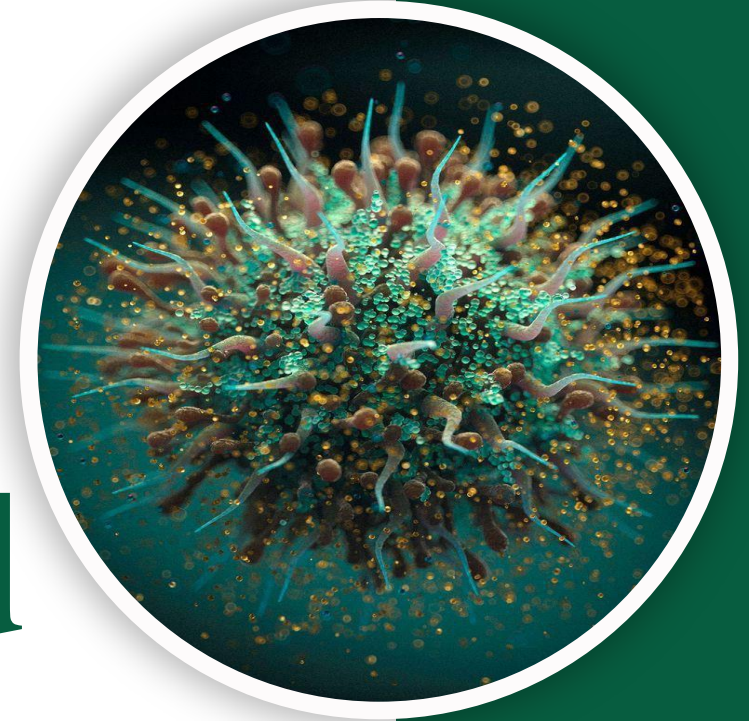


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(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)



Endocrine Pathology | FINAL 1

Diseases of the Pituitary Gland



Written by : Dopamine Scientific
Team

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Maria Baroudi

Diseases of the endocrine system lecture 1: Pituitary gland

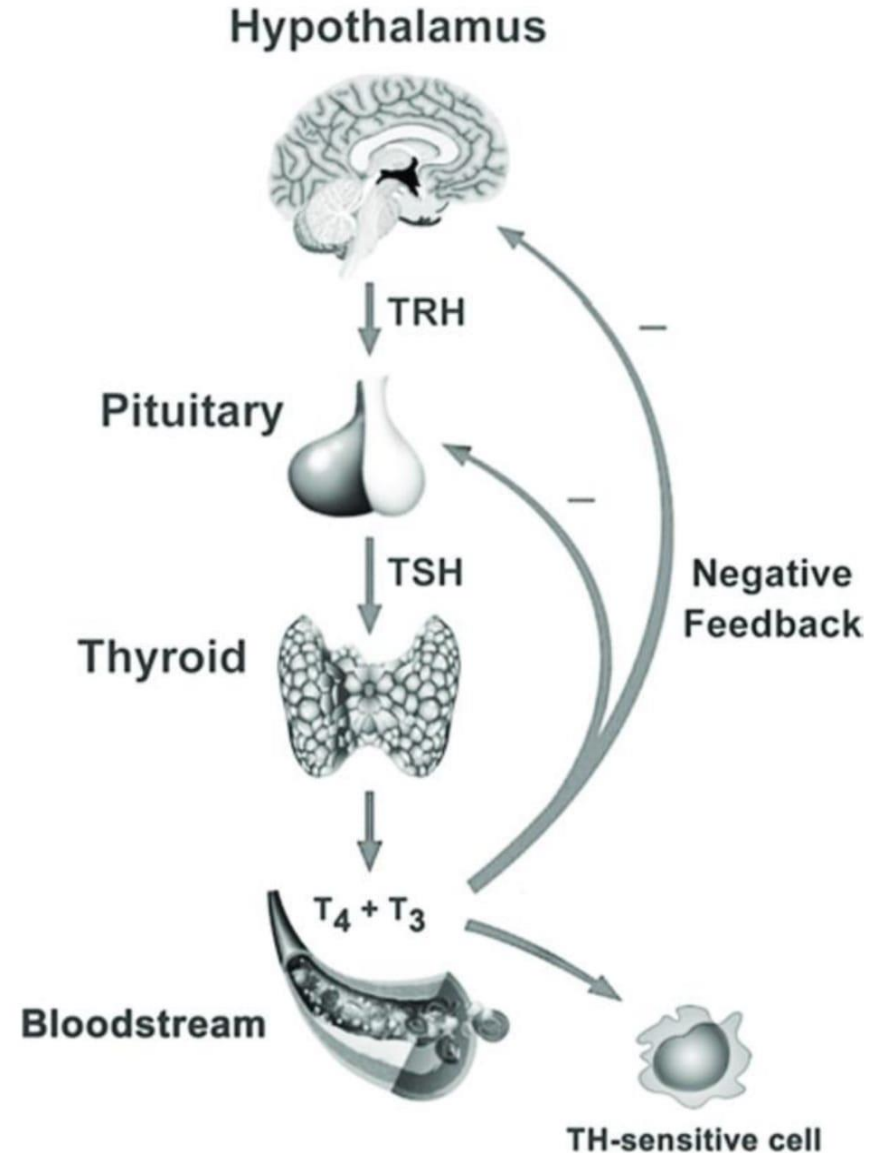
Dr Heyam Awad MD, FRCPath

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..

Example

- TRH (thyroid releasing hormone) and TSH (thyroid stimulating hormone) 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

(general rules that apply to the endocrine system as a whole)

The diseases of the endocrine system can be due to:

1. Mass effect

An increase in the size of the gland leads to the appearance of a mass that affects the surrounding tissues.

2. Disordered hormonal production (Under ~~hypo~~- or overproduction-hyper)

3. End organ resistance to the effect of the hormone

- the gland & its hormonal secretion is normal, also no masses are present, but the targeted organ is not responding - results are the same as the absence of the hormone (type 2 Diabetes)

*Remember: the hormone is a substance secreted from the gland, travels through the blood, & reaches the end organ.

- mainly focusing on the first 2 points.

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
- In general, tumors are divided into:
 - Neoplastic: all cells are mutated---> monoclonal (most neoplasms are derived from one original abnormal cell), can be benign or malignant.
 - Non-neoplastic: hyperplasia but no mutation & not clonal.

Endocrine system diseases general principles/3

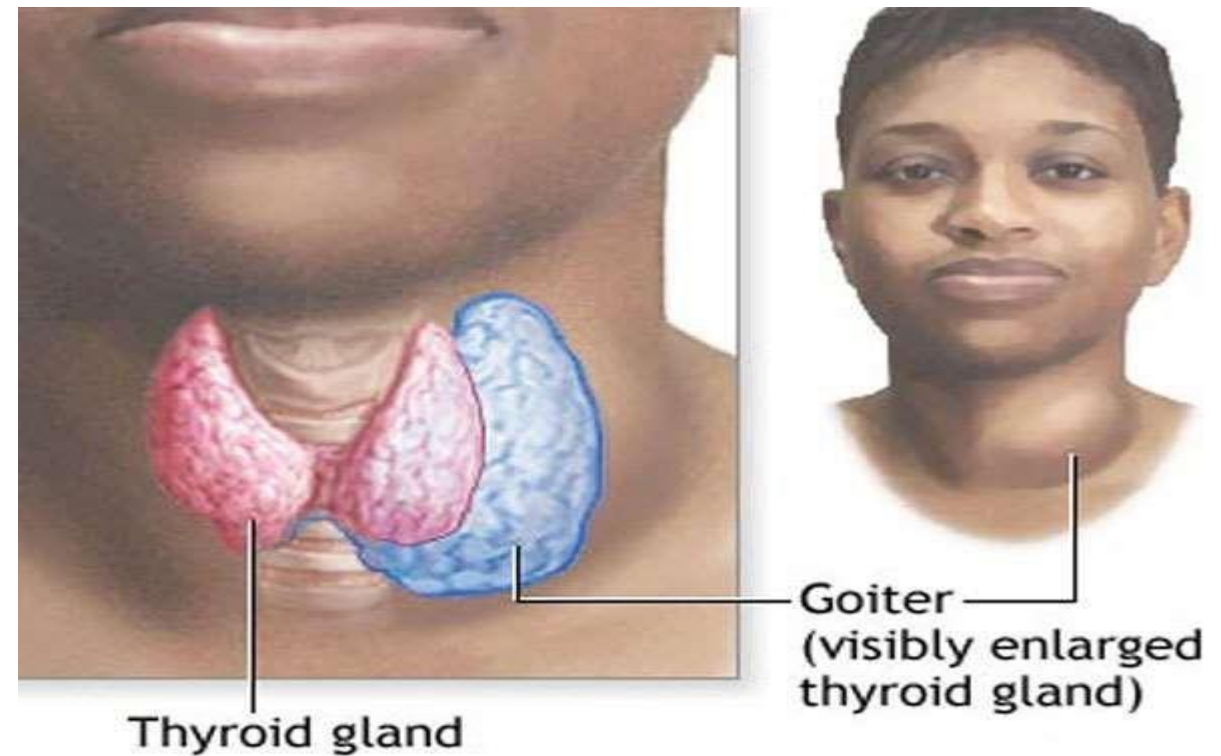
- The other group of diseases affecting endocrine glands are: abnormal hormonal secretion
- This can be over or under production due to several causes that will be discussed later
- **IMPORTANT NOTE: there is no relation between mass effect and hormonal abnormalities.**
- Patients might have a mass with normal, low or high hormonal secretion.
- Also hormone overproduction **is not always** associated with a mass
- The gland might have the size of a watermelon without oversecretion, while others might be too small with terrible oversecretion.

REMEMBER

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

Mass effect is not related to the hormonal level.

- Goiter: enlarged thyroid gland. Hormonal production can be:
 - Hyper - Hypo - Normal



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.

Dr. Heyam already mentioned this ,so she skipped it

PITUITARY GLAND: THE ORCHISTRA MAESTRO

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

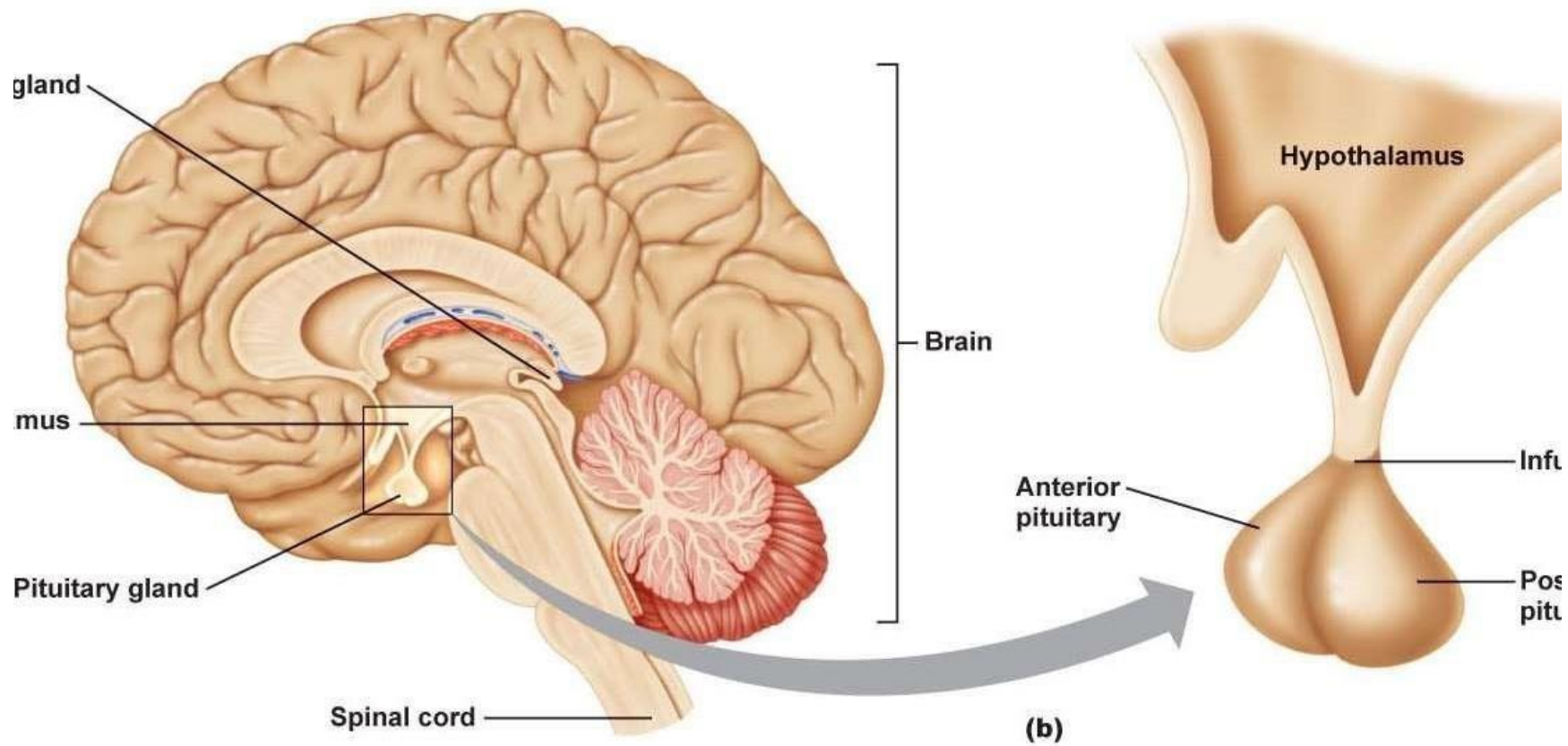
The next few slides were explained in physio.



Pituitary gland

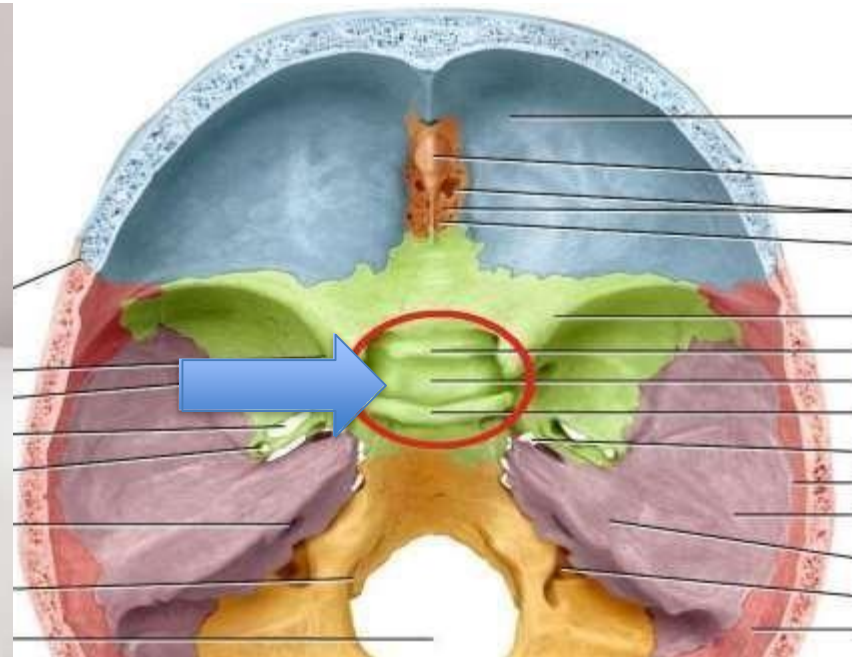
- Small, bean shaped structure that lies at the base of the brain within the sella turcica.

Pituitary gland



سيكوتلا جرسلا = 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.

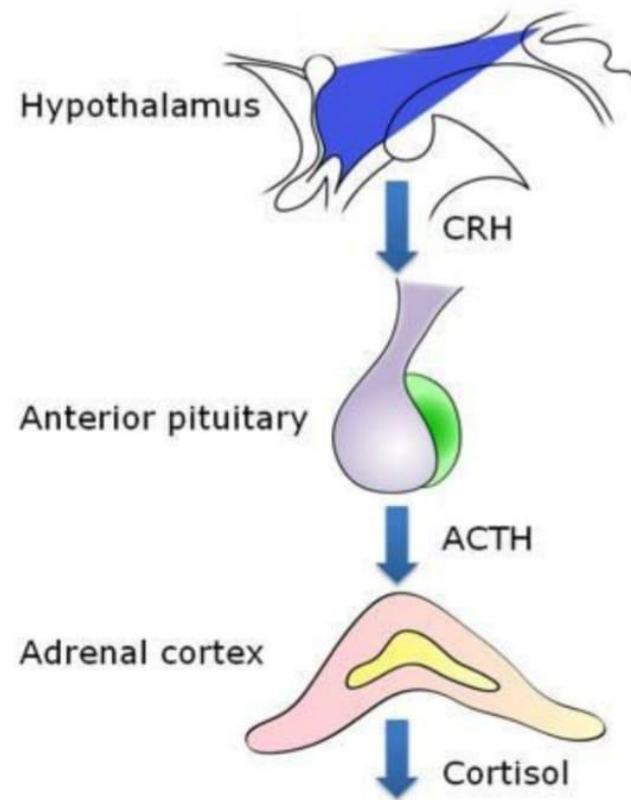


The hypothalamus (المهاد تحت) controls the pituitary (الغدة النخامية)

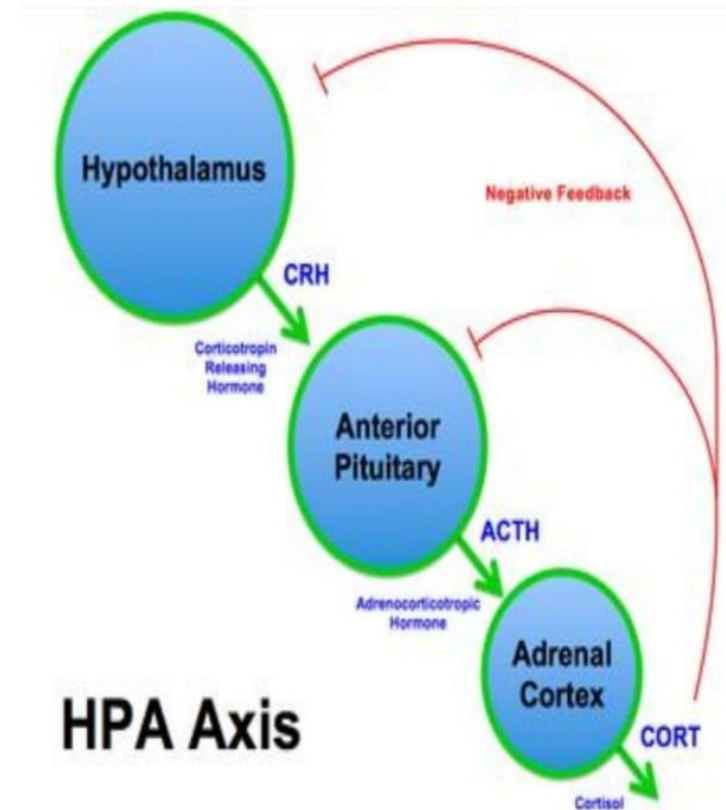
The production of most pituitary hormones is controlled by positively and negatively acting

factors from the hypothalamus which are carried to the anterior pituitary by a portal **vascular system**.

Examples of hypothalamic- pituitary axis.



F. Gaillard
© Podopostu.org

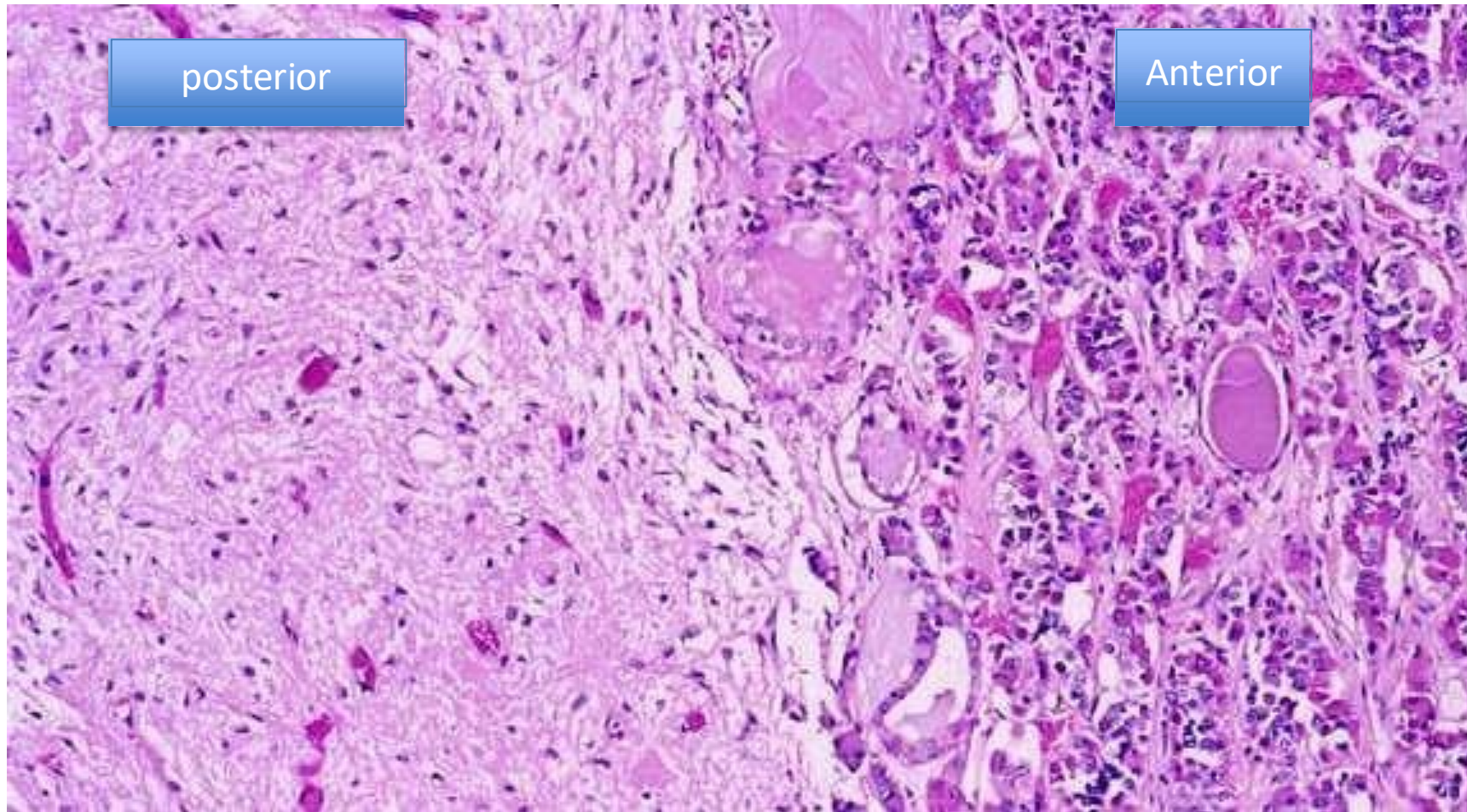


- The pituitary gland is composed of two morphologically and functionally distinct components: the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis)
- The anterior pituitary constitutes about 80% of the gland.

Anterior versus posterior pituitary

Posterior:
Stores
hormones only.

It is
neural
tissue



Anterior:
release &
synthesize
hormones

It is
epithelial
tissue

ANTERIOR VERSUS POSTERIOR PITUITARY LOBES

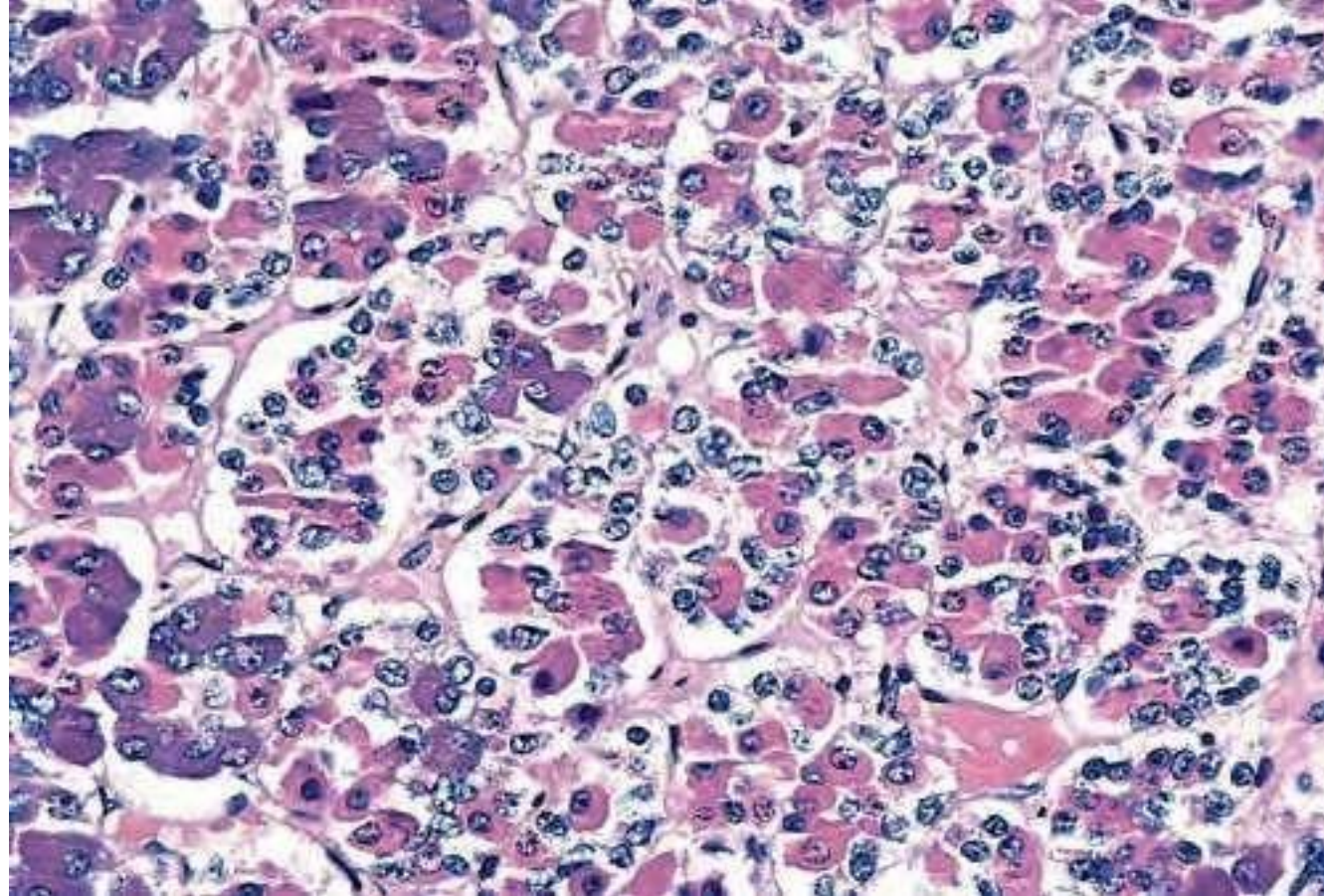
	ANTERIOR PITUITARY	POSTERIOR PITUITARY
histology	Epithelial cells	Glial cells and neuronal axons
Embryological origin	Oral mucosa (epithelial in origin)	Neural crest (neural in origin)
Hormones secreted	TSH, PRL, ACTH, GH, FSH , LH.	ADH and oxytocin (<i>synthesized in hypothalamus but stored in posterior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

Anterior pituitary

skipped

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

Anterior pituitary/ epithelial cells



- Skipped, but you can take a look at the glandular tissue of the anterior Pituitary, **remember:**
 - chromophils
 - Basophils & acidophils
 - chromophobes

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 (oxytosin 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, or even hyperplasia
- 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 the level of pituitary hormones is unaffected = resulting in normal hormonal levels.

- NOTE: Pituitary carcinomas are rare and usually non-secretory.
- In the whole endocrine system, carcinomas are rare. However, carcinomas are more common in the thyroid gland.
- Carcinomas are usually non-secretory.
- Carcinomas are difficult to be diagnosed histologically.

Mass effects of pituitary adenomas or carcinomas

Signs and symptoms :

- *Radiographic abnormalities of sella turcica: sellar expansion, bony erosions. (destruction to the bone of the sella turcica)

- *Compression of the optic chiasm **can be caused by any sort of mass in the pituitary** (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, **can lead to loss of consciousness.**

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

- **general rule: any increase in volume inside the skull - mass, increase in CSF, hemorrhage & fluid (edema) - increases intracranial pressure; because the skull has tightly closed sutures, so no area for more volume.**

- *seizures.

- *Cranial nerve palsies. (Cavernous sinus & its content of nerves)

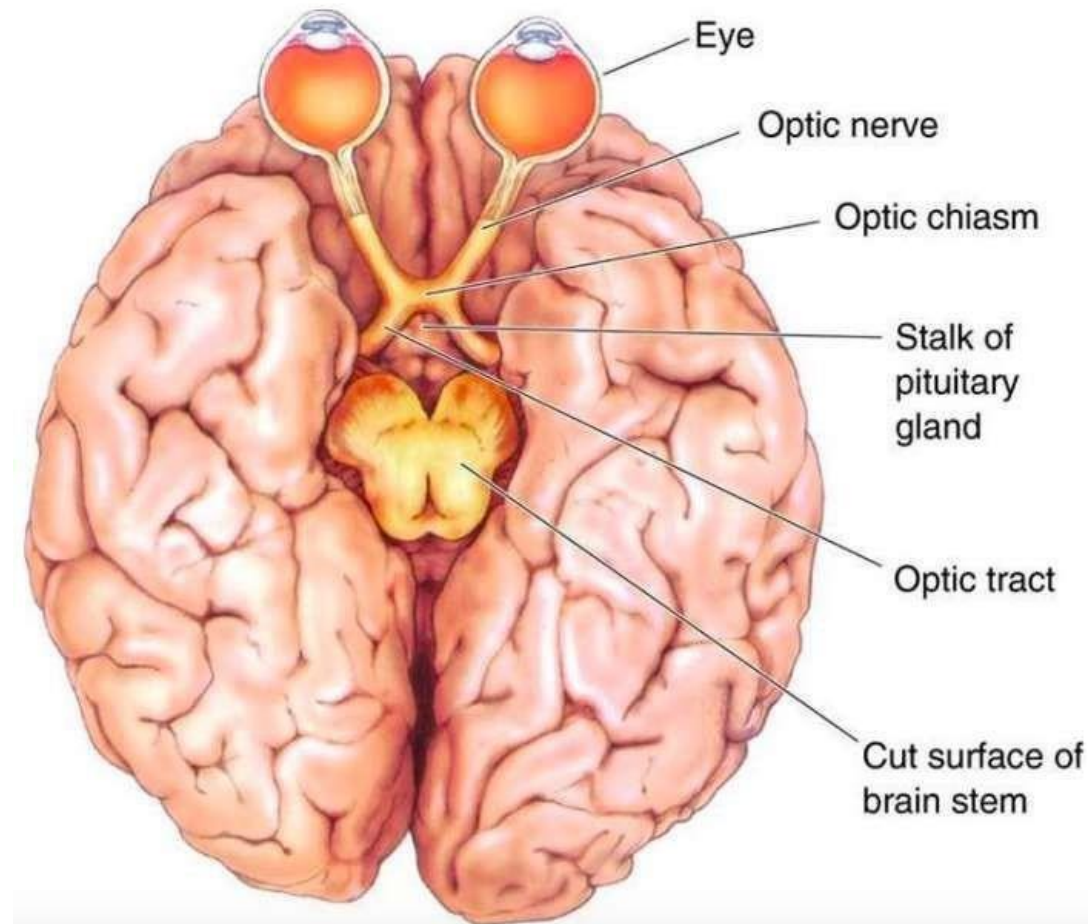
- ***pituitary apoplexy.. More details in a minute!**

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

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

- Adenoma: the gland enlarges gradually.
- If hemorrhage is present, rapid enlargement.

Pituitary adenomas

- Functional or nonfunctional.
- Functional: usually **one cell type** and one hormone produced. Sometimes can secrete more than one type of hormones
- Classified according to the hormones they produce.

Types of pituitary adenomas (according to the hormone produced)

- Prolactinomas.. 20-30%.. The most common
- Null cell adenoma... 20%.. Non-secretory non-functional
- 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% (more than one type of hormone)
- 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.

○ Why are most & least common important??

When you have a case, we usually go for the commonest cause & exclude the least common until proven otherwise.

E.g., problem in T4, think about thyroid before jumping to pituitary.

Pituitary adenomas

- In clinical practice, 10% of intracranial neoplasms are pituitary adenomas (not rare).
- But pituitary adenomas can be an incidental finding in 25% of autopsies. One out of every four people may have a pituitary adenoma without ever knowing about it during their lifetime. Why?
Because if the adenoma is **small and non-functioning**.smotpmys yna esuac ton yam ti ,
 - If it is **small** sah ti ,**not** tnacifingis a decudorp **mass effect** si ti gninaem ,**not** ot hguone egral **compress** eht .serutcurts gnidnuorrus
 - If it is **non-functioning** seod ti ,**not produce hormones**.smotpmys lacinilc esuac taht stnuoma ni
- Peak.. 4th to 6th decades.
- Mostly **single** lesions= solitary
- Can be divided into micro and macro adenomas according to size..
Cutoff point: 1cm.

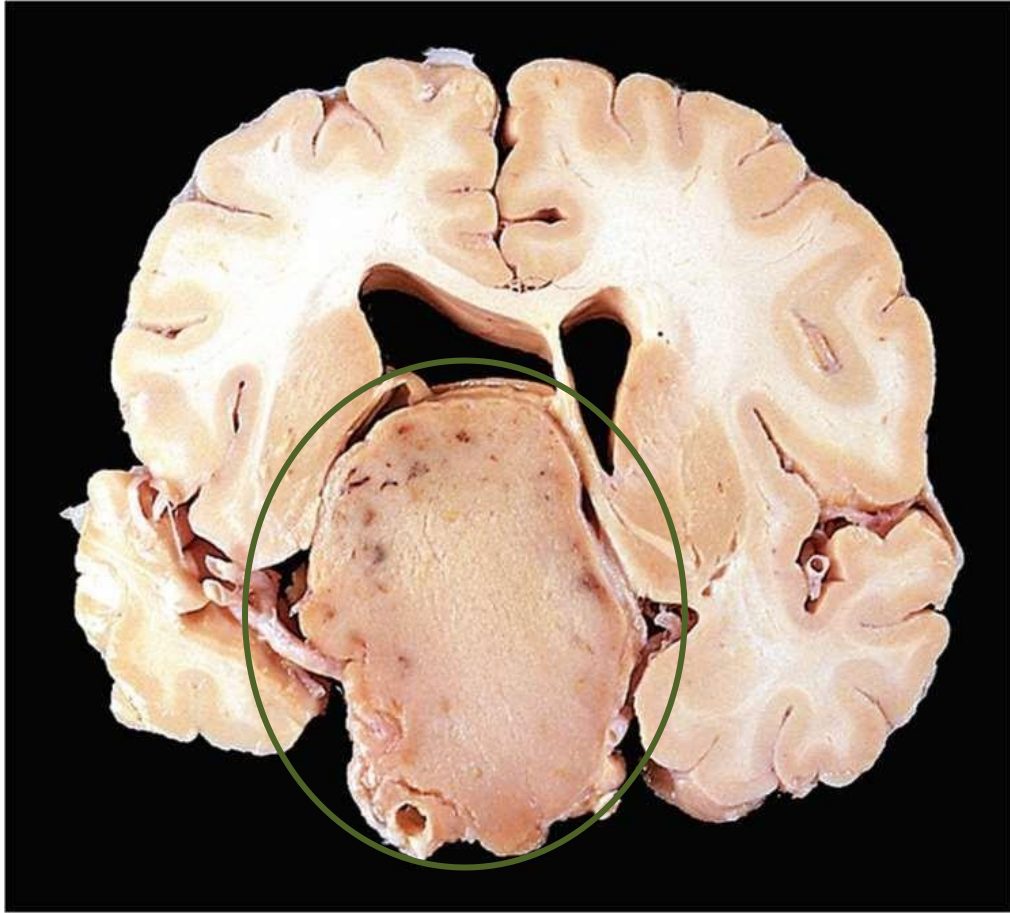
Macroscopic appearance

Gross features of adenomas

- The usual adenoma is a **well-circumscribed**, **usually soft** lesion that, if small, is confined by the sella turcica.

Which one is usually discovered as a macroadenoma?
non-secretory, no symptoms until mass effect is there.

Pituitary adenoma

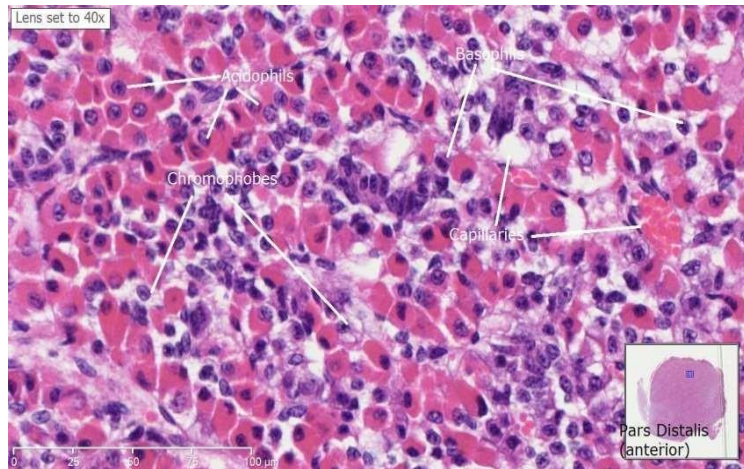


Kumar et al: Robbins Basic Pathology, 9e.
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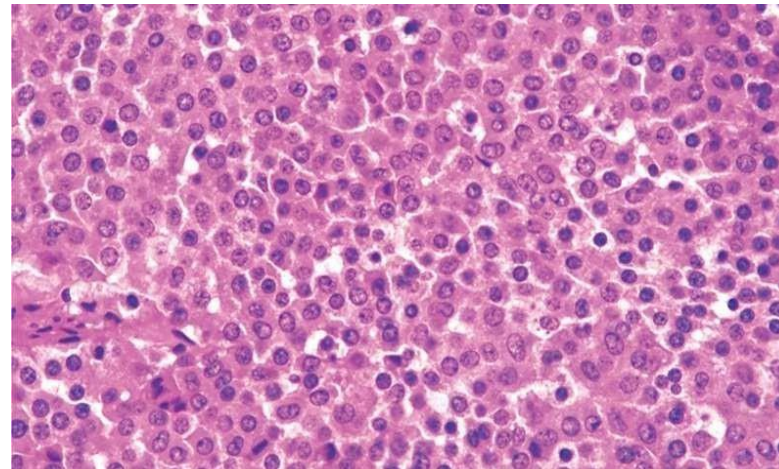
- We can draw a line around the borders of the tumor.
- Carcinoma has infiltrative characteristics, which is why they are immobile & solid; it has distant metastasis.
- Adenomas do not infiltrate or invade the surrounding tissues.

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?



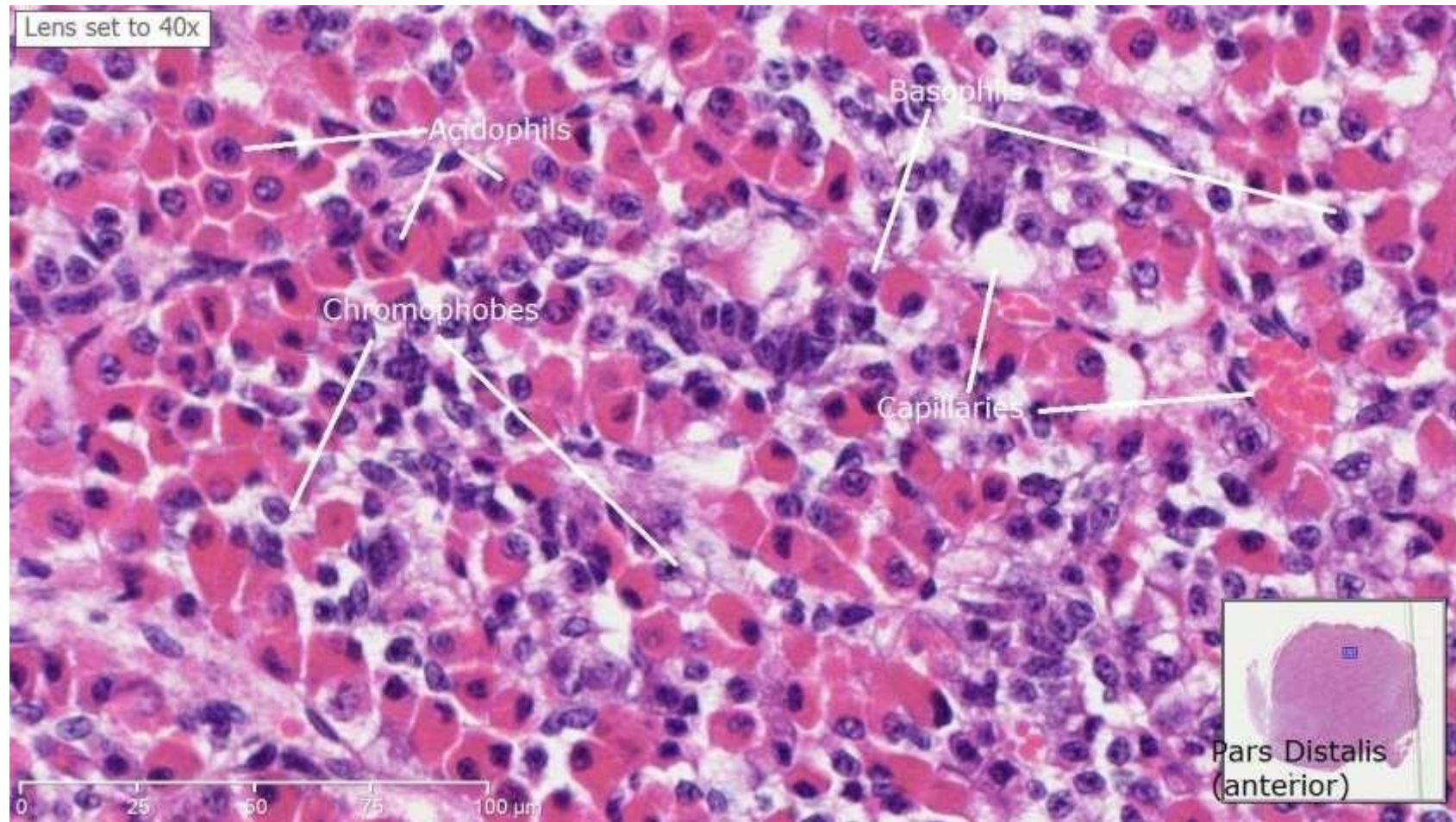
- Polymorphic: chromophils & chromophobes (normal)



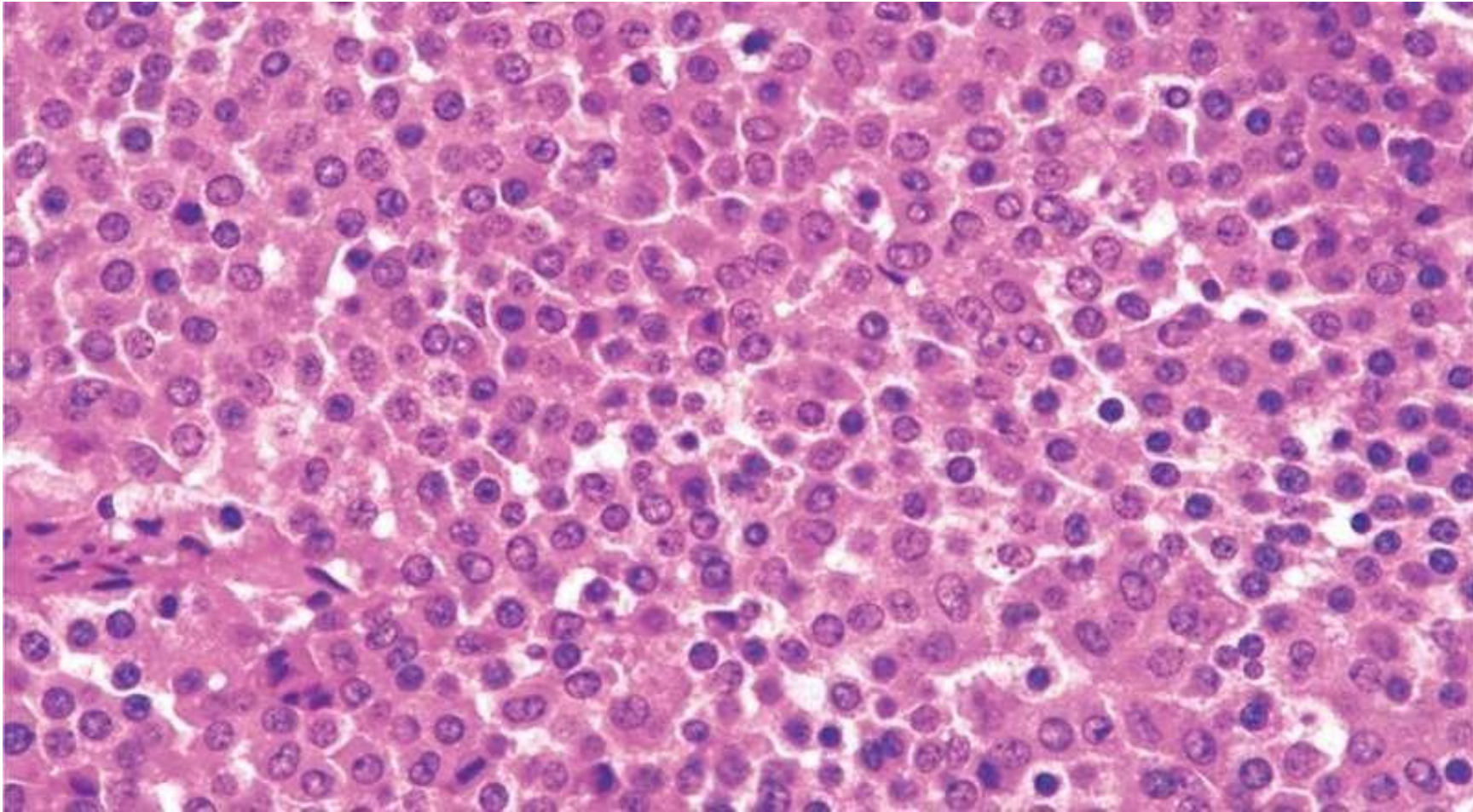
- monotonous/monoclonal: neoplasm (mostly adenoma).

- Mild atypia can still be seen in benign tumors.
- Therefore oligotypic, since aipya c ot tneiciffus ton esongaid .ycnangilam
- Malignancy si dehsilbatse ybinvasion into surrounding tissues and/or metastasis.

Normal pituitary.. Several cell types



Adenoma.. One cell type = monomorphic appearance



Symptoms of an adenoma may be due to:

- Mass effect caused by compression of surrounding structures.
- Hormonal production by a functioning adenoma such as:

1- prolactinomas

These are adenomas that produce prolactin= hyperprolactinemia.

Hyperprolactinemia causes:

- A. Amenorrhea (absence of menstrual cycle)
- B. Galactorrhea milk production (can occur in males)
- C. 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- loss of menstrual cycle, first we suspect pregnancy, then if she is taking any medications such as progesterone , lastly, prolactin levels. In males, sometimes symptoms are not clear until progression to macroadenoma.

2- Growth Hormone-Producing (Somatotroph) Adenomas

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 (**adults**) develop acromegaly, in which:

1. Growth is most conspicuous in soft tissues, skin, and viscera, and in the bones of the face (change in facial features), hands, and feet
2. Enlargement of the jaw (not due to bone enlargement but for soft tissue and small bone enlargement) results in its protrusion with separation of the teeth.
3. Enlarged hands and feet (bigger shoe size) with broad, sausage-like fingers

acromegaly



3- Corticotroph cell adenomas

increase in ACTH, high levels of cortisol.

- may be:

1. Clinically silent OR
2. May cause *hypercortisolism* = *increased cortisol*, manifested clinically as ***Cushing syndrome***

4- 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. *So, patients come with macroadenoma.*
- **May cause infertility due to hormonal imbalance.**
- **They can enlarge before being noticed, so mass effect may appear before hormonal effects.**

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.**

When a pituitary adenoma produces only one type of hormone (monomorphous), what happens to the secretion of other hormones?

Initially, the secretion of other hormones is often normal. However, as the adenoma increases in size, it can compress the surrounding normal pituitary tissue, leading to hypopituitarism.

This is especially common in nonfunctional pituitary adenomas, which do not secrete detectable hormones. As a result, they are often diagnosed late, only after their mass effect causes symptoms due to pressure on nearby structures, including hormone deficiencies.

Hyperpituitarism

The doctor didn't
mention this slide

- MOST COMMON CAUSE: functional adenoma.
- Other causes:
- Hyperplasia (non-neoplastic enlargement of the pituitary)
- Carcinoma
- Secretion of pituitary hormones by nonpituitary tumors. (Ectopic production of pituitary hormones)
- Hypothalamic disorders.

Hypopituitarism:

Occurs if there is a **Loss of at least 75% of the anterior pituitary** .(من رحمة ربنا فينا!)

Causes: **anything that destroys the pituitary (infection ,...)**

- 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, **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.
- The enlarged gland is thus vulnerable to ischemic injury, especially in women who experience significant hemorrhage and hypotension during the postpartum period.

- ✓ **After significant postpartum hemorrhage** **hypotension, tachycardia, and coagulopathy** → **Sheehan's syndrome**
- ✓ Normal postpartum bleeding should be distinguished from significant postpartum hemorrhage, which is an abnormal condition.
- ✓ Pituitary enlargement during pregnancy is a normal physiological change, but postpartum hemorrhage and ischemic injury are pathological.
- ✓ Sheehan syndrome doesn't occur in every pregnancy; severe hemorrhage may result due to several causes such as placenta previa or severe bleeding during an operation.

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 (decreased production)

causes *diabetes insipidus* (*DI*) characterized by **excessive urination (polyuria)** – loss of fresh water without sodium so the patient will have hypernatremia – 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: Any damage or destruction affecting the hypothalamus or pituitary can cause central DI, including infiltration by metastatic tumors or other destructive lesions.

a. Head trauma

b. Neoplasms.

c. Inflammatory disorders

d. Surgical procedures of the hypothalamus and pituitary.

e. Idiopathic.

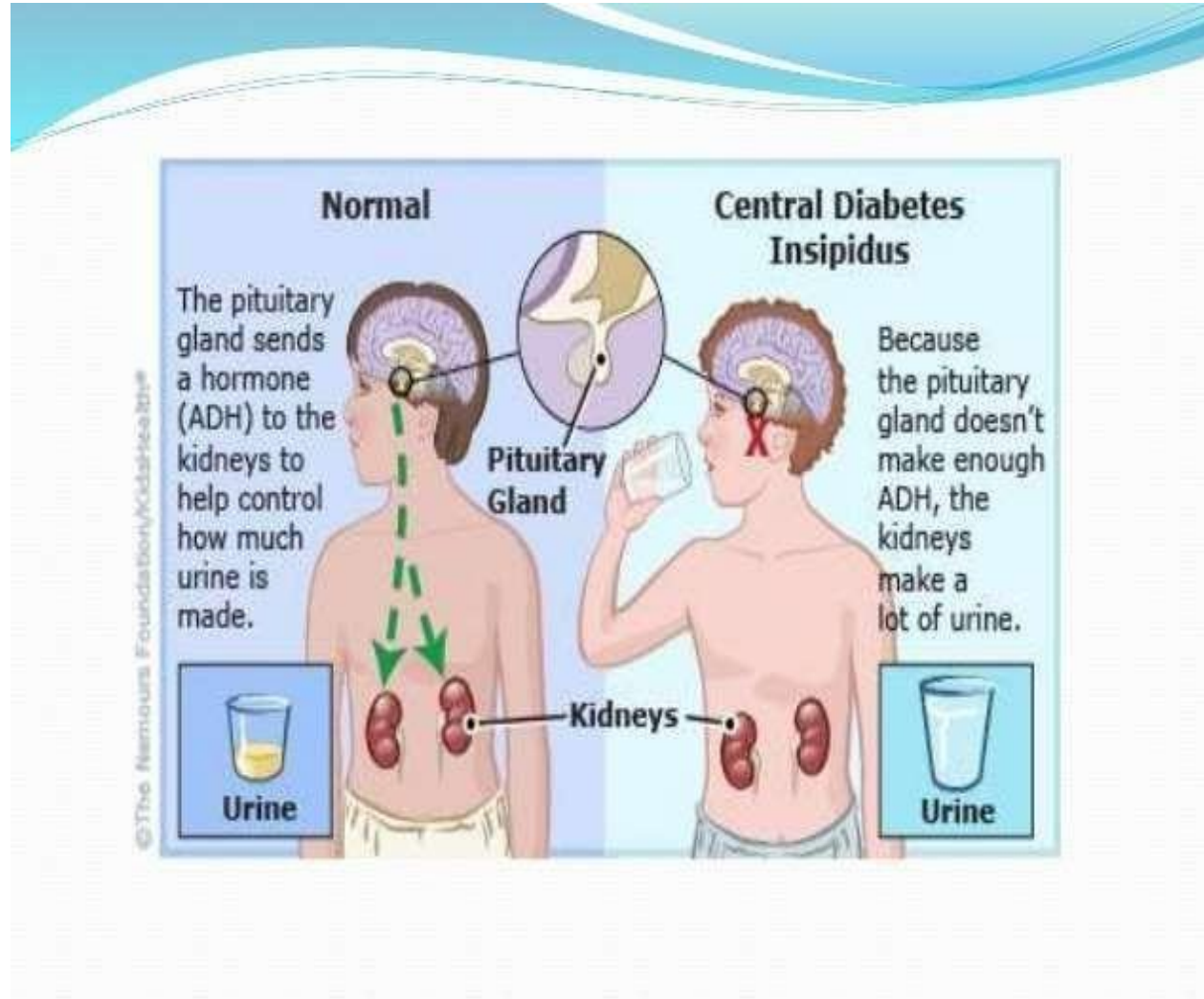
Note: Diabetes insipidus from ADH deficiency is designated as central DI, to differentiate it from nephrogenic DI

It is called diabetes insipidus because, like diabetes mellitus, it causes **polyuria and polydipsia**.

However, the urine in DI contains excessive **free water**,
erofereht si ti ;esoculg ssecxe tuohtiw **dilute urine** naht rehtar
.MD ni sa eniru hcir-esoculg

- 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** *water retention* → *dilution of plasma sodium* → *hyponatremia* → *edema* ,with resultant **hyponatremia**.
- The most common causes of SIADH include;
 - a. The secretion of **ectopic** ADH by malignant neoplasms. **Main cause.**
 - b. Non-neoplastic diseases of the lungs. *see next slide.*
 - c. local injury to the hypothalamus or neurohypophysis *can rarely stimulate ADH secretion.*
- The clinical manifestations of SIADH are dominated by hyponatremia, cerebral edema, and resultant neurologic dysfunction.

Ectopic hormone production (paraneoplastic syndrome): a malignant tumor may produce a hormone that is not normally produced by that tissue, e.g. **lung tumors producing ADH.**

Lung disease is an important cause of increased ADH; non-neoplastic lung diseases can also increase ADH secretion, although **malignant lung disease is the most important cause.**

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.
 - **Amenorrhea →first rule out pregnancy →then medications →then prolactin.**
 - Her vision is affected (**optic chiasm compression**) 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.
- ❑ It's most likely large because it caused mass effect.**

Answer : D

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

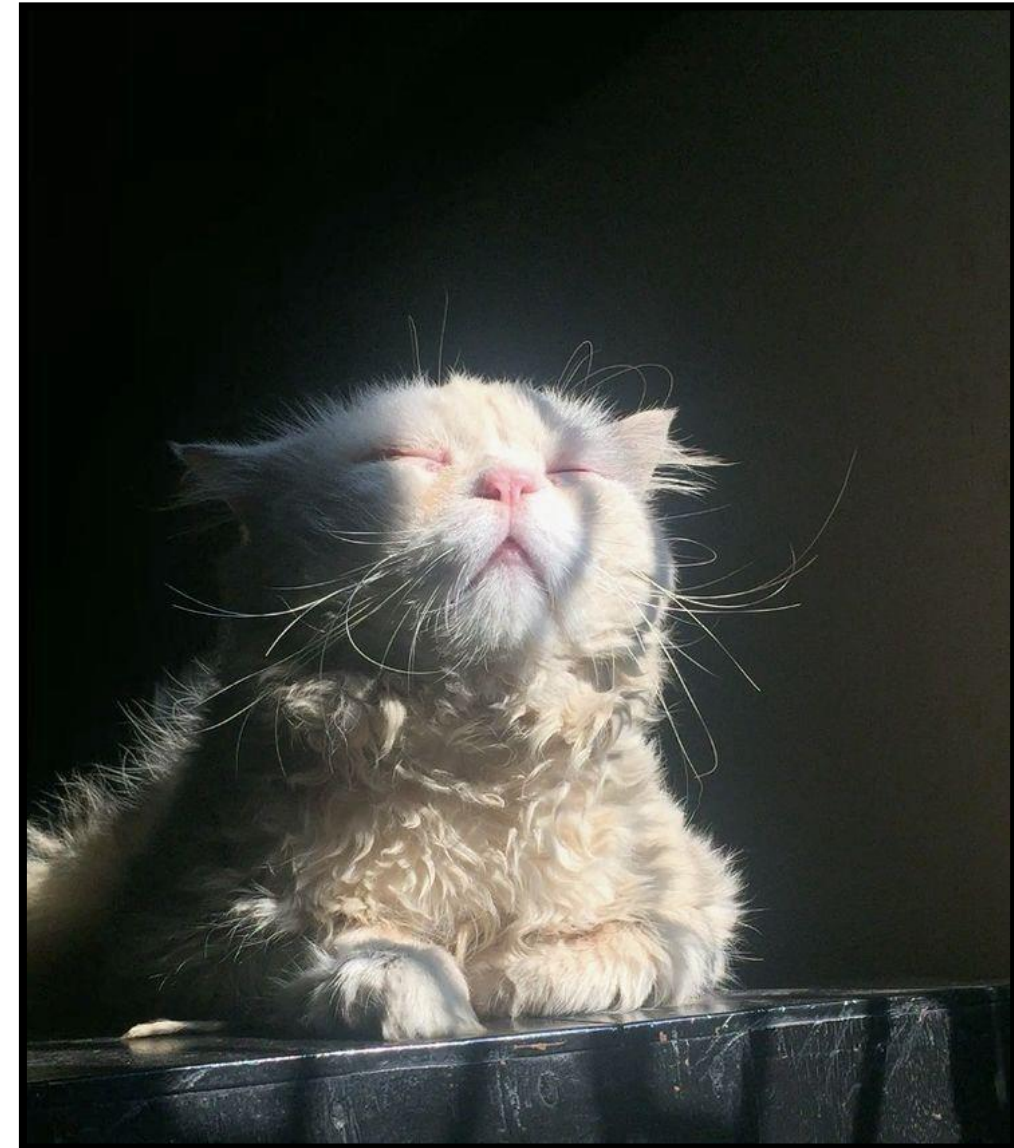
- A 41-year-old man has been **drinking large quantities of water**--up to 20 liters per day--for the past week. On physical examination he has **diminished skin turgor and dry mucous** membranes. A deficiency of which of the following hormones is most likely present in this man?
- A Vasopressin = ADH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

Check your understanding with past question:

An X ray of a 55-year-old female shows the Sella turcica with associated bony erosions. She complained of vision problems. The MOST COMMON cause of her symptoms is :

- A) Pituitary macroadenoma, Prolactinoma type
- B) Pituitary microadenoma, prolactinoma type
- C) Prolactinoma that can be of any size
- D) Non-functioning pituitary macroadenoma
- E) Non-functioning pituitary adenoma of any size

رسالة من الفريق العلمي:



قال رسول الله

«إنها ليست بنجس

إنها من الطوافين

عليكم والطوافات»

أي: إنها حيوان طاهر، وليست فيها نجاسة؛ «إنها من الطوافين عليكم والطوافات»، والطوافون والطوافات هم الخدم، وسُموا بذلك؛ لكثرة دخولهم وطوافهم في البيوت على مواليتهم، وشبهه بهم القِطَطَ لكثرة دخولها ووجودها في البيوت

إرواء الغليل للشيخ الألباني ١٧٣

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			