

# In the name of GOD

*Neuroendocrine*

*&*

*Endocrine system*

*For medicine students*

*Dr. Saeednia*

# Neuro endocrine & Endocrine

Hypophysis gland

Pineal body

Pancreatic islets

Thyroid gland

Parathyroid gland

Suprarenal gland

## Physiology of body controlled by:

- A. Nervous system:  
neurotransmitter  
secretion
- B. Endocrine system:  
hormone secretion

# Neuro endocrine & Endocrine

## *Hypophysis gland*

Pineal body

Pancreatic islets

Thyroid gland

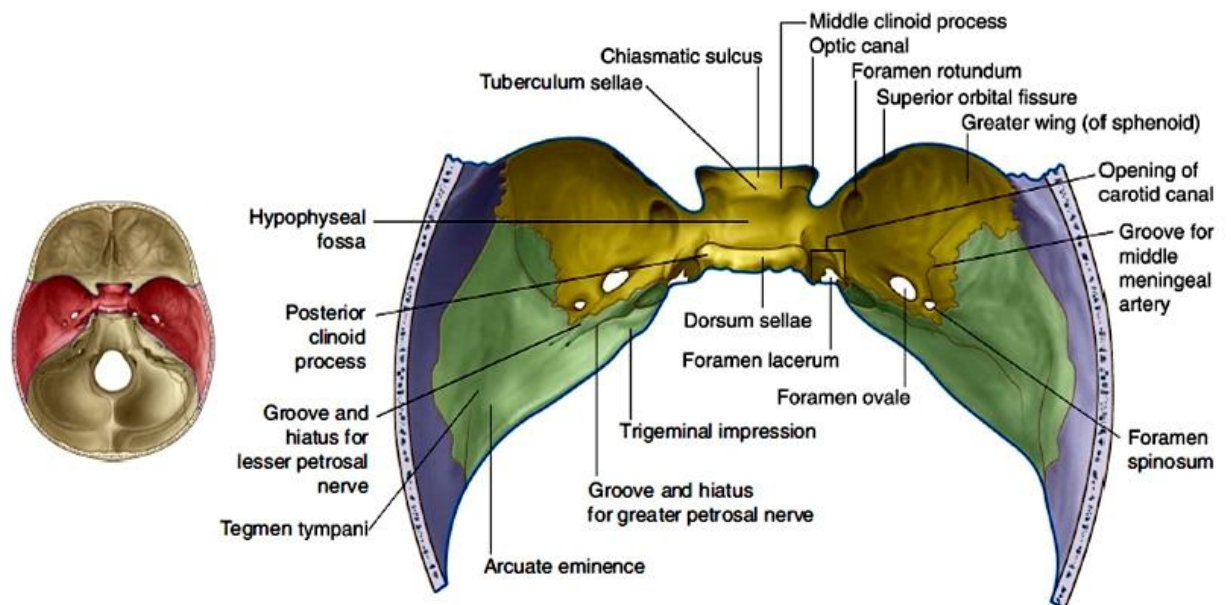
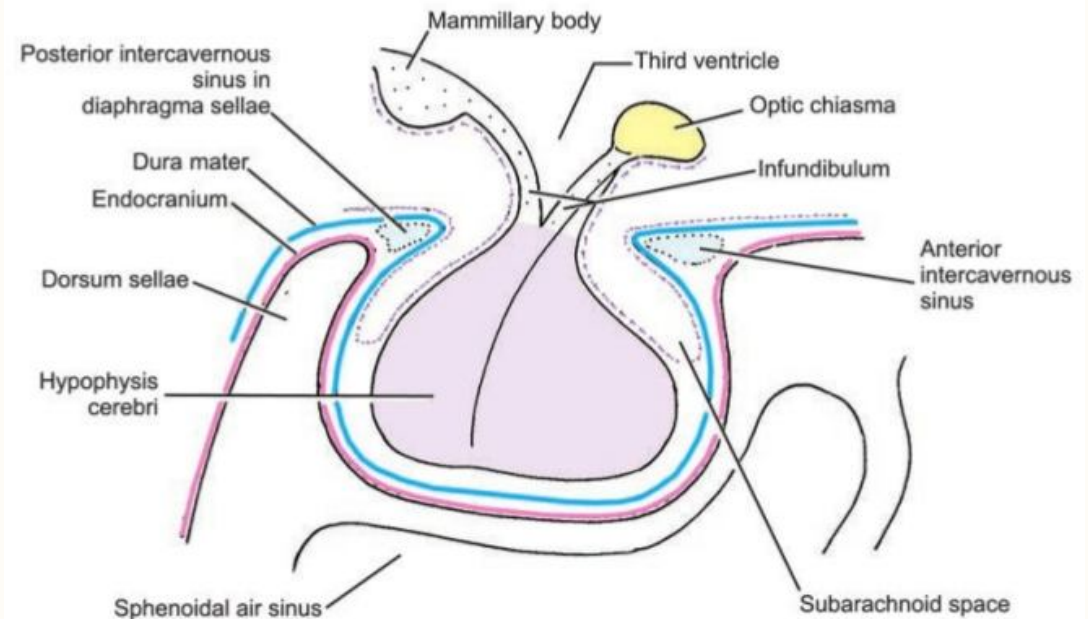
Parathyroid gland

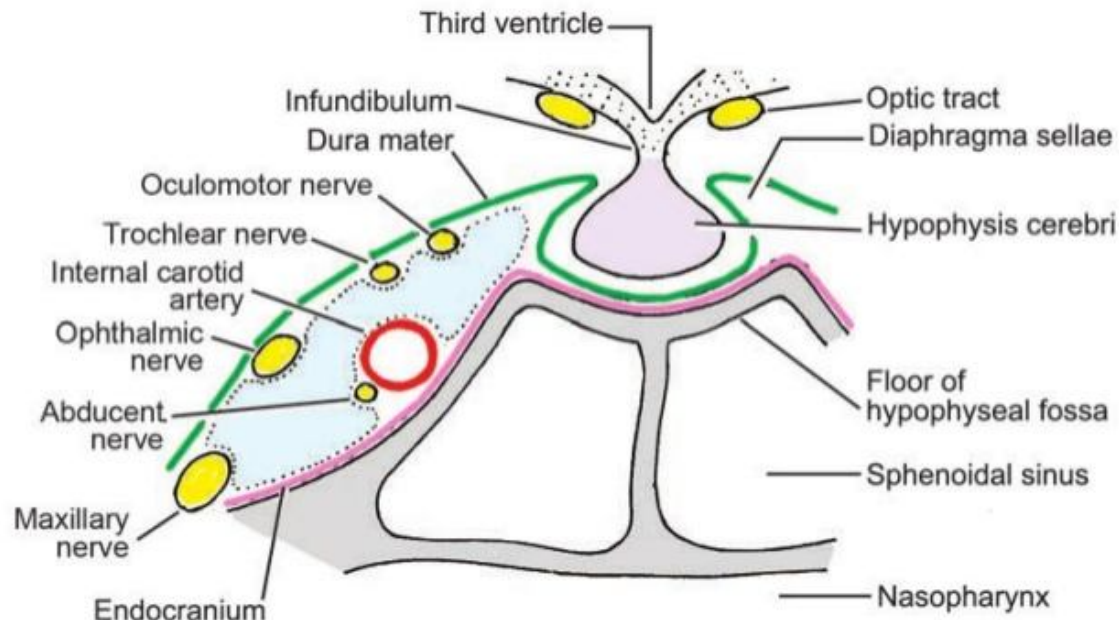
Suprarenal gland

## ***Sella turcica***

Sup. Surface of sphenoid body  
Just posterior to the chiasmatic

consists of a deep central area  
(the hypophyseal fossa)  
containing the pituitary





### ***Hypophysis correlation:***

Ant. : Optic chiasma

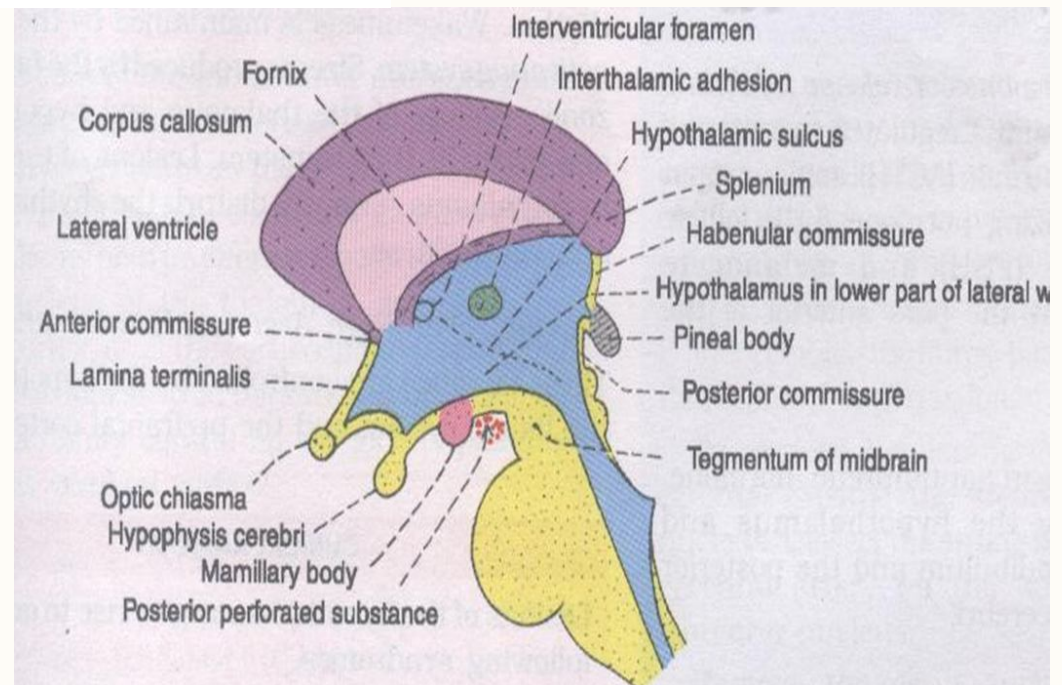
Post. : Mamillary body

Sup. : Hypothalamus

Lat. : Cavernous sinus:

Nerve= 3/4/6/ophthalmic/maxillary

Artery= int. carotid





## Regions of the hypophysis (pituitary gland)

### Adenohypophysis:

Pars tuberalis

Pars distalis (ant. Lobe)

Pars intermedia

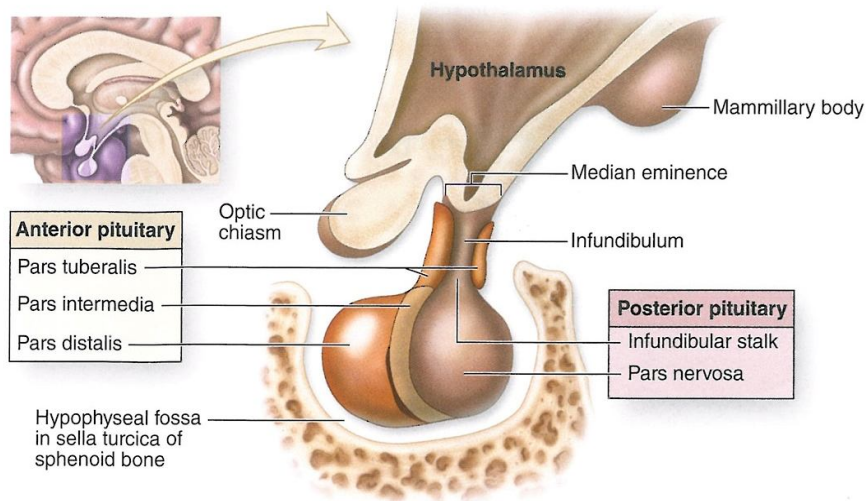
### Neurohypophysis:

Infundibulum =

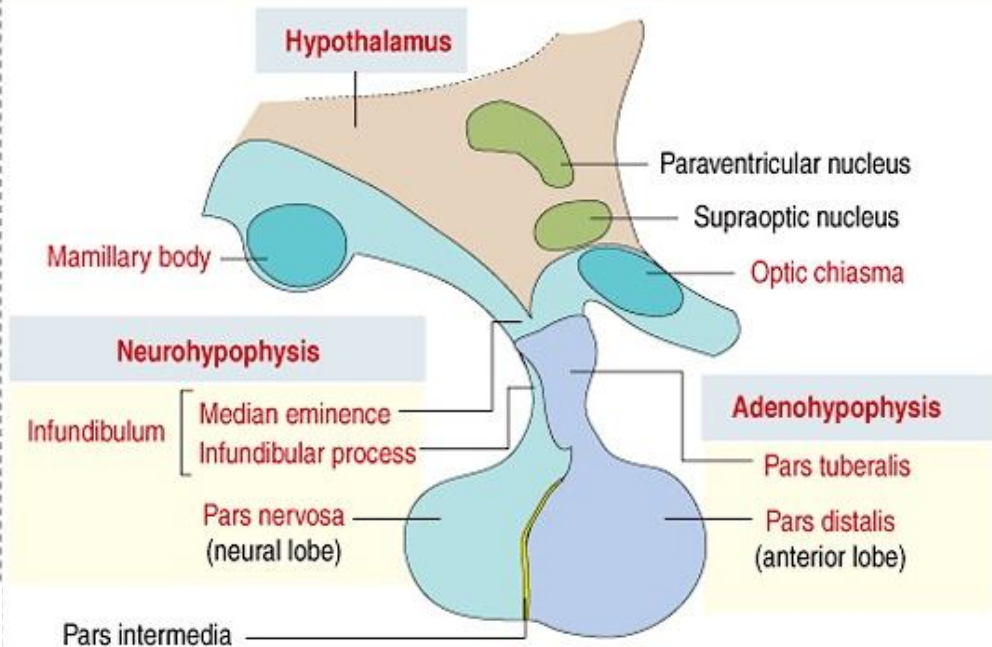
Median eminence

Infundibular process

Pars nervosa (neural lobe)



The **hypothalamus** is divided into two symmetrical halves by the third ventricle. It is limited rostrally by the **optic chiasma**, caudally by the **mamillary bodies**, laterally by the **optic tracts**, and dorsolaterally by the **thalamus**.



### Major subdivisions of the hypophysis

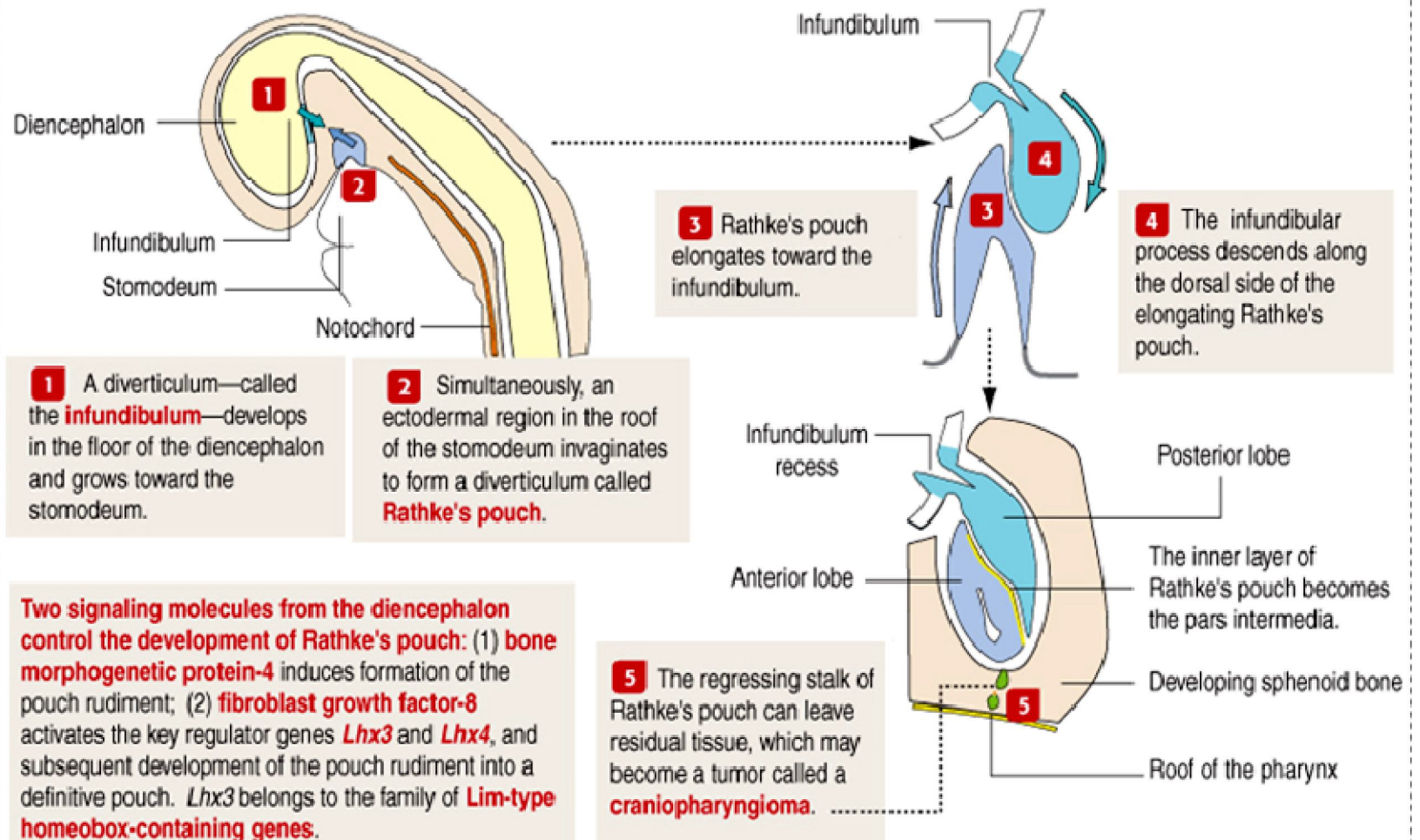
The **adenohypophysis** is formed by three major subdivisions: (1) the **pars distalis**, or **anterior lobe**, the main glandular epithelial component, (2) the **pars tuberalis**, a collar-like nonsecretory tissue enveloping the infundibulum of the neurohypophysis; (3) the **pars intermedia**, a narrow wedge forming a cap around the pars nervosa (neural lobe).

The **neurohypophysis** consists of two parts: the **pars nervosa**, or neural lobe, and the **infundibulum**. The infundibulum is formed by two structures: (1) the **median eminence**, a funnel-shaped extension of the hypothalamus; and (2) the **infundibular process**.

## Development of the hypophysis

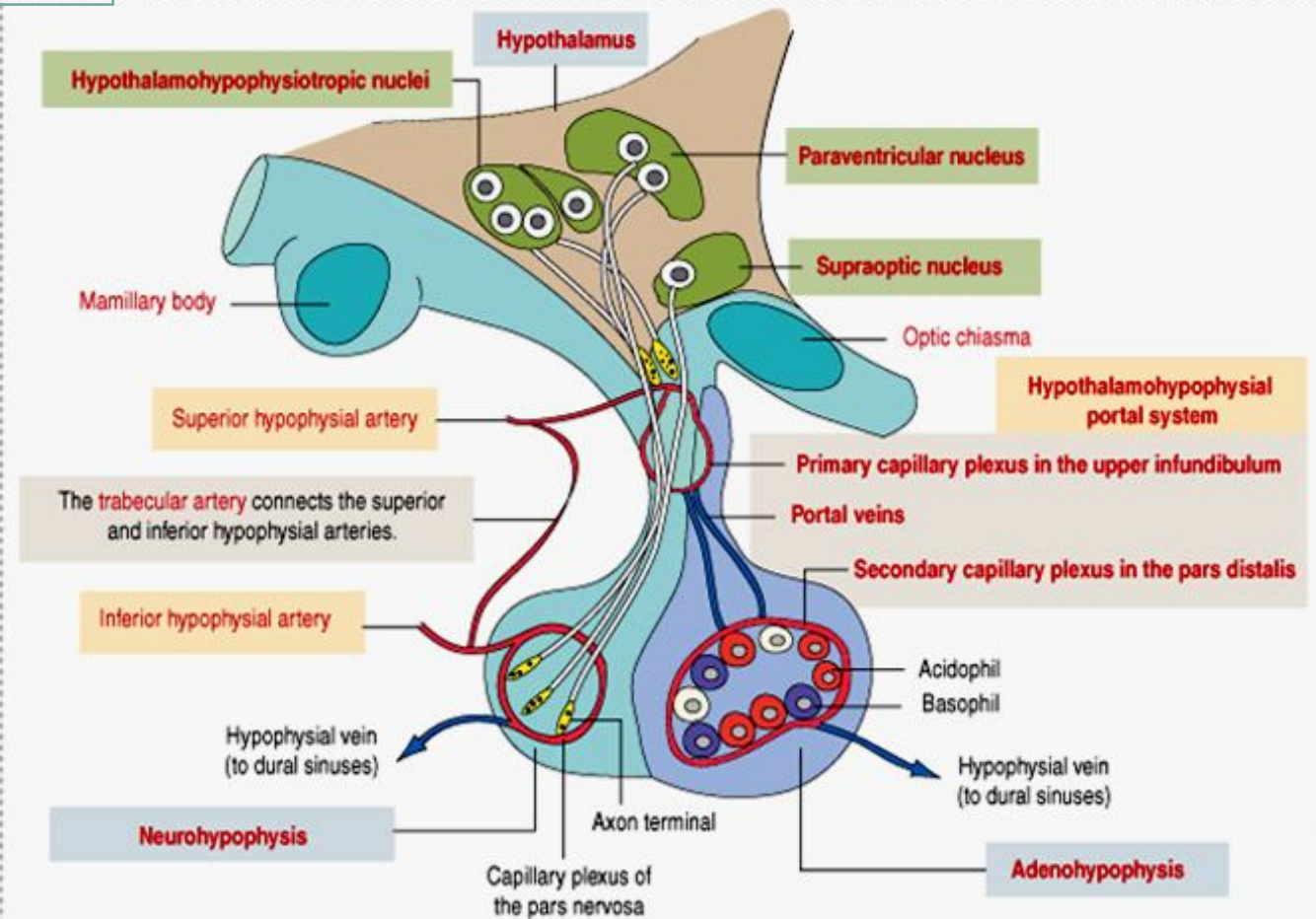
- Rathkes pouch : 3 week  
Adenohypophysis + pars tuberalis
- infundibulum : stalk + neurohypophysis

Pharyngeal hypophysis / craniopharyngioma





## Blood supply to the hypophysis



### Blood supply to the hypophysis

The **superior hypophyseal artery** forms a **primary capillary plexus** in the infundibulum (formed by the median eminence and infundibular stem). The primary capillary plexus receives releasing and inhibitory hormones from the neuroendocrine **hypothalamohypophysiotropic nuclei**.

The primary capillary plexus is drained by **portal veins**.

Portal veins supply blood to the **secondary capillary plexus**, with which basophils and acidophils are associated.

By this mechanism, hypothalamic releasing and inhibitory factors act directly on cells of the pars distalis (anterior

hypophysis) to regulate their endocrine function.

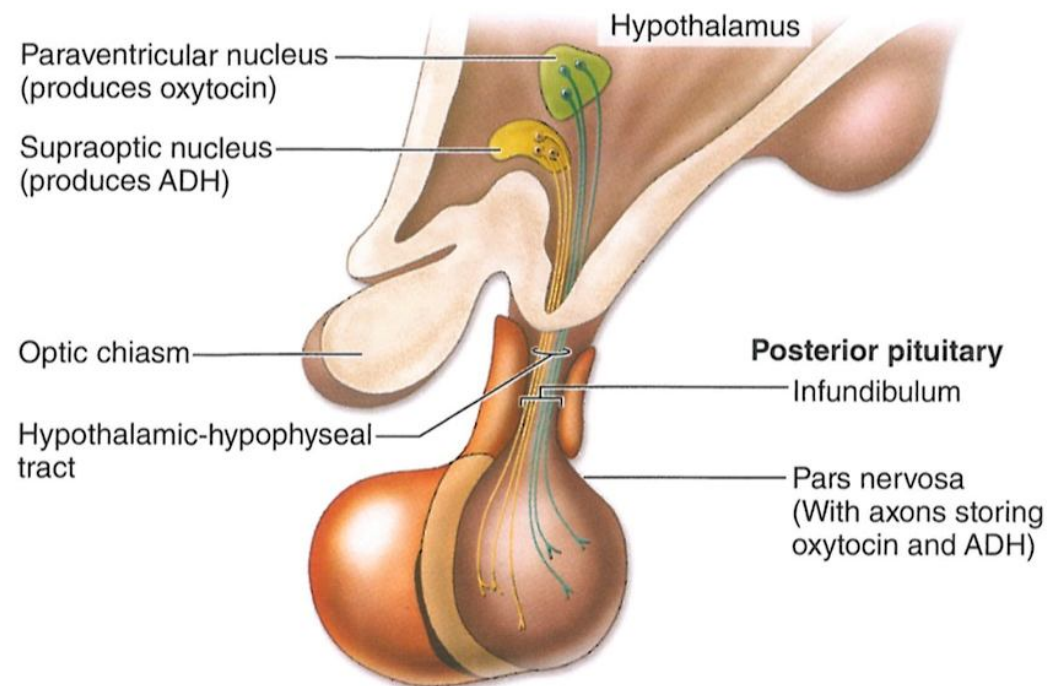
The primary and secondary capillary plexuses linked by the portal veins form the **hypothalamohypophysial portal system**.

The **inferior hypophyseal artery** supplies the pars nervosa, forming a capillary plexus, which collects vasopressin (antidiuretic hormone) and oxytocin produced by neuroendocrine cells of the supraoptic and paraventricular nuclei, respectively.

The superior and inferior hypophyseal arteries are connected by the **trabecular artery**.

### *Hypothalamic-hypophyseal tract:*

- ❖ Neurosecretory cell of the supraoptic & paraventricular nuclei that producing and releasing hormones In neural lobe
- ❖ Neurosecretory cell of the hypothalamus producing, releasing and inhibiting hormones in median eminence
- ❖ Pars distalis (ant. Lobe) that producing and releasing hormones by chromophil cells





### 3 types of cells in ant. Hypophysis:

#### Pars distalis:

Chromophobes

Chromophils :

#### Basophil:

Corticotrophs / POMC = ACTH +  $\beta$  - lipotropin

Gonadotrophs / FSH + LH

Thyrotrophs

#### Acidophil:

Somatotrophs / growth hormones

Lactotrophs / prolactin

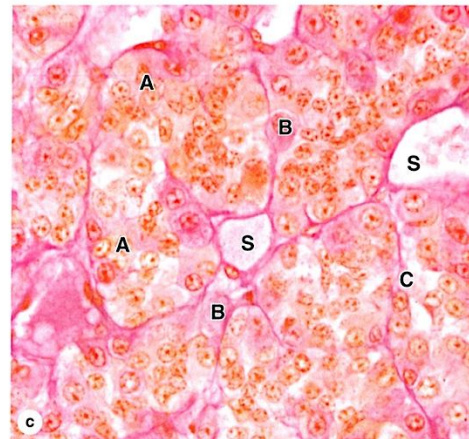
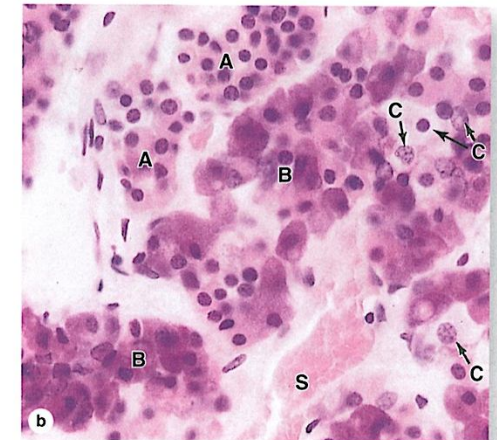
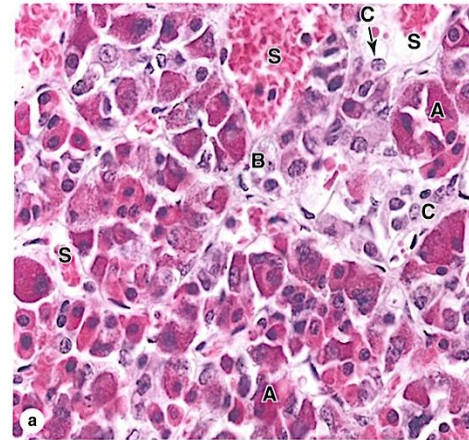
**Pars tuberalis:** Gonadotrophs

#### Pars intermedia:

From dorsal wall of hypophyseal pouch

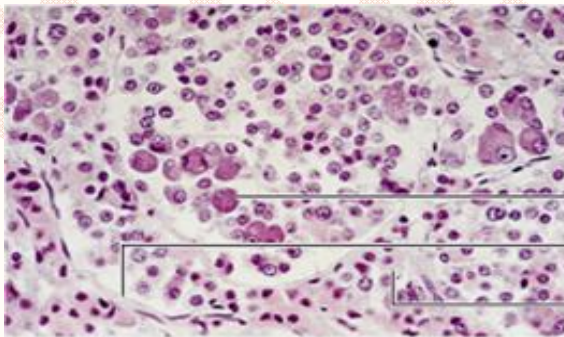
Rathkes cyst

POMC = two forms of MSH =  $\gamma$  - LPH +  $\beta$  - endorphin



(a, b) Most general staining methods simply allow the parenchymal cells of the pars distalis to be subdivided into acidophil cells (A), basophils (B), and chromophobes (C) in which the cytoplasm is poorly stained. Also shown are capillaries and sinusoids (S) in the second capillary plexus of the portal system. Cords of acidophils and basophils vary in distribution and number in different regions of the pars distalis, but they are always closely associated microvasculature that carries off secreted hormones into the general circulation. X400. H&E. (c) The same area is seen after staining with Gomori trichrome. X400.

## basophil, acidophil, and chromophobe cells in the anterior hypophysis



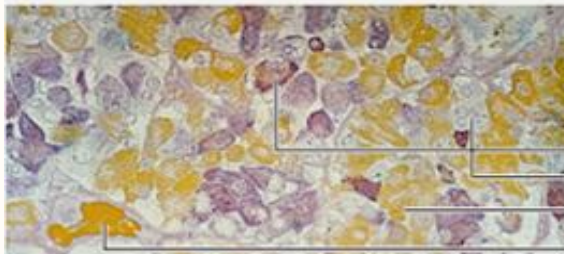
### Hematoxylin-eosin staining (H&E)

The anterior hypophysis consists of clusters of epithelial cells adjacent to fenestrated capillaries. With hematoxylin and eosin (H&E), the cytoplasm of **basophils** stains **blue-purple (glycoproteins)** and **acidophils** stain **light pink (proteins)**. Chromophobe cells display a very light pink cytoplasm.

Basophil

Fenestrated capillary

Acidophil



### Trichrome stain (aniline blue, orange G, and azocarmine)

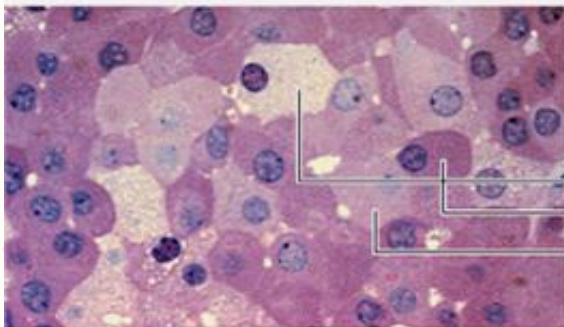
With the trichrome stain, the cytoplasm of **basophils** stains **blue-purple** and **acidophils** **orange**. **Chromophobe cells** stain **light blue**. Red blood cells in the lumen of the capillaries stain **deep orange**.

Basophil

Chromophobe

Acidophil

Red blood cells



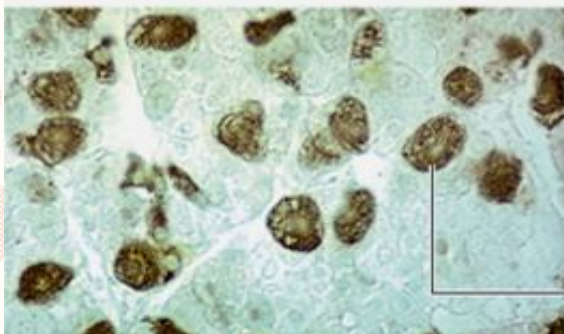
### Plastic section stained with basic fuchsin and hematoxylin

The polygonal shape of the epithelial cells of the anterior hypophysis is well defined in this preparation. The cytoplasm of **basophils** stains **dark pink**, **acidophils** stain **light pink**, and **chromophobe cells** are **unstained**.

Chromophobe

Basophil

Acidophil



### Immunohistochemistry (immunoperoxidase)

An antibody against the  $\beta$  chain of follicle-stimulating hormone (FSH) has been used to identify gonadotrophs within the anterior hypophysis in this illustration.

The use of specific antibodies against hormones produced in the anterior hypophysis has enabled (1) the precise identification of all hormone-producing cells of the anterior hypophysis; (2) the identification of hormone-producing **adenomas**; and (3) the elucidation of the negative and positive feedback pathways regulating the secretion of hypophysial hormones.

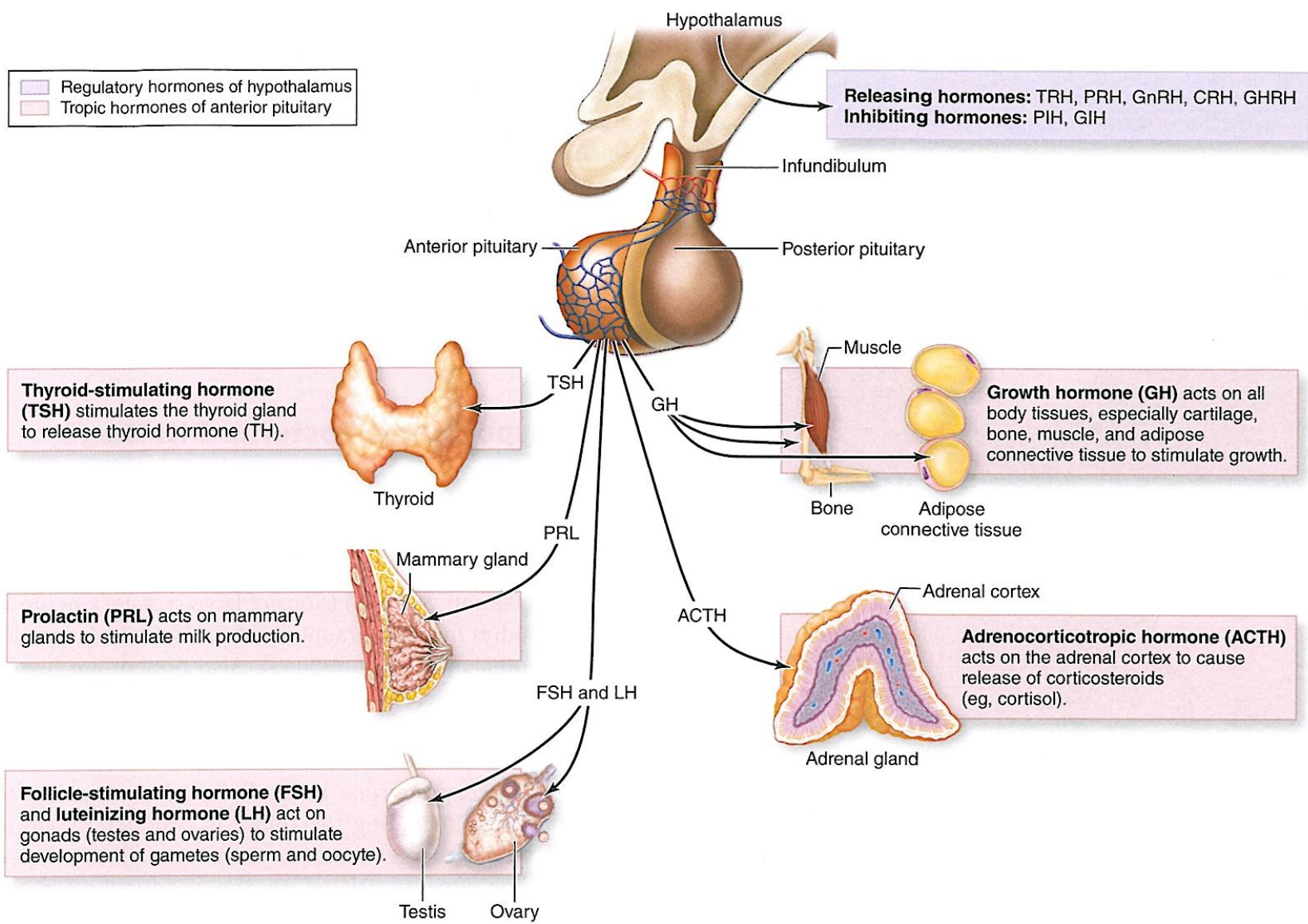
FSH-secreting cell (classified as basophil by H&E staining)



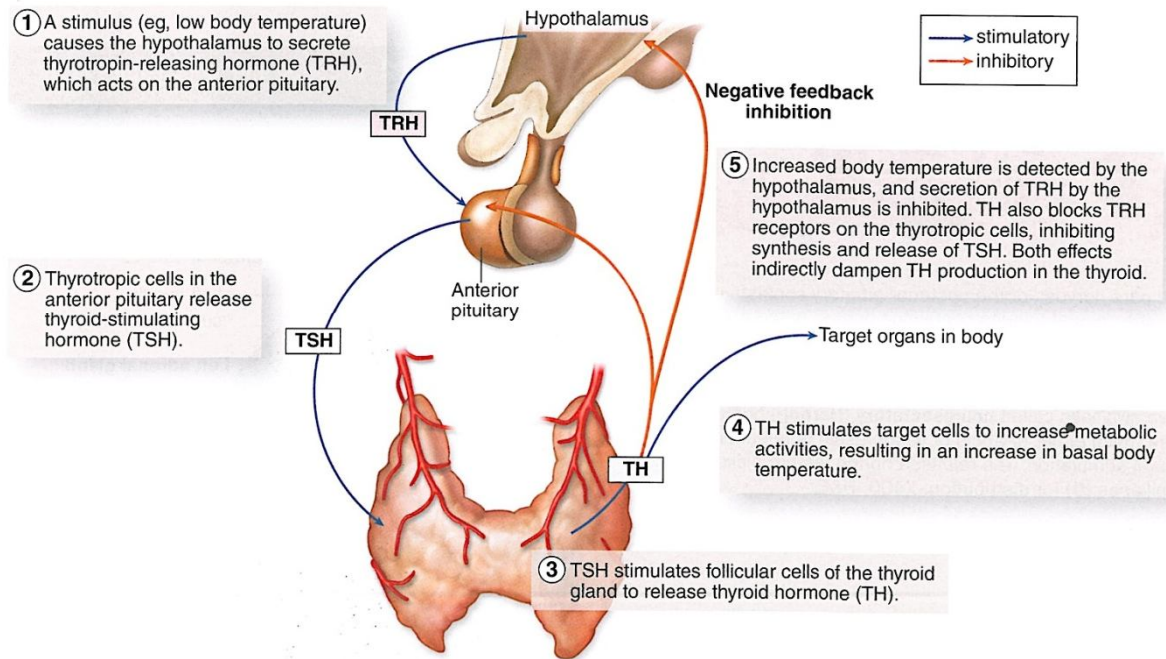
**TABLE 20–1****Major cell types of the anterior pituitary and their major functions.**

Cell Type	% of Total Cells	Hormone Produced	Major Function
Somatotrophs	50	Somatotropin (growth hormone, GH), a 22-kDa protein	Stimulates growth in epiphyseal plates of long bones via insulin-like growth factors (IGFs) produced in liver
Lactotrophs (or mammotrophs)	15-20	Prolactin (PRL), a 22.5-kDa protein	Promotes milk secretion
Gonadotrophs	10	Follicle-stimulating hormone (FSH) and luteinizing hormone (LH; interstitial cell-stimulating hormone [ICSH] in men), both 28-kDa glycoprotein dimers, secreted from the same cell type	FSH promotes ovarian follicle development and estrogen secretion in women and spermatogenesis in men; LH promotes ovarian follicle maturation and progesterone secretion in women and interstitial cell androgen secretion in men
Thyrotrophs	5	Thyrotropin (TSH), a 28-kDa glycoprotein dimer	Stimulates thyroid hormone synthesis, storage, and liberation
Corticotrophs	15-20	Adrenal corticotropin (ACTH), a 4-kDa polypeptide Lipotropin (LPH)	Stimulates secretion of adrenal cortex hormones Helps regulate lipid metabolism





**FIGURE 20-10 Negative feedback loops affecting anterior pituitary secretion.**



**TABLE 20-2**

**Hypothalamic hormones regulating cells of the anterior pituitary.**

Hormone	Chemical Form	Functions
Thyrotropin-releasing hormone (TRH)	3-amino acid peptide	Stimulates release of thyrotropin (TSH)
Gonadotropin-releasing hormone (GnRH)	10-amino acid peptide	Stimulates the release of both follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Somatostatin	14-amino acid peptide	Inhibits release of both somatotropin (GH) and TSH
Growth hormone-releasing hormone (GHRH)	40- or 44-amino acid polypeptides (2 forms)	Stimulates release of GH
Dopamine	Modified amino acid	Inhibits release of prolactin (PRL)
Corticotropin-releasing hormone (CRH)	41-amino acid polypeptide	Stimulates synthesis of pro-opiomelanocortin (POMC) and release of both $\beta$ -lipotropin ( $\beta$ -LPH) and corticotropin (ACTH)



## Growth hormone

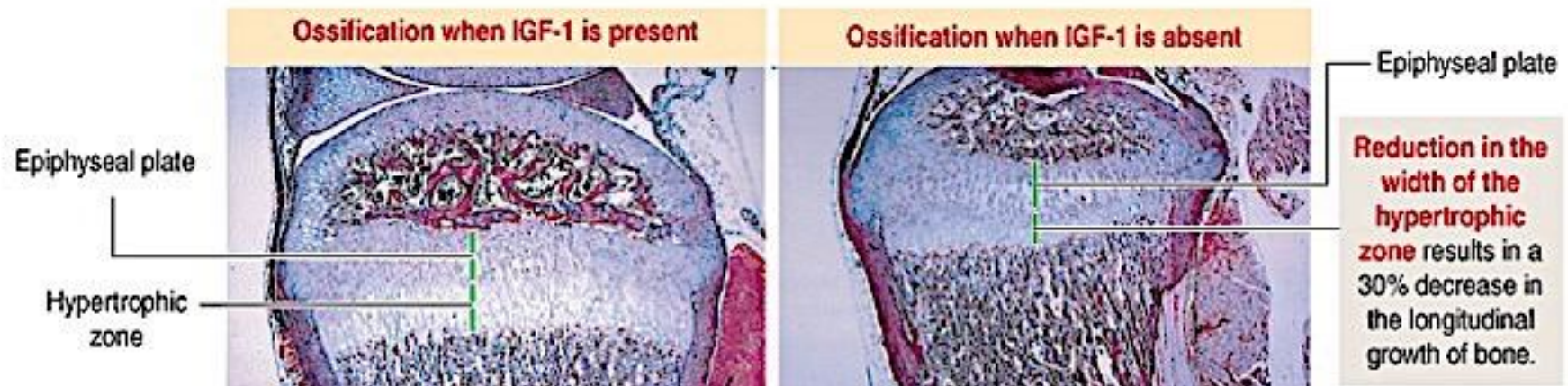
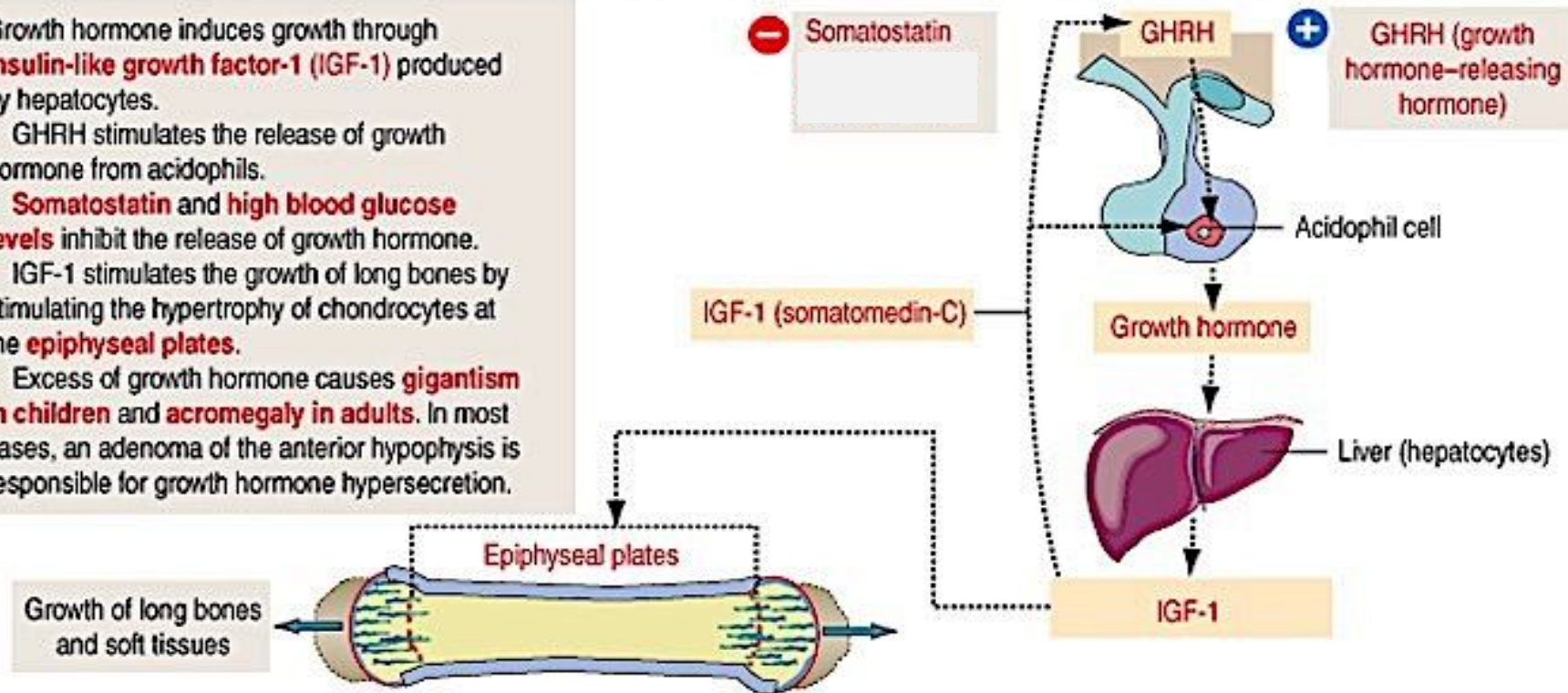
Growth hormone induces growth through **insulin-like growth factor-1 (IGF-1)** produced by hepatocytes.

GHRH stimulates the release of growth hormone from acidophils.

**Somatostatin** and **high blood glucose levels** inhibit the release of growth hormone.

IGF-1 stimulates the growth of long bones by stimulating the hypertrophy of chondrocytes at the **epiphyseal plates**.

Excess of growth hormone causes **gigantism in children** and **acromegaly in adults**. In most cases, an adenoma of the anterior hypophysis is responsible for growth hormone hypersecretion.



## Prolactin

Prolactin stimulates lactation post partum.

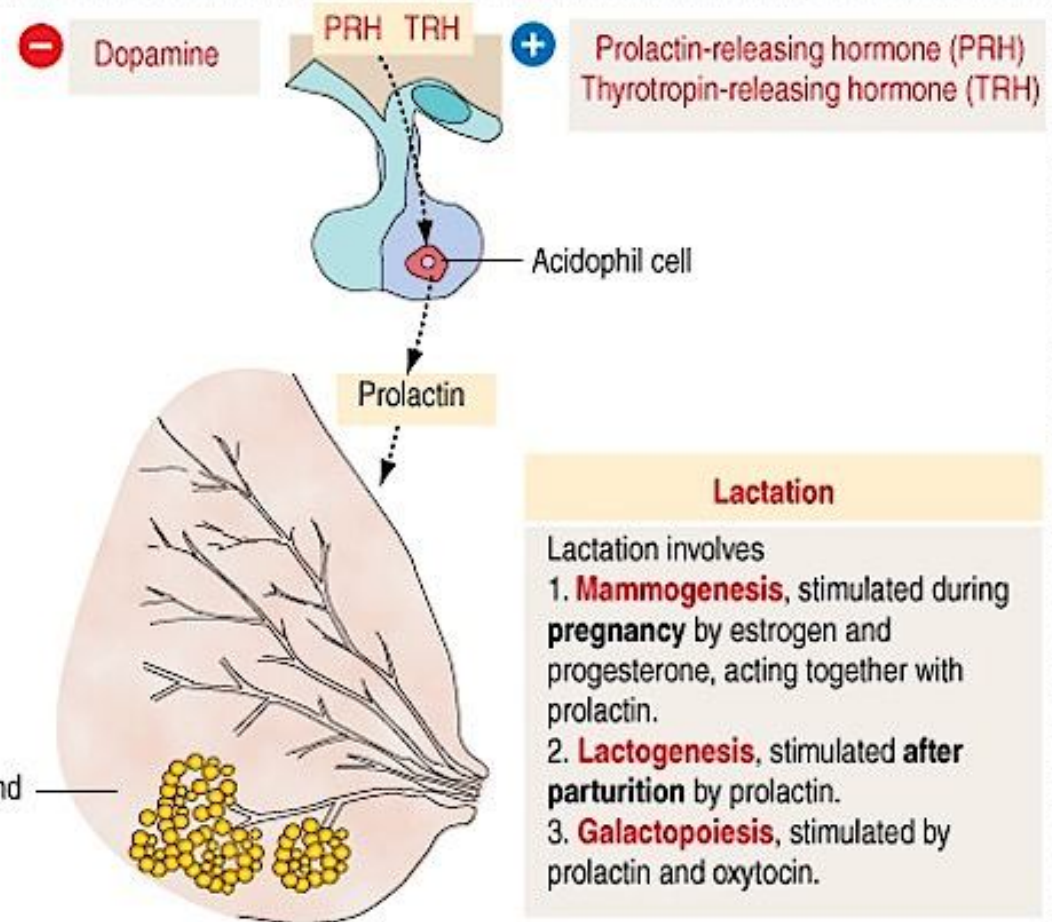
The secretion of prolactin by **acidophils** is regulated primarily by inhibition rather than by stimulation.

**Dopamine** is the main inhibitor of prolactin secretion.

**Suckling during lactation** is the major stimulus of prolactin secretion.

A prolactin-secreting adenoma of the anterior hypophysis causes **hyperprolactinemia**, which in turn accounts for **galactorrhea** (nonpuerperal milk secretion).

Hyperprolactinemia leads to reversible **infertility** in both females and males.





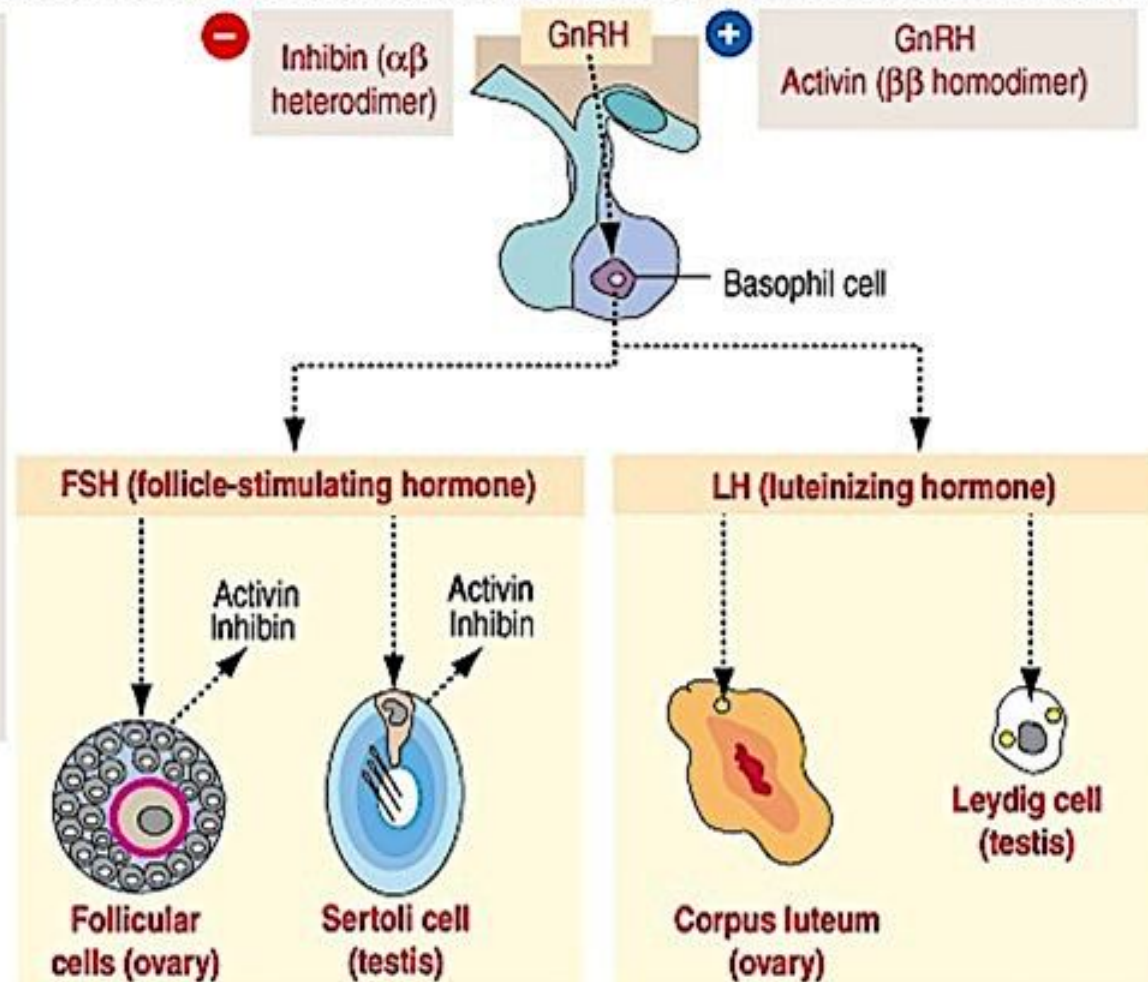
## Gonadotropins (FSH and LH)

Neurons in the **arcuate nucleus** of the hypothalamus secrete **GnRH** (gonadotropin-releasing hormone). GnRH is secreted in pulses at 60- to 90-minute intervals and stimulates the pulsatile secretion of **gonadotropins** by the basophilic gonadotrophs.

**In the female**, FSH stimulates **follicular cells** of the ovarian follicle to proliferate and secrete **estradiol**, **inhibin**, and **activin**. LH stimulates progesterone secretion by the **corpus luteum**.

**In the male**, FSH stimulates **Sertoli cell** function in the seminiferous epithelium (synthesis of **inhibin**, **activin**, and **androgen-binding protein**). LH stimulates the production of **testosterone** by **Leydig cells**.

A lack of FSH and LH in females and males leads to **infertility**.



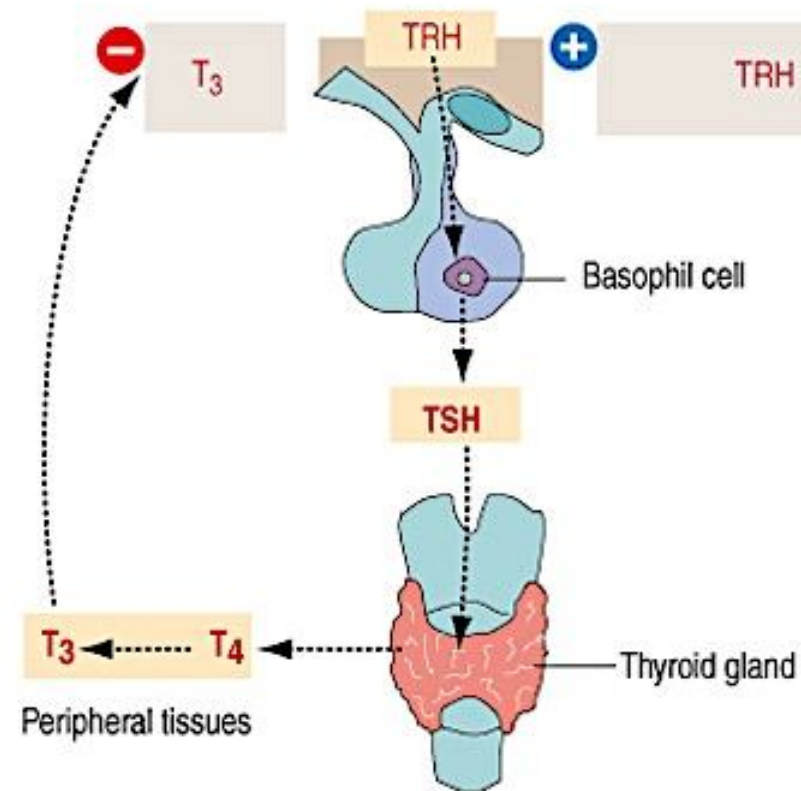


## Thyroid-stimulating hormone (TSH)

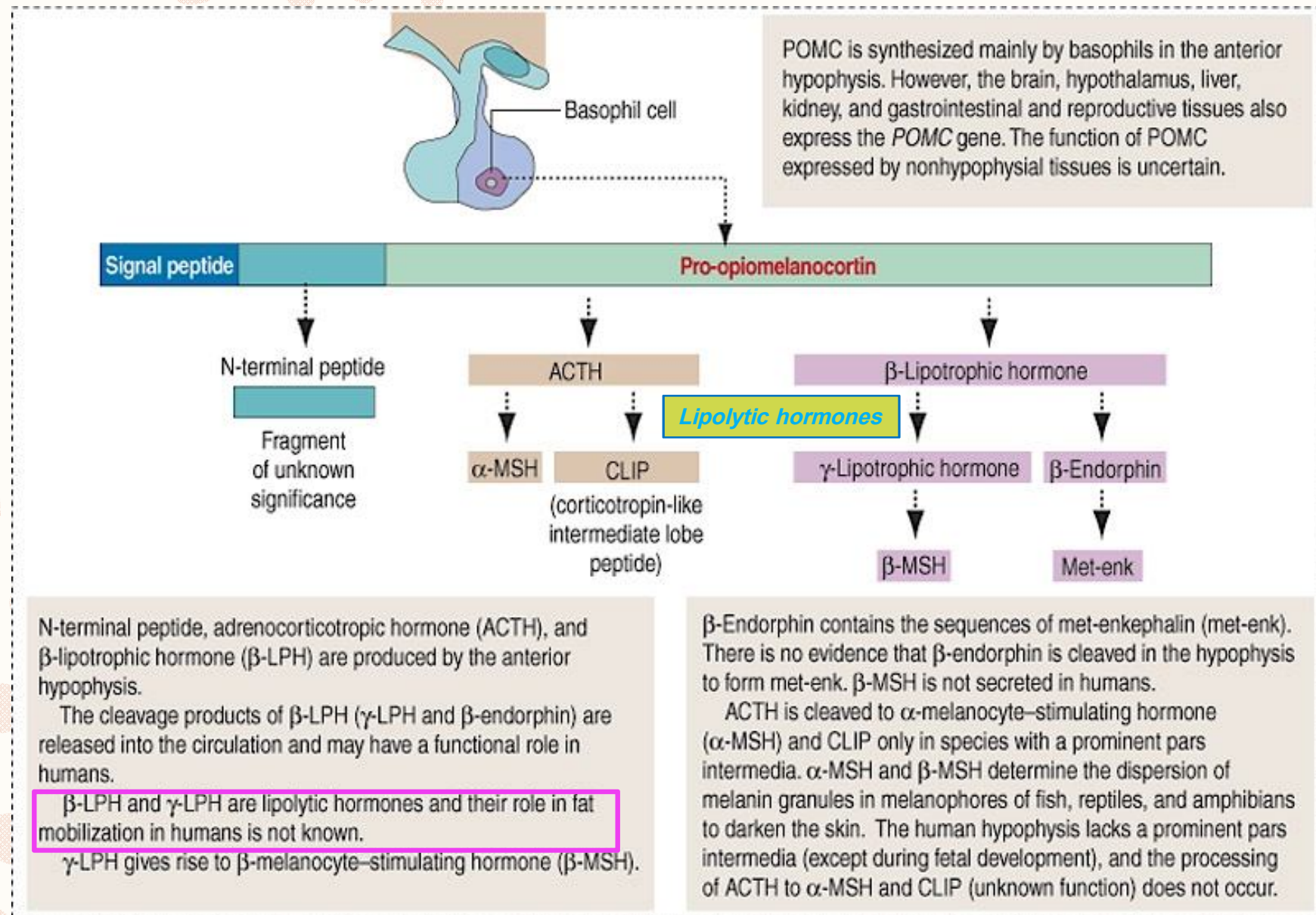
Thyrotropin-releasing hormone (**TRH**), a tripeptide, modulates the synthesis and release of **TSH** (thyroid-stimulating hormone) from basophils.

TSH is a glycoprotein that binds to a receptor in the plasma membrane of thyroid follicular epithelial cells. The hormone-receptor complex stimulates the formation of cAMP. The production of the thyroid hormones **T<sub>3</sub>** (triiodothyronine) and **T<sub>4</sub>** (thyroxine) is stimulated by cAMP.

Some **T<sub>4</sub>** is converted to **T<sub>3</sub>** in peripheral tissues. **T<sub>3</sub>** is more active than **T<sub>4</sub>** and has a negative feedback (inhibitory) action on TSH synthesis and release.



## Processing of pro-opiomelanocortin (POMC)





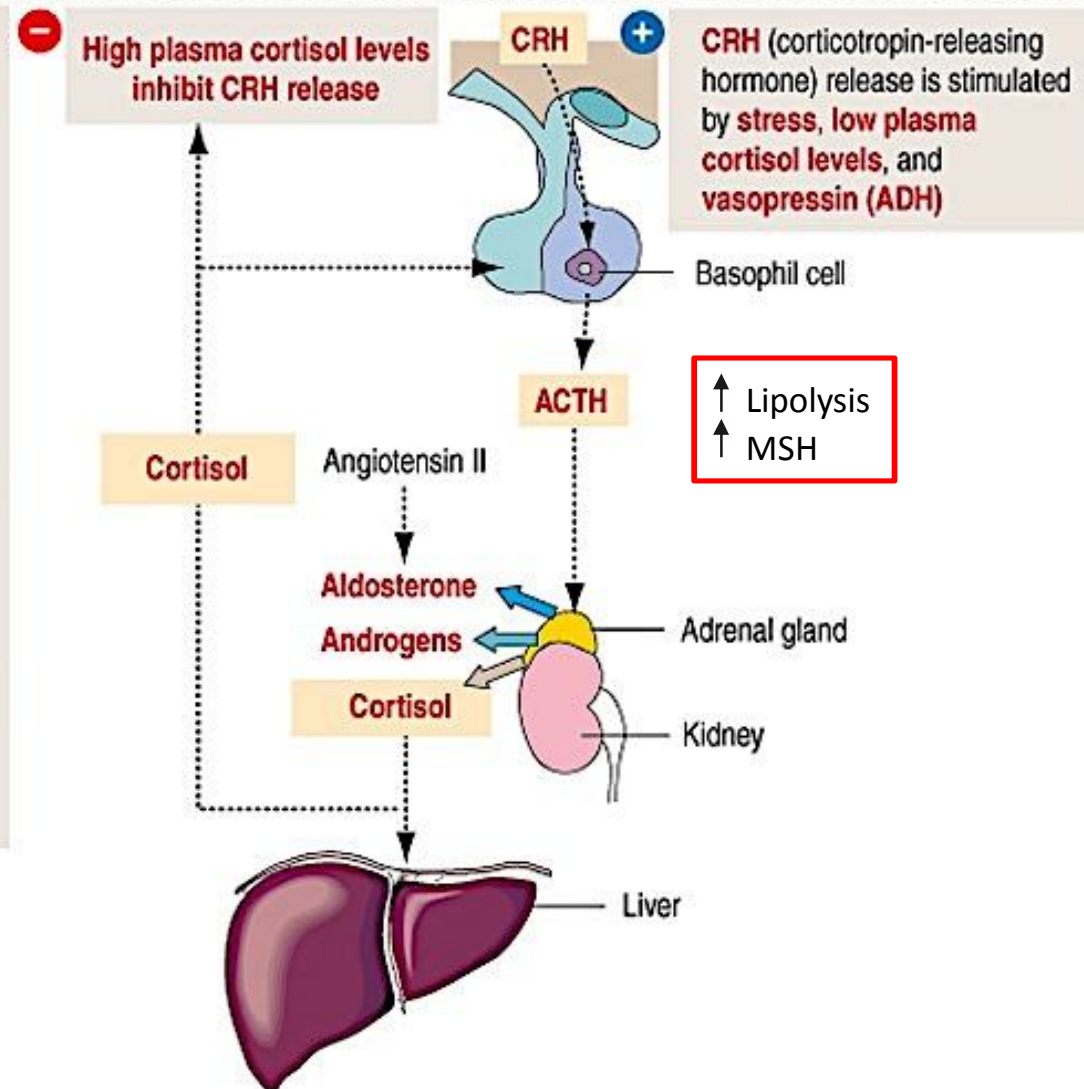
## Adrenocorticotrophic hormone (ACTH)

ACTH controls predominantly the function of two zones of the adrenal cortex (**zona fasciculata** and **zona reticularis**). The zona glomerulosa is regulated by **angiotensin II** derived from the processing of the liver protein angiotensinogen by the proteolytic action of renin (kidney) and converting enzyme (lung).

**ACTH stimulates the synthesis of cortisol** (a glucocorticoid) and androgens. Cortisol and other steroids are metabolized in liver.

Low levels of cortisol in blood, stress, and vasopressin (antidiuretic hormone [ADH]) stimulate ACTH secretion from basophils by stimulation of CRH release (positive feedback). **Cortisol is the dominating regulatory factor.**

**ACTH increases the pigmentation of skin.** Skin darkening in Addison's disease and Cushing's disease is not determined by melanocyte-stimulating hormone (MSH), which is not normally present in human serum.



### 3 types of cells in ant. Hypophysis:

#### Pars distalis:

Chromophobes

Chromophils :

#### Basophil:

Corticotrophs / POMC = ACTH +  $\beta$  - lipotropin

Gonadotrophs / FSH + LH

Thyrotrophs

#### Acidophil:

Somatotrophs / growth hormones

Lactotrophs / prolactin

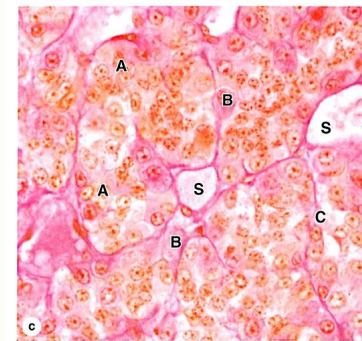
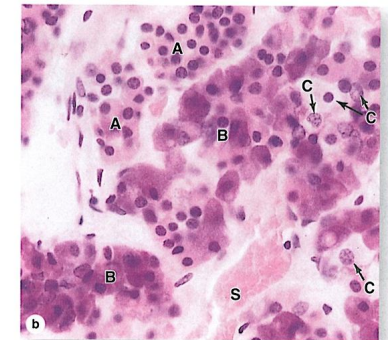
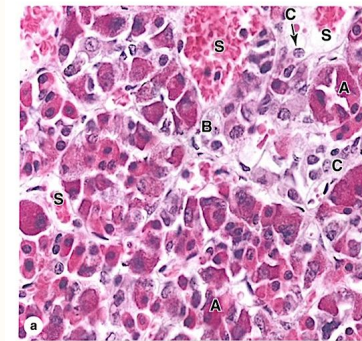
**Pars tuberalis:** Gonadotrophs

#### Pars intermedia:

From dorsal wall of hypophyseal pouch

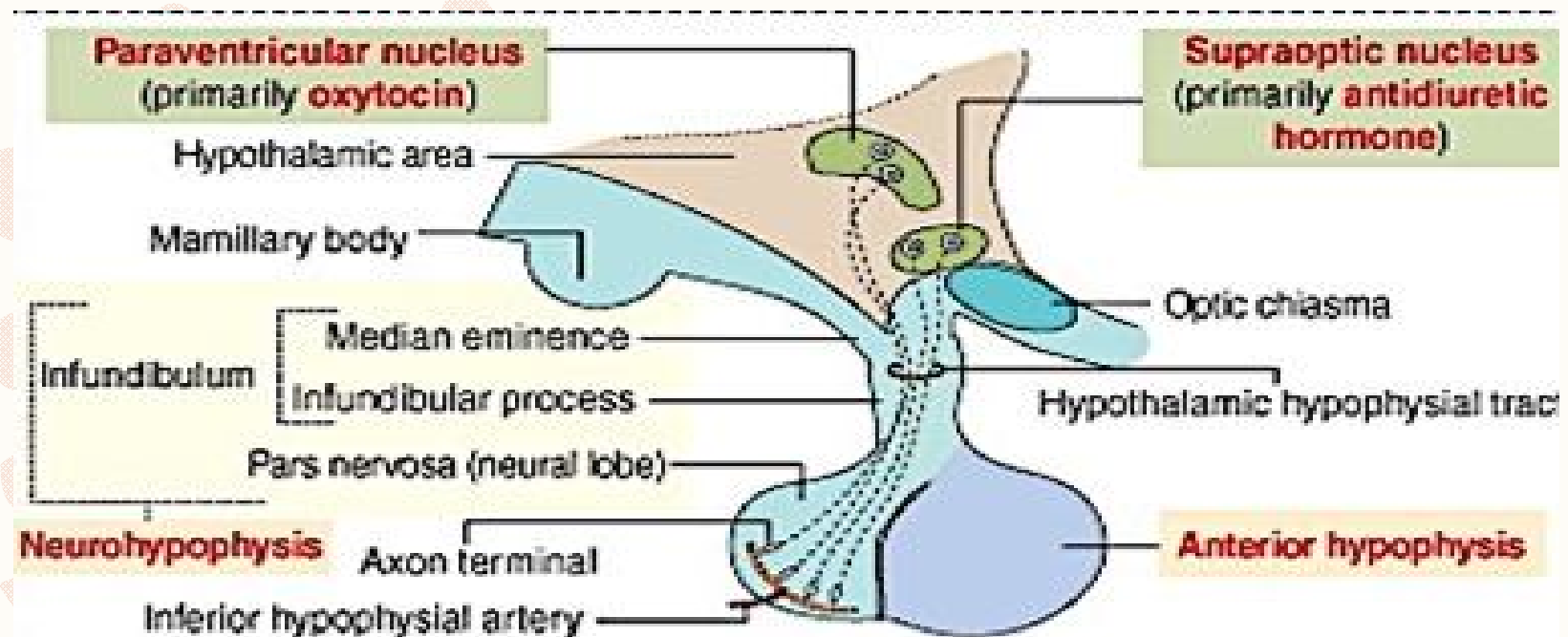
Rathkes cyst

POMC = two forms of MSH =  $\gamma$  - LPH +  $\beta$  - endorphin



(a, b) Most general staining methods simply allow the parenchymal cells of the pars distalis to be subdivided into acidophil cells (A), basophils (B), and chromophobes (C) in which the cytoplasm is poorly stained. Also shown are capillaries and sinusoids (S) in the second capillary plexus of the portal system. Cords of acidophils and basophils vary in distribution and number in different regions of the pars distalis, but they are always closely associated microvasculature that carries off secreted hormones into the general circulation. X400. H&E. (c) The same area is seen after staining with Gomori trichrome. X400.

## Neurohypophysis



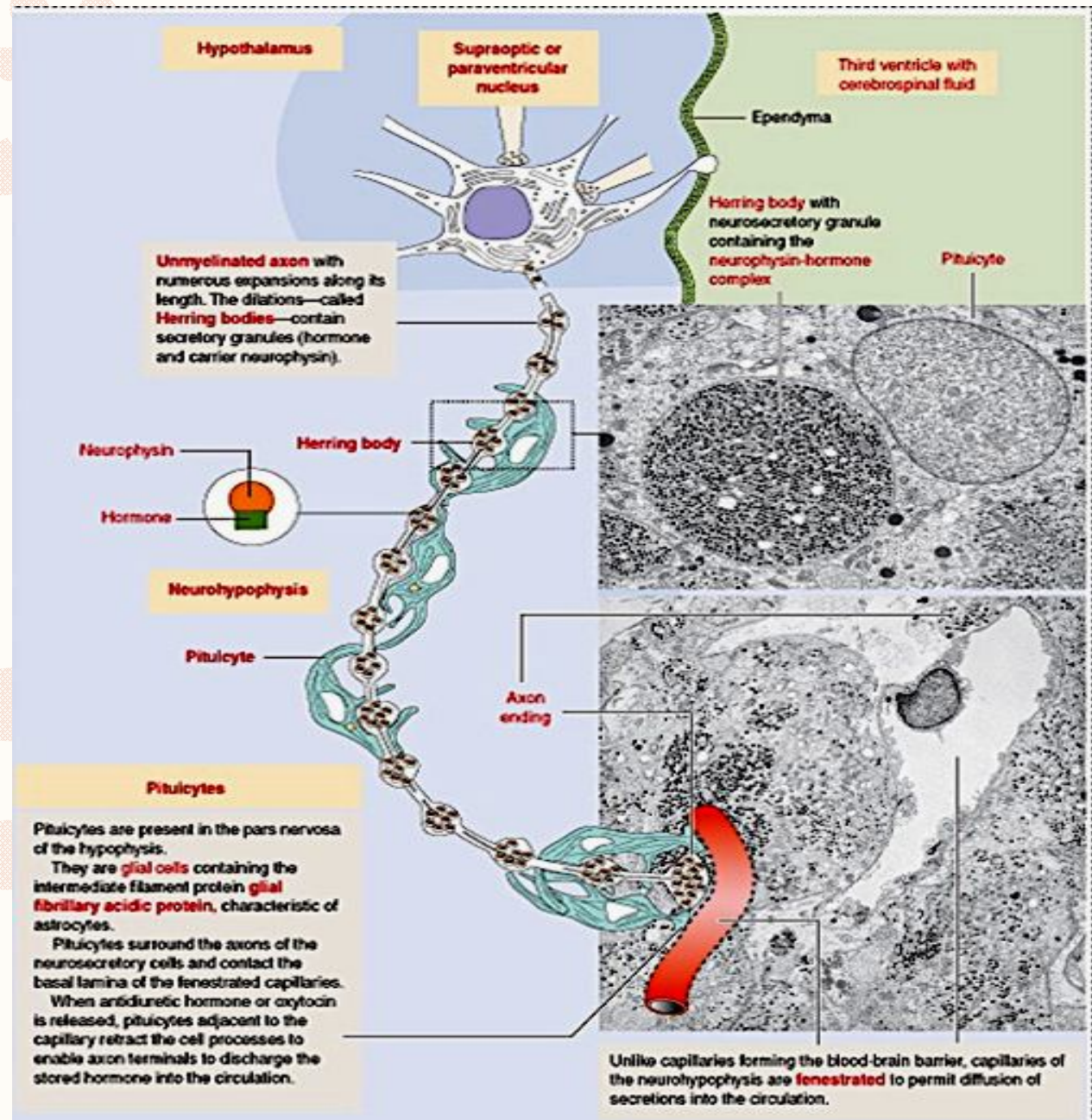
The hormones **antidiuretic hormone** (or **arginine vasopressin**) and **oxytocin** are synthesized in the neurons of the **supraoptic** and **paraventricular nuclei**, respectively.

The hormones are transported along the axons forming the **hypothalamic hypophyseal tract**, together with the carrier protein **neurophysin**, and are released at the axon terminals. The hormones enter **fenestrated capillaries** derived from the inferior hypophyseal artery.



## Structure and function of the neuroendocrine cell

- ❖ Supraoptic & paraventricular nucleus in Hypothalamus secrete ADH & oxytocin & neurophysin (hormone transporter)
- ❖ Pituicyte (glial cells)
- ❖ Herring body = secretory granules in axonal end

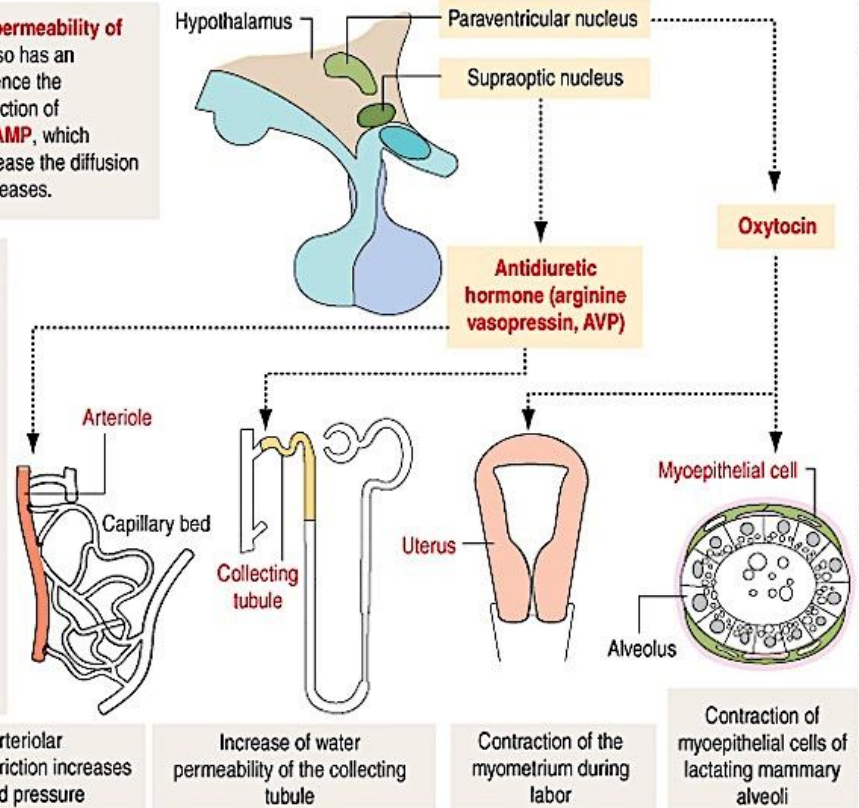


## Antidiuretic hormone and oxytocin

**Antidiuretic hormone** increases the **permeability of the collecting tubule to water** and also has an **arteriolar vasoconstrictive** action (hence the alternative name **vasopressin**). The action of antidiuretic hormone is mediated by **cAMP**, which stimulates membrane channels to increase the diffusion of water. Consequently, urine flow decreases.

**Oxytocin** acts on **uterine contraction** and **milk release**.

Estrogens increase the response of the myometrium to oxytocin; progesterone decreases the response. During lactation, oxytocin release is mediated by a neurohumoral reflex triggered by suckling. Suckling activates sensory receptors in the nipple and areola. Sensory fibers are linked to the hypothalamic neurons producing oxytocin. When the stimulus arrives, an action potential transmitted along the axons of the paraventricular neurons extending into the pars nervosa causes the release of oxytocin into the blood.



**TABLE 20-3**

### Hormones of the posterior pituitary.

Hormone	Function
Vasopressin/antidiuretic hormone (ADH)	Increases water permeability of renal collecting ducts
Oxytocin	Stimulates contraction of mammary gland myoepithelial cells and uterine smooth muscle

# Neuro endocrine & Endocrine

Hypophysis gland

***Pineal body***

Pancreatic islets

Thyroid gland

Parathyroid gland

Suprarenal gland



## *The pineal body:(epiphysis cerebri / third eye)*

Pine cone - shaped organ

From neuroectoderm in post. Wall of 3th ventricle

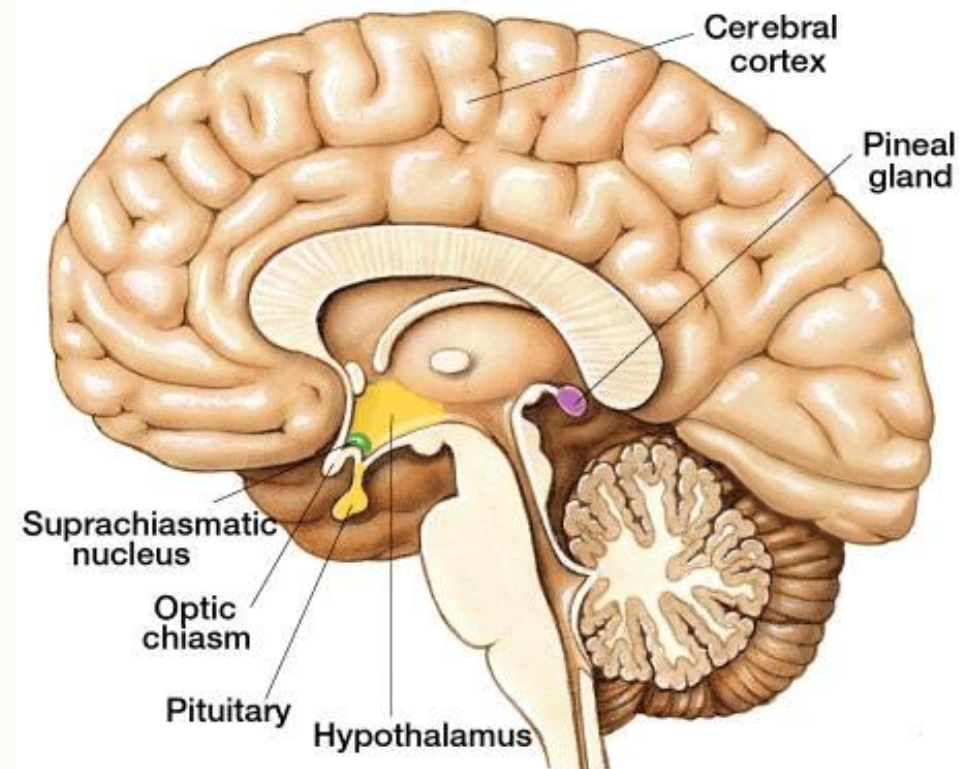
Secretory cell = pinealocytes / basophilic cytoplasm/  
many mitochondria / secretory vesicles / long cytoplasmic processes /  
dilation at the end / near capillaries /secretion of melatonin / glial cells /  
modifies astrocyte / brain sand (calcium + magnesium)

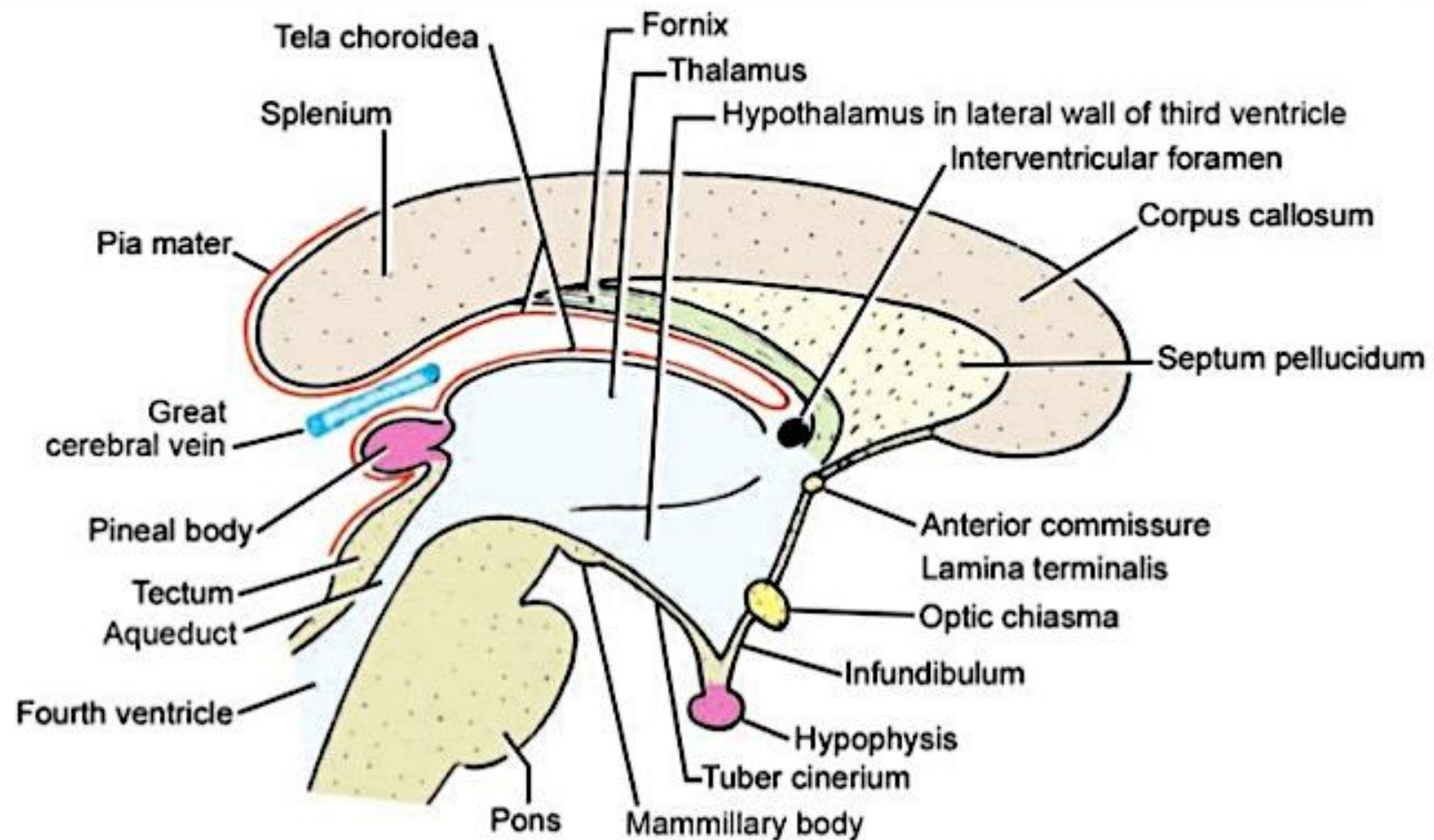
Pineal body correlations:

Sup. = splenium of corpus callosum

Inf. = tectum of midbrain

Ant. = thalamus





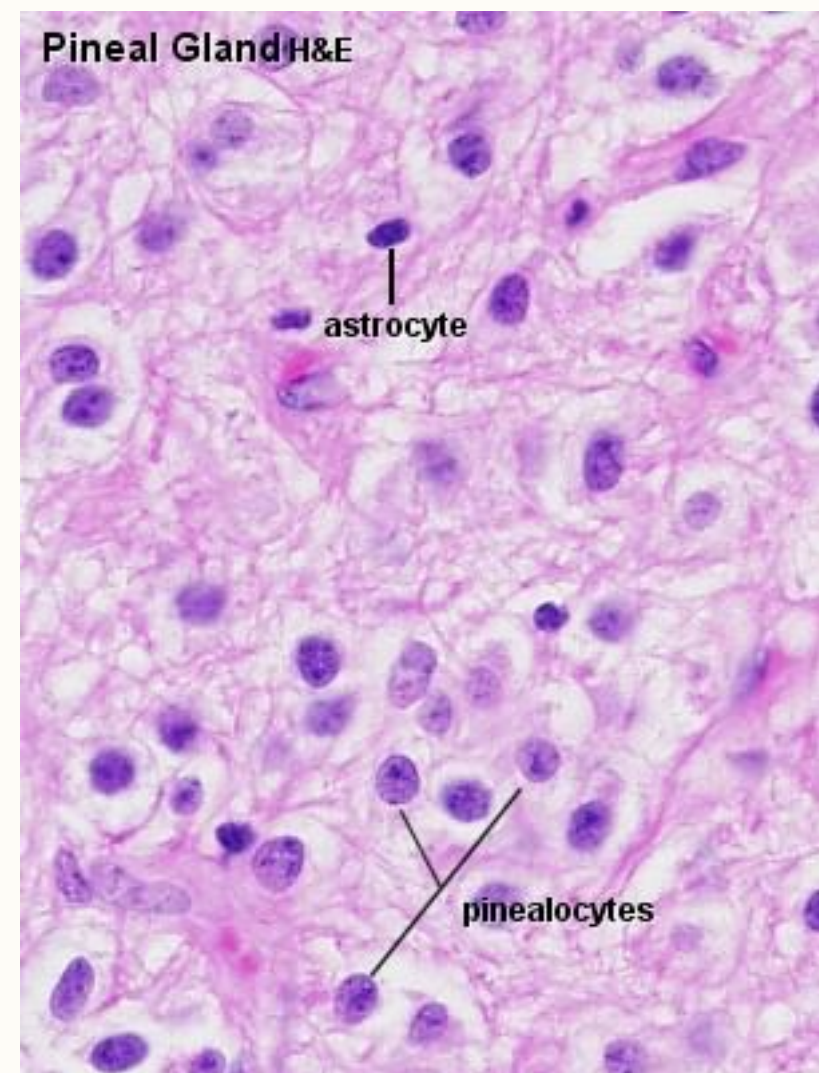
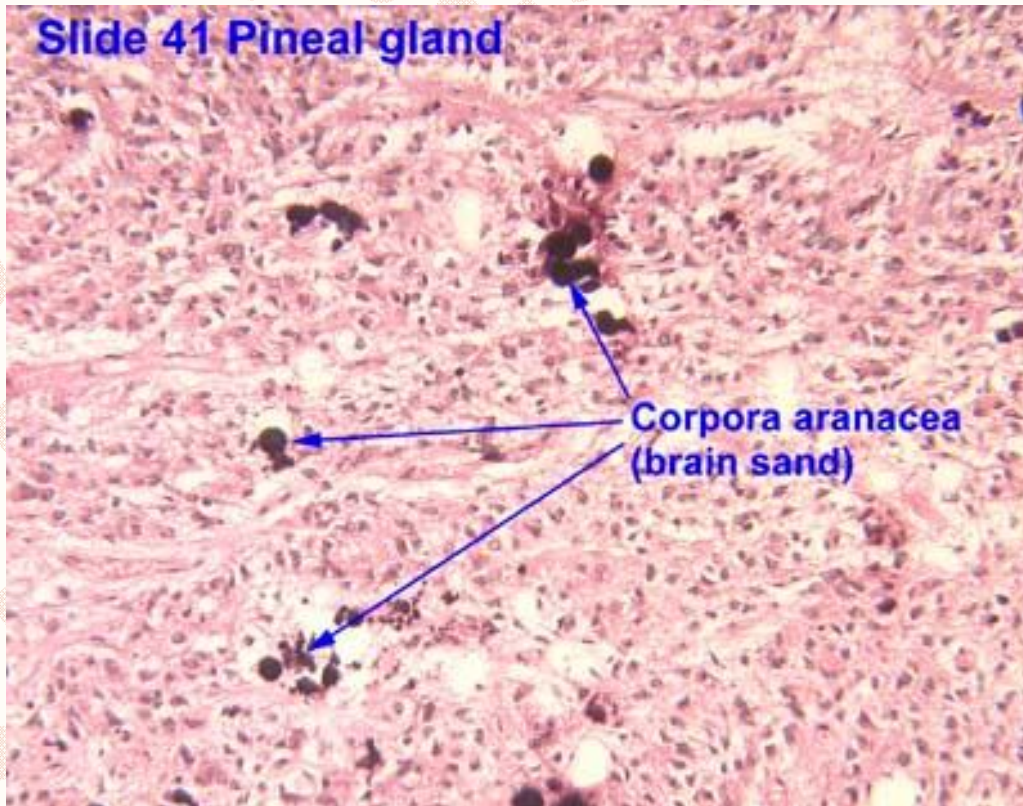
**46.6:** Diagram to show the position of the hypophysis cerebri and of the pineal body relative to the third ventricle of the brain



## CLINICAL CORRELATION

1. Tumours of the pineal gland can press on the tectum of the midbrain.
2. This can damage the oculomotor nucleus and can thus lead to paralysis of the oculomotor nerve.
3. Pressure of the tumour may obstruct the aqueduct and cause hydrocephalus.



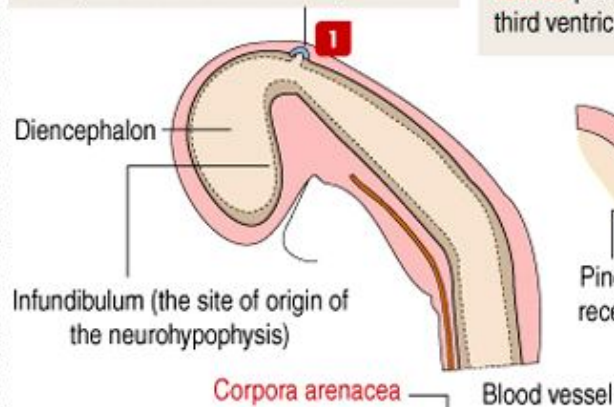




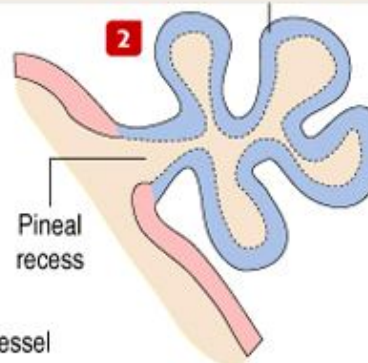
## Development of the pineal gland

Dorsal out pouching of diencephalon : 7 week  
Pineal recess

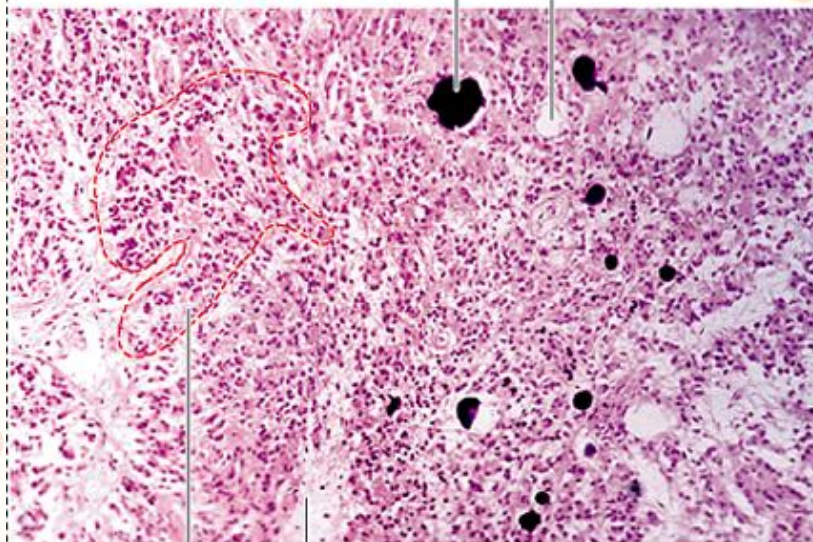
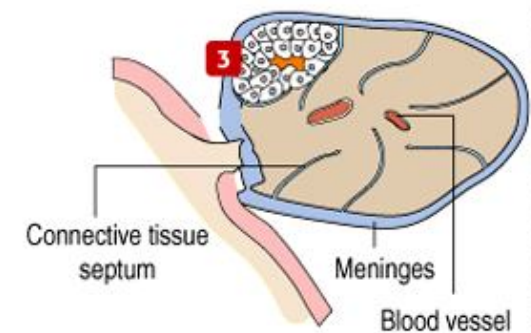
**1** A dorsal diverticulum, an outpocketing of the diencephalon, initiates the formation of the pineal gland during the 10th week of development.



**2** The wall of the vesicular evagination thickens. The lumen is occluded, except at the base of the outpocketing, where the **pineal recess** persists and communicates with the third ventricle in the adult.



**3** The pineal gland becomes a compact structure containing two cell types derived from the primordial neuroepithelial cells: (1) **pinealocytes**; and (2) **glial-like interstitial cells**. Meninges envelop and invade the developing pineal gland, forming **connective tissue septa**.



Cluster of pinealocytes      Connective tissue septum

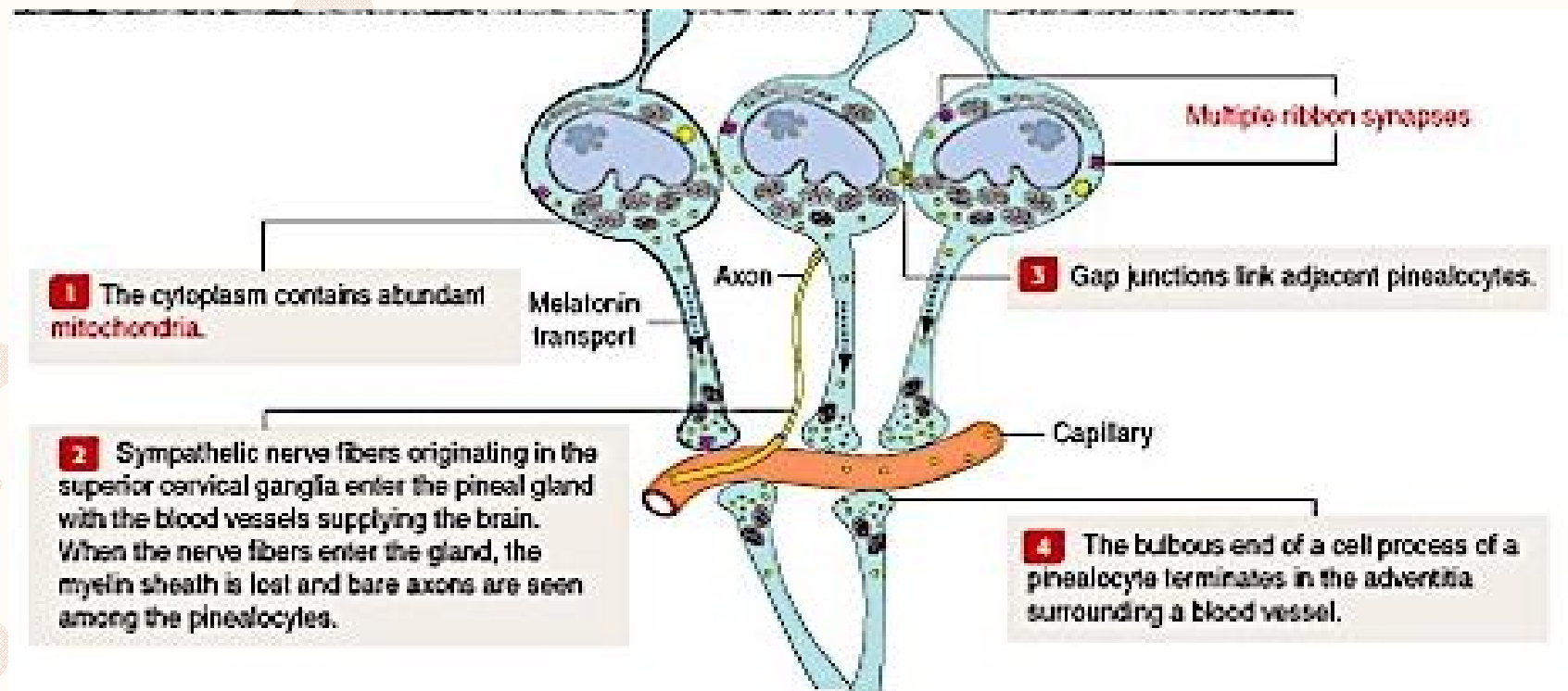
### The pineal gland

The pineal gland (so-called because it resembles a pine cone) consists of **melatonin-secreting pinealocytes** arranged in solid cords enclosed by processes derived from the **glial-like interstitial cells**. Cell processes projecting from the pinealocytes surround the blood vessels.

A typical feature of the histology of the pineal gland is the presence of calcium deposits, called **corpora arenacea** ("brain sand"), found in the extracellular space.

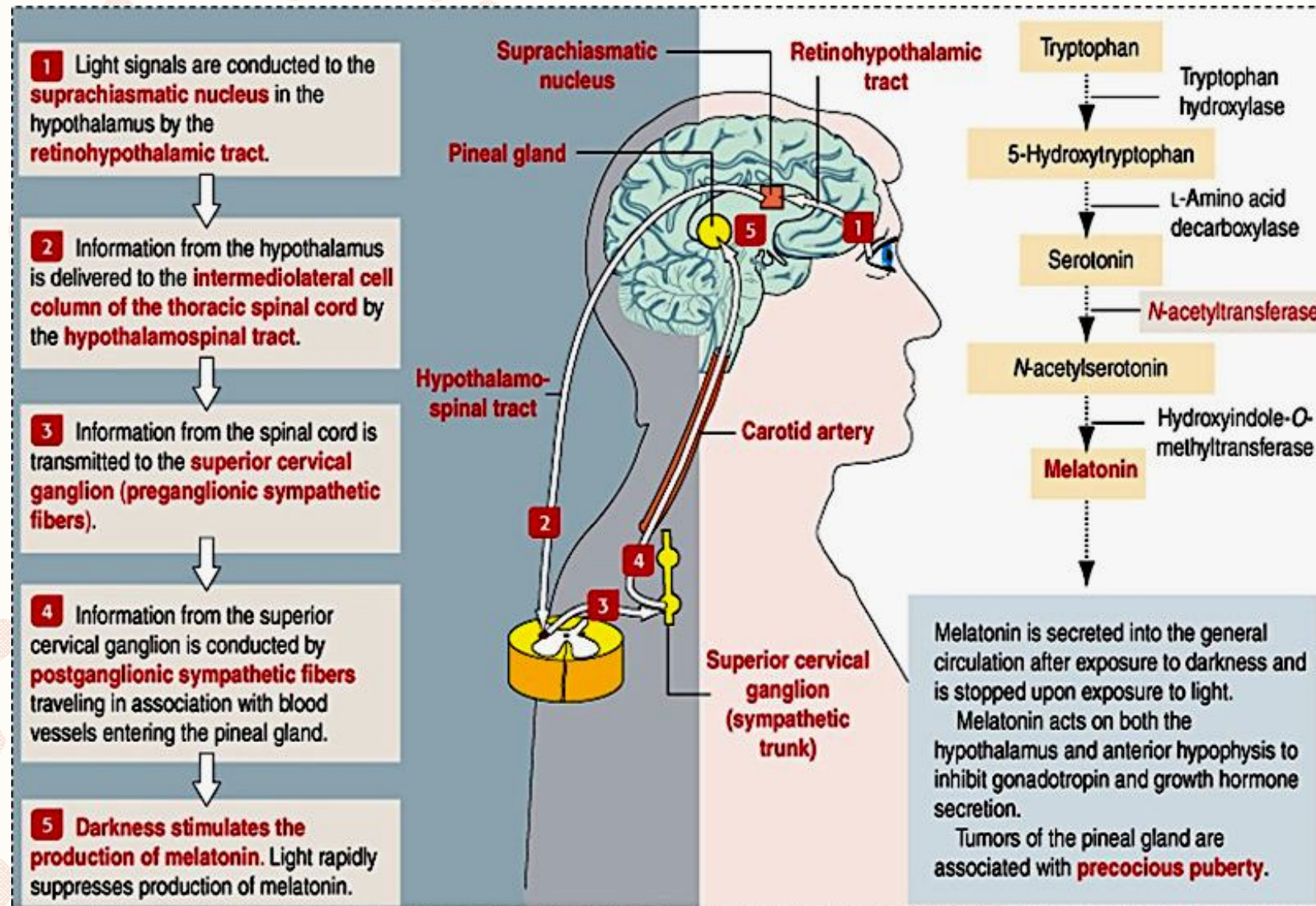
The nerve input to the pineal gland is from the **postganglionic sympathetic nerve fibers** derived from the **superior cervical ganglion**.

## Structure of the pinealocytes





## Synthesis and secretion of melatonin



# Neuro endocrine & Endocrine

Hypophysis gland

Pineal body

***Pancreatic islets***

Thyroid gland

Parathyroid gland

Suprarenal gland

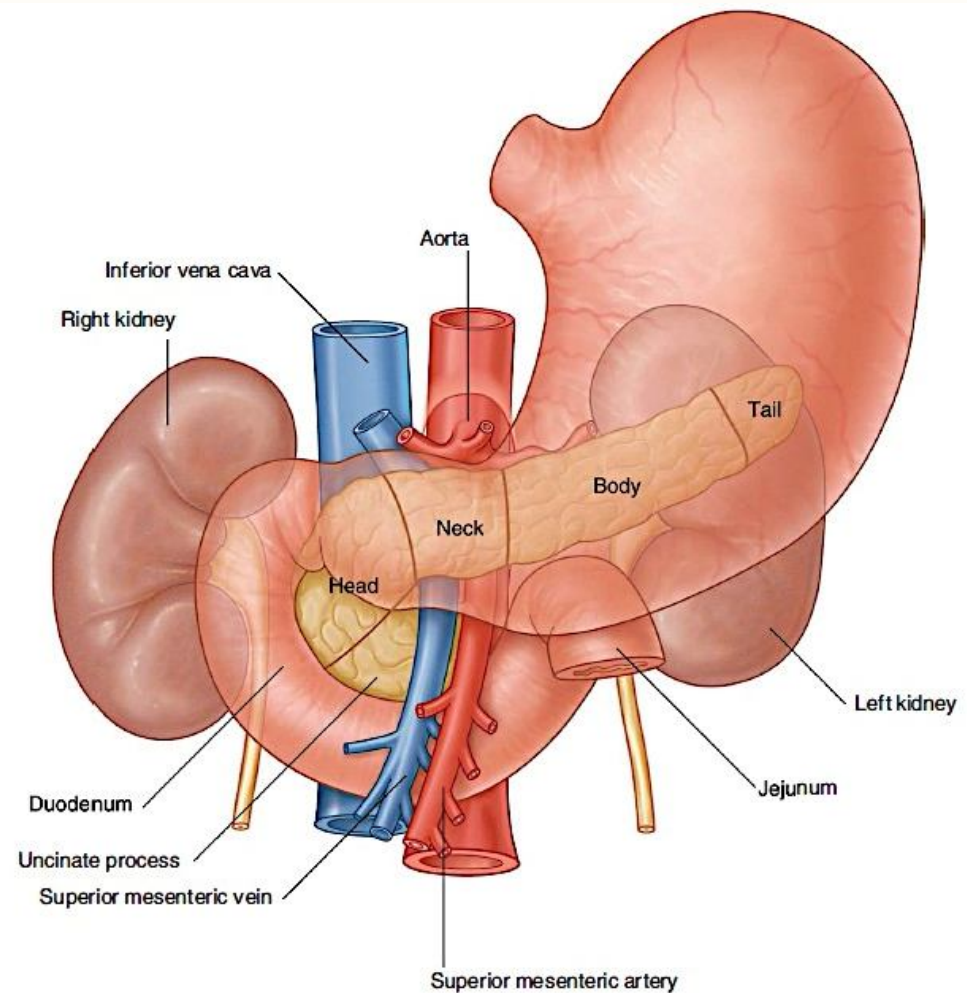
## ***Pancreas:***

The pancreas lies mostly posterior to the stomach

It extends across the posterior abdominal wall from the duodenum, on the right, to the spleen, on the left

consists of a head, uncinate process, neck, body, and tail

retroperitoneal except for a small part of its tail



**Fig. 4.98** Pancreas.



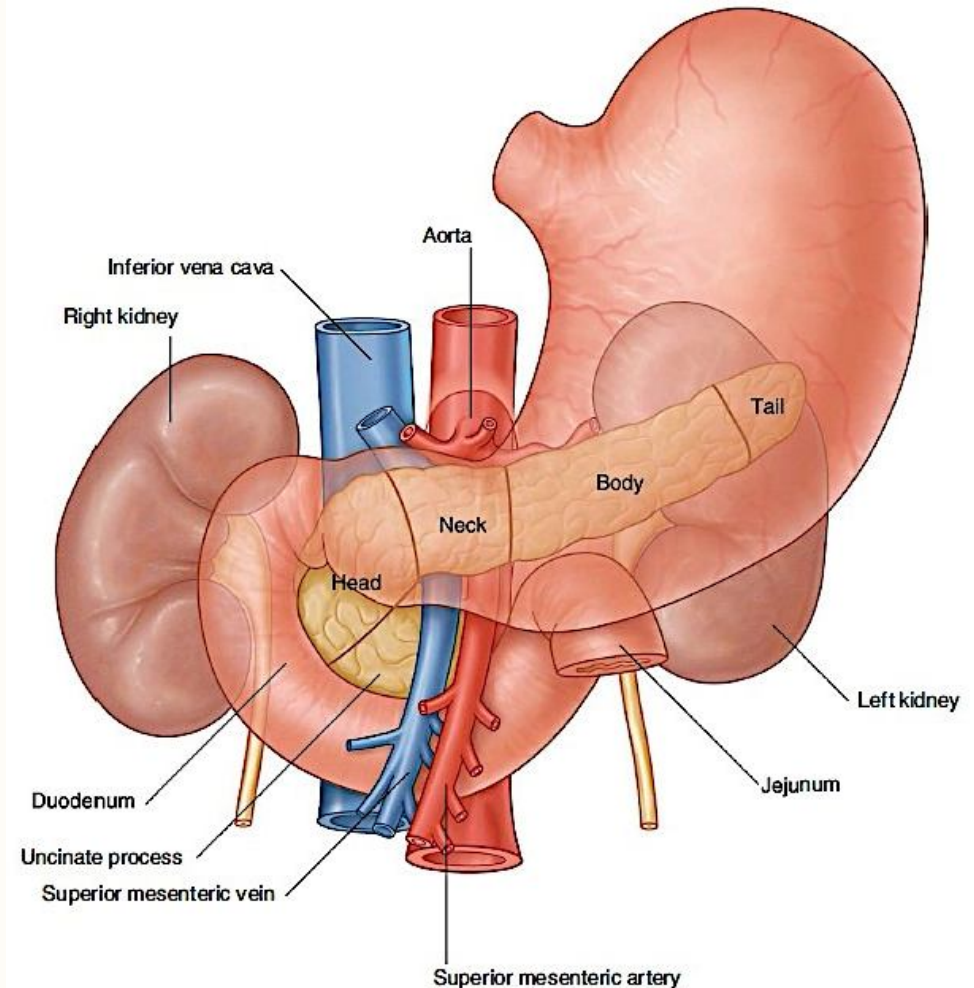
The **head** of the pancreas lies within the C-shaped concavity of the duodenum.

Projecting from the lower part of the head is the **uncinate process**, which passes posterior to the **superior mesenteric vessels**.

The **neck** of the pancreas is anterior to the superior mesenteric vessels. Posterior to the neck of the pancreas, the superior mesenteric and splenic veins join to form the portal vein.

The **body** of the pancreas is elongate and extends from the neck to the tail of the pancreas.

The **tail** of the pancreas passes between layers of the splenorenal ligament.



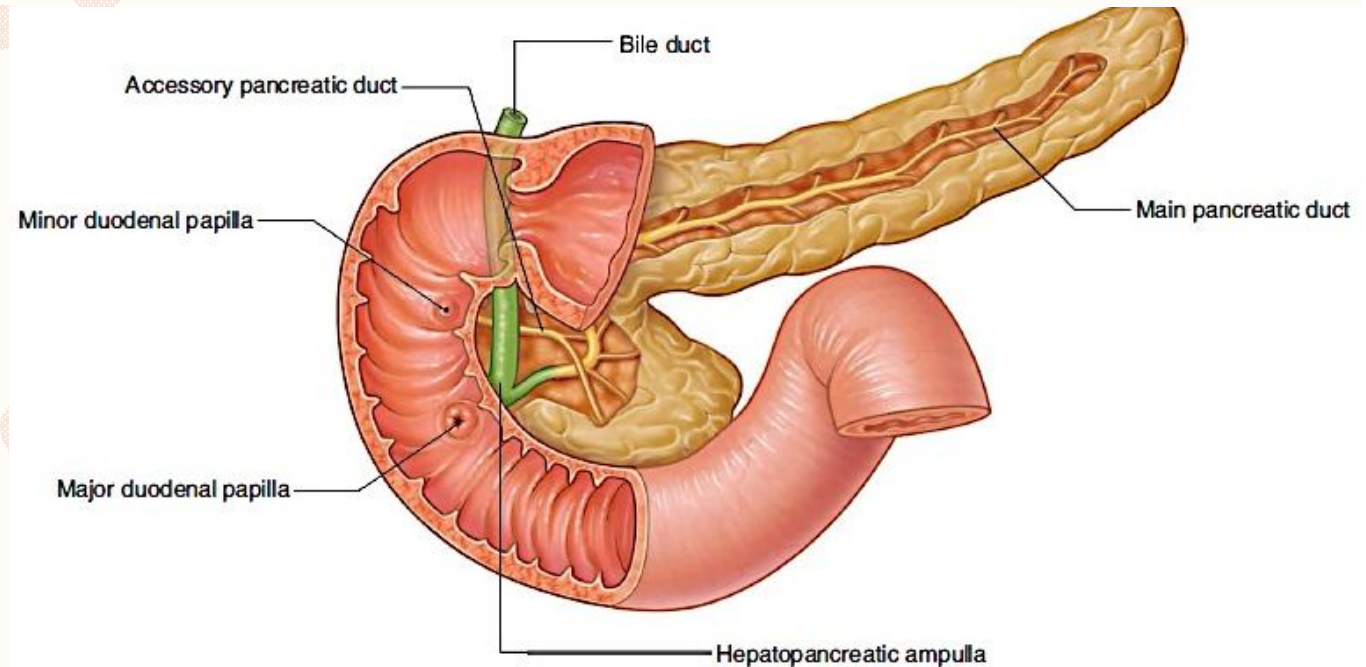
## The pancreatic duct:

In the tail of the pancreas  
In the body at the right  
In the head turns inferiorly

In the lower part of the head joins the bile duct / the hepatopancreatic ampulla (ampulla of Vater) / the descending (second) part of the duodenum at the major duodenal papilla

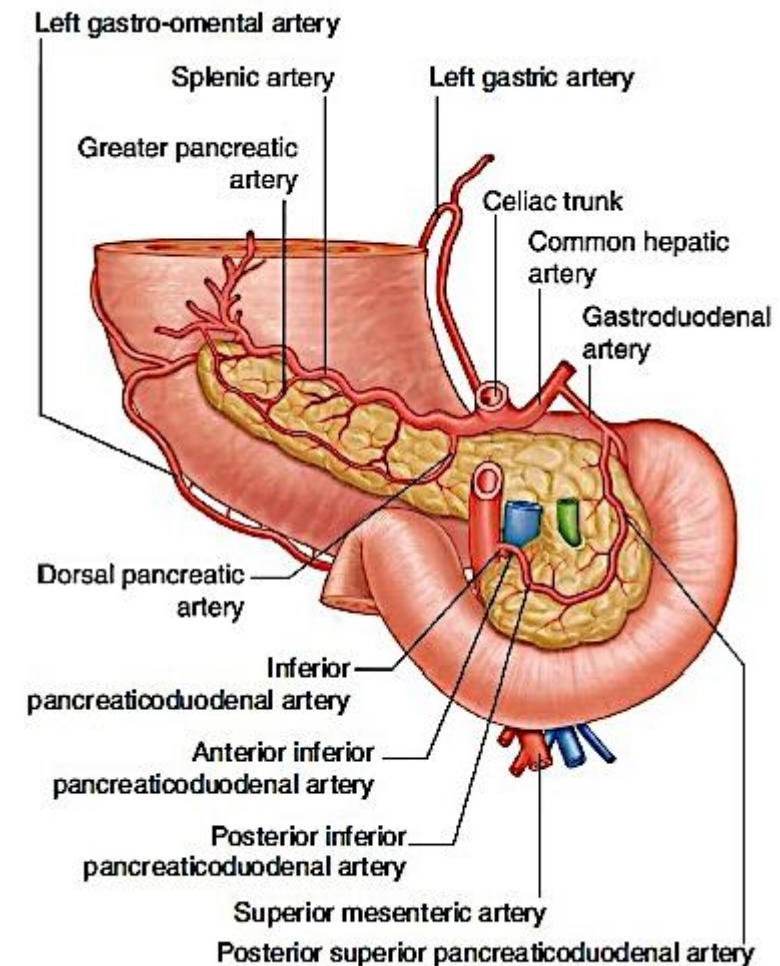
sphincter of ampulla (sphincter of Oddi) / smooth muscles.

The accessory duct empties into the minor duodenal papilla.



### ***the pancreas artery :***

- **gastroduodenal artery** from the common hepatic artery (a branch of the celiac trunk)
- **anterior superior pancreaticoduodenal artery** from the gastroduodenal artery
- **posterior superior pancreaticoduodenal artery** from the gastroduodenal artery
- **dorsal pancreatic artery** from the inferior pancreatic artery (a branch of the splenic artery)
- **great pancreatic artery** from the inferior pancreatic artery (a branch of the splenic artery)
- **anterior inferior pancreaticoduodenal artery** from the inferior pancreaticoduodenal artery (a branch of the superior mesenteric artery)
- **posterior inferior pancreaticoduodenal artery** from the inferior pancreaticoduodenal artery (a branch of the superior mesenteric artery)



**Fig. 4.101** Arterial supply to the pancreas. Posterior view.



## In the clinic

### Pancreatic cancer

Pancreatic cancer accounts for a significant number of deaths and is often referred to as the "silent killer."

Malignant tumors of the pancreas may occur anywhere within the pancreas but are most frequent within the head and the neck. There are a number of nonspecific findings in patients with pancreatic cancer, including upper abdominal pain, loss of appetite, and weight loss.

Depending on the exact site of the cancer, obstruction of the bile duct may occur, which can produce obstructive jaundice. Although surgery is indicated in patients where there is a possibility of cure, most detected cancers have typically spread locally, invading the portal vein and superior mesenteric vessels, and may extend into the porta hepatis. Lymph node spread also is common and these factors would preclude curative surgery.

Given the position of the pancreas, a surgical resection is a complex procedure involving resection of the region of pancreatic tumor usually with part of the duodenum, necessitating a complex bypass procedure.

## Pancreas:

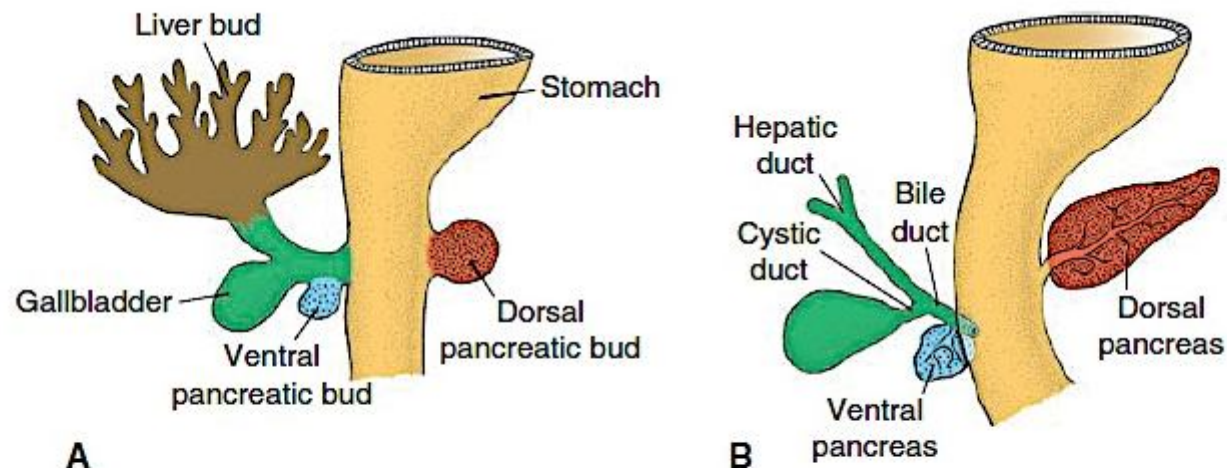
From endodermal lining of duodenum

Dorsal bud : in dorsal mesentery

Ventral bud : close to the bile duct

Rotation of duodenum to right and become C shape

Ventral bud moves dorsally and lie below and behind of dorsal bud



**Figure 15.19** Stages in development of the pancreas. **A.** 30 days (approximately 5 mm). **B.** 35 days (approximately 7 mm). Initially, the ventral pancreatic bud lies close to the liver bud, but later, it moves posteriorly around the duodenum toward the dorsal pancreatic bud.

Fusion dorsal and ventral bud

Ventral bud : uncinete process & inf. Part of head

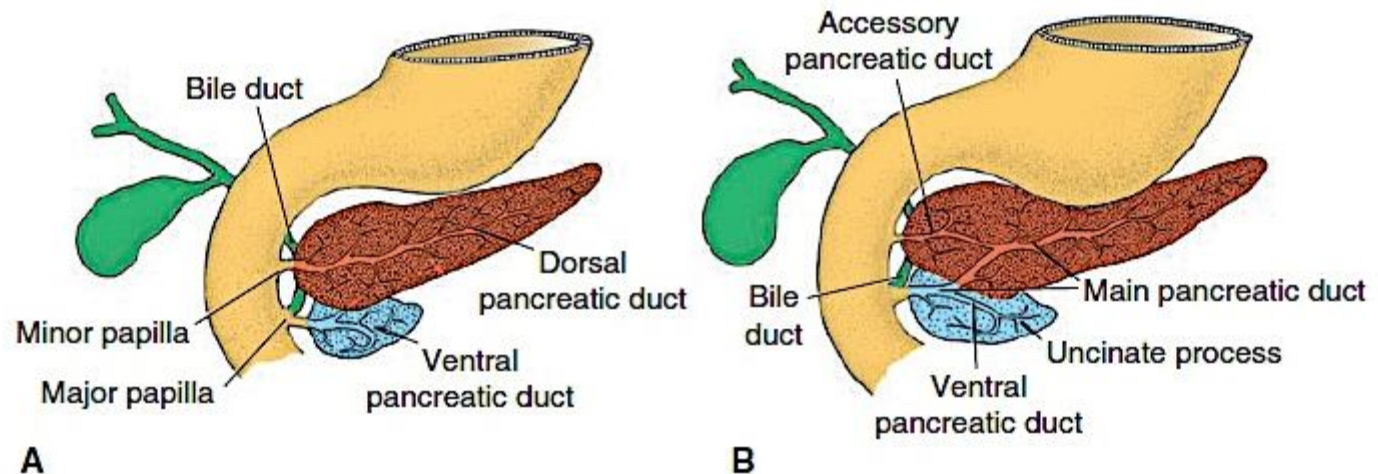
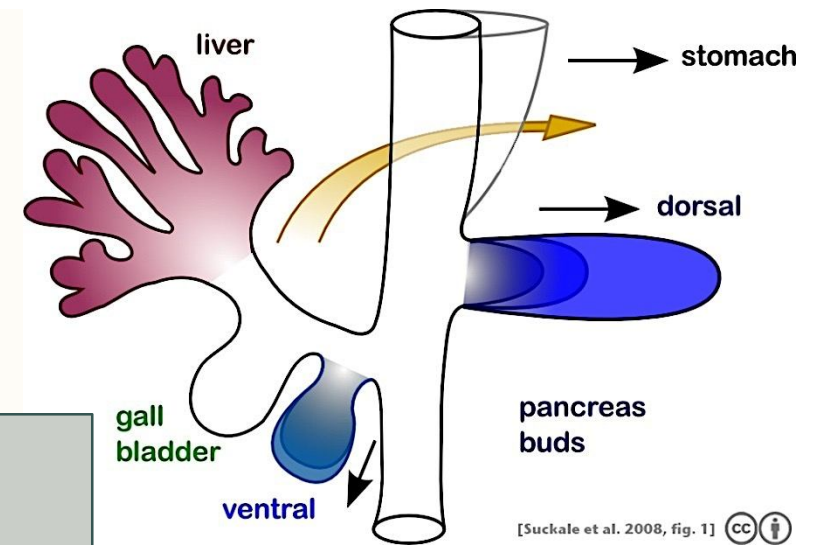
Dorsal bud : the remain of gland

The main pancreatic duct of wirsung : (papilla major)

Is formed by distal part of dorsal bud & entire ventral bud

The accessory duct of santorini: (papilla minor)

Is formed by proximal part of dorsal bud





## ***Islet of pancreas (langerhans):***

In 3 month

From parenchymatus tissue of pancreas

Insulin secretion : 5 month

Glucagon & somatostatin secreting cells : from parenchymal cell

Visceral mesoderm : connective tissue

## ***Molecular regulation:***

Dorsal bud:

Notochord & endothelium of dorsal aorta : FGF2 / ACTIVIN +  $\rightarrow$  SHH – in gut

Ventral bud:

Visceral mesoderm

***Islet of pancreas (langerhans):***

***Expression of PAX4 & PAX6 in cells =  $\beta$  cell /  $\delta$  cell /  $\gamma$  cell***

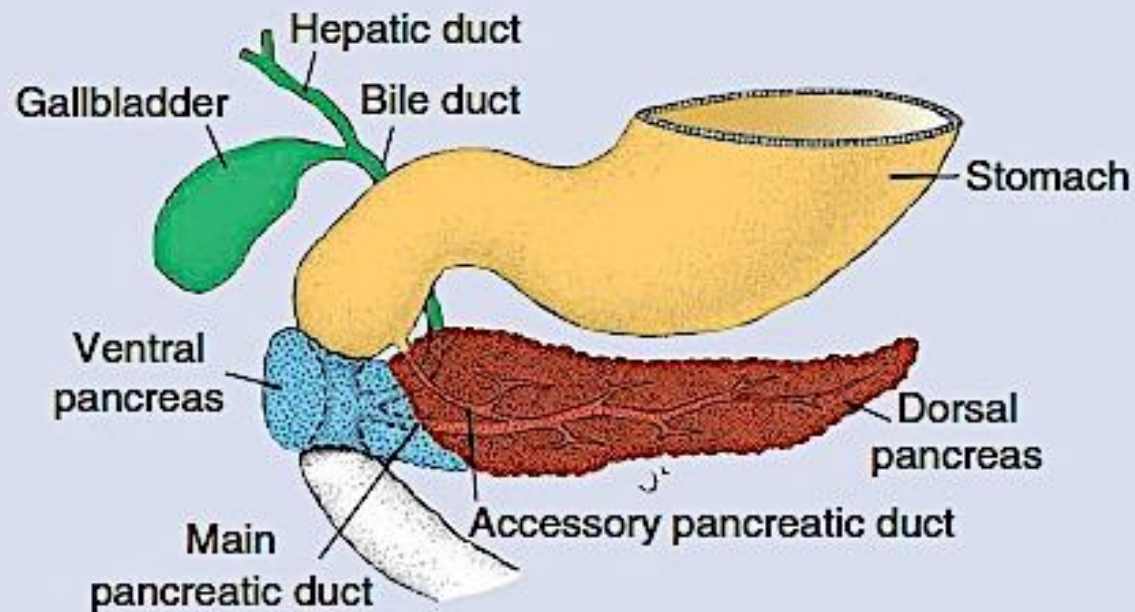
***Expression of PAX6 in cells =  $\alpha$  cell***

## Annular pancreas:

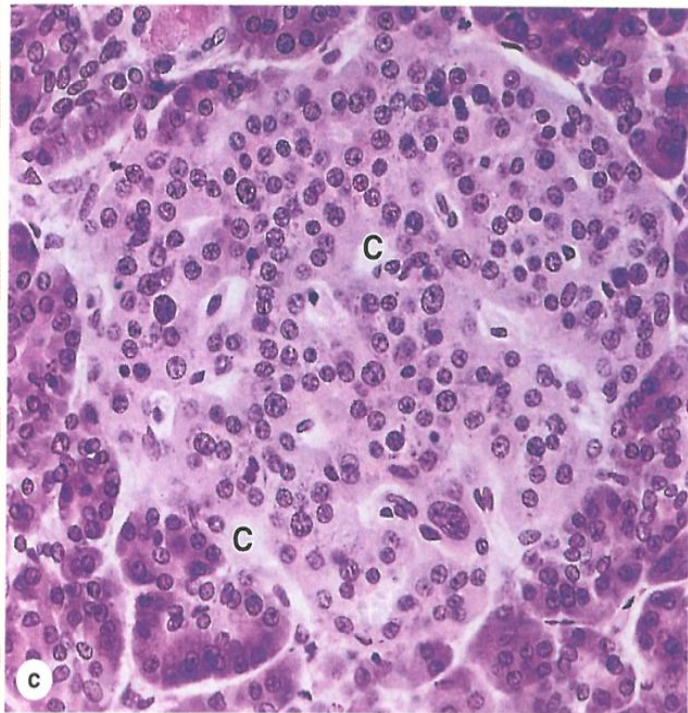
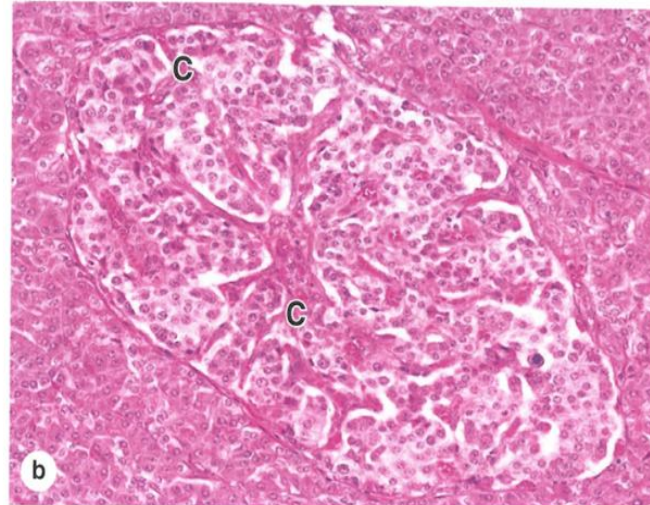
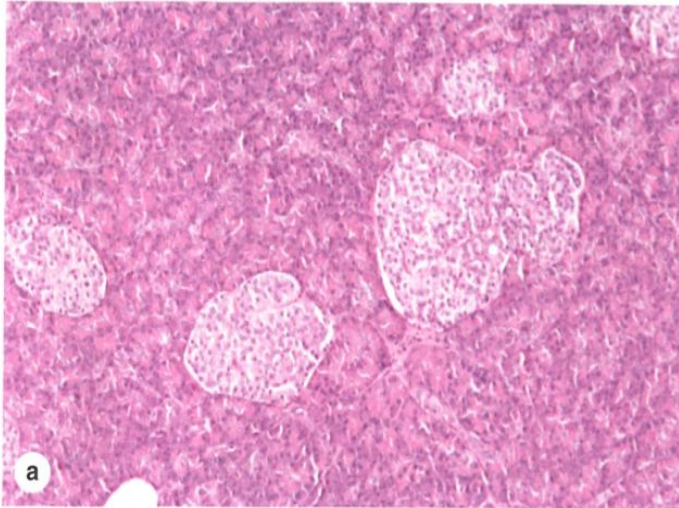
The right portion migrate along normal its route but the left migration in the opposite direction

## Accessory pancreatic tissue :

In mucosa of stomach & Meckle 's diverticulum



**Figure 15.23** Annular pancreas. The ventral pancreas splits and forms a ring around the duodenum, resulting in duodenal stenosis.



### ***Pancreatic islets:***

Compact ovoid mass in acinar tissue

Diameter = 100-200  $\mu m$

The cells = several hundred

1 million islets

Mostly in the tail

Reticular capsule surround each islet

More lightly stained than acinar

Routine stains = Trichrome stains

Cells of islet = acidophilic / basophilic

Acinar cells arranged in cord

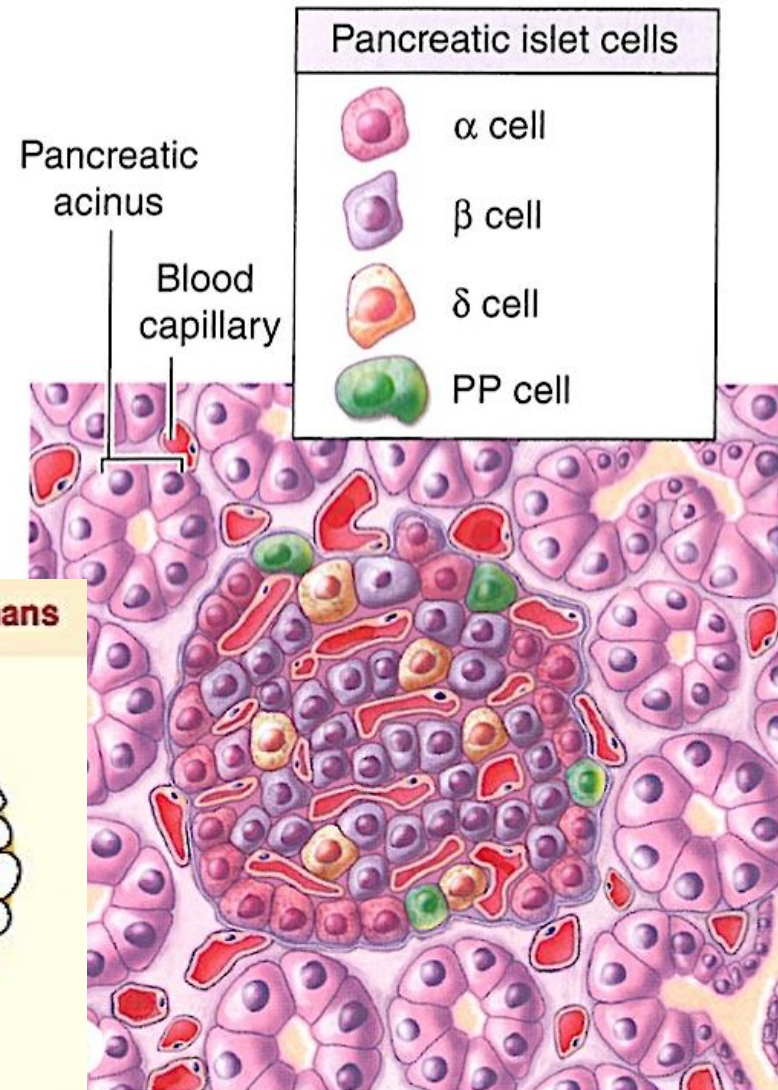
Fenestrate capillary



The major islet cells are most easily identified and studied by immunohistochemistry:

- $\alpha$  or **A cells** secrete primarily **glucagon** and are usually located peripherally.
- $\beta$  or **B cells** produce **insulin** (L. *insula*, island), are the most numerous, and are located centrally.
- $\delta$  or **D cells**, secreting **somatostatin**, are scattered and much less abundant.

A minor fourth cell type, more common in islets located within the head of the pancreas, are **PP cells**, which secrete **pancreatic polypeptide**.



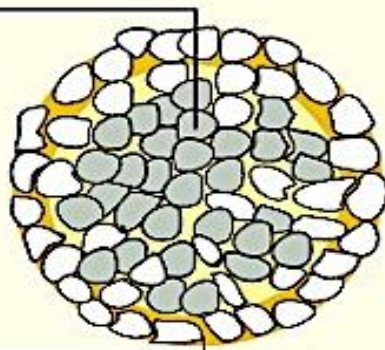
### Topographic distribution of endocrine cells in the islet of Langerhans

#### Core

Insulin-producing B cells predominate in the core.

#### Mantle

Other cells—A, D, and F cells—are present in the mantle.



**TABLE 20-4****Major cell types and hormones of pancreatic islets.**

Cell Type	Quantity (%)	Hormone Produced	Hormone Structure and Size	Hormone Function
$\alpha$	~20	Glucagon	Polypeptide; 3500 Da	Acts on several tissues to make energy stored in glycogen and fat available through glycogenolysis and lipolysis; increases blood glucose content
$\beta$	~70	Insulin	Dimer of $\alpha$ and $\beta$ chains with S-S bridges; 5700-6000 Da	Acts on several tissues to cause entry of glucose into cells and promotes decrease of blood glucose content
$\delta$ or D	5-10	Somatostatin	Polypeptide; 1650 Da	Inhibits release of other islet cell hormones through local paracrine action; inhibits release of GH and TSH in anterior pituitary and HCl secretion by gastric parietal cells
PP	Rare	Pancreatic polypeptide	Polypeptide; 4200 Da	Stimulates activity of gastric chief cells; inhibits bile secretion, pancreatic enzyme and bicarbonate secretion, and intestinal motility



1

Sympathetic and parasympathetic nerve endings are closely associated with about 10% of  $\alpha$ ,  $\beta$ , and  $\delta$  cells and can also function as part of the control system for insulin and glucagon secretion. Gap junctions transfer the autonomic neural stimulus to the other cells. Sympathetic fibers increase glucagon release and inhibit insulin release; parasympathetic fibers increase secretion of both glucagon and insulin.



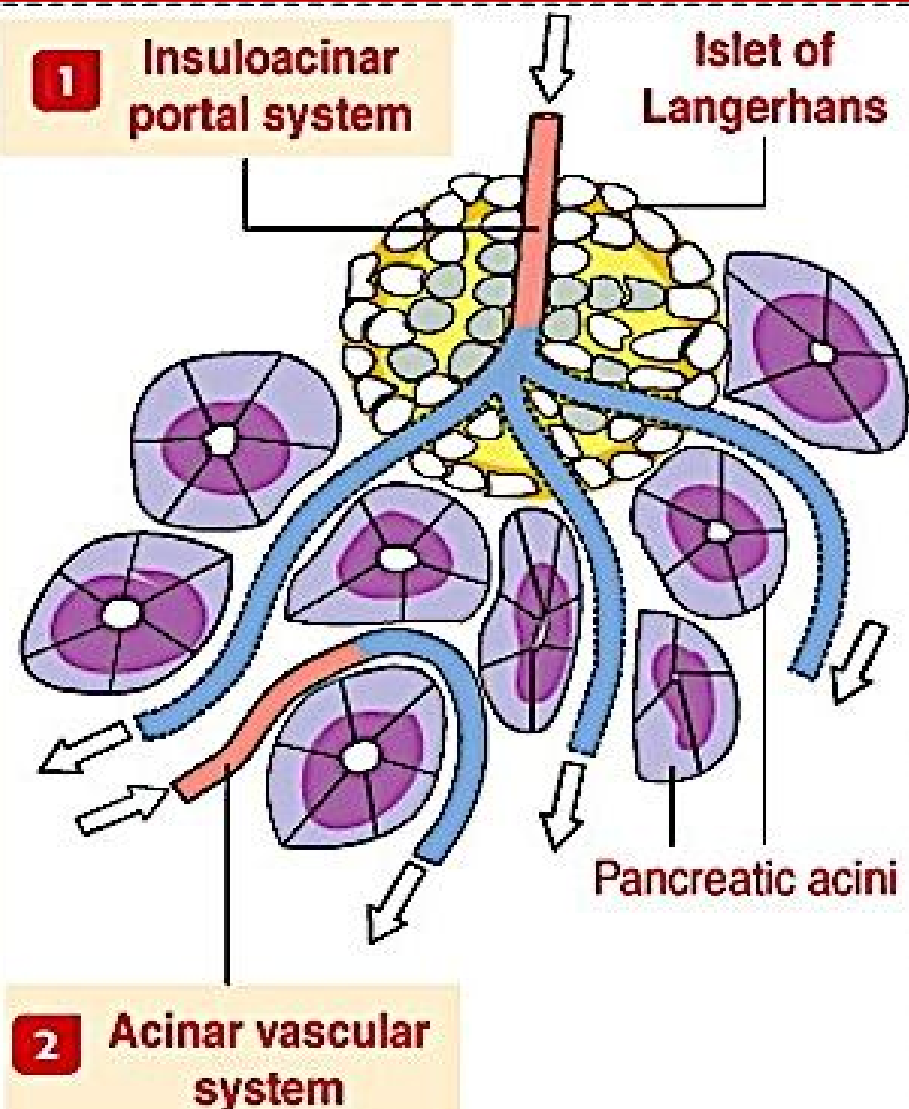
## Blood supply to the islets of Langerhans and cell distribution

### Dual blood supply: Acinar and insuloacinar vascular systems

**1** Each islet of Langerhans is supplied by afferent arterioles, forming a network of capillaries lined by fenestrated endothelial cells. This network is called the **insuloacinar portal system**.

Capillaries leaving the islet supply blood to the pancreatic acini surrounding the islet. This vascular system enables a local action on the exocrine pancreas of hormones produced in the islet.

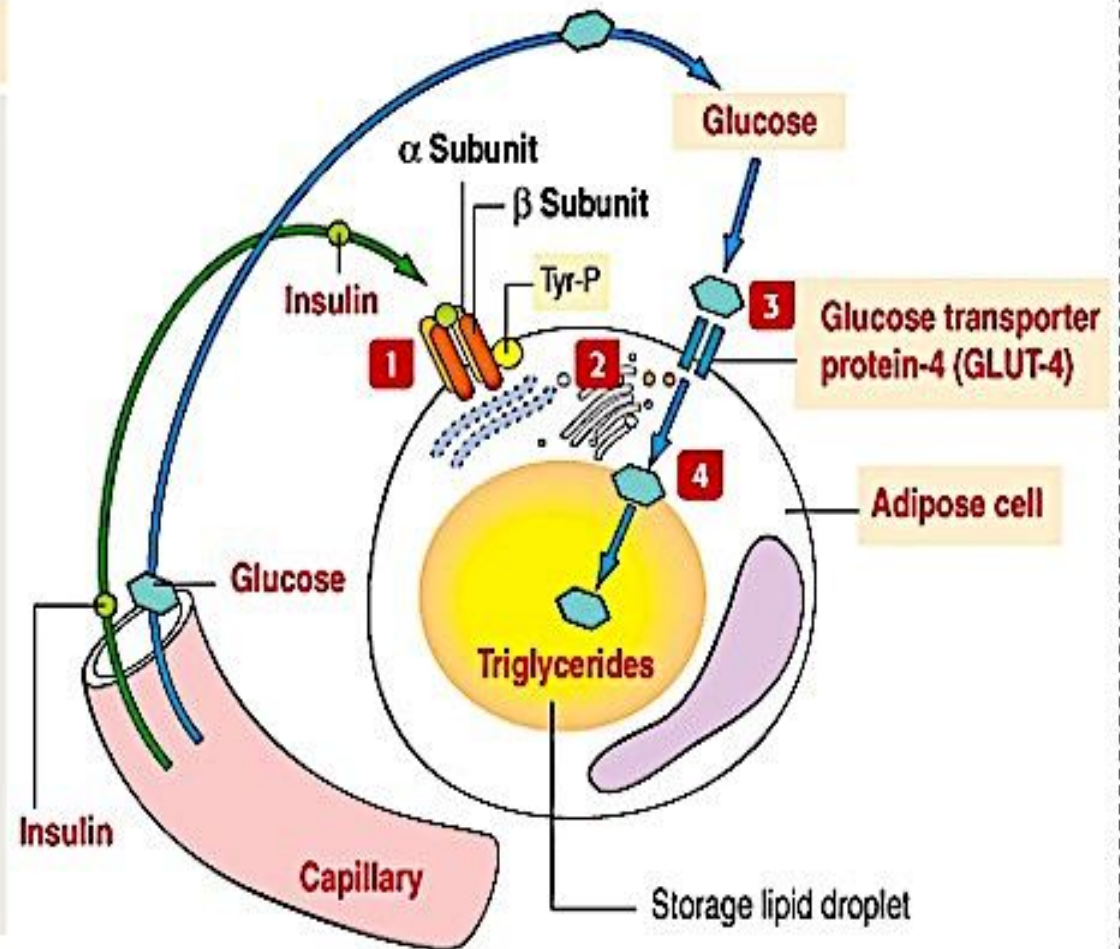
**2** An independent arterial system, the **acinar vascular system**, supplies the pancreatic acini.



## Adipose cell, lipid storage, and insulin

### Mechanism of action of insulin in an adipose cell

- 1** Insulin binds to the  $\alpha$  subunit of the insulin receptor and activates the autophosphorylation (**Tyr-P**) of the adjacent  $\beta$  subunit (a tyrosine kinase).
- 2** An activated insulin receptor stimulates DNA synthesis, protein synthesis, and the translocation of insulin-dependent **glucose transporter protein-4 (GLUT-4)** from the Golgi apparatus to the plasma membrane.
- 3** GLUT-4 translocation facilitates the cellular uptake of glucose.
- 4** This mechanism demonstrates that in diabetic individuals, a lack of insulin decreases the **utilization of glucose** in target cells.



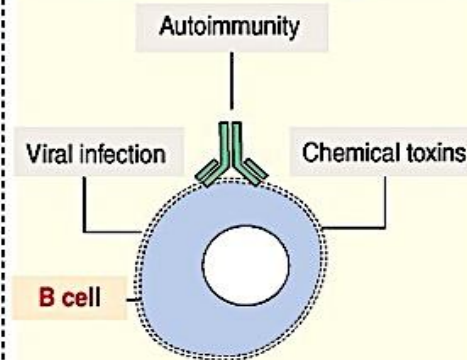


## >> MEDICAL APPLICATION

**Diabetes mellitus** is characterized by loss of the insulin effect and a subsequent failure of cells to take up glucose, leading to elevated blood sugar or **hyperglycemia**. **Type 1 diabetes** or **insulin-dependent diabetes mellitus (IDDM)** is caused by loss of the  $\beta$  cells from autoimmune destruction and is treated by regular injections of insulin. In **type 2 diabetes** or **non-insulin-dependent diabetes mellitus (NIDDM)**,  $\beta$  cells are present but fail to produce adequate levels of insulin in response to hyperglycemia and the peripheral target cells “resist” or no longer respond to the hormone. Type 2 diabetes commonly occurs with obesity, and poorly understood, multifactorial genetic components are also important in this disease’s onset.

### Diabetes mellitus: Clinical forms

#### Type 1 (insulin-dependent diabetes mellitus, IDDM)



**Lack of insulin** because of a destruction of B cells

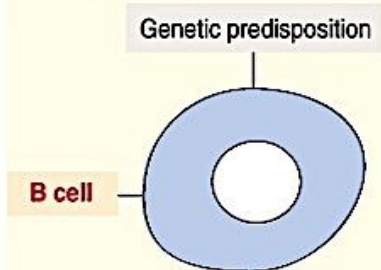
Individuals with IDDM require exogenous insulin to maintain life because there is no pancreatic insulin production.

B cells are damaged by the action of cytokines and autoantibodies produced by inflammatory cells.

Patients with IDDM are susceptible to ketosis.

Although 90% of the cases of IDDM begin in childhood (**juvenile diabetes**), it can develop at any time of life.

#### Type 2 (non-insulin-dependent diabetes mellitus, NIDDM)



**Insufficient insulin secretion** relative to glucose levels.

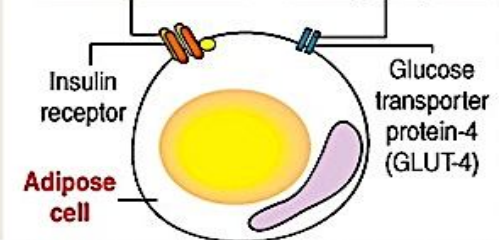
Individuals with NIDDM do not need exogenous insulin to maintain life.

A decrease in tissue response to insulin is often seen.

#### Insulin resistance of peripheral target tissues

Decrease in the number of insulin receptors

Deficient postreceptor signaling





## Clinical aspects of types 1 and 2 diabetes: Late complications

A major target of diabetes is the **vascular system**. **Atherosclerosis** of the aorta and large and medium-sized blood vessels leads to myocardial and brain infarctions and gangrene of the lower extremities. **Arteriosclerosis** (thickening of the wall of the arterioles) is associated with hypertension.

Myocardial infarct

Loss of B cells (islets of Langerhans)

Urinary bladder neuropathy (alteration in the autonomic nervous system)

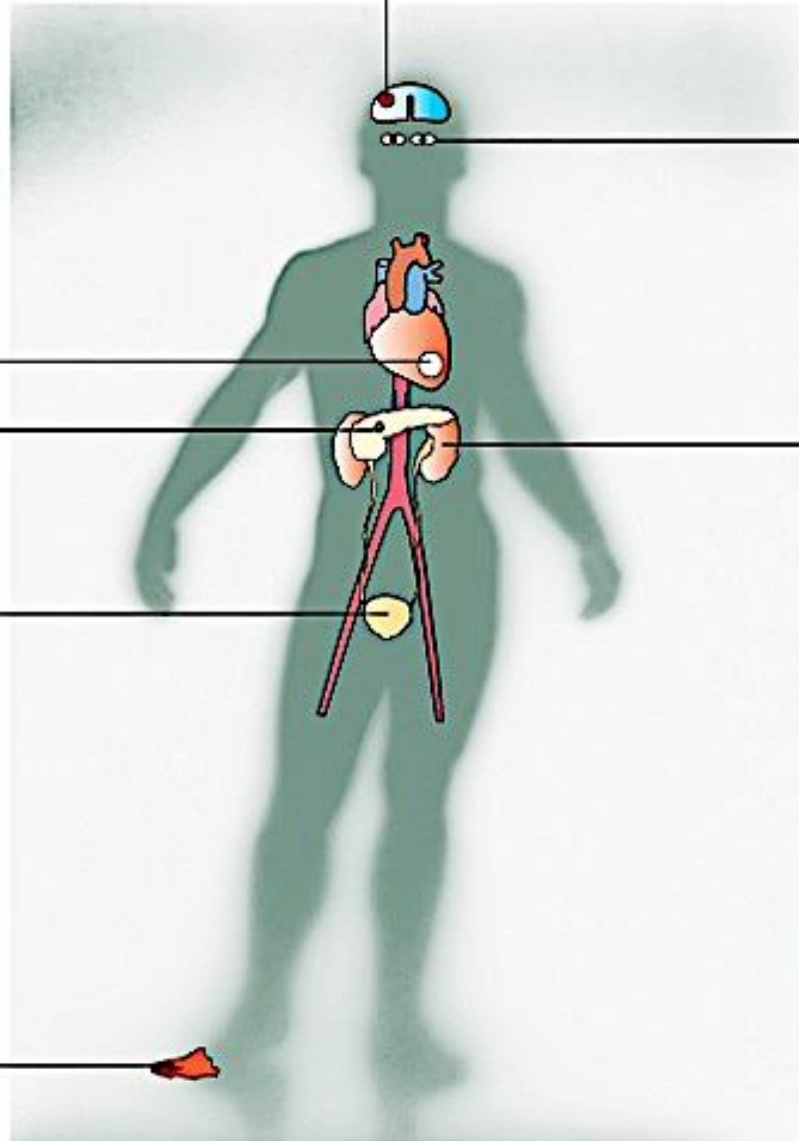
**Gangrene** caused by blood vessel obstruction as a consequence of vascular arteriosclerosis

Cerebral infarcts and hemorrhage

Eye complications of diabetes can cause total blindness. Damage of the retina (**retinopathy**), opacity of the lens (**cataract**), or **glaucoma** (impaired drainage of the aqueous humor) is frequently observed.

**Glomerulosclerosis**, **arteriosclerosis**, and **pyelonephritis** are frequently seen kidney diseases in diabetic patients. The most significant damage to the kidney is the **diffuse thickening of the basal lamina of the glomerular capillaries and proliferation of mesangial cells**.

This glomerular change is known as the **Kimmelstiel-Wilson lesion**.



# Neuro endocrine & Endocrine

Hypophysis gland

Pineal body

Pancreatic islets

---

***Thyroid gland***

Parathyroid gland

Suprarenal gland

# Thyroid gland

25 gram

Located in ant. Part of neck

Between C5 – T1

Have Two lobes & Isthmus

**Apex** = oblique line of thyroid cartilage

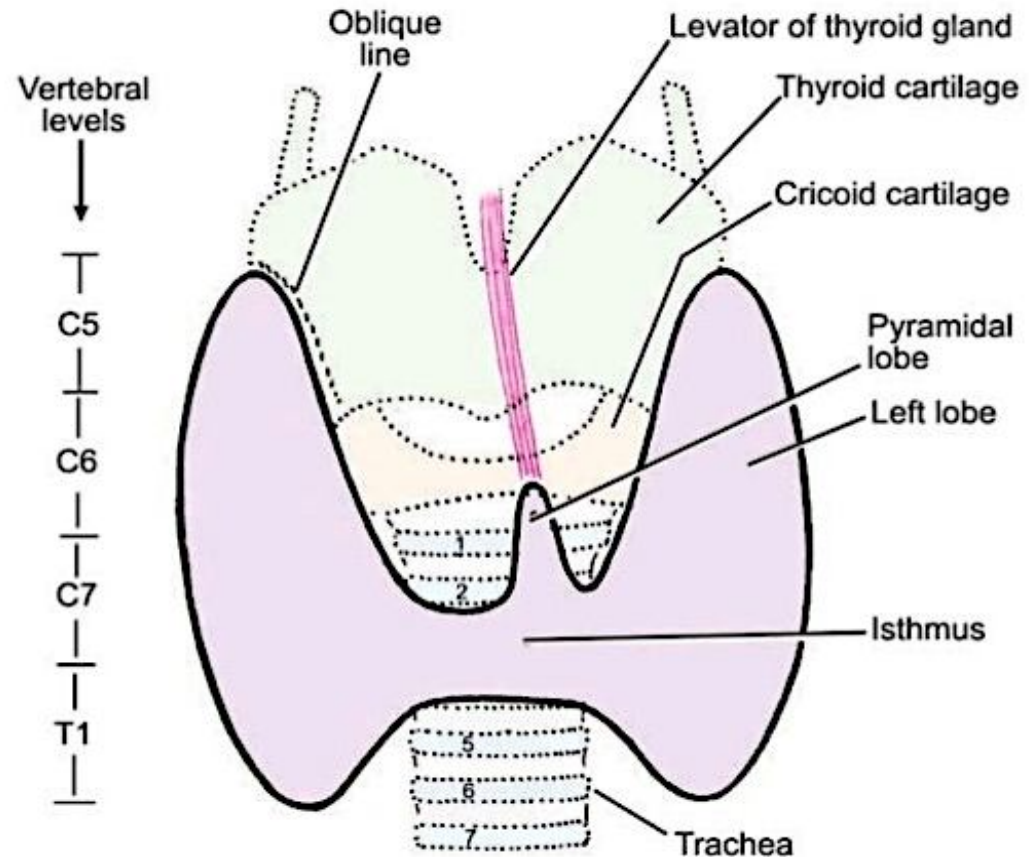
**Base** = T1

**Surfaces** =

**med.** = trachea / larynx

**Lat.** = antero lateral neck muscles

**Post.** = carotid sheath



46.7: Outline of the thyroid gland as seen from the front, and its relationship to the larynx and trachea



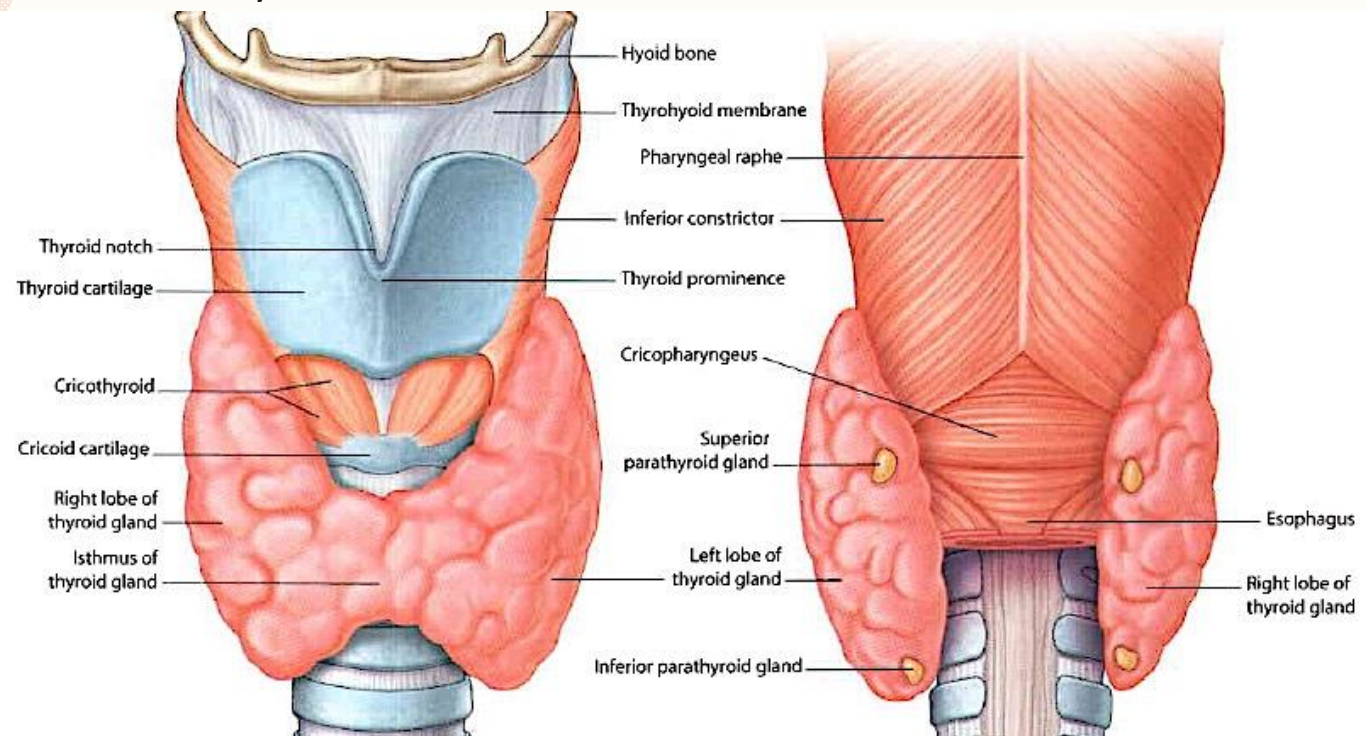
### **Post. Correlations:**

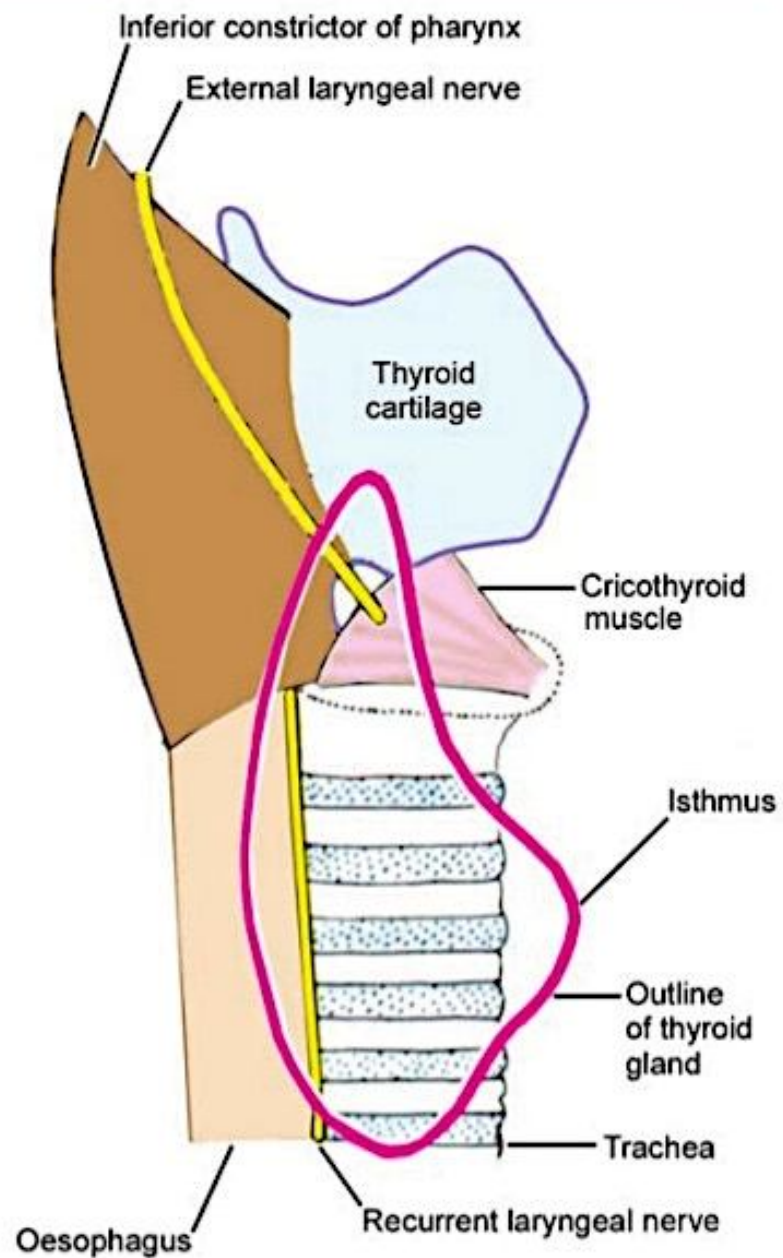
the trachea, the cricoid cartilage, and the lower part of the thyroid cartilage

### **Ant. Correlations:**

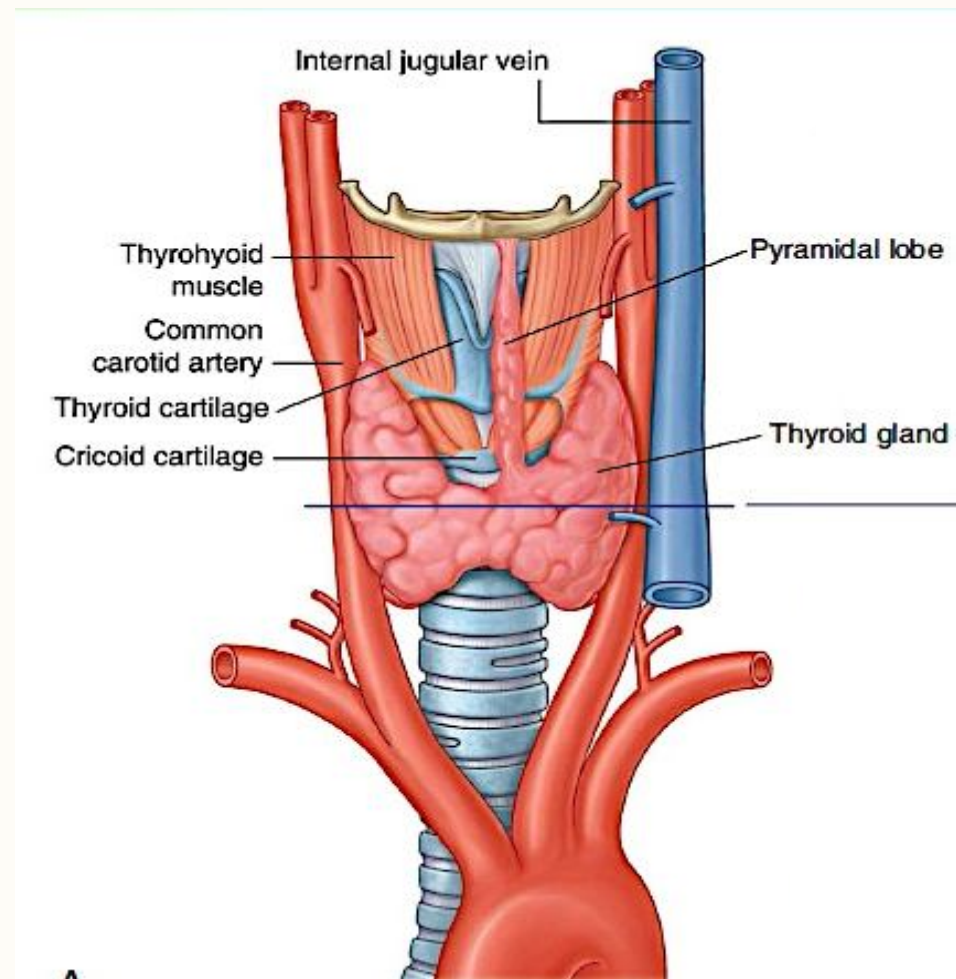
sternohyoid / sternothyroid / omo-hyoid muscles

- Located in the visceral compartment of the neck
- surrounded by the pretracheal layers of fascia

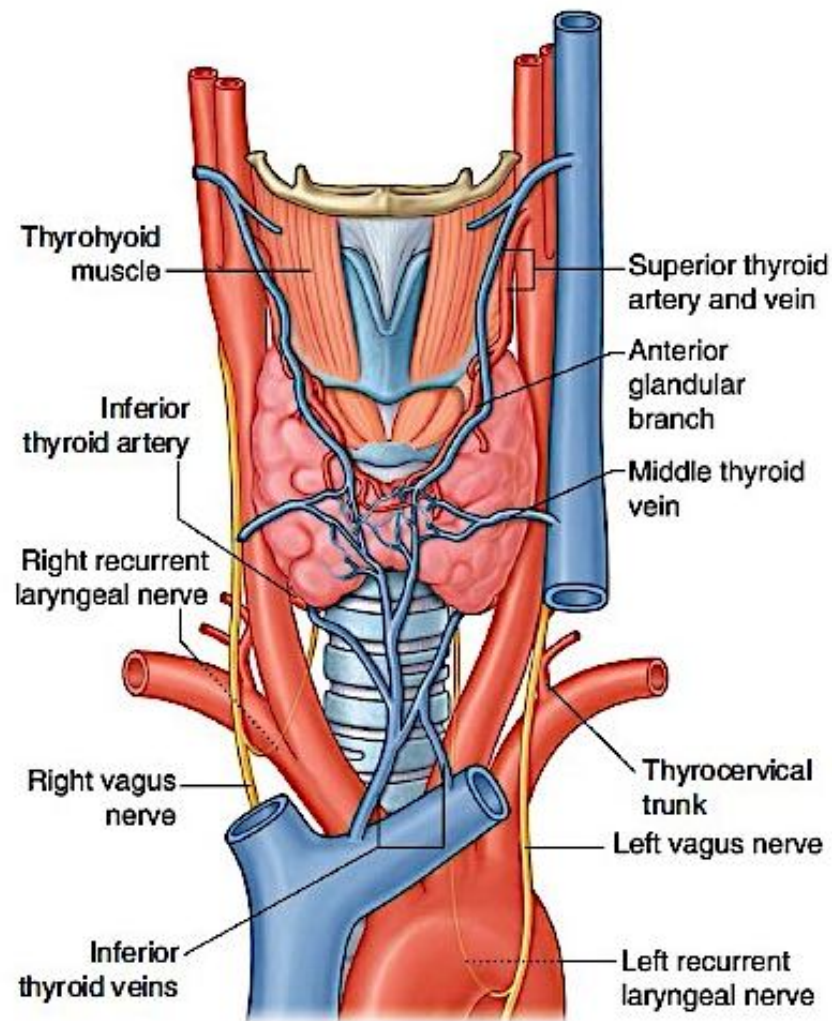




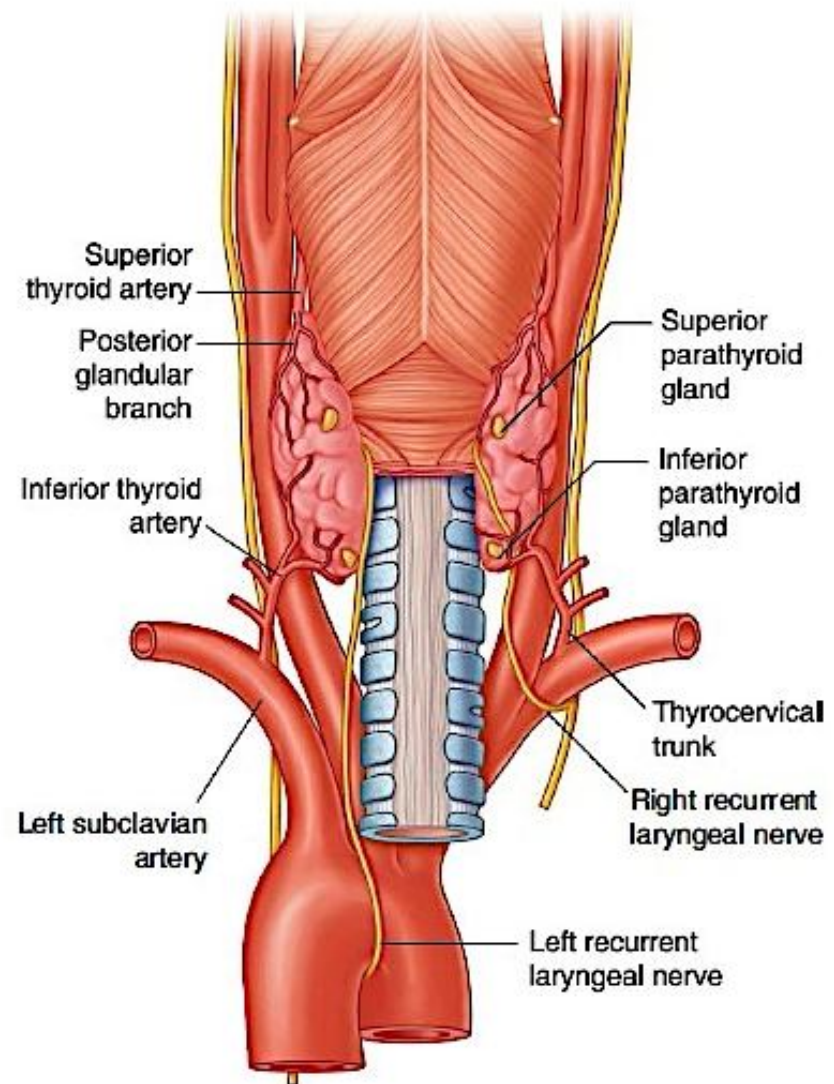
**46.9A:** Medial relations of the thyroid gland. The outline of the gland is shown in pink line







**Fig. 8.175** Vasculature of the thyroid: anterior view.



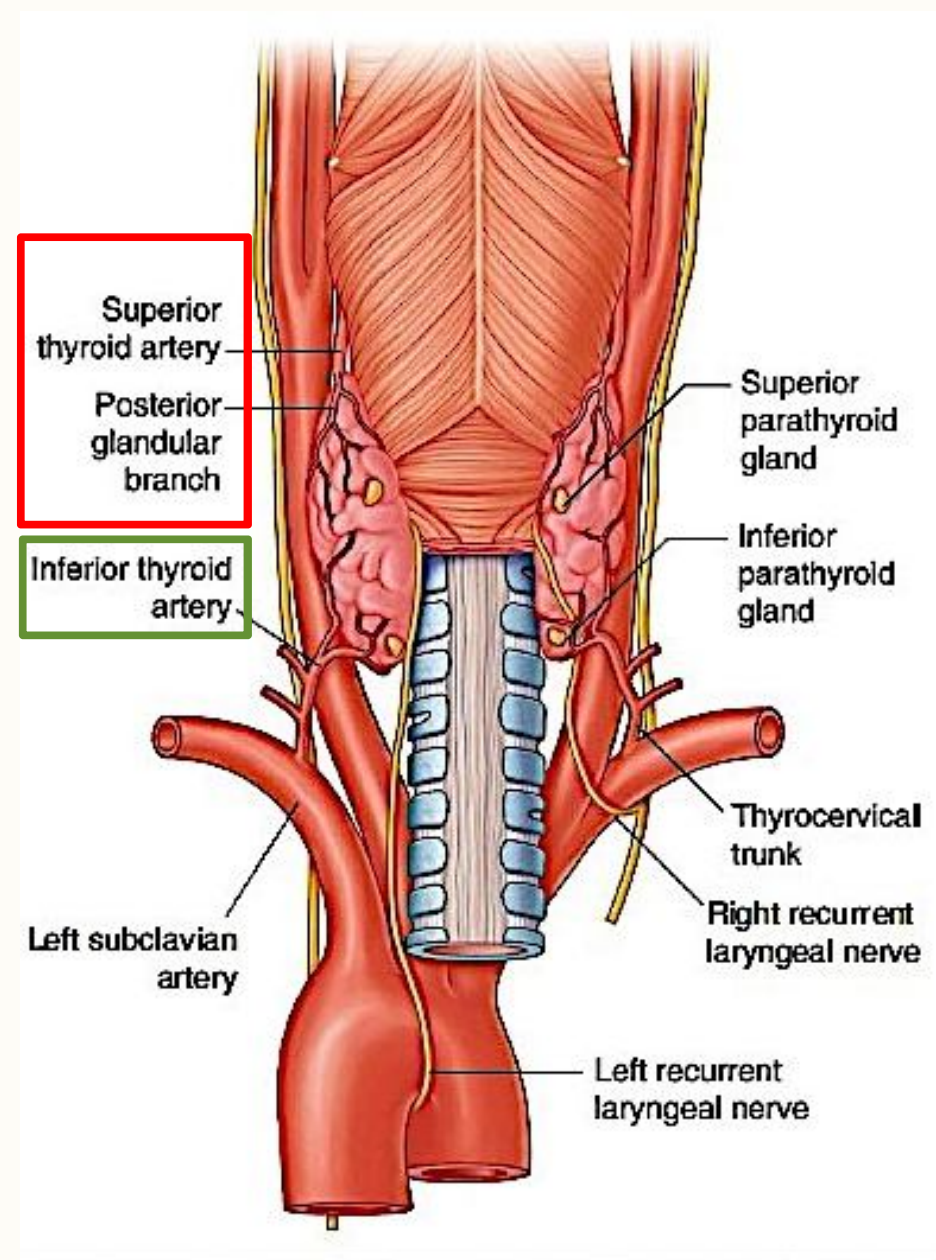
**Fig. 8.176** Superior and inferior thyroid arteries and left and right recurrent laryngeal nerves: posterior view.

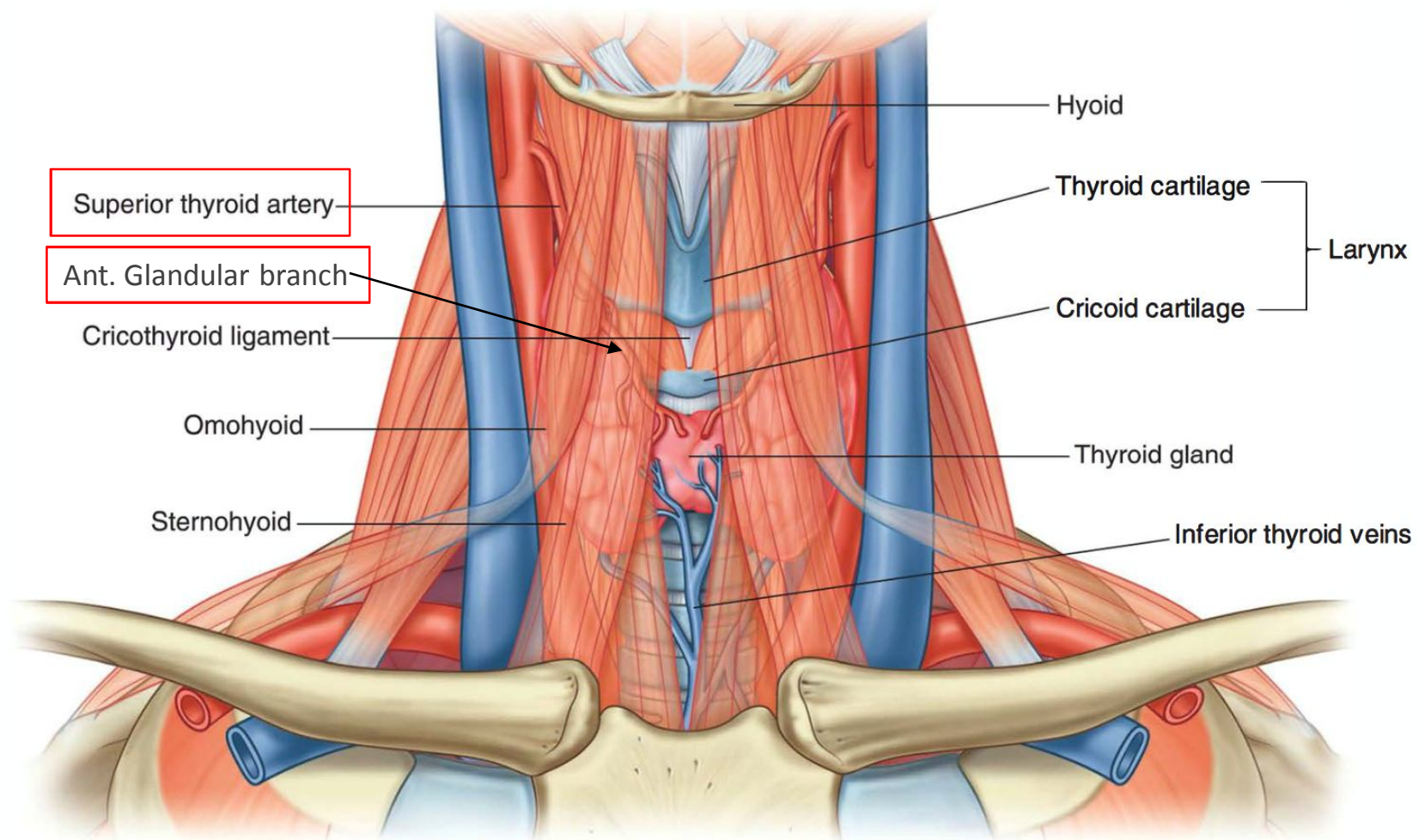


## Superior thyroid artery :

is the first branch of the external carotid artery  
It descends, passing along the lateral margin of the thyrohyoid muscle reach the superior pole of the lateral lobe of the gland divides into anterior and posterior glandular branches:

- The anterior glandular branch passes along the superior border of the thyroid gland and anastomoses with its twin from the opposite side across the isthmus
- The posterior glandular branch passes to the posterior side of the gland and may anastomose with the inferior thyroid artery





**Fig. 8.13** Larynx and associated structures in the neck.

## Inferior thyroid artery :

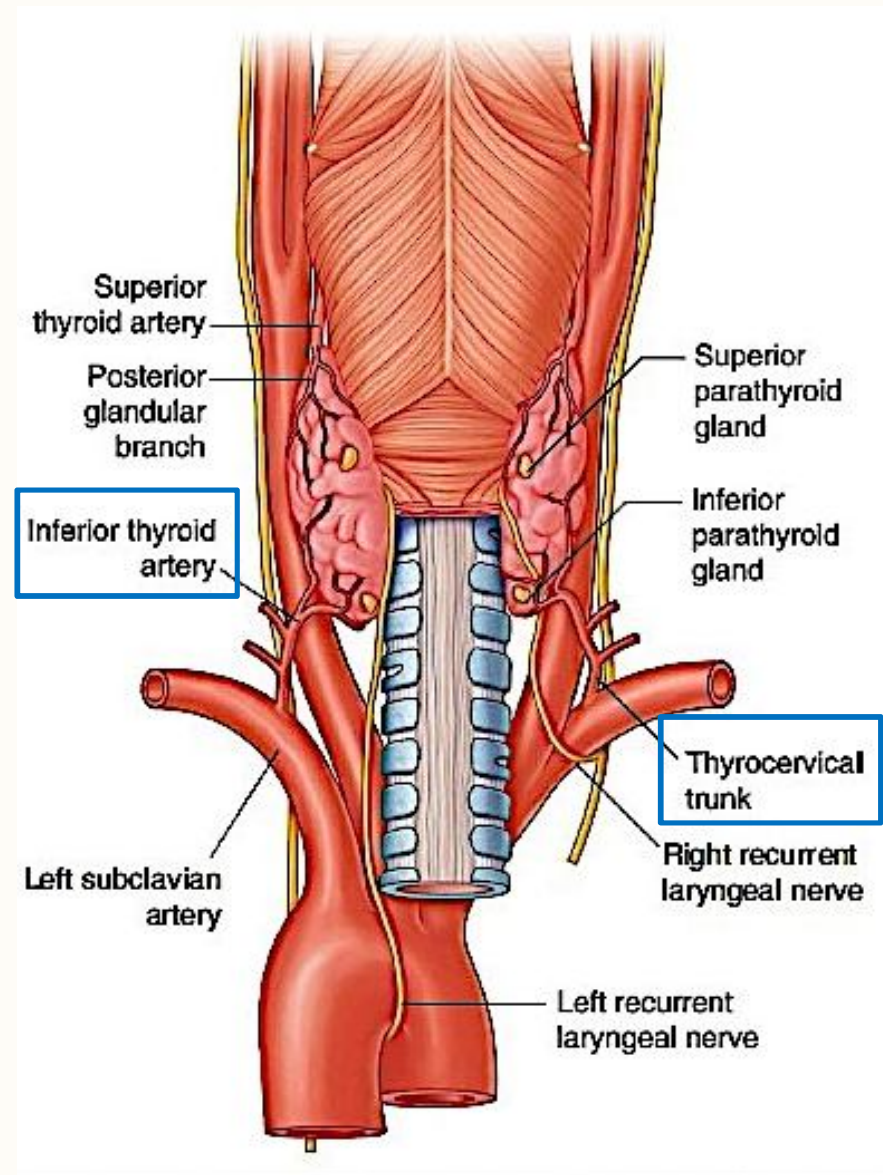
- branch of the thyrocervical trunk arises from the first part of the subclavian artery
- ascends along the medial edge of the anterior scalene muscle
- passes posteriorly to the carotid sheath reaches the inferior pole of the lateral lobe of the thyroid gland.

the inferior thyroid artery divides into :

**an inferior branch /** the lower part of the thyroid gland and anastomoses with the posterior branch of the superior thyroid artery

**an ascending branch /** the parathyroid glands

a small **thyroid ima artery** arises from the brachiocephalic trunk or the arch of the aorta and ascends on the anterior surface of the trachea to supply the thyroid gland





## Venous drainage

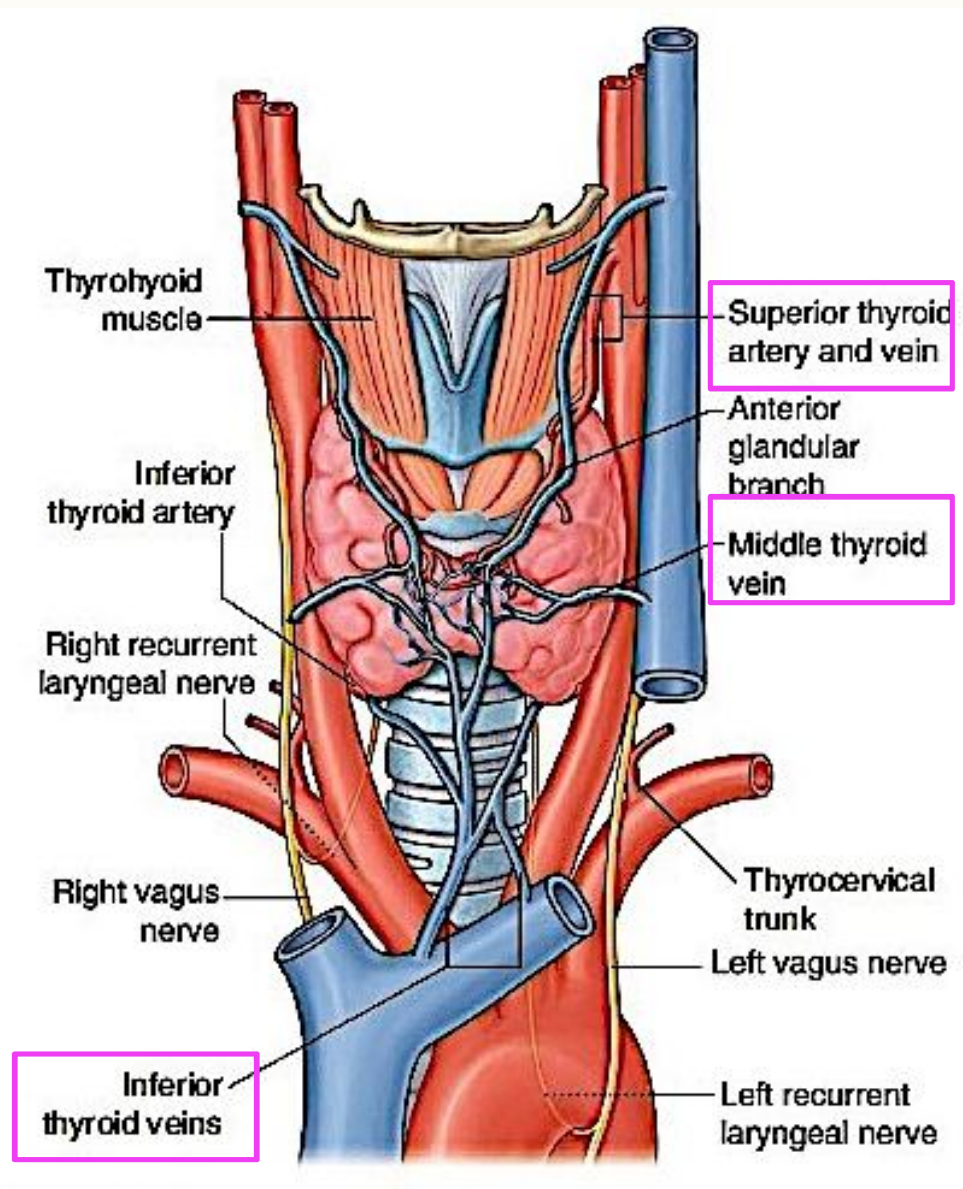
Three veins drain the thyroid gland :

The superior thyroid vein primarily drains the area supplied by the superior thyroid artery.

The middle and inferior thyroid veins drain the rest of the thyroid gland.

The superior and middle thyroid veins drain into the internal jugular vein

the inferior thyroid veins empty into the right and left brachiocephalic veins



## *Lymphatic drainage of the thyroid gland*

paratracheal nodes / deep cervical nodes along the internal jugular vein.

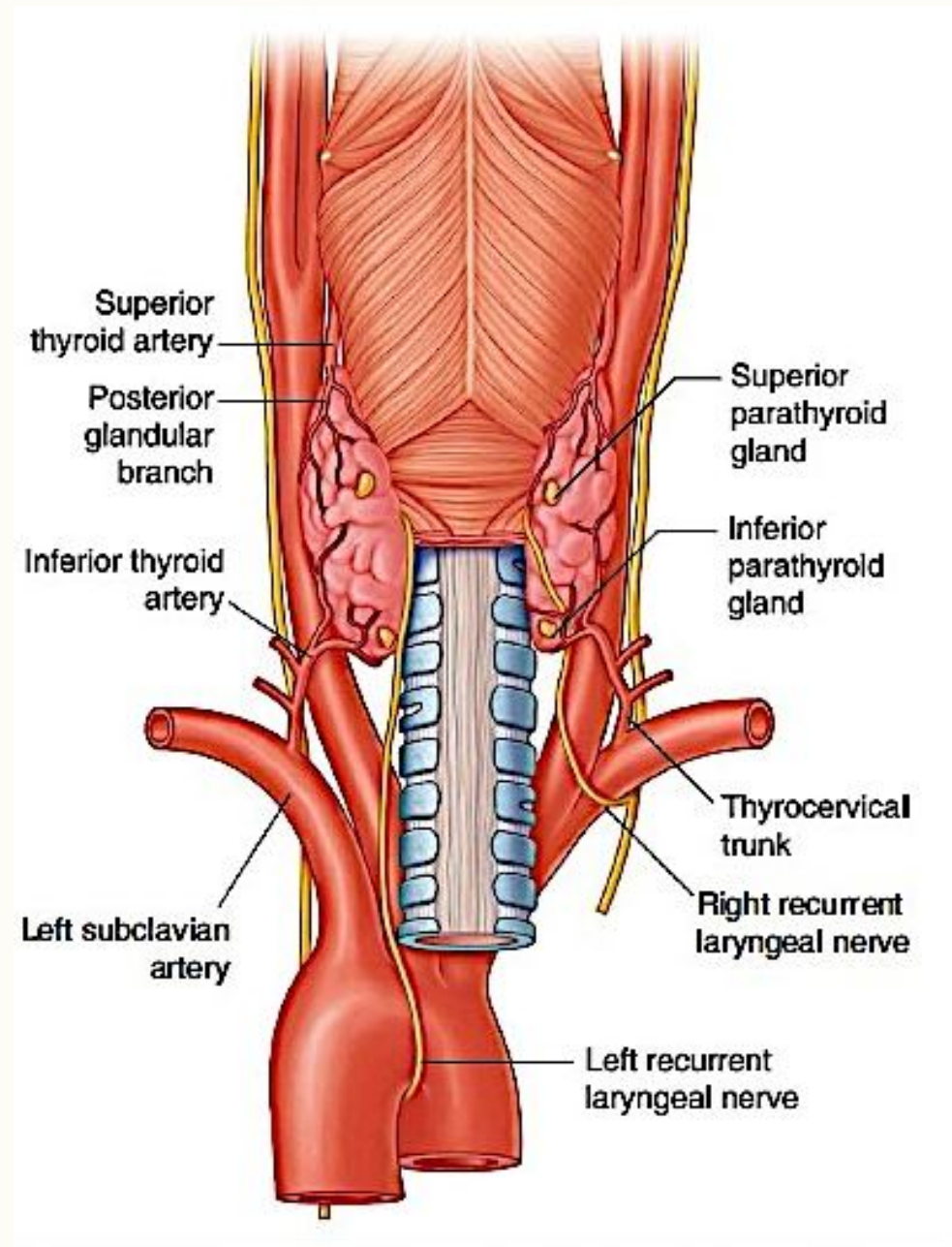
## *Recurrent laryngeal nerves*

*the vagus nerve [X] :*

*looping around the subclavian artery on the right*

*the arch of the aorta on the left*

- ascend in a groove between the trachea and esophagus
- They pass deep to the posteromedial surface of the lateral lobes of the thyroid gland



## *Thyroid gland:*

Proliferation of epithelium in the floor of pharynx

Between tuberculum impar & copula (foramen cecum)

Migration in front of pharyngeal gut

Thyroglossal duct

Migration in front of thyroid bone

Reach to final position in front of trachea = 7 week

Begins to function (follicular cell with colloid) = 3 month

