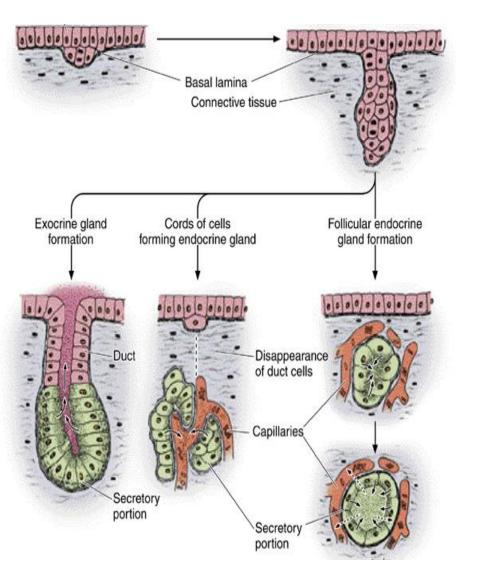
# Glands



### 1-Exocrine (has ducts): e.g.

Salivary glands,

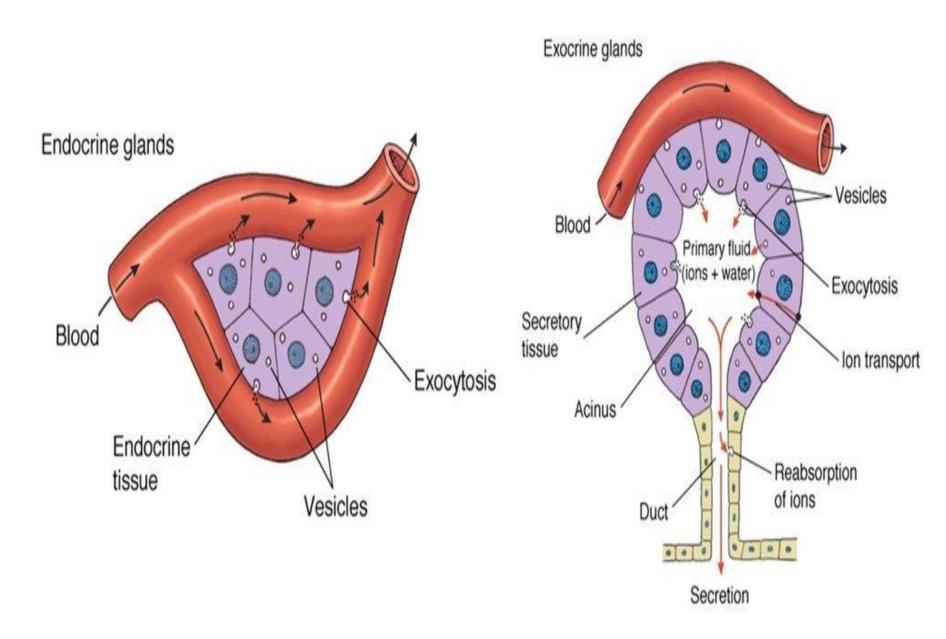
Secrete saliva in the mouth cavity through ducts.

## **2-Endocrine (no ducts):**

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

### <u>3-Mexocrine:</u> e.g. Pancreas Secretes digestive enzymes in the intestine & insulin hormone to the blood

# Glands



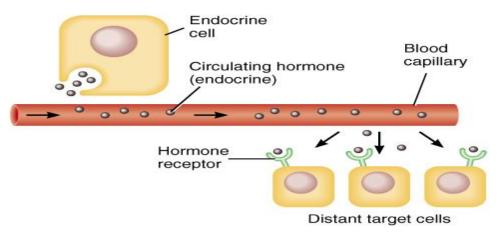
# **Endocrine system**

□ The endocrine system is a control system of ductless **glands** that secrete hormones within specific organs.

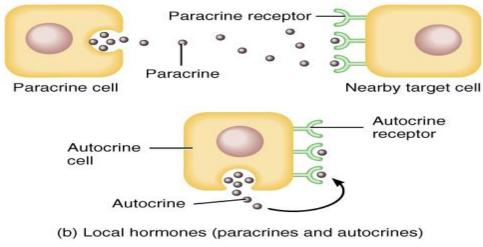
Hormones a small chemical act as "**messengers**," can enter the bloodstream and cause an action at **Target cells or tissue** (Specific cells affected by a hormone)

### **Patterns of Hormone Action**

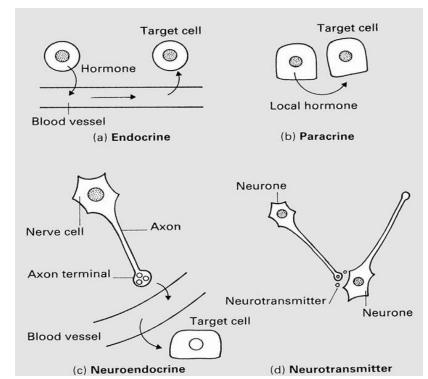
- **\* Paracrine:** Hormones that affect neighboring cells
- **Autocrine:** Hormones that act on the cells that secrete them
- \* Neuroendocrine
- \* Neurotransmitter



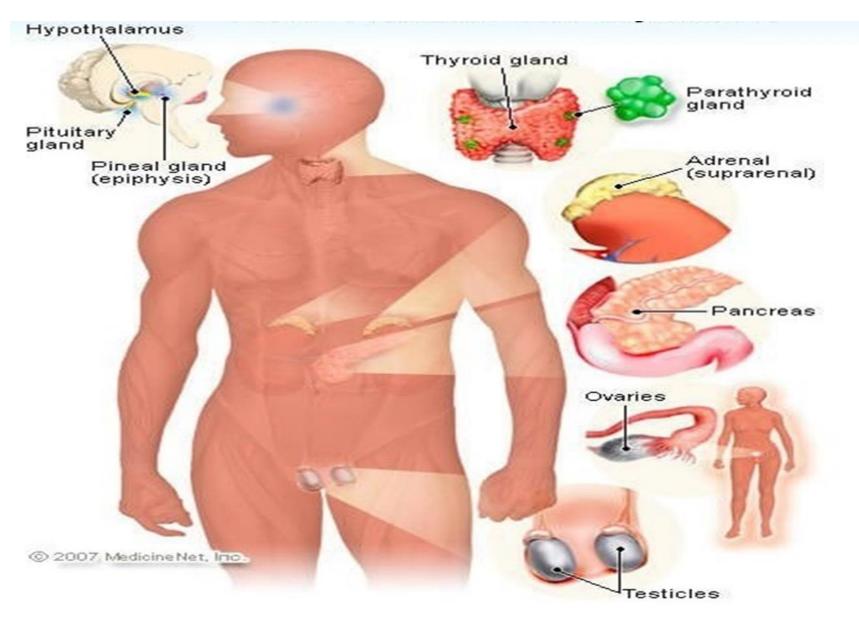
(a) Circulating hormones (endocrines)



C John Wiley & Sons, Inc.



# **Endocrine glands**



# **Introduction to the Endocrine System**

### The endocrine system

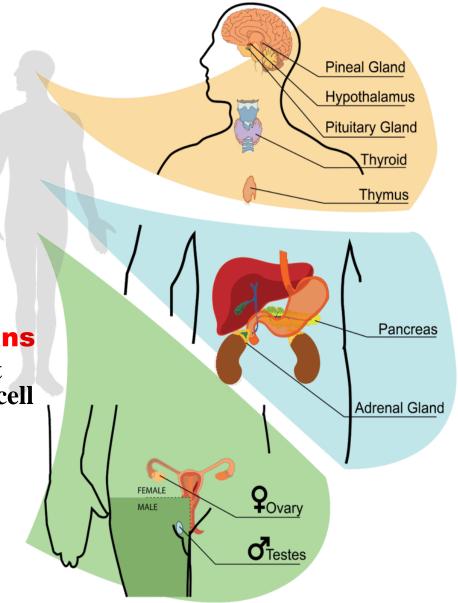
- \* Principle glands :
- Hypothalamus
- Pituitary gland
- Pineal body
- Thyroid gland & Parathyroid
- Suprarenal gland (adrenal)
- Pancreas
- Gonads (testis, ovary) + placenta

#### Sector States States

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

### \* Local Hormones

- GIT (Diffuse neuroendocrine system)
- Neurotransmitter (nerve ending)

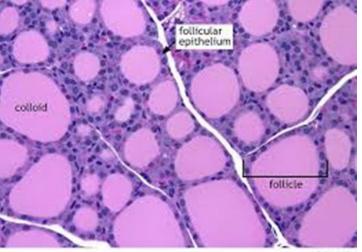


## **Basic structure of endocrine glands**

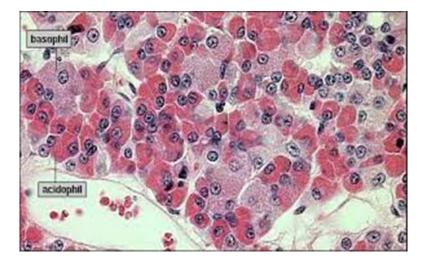
### Stroma

- $\succ$  CT inside the gland
- ➤ CT capsule
- Loose tissue
- Parenchyma= cells
- > Cells
- Plexus of blood vessels

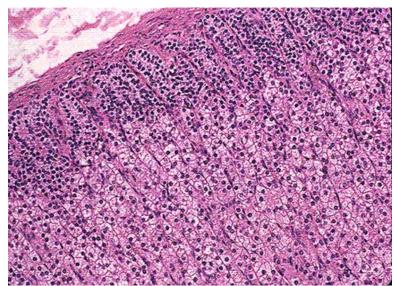
#### Follicles



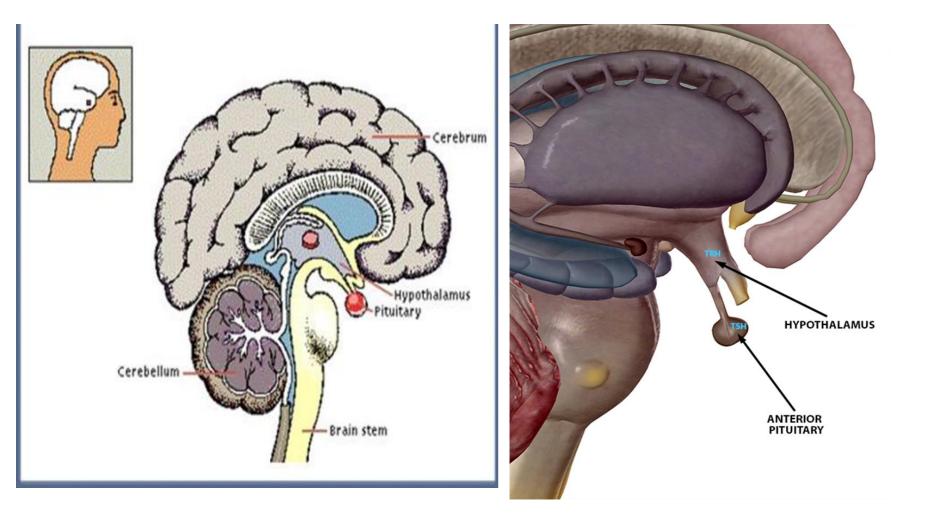
Cords



#### Cords



# **Pituitary gland**

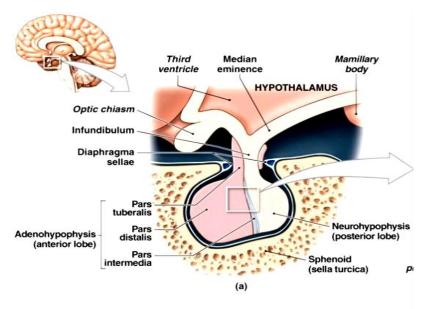


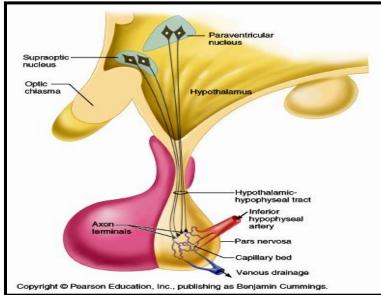
# **Pituitary gland**

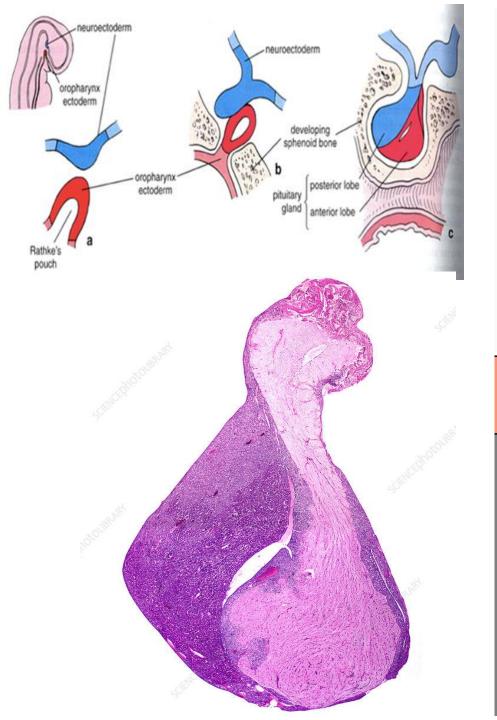
- □ The pituitary gland (hypophysis Cerebri) is attached to the bottom of the hypothalamus by a slender stalk called the infundibulum.
- □ The pituitary gland consists of **two major regions**:
- Anterior pituitary gland (anterior lobe or adenohypophysis)
- \* **Posterior** pituitary gland (posterior 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 because it is the main place for everything that happens within the endocrine system.

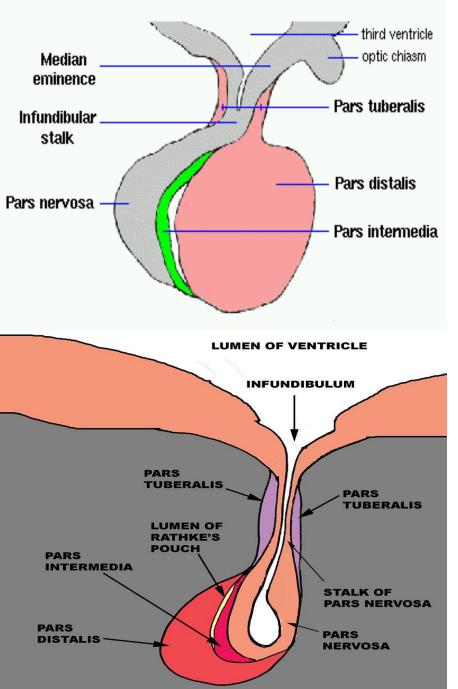
# Pituitary gland (Hypophysis Cerebri)

- Lies in the sella turcica(bony cavity of sphenoid)
- Covered by diaphragma sellae(fold of dura mater)
- Stroma : surrounded by a thin connective tissue capsule/ loose connective tissue between the capsule and the periosteum.
- **Parenchyma :** it has a **dense plexus** of veins
- epithelial component:
- adenohypophysis (anterior pituitary)
- neural component:
- Neurohypophysis (posterior pituitary).









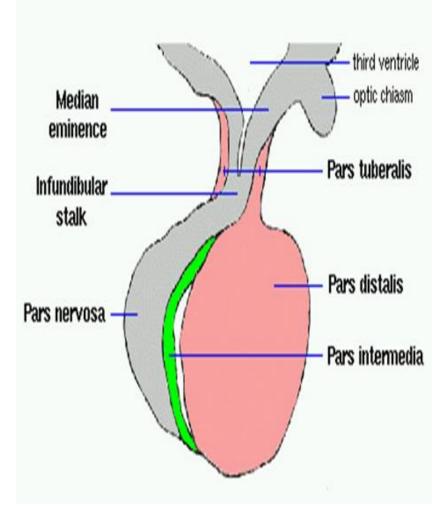
	Adenohypophysis (glandular part)	Neurohypophysis (nervous part)
Derived from	Oral ectoderm	Neural ectoderm 3 <sup>rd</sup> ventricle
	pinched off ( <b>Rathke's</b> pouch)	Connected with the brain by <b>neural stalk</b> (infundibulum)
Stain	Dark	Pale
Consist of	Glandular epithelium in the form of irregular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

# Adenohypophysis

### 1. Pars Tuberalis

### **2- Pars Intermedia**

3. Pars distalis



# Adenohypophysis

## **1.** 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
- Stem cells or exhausted chromophils

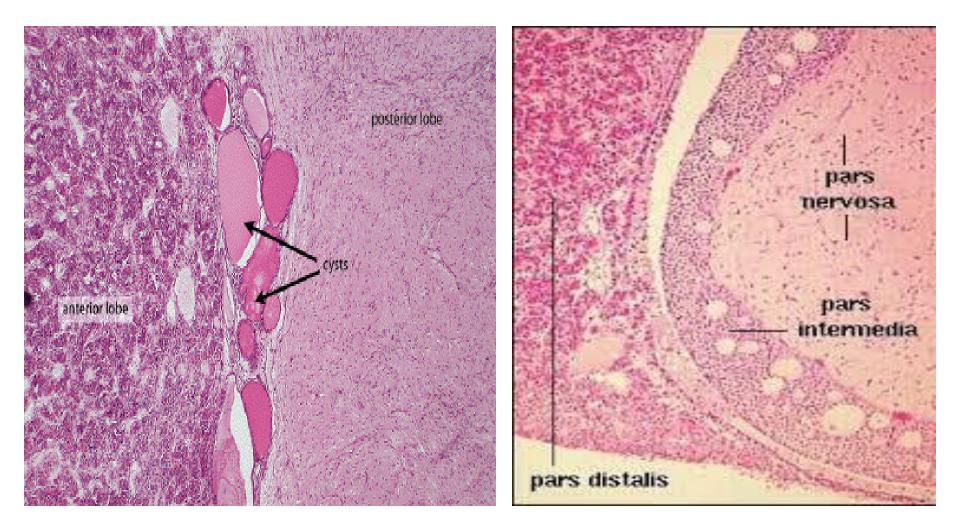
### **<u>2- Pars Intermedia</u>**

- □ In human/ unclear function
- □ contains **chromophobic** cells surrounding **colloid-filled cysts**
- □ In animals / the basophilic cells produce melanocyte stimulating hormone (MSH)

## **2- Pars intermedia**

			Pars distalls
	In humans	In animals	- Stalk of the pars nervosa - Pars tuberalis
Develop ment	rudimentary	Well developed	Pars nervosa
Arrange ment Of Cells	cords	Layers and cysts	
Function	Non specific and unknown	MSH (melanocytes- stimulating hormone)	PP PA
			col

### **Pars Intermedia**



### <u> 3- Pars distalis</u>

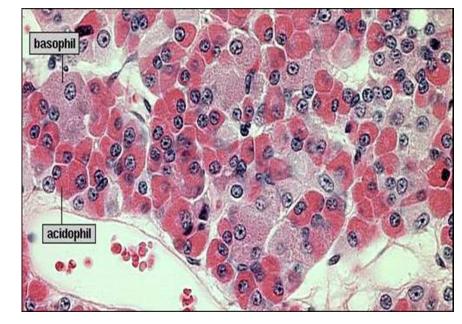
- Stroma : CT capsule, reticular fibers.
- Parenchyma
- **Cells** cords of epithelial cells
- + fenestrated sinusoids

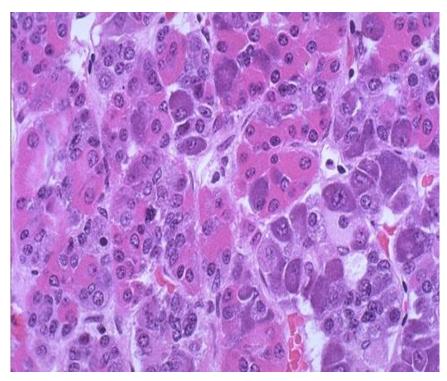
**staining characteristics** the cells are of two types :

- I- chromophobes 52%
- (which do **not stain intensely**).
- 2. chromophils 48%

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

- **basophils 11%** (darkly pink stained)
- acidophils 37% (eosinophilic or reddish stained)





# **Cells of pars distalis**

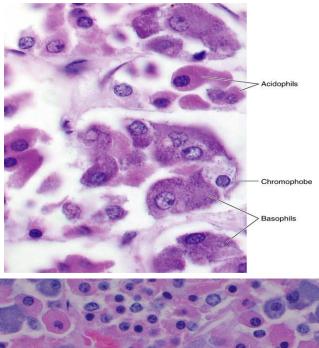
#### **Chromophils**

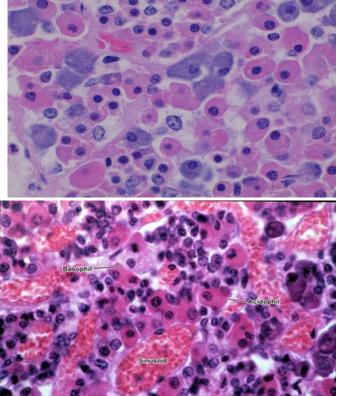
#### Chromophobes

Function	Endocrine cells	Stem cells or exhausted chromophils
Affinity for stain	Great	Weak
Size & shape	Large , polyhedral	Small, rounded
Percentage	<ul><li>48%</li><li>11% basophils</li><li>37% acidophils</li></ul>	52%

### **Identification of the cells**

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

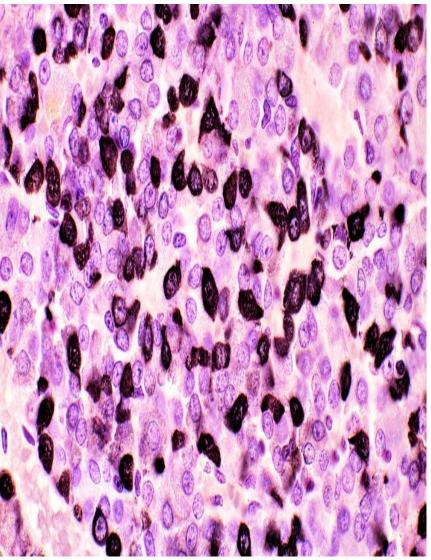


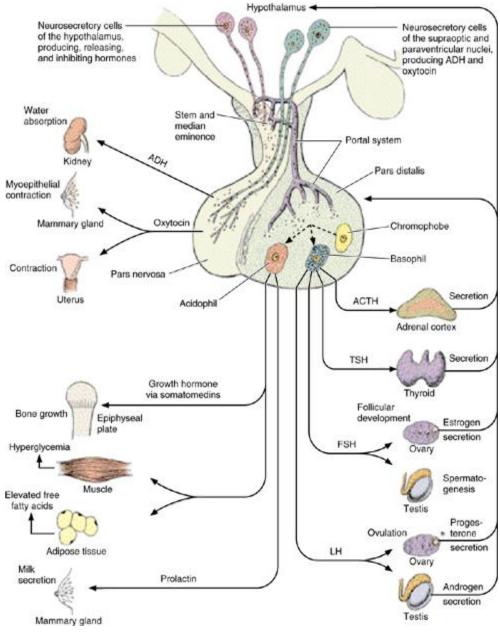


## **Adenohypophysis hormones**

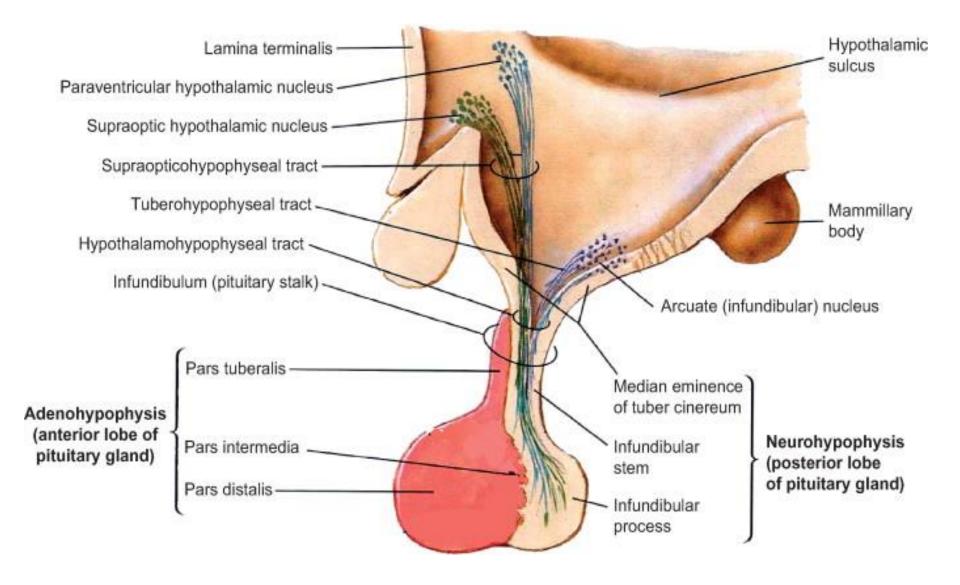
Cells		%	Function
Chromophobes		52%	degranulated cell, under-development cell (They are now thought to represent acidophil and basophilic cells in inactive or recently <b>degranulated</b> stage)
	gonadotropic cells		FSH LH
Basophils	thyrotrophic cells	11%	ТЅН
	corticotroph cells		АСТН
Acidophils	somatotrop cells		<b>GH</b> or somatotropic hormone (STH)
	mammotroph cells	37%	<b>Prolactin</b> (PR) or lactogenic hormone (LTH)
			Large in lactation & small in males & non pregnant

#### Immunohistochemical localization of growth hormone





# Neurohypophysis



## Neurohypophysis (Pars nervosa)

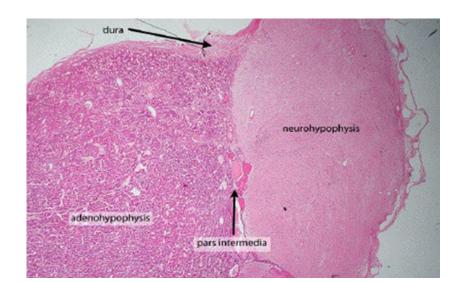
### **Two parts**

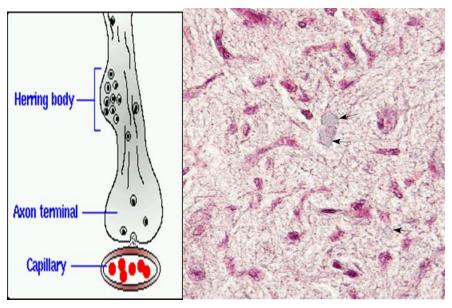
Infundibulum, a slender stalk of nerve tissue that suspends the pituitary gland from the base of the brain pituitary stalk The Pars Nervosa, is connected directly with the Hypothalamus of the brain by axons

#### 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

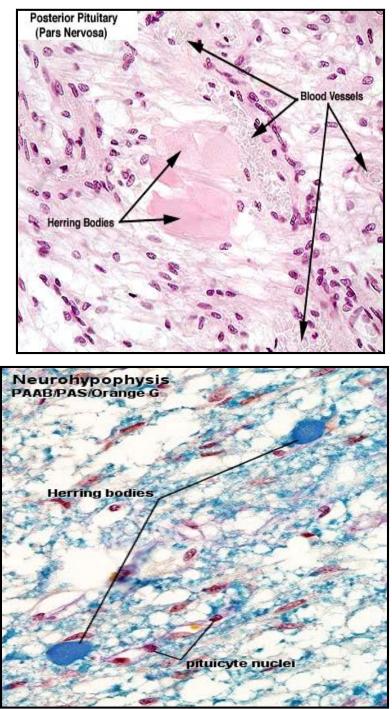




#### Neurosecretory cells = supraoptic & paraventricular nuclei

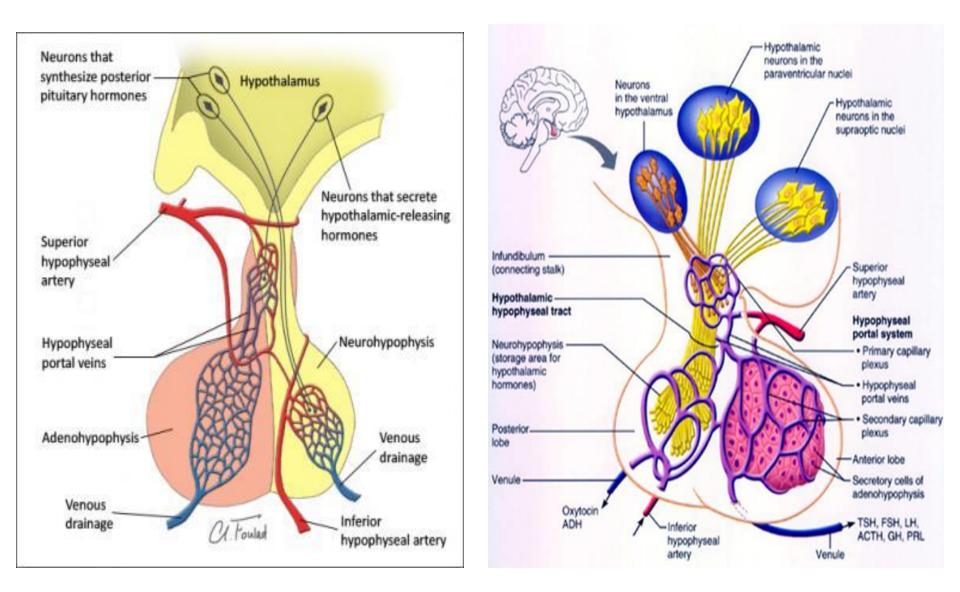
forms **Herring bodies** i.e. a dilatation of the axon near the terminals/ contain either

- 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
- 1. ↑ reabsorption of water from collecting tubules
   → hypertonic hypovolaemic urine
   (↓ ADH→ diabetes insipidus)
- Pituicyt is a glial cell of the posterior pituitary. 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

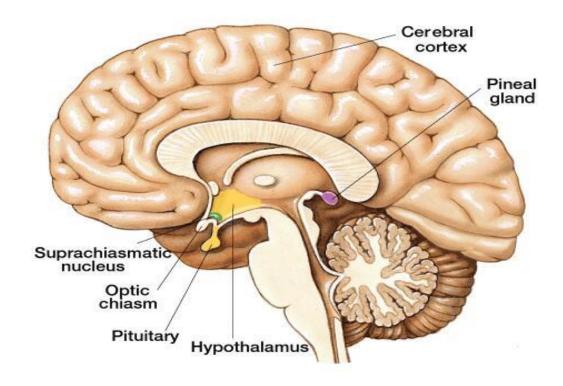


### **Blood supply of pituitary gland**

Releasing and inhibiting hormones Pass to hypophyseal portal system to pars distalis



## Pineal body (Epiphysis cerebri)



□It is embedded in between the cerebellum and cerebrum.

The shape is flattened stalk like structure hence it is called epiphysis.The name is derived from its **pinecone** like structure.

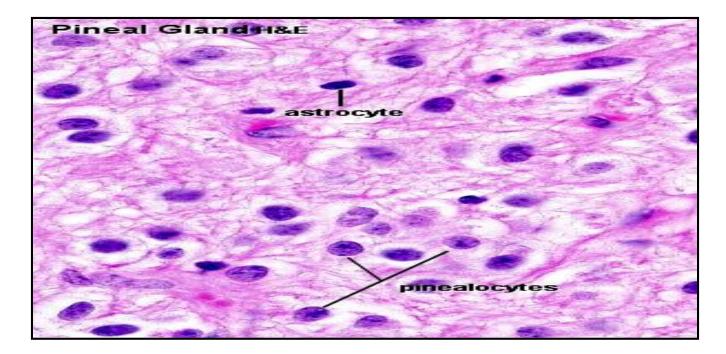
□known as 'third eye' as this gland receives its stimuli through vision

## **Pineal gland**

 $\Box$  Stroma: pia mater  $\rightarrow$  septa ( BVs & unmyelinated nerve fibers

**Paren**chyma: Two types of cells are present:

- 1. glial cells (astrocytes 5%) with small dark nuclei
- **2. pinealocytes** (95%), are **large** and **lightly** stained have larger, lighter and round nuclei secrete **melatonin**



Pineal GlandBlac		
astro-yto	Pinealocytes	Astrocytes (neuroglia)
	large irregular	elongated and denser
Nuclei		
Cytoplasm	pale basophilic	
Function	Melatonin secretion	Supportive & nutritive

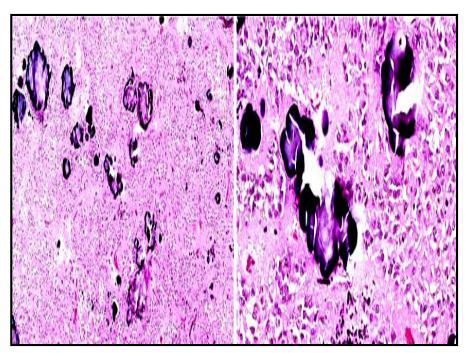
**Function :** Pineal gland controls the sex drive, hunger, thirst and the biological clock which determines the body's normal aging process.

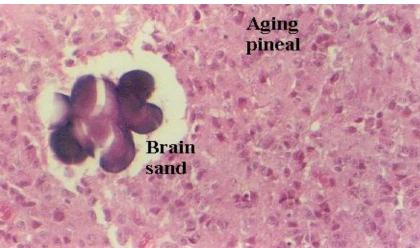
- 1. It is a neurosecretory cell the gland secretes melatonin.
- 2. It controls sleepiness and wakefulness.
- melatonin is involved in daily cycles or circadian rhythms.
   Levels are high at night as we grow sleepy & low at day light as we awake. The pineal body is directly light sensitive;

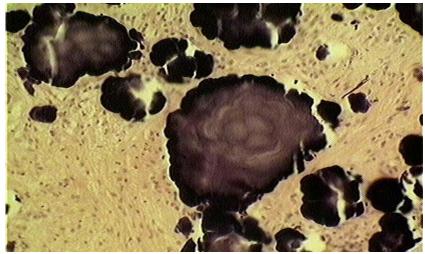
# **Pineal body with aging**

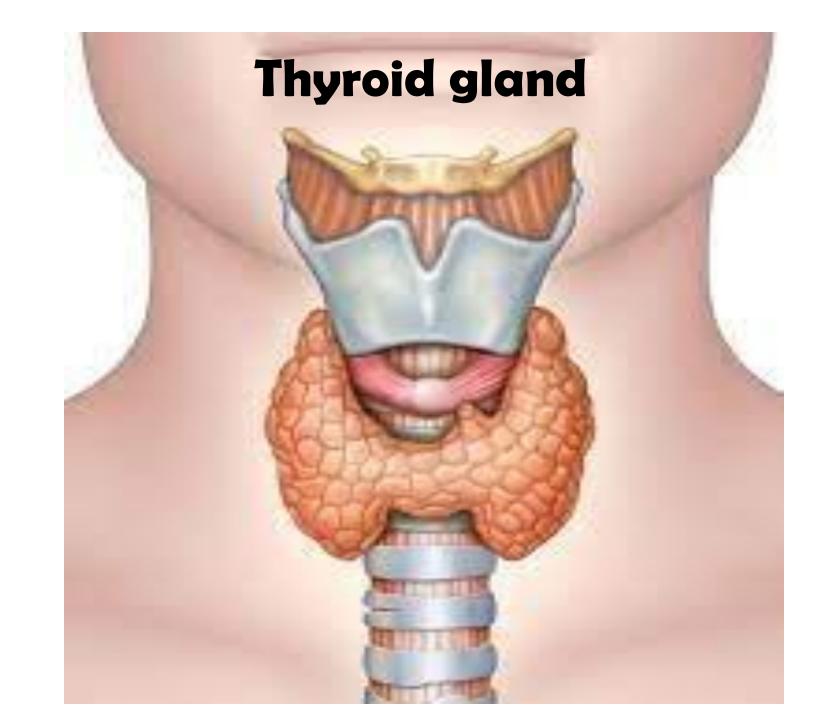
Fibrosis

- Calcification = formation of calcified bodies = (brain sand)
- Brain Sand, (areas of calcification) that are easily seen with the microscope.
- These are **not a degenerative** change







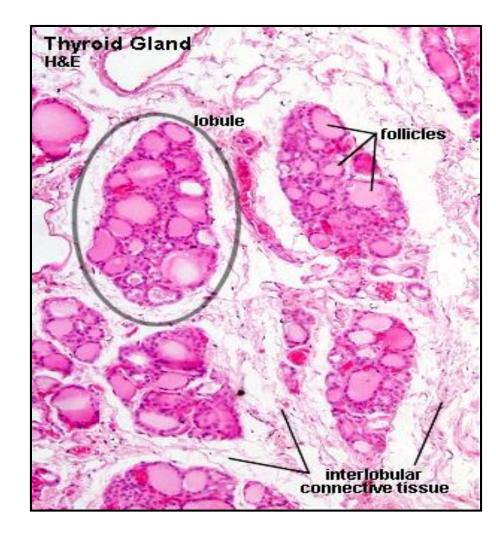


# **Thyroid gland**

### Structure

### Stroma

- Thyroid gland is covered by
- double capsule
- Outer: deep cervical fascia Inner: true CT capsule
- incomplete septa
- reticular fibers



## 

**lobules** surrounded by interlobular **connective tissue** each lobule is composed of a number of : Follicles + Blood vessels

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



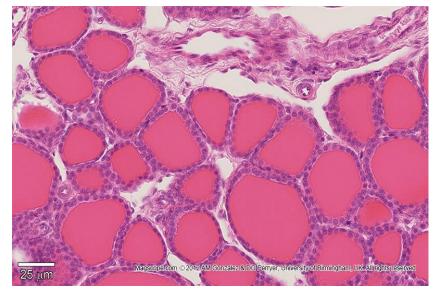
Thyroid capillary beds SEM

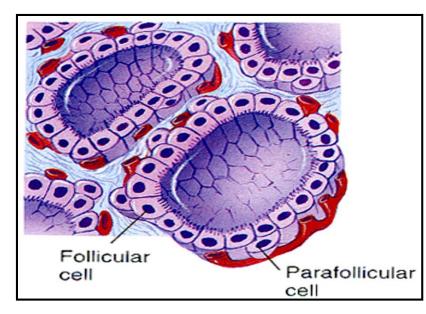
## **Cells of thyroid follicles**

- ☐ Follicular cells: a simple cuboidal epithelium
- Parafollicular cells (or "C cells") parafollicular cells are scattered among follicular cells and in spaces between the spherical follicles, they secrete calcitonin. – 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

### □ Interfollicular cells

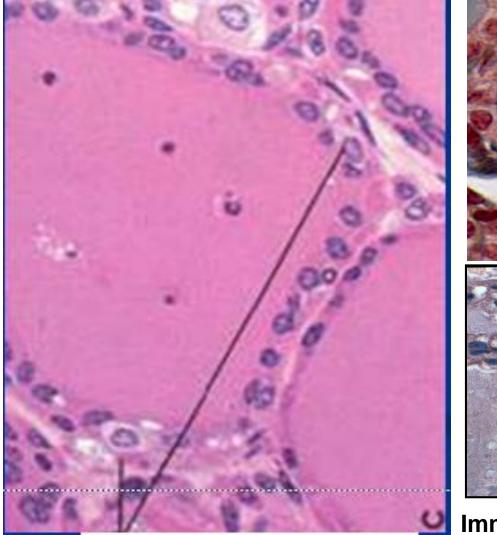
Superficial cut of the follicles

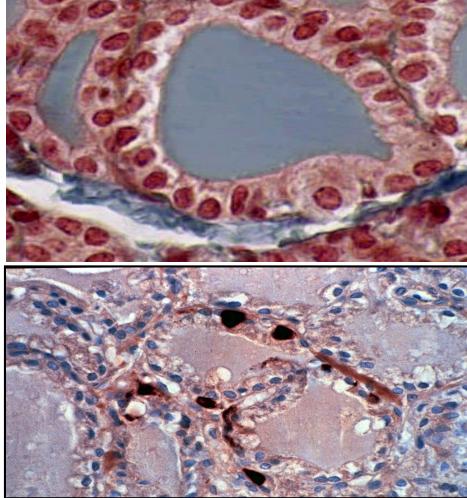




	Follicular cells	Parafollicular cells
Size	smaller	larger
Number	numerous	Few
Extension	Reach the lumen	Do not
Stain	basophilic	pale
Secretion	<ul> <li>Stored extracellularly in the lumen</li> <li>Secrete T3 &amp;T4</li> </ul>	<ul> <li>Stored intracellularly in small basal secretory granules</li> <li>Secrete calcitonin</li> </ul>
Lysosomes & phagosomes	abundant	Few in number

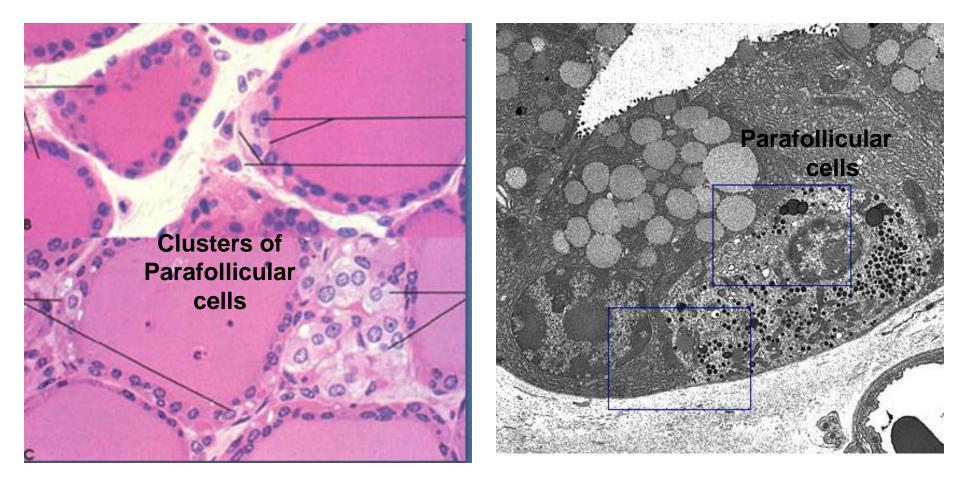
## **Parafollicular cells**



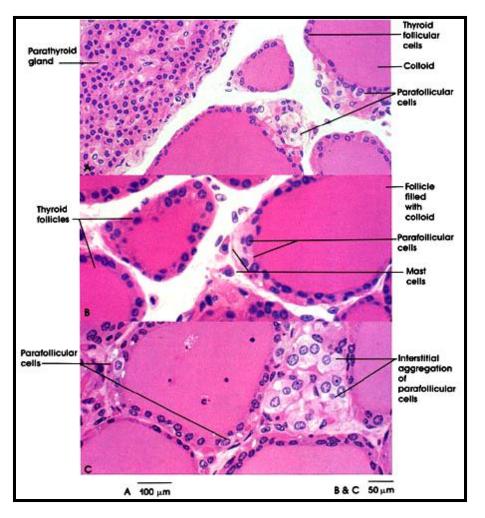


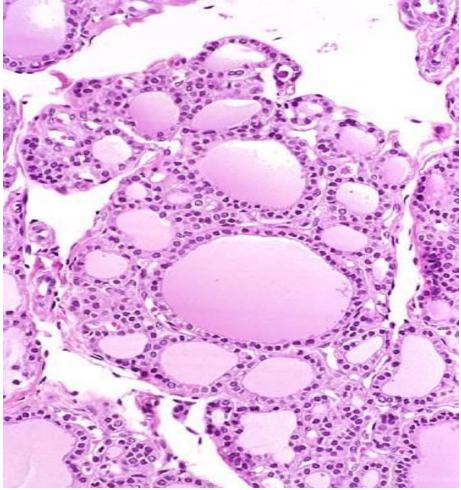
Immunocytochemical localization of calcitonin in C cells

## **Parafollicular cells**



# **Interfollicular cells**





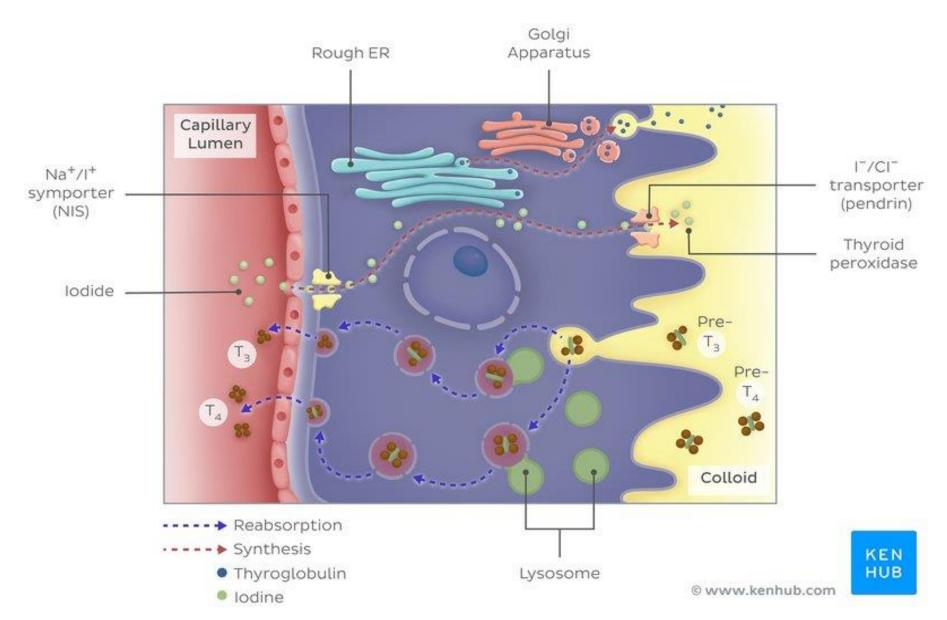
#### **Correlates EM structure of follicular** cells to its function.

- rER.

- **Microvillous border**
- endocytotic vesicles.
- lysosomes.

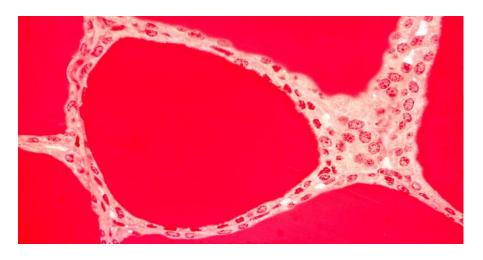
- Synthesis of thyroglobulin. → ●
- **Golgi apparatus** — add carbohydrate and form the vesicles.
- **exocytotic vesicles** dischargeThyroglobulin into the lumen
  - Follicular cells trap the iodide and liberate it as iodine in the follicular lumen
  - Surface area
    - iodination takes place **extracellularly.**
  - $\rightarrow$  reabsorb thyroglobulin.
    - hydrolyse thyroglobulin to thyroxine
    - thyroxine which is released into the fenestrated blood capillaries

# Follicular cells synthesis of T3 & T4



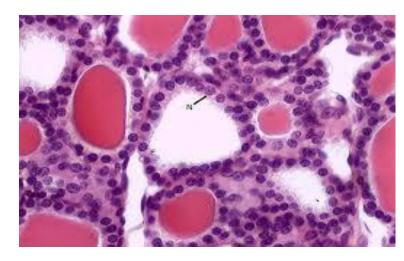
#### **Functional states of thyroid follicles**

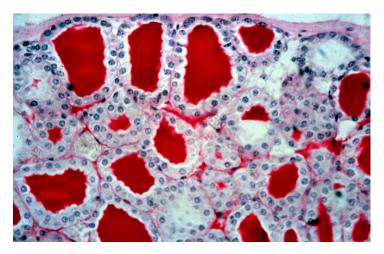
(variable - depending on the functional state) not secreting T3/T4 (inactive), the epithelial cells range from low columnar to cuboidal cells. When active, the epithelial cells become tall columnar cells.



#### hypoactive

Normal

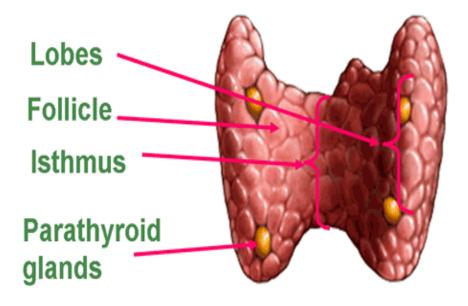


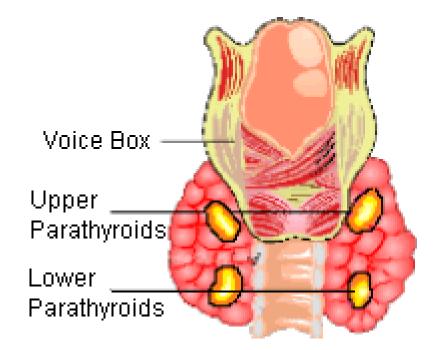


hyperactive

## **Parathyroid gland**

### THYROID





# Structure of parathyroid gland

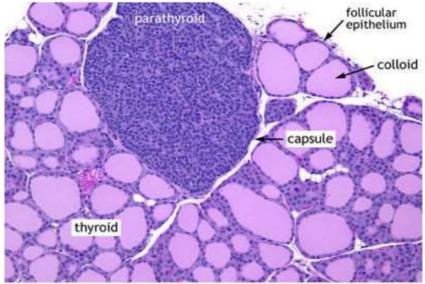
#### Stroma

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

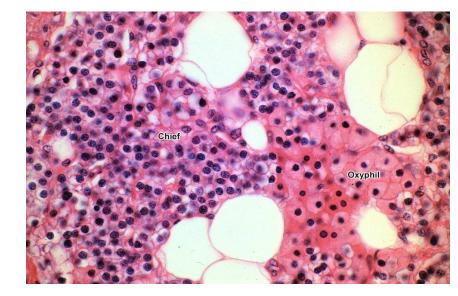
#### **Parenchymal cells**

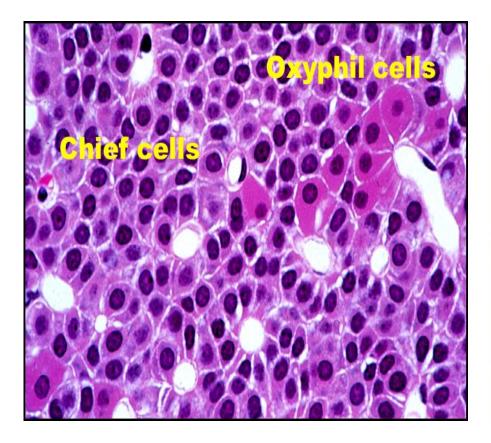
Two types of cells arranged in anastomosing **cords** surrounded by abundant **capillaries** 

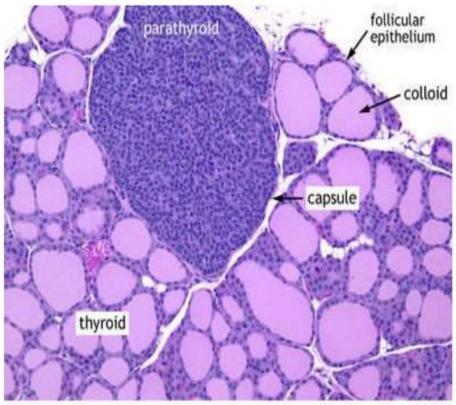
- Chief cells
- Oxyphil cells



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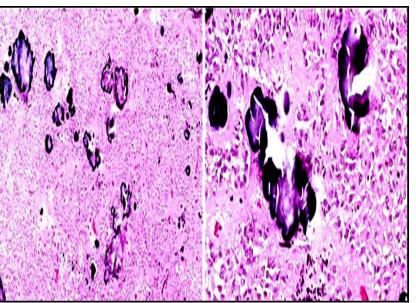


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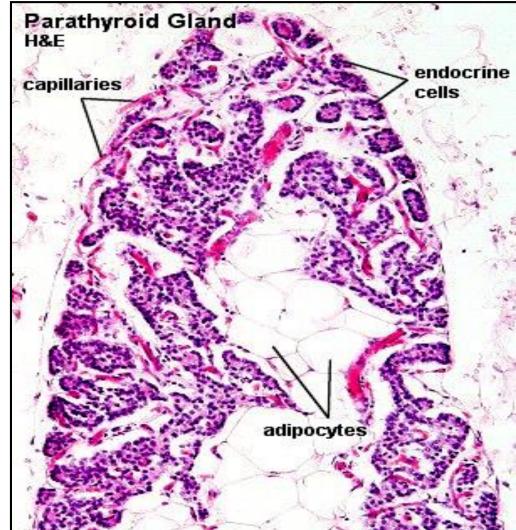
	Chief cells (principal)	Oxyphil cells
size	Small polygonal	Large polygonal
number	numerous	few
Stain	Faint acidophilic	Deep acidophilic
nucleus	Large vesicular	Small dense
Function	Parathyroid hormone (↑ Blood Ca level)	unknown

### Parathyroid gland in old people

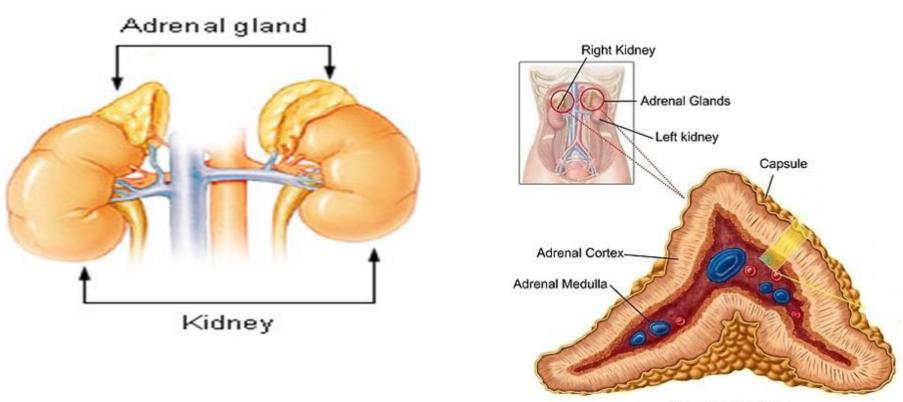
- Increase number of fat cells
- Increase number of oxyphil cells



Pineal gland with in old age

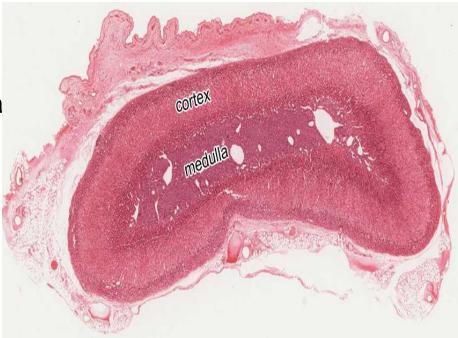


#### **ADRENAL GLANDS** or suprarenal gland



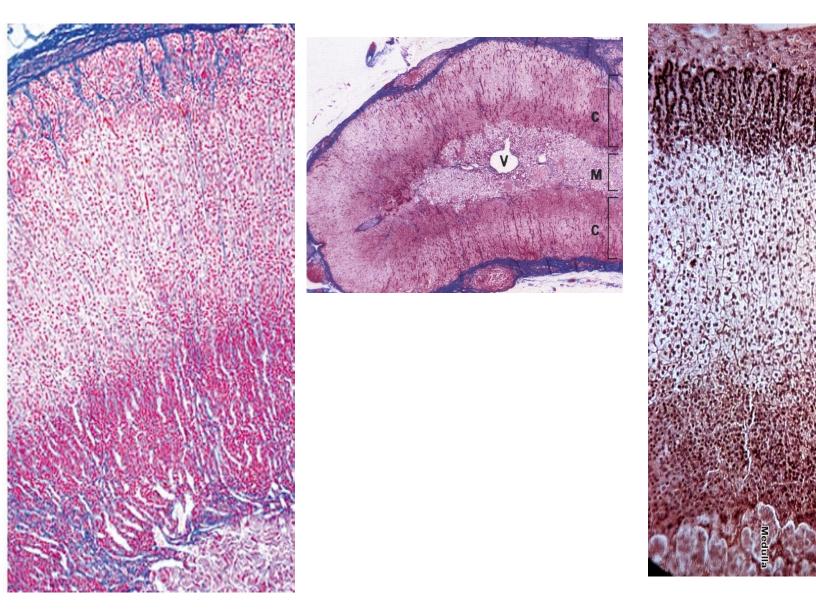
**Transverse Section** 

- **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 ( <b>mesodermal)</b>	Neural crest ( <b>ectodermal)</b>

#### ADRENAL GLANDS or suprarenal gland



#### **Zones of the cortex**

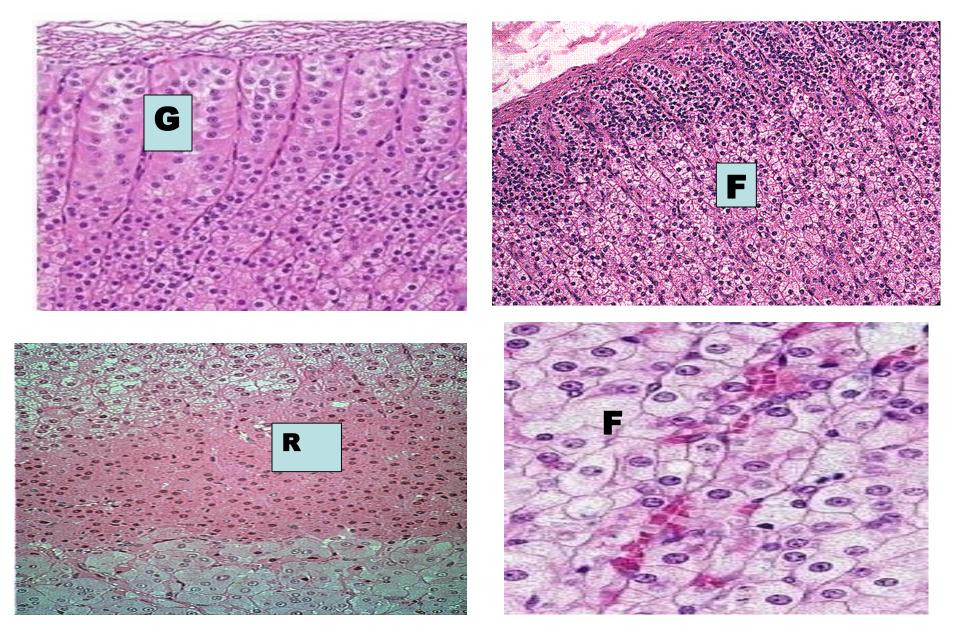
<u>**1. zona glomerulosa (15%)</u></u> /small rounded cells groups (clusters) or curved columns. The smallest cells, their nuclei are dark and round, and the cytoplasm is light basophilic// not influenced by ACTH// mineralocorticoid</u></u>** 

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:
- 1. Dark cells: pyknotic nuclei, excess lipofucsin pigment suggesting cellular degeneration.
- 2. Light cells: pale with pale staining nuclei

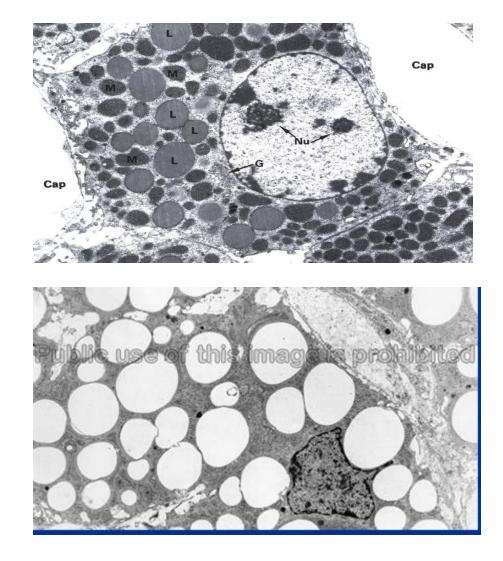
#### **Zones of the cortex**



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
Lipid droplets	few	numerous	less
Function	mineralocorticoids	glucocorticoids	Sex hormones

# 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)

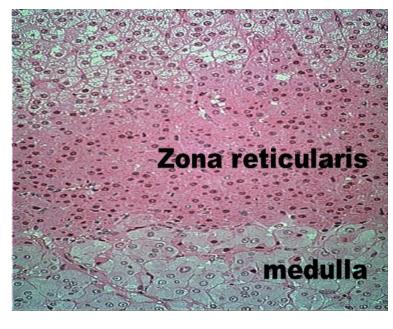


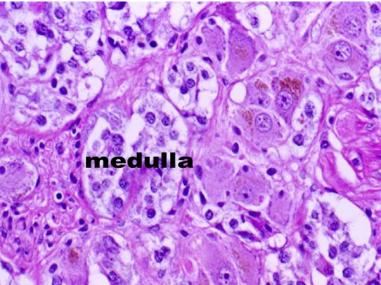
# **Adrenal medulla**

 -not sharply delimited from the cortex.
 -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.

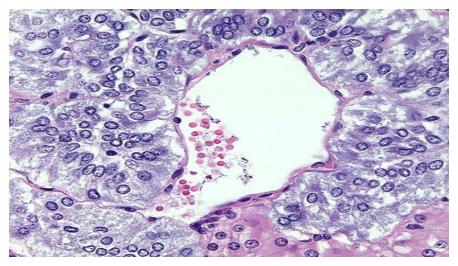
- -Catecholamines adrenaline and noradrenaline
- -Chromaffin cells are, like **ganglion cells** of the PNS, derived from **neural crest** cells.
- It includes 3 types of cells:
  - 1- Chromaffin cells
  - 2- Sympathetic ganglion cells
  - **3- Lymphocyte like cells**





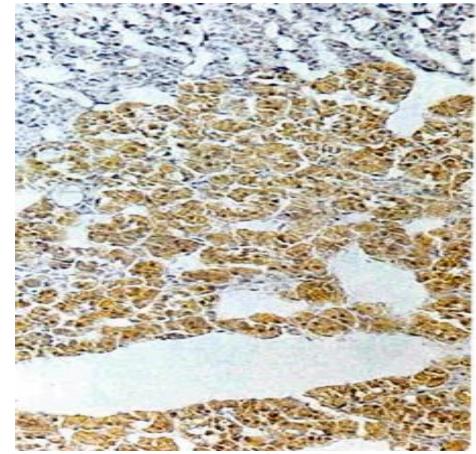
#### **Chromaffin cells**

#### 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**

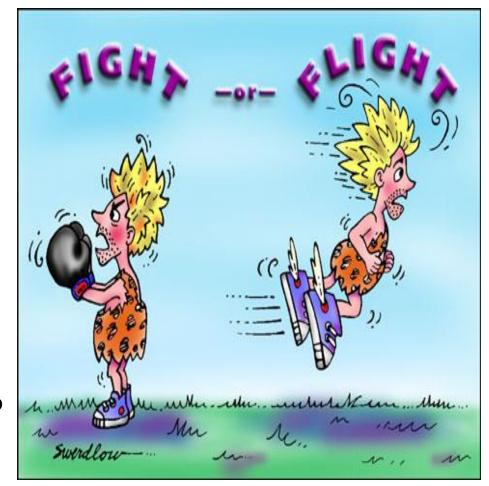
Granules in:	Epinephrine-secreting cells	Norepinephrine- secreting cells
Size	Small	larger
Contents	Fill the granule	Do not
	<b>E M</b> <b>protein synthesizing cells:</b> rER mitochondria prominent Golgi membrane-limited electron- dense granules of either epinephrine or norepinephrine	0.00

# **Function of adrenal medulla**

 epinephrine and norepinephrine → vasoconstriction, hypertension, ↑ heart rate & metabolic rate

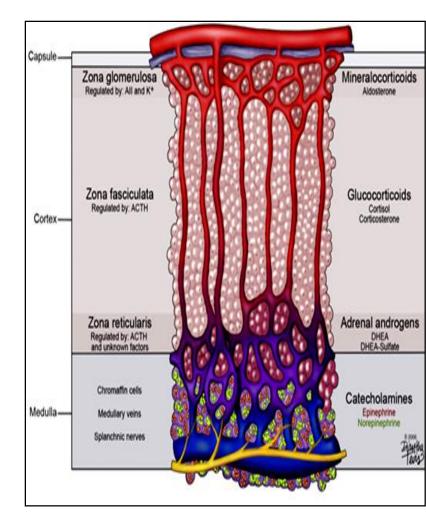
# Clinical hints of medulla

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**

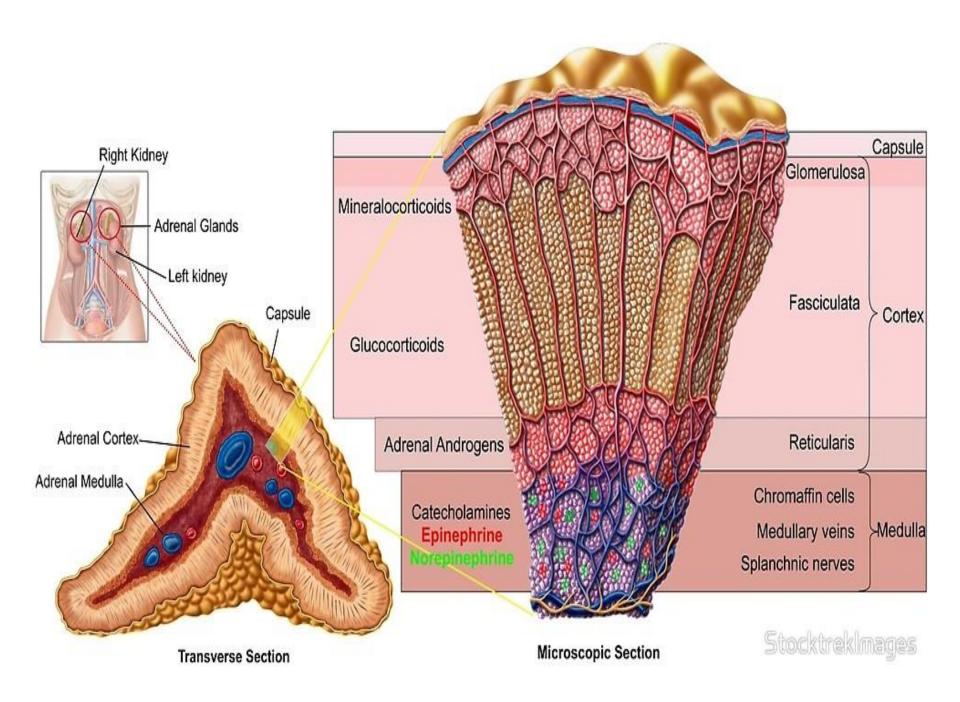


#### **Control of the Adrenal Cortex**

- The secretion of glucocorticoids is controlled initially through the release of corticotropin-releasing hormone in the median eminence, followed by secretion of (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**

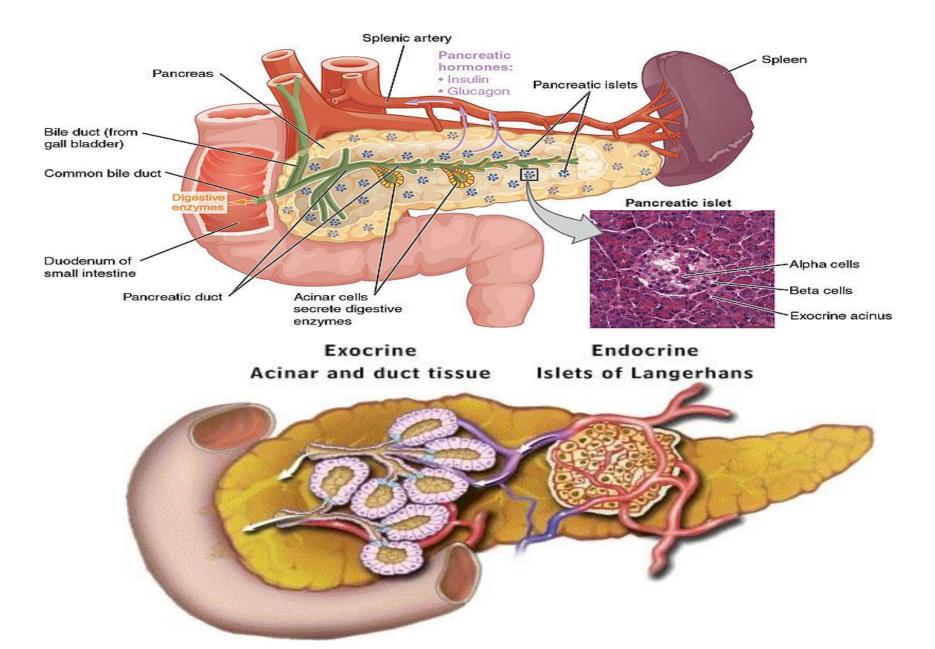
- Because of the feedback mechanism of adrenal cortex control, patients who are treated with corticoids for long periods should never stop taking these hormones suddenly:
- secretion of ACTH in these patients is inhibited, and thus the cortex will not be induced to produce corticoids, causing a severe 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**



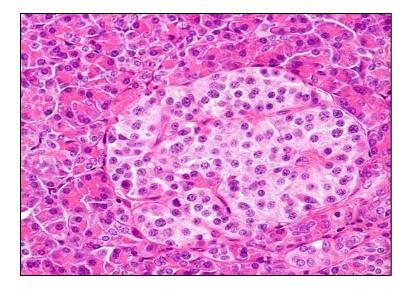
### PANCREAS

- □ Exocrine and endocrine gland.
- □ The exocrine part produces pancreatic juice.
- □ The endocrine part, ~1%, consists of the cells of the **islands of** Langerhans.

### **Endocrine part:** Islets of Langerhans

Masses of pale staining cells scattered between the pancreatic acini

- They are more in the **tail** than head of pancreas
- The cells are separated by fenestrated capillaries (highly vascularized)
- Cells of islets of Langerhans are Alpha, Beta, Delta, F (PP) cells



# **Structure** :of the islands of Langerhans.

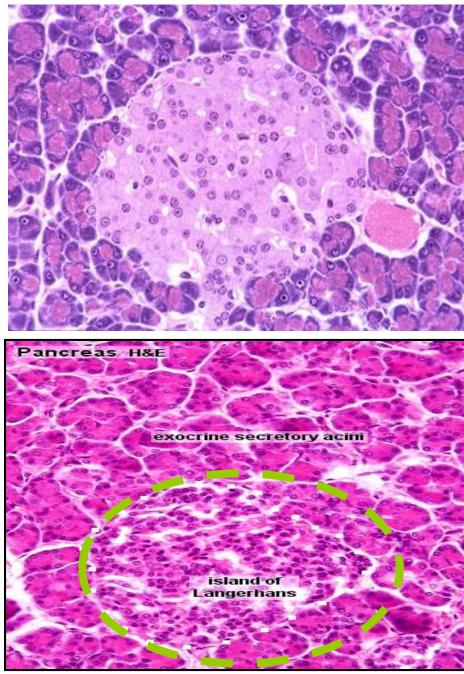
# Stroma:

Surrounded by thin capsule

#### Parenchyma

#### cellular composition of the islands

- □ 70% beta-cells, insulin. Insulin stimulates
- □ 20% alpha-cells, glucagon.
- □ 5- 10 % delta-cells which secrete somatostatin,
- **Given Set F- cells (PP)**



#### Beta (B) cells (70%):

- Produce **insulin** which **lower** blood sugar
- Cells are small in size, most numerous cell type, central in location in islets
- Stain blue
- EM: appear in two functional stages active & resting
- When active synthesize insulin. When resting packed with granules storing insulin
- Cells divide at very slow rate

#### <u>Alpha (A) cells (20%):</u>

- Produce glucagon which increase blood sugar insuling
- Cells larger in size, fewer in number, peripheral location in Islets
- Stain **pink**

Alpha cells

**Beta cells** 



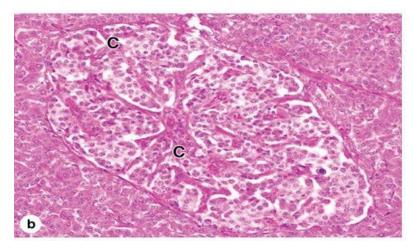


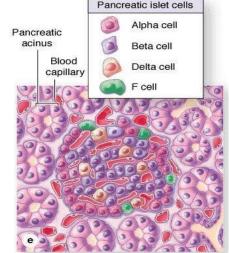
#### **Delta cells:**

- Secret somatostatin (growth inhibiting factor)
- Cells scattered at periphery and less abundant

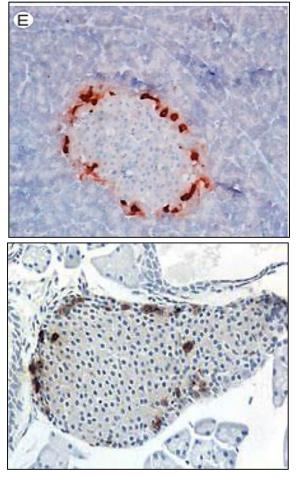
### F (PP) cells:

- Very few
- Secrete pancreatic polypeptide h.
- Regulate exocrine pancreas secretions



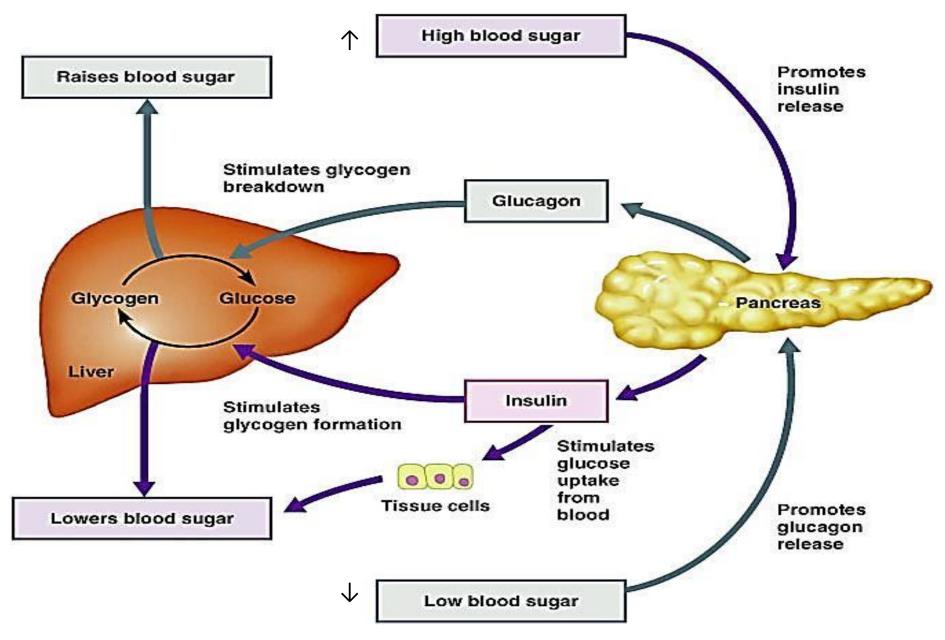


Delta cells

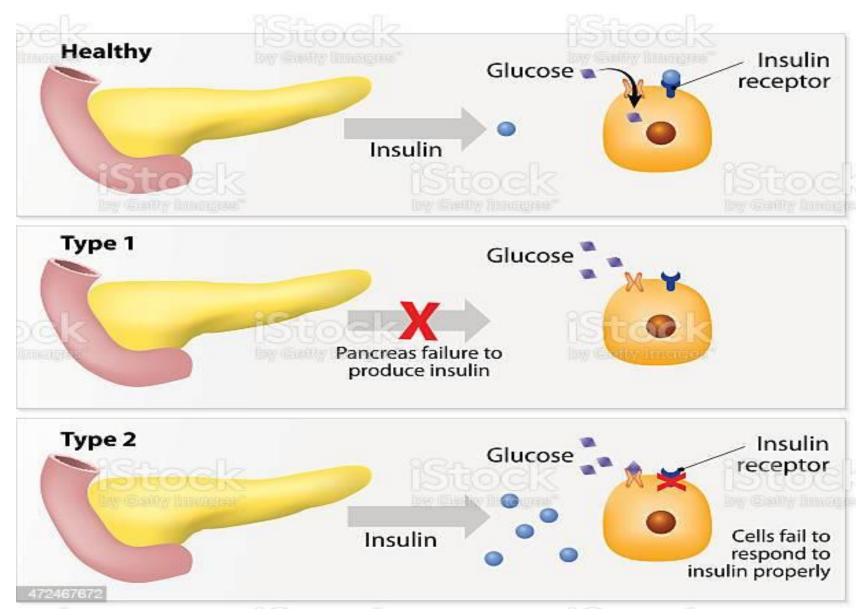


**PP cells** 

# **Regulation of blood glucose level**



### **DIABETES MELLITUS**

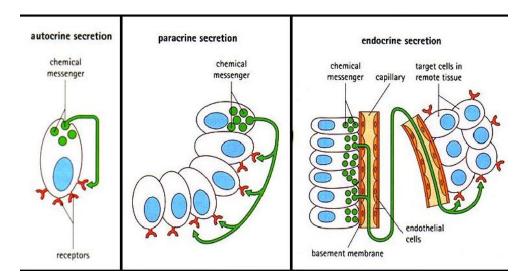


# **Diffuse neuroendocrine system**

- 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  $\rightarrow$  target organ
- 2. Paracrine → surrounding tissue
- 3. Autocrine  $\rightarrow$  themselves
- 4. Neuroendocrine → neurosecretion



# **Distribution of APUD cells**

# GIT (enteroendocrine cells) :

G cells EC cells ECL cells D cells S cells

#### Respiratory system

Bronchial Kulchitsky cells Small granule cells Neuroepithelial bodies among tracheobronchial epithelium.

#### Other sites

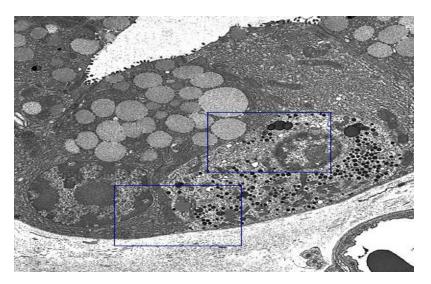
- **1. Myocardium:** → cardiodilatins and atrial naturetic polypeptides
- 2. Hypothalamus: supraoptic and paraventricular nuclei → oxytocin and vasopressin

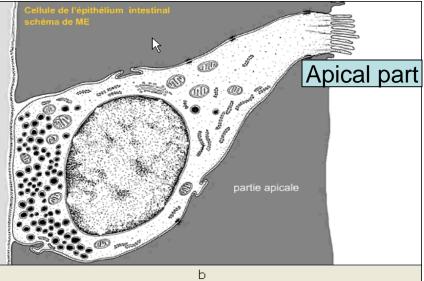
#### 3. Endocrine system:

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

# **Microscopic features**

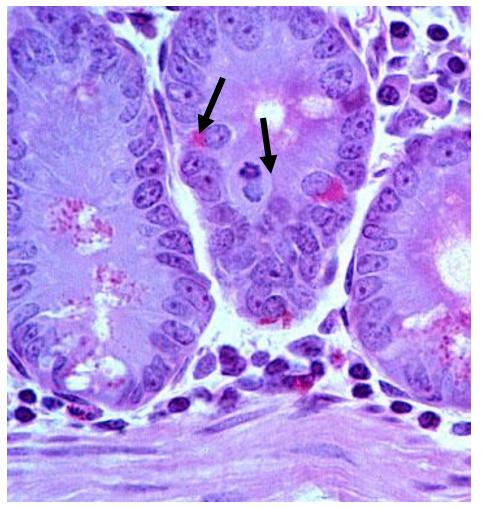
- Two types:
- 1. Open type
- 2. Closed type
- Electrolucent cytoplasm
- Few small secretory granules at the base or vascular pole
- Small infranuclear Golgi
- Sparse rER

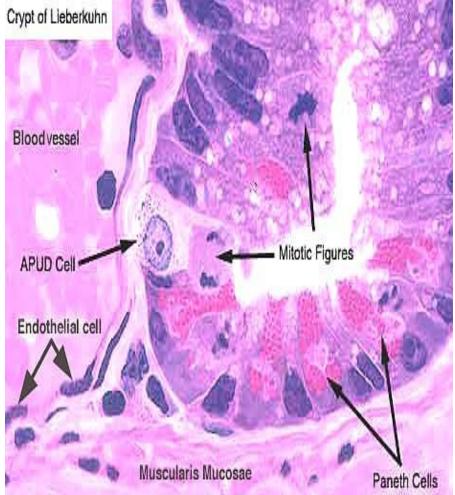




APUD of small intestine

# **Enteroendocrine cells**

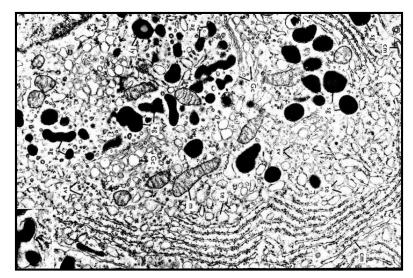




#### **General histological structures**

# Protein , polypeptide & a.a secreting cells

- Active nucleus
- ✤ Basophilic cytoplasm
- Numerous ribosomes & rER
- Prominent golgi & numerous mitochondria
- Secretory granules



#### **Steroid secreting cells**

- Active nucleus
- Acidophilic cytoplasm
- > Numerous **sER**
- numerous mitochondria with tubular cristae
- Numerous lipid droplets

