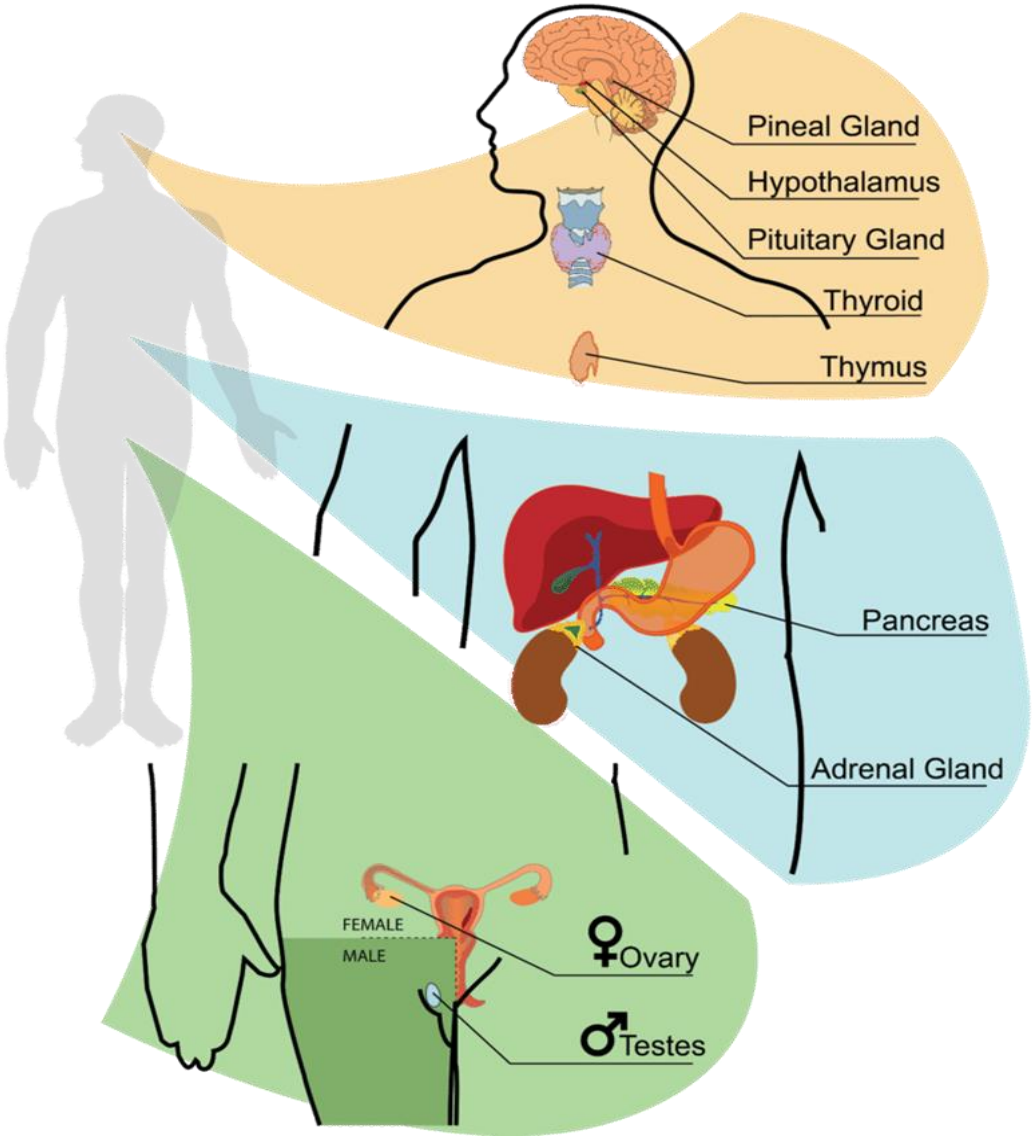
Endocrine Histology



Glands

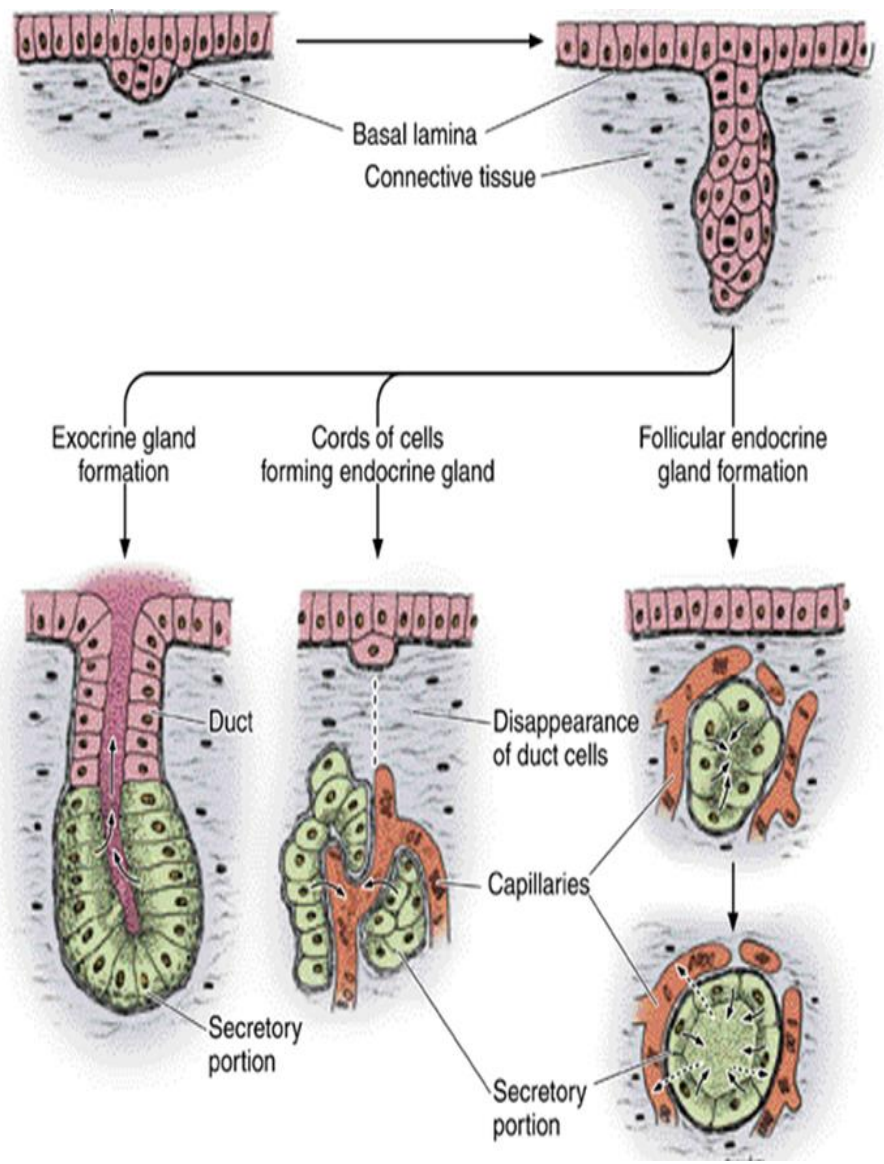
1-Exocrine (has ducts) : e.g.Salivary glands,

Secrete saliva in the mouth cavity through ducts.

2-Endocrine(has no ducts):

e.g. Thyroid ,pituitary glands. Secrete hormones directly into the blood.

3-Mixed: e.g. Pancreas ,Secretes digestive enzymes in the intestine & insulin hormone to the blood



The endocrine system

- The endocrine system provides connection from the hypothalamus of the brain to all the organs that maintain a constant temperature, maintain homeostasis , reproduction , or perform the basic actions and functions that are essential for life.
- The endocrine system is a control system of ductless glands that secrete hormones within specific organs.
- Hormones a small chemical act as "messengers," can enter the blood stream and cause an action at a distant location in the body.
- Hormones can be chemically classified **into :**

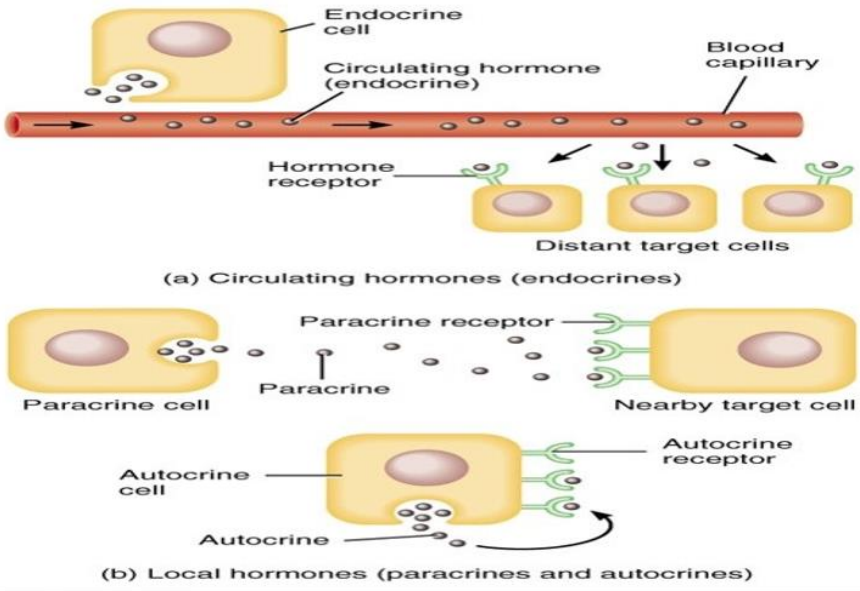
1. **Protein** : Hormones that are modified amino acids.
2. **Steroids**: Hormones that are lipids synthesized from cholesterol.

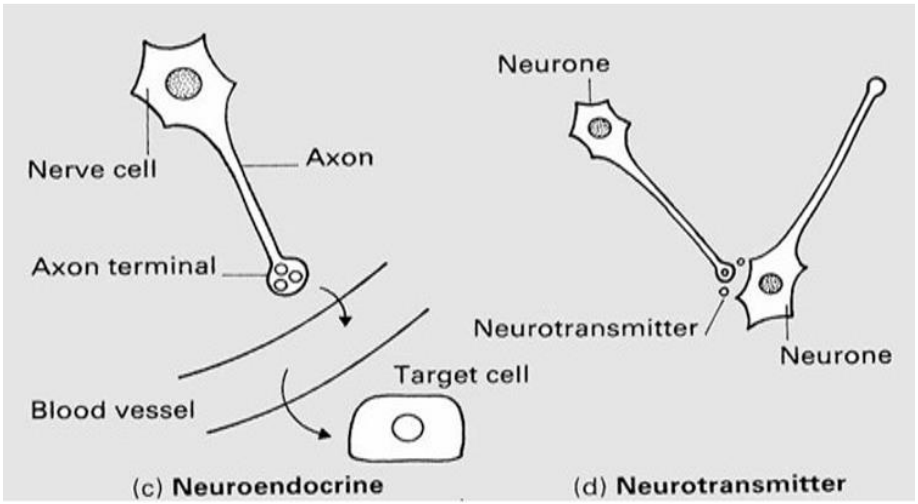
Patterns of Hormone Action

<u>Target cells or tissue</u>:

Specific cells affected by a hormone

- Endocrine : circulated by blood to **distant** target cells
- Paracrine : Hormones that affect **neighboring** cells
- Autocrine : Hormones that act on the cells that secrete them
- Neuroendocrine
- Neurotransmitter



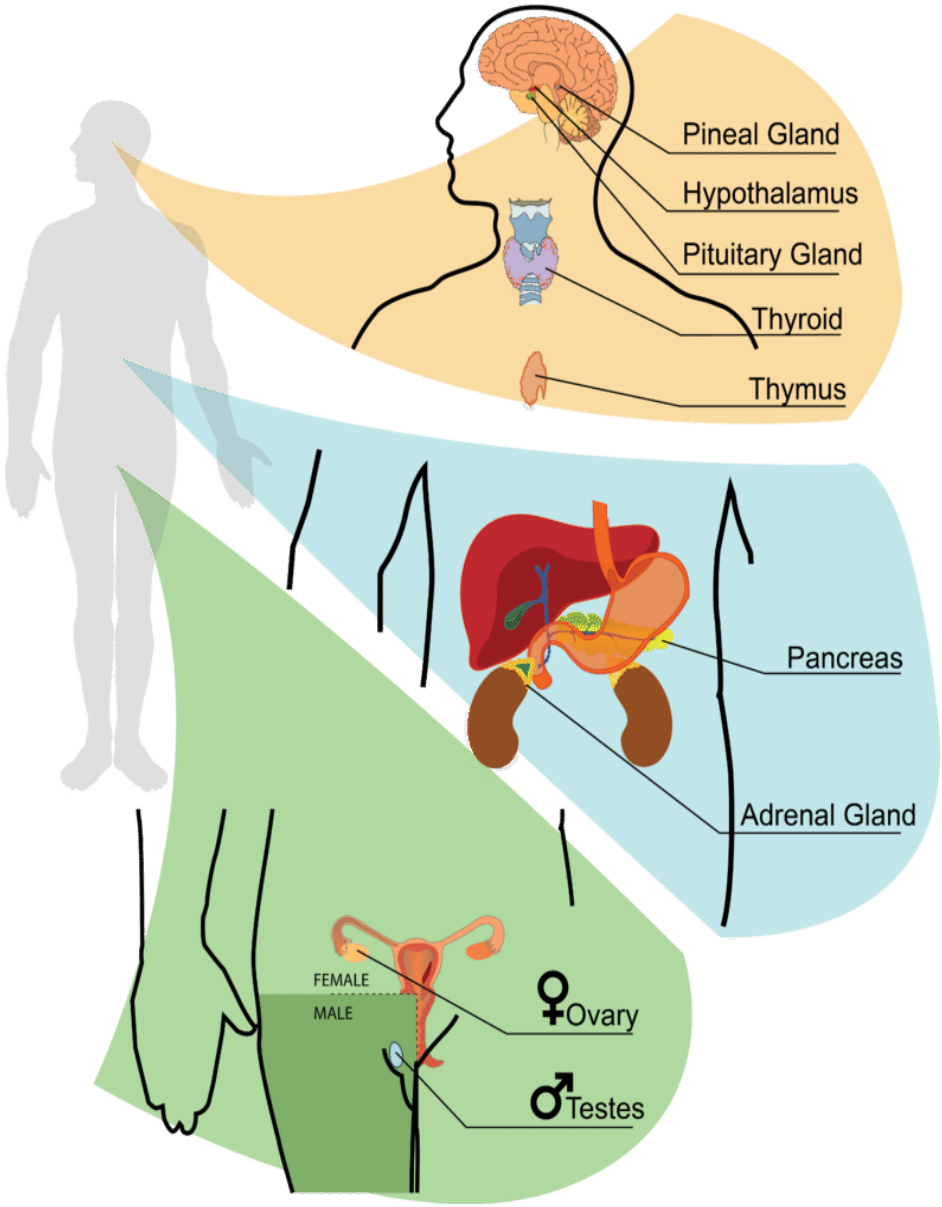


Introduction to the Endocrine System

The endocrine system

- **Principle glands :**
  - Hypothalamus
  - Pituitary gland
  - Pineal body
  - Thyroid gland & Parathyroid
  - Suprarenal gland (adrenal)
  - Pancreas
  - Gonads (testis, ovary) + placenta
- **Local Hormones**
  - GIT (Diffuse neuroendocrine system)
  - Neurotransmitter (nerve ending)
- **Others**

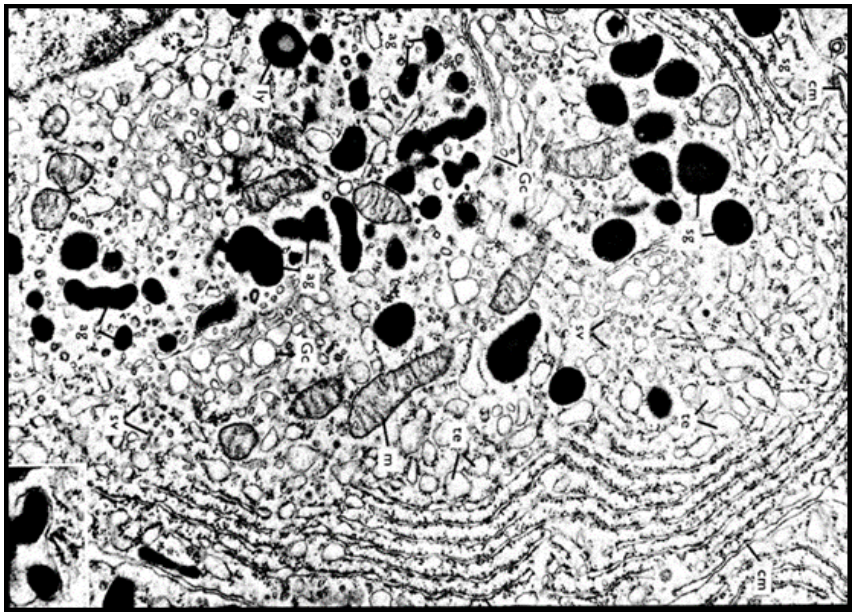
Kidney (erythrop + renin) , heart (ANF)
Thymus (hormone stimulate T cell maturation) & adipose (leptin)



General histological structures

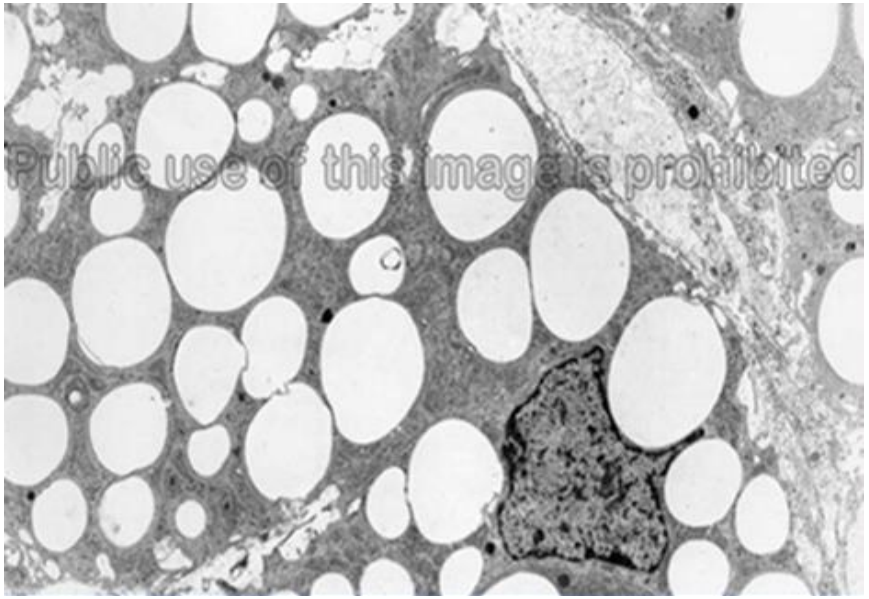
Protein secreting cells

- Active nucleus with prominent nucleolus
- **Basophilic** cytoplasm
- Numerous ribosomes & rER
- Prominent golgi & numerous mitochondria
- Secretory granules (stored hormones)



Steroid secreting cells

- Active nucleus prominent nucleolus
- **Acidophilic** cytoplasm
- Numerous sER
- numerous mitochondria
- Numerous lipid droplets (Not stored hormones)



Basic structure of endocrine glands

❑ Stroma

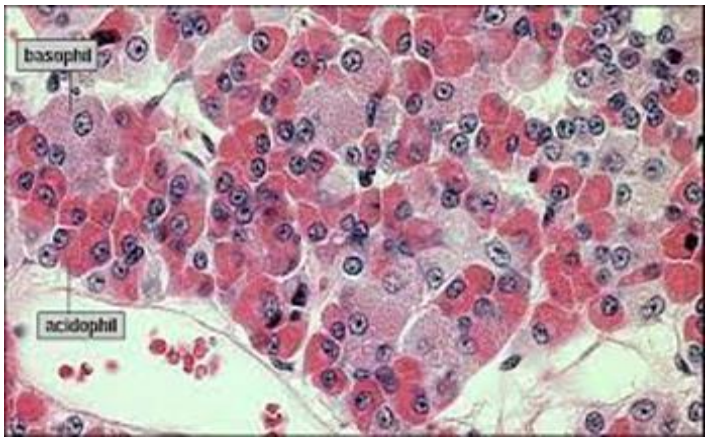
CT inside the gland

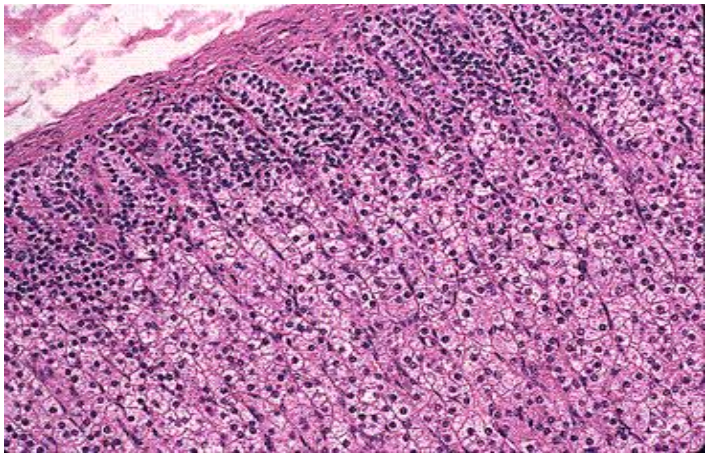
- ➢ CT capsule & C.T septa
- ➢ Loose tissue

❑ Parenchyma

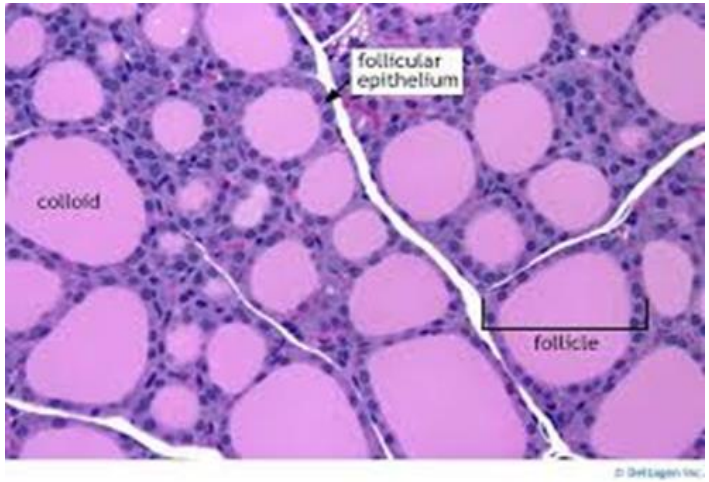
- ➢ Plexus of blood vessels
- ➢ Cells (cords or follicles)

Cords



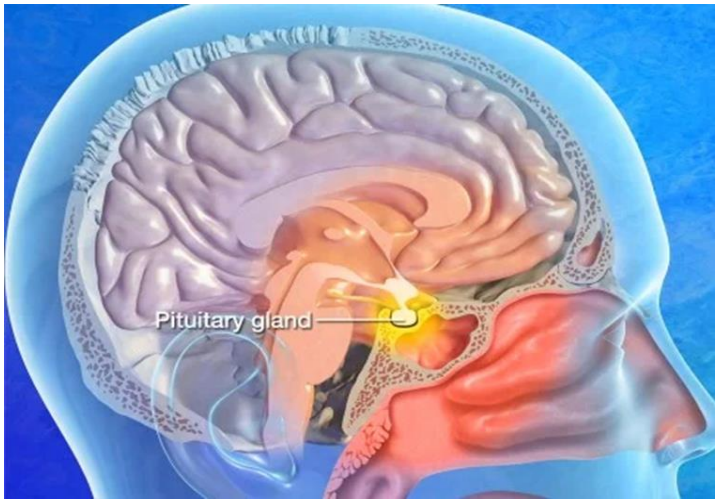


Follicles

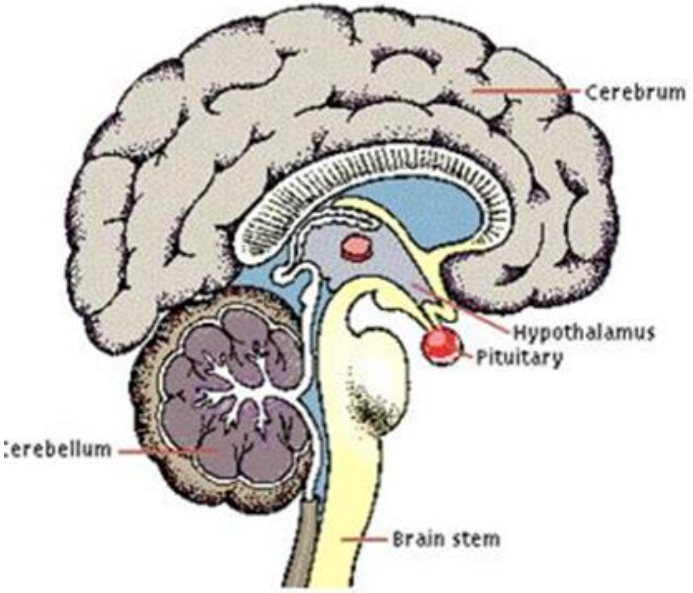


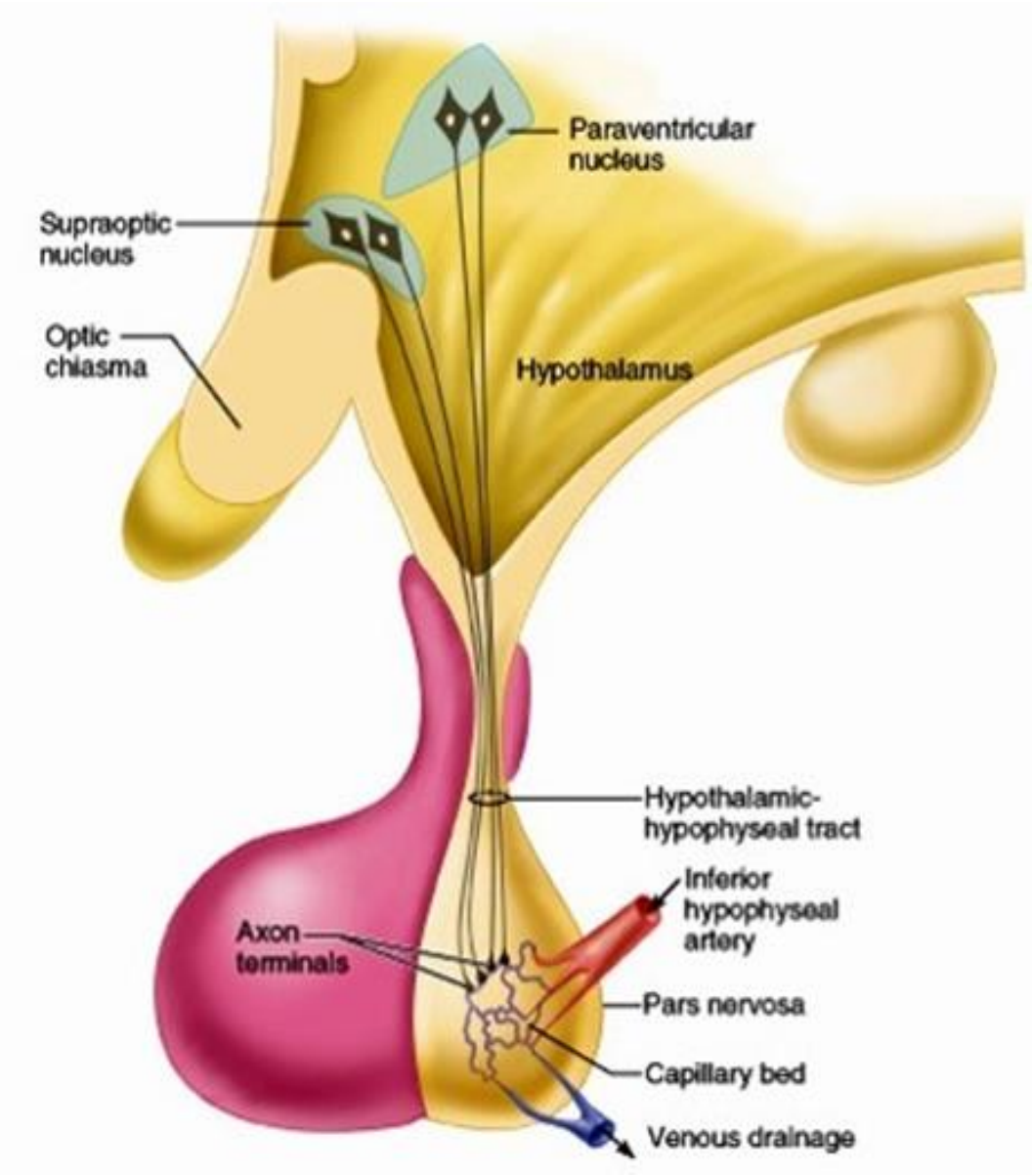
Pituitary gland
(Hypophysis Cerebri)

Site : The pituitary gland (hypophysis) is found in the inferior part of the brain and is connected to the bottom of the hypothalamus by a slender stalk called the infundibulum.



- The pituitary gland consists of **two major regions:**
  - Anterior pituitary gland (anterior lobe or adenohypophysis)
  - Posterior pituitary gland (posterior lobe or neurohypophysis).
- The Anterior pituitary is involved in sending hormones that control all other hormones of the body so referred to as the **master gland**




Paraventricular nucleus
Supraoptic nucleus
Optic chiasma
Hypothalamus
Hypothalamic-hypophyseal tract
Inferior hypophyseal artery
Axon terminals
Pars nervosa
Capillary bed
Venous drainage

Pituitary gland

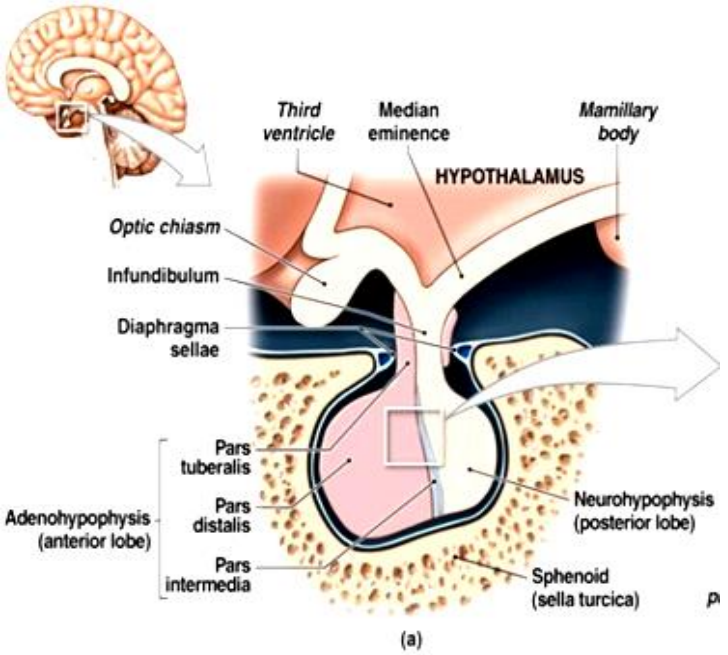
Site : Lies in the **sella turcica** (bony cavity of sphenoid)

Covered by **diaphragma sellae** (fold of dura mater)

Size : 0.5 gm

Stroma : surrounded by a **thin connective tissue** capsule/ loose connective tissue between the capsule and the periosteum.

Parenchyma : it has a **dense plexus** of thin-walled veins + Cells



- **epithelial component:**

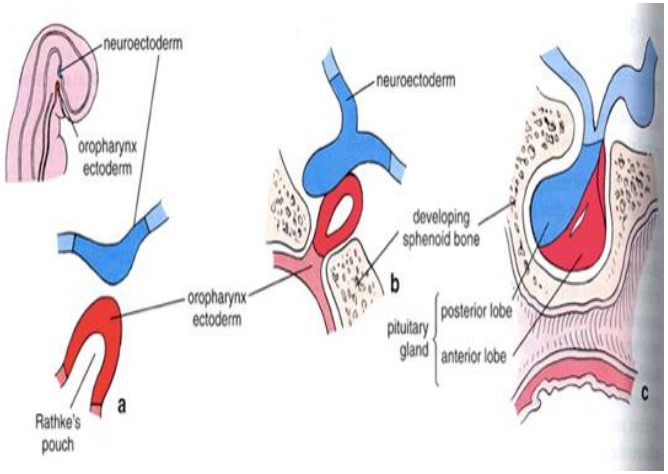
adenohypophysis (anterior pituitary)

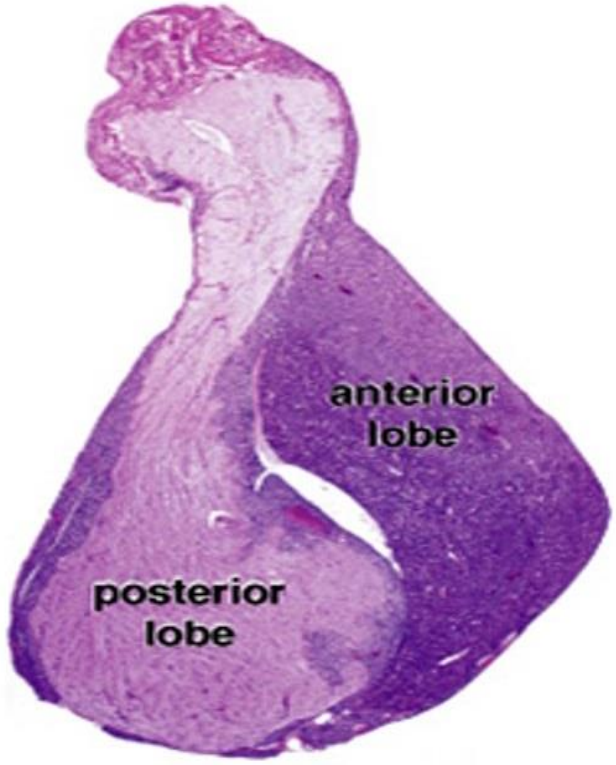
- **neural component:**

Neurohypophysis (posterior pituitary).

Development

	Adenohypophysis (glandular part)	Neurohypophysis (nervous part)
Derived from	Oral ectoderm	Neural ectoderm 3rd ventricle
	pinched off (Rathke's pouch)	in contact with the brain by neural stalk (infundibulum)
Stain	Dark	Pale
Consist of	Glandular epithelium in the form of irregular branching cords	Nerve fibers





Adenohypophysis

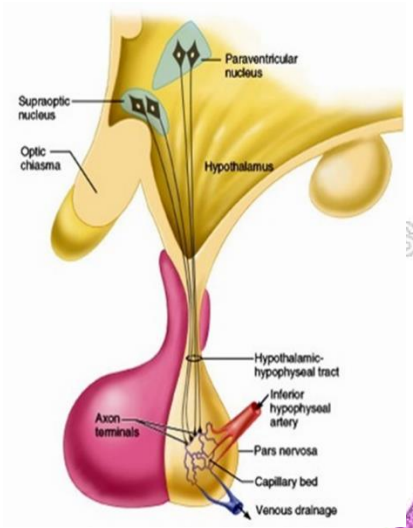
1. Pars distalis

2. Pars Tuberalis

- Highly vascular region containing the veins of the hypophyseal portal system and wraps the pituitary stalk (infundibulum).
- Principal cells of the pars tuberalis are chromophobes

3- Pars Intermedia

- contains basophil and chromophobe cells surrounding colloid-filled cysts, the nature of the colloid is yet to be determined.
- In human/ unclear function
- In animals / the basophilic cells produce melanocyte stimulating hormone (MSH)



1- Pars distalis

Stroma : CT capsule, reticular fibers.

Parenchyma

Fenestrated sinusoids

+ Cell cords of epithelial cells

Staining characteristics the cells are of

two types :

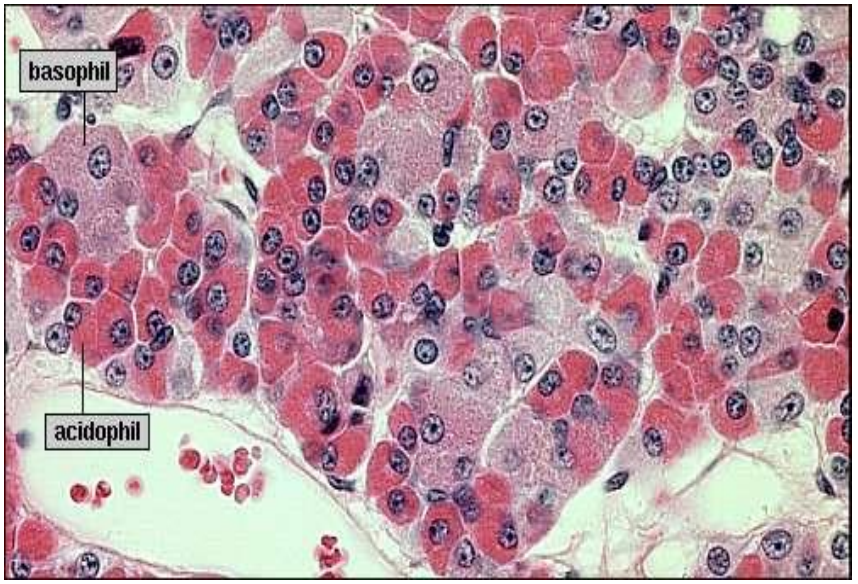
1- **Chromophobes** 52%

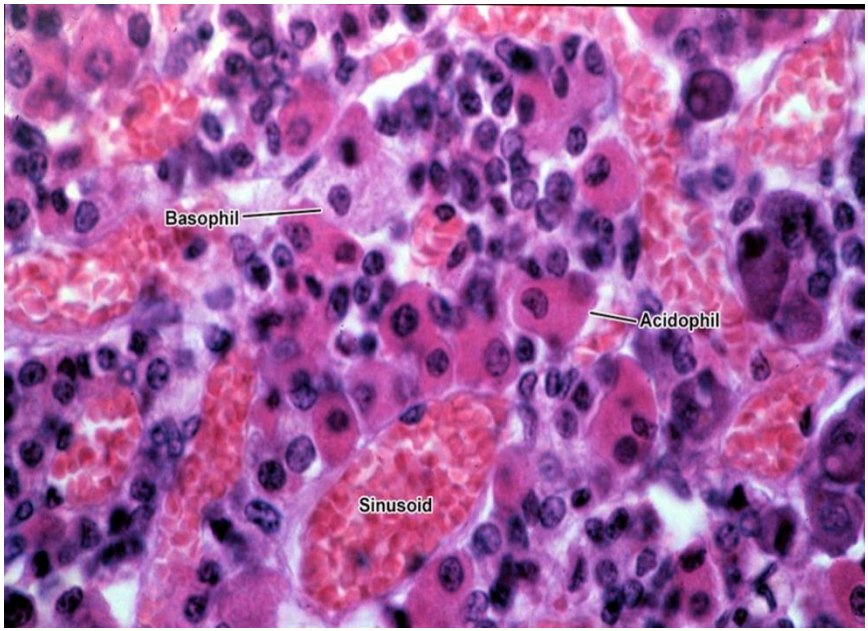
(which do **not stain intensely**).

2- **Chromophils** 48%

(having **densly** stained cytoplasmic **granules**)

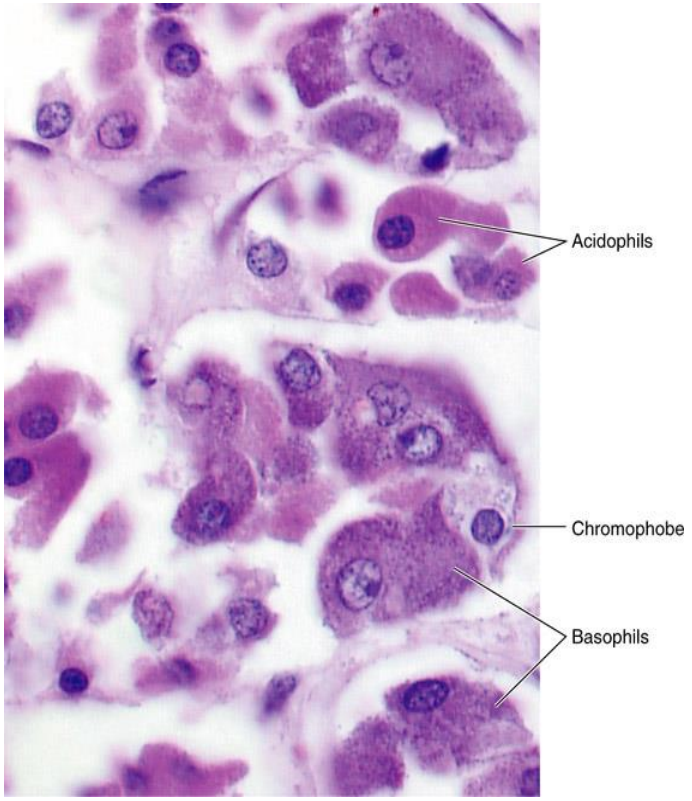
- **Basophils 11%** (darkly stained)
- **Acidophils 37%** (pink stained)





Cells of pars distalis

	Chromophils	Chromophobes
Function	Endocrine cells	Stem cells or exhausted chromophils Present mainly in pars tuberalis
Affinity for stain Size & shape	Great Large , polyhedral	Weak Small, rounded
Percentage	48% 11% basophils, 37% acidophils	52%
Organelles Granules	Of protein secretion Contain granules	Few Degranulated cells or reserve cells



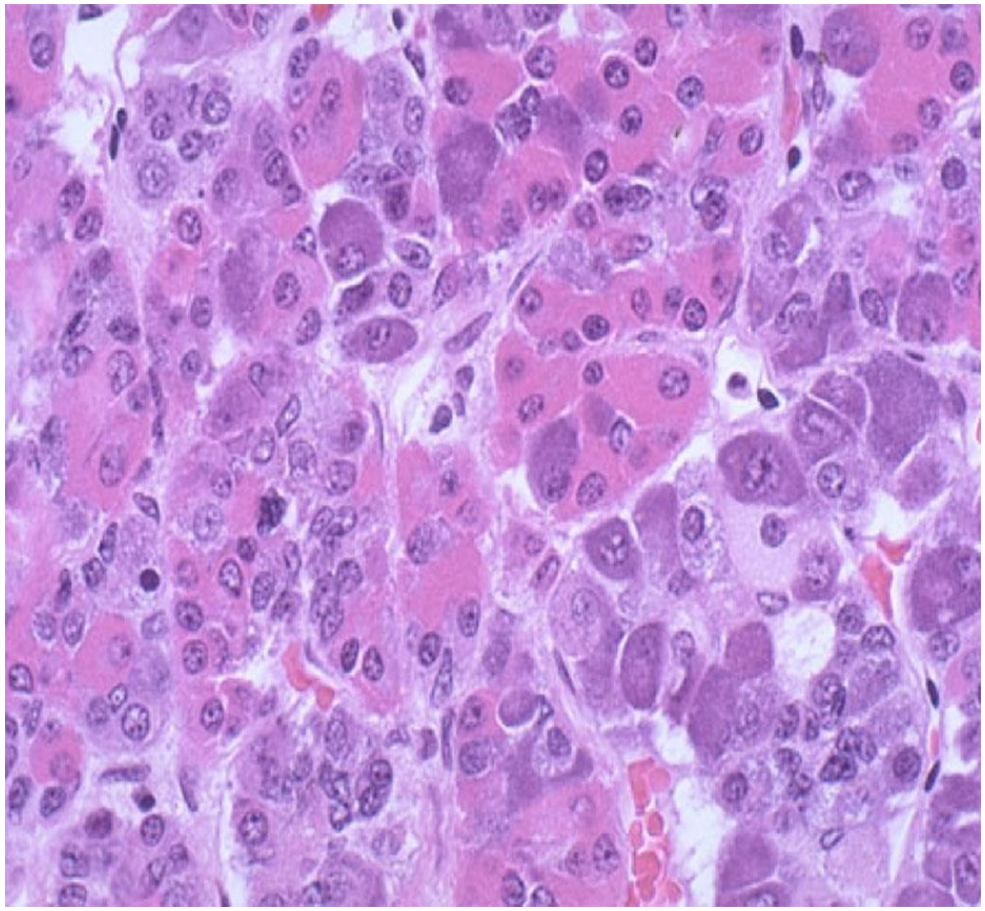
Identification of the cells

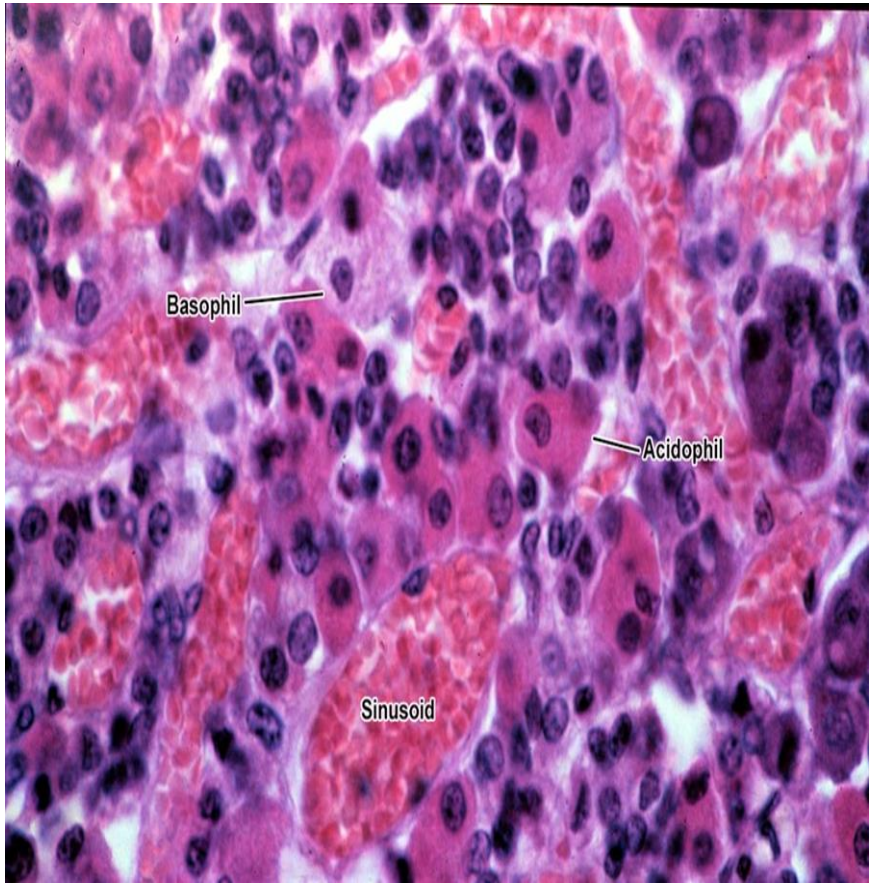
- Routine stains
- Special stain
- Immuno-histochemistry
- Transmission electron microscope

Adenohypophysis hormones

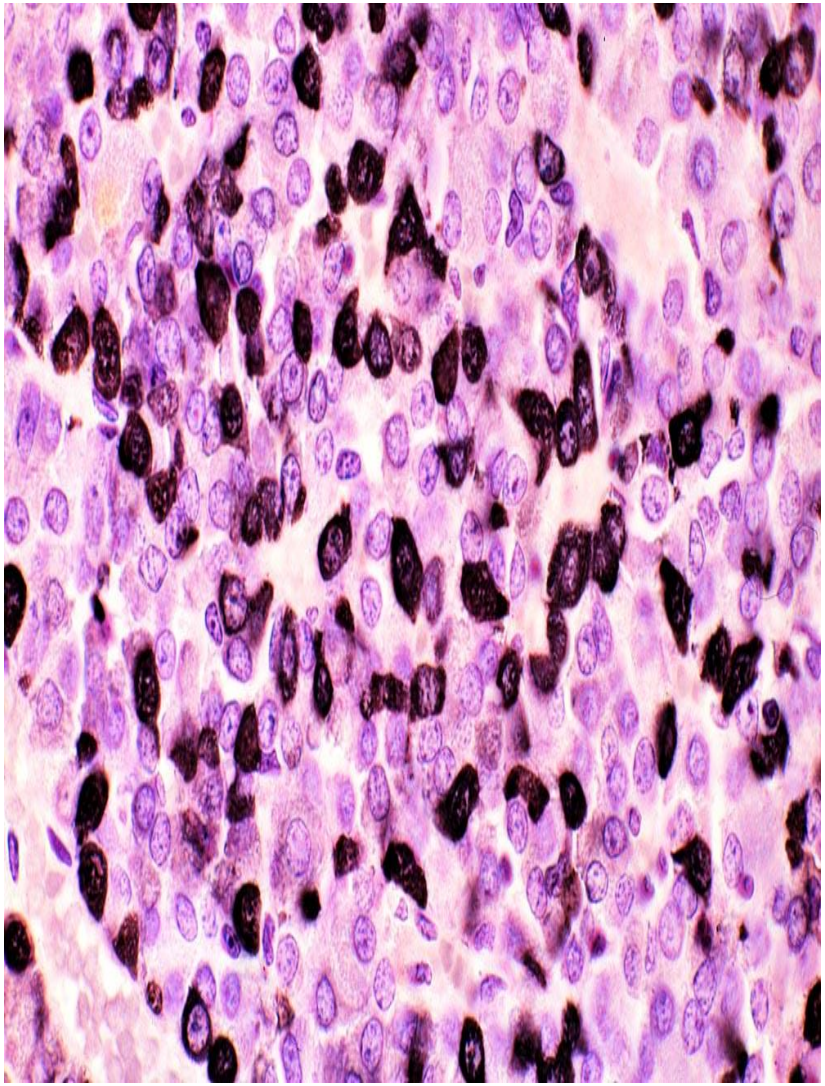
Cells		%	Function
Chromophobes		**52%**	degranulated cell, under-development cell (They are now thought to represent acidophil and basophilic cells in a **dormant** or recently **degranulated** stage)
Basophils	**Gonadotropic cells**	**11%**	FSH LH
	Thyrotropic cells		TSH
	Corticotropic cells		ACTH
Acidophils	**Somatotropic cells**	**37%**	GH or somatotropic hormone (STH)
	Mammotropic cells = Erdheim cells **crinophagy**		Prolactin (PR) or lactogenic hormone (LTH) Large in lactation & small in males & non pregnant

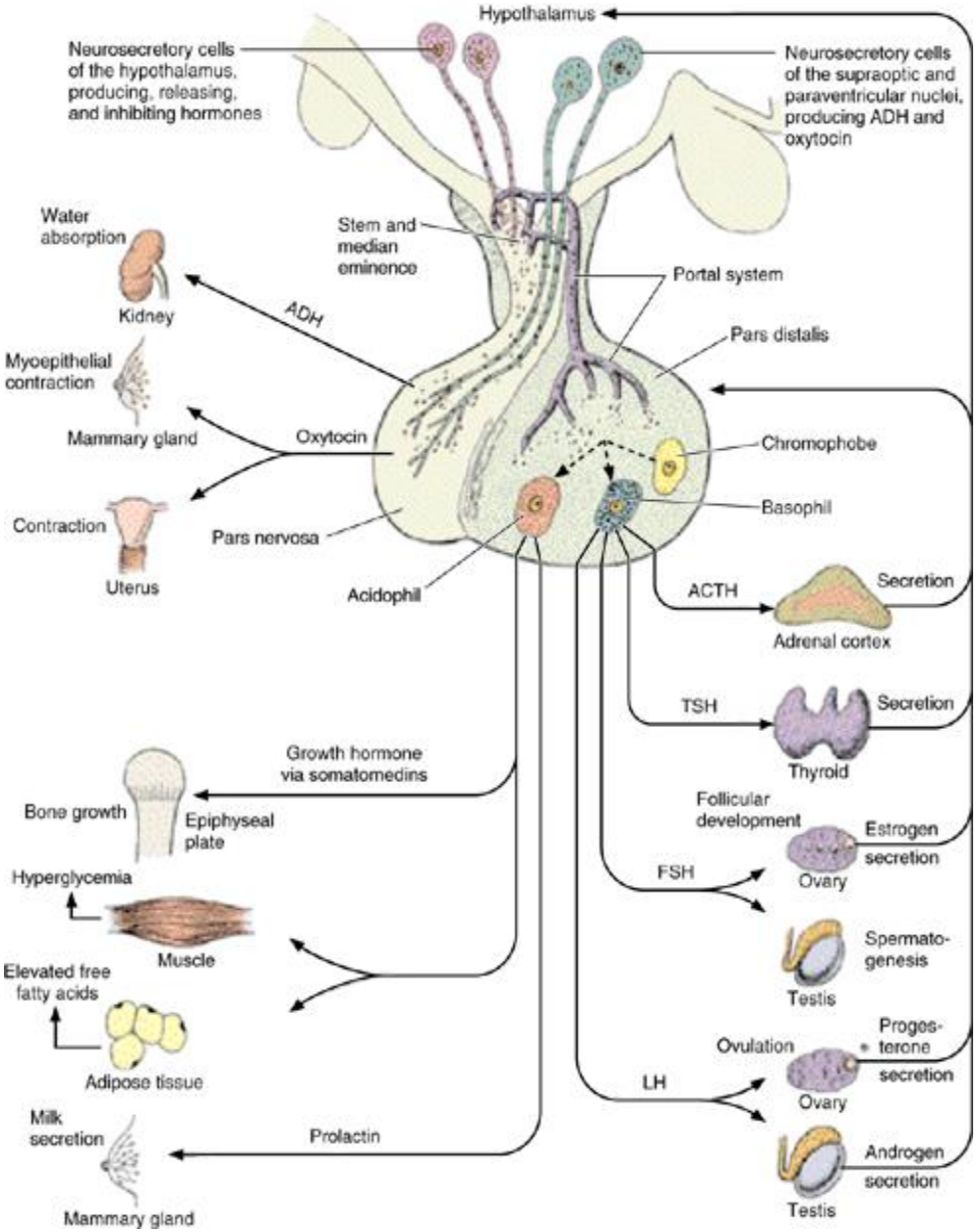
Anterior pituitary (H&E stain)





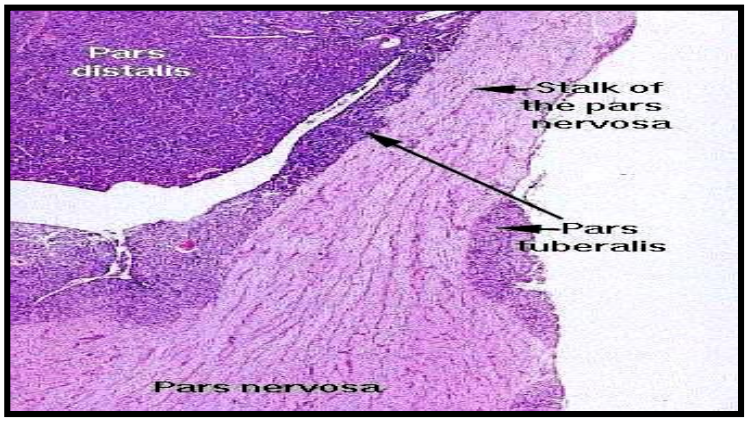
Immunohistochemical localization of growth hormone

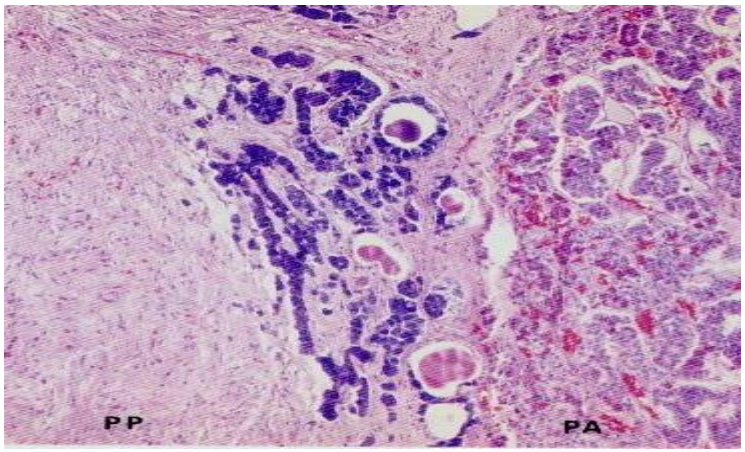


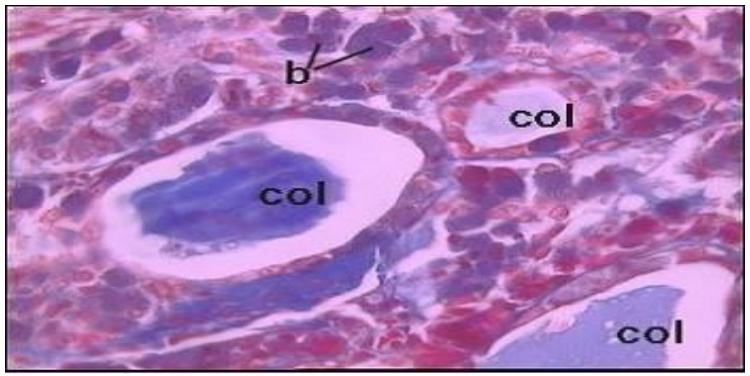


2- Pars intermedia

	In humans	In animals
Development	rudimentary	Well developed
Arrangement	cords	Layers and cysts
Cells	Cuboidal Faint basophilic	Cuboidal basophilic
Function	Non specific and unknown function	MSH (**melanocytes-stimulating hormone)**







Neurohypophysis (Pars nervosa)

Two parts

Infundibulum, a slender stalk of nerve tissue that suspends the pituitary gland from the base of the brain **pituitary stalk**

The Pars Nervosa, is connected directly with the Hypothalamus of the brain by axons

components

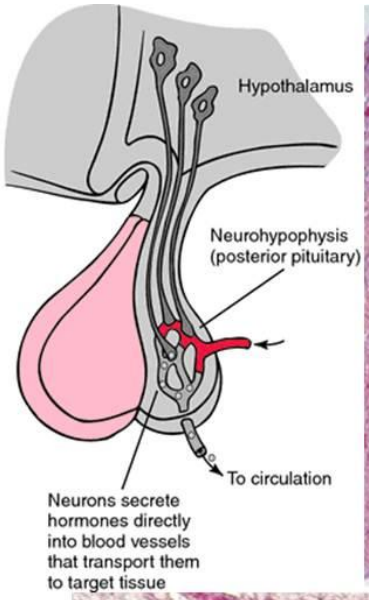
1- unmyelinated axons:

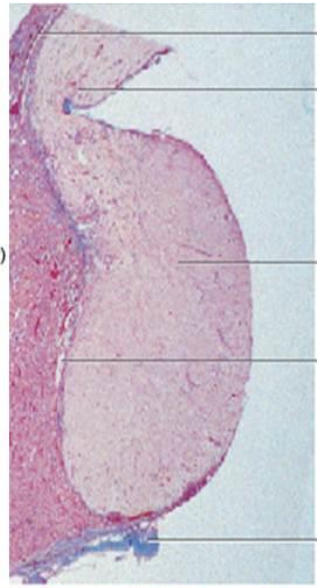
- of neurosecretory cells present in supraoptic and paraventricular nuclei of hypothalamus
- Transmit secretion through hypothalamo-hypophyseal tract.

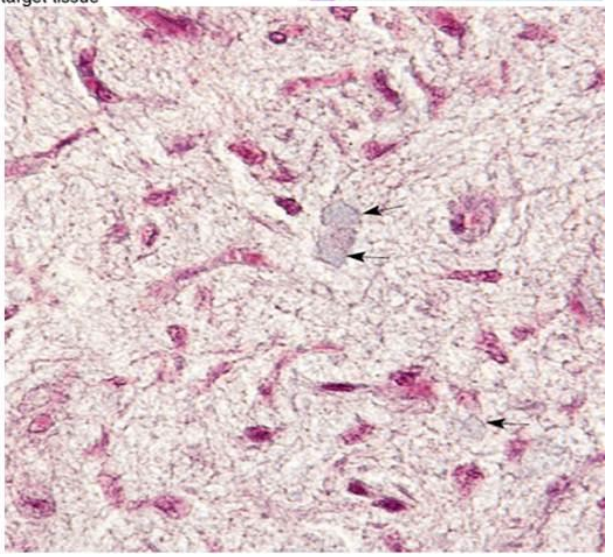
2- Herring bodies: homogeneous red bodies stored in dilated terminal ends of these axons

3-Pituicytes: modified branched glial cells having supportive , nutritive and insulating function.

4-Rich blood capillary plexus







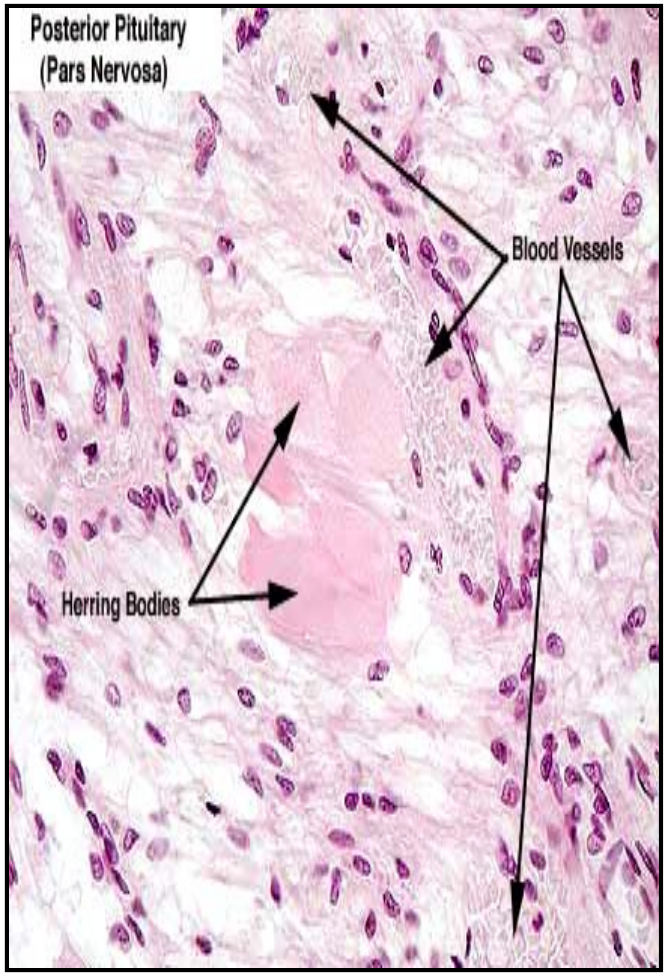
- **Neuro-secretory cells** forms **Herring bodies** i.e. **granules/accumulations form** a dilatation of the axon near the terminals/ contain either

❖ **Oxytocin** stimulate contraction of
1. Smooth muscle of uterus
2. Myoepithelial cells of mammary glands

❖ **Antidiuretic hormone** (ADH) (vasopressin) increasing reabsorption of water in renal tubule and causing the constriction of arterioles to increase blood pressure (Supraoptic nuclei)
1. Contraction of smooth muscle of BVs→ ↑ BP
2. ↑ reabsorption of water from collecting tubules → hypertonic hypovolaemic urine

(↓ ADH→ diabetes insipidus)

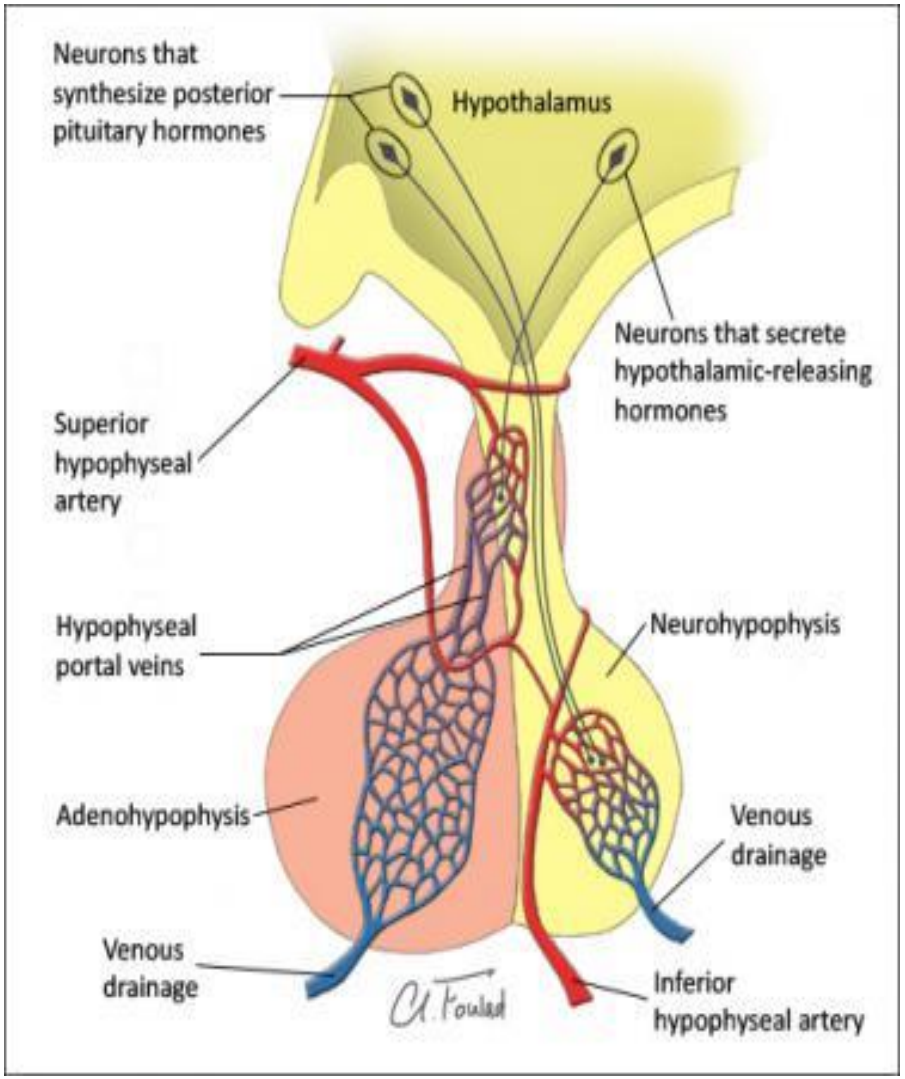
Pituicyte is a **glial cell** of the posterior pituitary. They generally **stain dark purple**, They are similar to the **astrocytes** /glial cells of the CNS. irregular with **processes** / cytoplasm contain pigment granules / function: provides **metabolic support** of nerve fibres

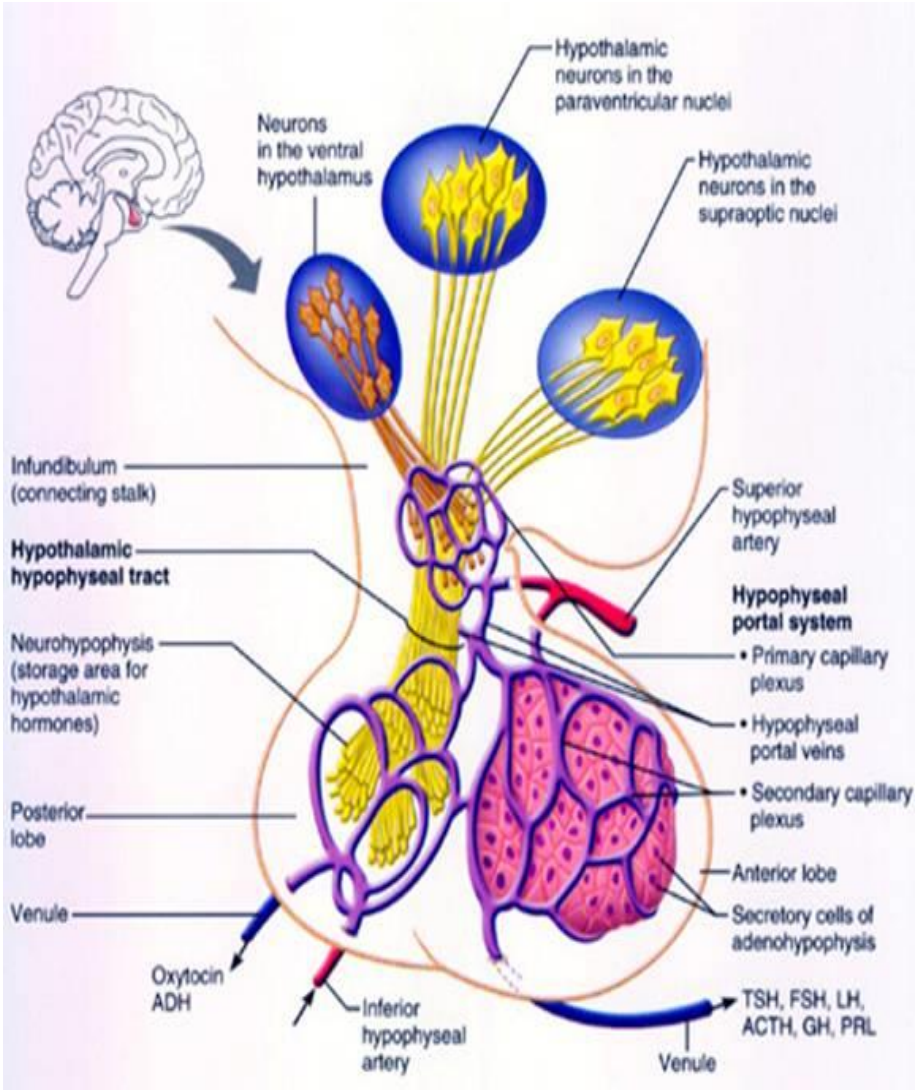


Blood supply of pituitary gland

Releasing and inhibiting hormones

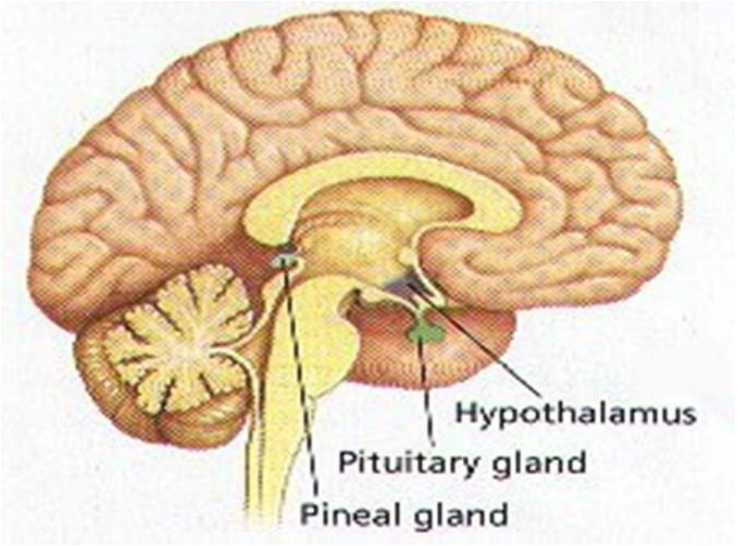
Pass to hypophyseal portal system to pars distalis





Pineal body (Epiphysis cerebri)

- Small pine-cone shaped
- Rice grain in size



Stroma:

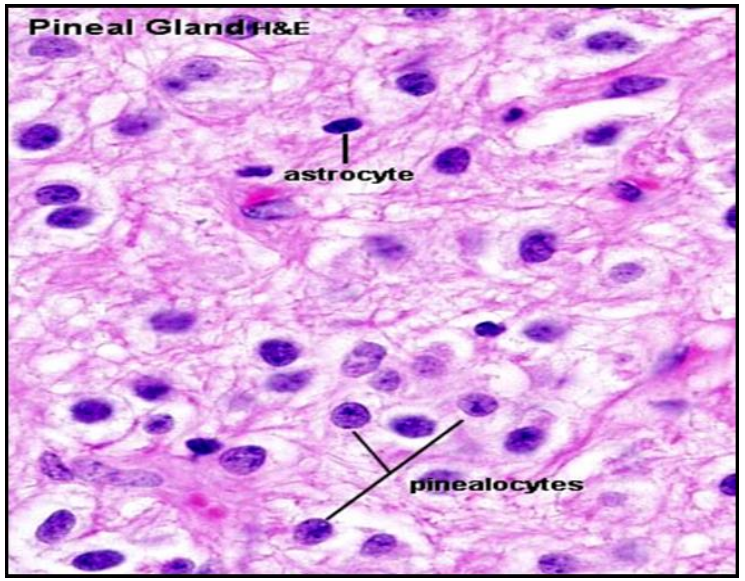
Pia mater → Septa (BVs & unmyelinated nerve fibers

Parenchyma:

Blood vessels + Two types of branching cells

1. glial cells (astrocytes 5%), small dark nuclei

2. pinealocytes (95%), are large and lightly stained have larger, lighter and round nuclei secrete melatonin



- melatonin - is involved in daily cycles or circadian rhythms. Levels are high at night as we grow sleepy & low at day light as we awake. The pineal body is directly light sensitive;

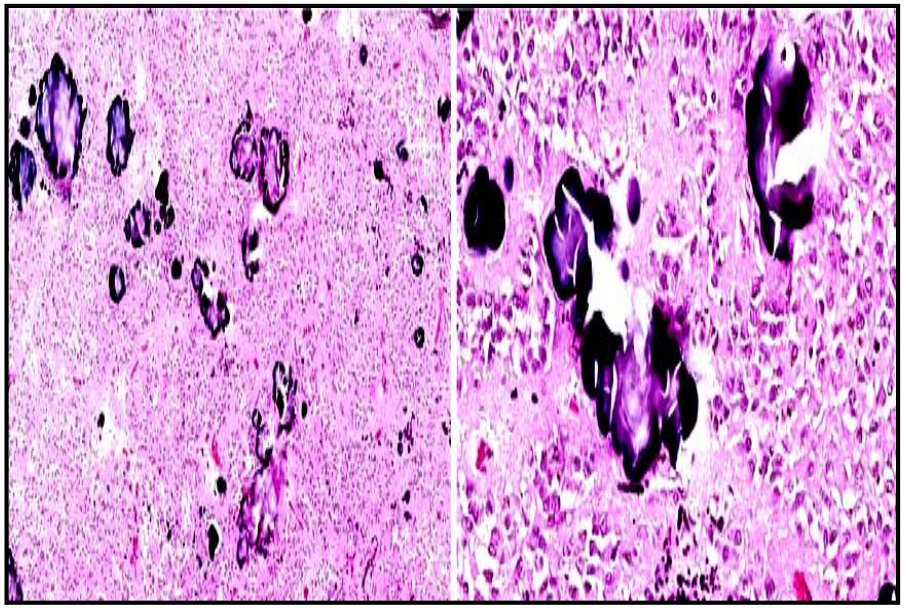
	Pinealocytes	**Astrocytes (neuroglia)**
Nuclei	large irregular with prominent nucleoli	elongated and denser
Cytoplasm	pale basophilic	Dark
Function	Melatonin secretion	Supportive & nutritive

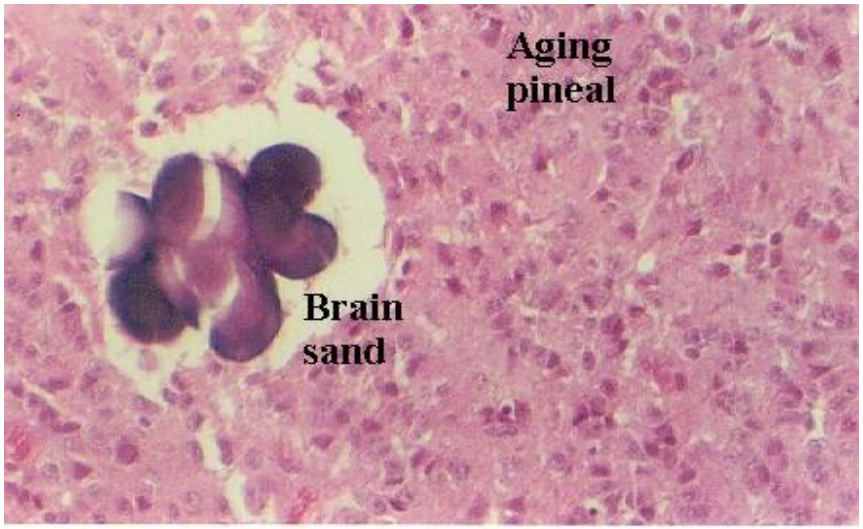
Pineal body with old age

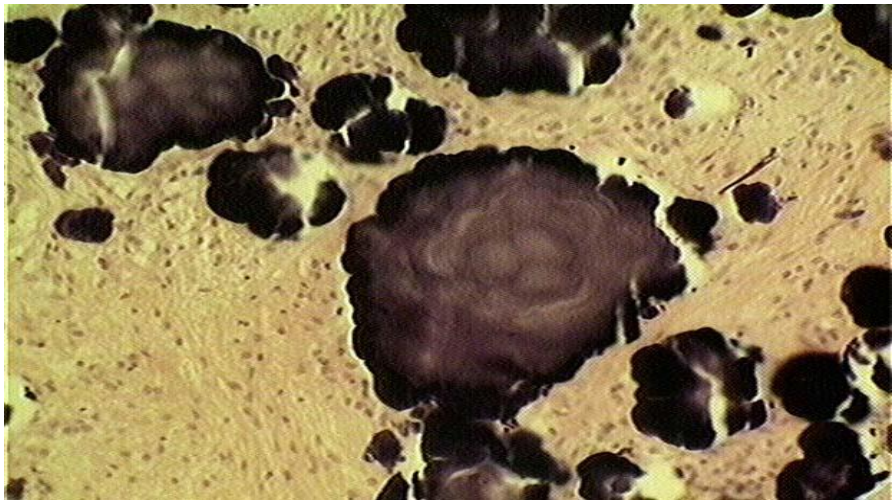
- ↑ fibrosis
- ↑ formation of calcified bodies

(brain sand)

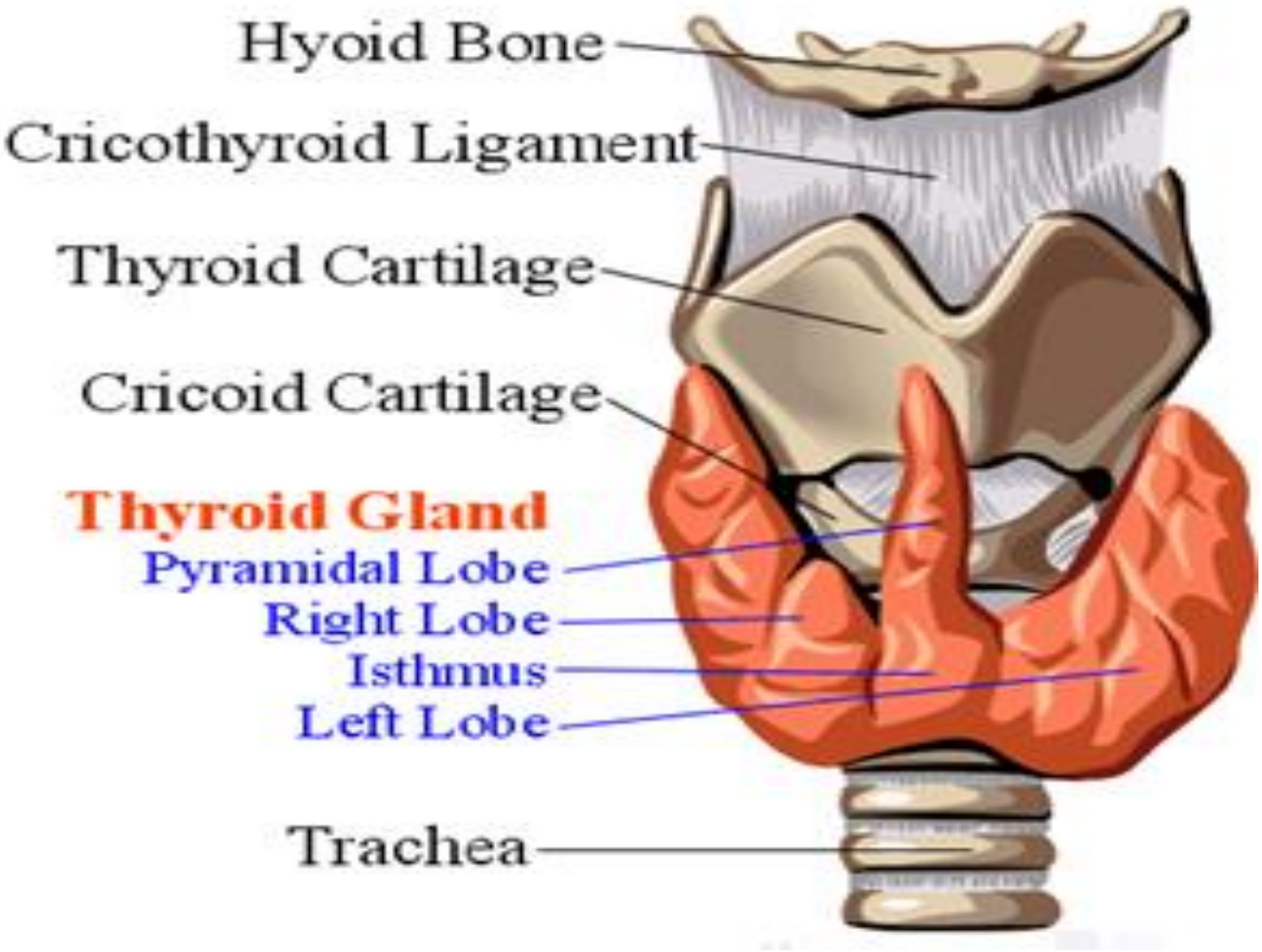
Brain Sand (areas of **calcification**) that are easily seen with the microscope. **not a degenerative** change; **not** pathological







Thyroid gland



Thyroid gland histology

Stroma

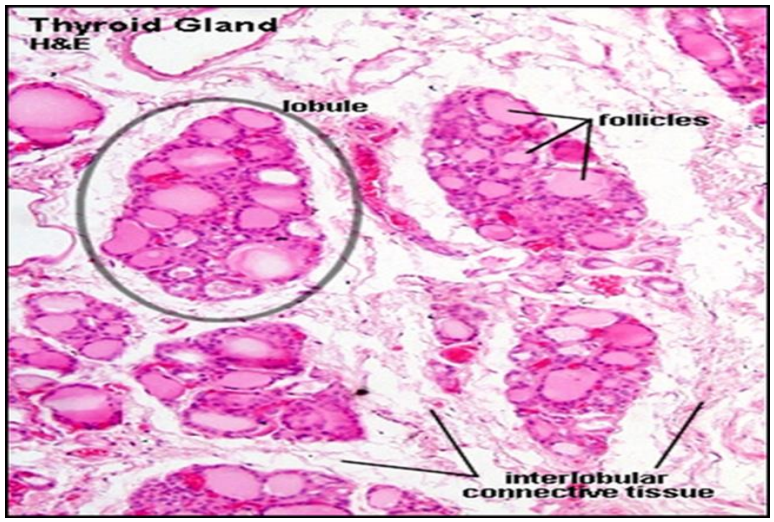
Thyroid gland is covered by a **double capsule**

- Outer: deep cervical fascia
- Inner: true CT capsule

incomplete septa **lobules**

surrounded by interlobular **connective tissue**

+ reticular fibers



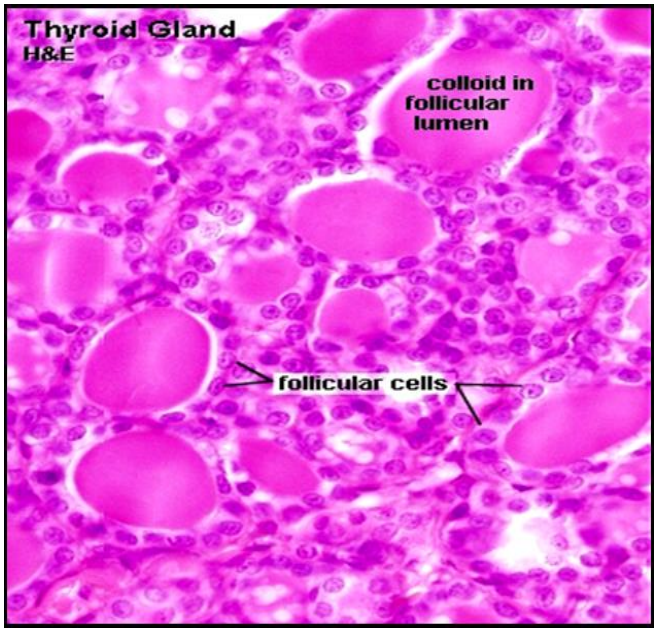
Parenchyma

1. **Blood vessels**
2. **Follicles**
   - Follicular cells
   - Parafollicular
   - Interfollicular cells

Thyroid capillary beds SEM

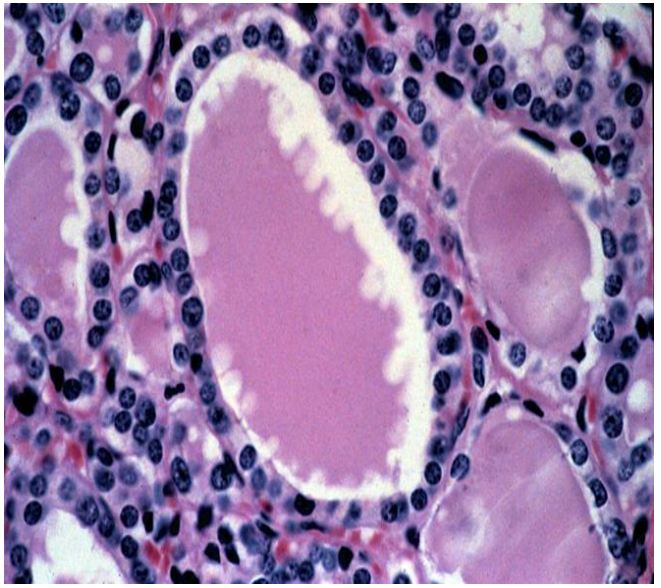
Parenchyma

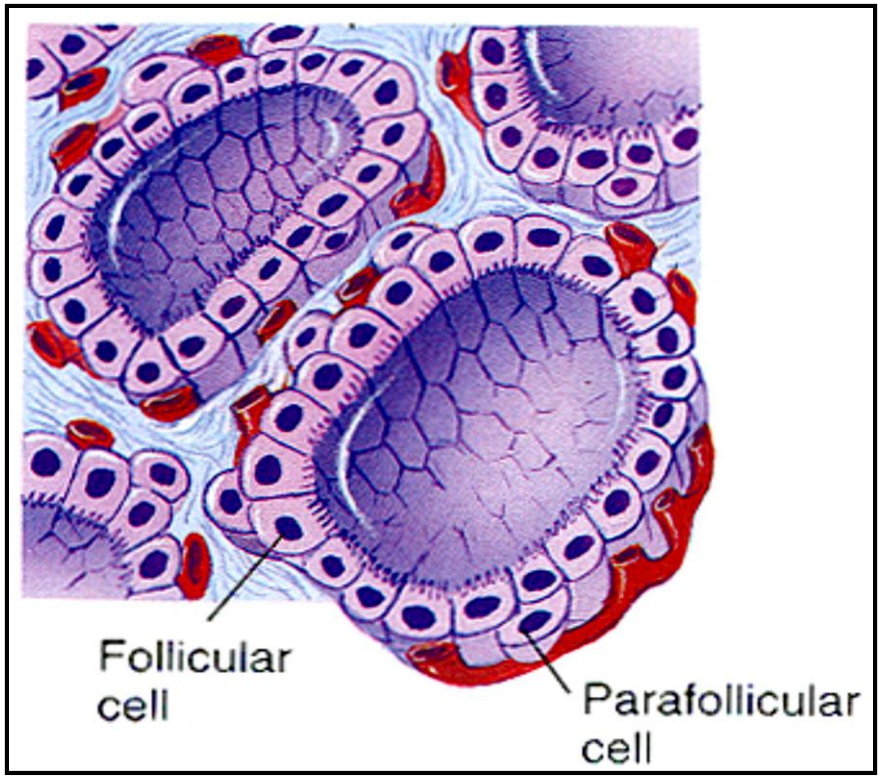
- **Follicles** the **structural and functional** building block of the thyroid gland **spherical** in shape
- separated by scant **interfollicular connective tissue**.

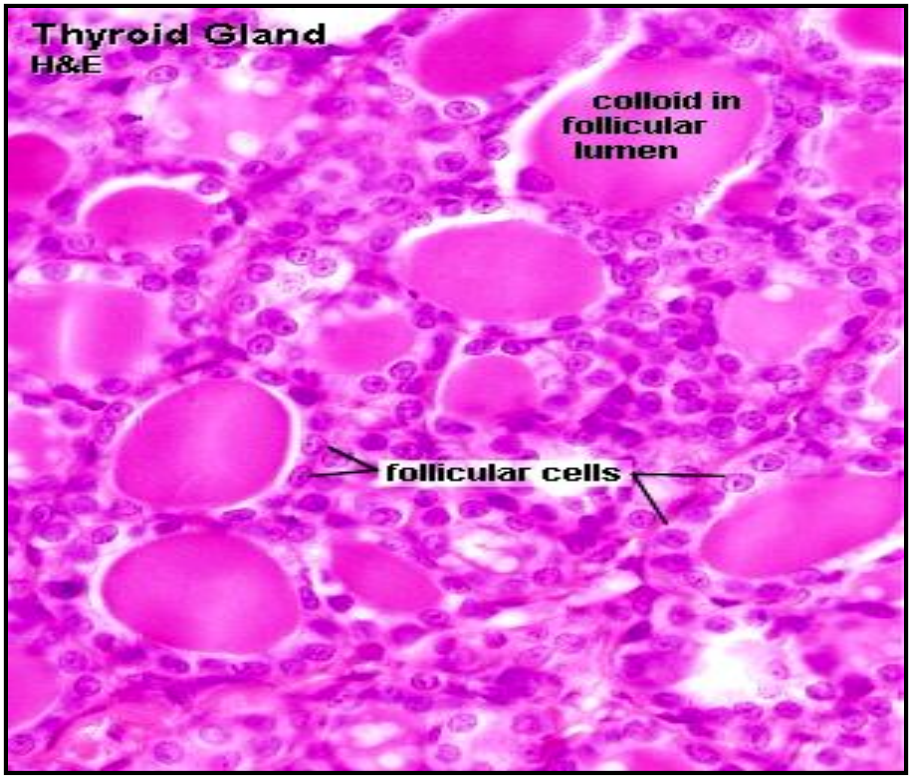


Follicular epithelial cells

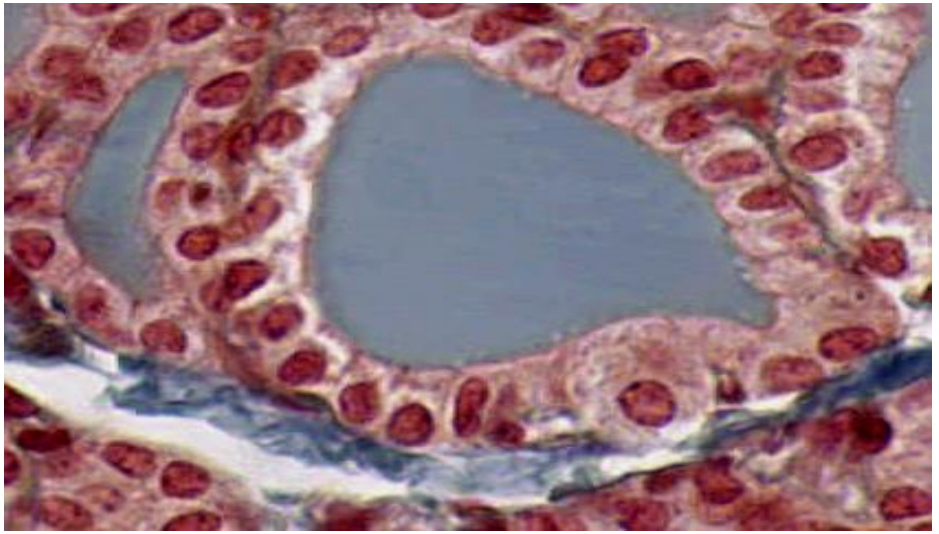
- **Follicular cells**: a **simple cuboidal epithelium** (variable - depending on the functional state) secreting **T3/T4**
- **Parafollicular cells** (or "**C cells**")= clear cell parafollicular cells are **scattered among** follicular cells and in **spaces** between the spherical follicles, –**large, pale stain** and **few** in number , No direct contact with the follicular lumen, They are **always** situated within the **basement membrane**, which surrounds the entire follicle , secrete **calcitonin**.
- **Interfollicular cells**

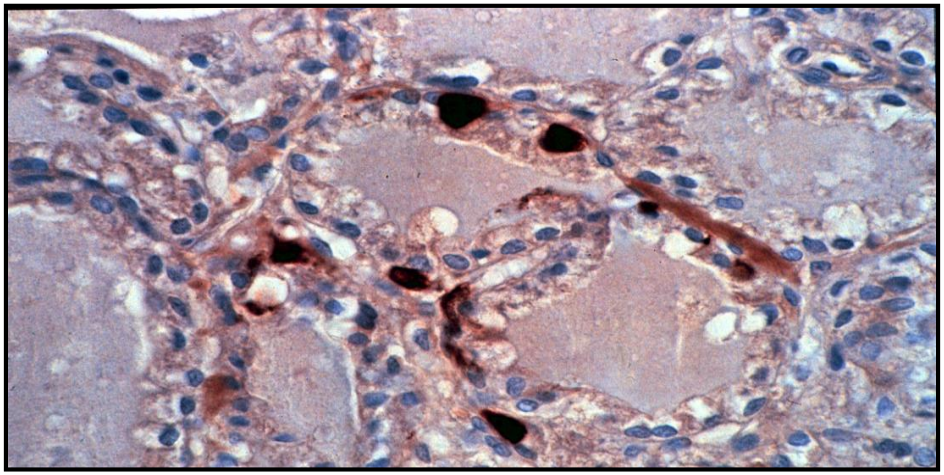



Follicular cell
Parafollicular cell


Thyroid Gland
H&E
colloid in follicular lumen
follicular cells

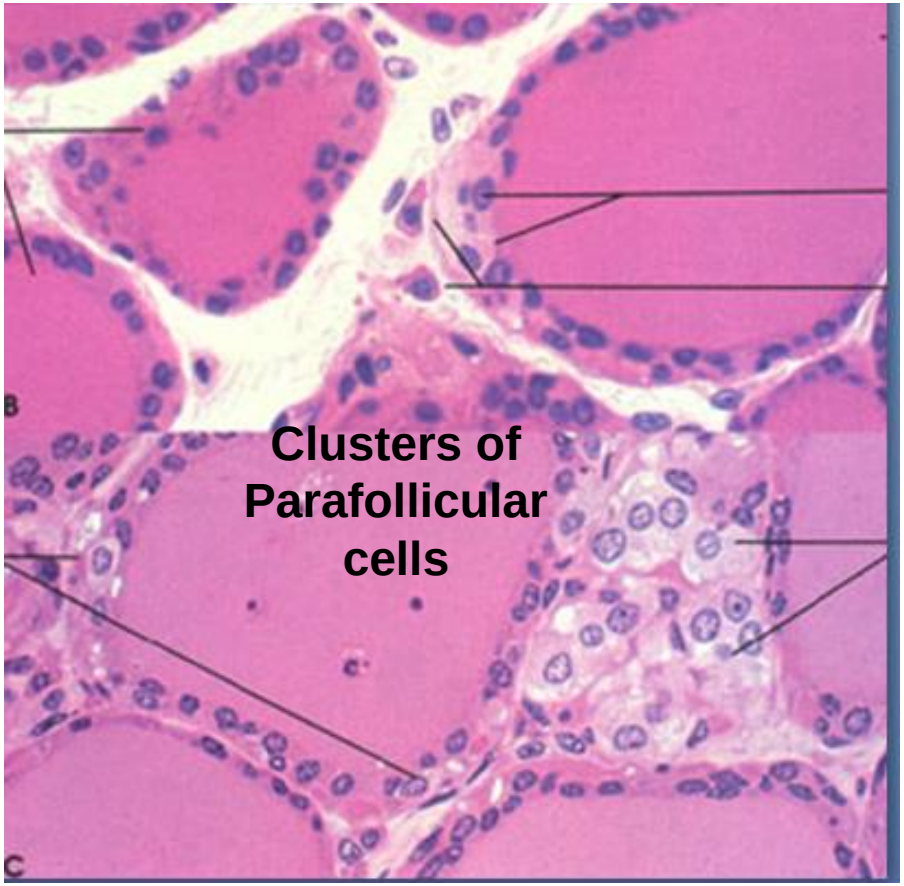
Parafollicular cells

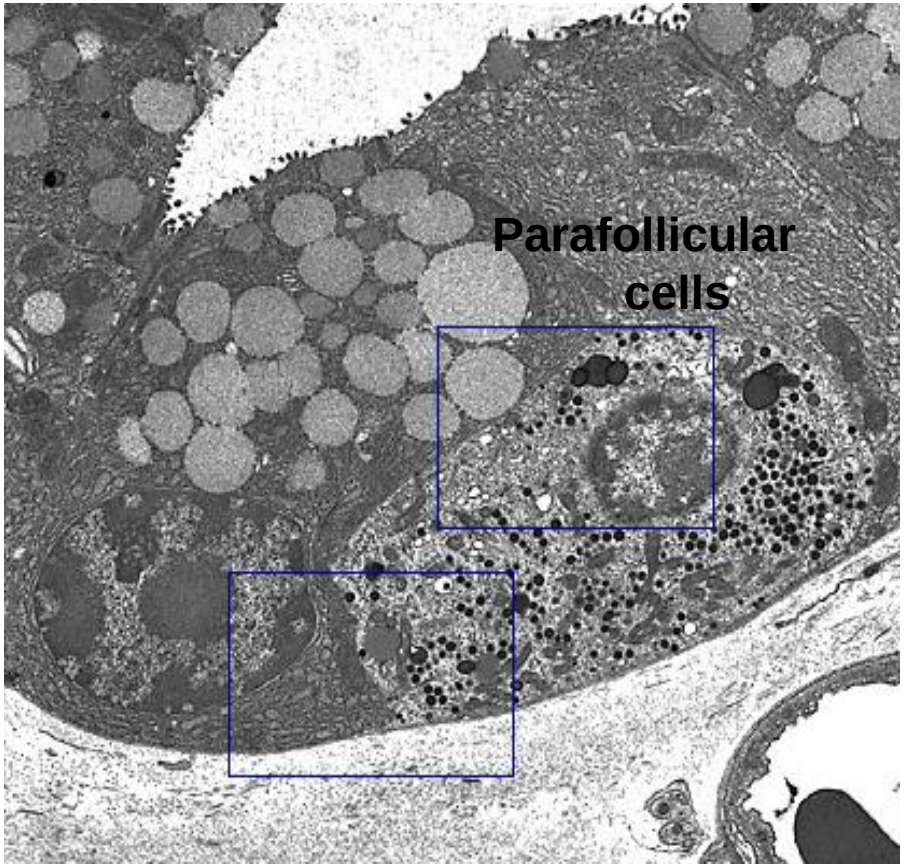




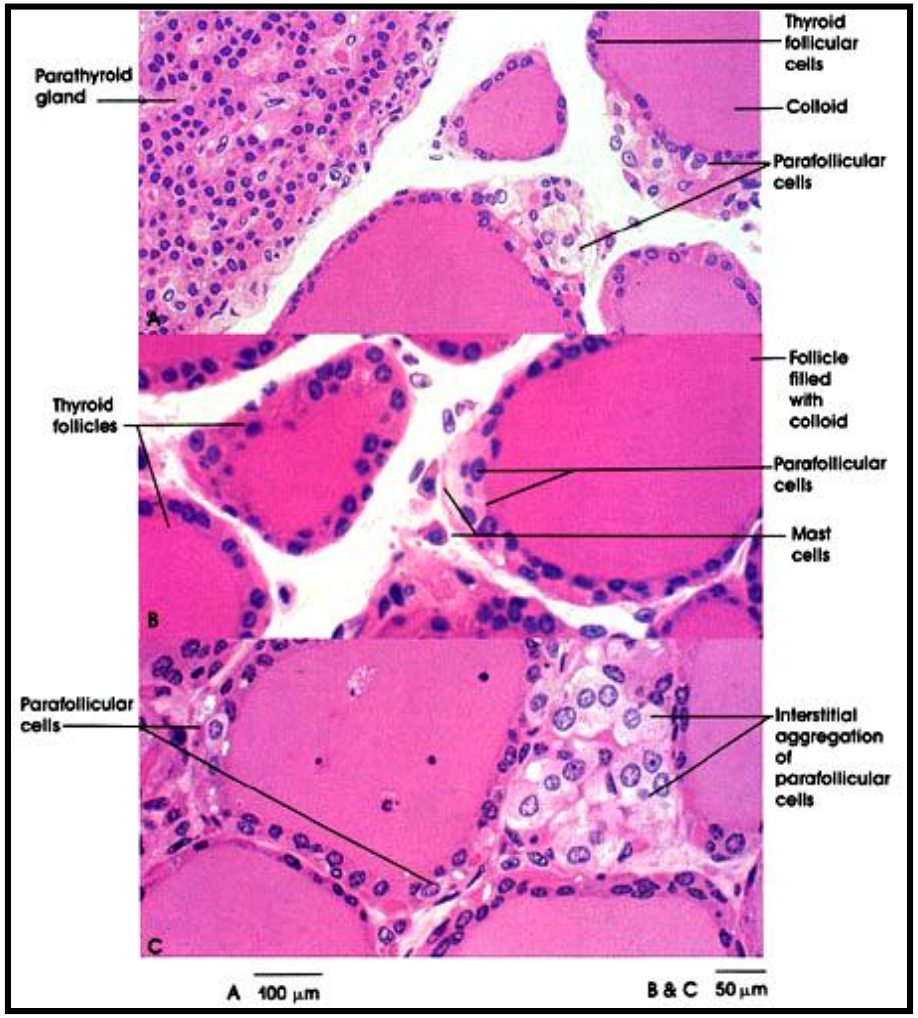
Immunocytochemical localization of calcitonin in C cells

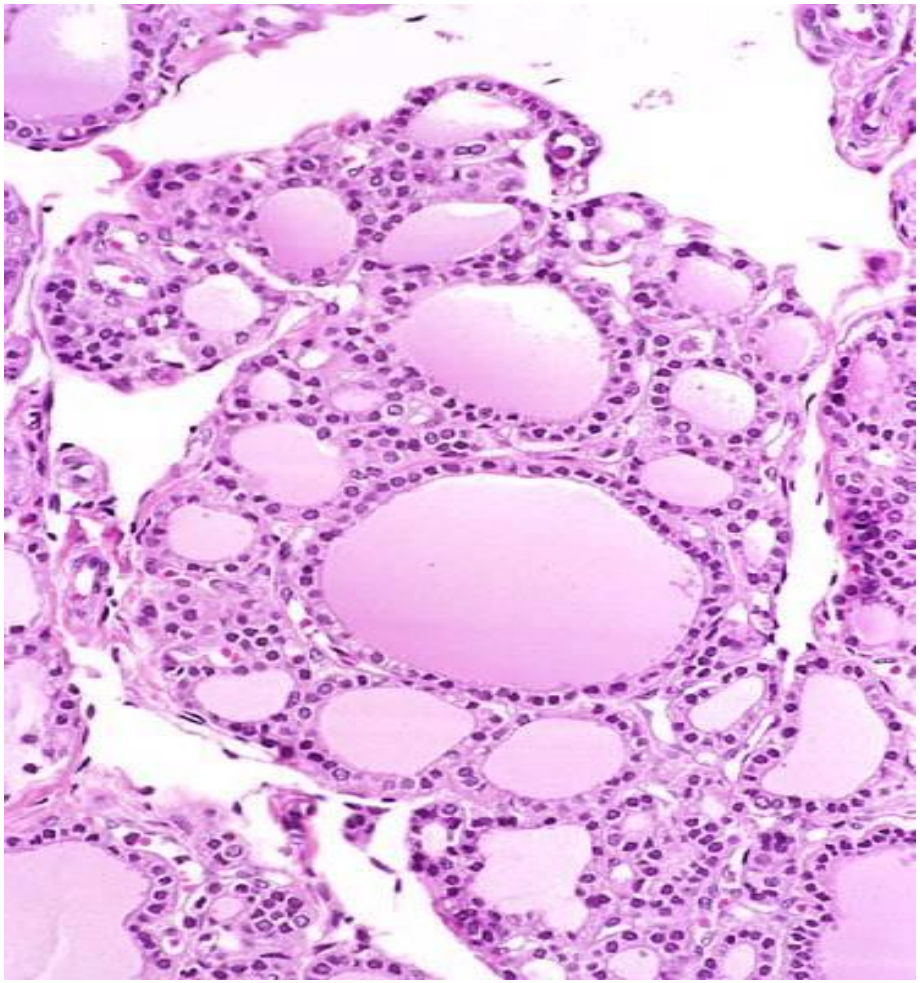
Parafollicular cells





Interfollicular cells



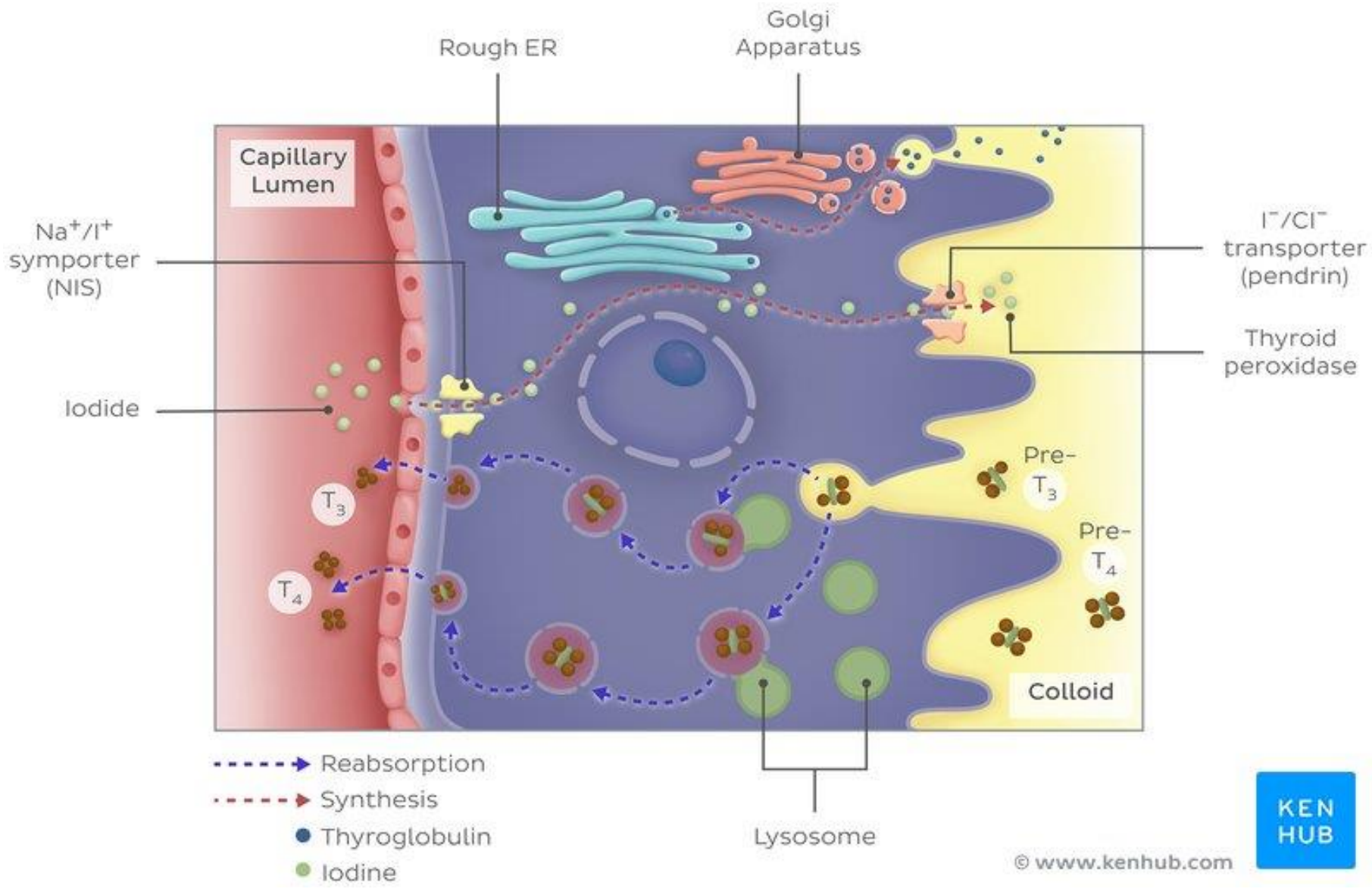


	Follicular cells	**Parafollicular cells**
Size	Smaller	larger
Number	numerous	Few
Extension	Reach the lumen	Do not
Stain	basophilic	pale
Secretion	•Stored extracellularly in the lumen •Secrete **T3 &T4**	•Stored intracellularly in small basal secretory granules •Secrete **calcitonin**
Lysosomes & phagosomes	**abundant**	**Few in No**

Correlates EM structure of follicular cells to its function.

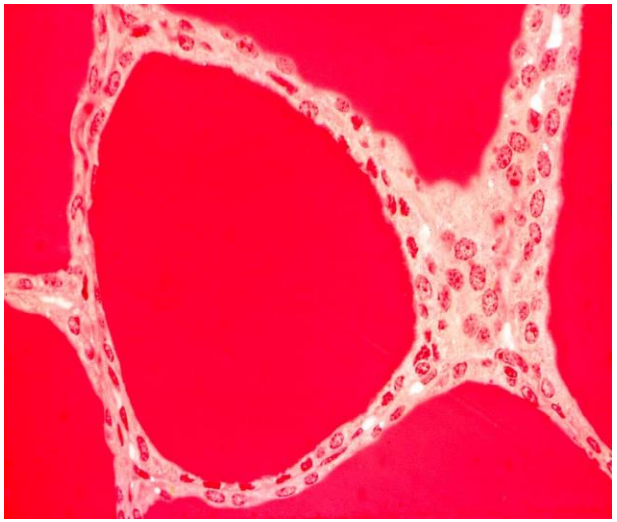
- **rER.** — Synthesis of thyroglobulin.
- **Golgi apparatus** — and form the vesicles.
- **Exocytotic vesicles** — dischargeThyroglobulin into the lumen
- Follicular cells trap the iodide and liberate it as iodine in the follicular lumen
- **Microvillous border** — Surface area ↑
- iodination takes place extracellularly.
- **Endocytotic vesicles.** — reabsorb thyroglobulin.
- **Lysosomes.** — hydrolyse thyroglobulin to thyroxine ↓
- thyroxine which is released into the fenestrated blood capillaries

Follicular cells synthesis of T3 & T4

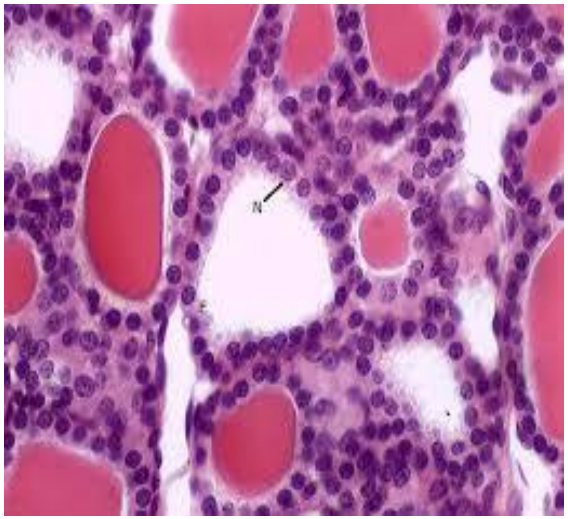


Functional states of thyroid follicles

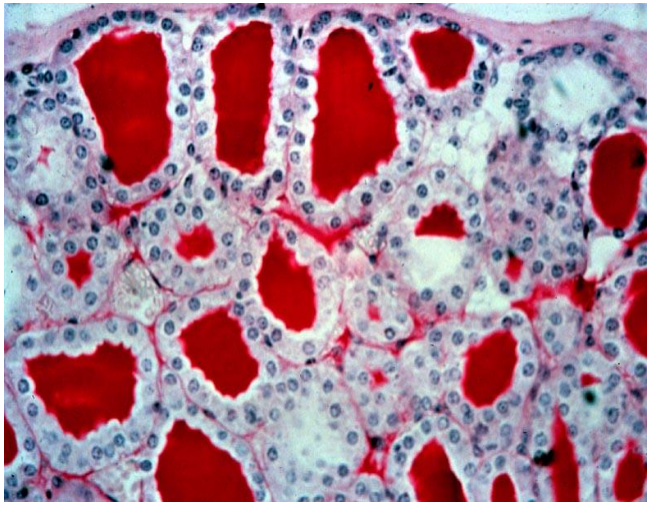
(hypoactive)



Normal



(hyperactive)



Iodine deficiency goiter

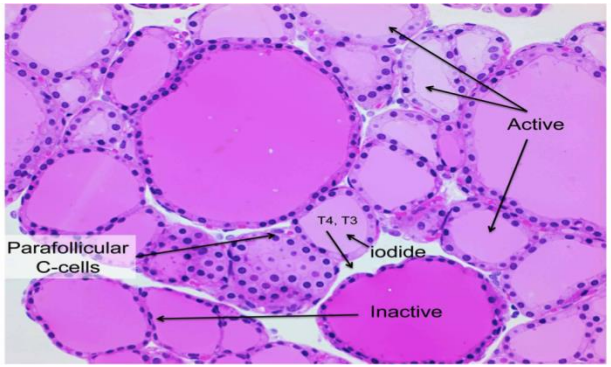
Hypertrophy of thyroid gland

↓ iodine in diet →↓ T3 &T4 →↑ TSH

Hypothyroidism

In children → cretinism (dwarf & mental retardation)

In adults → myxedema

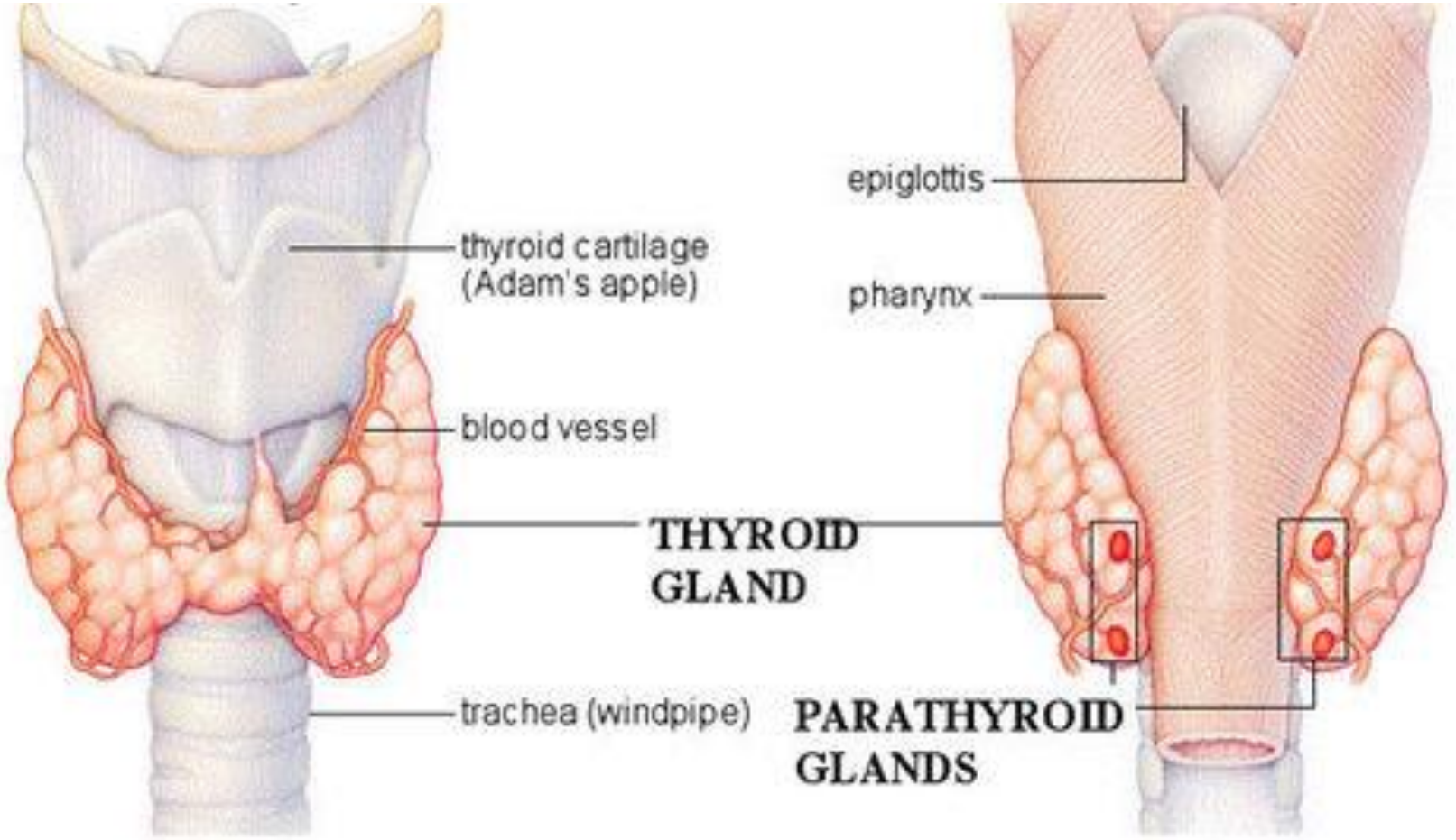


Hyperthyroidism (thyrotoxicosis)

Grave's disease or **exophthalmic goiter**

autoimmune disorder

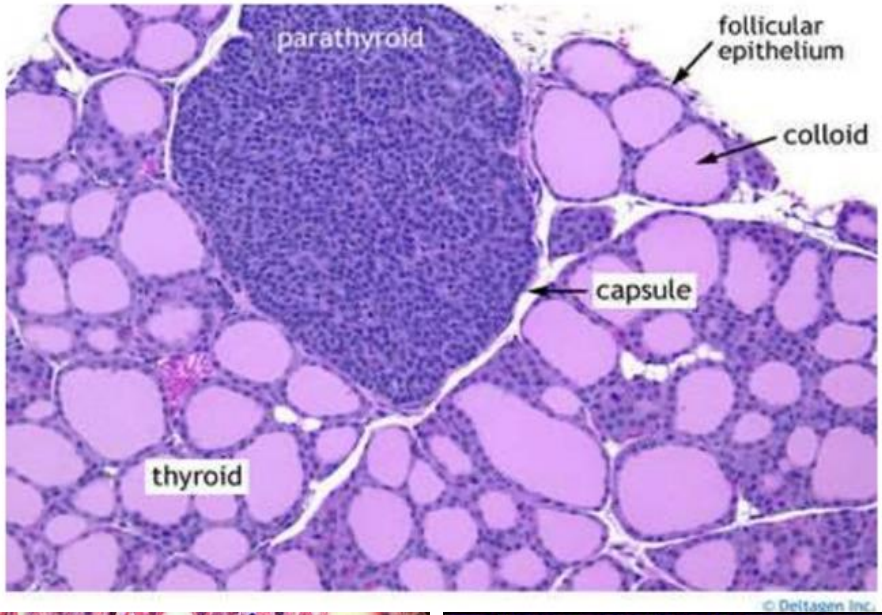
Parathyroid gland



Parathyroid gland

Stroma : C.T. capsule + thin septa

- Each parathyroid gland is surrounded by a thin **connective tissue capsule**, **delicate connective tissue septa with** a considerable number of fat cells infiltrate the gland

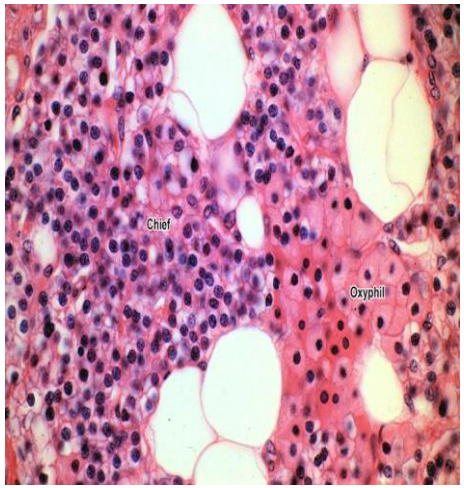


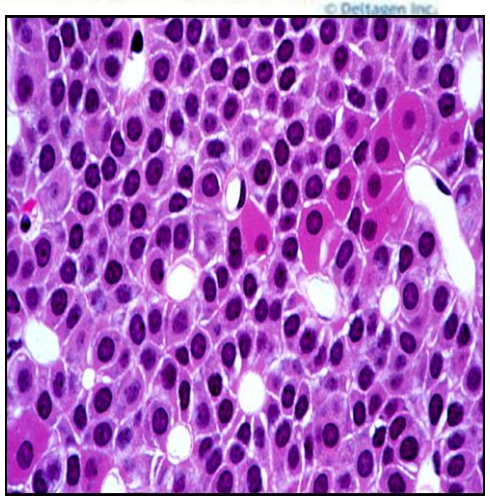
Parenchyma :

Abundant capillaries +

Parenchymal cells are arranged in anastomosing **cords** contain **Two types of** cells arranged in cords separated by blood vessels

- **Chief cells**
- **Oxyphil cells**

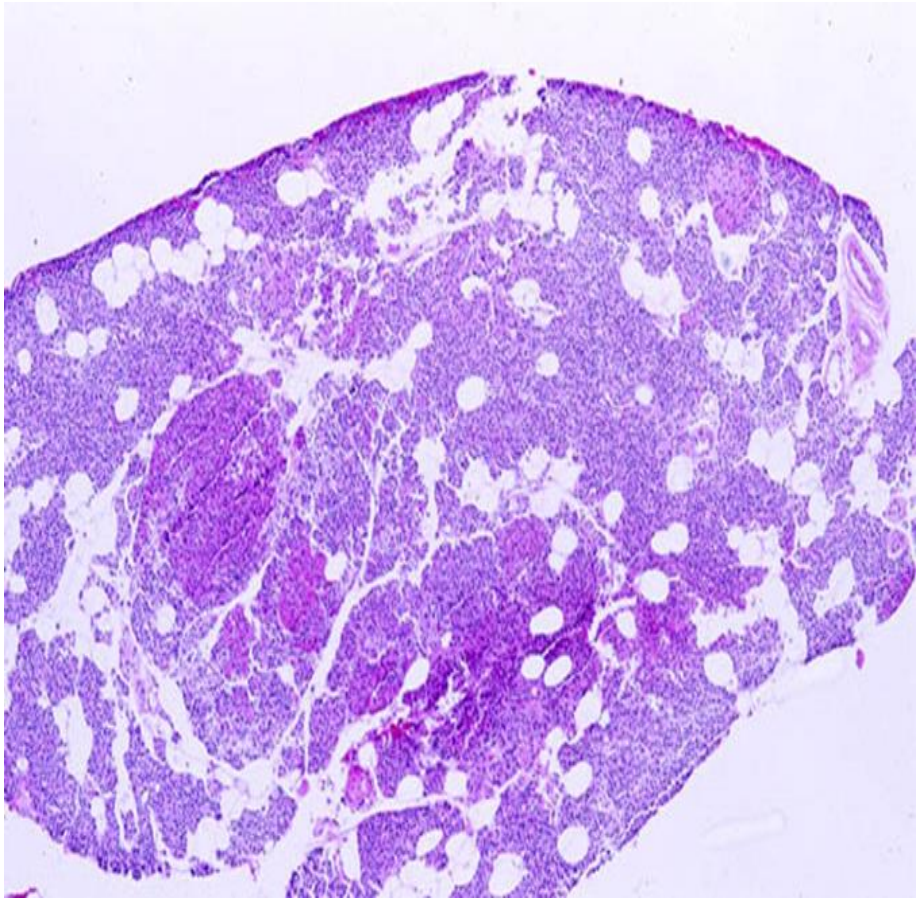


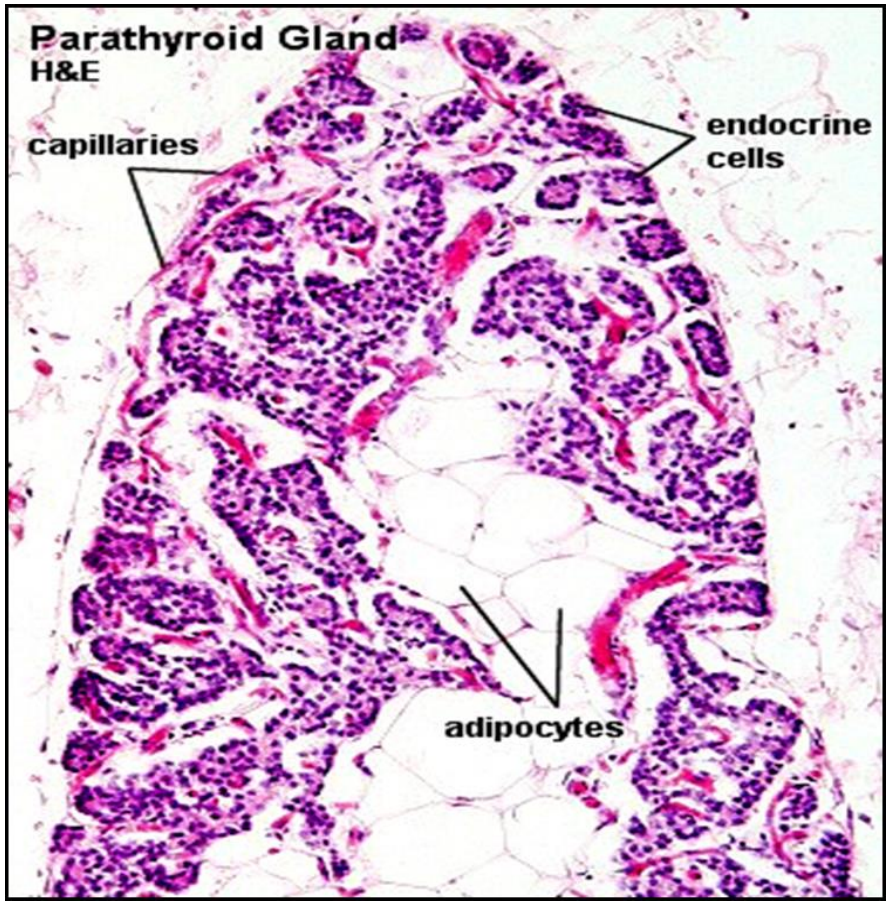


	Chief cells (principal)	**Oxyphil cells**
size	Small polygonal	Large polygonal
number	numerous	few
Stain	Faint acidophilic	Deep acidophilic
nucleus	Large vesicular	Small dense
rER	more	sparse
mitochondria	Moderate number	numerous
Function	Parathyroid hormone (↑ Blood Ca level)	unknown

Parathyroid gland with old age

- Fibrosis increase
- Increase number of fat cells





Regulation of blood calcium level

↓ Blood Ca++ level ⇨ ↑ PTH → ↑ Blood Ca ++ level through:

1. bone: ↑ osteoclasts
2. kidney: ↑ Ca ++reabsorption
3. intestine: ↑ Ca ++ ⇨ absorption

↑↑ Blood Ca ++level ↑ Calcitonin ⇨ ↓↓ Ca++ level by ↓activity of osteoclast

Hyperparathyroidism

↑ Parathyroid hormone →

1.bone fracture

2.Calcification of several organ

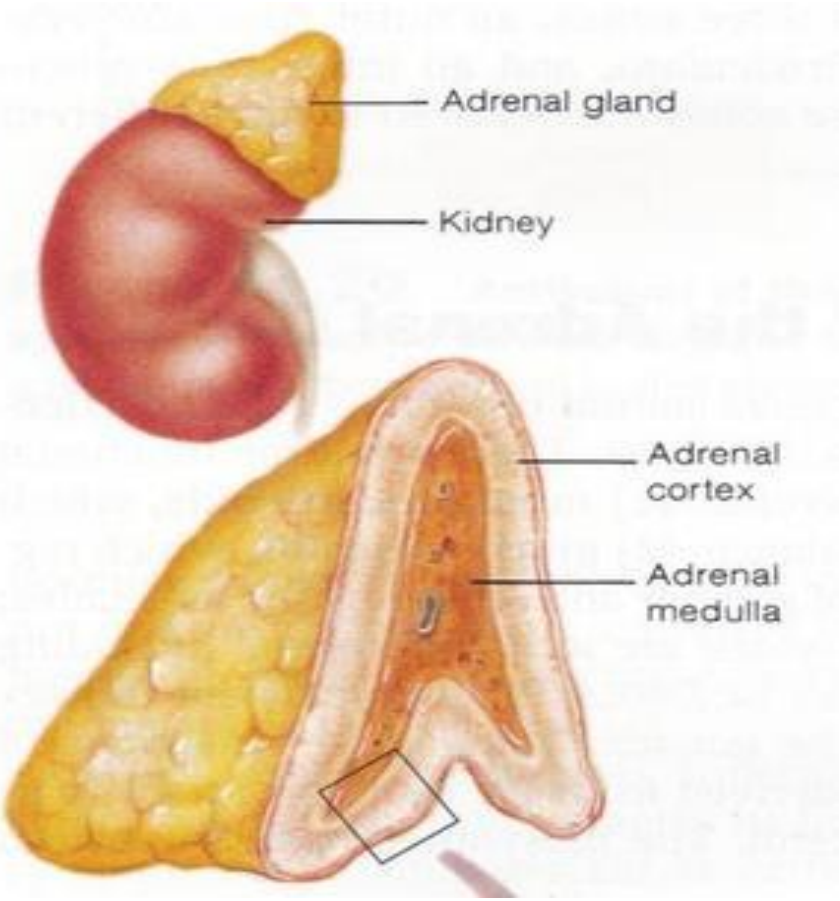
Hypoparathyroidism

↓ Parathyroid hormone →

1.bones become denser

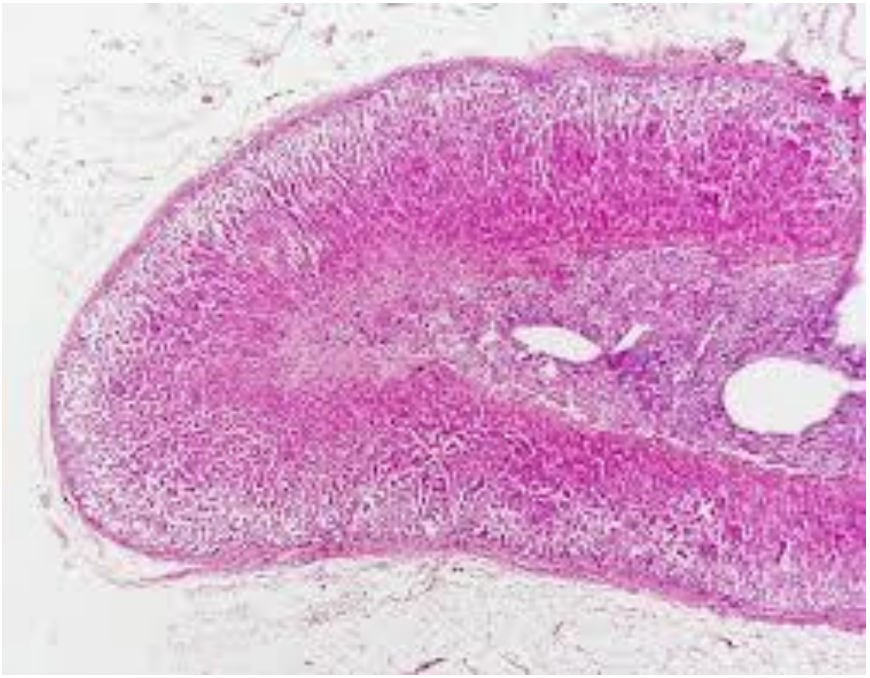
2. excitability of nervous system → tetany

ADRENAL GLANDS
or suprarenal gland



Stroma : The gland is surrounded by a **thick connective tissue capsule**.

- Vessels and nerves reach the medulla by way of connective tissue **trabeculae** which extend from the capsule towards the medulla.



Parenchyma : consist of

- ❑ outer **cortex** (the main part)
- ❑ inner **medulla 10%**

	Cortex	**Medulla**
Colour	Yellow	Reddish-brown
Position	Peripheral	Central
Origin	Coelomic mesoderm (mesodermal)	Neural crest (ectodermal)

Zones of the cortex

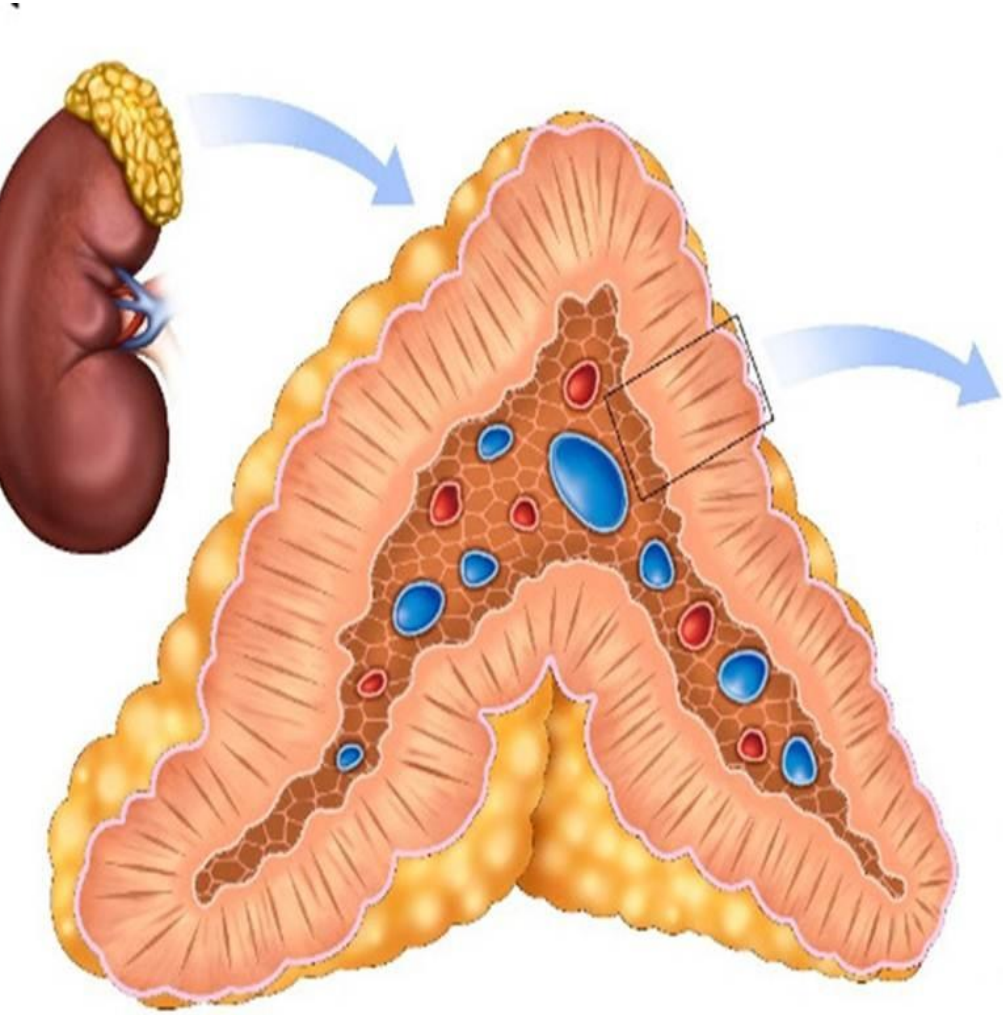
1. **zona glomerulosa** (**15%)** small rounded cells groups (clusters) or curved columns. The smallest cells, their nuclei are dark and round, and the cytoplasm is light basophilic// not influenced by ACTH// mineralocorticoid

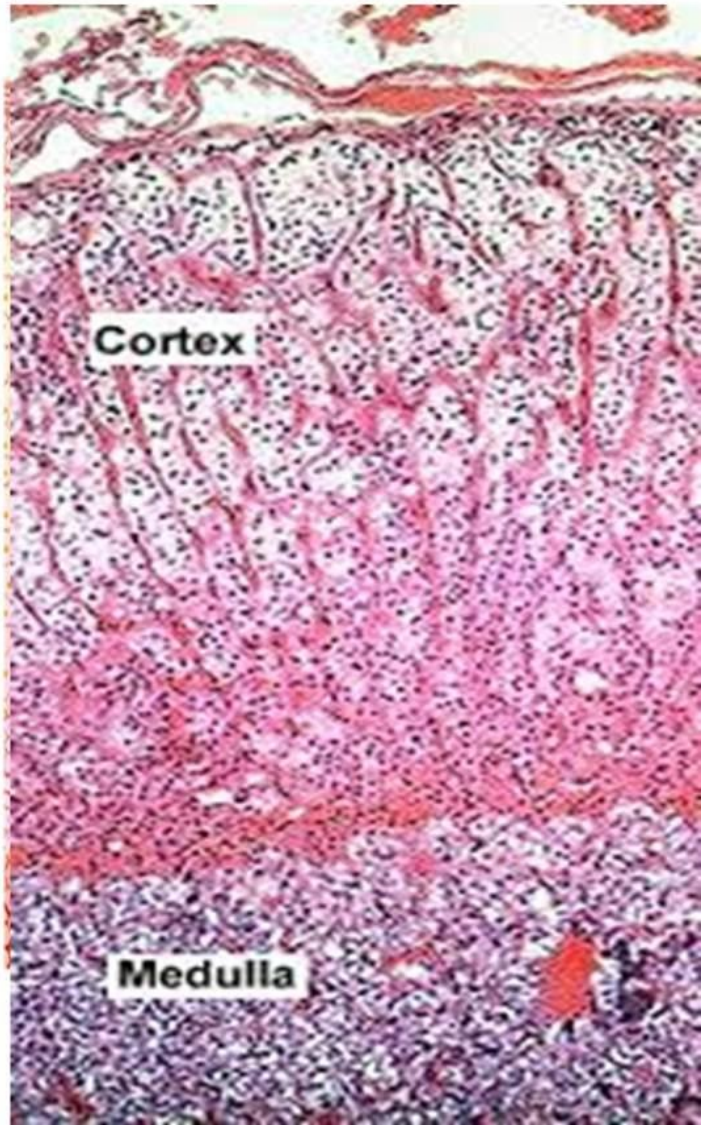
2- zona fasciculata (65%) consists of radially arranged cell cords separated by fenestrated sinusoid capillaries. The nucleus is light and typically located centrally. The cytoplasm is also light and often has a characteristic foamy or spongy appearance (lipid droplets) spongiocytes// glucocorticoids

3- zona reticularis (7%).

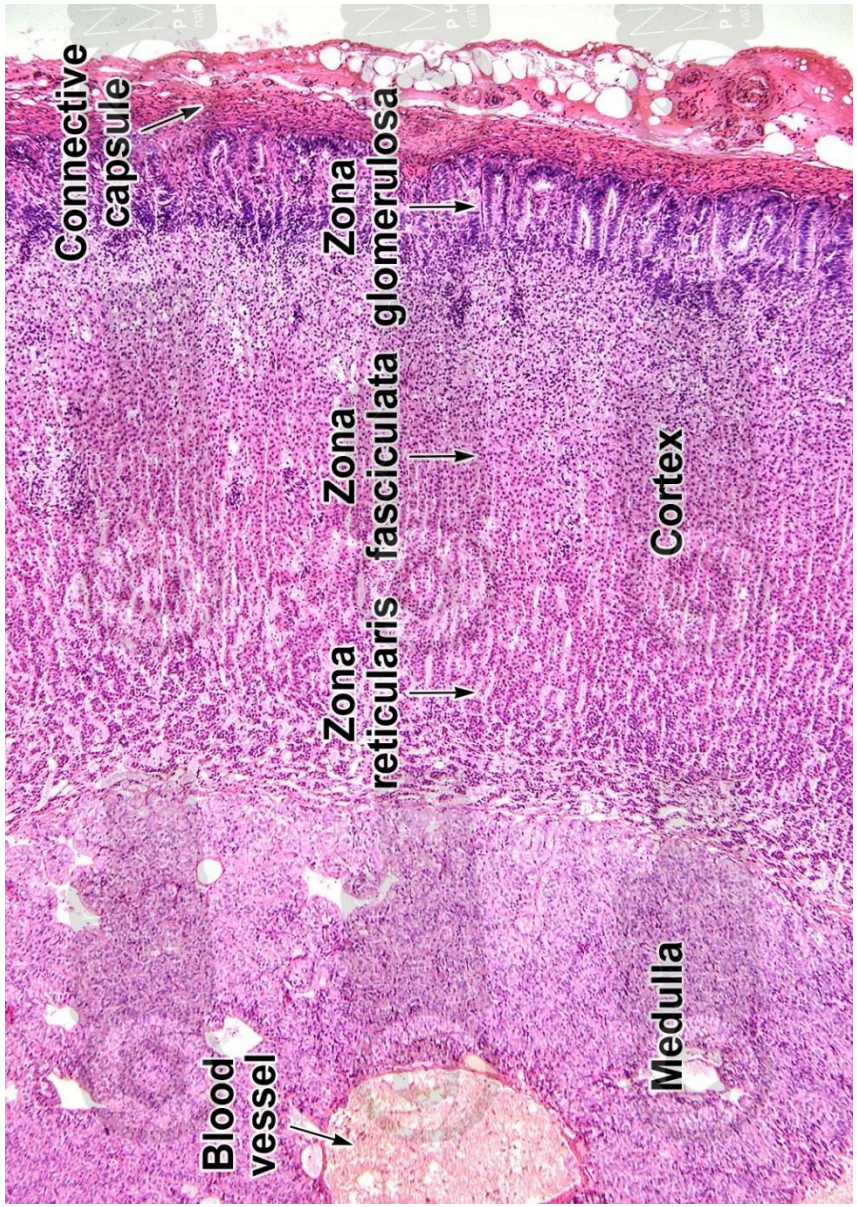
- Outer cells: like zona fasciculata but with fewer lipid droplets
- Inner cells: two types:
  - Dark cells: pyknotic nuclei, excess lipofucsin pigment suggesting cellular degeneration.
  - Light cells: pale with pale staining nuclei

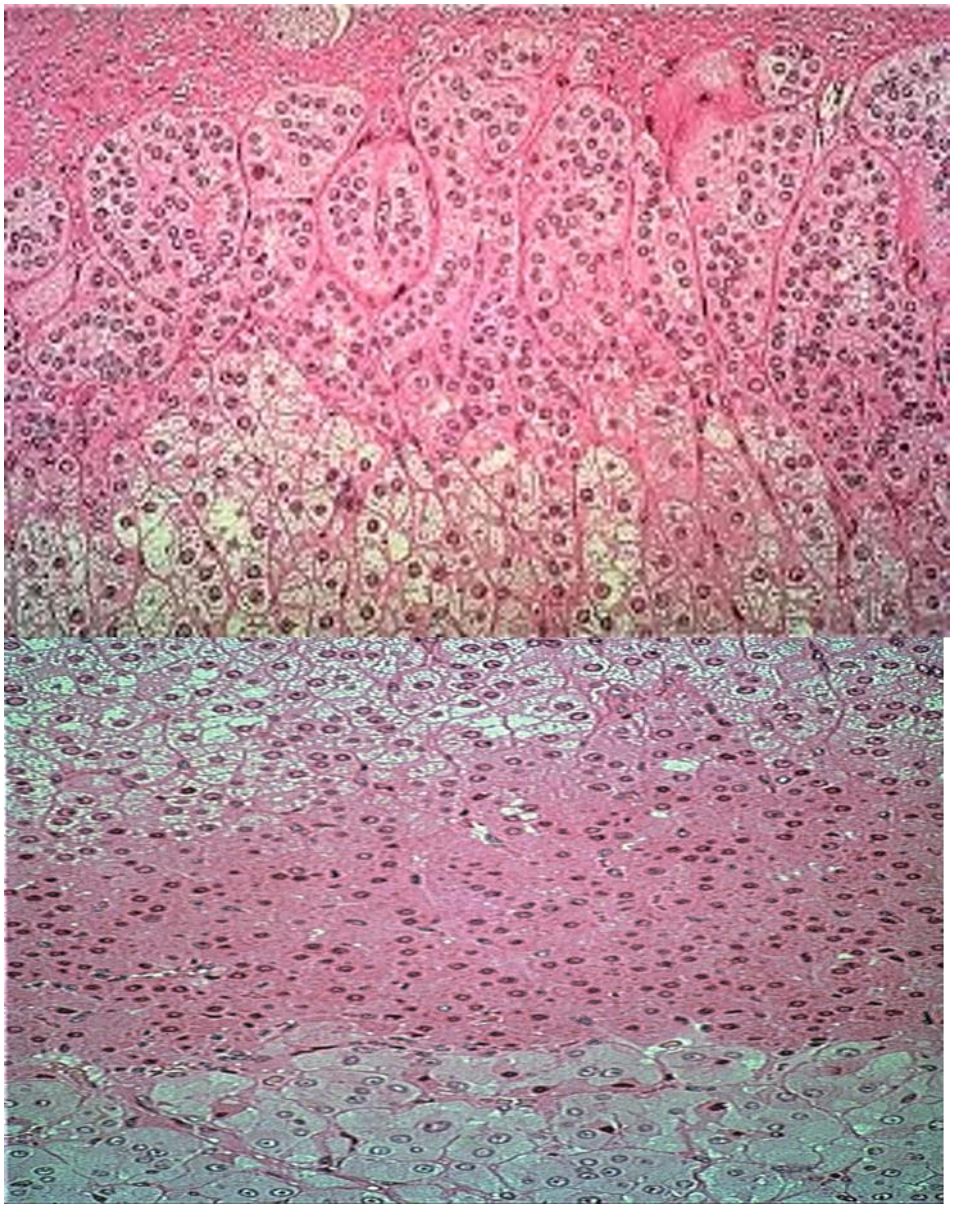
Zones of the cortex





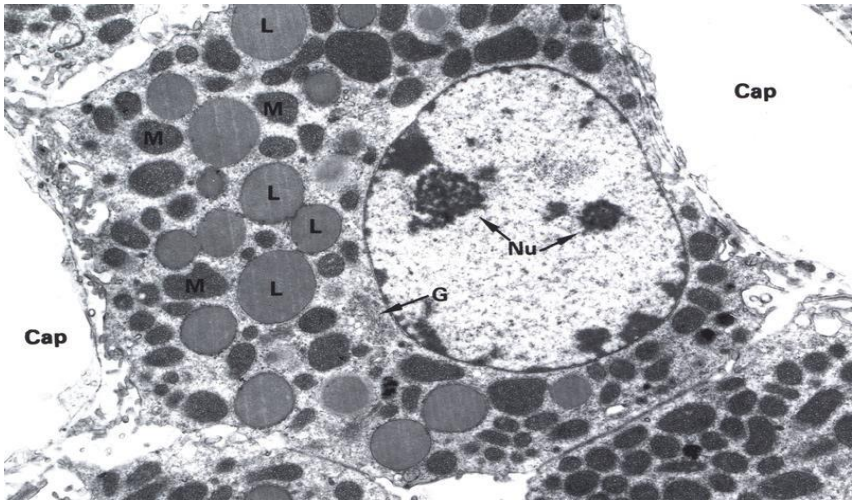
Zones of the cortex

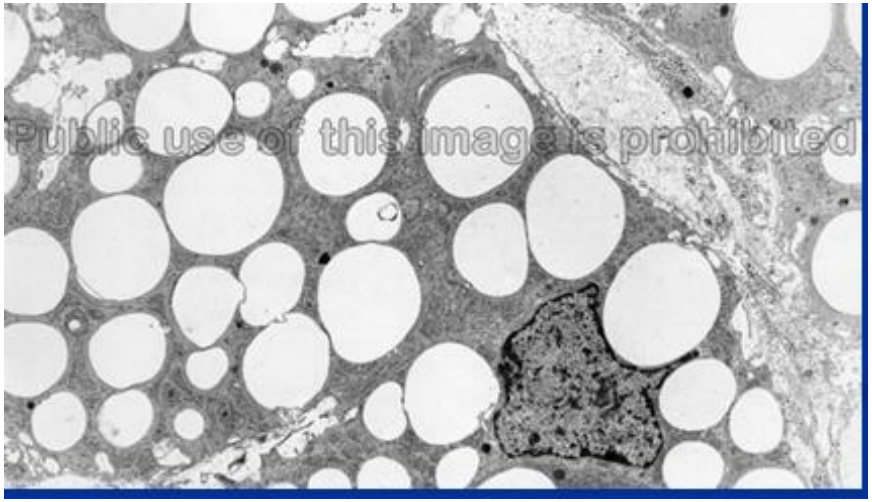




Cells in adrenal cortex are steroid secreting cells

- Extensive smooth ER
- Mitochondria with
- tubular cristae
- Golgi apparatus
- Lipid droplets
- Spongiocytes in zona fasiculata
  (highly vacuolated cells due to lipid droplets)





Cortex	**Z. Glomerulosa**	**Z. Fasciculata = Spongiocytes**	**Z. Reticularis**
% of volume	15%	65%	7%
Shape of cells **Arrangement**	Columnar or pyramidal cells Closely packed rounded or arched clusters	Polyhedral Cords 1 or 2 cell thick	Polyhedral Anastmosing Irregular cords
Cytoplasm (Acidophilic)	Slightly vacuolated	Numerous vacuoles (spongiocytes)	Less vacuoles
Lipid droplets	few	numerous	less
Function	Mineralocorticoids Aldosterone	Glucocorticoids = Cortisol	**Sex hormones =Androgens**

Adrenal medulla

- Not sharply delimited from the cortex.

It includes 3 types of cells:

1- Chromaffin cells

2- Sympathetic ganglion cells

3- Lymphocyte like cells

- Cells are arranged in strands or small clusters with capillaries and venules, weakly basophilic.
- Chromaffin cells, granules of these cells can be stained with potassium bichromate.
- Catecholamines adrenaline and noradrenaline
- Chromaffin cells are, like ganglion cells of the PNS, derived from neural crest cells.

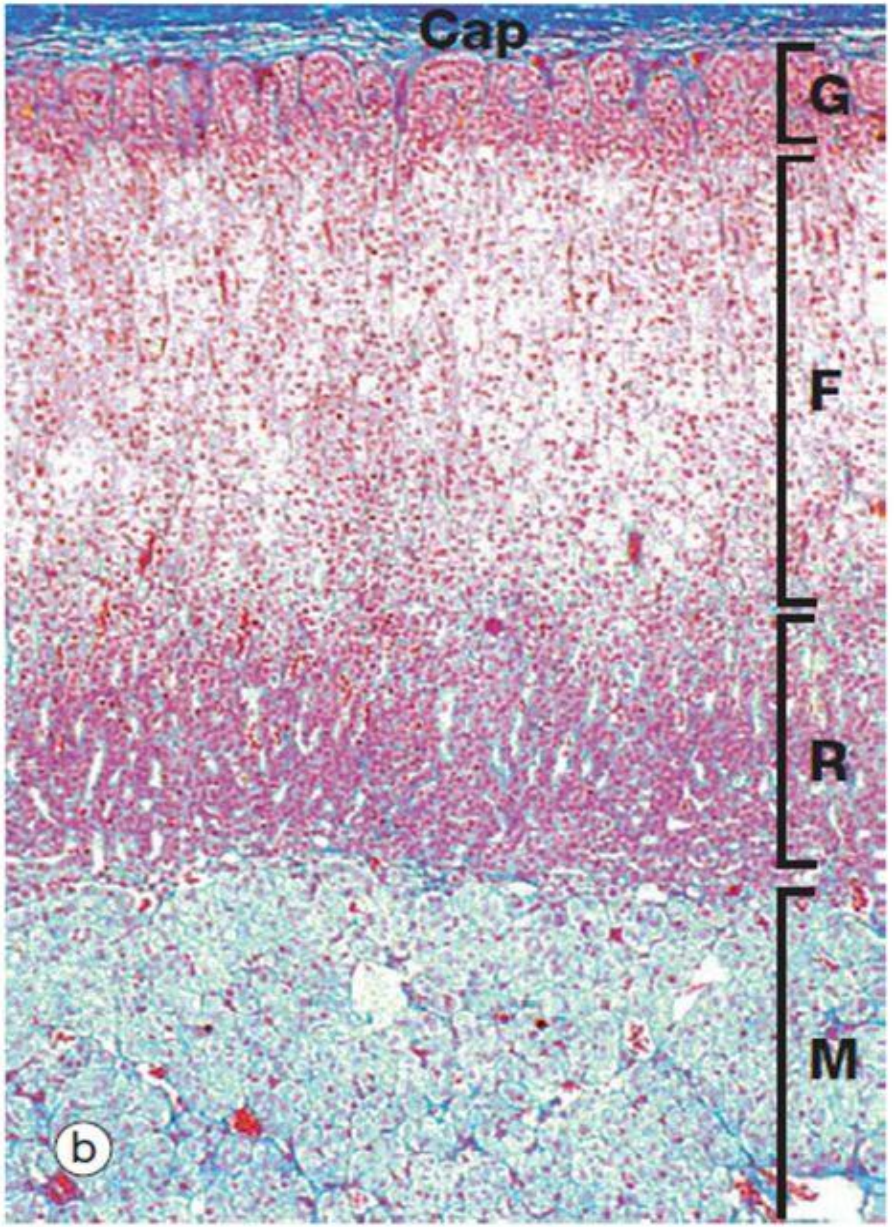
connective tissue capsule (Cap)

Outer zona glomerulosa (G) - mineralocor-ticoids.

The middle zona fasciculata (F) has linearly arranged cells that secrete glucocorticoids.

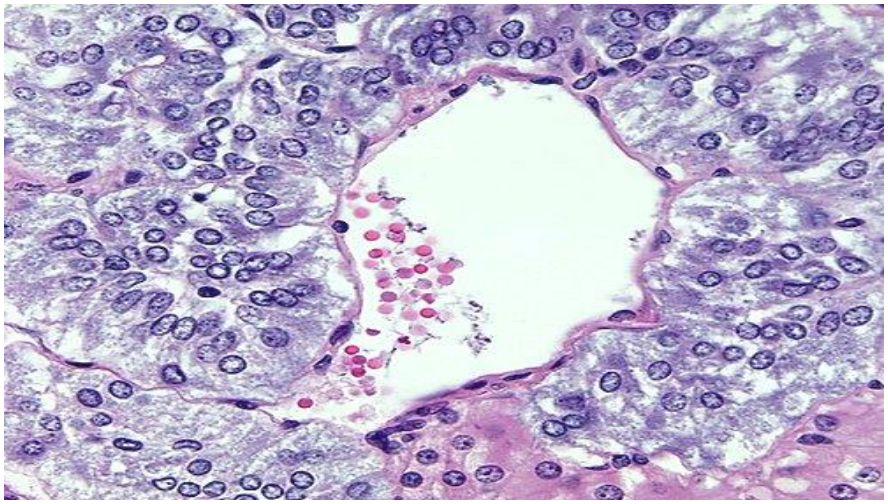
The inner zona retuclaris (R) cells form a cell network and secrete weak androgens.

inner medulla (M).



Chromaffin cells

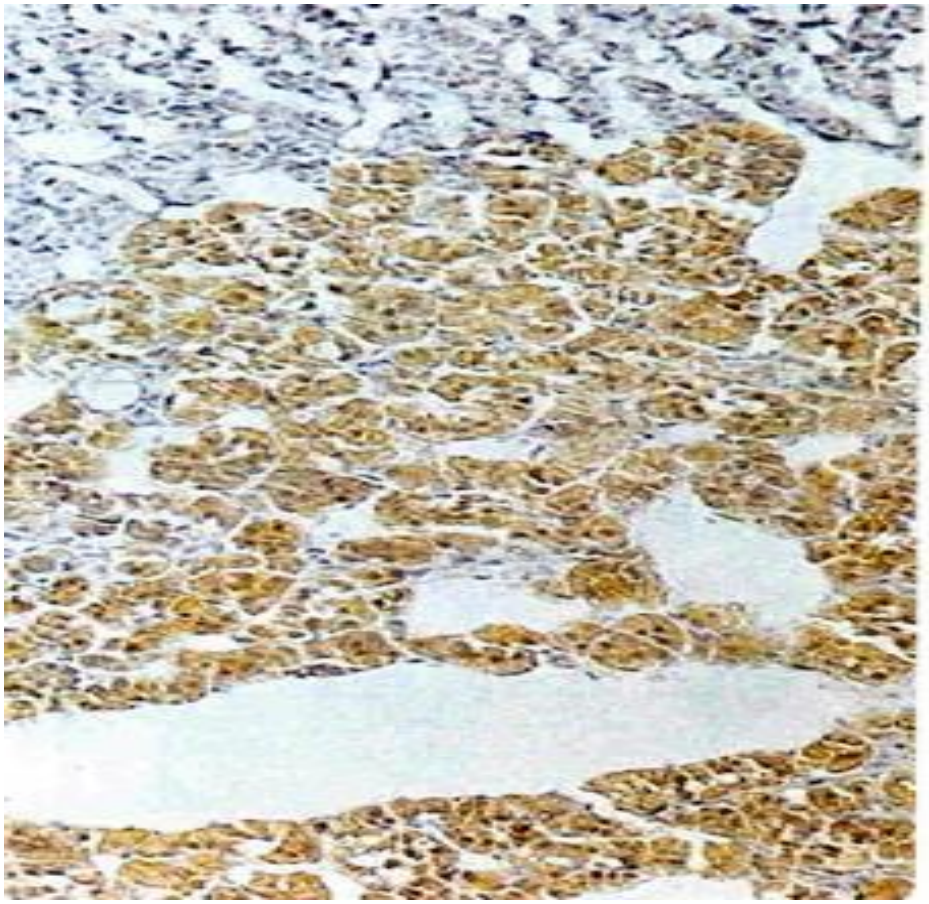
epinephrine cells & nor epinephrine cells



LM: large ovoid cells

large spherical nuclei

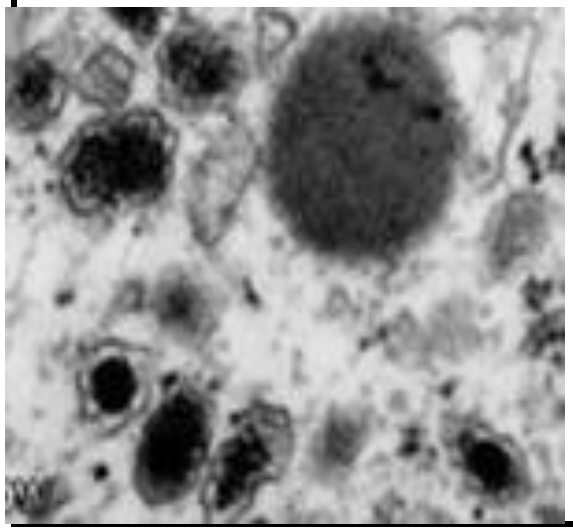
- pale basophilic cytoplasm
- arranged in rounded groups or short cords intimately related to BVs



Chromaffin reaction

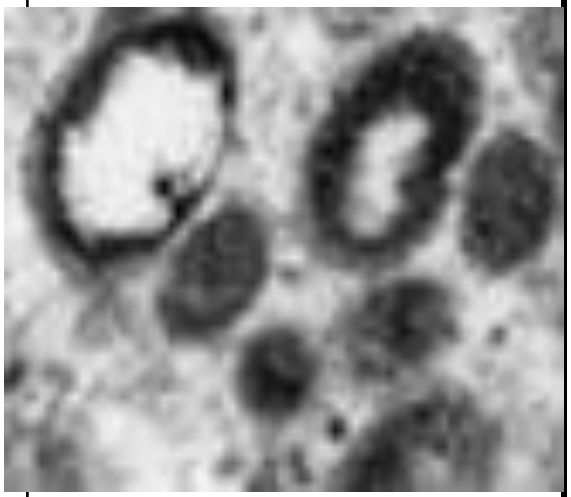
Granules of epinephrine & norepinephrine

Granules in:	Epinephrine-secreting cells	Norepinephrine-secreting cells
Size	Small	larger
Contents	Fill the granule	Do not



E M

protein synthesizing cells:
rER
mitochondria
prominent Golgi
membrane-limited electron-dense granules of either epinephrine or norepinephrine

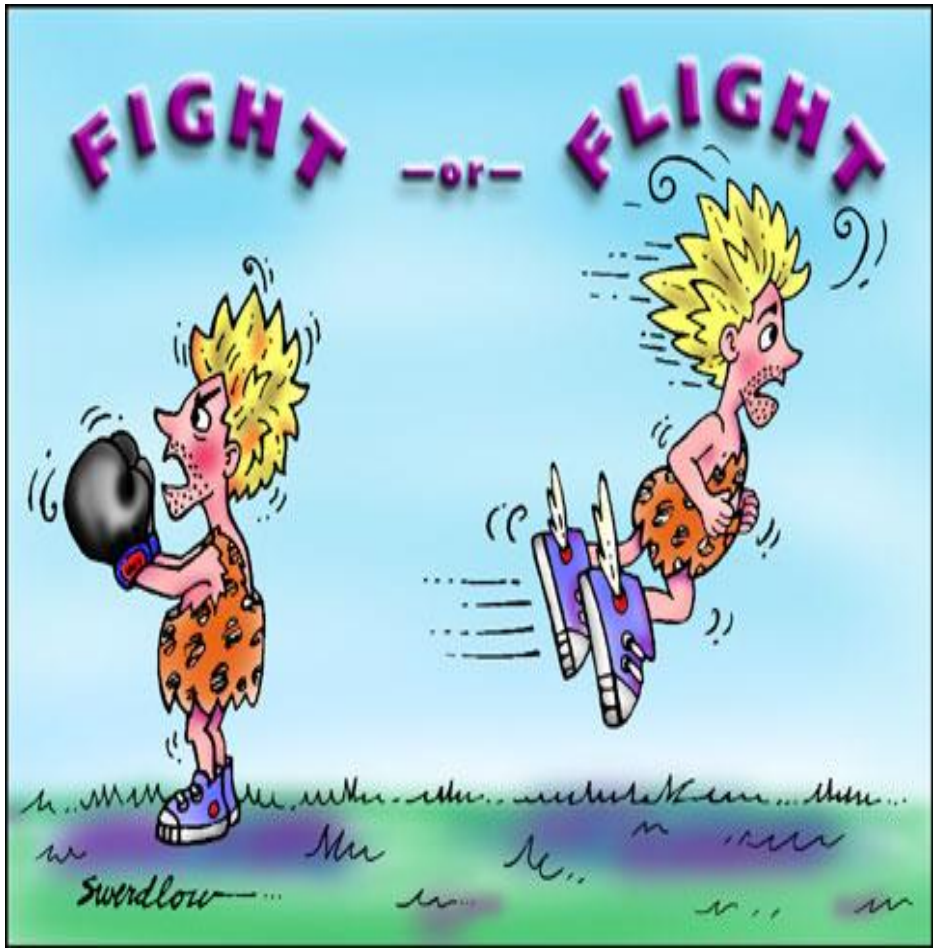


Function of adrenal medulla

- epinephrine and norepinephrine → vasoconstriction, hypertension, ↑ heart rate & metabolic rate
- Clinical hints of medulla
  - Pheochromocytoma

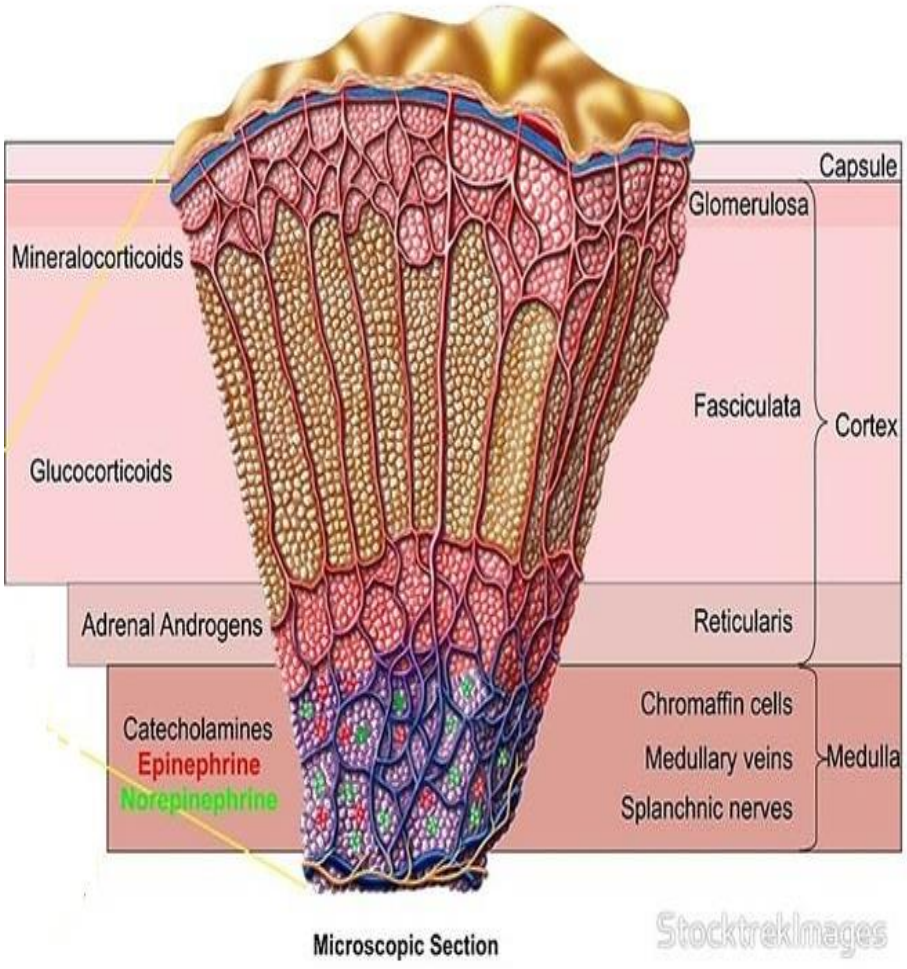
(tumour of chromaffin cells)

  - → paroxysmal elevation of BP



Blood supply of adrenal gland

- The adrenal glands are supplied by several arteries ,these arteries can be divided into:
- ❖ **Cortical arteries**, arteries that irrigate the capsule; branching into capillaries that irrigate the gland cells of the cortex and that eventually reach the medullary capillaries;
- ❖ **medullary arteries**, which pass through the cortex and form an extensive capillary network in the medulla.
- The cells of the medulla are, thus, bathed with both arterial blood from the medullary arteries and venous blood originating from the capillaries of the cortex.
- Capillaries of the medulla, together with capillaries that supply the cortex, form the medullary veins, which join to constitute the **adrenal** or **suprarenal vein**



Control of the Adrenal Cortex

- The secretion of glucocorticoids is controlled initially through the release of corticotropin-releasing hormone in the median eminence, followed by secretion of adrenocorticotropic hormone (ACTH, corticotropin) by the pars distalis of the hypophysis
- Free glucocorticoids may then inhibit ACTH secretion. The degree of pituitary inhibition is proportionate to the concentration of circulating glucocorticoids; inhibition is exerted at both the pituitary and hypothalamic levels
- Aldosterone secretion is controlled primarily by renin-angiotensin and secondarily by ACTH.
- **MEDICAL APPLICATION**
- Because of the feedback mechanism of adrenal cortex control, patients who are treated with corticoids for long periods should never stop taking these hormones suddenly:
- secretion of ACTH in these patients is inhibited, and thus the cortex will not be induced to produce corticoids, causing a severe misbalance in the levels of sodium and potassium.

Control of adrenal Medulla

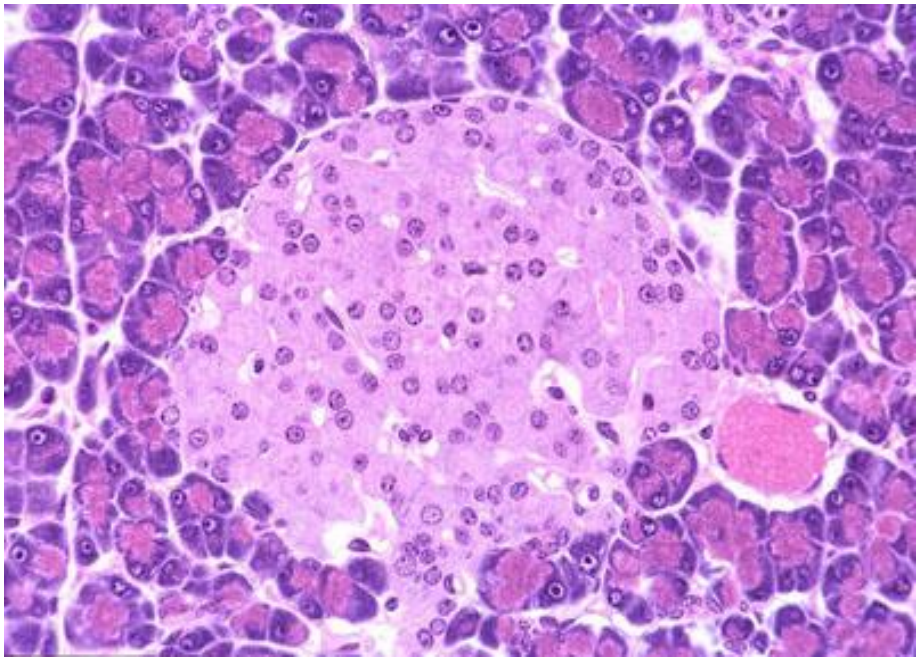
- The adrenal medullary cells are innervated by cholinergic endings of preganglionic sympathetic neurons.
- Epinephrine and norepinephrine are secreted in large quantities in response to intense emotional reactions, such as fright, that are part of an alarm reaction

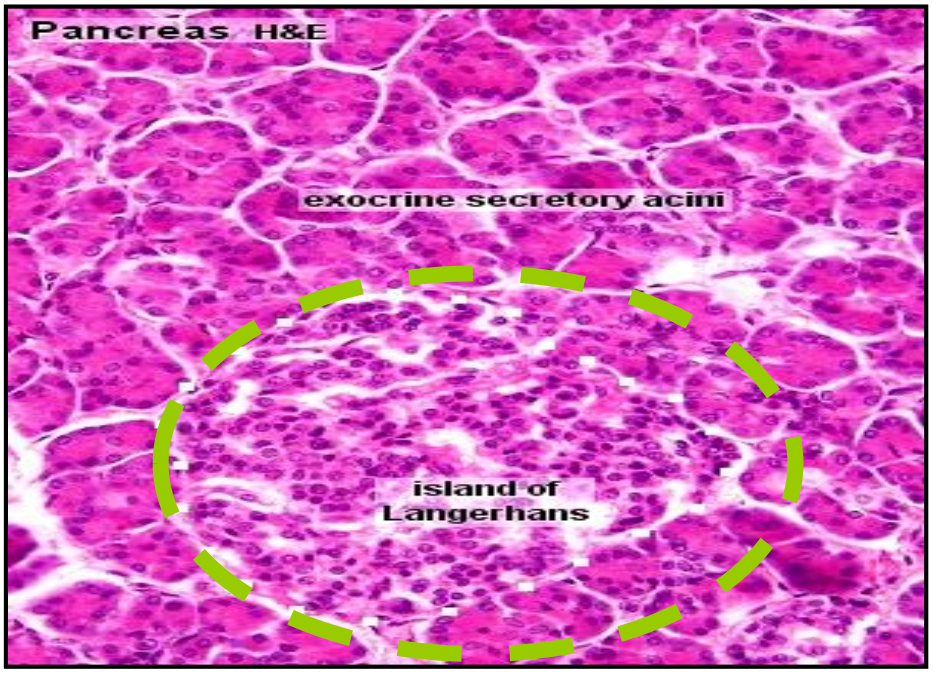
(the fight-or-flight response).

- Secretion of these substances is mediated by the preganglionic fibers that innervate medullary cells.
- Glucocorticoids produced in the cortex, which reach the medulla through capillaries that bathe cells of the cortex, constitute another mechanism of control.

PANCREAS

- exocrine and endocrine gland.
- The exocrine part produces about 1.5L of pancreatic juice every day.
- The endocrine part consists of the cells of the **islands of Langerhans**.
- The pancreas has **thin** capsule
- **cellular composition of the islands**
- **- 70% beta-cells**, **insulin**. Insulin stimulates
- **- 20% alpha-cells**, **glucagon**.
- **- 5- 10 % delta-cells** which secrete **somatostatin**





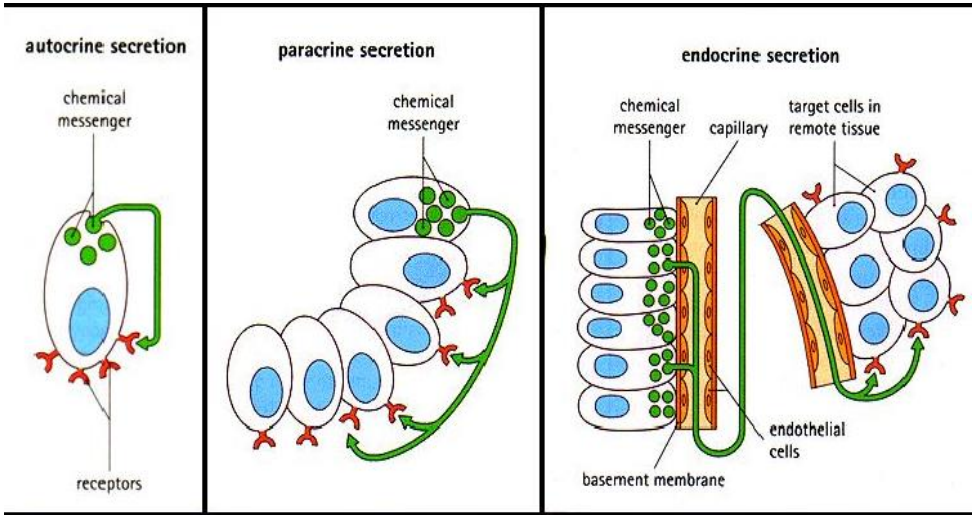
Diffuse neuroendocrine system

- Apudocytes or APUD cells
- Classification according to staining activity

1. Argentaffin cells: ppt silver in absence of reducing agent
2. Argyrophilic cells: ppt silver in presence of reducing agent
3. Chromaffin like cells: bind K dichromate

Mode of action

1. Endocrine → target organ
2. Paracrine → surrounding tissue
3. Autocrine → themselves
4. Neuroendocrine → neurosecretion



Distribution of APUD cells

1. GIT (enteroendocrine cells) :
   G cells EC cells
   ECL cells D cells
   S cells
2. Respiratory system
   Bronchial Kulchitsky cells
   Small granule cells
   Neuroepithelial bodies
   among tracheobronchial epithelium.

3. Other sites

- **Myocardium:** → cardiodilatins and atrial naturetic polypeptides
- **Hypothalamus:** supraoptic and paraventricular nuclei → oxytocin and vasopressin
- **Endocrine system:**

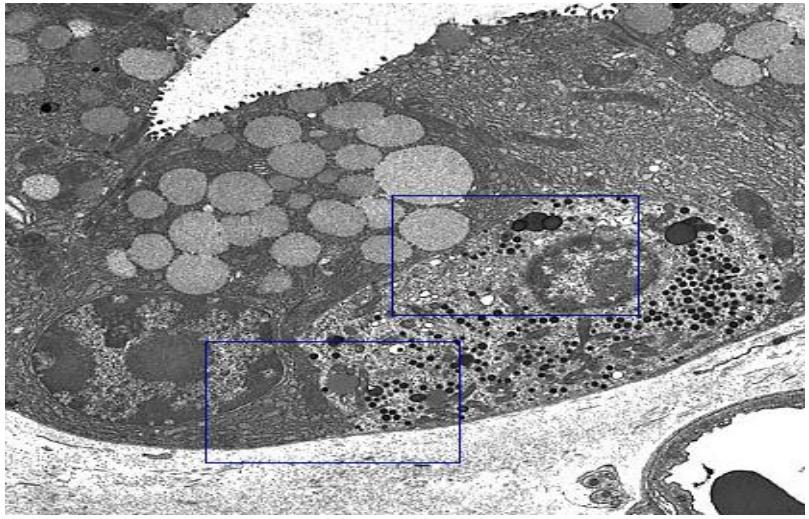
pinealocytes, parafollicular cells, chief cells, cells of islets of Langerhans and some adenohypophyseal and adrenal medullary chromaffin cells

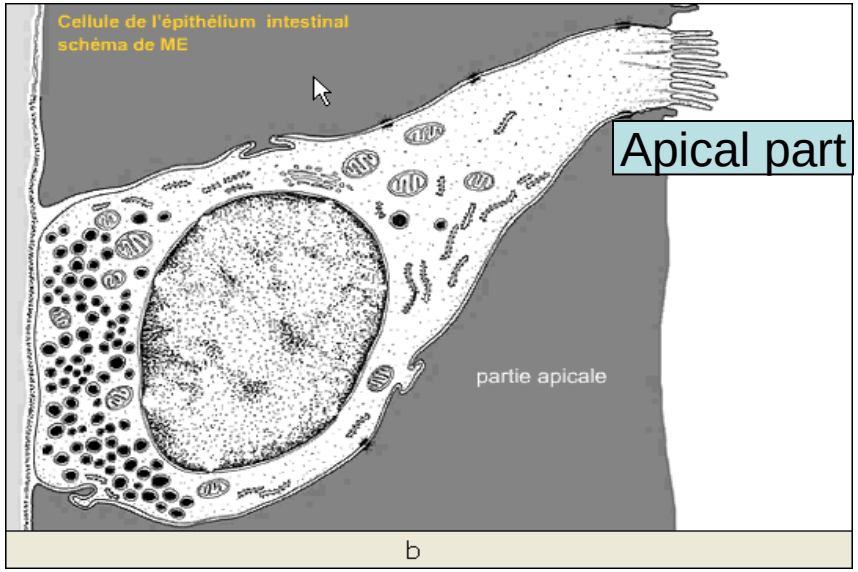
Microscopic features

Two types:

1. Open type
2. Closed type

- Electrolucent cytoplasm
- Few small secretory granules at the base or vascular pole
- Small infranuclear Golgi
- Sparse rER





APUD of small intestine

Entero-endocrine cells