

Diseases of the endocrine system 2019
lecture 1: Pituitary gland

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Notes

- Office hours: Sunday and Monday: 11-12, in the histopathology section room, faculty of medicine, ground floor.
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- Please ask me about anything you don't understand. If you need an appointment outside the office hours, please let me know.

Topics to be covered in the pathology lectures of this course:

- Pituitary gland.
- Thyroid gland.
- Parathyroid gland
- Adrenal gland
- Endocrine pancreas and Diabetes
- MEN syndromes.

- Reference: Robbins basic pathology, 10th edition

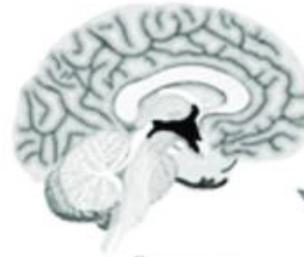
ILOS of this lecture

- 1. list the differences between the anterior and posterior pituitary.
- 2. list the hormones secreted by the pituitary and their functions.
- 3. describe the diseases of the anterior and posterior pituitary gland; their pathogenesis and clinical features.
- 4. compare the histological features of pituitary adenomas, atypical adenomas and carcinomas.

Introduction to the endocrine system

- The endocrine system is composed of glands , distributed on various anatomical locations, that work together to **maintain homeostasis (body's metabolic equilibrium)**.
- Endocrine glands secrete **hormones**, that circulate in the blood to reach and affect the function of target cells.
- Most hormones are secreted in response to **trophic factors** that are secreted in response to certain metabolic needs.
- production of hormones downregulates the activity of the gland that secretes the trophic hormone= negative feedback or **feedback inhibition**.
- See example on next slide..

Hypothalamus



↓ TRH

Pituitary



↓ TSH

Thyroid



T₄ + T₃

Bloodstream



TH-sensitive cell

Negative Feedback

example

- TRH and TSH are the trophic hormones responsible for stimulation of thyroid hormone production (T3 and T4)
- Once there is enough T3 and T4 ,the TRH and TSH are decreased.
- This maintains the balance of these hormones .



Endocrine system diseases general principles/1

The diseases of the endocrine system can be due to:

1. Mass effect
2. Disordered hormonal production (Under or over production)
3. End organ resistance to the effect of the hormone.

Endocrine system diseases

general principles/2

- Mass effect means an enlargement of the gland which can compress adjacent structures.
- Mass effect can be due to neoplastic or non-neoplastic conditions
- Neoplastic include: adenoma and carcinoma
- Non neoplastic= hyperplasia

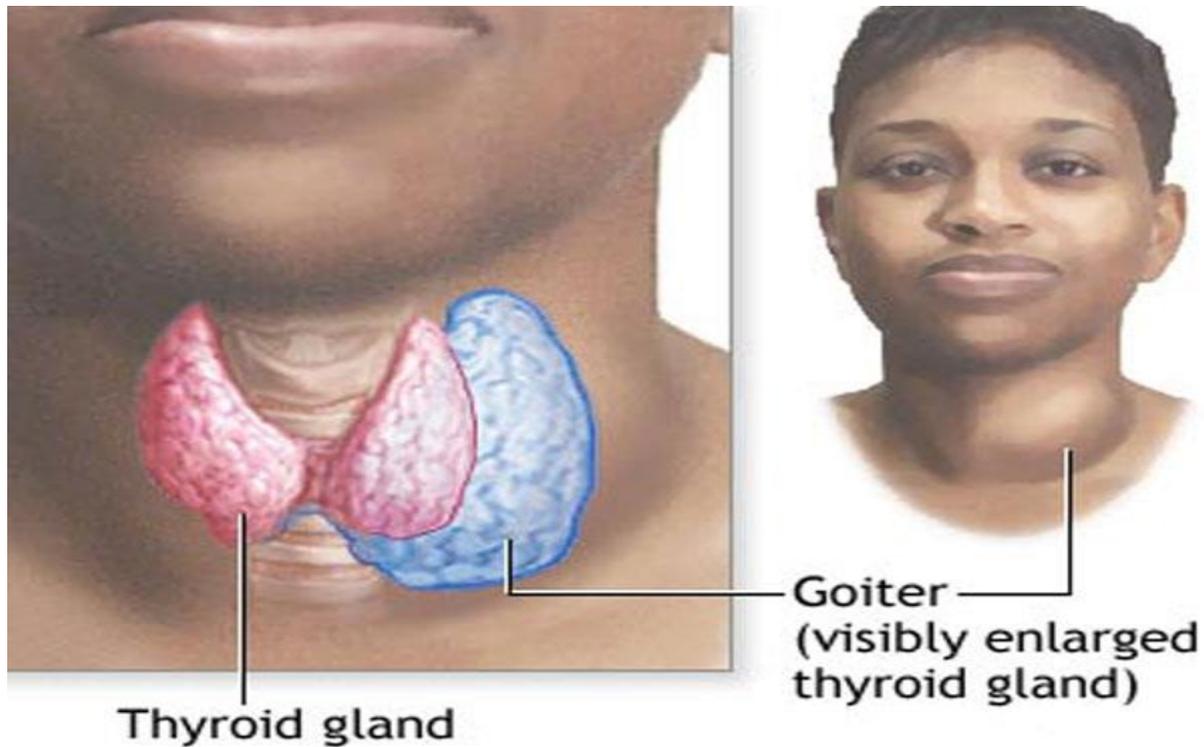
Endocrine system diseases

general principles/3

- The other group of diseases affecting endocrine glands are: abnormal hormonal secretion
- This can be over or under production due to several causes that will be discussed later
- IMPORTANT NOTE: there is no relation between mass effect and hormonal abnormalities.
- Patients might have a mass with normal, low or high hormonal secretion.
- Also hormone overproduction **is not always** associated with a mass

REMEMBER

- A large gland doesn't predict hormonal level !!



Endocrine system diseases

general principles/4

- **End organ resistance** means that the gland is secreting the hormone but the target organ is not responding to it . This occurs in some types of diabetes.

PITUITARY GLAND: THE ORCHISTRA MAESTRO

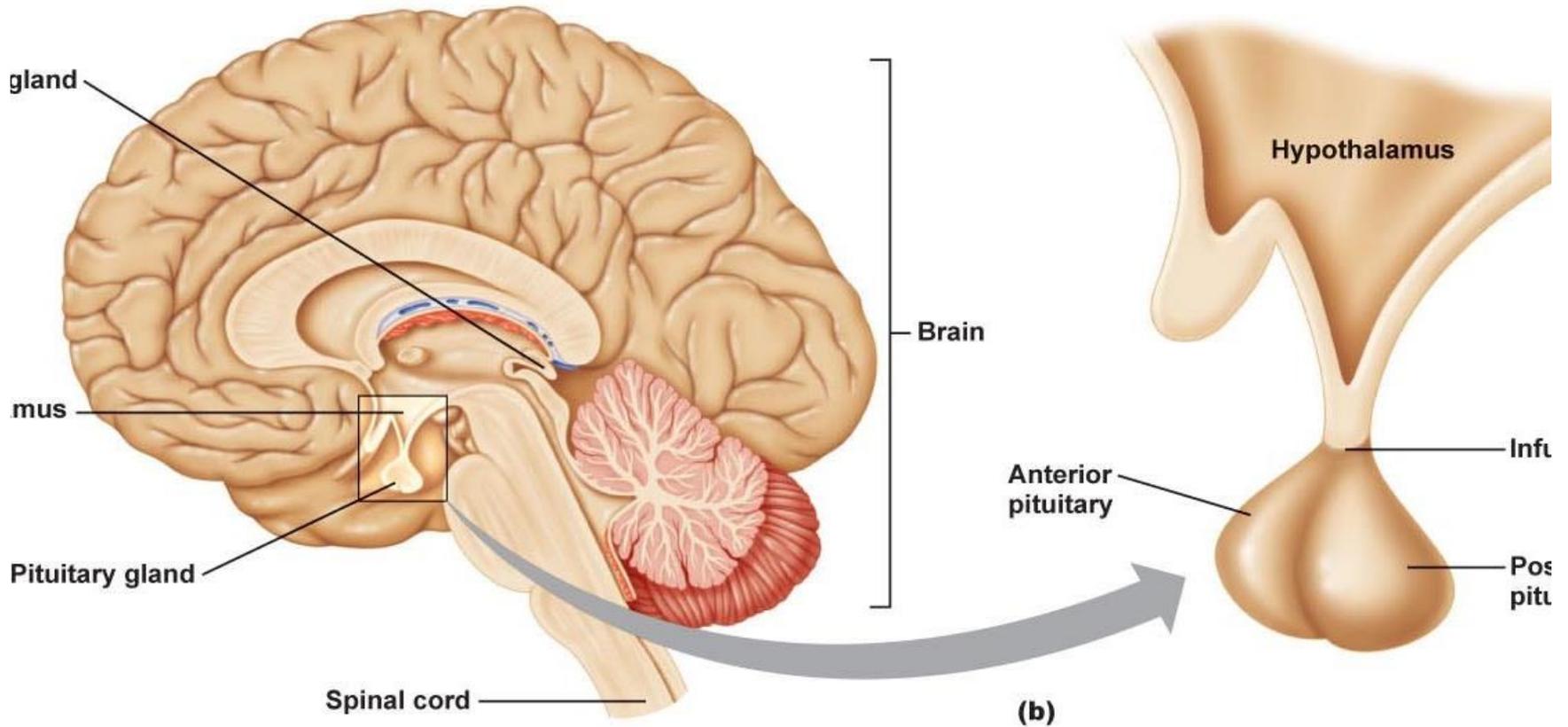
- The hormones secreted from the pituitary gland control levels of hormones secreted from all other endocrine glands.



Pituitary gland

- Small, bean shaped structure that lies at the base of the brain within the sella turcica.

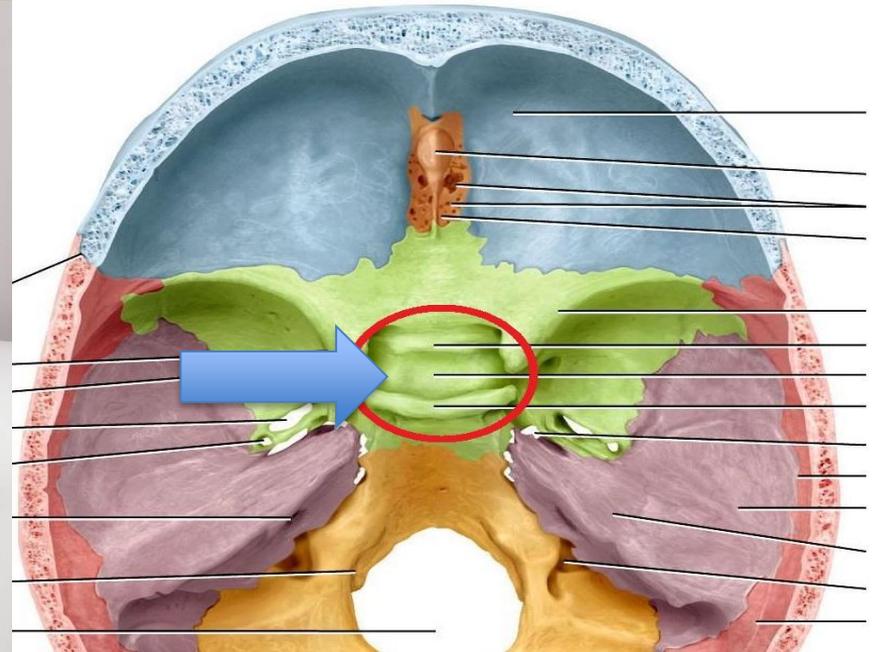
Pituitary gland



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السَّرَجُ التُّرْكِيُّ = Sella turcica = pituitary fossa

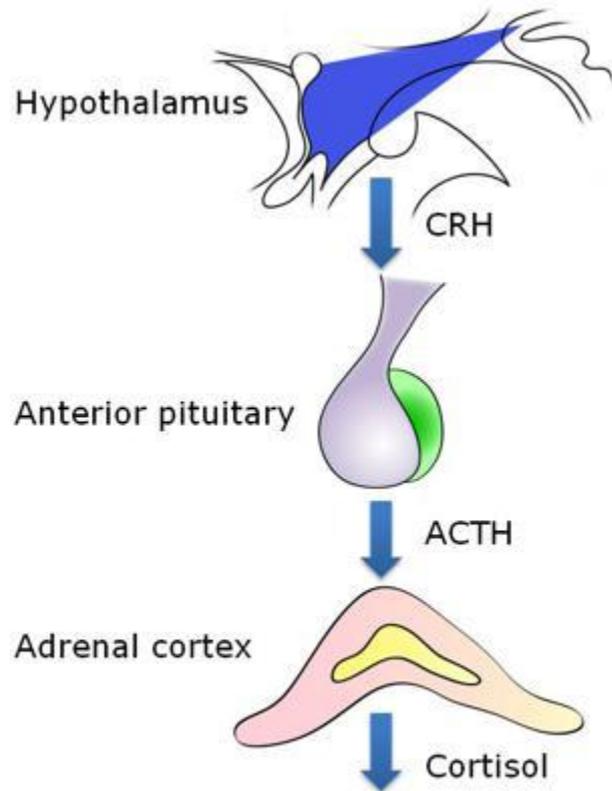
- The **sella turcica** (Latin for Turkish seat) is a saddle-shaped depression in the body of the sphenoid bone of the skull.



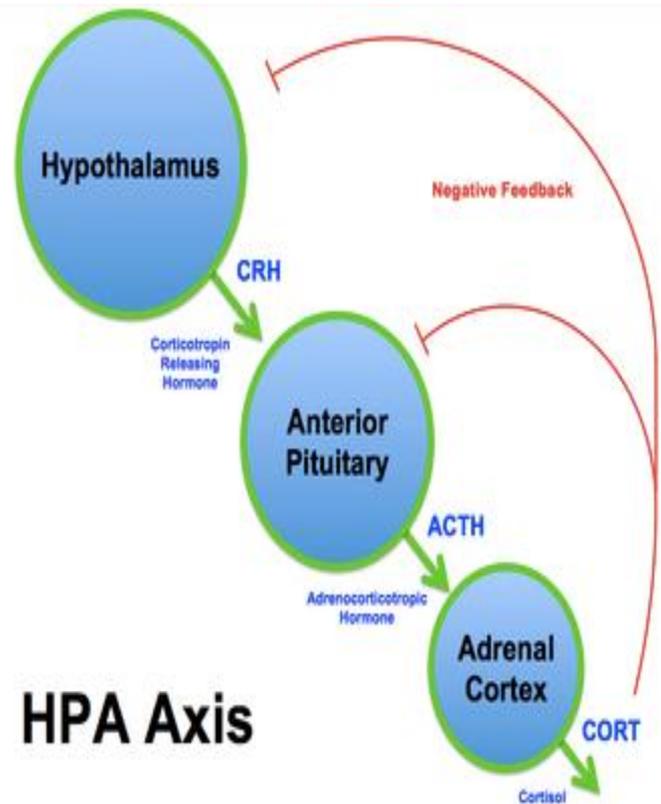
The hypothalamus (تحت المهاد) controls
the pituitary (الغُدَّة النُّخَامِيَّة)

The production of most pituitary hormones is controlled by positively and negatively acting factors from the hypothalamus which are carried to the anterior pituitary by a **portal vascular system**.

Examples of hypothalamic- pituitary axis.

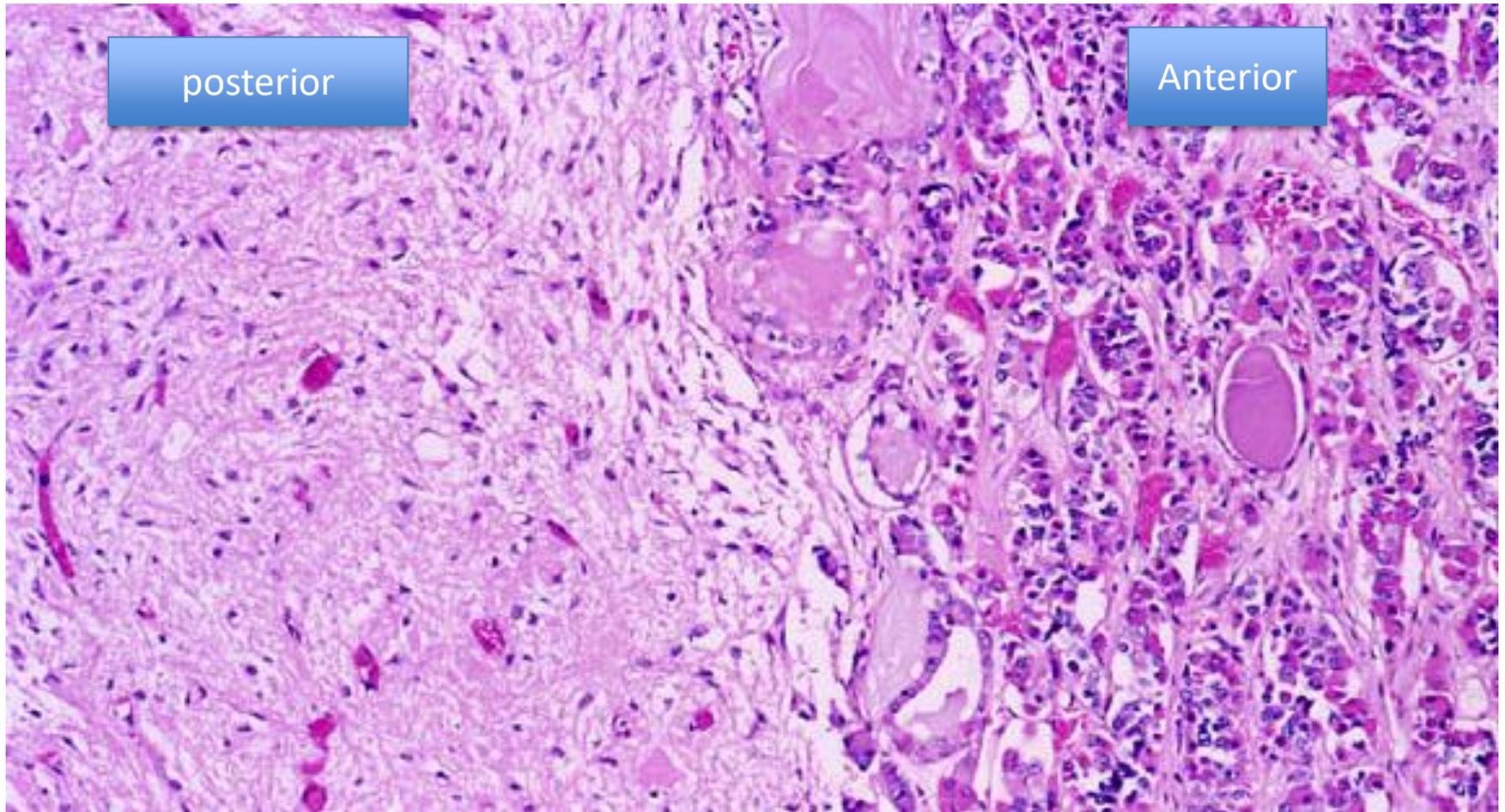


F Caillard
2006
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- The pituitary gland is composed of two morphologically and functionally distinct components: the **anterior lobe (adenohypophysis)** and the **posterior lobe (neurohypophysis)**
- The *anterior pituitary* constitutes about 80% of the gland.

Anterior versus posterior pituitary



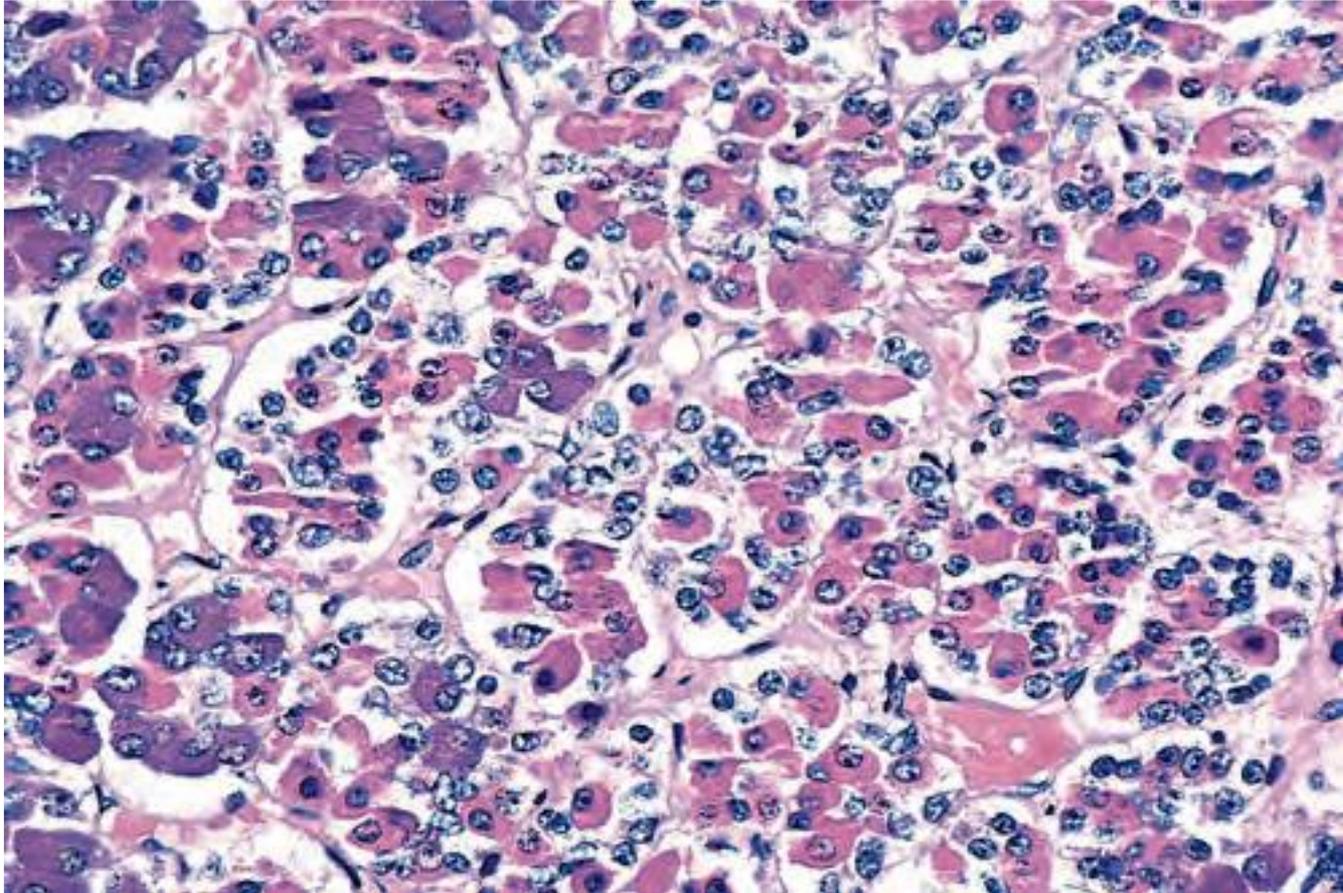
ANTERIOR VERSUS POSTERIOR PITUTARY LOBES

	ANTERIOR PITUITARY	POSTERIOR PITUITARY
histology	Epithelial cells	Glial cells and neuronal axons
Embryological origin	Oral mucosa	Neural crest
Hormones secreted	TSH, PRL, ACTH, GH, FSH , LH.	ADH and oxytocin <i>(synthesized in hypothalamus but stored in posterior pituitary)</i>

Anterior pituitary

- The anterior pituitary is composed of epithelial cells that secrete trophic hormones like: TSH, PRL, ACTH..

Anterior pituitary/ epithelial cells



Posterior pituitary

- The *posterior pituitary* consists of **modified glial cells** (*pituicytes*) and axonal processes extending from the hypothalamus through the pituitary stalk to the posterior lobe (*axon terminals*).
- The posterior pituitary secretes: *oxytocin* and *antidiuretic hormone* (ADH, also called *vasopressin*).
- These (*oxytocin* and ADH) are actually synthesized in the hypothalamus and stored within the axon terminals in the posterior pituitary

Diseases of the anterior pituitary gland

1. Mass effect

- Masses that can affect the pituitary: adenomas or carcinomas
- Adenomas can be **secretory** (secrete one of the pituitary hormones) in this case the level of that hormone will increase = **hyperpituitarism**
- OR adenomas can be **non secretory** so level of pituitary hormones unaffected = **normal hormonal levels**
- HOWEVER, if a non-secretory adenoma enlarges to the extent it **compresses** the surrounding normal pituitary tissue then level of hormone secretion from the normal tissue will be decreased resulting in **hypopituitarism**

- NOTE: pituitary carcinomas are rare and usually non-secretory.

Mass effects of pituitary adenomas or carcinomas

Signs and symptoms :

*Radiographic abnormalities of sella turcica :sellar expansion, bony erosions.

*Compression of the optic chiasm (the X-shaped structure formed at the point below the brain where the two optic nerves cross over each other) resulting in visual field abnormalities. (see next slide)

*elevated intracranial pressure: headache, nausea, vomiting.

Note: any mass in the cranium (inside the skull) can cause increased intracranial pressure

*seizures.

*Cranial nerve palsies.

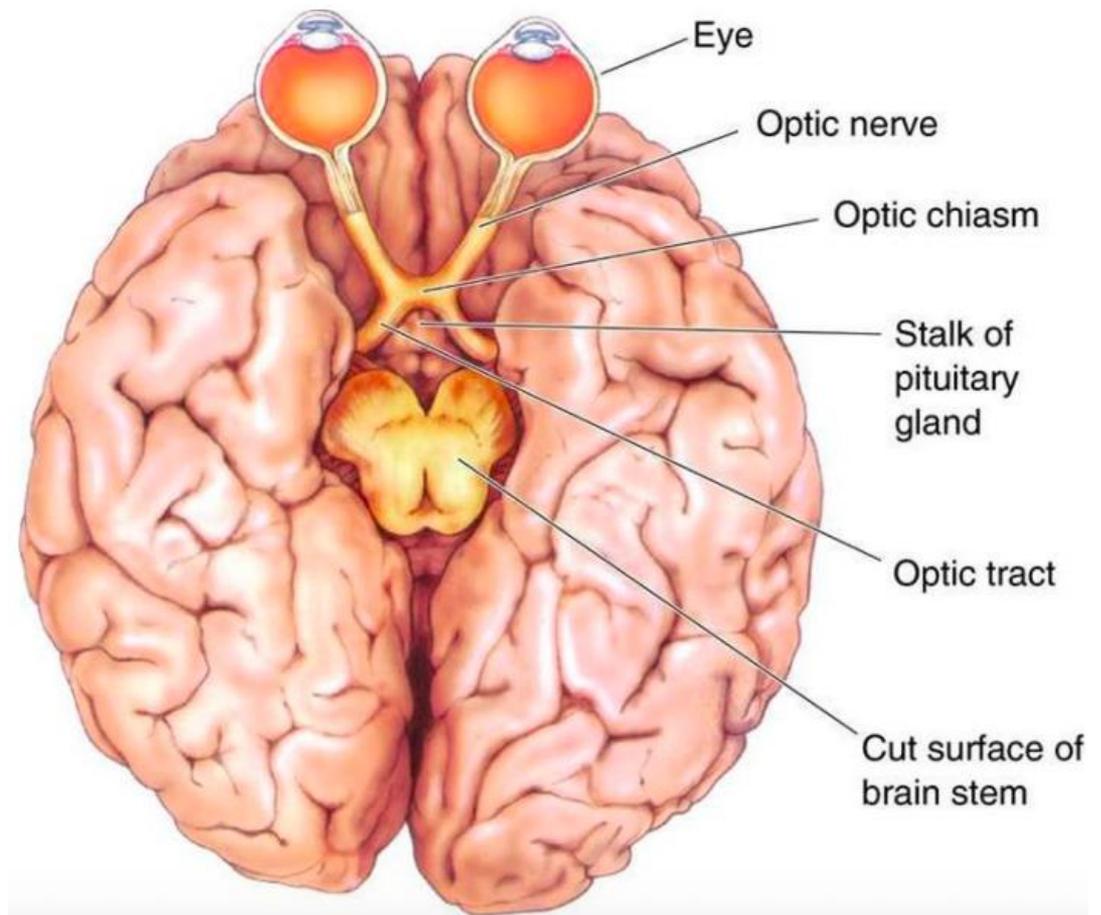
***pituitary apoplexy.. More details in a minute!**

The optic chiasm is the X shaped structure formed by cross-over of the optic nerves.

The pituitary is very close to this chiasm

So: a mass in the pituitary can compress the chiasm.. This will affect vision.

Note: because of this cross over, the right optic nerve supplies the left eye and vice versa.. So a defect in the right optic nerve will cause visual field defect in the left eye (the contralateral eye)



Pituitary apoplexy=السكتة النخامية

- Acute hemorrhage into an adenoma, which causes **rapid enlargement** of the lesion. This will result in decreased consciousness.
- This is a neurosurgical emergency.... Can cause sudden death.
- The word apoplexy means anger or rage.
- Apoplexy in medicine: is bleeding within internal organ.. Example: ovarian apoplexy, pituitary apoplexy.

Pituitary adenomas

- Functional or nonfunctional.
- Functional: usually **one cell type** and one hormone produced.
- Classified according to the hormones they produce.

Types of pituitary adenomas

- Prolactinomas.. 20-30%.. The most common
- Null cell adenoma... 20%.. Non secretory
- ACTH cell adenoma.. 10-15%
- Gonadotroph cell adenoma... 10-15%
- GH cell adenoma... 5%
- Mixed GH/Prolactin adenoma.. 5%
- TSH cell adenoma... 1%.. Least common
- pleurihormonal... 15%
- AS USUAL: DON'T MEMORISE THE NUMBERS!. The most common one is important and the fact that TSH adenomas are the rarest is also important.

notes

- 1. TSH adenomas are rare.. So if you have a patient with hyperthyroidism it will be very rare that the cause of his disease is related to the pituitary.
- 2. pleuri-hormonal adenomas do exist.. So a pituitary adenoma, although usually produces one hormone, it might secrete more than one type of hormones and patients will have symptoms related to the hormones secreted.

Pituitary adenomas

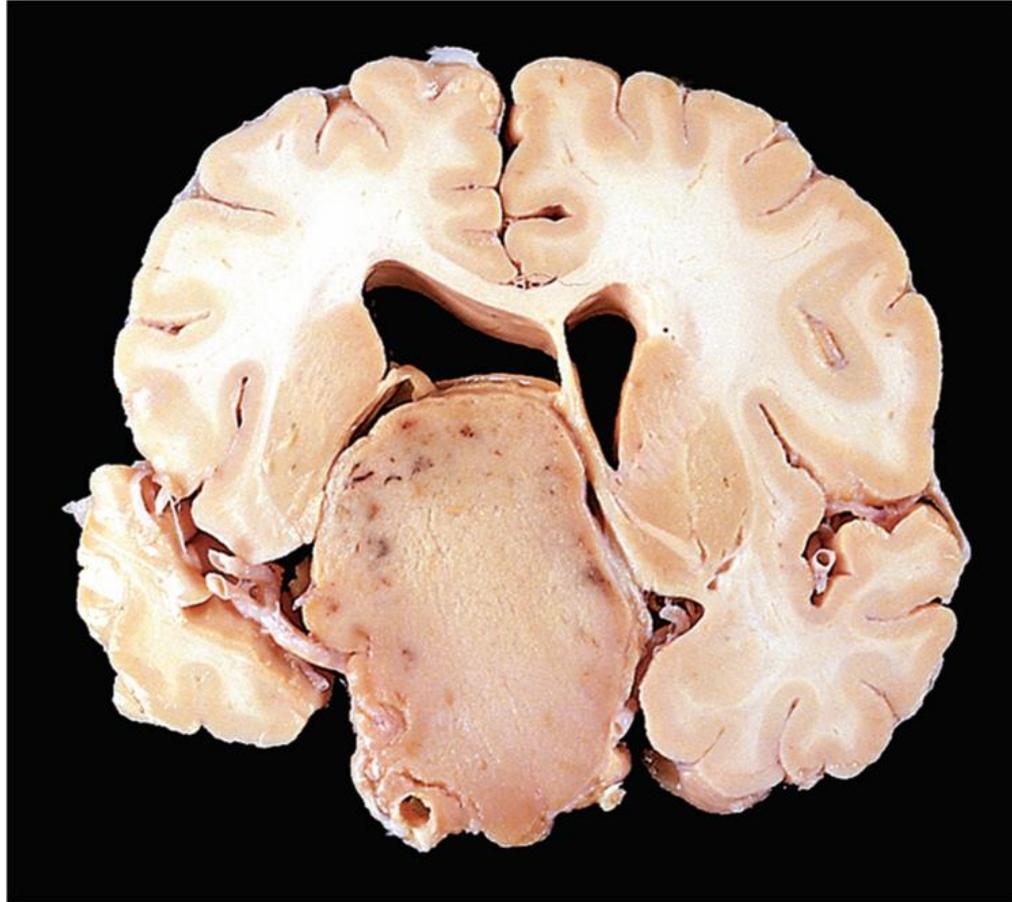
- In clinical practice 10% of intracranial neoplasms are pituitary adenomas.
- But pituitary adenomas can be an incidental finding in 25% of autopsies.
- Peak.. 4th to 6th decades.
- Mostly **single** lesions= solitary
- Can be divided into micro and macro adenomas according to size.. Cutoff point: 1cm.

Macroscopic appearance

Gross features of adenomas

- The usual adenoma is a **well-circumscribed**, lesion that if small, is confined by the sella turcica
- In 30% of cases, the adenomas are non-encapsulated and infiltrate adjacent bone, dura and brain.

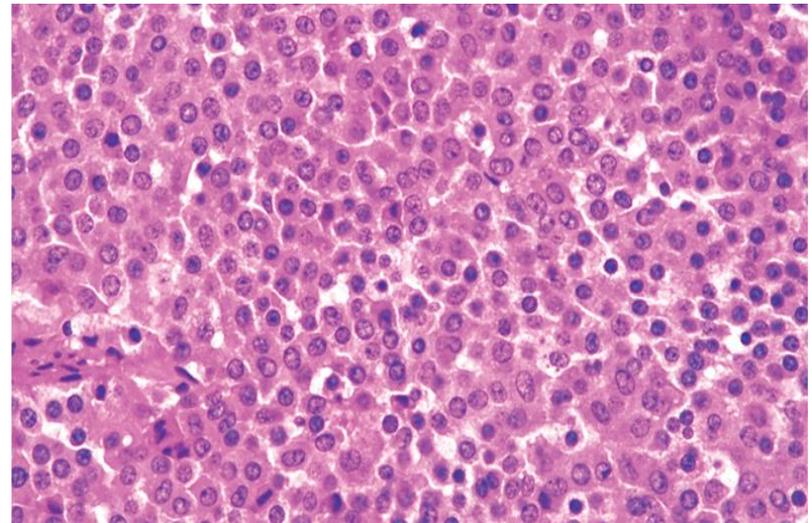
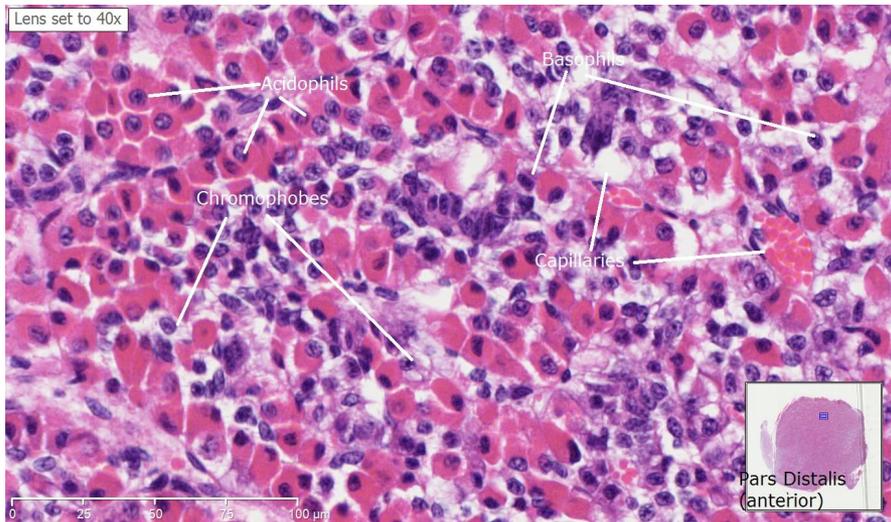
Pituitary adenoma



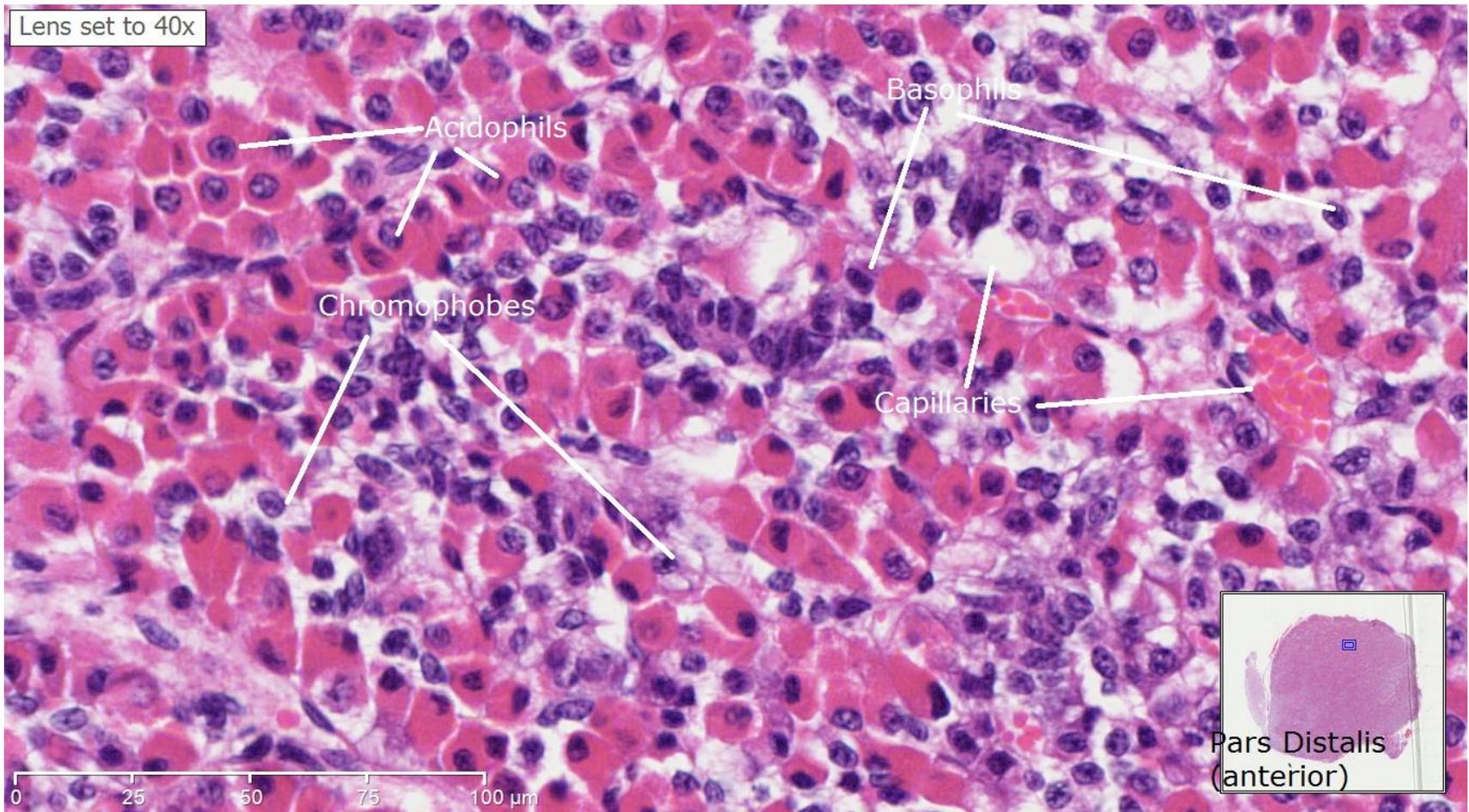
Kumar et al: Robbins Basic Pathology, 9e.
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Pituitary adenoma

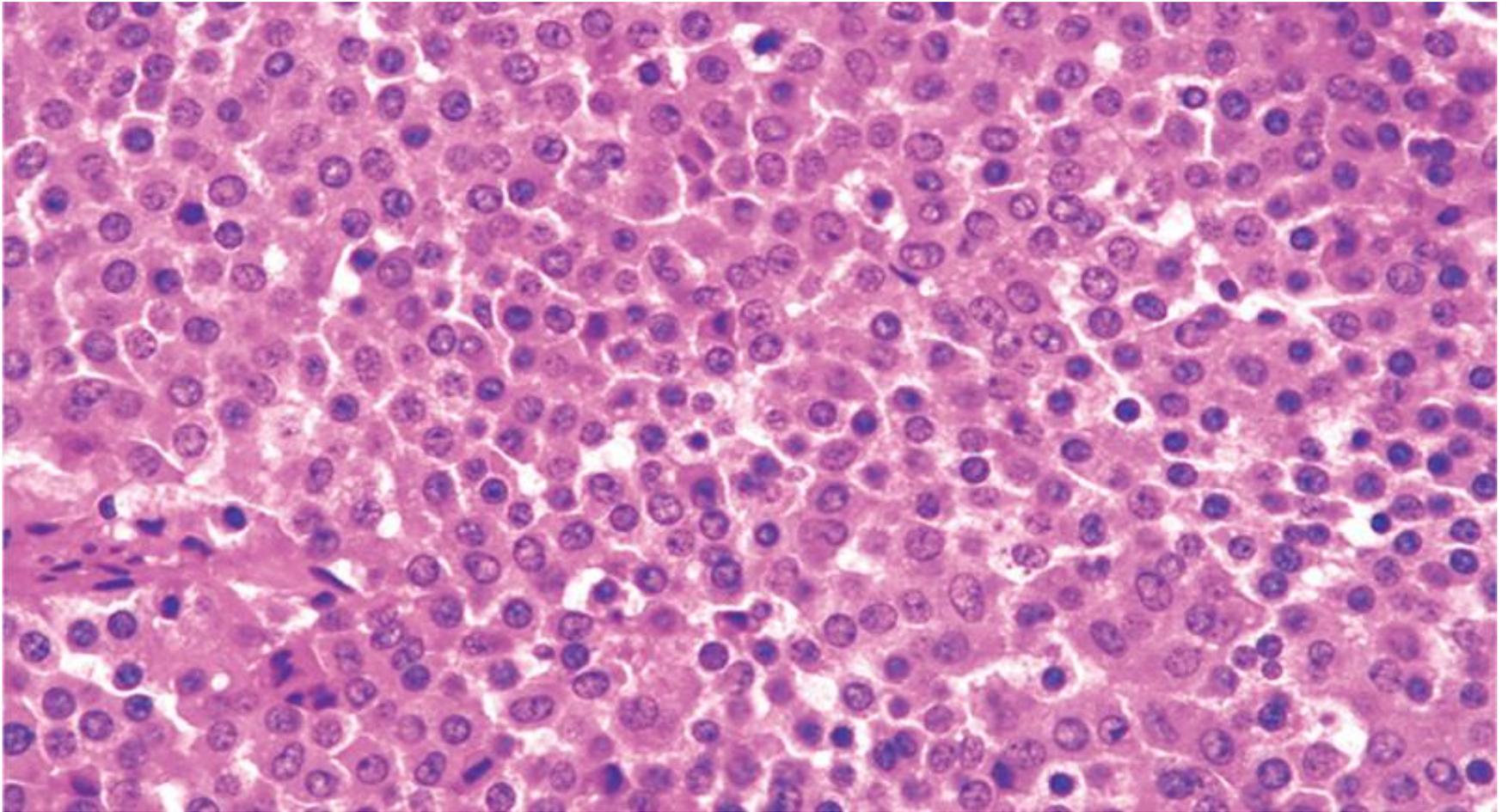
- Monomorphic: one cell type.. All cells look similar, whereas in the normal pituitary several cell types exist.
- Can you see the difference between these two pics?



Normal pituitary.. Several cell types



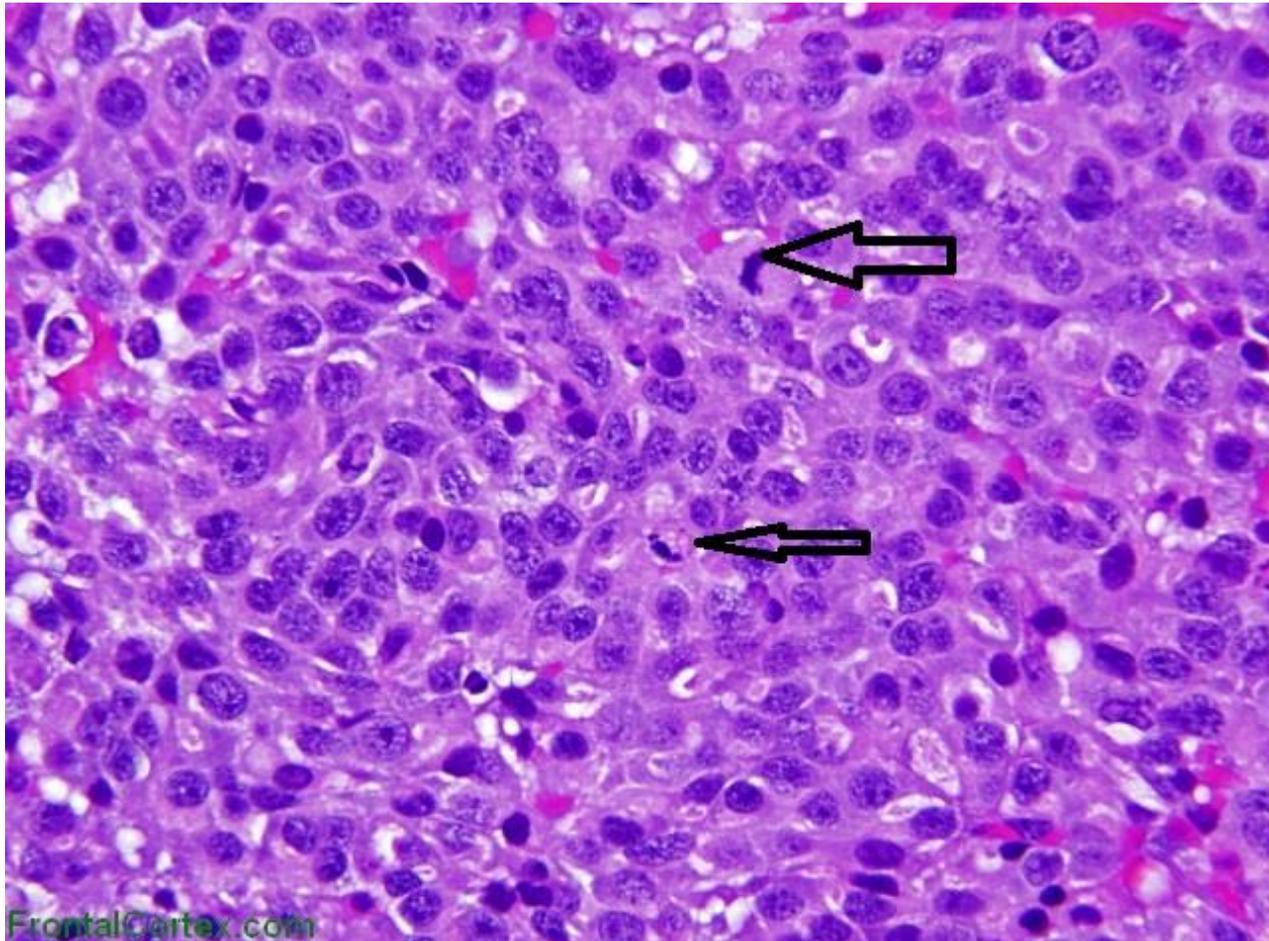
Adenoma.. One cell type =
monomorphic appearance



Notes

- Cellular **monomorphism** and the **absence of a significant reticulin network** distinguish pituitary adenomas from non-neoplastic anterior pituitary parenchyma
- **The functional status of the adenoma cannot be reliably predicted from its histologic appearance.**
- Adenomas that have *TP53* mutations demonstrate brisk mitotic activity and are called **atypical adenomas to reinforce their potential for aggressive behavior.**

Atypical adenoma with increased mitosis.. These have TP53 mutation and are aggressive



- *prolactinomas*

*These are adenomas that produce prolactin.=
hyperprolactinemia*

Hyperprolactinemia causes:

- a. Amenorrhea and galactorrhea,
- b. Loss of libido, and infertility

- prolactinomas usually are diagnosed **at an earlier stage in women of reproductive age** than in other persons .. Because they are more likely to have obvious symptoms

Other causes of hyperprolactinemia

- a. Pregnancy, and high-dose estrogen therapy,
- b. Dopamine-inhibiting drugs (e.g., reserpine).
- c. Any mass in the suprasellar compartment may disturb the normal inhibitory influence of hypothalamus on prolactin secretion, resulting in hyperprolactinemia-a mechanism known as the *stalk effect*.

Growth Hormone-Producing (Somatotroph) Adenomas

- May be quite large at time of diagnosis because the clinical manifestations of excessive growth hormone may be subtle,
- Small amounts of immunoreactive prolactin often are present as well.

clinical manifestations.

Increased growth hormone can cause Gigantism or acromegaly:

If a growth hormone-secreting adenoma occurs before the epiphyses closes (in children) it causes *gigantism.*

- gigantism: generalized increase in body size, with disproportionately long arms and legs.

gigantism



acromegaly

If elevated levels of growth hormone persist, or develop **after closure** of the epiphyses, affected persons develop acromegaly, in which:

1. Growth is most conspicuous in soft tissues, skin, and viscera and in the bones of the face, hands, and feet
2. Enlargement of the jaw results in its protrusion with separation of the teeth.
3. Enlarged hands and feet with broad, sausage-like fingers

acromegaly

acromegalypictures.com

- acromegaly



Corticotroph cell adenomas

- may be:

1. Clinically silent OR

2. May cause *hypercortisolism* = increased cortisol, manifested clinically as ***Cushing syndrome***

- Large, clinically aggressive corticotroph cell adenomas may develop after surgical removal of the adrenal glands for treatment of Cushing syndrome, this condition is *Nelson syndrome*.

The reason is the metabolic demands and the loss of the feedback mechanism.

***Because ACTH is synthesized as part of a larger pro-hormone substance that includes melanocyte-stimulating hormone (MSH), hyperpigmentation may be a feature.**

Gonadotroph LH]-producing and FSH adenomas

- Can be difficult to recognize, because they secrete hormones inefficiently, and the secretory products usually do not cause a recognizable clinical syndrome.

Pituitary carcinomas

- *are exceedingly rare and in addition to local extension beyond the sella turcica, these tumors virtually always demonstrate **distant metastases.***
- **As a general rule: Most endocrine carcinomas are diagnosed depending on behavior (presence of metastases) and not on histological appearance. i:e under the microscope adenoma and carcinoma can look similar.. You need to know the clinical information and check if the patient has metastatic disease in order to call the lesion metastatic.**

- Second type of disease that affect the pituitary other than mass effect is hormonal over or under production

Hyperpituitarism

- MOST COMMON CAUSE: functional adenoma.
- Other causes:
- Hyperplasia
- Carcinoma
- Secretion of pituitary hormones by nonpituitary tumors.
- Hypothalamic disorders.

Hypopituitarism:

Occurs if there is **Loss of at least 75% of anterior pituitary**

Causes:

- a. *Congenital* absence(exceedingly rare)
- b. Hypothalamic tumors, associated with posterior pituitary dysfunction.
- C . Nonfunctioning pituitary adenomas .. Most common/
remember that this occurs when the adenoma compresses normal pituitary tissue and affects its function.
- d. Ischemic necrosis of the anterior pituitary, e;g Sheehan syndrome(see next slide)
- e. Ablation of the pituitary by surgery or irradiation
- f. Inflammatory lesions such as sarcoidosis or tuberculosis
- g. Trauma and Metastatic neoplasms involving the pituitary.

Sheehan syndrome, or postpartum necrosis of anterior pituitary, is the most common form of clinically significant ischemic necrosis of the anterior pituitary.

- During pregnancy, the anterior pituitary enlarges considerably, because of an increase in the size and number of prolactin-secreting cells and this physiologic enlargement is not accompanied by an increase in blood supply from the low-pressure portal venous system.
- The enlarged gland is thus vulnerable to ischemic injury, especially in women who experience significant hemorrhage and hypotension during the postpartum period
- Note: Sheehan syndrome is named after a British **pathologist** who described the condition.

POSTERIOR PITUITARY SYNDROMES.

- Impairment of oxytocin synthesis and release has not been associated with significant clinical abnormalities.
- The clinically important posterior pituitary syndromes involve ADH= vasopressin

ADH deficiency

causes *diabetes insipidus (DI)* characterized by **excessive urination (polyuria)** caused by an inability of the kidney to properly resorb water from the urine

SO: patients are thirsty and have polydipsia= excessive drinking



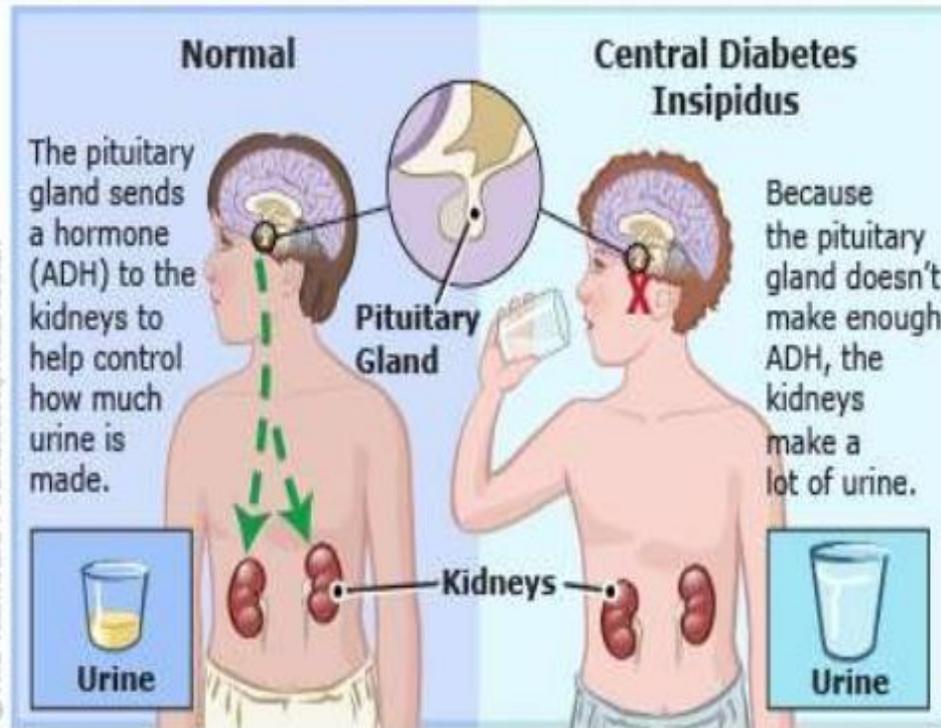
Diabetes insipidus can result from several causes,

- a. Head trauma, Neoplasms,
- b. Inflammatory disorders and surgical procedures of the hypothalamus and pituitary,
- c. The condition may be idiopathic.

Note:- Diabetes insipidus from ADH deficiency is designated as *central DI*, to differentiate it from *nephrogenic DI*

- The clinical manifestations of DI include:
 - a. The excretion of large volumes of **dilute** urine with an inappropriately **low specific gravity**
 - b. **Serum sodium and osmolality are increased** as a result of excessive renal loss of **free water** resulting in thirst and polydipsia
- Patients who can drink water generally can compensate for urinary losses; patients who are bedridden, or are limited in their ability to obtain water may develop life threatening dehydration.

DI



Increased ADH= Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

In (*SIADH*) ADH excess is caused by several extracranial and intracranial disorders.

- This condition leads to **resorption of excessive amounts of free water, with resultant hyponatremia.**
- The most common causes of SIADH include;
 - a. The secretion of **ectopic** ADH by malignant neoplasms
 - b. Non-neoplastic diseases of the lung
 - c. local injury to the hypothalamus or neurohypophysis.
- The clinical manifestations of SIADH are dominated by hyponatremia, cerebral edema, and resultant neurologic dysfunction.

CHECK YOUR UNDERSTANDING/ Q1

- A 31-year-old woman, who has two healthy children, notes that she has had **no menstrual periods** for the past 6 months, but she is not pregnant and takes no medications. Within the past week, she has noted **some milk production** from her breasts. She has been bothered by **headaches** for the past 3 months. After nearly hitting a bus while changing lanes driving her vehicle, she is concerned with **her vision**. Which of the following laboratory test findings is most likely to be present in this woman?
 - A Increased serum cortisol
 - B Lack of growth hormone suppression
 - C Increased serum alkaline phosphatase
 - D Hyperprolactinemia
 - E Decreased serum TSH

Explanation of the case in the question.

- This patient has amenorrhea and galactorrhea.. These are manifestations of increased prolactin.
- Her vision is affected because of the mass effect of the prolactinoma.
- The headache is caused by the increased intracranial pressure caused by the mass (any increase in the components of the brain: brain tissue, fluid, blood or CSF will result in increased intracranial pressure).. Headache is one of the manifestations of increased intracranial pressure.

CHECK YOUR UNDERSTANDING/ Q2

- A 33-year-old previously healthy man has lateral **visual field deficits**, but his residual vision is 20/20. **His facial features have changed** over the past year. His **shoe size has increased**. A head CT scan reveals **enlargement of the sella turcica**. Which of the following hormones is most likely being secreted in excessive amounts in this man?
 - A Antidiuretic hormone
 - B Prolactin
 - C ACTH
 - D **Growth hormone**
 - E Luteinizing hormone

CHECK YOUR UNDERSTANDING/ Q3

- A 41-year-old man has been **drinking large quantities of water**--up to 20 liters per day--for the past week. On physical examination he has **diminished skin turgor and dry mucous** membranes. A deficiency of which of the following hormones is most likely present in this man?
- A **Vasopressin = ADH**
- B Oxytocin
- C TSH
- D Growth hormone
- E Prolactin

