ENDOCRINE SYSTEM

Anatomy & Histology

Lec. Enter no.

WRITER: هي لله

CORRECTOR: فاعل خير

DOCTOR: غادة ابو الغنم

ما ينطق به الدكتور من شرح سيكون باللون الاحمر
وما يكون مهم في شرح الدكتور يكون باللون البنفسجي
ما يكون مهم في السلايدات يكون بخطين أو بخط

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.

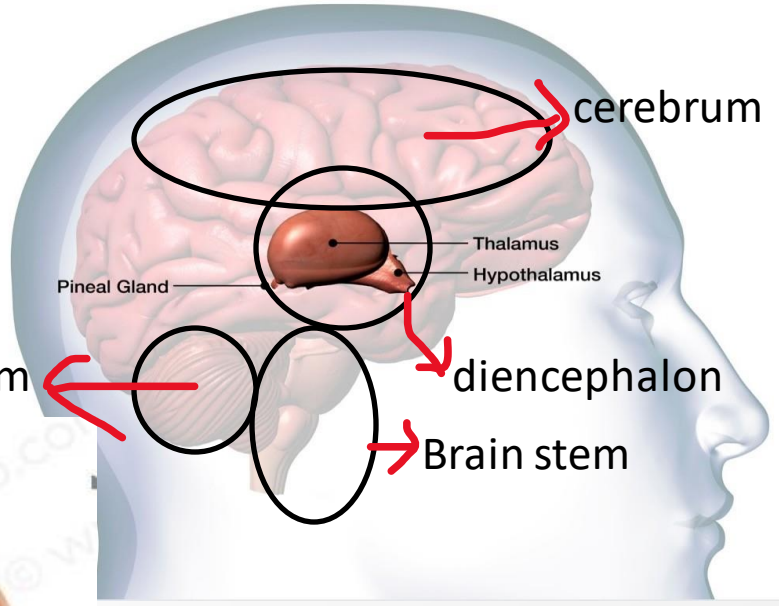
Ventricles are spaces within the brain that contain cerebrospinal fluid.

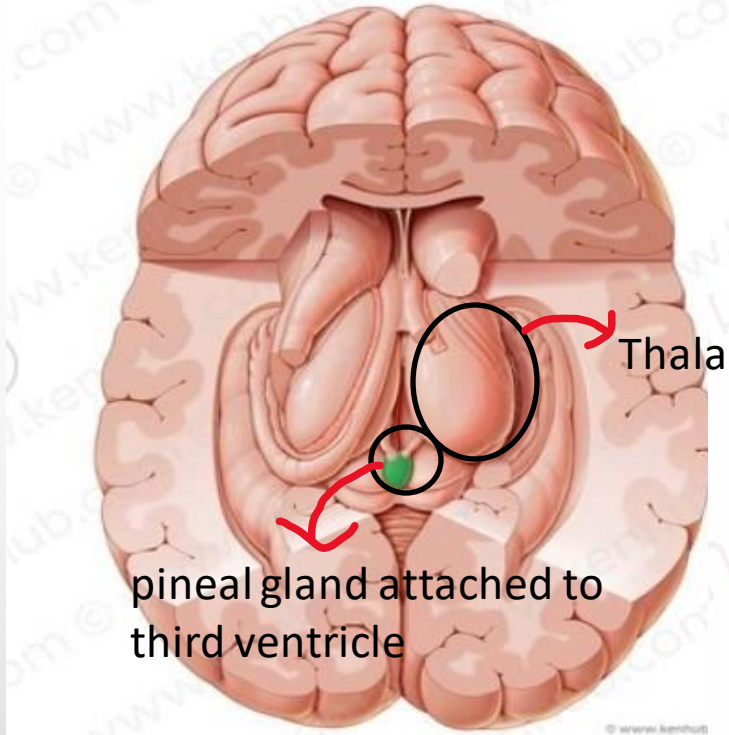
- Resides between the thalamic bodies.

- Has a rich blood supply

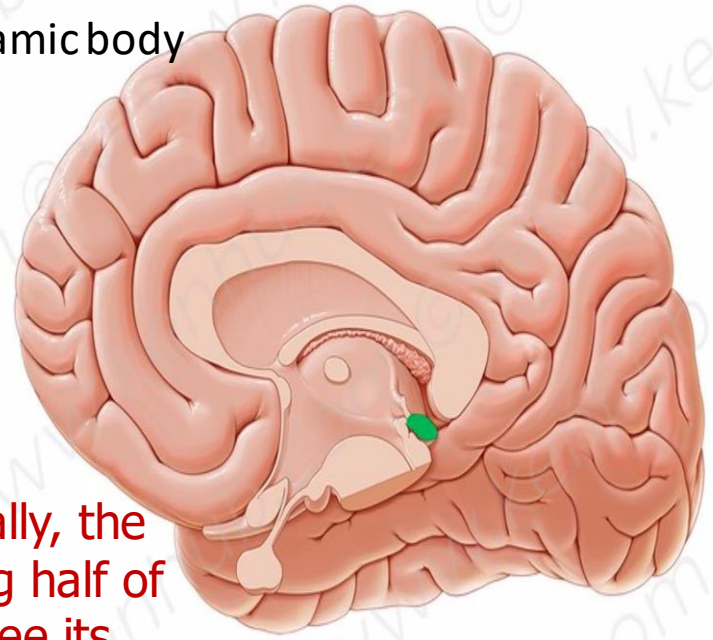
- it has adrenergic receptors, so Innervated by postganglionic sympathetic nerve fibers (SCG). it also has parasympathetic but we will discuss more about sympathetic.

- Covered by connective tissue of the pia mater (septa).The innermost layer of the meninges, and the most delicate one.





Inferior view



This is how it looks like laterally, the only way to see it is removing half of the brain that's only way to see its actually

Septa divide the gland into smaller compartments and allow large blood vessels to enter the gland. These vessels then break down into smaller capillaries to support the gland's secretion processes. This process is important for the production of melatonin, a hormone crucial for regulating our daily cycle

LOCATION/BLOOD SUPPLY

Location

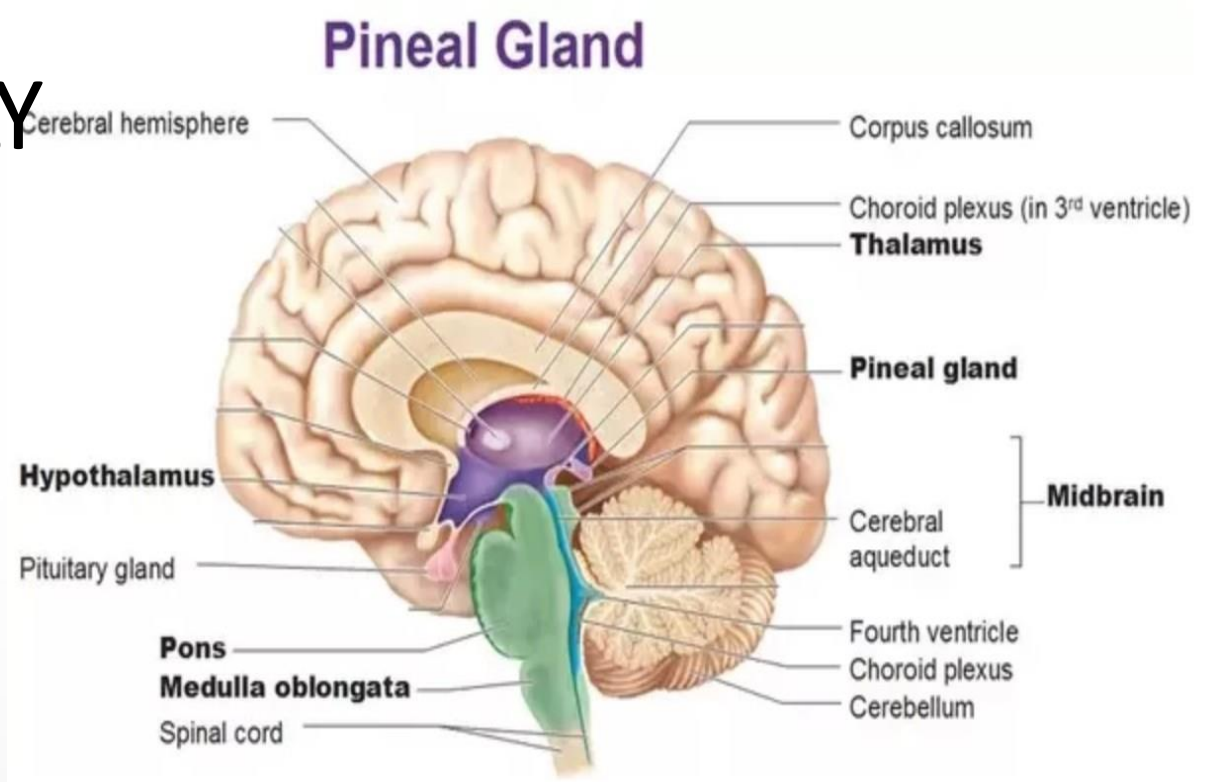
Is a midline structure, located between the two cerebral hemispheres. We have as we said to remove right or left hemispheres to see it.

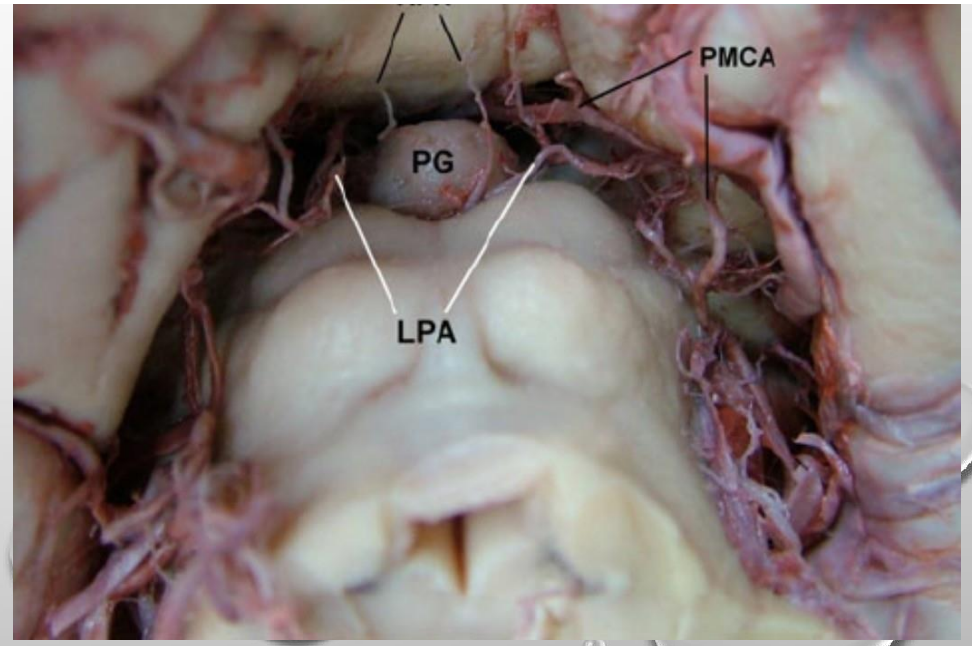
It is attached by a stalk to the posterior wall of third ventricle.

It is further closely related to the midbrain. (see picture 2)

Blood supply It is only second to kidneys in terms of how well vascularised it is.

• Lateral and medial pineal artery branches of the posterior choroidal arteries which are branches of posterior cerebral artery which is branch of terminal branch of basilar artery.





Organogenesis

- 7th-8th week Of gestation. الحمل

- Develops from neuroectoderm (brain tissue) (take its origin from 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, within this cavity, the parenchymal cells forms the secretory cells and the innervation also takes place.

Because they form gradually, they will be formed first as tubules and then those tubules will give rise to the final cells that they are called pinealocytes.
Side by side, the evolution of secretory cells will be also accompanied by the development of the innervation of this gland.

- 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.

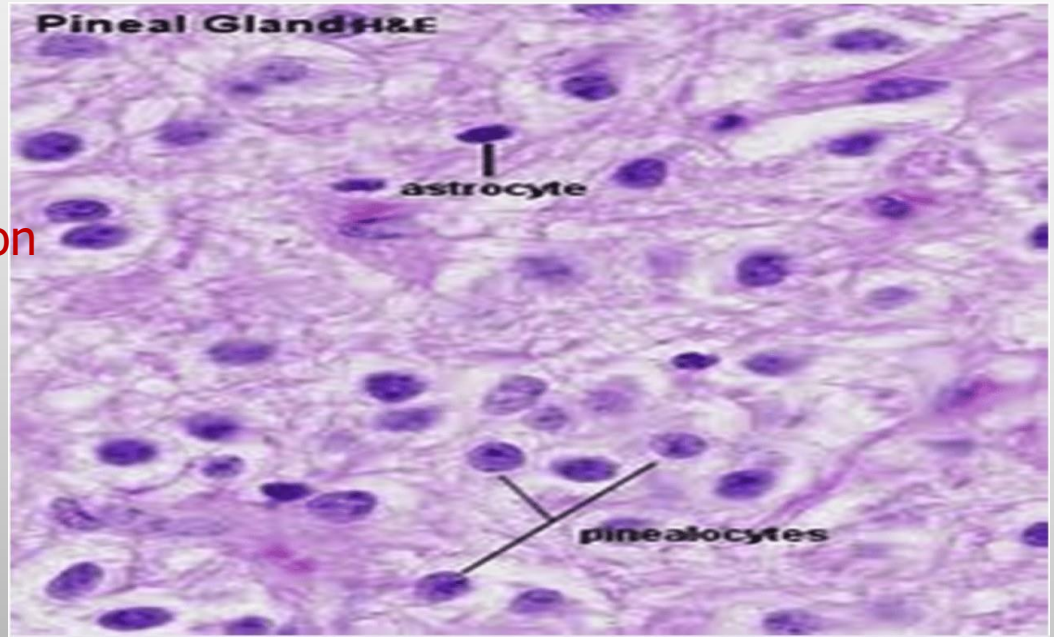
When we are born, this gland is said to be not fully mature, so it actually takes quite some time for this gland to reach its full secretory mode within the first decade of life. However, there is also evidence that from birth to 2 years of age, this period of time seems to be quite critical for its growth and function.

Histology

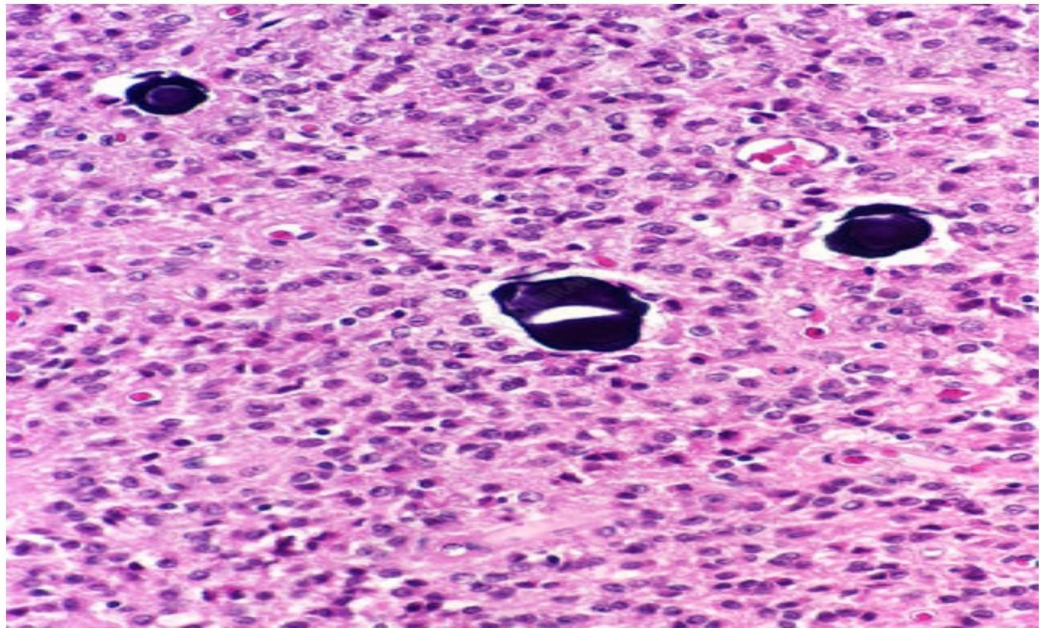
- Prominent and abundant secretory cells-pinealocytes.
- Slightly basophilic cytoplasm and irregular euchromatic nuclei
- Secretory vesicles, many mitochondria, and long cytoplasmic processes.
- Produce **melatonin**: a low-molecular-weight, derived of serotonin which is a tryptophan derivative.
- Unmyelinated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

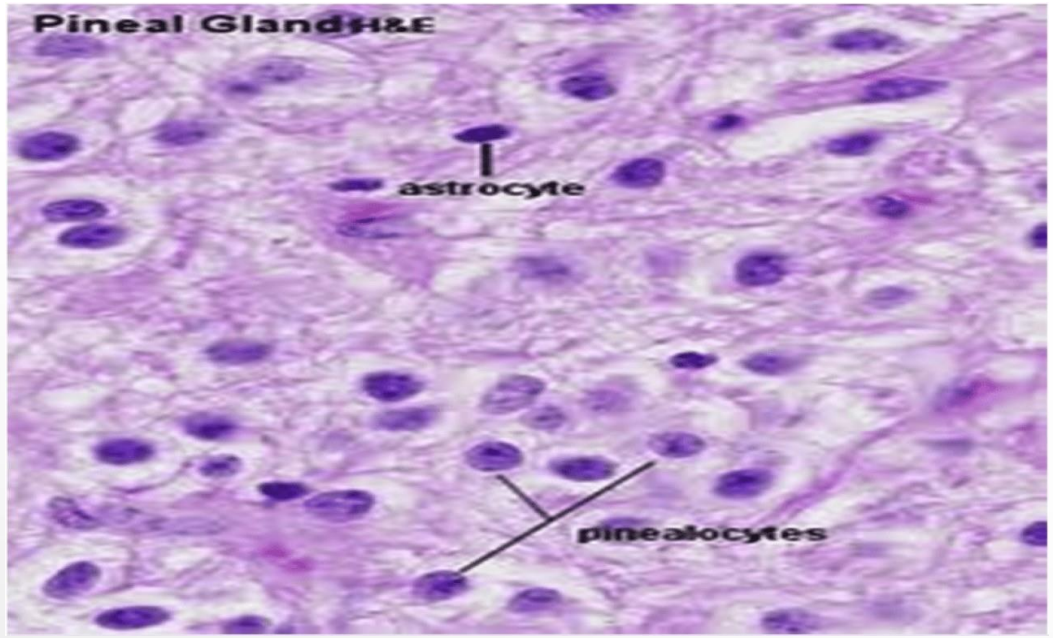
Both are stained with H&E stain and visualized by bright field like microscope.

High magnification



Low magnification





"Euchromatic" refers to the lightly stained regions of chromatin within the nucleus of a cell. These regions contain actively transcribed genes and are associated with the expression of genetic information. In the context of pinealocytes, larger euchromatic nuclei suggest that these cells are actively involved in gene expression and protein synthesis, which may be related to their secretory functions.

We will see a lot of cells, but if you pay attention, you will notice that some of those nuclei are different from the others and that's correct.

Most of the cells are pinealocytes (principal cells) those are the one that they are incharge of synthesis and release of melatonin.

However, we do have some glial cells up to 5% of the total cell population, so most of those cells are astrocytes.

How can I distinguish between them? simply the astrocytes have darker, smaller and more flattened nuclei, Whereas the ones for pinealocytes are the ones with larger euchromatic nuclei, and those are the most numerous.

The pinealocytes cytoplasm is slightly basophilic, it has secretory vesicles which is expected for any other endocrine cell, many mitochondria which is also expected.

These cells have long cytoplasmic processes, and upon closer inspection between the cells, linear structures can be observed. Although initially resembling filaments, these structures are actually more like linear formations.

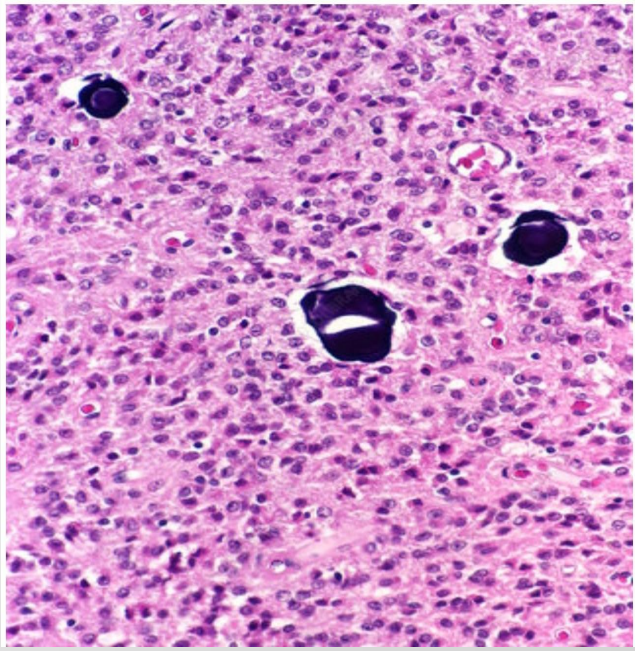
From chatGPT about linear structures:

linear structures between the cells could be pineal gland trabeculae or septa. These are thin, fibrous connective tissue partitions that extend into the gland, providing structural support and organization by dividing the glandular tissue into compartments. They may appear as linear formations when observed between cells. These structures play a role in supporting the gland's architecture and function.

This explanation seems to be logically correct but I don't know if it is scientifically correct according to previous picture.

Histology

• Has interstitial glial cells (modified astrocytes) which represent 5% of the cells---- elongated nuclei more heavily stained than those of pinealocytes and found in perivascular areas.



• Microglial cells are present too.

• **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.

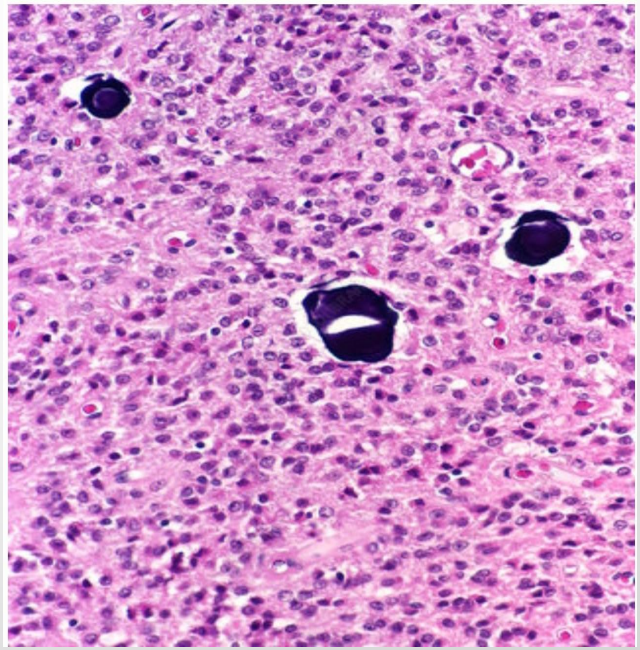
Another important feature of pineal gland are those dark regions, they are actually not that dark in higher magnified images, they appear more or less purplish.

They are called brain sand or corpora arenacea. These are simply concretions of calcium and magnesium salts. These salts bind to some extracellular proteins and then grow in size by accretion.

This happens because the gland tends to deposit calcium over time. There is clear evidence that the number and size of these brain sands increase with age. Therefore, we can use the size and amount of brain sand to tell which pineal gland is older than the other.

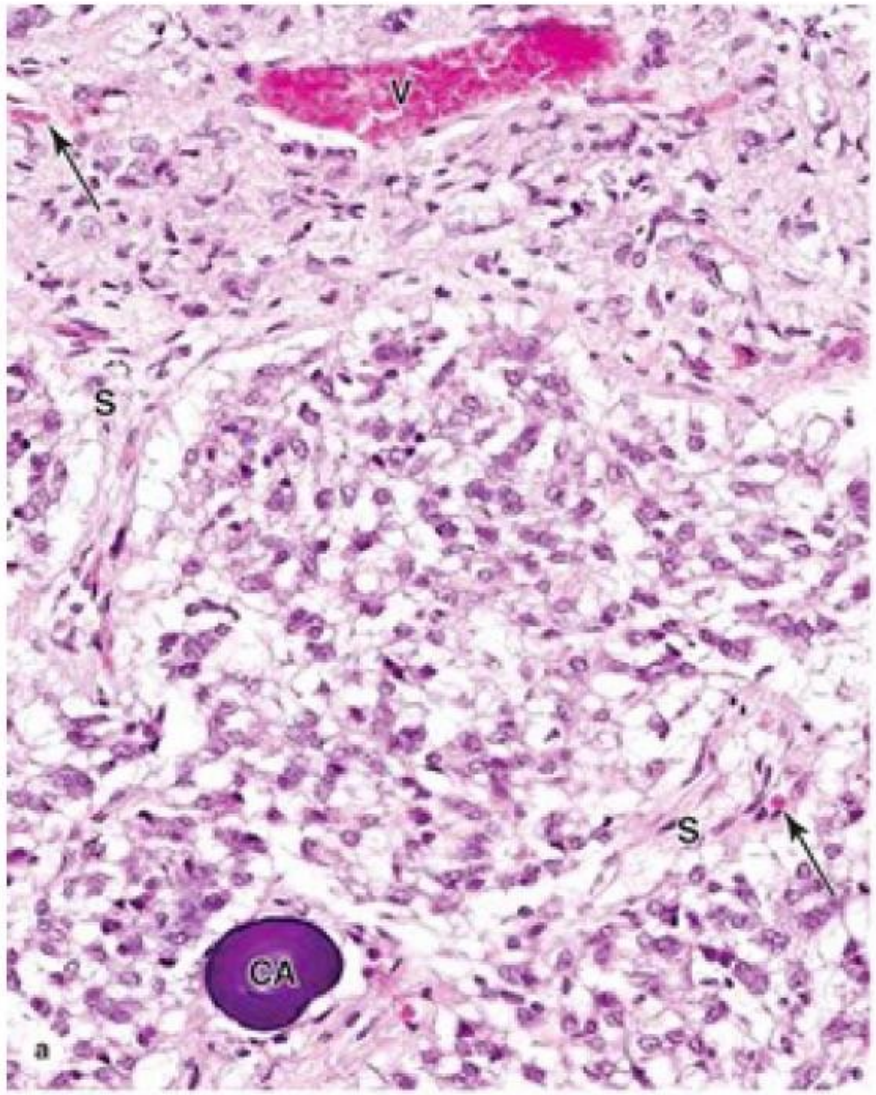
They can also be easily seen in brain radiographs, appearing as whitish regions. This allows us to locate the pineal gland by detecting brain sands.

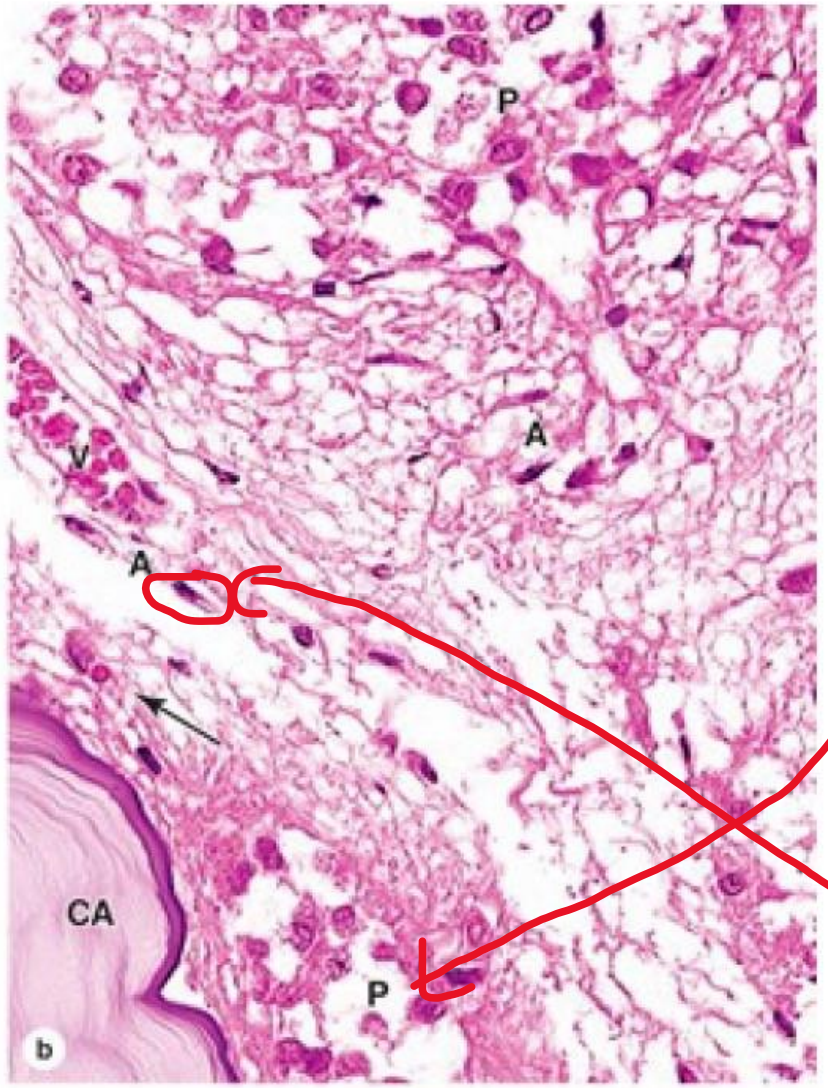
However, although they tend to increase in size and number with age, there is no apparent effect on the gland's function.



In this image, it is quite clear that there is some connective tissue surrounding a tiny compartment of cells. Most of the cells, even at this low magnification, are pinealocytes. The darker, smaller ones are astrocytes and other glial cells.

I can see brain sands or CA also.





You can see the waviness here, which is due to the accretion of calcium and magnesium. This process is evident as the deposits expand and become larger.

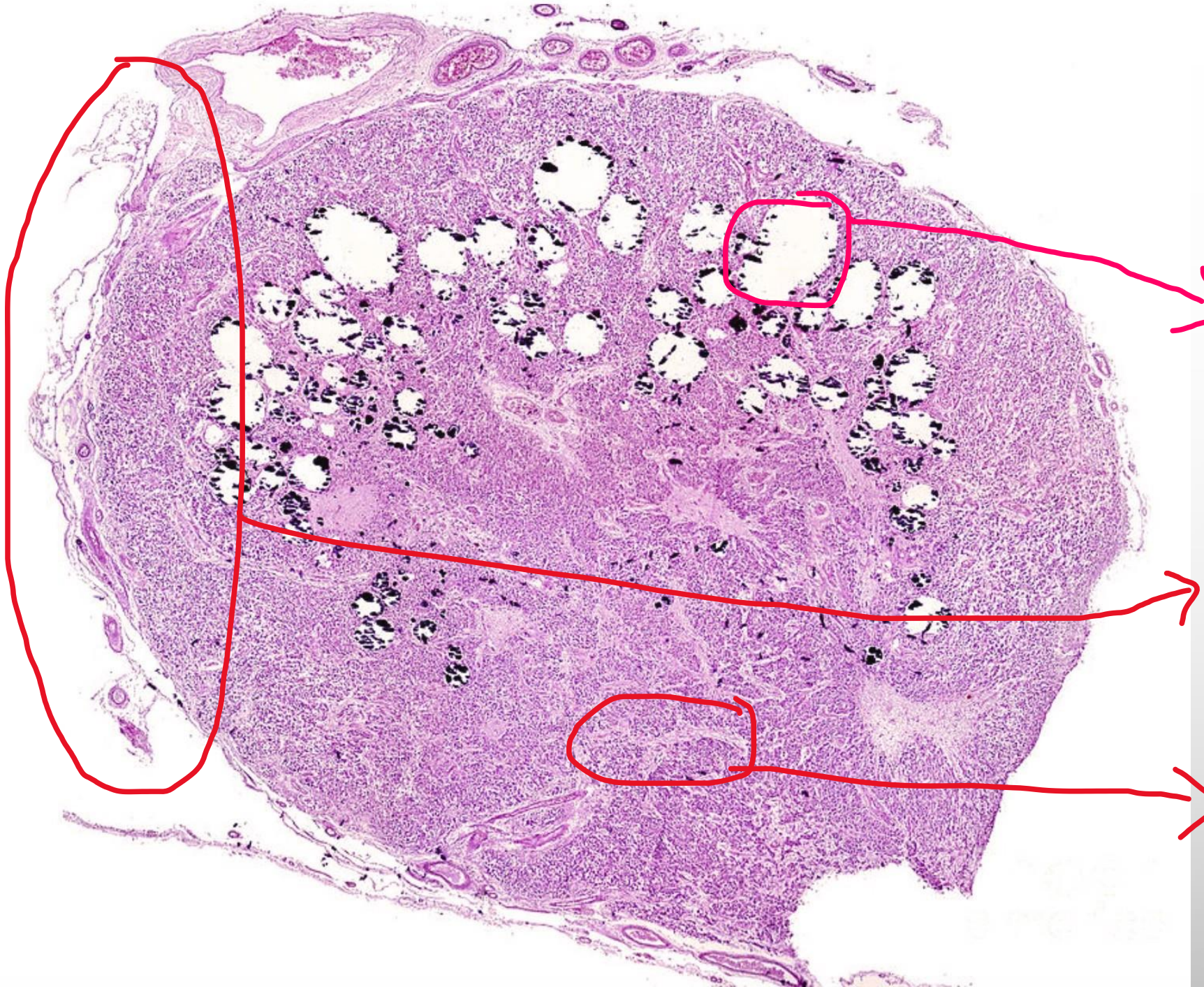
Most of the cells are pinealocytes,

while the flatten one are astrocytes.

• (A) pinealocytes surrounded by septa (S) venules (V) and capillaries (arrows). Extracellular mineral deposit: corpus arenaceum (C A) (marker for the pineal).

There are sinusoids throughout the structure of the gland. Since this is an endocrine gland, the high density of blood vessels is quite expected.

• (B) pinealocytes (p) fewer astrocytes (a)



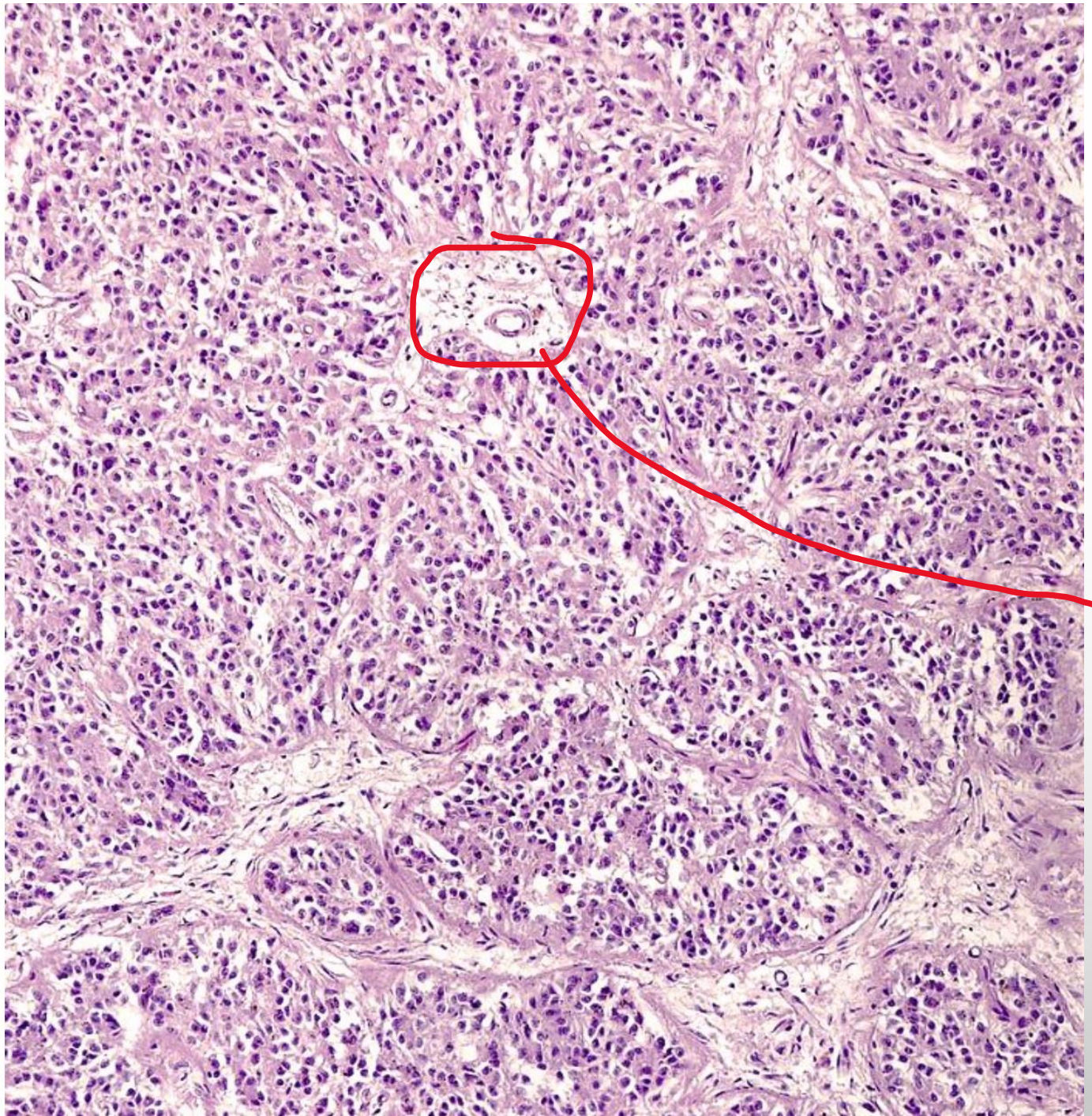
Low magnification.

A lot of brain sands and their size is quite huge.

You might wonder why there are whitish spaces instead of being filled with magnesium and calcium. This is simply due to the fact that they were washed away during histological preparations.

This is the connective tissue wrap derived from the pia mater. On the side here, we observe numerous blood vessels.

Deeper inside, we see the stroma or connective tissue that further divides the gland into smaller compartments.



High magnification.

We can recognize the connective tissue that divides the gland into smaller compartments.

Here, we observe a blood vessel running into it.

most of the cells are simply pinealocytes.

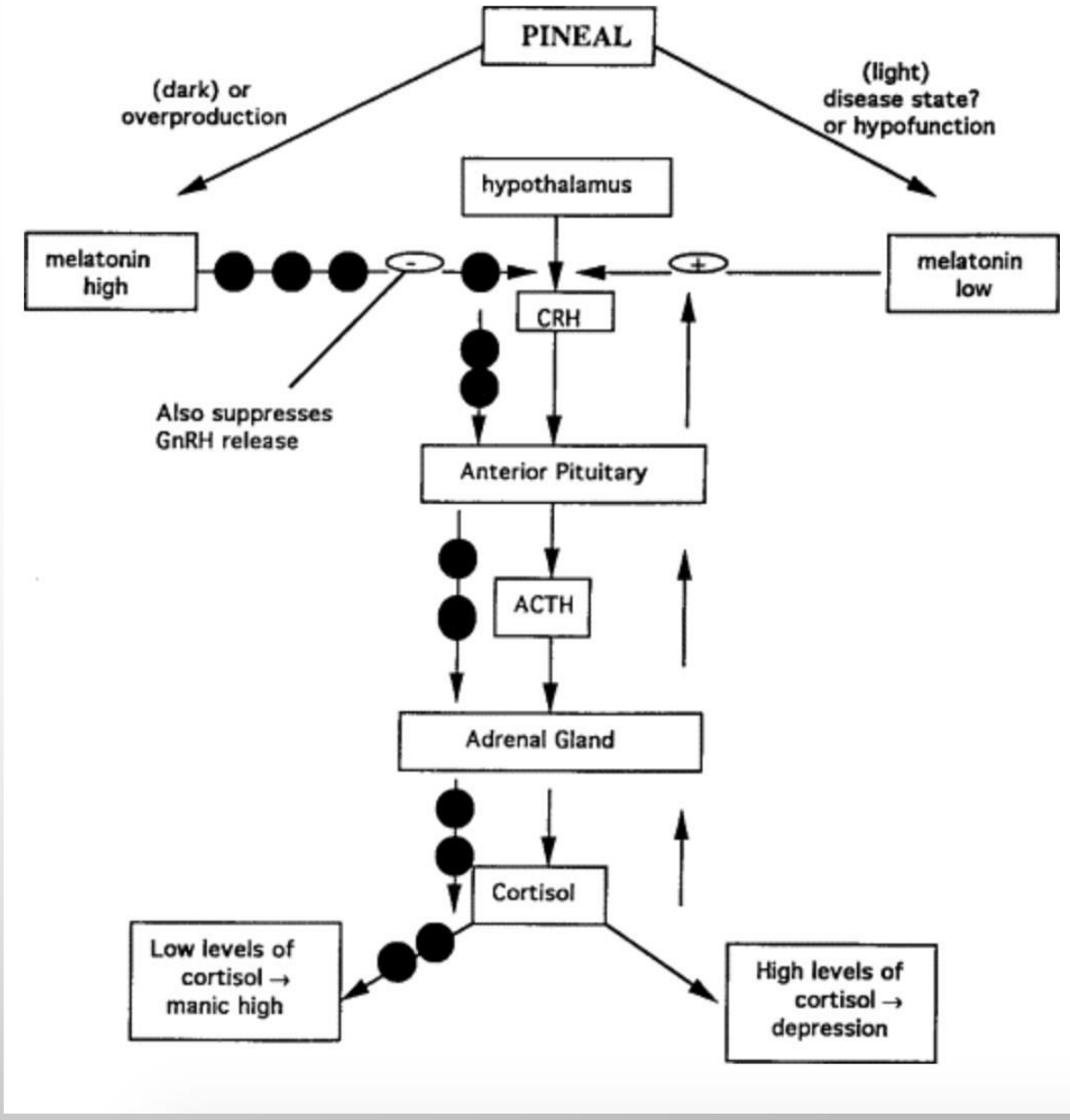
Pineal Gland Functions

• 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.



So, here will be discussing what the melatonin hormone do in general:

Melatonin hormone has inhibitory function on number of glands as you can see on the pituitary, parathyroid, adrenal, and the hypothalamus itself also!! So after being release by the pineal gland either to go into the bloodstream or the CSF it will circulate and reach on number of target cells

Okey, I get how is the general function but when it secreted in the highest of the most?

It secretes in the dark hours

Alright, but I didn't get exactly how it going to do the inhibitory effect?

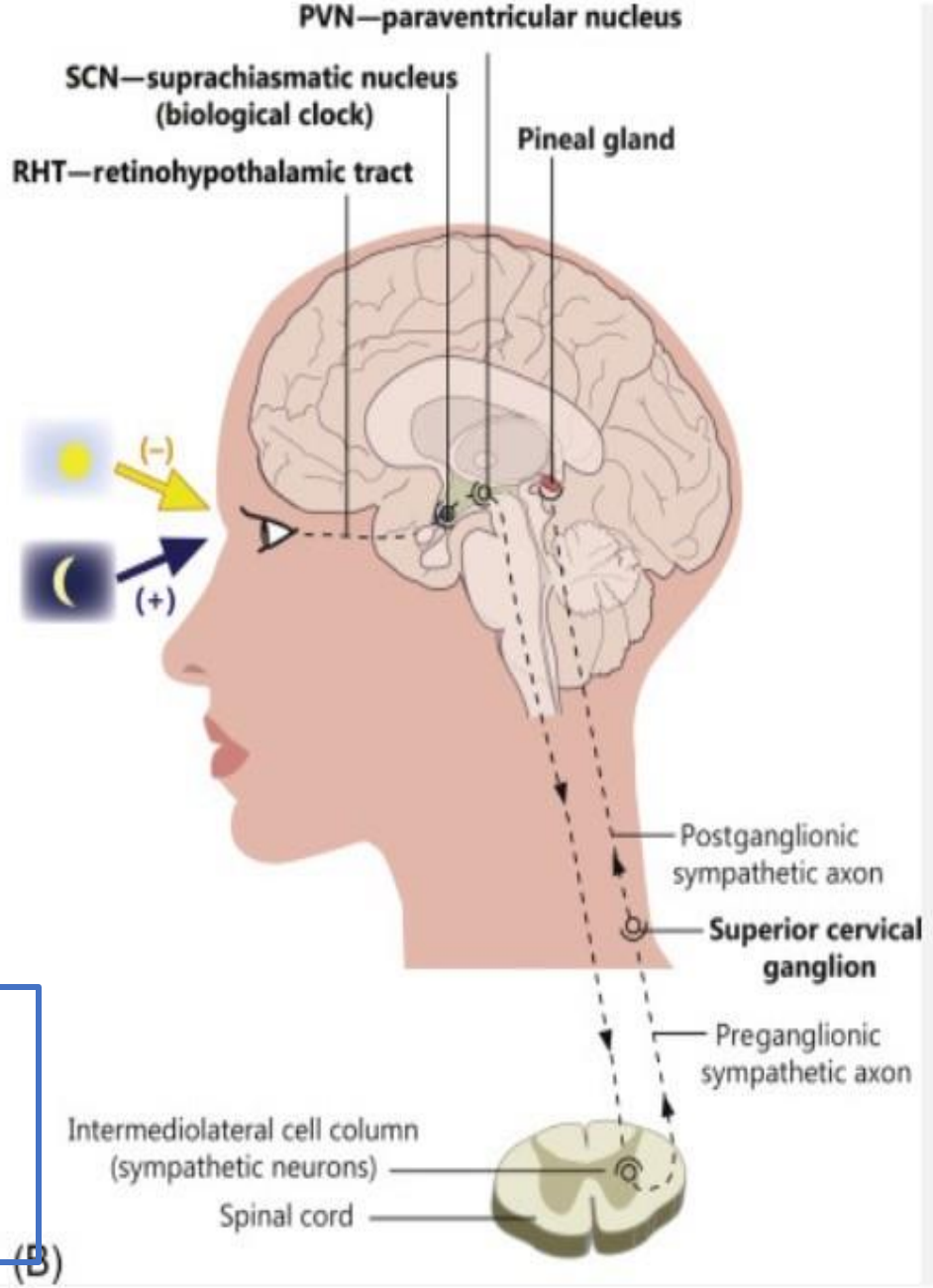
Melatonin inhibits the release of hormones directly or simply affecting the releasing hormones from the hypothalamus and this is regarding the pituitary, adrenal, hypothalamus axis.

To more understanding let's make a comparison between the dark and light hours to see how the melatonin actually work???

Dark hours	Light hours
So, as you can see in the image before, when the concentration [Melatonin] is higher this will lead an inhibition of CRH and it will lead to less excitation for the anterior pituitary to release the ACTH. So, when we have less ACTH going to the adrenal gland that will lower the [cortisol] and usually happens in dark hours	On the other hand, we will have less Melatonin will relief its inhibitory function on the axis that shown in the doctor's slide. So, we will have CRH, more ACTH, more excitation in Adrenal gland, and we will have higher cortisol in the blood

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 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.

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

Okey, I understand the function but the dark and light hours, how pineal knows there is light or dark, does it have eyes 😂, No , let's find out how it knows?

It simply a close association and connection between the visual system and the pineal gland. So, simply our retina is the one can tell us when it is dark or when it is light. So, simply Melatonin is released, and its concentration has detected a less light and then will be transferred to the pineal gland.

How will being transferred to the pineal gland?

By what we called it retino-hypothalamic nuclei which ones the supraoptic chiasmatic nucleus and the paraventricular nucleus so this 2 hormones will do a rely for this tract
Now, from there this message will also be taken all the way down to the spinal cord so from the spinal cord from the preganglionic and then to the postganglionic to the superior cervical ganglion we will have the final ural impulses that will eventually end in the pineal gland and then this will deliver the message to the pineal gland of what's going on outside the human body.

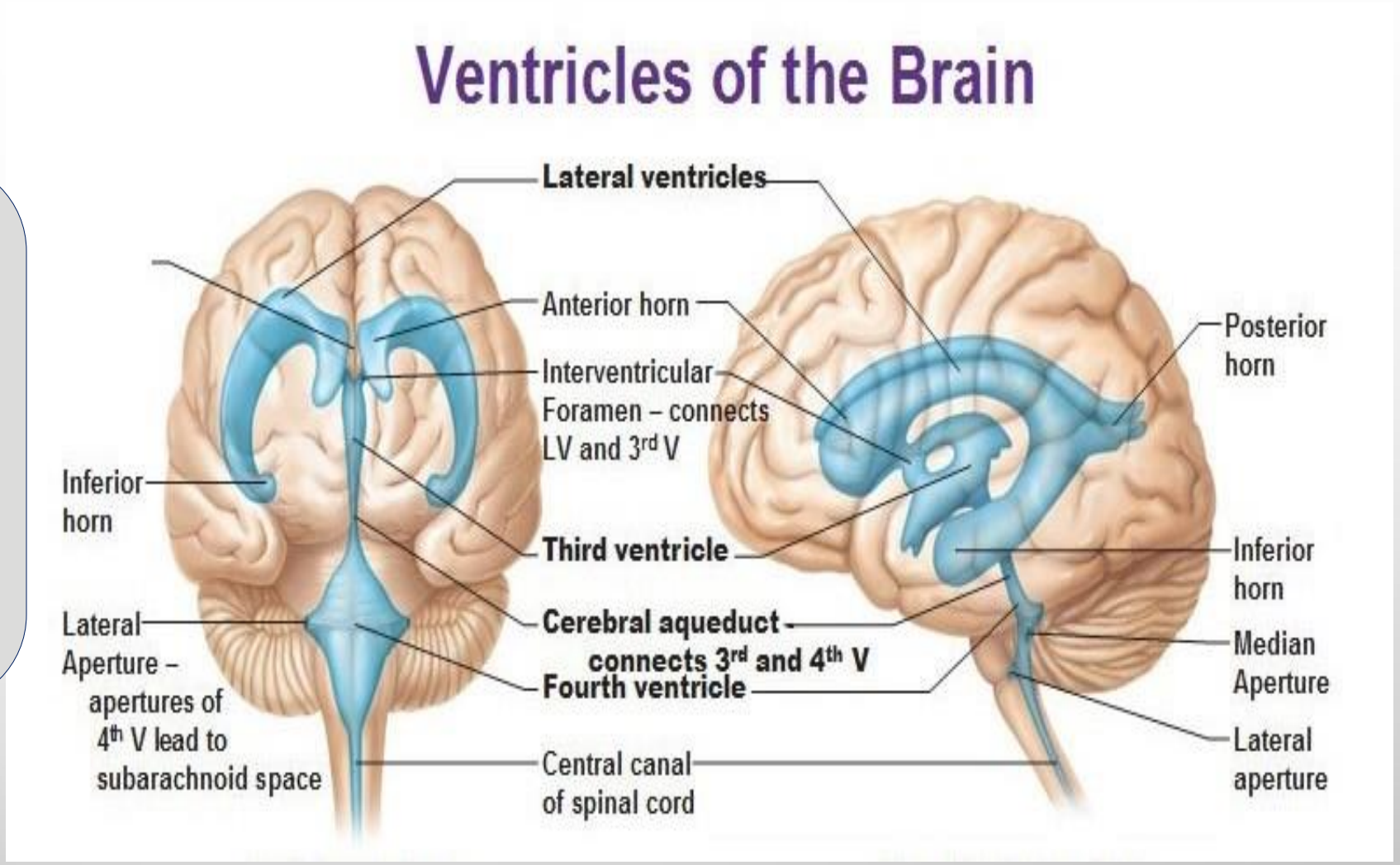
Quick recap:

Enter the light → retina → retino-hypothalamo tract → nuclei in the hypothalamus → they will rely this sensory information → from there it will descend to the spinal cord → they will do a rely of this message → to the preganglionic → we will have that being transferred → postganglionic neurons in the superior cervical ganglin → those postgangsympathatic axons will → letting know the pineal what the time now

So, simply the pineal gland it's a neuroendocrine transducer so it translated sensory inputs eventually into an endocrine product which will affect our wake-sleep cycle, it will affect our circadian rhythm

Pineal Glands

You can see the ventricles because we have talked about the third ventricle and its association with the pineal gland so you can relate this image when you look at it.

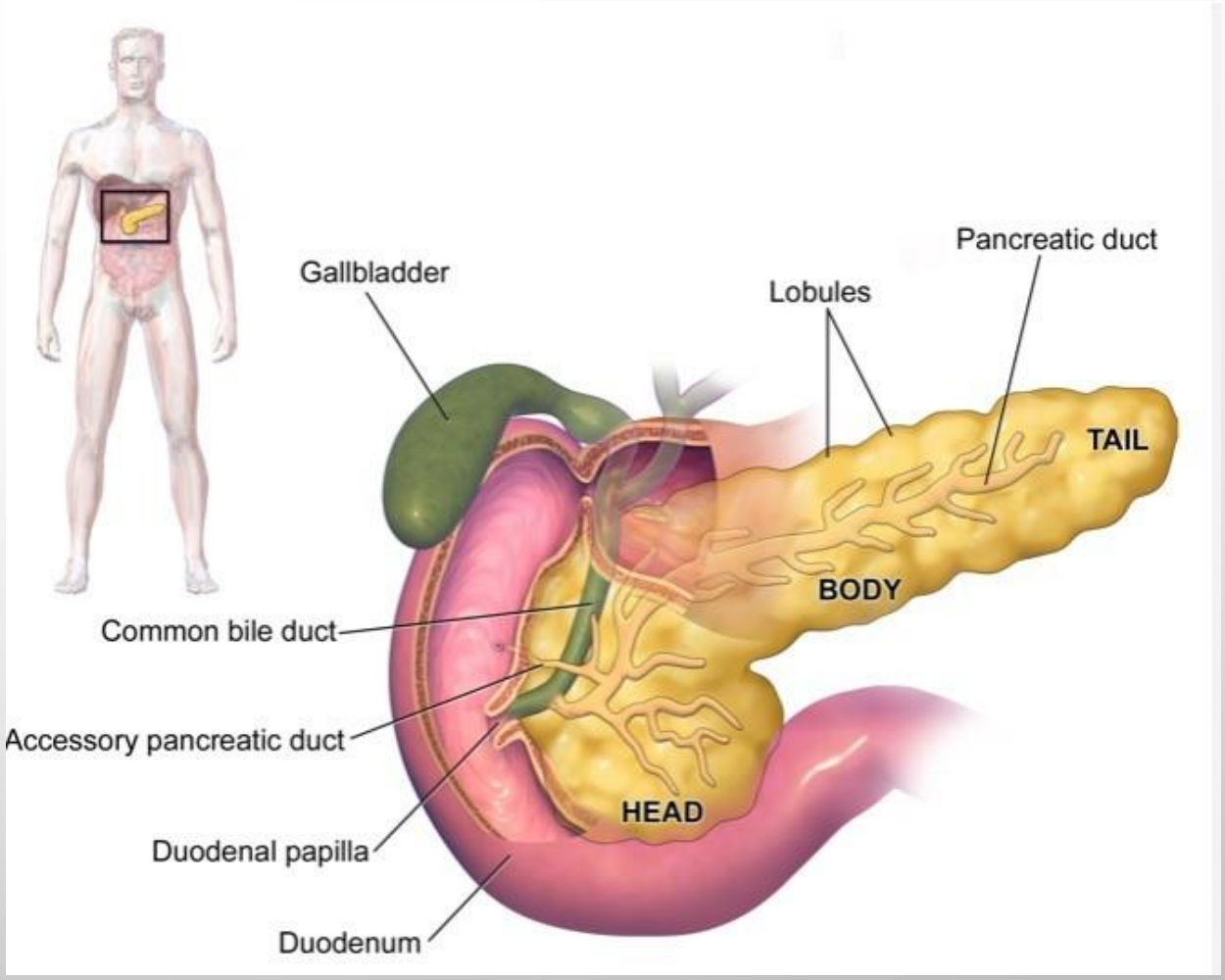


The pancreatic islets (Islets of Langerhans)

• 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 and contain several hundred cells, but some have only a few cells.

• The pancreas has more than 1 million islets (mostly in tail region).



ISLETS OF LANGERHANS PANCREAS

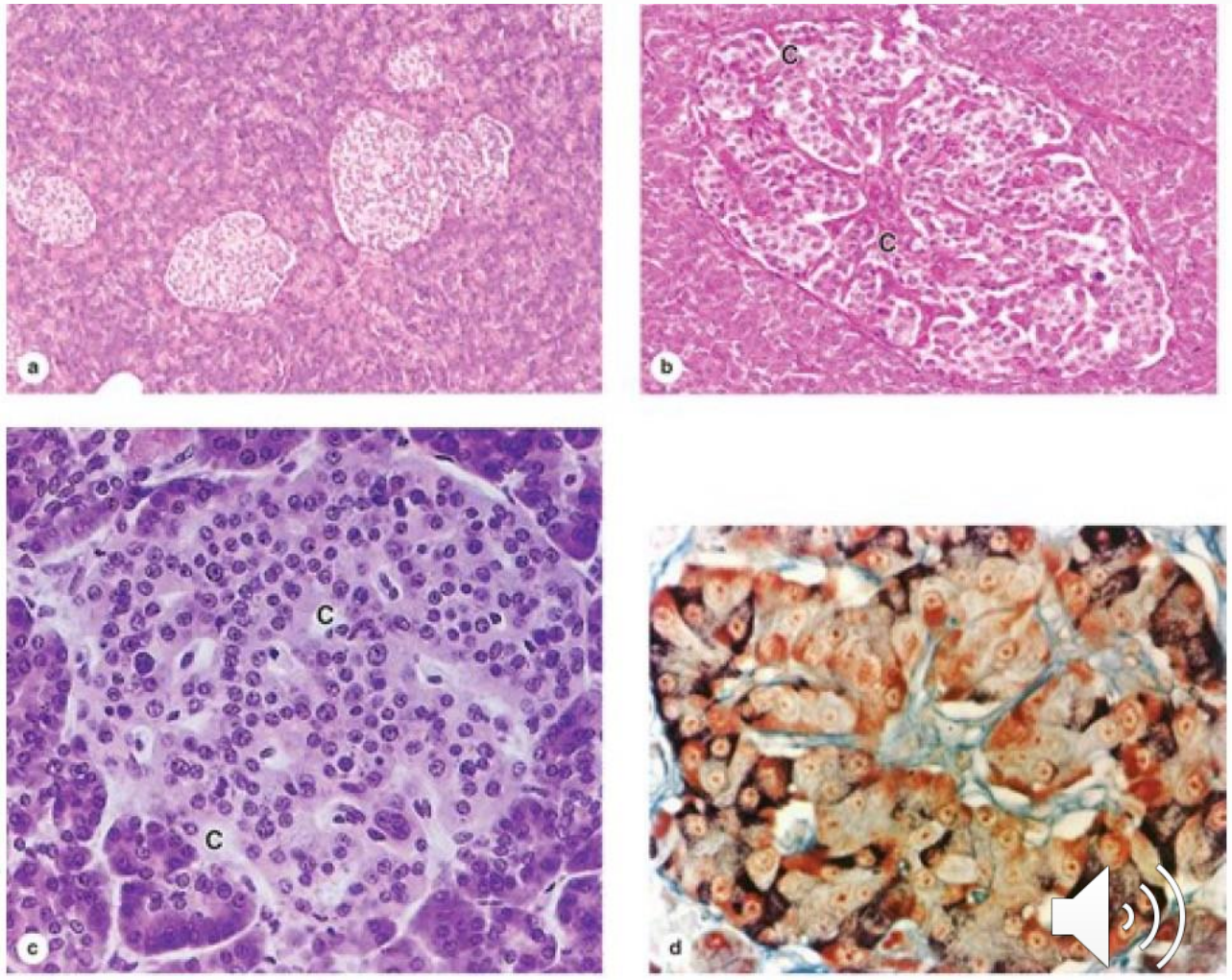
Now let's talk about the Islets of Langerhans in the Pancreas

The Pancreatic Islets (Islets of Langerhans)

- 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.

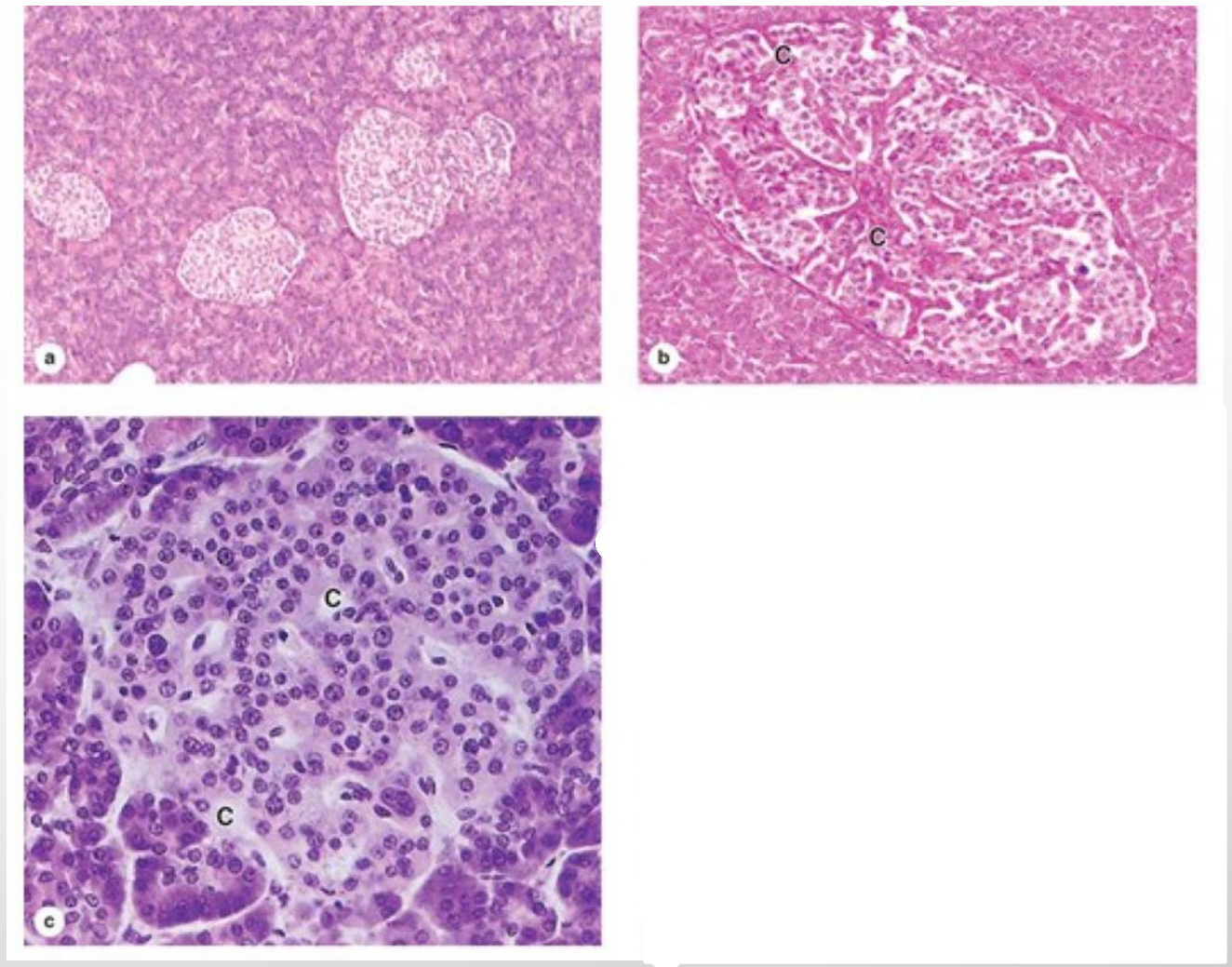
- Have the same embryonic origin as the pancreatic acinar tissue: in epithelial outgrowths from endoderm of the developing gut.



(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.

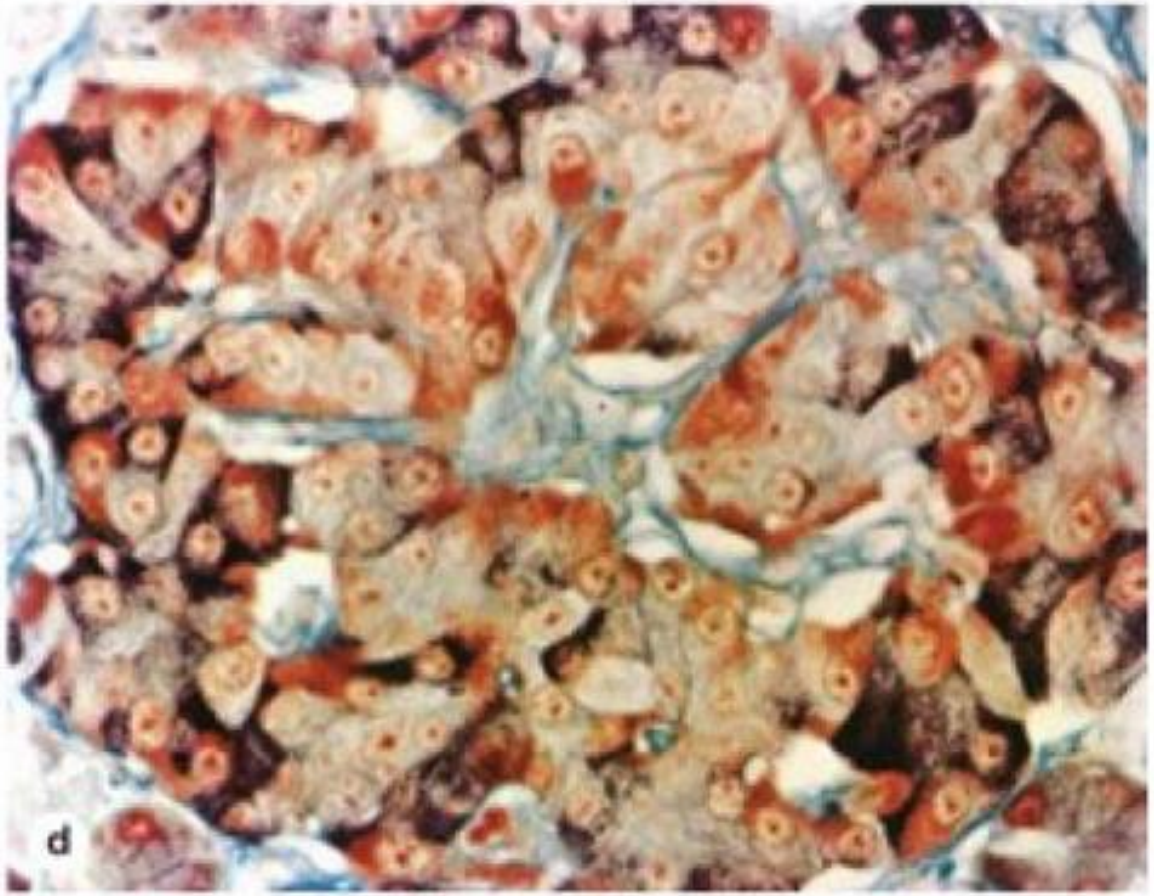
So, previously have studied the pancreas in the GI, basically it's an exocrine gland mainly but side by side it also has endocrine function as well because it does have some of its secreted cells that they synthesize and they release hormones just like the exocrine ones where they synthesize and release enzymes plus other molecules so is estimated that endocrine part of the pancreas to be 1%-2% of its total volume so we have many of these islands scattered throughout the entire structure of the pancreas however we have some concentration of specific cells within specific regions of the pancreas and we will just discuss this shortly, now pancreas if you recall it was actually derived from endoderm both for the exocrine and the endocrine portion.

so these three images that we're looking at, this is simply these three are H&E stain sections, this low magnification, slightly higher this is the highest and as you can see the endocrine cells they do stain less basophilic than the surrounding exocrine ones, in addition, we does see that these cells are actually arranged into quarts as you can see so they are lined up in quarts and they are bordered and surrounded by the sinusoidal capillaries to pick up their secretion.



Histology of the 4th image:

Now, this is a nice special stain. It is a modified aldehyde fuchsin that distinguish these two subpopulation are the most common in the islets of Langerhans so this is one of them
The blue greenish color it's for the reticular support within the islets because as just like any other endocrine parts this is what we usually see as a supportive connective tissue, now we do see that some of the cells do have a brownish orangish color those are the beta cells and later we will get to know the difference of populations and which molecules are being secreted or which hormones are being secreted from which cell population.



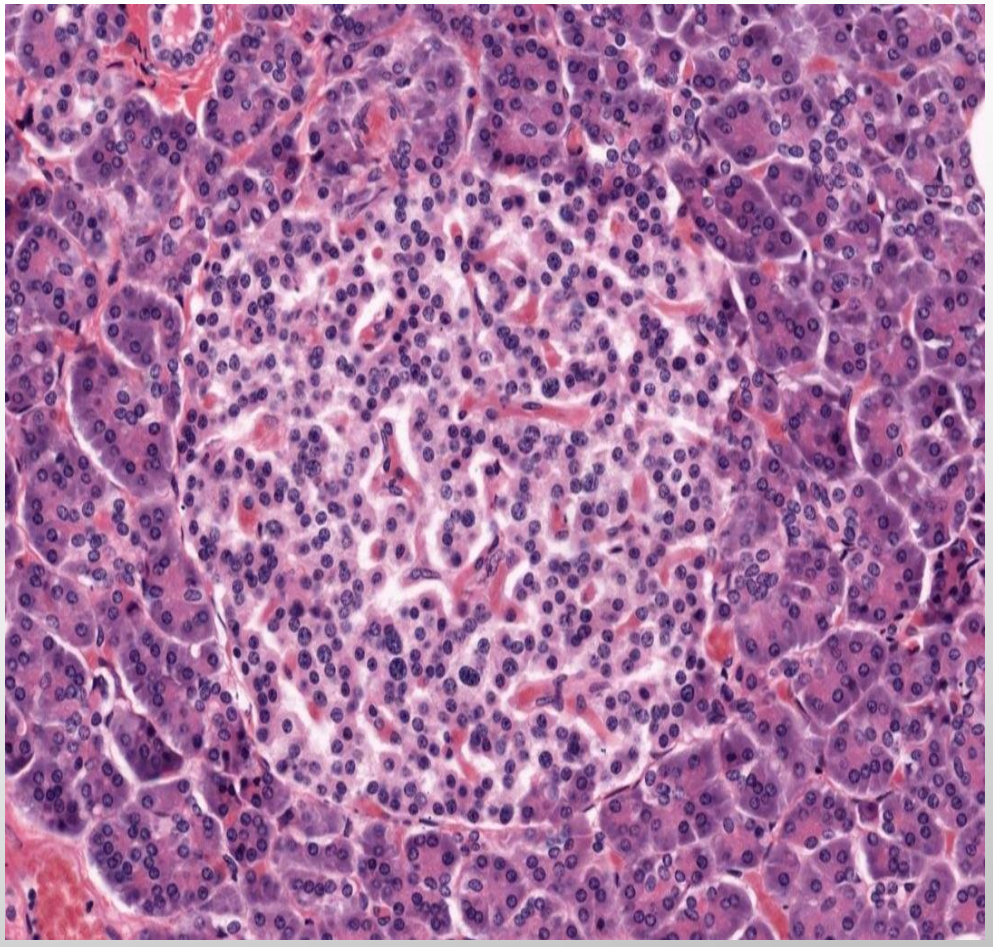
The Pancreatic Islets (Islets of Langerhans)

• 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.

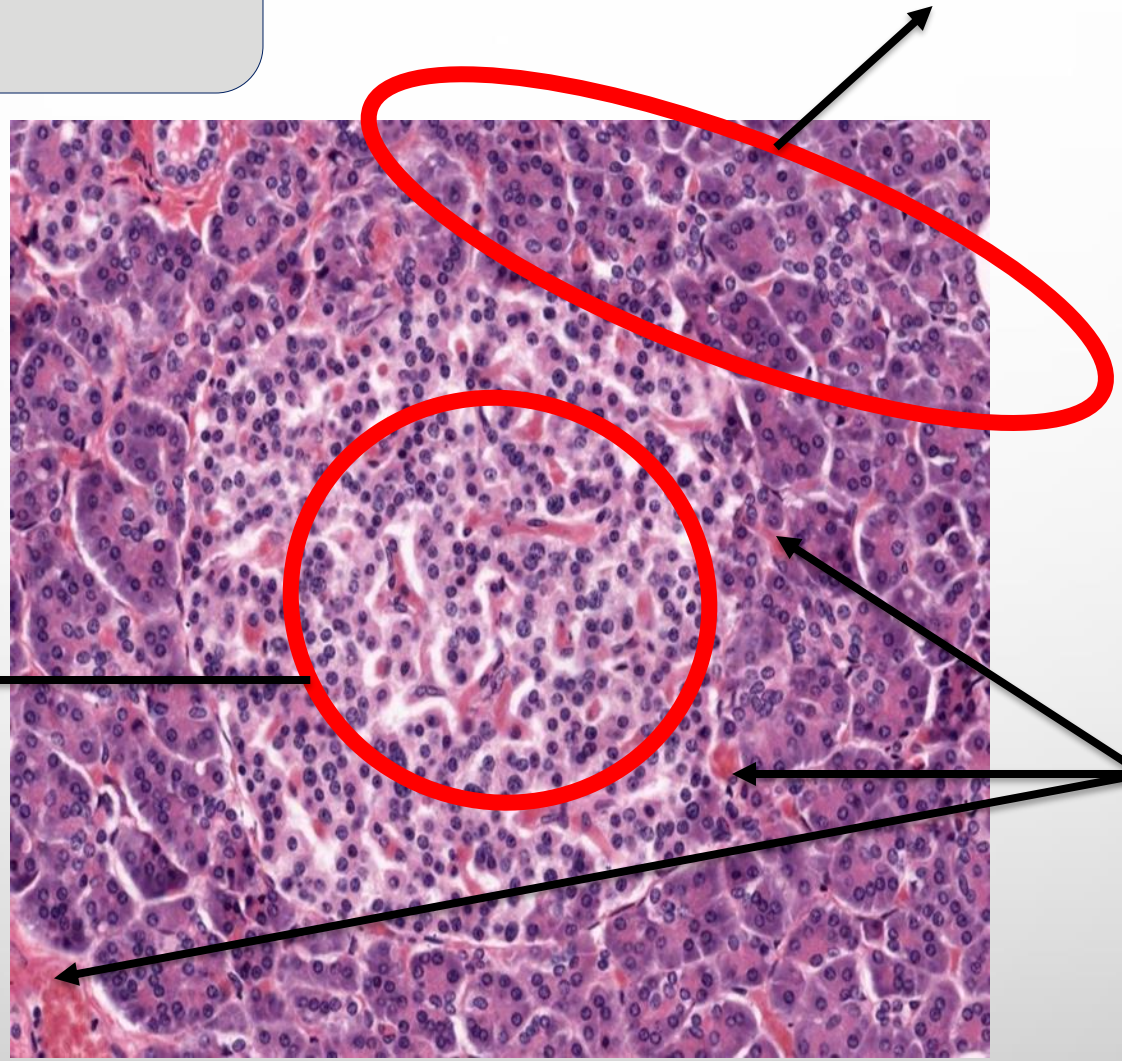
• Most islet cells are acidophilic or basophilic with fine cytoplasmic granules.

• Active polypeptide-secreting cells, with secretory granules that vary in size, morphology, and electron density from cell to cell.



Now, this is another H&E stain but in this one the sinusoids are quite clear, and this is the whole islets of Langerhans

The exocrine parts of the pancreas



The cords of the endocrine cells inside

We can see the extensive capillary Network inside that's these cells use to deliver their products to deliver their hormones towards the systemic circulation

Cells

This diagram it shows us the four major cell subpopulations.

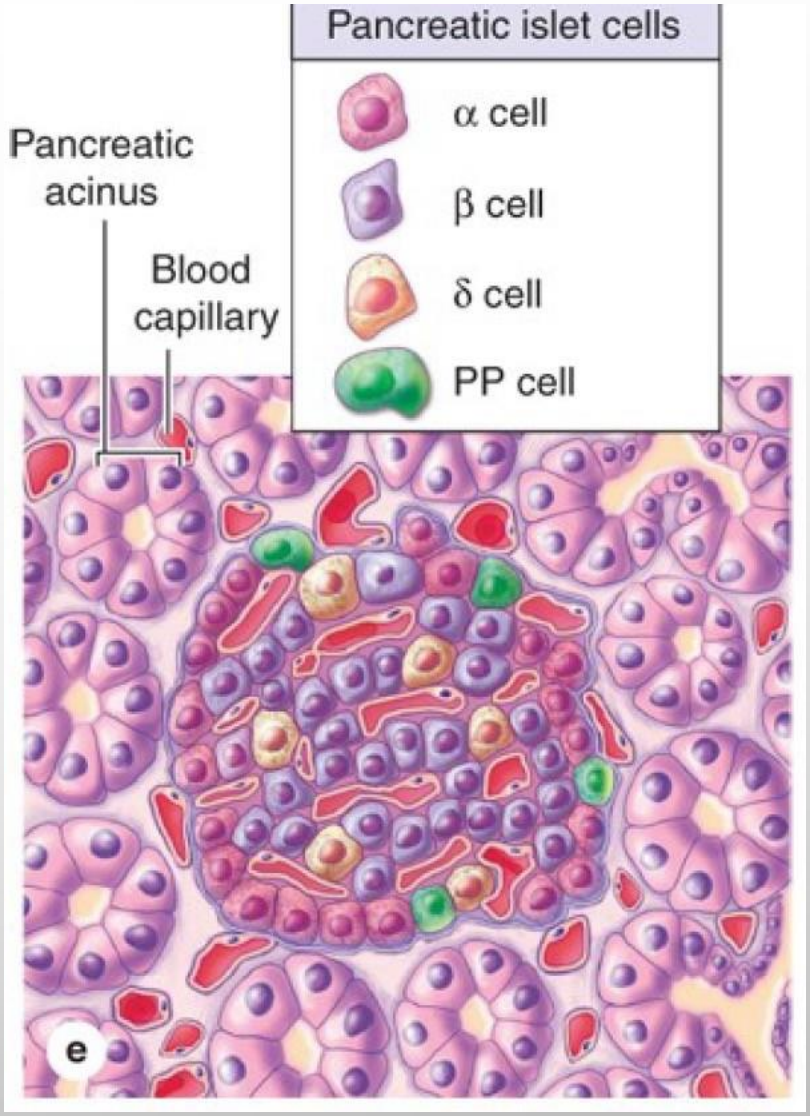
The Major islet cells:

1. a or A cells secrete primarily glucagon and located peripherally.

2. b or B cells produce insulin (l. Insula, island), most numerous, and located centrally.

3. d or D cells, secreting somatostatin, are scattered and much less abundant.

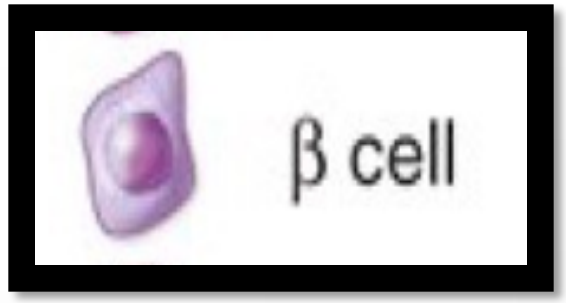
4. PP cells secrete pancreatic polypeptide, more common in islets located within the head.



Do you we have more than that?

YES!!!, but they're less common and they're much less numbered.

The alpha / A cells those are the ones in charge of the sense and release of glucagon and we've studied this in glucose metabolism

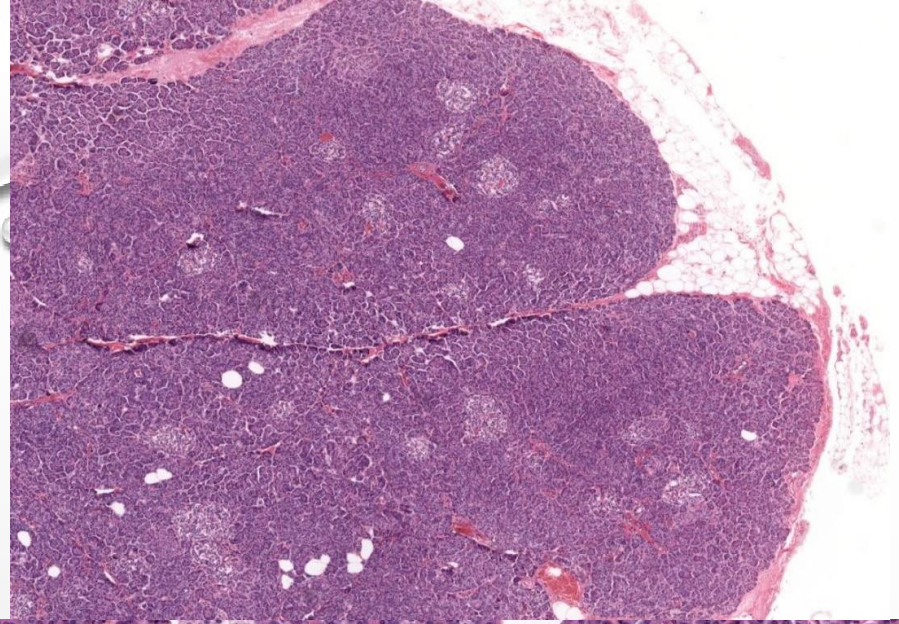


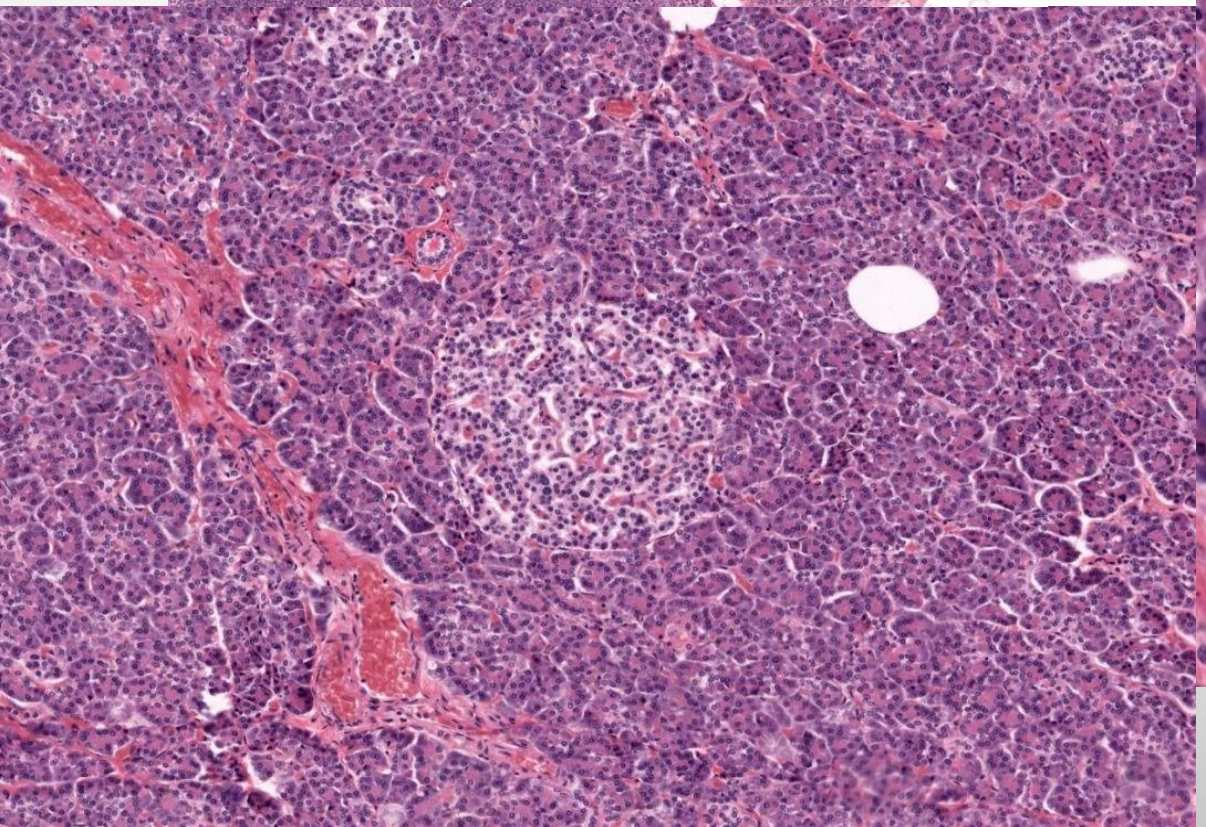
The beta/ B cells those are the ones in charge of insulin and the diabetes has been discussing extensively in almost all the disciplines of the system and can see the beta cells seems to occupy a more central location whereas the alpha are more in the outside

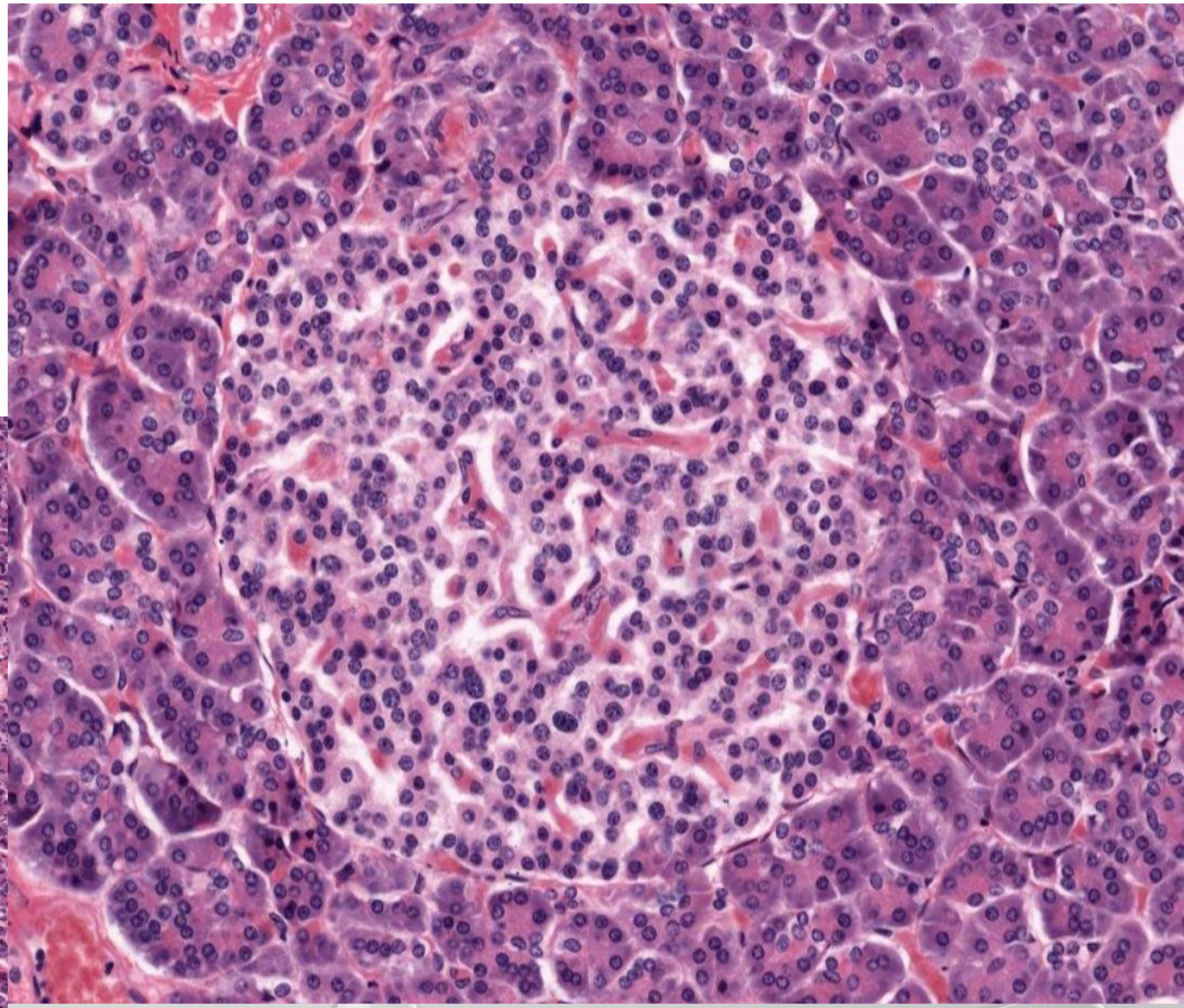
Now, the third type are the delta or the D cells those are responsible for the somatostatin.

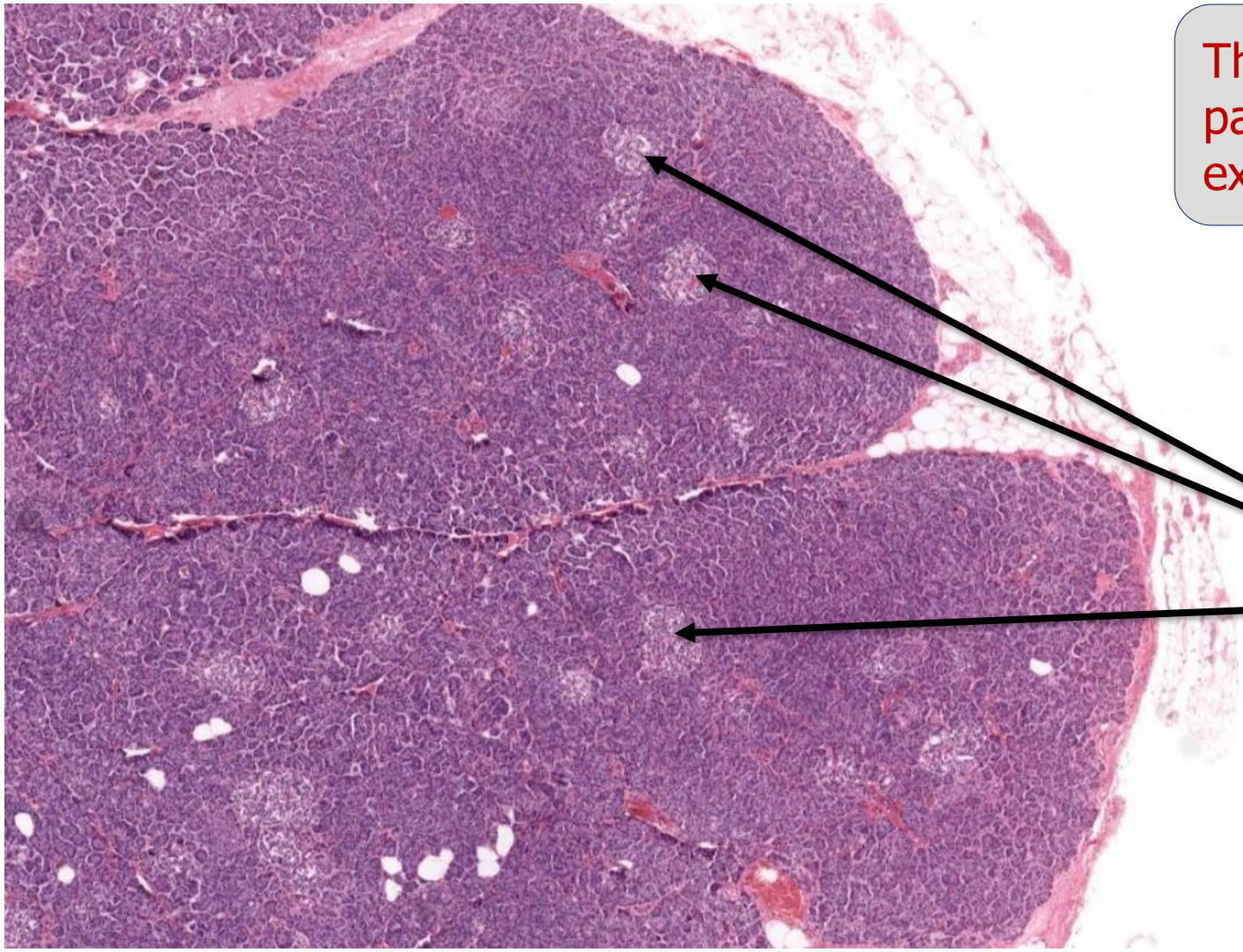
we have other small numbered ones so the PP cells those they secrete the pancreatic polypeptide and those seem to be more concentrated in the head region of the pancreas

Note: So, you can see that the alpha and the beta are the most numerous than the less numbered ones are the delta and the PP cells



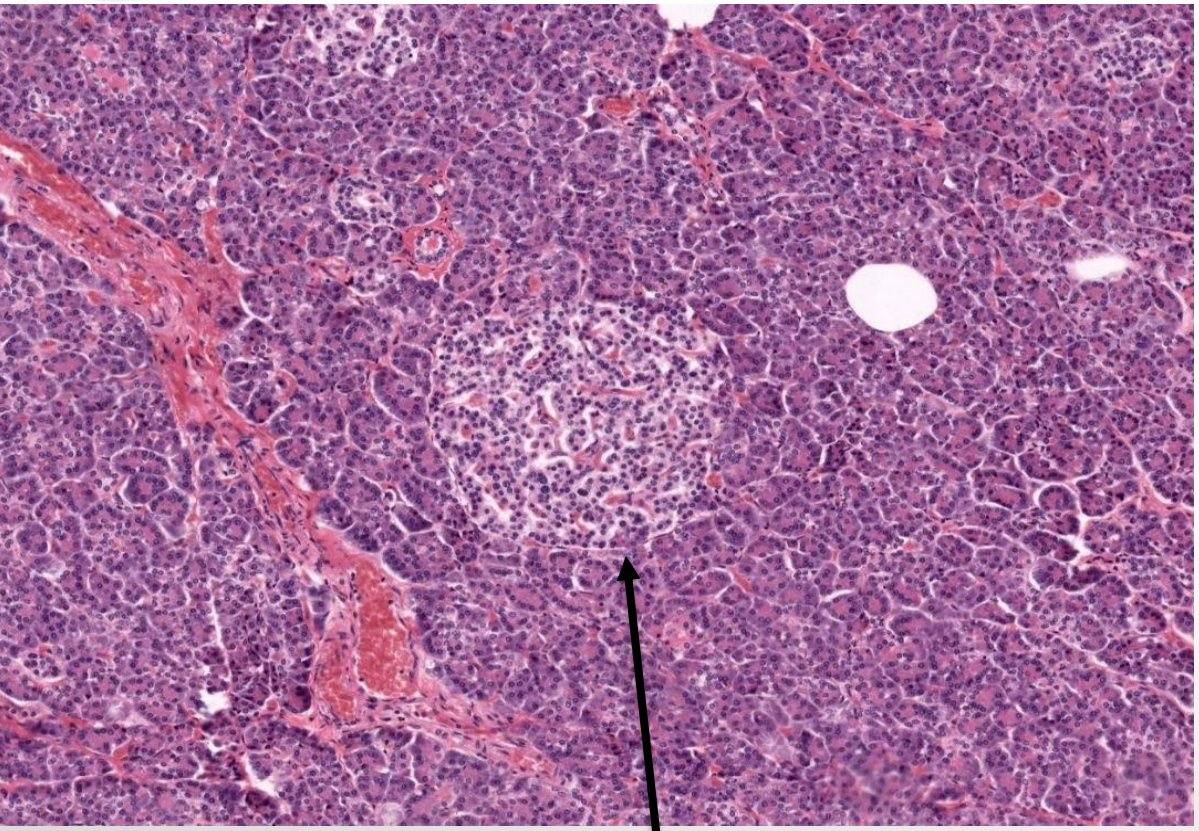




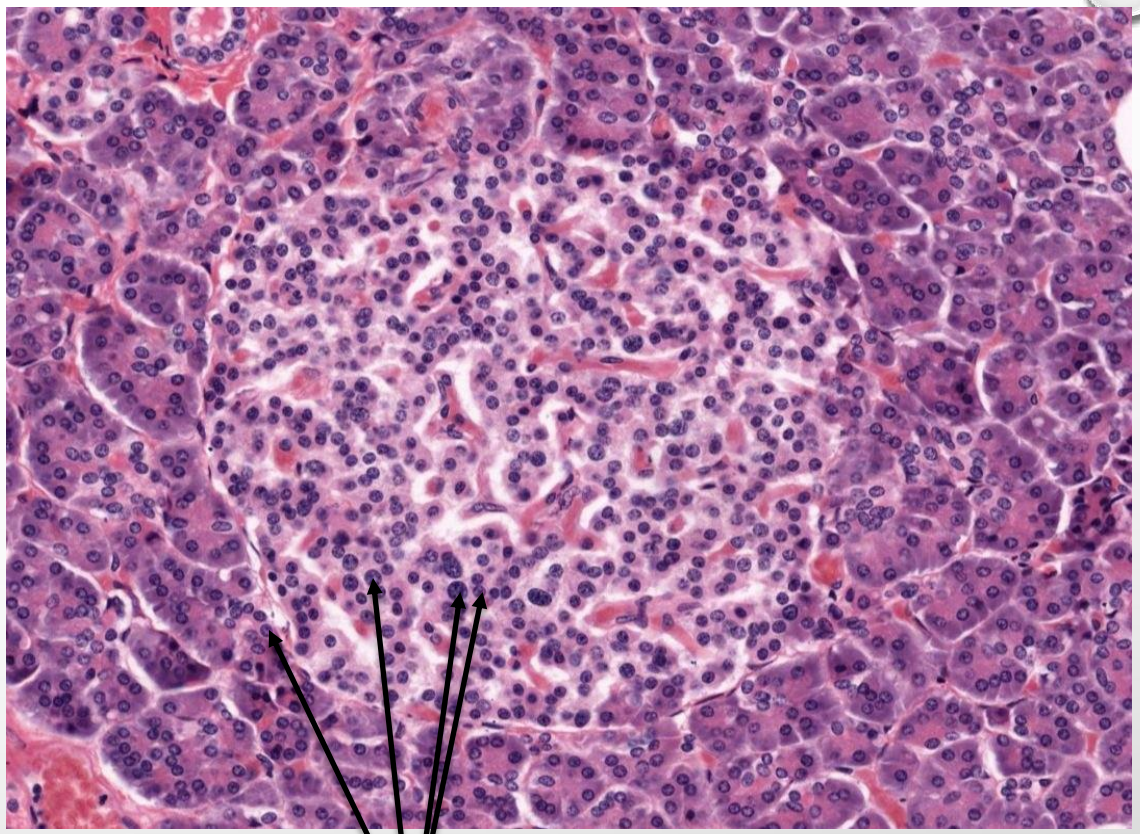


This is low magnification of the pancreas, what we mostly is the exocrine S9

The Islets of the pancreas

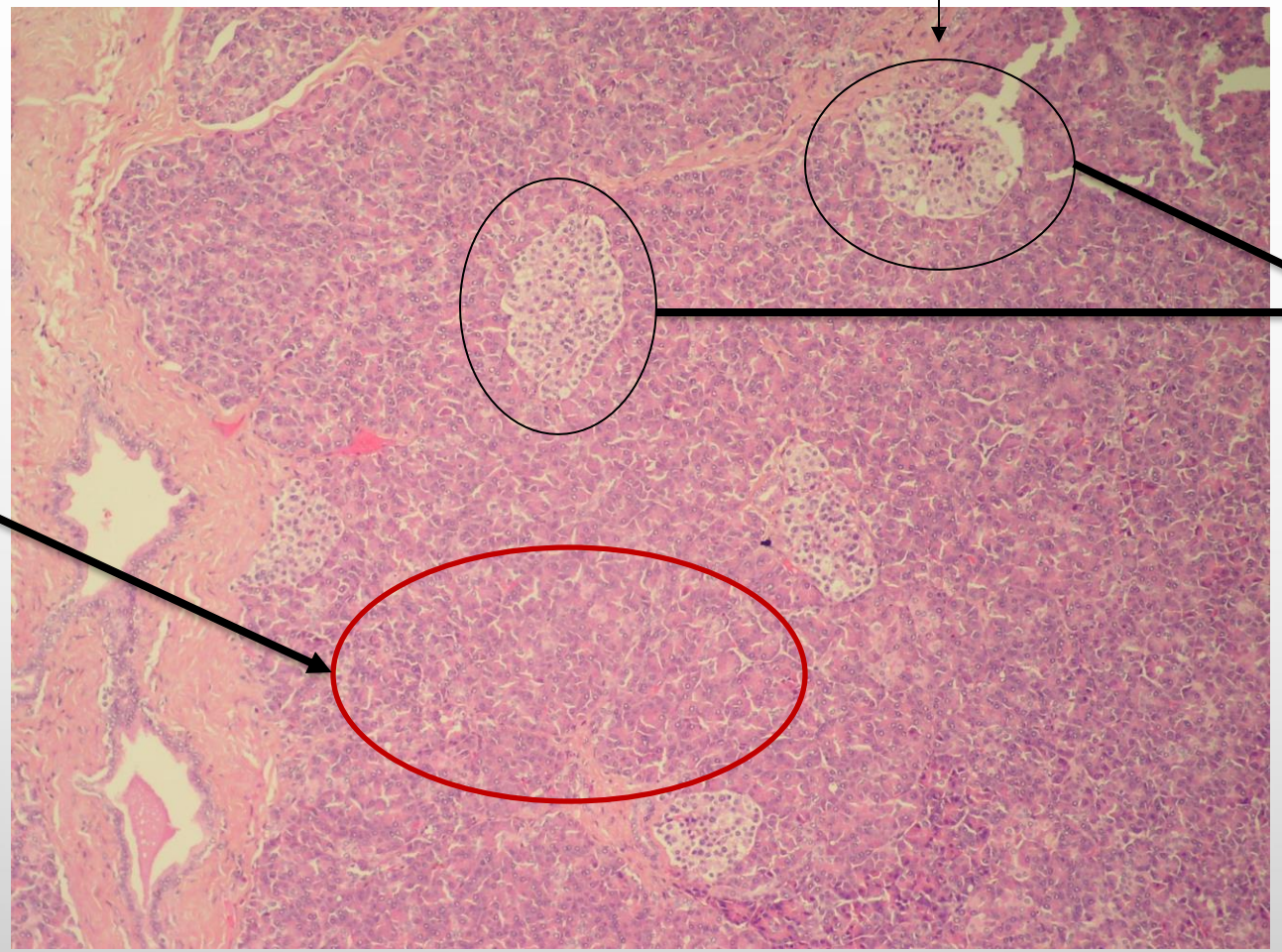


Supporting by the reticular tissue and distinguish the fenestrated capillaries



Cords of the Cells and fenestrated capillaries inside

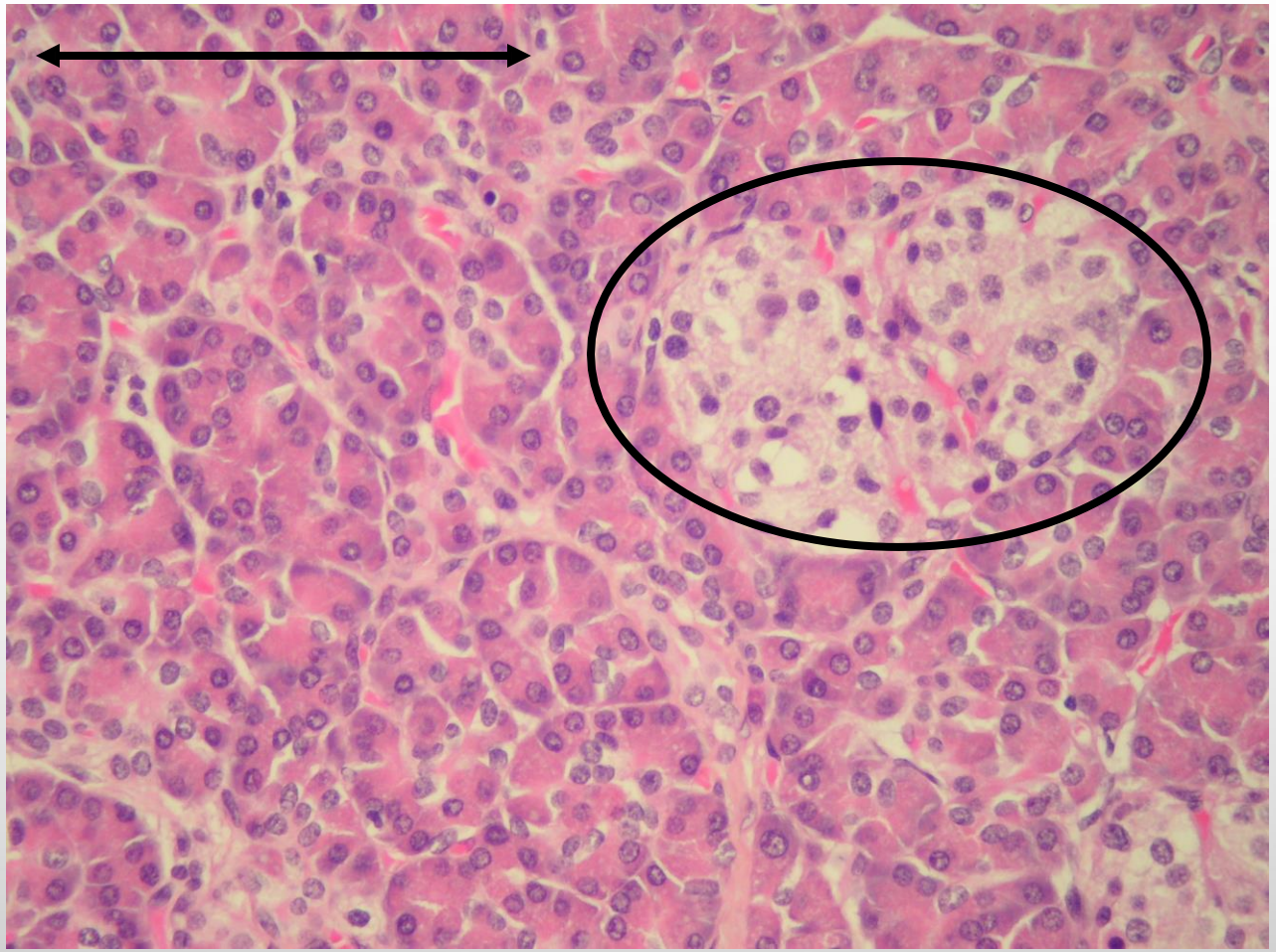
PANCREAS (EXOCRINE &ENDOCRINE)



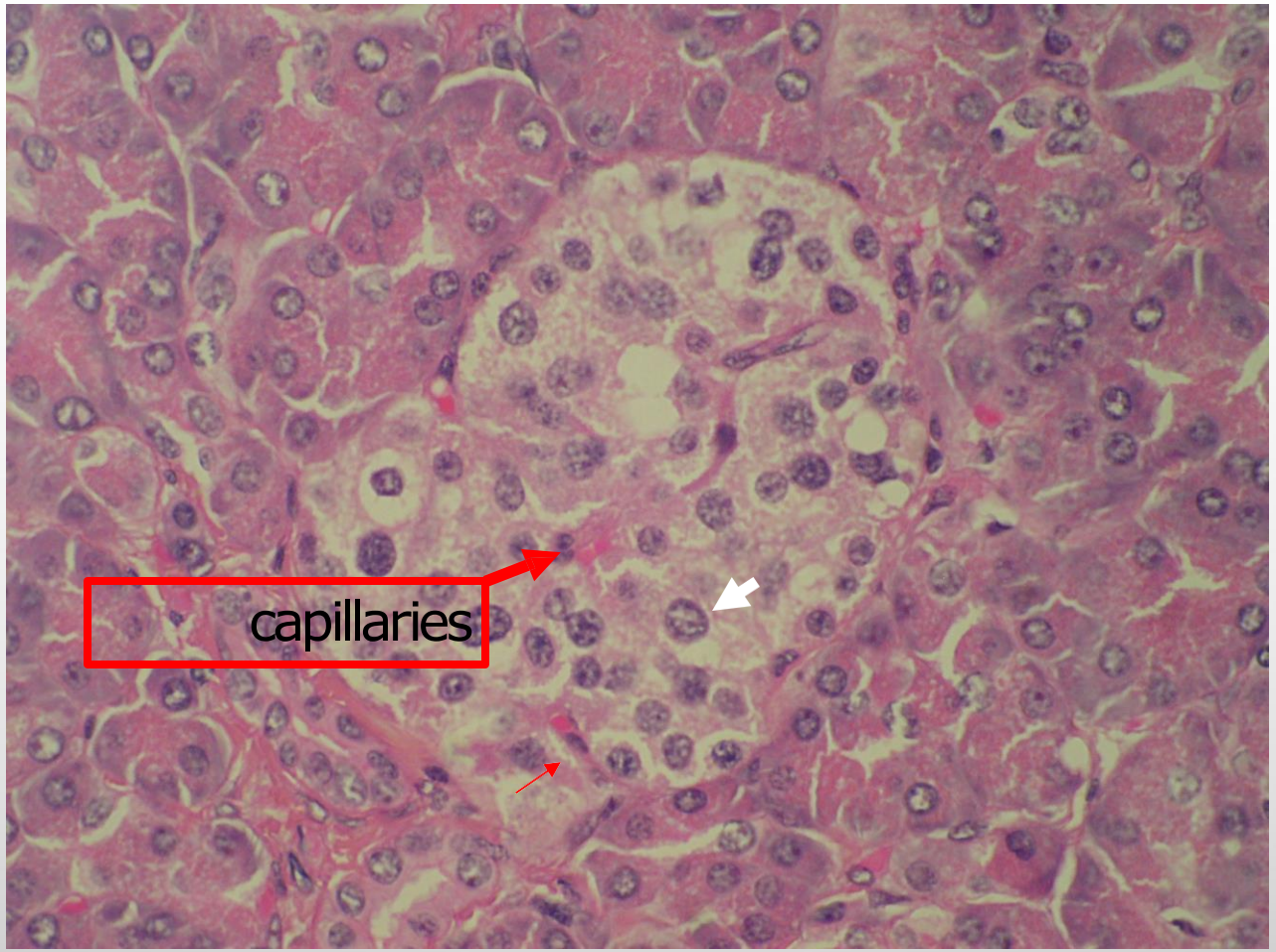
Exocrine S9

Endocrine cells

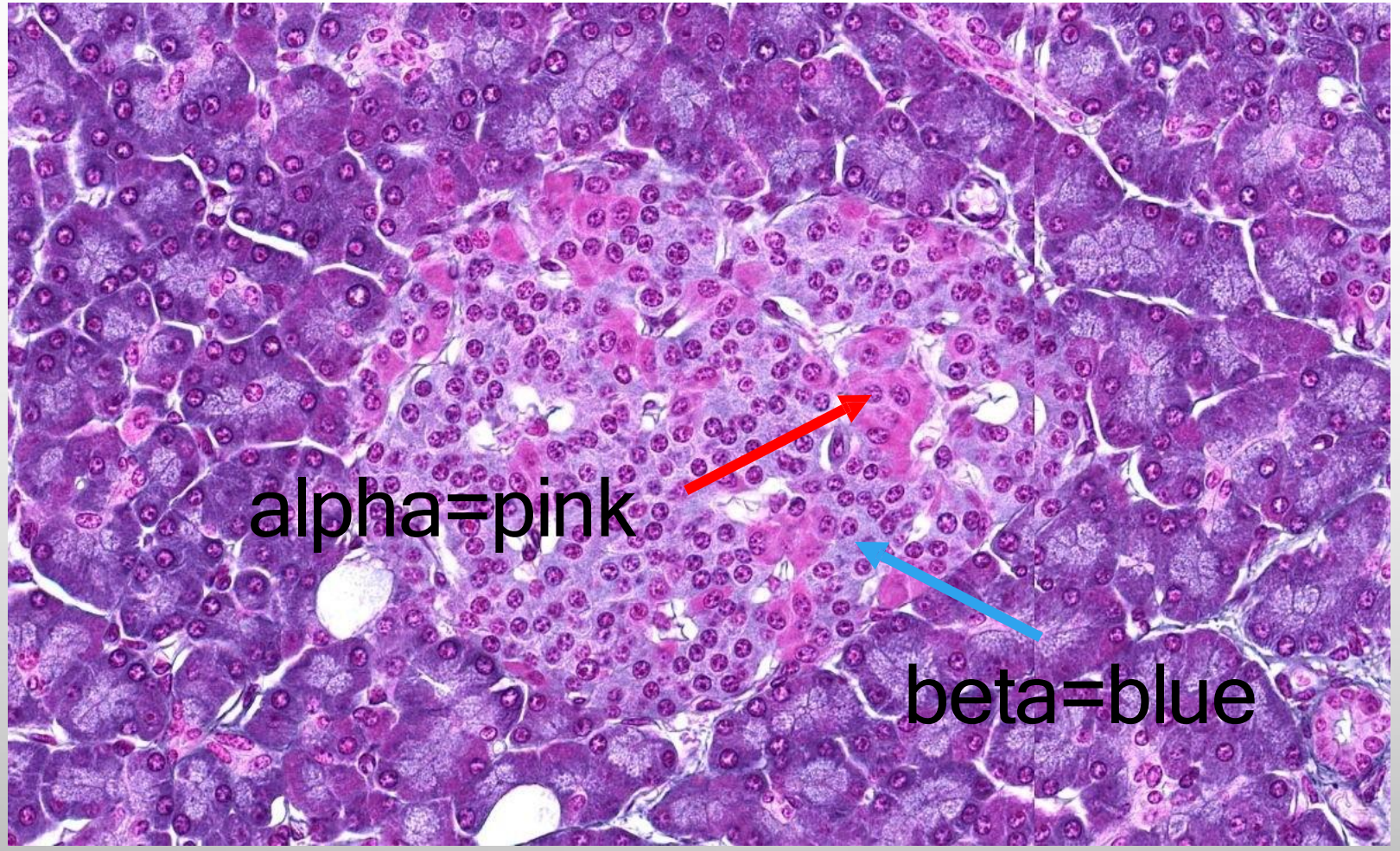
EXOCRINE PART &ENDOCRINE (ISLET OF LANGERHANS)



TYPES OF ENDOCRINE CELLS



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



Cell Type	Quantity (%)	Hormone Produced	Hormone Structure and Size	Hormone Function
α	~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
β	~70	Insulin	Dimer of α and β 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
δ 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