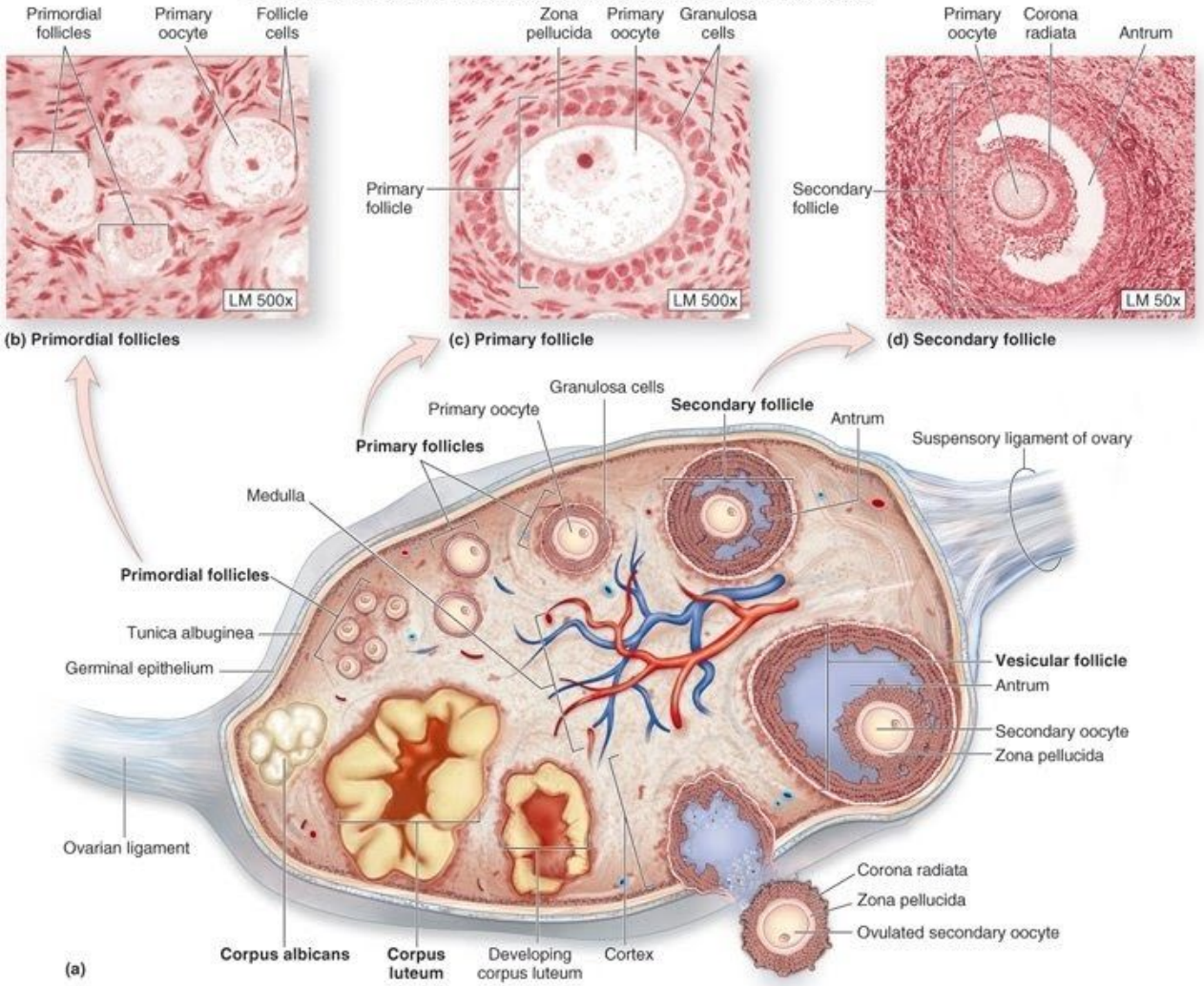
Each follicle contains a developing ovum

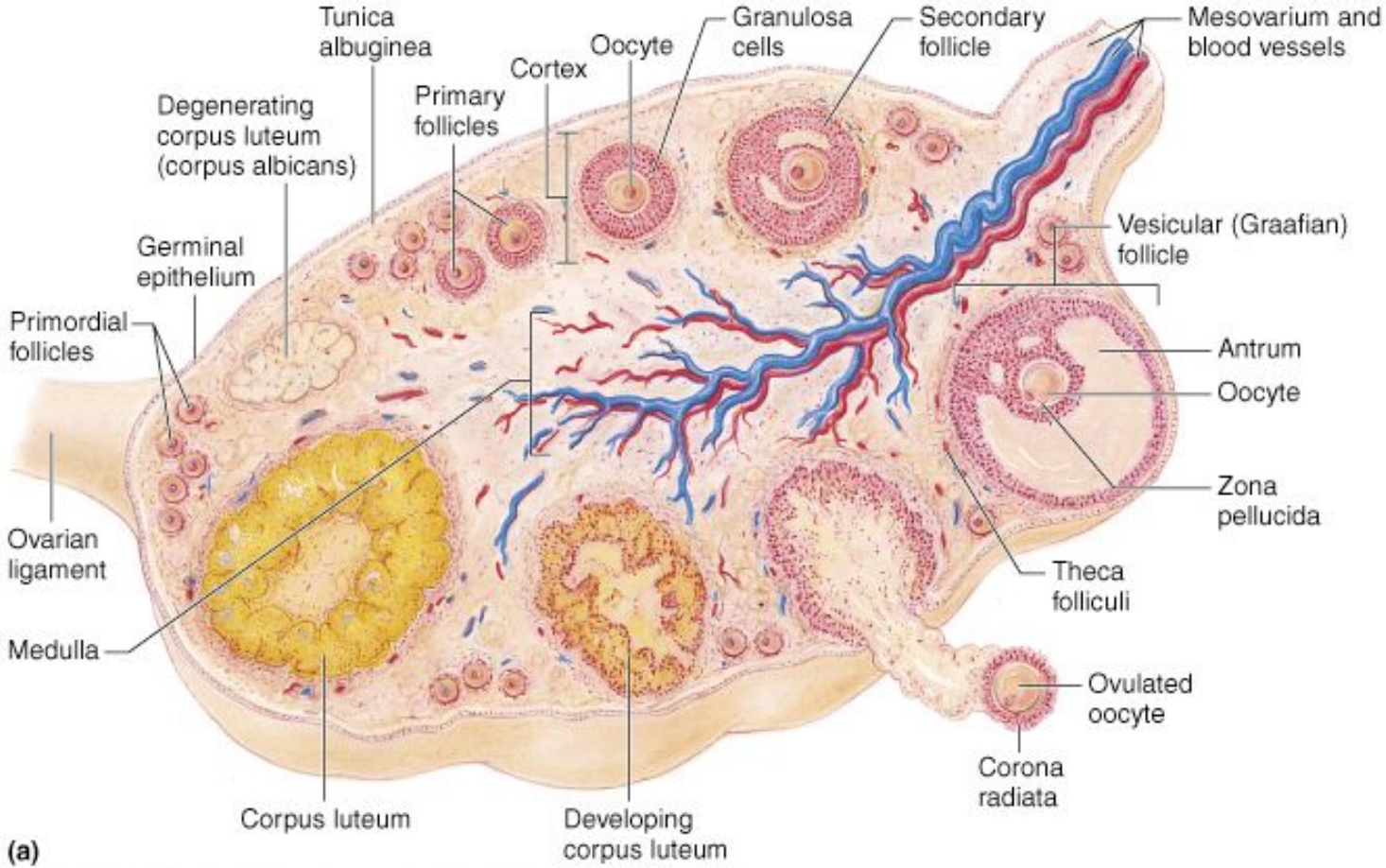
Medulla:- inner small part

Hilum:- area where ovary attaches top mesentery

Site of entry of blood vessels and lymphatics

Contains some remnants of mesonephric ducts and hilus cells similar to interstitial cells of testis





Functions of ovaries :-

- **Gametogenic : oogenesis**
- **Endocrine : secretion of ovarian hormones (estrogen and progesterone)**

OOGENESIS

Process of formation of ova from primitive germ cells

Phases :- fetal oogenesis

Postnatal and prepubertal oogenesis

Pubertal oogenesis

Fetal oogenesis

Fetal ovary begins oogenesis by 10 wks of gestation (spermatogenesis begins at puberty)

When bipotential gonads differentiate into ovaries in genetic female (44 +XX) embryo by 10th wk of gestation, primitive germ cells undergoes mitosis to form oogonia

Oogonia are the stem cells from which ova are derived (only female cell in which both X chr are active)

Oogonia proliferate by mitosis forms primary oocytes (process begins at 15th wk and reaches peak b/w 20 and 28 wk of gestation)

Primary oocytes (diploid) enters prophase of first meiotic division and remain in this state until ovulation occurs after puberty

Primary oocytes enveloped by single layer of flat granulosa cells → primordial follicles (granulosa cells formed by proliferation of coelomic epithelium , cortical cells)

Primordial follicle is fundamental reproductive unit of ovary

Many germ cells undergo atresia and at term only 2 million germ cells are present (most of them developed into primordial follicles,oogonia and primary oocytes

Postnatal oogenesis and prepubertal oogenesis

By 6 mnths postpartum, all of the oogonia → primary oocytes and primordial follicles

By onset of puberty, two ovaries contain 3 lakh primordial follicles

Pubertal oogenesis

After puberty, oogenesis occurs once every 28 days till menopause

Every mnth, in each ovary more than 1 primordial follicle start undergoing maturation but one reaches maturity and rest undergo atresia at diff stage of develop.

Different stages of maturation of primordial follicle into graafian follicle→ folliculogenesis

Just before ovulation, primary oocytes completes first meiotic division→ **secondary oocyte and first polar body**

First polar body soon fragments and disappears

Secondary oocyte (haploid) immediately begins the second meiotic division, stops at metaphase and is completed only if fertilization occurs. After fertilization, second polar body is formed and extruded out. Fertilized ovum proceeds to form new individual

Pubertal oogenesis versus spermatogenesis

Female cannot form oogonia beyond 28 wks of gestation

Male produces spermatogonia and primary spermatocytes continuously throughout life

Meiosis in female results in the formation of one viable oocyte .primary spermatocyte → 4 spermatozoa

Endocrine function of ovaries

Estrogens:-

Naturally occurring estrogens :- oestradiol (physiologically most potent). Accounts for >90% of circulating estrogens

oestrone :- weak

Oestriol:- degradation product of estradiol and estrone . weakest

In normal non-pregnant female, estrogens are mainly secreted by theca interna and granulosa cells of ovarian follicles

Small quantity also produced by adrenal cortex, breast, some areas of brain, placenta (during pregnancy), sertoli cells

Estrogens mainly synthesized from cholesterol

Progesterone and testosterone are synthesized first and then converted to estrogens

- **Δ5 and Δ4 pathway**

FSH and LH from anterior pituitary stimulate the synthesis of female sex hormones by acting on the receptors

- Theca cells have many LH receptors. LH increases the conversion of cholesterol to androstenedione via cAMP
- Granulosa cells possess FSH receptors . FSH facilitates secretion of estradiol by acting on the receptors through activation of cAMP → increases the activity of aromatase

Granulosa cells also acquire LH receptors

- There exists an interaction b/w theca interna and granulosa cells for estrogen synthesis. Theca interna provide androstenedione to granulosa cells for the synthesis of estradiol
- Stromal tissues of ovary secretes small amount of androgens and estrogens

➔ **In early follicular phase → 36 μg/day**

➔ **Just before ovulation→ 380 μg/day**

➔ **Mid luteal phase → 250μg/day**

➔ **After menopause, → 50μg/day**

98% plasma bound & 2% free

60% → albumin

38% → beta globulin (gonadal steroid binding globulin)

- **Metabolised in liver**
- **Estradiol and estrone → estriol**
- **Conjugated with glucuronic acid and sulphuric acid in liver and excreted into urine and bile**

Functions of estrogen

Reproductive actions :-

- During embryonic life → no effect on sex differentiation
- Pre-pubertal stage → estrogen secreted in small amount, little physiological actions
- At puberty:-

➢ Growth and development of genital organs

Ovaries increase in size and ovarian cycles start

Fallopian tubes become functional, epithelium becomes

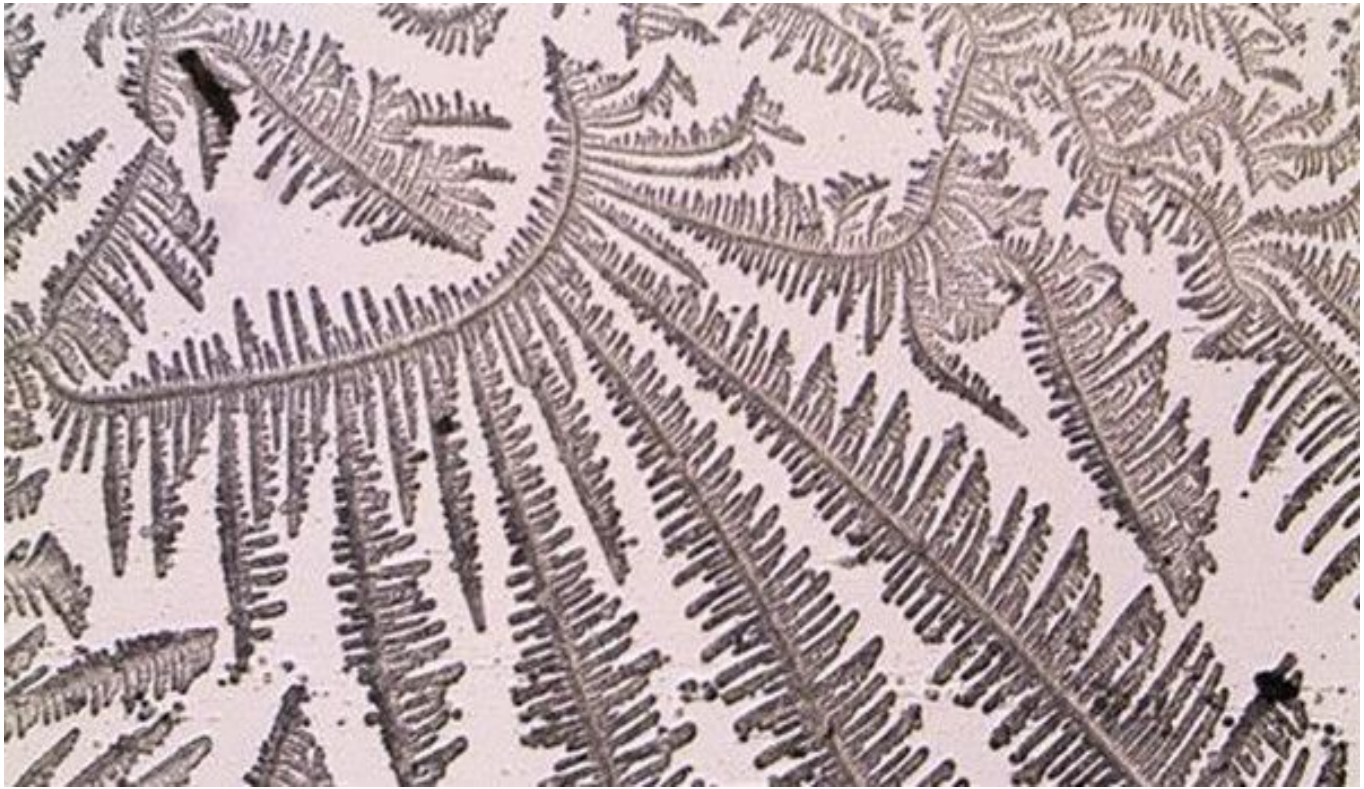
more ciliated, motility increases at the time of ovulation

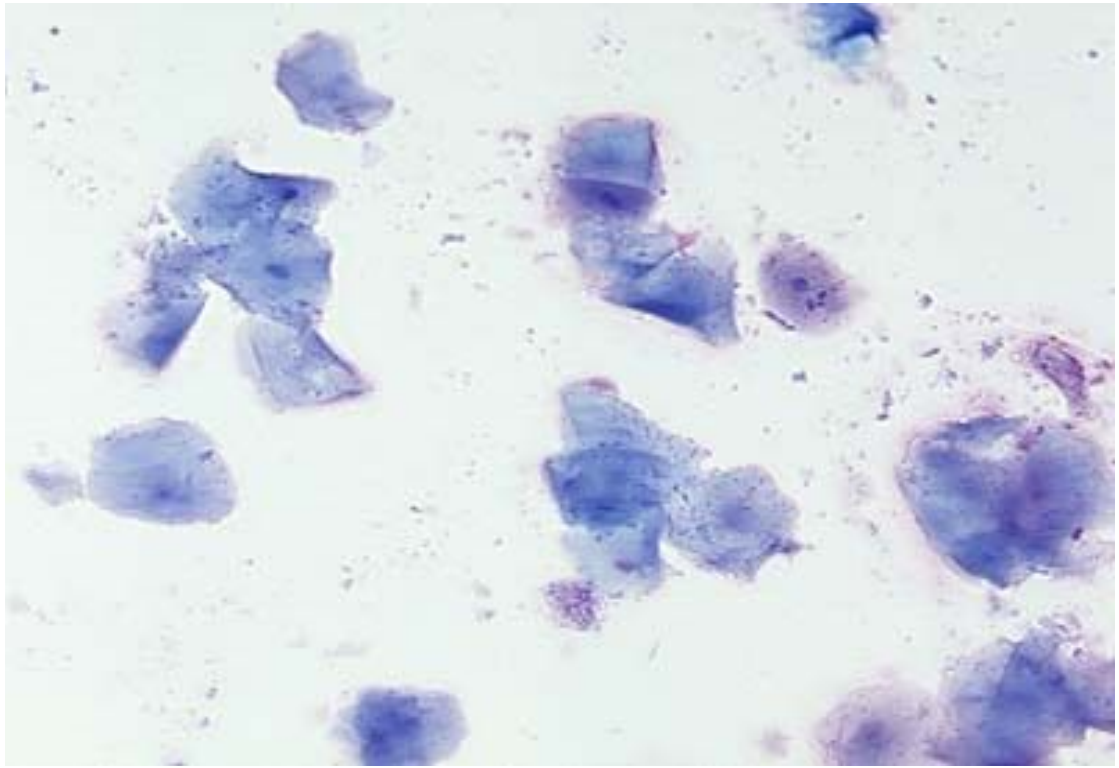
Uterus enlarges in size, muscle fibres become active and excitable

endometrium gets thickened due to increase in stroma and blood flow, rhythmic cyclic changes occur with onset of menstruation

Cervix also enlarges and undergoes cyclic changes

Vagina increases in size ,epithelium increase in size(cuboidal→ cornified squamous epithelium), sensitive to estrogen→ show cyclic changes during sexual cycle





External genitalia

Increase in size of clitoris

Labia majora and minora increase in size and get widened

- ➢ Appearance of secondary sex characters
- ➢ Ductal growth and fat deposition of breast

Other actions

- **Effect on bones:-** by its osteoblastic activity, estradiol accelerates the linear growth of bones at puberty

Epiphyseal centres more sensitive to estrogen than

testosterone → average height of females is little less than males

- **Enlarges the hip and widens the inlet of pelvic bone to facilitate childbirth**
- **Maintains the balance b/w bone formation and bone resorption**

Promotes bone formation by deposition of bone matrix by calcium and phosphate retention

Inhibits bone resorption by inhibiting production of osteoclasts and their activity

Loss of estrogen action after menopause→ osteoporosis

- **Effect on metabolism:-**

Protein :- cause positive nitrogen balance due to growth promoting effect

Increase hepatic synthesis proteins like TBG, CBG, VLDL, HDL etc

Fat :- fat deposition in S/C tissues, breasts and thighs

Lowers plasma cholesterol and LDL due to increase in LDL receptors

- **Water and electrolyte balance:- cause salt and water retention**
- **On vasculature :- vasodilator effect → local release of NO, PGE2 etc**

Anti Vasoconstrictor effect:- inhibition of endothelin release

Loss of vasodilator effect in postmenopausal women→ increased risk of coronary heart d/s

- **On CNS:- increase in libido, improves memory and learning**

- **On skin:- makes the skin soft and vascular**

Makes sebaceous glands secretion thin and inhibits formation of blackheads and acne

Mechanism of action of estrogens:- enters into cell and bind with cytoplasmic receptors

Estrogen receptors → ERα and ERβ

Synthetic estrogens :-

Ethinyl derivatives of oestradiol :- diethylstilbestrol and ethinyl estradiol

Plant estrogens

Therapeutic uses of estrogenic preparations:-

- To reduce menopausal symptoms like hot flushes
- To prevent postmenopausal osteoporosis
- To prevent atherosclerosis and incidence of heart attacks and strokes
- As contraceptives

Side effects:- stimulate growth of endometrium and breast→ incidence of Ca breast and uterus

Progesterone

- Maintains pregnancy
- Biologically called prostagen or gestagen
- In nonpregnant women, mainly secreted by corpus luteum and during pregnancy by placenta
- Synthesized from cholesterol, important intermediary compound for the production of estrogens and androgens

- In early follicular phase:- plasma conc very low (0.9ng/ml)
- Preovulatory phase:- level starts rising (secretion from granulosa cells)
- Mid luteal phase :- reaches to peak value (18ng/ml)
- At the end of cycle,level fall to minimum
- During pregnancy, level rises further
- After menopause,fall to minimum (0.2ng/ml)
- 98% protein bound (80%--> albumin, 18%--> transcortin ,cortisol binding globulin)

In the liver, progesterone metabolized to pregnanediol and 17 α-OH progesterone → pregnanetriol

Metabolites conjugated with glucuronic acid and sulphuric acid forms water soluble substances and excreted to urine and bile

Functions of progesterone:-

Reproductive actions:- mainly on reproductive organs primed by estrogens

Action on uterus :-

Endometrium :- proliferation of endometrial cells

Thickness also increases

Endometrial glands become tortuous and contain fluid provide nutrition to blastula if fertilization occurs

Spiral arteries become more coiled

Stroma of endometrium become edematous

Progesterone is responsible for secretory phase of endometrial cycle and prepares the endometrium to receive the zygote

- Decreases the uterine motility

Has antiestrogenic effect on myometrial cells, decreasing the excitability sensitivity to oxytocin and spontaneous electrical activity and increasing membrane potential

Decreases the synthesis of voltage dependent calcium channel proteins

Decreases the no. of estrogen receptors in myometrium

- Cervical secretion become thick and viscid, ferning pattern disappears

Vagina :- epithelium becomes thickened and infiltrated with leucocytes, secretion become thick and viscid

Fallopian tube:- increases the beating rate of cilia towards uterus, rich in secretion that provide nutrition

Breast :- lobular and alveolar growth of breast

- **Thermogenic effect :- increases basal body temperature by 0.5^0C in postovulatory phase (thermogenic steroid)**
- **Decreases appetite and produces somnolence**
- **Increases the sensitivity of respiratory centre to CO_2 stimulation (pCO_2 slightly less in woman during luteal phase)**

- Decreases HDL → proatherogenic agent
- Large doses of progesterone → natriuresis , blocking action of aldosterone on kidney

Mechanism of action

Progesterone receptors present in cytoplasm

Synthetic steroid mifepristone binds to progesterone receptors and blocks the DNA binding site → antiprogesterone drug

Other ovarian hormones :-

Inhibin :- **inhibits FSH release**

Activin:- **activate FSH release from anterior pituitary**

Relaxin:- **produced by corpus luteum , uterus, placenta, mammary glands**

Relaxes pubic symphysis and pelvic joints, softens and dilate cervix and facilitates delivery

In nonpregnant state→ secreted from corpus luteum and endometrium during secretory phase

Ovarian androgens :- small amount of testosterone secreted during biosynthesis of estrogen and progesterone

Main source of androgens in female → adrenal cortex

Responsible for acne, libido and pubic hair

FEMALE SEXUAL CYCLE

Birth to puberty :- primary and accessory sex organs remain quiescent

Puberty → b/w 12 and 14 yrs of age

Puberty to menopause:- sexual cycle starts ,repeats every 28 days

Occurrence of first menstrual cycle → **menarche**

Permanent stoppage of menstrual cycle → **menopause**

Period b/w menarche and menopause → reproductive period

post menopausal period:- after menopause (45-50yrs)

Female sexual cycle ceases

- **Rhythmical changes occur in ovaries, uterus, cervix and vagina**
- **Components:-**

➔ **Ovarian cycle**
➔ **Endometrial cycle**
➔ **Changes in cervix**
➔ **Changes in vagina**
➔ **Other changes during sexual cycle**
➔ **Changes in gonadotropin secretion**

Duration of sexual cycle is 28 days (20-40)

First day of menstruation taken as first day to each component of female sexual cycle

OVARIAN CYCLE

Refers to rhythmic changes occurring in ovaries during each female sexual cycle of about 28 days (20-40 days)

- **During each cycle, single mature ovum is released from ovary**
- **Ovarian changes completely depend on gonadotropic hormones (FSH and LH)**

Both FSH & LH stimulate ovarian target cells by combining with its own receptors and activate cAMP

OVARIAN CYCLE divides into

- Preovulatory phase or follicular phase
- Ovulation
- Postovulatory phase or luteal phase

Preovulatory phase or follicular phase

- Extends from 5th day of cycle till the time of ovulation (at 14th day)

Generally lasts for 8-9 days (10-25 days)

- **Mostly under the influence of FSH . LH also helps in maturation of follicle in the latter part**
- **During this phase, 10-15 primordial follicles start maturing, one follicle matures fully and rest undergoes atresia .Process of maturation of follicle → folliculogenesis**

Phases of folliculogenesis

1. **Primordial follicles:-** **fundamental reproductive units of ovary**

At the time of puberty, both ovaries → 3 lakh

- Primordial follicles formed in fetal life. Consists of primary oocyte in prophase of first meiotic division surrounded by single layer of spindle shaped/flat cells (granulosa cells)
- Both granulosa cells and primary oocyte enveloped in basal lamina
- Granulosa cells provide nutrition to primary oocyte (birth to puberty), also secrete **oocyte maturation inhibiting factor (OMIF)** which keeps ovum in immature stage till puberty
- Under the influence of FSH and LH, follicles start growing → primary follicles

2. Primary follicle:-

- Granulosa cells become columnar and undergo mitotic division to form multi layered **stratum granulosum**
- Oocyte enlarges (20 μ in size)
- Homogeneous membrane appears b/w s.granulosum and oocyte → **zona pellucida** (consists of glycoprotein)

3. Secondary follicle:-

- Granulosa cells undergo further proliferation
- Oocyte further increases in size (100 μ),nucleus larger and vesicular
- Thecal folliculi or follicular sheath formed outside the

basal lamina from spindle shaped cells from stroma

- Theca folliculi → theca interna (inner rim of secretory cells) and theca externa (outer rim of thickly packed spindle cells)
- Independent blood supply

4. Tertiary follicle:-

- Formation of antrum:- after proliferation, granulosa cells start secreting follicular fluid, formation of cavity in stratum granulosum → antrum or follicular cavity
- Fluid → liquor folliculi contain estrogen
- Granulosa cells continue to proliferate and size of follicle increases

- Theca cells proliferate rapidly. Theca interna → theca interstitial cells (steroidogenic cells synthesize and secrete androstenedione in response to FSH and LH)
- Upto this stage, follicular growth is mainly stimulated by FSH alone

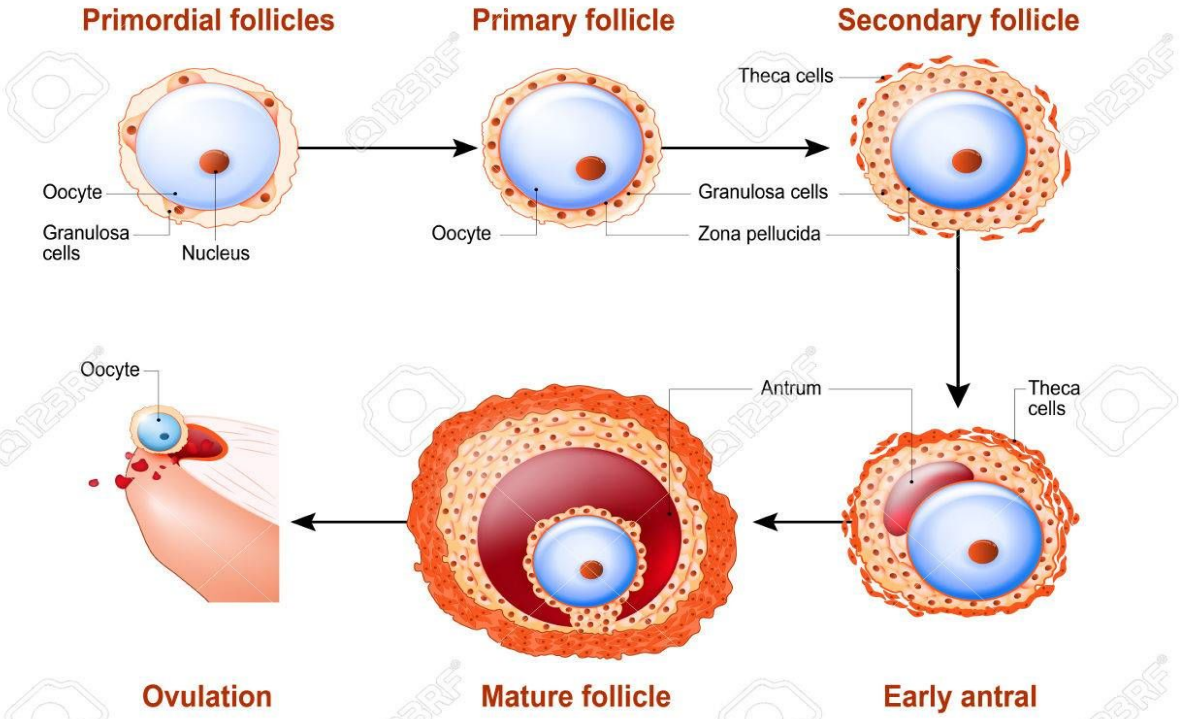
5. Graafian follicle:-

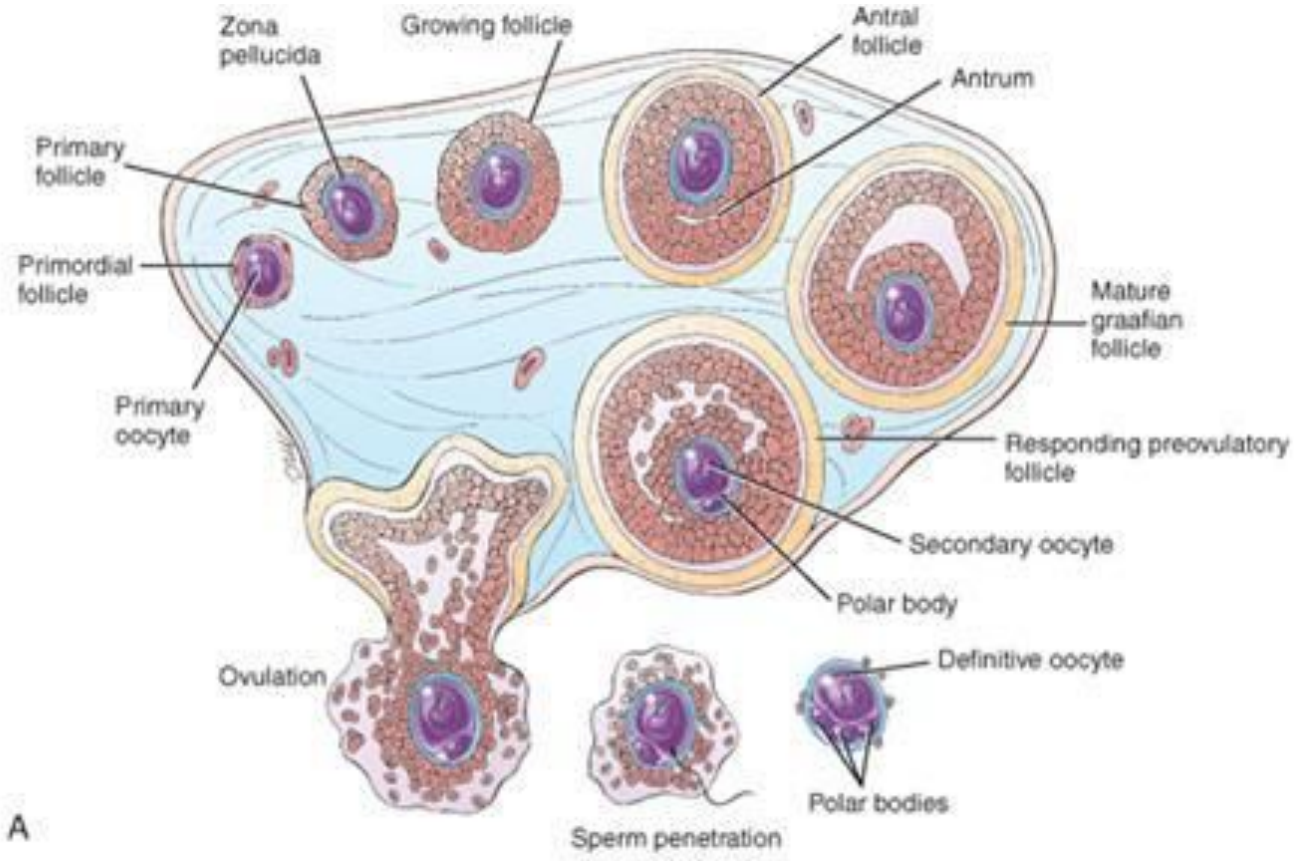
- After about 7th day of sexual cycle, one of the tertiary follicle increases in size (in response to FSH and LH) and forms graafian/antral/ vesicular follicle
- Rest of follicles degenerate and atrophied by apoptosis

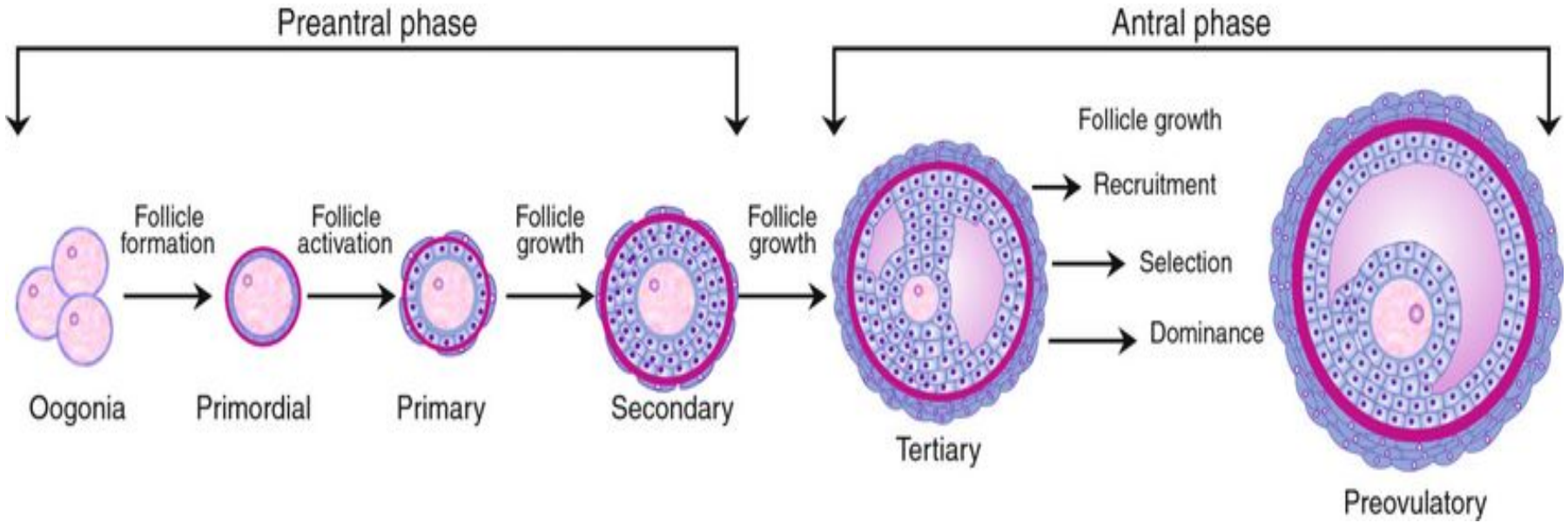
- Size of follicle increases to 2-5mm (granulosa and theca proliferation). It extends through the whole thickness of cortex of ovary. At one place, encroaches upon tunica albuginea and bulges out of the surface into peritoneal cavity
- Antrum become larger and distended with fluid. Follicular fluid surrounds the ovum all except one point (eccentric position). Ovum covered by a layer of cells → **corona radiata**, remains in contact with granulosa cells only at **cumulus oophorus**
- Thickness of theca interna become double with rich network of capillaries

- Estrogen secreting cells of theca interna increases (cells of theca glands)
- Just prior to ovulation, primary oocyte of fully matured graafian follicle completes first meiotic division and forms secondary oocyte (n) and first polar body

THE MATURATION OF A FOLLICLE




Zona pellucida
Growing follicle
Antral follicle
Antrum
Primary follicle
Primordial follicle
Mature graafian follicle
Primary oocyte
Responding preovulatory follicle
Secondary oocyte
Polar body
Ovulation
Definitive oocyte
Polar bodies
Sperm penetration
A


Preantral phase
Antral phase
Follicle formation
Follicle activation
Follicle growth
Follicle growth
Follicle growth
Recruitment
Selection
Dominance
Oogonia
Primordial
Primary
Secondary
Tertiary
Preovulatory

Ovulation

- Release of secondary oocyte from the ovary (following rupture of graafian follicle) into the peritoneal cavity
- In normal 28 day cycle, occurs 14 days after onset of menstruation (early on day 15)
- Ovulation caused by LH surge at mid cycle in response to an elevation in plasma estradiol conc
- Onset of LH surge → 34-36 hrs before ovulation
- Peak of LH surge → 12-24 hrs before ovulation (increases 6-10 fold)

- **Ovulatory peak of FSH (2-3 fold increase) → 2 days prior to ovulation (stimulated by progesterone)**
- **FSH increases granulosa cell LH receptors**
- **<u>Changes in graafian follicle</u>:- LH & FSH**

Rapid swelling of follicle:- few days before ovulation

Rapid growth of new BV into the follicle wall and PGs secreted into follicular tissue → cause diffusion of plasma into follicular fluid → further swelling

Formation of stigma:- outer wall stretched due to rapid swelling → forms a thin avascular area (stigma) over the most convex point

Release of proteolytic enzymes from lysosomes in the theca externa cells → activated by progesterone

Dissolution of capsular wall by proteolytic enzymes

Rupture of graafian follicle:- simultaneous stretching and enzymatic dissolution of follicular wall → degeneration of stigma. Within 30 min, fluid begins to ooze from stigma followed soon by rupture of follicle wit release of ovum surrounded by corona radiata into peritoneal cavity near fimbriated end.

Only one ovum is released from any one of two ovaries during each sexual cycle

Determination of ovulation time :-

Basal body temperature estimation:- slightly falls (0.3-0.5^{0}C) just prior to ovulation and increases slightly after ovulation

Hormonal excretion in urine:- urinary excretion of end products of estrogen increases to peak at the time of ovulation and end products of progesterone increases after ovulation

Hormone levels in plasma :- plasma conc of LH & estrogen → increased and FSH decreased at the time of ovulation

Progesterone increased after ovulation

Postovulatory phase:-

- **Luteal phase of ovarian cycle**
- **Constant period of 14 days**

<u>Formation of Corpus Haemorrhagicum:-</u> following ovulation, outer wall of graafian follicle collapses and filled with blood

Minor bleeding from follicle into the abdominal cavity cause peritoneal irritation and fleeting lower abdominal pain → mittelschmerz

Formation of Corpus Luteum:-

Granulosa cells and theca cells of follicle lining begin to proliferate and clotted blood rapidly replaced with yellowish lipid rich luteal cells → luteinization → corpus luteum

- **LH responsible for luteinization**
- **Lutein cells secrete large amounts of progesterone and estrogen to lesser extent**
- **Progesterone has negative feedback on FSH nd LH secretion**

Formation of Corpus Albicans :-

If there is no fertilization and pregnancy occurs, CL begins to regress after 24th day of sexual cycle and replaced by whitish scar tissue

Occurs due to falling levels of LH and FSH and Inhibin secreted by lutein cells

On 26th day, levels of Estrogen, Progesterone and Inhibin falls→ removes feedback inhibition of ant pituitary→ FSH and LH secretion begins and next ovarian cycle is initiated

Corpus Luteum of Pregnancy:-

If fertilization occurs, corpus luteum persists and become major source of estrogen and progesterone till 3rd month of pregnancy after that placenta takes over the function

Endometrial cycle (uterine cycle)

Cyclic changes occuring in the endometrium during active reproductive period in females leading to recurrent monthly bleeding per vaginum (menstruation)

Brought about by cyclic production of estrogens and progesterone by the ovaries

Phases

- Menstrual phase (1st to 5th day)
- Proliferative phase (6th to 14th day)
- Secretory phase (15th to 28th day)

Proliferative phase :- preovulatory phase of endometrium

- Follows phase of menstruation, thin basal layer of original endometrium left
- Estrogen secreted by developing graafian follicle in the ovary
- Proliferative phase coincides with follicular phase of ovarian cycle

- **Changes in endometrium**

➔ **Epithelial cells grows and re epithelialize the endometrial surface**

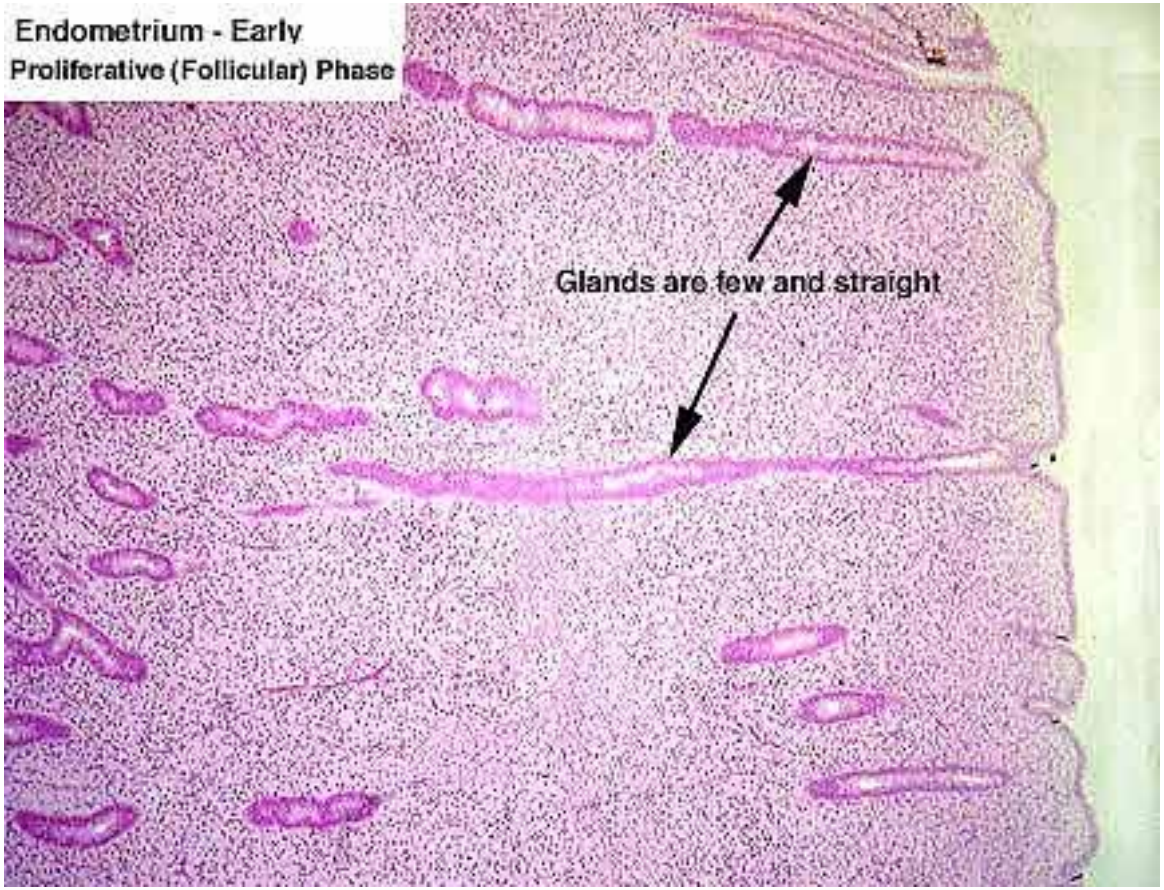
➔ **Thickness of endometrium increases to 3-4 mm**

➔ **Mitosis of stratum basale regenerates the stroma of stratum functionale**

➔ **Angiogenesis in S functionale → proliferation of BV → spiral arteries**

➔ **Endometrial glands grows contain glycogen, nonsecretory**

➔ **Ovulation occurs at the end of this phase**


Endometrium - Early
Proliferative (Follicular) Phase
Glands are few and straight

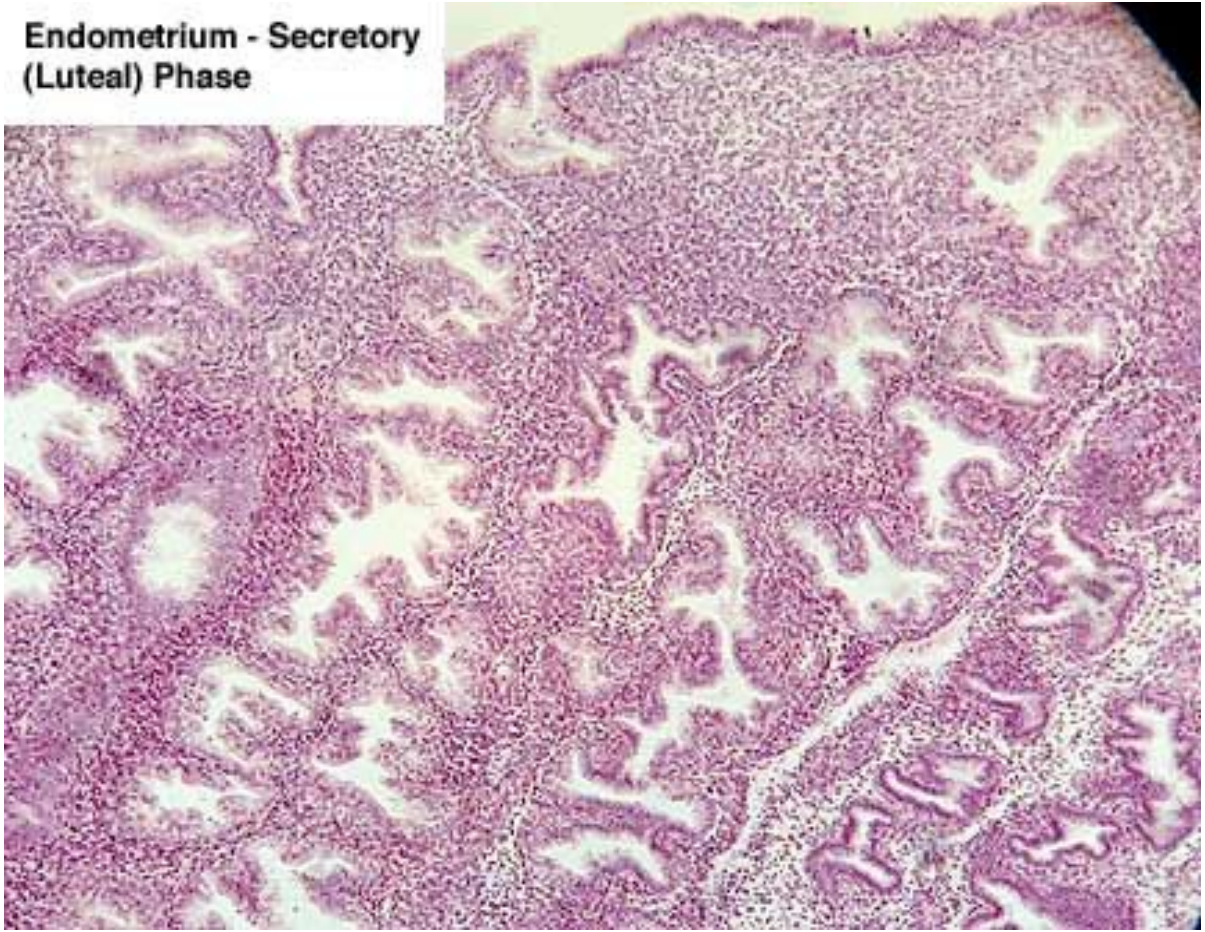
Secretory phase:- coincides with luteal phase of ovarian cycle

- Both estrogens and progesterone secreted by corpus luteum are responsible
- Changes in endometrium :-

➔ Additional proliferation of cellular stroma caused by estrogens

➔ Differentiation of endometrium :- elongation and coiling of endometrial glands . glands become secretory and secrete thick viscous fluid containing glycogen → effect of progesterone

- ➔ Blood supply of endometrium increases and promotion of spiralling of blood vessels→ effect of progesterone
- ➔ **Corkscrew shaped glands and increased vascularity**
- ➔ Thickness of endometrium increases to 5-6 mm → thickened endometrium with large amounts of nutrients ready to provide appropriate condition for implantation
- ➔ If fertilization doesn't occur, corpus albicans forms and on 26th day ,levels of estrogen and progesterone level declines → end of secretory phase


Endometrium - Secretory
(Luteal) Phase

Menstrual phase:- bleeding phase

- 24 hrs before the end of menstrual phase, sharp decline in plasma levels of estrogen and progesterone→ responsible for menstrual bleeding

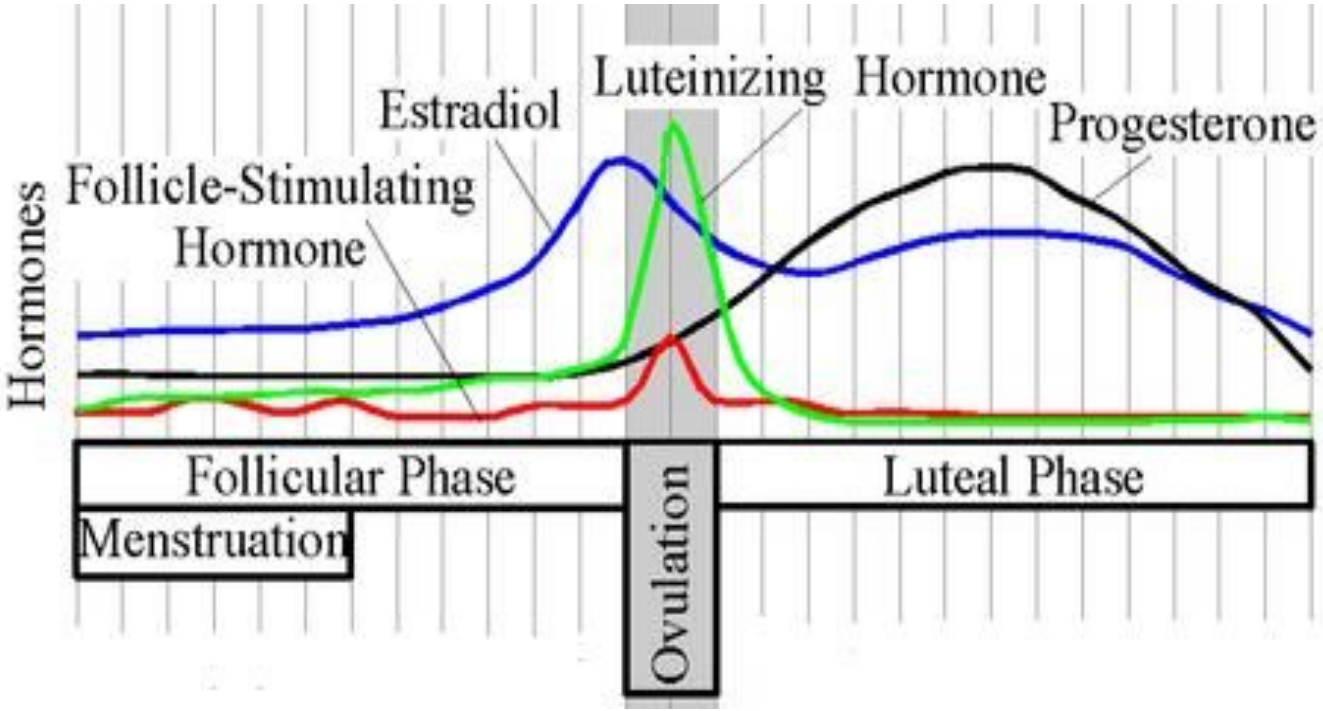
➔ Intense spasm of spiral arteries → hypoxia and ischemia (mediated by local production of PGs)

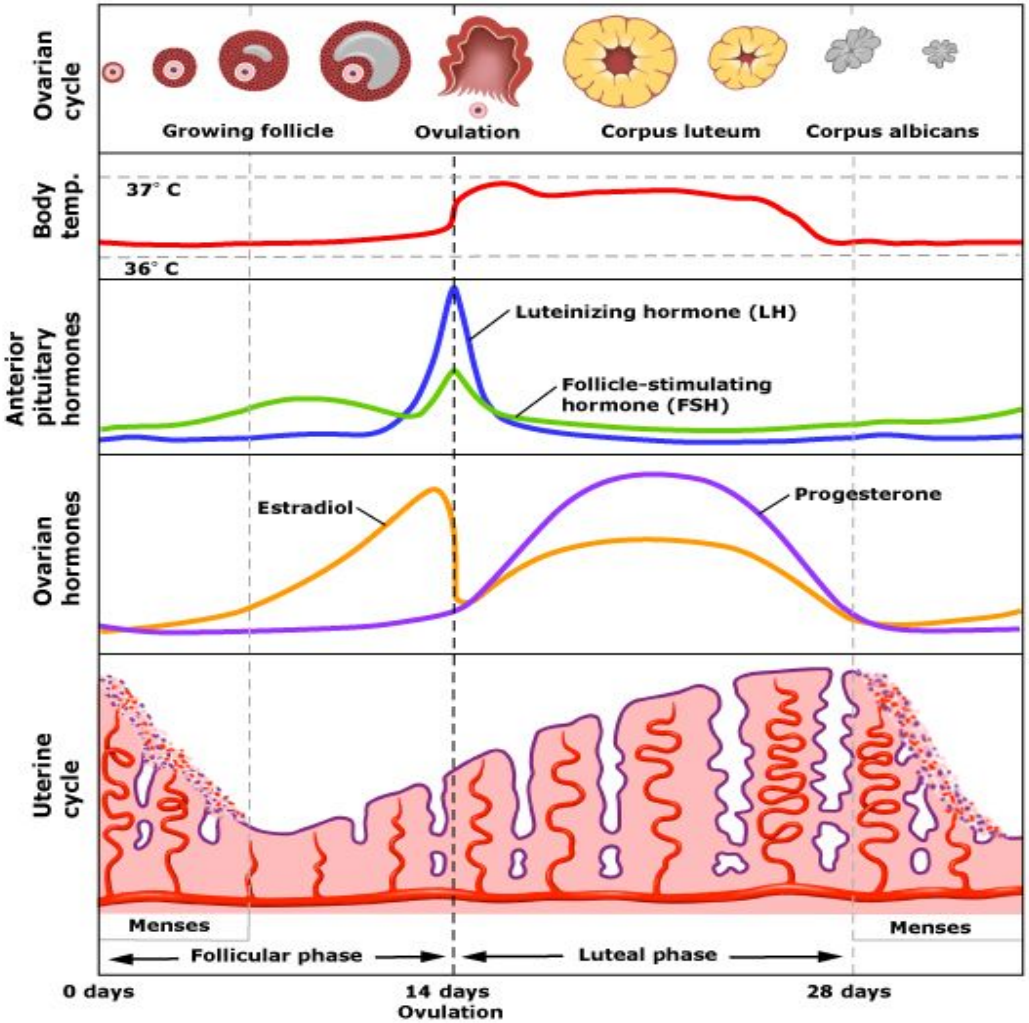
➔ Necrosis of S functionale and spiral arteries

➔ Blood vessels get open up → seepage of blood into surrounding endometrial necrotic tissue

➔ Separation of necrotic tissue starts gradually from underlying basal viable tissue and later sloughed off.

- ➔ Endometrial debris contains necrosed sloughed off tissue, blood, serous fluid and large amounts of PGs and fibrinolysins
- ➔ Average amount of blood loss → 30ml
- ➔ Menstrual blood immediately get clotted inside the uterine cavity but soon get liquified by fibrinolysin
- ➔ PGs cause further spasm of spiral arteries and also produce contraction of myometrium
- ➔ About two-third of superficial endometrium is sloughed off and only a thin basal layer (2 mm thick) is left behind


Hormones
Follicle-Stimulating Hormone
Estradiol
Luteinizing Hormone
Progesterone
Follicular Phase
Menstruation
Ovulation
Luteal Phase

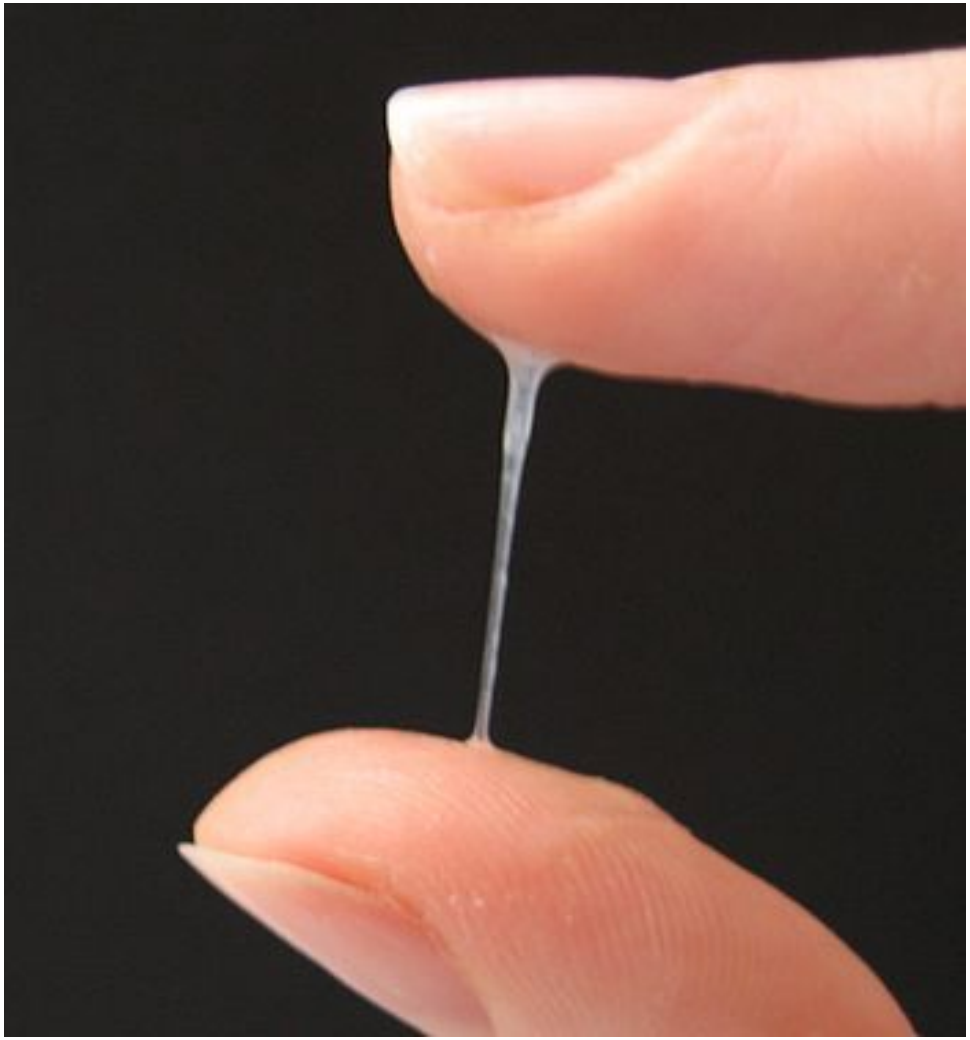

Ovarian cycle
Growing follicle
Ovulation
Corpus luteum
Corpus albicans
Body temp.
37° C
36° C
Anterior pituitary hormones
Luteinizing hormone (LH)
Follicle-stimulating hormone (FSH)
Ovarian hormones
Estradiol
Progesterone
Uterine cycle
Menses
Menses
Follicular phase
Luteal phase
0 days
14 days
Ovulation
28 days

Cyclic changes in cervix:-

- During menstruation phase, cervical mucosa doesn't undergo desquamation like that of endometrium
- During proliferative phase, secretion of endocervical mucosa become thin , watery and alkaline. At the time of ovulation, cervical mucus is thinnest and elasticity is maximum, can be stretched like long ,thin, elastic thread (spinnbarkeit effect)

  Fern pattern of mucosa → fern test

- During secretory phase, cervical secretion decreases, → thick, tenacious and cellular, disappearance of fern pattern



Cyclic changes in vagina :-

- **In the proliferative phase, vaginal epithelium becomes thickened and cornified**

Cornified cells and maturing cells accumulate glycogen. Vaginal smear shows large eosinophilic cornified cells having small pyknotic nucleus or it may be absent

- **In the secretory phase, vaginal epithelium proliferates and get infiltrated with leucocytes and secretion become thick and viscid**

Other changes during sexual cycle

Changes in fallopian tubes:-

Follicular phase :- increase in no of cilia and secretory epithelial cells and increase in vascularization of fimbria

At the time of ovulation:- motility increases

Luteal phase:- increase in secretion of epithelial cells → provide nutrition to ovum,incoming sperm and zygote if fertilization occurs

Changes in breast:-

Follicular phase :- ductal growth (estrogen)

Secretory phase :- lobular and alveolar growth (progesterone)

Premenstrual weight gain:- salt and water retention by estrogen

Oestrous cycle:-

- **In all other mammals except primates**
- **Oestrous → 'heat'**
- **Only period when sexual interest is aroused in female animals**
- **Happens at the time of ovulation and coincides with male's sexual desire**
- **Bleeding per vaginum doesn't occur**

<u>Spontaneous ovulation</u>

<u>Reflex ovulation</u>→ brought about by neuro endocrinal reflex aroused by copulation

Hormonal control of female sexual cycle

Hypothalamo-hypophyseal-gonadal axis

- **Role of hypothalamus**

Regulates the secretion of gonadotropins (FSH and LH) through GnRH . LHRH predominantly secreted from cells of arcuate nucleus and preoptic area

Reaches the ant pituitary through hypothalamo-hypophyseal portal system and stored as small granules

- Release of GnRH influenced by dopamine, ratio of FSH and LH, gonadal hormones, dark and light cycles operating through melatonin (released from pineal gland)
- Role of anterior pituitary

By releasing gonadotropins

Regulates ovarian cycle

Regulation of gonadotropins

<u>Gonadal hormones:-</u> estrogen and progesterone regulate its secretion by their feedback effect

- **Estrogen in high conc (just before ovulation), inhibit release of FSH by negative feedback effect and promotes LH release by positive feedback effect**
- **High levels of estrogen and progesterone in mid luteal phase inhibit secretion of LH and FSH (negative feedback)**
- **Low levels of estrogen and progesterone (menstrual phase) increase the secretion of FSH and LH (postive feedback)**

Oral contraceptives (contains high con of gonadal hormones) inhibit gonadotropin release by negative feedback and prevent ovulation

Human chorionic gonadotropins (HCG):-

- Glycoprotein secreted by syncytiotrophoblasts during early pregnancy
- Like LH, HCG maintains functional state of CL and elevates gonadal hormones → inhibition of gonadotropin release

Prolactin:- mammotropic hormone secreted from ant pituitary during lactation

Inhibit GnRH release and thus lowers basal secretion of FSH and LH (lactational amenorrhoea)

- **Role of ovaries**

By secreting gonadal hormones

Estrogen:- plasma conc of E starts rising from first day of cycles reaches to peak just before ovulation → estrogen surge

Within 24 hrs, LH surge takes place at mid cycle → estrogen has positive feedback effect

E increases sensitivity and responsiveness of gonadotrophs to GnRH

- E through positive feedback effect responsible for ovulation
- Responsible for proliferative phase of endometrial cycle

Progesterone :-

- After ovulation, formation of corpus luteum → estrogen and progesterone high (rises markedly)
- High levels of gonadal hormones inhibit gonadotropin release
- Progesterone prepares estrogen primed endometrium for implantation → secretory phase

- If fertilization doesn't occur, corpus luteum involutes and levels of E & P decline → menstruation
- Negative feedback effect on ant pituitary and hypothalamus abolishes → increase in gonadotropins → next ovarian and endometrial cycle starts

If fertilization occurs, HCG levels rises, maintains corpus luteum → levels of E & P remain high and by negative feedback effect FSH & LH remain low

Menopause

Human ovaries become unresponsive to gonadotropins and secretion of ovarian hormones declines with advancing age→ permanent stoppage of menstrual cycle (45-55yrs)

- **Decrease in no of primordial follicles → ovaries no longer secrete progesterone and estrogen level decreases**
- **High plasma level of FSH and LH**
- **During premenopausal period, FSH level increases before rise in LH → irregular menstrual cycle**

- **Loss of ovarian functions :-**

➔ **Hot flushes :- associated with LH surge**

➔ **Osteoporosis, ischemic heart d/s, renal d/s**

<u>Hormonal replacement therapy</u>

Estrogen 1-21 days and progesterone added from 14-21 days

Side effects :-

- **Fluid retention, weight gain, HTN, thrombosis**

Abnormalities of female sexual cycle:-

- Abnormalities of ovarian functions
- Abnormalities of menstruation

Abnormalities of ovarian functions

Hypogonadism :- Kallmann's syndrome (hypogonadotropic hypogonadism)

GnRH resistance

Aromatase deficiency

Ovariectomy:-

Atrophy of genital apparatus

Stoppage of menstruation

Breast changes

Vasomotor changes:- hot flushes

Emotional disturbances → irritability and depression

Hypersecretion of ovaries:-

Precocious puberty

Abnormalities of menstruation

Anovulatory cycle:- menstrual cycle normal but ovulation doesn't occur

Main cause of female infertility

Amenorrhoea:- absence of menstrual bleeding

Primary :- bleeding has never occurred

Secondary :- cessation of menstrual cycle in women who previously has normal and regular cycles

Pregnancy is the most common cause

Hypomenorrhoea :- scanty menstruation

Menorrhagia :- abnormally profuse bleeding during normal regular cycles

Metrorrhagia:- occurrence of uterine bleeding in b/w the periods

Oligomenorrhoea :- infrequent and reduced frequency of menstruation

Polymenorrhoea :-

Dysmenorrhoea :-

Premenstrual syndrome (PMS)

About 7-10 days before the end of cycle, irritability , lack of concentration, feeling of depression, headache, and constipation

PHYSIOLOGY OF PREGNANCY

Fertilization:-

- Fusion of male and female gametes
- Takes place at ampulla of fallopian tube
- Before fertilization, ovum and sperms reach the ampulla for fertilization
- 1. Transport of gametes

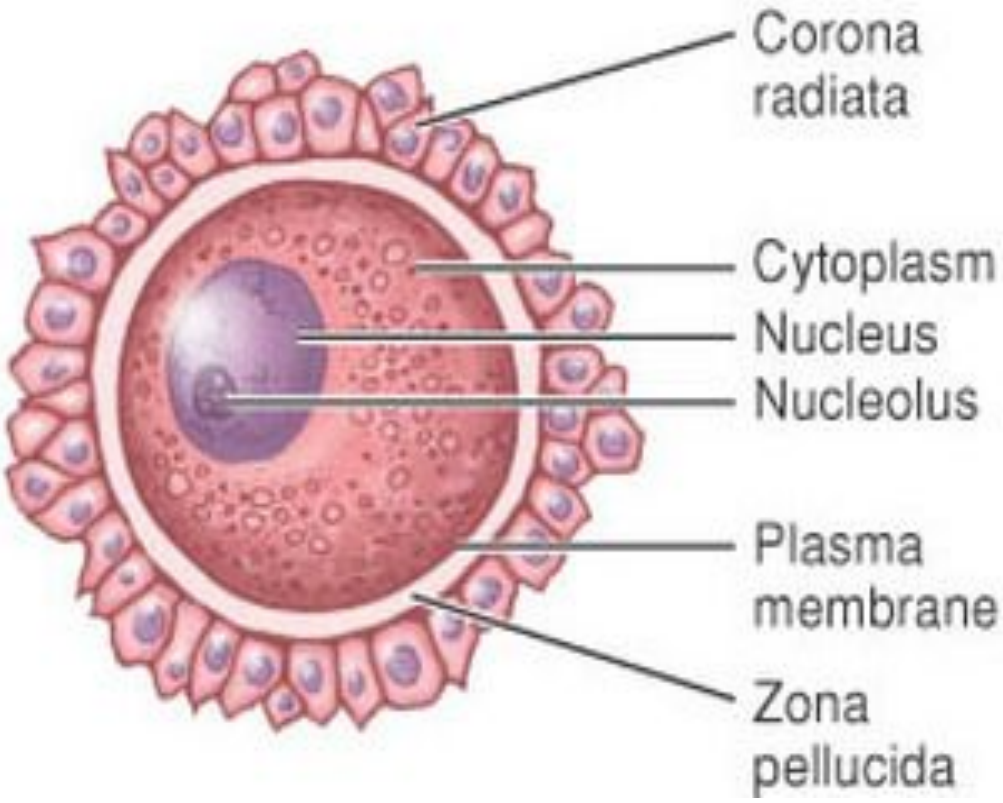
Transport of ovum

At the time of ovulation, ovum is directly expelled into peritoneal cavity, taken up by fimbriae of infundibulum

Ciliated epithelium and smooth muscle contractions present in the wall of fallopian tube helps in the transport of ovum

Structure of ovum :- secondary oocyte surrounded by zona pellucida (glycoproteins) surrounded by corona radiata (granulosa cells arranged in multilayers held together by matrix composed of hyaluronic acid)

Fate of ovum:- ovum held up at ampulla for 2-3 days. Remain viable for 6-24 hrs after ovulation. → if viable sperm penetrates it. Fertilization takes place and leading on to pregnancy. If doesn't occur, ovum dies out and degenerates


Corona radiata
Cytoplasm
Nucleus
Nucleolus
Plasma membrane
Zona pellucida

Transport of sperms in female genital tract

- After ejaculation, several millions sperms (200 million /ejaculation) get deposited in vagina
- 50-100 sperms manage to reach onto ovum and only one is able to penetrate it→ depends on several factors that affect transportation and accessibility of sperm to ovum
- Motility of sperms :-

Flagellar movt in fluid medium → 1-4mm/min

In 30-60 min → reaches fallopian tube

Depends on

- pH of fluid medium
- Cervical mucus secretions
- Fluid currents
- Temperature
- Hormones

pH of fluid medium

- Neutral and alkaline pH enhances activity of sperms
- Vaginal fluid is acidic→ immediately sperm activity inhibited and sperms become non-motile

- Alkaline semen neutralizes vaginal acidic pH → in less than 60 min after ejaculation, sperms become active & activity increases in cervix and in the body of uterus

(principal piece of sperm tail contain alkaline sensitive calcium channels)

Cervical mucus secretions

Acts as a mechanical barrier for sperms (proliferative phase → become thin and watery favours the passage of sperms)

Fluid currents

In vaginal and uterine cavity, currents are set up by ciliary movements towards exterior (antagonistic direction), further resist sperm motility

Temperature

- **With rising temperature, activity of sperms increases, life span decreases**
- **In ejaculated semen, maximum life span of sperm is 24-48 hrs at body temperature (at lower temperature, semen can be stored)**

Hormones

Oxytocin :- during coitus, stimulation of female genital tract → release of oxytocin from neurohypophysis→ causes propulsive movt of uterus → help to aspirate seminal fluid from vagina into fallopian tube

Estrogen :- makes cervical secretion thin and watery → favours transport of sperms

Prostaglandins :- present in semen increases female genital tract movements

Progesterone:- further stimulates sperm motility

2. Sperm capacitation :-

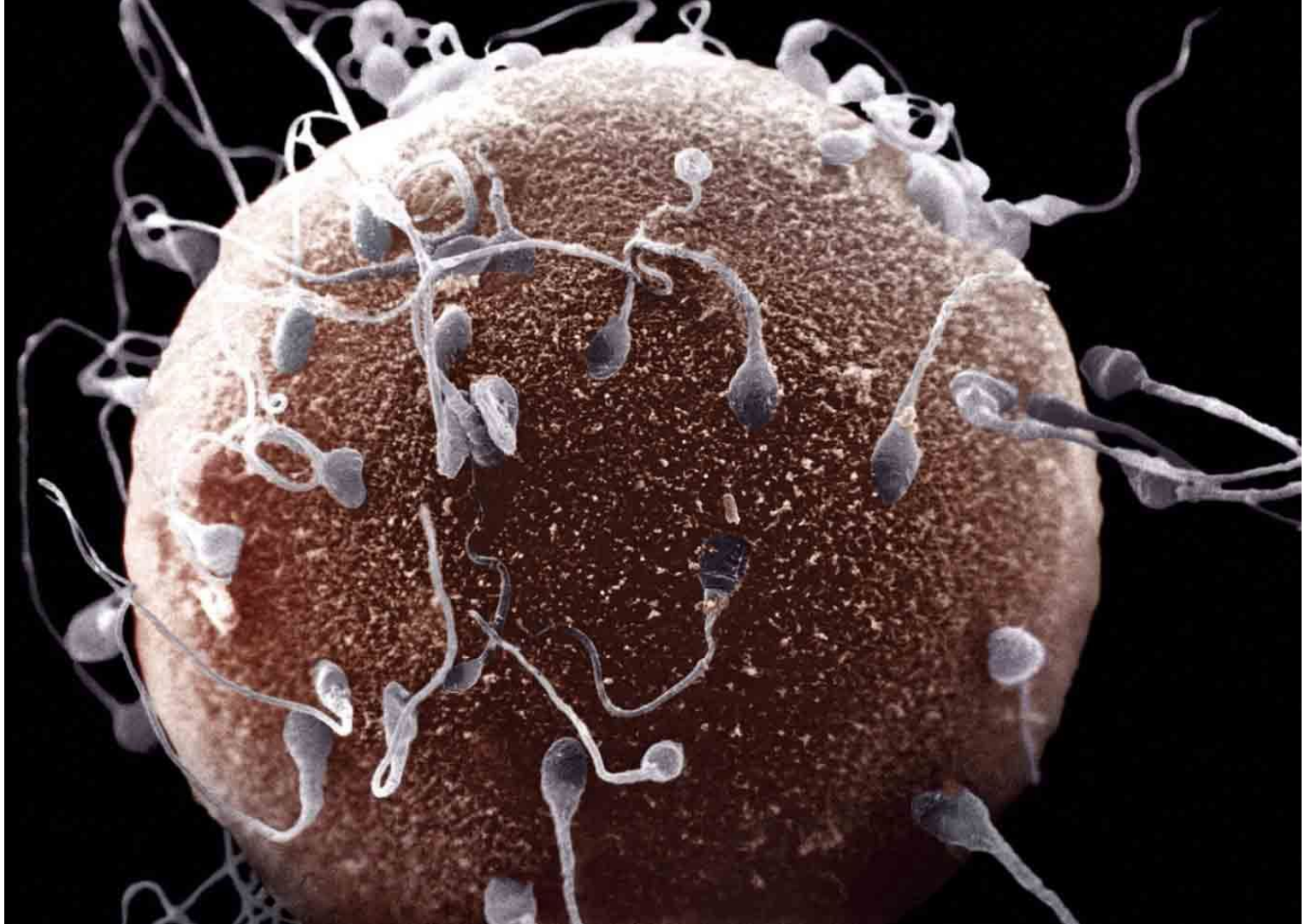
- Process that makes a sperm to fertilize an ovum
- Takes about 1-10 hrs (capacitation period)
- Occurs due to removal of certain factors that normally remain quiescent in male genital tract
- In female genital tract, cholesterol contents of acrosomal membrane decreases and it becomes weak → release of enzymes from head (in male genital tract, acrosomal membrane remains very tough because of high cholesterol content)
- Membrane of sperm becomes permeable to calcium ions

Influx of calcium → makes flagellar movt more strong and whipish (hyperactivation of sperms) & triggers the release of enzymes from acrososme

3. Fusion of gametes :-

Chemoattraction:- occurs by substances produced by ovum

Ovaries produce certain odorant molecules that interact with olfactory receptors present on sperm and is the cause of motility (chemotaxis)



Penetration of sperm through ovum coverings :-

Sperm passes through corona radiata and zona pellucida before reaches the oocyte

Penetration of corona radiata :- by release of hyaluronidase and other proteolytic enzymes present in acrosome and hyperactivation of sperm

Hyaluronidase polymerises hyaluronic acid present in matrix holding granulosa cells

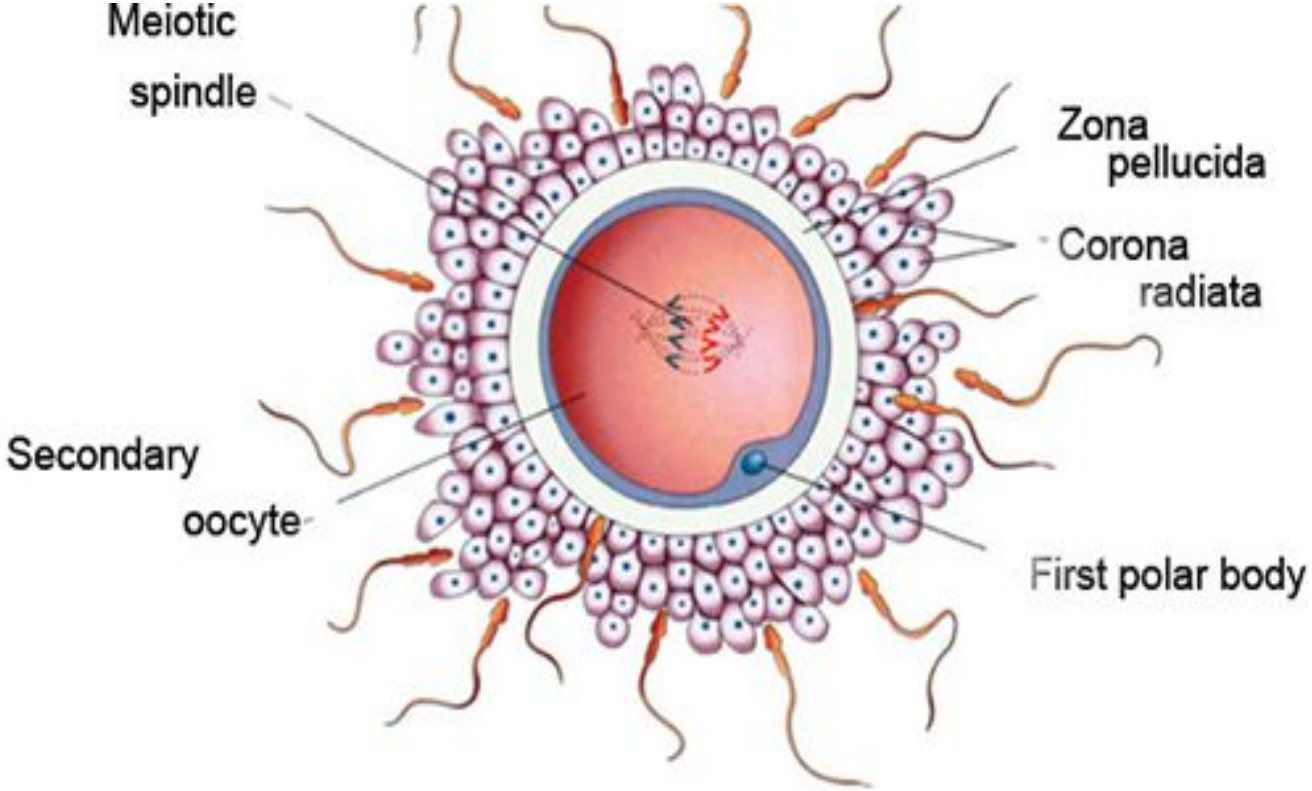
Proteolytic enzymes digest away the proteins of structural tissues

Hyperactivation of sperms produces penetrating thrust on the ovum due to vigorous lashing of sperm's tail

Binding of sperm to zona pellucida :- after passing through corona radiata many sperms make contact with zona pellucida by binding to receptor protein zona pellucida glycoprotein → triggers acrosomal reaction

Acrosomal reaction:- release of acrosin (protease enzyme) from anterior membrane of acrosome

Acrosin opens the penetrating pathway for passage of sperm head into perivitelline space (space b/w zona pellucida and oocyte membrane)

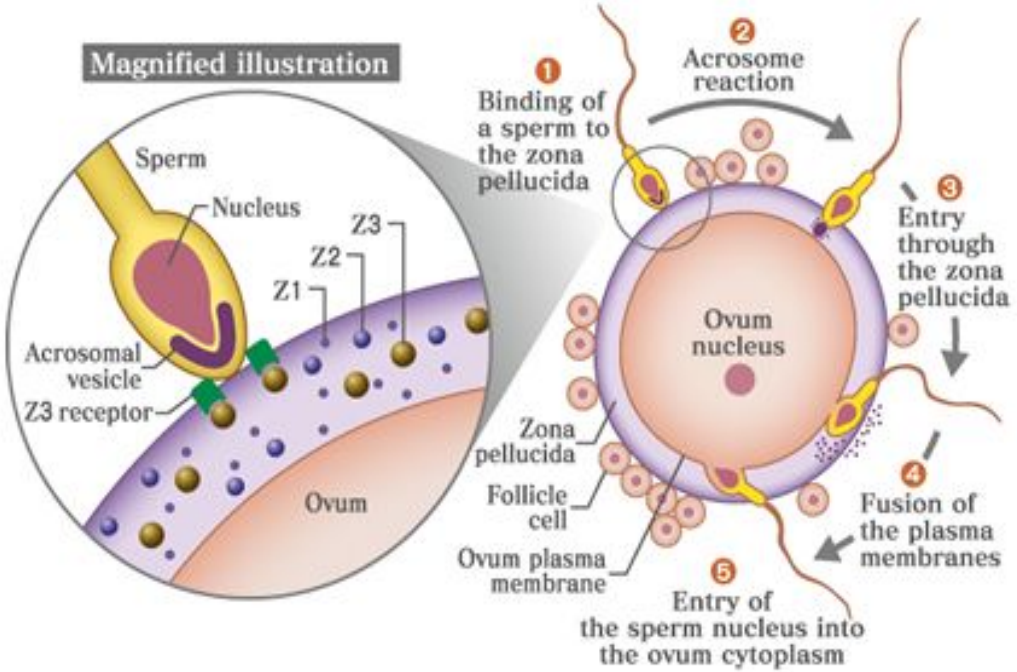

Meiotic
spindle
Zona
pellucida
Corona
radiata
Secondary
oocyte
First polar body

For effective penetration by the sperm, acrosomal reaction should takes place at zona pellucida (lifespan of acrosomal reacted sperm is very short)

Fusion of sperm with oocyte :-

Equatorial region of acrosome → site of initial contact b/w sperm and vitelline membrane

Fertilin (protein present in acrosome-reacted sperm) interacts with protein present on vitelline membrane and within 30 minutes membranes of sperm and oocyte fuse, genetic material of sperm enters into oocyte and cause fertilization and embryo begins to develop


Magnified illustration
Sperm
Nucleus
Z3
Z2
Z1
Acrosomal vesicle
Z3 receptor
Ovum
1 Binding of a sperm to the zona pellucida
2 Acrosome reaction
3 Entry through the zona pellucida
Ovum nucleus
Zona pellucida
Follicle cell
Ovum plasma membrane
4 Fusion of the plasma membranes
5 Entry of the sperm nucleus into the ovum cytoplasm

Only one sperm can enter into oocyte, further entry of sperms is prevented by ovum activation

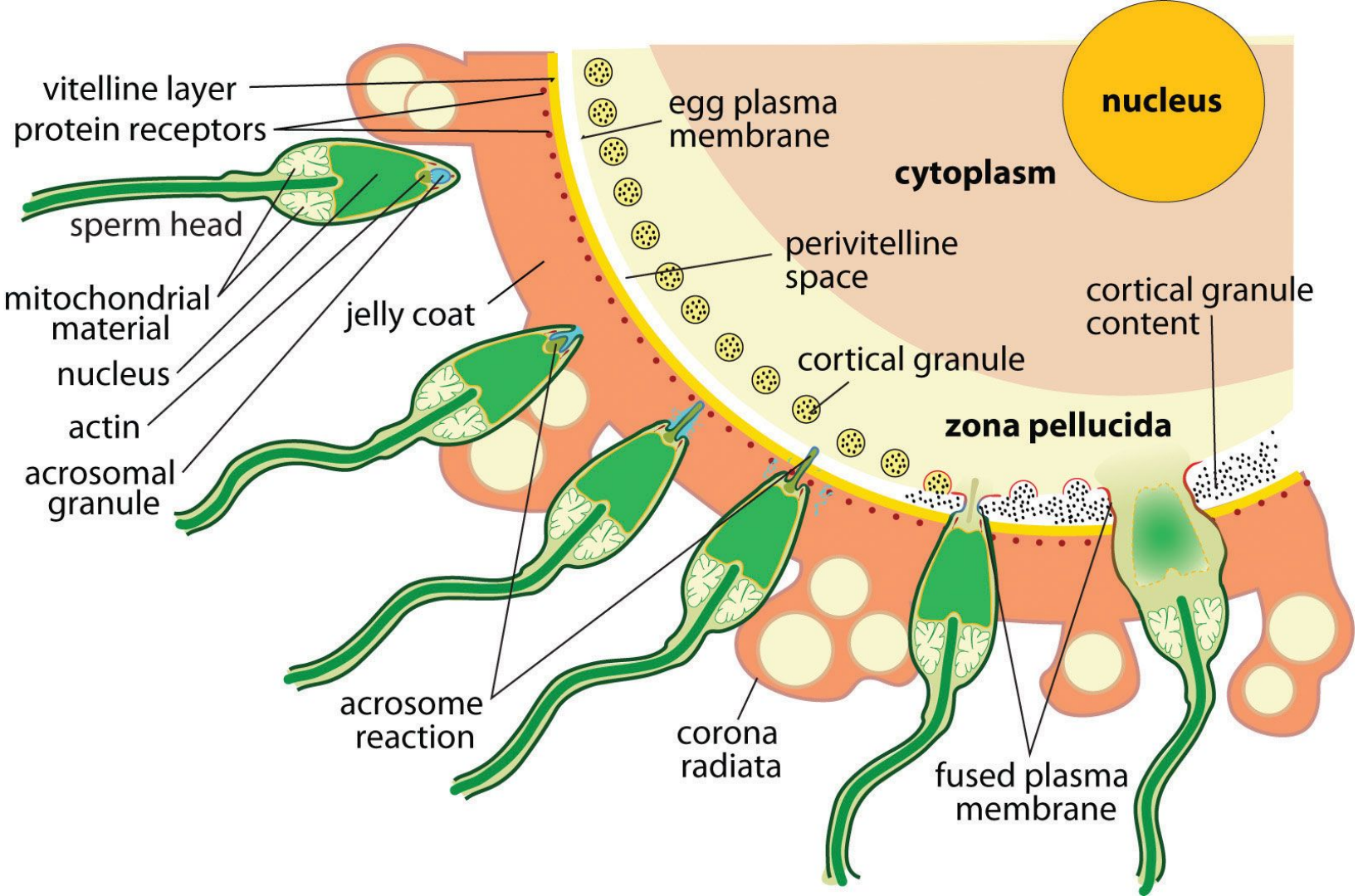
Ovum activation :-

Membrane potential of ovum decreases (depolarization), followed by some structural changes in zona pellucida

Release of calcium from intracellular egg reserve leads to exocytosis of cortical granules into perivitelline space

Vitelline block to polyspermy :- cortical granules prevent further entry of sperm into ovum

Zona blockade to polyspermy :- cortical granules contain glycosidases (causes alteration in ZP receptor protein)


vitelline layer
protein receptors
sperm head
mitochondrial material
nucleus
actin
acrosomal granule
jelly coat
egg plasma membrane
nucleus
cytoplasm
perivitelline space
cortical granule content
cortical granule
zona pellucida
acrosome reaction
corona radiata
fused plasma membrane

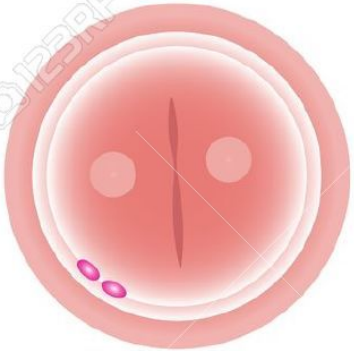
and proteases (degrades ZP) → causes loss of affinity of sperm for zona pellucida and thus prevent polyspermy

Implantation:-

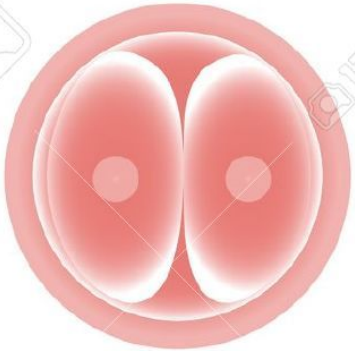
- **Formation of blastocyst :-** fertilized ovum starts dividing immediately → morula (16 cell stage) & blastocyst (100 cell stage)

Inner cell mass surrounded by layer of trophoblast, covered by zona pellucida

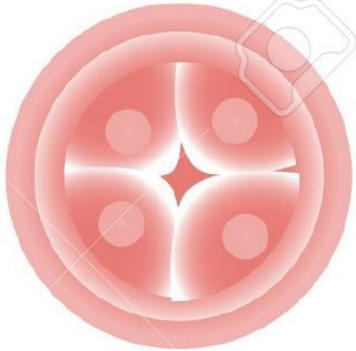
- Trophoblast cell layer has great sticking property to epithelial cells of fallopian tube → presence of zona pellucida prevents implantation in fallopian tube



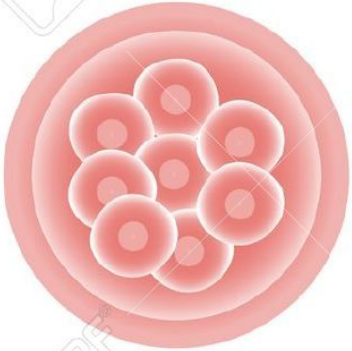
ZYGOTE



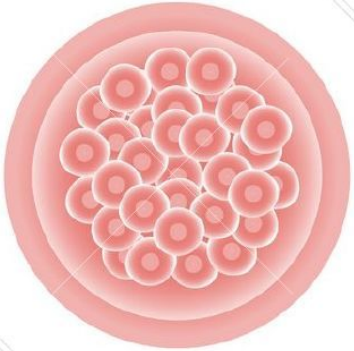
2 CELL STAGE



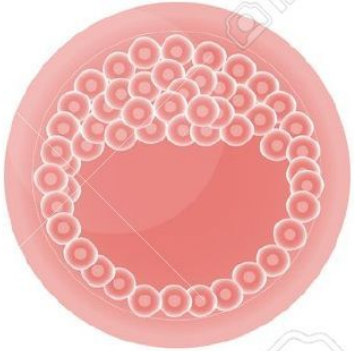
4 CELL STAGE



8 CELL STAGE



MORULA
(72 HOURS)



BLASTOCYST
(4 DAYS)

- **Transportation of blastocyst in uterine cavity :-**

In next 3-4 days, blastocyst is transported into uterine cavity (transportation assisted by fluid currents and ciliary movements of fallopian tube and uterus)

In uterine cavity, it floats for some time → zona pellucida layer disappears and trophoblast cell layer is exposed

Ectopic pregnancy :- incase of injury/ incapable movement of fallopian tube. Embryo implants within fallopian tube itself (chromosomal abnormalities, endocrinal abnormalities, congenital /acquired defect in uterus)

- **Implantation of blastocyst in the endometrium:-**

Trophoblasts due to high sticking property, come in contact with hormonally prepared endometrium of uterus

Inner layer of trophoblast → cytotrophoblast

Outer layer → syncytiotrophoblast

Syncytiotrophoblast secrete proteolytic enzymes that digest and liquefy the endometrium cells → blastocyst erodes and burrows into endometrium ⇒ implantation

Blastocyst goes deeper and deeper into uterus mucosa till whole of it lies within endometrium → endometrial implantation

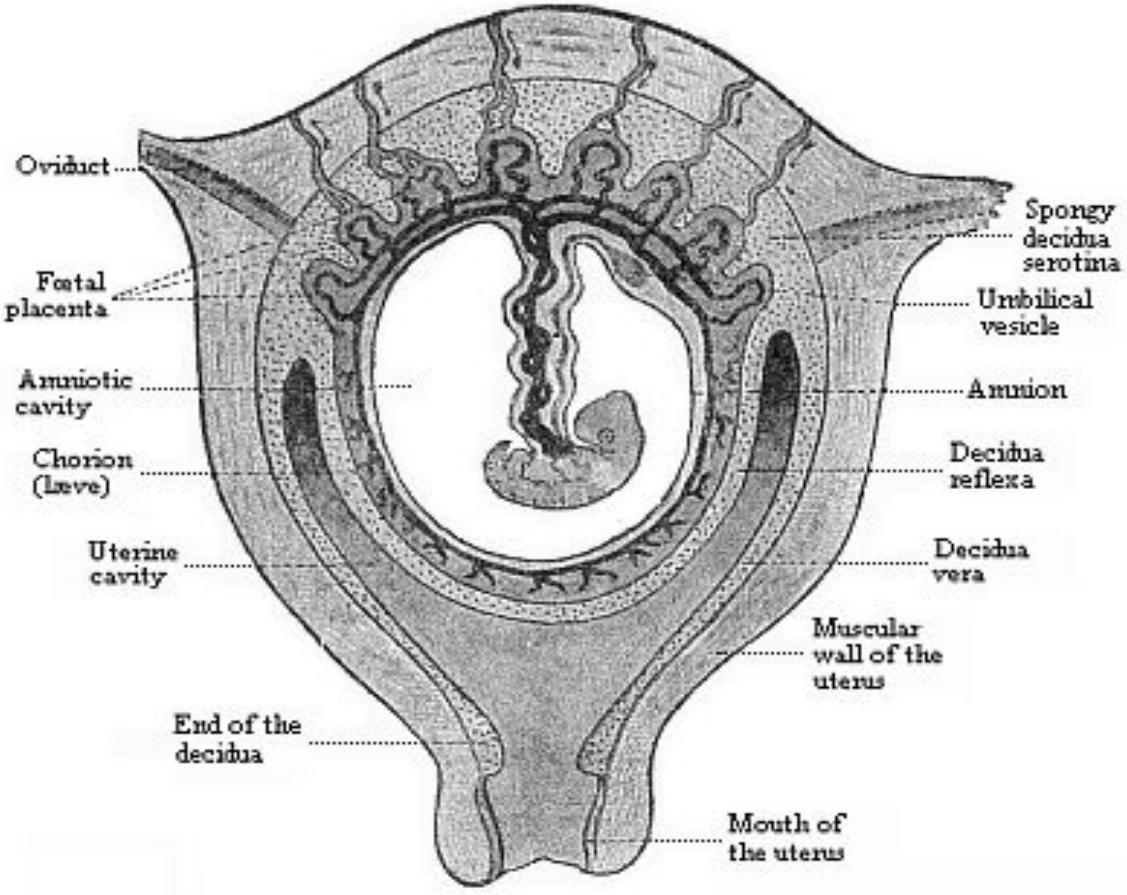
Normal site of implantation → dorsal wall of uterus

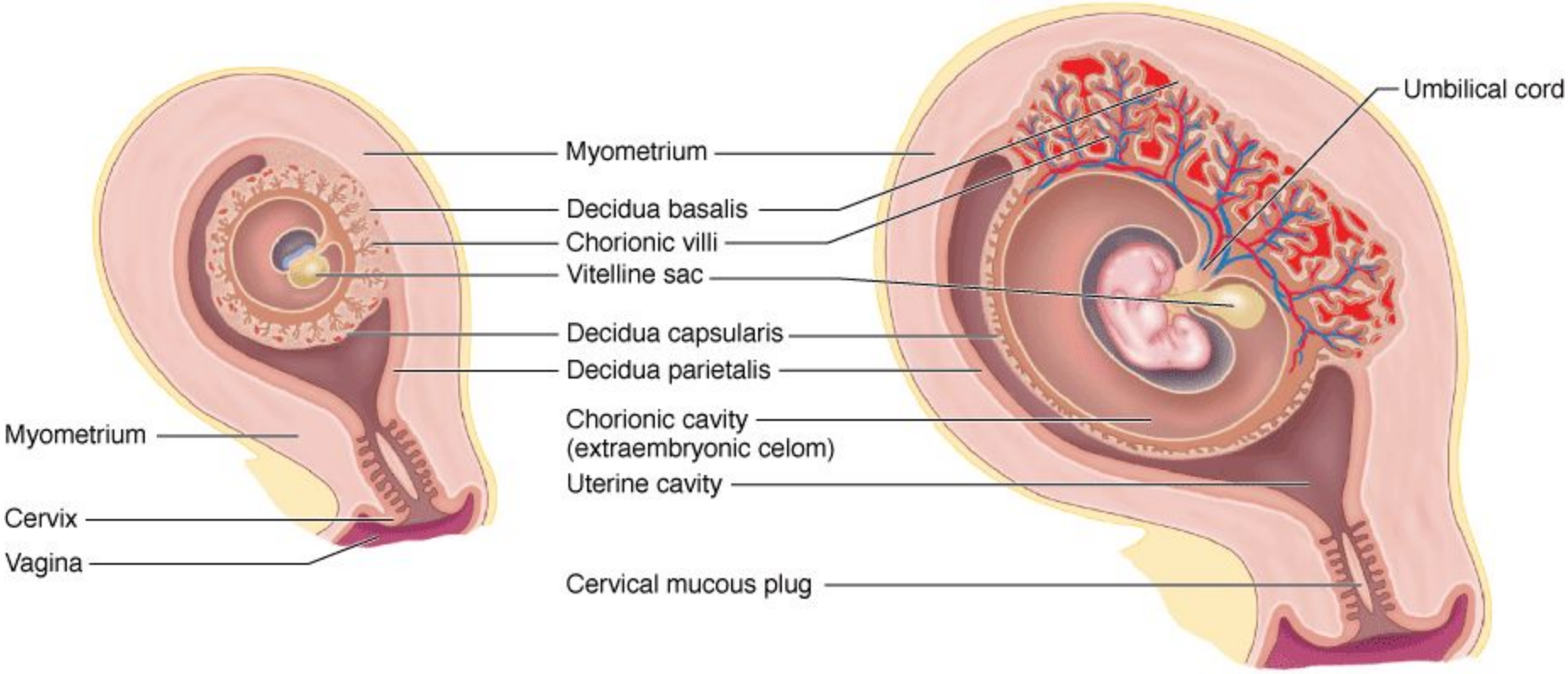
- **Decidual reaction :-**

After implantation, endometrium is called as decidua

Stromal cells of endometrium get enlarged, become vacuolated and filled with glycogen and lipids → decidual cells ⇒ decidual reaction

Stored glycogen and lipids → source of nutrition for the embryo till placenta takes up this function


Oviduct
Fœtal placenta
Amniotic cavity
Chorion (laeve)
Uterine cavity
End of the decidua
Mouth of the uterus
Muscular wall of the uterus
Decidua vera
Decidua reflexa
Amnion
Umbilical vesicle
Spongy decidua serotina



Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition:* http://www.accessmedicine.com

PLACENTA

- Temporary organ formed during pregnancy
- Important link between mother and fetus
- Decidual part where placenta is to develop → decidua basalis
- Placenta attains full size by 12 weeks
- After 12 wks, fetus and placenta function as a single unit (fetoplacental unit) especially for the synthesis of steroid hormones
- Placental villi
- After birth of the baby, placenta shed off along with decidua

Placental membrane

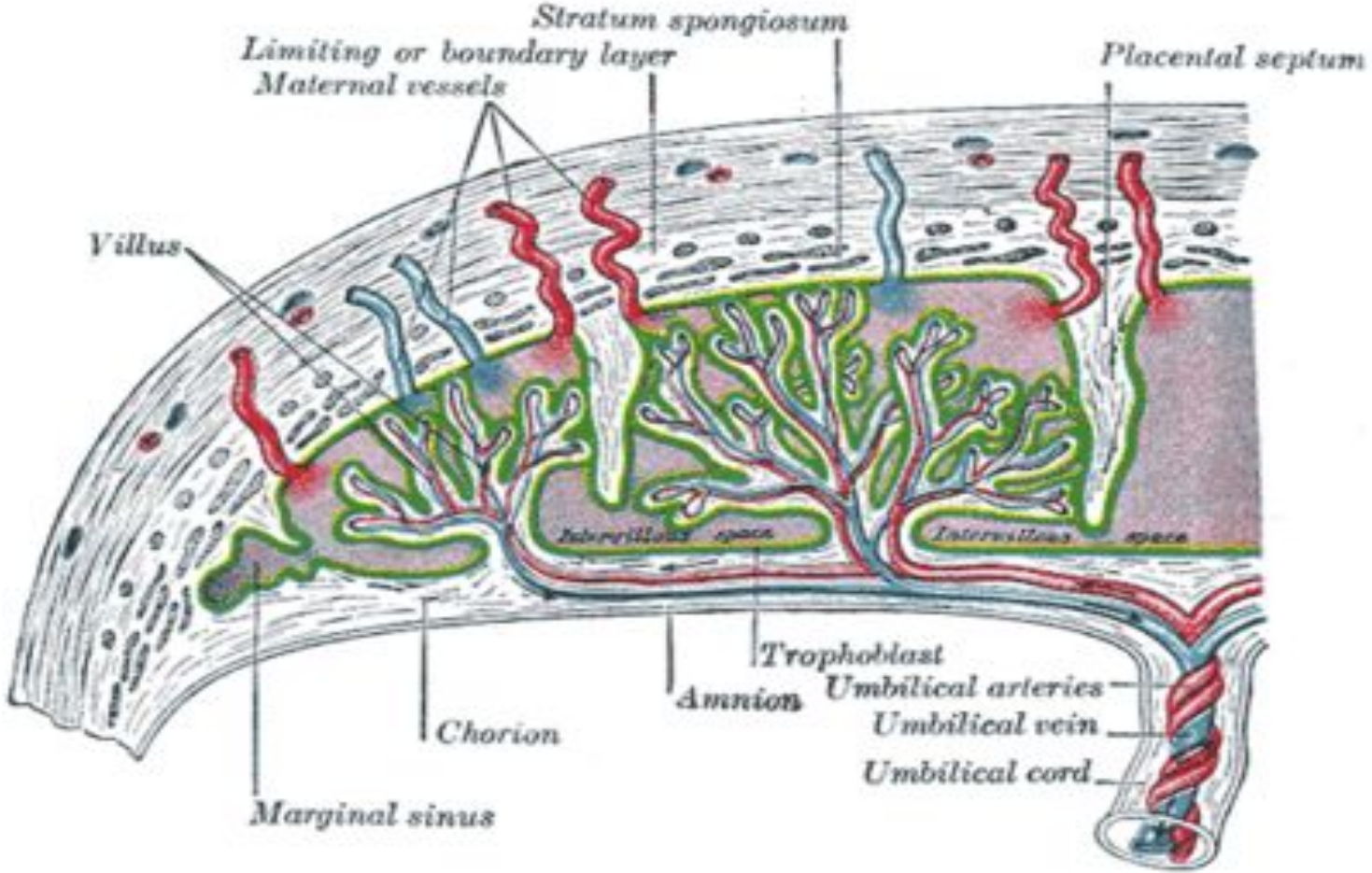
- Maternal and fetal blood do not mix with each other, separated by placental membrane
- Layers -- from fetal side

➔ Endothelium of fetal blood vessels and its basement membrane

➔ Surrounding mesenchymal tissue

➔ Cytotrophoblast and its basement membrane

➔ syncytiotrophoblast


Stratum spongiosum
Limiting or boundary layer
Maternal vessels
Placental septum
Villus
Trophoblast
Umbilical arteries
Amnion
Umbilical vein
Chorion
Umbilical cord
Marginal sinus

Functions of placenta

- Respiratory function
- Nutritive and storage function
- Excretory function
- Immunological function
- Endocrine function

Respiratory function

- Diffusion of oxygen from maternal blood to fetal blood
- Increased extraction due to

➔ Affinity of HbF for O_2 is very high

➔ Hemoglobin content more in fetus than in mother

➔ Double Bohr effect → ODC shift to right on maternal side and shift to left on fetal side

- Diffusion of CO_2 from fetal blood to maternal blood

Nutritive and storage function

- Substances of molecular wt less than 1000 can easily pass through placental barrier
- Glucose transported by carrier mediated facilitated diffusion
- Amino acids and ascorbic acid actively transported
- Fatty acids by simple diffusion but more slowly than glucose
- During early pregnancy, glucose, Na^{+}, Ca^{2+}, iron etc are stored in placenta and utilized by fetus in later pregnancy

Excretory function

Urea, uric acid, creatinine diffuse across placenta to maternal blood and excreted by maternal kidneys→ act as fetal kidney

Immunological function

- **Placenta protects the fetus from incompatibility b/w mother and fetus**
- **Prevents immunological maternal attacks by destroying T lymphocytes**
- **Partially responsible for prevention of rejection of fetal tissue**

- **Crossing of maternal antibodies through placenta to fetus provides passive immunity (IgG from 14 wks onwards)**

Endocrine function

Synthesizes hormones

- ➔ **Human Chorionic Gonadotropin (hCG)**
- ➔ **Human chorionic somatomammotropin (HCS)**
- ➔ **Human chorionic thyrotropin (HCT)**
- ➔ **Placetal estrogens**
- ➔ **Placental progesterone**
- ➔ **relaxin**

Human Chorionic Gonadotropin (hCG)

- Glycoprotein formed by syncytiotrophoblast
- Can be detected in blood by about 6th day of pregnancy by radioimmunoassay
- By about 14th day it can be estimated in urine of pregnant woman
- Peak level → 6-9 wks
- Declines by 16-20wks
- Detection of hCG in urine basis of immunological test of pregnancy
- Level increased in multiple pregnancies, Down syndrome

Functions

- Maintenance of corpus luteum of pregnancy
- Increases estrogen and progesterone secretion from ovary
- In male fetus, stimulates Leydig cells to secrete testosterone. Helps in descent of testis
- Stimulates maternal thyroid gland function (structural similarity to TSH)
- Immunosuppressive action helps in maintenance of pregnancy

Human chorionic somatomammotropin (HCS)

- Also formed in syncytiotrophoblast
- Secreted by 5th wk of pregnancy onwards
- Functions :-

➔ Lactogenic function:- has milk producing effect and also causes slight enlargement of breasts

➔ Mild growth promoting activity (maternal growth hormone of pregnancy)

➔ Responsible for diabetogenic state of mother in pregnancy by producing insulin resistance

Human chorionic thyrotropin (HCT)

- Glycoprotein similar to pituitary TSH
- Physiological function in pregnancy not known

Estrogen and progesterone

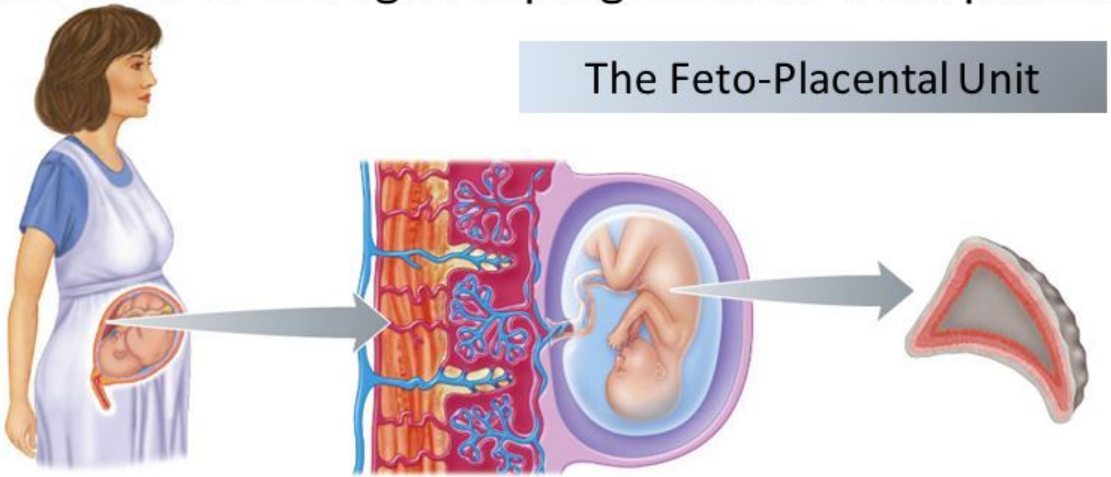
- Fetoplacental unit :- by 12th wk of development, fetus and placenta function as a single unit

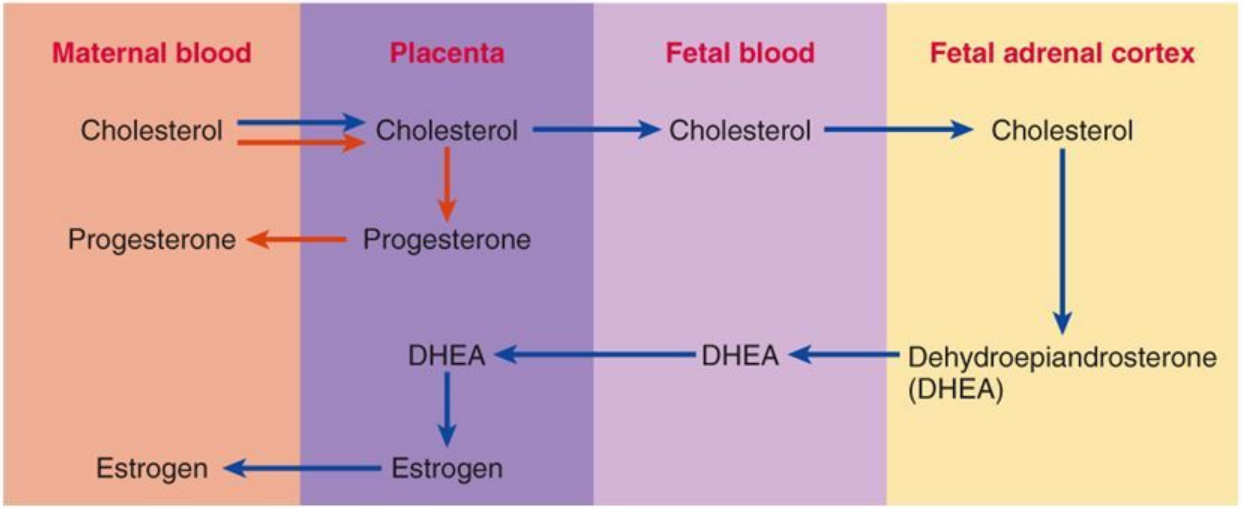
★ Important role in steroidogenesis esp synthesis of estrogen and progesterone

★ From mother cholesterol enters placenta → pregnenolone and progesterone formed

- ★ **Progesterone reaches fetal adrenals → cortisol and corticosterone**
- ★ **Pregnenolone reaches fetal adrenals and liver→ DHEAS and 16-OH DHEAS**
- ★ **16-OH DHEAS → estriol (principal estrogen formed by fetoplacental unit**

secretion of estrogen & progesterone from placenta





Relaxin

- Relaxes pelvic ligaments
- Causes dilatation and softening of cervix
- Reduces uterine contractility and maintains pregnancy

Inhibin and GnRH

- GnRH stimulates and inhibin inhibits secretion of HCG
- Regulates HCG secretion

Pregnancy tests

- Detection of hCG quantitatively or qualitatively in urine or blood → basis of pregnancy tests
- Biological tests and immunological tests
- Immunological tests are now used
- Gravindex test → based on latex agglutination inhibition technique

➔ Absence of agglutination indicates positive test

Immunological test /Gravindex test

- Antibodies are prepared by injecting urine of pregnant woman containing HCG into rabbits (HCG antiserum)

A drop of urine of pregnant woman

+

A drop of HCG antiserum

+

HCG coated latex particles

→ No agglutination (positive pregnancy test)

→ antibodies are not available to react with hCG coated latex particles because it has been used up by the HCH present in the urine sample

- False positive results in

➢ Choriocarcinoma
➢ Vesicular mole
➢ Testicular tumour in male

Amniocentesis

- Volume of amniotic fluid surrounding the fetus at 36 wk→ 800-1000ml
- Procedure done at 14-18wks of gestation
- Advantages :-

➔ Early detection of genetic disorders such as Down's syndrome, sickle cell disease etc

➔ Prenatal estimation of lecithin: sphingomyelin ratio in amniotic fluid → predict chances of developing respiratory distress syndrome (<1.5 → risk is high)

Physiological changes during pregnancy

Average duration of pregnancy → 280 days (40wks)

Hematological changes

- **Total blood volume increases by 30%**
- **Plasma volume increases relatively more than red cell volume → hemodilution → physiological anemia of pregnancy**
- **RBC count, Hb, PCV decreases ;ESR and reticulocyte increases**

- Total plasma protein decreases
- Hypercoagulable state

Cardiac output increases from 5 to 7 L/min at 20 wks of gestation