Endocrine System

It contains glands with no ducts, but their hormones are carried directly to the blood by blood sinusoids or fenestrated blood capillaries. It includes:

1-Glands: e.g: pituitary, supra renal, thyroid,parathyroid &pineal body.

2-Masses of cells: e.g:ovary,testis,thymus,….

3-Scattered cells: all over the body:e.g.:APUD.

- Hormones are:

- Chemical substances
- Secreted by special cells
- Affect distant organs
- They regulate the biochemical reactions in the body
- They regulate the processes of the body as the growth, maturation , regeneration & reproduction
- Chemical structure of hormones:

Protein (polypeptide) hormones	Steroid hormones	Amino acid hormones
1- Hormones secreted by anterior pituitary - FSH (follcle stimulating hormone) - TSH (thyroid stimulating hormone) - ACTH (adrinocorticotrophic hormone) - LH (leutinizing hormone) - PRL (prolactin) - GH (growth hormone) 2- Hormone secreted by posterior pituitary - ADH - OXYTOCIN 3- Insulin & glucagon (pancreas) 4- Parathyroid hormone 5- Hypothalamic hormones 6- Calcitonin hormone	1- Adrenal cortex hormones - Cortisol - Aldosterone 2- Gonadal hormones - Ovary: - Estrogen - Progesterone - Testes : Testosterone	- Thyroxine - Adrenaline - Noradrenaline

- Interrelation between the endocrine system & the Nervous system

Hypothalamo - Hypophyseal portal circulation	Hypothalamo – Hypophyseal tract
- **Blood** system (vascular connection) - Connect between **hypothalamus** and **anterior** pituitary - Carry **Releasing & Inhibiting** hormones secreted from the hypothalamus to affect anterior pituitary - ex **TSH** ---thyroid stimulating hormone **FSH** ---follicle stimulating hormone **ACTH** ---adrinocorticotrophic hormone	- **Nervous** connection - Connect between **hypothalamus** and **posterior** pituitary - Carry the **2** hormones **formed in** the **hypothalamus** **ADH**----in **Supraoptic** nucleus **Oxytocin**—in **paraventricular** nucleus in hypothalamus **to** **Posterior** pituitary to be **stored** then **released**

- Mechanism of action of hormones:

- The hormone to exert its action should BIND to RECEPTOR
- The receptors of hormones are:
  1- Large proteins
  2- Specific receptor for single hormone (key and lock)

3- Located either on:
   - Surface of cell -----for protein hormones
   - Cytoplasm----------for steroid hormones
   - Nucleus----------for thyroid hormones

4- They are dynamic
   - May increase --- up regulation --- decrease hormone level
   - May decrease --- down regulation --- increase hormone level.

- Mechanism of action of hormones:

According to chemical nature of hormone:

1- Protein hormones & polypeptides, glycoprotein hormones (NON GENOMIC action):

- The hormone is named (1st messenger)
- Hormone combine with receptor on cell membrane (protein can not cross cell membrane) form hormone receptor complex the hormone receptor complex act through 2nd messenger formed which may be:

Adenyl cyclase -- c-AMP 2nd messenger system	**Inositol- diacyl glycerol 2nd messenger system**	**c-GMP 2nd messenger**
Hormone + receptor ↓ Receptor bind to G protein ↓ G protein activates ADENYL CYCLASE enzyme ↓ ++++ transformation of ATP to c-AMP (2nd messenger) (cause the effect) ↓ c-AMP activates PROTEIN KINASE ↓ Phosphorylates proteins in cell (add phosphate group to it) Change chemical reactions Cause the effect ↓ Phosphodiestrase break c-AMP to AMP	Hormone + receptor Activates enzyme PHOSPHOLIPASE – C This enzyme increase break down of phospholipid in the cell membrane into two 2nd messengers IP3 , & DAG 1- Inositol tri phosphate (IP3) Increase mobilization of Ca++ from mitochondria & endoplasmic reticulum (it perform the effect) 2- Di acyl glycerol (DAG) Activate **protein kinase C** Protein kinase C phosphorylates proteins	

2-Steroid hormones

- (GENOMIC action ---- activate the GENES to inrease protein formation ----form action of hormone).
- Steroid hormone pass cell membrane bind to receptor in the cytoplasm to form hormone receptor complex the complex enter the nucleus get incorporated with the DNA cause transcription of DNA & form mRNA-(2nd messenger mRNA –cause protein formation---form hormone action

3-Thyroid hormone (GENOMIC action):

- They are very small and can pass cell membrane so they pass cell membrane & nuclear membrane
- Bind to receptor in nucleus
- Increase transcription of DNA to form mRNA (2nd messenger)
- Increase protein formation---form hormone action

- Feed back control of hormones:

- Def: It is the mechanism by which the ENDOCRINE system MAINTAIN the LEVEL of the HORMONE secreted by certain gland CONSTANT in blood.

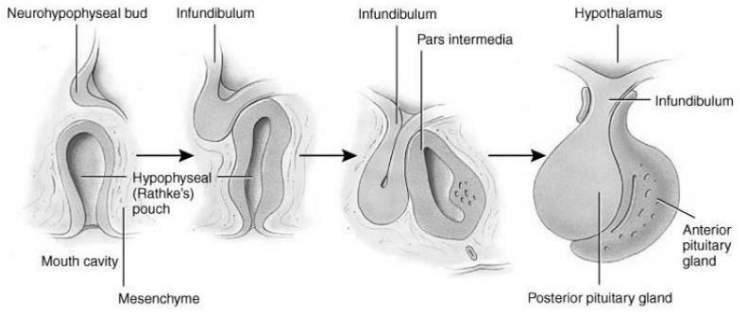
- Negative feed back:

- If the HORMONE level INCREASE in blood ---- the HORMONE inhibit the GLAND to decrease its secretion.
- Types of negative feed back:

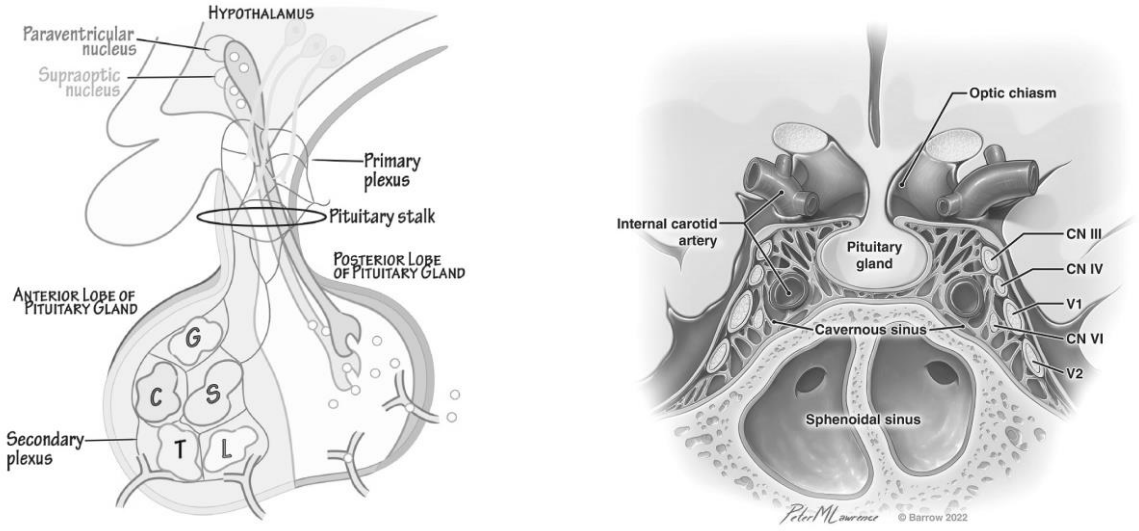
Short –short loop (Ultra short)	Short loop	Long loop
Hormone inhibit itself	Hormone inhibit its releasing hormone	Hormone inhibit hypothalamus and pituitary

- Positive feed back:

- Increase the LEVEL of hormone -----stimulate secretion of the other hormone.
- Eg increase estrogen ----- increase LH



Development of pituitary



Pituitary gland

Quizlet / Ditki / Research gate

ANATOMY OF THE PITUITARY GLAND

Embryological preview:

- It develops from two sources; Rathke's pouch (at the roof of stomodeum or future mouth) and infundibulum (at the floor of diencephalon or future hypothalamus).
- Rathke's pouch grows towards the diencephalon. The part connecting it to the stomodeum disappears, while the cranial part enlarges forming ant lobe of pituitary.
- An extension from the floor of diencephalon descends to meet the pouch and forms the post lobe of pituitary. The infundibulum between the diencephalon and the pituitary remains containing the nerve fibers connecting both.

- It is the Master of the endocrine gland, measuring 12 X 8 X 6 mm and weighting 0.5 gm
- The pituitary gland is connected to the hypothalamus by a stalk passing through the diaphragma sellae

Relations: it lies in the pituitary fossa with the following relations:

Ant: tuberculum sellae.
Post: dorsum sellae.
Sup: diaphragma sellae and optic chiasma
Inf: sphenoid air sinuses.
Lat: cavernous venous sinus.

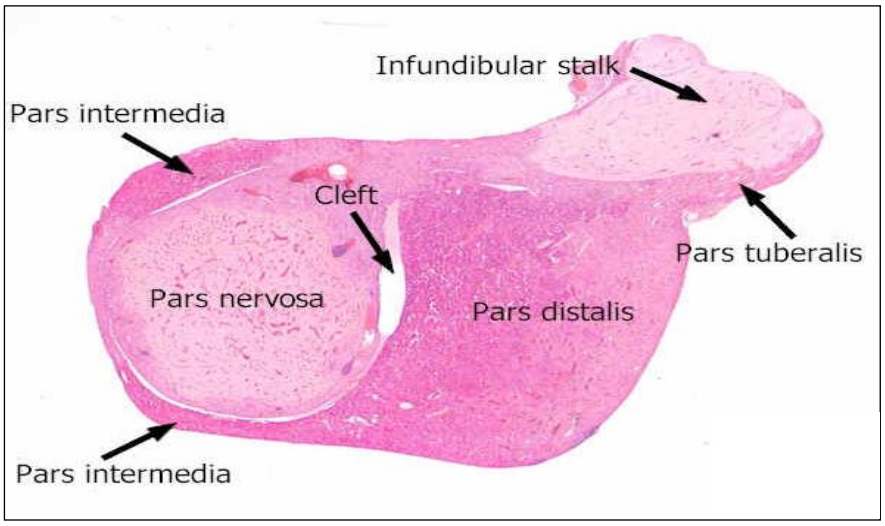
- Histology of the pituitary gland

A- Adenohypophysis:

- Adenohypophysis: (Pars distalis, Pars tuberalis &Pars intermedia).

B- Neurohypophysis:

Neurohypophysis: It includes Pars nervosa, & Infundibulum.



Pituitary gland

I) Pars distalis

- It is formed of cells classified into 2 groups:

Chromophobes & Chromophils.

Chromophobes (52%):

- Small cells with pale cytoplasm which has mild affinity for stains.
- Some cells are granular may secrete hormones.
- Some cells are non granular & are considered as stem cells.

Chromophils (48%)

They are classified into:

A) Acidophils (37%).

B) Basophils(11%)

A) Acidophils (37%)

- They are medium sized cells between chromophobes &basophils

Cell type	a) Somatotrophs	b) Mammotrophs
Hormone	- Growth hormone (If increased before closure of epiphysis, it causes gigantism, if after closure, it causes acromegaly. - If it decreased, it causes dwarfism.	Prolactin (Milk secretion)
L.M.	- Spherical cells with central rounded nuclei &acidophilic granules.	Oval cells with oval nuclei & acidophilic granules
E.M.	Golgi, mitochondria, rER & secretory granules	Mitochondria, golgi, rER, secretory graules which enlarge during pregnancy & lactation
Special stain	Orange G (Orangeophil)	Carmine (Carminophil)

B) Basophils (11%)

They are the largest cells classified into 3 types:

Cell type	Thyrotrophs	Corticotrophs	Gonadotrophs	
Hormones	TSH (Thyroid stimulating hormone), T_3 & T_4	ACTH (Adrenocorticotrphic hormone), MSH (Melanocyte stimulating hormone) Endorphin, Lipotropic factor.	FSH secreting cells	LH secreting cells
L.M.	Rounded cells with rounded nuclei.	Oval cells with eccentric nuclei.	FSH LH Rounded cells with rounded nuclei	
E.M.	All cells have mitochondria, golgi, rER& secretory granules.			

II) Pars Tuberalis

-Basophilic cells.

-Unknwon functions, but some secrete gonadotrophins (FSH&LH)

III) Pars Intermedia

- Basophilic cells
- Rudimentary in man, but in some species, they secrete melanocyte stimulatin hormone

Neurohypophysis

- It is formed of two parts which are:

I) Infundibulum.

II) Pars Nervosa.

I) Infundibulum:

- It connects the hypothalamus with pars nervosa.

II) Pars Nervosa:

- It does not secrete hormones.
- It contains:

a) Pituicytes: They are supporting neuroglial cells**.**

b) Nerve fibers (no nerve cells):

- Axons of secretory cells of hypothalamus.
- They carry neurosecretion to blood capillaries.

c) Herring bodies:

- They are acidophilic bodies containing the accumulated secretions in axon terminals of nerve fibers.
- They contain two hormones: oxytocin &vasopressin.

d) Fenestrated blood capillaries:

- They are surrounded by Herring bodies.

Functions of pars nervosa:

- It is the site of storage of ADH &Oxytocin secreted by supraoptic & paraventricular nuclei of hypothalmus.

- Hormones secreted by the anterior pituitary

They are:

1- T.S.H.
2- A.C.T.H.
3- F.S.H.
4- L.H.
5- G.H.
6- P.R.L.

1- Thyroid stimulating hormone (TSH):

- TSH release is stimulated by thyrotrophin-releasing hormone (TRH) from the hypothalamus
- TSH release is inhibited by increase T_3 and T_4 , this is called negative feedback.
- Secretion of TRH is stimulated by cold and by stress, via the CNS.
- TSH acts on the thyroid gland.
- It stimulates the release of thyroid hormones (T_3 and T_4).
- It increases iodine uptake by the thyroid; and stimulates thyroid growth

2- Adrenocorticotropic hormone (A.C.T.H.):

- It is a Polypeptide hormone.

- ACTH is stimulated by corticotropin-releasing hormone (CRH) from the hypothalamus.
- It is inhibited by increased glucocorticoids (cortisol hormone) --- negative feedback.
- Secretion of ACTH is increased by stress.
- Secretion of the A.C.T.H. is pulsatile with a diurnal rhythm (high at 7.00am, low at midnight).
- It stimulates production and secretion of cortisol from the cortex of the adrenal gland.
- ACTH produces some increase in adrenal sex steroids and stimulates growth of the adrenal cortex.
- It stimulates Melanocyte-stimulating hormone and thus stimulates pigmentation of skin via actions on melanocytes.

3-Gonadotrophins (L.H , F.S.H)

Luteinizing hormone (LH), follicle-stimulating hormone (FSH):

- In Females:

- LH and FSH control growth and development of follicles.
- LH and FSH control ovulation.
- LH and FSH control synthesis of sex steroids by the ovary.
- LH and FSH control growth and secretion of the sex steroid progesterone by the **corpus luteum**

- In Males:

- LH controls testosterone production by the Leydig cells;
- FSH stimulates the Sertoli cells and sperm production

- Control:

- LH and FSH release is stimulated by hourly pulses of gonadotrophin-releasing hormone (GnRH) during reproductive life
- LH and FSH release is inhibited by sex steroid oestrogen --- negative feedback.
- Oestrogen causes positive feedback for LH at mid ovarian cycle causing LH surge at ovulation.
- In males, LH release is inhibited by negative feedback from testosterone;
- In females ovarian peptides (inhibin and follistatin) inhibit FSH.
- Cyclical variations in LH and FSH in menstrual cycle.

4-Growth hormone (GH) :

- It stimulates long bone and soft tissue growth.
- It acts via stimulating the release of Insulin growth factors (IGFs) from the liver and to a less extent by direct actions.
- It is essential for growth after 2 years postnatally,
- It only promotes growth if sufficient nutrition is available.
- Growth hormone exerts complex actions on metabolism (amino acid, fatty acid, glucose).
- It has insulin-like effects to promote amino acid uptake by liver and muscle and, therefore, promotes protein synthesis.
- If growth hormone is chronically increased, it has anti-insulin effects.
- It is one of the hormones that switches metabolism away from glucose use (increase blood glucose – diabetogenic) and it goes towards increased oxidation of fat (e.g. in starvation)

- Function of GH:

Metabolic action on protein	Metabolic action on carbohydrates	Metabolic action on fat	Action on growth
1-Anabolic * Increase protein formation * Positive nitrogen balance * Increase number of cells * Increase size of cells **MECHANISM:** 1-increase amino acid uptake 2-increase formation of mRNA 3-increase RNA translation to form proteins	1-Diabetogenic (Hyperglycemic) *increase blood glucose MECHANISM: 1-decrease glucose entry to cell 2-increase GLYCOGENOLYSIS Glycogen----glucose	1-Lipolytic - (increase lipolysis) - Increase fatty acid uptake by liver - Increase ketone body formation by liver-----may lead to ketosis (ketogenic)	- Increase growth of soft tissue ----as it is ANABOLIC on protein - Increase growth of long bones **Mechanism**: GH act on epiphyseal cartilage of bone --- indirectly through SOMATOMEDINS (insulin growth factors) GH ↓ Liver somatomedins ↓ Act on bones

- Somatomedins:

- Protein in nature
- Formed in liver
- Has insulin like action:
  - Increase glucose uptake by cell
  - Inhibit lipolysis
- Called sulfation factors
- Has prolonged action

- Control:

- Secretion is increased via the hypothalamus by hypoglycaemia, stress, and exercise.
- Hypothalamic factors that regulate growth hormone release are growth hormone-releasing hormone (GHRH).
- Hypothalamic factors that inhibit growth hormone release is somatostatin, (GHIH) which inhibits, its release.
- Systemic control is via negative feedback by growth hormone when its level increases it inhibit the release at the hypothalamus level.
- GH is secreted in pulsatile pattern:

Factors stimulate GH secretion	Factors inhibit GH secretion
1- Decrease caloric supply as in - Hypoglycemia - Starvation - Exercise - Stress 2- Sleep 3- GHRH	1- GHIH 2- Hperglycemia 3- Increase fatty acids 4- Obesity 5- Cortisol hormone 6- Old age

- Control of gh secretion is done by:

Hypothalamic control	Feed back control
- GHRH ---+++++ GH secretion from anterior pituitary - GHIH ---- _ _ _ GH secretion from anterior pituitary	- Short loop negative feed back: GH ----- on reaching normal level ----inhibits GHRH - Long loop feed back: GH ↓ Liver ↓ Somatomedins (IGF-1) ↓ +++ hypothalamus to secrete SOMATOSTATIN ↓ Inhibit GH secretion

- Disturbances of GH secretion:

Hypofunction of GH	Hyperfunction of GH	Hyperfunction of GH
1- Pituitary Dwarfism: Def: Dwarf due to decrease GH before puberty Causes: 1-Decrease GHRH 2-Decrease GH 3-Inability to form somatomedin C (Levi-Lorain dwarf) GH secretion is normal but person can not form Somatomedin C Features: 1-Symmetrical growth retardation (proportionate dwarf)---span = height 2-Retarded growth of soft tissue 3-Mentally, sexually normal	Gigantism: Def: Increase GH before union of the epyphysis (before puberty) Characters: 1-Symmetrical over growth of all bones (taller than normal but proportionate) 2-Over growth of soft tissue (splanchnomegally) 3-Hyperglycemia, glucosuria, DM 4-Hypogonadism due to pressure of the acidophill cells secreting GH on basophil cells secreting FSH	Acromegally: Def: Increase GH after union of epiphysis of long bones (after puberty) 1-Over growth of HANDS,FEET,FINGERS, 2-Over growth of skull flat bones: - Box shape - Prominent sheeks - Prominent nose - Prominent super cilliary ridge - Protruded lower jaw (proganthism) - Separated teeth Over growth of skin of scalp cause wrinkling—(buldog face

- Over growth of vertebrae---kyphosis
- Over growth of musclesmuscles and viscera
- This case may be due to tumor in pituitary leading to pituitary enlargement----- press on optic chiasma----visual field loss (bitemporal hemi anopia)
- Hyperglycemia-----glucosuria----DM
- GH is similar to PRL ----lead to Gynecomastia & milk production

- 5-- Prolactin (PRL):

- It is secreted by lactotroph cells.
- It plays a principal role in preparation for lactation.
- PRL stimulates the development and growth of secretory alveoli and milk production. in the breast
- PRL also inhibits the reproductive system at the level of the gonads (inhibits the effect of FSH and LH on the ovaries) (causes 'lactational amenorrhoea' in women after delivery of baby).

Normal level of prolactin is 5 ng/ml in male & 8 ng/ml in females

- Control:

- Secretion of PRL is increased by suckling.
- PRL release is inhibited by dopamine from the hypothalamus.
- PRL synthesis is stimulated by circulating oestrogen.
- Chlorpromazine drug stimulates PRL secretion.

- Physiologic variation of PRL in plasma:

Sleep	Pregnancy	Parturaition	Suckling	Stress
Rise at onset of sleep	- Rise gradually during pregnancy - Reach peak at parturition	After parturition PRL level returns to its normal level 8 ng/ml	- It forms SURGE (sharp rise)	- Physical or mental stress increase PRL secretion

- Disturbances of PRL secretion

Hypoprolactinemia	Hyperprolactinemia (increase PRL secretion)
- Rare - Occur if pituitary is damaged - The female may not lactate after labor	Causes: 1- Tumor of anterior pituitary 2- Intake of DOPAMINE blocking drugs as CHLORPROMAZINE Effects: • In males: Increased PRL has inhibitory effect on FSH on testes this leads to: - Sterility - Infertility - Impotence - Gynaecomastia (enlarged male breast) - Decrease libido • In females: 1-The high level of PRL------ INHIBIT the action of GONADOTROPINE (FSH) on the ovaries leading to ↓ No maturation of ova ↓ Ammenorrhea (no monthly period) ↓ Infertility ↓ Sterility 2-Galactorrhea (increase milk production in non lactating females)

Hormones secreted by the posterior pituitary

- ADH (vasopressin) = pressophysin

- Actions:

- It increases water reabsorption by acting on collecting ducts of kidney through (V2 receptor).
- It has a vascular pressor effects to constricting peripheral arterioles and veins through (V1 receptors)
- ADH acts on receptors in the glomerular mesangium to increase formation of the (PGE2) --- which is a vasodilator

- The action of the (PGE2) as a vasodilator antagonizes the vasoconstrictor action of the ADH on the renal tissue
- It acts through V3 receptors In anterior pituitary (Corticotrope cells) = cells which secrete ACTH

- Control of ADH:

Stimuli inhibit ADH secretion	Stimuli increase ADH secretion
1- Cold weather 2- Alcohol 3- Hypervolemia 4- Decrease osmotic pressure in plasma (plasma osmolarity) 5- Alpha agonists	1- Increase plasma osmolarity (increase osmotic pressure in plasma) 1% ↓ Stimulate osmoreceptors in hypothalamus ↓ Increase ADH secretion ↓ Increase water REABSORPTION in DISTAL tubules in kidney (FACULTATIVE) ↓ Return plasma osmolarity to normal 2- Hypovolemia: Decrease blood volume by 10% Decrease blood pressure +++ Carotid sinus baroreceptors → +++ Vasomotor center → +++ secretion of ADH → Vasoconstrition , increase blood pressure +++ Atrial receptors → +++ Vagus nerve → +++ ADH +++ BP (weak) 3- Stress increases ADH secretion as the it stimulates the release of CRH and the it is co-secreted with the ADH 4- Drugs (morphine nicotine) 5- Nausea (it stimulates the release of the ADH by an unknown cause) 6- Hot weather (as there will be more sweat so the ADH will decrease the urine output to preserve the water and blood volume)

- Diabetes insipidus:

Def: Caused due to defeciency of ADH

Causes:

1- Lesion in supraoptic nucleus ----(central diabetes insipidus)

2- Congenital defect in V2 receptors in kidney
kidney does not respond to ADH
(nephrogenic diabetes insipidus)

- Manifestation of diabetes insipidus (D.I.):

* Polyuria ----- increase volume of urine up to 10 liters /day-----specific gravity of urine ---very low
(1002-1004)
- Loss of water soluble vitamins
- Loss of electrolytes

* Polydepsia: drink large volume of water
* Increased BMR as more volume of water is heated

- Oxytocin (oxyphysin):

- Actions:

It causes contraction of uterine myometrium in childbirth and contraction of breast myoepithelium to eject milk.

- Control:

- The hormone release is stimulated by stretch of cervix/vagina during parturition (the Ferguson refl ex)
- The hormone release is stimulated by suckling—stimulation of the nipple causes the milk ejection.

Pineal Body (Epiphysis Cerebri)

- It is a cone shaped neuroendocrine gland.
- It is derived from neuroectoderm.
- **It is formed of:**
  - **Pinealocytes.**
  - **Astrocytes.**
  - **Fenestrated blood capillaries.**
  - **Brain sand (psammoma bodies).**

1) Pinealocytes:

- Structure:

- They are large branched cells with long tortuous processes which end by dilations on blood capillaries in the vascular septa.
- The nuclei are large pale with clear nucleolus.
- The cytoplasm is basophilic.
- By E.M:they are rich in mitochondria,golgi apparatus,rER& secretory granules.

- Functions: They secrete:

- Serotonin (at day time).
- Melatonin (at night):
  - ***** Regulates gonadal function to prevent precocious puberty.
  - * Antioxidant(protection of body cells).
  - * Regulation of sleep rhythm.

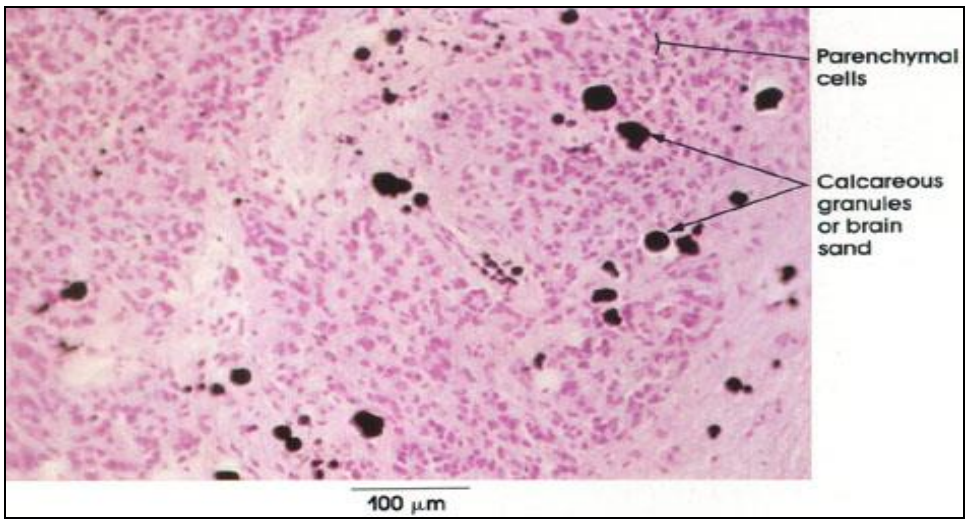
2) Astrocytes:

- They are neuroglial supporting cells.
- They are presented between pinealocytes.
- The nuclei are darker.
- They have long processes.
- They have many intermediate filaments.

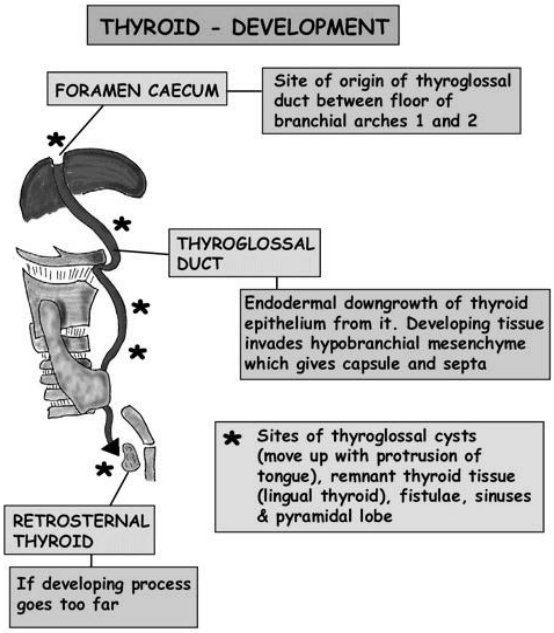
3) Fenestrated blood capillaries.

4) Brain sand (Psammoma bodies,corpora aranacea):

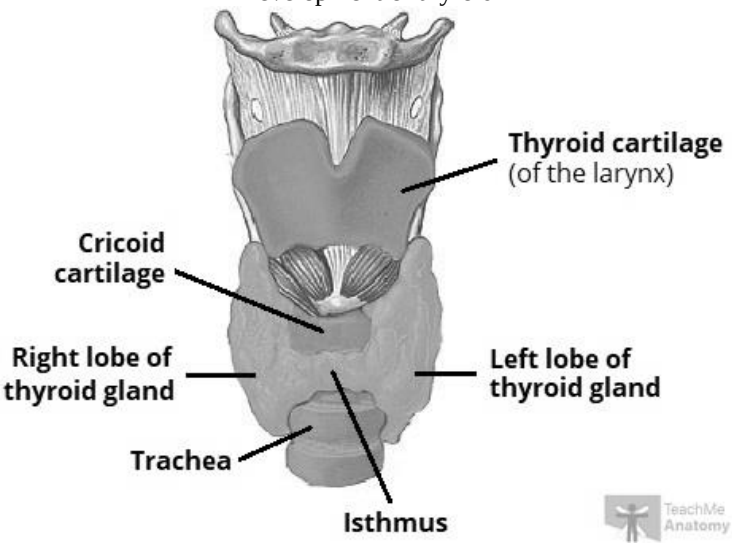
- They are calcified secretory products in concentric layers.
- They increase with age.
- They are land mark in x-ray to localize any mass in the brain,which may displaces its position.


Parenchymal cells
Calcareous granules or brain sand
100 µm

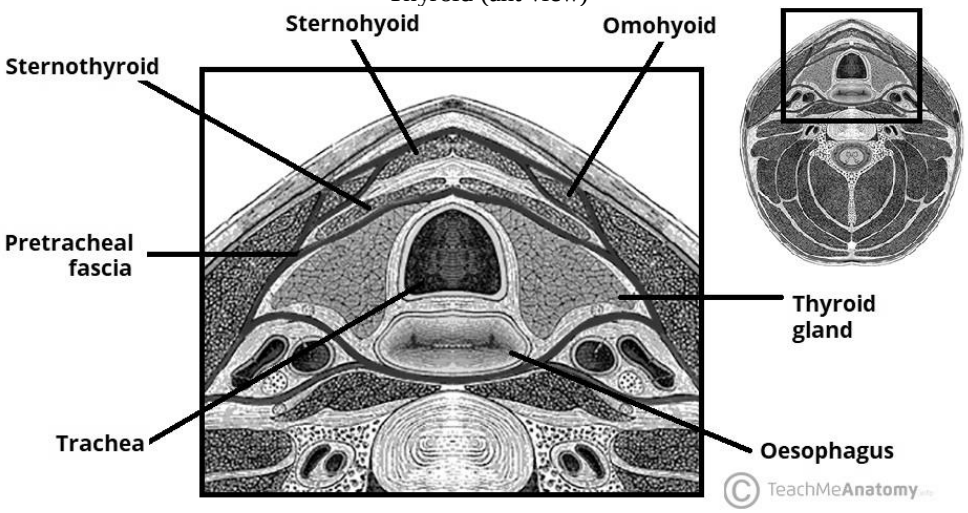
Pineal body



Development of thyroid



Thyroid (ant view)



Thyroid (transverse section)

Weebly / Teachmeanatomy

ANATOMY OF THYROID GLAND

Embryological preview:

- The endoderm of 1st pharyngeal arch develops into the mucous membrane of the ant 2/3 of tongue. While the endoderm of 3rd and 4th arches develops into the mucous membrane of the post 1/3 of tongue. The line between the ant 2/3 and post 1/3 of the mucous membrane of the tongue is called sulcus terminalis and it shows foramen cecum at its middle.
- From foramen cecum arises a thyroglossal duct which migrates caudally to reach the thyroid cartilage and forms the thyroid gland acini.
- the connective tissue and vessels arise from surrounding mesoderm.
- The duct connecting the thyroid to the tongue forms the pyramidal lobe above the isthmus and the rest disappears.

Congenital anomalies:

Aplasia or hypoplasia of thyroid: due to failure of development of thyroid acini.
Lingual thyroid: due to failure of extension of thyroglossal duct.
Mediastinal thyroid: the thyroglossal duct continue its migration to the thorax..
Thyroglossal cyst: persistence of part of thyroglossal duct with cyst formation. This cyst moves with the protrusion of tongue.

Relations: the thyroid gland has two lobes connected by an isthmus.

Lobe: pyramidal in shape, tracheal ring. It has:

Apex: at the C5 vertebra.
Base: at the level of T1vertebra (6th tracheal ring).
Ant border
Post border: related to parathyroid gland.
Lat (superficial) surface: related to skin, superficial fascia (containing platysma), deep investing fascia and sternohyoid, sternothyroid, omohyoid and sternomastoid muscles.
Posterolateral surface: related to carotid sheath.
Med surface: related to:

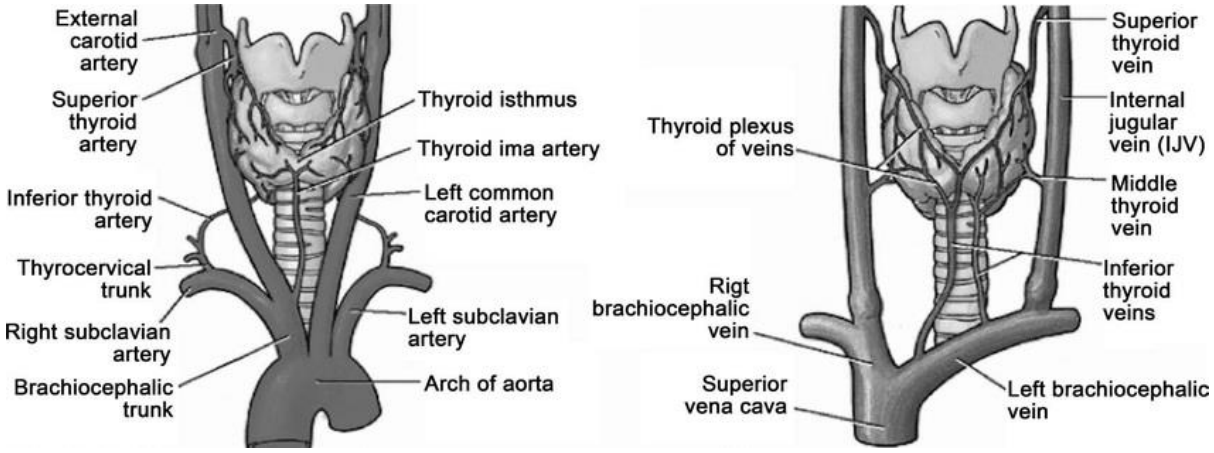
- larynx and pharynx (between C5-C6 vertebrae), trachea and esophagus (between C6 and T1 vertebra).
- External laryngeal nerve is related to the upper part of this surface and the recurrent laryngeal nerve is related to its lower part.

Isthmus: it has:

Upper border: presents a small pyramidal lobe.
Inferior border.
Anterior surface: related to skin, superficial fascia (containing platysma), deep investing fascia, and sternohyoid and sternothyroid muscles.
Posterior surface: related to tracheal rings 2-4.

Capsules of the gland:

Inner (true) capsule: formed of connective tissue.
Outer false capsule: derived from the pretracheal fascia and attached to larynx.



Blood supply of thyroid

Wikimedia

Blood supply of the thyroid gland:

Arteries:

Rt and Lt sup thyroid As (of ECA): supplies the apex and anterior aspect of the gland. the two arteries anastomose at the upper border of the isthmus.

Rt and Lt inf thyroid As (of thyrocervical trunk of subclavian A): supplies the base and the posterior aspect of the gland.

Thyroidea ima artery (of aortic arch): supplies the isthmus.

Veins:

Rt and Lt sup thyroid Vs: emerges from the apex of the thyroid lobe and usually drains to IJV.

Rt and Lt middle thyroid Vs: emerges from the middle of the lobe and drains to IJV.

Rt and Lt inf thyroid Vs: emerges from the base of the thyroid lobe. They unite forming a single vein and drains to Lt brachiocephalic V.

Applied anatomy:

- Due to the enclosement of thyroid gland within the pretracheal fascia connecting it to the larynx, the thyroid gland moves during swallowing. Enlargement of the thyroid gland may cause pressure symptoms on trachea and esophagus (difficulty in breathing and swallowing).
- The sup thyroid A is closely related to the external laryngeal N away from the gland, while the inf thyroid A is closely related to the recurrent laryngeal nerve near the gland. To avoid the nerve injuries during thyroidectomy the sup thyroid artery should be ligated near the apex. While the inf thyroid artery should be ligated away from the gland.
- Injury of external laryngeal nerve causes paralysis of cricothyroid muscle of larynx leading to loss of of high pitched voice. Injury of RLN causes paralysis to other muscles of larynx leading to hoarseness of voice.

- Histology of the thyroid gland

It is formed **of stroma & parenchyma.**

I) Stroma:

- Capsule: Two capsules (True& False):

True capsule: Inner capsule, firmly adherent to the gland**.**

- False: Outer capsule, formed of pretracheal fascia.

- Trabeculae: Thin,divide the gland into lobes &lobules &carry blood vessels.

- Reticular C.T: reticular cells &fibers in the background, stained with **Ag(silver).**

II) Parenchyma:

-It is formed of Thyroid follicles &Inter follicular tissue.

A) Thyroid follicles:

- The structural & functional units of the gland.
- Shape: oval or rounded.
- Lined with cubical epithelium, resting on thin basement membrane.
- Surrounding a lumen filled with acidophilic colloidal material called (iodinated glycoprotein).
- They are lined with two types of cells:

1) Follicular cells (98%):

- By L.M: Cubical cells with basophilic cytoplasm& central rounded nuclei.

- By E.M: The cells have:

- Apical micro villi.
- Tight junctions between adjacent cells**.**
- Mitochondria, supranuclear golgi apparatus, ribosomes, lysosomes &apical secretory vesicles.

Functions: Secretion of thyroid hormones (T_3 & T_4) under control of TSH.

2) Parafollicular (c-cells) (2%):

- By L.M:

- They are larger cells with paler cytoplasm, so called clear cells , stained with Ag.
- They are presented between the basement membrane & follicular cells.
- They don't reach the lumen of the follicle.

- By E.M:

-Mitochondria, rER, Golgi apparatus& basal secretory granules.

Functions: They secrete Thyrocalcitonin which decreases blood calcium.

B) Interfollicular Tissue:

- It is in between thyroid follicles.
- It contains; reticular C.T., interfollicular cells, C-cells & fenestrated blood capillaries.

- Hormones of the thyroid gland

- They are:

1-Thyroxine T4,T3

2-Calcitonin ----from para follicular cells

- Formation of the thyroid hormones:

- Iodide trapping: active iodide uptake by thyroid gland.
- Oxidation of iodide to iodine
- Binding of iodinated tyrosine with the glycoprotein(thyroglobulin).
- Iodination of tyrosine to form monoiodotyrosine(MIT),diiodotyrosine(DIT).
- Coupling of 2(DIT) to form T4 and 1(MIT) +1(DIT) to form T3.
- Release of thyroid hormones.
- Normal level of T_4, T_3:

	T4	T3
Total	8-12 ug/dl	0.15 ug/dl
Bound	99.98%	99.8%
Free	1- 6 ng/dl	0.3ng/dl

- Function of thyroid hormones:

Effect on metabolism	Effect on metabolism	Effect on metabolism	Effect on metabolism	Effect on metabolism	Effect on metabolism
Calorigenic	Carbohydrate metabolism	Fat metabolism	Protein metabolism	Vitamin metabolism	Basal metabolic rate
- Increase O_2 consumption - Increase heat production - Increase size & number of mitochondria - Increase ATP formation - Increase Na^+ K^+ ATPase enzyme	- Increase absorption of glucose by intestine - Increase gluconeogenesis Change amino acid----glucose - Increase glucose uptake by cells - Increase insulin	- Lipolysis--- mobilize lipids from stores - Deplete fat stores - Decrease cholesterol in plasma - Increase oxidation of fatty acids	- Anabolic--- increase protein formation (in normal dose) - On large dose ---catabolic	- Increase body needs for vitamins as thyroid hormone act as coenzymes - Help conversion of carotein to vitamin A	- Increase BMR - Responsible for normal BMR

- On Body system:

On GIT	On CVS	On CNS

- +++ motility of GIT
- +++ secretion of GIT
- +++ absorption of GIT
	- Increase HR:
	  - Thyroid hormone stimulates SAN
	  - Thyroid hormone has direct effect on excitability
	- Increase CO-- due to
	  - Increase metabolism
	  - Stimulate Beta adrenergic receptors
	  - Increase heat production
	- Increase pulse pressure Systolic – Diastolic
	- Increase systolic pressure due to increase CO
	- Decrease diastolic pressure due to peripheral vasodilation
	- Increase force of contraction – enzyme activity
		- Increase myelination and growth of neurones
		- Increase synaptic transmission (needed for wakfulness)

- Effect on growth:

- Essential for MENTAL development during first year post natal
- Needed for PHYSICAL linear growth , maturation of growth centers and eruption of teeth
- Needed for SEXUAL growth & maturation.

- Abnormalities of thyroid gland function:

- Hypothyroidism:

- Causes of hypothyroidism:

1- Causes in the thyroid gland. (primary)

Causes in pituitary origin (secondary)

Causes in hypothalamus (tertiary)

- Congenital absence of thyroid gland
- Chronic iodine defeciency
- Chronic thyroiditis
- Excessive antithyroid drugs
- Surgical removal of thyroid gland

2- Decrease TSH of the anterior pituitary

Decrease TRH of the hypothalamus

Hypothyroidism (adult)-(Myxoedema)	Hypothyroidism (infant)-(cretenism)
Characters: 1- BMR---Decreased to about 50% leading to: - Increase body weight - Can not tolerate cold weather - Coarse & sparse hair - Skin: Cold Dry: No sweat Puffy: Accumulate complex proteins water retention: Puffy skin Yellow: Why Liver need thyroid hormone to transfer Carotene: Vitamin A As the thyroid hormone is decreased carotene will not be transferred to vitamin A and remain under skin giving it the yellow color	- Delay in all normal growth milestones - Retarded physical , and mental , and sexual growth 1- Physical growth: - Dwarf (short) - Disproportionate –as span is retarded more than height as vertebrae not retarded - Umbilicus not central - Obese: Why: Because the skeletal growth is more inhibited than soft tissue growth - Delay eruption of teeth - Delay close fontanels - Delay sitting and walking - Increase body weight - Increase plasma cholesterol - Decrease activity of all body systems - Decrease metabolic rate, body temperature

Hypothyroidism (adult)-(Myxoedema)	Hypothyroidism (infant)-(cretenism)
2- CNS: - Slow mentation - Poor memory - Hypersomnia - Hyporeflexia 3- CVS: Decrease HR, CO Atherosclerosis Low voltage ECG 4- GIT: Constipation Loss of appetite 5- Blood: Increase serum cholesterol level 6- Non pitting oedema: Due to accumulation of the myxoedematous tissue 7- Decrease respiratory rate (decrease ventilation) 8- Eye: Puffiness Swelling face Night blindness---decrease vitamin A 9- Metabolism: - Decrease glucose absorption - Increase glycogen in liver & muscle - Non pitting oedema—myxoedematous accumulate	Facial features: - Ugly face - Swolen eye lid - Depressed nose , wide nostril - Enlarged protruded tongue - Thick dry skin deposit fat in supraorbital region - Pot belly abdomen due to enlarged liver and spleen Mental development: He is mentally retarded Sexual development: Delayed sexual development

Difference between GH dwarf and thyroid dwarf

Thyroid dwarf	GH dwarf
- Lack of thyroid hormone	- Lack of GH
- Disproportionate dwarf	- Proportionate dwarf
- Idiot	- Normal mentality
- Impotent	- Infantile shape
- Ugly	- Normal sexually

- Hyperthyroidism (thyrotoxicosis):

Excessive secretion of thyroid hormone

- Causes:

1-Acute thyroiditis---inflammation of thyroid---lead to increase secretion of the thyroid hormone

2-Tumor in thyroid gland

3-Graves disease---antibodies present against TSH receptors on the thyroid gland ----produce excess T_3, T_4----while they have no negative feed back

4-Excessive adminstration of thyroid hormones

5-Pituitary tumor

- Characters:

1-BMR---Increase BMR to 100%

Not tolerate hot weather

Warm flushed sweaty skin

2-CNS---Irritable. Tremors , insomnia , hyperreflexia
Increased excitability of nervous tissue

3-CVS---Tachycardia due to
-Direct stimulation of SAN
-Increase senstivity of the SAN to catecholamines

4-blood pressure: -Increase systolic –due to increase SV, CO
-Decrease diastolic—due to peripheral VD
-Increase pulse pressure

***Eyes: Exophthalmus**

- Antibodies against extra ocular muscles
- Cause hypertrophy of the muscles
- Push eye ball forward
- Press on optic nerve causing atrophy, blind

***GIT**---Diarrhea, hyperphagia

***Blood:**---Hyperglycemia

- Decrease cholesterol level
- Increase pulmonary ventilation
- Shift O_2 dissociation curve to right

On metabolism:

- Increase catabolism of protein of protein
- Hyperglycemia
- Decrease cholesterol level in blood

- GOITRE

- Def: enlarged thyroid (non inflammatory non neoplasmic)

- It may be associated with

- With normal , decreased or increased thyroid activity
- It is of three types

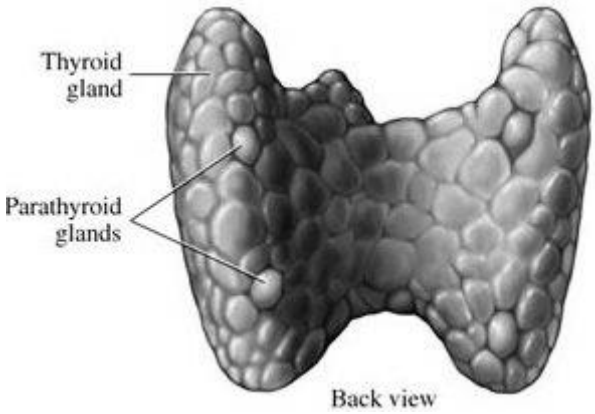
1- Physiologic: - During puberty
- During pregnancy
- Thyroid gland enlarges to form more thyroid hormone to meet the increased needs for thyroid hormone

2- Hypothyroidism: - In case of iodine deficiency
(colloid goitre) - Thyroid follicles filled with
- Thyroglobulin
- Thyroid hormones not formed

3- Hyperthyroid: - In TUMOR adenoma
(parenchymatous goitre) - Graves disease
Thyroid cells increase in size & number

- Goitergenic substances are :

Drugs block iodide trapping	Drugs block of iodine	Natural goitergens
- Monovalent anions: 1- Perchlorate, nitrate iodate Compete with iodine & Uptaken to follicles 2- Thiocynate Compete with iodine but They are not uptaken to follicles They lead to: - Decrease thyroid hormones - Increased TSH	- Thioria - Thiouracil - Thiocarbmide They compete with tyrosine Prevent formation of MIT, DIT Decrease thyroid hormones Increase TSH	- They are carrots, cabbage & turnips - They contain progoitrin --- & its converter is heat labile - The converter is heat labile - The progoitrin is converted to goitrin even if the food is cooked due to presence of bacteria activator in the intestine act as converter



Parathyroid glands

Medicocrazy

ANATOMY OF THE PARATHYROID GLANDS

- They are four small glands embedded in the posterior aspect of thyroid lobes.
- The sup parathyroid lies at the middle of the posterior border of thyroid lobe, while the inf parathyroid lies close to the inferior pole of thyroid lobe.

Embryological preview: the superior parathyroid develops from the 4th pharyngeal pouch while the inferior parathyroid develops from the 3rd pharyngeal pouch

Blood supply: inf thyroid As.

Applied anatomy: during thyroidectomy, its post part should be preserved to maintain the parathyroid glands.

- Histology of the parathyroid gland

- They are four small endocrine glands at the back of the thyroid gland.
- They are formed of stroma & parenchyma.

A) Stroma:

- Capsule: Thin, formed of C.T cells & fibers.

- Trabeculae: Thin, formed of C.T cells & fibers divide the gland into incomplete lobules, carry blood vessels.

- Reticular C.T.: Reticular cells & fibers, in the background ,stained with Ag.

B) Parenchyma:

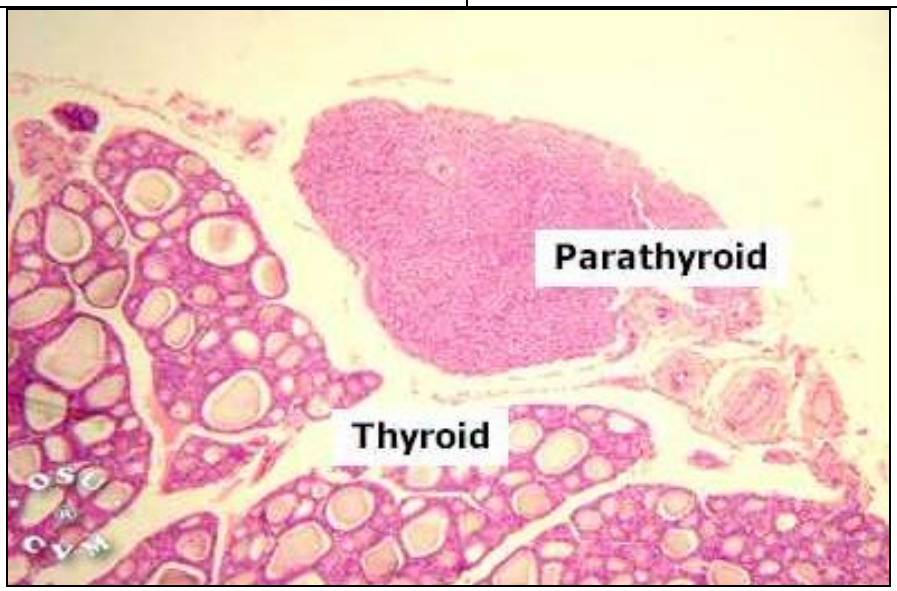
Two types of cells.

- Chief (Principal) cells

- Oxyphil cells.

a) Chief cells	b) Oxyphil cells
Small & more numerous.	Larger & less numerous, but No. increases with age.
Polygonal cells with central rounded nuclei.	Oval or rounded cells with eccentric nuclei.
Basophilic cytoplasm	**Acidophilic cytoplasm**
Fine granules	Acidophilic granules
By E.M: Mitochondria, rER, golgi & secretory granules.	Mitochondria

Functions: Secretion of parathyroid hormone (parathormone) which increase blood calcium.	Un known function.



Thyroid & parathyroid gland

Calcium homeostasis

Ca^{2+} has very important extracellular effects as

- Its effect on excitability of tissues
- Its effect on blood clotting
- It is an essential component of bone.

The condition Hypocalcaemia (i.e. total Ca2+ <1.2–1.5mM): Is very Dangerous :

- It Increases neuronal membrane excitability by increasing sodium permeability causing tetany (involuntary nerve-induced spasm of skeletal muscles)
- The Heart QT interval is increased ('prolonged QT') and heart failure may occur
- The condition of Hypercalcaemia is only dangerous in the long term due to
- It decreases neurone excitability
- The Calcium salts are rather insoluble, so urinary stones and tissue calcification occurs
- Attempts to secrete excess calcium via urine causes polyuria, which leads to dehydration and exacerbates the problem.

A fall in plasma Ca2+ is therefore more dangerous, short term, than a rise;

Amounts of calcium in the body:

- The main controlled parameter is plasma-ionized Ca^{2+}: 1.2mM.
- Plasma contains 2.5 mM total (2.4–2.6mM); 50% is ionized

Total body calcium:

- Normal adult contains 25 moles (1kg) of calcium
- **Bone calcium:**
  - 1% (250mmol) is rapidly exchangeable
  - 99% is hydroxyapatite bound to collagen: Slowly exchangeable.
  - Interstitial fluid calcium is freely exchangeable with plasma calcium.

Phosphorus

- 85% in the skeleton as hydroxyapatite
- 15% in soft tissues
- **Plasma:** Phosphate 0.2 mM; varies widely with age, sex, diet.

The hormones controlling calcium are:

1-Parathyroid hormone (PTH): From parathyroid gland
2-Calcitonin: From thyroid gland
3-Active vitamin D

- PTH:

- Actions of PTH (hypercalcemia, hyperphosphaturia, hypophosphatemia, hypocalcuria)

A-On bone

1- Rapid phase:

- Begins within minutes
- PTH activate receptors on osteocytes
- Increase permeability of osteocytic membrane to Ca^{++} from bone(move Ca^{++} from bone to blood)----increase Ca^{++} in blood
- It recognizes osteoblasts so that they become separated to allow calcium efflux from matrix and access of osteoclasts (which break down bone).

2- Slow phase

- It takes days to weeks
- PTH acts on osteoblasts----stimulate them to form—IL-6
- IL-6 stimulates osteoclasts -----resorb bone and release Ca^{++} to ECF
- Indirectly as osteoclasts have no receptors for PTH

B- On kidney

- PTH increase phosphate excretion in urine ----leading to its decrease in blood ---- lead to increase Ca^{++} in blood
- PTH ---activate 1-alpha hydroxylase enzyme ----which cause activation of vitamin D
- PTH increases reabsorption of Ca^{++} from distal tubules
- PTH increases Mg^{++} reabsorption

C- On intestine:

- PTH ---stimulate formation of active vitamin D through formation of 1-alpha hydroxylase enzyme---increase Ca^{++} in blood
- Ca^{2+} can be disturbed, when PTH is insufficient

* Deficiency:

1- Hypoparathyroidism this leads to —low plasma Ca2+, whixh leads to tetany.

2- Pseudohypoparathyroidism—there is resistance to PTH due to receptor defect (PTH levels are normal or increased)

- Excess hyperparathyroidism due to (tumours) - this causes raised plasma Ca^{2+}, bone destruction, urinary stones, & sluggish CNS.

- Action of vitamin D:

Mechanism of activation of vitamin D

Vitamin D (1-25 dihydroxycholicalceferol)

Ultra violet waves

Acts on

7-dehydrocholesterol (under skin)

To form

Cholecalceferol

Which

In liver change to -25 hydroxycholecalceferol (by 25 hydroxylase enzyme) by adding (OH group) at the 25^{th} carbon

Then

In kidney ---1-25 di hydroxycholecalceferol (1-alpha hydroxylase enzyme) by adding (OH group) at the first carbon

1-On kidney:

- It increases Ca^{++} reabsorption by distal tubules

2- On intestine:

- Vitamin D stimulate the formation of Calbindin D
- I ncreases absorption of Ca++

3-On bones:

- In high Ca^{++} --stimulates osteoblastic activity (increase Ca++ from blood to bone)
- In low Ca^{++} PTH ----- ++osteoblasts which ++IL-6 which will ++osteoclasts to ++++++Ca++ mobilization from the bone to the blood.

- In both conditions deficiency and excess of vitamin D, serum Ca^{2+} is approximately normal:

- **Defi ciency:**
  - Children: Rickets renal rickets;
  - Vitamin D-resistant rickets
  - Adults: Osteomalacia. Increasingly implicated in a range of chronic diseases (e.g. MS, diabetes)
- **Excess:** Vitamin D poisoning which leads to symptoms of hypercalcaemia.

- Calcitonin hormone

It is a Peptide hormone produced by C cells of thyroid and secreted in response to serum Ca^{2+} above normal range.

Its Principal function is to prevent hypercalcaemia and excessive bone breakdown.

- Action of calcitonin:

A- On bone:

- Stimulate osteoblasts
- Increase bone matrix
- Decrease bone resorption

- Decrease number and activity of osteoclasts

B-On kidney:

- It inhibits one alpha hydroxylase enzyme ----decrease active vitamin D
- It increases excretion of Ca++, PO4- in urine

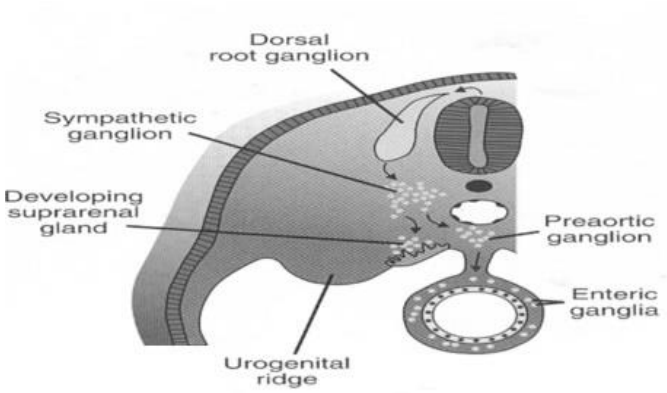
- Disturbance of calcium level in blood:

- Tetany:

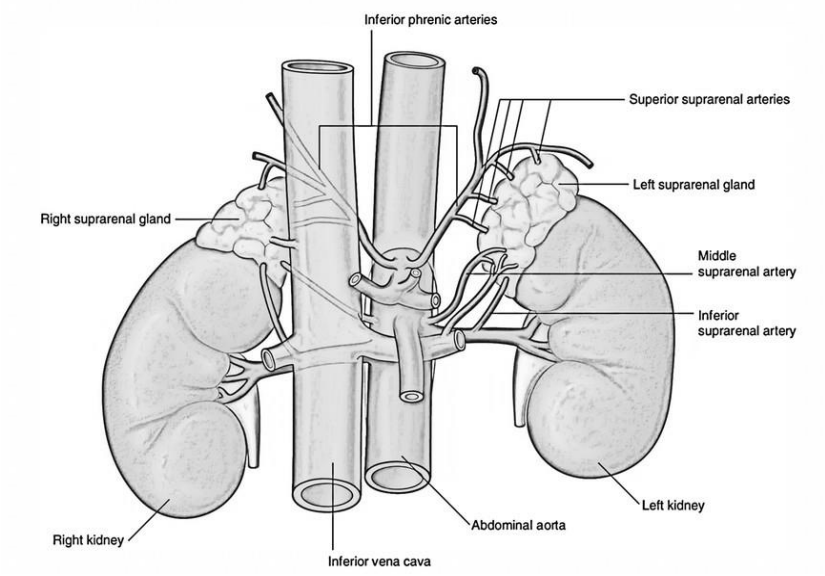
- Def: increase neuromuscular excitability due to decrease ionized Ca^{++}

- Mechanism:

The Decrease in the ionized Ca^{++} level in plasma which under normal conditions partially opposes the entry of sodium along the receptors on the muscle side at the neuromuscular junction will make the entry of sodium through these channels un opposed this will lead to increase Na^{+} permeability through these channels and ------increase excitability which appear as twitches and muscle spasm.



Development of suprarenal gland



Suprarenal glands

Earth's lab

ANATOMY OF THE SUPRARENAL GLANDS

Embryological preview:

- The cortex develops from mesodermal cells lining the coelomic cavity of lat plate mesoderm.
- The medulla is derived from migrating cells of neural crest.

	RT	LT
Shape & site	Triangular	Semilunar
Hilum	Directed sup	Directed inf
Relations		
Inferolateral	Rt kidney (doesn't reach the hilum)	Lt kidney (reaches the hilum)
Med	Coeliac ganglion	Coeliac ganglion
Ant	Liver & IVC	Stomach (separated by lesser sac)
Post	Rt crus of diaphragm	Lt crus of diaphragm

Blood supply

Arterial

- Sup suprarenal A (of inf phrenic A)
- Middle suprarenal (of aorta)
- Inf suprarenal (of renal A)

Venous: suprarenal V (the Rt drains into IVC, the Lt drains into Lt renal)

- Histology of the suprarenal glands (Adrenal glands):

-They are two endocrine glands in contact with upper border of both kidneys.

-They are formed of:

- Stroma:

a) Capsule: Thick, covered with adipose C.T.

b) Trabeculae: Thin, descend from the capsule to divide the cortex into compartments.

c) Reticular C.T.: Present in the background ,stained with Ag.

- Parenchyma: It contains cortex& medulla.

I) CORTEX:

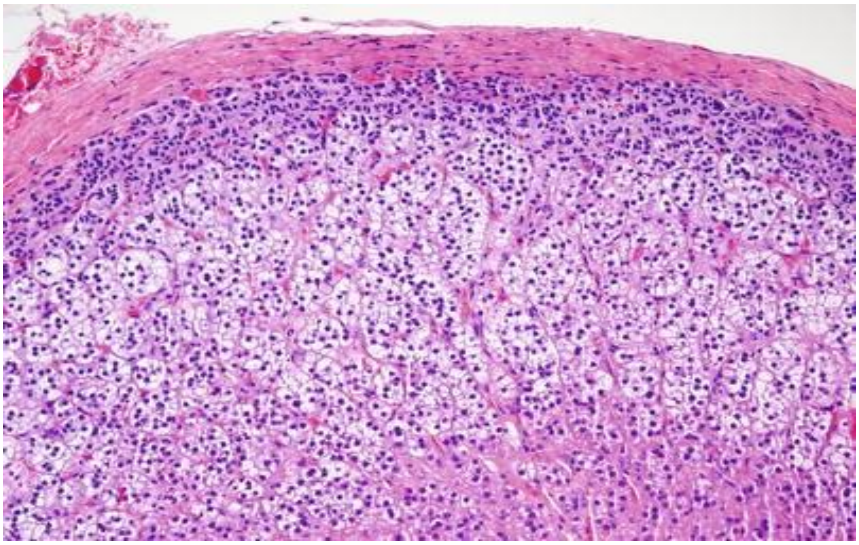
It is formed of three zones:

A) Zona glomerulosa:

- The narrowest zone just under the capsule.
- Formed of arched groups (Glomeruli)separated by fenestrated capillaries.
- The cells are columnar with basal oval nuclei &pale cytoplasm.
- E.M:Rich in mitochondria, golgi, sER& few fat droplets.
- Functions: secretes mineralocorticoids, mainly aldosterone, to regulate electrolytes & water balance under control of angiotensin II.

B) Zona fasciculata:

- The widest zone.
- Formed of narrow straight cords(fascicles) of polyhedral cells, with central rounded pale nucleus. Some cells have two nuclei.
- The cytoplasm is vacuolated, so they are called spongiocytes.
- E.M.: Mitochondria,golgi,sER,many fat droplets,vitamin C&cholesterol.
- Function: Secretion of glucocorticoids (cortisol), which regulate lipid,protein & carbohydrates metabolism under control of ACTH.



Suprarenal gland

C) Zona reticularis:

- The deepest zone.
- The cells are polyhedral with central rounded nuclei.
- The cytoplasm is acidophilic.

E.M.: Mitochondria, golgi, sER & few fat droplets.

Lipofuscin pigment is commonly seen in these cells.

- Function: Secretes androgens&small amounts of glucocorticoide under control of ACTH.

II) Medulla: It contains chromaffin cells& sympathetic nerve cells.

1) Chromaffin cells:

- They are modified sympathetic neurons.
- They are polyhedral cells, with basophilic granular cytoplasm, and central rounded pale nuclei.
- The granules are stained brown with chromium salts.
- E.M: mitochondria, golgi, rER& granules.
- There are two types of cells at ultrastructural level:

A) Adrenalin secreting cells: With homogeneous granules.

B) Noradrenalin secreting cells: With more dense granules &peripheral clear halo beneath the membrane.

2) Sympathetic nerve cells:

- They are stellate nerve cells scattered between chromaffin cells.
- They stimulate the secretory activity of chromaffin cells.

Functions of the medulla:

- **Actions:** Preparation for emergency physical activity. The adrenal medulla contributes only 10% of the total sympathetic nervous system response to stress and so, thus, is not vital
- **Receptors:** Adrenaline and noradrenaline act at adrenergic receptors
- **Stimuli:** Any stressful stimuli which activate the sympathetic nervous system (e.g. low blood pressure, haemorrhage, pain, low blood glucose, exercise, surgery, asphyxia)
- **Pathology:** Tumours of the adrenal medulla (phaeochromocytoma) constantly secrete catecholamines causing hypertension, tremor, anxiety, forceful heartbeat.

- Adrenal cortex hormones

- Cortisol

• Actions:

- It provides protection of the body in prolonged stress primarily to preserve glucose for the brain. Exerts widespread actions on many tissues
- Cortisol stimulates metabolism of:
  - Carbohydrates stimulates glucose production – may lead to hyperglycemia - opposes insulin actions – diabetogenic
  - Lipids stimulates lipolysis and ketogenesis (results in redistribution of fat to trunk if fatty acids are in excess)
  - Proteins stimulates gluconeogenesis

- Cardiovascular effects:

- Maintains the circulation via increased myocardial contraction; increases vascular tone
- Maintains plasma volume by preventing increased vascular permeability

- Skeletal muscle: Maintains ability to give sustained contractile responses

- **Ion control:** Promotes Na^+ retention and K^+ excretion
- **In the CNS:** Varied effects on mood and behaviour
- **Haemopoiesis:** Increases red blood cell production, so enhances oxygen-carrying capacity of blood

-Inflammatory response immune system: Immunosuppressive actions:

- Inhibits leucocyte translocation from blood to sites of tissue damage or infection
- Stimulates lymphocyte destruction
- Glucocorticoid selective drugs are used therapeutically to treat inflammatory diseases such as asthma and eczema (e.g. prednisone, betamethasone) but have some mineralocorticoid effects

- Reproduction and lactation: Inhibits, in part by inhibition of LH and PRL, release from the anterior pituitary gland (pregnancy is a nonessential metabolic drain on resources).

- Receptors: Glucocorticoid receptors (GR) are present in almost all cells. GRs are located in the cytoplasm of cells and migrate to the nucleus to regulate gene transcription when cortisol binds

- Control of output:

CRH (hypothalamus)----- ACTH (pituitary) ----- Cortisol (adrenal cortex)
Stress ----++++ seretion
Increase secretion at early morning and decrease at night

- Abnormal function:

- **Cortisol insufficiency—Addison's disease**
- **Cortisol excess—Cushing's syndrome**

- Aldosterone (regulation of body sodium and fluid volume)

• Receptors: Mineralocorticoid (MR) receptors are present in the nuclei of only a few cell types kidney collecting tubule epithelia, salivary and sweat glands

• Actions: In the kidney, aldosterone regulates ion transport in the kidney collecting tubules in order to stimulate reabsorption of Na+ in exchange for secretion of K^+, H^+, NH^{4+}. There is a 2h lag in the response to aldosterone as MR effects are via stimulating transcription of the Na/K ATPase protein. In salivary and sweat glands, aldosterone regulates ion transport to retain sodium

• Control of output: **The renin–angiotensin system**

-Abnormal function:

- **Hypoaldosteronism (in adrenal failure)** results in sodium loss, low blood volume, and low blood pressure
- **Hyperaldosteronism (Conn's syndrome)** results in excess sodium retention, water retention, and increased blood pressure.

*** Spironolactone (an aldosterone antagonist)** is used as an antihypertensive.

-Adrenal androgens (DHEA)

DHEA (dehydroepiandrosterone) is produced and released from the adrenal cortex zona reticularis. DHEA is a weak androgen which is a very minor component of adrenal secretions.

- Adrenal insuffi ciency

ACTH used in diagnosis of adrenal insufficiency (Addison's)

- Hyperaldosteronism:

- Definition

Excess production of the aldosterone hormone by the adrenal cortex.

- Causes

- Primary (cons syndrome)

- Adrenal cortical adenoma with autonomous production of aldosterone
- Primary adrenal cortical hyperplasia

- Secondary:

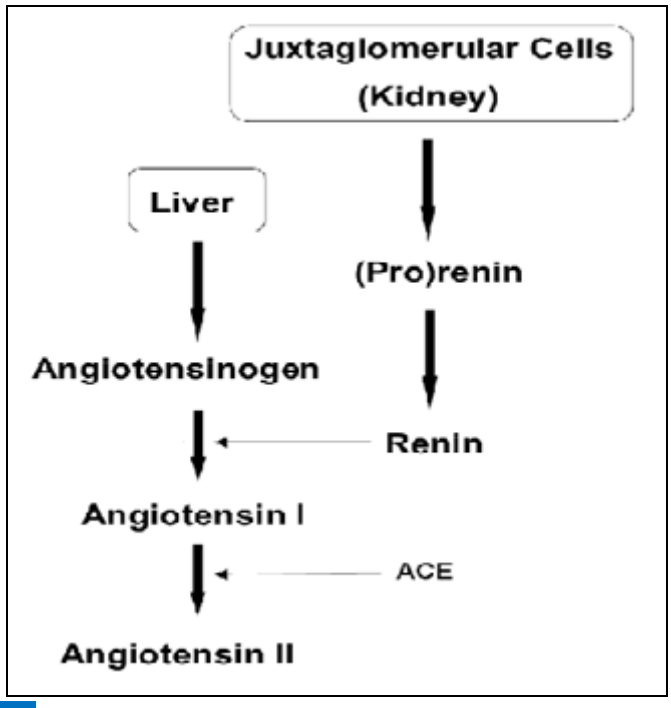
Normal response to activation of the renin–angiotensin system

- **Congestive heart failure**
- **Decreased renal perfusion (e.g. renal artery stenosis),** so the juxtaglomerular apparatus senses a lack of perfusion and produces more renin
- **Hypoalbuminaemia**-and, thus, reduced osmotic pressure within the vascular system, so reduced plasma volume and reduced renal perfusion
- **Pregnancy**-oestrogen induces increased plasma renin substrate.

Consequences

- **Sodium and water retention with potassium excretion leading to hypertension and hypokalaemia**
- **In primary hyperaldosteronism,** renin levels will be low (useful in the diagnostic process).

- Rennin angiotensin system

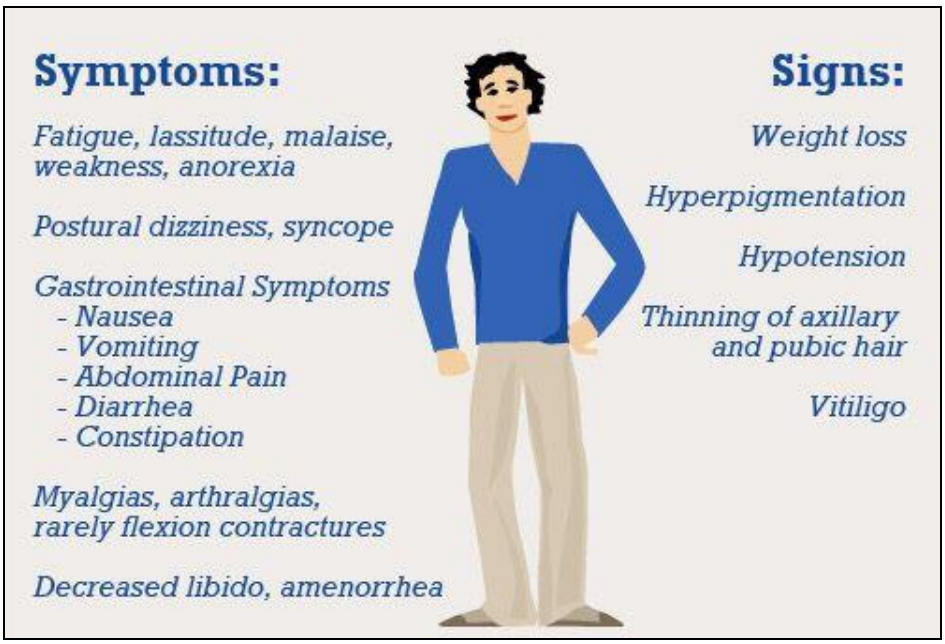


- Addison disease:

Addison's disease, (**primary adrenal insufficiency**) and **hypocortisism**, is a long-term endocrine disorder in which the adrenal glands do not produce enough steroid hormones.

- Causes:

- Decrease cortisol secretion and aldosterone is produced by autoimmune disease or TB
- Some medications
- Sepsis
- Bleeding in both adrenal glands
- Decreased ACTH



- Cushing's syndrome:

- Definition

Excess glucocorticoid hormones in the body, from whatever source.

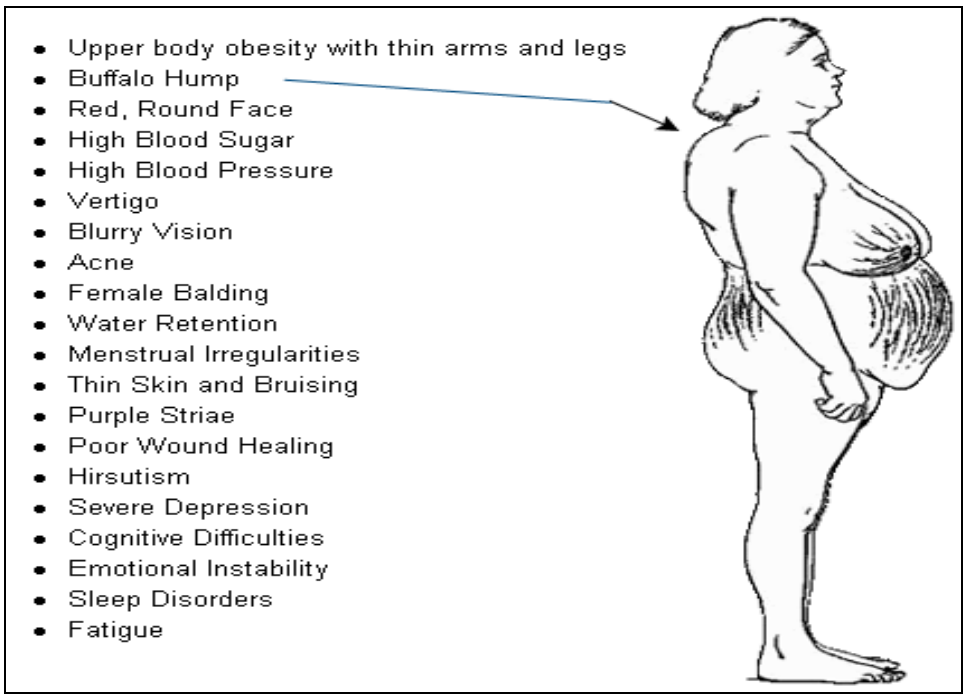
- Mechanisms

- Pituitary adenoma producing excess ACTH because it no longer responds to the normal feedback loop that inhibits ACTH release when cortisol level increases. The excess ACTH then stimulates the adrenal cortex to produce excess glucocorticoid hormones. This is also known as Cushing's disease
- Adenoma of the adrenal cortex which has become autonomous from the pituitary–adrenal feedback loop and produces excess glucocorticoids
- Excess ACTH administered by the medical profession or produced endogenously by a tumour (such as small cell lung cancer)
- Excess glucocorticoid steroids (e.g. prednisolone) administered by the medical profession. This was the most common mechanism for a few decades, since steroids were powerful drugs that could control severe allergic and inflammatory processes such as asthma or rheumatoid arthritis. Fortunately, more specific drugs are now available for some conditions, (e.g. asthma) and in others, 'steroid-sparing' immunosuppressants, (e.g. azathioprine) are used to reduce the risk or magnitude of Cushing's syndrome

- Complications of Cushing's syndrome

- Diabetes mellitus

- Proximal muscle weakness
- Decreased immunity to infections
- Osteoporosis
- Truncal obesity
- Hirsutism
- Depression, psychosis.



The stress response

- Stress:

- Defination : Any change or event that either disrupts, or threatens to disrupt, homeostasis to an unusual degree.

- Stressors

- Acute stressors:

- Extreme heat/cold
- Blood volume depletion by heavy bleeding, dehydration
- Hypoglycaemia
- Pain
- Surgical procedures
- Toxins from a bacterial infection
- Severe exercise, sleep deprivation

• Chronic stressors:

- Chronic infection, chronic pain
- Housing problems, marital problems
- Financial worries, difficulties at work.

- The stress response:

• The stress response is counter-homeostatic as:

- It raises blood pressure
- It raises blood sugar
- It raises ventilation.

• The purpose of these changes is to prepare the body to meet an emergency situation, and to allow him to survive this emergency, and return to normal homeostasis when the stress is no longer present

• It involves a short-term alarm reaction; and a more long-lasting resistance reaction.

- The acute alarm reaction

- The acute 'alarm reaction' (fight-or-flight) involves hypothalamic control by activation of:
  - • CNS outputs
  - • The sympathetic nervous system and adrenal medulla.
- The responses are immediate and mobilize the body's resources for immediate physical activity, and cause arousal of the cerebral cortex.

- The resistance response

If the stress is more sustained, more chronic responses occur to produce the resistance reaction. These involve :

- Slower results of the sympathetic stimulation
- Actions of various hormones that are more prolonged than those of the catecholamines.

* Sympathetic nerves stimulate juxtaglomerular cells of the kidney. This results in the production of angiotensin II which both causes vascular constriction and also stimulates mineralocorticoid (aldosterone) release which:
  - • Increases Na^+ reabsorption which causes water retention, maintains a high blood pressure, and counteracts fl uid loss
  - • Increases elimination (exchange) of H^+ ions (accumulate as a result of the increased catabolism).

*Increase release of glucocorticoids

* Hypothalamic TRH

Thyroid hormones increase the metabolic rate and the catabolism of glucose, fats, and proteins

* Hypothalamic GHRH

Increased liver breakdown of fats to fatty acids and glycerol

- • Increased liver conversion of glycogen to glucose.
- • By these means, the resistance reaction allows the body to continue fighting a stressor long after the effects of the acute alarm reaction. It produces the energy and circulatory changes required for the performance of strenuous tasks, fighting infection, avoiding fatal haemorrhage

- When the stress is prolonged

- • Within the hypothalamus, CRF, glucocorticoids, opioid peptides reduce GnRH secretion avoid risk of pregnancy and a further drain on metabolic resources
- • In the hippocampus, glucocorticoids act on glucocorticoid receptors to modify emotional reactions induce mild euphoria, diminishing the psychic effects of the stress.

- Chronic stress at different ages

- *In utero*: the stress of undernourishment leading to low birthweight is associated with a signifi cant increase in risk of hypertension, diabetes mellitus, and lower life expectancy
- Childhood: chronic stress in childhood is associated with retarded growth
- Old age: the morning peak of cortisol occurs earlier in the aged; the cortisol response to the stress of an operation is also prolonged.

The endocrine pancreas

- Structure: the islets of Langerhans

- The islets are diffusely distributed throughout the pancreas
- Islets comprise insulin cells (B cells), glucagon cells (A cells; somatostatin cells (D cells), and pancreatic polypeptide cells
- The endocrine pancreas regulates the availability of metabolic substrates.

- Plasma glucose concentrations

The 'normal' morning fasting blood glucose concentration is 4–5mM and rises up to 8mM after a meal.

- Hypoglycaemia (<3mM) causes: Dizziness, confusion, hunger, convulsions, coma; sympathetic activation
- Hyperglycaemia >8mM glucose causes osmotic effects; if >10 mM glucose is lost in urine with water (excess urine production = diabetes) thirst, abnormal glycation of proteins.

- Insulin:

- Synthesis

A protein hormone from the prohormone, proinsulin, cleaved to insulin + C peptide in secretory granules. Insulin comprises two chains linked by two S-S bonds; stored with zinc in granules.

- Mechanism of insulin secretion:

- Glucose enters the B cell (diffusion is facilitated by GLUT2)
- Metabolism of the glucose in the B cell produces ATP
- ATP closes ATP-dependent potassium channels present in the B cell membrane, which in turn depolarizes the B cell
- Depolarization causes Ca^{2+} entry; this in turn stimulates exocytosis of insulin
- Sulphonylurea drugs inhibit the ATP-dependent K^{+} channels and promote insulin release.

- Mechanism of insulin action:

- The insulin receptor is a tyrosine kinase-linked receptor
- Phosphorylation of insulin receptor substrate (IRS) proteins occurs which activates intracellular signalling cascades.

- Insulin promotes anabolism and controls use of metabolic substrates

- Acts to lower elevated plasma glucose
- Controls transport of glucose and amino acids into many types of cell
- Directs the use of glucose and amino acids and augments their oxidation to ATP
- Increases protein synthesis and inhibits proteolysis
- Supports growth and proliferation of many cell types.

- Diabetes mellitus :

Diabetes mellitus is, an incurable condition that is diagnosed as a chronic increase in blood glucose levels—hyperglycaemia. The condition is broadly divided into two types, depending on the underlying cause:

• Type 1 diabetes (formerly IDDM)

Is caused by an inability to synthesize sufficient insulin—the hormone responsible for stimulating uptake of glucose into cells. Insulin is usually synthesized in B cells of the islets of Langerhans in the pancreas, but they are destroyed by an autoimmune response early in the life of susceptible individuals (onset usually occurs before children reach 10 years of age).

The trigger for this response is believed to be due to an environmental stimulus in individuals with a genetic predisposition to the condition.

Although the child of a parent with type 1 diabetes is at increased risk of developing the disease, the risk is relatively small (<2% if the mother is affected, <6% if the father is affected) unless both parents have the disease, in which case genetic counselling should be sought.

• Type 2 diabetes (formerly NIDDM)

Includes a wide range of disorders that develop over many years, often later in life, ultimately leading to hyperglycaemia. In cases where a specific cause can be identified, reduced secretion of insulin or a reduction in the effectiveness of insulin to facilitate uptake of glucose into cells (so-called insulin resistance) is implicated. However, up to 98% of cases are 'idiopathic', meaning that no specifi c cause has been identified.

- Risk factors for diabetes

- Genetic factors
- An increasingly prominent risk factor for diabetes is obesity, probably due to down-regulation of insulin receptors in response to increased insulin production (hyperinsulinaemia).
- Gestational diabetes is a term relating to pregnant women who are diagnosed with hyperglycaemia during routine plasma glucose tests at about ~28 weeks gestation. Blood glucose levels typically return to normal within 6 weeks of birth, but the condition may be indicative of a predisposition to type 2 diabetes later in life for both mother and child. Babies of mothers with gestational diabetes are often born overweight because of the growth-stimulating effects of increased fetal insulin secretion in response to high glucose levels derived from the mother.

- Glucagon:

Peptide hormone that protects against a lack of metabolic substrates.

• Synthesis: Produced as prohormone, proglucagon, then cleaved to glucagons in secretory granules

• Produced: By A cells of the pancreatic islets

• Release: Increased in response to low plasma glucose.

• Actions: All in the liver (via Gs, cAMP); protects against

- Hypoglycaemia:

- When low plasma glucose
- When high amounts of protein ingested or when high demand for glucose (e.g. exercise).

- Effects in the liver depend on the concentration of glucagon in the plasma:

- Low amount of glucagons: Stimulates glycogenolysis
- Medium amount of glucagons: Stimulates gluconeogenesis
- High secretion of glucagons: Stimulates lipolysis, fatty acid oxidation, ketogenesis.

- Somatostatin:

Peptide hormone made in D cells of pancreas.

• Actions: Inhibits the secretion of both insulin and glucagons (paracrine action); role in the physiology of the islets is as yet uncertain.

- Other sites of hormone production

- Adipose tissue: Leptin
- Heart: Atrial nateuritic peptide
- Kidneys: - Erythropoietin
  - Renin angiotensin system

Adipose tissue: leptin

- It is produced in fat cells throughout the body
- Stimuli for its release: The accumulation of fat, correlates with body mass index ,& reflects the availability of metabolic substrates

• Actions:

- Acts on receptors in basal hypothalamus; inhibits neuropeptide Y action in hypothalamus and influences many other neurotransmitters involved in feeding behaviour
- Decreases appetite (signals satiety)
- Increases energy expenditure, sympathetic activity
- Decreases insulin secretion
- Mutations in leptin (ob) protein or receptor are a rare cause of human gross obesity; leptin resistance may be involved in human obesity

APUD Cells (DNES)

* They are **A**mine **P**recursor **U**ptake &**D**ecarboxylation cells.
* They can be stained with Ag,so called Argenaffin cells.
* They are derived from neuroectoderm,so they are called diffuse neuroendocrine system(DNES).
* Their secretions act as hormones or neurotransmitters.
* E.M: They have ribosomes,basal secretory granules or synaptic vesicles,rER.

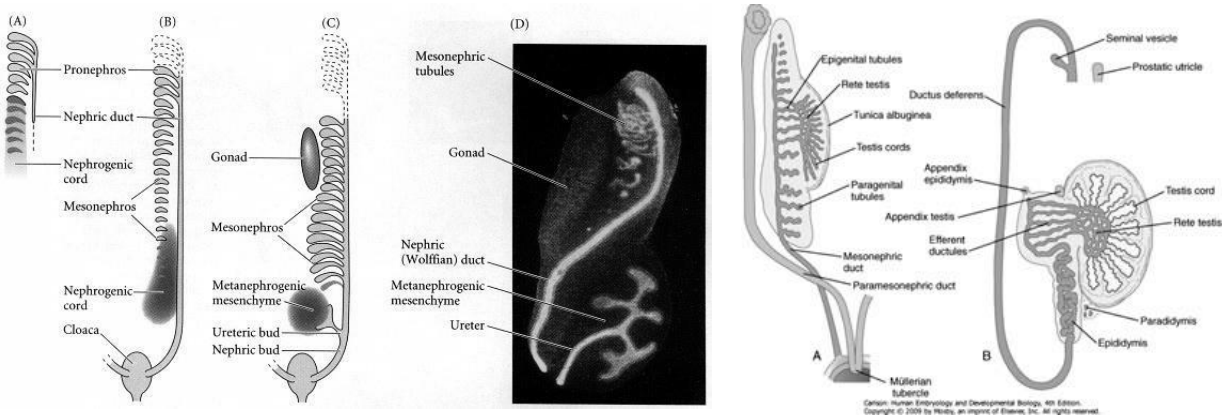
*** Sites:**

1) GIT: Stomach, intestine,pancreatic duct &common bile duct. They are called **enteroendocrine cells**:

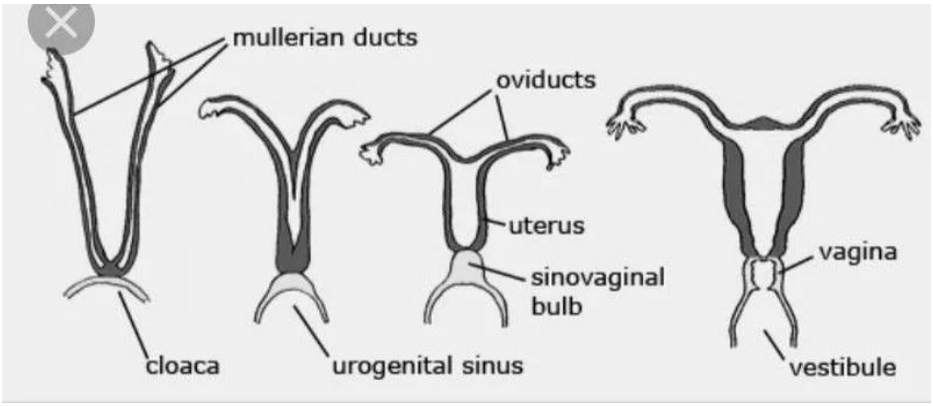
D-cells	Somatostatin
A cells	Glucagon
G-cells	Gastrin
S-cells	Secretin
N-cells	Neurotensin
E-cells	Endorphin

2) Respiratory tract: They secrete:
- Serotonin
- Calcitonin
- Catecholamines
- Enkephalins

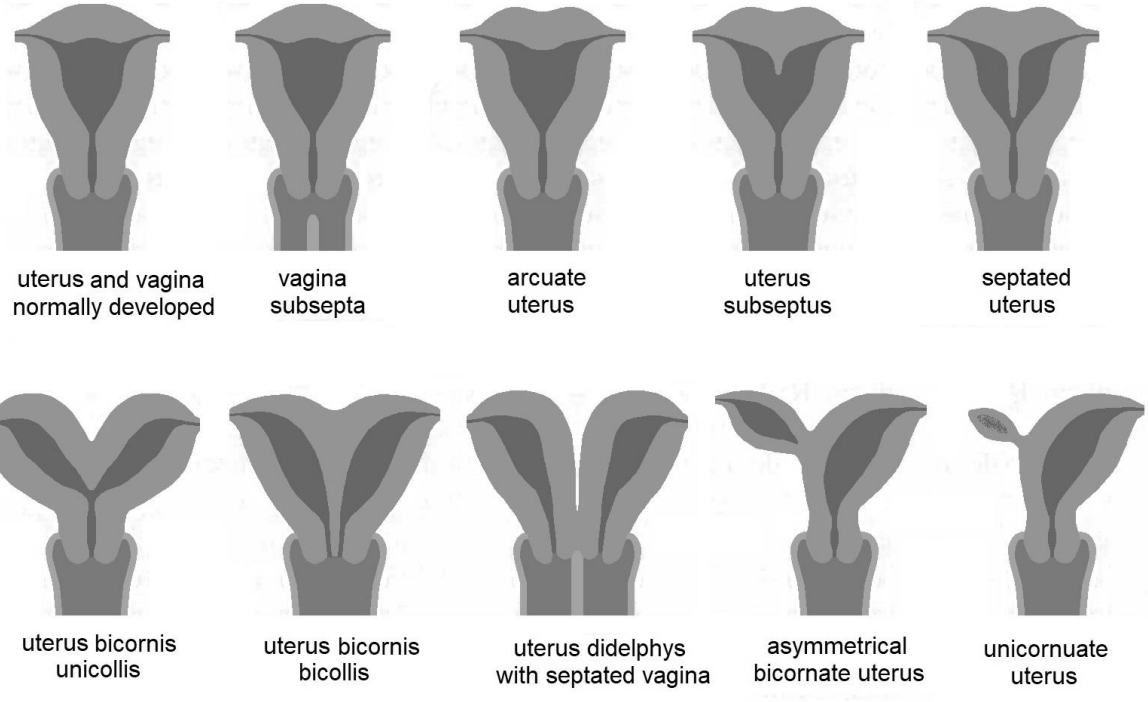
3) Suprarenal medulla: Chromaffin cells, which secrete catecholamines.
4)Pancreas: Islets of Langerhans
5)Thyroid gland: C-cells,which secrete calcitonin.
6)Pituitary gland: Corticotrophs, which secrete ACTH&MSH.
7)Kidney: Juxtaglomerular cells, which secrete renin.
8)Prostate: Prostatic endocrine paracrine cells (PEP),which secrete serotonin.
9)Skin: Merkles cells.



Mesonephros & mesonephric duct



Paramesonephric ducts



Uterine anomalies

IBiology / Duke / Medizzy / Wikemedia

EMBRYOLOGICAL PREVIEW OF THE GENITAL SYSTEM

Development of intermediate mesoderm: it passes into three successive stages called pronephros, mesonephros and metanephros (permenant kidney).

Pronephros: The intermediate mesoderm in the cervical region differentiates into pronephros (primitive kidney and ureter) with a formation of a pronephric duct which grows caudally to end in the primitive urogenital sinus (part of hind gut and future urinary bladder). This cervical kidney degenerates completely, the pronephric duct remains from the thoracic region downwards and is transformed into mesonephric duct.

Mesonephros: The intermediate mesoderm in the thoracic and upper lumbar region differentiates into mesonephros which attaches to the mesonephric duct. Its cranial part disappears, while the caudal part of mesonephros develops into efferent tubules of testis (in males) and degenerates in females (epoophoron and paroophoron).

The mesonephric (Wollfian) duct:

- The proximal part of mesonephric duct differentiates into epididymis, vas deferens, seminal vesicles and ejaculatory duct (in males) and degenerates in females.
- The caudal part of mesonephric duct gives rise to a ureteric bud and then differentiates into the trigone of urinary bladder, the upper ½ of prostatic urethra (in males) and the whole urethra (in females). It ends in the urogenital sinus which will complete the urinary bladder and urethra.

The paramesonephric (Mullerian) duct:

- It begins as an evagination from the neighboring mesodermal coelomic cells of lateral plate mesoderm into the intermediate mesoderm.
- The cranial 1/3 of the duct is vertical, the middle 1/3 is horizontal and the caudal 1/3 is vertical. The caudal 1/3 of the two paramesonephric ducts becomes in contact with each other.
- The paramesonephric ducts differentiates in females forming fallopian tubes, uterus and cervix.
- The caudal ends of the two ducts becomes in contact with the urogenital sinus. The urogenital sinus will form a thickened single cord called the vaginal plate which will grow cranially pushing the paramesonephric ducts. It will be canalized forming the vagina.
- The neighboring walls of the two ducts disappears forming a single cavity.
- The paramesonephric ducts degenerates in males forming the prostatic utricle.

Congenital anomalies:

Failure of fusion of the two paramesonephric ducts:

- ***Double uterus double cervix double vagina***
- ***Double uterus double cervix single vagina***
- ***Double uterus single cervix single vagina***
- ***Uterine septum***
- ***Arcuate uterus***

Failure of development of one paramesonephric duct (unicornuate uterus)

Atresia of the vagina: due to failure of vaginal canalization

Development of the external genitalia:

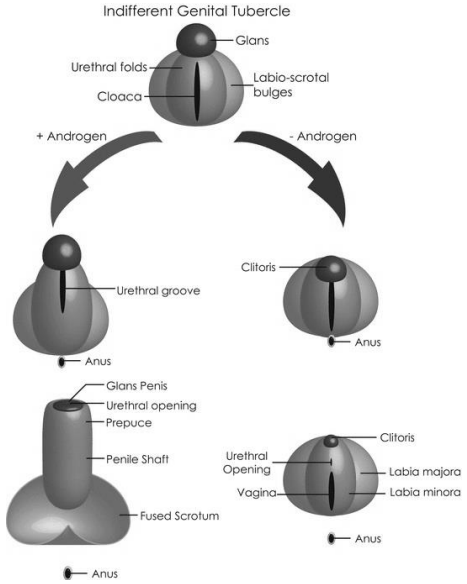
- The mesoderm ventral to the urogenital sinus grows forming genital tubercle (future penis or clitoris).
- The mesoderm at the side of the urogenital sinus forms genital swelling (future scrotum or Labium major).

Congenital anomalies: usually due to defect in hormones or its receptors

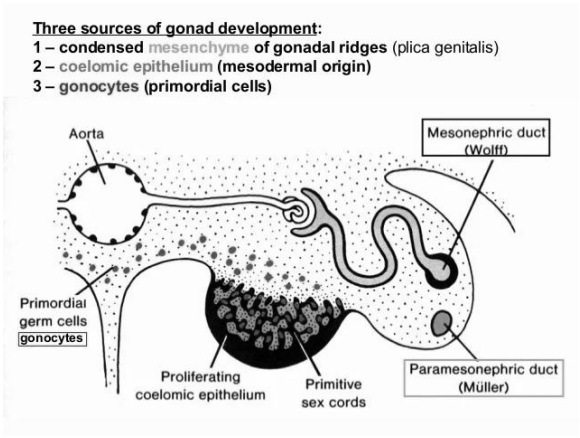
True Hermaphroditism (V. rare): the subject has the gonads and external genitalia of both sexes.

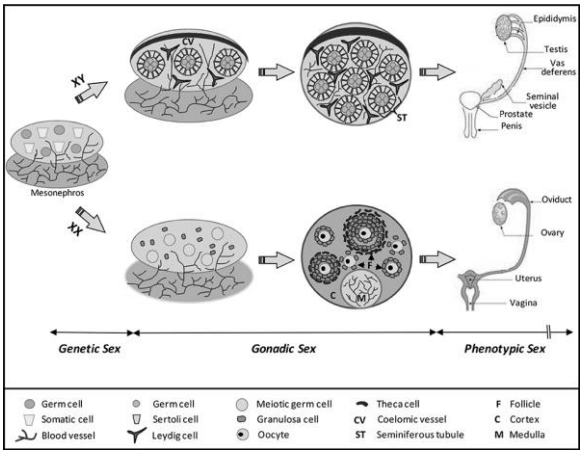
Pseudohermaphroditism: a subject with a gonad of a sex and external genitalia similar of the opposite sex

Ambiguous genitalia: The external genitalia is unclear whether it is for a male or a female.

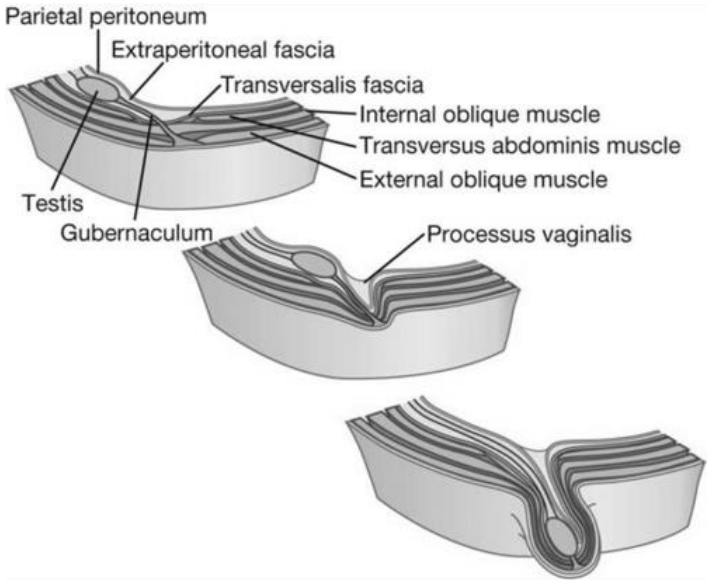


Genital tubercle & swelling





Gonads



Descend of testis

Springer link / fity club / Frontiersin / Quizlet

Development of the gonads: both gonads (testis & ovary) start as a thickening of the intermediate mesoderm at the level of mesonephros called genital ridge. The gonads are indifferent till the 6th week of development.

Development of the testis: the testis develops from 3 sources

The genital ridge differentiates into tunica albuginea of the testis & Leydig cells.

Sertoli cells are derived from cells originating from neighboring mesodermal coelomic cells of lateral plate mesoderm and penetrating the genital ridge

Spermatogonia are derived from endodermal cells from the caudal part of yolk sac which migrate to reach the genital ridge.

- The spermatogonia mix with Sertoli cells forming sex cords which remain solid till puberty when it canalize forming seminiferous tubules.

Descend of the testis:

- The testis development starts within the abdominal cavity. The spermatogenesis needs a temperature lower than the normal body temperature by 2-3°. Accordingly, the testis should migrate outside the abdominal cavity.
- The caudal part of the genital ridge forms a cord called Gubernaculum which traverses the muscles of the anterior abdominal wall (forming the inguinal canal) and drags the testis to the scrotum. The testis reaches the inguinal canal at the 7th month and enters the scrotum at birth.
- The testis pushes the different layers of ant abdominal wall through its way of descend forming layers of covering around it (coverings of spermatic cord and layers of scrotum).
- The testis drags its blood supply, nerves & lymphatics from abdomen to scrotum. These structures form the spermatic cord.

Congenital anomalies:

Sertoli only syndrome: failure of migration of Spermatogonia to the testis. The seminiferous tubules contain only Sertoli cells.

Undescended testis: The testis is present high along its normal course. If not treated rapidly, the spermatogonia will lose its ability to produce sperms.

Embryological development of the ovary: the ovary develops from 3 sources

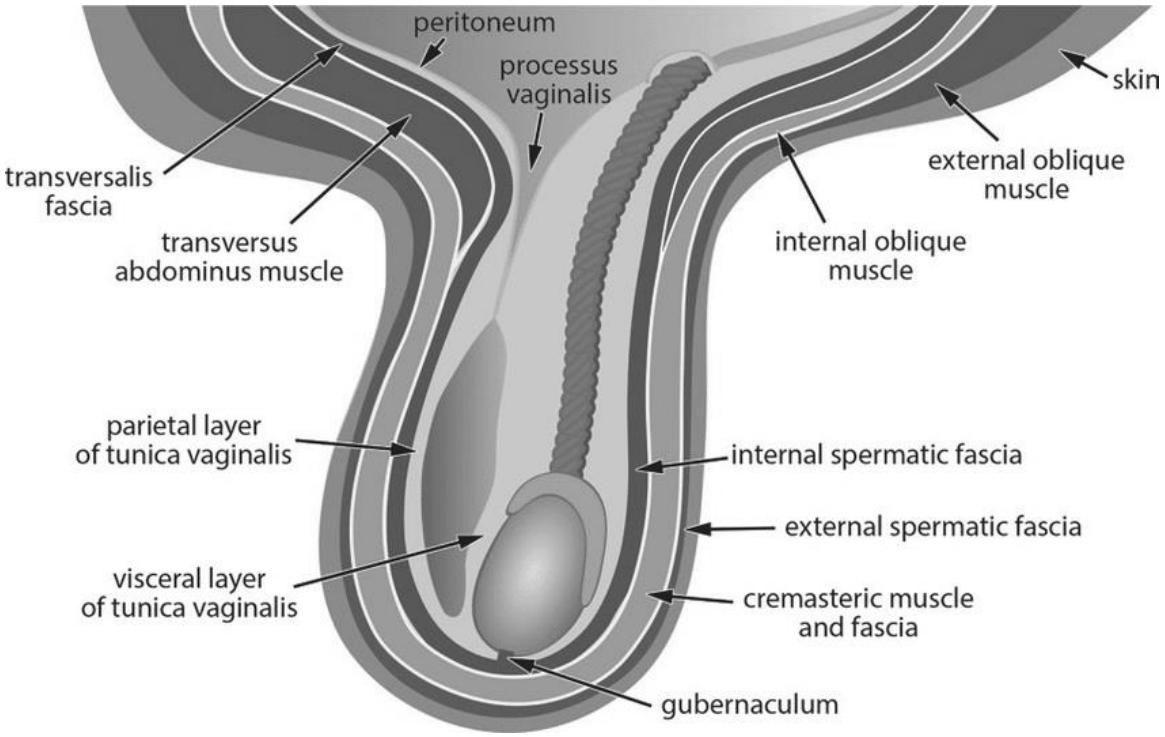
The genital ridge differentiates into the connective tissue of the ovaries.

Follicular cells are derived from cells originating from neighboring mesodermal coelomic cells of lateral plate mesoderm and penetrating the genital ridge

Oogonia are derived from endodermal cells from the caudal part of yolk sac which migrate to reach the genital ridge.

- The oogonia mix with follicular cells forming sex cords. which divides into separate follicles.
- The caudal part of the genital ridge forms a Gubernaculum which traverses the muscles of the anterior abdominal wall (forming the inguinal canal) reaching the labium major.
- The gubernaculum is attached to the uterotubal junction and is divided into 2 parts; cranial part between the ovary and the uterus which develops into round ligament of the uterus, and a caudal part between the uterus and labium major which develops into round ligament of uterus. Accordingly the ovary descends only to the side of uterus.

Congenital anomalies: ***Ovarian hypoplasia or dysgenesis:*** few or no germ cells are found in the ovaries.



Layers of scrotum

Researchgate

MALE GENITAL ORGANS

SCROTUM

Definition: skin fold suspended from ant abdominal wall. It is divided by incomplete septum into 2 compartments.

Layers of scrotum (from inside outwards):

Abdominal layer	Corresponding scrotal layer
Peritoneum (visceral & parietal)	Tunica vaginalis (visceral & parietal)
Fascia transversalis	Internal spermatic fascia
Transversus abdominis	---
Internal oblique	Cremasteric M & fascia
External oblique	External spermatic fascia
Deep membranous layer of fascia (Scarpa's fascia)	Continues as Dartos (Colle's) fascia
Superficial fatty layer	Replaced by Dartos M
Skin	Skin

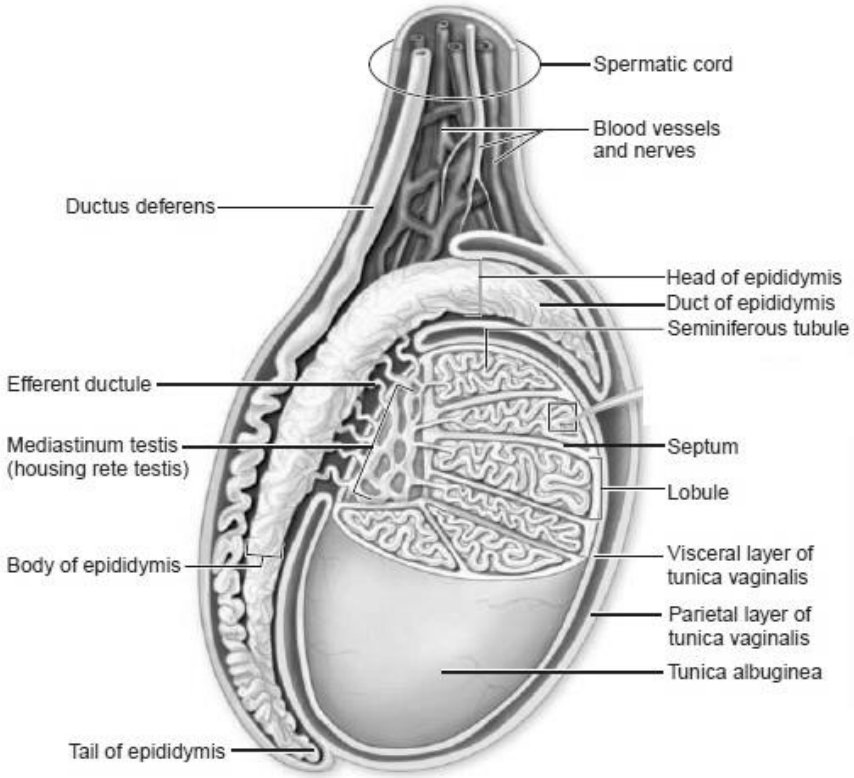
Applied anatomy: Infantile hydrocele: when the testis completes its descent, the peritoneal canal connecting peritoneum to tunica vaginalis degenerates (vestigue of processus vaginalis). Failure of degeneration leads to scrotal swelling which increases during standing and decreases by lying down.

Muscles of scrotum

Muscle	*Attachment*	*Action*	*NS*
Cremasteric (skeletal, nearly absent in females)	from internal oblique → U shaped loops → descend to scrotum → ascend back → pubic tubercle	• Elevates the testis (cremasteric reflex) • Tone → increase venous return of the testis	Genital branch of genitofemoral nerve (the Dartos M has only sympathetic innervation)
Dartos (smooth)	Between Dartos fascia & skin	Increase skin wrinkles → decrease surface area→ increase temperature	

Blood supply: branches from femoral, pudendal an inf epigastric As.

Lymphatic drainage: superficial inguinal lymph nodes.



Testis and epididymis

Quizlet

TESTIS

❖ It is the primary sexual organ of male. It measures 4X2X1 cm.
❖ It lies in the scrotum. The Lt is slightly lower than the Rt one.

Shape: has 2 surfaces (med and lat), 2 borders (ant and post) and 2 ends (sup and inf).

Internal structure:

- Each testis is divided into about 200 compartments.
- Each compartment contains about 2 seminiferous tubules (concerned with sperm formation).
- Each seminiferous tubule is about 2 feet (60 cm) long.
- The seminiferous tubules communicate forming rete testis.
- Rete testis gives rise to 15-20 efferent ductules which unite to form epididymis.
- The sperm formation takes about 2 months.

Coverings: (from inside outwards):

1) **Tunica albuginea:** thick fibrous capsule, firmly adherent to the testis. It is thicker posteriorly and forms mediastinum testis.
2) **Tunica vaginalis:** an extension from the peritoneum forming double layer of serous membrane (visceral and parietal).
3) **Scrotum**

Blood supply:

Arterial: mainly by testicular A (of abdominal aorta) and cremasteric A.

Venous: pampiniform plexus of Vs on the post wall of testis → 2-3 testicular Vs in inguinal canal → single testicular V at deep inguinal ring.

RT testicular V ends in IVC (in the same direction).

Lt testicular V ends in Lt renal V (perpendicular to its blood stream).

Applied anatomy: ***varicocele:*** dilated elongated tortuous Vs of the pampiniform plexus. It is more common on the Lt side because of:

- The direction of the venous drainage of the testicular Vs (perpendicular in Lt and in the same direction in the Rt).
- Longer Lt testicular V (lower Lt testis)
- The colon on the Lt side is usually filled with hard fecal matter causing pressure on Lt testicular V.

Lymphatic drainage: paraaortic lymph nodes.

- Histology of the testis

- It is a compound tubular, mixed gland present in the scrotum: Formed of: Glands & **Stroma:**

The capsule is formed of 3 coats:

(1) Tunica vaginalis:

It is a peritoneal fold formed of visceral & parietal layers. The 2 layers are lined with simple squamous epithelium.

(2) Tunica Albuginea:

A connective tissue thickened posteriorley---mediastinum testis, trabeculae arise from mediastinum testis ---divide testis into 250 lobules. Each lobule contains 1-4 Seminiferous tubules

(3) Tunica vasculosa:

Vascular C.T. lining tunica albuginea & the septa.

Reticular C.T.:

- Reticular cells & fibres.
- Present in the background. Stained with Ag.

Parenchyma:

(a) Exocrine part = Seminiferous tubules — sperms.

(b) Endocrine part = Leydig cells — testosterone.

The Seminiferous Tubules

- Convoluted tubules
- 50cm long & 200um in diameter.
- Lined with stratified epith = spermatogenic epith. formed of 2 types of cells: Sertoli cells and spermatogenic cells.

1] Sertoli cells:

L.M.

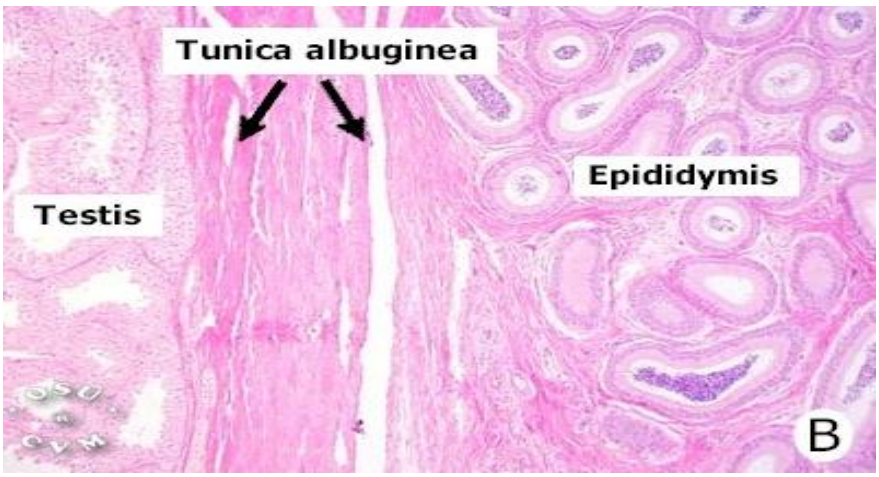
- Tall pyramidal cells, extend from the basement membrane to the lumen
- Have indistinct cell boundaries.
- Have pale oval or triangular basal nucleus with clear nucleolus.
- Have pale cytoplasm (rich in lipid droplets).

E. M.

- Rich in mit, G.A., S-ER, lysosomes, few r-ER, apical mirofilaments & microtubules & many fat droplets.
- Spermatogenic cells occupy pockets in the lateral wall of sertoli cells & head of sperms occupy apical infoldings in their cell membranes.
- The lateral borders of cells show tight junction at their basal parts to form the blood testis barrier.

Functions of Sertoli Cells:

1. Support & active translocation of spermatogenic cells towards the lumen.
2. Nutrition needed for differentiation of spermatogenic cells.
3. Phagocytic activity: digest residual bodies of spermiogenesis & degenerating germ cells.
4. Secrete testicular fluid which carry the non-motile sperms to the epididymis.
5. Secrete Androgen Binding protein (stimulated by FSH) which stimulates uptake & action of testosterone i.e. stimulates spermatogenesis.
6. Secrete Inhibin: inhibits FSH so inhibits spermatogenesis. Inhibin is used as male contraceptive.
7. Form the blood testis barrier.



- Testis & epididymis

The Blood Testis Barrier

It is formed by tight junctions between the basal parts of the adjacent Sertoli cells. It divides the seminferous tubule into 2 compartments:

1-Outer (basal) compartment: containing only spermatogonia.

2-Inner (adluminal) compartment: containing the rest of the spermatogenic cells So, tissue fluid formed by the capillaries in tunics vasculosa reach spermatogonia only & cannot reach other cells except through sertoli cells.

Functions of the blood testis barrier:

(1) Selection of nutrients & hormones for growth of the sperms.

(2) Protection of spermatogenic cells from any damaging substances present in the blood.

(3) Prevents auto- immune reactions: as it prevents antigens of differentiating sperms from reaching the blood.

(4) Protect spermatogenic cells from any circulating antisperm antibodies.

(5) Maintain high concentration of ABP (androgen binding proteins) in the adluminal compartment needed for spermatogenesis.

2] Spermatogenic cells:

(a) Spermatogonia: (12um)

Small cells with rounded nuclei that rest directly on the basement membrane, 2 types:

- Type A spermatogonia: - Dark
  - Pale

  - **Dark type A**: Dark nuclei & remain out of cycle (reserve cells).
  - **Pale type A**: Pale nuclei & act as stem cells.

  At puberty, they divide to give — type B.

- Type B spermatogonia:

  Larger cells with large darker nuclei they grow in size & give rise to 1ry spermatocytes.

(b) Primary spermatocytes:

Appear after puberty. The **largest cells (1 8um**) arranged .in 2 or 3 layers. Have large rounded nucleus with **diploid** Number of coiled **chromosomes (46**) each cell completes the first meiotic division to give 2ry spermatocyte

(c) Secondary spermatocytes:

Smaller cells with smaller nuclei. Have **haploid Number** of chromosomes **(23),** Difficult to be seen in sections as they rapidly enter 2nd meiotic division to give spermatids.

(d)spermatids:

Very small (8 um) cells with dark nuclei (**23chromosomes),** near the lumen. Each spermatid by **spermiogenesis** give mature sperm.

(e) Mature sperms:

60um long formed of: **Head** & **tail** (**neck**, **middle piece**, **principal piece** & **end piece)**.

- **Head**: **(5um**): Formed of condensed nucleus. Its anterior 2/3 is covered with head cap rich in hydrolytic enzymes.
- **Neck**: short segmen: Contains 2 centrioles.
- **Middle piece (5um**) beginning of flagellum (microtubules) surrounded by supporting fibres then mitochondria) sheath.
- **Principal piece (40um):** The flagellum surrounded by supporting fibres.
- **End piece** (**10um):** Only the flagellum

SUMMARY of spermatogenesis:

The process of formation of sperms takes about 64-70 days under control of FSH it includes 2 stages

1] Spermatocytogenesis:

Spermatogonia (20) mitosis----------Dark type A (reserve cells)

↓

Pale type A (stem cells)

↓ mitosis

Type B spermatogonia (2n)

↓ growth

1ry spermatocytes

↓ 1st meiotic division

2ry spermatocytes (1 n)

↓ 2nd meiotic division

Spermatids (1 n)

2] Spermiogenesis:

It is the change of spermatid into mature sperm by metamorphosis without cell division, it includes three phases:

1- Golgi phase: Golgi vesicles form acrosomal vesicles which fuse to form lone vesicle, centerioles migrateto the opposite pole.

2- Acrosomal phase: The nucleus becomes flat elongated and more condensed.

Acrosomal vesicle enlarged formed ----acrosomal capsurrounded by supporting fibers

Mitochondria aggregate spirally around the first part of flagellum --- middle piece where movement is generated.

3- Maturation phase:

Acrosomal cap enlarges to cover the anterior 2/3 of the nucleus---- head rich in hydrolytic enzymes to facilitate fertilization of ovum.

Excess cytoplasm pinch off as residual bodies, hagocytosed by Sertoli cells

Nucleus — head of sperm.

G.A —head cap. Centeriole-flagellum. Mitochondria — middle piece.

Factors Affecting Spermatogenesis

4 hormonal factors	4 non hormonal factors
1-LH	1-Temperature
2-FSH	2-Diet
3-Androgen	
4-Other hormones	

1- LH:

It stimulates the interstitial cells of leidig to secrete Testosterone.

2-FSH:

- Needed for late stages of spermatogenesis
- Needed for growth of testes
- Needed for growth of sertoli cells
- Stimulate the production of ABP (androgen binding protein)

3- Androgen (testosterone):

* Maturation of spermatids to spermatozoa
* It act on Sertoli cells causing development
* It is needed for maturation of sperms
* Needed development of germinal epithelium
* Needed for miosis

NB: The testosterone is kept in high concentration locally in the testes by:

1- Secretion of testosterone by leydig cells locally
2- Secretion of ABP by sertoli cells
3- Counter current mechanism (high amount of testosterone in vein ------diffuse to arterial blood ----reach testes
4- Other hormones:
   * Inhibin--- regulate secretion of FSH by anterior pituitary
   * Leptin----has a role in onset of puberty
   * Thyroxine—if decreased ---inhibit spermatogenesis

Non hormonal factors:

1-Temperature:

The optimum temperature for spermatogenesis is 32 – 35 degrees this is maintained by:

- Thin skin of scrotum
- Testes out side body
- No sub cutaneous fat
- Many sweat glands
- Counter current heat exchange between spermatic arteries & veins
- Dartos muscle---contract---pull testes near body---more warm in cold weather
- Relax--testes come far from the body--decrease temp.

2-Diet:

For normal function of TUBULES person should have BALANCED DIET which includes:

- Vitamin A , vitamin E , vitamin B, C

Factors that inhibit spermatogenesis:

1- Atomic radiation, or X ray large dose---irreversible damage of semeneferous tubules
2- O_2 lack & toxins

Function of testosterone :

1-during intra uterine life	2-on primary sex organs	3-on secondary sex organs	4-on secondary sex characters	5-metabolic effects
-Growth & development of wolfian duct to male urogenital sinus 2-development of male external genetalia 3-descend of testes into scrotum at 8th month of pregnancy by action of DHT	1-needed for spermatogenesis	1-essential for growth & maturation of -seminal vesicle -prostate 2-DHT needed for growth & maturation of external genetalia	1-Hair: -Beard appearance & mostache -increase body hair & decrease scalp hair. -appear of pubic hair 2-skin: -increase sebaceous glands--acne -thick skin 4-enlarge length of vocal cords – -deep low pitch voice 5-wide shoulder narrow pelvis & enlarged muscles 6-sexual desire &agression	1-retention of Na+, K+ 2-increase muscle bulk 3-deposit Ca++ in bones 4-increase growth spurt in puberty

Testicular function tests:

Semen analysis	Estimation of Gonadotropins in urine	Estimation of testosterone, FSH, LH in blood	Estimation of 17 ketosteroids in urine	Testicular biopsy
-volume:2-4ml/ejaculate -count 80-100 million/ml -PH—7.3-7.5 alkaline -specific gravity1028 -white color -60% of sperms should be motile	-pituitary gonadotropines secreted in urine -used to differentiate between PRIMARY)and SECONDARY hypog onadism 1-Primary hypogonadism—no testosterone –gonadotropines high 2-Secondary hypogonadism – decrease	-decrease testosterone level---with high gonadotropines (FSH) ----primary hypogonadism Decrease testosterone and decrease FSH, LH ---- hypogonadism due to pituitary or hypothalamic cause		Sample of testes is examined histologically -done in case of azospermia *if semeneferous tubules appear to have sperms---- azospermia due to duct obstruction *if semeneferous tubules does not contain sperms---testes can not form sperms

Oligospermia: Low sperm count ----below 50 million/ml---- Below 20 million -----infertility

Azospermia: Absent sperms in semen

Interstitial C.T.

The spaces between the seminiferous tubules contain loose c.t. rich in blood vessels, macrophages, fibroblasts, leydig cells & Myoid cells which are contractile cells, similar to smooth muscles to propel sperms towards ducts.

Interstitial cells of leydig: = [Endocrine part]

L.M.: Rounded cells with rounded nuclei & prominent nucleoli

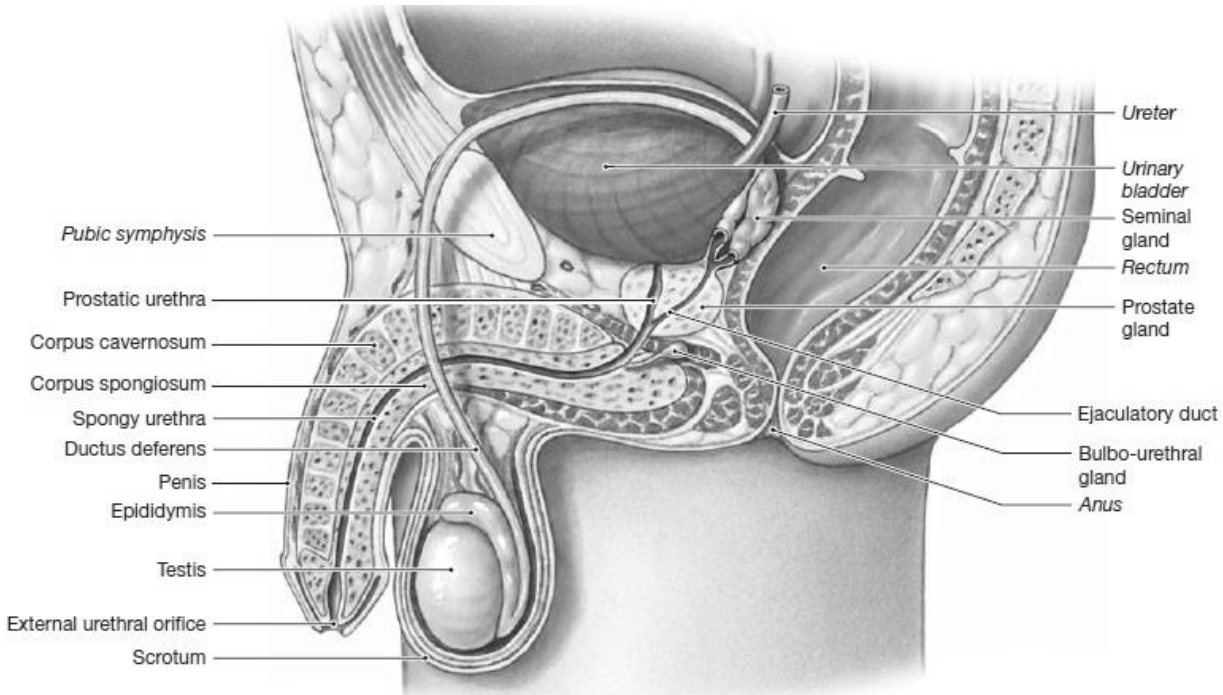
- Present in groups between the seminiferous tubules.
- Have acidophilic vacuolated cytoplasm

by EM: Rich in sER, mit, G.A. many fat droplets.

Function: Secrete testosterone

Capacitation:

- The process by which sperms acquire their full capacity for fertilization.
- Starts in the epididymis & become complete in the fallopian tube.



Male genital system

Martini

STRUCTURE OF MALE INTERNAL GENITAL ORGANS

EPIDIDYMIS

- ❖ It is 6 meters single coiled duct.
- ❖ It lies in the scrotum posterolateral to the testis separated from it by sinus of epididymis (space lined by tunica vaginalis).
- ❖ The sperms pass through epididymis in about 2 weeks, where it start to have its own movements.

Shape and parts: coma shape, divides into:

1) **Head:** attached to the upper pole of the testis
2) **Body**
3) **Tail:** attached to the lower pole of the testis continuous with the vas deference

- Histology of Genital ducts

- Intratesticular ducts

1- **Tubuli recti:** Straight tubules lined with sertoli cells

2- **Rete testis:** Branch and anastomose in the mediastinum testis lined with cuboidal cells

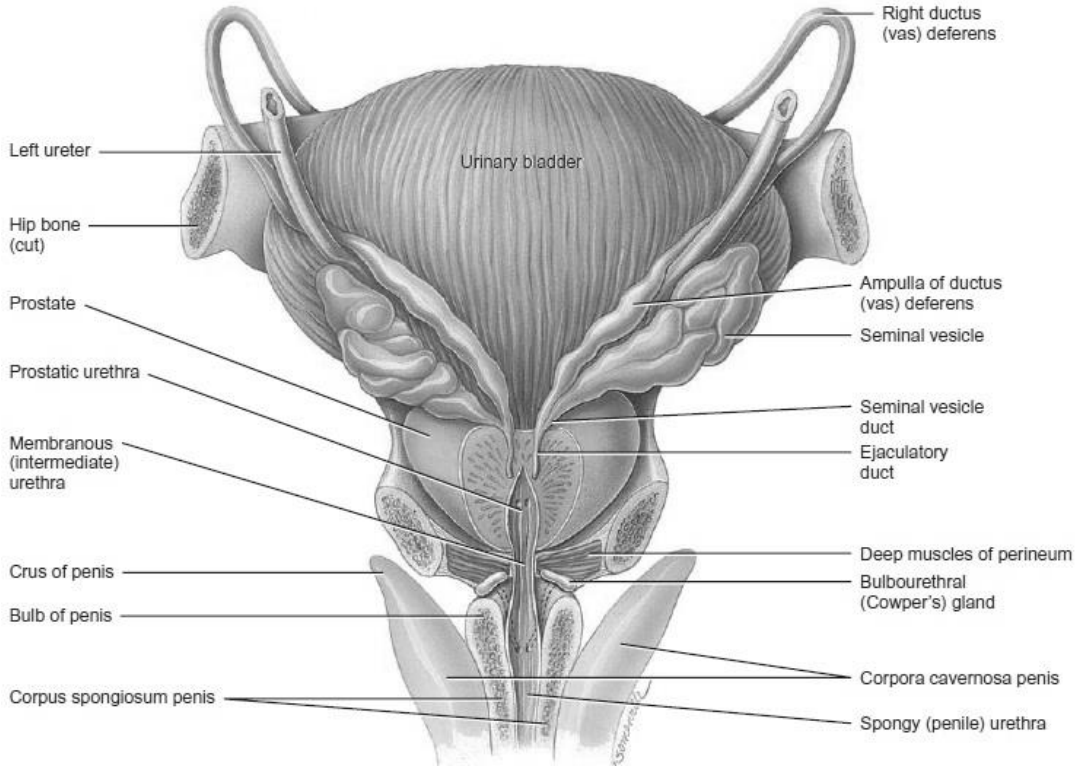
- Extratesticular ducts

1-Vasa efferentia:

10-20 tbules start in the testis but its main part is extratesticular and form the head of epidydimis, lined with festooned epithelium(tall columnar ciliated cells alternating with low columnar secretory cells.

2- Epididymis:

Formed of head (=vasa efferentia), body & tail. The body and tail contain a duct lined with pseudo stratified columnar ciliated epithelium with stereocilia (non- motile).



Vas deference, seminal vesicles, ejaculatory ducts and prostate (post view)

Tortora & Nielsen

VAS DEFERENCE

❖ It is 45 cm long duct. It has a thick muscular wall which can be felt by examination and narrow lumen.

Course & relations:

- It begins as a continuation of tail of epididymis.
- In the scrotum it ascends post to the testis.
- Passes through superficial inguinal ring, inguinal canal and deep inguinal ring.
- Passes behind the inf. epigastric a.
- In the pelvis: it crosses structures on the lat pelvic wall (external iliac vessels, umbilical A, lat umbilical ligament, obturator N and vessels and inf vesical A)
- Crosses above the end of the ureter then post to urinary bladder.
- Dilates to form ampulla of the vas med to seminal vesicle (for sperm storage).
- Ends behind the neck of the bladder by uniting with the seminal vesicle forming the ejaculatory duct.

- Histologically it is formed of:

- **Mucosa:** Ps. St. col. cil. epith. (with stereocilia) lost at its upper part.
  C.T. corium.
- **Musculosa:** Thick, 3 layers of smooth muscles inner long; middle circ., & outer long.
- **Adventitia**: Loose C.T.

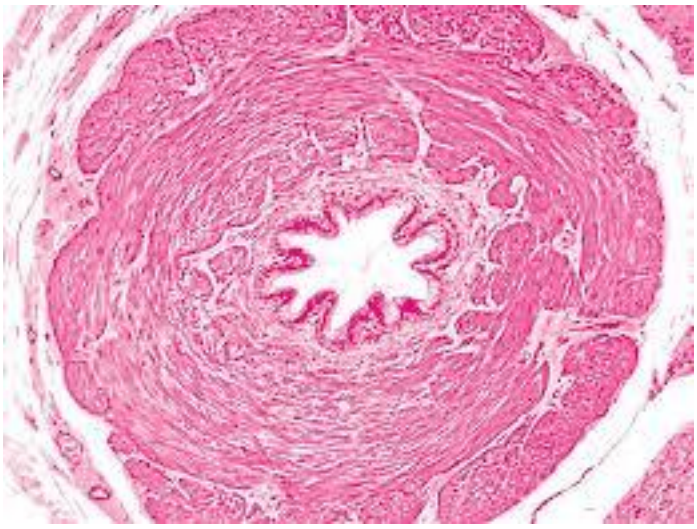


Fig (2): Vasdeferens

SPERMATIC CORD

- ❖ It is a sheath formed of extensions of anterior abdominal wall extending from inguinal canal to the testis
- ❖ It contains the vas deference, arteries, veins, lymphatics and nerves of the testis.

Coverings: (from inside outwards):

1) **Internal spermatic fascia** (from fascia transversalis)
2) **Cremasteric muscle and fascia** (from int oblique)
3) **External spermatic fascia** (from ext oblique so it covers it only outside the inguinal canal)

Contents:

1) **Vas deference**
2) **Vestigue (remnant) of processus vaginalis**
3) **Arteries:**
   - ***a)*** ***Testicular A*** (of aorta)
   - ***b)*** ***A to the vas*** (of inf vesical)
   - ***c)*** ***Cremasteric A*** (of inf epigastric)
4) **Pampiniform plexus of veins**
5) **Nerves:**
   - ***a)*** ***Sympathetic fibers*** (form testicular plexus around testicular A)
   - ***b)*** ***Parasympathetic fibers*** (to the vas)
   - ***c)*** ***Genital branch of genitofemoral N.***
6) **Lymphatics:** draining the testis to paraaortic lymph nodes.

SEMINAL VESICLES

- ❖ Paired inverted pear shaped male sexual gland formed coiled duct (6-8 inches)
- ❖ Its base is related to the ureter and medially related to the vas deference.
- ❖ It is responsible for about 70% of semen volume.
- ❖ The seminal vesicles secrete fructose which is the nutrient for the sperms.

- Histology:

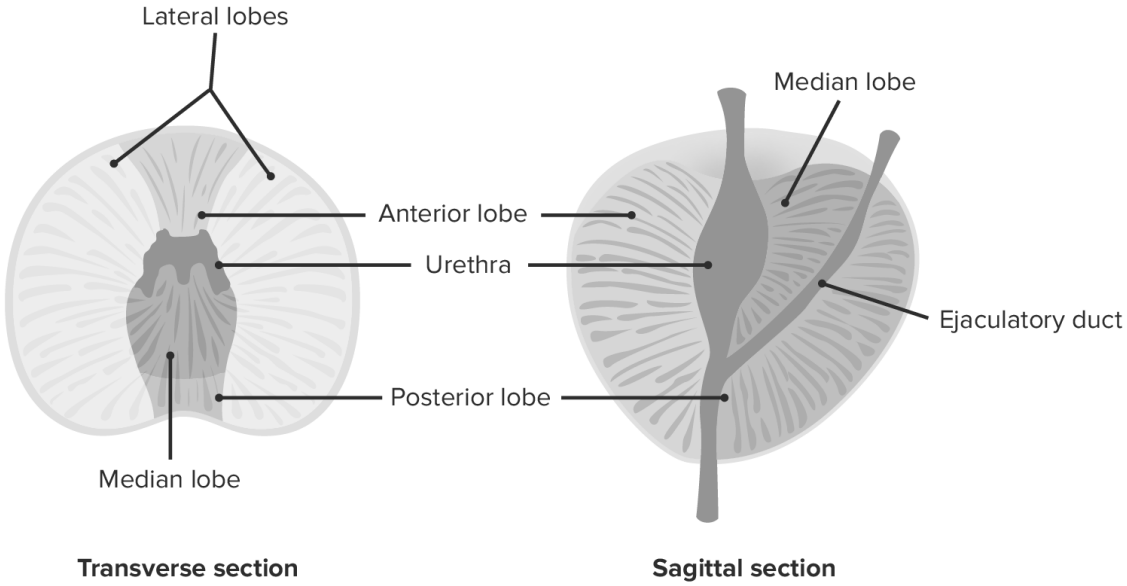
- Each gland is formed of mucosa, musculosa and adventitia.
- **Mucosa:** Highly folded formed of;
  a. Epithelial lining: Pseudostratified columnar epithelium.
  b. Lamina propria is a thin layer of fibroelastic C.T.
- **Musculosa:** Thin formed of inner circular and outer longitudinal smooth muscle.
- **Adventitia:** Formed of fibroelastic c.t.
- **Functions:**
  1. Add sperm-activating substances, such as fructose, citrate, proteins, and prostaglandins to seminal fluid.
  2. Provides bulk of seminal fluid (70%).

EJACULATORY DUCT

- ❖ Its apex unites with the ampulla of vas to form ejaculatory duct.
- ❖ It is 1 inch duct formed by union of ampulla of vas and seminal vesicle.
- ❖ It passes between the median and lat lobes of the prostate to opens in prostatic urethra (at seminal colliculus).

- Histology:

- Each is about 2 cm long, formed by union of the ductus deferens and the duct of the seminal vesicle. ***(fig.34)***
- The two ducts pierces the prostate to open on the seminal colliculus of the prostatic urethra.
  - It is one cm long formed by fusion of the ampulla of the vas with the duct of seminal vesicle.
  - Opens in the prostatic urethra
  - Lined with pseudo stratified columnar epithelium (no muscles)



Lobes of the prostate

Tortora & Nielsen / slide share

PROSTATE

- ❖ It is a single inverted cone male sexual gland.
- ❖ It secretes its product directly in the prostatic urethra.

Shape and relations:

Sup: related to urinary bladder, the base of the prostate surrounds the upper part of urethra which traverses it from base to apex nearer to its ant aspect.
Inf: the apex rests on the pelvic fascia (roof of the deep perineal pouch).
Ant: symphysis pubis and retropubic fat.
Post: rectum & rectovesical fascia.
Lat: levator prostatae.

Coverings:

True fibromuscular capsule: firmly adherent to the gland.
False fibrous sheath: formed by pelvic fascia and contains prostatic plexus of Vs.

Lobes:

Median lobe: post to the urethra & between the 2 ejaculatory ducts.
2 Lat lobes: lat to the urethra
Post lobe: connecting the 2 lat lobes post to urethra and inf to ejaculatory ducts.
Ant lobe (isthmus): fibromuscular band (no glandular tissue) connecting the 2 lat lobes ant to the urethra.

Blood supply:

Arterial: inf vesical and middle rectal As.
Venous: ***prostatic venous plexus:*** embedded in the false capsule, receives deep dorsal vein of penis and drains into internal iliac V. It is connected to vertebral plexus of veins (cancer prostate commonly spread to vertebral column).

Lymph drainage: internal iliac and external iliac lymph nodes.

Age changes:

- At birth it is just ducts.
- At puberty the hormones cause sudden increase in follicles.
- >50 years it shows benign hypertrophy. Usually the median lobe enlarges post to the bladder stretching the trigone (uvula vasica). Enlargement of the gland may also cause obstruction to the urethra.

- Histological structure of prostate

The gland consisted of stroma & parenchyma.

- Stroma:

1 - Capsule: The capsule is thick & fibromuscular.
2- Trabeculae: They arise from the under surface of the capsule dividing the gland into lobes & lobules. They are thick & fibromuscular.
3- Reticular network: Formed of reticular cells & fibers in the background, only demonstrated by Ag.

- Parenchyma:-

The prostate is formed of about 30-50 tubulo-alveolar glands, arranged in three concentric groups around the prostatic urethra:-

1- **PERIPHERAL LAYER (Main group):** About 70% of the glandular tissue. They give their secretions by means of ducts that open into prostatic sinuses on the posterior wall of the urethra.

2- SUBMUCOSAL LAYER: The middle zone, formed of medium sized acini that open by ducts into the prostatic sinuses.

3- MUCOSAL LAYER: In the central zone of the gland around the urethra. It is formed of small acini that secrete directly into the urethra.

- PROSTATIC ACINI are generally lined with columnar epithelium but some acini are lined with cuboidal, or pseudostratified columnar epithelium depending on level of testosterone. By E.M., the lining cells have well devloped rER. Golgi apparatus & mitochondria. Some acini especially in old contain prostatic concretion **(corpora amylacea)** which are dried secretion (usually calcified)

- FUNCTIONS OF PROSTATE:

1- Secretion of thin milky fluid rich in citric acid,fibrinolysin that liquefy the semen, acid phosphatase enzyme & minimal amount of Prostatic Specific Antigen (PSA).

2- It gives the semen its characteristic smell.

- CLINICAL NOTTES:

Senile prostate: It is a case accompanied by hyperplasia of acini of mucosal layer & leading to — difficulty in micturition (as this group is around the urethra).

Prostatic carcinoma: It usually starts in the peripheral layer of prostate , does not affect micturition except in late stages &, it may be accompanied by a high level of PSA

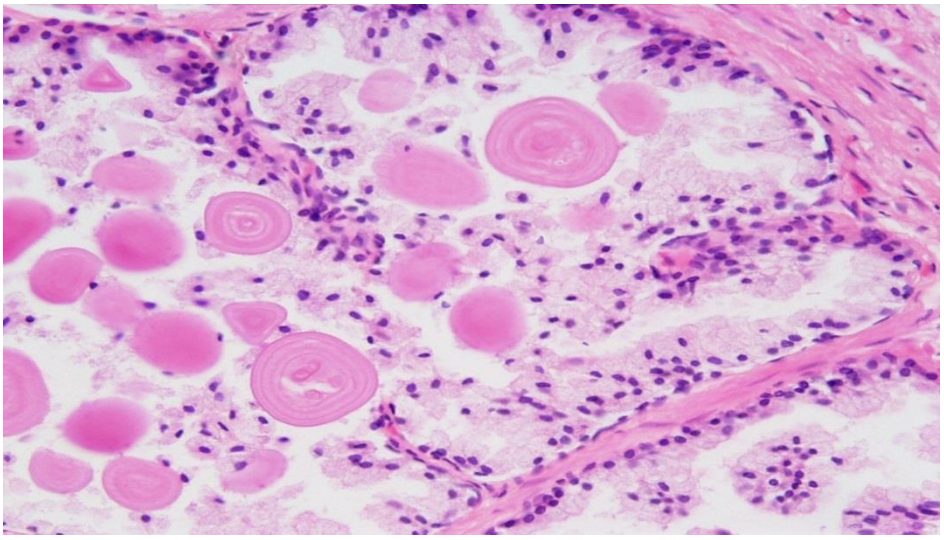


Fig (3): Corpora amylacea

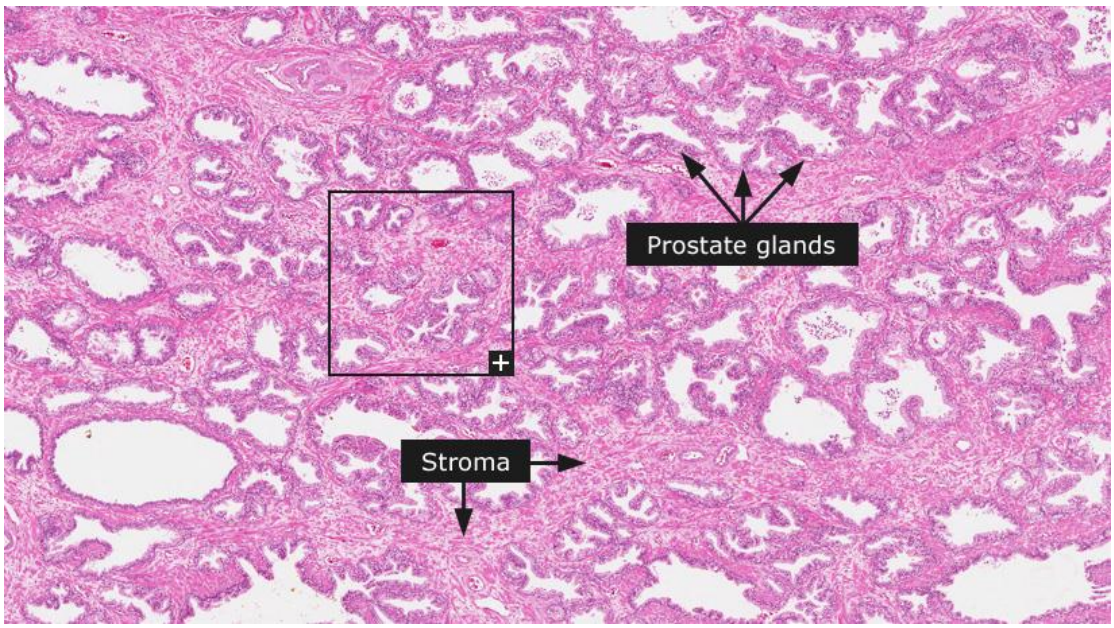


Fig (4): Prostate

BULBOURETHRAL GLANDS

- ❖ It is found at the sides of urethra inferior to prostate.
- ❖ It secretes mucoid secretion in the urethra.

Histology

- Formed of:

1. **Stroma:**

Thin C,T, capsule and Septa containing Skeletal and smooth muscle

2. Parenchyma:

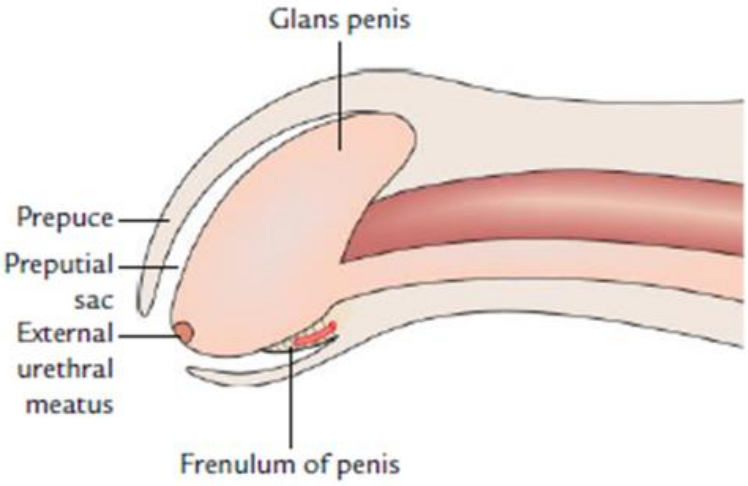
- Tubuloalveolar glands lined with mucus-secreting simple cuboidal or columnar epithelium.
- Ducts unite to form main duct lined by stratified columnar epithelium.

- Function: The secreted mucus is clear and acts as a lubricant.

Gland	Lining epithelium	Muscle
Prostate	Simple columnar but may differ according to activity.	Smooth muscle in capsule and septa.
Seminal vesicle	Pseudostratified columnar but may differ according to activity.	Smooth muscle arranged as Inner circular and outer longitudinal.
Bulbourethral gland	Simple cuboidal or columnar	Smooth and skeletal m

PENIS

- It is the male organ of copulation.
- It is formed of 3 cylindrical bodies; 2 corpora cavernosa formed of erectile tissue and a corpus spongiosum formed of spongy tissue & contains urethra.



- Histology:

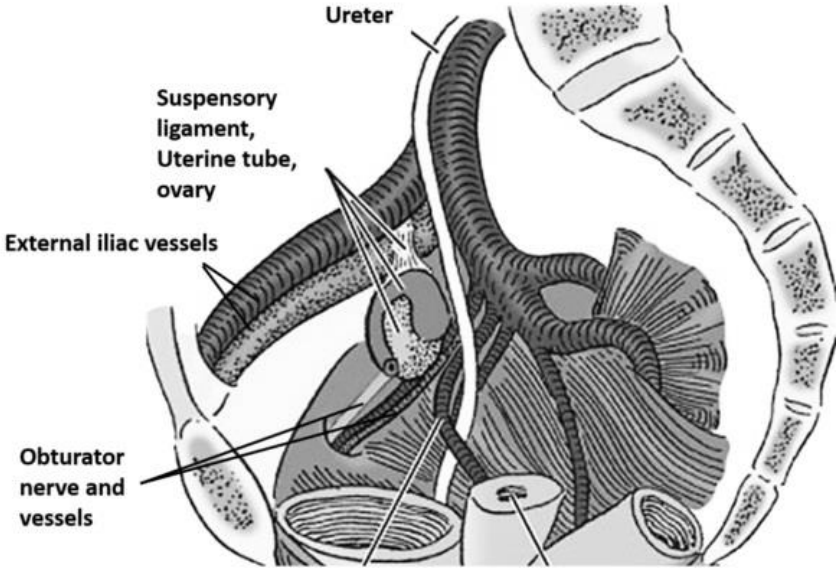
- Covered with skin with no subcutaneous fat with hairs only at it's root.
- Formed of erectile tissue in the form of: 2 corpora cavernosa. & a corpus spongiosum.
- Each corpus is formed of blood spaces blood
- Separated by c.t., smooth- muscles and elastic fibres.
- The 3 corpora are surrounded by tunica albuginea, fascia penis then skin.
- The 2 corpora covernosa are separated by incomplete septum.
- Corpus spongiosum contains the penile part of urethra.

Fig (6): Penis

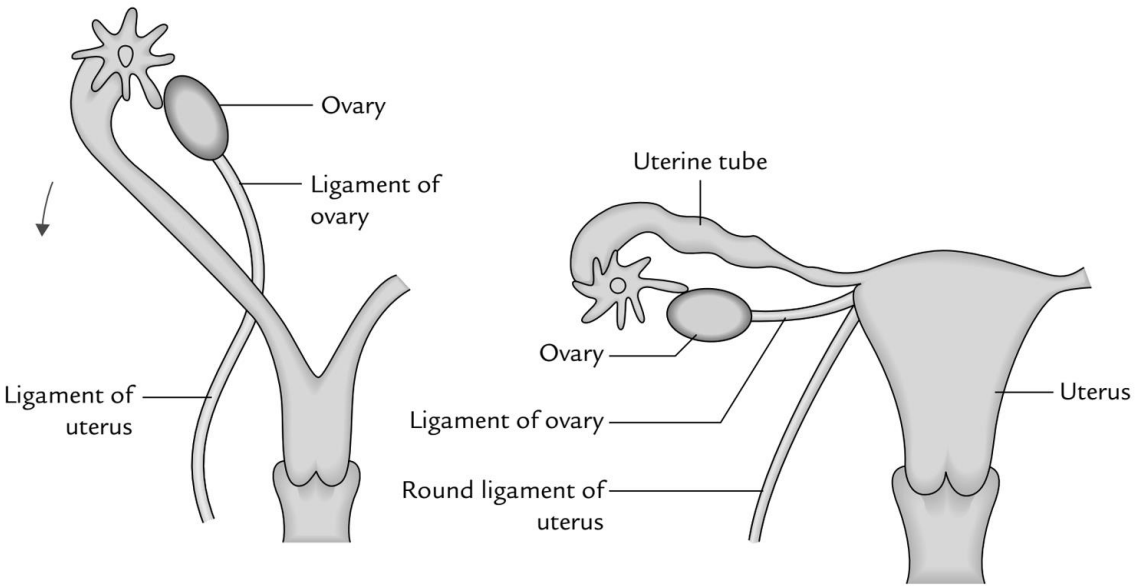
- Female genital System

The female genital system is composed of:

1. **Primary sex organs: 2 ovaries which have both exocrine (production of oocytes) and endocrine (secretion of female hormones) functions.**
2. **Secondary sex organs:**
   - **2** fallopian tubes.
   - Uterus.
   - Vagina.
   - External genitalia.
   - 2 mammary glands.



Ovarian fossa



Round ligament of the ovary and round ligament of the uterus

Anatomy QA / Slide share

OVARIES

Shape and position:

- Almond shape, 3 X 1.5 X 1 cm
- It is smooth prepubertal and shows irregular surface post pubertal
- It lies vertical in nullipara and horizontal in multipara (the sup pole becomes lat)

Parts and relations:

Sup (tubal) end: related to the fimbriae of the uterine tube. and is attached by suspensory ligament of the ovary to side wall of the pelvis.

Inf (uterine) end: attached by round ligament of the ovary to the uterus.

Ant border: attached by mesovarium to the upper surface of the broad ligament.

Post border: related to the uterine tube.

Lat surface: related to ovarian fossa (containing umbilical A, obturator N and vessels, ureter and internal iliac vessels).

Med surface: is related to the uterine tube.

- The uterine tube surrounds the sup, post and med aspects of the ovary.

Peritoneal coverings: It is completely covered with peritoneum except the site of the entrance of ovarian vessels (hilum of the ovary).

Peritoneal folds: mesovarium and suspensory ligament of the ovary.

Ligaments of the Ovary:

Suspensory ligament of the ovary: between the ovary and lat pelvic wall. It contains ovarian vessels.

Mesovarium: between the ovary and the sup surface of broad ligament. It contains ovarian vessels.

Round ligament of the ovary: between the inf end of ovary and the uterus.

Blood Supply:

Arterial: ***Ovarian A.***

- It is a branch of abdominal aorta
- It passes through the suspensory ligament of the ovary, then through the mesovarium
- It ends by anastomosing with the uterine A
- It supplies the ovary and lat part of uterine tube

Venous: pampiniform plexus → ovarian V. In the Rt side it ends in IVC, in the Lt side it ends in Lt renal V.

Lymphatic drainage: lat aortic lymph nodes.

- Histology:

- **Tunica albuginea is a layer of dense connective tissue under the germinal epithelium which is responsible for the whitish color of the ovary.**
- Underneath the tunica albuginea. 2 zones can be seen:

I. Outer cortex: Where ovarian follicles are present in the connective tissue stroma formed of spindle-shaped fibroblasts.

2. Inner medulla: Containing many blood vessels within a loose connective tissue.

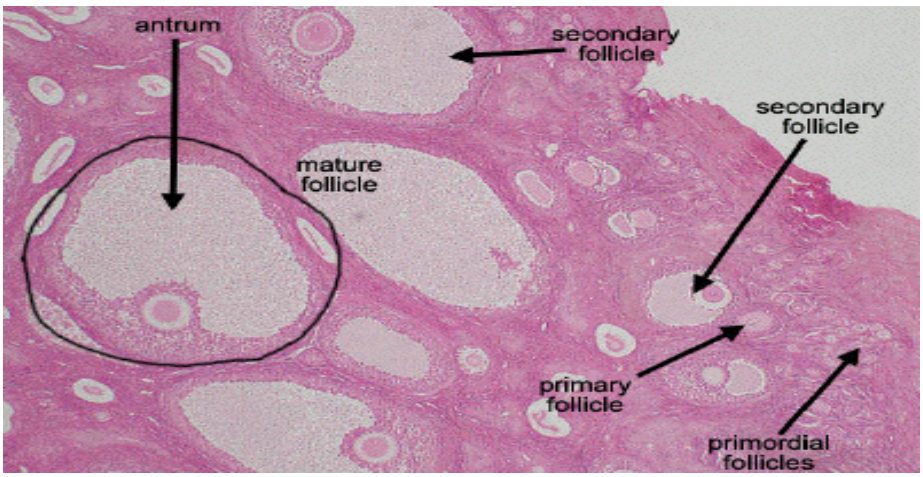


Fig (1): Ovary with ovarian follicles

- Ovarian Follicles

1. Primordial follicles:

- Contain **primary oocyte (25um)** arrested in the prophase of first meiotic division.
- Follicular cells form a simple squamous epithelium around the oocyte
- Is the only follicle present until puberty.

2. Primary follicles:

- Develop under the effect of **FSH**. **2 types**;

I - Unilaminar primary follicle

- Contains **a primary oocyte (40um).**
- Follicular cells form a simple cuboidal or columnar epithelium around the oocyte.

II - Multilaminar primary follicle:

- Contains **a primary oocyte (50um).**
- **Follicular cells** form a stratified epithelium around the oocyte called granulosa cells. The innermost layer is formed of columnar cells called **corona radiata.**
- **Zona pellucida** formed by both the oocyte and adjacent follicular cells, is a thick glycoprotein band surrounding the oocyte.
- **Theca folliculi**, a layer located outside the basement membrane is formed by the differentiation of the surrounding stromal cells. It is formed of 2 layers, cellular theca interna and fibrous theca externa.
- **Follicular fluid** secreted by granulosa cells accumulates in antral spaces between them.

3. Secondary follicle:

- Contains a **primary oocyte (120um).**
- Multiple antral spaces eventually coalesce to form a single antrum and the oocyte is pushed to one side.
- Usually only a single secondary follicle progresses to the mature follicle stage.

4. Mature Graafian follicle:

- For further maturation both FSH and LH are needed.
- The follicle is about 2 cm in diameter and bulges on the surface of the ovary.

- It is formed of:
  - i. **Primary oocyte** that completes Meiosis I with the formation of a **secondary oocyte** and first polar body just before ovulation.
  - ii. **Zona pellucida:** Glycoprotein layer.
  - iii. **Corona radiata:** Columnar cells surrounding the oocyte. They send tiny processes through zona pellucida to make contact with microvilli arising from oocyte through gap junctions.
  - iv. **Cumulus oophorus:** Group of granulosa cells surrounding corona radiate & connecting it to the granulosa cells.
  - v. **Granulosa cells:** 3-4 layers of polyhedral cells lining the follicular cavity.
  - vi. **Thick basement membrane.**
  - vii. **Theca interna:** Formed of cells that secrete androgen which is converted to estrogen by aromatase enzyme secreted by granulosa. cells.
    By EM, they show abundant sER, mitochondria and numerous lipid droplets. (steroid secreting cell).
  - viii. **Theca externa:** Formed of flattened connective tissue cells.

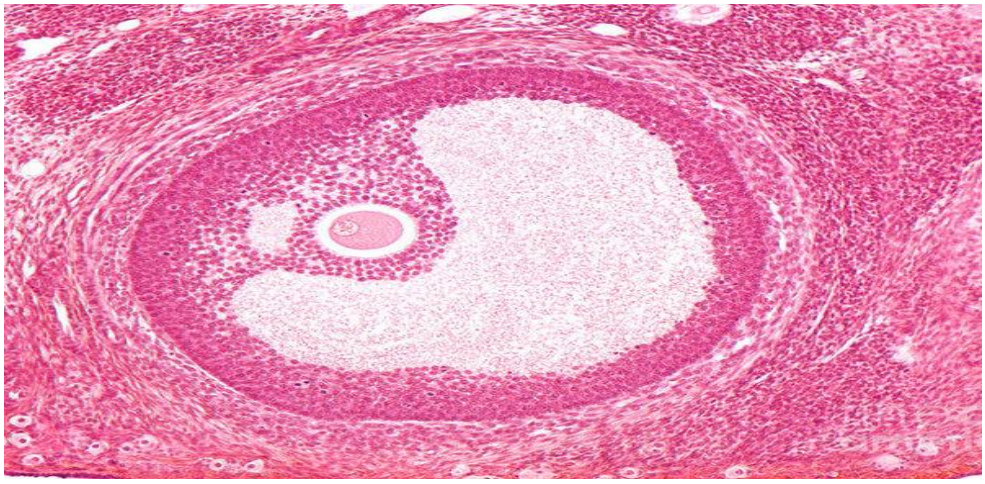


Fig (2): Mature graafian follicle

- **Fate of mature Graafian follicle (ovulation):**
  - Ovulation is stimulated by luteinizing hormone (LH) from the pituitary gland. It takes place at Day 14 of a 28 day ovarian cycle.
  - The Graafian follicle ruptures, releasing the haploid secondary oocyte, cumulus oophorus, follicular fluid, and blood.
  - Oocyte and the surrounding cumulus are transported through the oviduct to the ampulla to wait for fertilization. Fertilization triggers the completion of meiosis II and the formation of an ovum.
  - Granulosa and theca interna cells begin formation of corpus luteum.

5. Atretic follicles:

The process of follicular atresia begins before birth and continues throughout the life of a woman. Of the 2 million primordial follicles present at birth, only about 450,000 follicles remain at puberty and about 450 of those will be ovulated. The remainder degenerate, thereby producing more atretic than "normal" follicles.

- Corpus Luteum

- The corpus luteum is a temporary endocrine gland that lives for about 12 days.
- Functional during the second half of the ovarian cycle.
- Its formation is stimulated by luteinizing hormone (LH) secreted by the pituitary gland.
- Composed of:

- Granulosa lutein cells

- Form from cells in the granulosa layer, which enlarge and become rich in sER, mitochondria and lipid droplets (steroid secreting cell).
- Secrete progesterone hormone.

- Theca lutein cells:

- Form from theca interna cell.
- Typical steroid secreting cells but smaller than granulosa lutein cells.
- Secrete estrogen hormone.

- Fate of corpus luteum:

- **If pregnancy does not occur**: No further hormonal stimulation takes place and the cells of the corpus luteum degenerate after 12 days. This is called corpus luteum of menstruation
  Its **cellular remnants** are phagocytosed by macrophages. Fibroblasts invade the area and produce a scar of dense connective tissue called the corpus albicans.
- **If pregnancy occurs:** The corpus luteum, enlarges and it is known as the corpus luteum of pregnancy.
  This structure is functional for the first trimester of pregnancy, until the placenta is formed.
  After that it degenerates and replaced by corpus albicans.

- Types of corpus luteum:

1. Corpus hemorrhagicum: in animals, the cavity of corpus luteum is filled with blood.
2. Corpus luteum of menstruation.
3. Corpus luteum of pregnancy.
4. Corpus albicans.

- Ovogenesis

- Definition: Development of primordial germ cells (oogonia) to mature ovum.

- Oogonia develop in the yolk sac and migrate to developing ovary.

- Stages:

1. **Proliferation:** Division of oogonia by mitosis to give large number of cells during the first 3 months of intrauterine life.
2. **Growth:** oogonia grow ---- primary oocytes which enter prophase of meiosis I. At birth and till puberty all follicles contain primary oocytes.
3. **Maturation:** At puberty and just before ovulation, the 1ry oocyte completes the

first meiotic division ---2ry oocyte and first polar body each has 23 d chromosomes. After fertilization the 2ry oocyte ---ovum and second polar body, each has 23 s chromosomes.

- Function of estrogen hormone :

- Action:

A- In embryonic life: Full development of uterus & vagina

B- In prepubertal life: Negative feed back on GnRH-----due to hypersenstivity of hypothalamus

C- During puberty:

1- On Primary sex organs

* Growth of the ovarian follicles at beginning of cycle
* Stimulate LH surge------Ovulation -----corpus leuteum formation

2- On Secondary sex organs

Uterus:

1- Regeneration of the endometrium
2- Proliferation of epithelium
3- Growth of glands (minimal Secretion
4- Increase blood flow of uterus
5- Increase actin & myosin
6- Increase senstivity to Oxytocin hormone
7- Increase excitability of uterus---spontaneous contraction

Cervix: The cervix secretion is:
- Thin
- Alkaline
- Can be stretched
- Protective for sperms
- Help movement of sperms

Vagina:

- Increase layers of vagina (stratification)
- Increase resistance to infection
- Deposit glycogen---change to lactic acid----kill bacteria

Fallopian tubes:

- Increase motility
- Increase cilia action
- Push ova towards uterus

Breast:

- Enlargement of breast at puberty
- Deposit fat in breast
- Stimulate growth of ducts
- Stimulate growth of nipple
- Stimulate pigmentation of areola
- Increase blood flow of breast

External genetalia: Stimuate its growth

3- On Secondary sex characters

Hair:

- Less body hair

- Increase scalp hair
- Pubic hair has a straight upper boarder

Voice:

- High pitched voice
- No effect of estrogen on vocal cords

Body configuration:

- Narrow shoulder
- Wide pelvis
- Characteristic fat distribution

Skin:

- Soft skin
- Smooth skin
- Fluid sebaceous secretion----inhibit acne formation

Behaviour: Increase libido

Metabolism:

- Anabolic on: * Bones
  * Sexual organs
- Stimulate union of epiphysis

Systemic action:

- Estrogen lower the Cholesterol level-----prevent atherosclerosis
- Salt & water retention

- Progesterone:

Action:

1- On secondary sex organs:

Uterus:

- Control the second half of the menstrual cycle (secretory phase)
- Prepare the endometrium for implantation of fertilized ovum by increasing its thickness
- Help formation of placenta
- MAINTAIN pregnancy by:
  - Cause hyperpolarization of the muscle of uterus (myometrium)----- decrease uterine contractions
  - Decrease senstivity of the myometrium to estrogen
  - Decrease number of estrogen receptors

2-Crevix:

Under effect of progesterone the cervical mucus is

- Increase mucus secretion
- Thick
- Viscid
- Cellular
- Not help movement of sperms

3-fallopian tubes: Increase mucus secretion ----for nutrition of the fertilized ovum

4-Vgina:

- Thick proliferation
- Leukocyte infiltration

5-mammary glands:

- Stimulate the growth of the secretory alveoli
- Stimulate the growth of ducts
- Help lactation (lesser extent)

2-On the ovary: Progesterone inhibit LH ----inhibit ovulation

3-Thermogenic action:

It cause increase in the basal body temperature by 0.5 degrees at time of ovulation by:

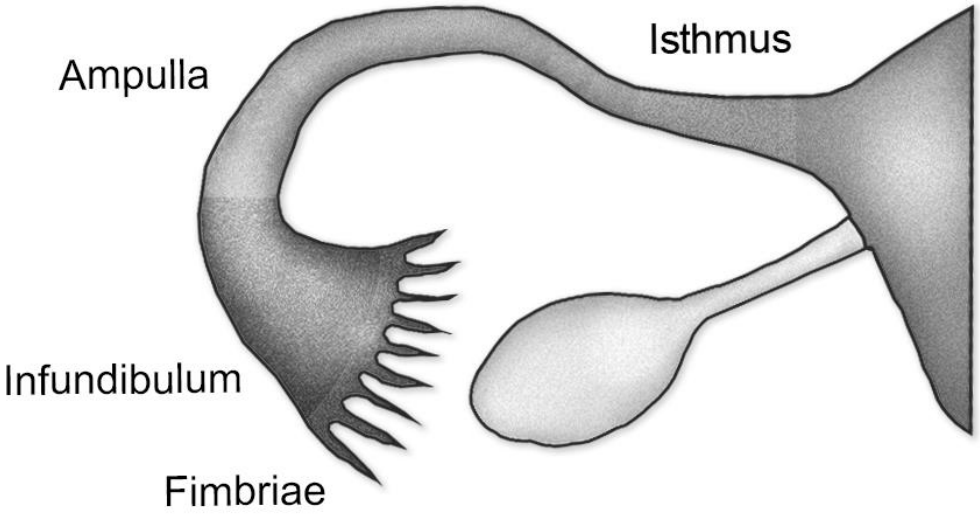
- Direct action on heat regulating center in hypothalamus
- Permissive action on thyroid hormones

4-Effect on respiration: Increase respiratory rate

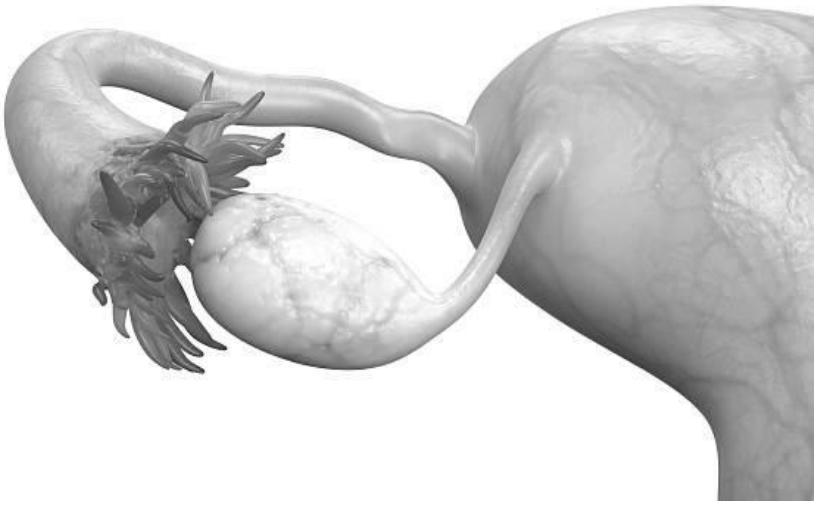
5-Effect on appetite: Stimulate appetite

6-Give the mother the maternal behaviour

7-In large amounts it may cause SODIUM , WATER retention



Parts of Uterine tube



Relations between uterine tube and ovary

Pinterest / Webteb

UTERINE (FALLOPIAN) TUBE

❖ 10 cm tube extending from the uterus medially to the ovary laterally. It is the normal site of fertilization.

Parts and relations:

Infundibulum:

- It is funnel shape; 3 cm in length and 3 mm in diameter.
- It shows an opening in the peritoneal cavity.
- It has 20-30 projections (fimbriae) surrounding the sup, post and med aspects of the ovary. A large fimbria is attached to the sup end of the ovary and guides the oocyte to the cavity of the tube.

Ampulla: it is largest part of the tube; 5 cm in length and 4 mm in diameter. It is the normal site of fertilization.

Isthmus: 2 cm in length and 2 mm in diameter

Uterine (intramural) part: It is the narrowest part of the tube; 1 cm X 1 mm in diameter. Its cavity is continuous with the uterine cavity.

Peritoneal coverings: completely covered by peritoneum. It is the only structure piercing the peritoneum.

Blood Supply:

Arterial: med ⅔ by uterine A and Lat ⅓ by ovarian A.

Venous: corresponds to the As.

Lymphatic Drainage: lat aortic lymph nodes.

Applied Anatomy:

- It is the normal site of fertilization
- It is the most common site for ectopic pregnancy
- It is the only structure piercing the peritoneum. Its cavity is connected to the peritoneal cavity (hence the easier ascending peritonitis in females).
- Occlusion of uterine tubes is a common cause for infertility.
- Ligation of uterine tubes is an irreversible method for contraception.

- Histology: The oviducts have four subdivisions; Infundibulum, Ampulla, Isthmus & Intramural (interstitial).

- **Structure:**

- **Mucosa:** It has many folds especially in the infundibulum.
  a) Epithelium. Simple columnar ciliated cells and secretory cells.
  b) CT corium.
- **Muscularis mucosa :** inner circular , outer longitudinal smooth muscle layers.
- **Serosa:** Loose C.T. covered by simple squamous epithelium

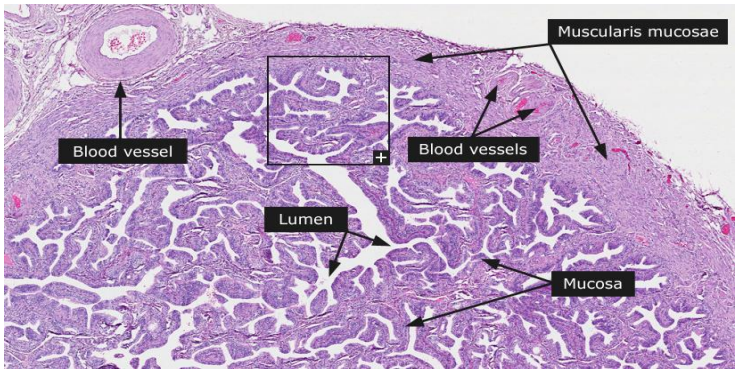
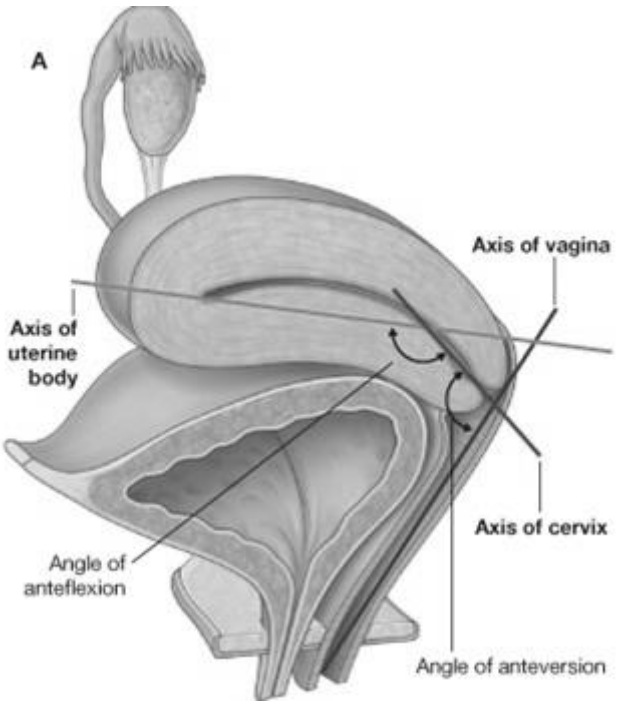
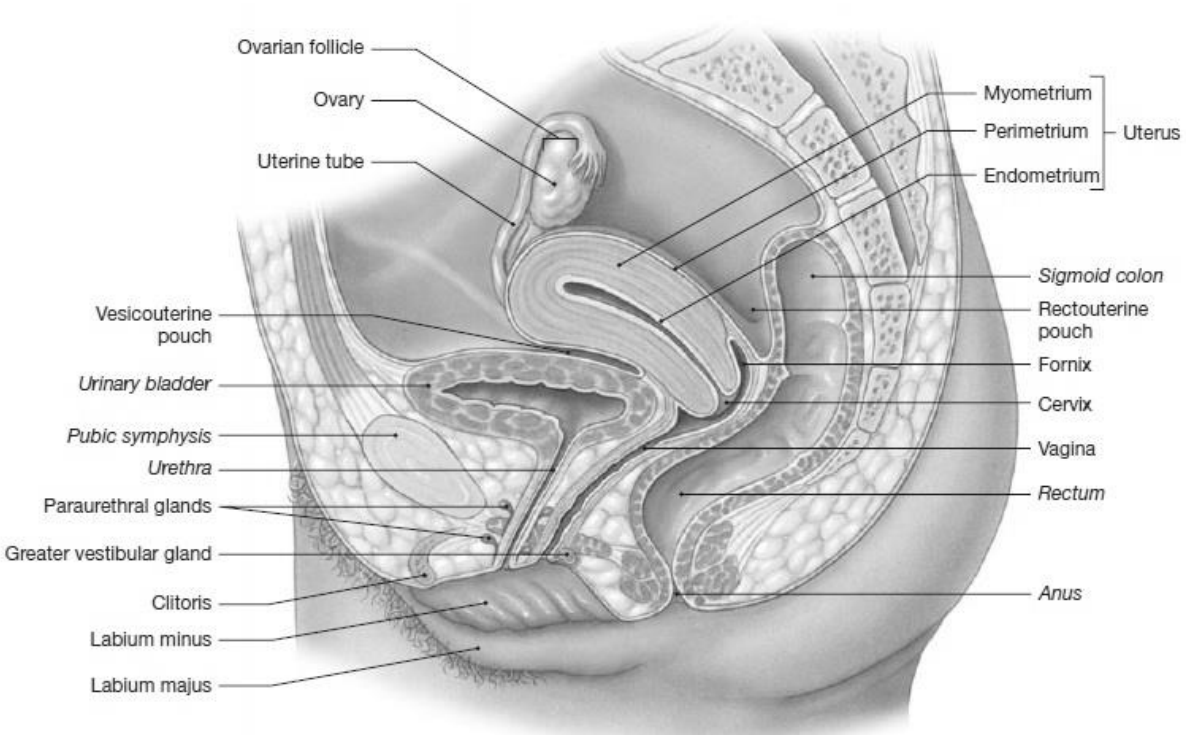


Fig (3): Fallopian tube



AVF uterus



Relations and pouches of the uterus

slide share / Martini

FEMALE GENITAL ORGANS

UTERUS

❖ Pear shaped muscular organ, in the center of the female true pelvis.

Position: dextrorotated (slightly rotated to the Rt) anteverted anteflexed (AVF).

N.B.: Antevertion: is ant bending between the cervix and vagina, the angle is 90º. Anteflexion: is ant bending between the body and cervix, the angle is 170º. In 20% of females the uterus is retroverted retroflexed (RVF).

Parts and relations:

1) **Fundus:** upper part of the uterus above the level of the 2 uterine tubes.
2) **Body:** 3x2x1 inches (post pubertal). The body: cervix length ratio is 1:1 prepubertal, and 2:1 – 3:1 post pubertal. The body shows:
   Ant surface: directed downwards, related to the urinary bladder (sup surface) separated from it by uterovesical pouch.
   Post surface: related to small intestines and pelvic colon.
   2 Lat borders: attachment of broad ligament (with the uterine A inside it).
3) **Isthmus:** junction between body and cervix. In pregnancy it forms the lower uterine segment.
4) **Cervix** (neck): fusiform canal 1X1 inches. It shows:
   Supravaginal part: related to:
   Ant: urinary bladder (base)
   Post: rectum separated from it by rectovaginal pouch containing sigmoid colon and small intestines.
   Lat: uterine A & ureter (crossing each other).
   Vaginal part: surrounded by 4 vaginal fornices: ant, post, and 2 lat.
   Internal os: opening connecting the cavity of the uterus to that of cervix.
   External os: opening of the cervix in the vagina in contact with its post wall.

Peritoneal coverings: the fundus and body are completely covered with peritoneum. The supravaginal cervix is covered posteriorly, anteriorly it is in direct contact with urinary bladder.

Peritoneal pouches:

Uterovesical pouch: reflection of peritoneum from sup surface of the bladder to the ant surface of the body of uterus.

Rectovaginal (Douglas) pouch: reflection of peritoneum from rectum to the post surface of the vag. It is the most dependent part of female peritoneum, it contains sigmoid colon and small intestines.

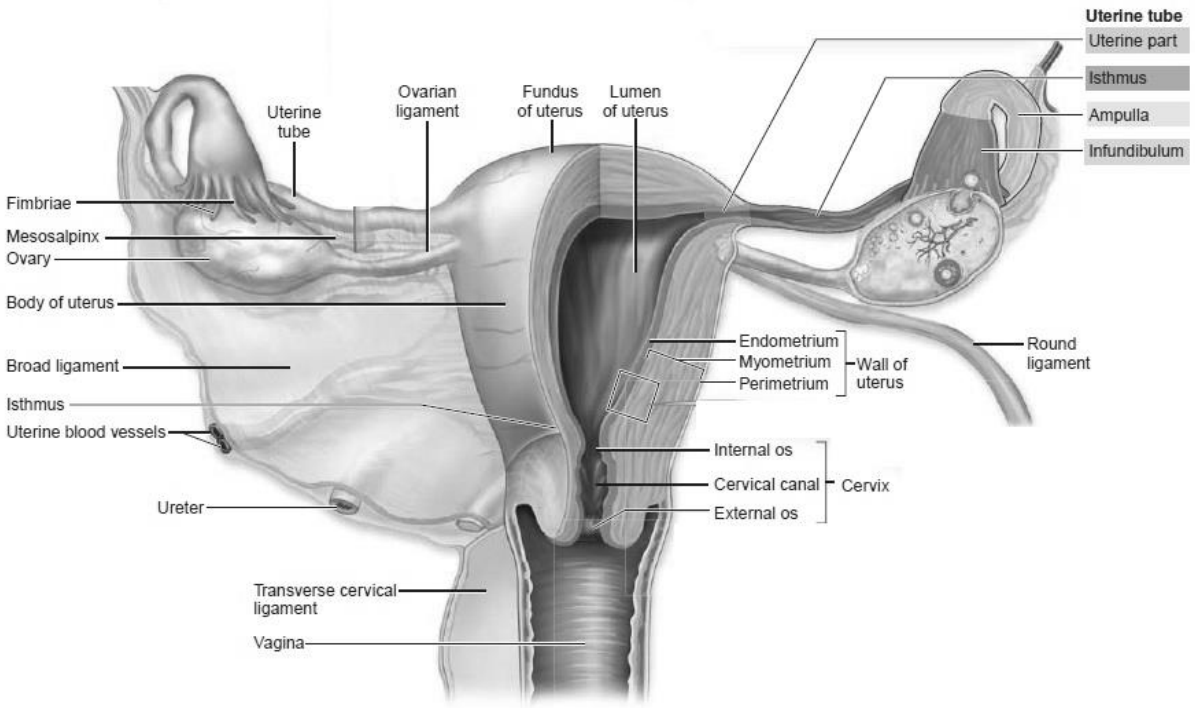
Peritoneal folds: broad ligament and ant ligament of the cervix.

Blood supply:

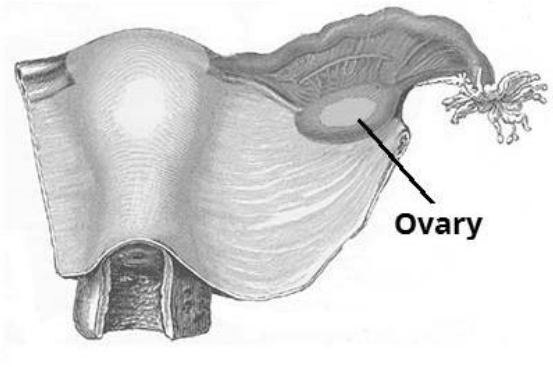
Arterial: ***uterine A*** (tortuous):

- A branch of internal iliac A (ant division).
- Enters the broad ligament through its post border.
- It passes to the uterus and ascends along its lat border (crosses the ureter 1 inch above the cervix) to reach the fundus.
- Turns below the uterine tube and ends by anastomosing with the ovarian A.
- It supplies the uterus and med part of uterine tube.

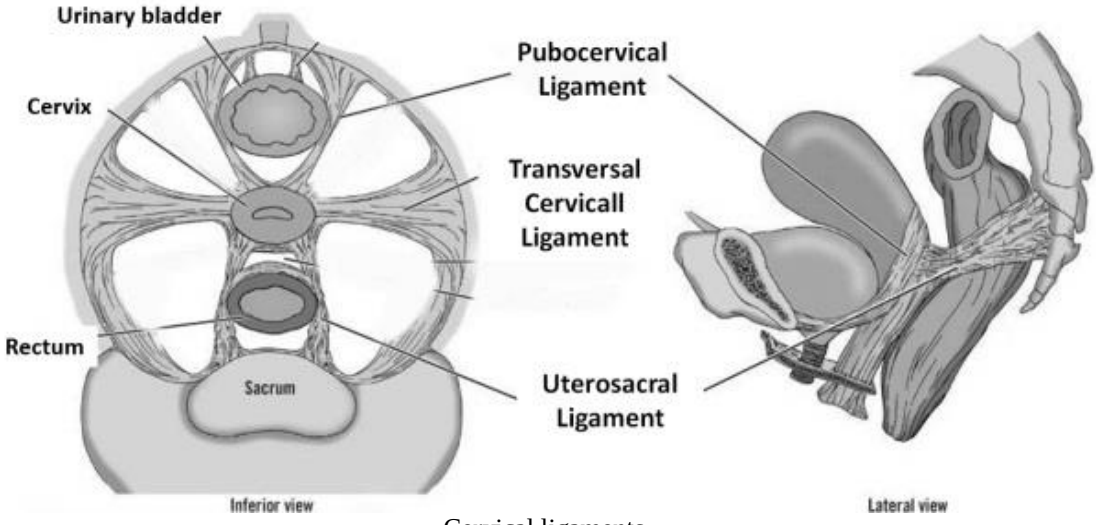
Venous: uterine V drains into internal iliac V



Broad ligament



Parts of broad ligament



Cervical ligaments

Quizlet / Teachmeanatomy / Anatomy QA

Ligaments of the uterus:

1) **Broad ligament:** peritoneal fold between the lat border of uterus and lat pelvic wall.

Relations:

Ant border: free and contains uterine tube (med ¾).

Post border (root): attached to the pelvic floor (levator ani)

Med border: attached to the uterus (lat border).

Lat border: attached to the lat pelvic wall. It crosses external iliac vessels, umbilical A and obturator N and vessels.

Upper surface:

- Related to small intestines.
- Pierced (near the lat border) by the uterine tubes.
- It has a fold called mesovarium connecting it to the ovary.

Lower surface: related to the urinary bladder.

Contents:

a) Uterine tubes: in its free ant border.

b) Ureter: passes in the root and crossed by uterine A.

c) Uterine A.

d) Ovarian vessels: passes through the suspensory ligament of the ovary then through mesovarium to the ovary.

e) Round ligament of the ovary: between the ovary and uterotubal junction. It projects through the upper surface.

f) Round ligament of the uterus: between uterotubal junction → broad ligament → inguinal canal → labium majus. It projects through the lower surface.

g) Epoophoron and paraoophoron: embryological remnants.

h) Autonomic plexus, lymphatics and connective tissue

Parts:

Mesovarium: extension from the upper surface of broad ligament connecting it to the ovary. It contains ovarian vessels, autonomic plexus, lymphatics and connective tissue.

Suspensory ligament of the ovary (infundibulopelvic ligament): between the mesovarium and lat pelvic wall. It contains ovarian vessels.

Mesosalpinx: between uterine tubes, round ligament of the ovary and mesovarium.

Mesometrium: between the uterus, round ligament of the ovary and lat pelvic wall.

2) **Round ligament of the ovary:** between the ovary and uterotubal junction.
3) **Round ligament of the uterus:** attached to uterotubal junction → passes inside broad ligament → inguinal canal → labium majus. It is the cause of angle of anteversion.
4) **Pubocervical ligaments:** between the cervix and the body of pubis.
5) **Transverse cervical (Mackenrodt) ligament:** between the cervix and lateral pelvic wall
6) **Uterosacral ligament:** between the cervix and S1-2 vertebrae.

- **Histologically**, fundus and body are similar but different from cervix.

- Fundus & body:

Their wall is formed of three layers:

1. **Endometrium, or mucosa**: Formed of:
   - Epithelium: mix of ciliated and secretory simple col. cells
   - Lamina propria containing simple tubular glands.
   - The epithelium of the uterine glands is similar to the superficial epithelium, but ciliated cells are rare within the glands.
   - The connective tissue of the lamina propria is rich in fibroblasts and ground substance.

   The endometrial layer can be subdivided into two zones:

   (1) The basal zone
   - The deepest one.
   - Contains lamina propria and the closed tips of the uterine glands.
   - Not changed during menstrual cycles.
   - Supplied by straight arteries.

   (2) The **functional zone**
   - Contains the remainder of the lamina propria and the glands, as well as the surface epithelium.
   - It undergoes profound changes during the menstrual cycles.
   - Supplied by spiral arteries.

2. **Myometrum,** a thick smooth muscle , 3 zones are poorly defined;
   - Submucosal layer: inner part formed of longitudinal muscle fibres.
   - Vascular layer: middle part formed of circular & oblique muscle fibres arranged around blood vessels.
   - Supravascular layer: Outer part formed of longitudinal fibres.
3. **Perimetium**: Loose C.T. covered by simple squamous mesothelium.

- Endometrial changes during menstrual cycle

The duration of the menstrual cycle is variable but averages 28 days.

- The Menstrual (destructive) Phase

- From 1st— 5th day of bleeding.
- When fertilization of the oocyte does not occur and there is rapid decrease of blood levels of progesterone and estrogens.
- This leads to breakdown of spiral blood vessel walls and bleeding begins --- detaching part of the functional layer.
- At the end of the menstrual phase, the endometrium is usually reduced to a thin layer (0.5 mm) made mainly of basal zone.

- Proliferative (follicular-estrogenic) phase:

- From 5th---14th days
- Under control of estrogen produced by ovarian follicles stimulated by FSH
- The endometrium is covered by simple columnar epithelium
- The glands are narrow and straight.

- The blood vessels are regenerated.
- At the end of the proliferative phase, the endometrium is 2-3 mm thick.

- Secretory (Luteal-progestational) phase:

- From 14th day to onset of next cycle.
- It results from the action of progesterone secreted by the corpus luteum.
- The amount of glycoprotein secretory products dilate the lumens of the glands so become highly coiled.
- The blood vessels are congested.
- The endometrium reaches its maximum thickness (5 mm) as a result of the accumulation of secretions and of edema in the stroma.

- Cervix of Uterus

- The mucosa is formed of epithelial lining consists of a mucus-secreting simple columnar epithelium.
- Under the epithelium connective tissue contains the mucous **cervical glands,** which are branched tubuloalveolar.
- This mucosa does not undergo remarkable changes during the menstrual cycle.
- Under the mucosa, the wall is made of dense connective tissue (85%) with many elastic fibres & few smooth muscle fibers .
- The external aspect of the cervix that bulges into the lumen of the vagina is covered with stratified squamous epithelium.
- At the time of ovulation, the mucous secretions are watery and allow penetration of the uterus by sperm.
- In the luteal phase or in pregnancy, the progesterone levels alter the mucous secretions so that they become more **viscous** to prevent the passage of sperm, as well as microorganisms.

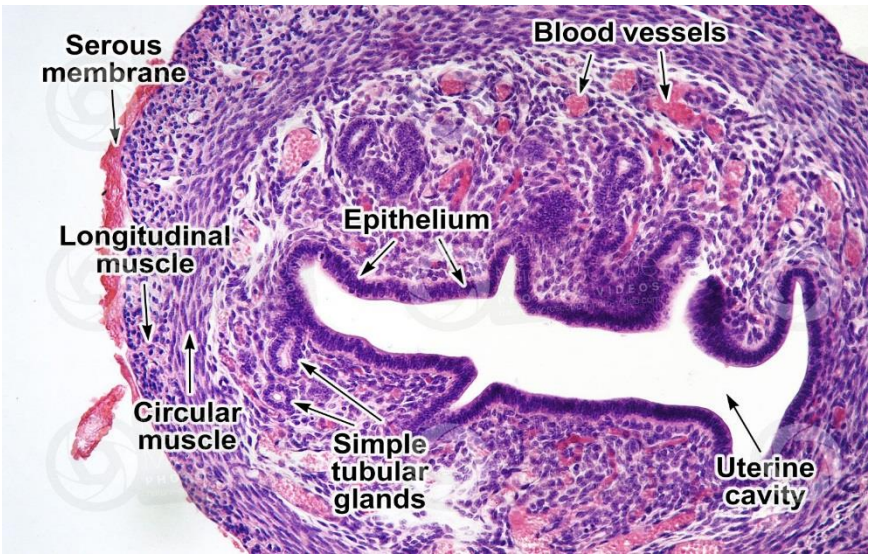


Fig (4): Uterus

- The menarche - the menopause

- Menarche: Beginning of the reproductive period in the female usually about 9-12 years

- Menopause is the progressive decline in the female reproductive system.
- Numbers of oocytes in the ovaries are depleted by atresia
- Ovarian responsiveness to LH and FSH decreases
- Cycles become anovular and irregular
- Oestrogen and progesterone concentrations fall.
- FSH and LH circulating concentrations are high because of the loss of negative feedback inhibition by oestrogen but no LH surge occurs
- The loss of ovarian steroids results in: vaginal dryness, uterine muscle fibrosis, loss of breast tissues, depression, night sweats, hot flushes
- Increased risk of myocardial infarction, increased bone resorption, and resulting bone weakness
- The changes can be treated with hormone replacement therapy.

- Vagina:

- Histology: The wall of the vagina is devoid of glands. The mucus found in the lumen of the vagina comes from the glands of the uterine cervix.

Mucosa:

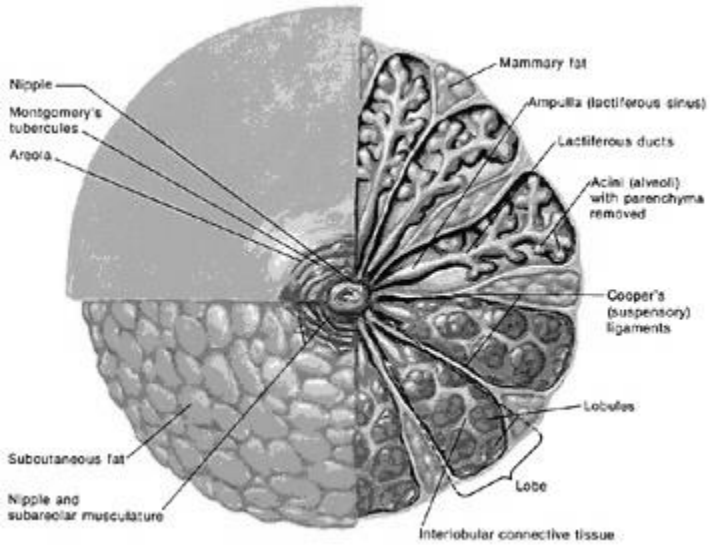
- The epithelium of the vaginal mucosa of an adult woman is **non-keratinized stratified squamous.**
- Stimulation by estrogen: synthesizes and accumulates a large quantity of glycogen, which is deposited in the lumen of the vagina when the vaginal cells desquamate. Bacteria in the vagina metabolize glycogen and form lactic acid, which is responsible for the usually low pH of the vagina.
- The acidic vaginal environment provides a protective action against some pathogenic microorganisms.
- The lamina propria of the vaginal mucosa is composed of loose connective tissue that is very rich in elastic fibers. Among the cells present are lymphocytes and neutrophils in relatively large quantities.

Musculosa:

- Formed of inner circular and outer longitudinal muscle fibers.

Adventitia:

- Connective tissue containing; thick elastic fibers explaining the great elasticity of the vagina, blood vessels & nerves.



Mammary gland

Praborini

ANATOMY OF THE MAMMARY GLAND

Position:

- From side of sternum to midaxillary line & from 2-6 ribs.
- It rests on pectoralis major (covered by pectoral fascia) & serratus ant.
- Has an extension to the axilla (axillary tail).

Structure:

- It is formed of skin, mammary glands, suspensory ligament and superficial fascia containing fat (causing smooth contour).
- It has no capsule.

The Skin: shows the nipple & areola

The nipple is a conical projection at the level of 4th intercostal space. It is pinkish in color, and irreversibly darkens during the first pregnancy (medicolegal importance).

The areola is a light brown skin surrounding the nipple.

The Glands give lactiferous ducts from each lobe, which dilates below the areola (lactiferous sinus), then narrow again to open separately at the nipple.

Suspensory ligament of breast (Cowper's ligament): fibrous strands extending between skin & pectoral fascia, dividing the breast into 15-20 lobes.

Blood supply:

- Mammary branches of lat thoracic & intercostal As.
- Perforating branches of internal thoracic A.

Lymphatic drainage:

- Mainly to axillary lymph nodes (ant, central & apical) → supraclavicular lymph nodes.
- Some lymphatics pass to infraclavicular, internal thoracic & abdominal lymph nodes.

Applied anatomy: cancer breast is the world wide most common cancer in females (25% of diagnosed cancers in females). Efforts are directed towards early detection through regular examination & mammography. In detected cases, examination of lymph nodes is extremely important to grade the disease.

- Histology: Each mammary gland is an exocrine compound alveolar apocrine gland.

- Resting mammary gland:

1- Stroma:

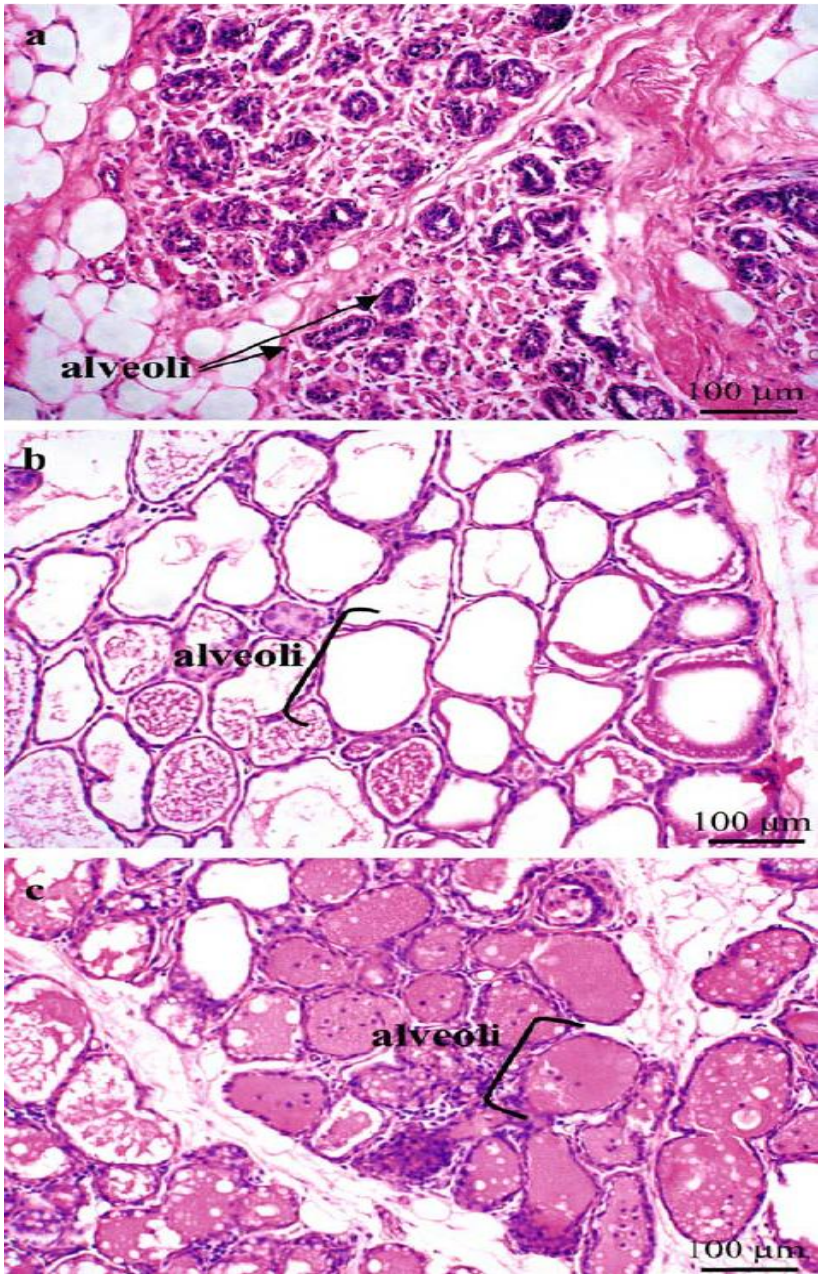
- No capsule but **covered by skin** with nipple and areola.
- The nipple: conical elevation formed of dense CT and smooth muscle covered by pigmented skin.
- It contains openings of lactiferous duct.
- The areola: circular region of pigmented skin containing modified sebaceous glands (**Montgomery glands**).
- Interlobar septa extend inwards from subcutaneous tissue, formed of dense connective tissue and adipose tissue.
- The gland is divided to 15-25 lobes.
- Intralobular connective tissue is loose with no fat cells.

2- Parenchyma:

- Each lobe is drained by its own lactiferous duct leading directly to the nipple, where it opens onto its surface. Before reaching the nipple, each of the ducts is dilated to form a lactiferous sinus then become narrow again.
- Near the opening at the nipple, lactiferous ducts are lined by a **stratified squamous epithelium**.
- The lactiferous sinus and the lactiferous ducts are lined by **stratified cuboidal epithelium**.
- The smaller ducts leading to the lactiferous duct are lined **by a simple cubical or columnar epithelium.**

- Lactating (Active) Mammary Glands

- The mammary glands undergo intense growth as a result of the action of estrogen, progesterone, prolactin, and human placental lactogen.
  Changes:
- Proliferation of alveoli at the ends of the terminal ducts. They are lined **by cubical epithelium**.
- **Fat droplets** and secretory vacuoles containing milk proteins
  Seen in apex of alveolar cells
- By EM the cells are rich in rER & Golgi (**Protein synthesis)** and sER, mitochondria (**Lipid synthesis).**
- **Stellate myoepithelial cells** are found between the alveolar epithelial cells & the basal lamina.
- **Milk** appears acidophilic with dissolved fat droplets in alveoli.
- **The CT septa are thinner** with **less fat cells**.
- The connective tissue surrounding the alveoli contains many **lymphocytes** and **plasma cell**, responsible for the secretion of immunoglobulins (secretory IgA) that give passive immunity to the newborn.



Mammary gland

- Breast development in pregnancy and lactation, and its hormonal control:

- Mammary glands develop and the alveoli mature in response to placental hormones (placental lactogen, oestrogen, and progesterone) during pregnancy
- Massive development of the tubero-alveolar structure of the epithelium and ducts occurs to give 12–20 galactopoietic units, emptying into a common sinus at the nipple.

- Lactogenesis—prolactin and other hormones

Prolactin stimulates milk production. Its release is inhibited by dopamine, and dopamine agonists can be used to inhibit lactation.

- The maintenance of lactation depends on maternal prolactin release elicited by the suckling stimulus
- The first milk (colostrum) formed in the mother's breast contains an abundance of antibodies to protect the fetus against any local infections. The antibodies are of the IgA type, which are able to readily pass across the gut epithelium of the baby.

- Milk-ejection reflex—oxytocin

- The ejection of milk is stimulated by oxytocin released from the posterior pituitary, & elicited by suckling
- Oxytocin acts to contract the myoepithelial cells surrounding the alveoli within the breast which, together with the negative pressure of suckling at the nipple, ensures milk ejection.

- Puberty

- Def: Puberty is the time in life when a boy or girl becomes sexually mature. It usually happens between ages 10 and 14 for girls and ages 12 and 16 for boys. It causes physical changes, and affects boys and girls differently.

- In girls:

- The first sign of puberty is usually breast development.
- Then hair grows in the pubic area and armpits.
- Menstruation (or a period) usually happens last.

- In boys:

- Puberty usually begins with the testicles and penis getting bigger.
- Then hair grows in the pubic area and armpits.
- Muscles grow, the voice deepens, and facial hair develops as puberty continues.

Both boys and girls may get acne. They also usually have a growth spurt (rapid increase in height) that lasts for about 2 or 3 years. This brings them closer to their adult height, which they reach after puberty.

- Mechanism:

GnRH neurons of the hypothalamus control the initiation of puberty. The pulsatile secretion of GnRH by these neurons causes the changes of puberty. It is thought that release of neurokinin B and dynorphin help to generate the pulsatile secretion of GnRH. GnRH causes the release of LH and FSH from the gonadotropic cells of the anterior pituitary gland. FSH and LH affect the Leydig and Sertoli cells in the testes and the theca and granulosa cells of the ovary.

The zona reticularis of the adrenal cortex produced the hormones responsible for adrenarche and function separately from the hypothalamic-pituitary-gonadal axis.

- Precocious puberty and delayed puberty

- Precocious puberty (early puberty) can arise from:

1- Tumours of the posterior hypothalamus
2- Activating mutations of the LH receptor
3- Thecal, granulosa, or Leydig cell tumours
4- Gonadotrophin-secreting tumours

- Delayed puberty can arise from:

1- Kallmann's syndrome—
2- Deficit in formation of GnRH neurones in the developing brain which results in GnRH, LH, and FSH deficiency.