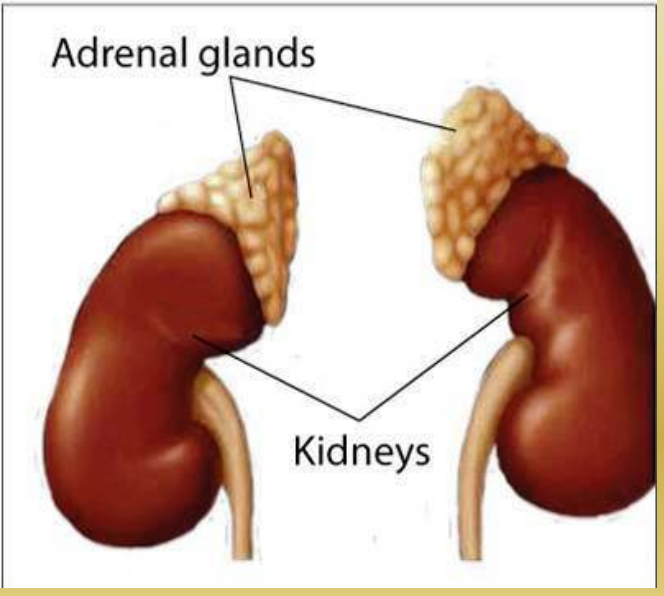


Lecture 5 Diseases of adrenal gland

By Dr.Esraah Alharris
PhD(path), MSc(path), MBChB

The objectives of this lecture

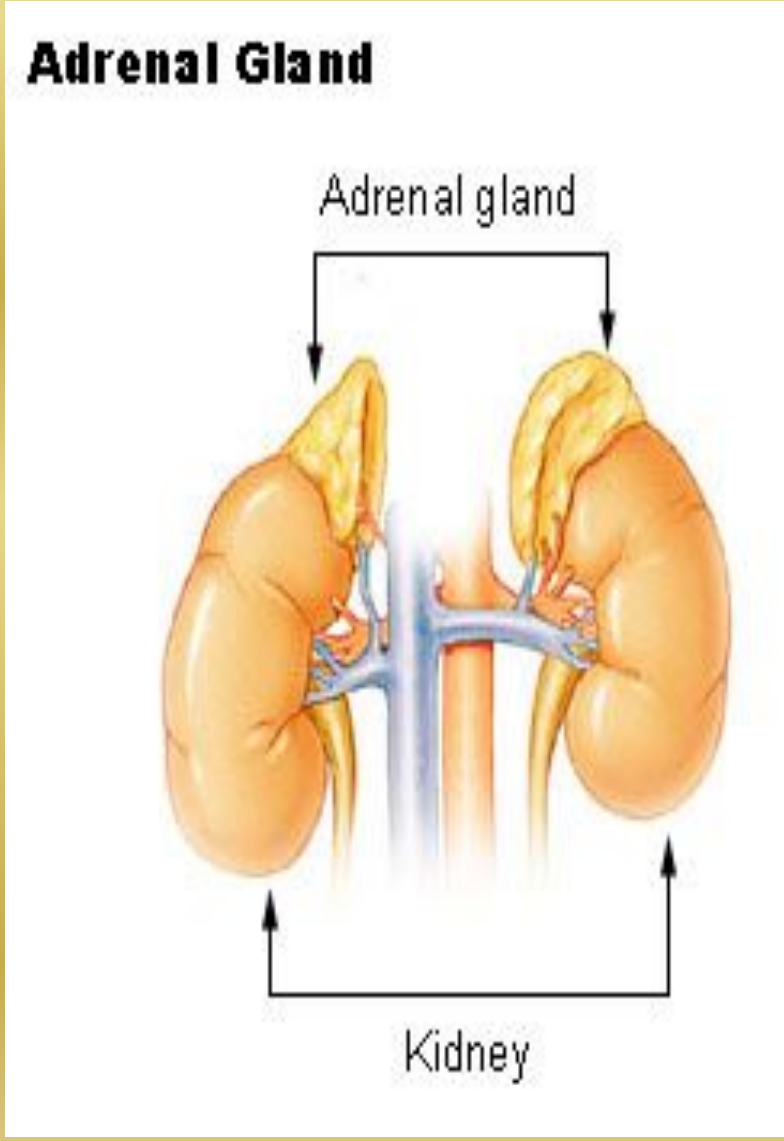
- To review the anatomy, histology and physiology of adrenal gland
- To classify the adrenal disorders
- To show the gross and microscopical pathological features for different adrenal functional disorders

CASE

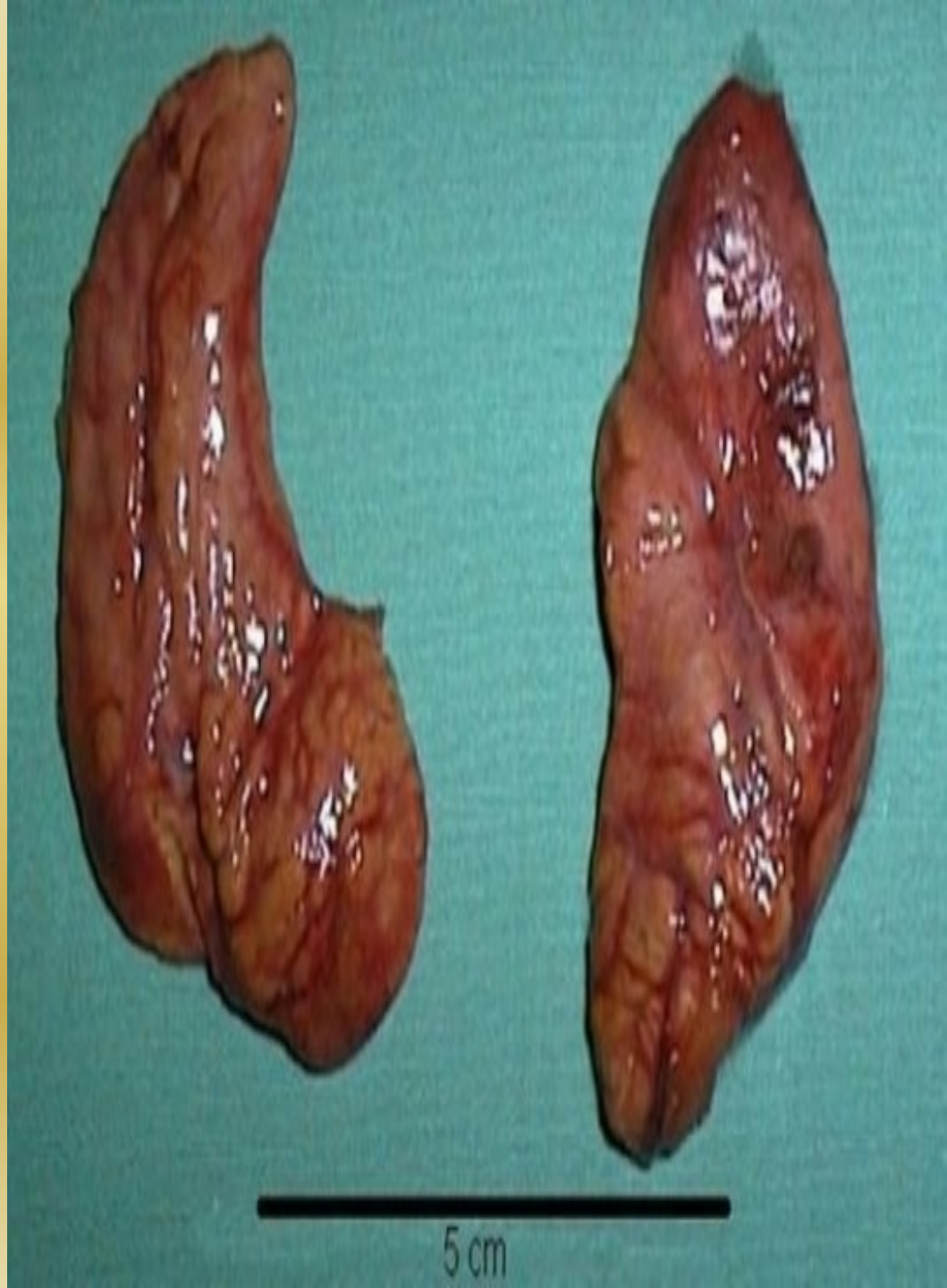
A 55-year-old woman presents with increasing muscle weakness and fatigue. Physical examination finds an obese adult woman with purple abdominal stria and increased facial hair. The excess adipose tissue is mainly distributed in her face, neck, and trunk. Laboratory evaluation finds increased plasma levels of cortisol and glucose. Which of the following is the most likely diagnosis?

1. Addison's disease
2. Bartter's syndrome
3. Conn's syndrome
4. Cushing's syndrome
5. Schmidt's syndrome

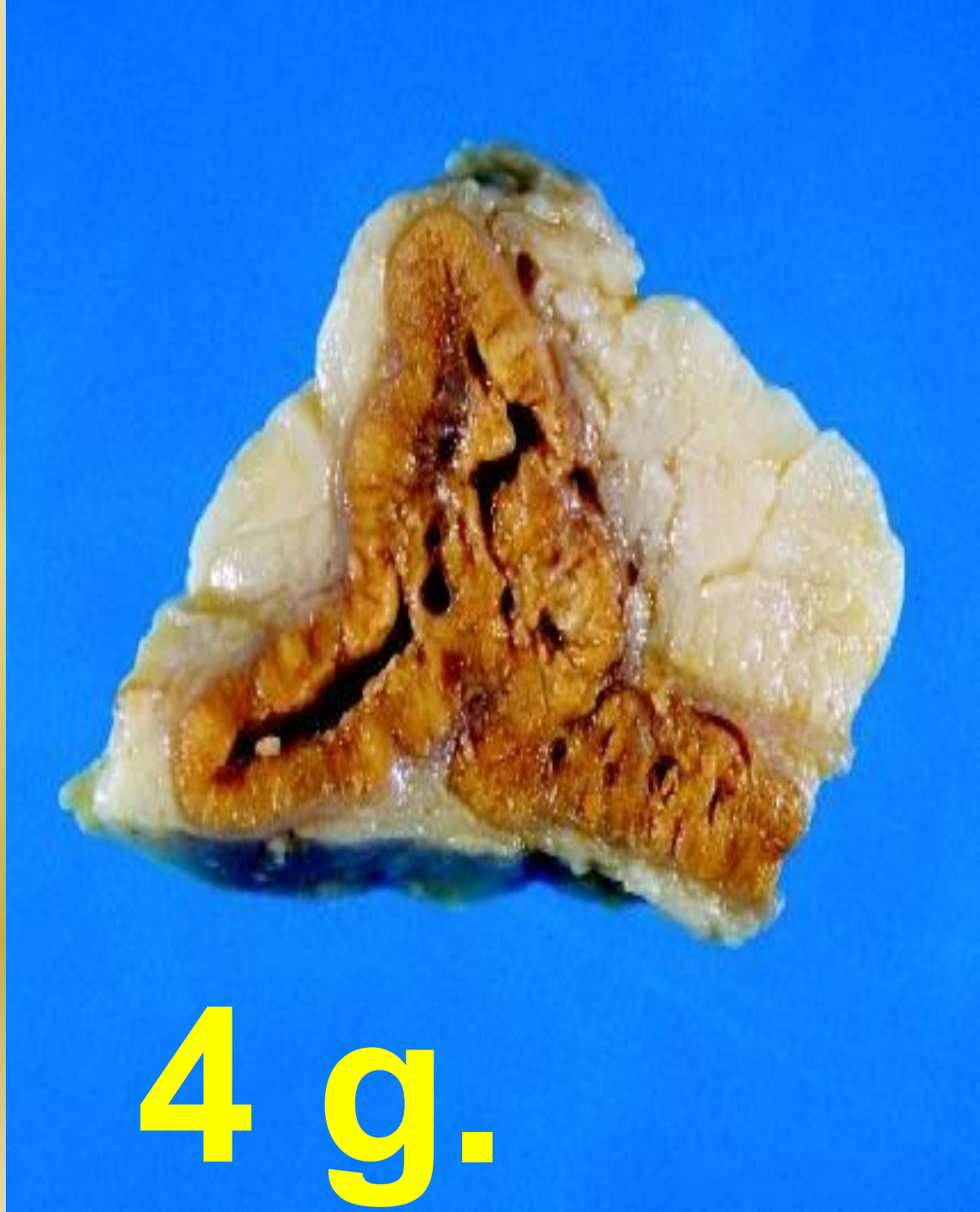
- Adrenal glands are triangular shaped endocrine glands that measure about 3 inches in length, and a half inch in height.
- The two glands are separated with one being on each kidney.



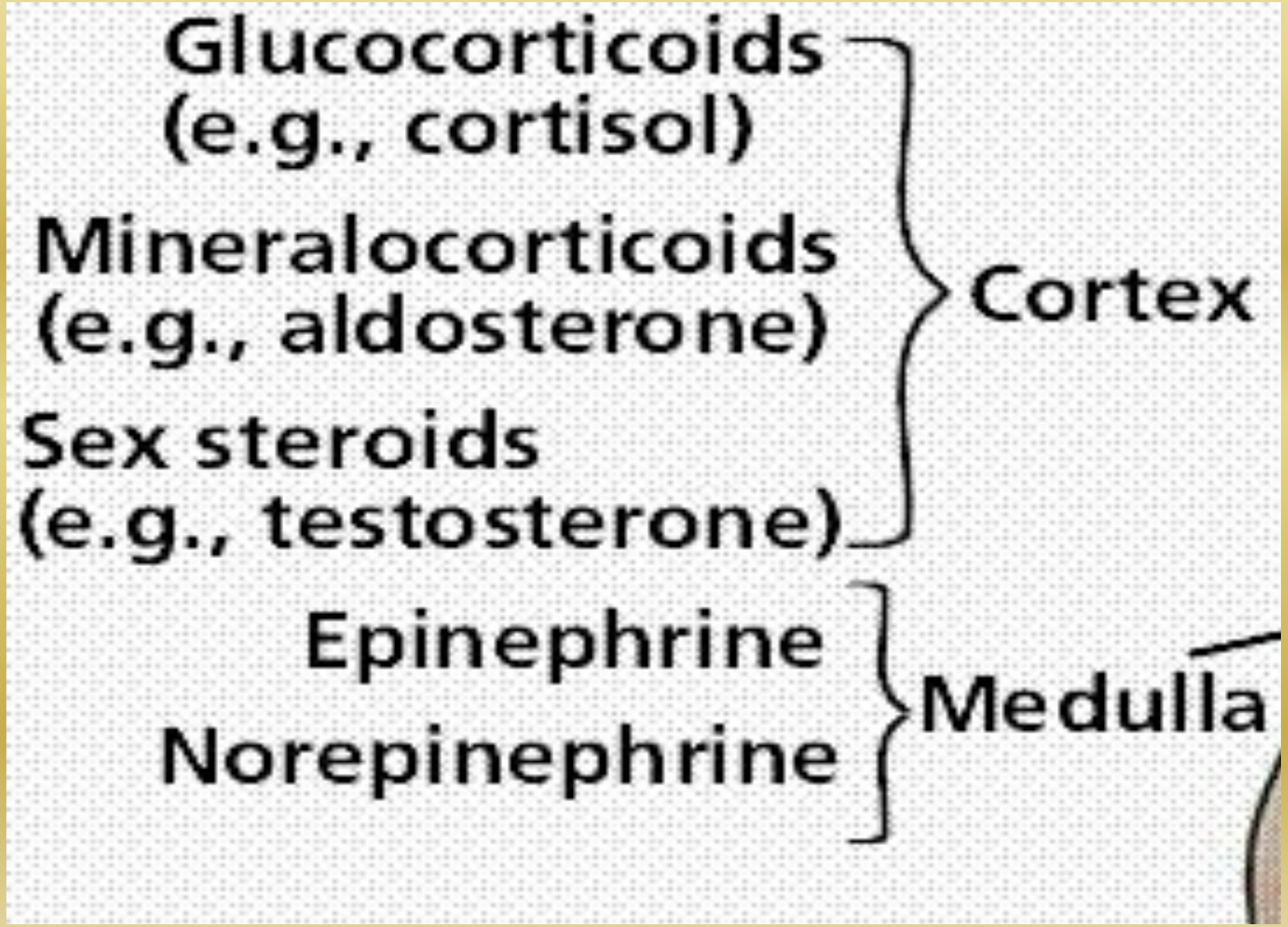
Right is usually flatter and much less triangular. Think of the liver is squishing it.



They are made up of an inner layer called the *adrenal medulla* and an outer layer called the *adrenal cortex*.

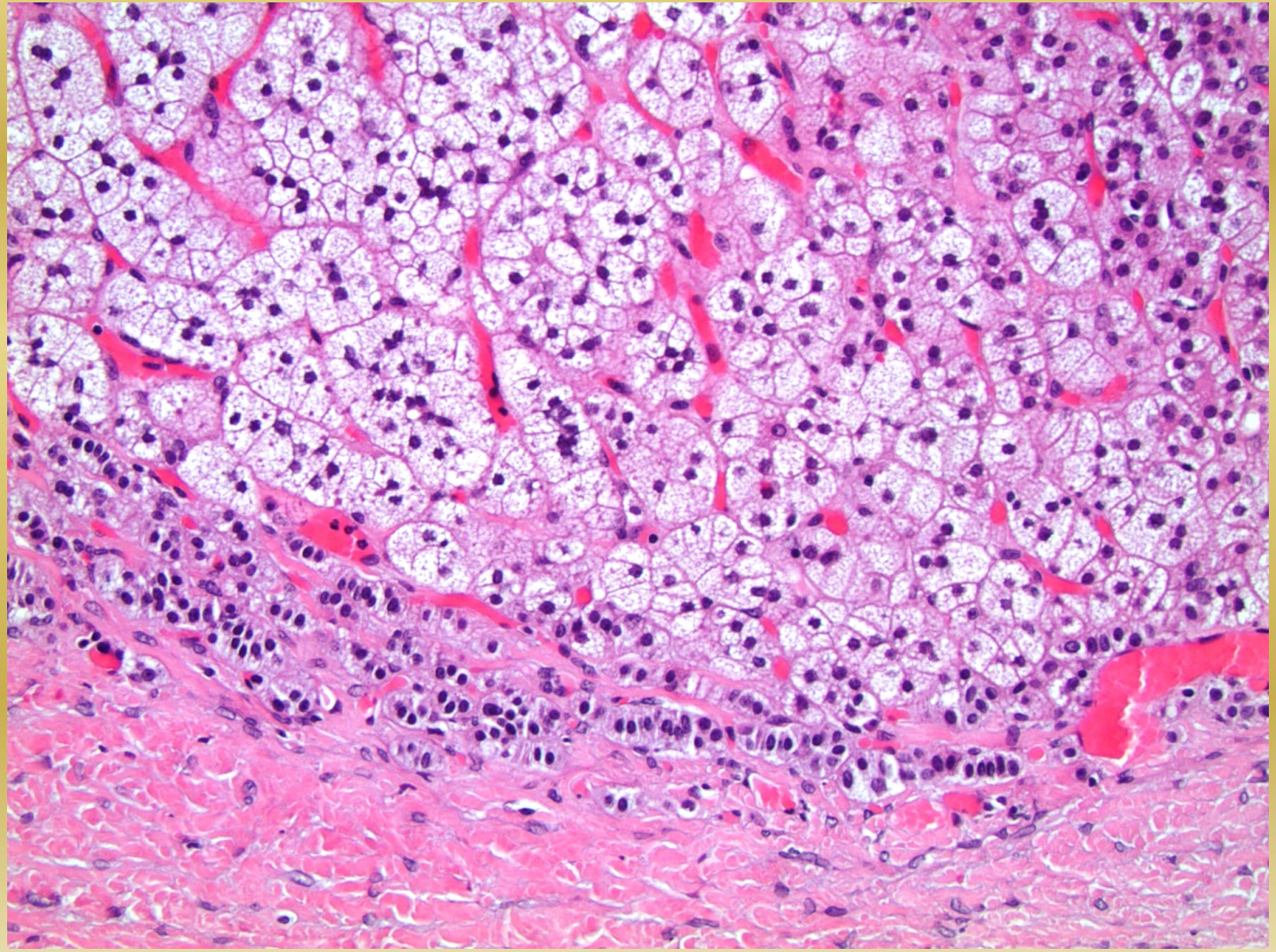


4 g.

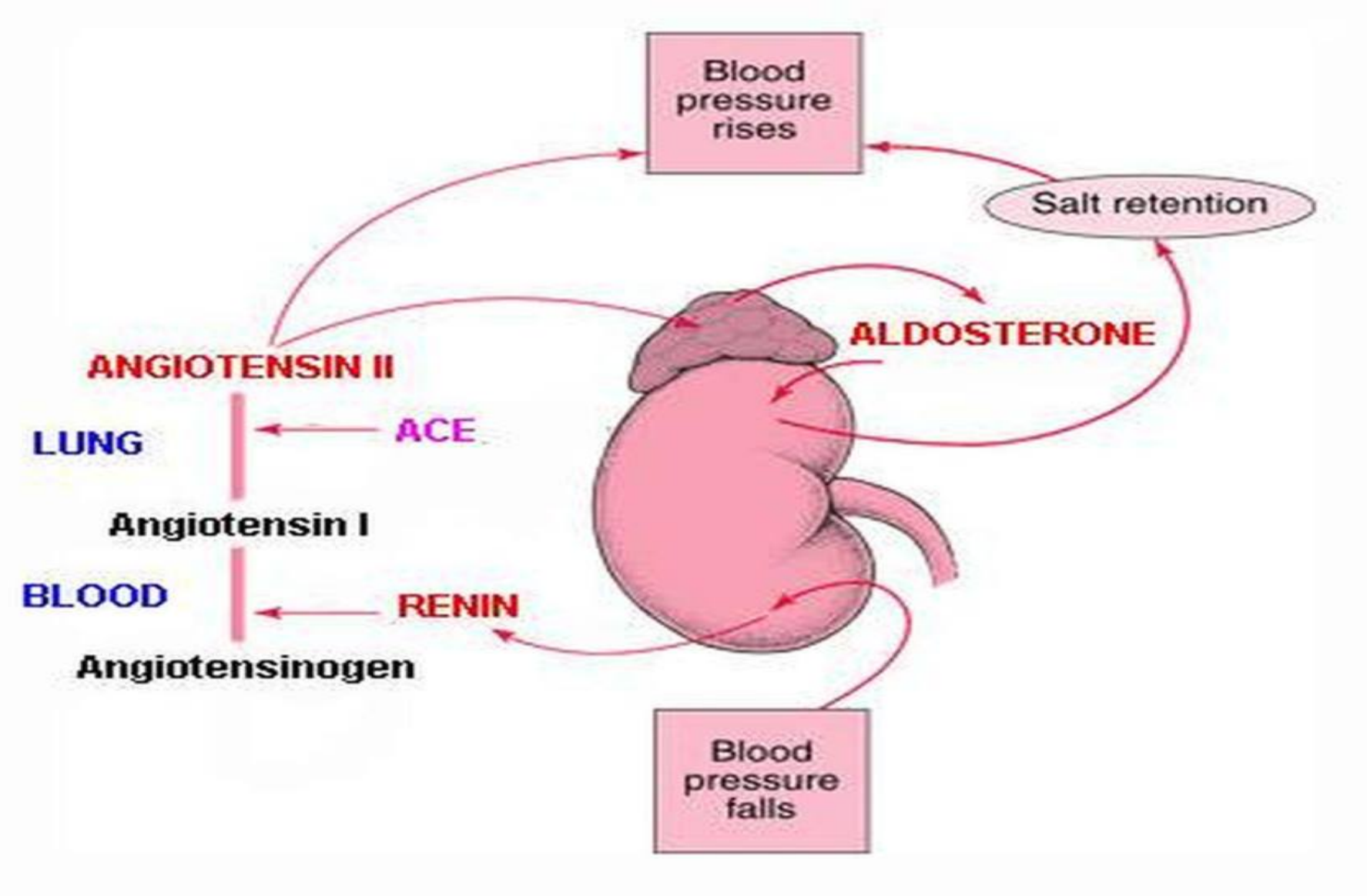

Glucocorticoids
(e.g., cortisol)
Mineralocorticoids
(e.g., aldosterone)
Sex steroids
(e.g., testosterone)
Cortex
Epinephrine
Norepinephrine
Medulla

- **G**lomerulosa (**Salt**), mineralocorticoids
  - ALDOSTERONE Regulates electrolyte & fluid homeostasis
- **F**asciculata (**Sugar**), glucocorticoids
  - CORTISOL Stim. gluconeogenesis & ↑ blood glucose
- **R**eticularis (**Sex**), gonadocorticoids
  - ANDROGENS, ESTROGENS

Normal adrenal histology

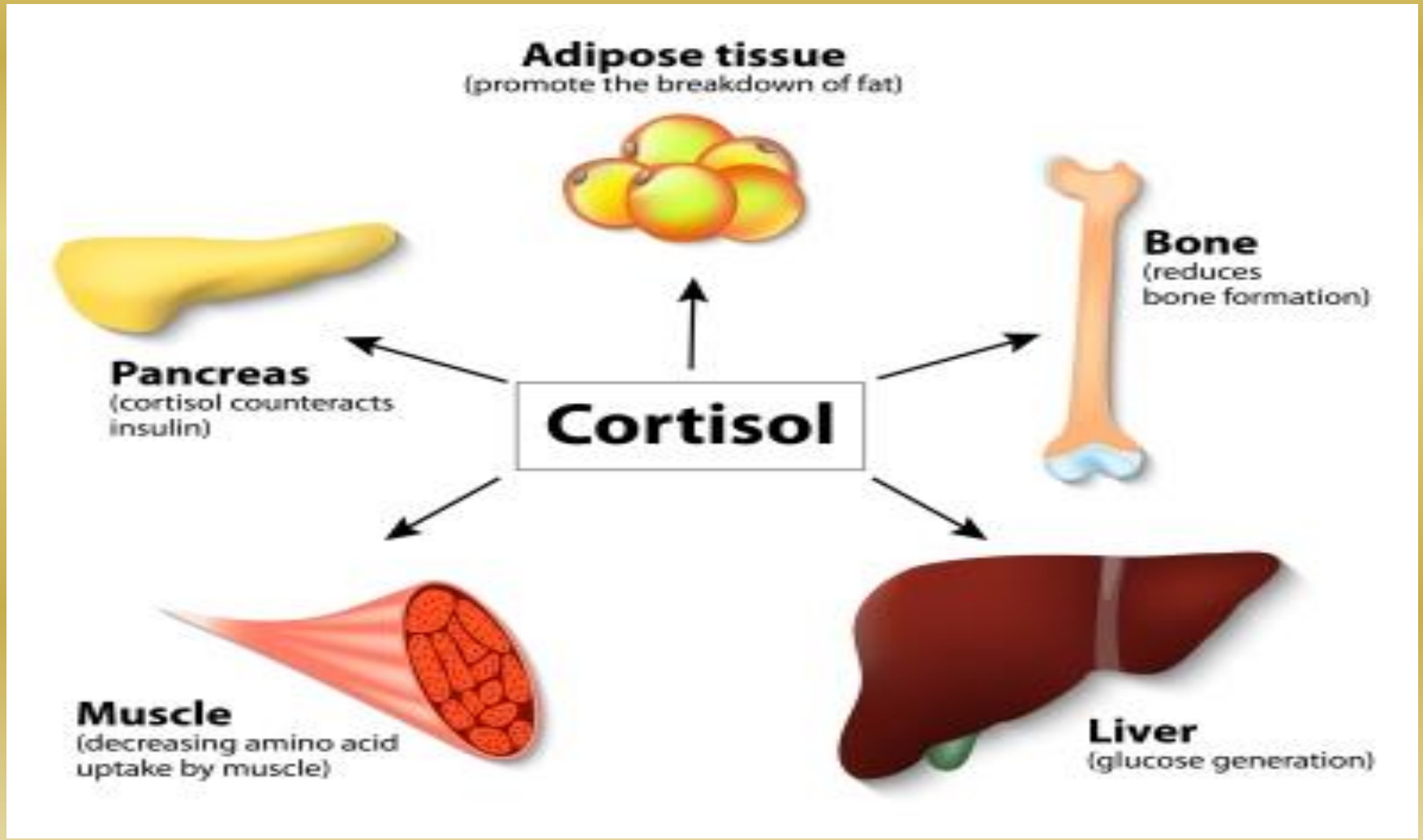


ALDOSTERONE



CORTISOL

It is released in response to stress and low blood-glucose concentration.



- Adrenal Medulla
  - Epinephrine
    - Adrenaline
  - Function
    - Prolong & ↑ SNS (sympathetic nervous system) response to stress

- Adrenal Medulla
  - Norepinephrine
  - Function
    - Prolong & ↑ SNS (sympathetic nervous system) response to stress

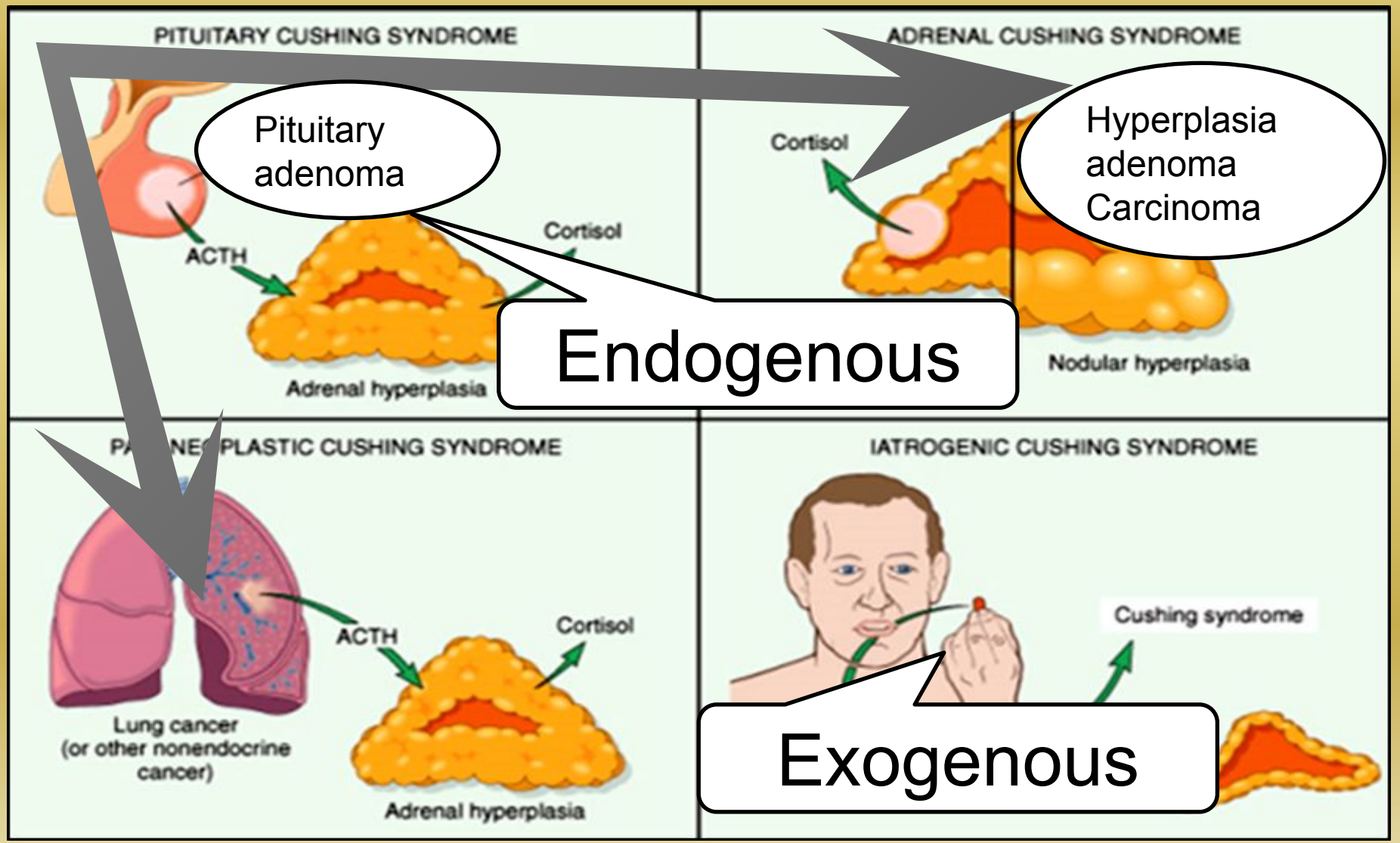
Adrenal cortex

Adrenocortical hyperfunction:

1- Cushing's syndrome Excess corticosteroids
2- Conn's syndrome Excess aldosterone
3- Adrenogenital syndrome Excess androgen

CUSHING SYNDROME

Causes : *very important*



1- Administration of exogenous glucocorticoids
(<u>most common cause</u>)
Suppress endogenous ACTH and result in cortical atrophy

2- Pituitary ACTH hypersecretion (Cushing disease) typically occurs pituitary adenoma.

- **Serum ACTH is elevated and is not suppressed by low-dose dexamethasone challenge but is reduced by high-dose challenge.**

3- Primary adrenal neoplasms

ACTH-independent Cushing syndrome

Adenoma

Carcinoma

ACTH levels are quite low (feedback inhibition), and dexamethasone challenge has no effect on cortisol levels.

4- Ectopic ACTH secretion (non-pituitary non adrenal tumors)

Commonly associated with :-

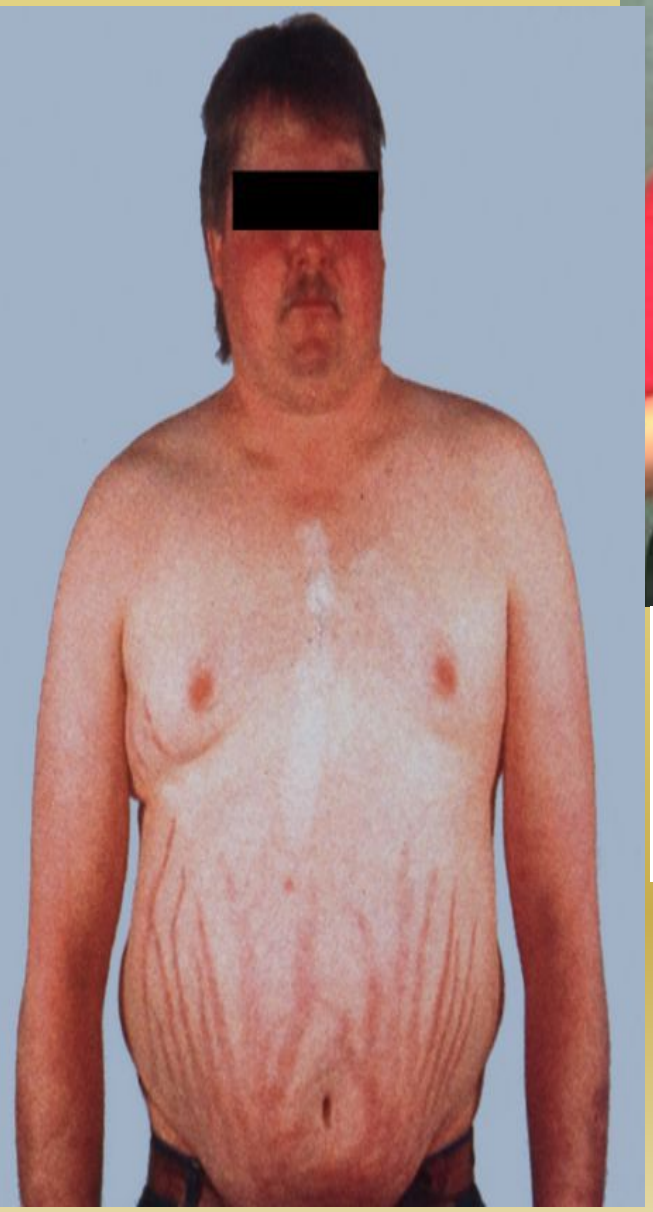
- lung small cell carcinoma
- Carcinoid tumors
- thyroid medullary carcinoma
- islet cell tumors
- Rarely, due to ectopic secretion of (CRF) Corticotrophin releasing factor.

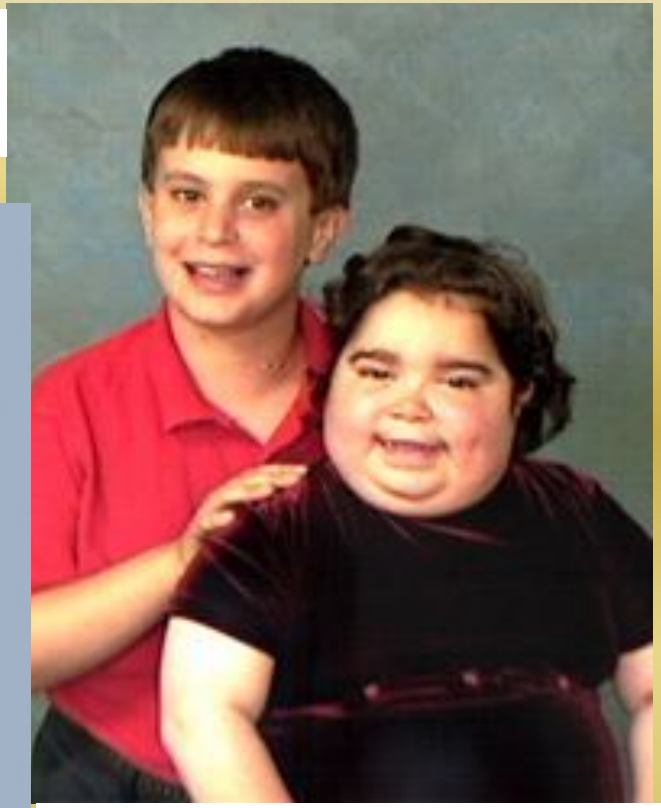
Serum ACTH is elevated and its secretion is completely insensitive to either low-dose or high-dose dexamethasone.

Clinical Course :-
Cushing syndrome develops slowly, and early manifestations (hypertension and weight gain) are non-specific

central obesity, moon facies,
fat accumulation on the posterior neck and back (so-called “buffalo hump”)
• Atrophy of type 2 fast-twitch myofibers with decreased muscle mass and proximal muscle weakness
• Hyperglycemia, glucosuria, and polydipsia (secondary diabetes)
• Poor wound healing and abdominal striae due to catabolic effects on collagen

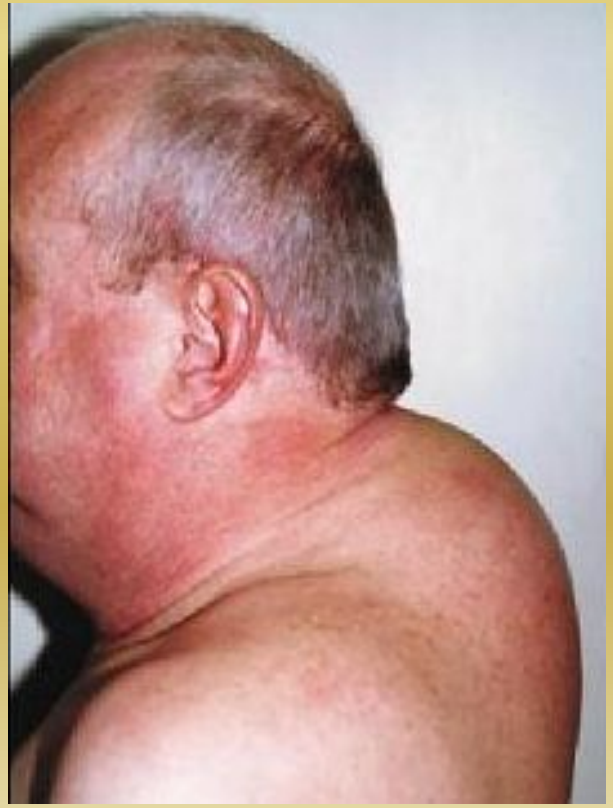
STRIAE





MOON FACIES

BUFFALO HUMP



- Bone resorption and osteoporosis with increased risk of fractures
- Increased risk of infection due to immunosuppression
- Hirsuitism and menstrual abnormalities
- Mental disturbances including depression and frank psychosis

Conn's syndrome Excess aldosterone

- Primary idiopathic hyperaldosteronism 60% of cases
- Adrenocortical neoplasm (35% of cases); usually solitary aldosterone-secreting adenomas (Conn syndrome), typically arising in middle age with a female to male ratio of 2:1.
- Adrenocortical carcinoma is a rarer.
- Hereditable

Clinical Course:-

- Hypertension is the major feature

- Hypokalemia, when present, results from renal potassium wasting causing a variety of neuromuscular manifestations, including weakness, paresthesias, visual disturbances, and occasionally tetany

Adrenogenital Syndromes

Disorders of sexual differentiation (e.g., female virilization or male precocious puberty) can be caused by primary gonadal or adrenal disorders.).

- **Androgen-secreting adrenal cortical neoplasms are more likely to be carcinomas than adenomas.**
- **Congenital adrenal hyperplasia (CAH)**

Hyperadrenalism

Pathological features:-

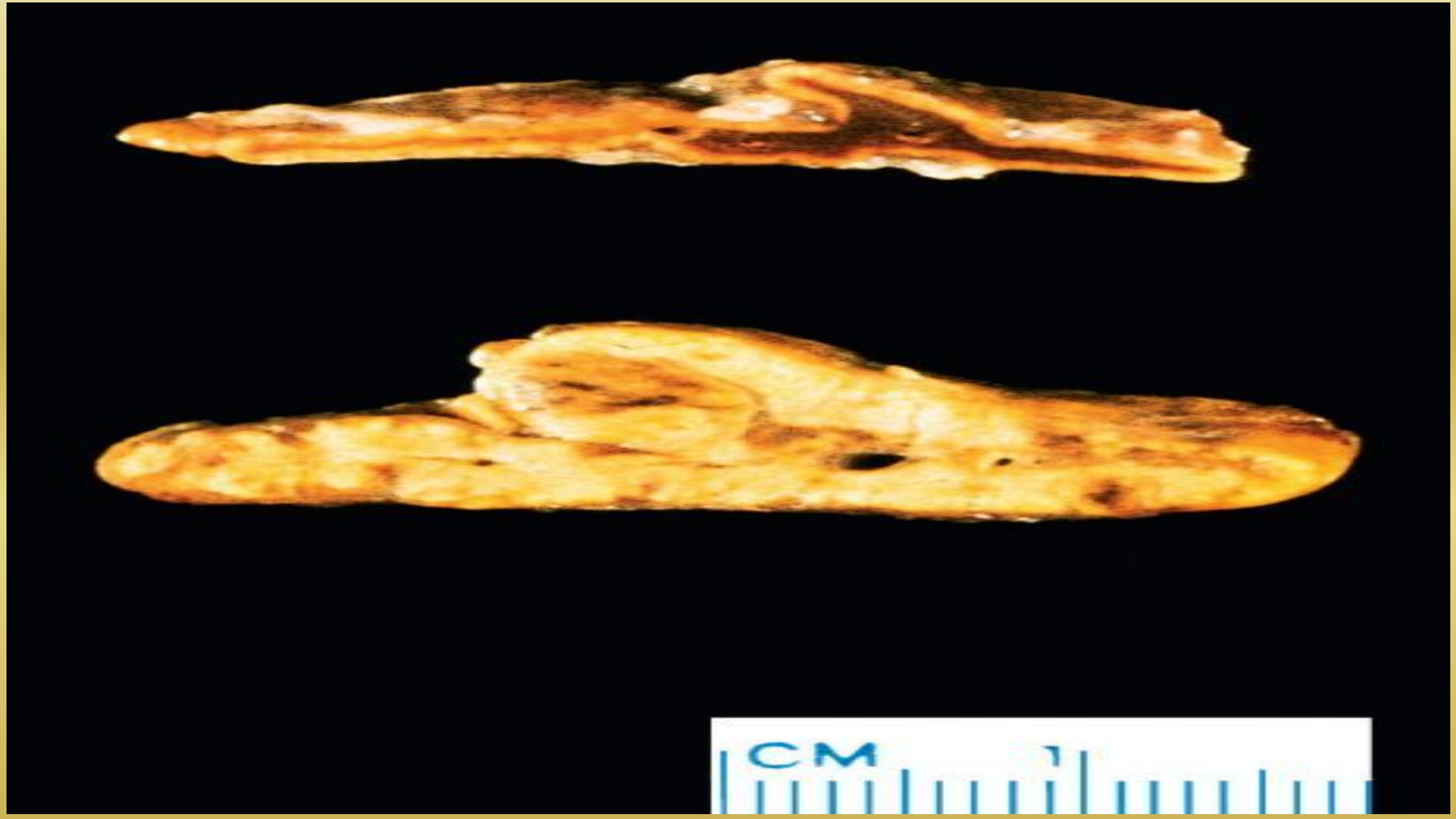
There is one of four changes in the adrenal glands, which depends on the cause.

1. Cortical atrophy

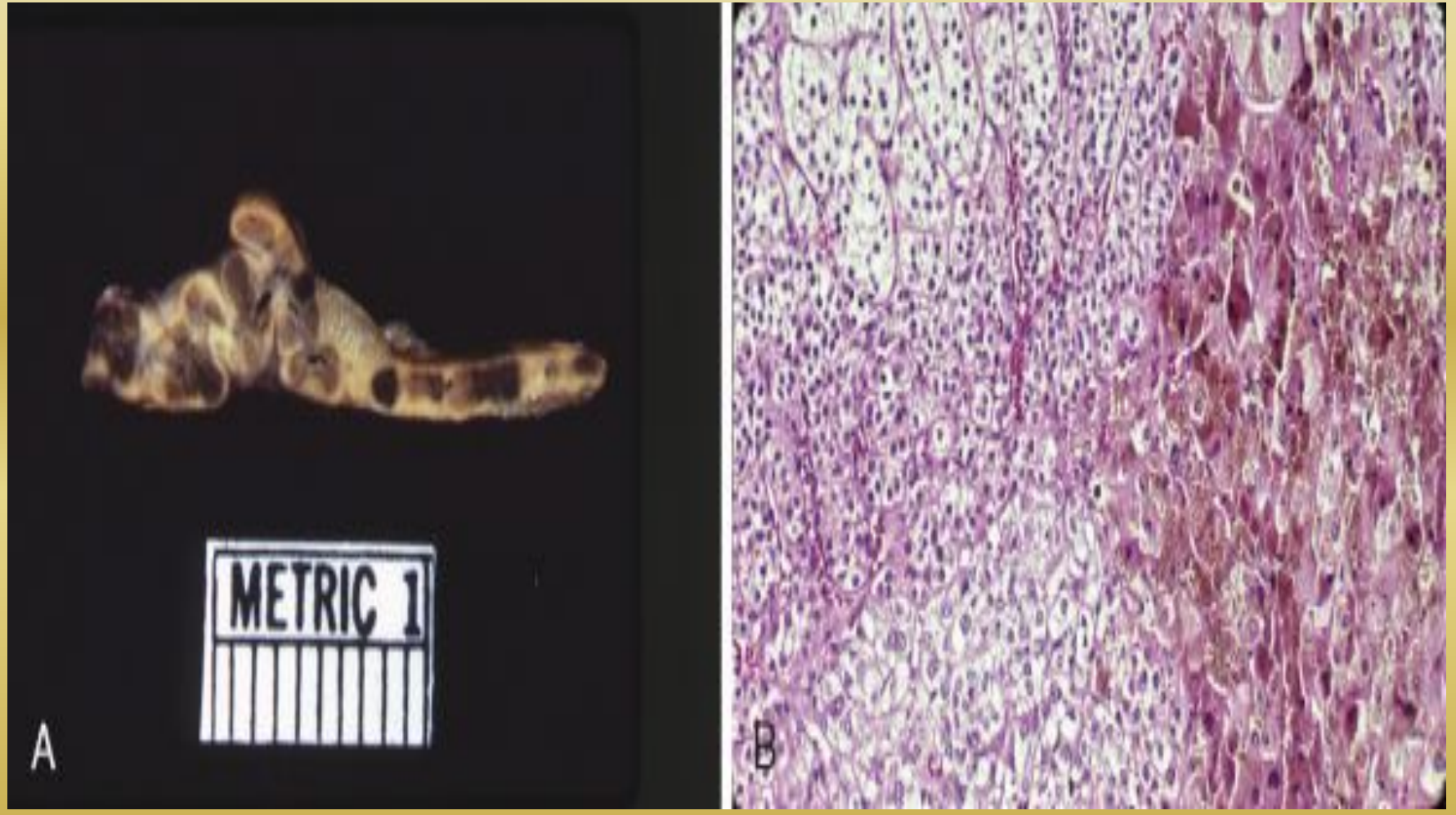
2. Diffuse hyperplasia

3. Nodular hyperplasia

4. Adenoma, rarely a carcinoma

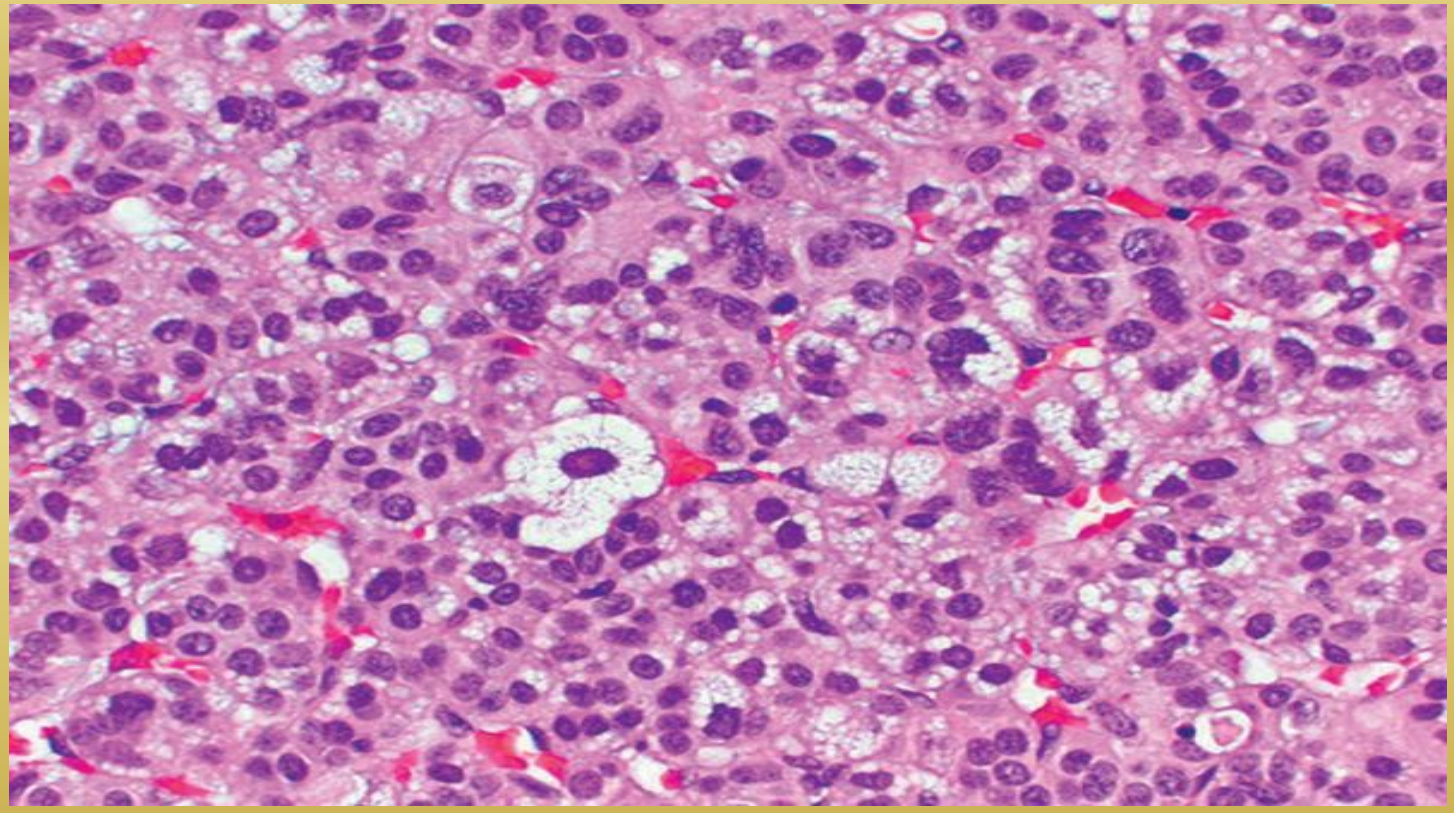


Diffuse hyperplasia of the adrenal contrasted with normal adrenal gland. In cross-section the adrenal cortex is yellow and thickened, and a subtle nodularity is seen



A, Primary pigmented nodular adrenocortical disease showing prominent pigmented nodules in the adrenal gland.
B, On histologic examination the nodules are composed of cells containing lipofuscin pigment, seen in the right part of the field.

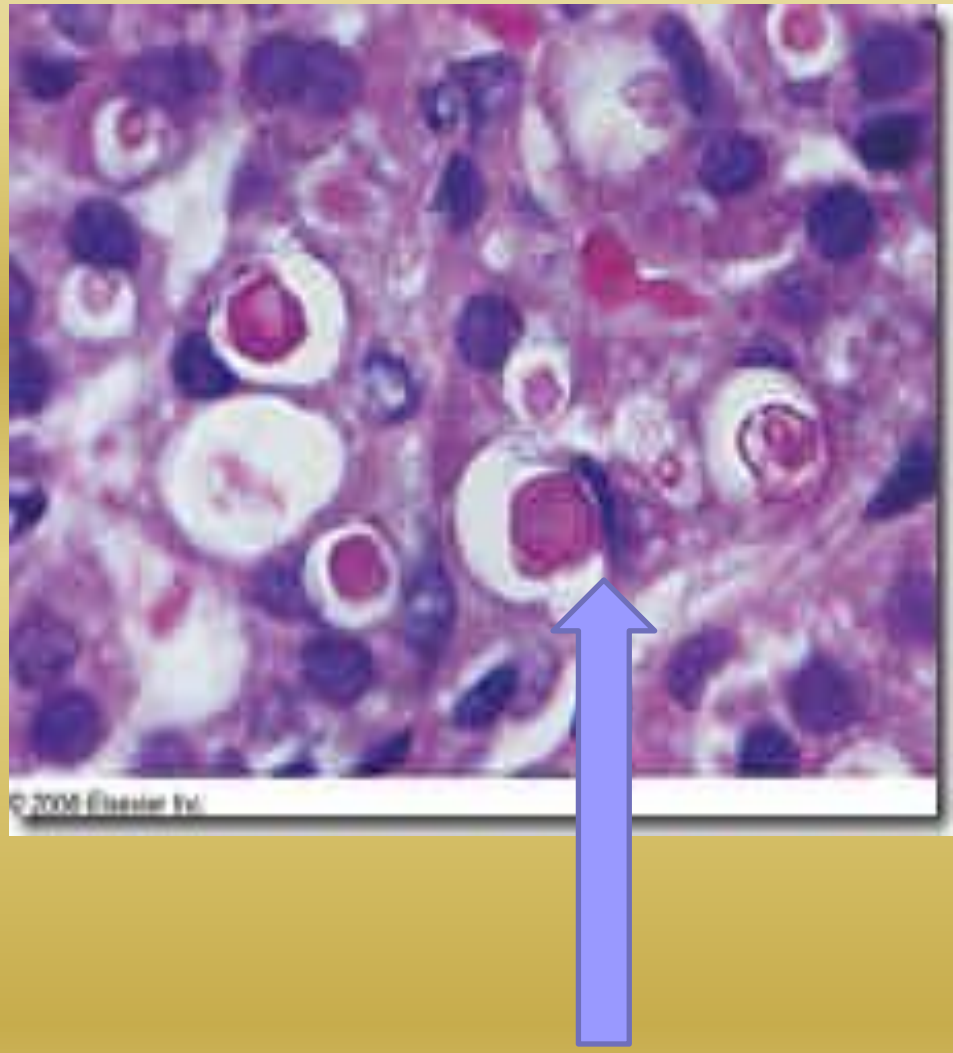
Aldosterone-producing adenomas



The neoplastic cells are vacuolated because of the presence of intracytoplasmic lipid. There is mild nuclear pleomorphism. Mitotic activity and necrosis are not seen

- **Hyperaldosteronism**
- **Adrenal adenoma;**

vacuolated cells with lipid contents & **spironolactone** inclusion bodies



Adrenal hypofunction:

Primary (adrenocrtical) or,
Secondary (ACTH deficiency).

Primary insufficiency is divided into acute & chronic.

Adrenal hypofunction:

- A- Acute adrenal insufficiency:
- *Massive adrenal hemorrhage including Waterhouse-Friderichsen syndrome*
- *Sudden withdrawal of long-term corticosteroid therapy*
- *Stress in those with chronic adrenal insufficiency.*

B- Chronic “Addison´s disease”:

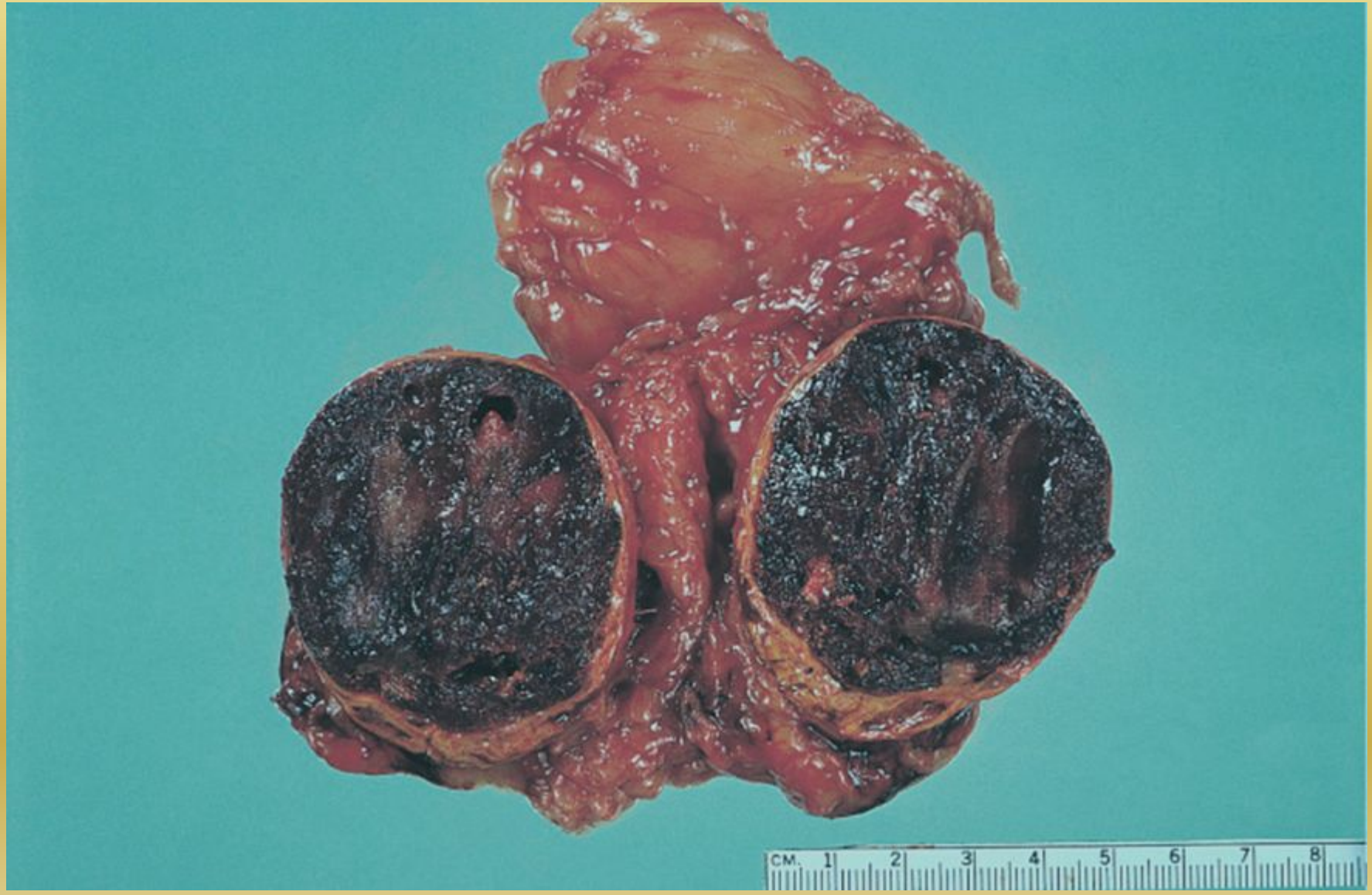
Destruction of 90% of adrenal cortex gradually:

1- Autoimmune inflammation

2- Chronic Infection TB , AIDS

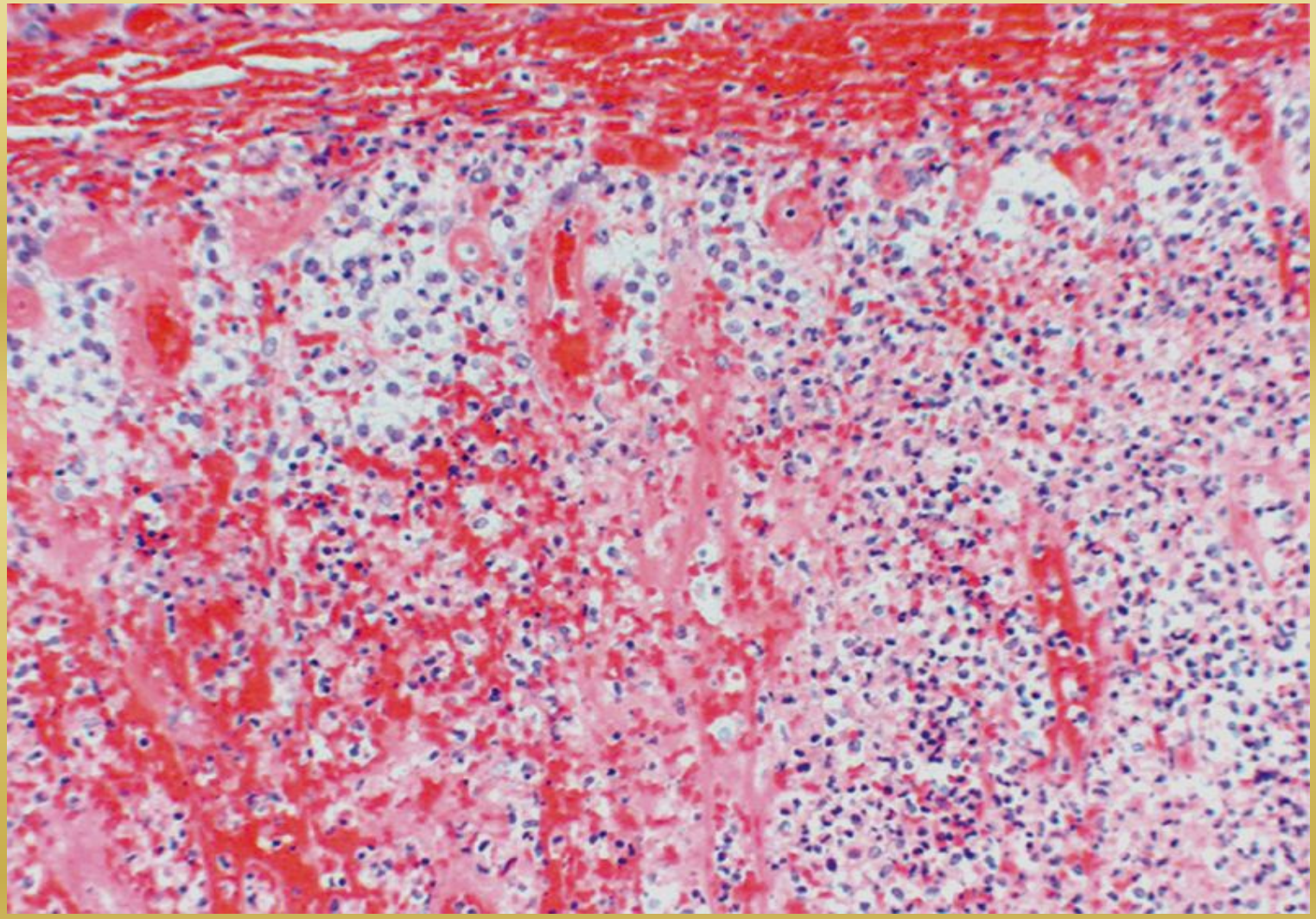
3- Bilateral metastatic tumour

Hemorrhage Adrenal



Adrenal gland massively replaced by hemorrhage. There was no evidence of a tumor in any of the many sections taken.

Adrenal hemorrhage



Acute adrenal insufficiency caused by severe bilateral adrenal hemorrhage in an infant with overwhelming sepsis (Waterhouse-Friderichsen syndrome). At autopsy the adrenals were grossly hemorrhagic and shrunken; microscopically, little residual cortical architecture is discernible.

Addison’s Disease

- **Pathophysiology**

Primary

- *Autoimmune adrenalitis (the most common cause;* 70% of cases*)*
- *Tuberculosis & fungal infections*
- *AIDS*
- *Metastatic cancers* (lung and breast)

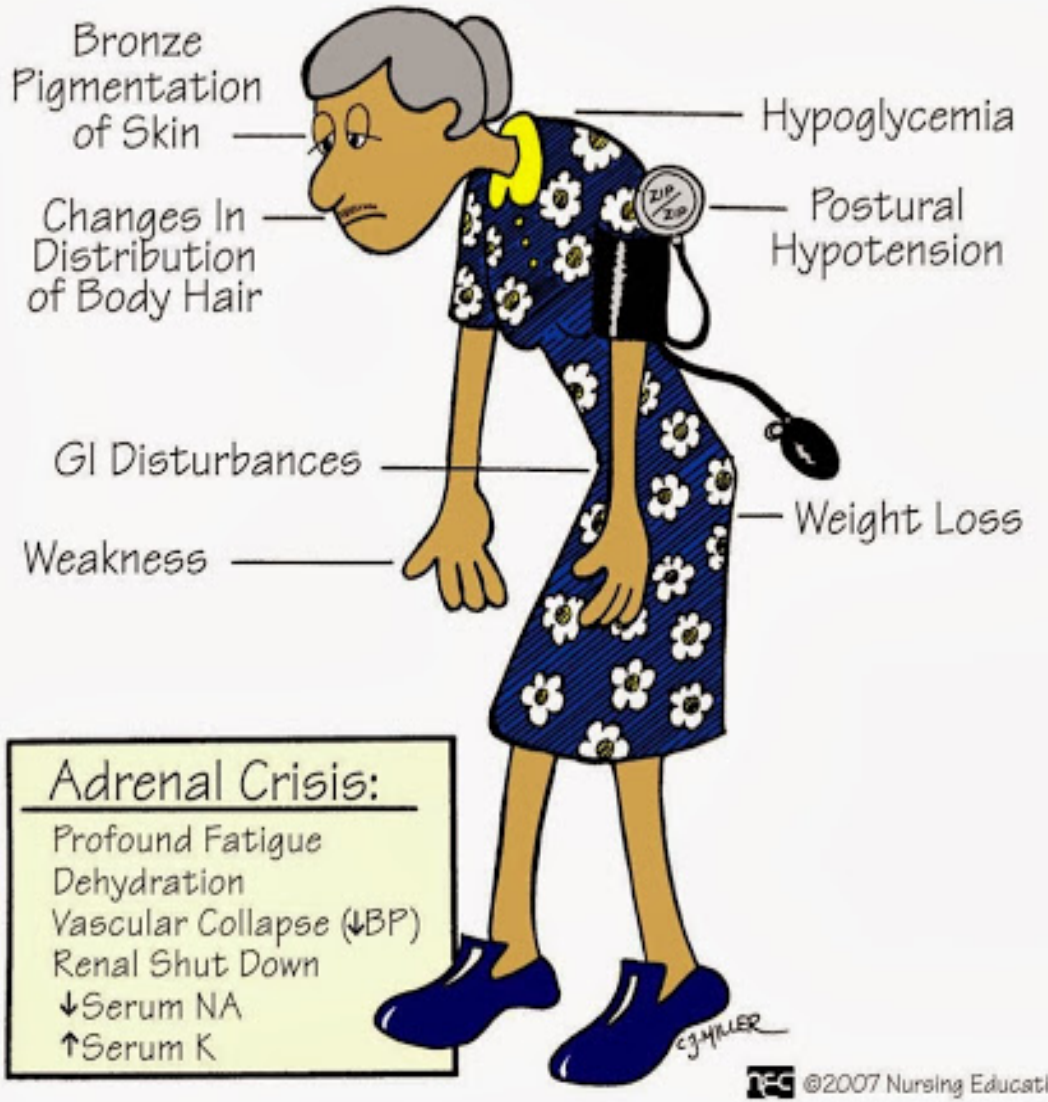
Secondary

- ↓ ACTH from pituitary
- ↓ hypothalamus stimulation

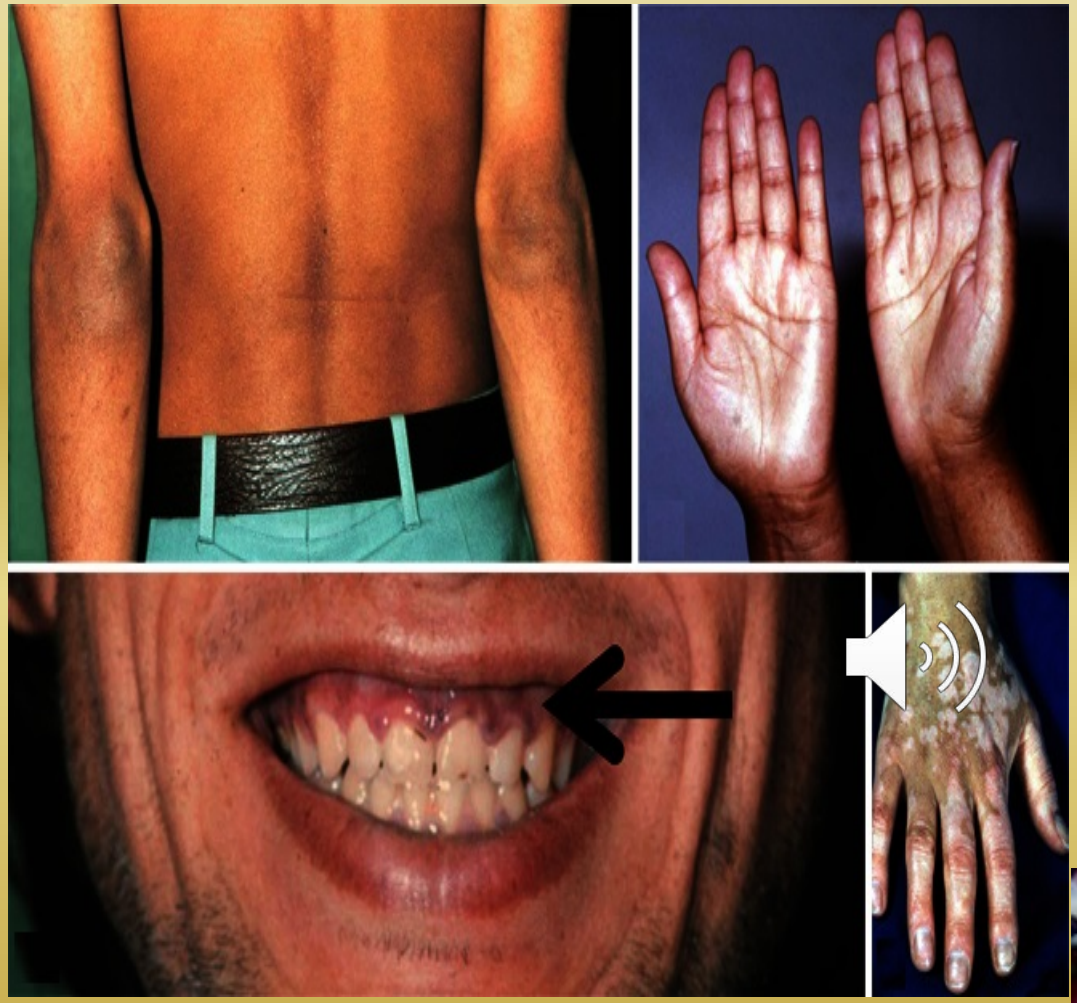
Addison's Disease: Signs & Symptoms

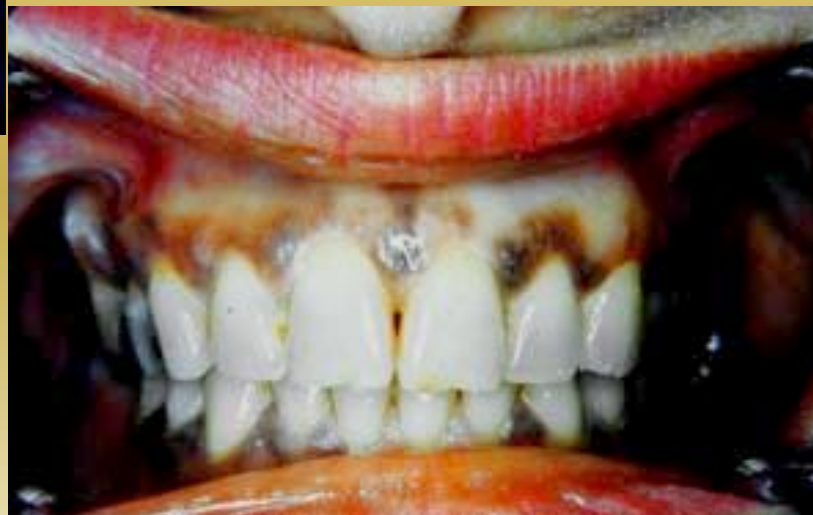
- Hypotension
  - Lack of aldosterone
  - Na+ & H2O loss
  - K+ reabsorption
- Tachycardia
- Bronze coloration of skin due to loss of cortisol feedback on the pituitary), to both ACTH and MSH
- Hypoglycemia
- Fatigue, muscle weakness
- Weight loss
- ↓ tolerance for stress
  - Anxious
  - Irritable
  - Confused
- Pulse
  - Weak
- GI upset
  - N/V
  - Anorexia

ADDISON'S DISEASE



Acute stresses (e.g., trauma or infection) can precipitate acute adrenal crisis, with rapid progression to death unless corticosteroid therapy is promptly initiated.





Addison disease oral pigmentation

Secondary adrenocortical insufficiency

Hypothalamic or pituitary disorder leading to diminished ACTH production (e.g., tumor, infection, infarction);
can be an isolated deficiency or associated with decreased levels of other pituitary hormones (panhypopituitarism).
It is distinguished from primary hypoadrenalism by:

- **Absence of hyperpigmentation**
- **Near-normal aldosterone levels since production is largely independent of ACTH; thus, hyponatremia and hyperkalemia are not features of secondary adrenocortical insufficiency.**

Thank You