Diseases of the endocrine system lecture 1

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FRCPath

- Lectures will be available on the university website before they are given.
- Office hours: Sunday and Monday 1-3.
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- Slides on the website will contain ALL the material needed for the exam
- I encourage you to read from the book though!
- A short version of each lecture will be used for demonstration purposes during lecture hours.

Six lectures

- Pituitary gland.
- Thyroid gland 1
- Thyroid gland 2
- Parathyroid gland
- Adrenal gland
- Endocrine pancreas & diabetes

- Reference: Robbins basic pathology, 9th edition

Endocrine system diseases general principles/1

The diseases of the endocrine system can be due to

1. Mass effect or 2. disordered hormonal production (Under or over production)

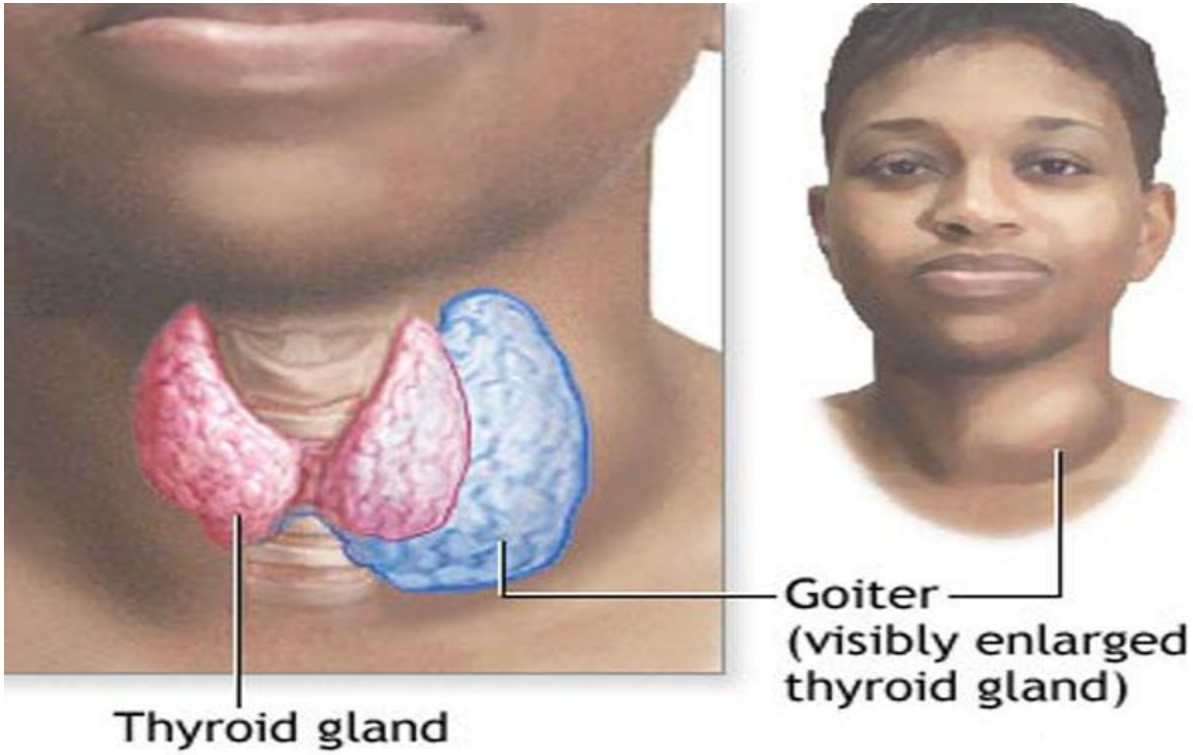
- Mass effect means an enlargement of the gland which can compress adjacent structures.
- Mass effect can be due to neoplastic or non-neoplastic conditions
- Neoplastic include: adenoma and carcinoma
- Non neoplastic= hyperplasia

Endocrine system diseases general principles/2

- 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

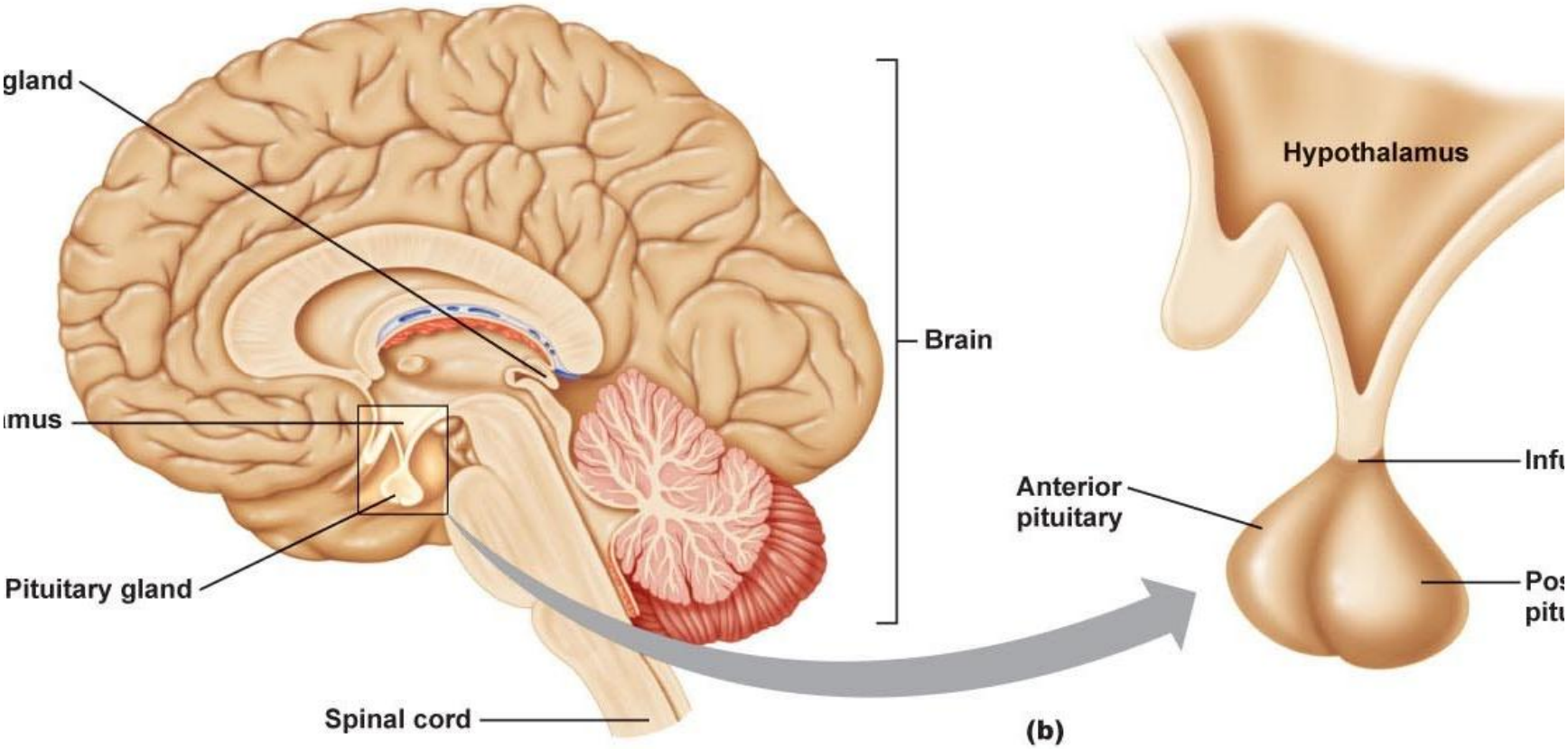
- A large gland doesn't predict hormonal level !!



PITUITARY GLAND: THE ORCHISTRA MAESTRO

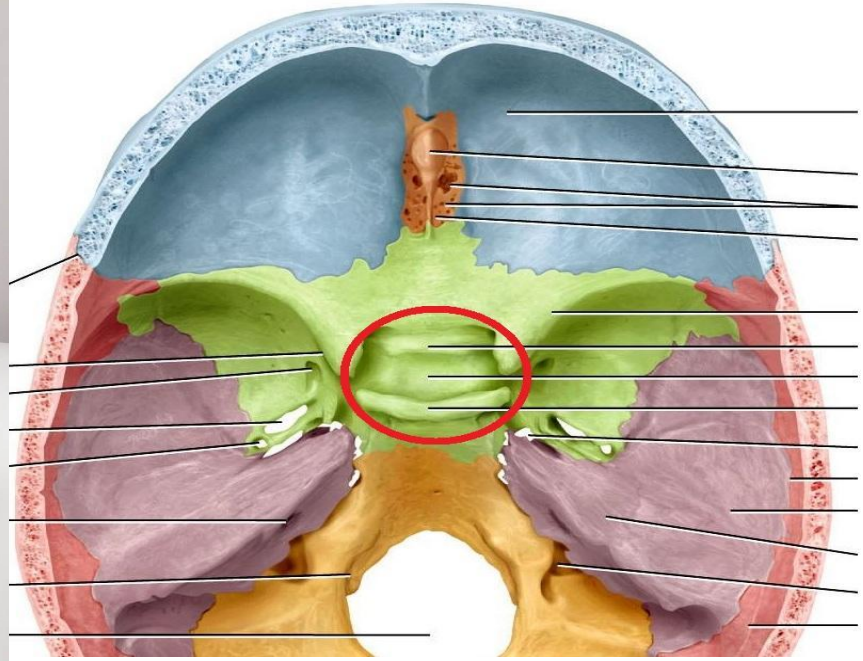
- The hormones secreted from the pituitary gland control levels of hormones secreted from all other endocrine glands.

Pituitary gland



اَلسَّرْجُ التُّرْكِيُّ= Sella turcica = pituitary fossa

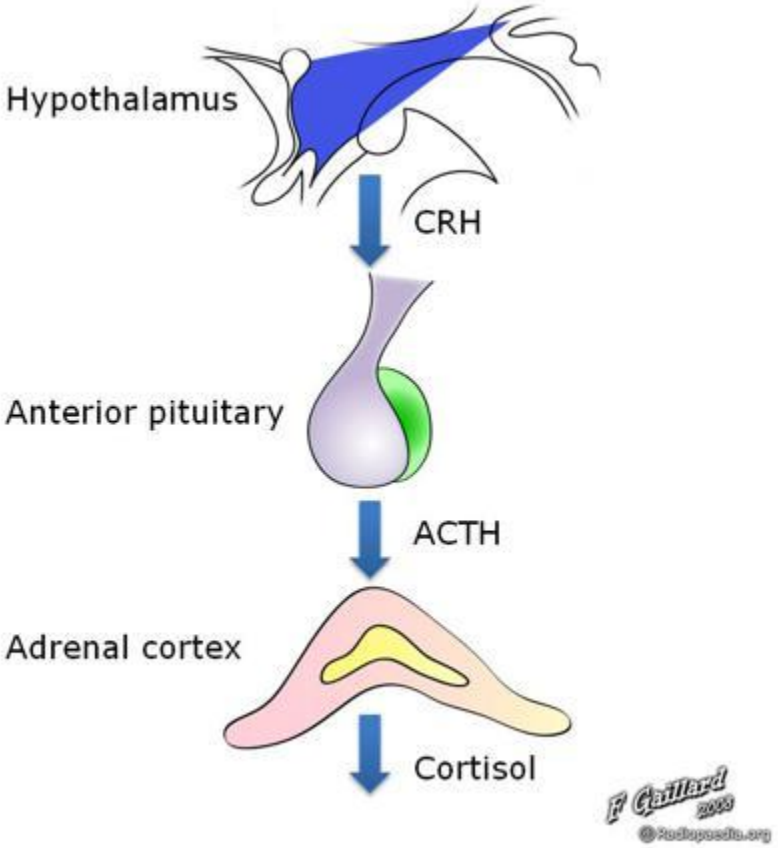
- The **sella turcica** (Latin for Turkish seat) is a saddle-shaped depression in the body of the sphenoid bone of the skull

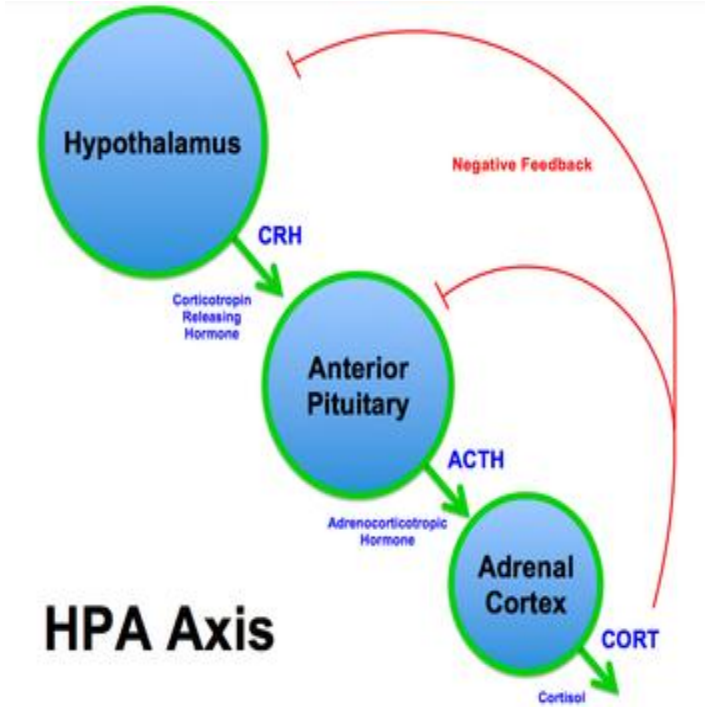


The hypothalamus (تحت المهاد) controls the pituitary (الْغُدَّة النُّخَامِيَّة)

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.**

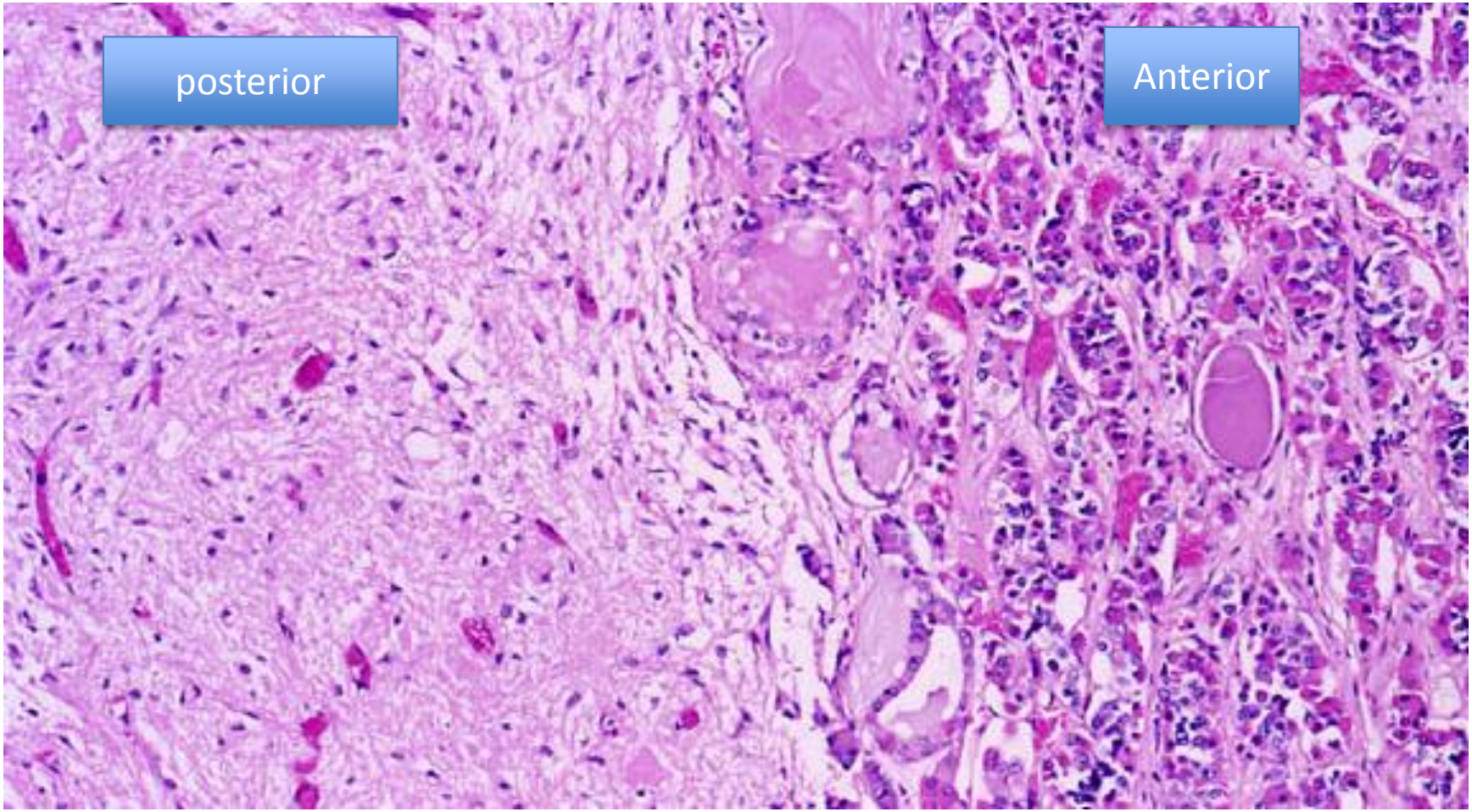
Examples of hypothalamic- pituitary axis





- 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.

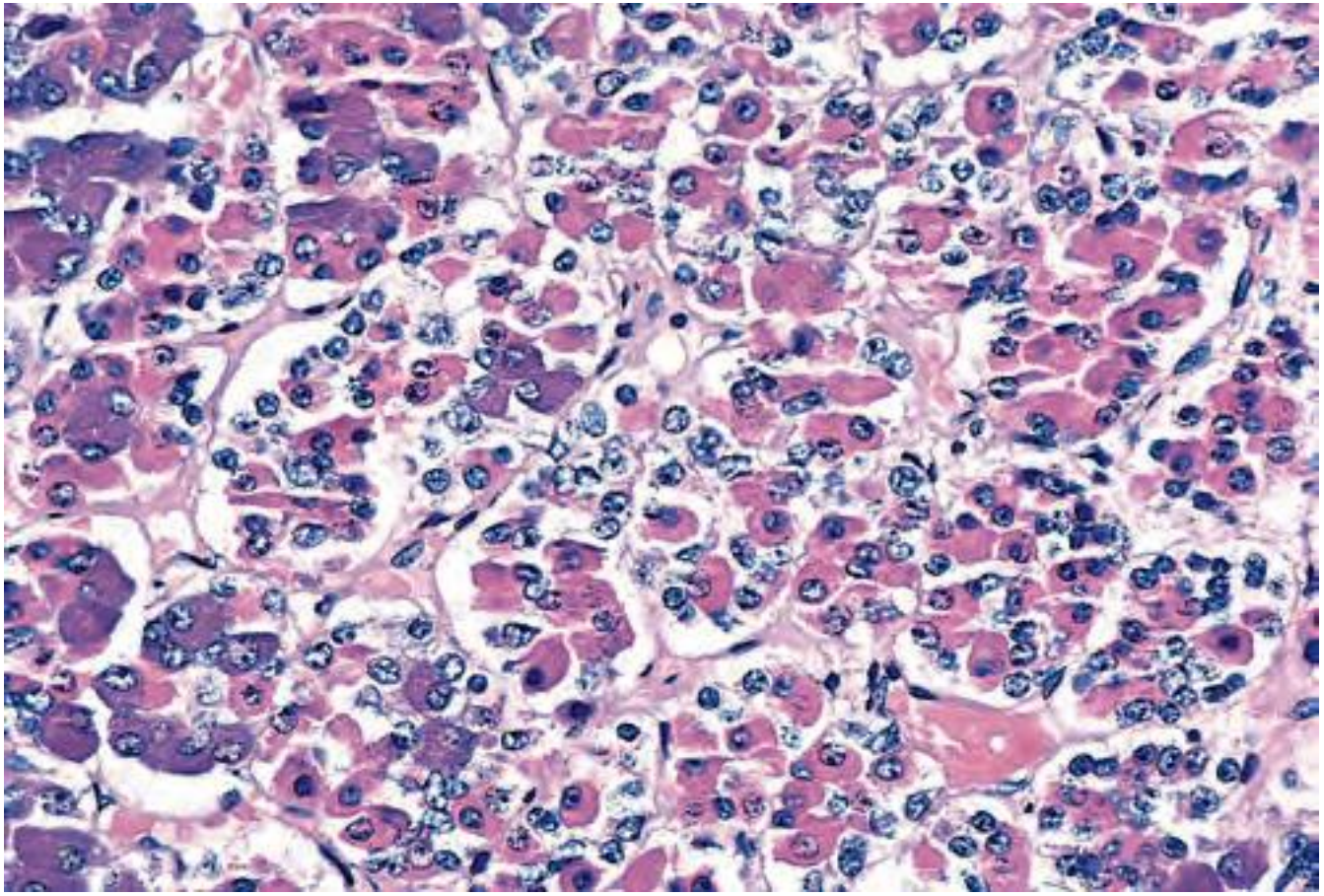
Anterior versus posterior pituitary



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 (*synthesized in hypothalamus but stored in posterior pituitary*)

Anterior pituitary/ epithelial cells



Posterior pituitary

- The *posterior pituitary* consists of **modified glial cells** (termed *pituicytes*) and axonal processes extending from the hypothalamus through the pituitary stalk to the posterior lobe (*axon terminals*).

- Two peptide hormones are secreted from the posterior pituitary, *oxytocin* and *antidiuretic hormone* (ADH, also called *vasopressin*).

- These (oxytosin and ADH) are actually synthesized in the hypothalamus and stored within the axon terminals residing 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: PITUITAY CARCINOMAS ARE RARE AND USUALLY NON_SECRETORY.

Mass effects of pituitary adenomas or cacinomas

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.

*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.. See next slide

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/Prolactn adenoma.. 5%
- TSH cell adenoma… 1%.. Least common
- pleurihormonal… 15%

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.. 4^{th} to 6^{th} decades.
- Mostly **single** lesions= solitary
- Can be divided into micro and macro adenomas according to size.. Cutoff point: 1cm.

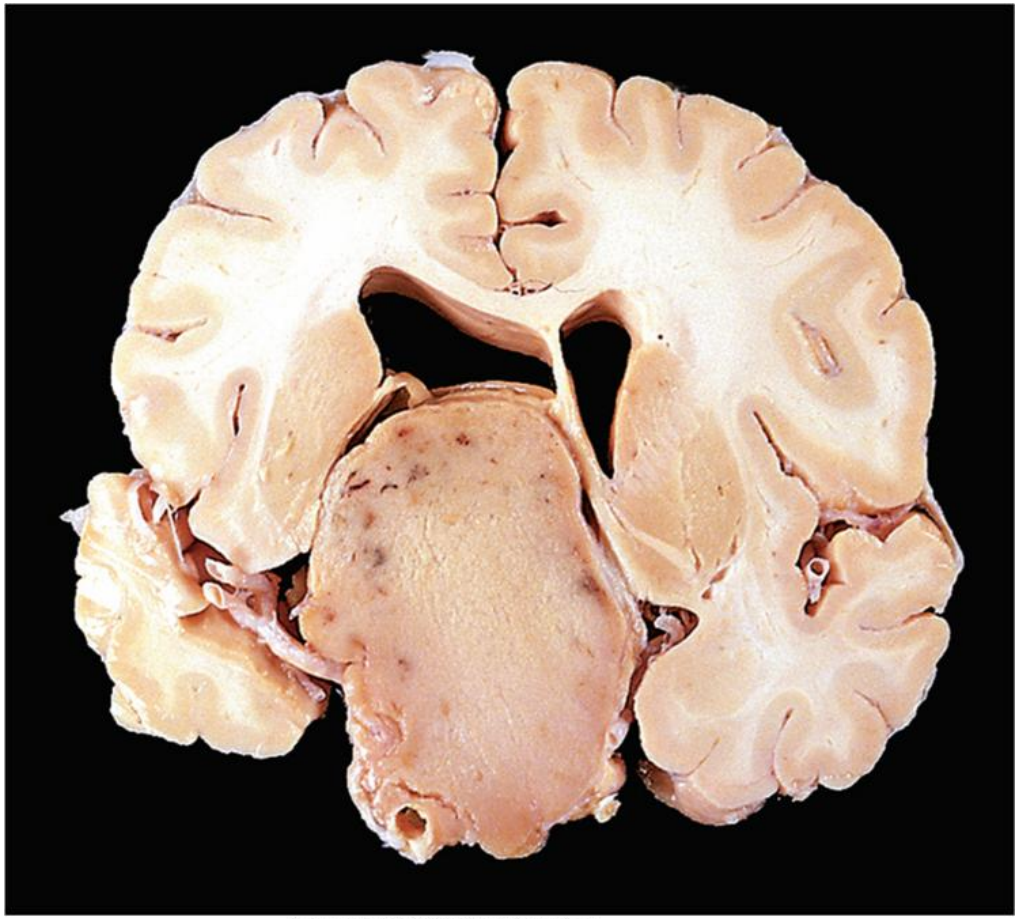
Macroscopic appearance

Gross features of adenomas

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

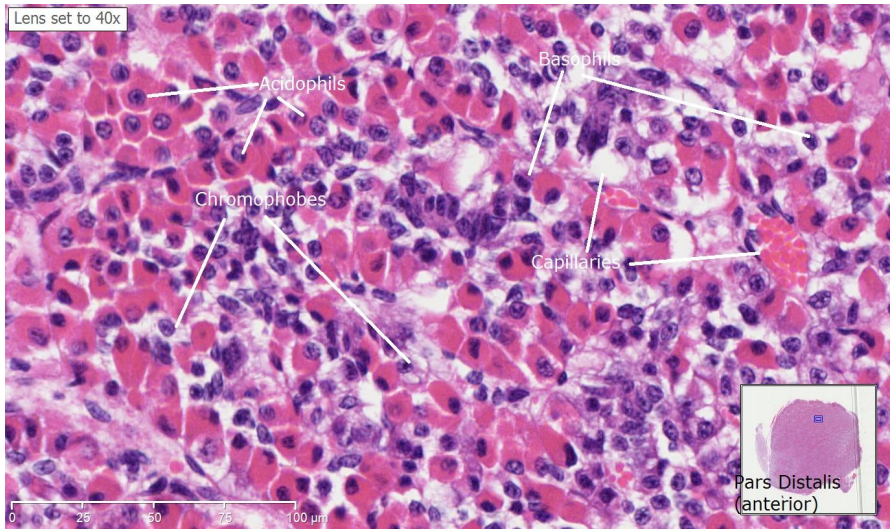
- In 30% of cases, the adenomas are non-encapsulated and infiltrate adjacent bone,dura and brain.

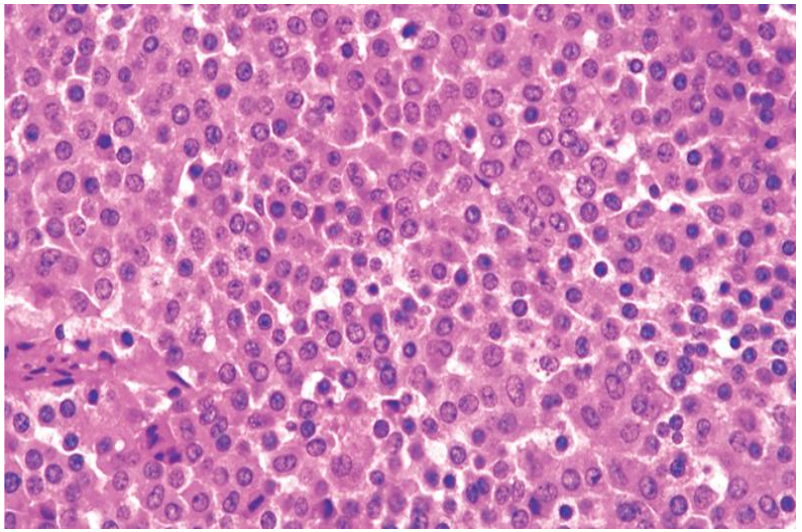
Pituitary adenoma



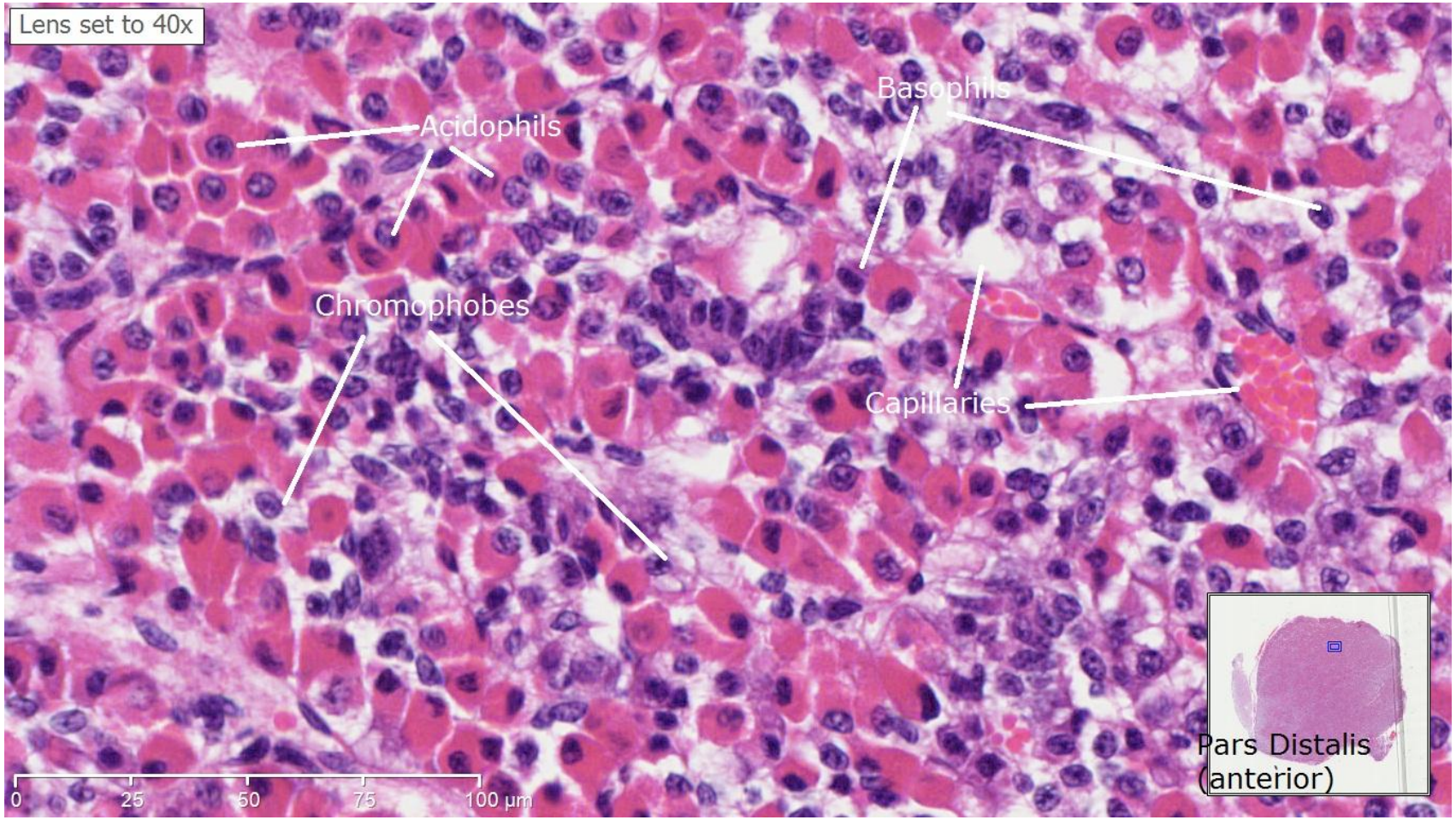
Pituitary adenoma

- Monomophic: 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?

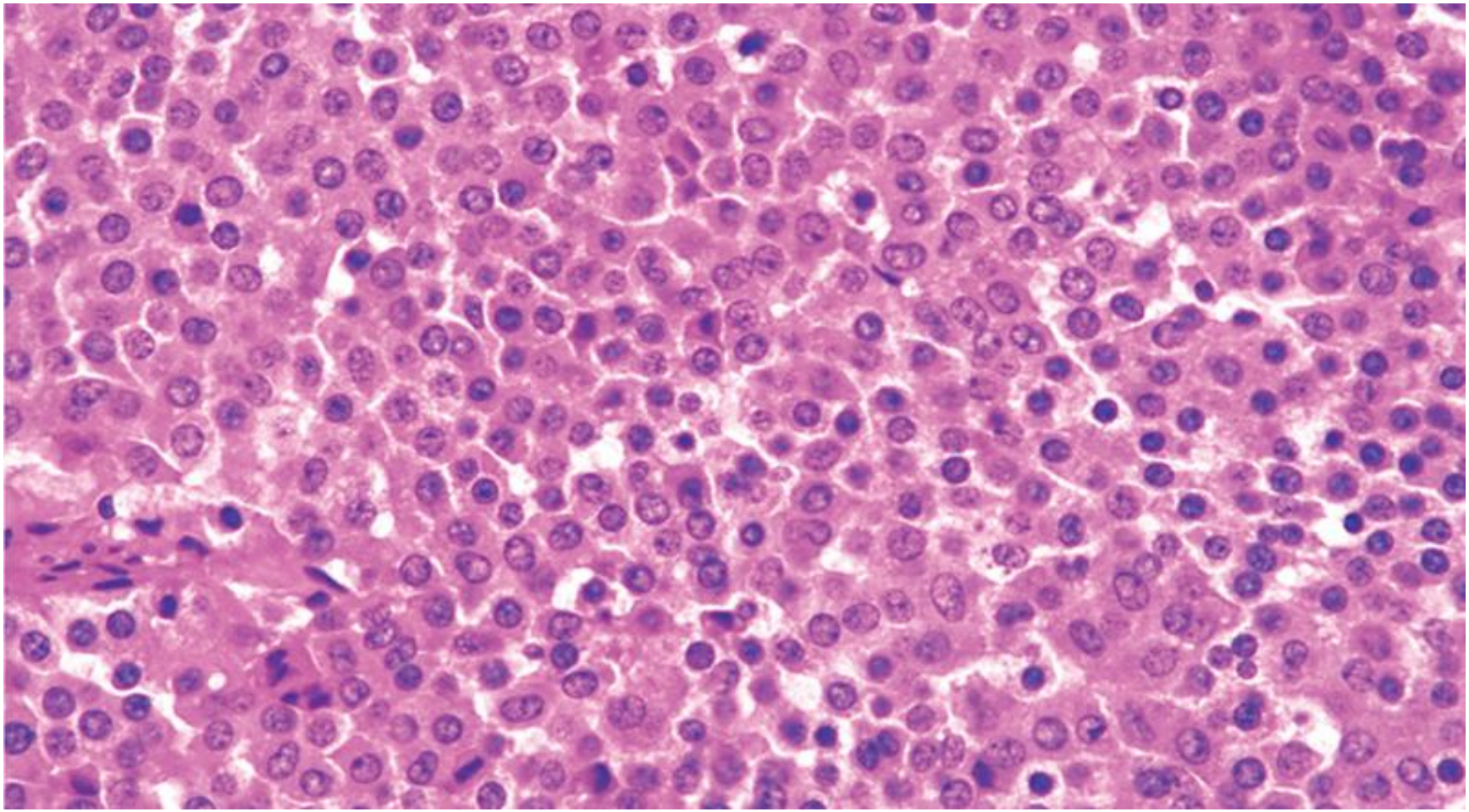




Normal pituitary.. Several cell types



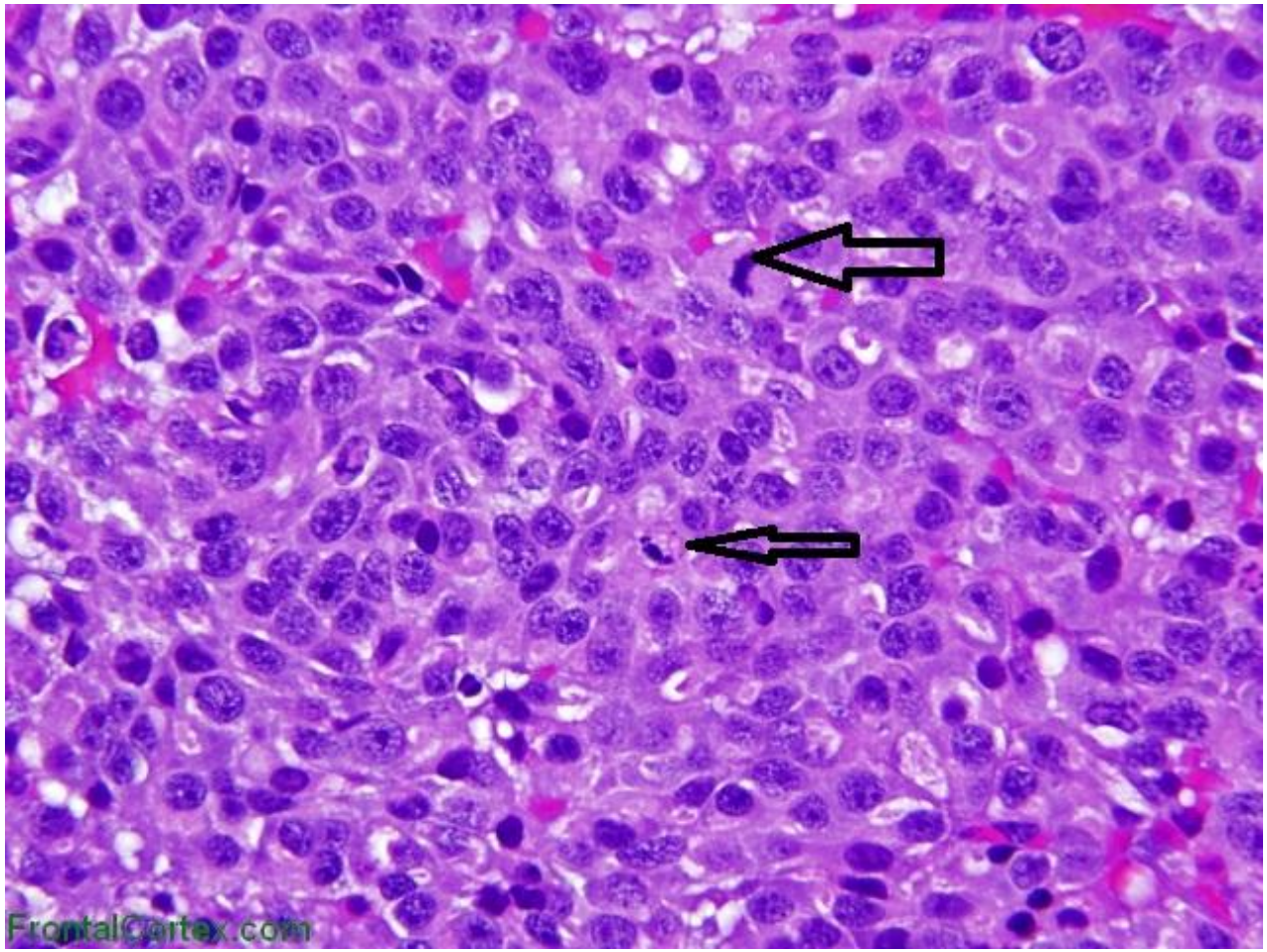
Adenoma.. One cell type = monomorphic appearance



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 designated **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

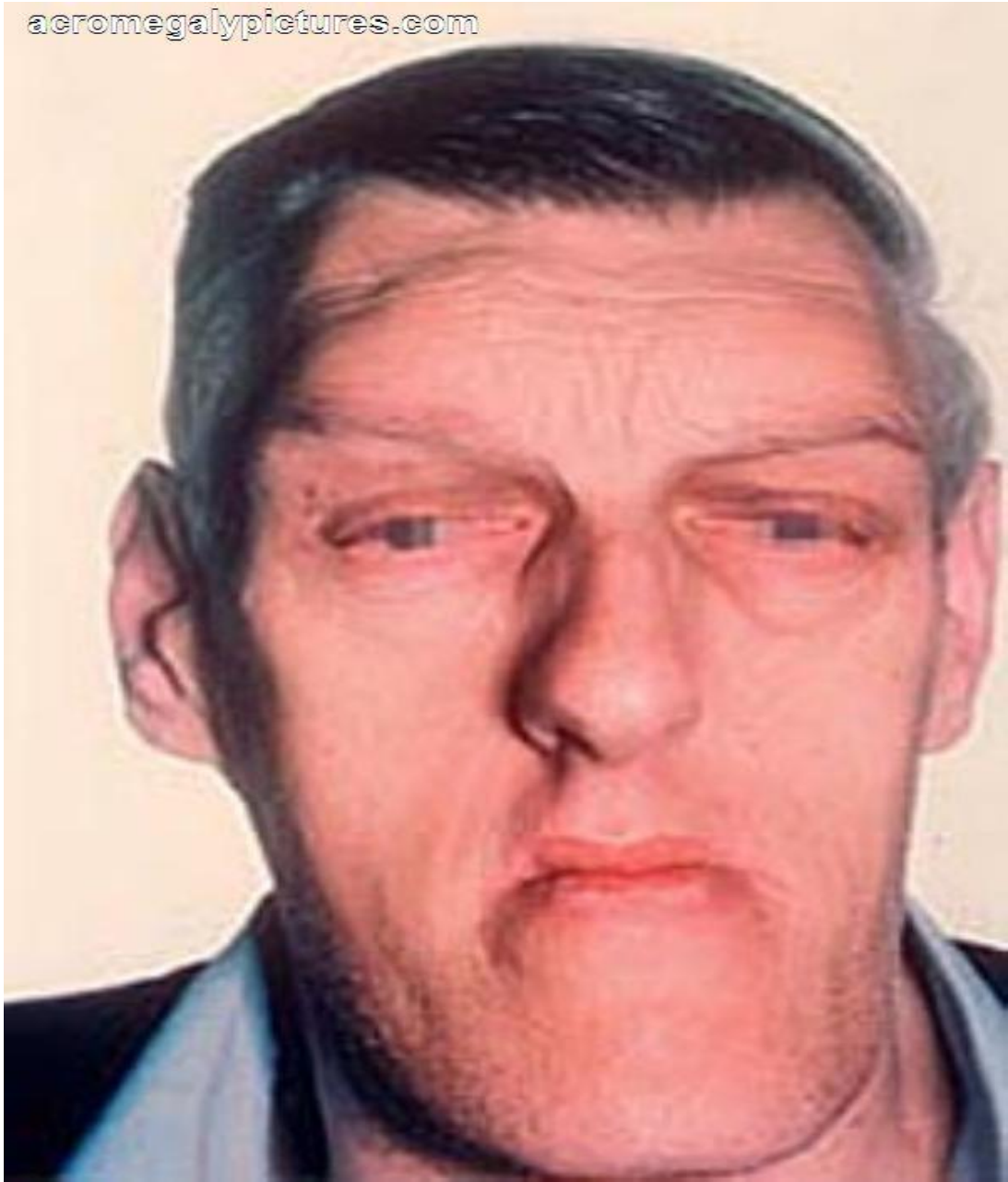
If elevated levels of growth hormone persist, or develop after closure of the epiphyses, affected persons develop *acromegaly,* in which:

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



Corticotroph cell adenomas

- **may be:**

1.Clinically silent OR

2. May cause *hypercortisolism= increased cortisol , m*anifested 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*.

***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 i*n addition to local extension beyond the sella turcica, these tumors virtually always demonstrate **distant metastases.**

- **As a general rule: all endocrine carcinomas are diagnosed depending on behavior (presence of metastases) and 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. C*ongenital* 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

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*

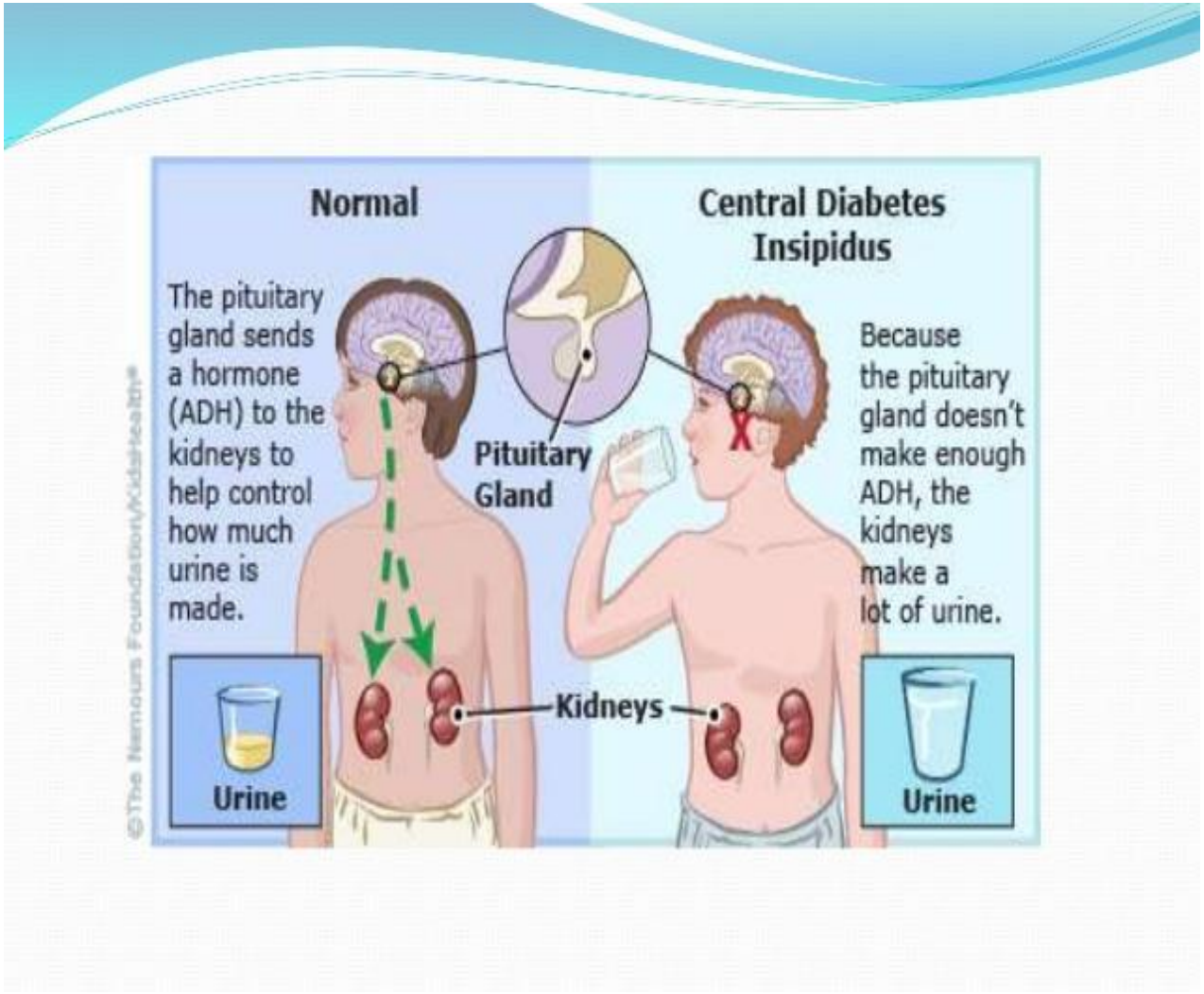
- The clinical manifestations of DI include:

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 obtunded, bedridden, or otherwise limited in their ability to obtain water may develop life threatening dehydration.

DI


Normal
Central Diabetes Insipidus
The pituitary gland sends a hormone (ADH) to the kidneys to help control how much urine is made.
Pituitary Gland
Because the pituitary gland doesn't make enough ADH, the kidneys make a lot of urine.
Kidneys
Urine
Urine
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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.

Diabetes Insipidus		SIADH
- High Urinary Output		- Low Urinary Output
- Low Levels of ADH		- High Levels of ADH
- Hypernatremia	VS	- Hyponatremia
- Dehydrated		- Over Hydrated
- Lose too much fluid		- Retain too much fluid

* Both will present with excessive thirst

CHECK YOUR UNDERSTANDING

- 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

- 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

- 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. Laboratory studies show sodium 162 mmol/L, potassium 4.1 mmol/L, chloride 121 mmol/L, and bicarbonate 27 mmol/L. His serum glucose is 75 mg/dL and creatinine 1.0 mg/dL. His serum osmolality is 343 mOsm/kg. 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