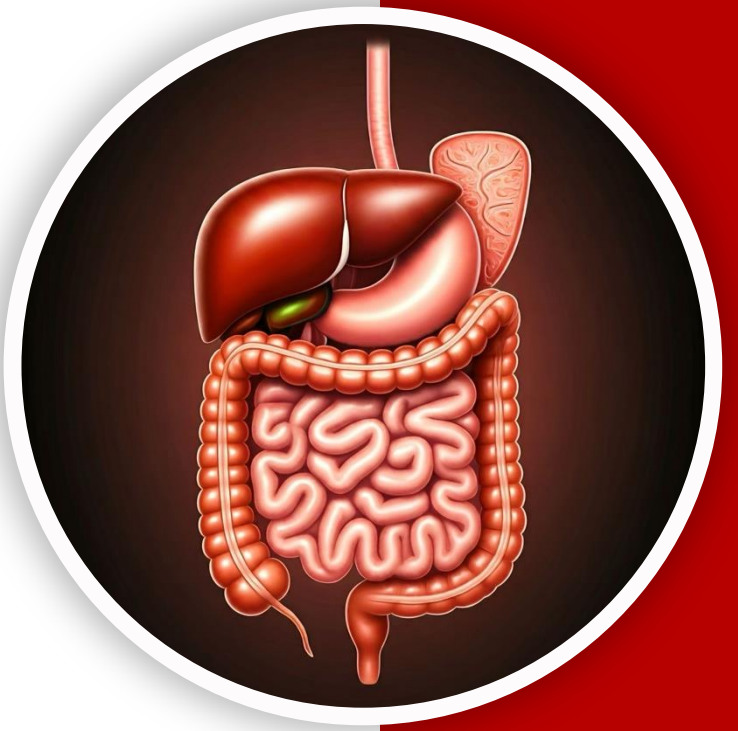
بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Endocrine Anatomy, Histology & Embryology | MID 6

Pineal gland and islets of Langerhans



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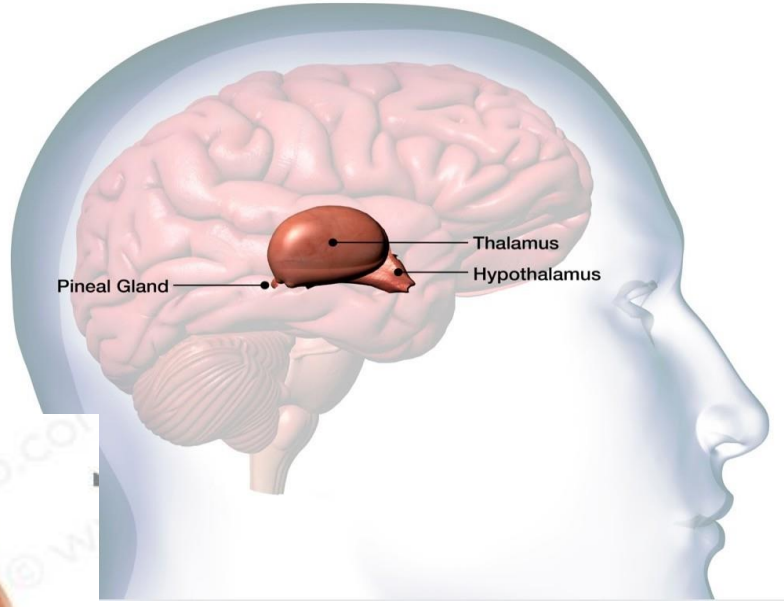
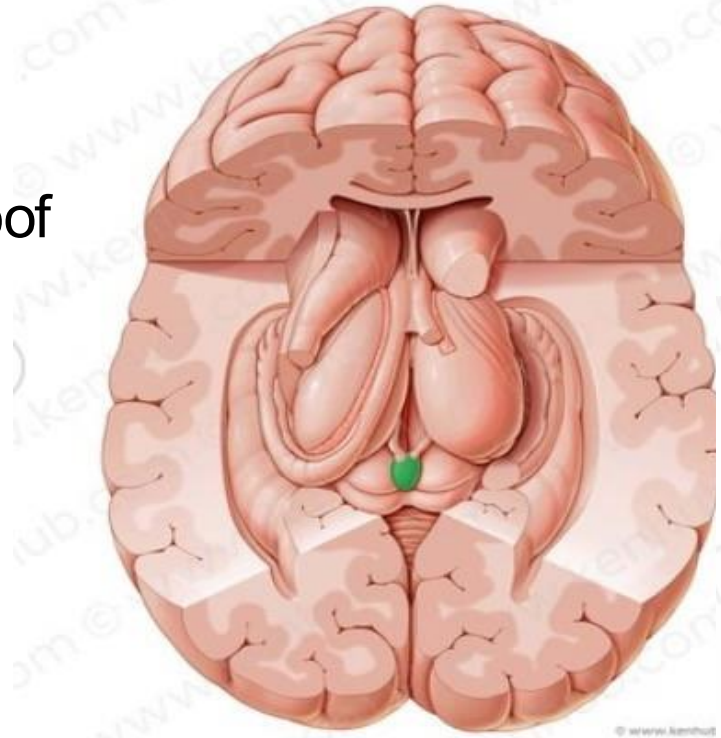
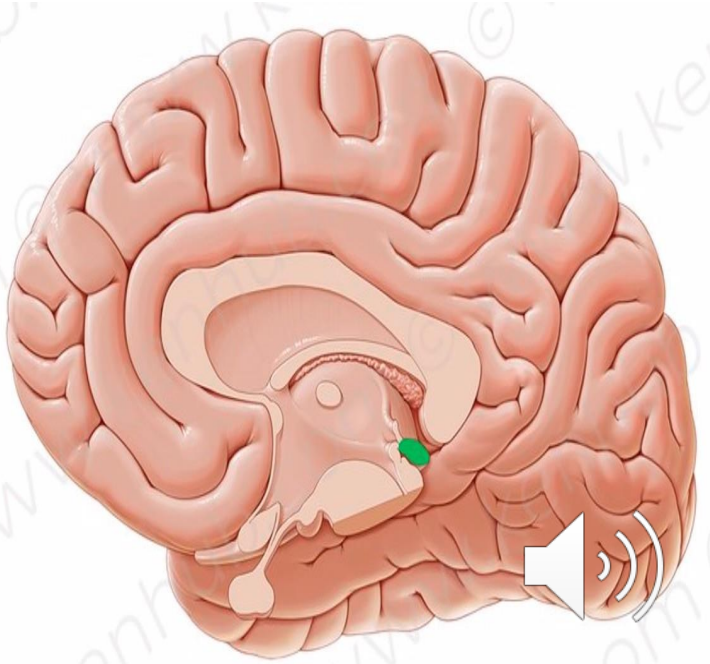
Pineal Gland

Pineal Gland

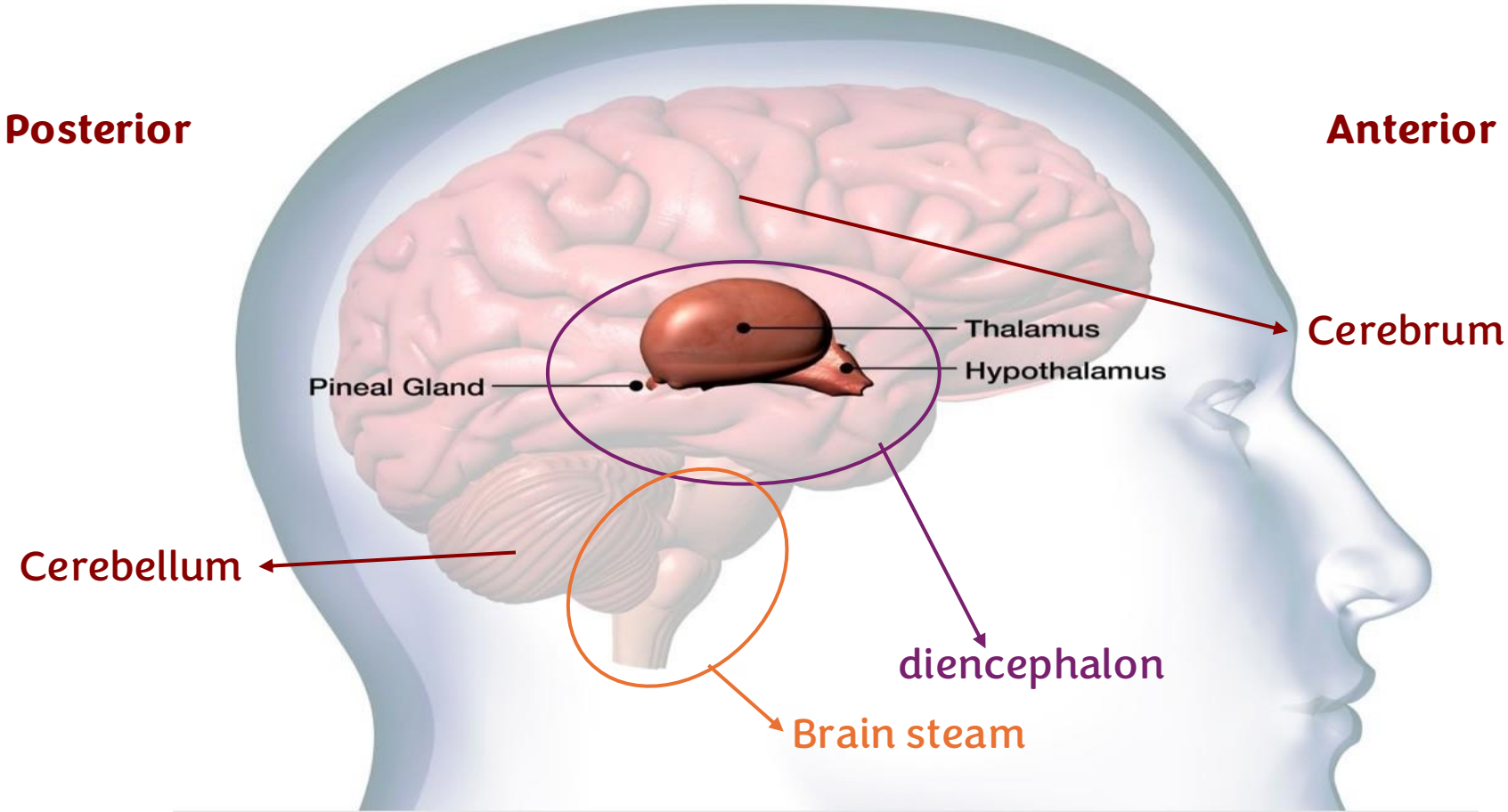
- A small, pine cone-shaped organ (5-8 mm by 3-5 mm)
- Also known as the epiphysis cerebri
- Posteriorly from the posterior end of the roof of the third ventricle of the brain.
- Resides between the thalamic bodies.
- Has a rich blood supply
- Innervated by postganglionic sympathetic nerve fibers (SCG).
- Covered by connective tissue of the pia mater (septa).





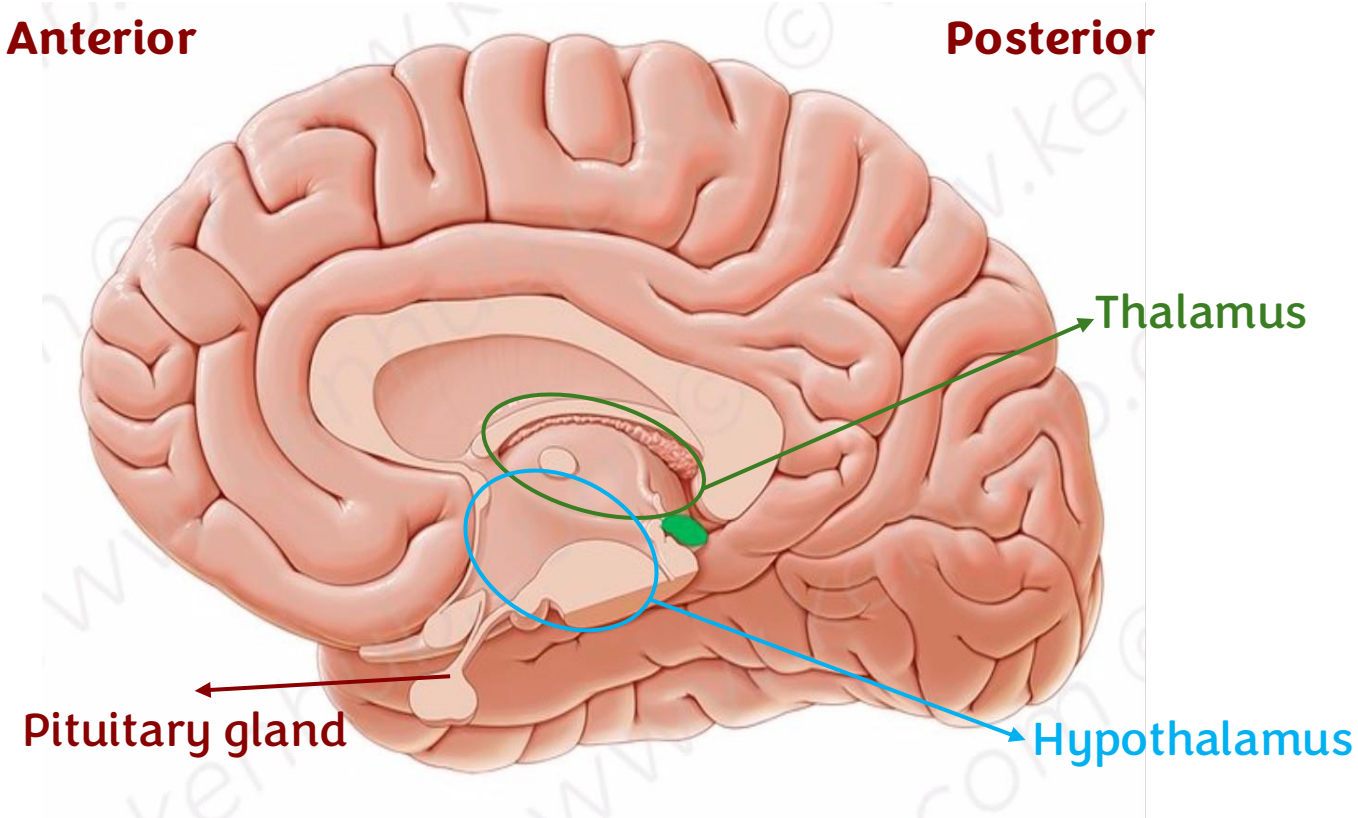


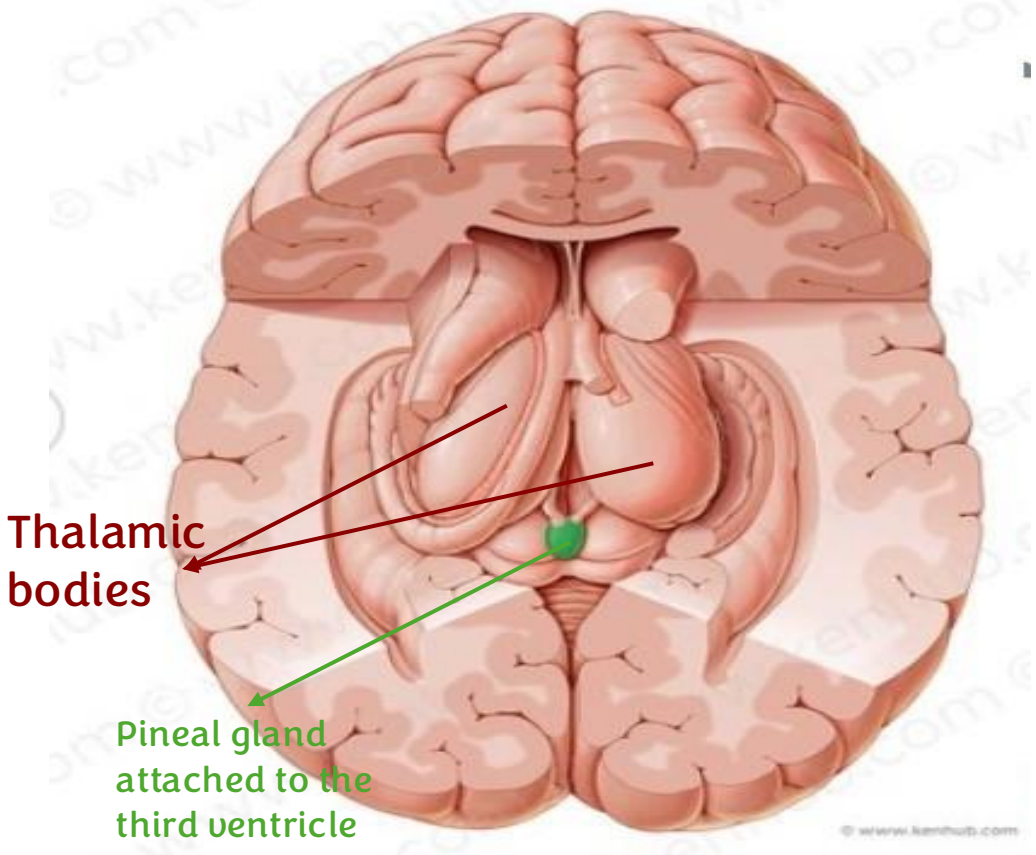
- The **diencephalon** includes important structures such as the **thalamus** and the **pineal gland**. The pineal gland is found between the bodies of the thalamus sticking from the **third ventricle**.
- The **ventricles** are cavities within the brain that contain **cerebrospinal fluid (CSF).**
- The **pineal gland**, part of the epithalamus, has a rich vascular supply. It is covered by a layer of the **meninges**, specifically the delicate innermost layer called the **pia mater .** This connective tissue sends septa that further divide the gland into smaller compartments. These septa allow larger blood vessels to enter the gland and then branch into smaller capillaries to pick up the secretion of the gland, which is the hormone melatonin, an important hormone for our daily cycle.
- The pineal gland also contains **adrenergic receptors**, allowing it to receive **postganglionic sympathetic innervation**. Additionally, it has some **parasympathetic innervation**.



In terms of its location, The pineal gland can only be seen clearly after removing one half of the brain.
And it's located centrally

This is how it looks from an inferior view; that is, when viewed from below.



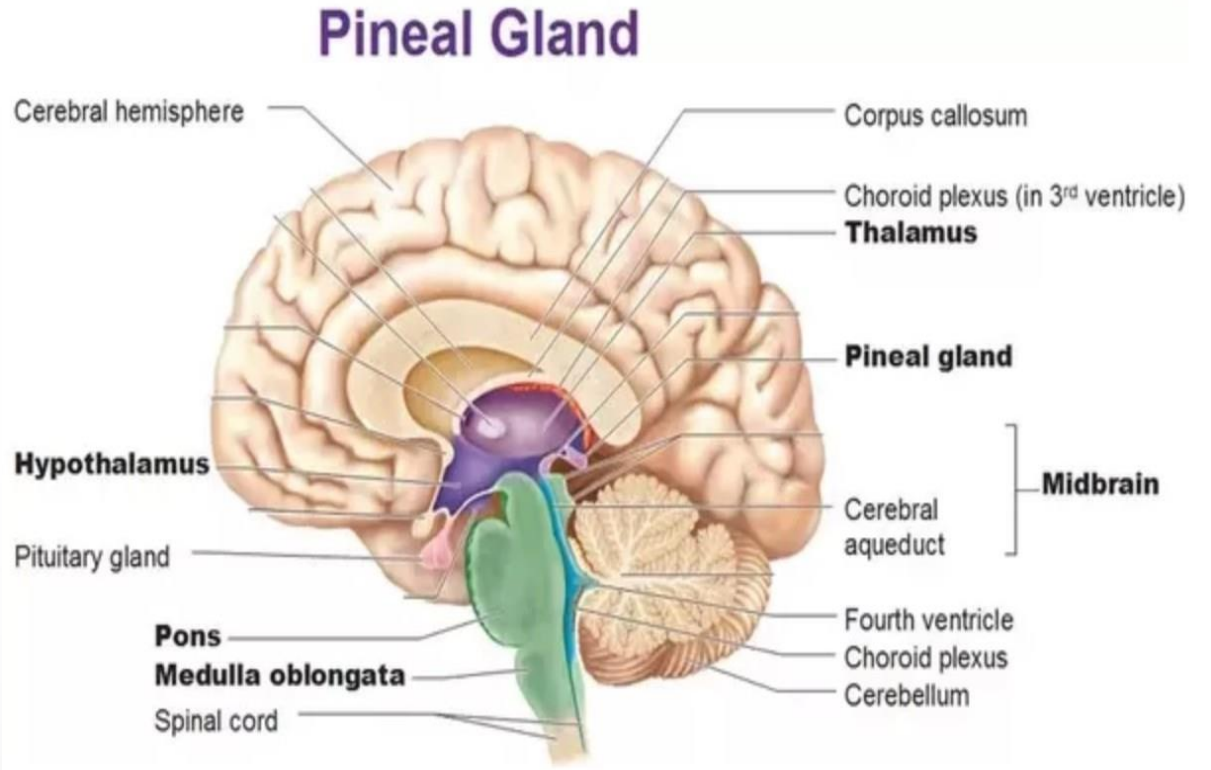


LOCATION/BLOOD SUPPLY

Location

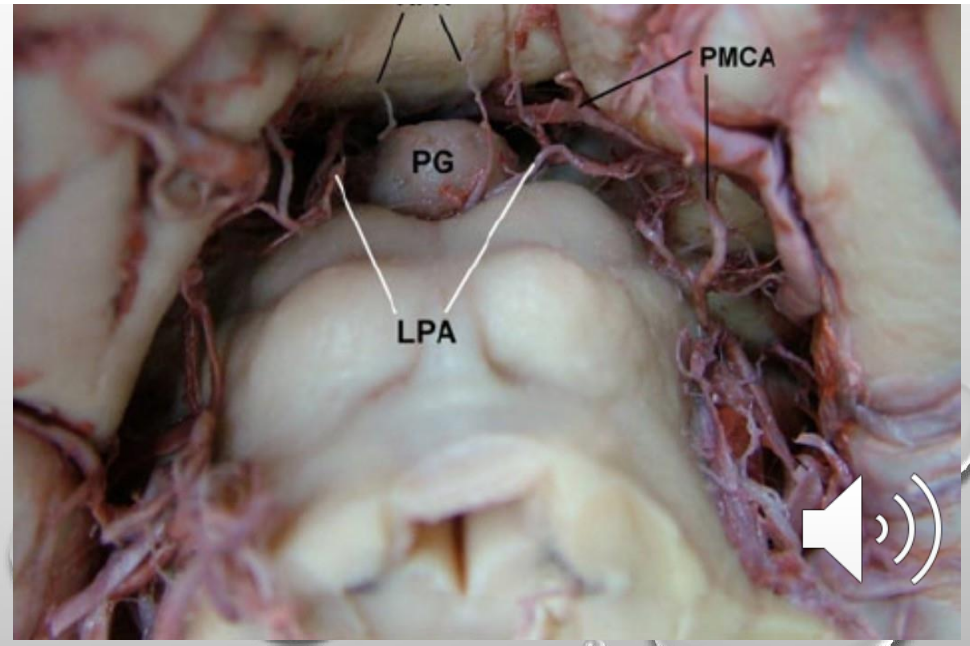
Is a midline structure, located between the two cerebral hemispheres.

It is attached by a stalk to the posterior wall of third ventricle , and it's further related to the midbrain.



Blood supply

- Lateral and medial pineal artery branches of the posterior choroidal artiers which are branches of posterior cerebral artery and the posterior cerebral artery is the terminal branch of basiliar artery.
- Although the pineal gland is extremely small, it has a very rich blood supply. It is considered second only to the kidneys in terms of how well vascularized it is.



Organogenesis

During organogenesis, the pineal gland begins to develop around the seventh week of gestation. It originates from the neuroectoderm, which is expected since it is part of brain tissue. Specifically, it arises from the posterior wall of the third ventricle, a region with which it remains closely associated.

In this area, the neuroectoderm thickens and forms a small cavity that stays connected to the third ventricle. Within this cavity, the cells that will eventually become the secretory (parenchymal) cells develop gradually. Initially, these cells are organized as tubules, which later differentiate into the mature cells known as pinealocytes

At the same time, as these secretory cells are developing, the gland also acquires its postganglionic sympathetic innervation. Thus, the maturation of the gland's cellular components occurs alongside the development of its nerve supply.

At birth, the pineal gland is not fully mature and requires additional time to reach its full secretory capacity. Although it continues developing throughout the first decade of life, the period from birth to about two years of age is considered especially critical for its growth and functional development

Organogenesis

- 7th-8th week.
- Develops from neuroectoderm (posterior wall of the third ventricle).
- Neuroepithelium that lines the roof of the third ventricle thickens, then the gland is formed as a small cavity that is connected to the third ventricle. Gradually, the parenchymal cells forms the secretory cells and the innervation also takes place.
- The development of the mature gland is seen in the first decade of life; the pineal gland will increase in size from birth to about 2 years in age.

Histology

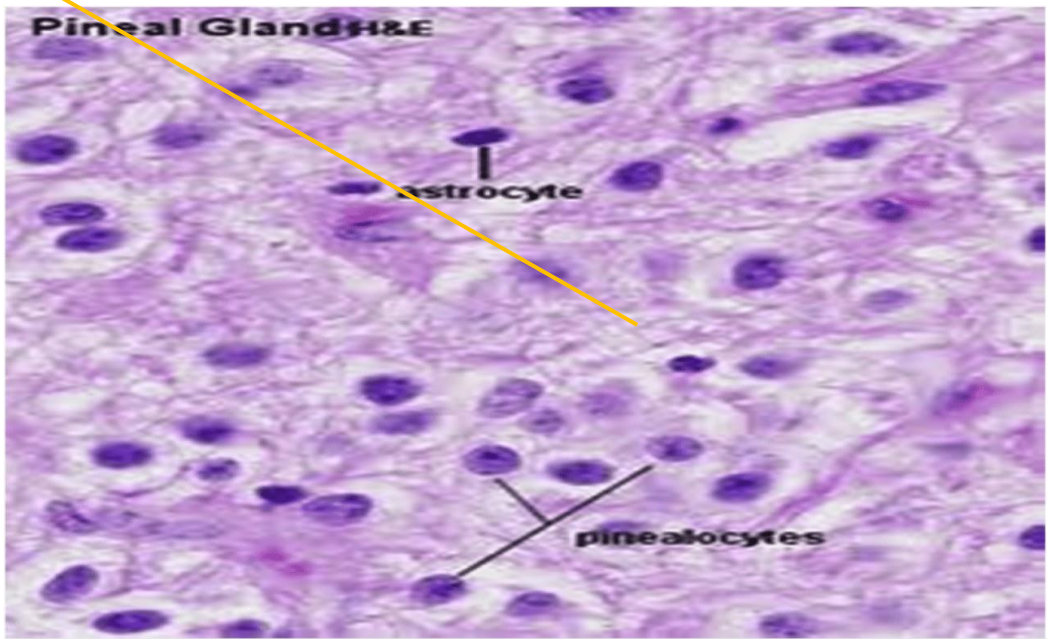
Stained by H&E and visualized by a bright field microscope

- Prominent and abundant secretory cells-**pinealocytes**.
- Slightly **basophilic** cytoplasm and **irregular** euchromatic nuclei
- The pinealocytes have Secretory vesicles (which is expected for any other endocrine cells) , many mitochondria, and long cytoplasmic processes.
- Produce **melatonin:** a low-molecular-weight, a **tryptophan derivative**→ **EXPLANATION:** melatonin is derivative of serotonin and serotonin is derivative of tryptophan amino acid .
- Unmyelinated **sympathetic** nerve fibers enter the pineal gland and end among pinealocytes (some form synapses)

They are in charge of the synthesis and release of the melatonin

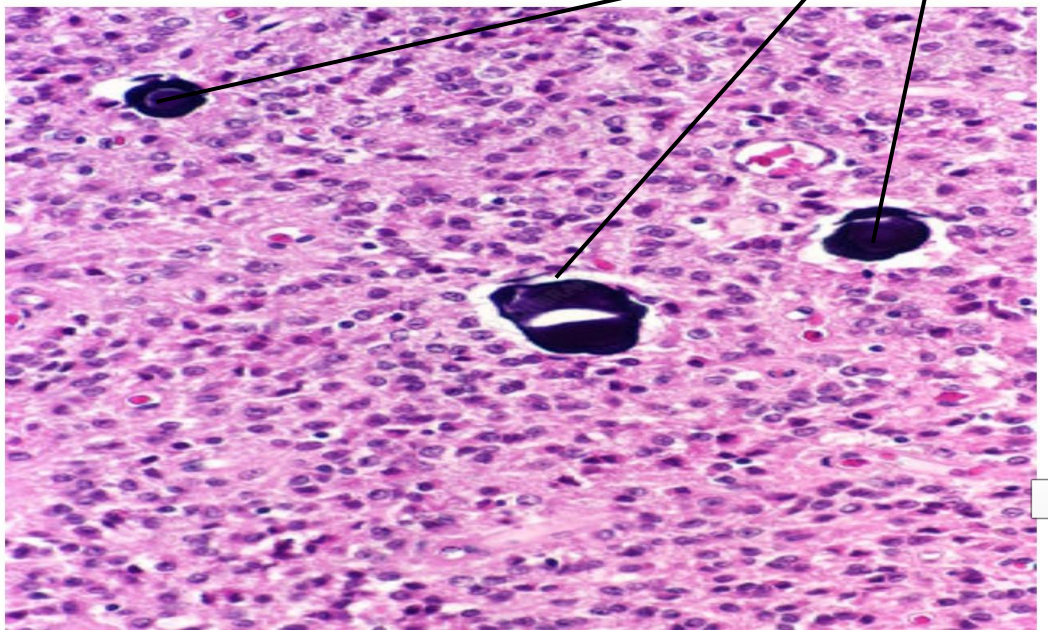
long cytoplasmic processes

Higher magnification



Lower magnification

Corpora arenacea



Histology

- Has interstitial glial cells (modified astrocytes) which represent 5% of the cells ,,, how to distinguish them? The astrocytes have elongated (flattened) nuclei more heavily stained than those of pinealocytes and found in perivascular areas , Whereas the ones for the ones for pinealocytes are the one with the larger euchromatic nuclei and those are the most numerous.
- Microglial cells are present too.
- Another important feature of the pineal gland is the presence of dark regions seen at low magnification. However, at higher magnification, these areas are not truly dark; instead, they appear more purplish and are known as **Corpora arenacea, or brain sand (**concretions of calcium and magnesium salts), formed by mineralization of extracellular protein deposits---glands accumulate calcium from blood.
- May appear during childhood and gradually increase in number and size with age.
- **No apparent effect** on the gland's function.

Corpora arenacea

Corpora arenacea (brain sand) are calcified concretions composed mainly of calcium and magnesium salts. These deposits form when the salts accumulate on extracellular proteins and gradually increase in size through accretion.

Over time, the pineal gland tends to deposit more calcium, so both the number and size of these calcifications increase with age. Because of this, they can be used as an approximate indicator of the gland's age—older pineal glands typically contain more and larger corpora arenacea.

These structures are also visible on brain radiographs, where they appear as whitish areas. This makes it possible to identify the location of the pineal gland by detecting these calcifications.

Despite their increase with age, corpora arenacea do not appear to have any significant effect on the gland's secretory function.

Images from the histology textbook

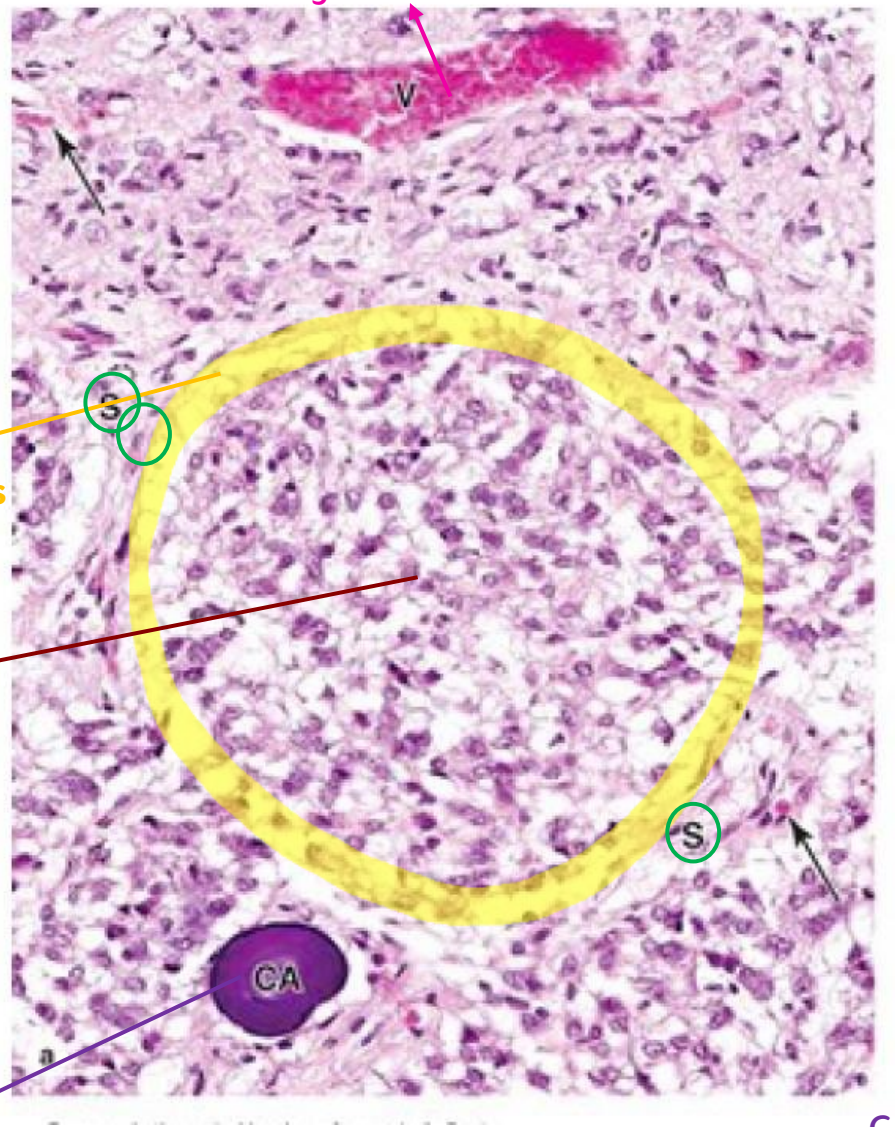
Big Blood vessel

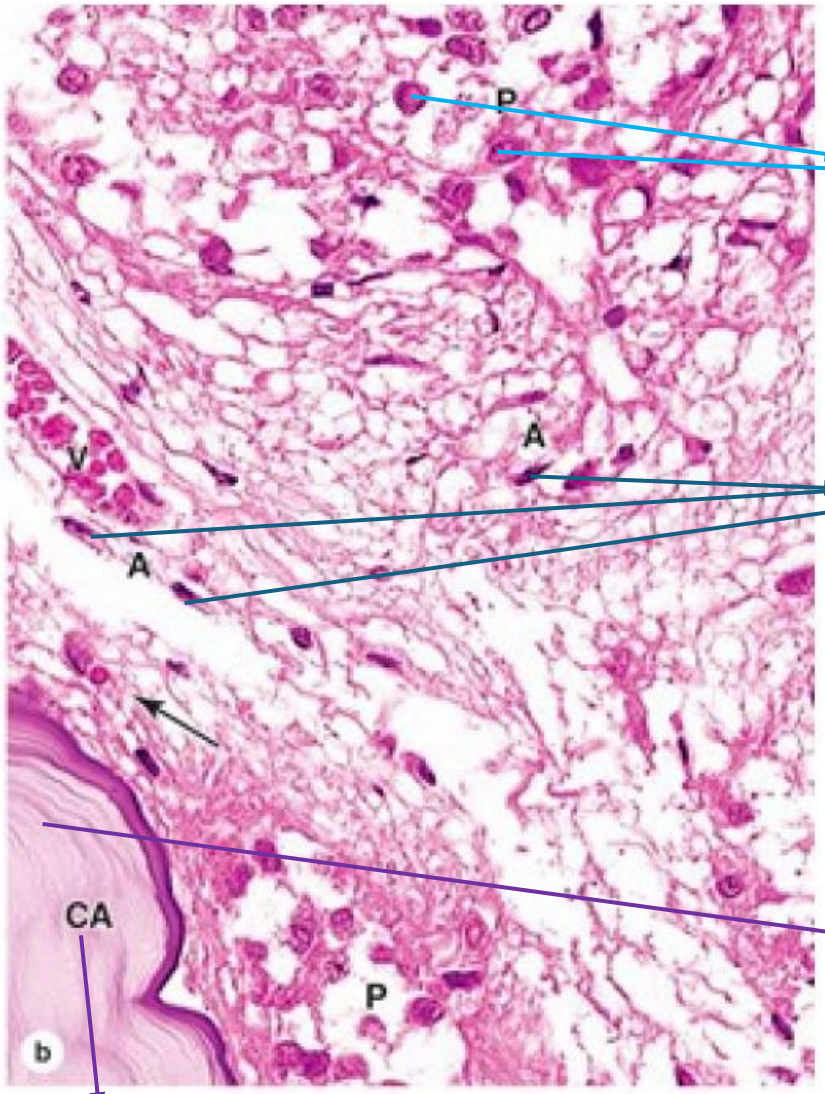
We have sinusoids throughout the structure of the gland

Connective tissue surrounding tiny compartment of the cells

We can see here at low magnification, most of the cells observed are pinealocytes. The smaller, darker-staining cells represent astrocytes and other glial cells

Corpora arenacea





Pinealocytes

The flattened ones are astrocytes

This wavy appearance is due to the continuous accretion of calcium and magnesium salts, which accumulate over time as the deposits expand and increase in size

Corpora arenacea

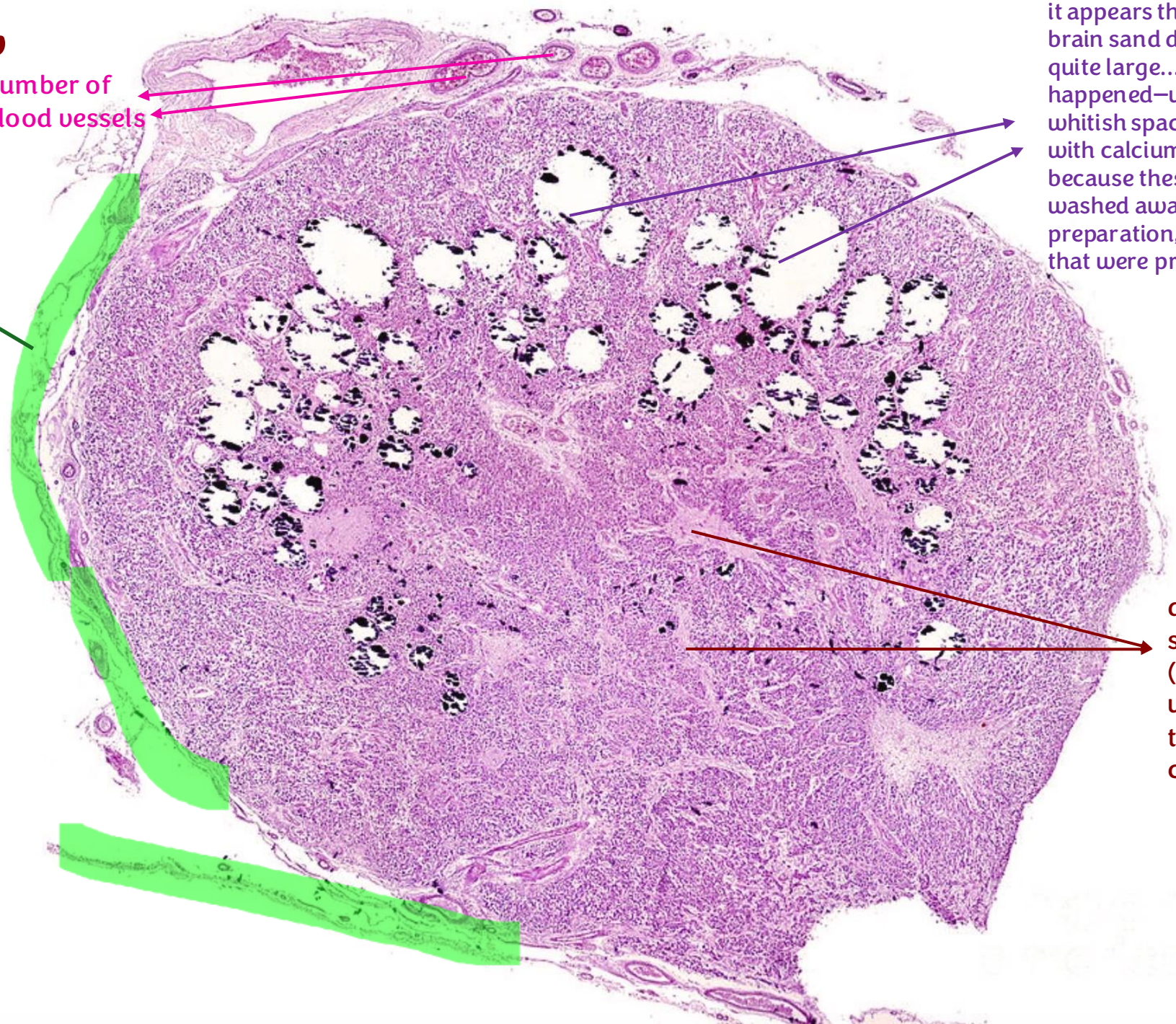
- (A) pinealocytes surrounded by septa (S) venules (V) and capillaries (arrows). Extracellular mineral deposit: corpus arenaceum (C A) (marker for the pineal).
- (B) pinealocytes (p) fewer astrocytes (a)

that's at a very low magnification

number of blood vessels

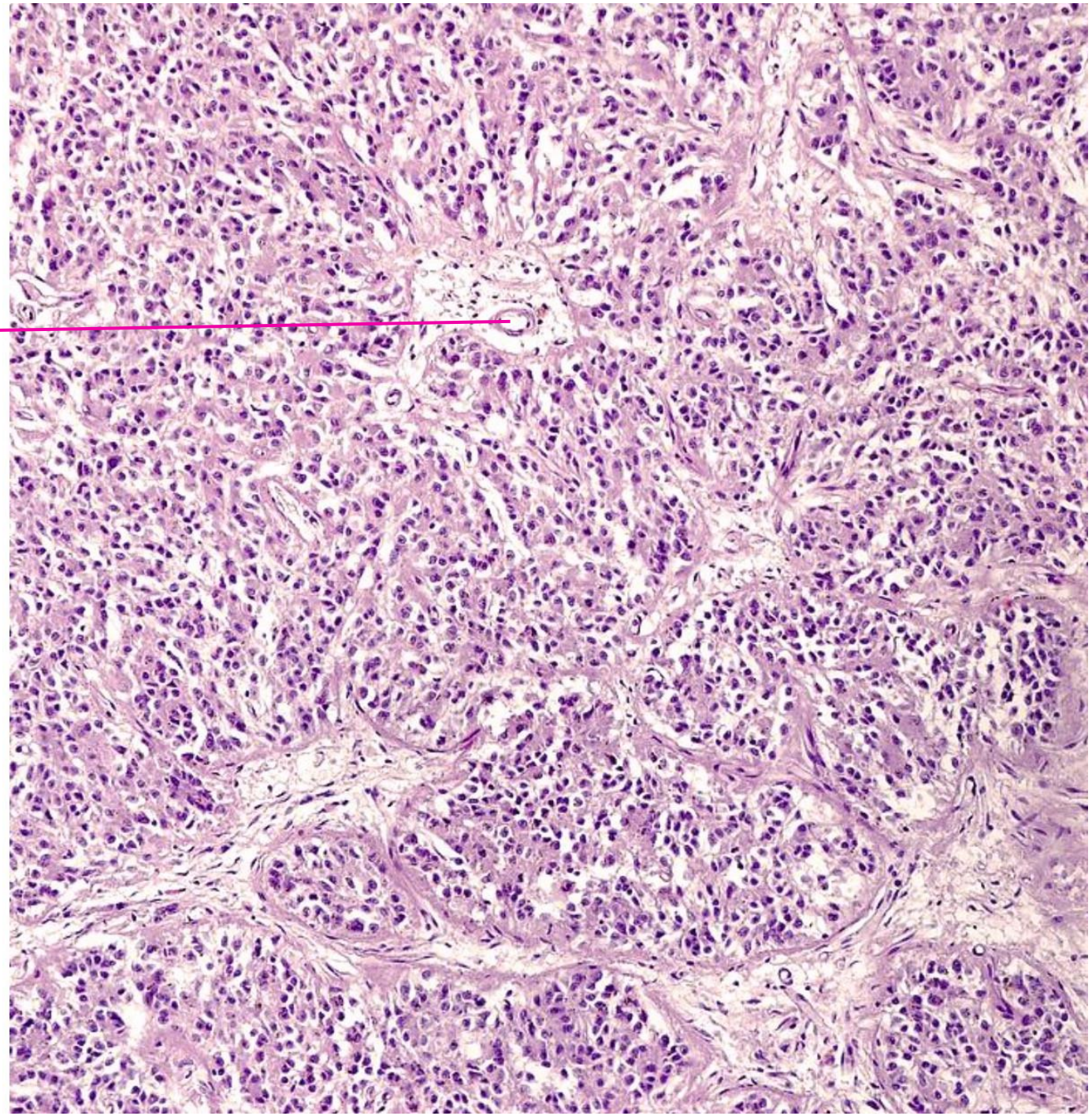
this is the connective tissue capsule, which originates from the pia mater

it appears that there are numerous brain sand deposits, and their size is quite large... you might wonder what happened—why do we see empty whitish spaces instead of being filled with calcium and magnesium? this is because these mineral deposits were washed away during histological preparation, leaving behind the spaces that were previously occupied by them



deeper inside, we can see the stroma (connective tissue), which further divides the gland into smaller compartments

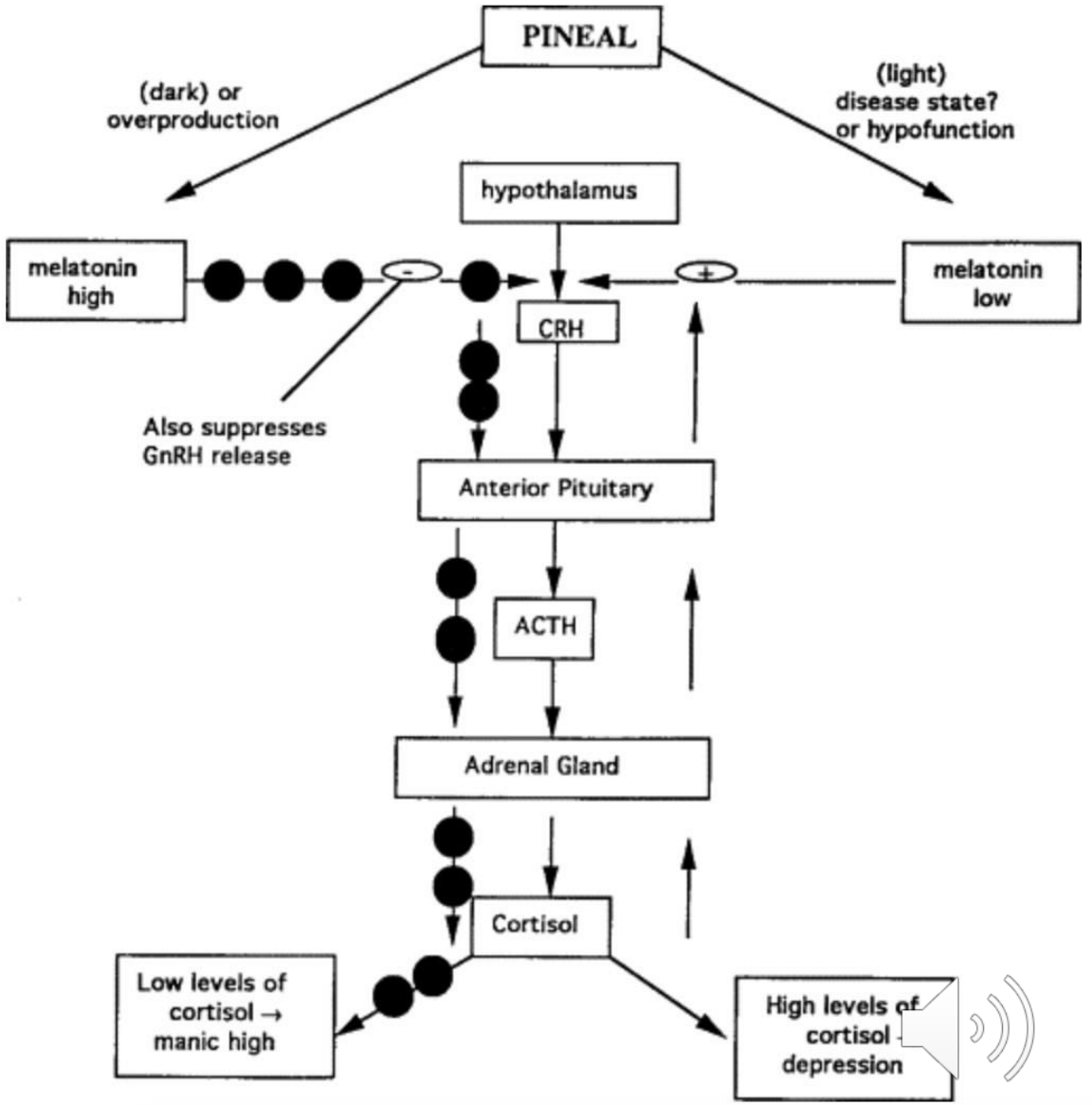
Blood vessel



now at a higher magnification, we again recognize the connective tissue that divides the gland into smaller compartments, along with the cells within them

Pineal Gland Functions

- Influences the activities of the **pituitary** gland, the Islets of Langerhans of the pancreas, the parathyroids, the adrenals, and the gonads.
- The pineal secretions, reach their target organs via bloodstream or cerebrospinal fluid.
- Their actions are mainly inhibitory.
- Directly inhibit the production of hormones or indirectly inhibit the secretion of releasing factors by the hypothalamus.

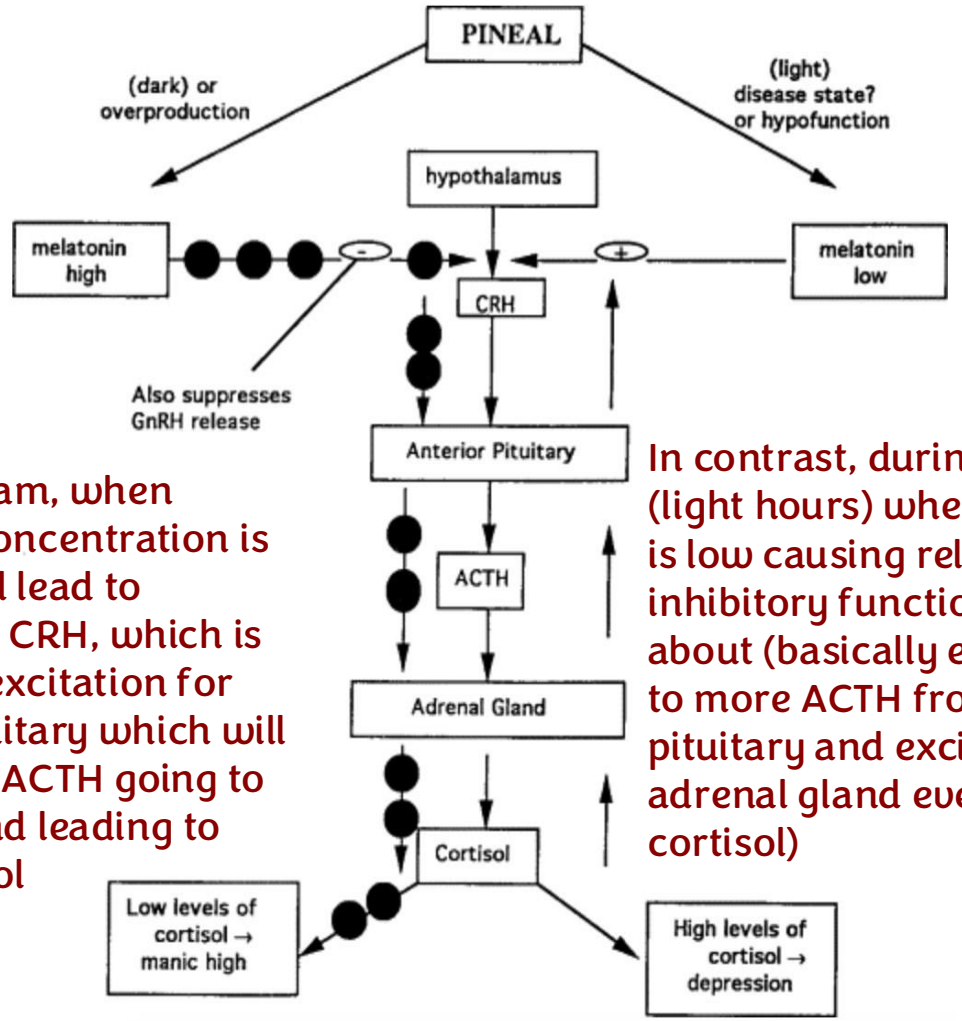


Here we will be discussing what the melatonin hormone does in general.

Melatonin hormone has a inhibitory function on a number of glands (such as pituitary, parathyroid, adrenal and even the hypothalamus itself).

After its release by the pineal gland in the bloodstream or the cerebrospinal fluid, it will circulate and reach a number of target cells, its mostly secreted in the dark(at night).

high melatonin has an inhibitory effect by inhibiting the release of the hormones directly OR effecting the releasing hormone from the hypothalamus
(Melatonin exerts its inhibitory effects at both levels: it acts directly on the anterior pituitary gland to suppress hormone secretion and acts upstream on the hypothalamus to inhibit the release of specific releasing hormones)



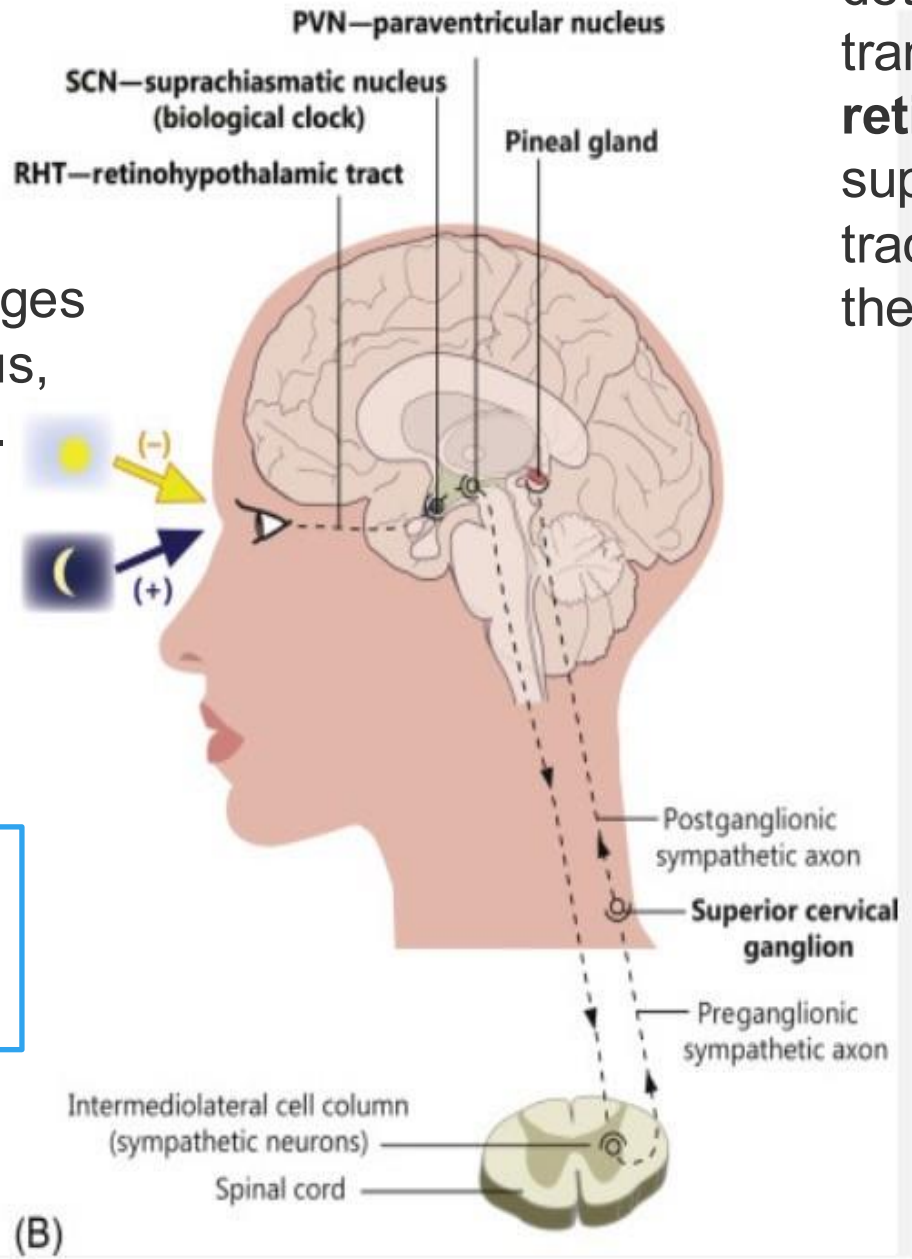
in this diagram, when melatonin concentration is high this will lead to inhibition of CRH, which is lead to less excitation for anterior pituitary which will give me less ACTH going to adrenal gland leading to lower cortisol

In contrast, during the day (light hours) where melatonin is low causing relief to the inhibitory function we talked about (basically excitation lead to more ACTH from the pituitary and excitation of the adrenal gland eventually more cortisol)

Melatonin release is **promoted** by darkness and **inhibited** by daylight.

Diurnal fluctuation in blood melatonin levels---rhythmic changes in the activity of the hypothalamus, PG, and other endocrine tissues.

The pineal gland---a neuroendocrine transducer, converting sensory input into variations in many hormonal functions.



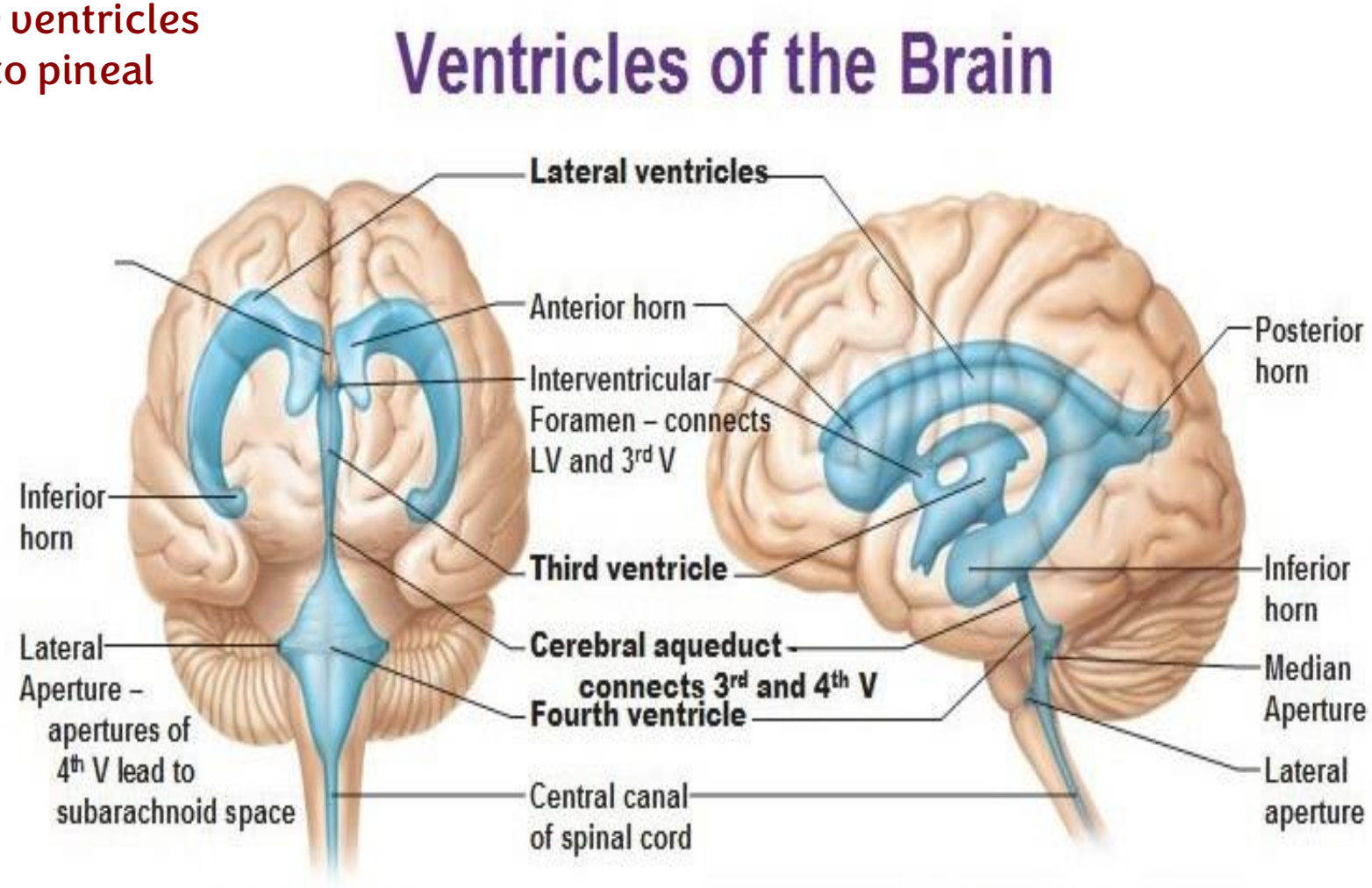
The cycle of light and darkness is detected within the retinas and transmitted to the pineal via the **retinohypothalamic tract**, the suprachiasmatic nucleus, and the tracts of sympathetic fibers entering the pineal G.

So how does melatonin know when its dark or light outside? By a close connection between our visual system and the pineal gland, so it's our retina that's telling us if its dark or light! The less light detected by our retina the more melatonin produced, which gets transferred to pineal gland by retinohypothalamic tract, which will also relay in the hypothalamic nuclei (specifically in the suprachiasmatic nucleus and the paraventicular nucleus) then the message will be taken down to the spinal cord, from the spinal cord—> preganglionic —> postganglionic neurons in the superior cervical ganglion, then to pineal gland which will finally deliver the message to the pineal of what's happening outside the body!!

- to recap:
- From the retinas —>retinohypothalamic tract —> goes to nuclei in hypothalamus —> relays the sensory the information —> descends to spinal cord —> preganglionic —> postganglionic in the superior cervical ganglion—> synapses with pineal gland —> pineal gland is able to tell if its dark or light and produces melatonin accordingly !!!!
- Essentially the pineal gland is a neuroendocrine transducer, translation a sensory input to an endocrine product(melatonin) effecting the sleep-awake cycle (the circadian rhythm).

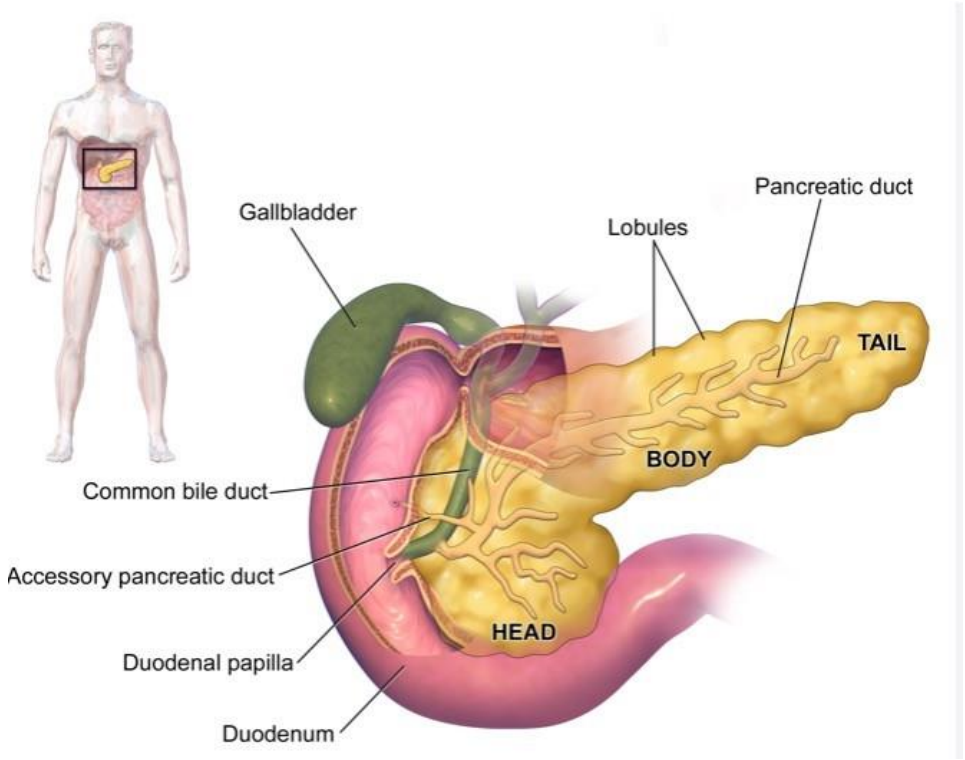
Pineal Glands

Image to see the ventricles and its relation to pineal gland!!!



The pancreatic islets (Islets of Langerhans)

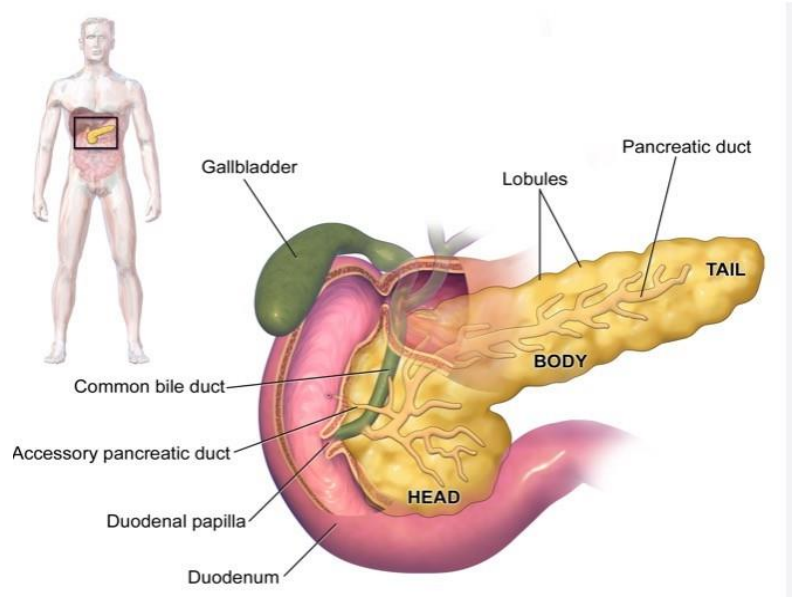
- Are compact spherical or ovoid masses of endocrine cells embedded within the acinar exocrine tissue of the pancreas.
- Most islets are 100-200 μm in diameter **making it relatively large under the microscope** and contain several hundred cells, but some have only a few cells.
- The pancreas has more than 1 million islets (mostly in tail region).



The pancreatic islets (Islets of Langerhans)

•The surrounding **exocrine pancreas** stains **intensely basophilic** due to its abundant rough endoplasmic reticulum (RER) and numerous protein-rich secretory granules. In contrast, the **islets of Langerhans** stain **less basophilic** and therefore appear **relatively acidophilic (paler)** than the surrounding exocrine tissue, allowing them to be readily distinguished on histological sections. *(The islets are also **highly vascular**, containing numerous **fenestrated capillaries** that facilitate the rapid release of hormones into the bloodstream.)*

•The apparent size of an islet in a histological section depends on the **plane of section**: a **central cut** appears larger, whereas a **peripheral cut** appears smaller.



•The **entire pancreas**, including both the **exocrine** and **endocrine** components, develops from the **endoderm**. *(Specifically, it arises from the **dorsal and ventral pancreatic buds**, which later fuse to form the definitive pancreas.)*

- Although both components share the same embryological origin, different developmental pathways and molecular signaling mechanisms determine whether precursor cells differentiate into **exocrine** or **endocrine** pancreatic tissue. *(The endocrine cells subsequently aggregate to form the **islets of Langerhans**, whereas the exocrine cells differentiate into the **pancreatic acini and ductal system**.)*

ISLETS OF LANGERHANS PANCREAS

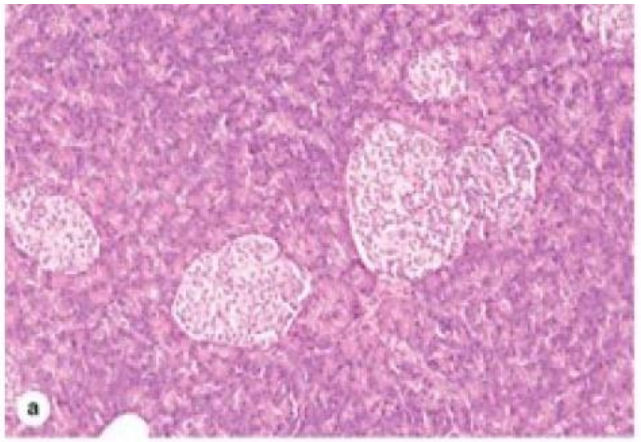
The Pancreatic Islets (Islets of Langerhans)

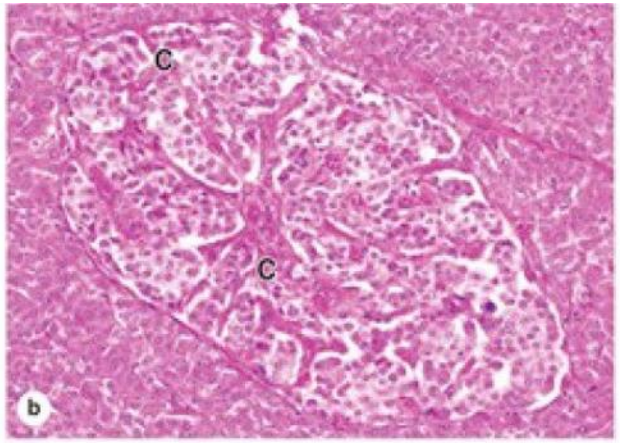
MAINLY EXOCRINE but 1% of it is endocrine cause SOME of its secretory cells synthesize and release hormones.

Scattered among exocrine parts is islets of langerhans, now structure wise they look totally different, and around them like a small "nest" made up of reticular fibers surrounding them
Now if u look closely the parenchyma of these islets are sinusoids,

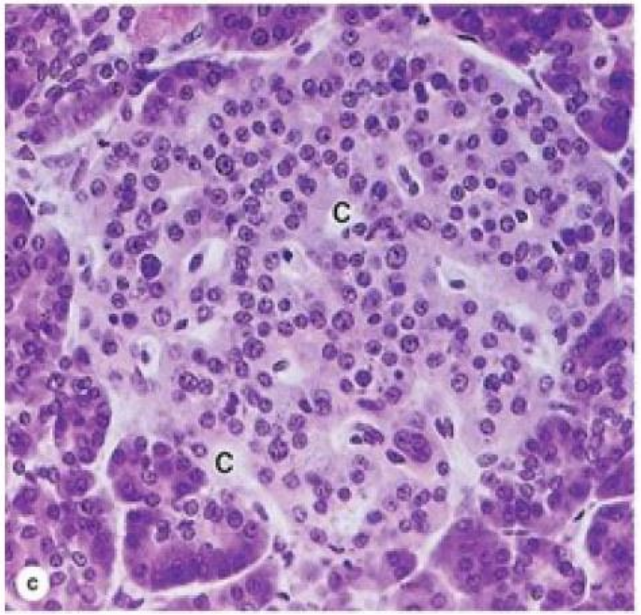
- They only constitute 1-2% of the organ's total volume.
- A thin reticular capsule surrounds each islet, separating it from the adjacent acinar tissue.
- Have the same embryonic origin as the pancreatic acinar tissue: in epithelial outgrowths from **endoderm** of the developing gut.

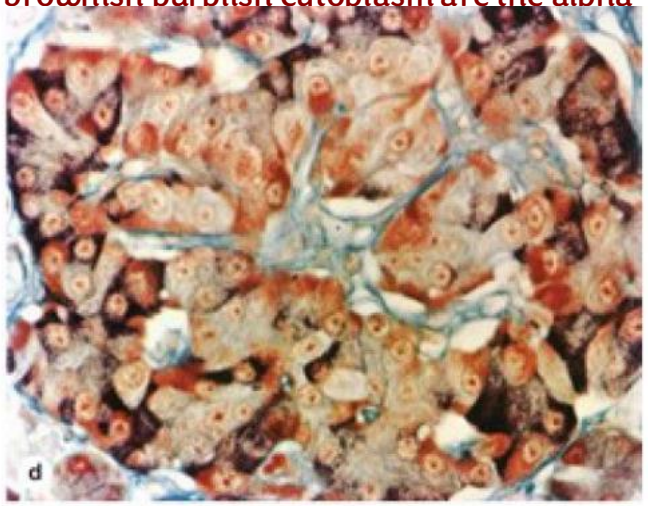
Endocrine cells stain less basophilic than exocrine ones plus arranged in cords and lined up and surrounded by fenestrated capillaries.





Special stain! Modified aldehyde fuchsin, the blue greenish color is reticular support
The brownish purplish cytoplasm are the alpha cell





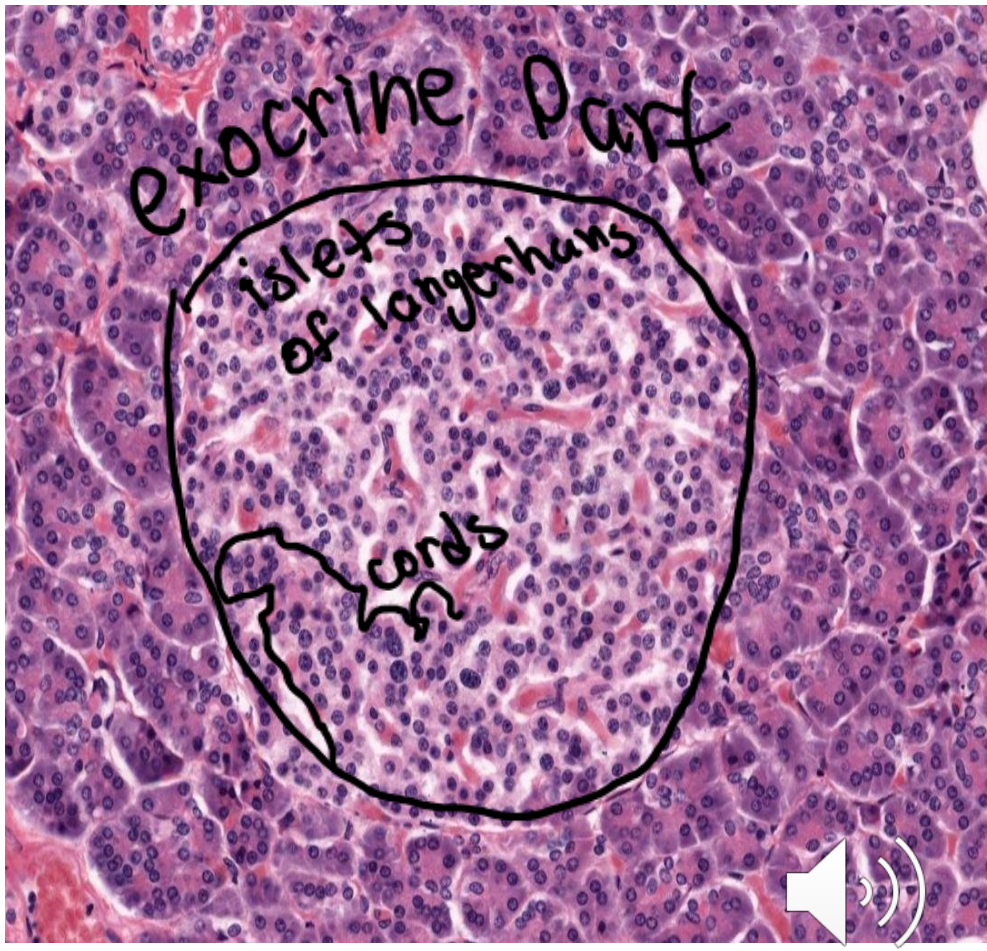
The golden-brownish /orangish are the beta cells

(a-c) H&E staining at different magnifications.
(d) An islet prepared with a modified aldehyde fuchsin stain shows that granules in the peripheral **α cells** are a deep brownish purple and the central **β cells** granules are brownish orange. Reticulin connective tissue of the islet capsule and along the capillaries stains green in this preparation.

The Pancreatic Islets (Islets of Langerhans)

- The cells of islets are polygonal or rounded, smaller, and more lightly stained than the surrounding acinar cells,
- Arranged in cords separated by fenestrated capillaries.
- Most islet cells are acidophilic or basophilic with fine cytoplasmic granules.
- Active polypeptide-secreting cells, with secretory granules that vary in size, morphology, and electron density from cell to cell.

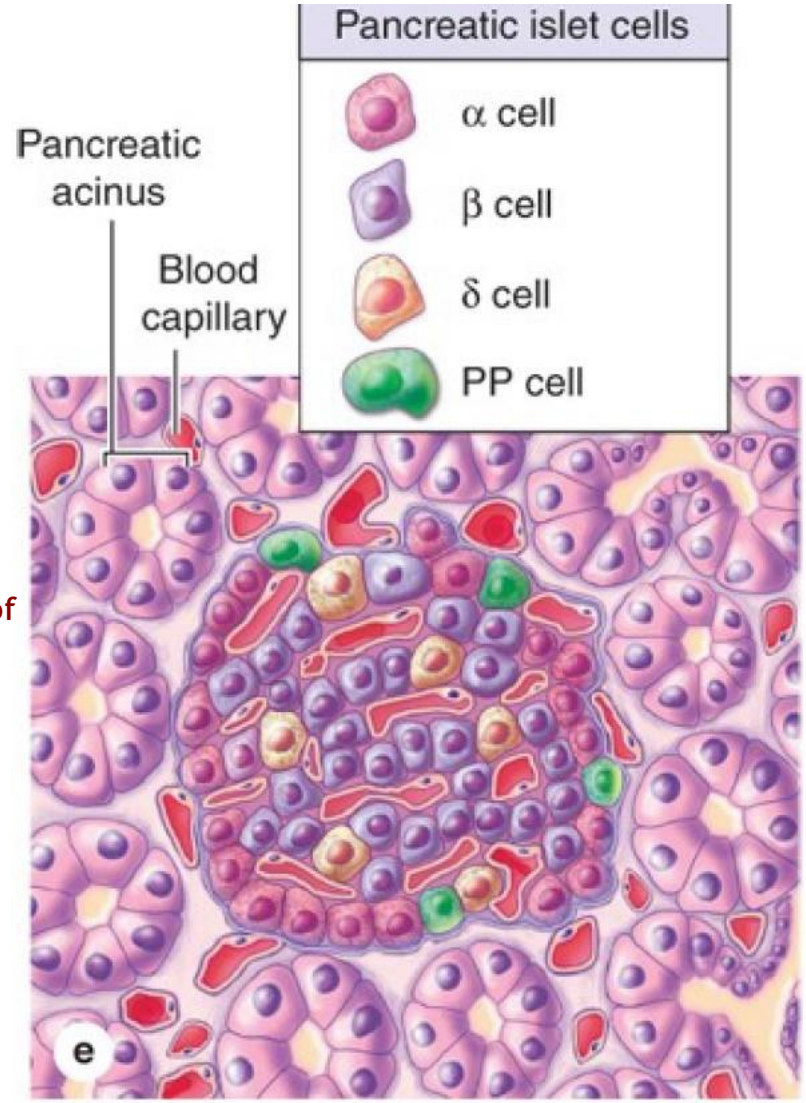
Also H&E stain but this one the sinusoids are clear

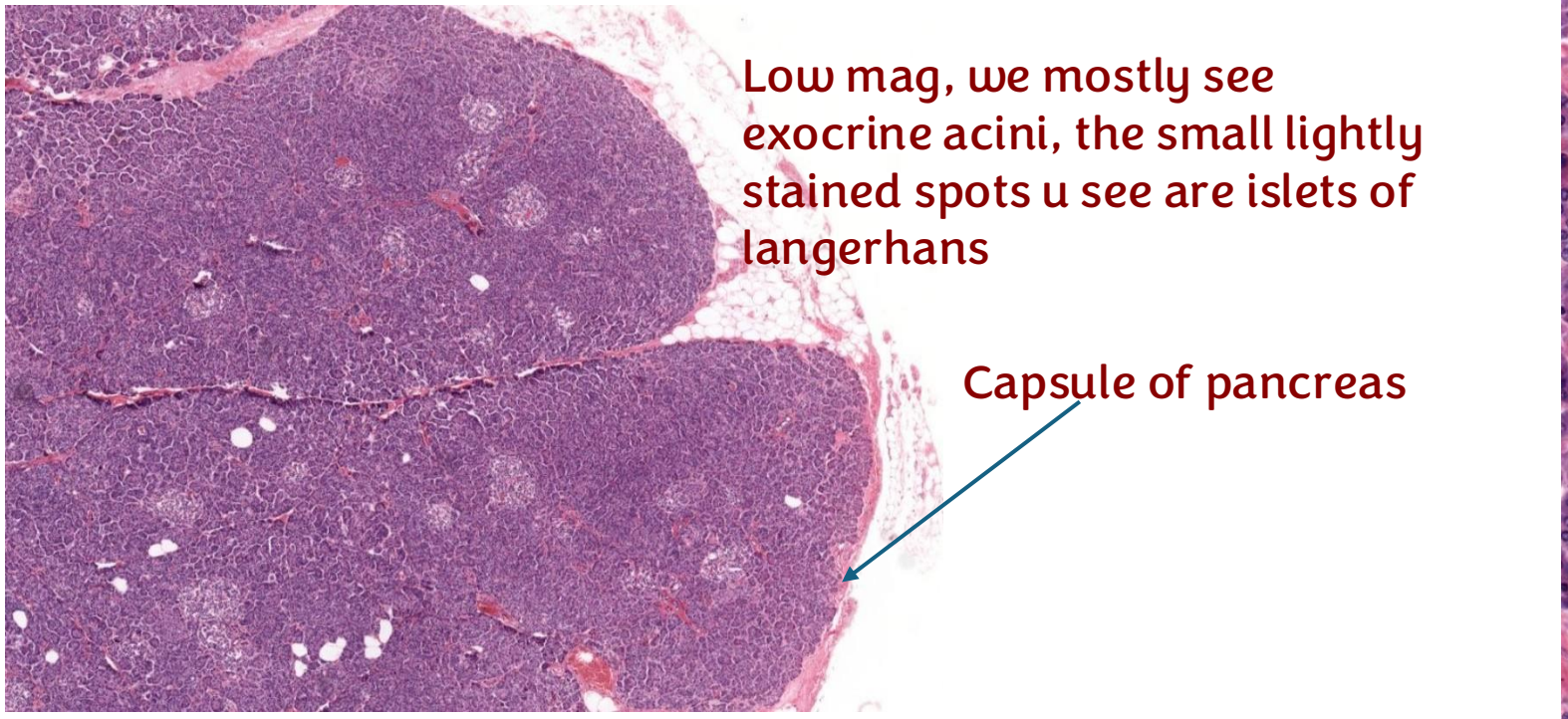


Cells

The Major islet cells:

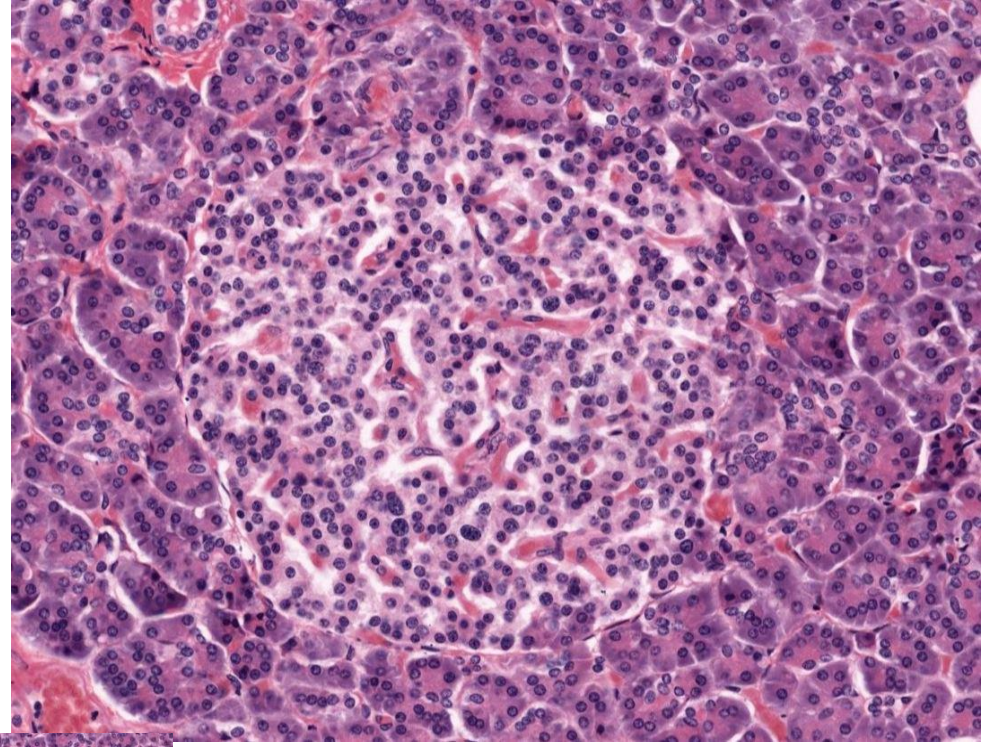
1. α or A cells secrete primarily **glucagon** and located peripherally. Lowers glucose, BUT glucagon doesn't work alone
2. β or B cells produce **insulin** (l. Insula, island), most numerous, and located centrally. Elevating glucose, insulin is the maestro of elevated sugar lvl
3. δ or D cells, secreting **somatostatin**, are scattered and much less abundant.
4. **PP** cells secrete **pancreatic polypeptide**, more common in islets located within the head.

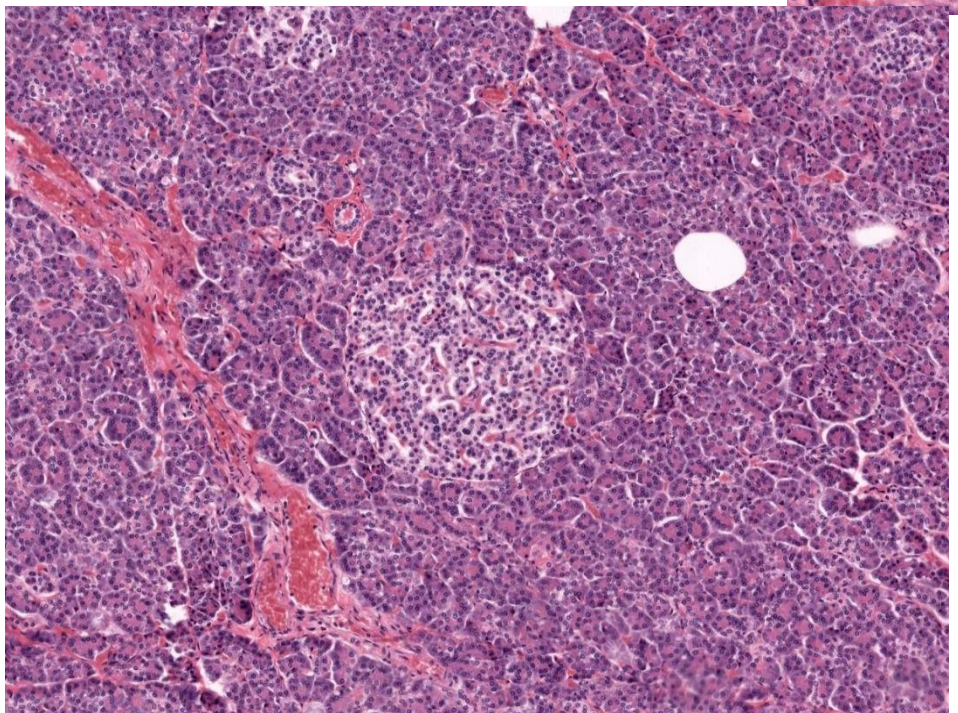




Low mag, we mostly see exocrine acini, the small lightly stained spots u see are islets of langerhans

Capsule of pancreas

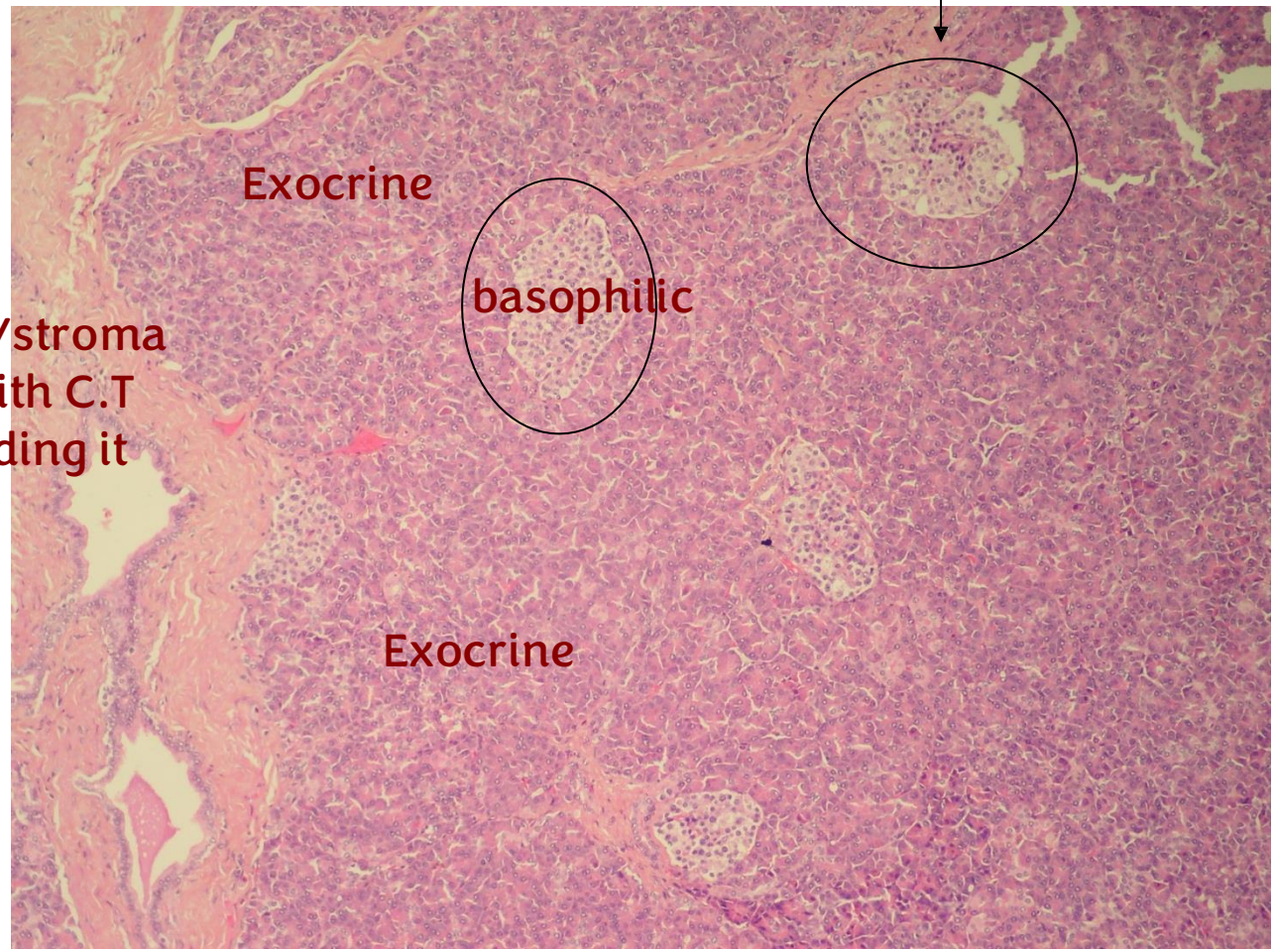




Enlarged

Lots of exocrine and lightly stained areas (islets)

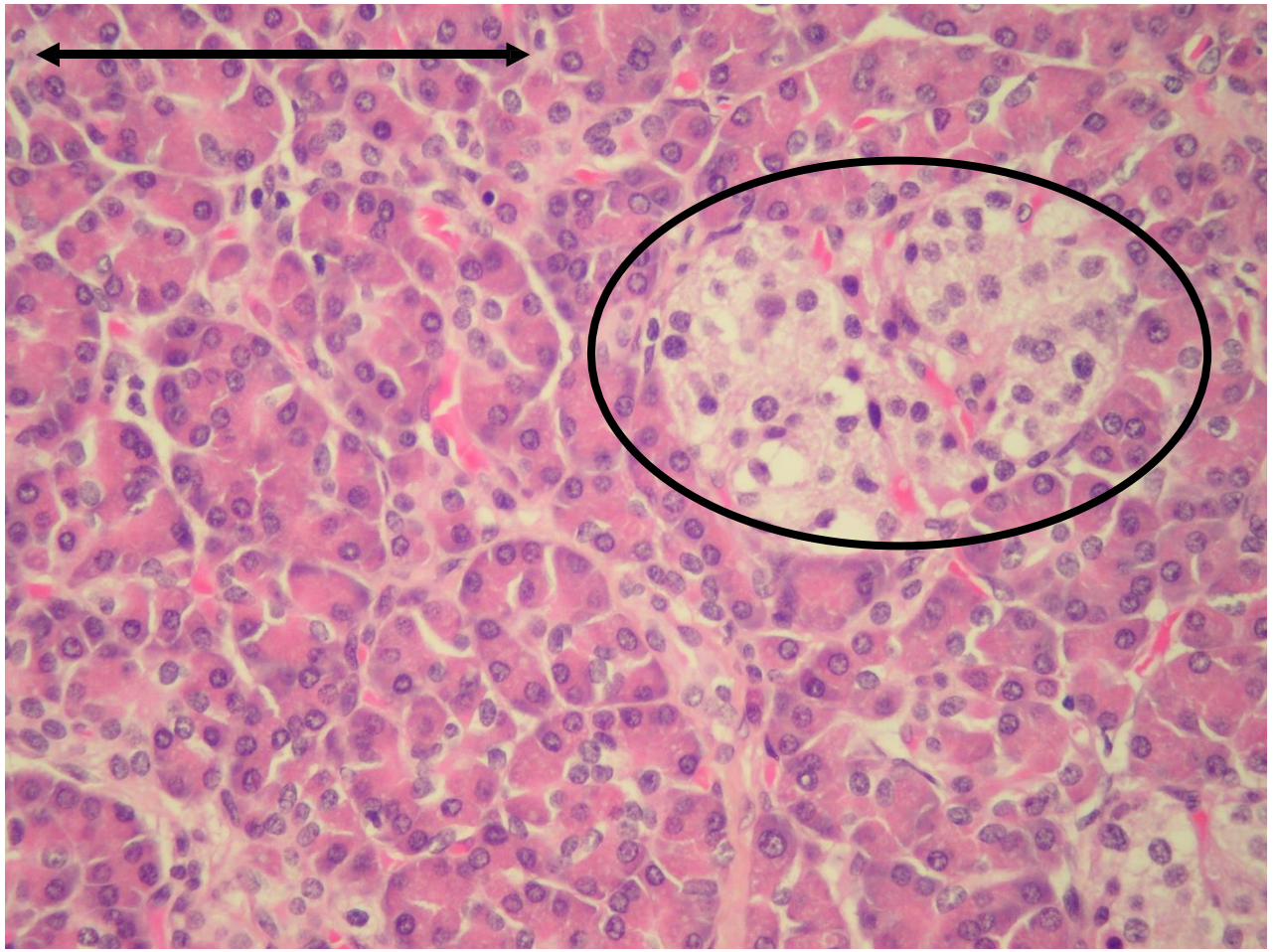
PANCREAS (EXOCRINE &ENDOCRINE)



Capsule/stroma inside with C.T surrounding it

Low mag. image, the lightly stained ones are islets

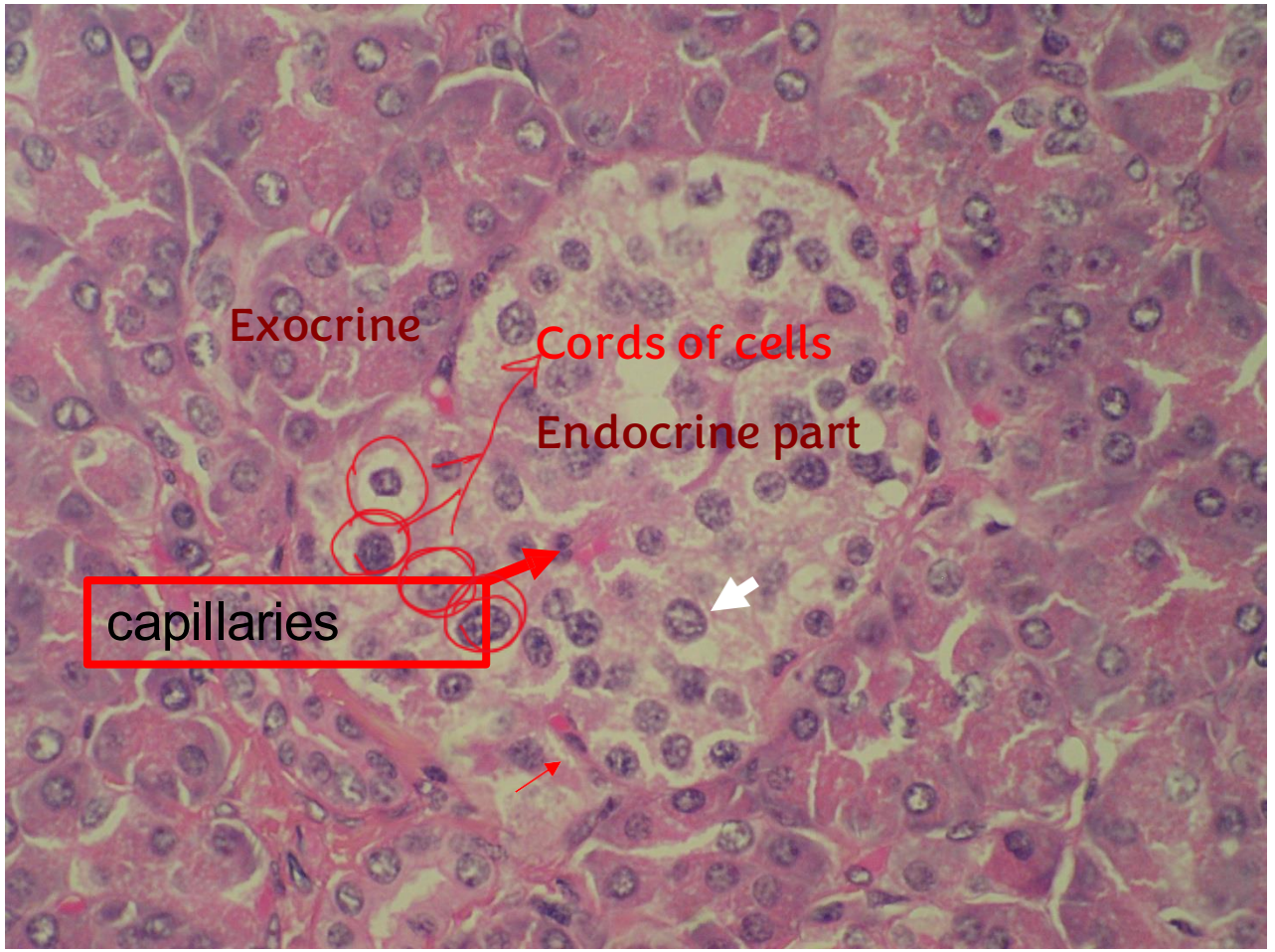
EXOCRINE PART &ENDOCRINE (ISLET OF LANGERHANS)



High mag. Islets plus capillaries inside

TYPES OF ENDOCRINE CELLS

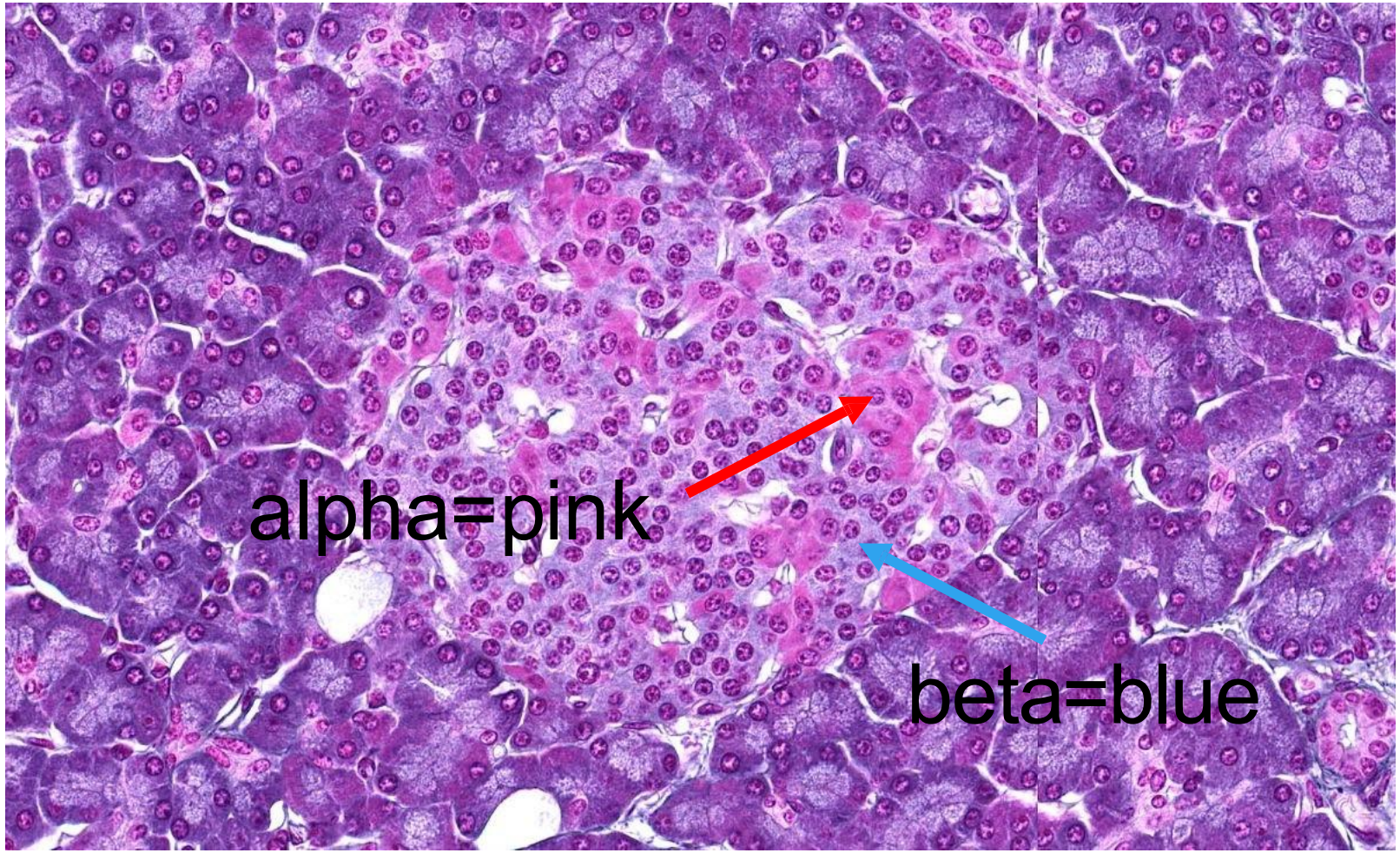
Same as previous!



Special stain!!

Islets of langerhans-Gomri's stain alpha Cs=pink, beta Cs=blue

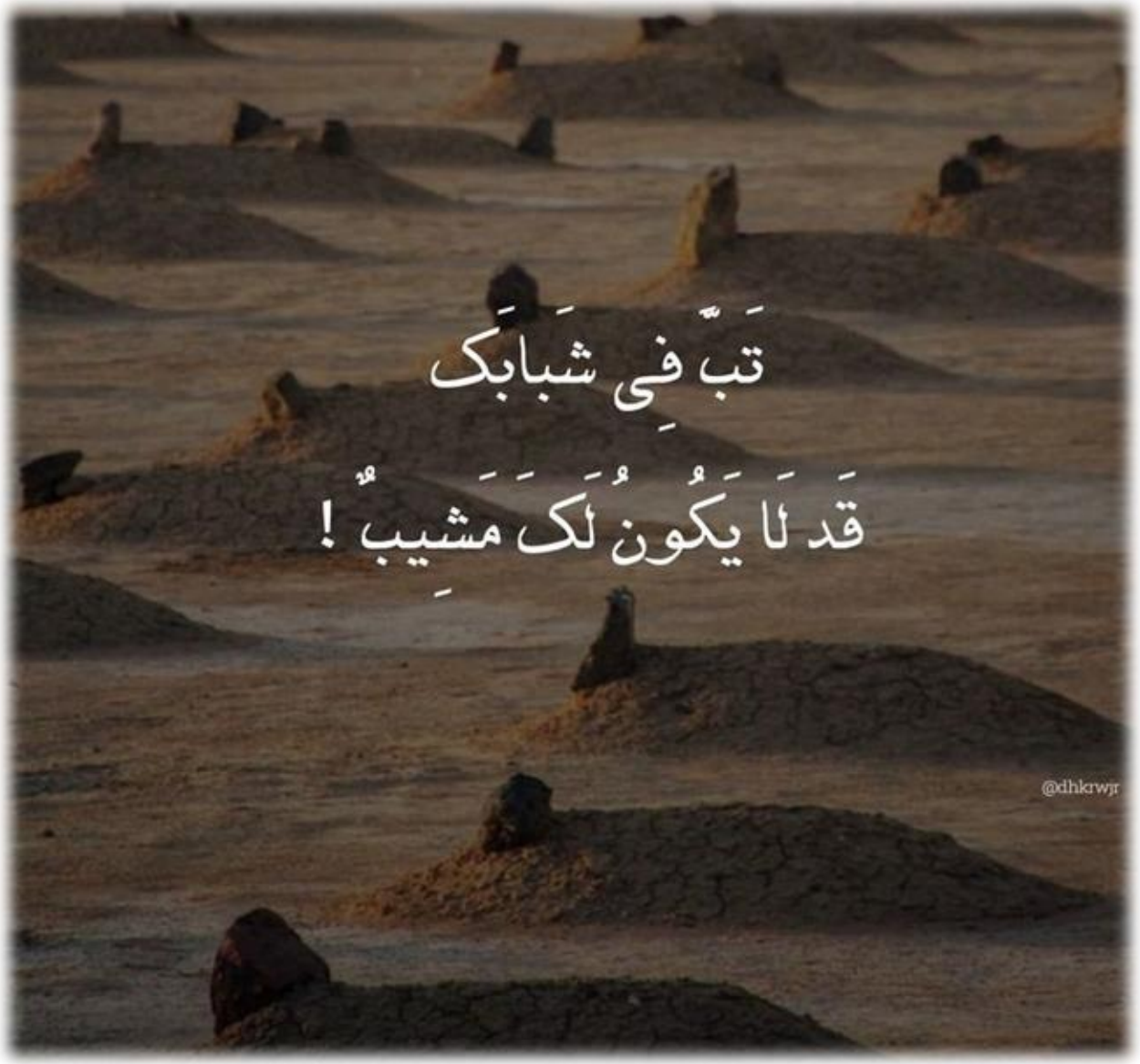
Eosinophilic cells are the alpha cells



We see diff types of cells and %, MEMORIZE IT PLUS THE FUNCTIONS!!!!!! </3

Cell Type	§uantity (%)	Hormone Produced	Hormone Structure and Size	Hormone Function
α	-20	Glucagon	Polypeptide; 3500 Da	A¢ts on several tissues to make energy stored in glycogen and fat available through glycogenolysis and lipolysis; increases blood glucose content
β	-T0	Insulin	Dimer of a and § chains with S-S bridges; 5700-6000Da	Acts on several tissues to cause entry of glucose into cells and promotes decrease of blood glucose content
6 or D	5-10	Somatostatin	Polypeptide; 1650 Da	Inhibits release of other islet ¢ell hormones through local paracrine action; inhibits release of Gh and TSh in anterior pituitaiy and HCl secretion by gastrit parietal cells
FP	Rare	Pancreatic polypeptide	Polypeptide; 4200 Da	Stimulates activity of gastric ¢hief cells; inhibits bile secretion, pancreatic enzym e and bicarbonate secretion, and intestinal m o tility

رسالة من الفريق العلمي:



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			