PATHOLOGY OF ENDOCRINE SYSTEM

PITUITARY GLAND

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Endocrine system lectures 2022

Objectives:

1. Identifying the Hyperpituaritism and Hypopituarisim
2. Knowing the Causative agents regarding Hypopituarisim
3. Sheehan Syndrome
4. Knowing the posterior Hypopituarisim and the difference regarding point B and A in 41-42 Slides.

The Endocrine system is divided into :

1-Endocrine organs which are entirely dedicated to production of hormones e.g pituitary, thyroid , parathyroid & adrenal .

2- Endocrine components in clusters in organs having mixed functions, e.g. pancreas, ovary & testes.

3-Diffuse endocrine system, comprising scattered cells within organs or tissues acting locally on adjacent cells without entry into blood stream (Paracrine: any cell that affect the adjacent one).

Classification of Hormones

A- Hormones that trigger biochemical signals upon interacting with cell surface receptors:

Leads to an increase in intracellular molecules, termed second messenger (cAMP) , production of mediators from membrane phospholipid ⇑ in the intracellular calcium ⟹ proliferation, differentiation, survival, functional activity of the cells.

1- peptide hormones: Growth hormones, and insulin.

2- small molecules: epinephrine.

1+2 => related to the cell surface receptors.

B- Hormones that diffuse across the plasma membrane and interact with intracellular receptors:

Lipid -soluble hormones include:

steroids (estrogen, progesterone, glucocorticoids), retinoids, thyroxine.

They go directly inside the cell and affect the cell.

Disease divided into :

1- Diseases of overproduction of secretion (Hyperfunction)

2- Diseases of underproduction (Hypofunction)

3- Mass effects (Tumors) because the skull is a limited space that would compress adjacent CNS organs.

N.B. Correlation of:

1-Clinical picture. (Symptoms)

2- Hormonal assays

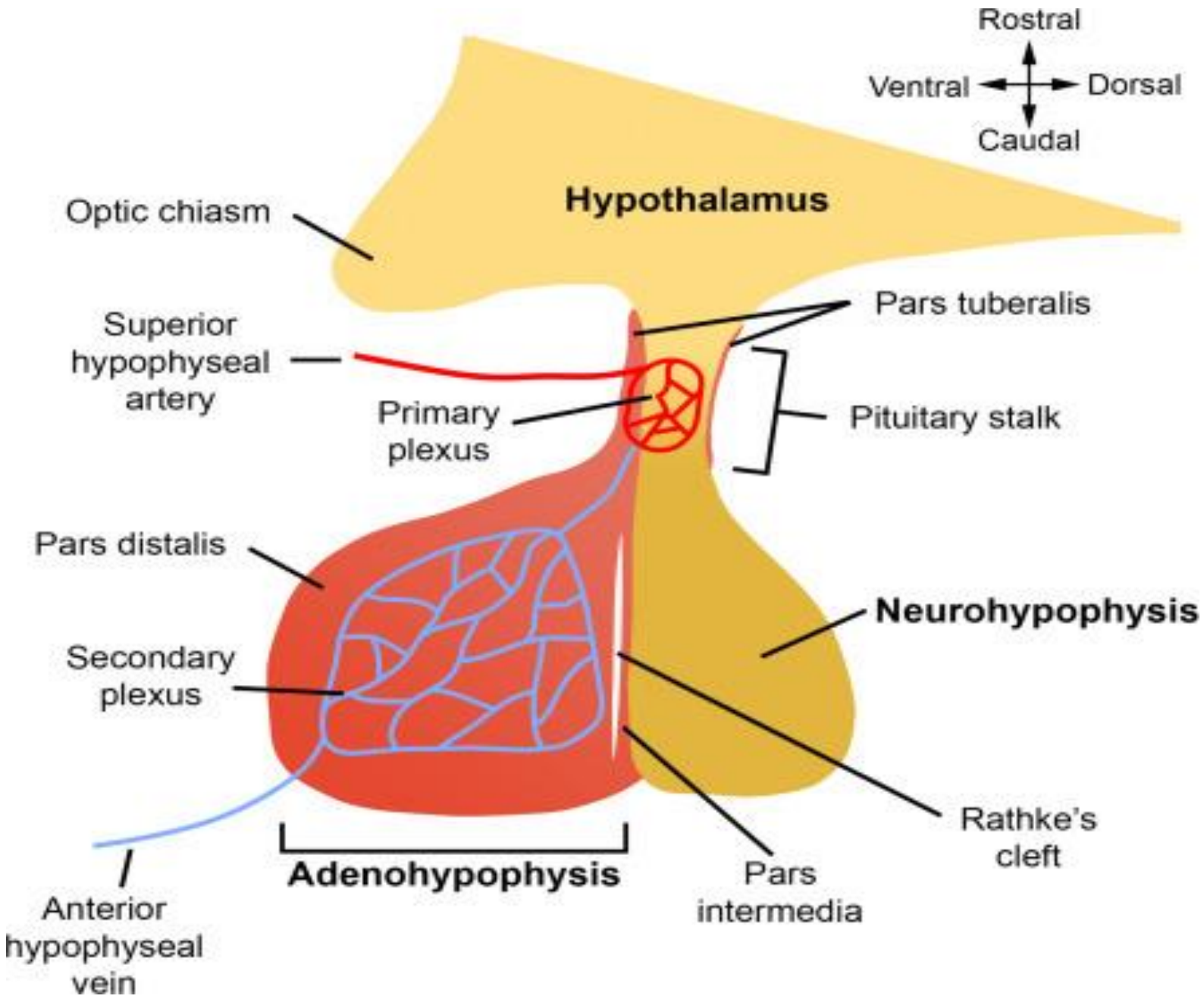
3- Biochemical findings together

4-Pathological picture are of extreme importance in most conditions.

PITUITARY GLAND:

The Mother of the Endocrine Glands.

N.B: The size of the pituitary would DOUBLE during pregnancy


Rostral
Ventral
Dorsal
Caudal
Hypothalamus
Optic chiasm
Pars tuberalis
Superior hypophyseal artery
Primary plexus
Pituitary stalk
Pars distalis
Neurohypophysis
Secondary plexus
Rathke's cleft
Adenohypophysis
Pars intermedia
Anterior hypophyseal vein

- The pituitary lies in sella turcica & weighs about 0.5 gm. It is connected to the HYPOTHALAMUS through its stalk, and composed of :

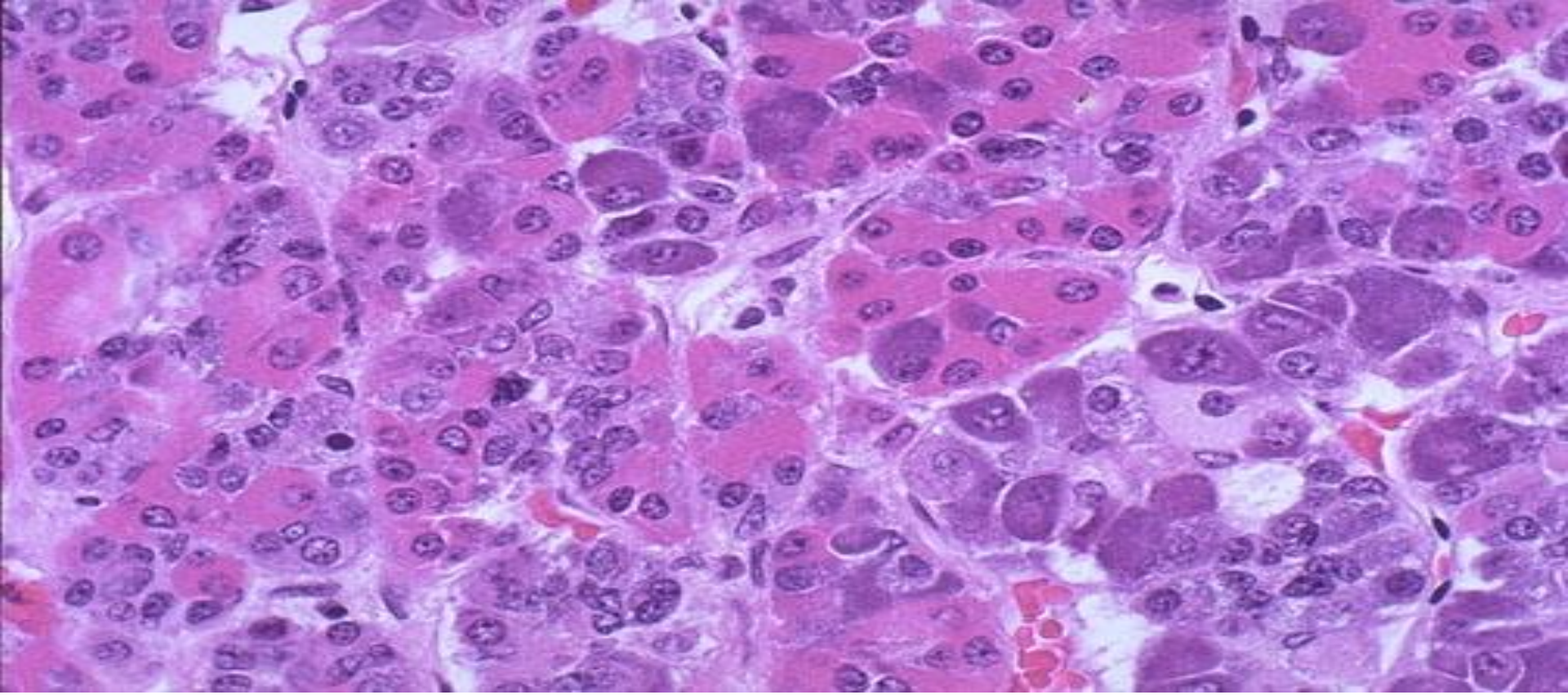
A-ADENOHYPOPHYSIS- (80%) developed from Rathke's pouch (Embryological Origin). It's blood supply is through venous plexus from hypothalamus. It is controlled under Hypothalamic - Hypophyseal feed back control.

Produce: GH,PROLACTIN,ACTH,FSH,LH,TSH. All of them are acting on another tisseus and Glands. (Specific)

B- NEUROHYPOPHYSIS developed from the floor of the third ventricle & consists of modified glial cells & axons from cell bodies in hypothalamus.

It has its own blood supply.

Produce: oxytocin & ADH



This is Adenohypophysis

Mixture of Cells. Clusters of cells that have variable colors.

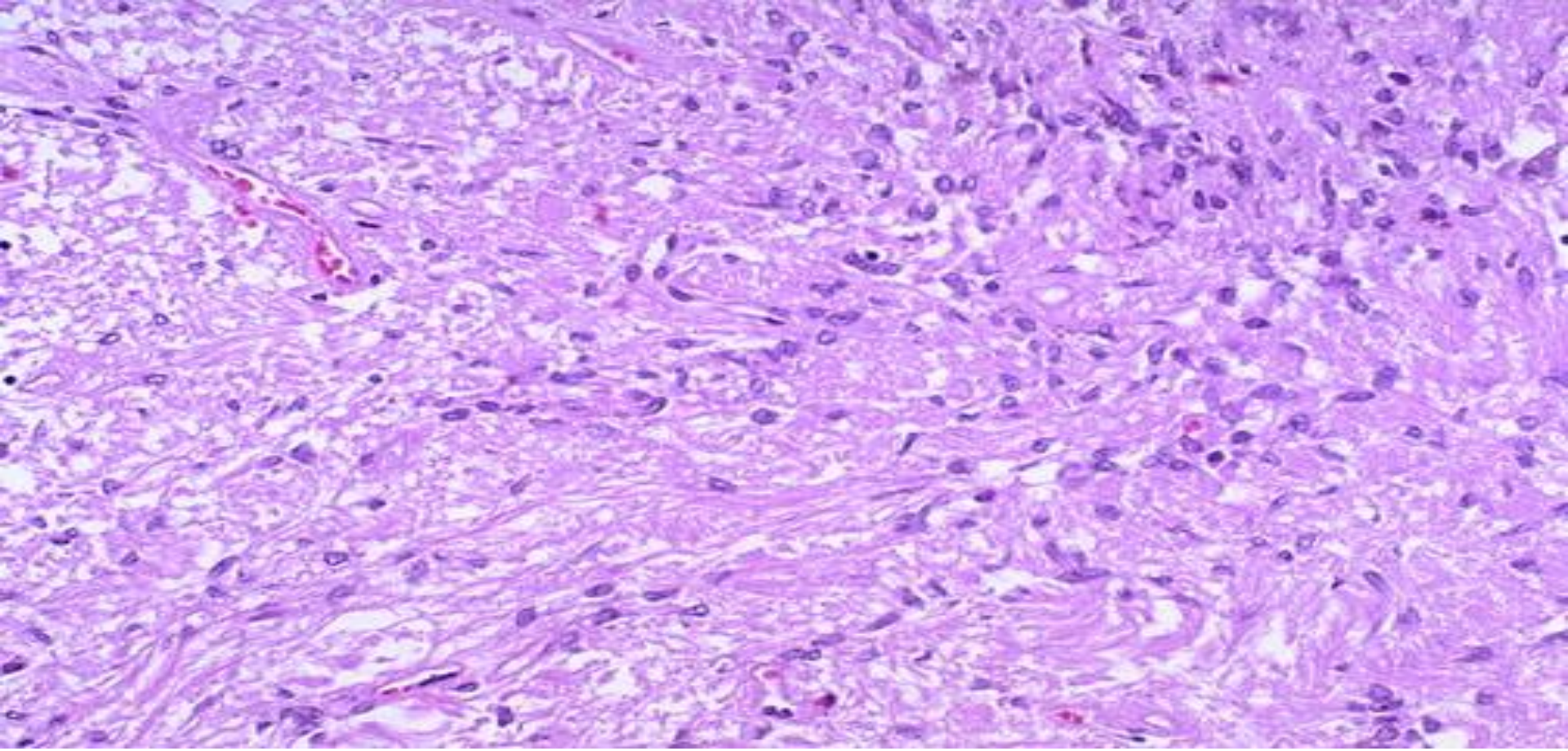
The **pink acidophils** secrete growth hormone (GH) and prolactin (PRL)

The **dark purple basophils** secrete corticotrophin (ACTH), thyroid stimulating hormone (TSH), and gonadotrophins follicle stimulating hormone-luteinizing hormone (FSH and LH) .

The **pale staining chromophobes** have few cytoplasmic granules, but may have secretory activity.

مش مهم نحفظ شو بفرزو بس انهم خليط من الخلايا

و نعرف انه ال GH and Prolactin يتم إفرازهم من نفس الخلية و دايما مع بعض

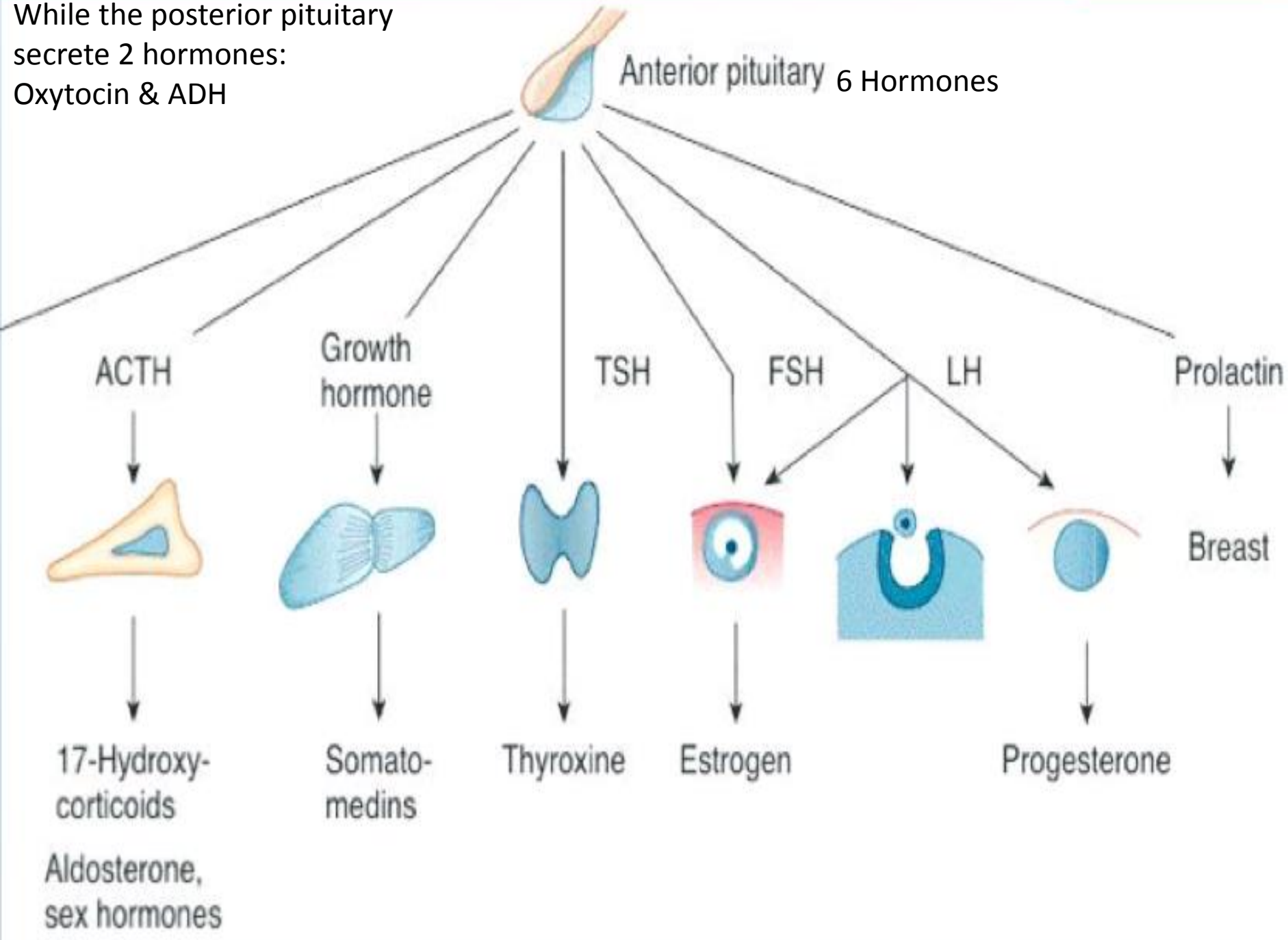


Neural cells Composed of Axons

The **neurohypophysis** shown here resembles neural tissue, with glial cells, nerve fibers, nerve endings, and intra-axonal neurosecretory granules.

The hormones **vasopressin** (antidiuretic hormone, or ADH) and **oxytocin** made in the hypothalamus (supraoptic and paraventricular nuclei) are transported into the intra-axonal neurosecretory granules in the neurohypophysis where they are released.

While the posterior pituitary secrete 2 hormones:
Oxytocin & ADH



CELLS & SECRETIONS :

A- Anterior pituitary (Adenohypophysis)

1- Somatotrophs from acidophilic cells → Growth H.
2- Lactotrophs from acidophilic cells → Prolactin
3- Corticotrophs from basophilic cells → ACTH,POMC derived peptides.
4- Thyrotrophs from pale basophilic cells → TSH
5- Gonadotrophs from basophilic cells → FSH, LH

B- Posterior pituitary (Neurohypophysis)

1- Oxytocin
2- ADH (AntiDiuritic Hormone)

HYPERPITUITARISM & PITUITARY ADENOMA

Pathology Starts Now:

In most cases, excess is due to ADENOMA (Most common Presentation)

arising in the anterior lobe.

Adenoma: single mass, well Circumscribed with well defined borders. Lined capsule.

Existance of the MITS may indicate the Carcinoma type.

Less common causes include :

* Hyperplasia
* Carcinoma
* Ectopic hormone production
* Some hypothalamic disorders

Incidence of pituitary adenomas:

- 10% of all intracranial neoplasms
- 25% are incidental
- 3% occur with MEN syndrome
- Most occur between 30-50 years of age

Behaviour of pituitary adenomas :

- Primary pituitary adenomas usually benign.
- Radiological changes in sella turcica .
- May or may not be functioning:
- The non Functioning (20%)

. If functional (80%).

the clinical effects are secondary to the hormone produced.

- More than one hormone can be produced from the same cell or just one hormone (monoclonal).

CLINICAL FEATURES of PITUITARY ADENOMA:

1- Symptoms of hormone production.

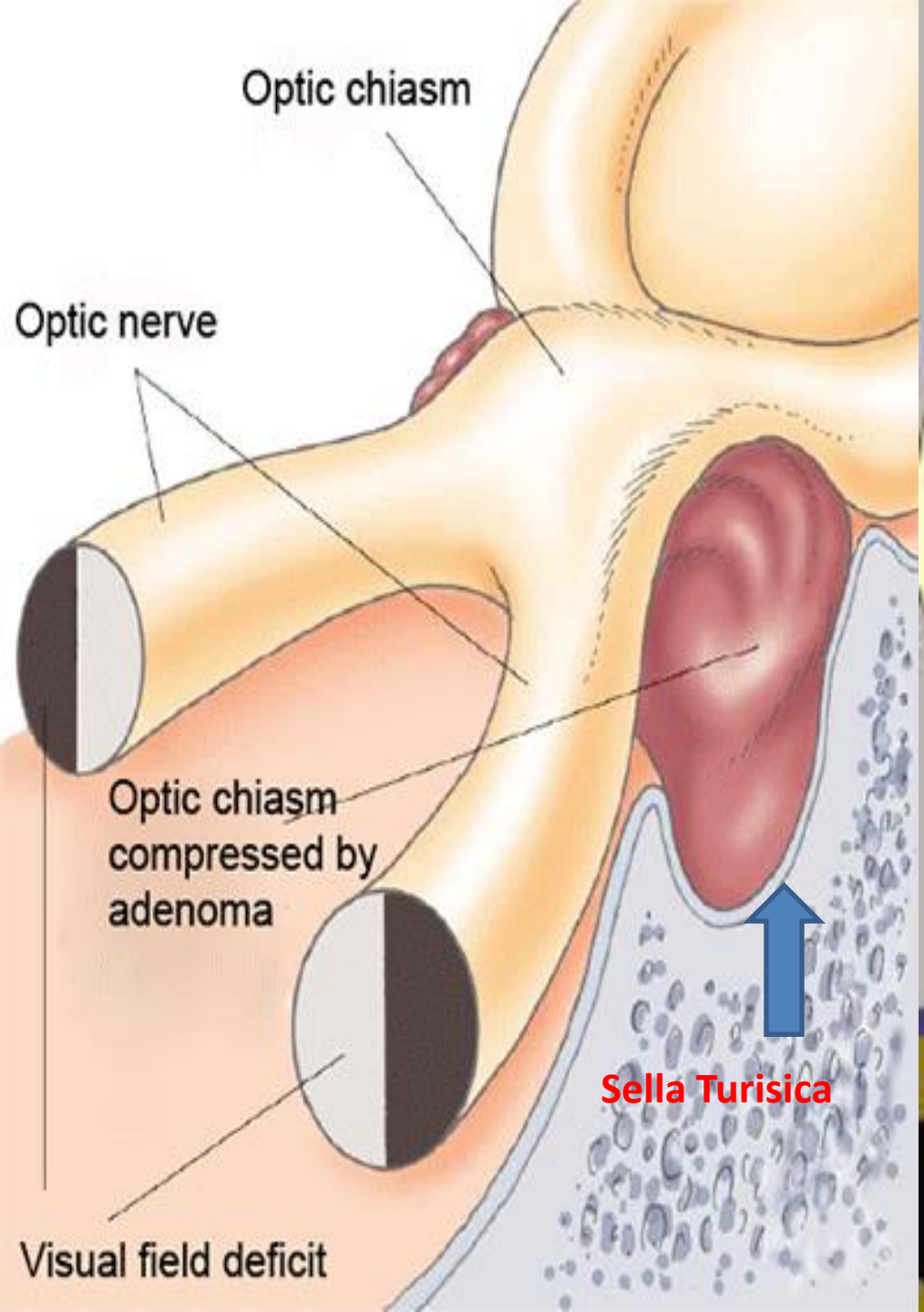
Ex: symptoms are similar to the over production of a hormone.

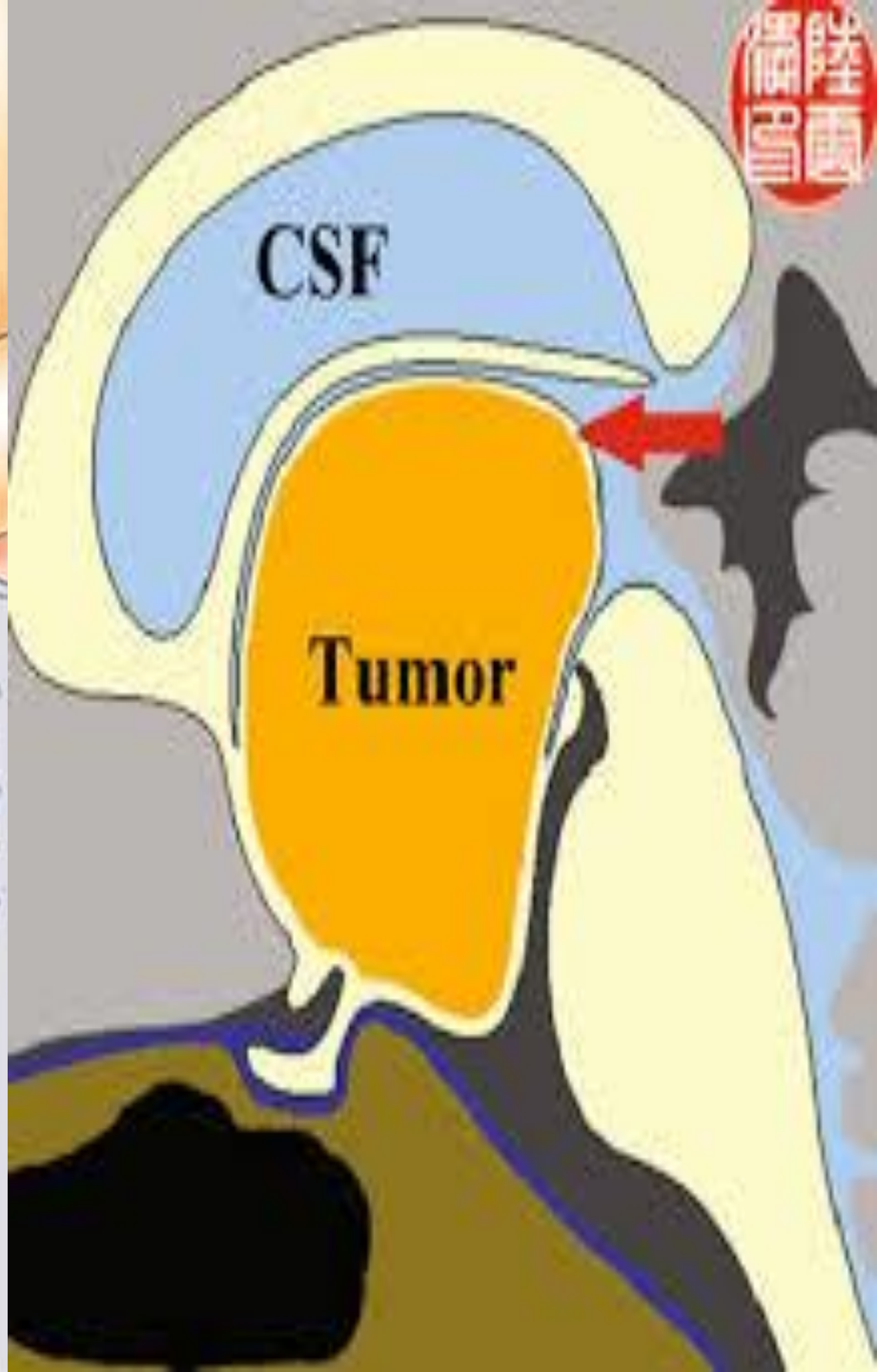
2- Visual field abnormalities (pressure on optic chiasma above sella tursica). (Mass Effect)

3- Elevated intracranial pressure (blockage of CSF flow): Headache , nausea , vomiting. (Mass Effect)

4- Hypopituitarism (result from pressure on adjacent pituitary): Diabetes insipidus . (Mass Effect)

5-Cranial nerve palsy (invasion to brain). (Mass Effect)


Optic chiasm
Optic nerve
Optic chiasm compressed by adenoma
Visual field deficit
Sella Turisica


CSF
Tumor

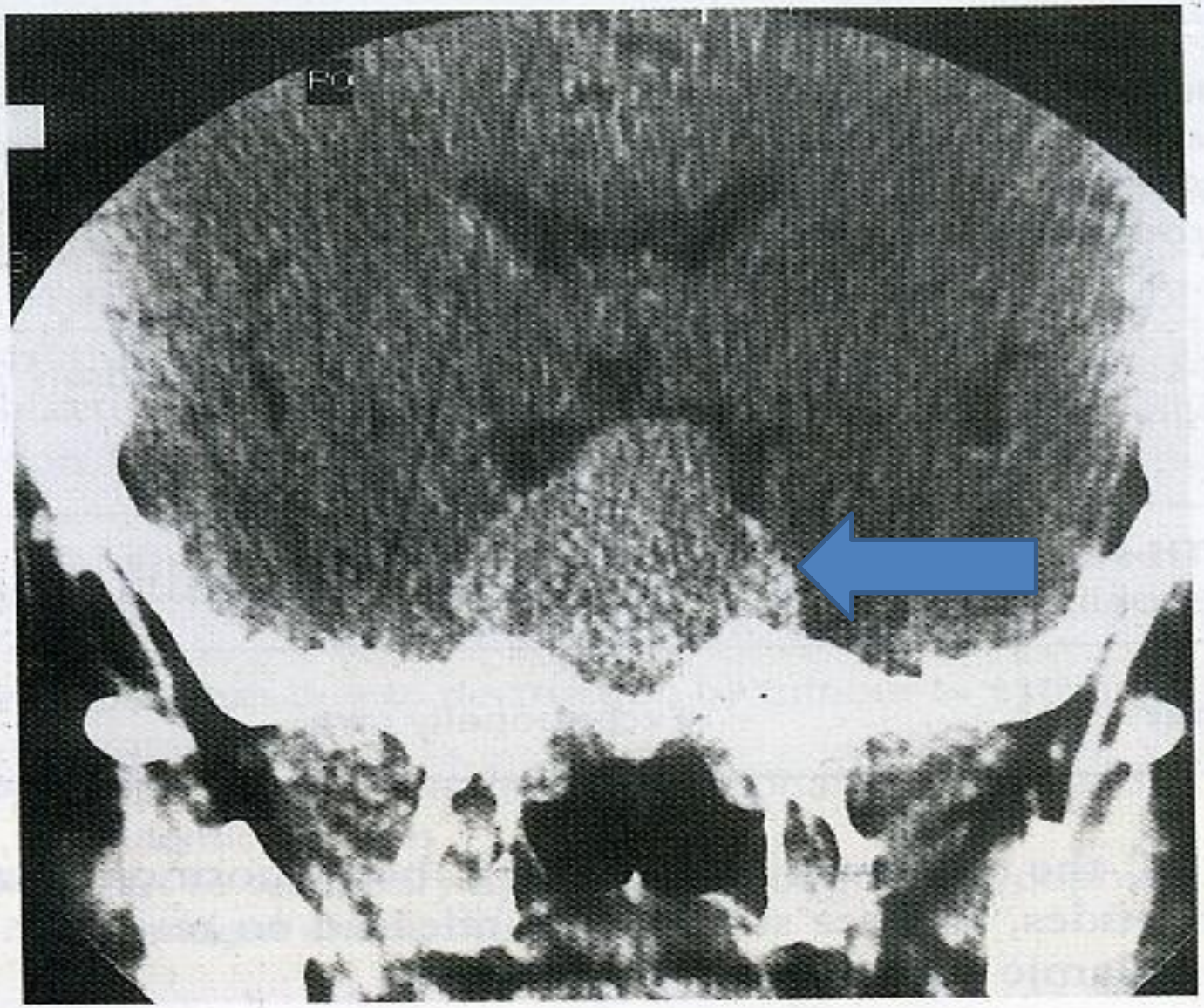
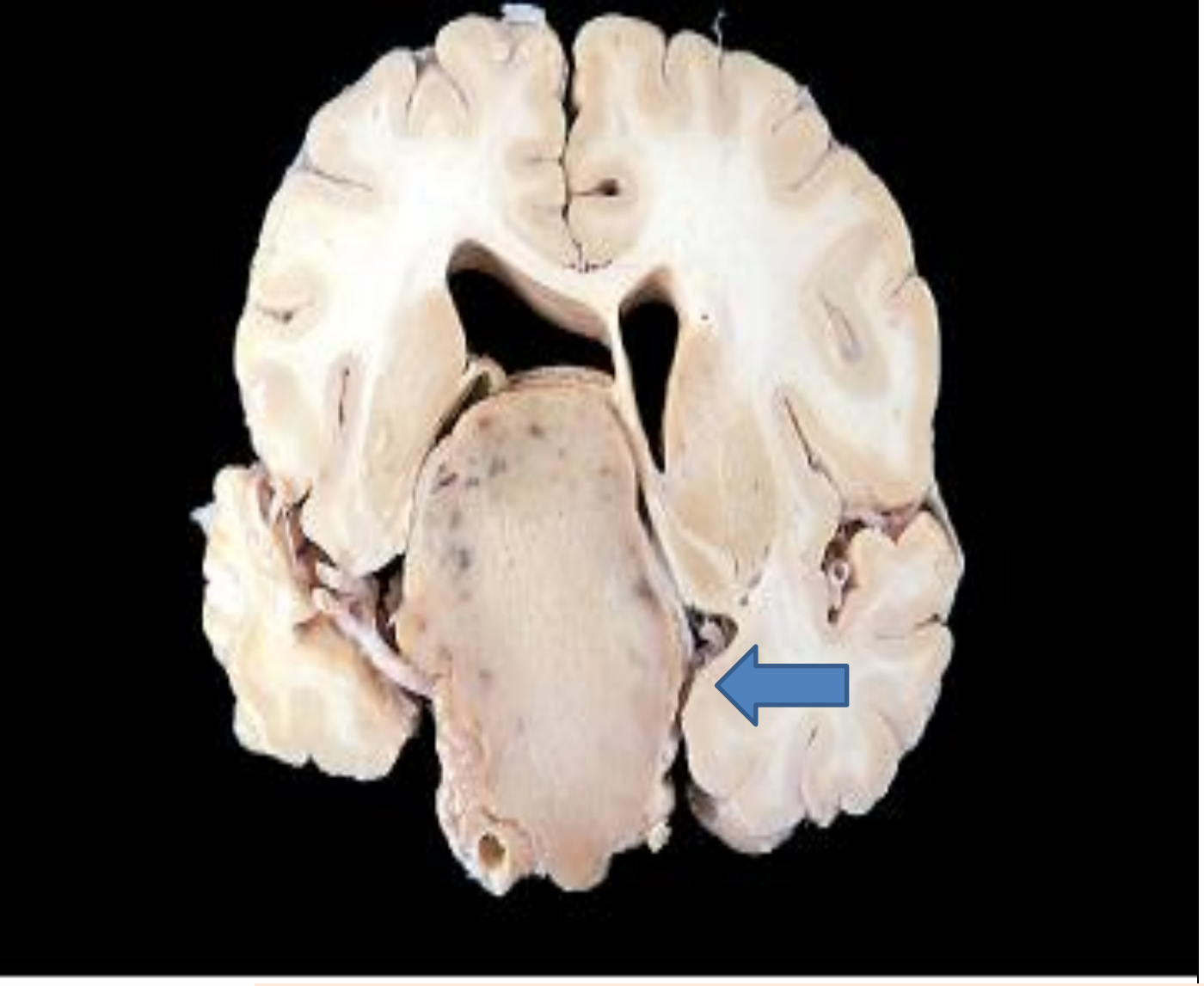


Fig. 17.8 Coronal plane CT scan of the pituitary fossa showing a pituitary adenoma. The sella turcica is widened by a pituitary adenoma which is compressing the optic chiasma and hypothalamus.



Clinical Presentation is the Mass effect of pituitary adenoma.

Morphology of pituitary adenomas :

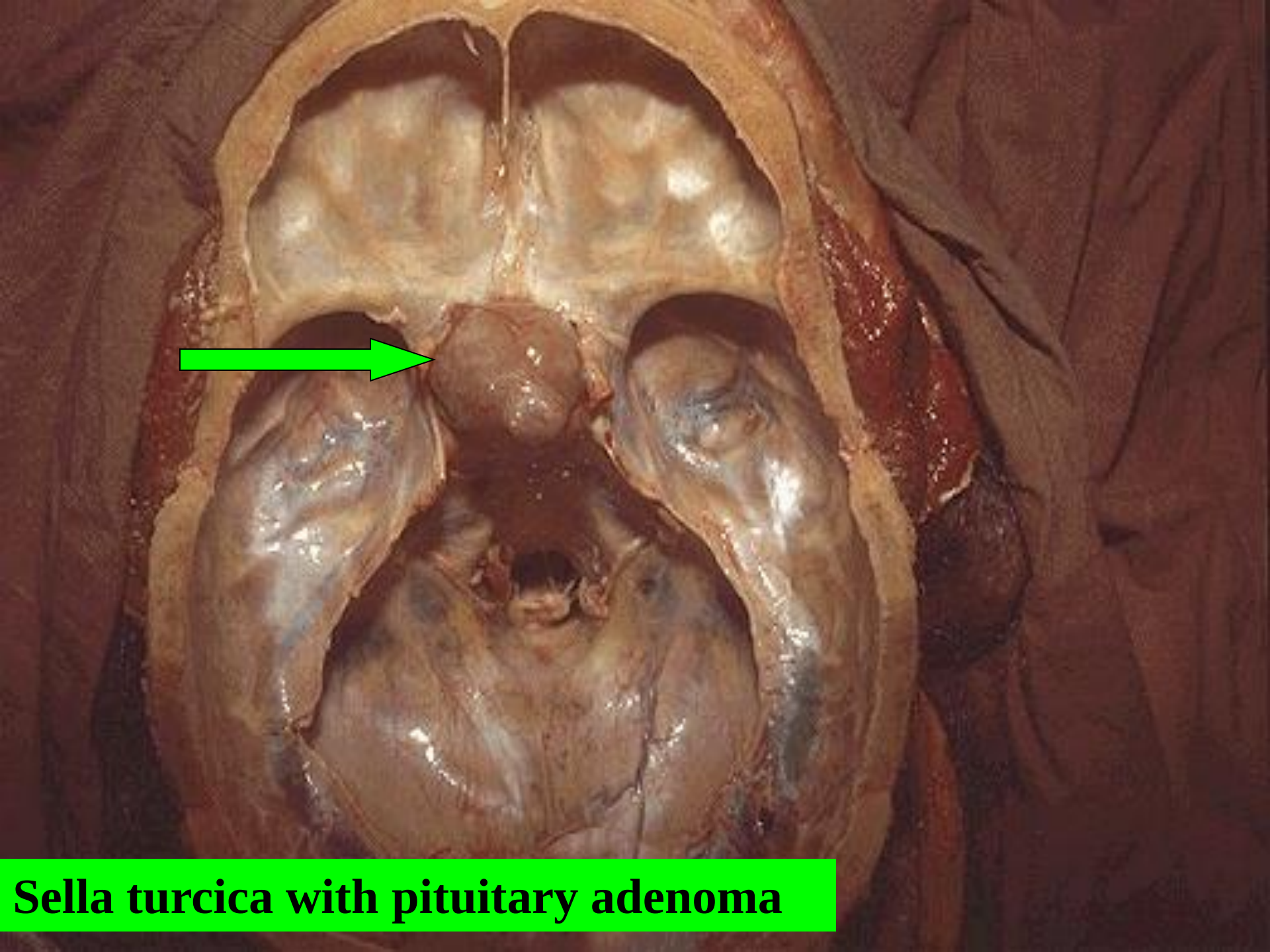
- Well circumscribed, invasive in up to 30%
- Size 1cm. or more, specially in nonfunctioning tumor. If more than 1cm is it mostly Functioning.
- Hemorrhage & necrosis seen in large tumors .

Microscopic picture:

- Uniform cells, one cell type (monomorphism)
- Absent reticulin network

Reticulin: is a type of stain that would detect the network between the cells.

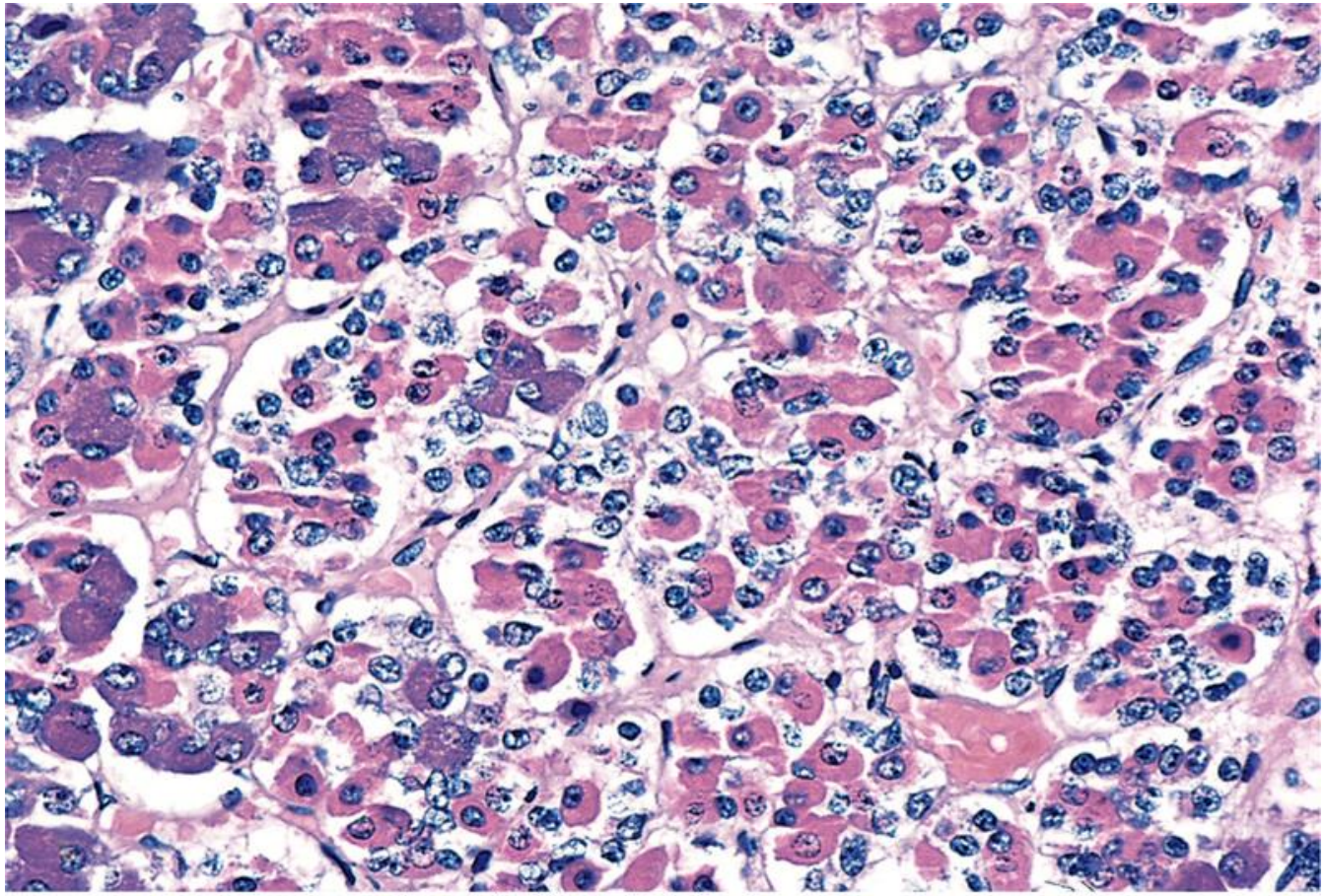
- Rare or absent mitosis. Also we said that the difference between the adenoma and the Carinoma is the MITS.

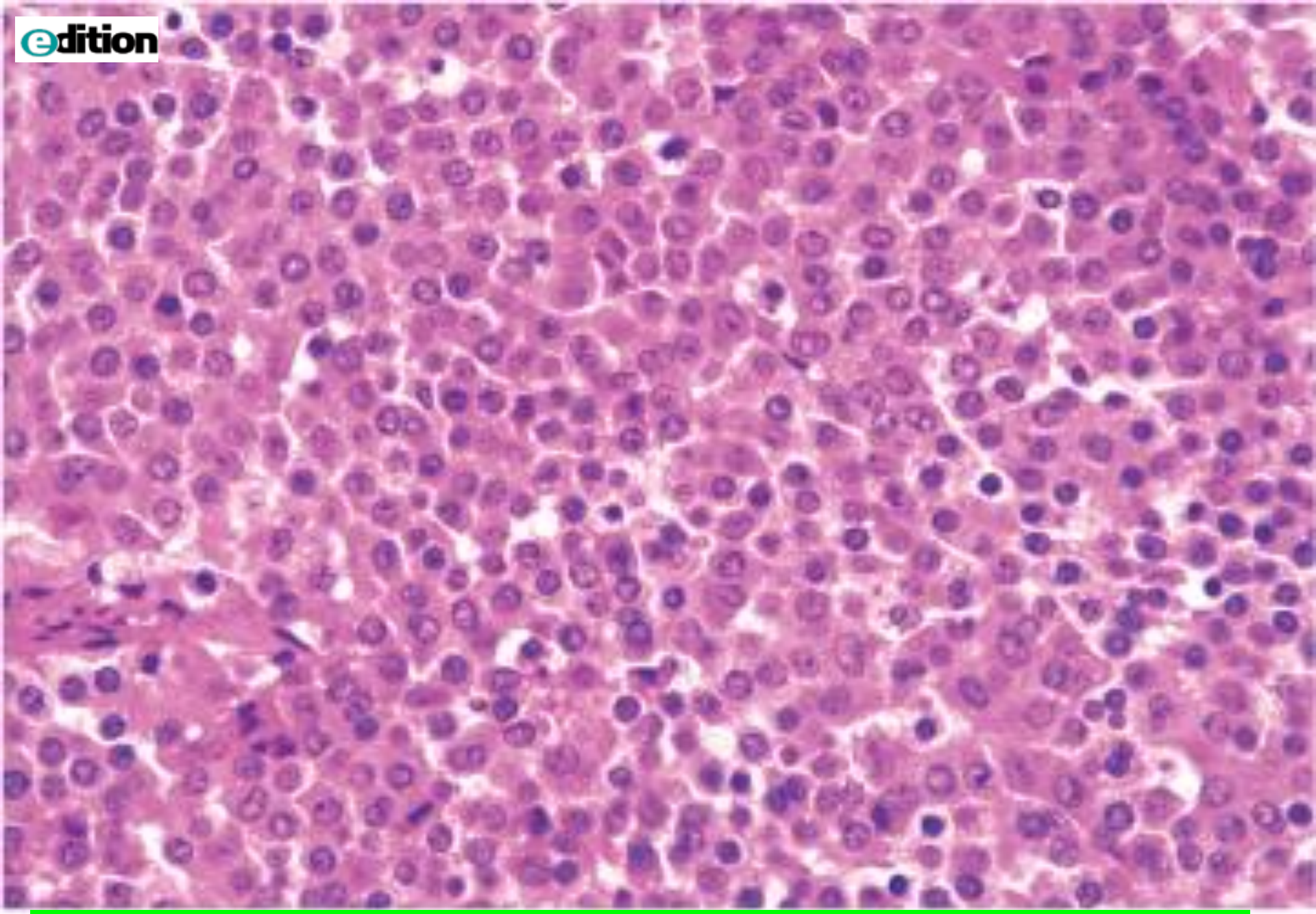


Sella turcica with pituitary adenoma

Normal pituitary gland

Composed of a mixture of variably colored cells.
Acidophilic and Basophilic cells





Uniform cells of pituitary adenoma

Types of Pituitary Adenomas

- Previously classified according to histological picture e.g :

  Acidophilic Adenoma

- Now according to immunohistochemical findings & clinical picture ….. e.g.

  Growth hormone secreting adenoma

Prevalence of Pituitary Adenoma

Adenoma Type	Prevalence (%)
GH cell adenoma	15
PRL cell adenoma **MOST**	30 ⟸
GH and PRL cell adenoma **Compound**	7 ⟸
ACTH cell adenoma	10
Gonadotroph cell adenoma	10
Nonfunctioning adenoma	20 -25 ⟸
TSH cell adenoma **LEAST**	1 ⟸
Unclassified adenoma	2

ACTH=Adrenocorticotropic hormone;
GH=Growth hormone; PRL=Prolactin;
TSH=Thyroid-stimulating hormone

1- PROLACTINOMA :

- 30% of all adenomas, chromophobe or w. acidophilic

- Functional even if microadenoma, but amount of secretion is related to size.

The cut point between the Macroadenoma and Microadenoma is 1cm.

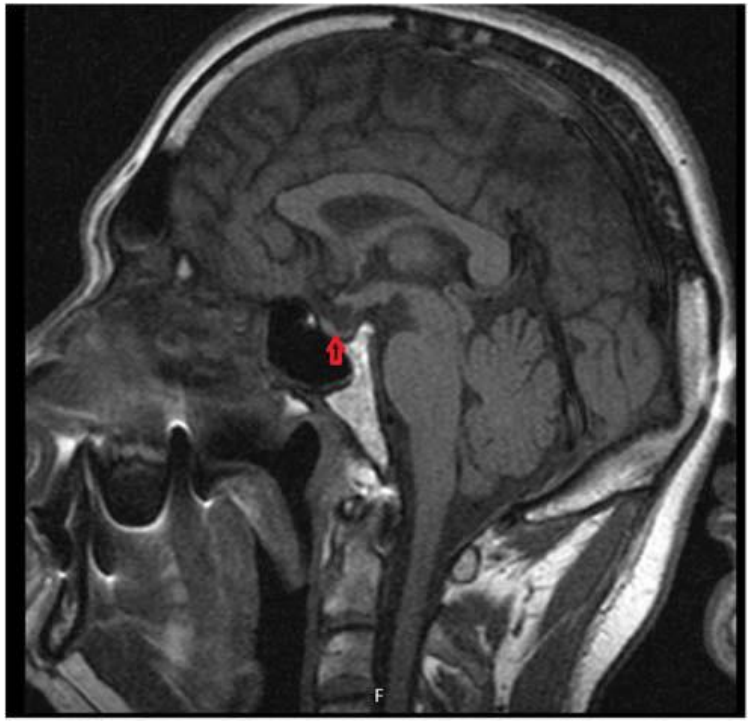
- Mild elevation of prolactin does NOT always indicate prolactin secreting adenoma !

Other causes of ↑ prolactin include :

- estrogen therapy (Ex: OCP)
- pregnancy
- certain drugs, e.g reserpine (dopamin inhibitor).
- hypothyroidism. So the pituitary is trying to make TSH in high amounts it will undergo Hyperplasia. So it will secrete Prolactin as added hormone due to the hyperplasia. So we need to test the TSH in this condition to role out Hypothyroid.
- mass in suprasellar region ? (Next slide)

- Any mass in the suprasellar region may interfere with normal prolactin inhibition → ↑ Prolactin

(STALK EFFECT)



Symptoms : (Female)

- Galactorrhea
- Amenorrhea
- Decrease libido (+male)
- Infertility (+male)

Treatment:

Bromocreptine (dopamine agonist);cause shrinkage of neoplasm & regression of hyperplasia in most causes.

So adenoma can be treated with drug and not an invasive procedure

2- Growth hormone secreting adenoma :

- 40% Associated with GNAS 1 gene mutation
- Persistent secretion of GH stimulates the hepatic secretion of insulin-like growth factor I (IGF-I) → many of clinical effects
- Initial investigation : measurement of GF & IGF-I which is increased.
- Confirm by failure to suppress GH production in response to an oral load of glucose. So we make the patient fast for 8 – 12 hours then we give a specific dose of glucose orally, then we measure whether the GH had been suppressed or not!

Structure :

Composed of granular ACIDOPHILIC cells and may be mixed with prolactin secretion.

Symptoms :

May be delayed so adenomas are usually large

Produce GIGANTISM (children) or ACROMEGALLY (adults).

Diabetes, arthritis, large jaw & hands, osteoporosis, ↑BP, HF…..etc

3- Corticotroph cell adenoma

- Usually microadenomas
- Higher chance of becoming malignant
- Chromophobe or basophilic cells
- Functionless (if it is small tumor) or Cushing 's Disease (↑ ACTH in case of malignant tumor)
- Bilateral adrenalectomy or destruction may result in aggressive adenoma:

Nelson's Syndrome (Reduction of the feedback of the steroid hormone).

- After nelson's syndrome, the receptors of ACTH would be gone, so there would a hyperplasia in the pituitary. that would result in an increase of the size of the pituitary.
- ↑ ICP (Due to the Hyperplasia)

- Difference between the Cushing Syndrome and the Cushing Disease:

- Cushing Syndrome: Associated with a pathology matter with Adrenal gland.

- Cushing Disease: Associated with the Central causetive agent and it’s the piuitary.

4- Non functioning adenoma, 20-25% silent or null cell ,nonfunctioning & produce mass effect only.

5- Gonadotroph producing LH &FSH, (10-15%)- Function silent or is minimal , late presentation mainly mass effect produced.

Produce gonadotrophin α subunit, β- FSH & β-LH.

6- TSH producing, (1%) rare cause of hyperthyroidism.

7- Pituitary carcinoma, Extremely rare, diagnosed only by metastases.

HYPOPITUITARISM : Loss of hormones

- Loss of > 75% of ant. Pituitary → Symptoms
- Congenital or acquired, intrinsic or extrinsic

- Acquired causes include :

1- Nonsecretory pituitary adenoma: we have a mass that doesn't produce anything, but it has a mass effect on the adjacent structure

2- SHEEHAN'S SYNDROME: Associated with pregnancy. And there would be a Post pratum hemorrhage and therefore it would decrease the blood supply going to the pituitary causing necrosis of the gland, and the female would undergo this syndrome. The presentation would appear after 7-8 months with an inability to lactate due the necrosis (destruction) of the pituitary.

3- Ischemic necrosis e.g. sickle cell anemia, DIC

4- Pituitary apoplexy: A condition where there is a spontaneous bleeding of hemorrhage due to tumor. Clinical presentaion would be a headache, N+V, double vision or loss in vosion. A long with changes in the mental status.

HYPOPITUITARISM Cont.

5- Iatrogenic by radiation or surgery

6- Autoimmune (lymphocytic) hypophysitis

7- Hypothalamic mass

8- Inflammatory e.g sarcoidosis or TB

9- Empty Sella Syndrome :

Radiological term for enlarged sella tursica, with atrophied or compressed pituitary.

May be primary due to downward bulge of arachnoid into sella floor compressing pituitary.

Secondary is usually surgical.

10- Infiltrating diseases in adjacent bone causing compressoin e.g. Hand Schuller – Christian Disease

Metastatic tumors

11- Craniopharyngioma: which is a benign tumor in the sella tursica

- Symptoms of hypopituitarism:
  - Dwarfism (Pituitary Dwarf) in children. Due to improper release of Growth Hormone.
  - Effect of individual hormone deficiencies.
  - Amenorrhea & no lactation (Ex. Sheehan syndrome)
  - Loss of Melanocyte Stimulating Hormone (MSH) → Decreased pigmentation

Craniopharyngioma :

* 1-5 % of intracranial neoplasms
* Derived from remnants of Rathke's Pouch
* Suprasellar or intrasellar, often cystic with calcification
* Children or adolescents most affected
* Symptoms may be delayed ≥ 20yrs (50%)
* Symptoms of hypofunction or hyperfunction of pituitary and /or visual disturbances, diabetes insipidus
* Benign & slow growing

POSTERIOR PITUITARY SYNDROMES:

A- ADH deficiency : Diabetes Insipidus

Polyuria, polydipsia, hypernatremia & dehydration.

Urine is dilute, due to inability to reabsorb water from the collecting tubules.

Treatement? Drink a lot of water along with drugs.

Causes :-

Head trauma, tumors & inflammations in

pituitary or hypothalamus…etc.

B- Syndrome of inappropriate ADH secretion (SIADH):

- Part of paraneoplastic Syndrome (Most common cause): Small Cell Cacrcinoma of Lung
- Causes excessive resorption of water→ hyponatremia, cerebral edema.

C-Abnormal oxytocin secretion :

Abnormalitis of synthesis & release have not been associated with any significant abnormality.