

Endocrine system

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Symptoms of pituitary disease

- ▶ Hyperpituitarism
- ▶ Hypopituitarism
- ▶ Local mass effect

Local mass effects

- ▶ Expansion of sella turcica, bony erosion, and disruption of the diaphragma sellae
- ▶ Bitemporal hemianopsia
- ▶ ↑ ICP: headache, nausea, and vomiting
- ▶ Invasive pituitary adenoma:
 - ❑ Seizures, hydrocephalus, or cranial nerve palsy
- ▶ Pituitary apoplexy:
 - ❑ Acute hemorrhage into an adenoma

Hyperpituitarism

- ▶ Excessive secretion of trophic hormones
- ▶ **Causes:**
 - ▶ Anterior pituitary adenoma, most common
 - ▶ Pituitary hyperplasia
 - ▶ Pituitary carcinoma

PITUITARY ADENOMAS

- ▶ Classified on the basis of hormone(s) produced by the neoplastic cells
- ▶ Most pituitary adenomas are isolated lesions
- ▶ 3% are associated with MEN-1

MEN 1

Pituitary
adenoma

Parathyroid
hyperplasia

Pancreatic
tumors

MEN 2A

Parathyroid
hyperplasia

Medullary
thyroid
carcinoma

Pheo-
chromo-
cytoma

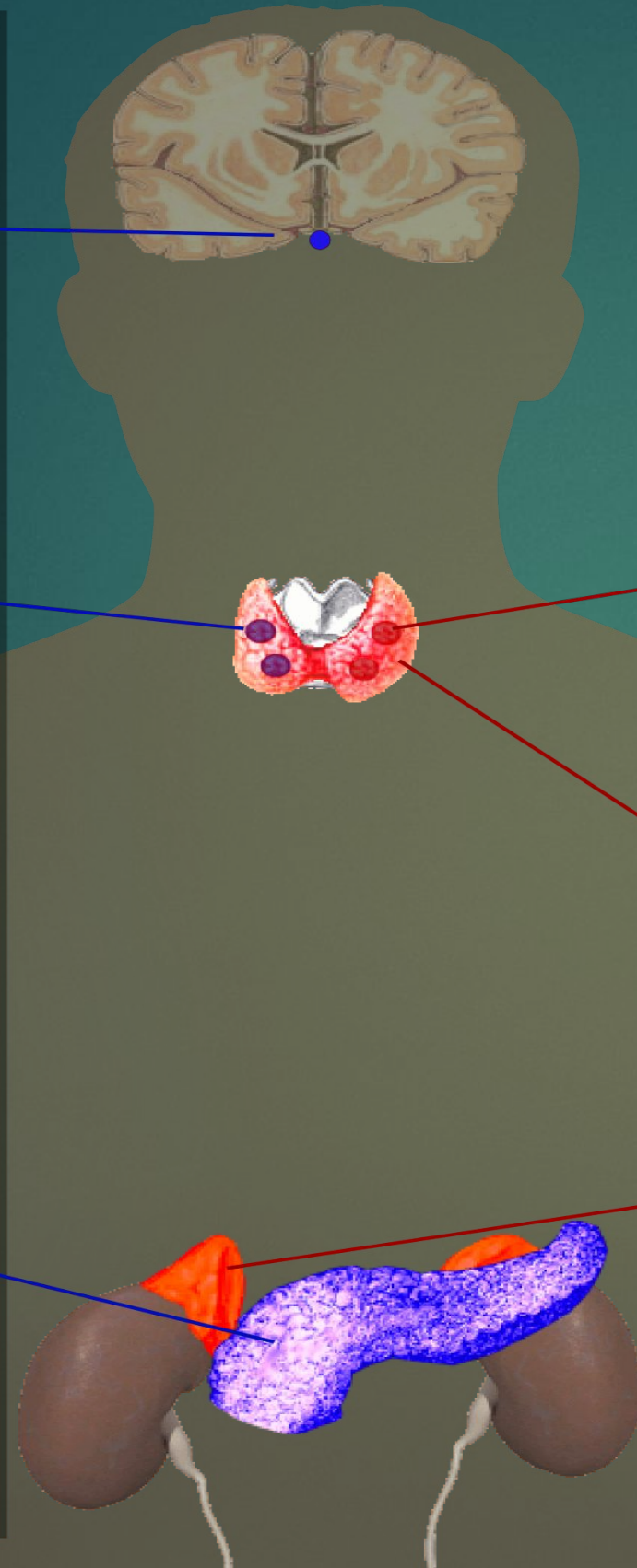
MEN 2B

Mucosal
neuromas

Marfanoid
body
habitus

Medullary
thyroid
carcinoma

Pheo-
chromo-
cytoma



PITUITARY ADENOMAS

- ▶ Pituitary adenomas can be:
 - ❑ Small (microadenoma) <1 cm in diameter
 - ❑ Large (macroadenoma) > 1 cm in diameter

Classification of Pituitary Adenomas

Prolactin cell (lactotroph) adenoma

Growth hormone cell (somatotroph) adenoma

TSH cell (thyrotroph) adenomas

ACTH cell (corticotroph) adenomas

Gonadotroph cell adenomas

Mixed (plurihormonal) adenomas

GH-prolactin (Mammo-somatotroph) adenomas

Null-cell adenoma

Hormone-negative adenomas

Absence of hormones by IHC & E/M

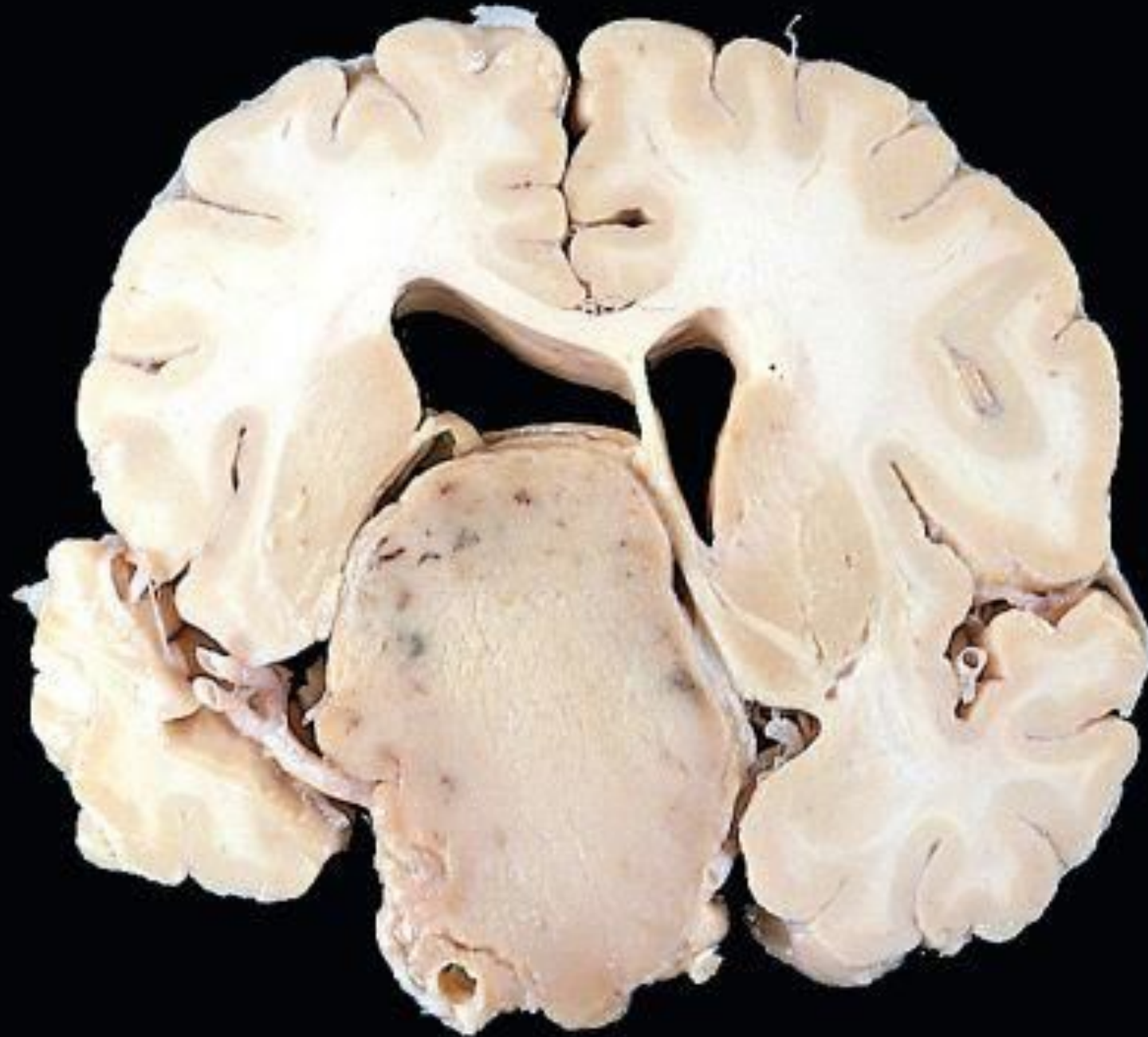
Clinical picture

- ▶ 10% of intracranial neoplasms
 - ▶ 25% of routine autopsy studies
 - ▶ Usually in adults, peak incidence 30s-50s
-
- _ Hyperpituitarism
 - _ Hypopituitarism (destruction of adjacent gland)
 - _ Mass effect

Morphology

- ▶ A well-circumscribed and encapsulated
- ▶ Soft and gelatinous
- ▶ Microadenomas: confined by sella turcica
- ▶ Macroadenomas may
 - ❑ Compress optic chiasma & adjacent structures
 - ❑ Extend into the cavernous & sphenoidal sinuses
- ▶ Invasive adenomas 30%
 - ❑ Infiltrate adjacent bone, dura, and brain

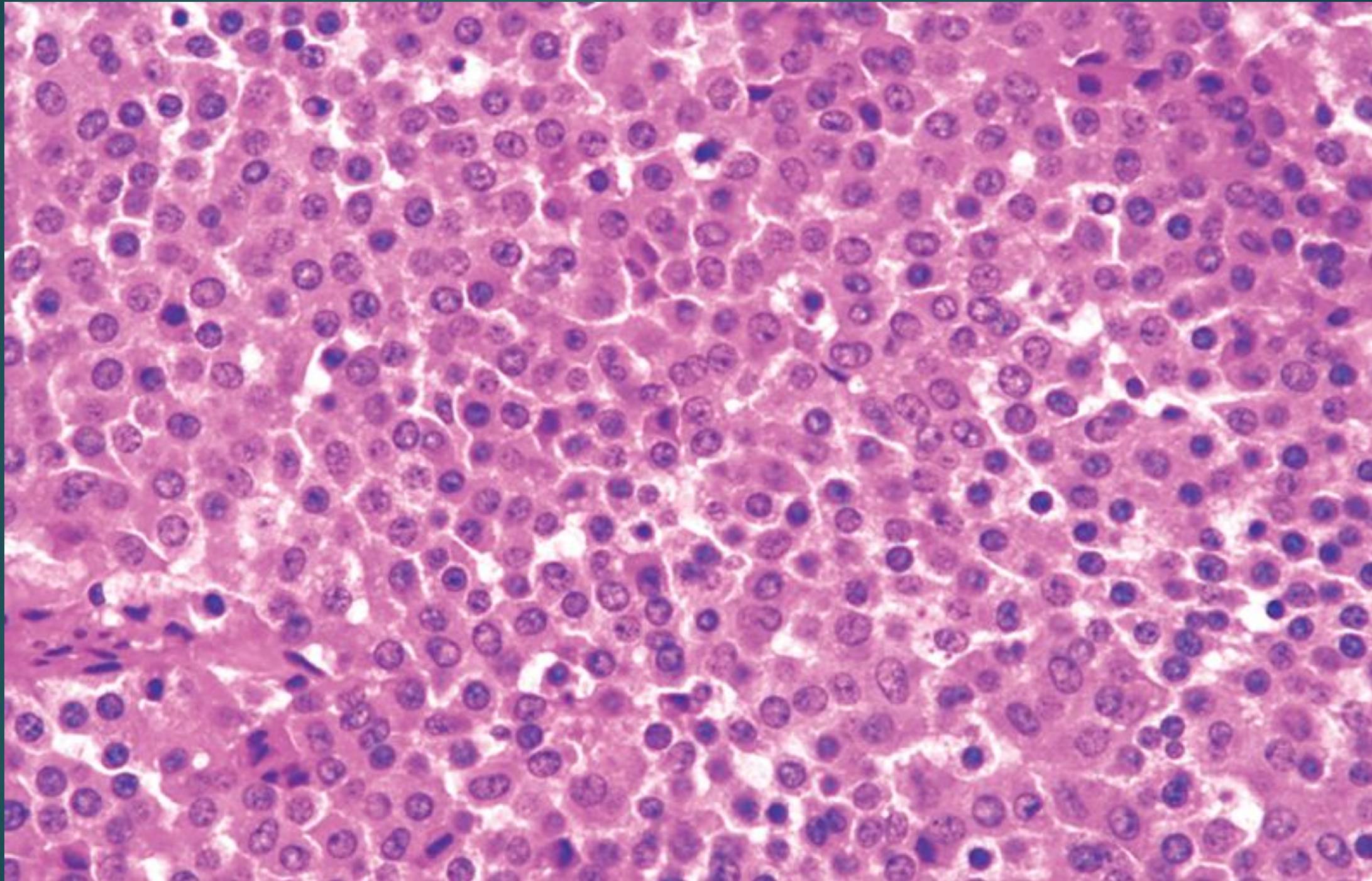
**Large pituitary adenoma



**Microscopic appearance

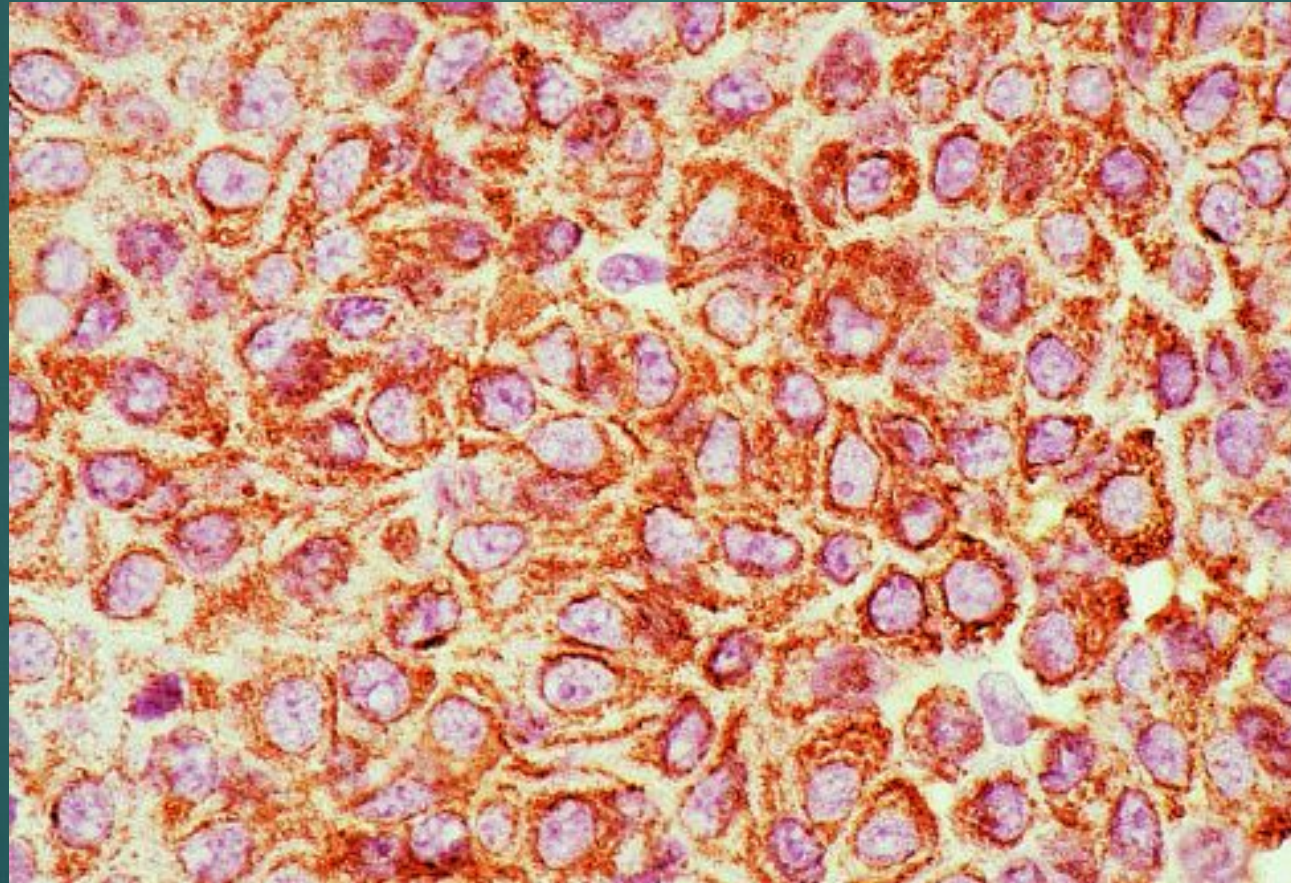
- ▶ Uniform monomorphic cells
- ▶ Arrayed in sheets cords, or papillae
- ▶ Their cytoplasm may be acidophilic, basophilic, or chromophobic
- ▶ The nuclei may be uniform or pleomorphic
- ▶ Mitotic activity is usually scanty

****Pituitary adenoma**



Monomorphism of cells and absence of reticulin network

**ACTH cell adenoma



Prolactinomas

- ▶ The most common type of pituitary adenoma
- ▶ May be micro- or macroadenoma
- ▶ Females of reproductive age usually present early with symptoms of hyperprolactinemia:
 - ▶ Amenorrhea- Galactorrhea
 - ▶ Loss of libido and infertility
- ▶ Serum prolactin > 200 ng/ml is diagnostic

Other causes of hyperprolactinemia

- ▶ Pregnancy
- ▶ High-dose estrogen therapy
- ▶ Anti-psychotic drugs
- ▶ Liver cirrhosis
- ▶ Renal failure
- ▶ Hypothyroidism
- ▶ Dopamine-inhibiting drugs (e.g., reserpine)



Autonomous production of prolactin occurs with pituitary adenomas; these so-called prolactinomas are the most common functioning pituitary adenomas, accounting for 60% of all pituitary tumors. They are usually microadenomas when they occur in women and macroadenomas in men, usually presenting with visual field deficits, etc. Macroadenomas can obstruct the pituitary stalk, increasing prolactin release by blocking dopamine transport from hypothalamus (stalk effect). Other examples are tumors, such as craniopharyngioma, meningioma, and dysgerminoma; empty sella; and trauma.

Diagnosis

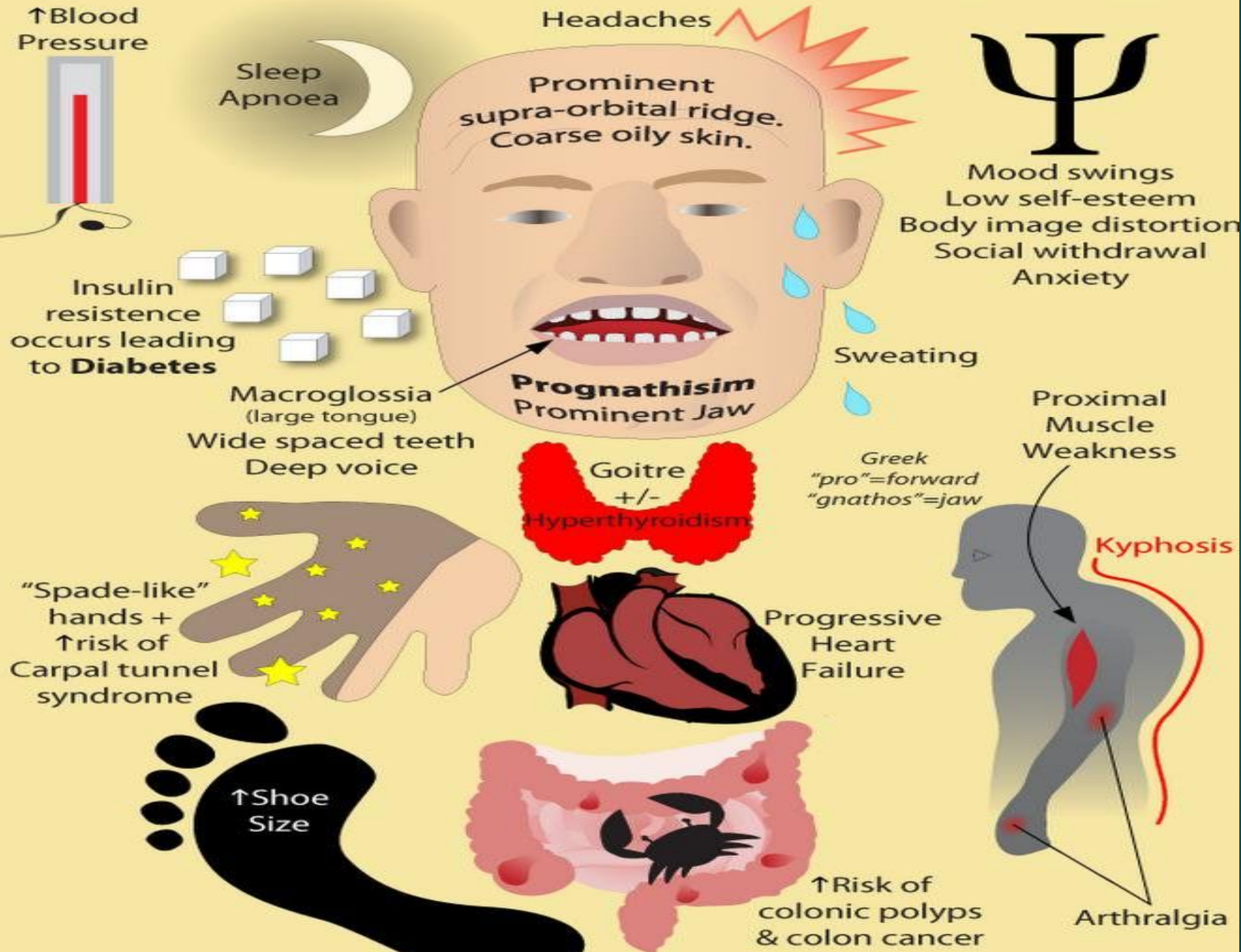
- _ Always exclude states such as pregnancy by pregnancy test , exclude drug induced hyperprolactinemia and hypothyroidism
- _ Prolactine level
- _ Imaging studies : CT and MRI

Growth Hormone-Producing Adenomas

- ▶ The 2nd most common adenoma
- ▶ May be quite large at time of diagnosis
- ▶ **Clinical picture:**
 - ▶ Children (gigantism)
 - ▶ Adults (acromegaly)
 - ▶ Abnormal glucose tolerance and DM
 - ▶ Generalized muscle weakness
 - ▶ Hypertension, osteoporosis, and CHF

Acromegaly

Caused by over-secretion of **growth hormone (GH)** from the **pituitary gland**.
The condition is rare and tends to present between 30 and 50 years of age.



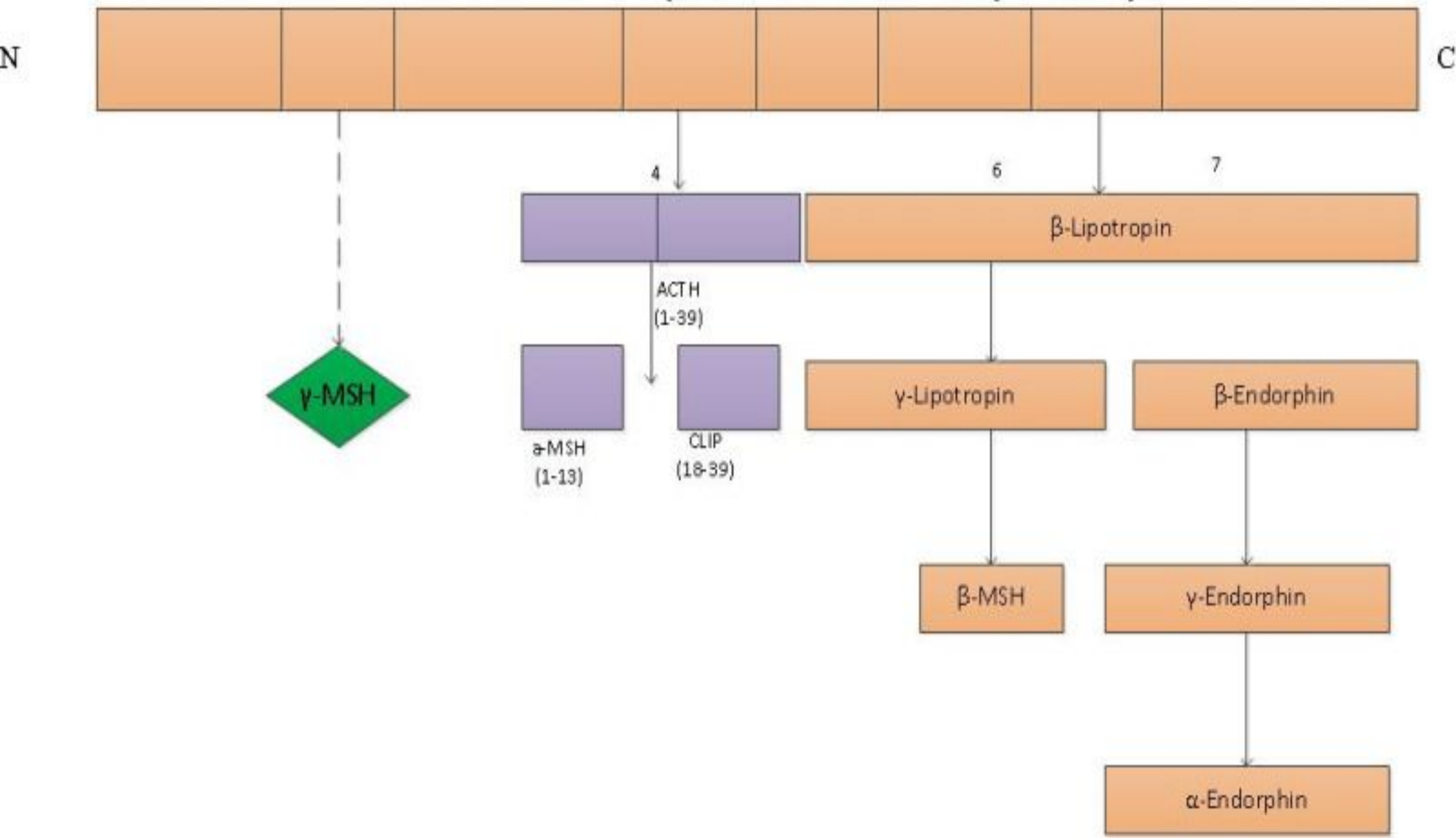
Diagnosis

- _ Patients with acromegaly have symptoms for an average of 9 years before the diagnosis is made.
- _ The best initial test is IGF-1 level.
- _ Confirmatory testing involves the measurement of GH after 100 g of glucose is given orally; this test is positive if GH remains high (>5 ng/mL) and suggests acromegaly. Normally a glucose load should completely suppress levels of GH.
- _ Radiologic studies such as CT scanning and MRI are used to localize the tumor but should be done only after GH excess is documented biochemically

Corticotroph Cell Adenomas

- ▶ Most are small (microadenomas)
- ▶ ACTH stains positive with PAS stains
- ▶ May be clinically silent or may cause hypercortisolism (Cushing disease)
- ▶ Hyperpigmentation due to ↑ MSH
- ▶ Nelson syndrome

Pro-opiomelanocortin(POMC)



Nelson syndrome

- ▶ The development of large destructive pituitary adenoma after surgical removal of the adrenal glands
- ▶ Loss of inhibitory effect of adrenal cortisol
- ▶ Hypercortisolism does not develop

**Gonadotroph (LH & FSH) adenomas

- ▶ Most frequent in middle-aged M & F
- ▶ Usually macroadenoma
- ▶ FSH is usually the predominant hormone

Classification of pituitary adenoma

Cell Type	Hormone	Tumor Type	Syndrome
Corticotroph	ACTH	ACTH cell (corticotroph) adenoma	Cushing Dz Nelson syndrome
Somatotroph	GH	GH cell (somatotroph) adenoma	Gigantism (children) Acromegaly (adults)
Lactotroph	Prolactin	Prolactin cell (lactotroph) adenoma	Galactorrhea Amenorrhea Sexual dysfunction Infertility
Thyrotroph	TSH	TSH cell (thyrotroph) adenoma	Hyperthyroidism
Gonadotroph	FSH, LH	Gonadotroph, Most of “null cell”, adenomas	Hypogonadism, mass effects, and hypopituitarism

Pituitary carcinoma

- ▶ Exceedingly rare
- ▶ Local extension beyond the sella turcica
- ▶ Always have distant metastases

Hypopituitarism

- ▶ Deficiency of trophic hormones
- ▶ Occur with loss of $\geq 75\%$ of anterior pituitary

Causes

Ischemic necrosis of pituitary

Surgery, radiation, trauma

Inflammation (sarcoidosis or tuberculosis)

Metastatic neoplasm

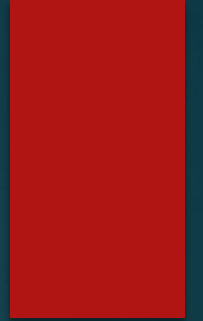
Nonfunctional pituitary adenomas

Congenital (exceedingly rare)

Hypothalamic lesions or tumors

❑ Associated with posterior pituitary as DI

Ischemic necrosis of anterior pituitary



- ▶ **Sheehan syndrome (postpartum necrosis)**
 - ❑ The most common form
 - ❑ The physiological enlargement of the gland without ↑ in blood supply
- ▶ **Other causes:**
- ▶ DIC, Sickle cell anemia, ↑ ICP, traumatic injury, and shock of any origin

Clinical manifestations of hypopituitarism

Deficient hormone	Manifestation
GH	Children may develop growth failure (pituitary dwarfism)
FSH, LH or (GnRH)	Amenorrhea and infertility in women Decreased libido, impotence with loss of pubic and axillary hair in men
TSH	Hypothyroidism
ACTH	Hypoadrenalism
Prolactin	Failure of postpartum lactation

Posterior pituitary hormones

- ▶ Oxytocin:
 - ▶ Contraction of smooth muscle in pregnant uterus and around the lactiferous ducts
 - ▶ No clinical syndromes
- ▶ Antidiuretic hormone (ADH):
 - ▶ Diabetes insipidus DI, ADH deficiency
 - ▶ SIADH: $\uparrow$ of inappropriate ADH secretion

Physiologic effects of oxytocin

- Two target tissues both involved in neuroendocrine reflexes
- During delivery
 - ✓ baby's head stretches cervix
 - ✓ hormone release enhances uterine muscle contraction
 - ✓ baby & placenta are delivered
- After delivery
 - ✓ *Oxytocin* stimulates contraction of the uterus and ejection (let-down) of milk from the breasts.
 - ❖ Nursing a baby after delivery stimulates oxytocin release, promoting uterine contractions and the expulsion of the placenta (Clinical Application).
 - ❖ suckling & hearing baby's cry stimulates milk ejection



Uterus



Mammary glands

Control of oxytocin secretion

Stimuli

- Stimulation of the “touch receptor” around the nipples
- Milk let-down or “milk ejection reflex” (latent period: 30-60 seconds)
- Genital tract stimulation

Inhibition

- Milk let-down can be inhibited by emotional stress and psychic factors such as fright
 - ✓ NE & Epi inhibit its secretion
 - ✓ Ethanol
 - ✓ enkephalins

Vasopressin

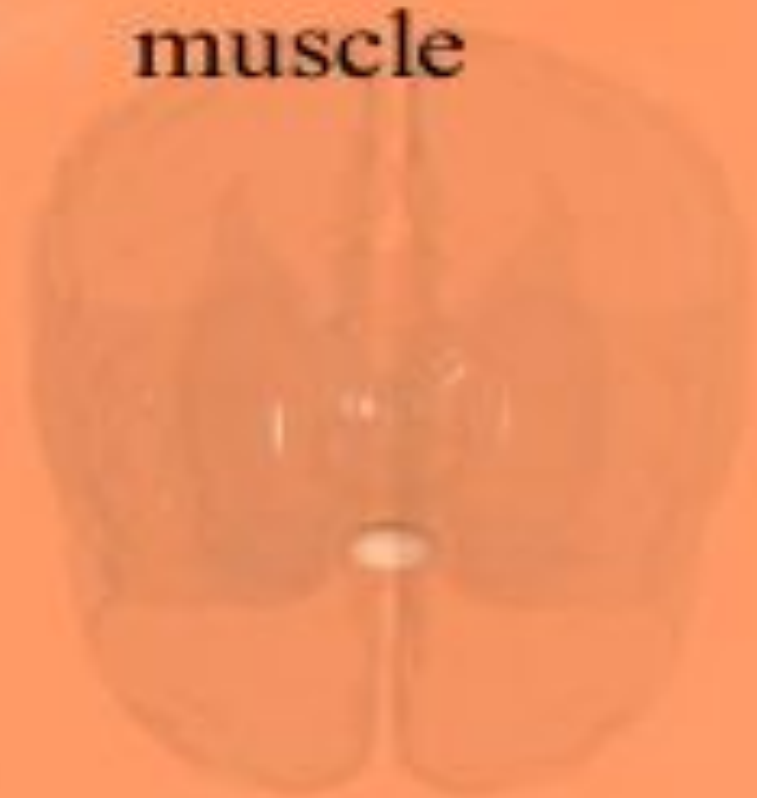
- Antidiuretic hormone V_2 -receptor:
collecting duct and distal convoluted tubule
- Vasopressor hormone V_1 -receptor:
vascular smooth muscle



Vasopressin

Decreases water excretion by kidneys (V_2 receptors)

Constricts blood vessels (V_1 receptors)- arteriolar smooth muscle



Vasopressin (ADH) Secretion

Secretion is Stimulated by:

1. Large decreases in blood volume
2. Decreases in blood pressure
3. Pain, fear, trauma, and stress

ADH

- ▶ A nonapeptide hormone synthesized in the supraoptic nucleus in response to:
 - _ ↑ plasma oncotic pressure
 - _ Left atrial distention
 - _ Exercise, and certain emotional states
- ▶ ADH acts on the collecting tubules of kidney to promote the resorption of free water

Diabetes insipidus

▶ Central DI, ADH deficiency

- ❑ Head trauma
- ❑ Neoplasms of hypothalamus & pituitary
- ❑ Inflammation of hypothalamus & pituitary
- ❑ Surgery of hypothalamus or pituitary
- ❑ Idiopathic

▶ Nephrogenic DI

- ▶ Renal tubular unresponsiveness to ADH
- ▶ Idiopathic or it can be secondary to hypercalcemia, hypokalemia, sickle cell disease, amyloidosis, myeloma, pyelonephritis, sarcoidosis, or Sjögren syndrome. Drugs (lithium, colchicine) are among the most common causes of nephrogenic DI.

Manifestations of DI

- ▶ polyuria,
- ▶ excessive thirst,
- ▶ polydipsia (16–20 L/d),
- ▶ hypernatremia with high serum osmolarity and coexisting low urine osmolarity and urine specific gravity

Diagnosis.

- _ The water deprivation test compares Uosm after dehydration versus Uosm after vasopressin.
- _ In a normal person, the response to fluid restriction is to increase urine osmolality and decrease urine volume.
- _ In DI, the urine volume remains high despite volume depletion

SIADH

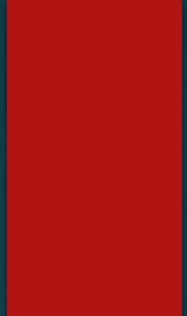
- ▶ ADH excess is caused by several extracranial and intracranial disorders
- ▶ Causes:
- ▶ Ectopic ADH production by malignant neoplasms (particularly **SmCC of lung**)
- ▶ Non-neoplastic diseases of the lung
- ▶ Drugs such as chlorpropamide, and carbamazepine can induce SIADH.

Manifestations

- ▶ In general, increased ADH causes water retention and extracellular fluid volume expansion.
- ▶ The water retention and sodium loss both cause hyponatremia, which is a key feature in SIADH.
- ▶ concentrated urine ($U_{osm} > 300 \text{ mOsm}$)
- ▶ When hyponatremia is severe ($\text{sodium} < 120 \text{ mOsm}$), or acute in onset, symptoms of cerebral edema become prominent (irritability, confusion, seizures, and coma).

Diagnosis:

- 1_ Hyponatremia
- 2_ Plasma osmolality is less than 270 mOsm/kg
- 3_ Urine Na Conc. Is more than 20 mEq/l



	Psychogenic polydipsia	Diab. insipidus	SIADH
Plasma osmolality	↓	↑	↓
Serum sodium	↓	↔ or ↑	↓
Urine osmolality	↓	↓	↑
Urine sodium	↔	↔	↑

اللهم إن أًصبت فمناك وحدك
وإن أخطأت فمن نفسي ومن الشيطان