Endocrine system
lecture 5 Adrenal gland

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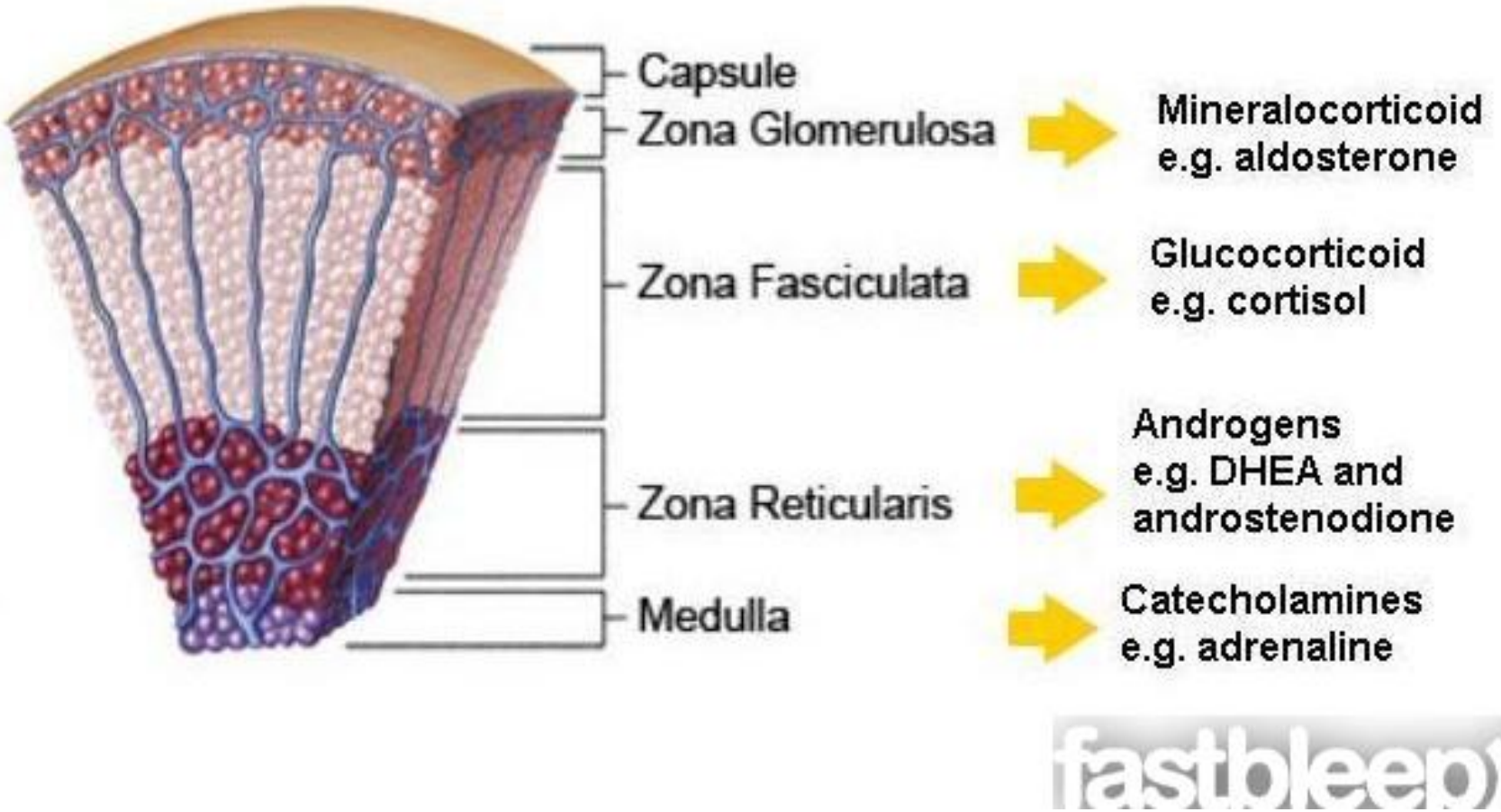
FRCPath

Adrenal gland

- الغُدَّةُ الكُظْرِيَّة
- **الغدة فوق الكلوية**

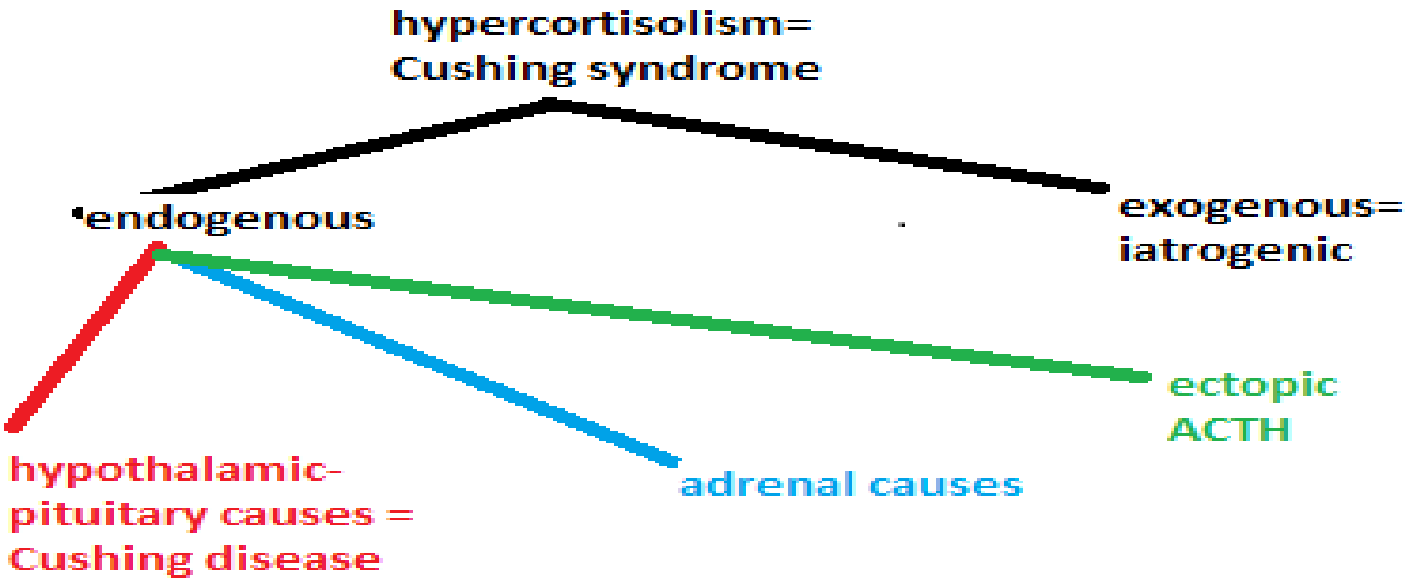
Adrenal gland



Adrenal cortex

- Hyperadrenalism :
  *Hypercortisolism,
  *hyperaldosteronism.
  * adrenogenital syndromes (will not be discussed here)
- Hypoadrenalism:
  *acute adrenal insufficiency
  *chronic adrenal insufficiency (Addison disease)
  *secondary adrenal insufficiency.
- Masses = Neoplasms
  * adenoma
  *carcinoma

hypercortisolism

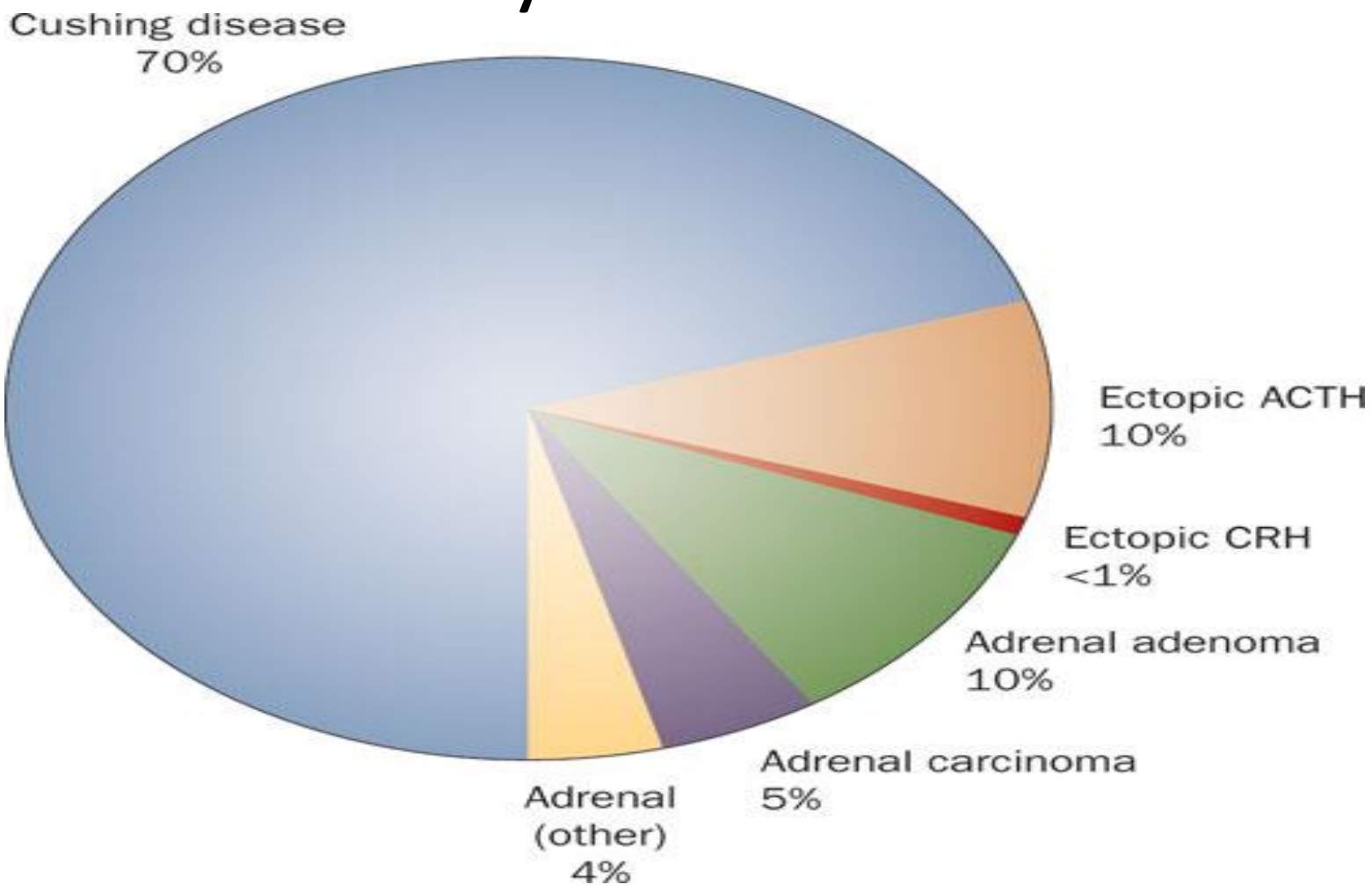


Hypercortisolism (Cushing Syndrome)

- Exogenous : if you treat patients with glucocorticoids (Iatrogenic) : this is the most common cause of Cushing syndrome.
- Endogenous causes

A. Hypothalamic-pituitary diseases causing hypersecretion of ACTH (Cushing disease)
B. Primary adrenal hyperplasia and neoplasms
C. Secretion of ectopic ACTH by nonpituitary tumors

Causes of endogenous Cushing syndrome



HYPOTHALAMIC- PITUITARY CAUSES CUSHING DISEASE

-70% of cases of spontaneous, endogenous Cushing syndrome are due to Cushing disease.

- Occurs most frequently during young adulthood (the 20s and 30s)
- mainly affecting women.

CUSHING DISEASE

-majority of cases are due to pituitary ACTH-producing *adenoma*

- In the remaining patients, the anterior pituitary contains areas of *corticotroph cell hyperplasia* which may be: primary or, less commonly, secondary to CRH producing tumor

MORPHOLOGY

The adrenal glands in Cushing disease show bilateral nodular cortical hyperplasia secondary to the elevated levels of ACTH ("ACTH-dependent" Cushing syndrome).

Because ACTH is high.. There is hyperplasia of the adrenals which is nodular.

However, bilateral diffuse hyperplasia can occur.

Nodular cortical hyperplasia

PRIMARY ADRENAL HYPERPLASIA AND NEOPLASMS

- 10% to 20% of cases of endogenous Cushing syndrome are due to primary diseases in the adrenal gland.
- *This is called ACTH-independent Cushing syndrome,* because of the low serum levels of ACTH
- It is caused by adrenal adenoma or carcinoma.
- Can also be caused by primary hyperplasia but this is very rare.

ECTOPIC ACTH BY NONPITUITARY TUMORS

- mostly caused by *small cell carcinoma of the lung*,
- The adrenal glands undergo bilateral hyperplasia due to elevated ACTH,

Changes in adrenal in cases of Cushing syndrome:

1) Cortical atrophy :If the syndrome results from exogenous glucocorticoids ,suppression of endogenous ACTH results in bilateral cortical atrophy**.**

- The zona glomerulosa is of normal thickness because it functions independently of ACTH

2) Diffuse and nodular hyperplasia: Is found in 60% to 70% of Cases of endogenous Cushing syndrome.

- Secondary hyperplasia is found in patients with ACTH- dependent Cushing syndrome (due to Cushing disease or ectopic production of ACTH)

Primary adrenocortical neoplasms

- Are more common in women in their 30s to 50s.

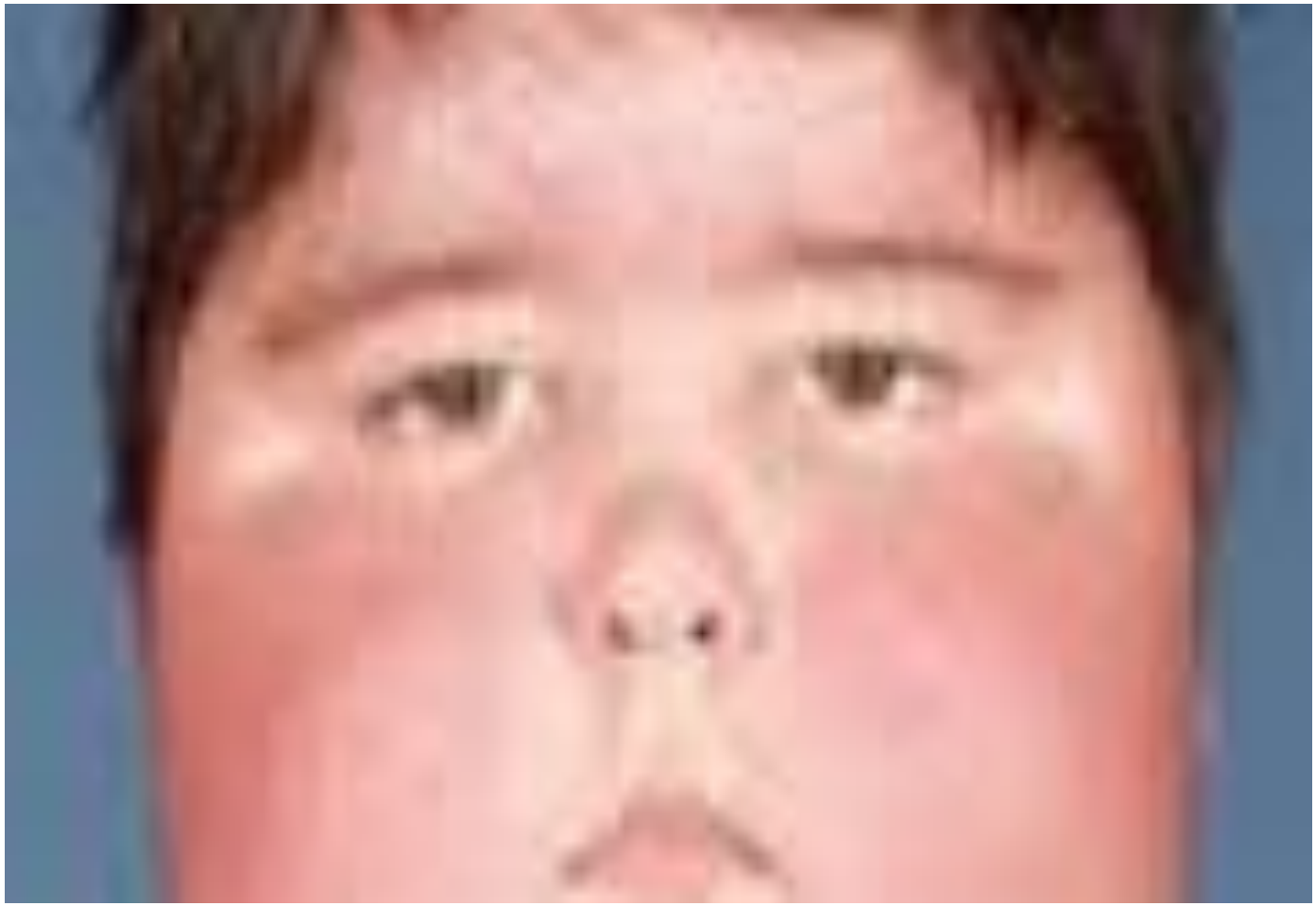
a. Adrenocortical adenomas: Are yellow tumors surrounded by thin capsules, and most weigh less than 30 g

b. Carcinomas tend to be nonencapsulated masses , exceeding 200 to 300 g in weight,

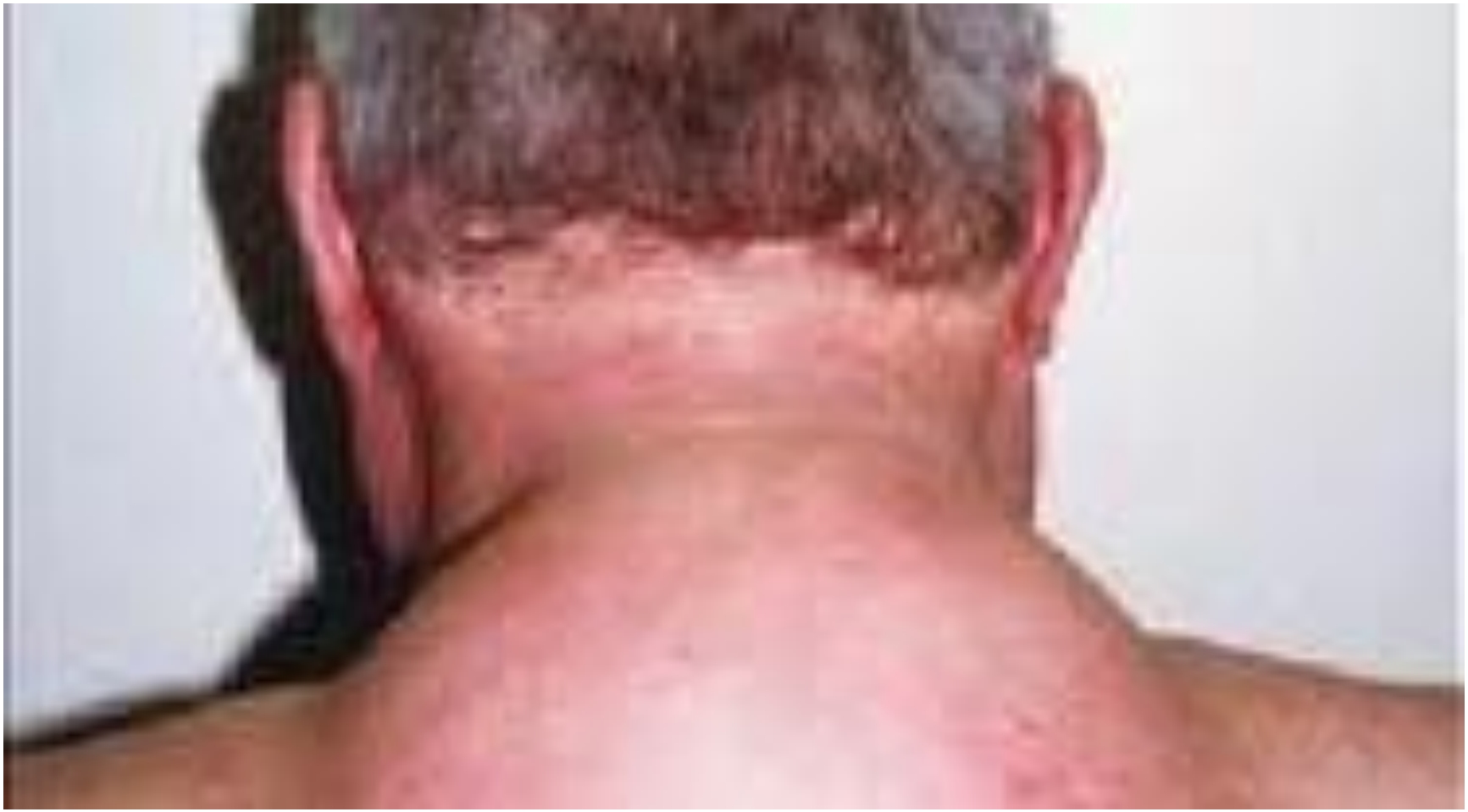
CLINICAL MANIFESTATIONS OF CUSHING SYNDROME

a. Hypertension and weight gain
b. truncal obesity, "moon facies,“ accumulation of fat in the posterior neck and back ("buffalo hump") .
c. Glucocorticoids induce gluconeogenesis with resultant *hyperglycemia, glucosuria,* and *polydipsia,*
d. The catabolic effects on proteins cause loss of collagen and resorption of bone and bone resorption results in *osteoporosis and* susceptibility to fractures.
e. The skin is thin, fragile, and easily bruised; cutaneous striae are particularly common in the abdominal area
f. Patients are at increased risk for a variety of infections.
g. Hirsutism and menstrual abnormalities
h. Mental disturbances ,mood swings, depression, psychosis

Moon face

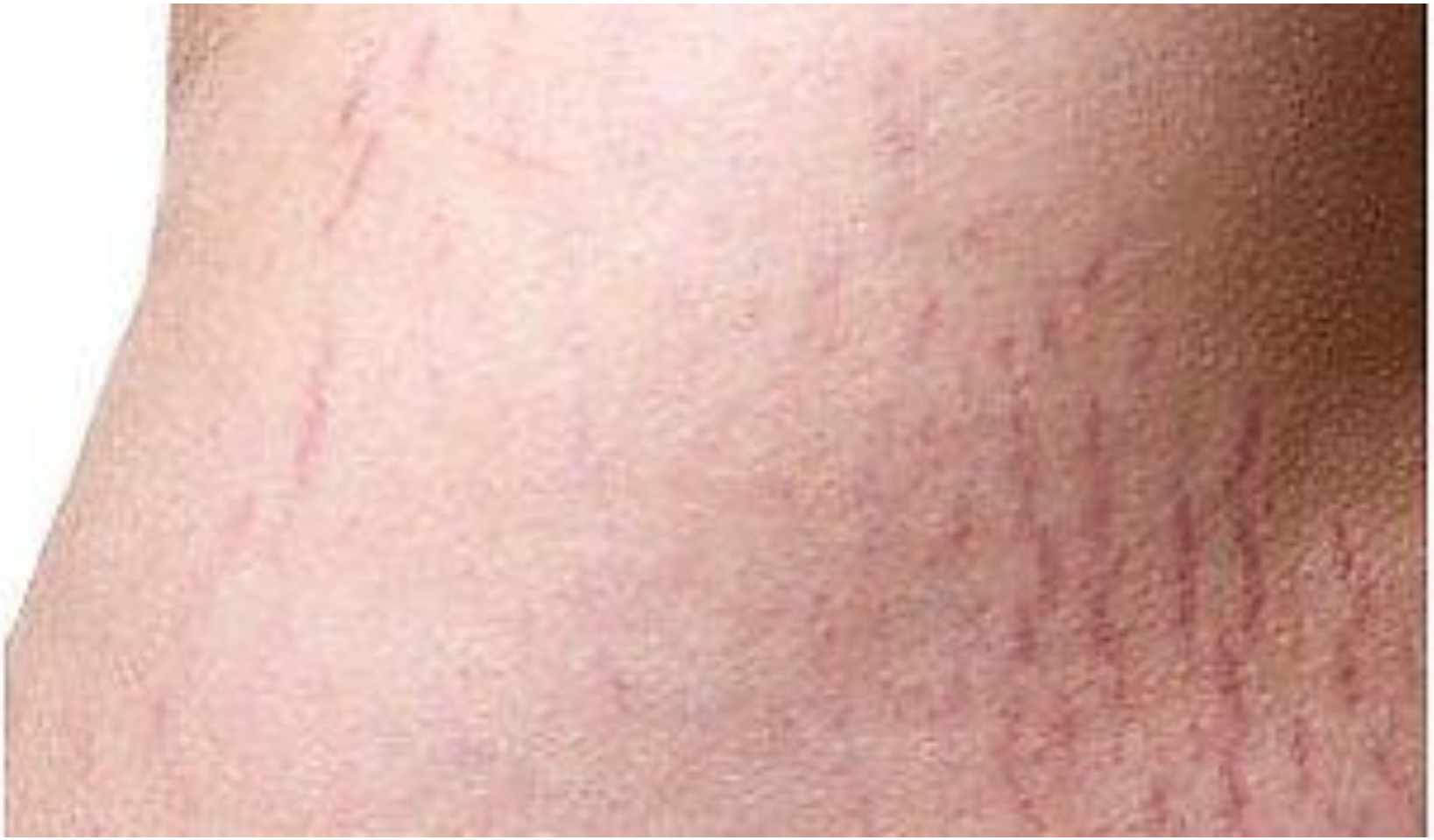


Buffalo hump



buffalo

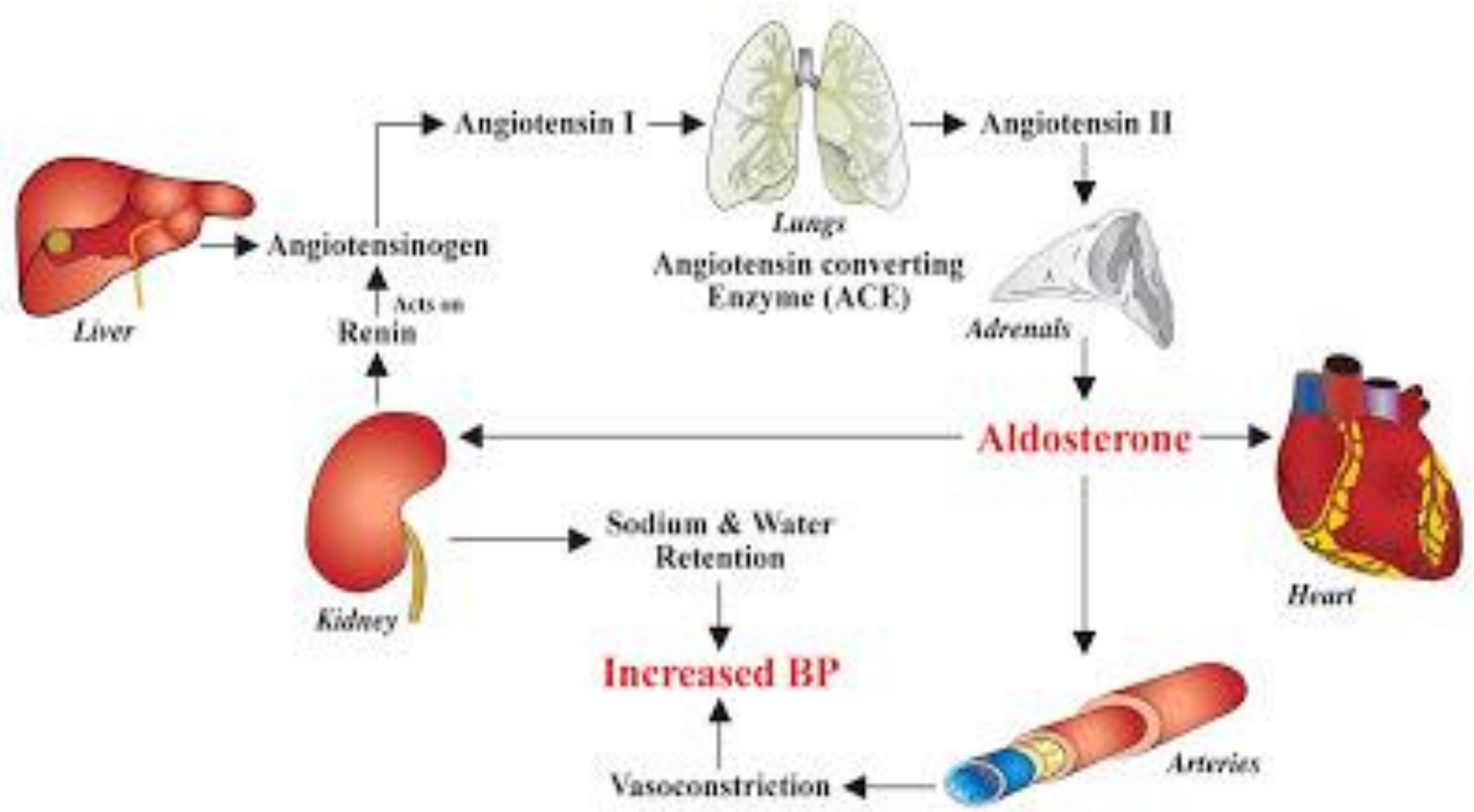
stria



aldosterone

- The **renin–angiotensin–aldosterone system** (**RAAS**) is a hormone system that is involved in the regulation of the plasma sodium concentration and arterial blood pressure.

RAAS


Angiotensin I
Angiotensin II
Lungs
Angiotensin converting Enzyme (ACE)
Liver
Angiotensinogen
Acts on
Renin
Adrenals
Aldosterone
Heart
Kidney
Sodium & Water Retention
Increased BP
Vasoconstriction
Arteries

HYPERALDOSTERONISM

Primary hyperaldosteronism:

- autonomous overproduction of aldosterone with secondary suppression of renin- angiotensin system and decreased plasma renin activity

Secondary hyperaldosteronism:

- Secondary to activation of renin-angiotensin system characterized by increased levels of plasma renin

CAUSES OF SECONDARY HYPERALDOSTERONISM

a. Decreased renal perfusion(renal artery stenosis)

b. Arterial hypovolemia and edema e.g heart failure

c. Pregnancy (caused by estrogen-induced increases in plasma renin substrate

PRIMARY HYPERALDOSTERONISM

a. Bilateral idiopathic hyperaldosteronism,

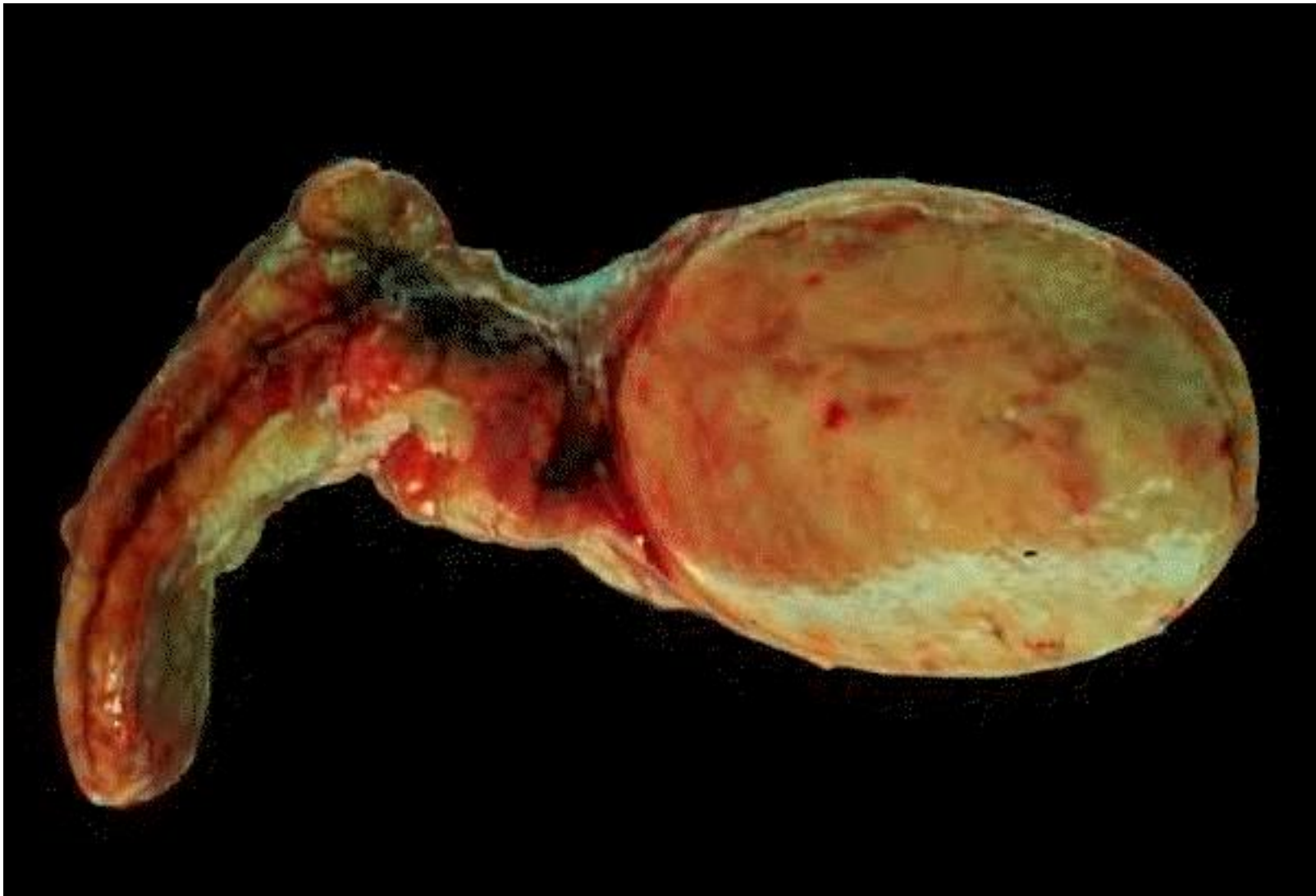
- bilateral nodular hyperplasia of adrenals
- the most common underlying cause (60% of cases)

b. Adrenocortical neoplasm, adenoma (the most common cause) or, rarely, an adrenocortical carcinoma.

- In approximately 35% of cases, the cause is a solitary aldosterone-secreting Aldosterone-producing adrenocortical adenoma referred to as *Conn syndrome*

c. Rarely, familial hyperaldosteronism may result from a genetic defect that leads to overactivity of the *aldosterone synthase* gene, *CYP11B2.*

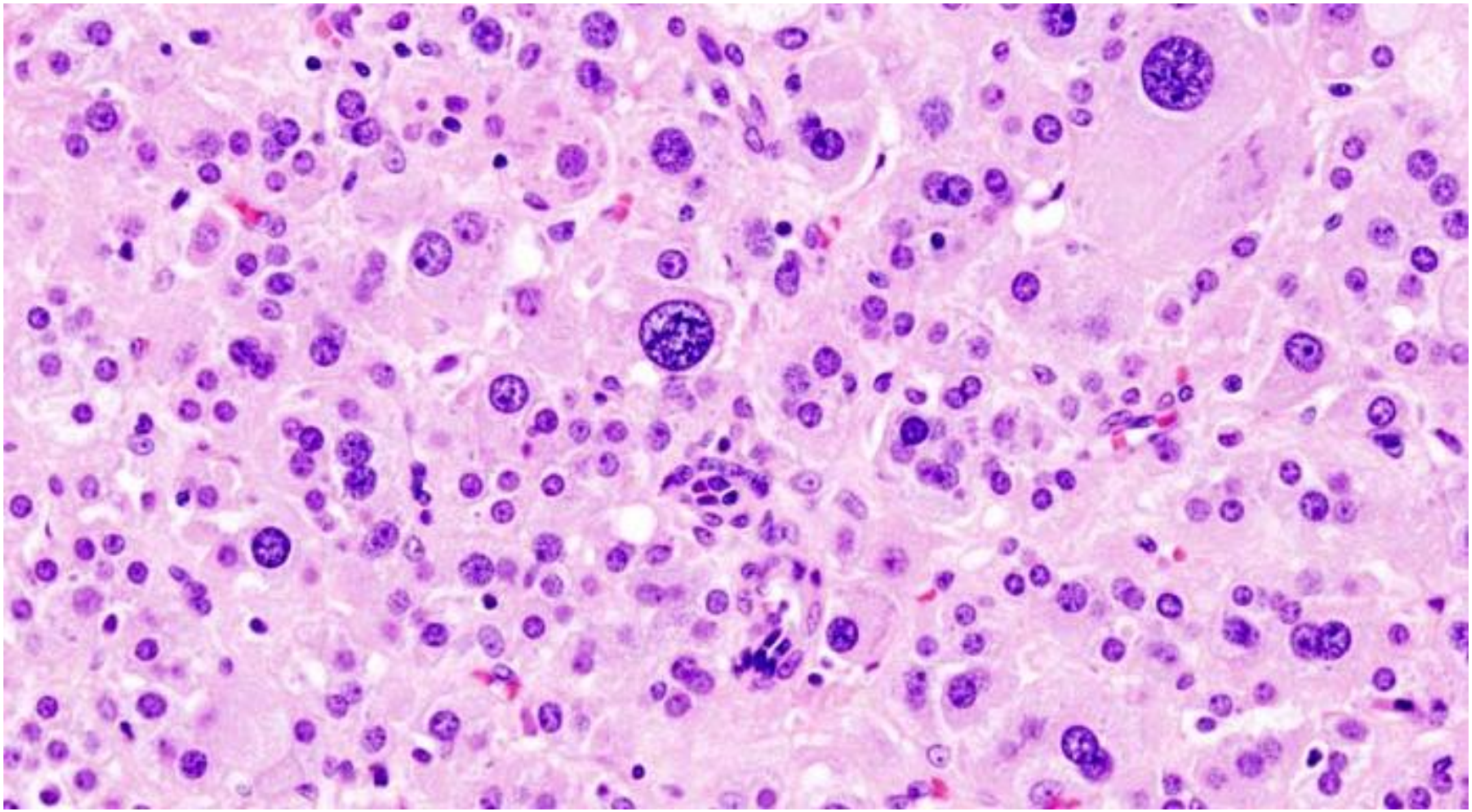
Adrenocortical adenoma



Features of adrenocortical adenoma

- Solitary
- Encapsulated
- Well circumscribed
- Histology: can show endocrine atypia
- May contain spironolactone bodies if treated with spironolactone… see next slides for details

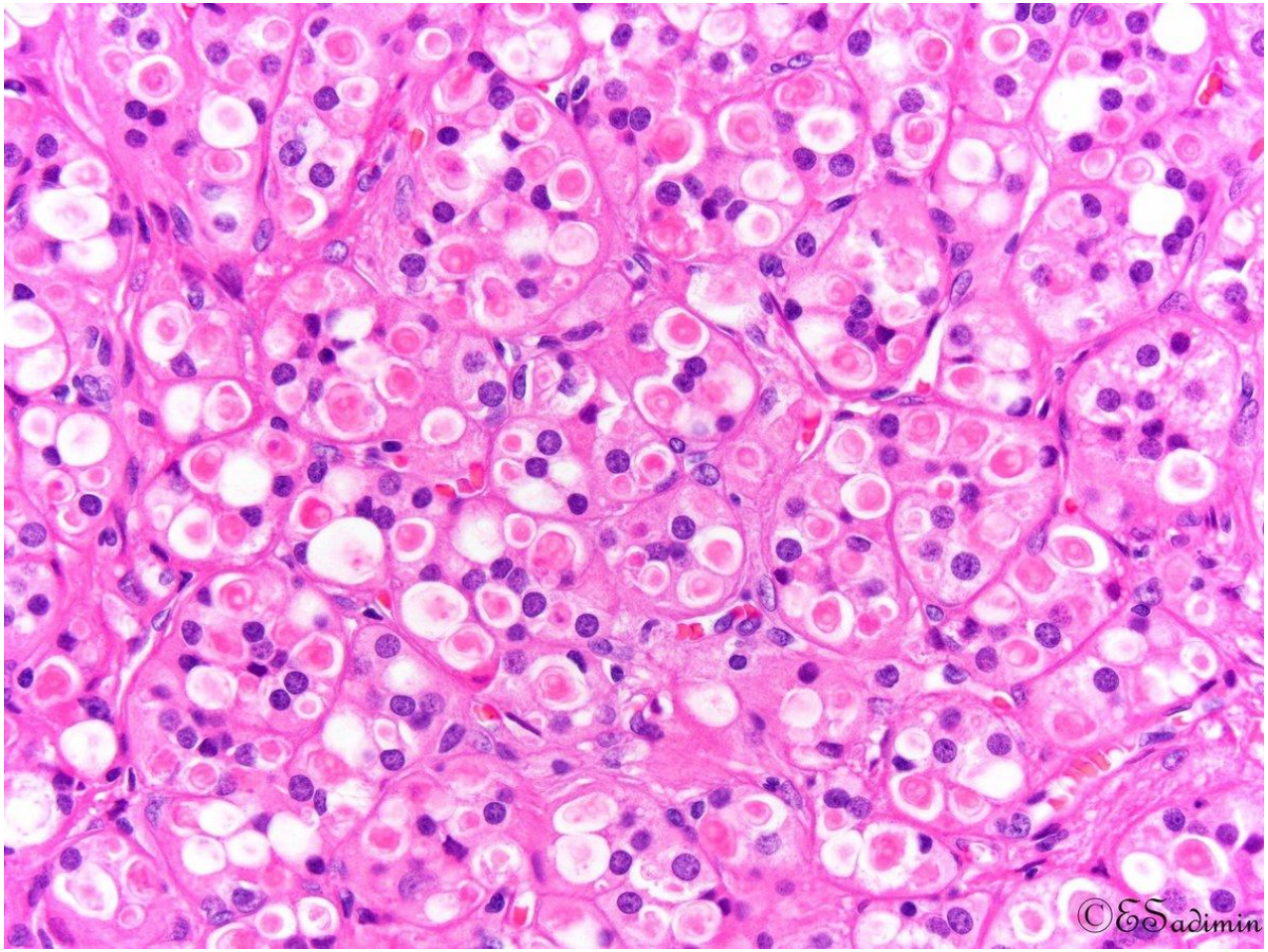
Adrenocortical adenoma/ note the endocrine atypia



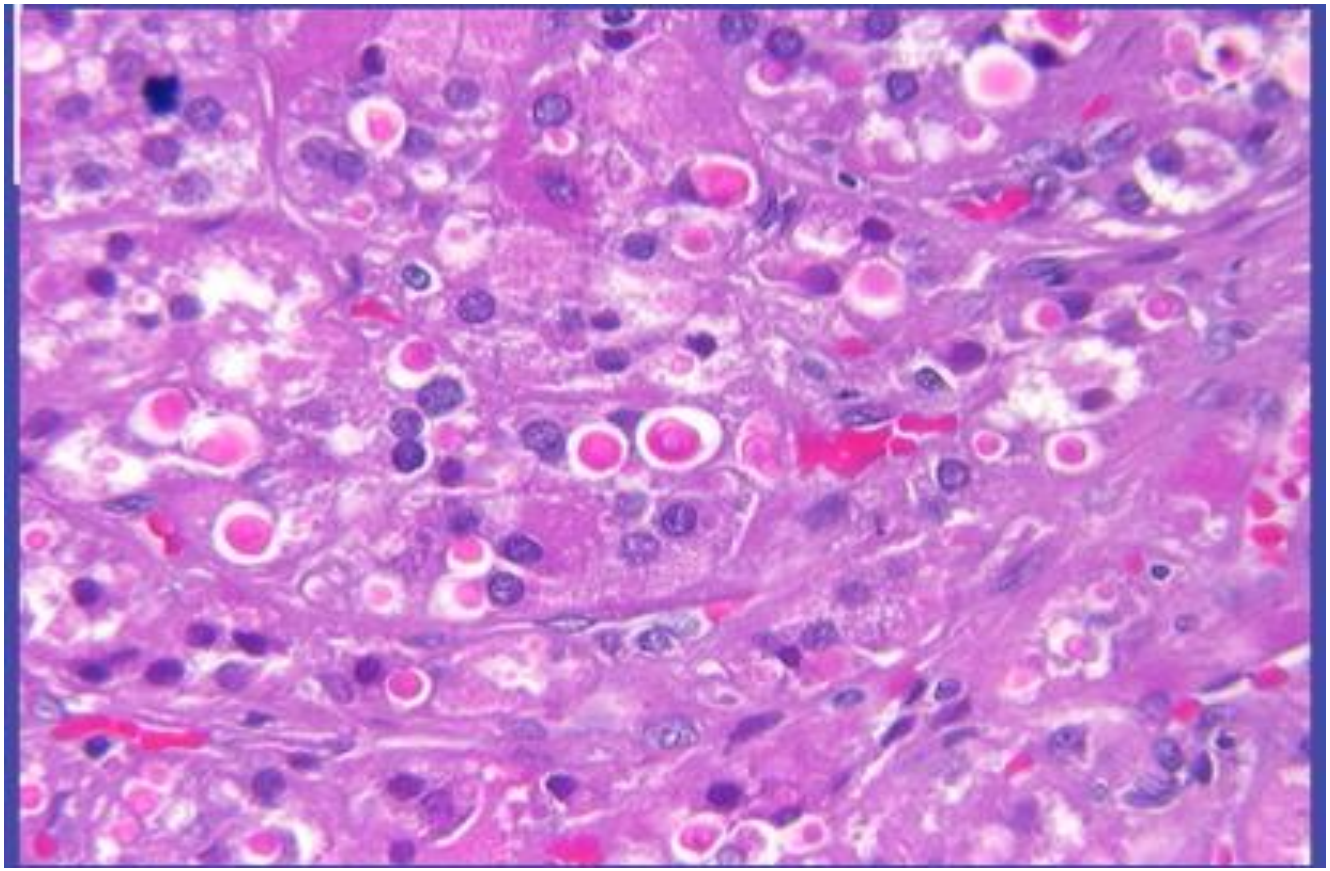
Spironolactone bodies

- Aldosterone producing adenomas contain eosinophilic, laminated cytoplasmic inclusions= spironolactone bodies which appear after treatment with spironolactone (an aldosterone antagonist)

Spironolactone bodies



Spironolactone bodies



CLINICAL FEATURES OF HYPERALDOSTERONISM

The clinical hallmark is hypertension

- Hyperaldosteronism may be the most common cause of secondary hypertension
- *Hypokalemia*

Adrenal insufficiency

- = decreased hormonal production from the adrenal
- Divided into three types

1. Acute insufficiency
2. Chronic insufficiency= Addison disease
3. Secondary insufficiency

Acute Adrenocortical Insufficiency :

Occurs in the following situations:

a. Crisis in patients with chronic adrenocortical insufficiency precipitated by stress

b. In patients maintained on exogenous corticosteroids .. Sudden withdrawal, or stress

c. Massive adrenal hemorrhage

.

Massive adrenal hemorrhage

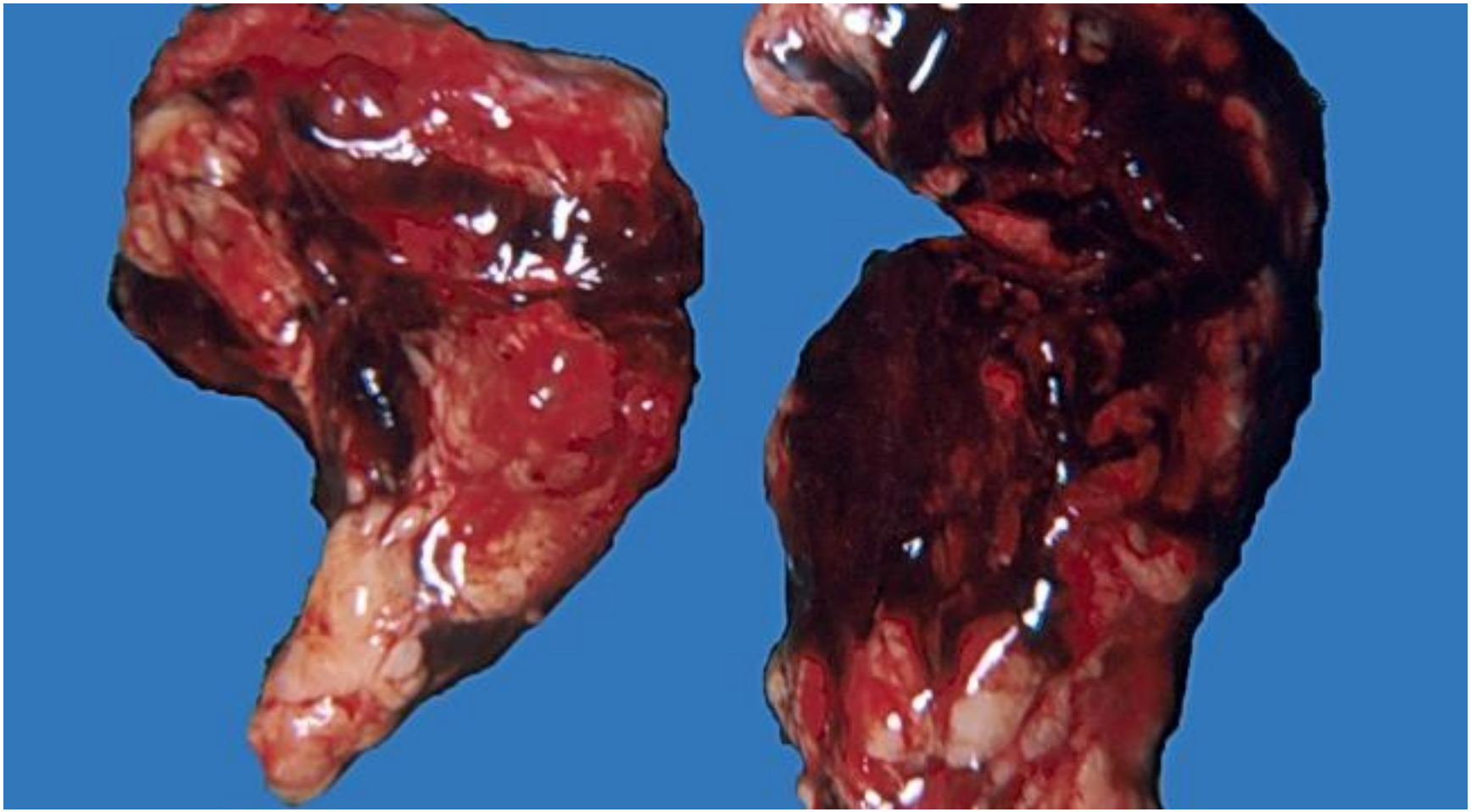
may destroy enough of the adrenal cortex to cause acute adrenocortical insufficiency.

- This condition may occur :

1. In patients maintained on anticoagulant therapy
2. Patients suffering from sepsis : a condition known as the Waterhouse-Friderichsen syndrome

- Sepsis due to: *Neisseria meningitidis* ,*Pseudomonas* spp., , and *Haemophilus influenzae*
- *Underlying cause???* unclear but probably involves endotoxin-induced vascular injury .

Massive adrenal hemorrhage



primary chronic adrenocortical insufficiency **(Addison disease)**:

-uncommon disorder resulting from **progressive destruction** of the adrenal cortex.

Causes:

- Autoimmune adrenalitis.
- Infections
- Metastatic tumors

ADDISON DISEASE

1. Autoimmune adrenalitis

- 60% to 70% of Addison disease cases and is the most common cause of primary adrenal insufficiency in developed countries.
- There is autoimmune destruction of steroid-producing cells, and autoantibodies to several key steroidogenic enzymes have been detected in affected patients

Addison disease

2. Infections,: Tuberculosis and Fungal infections

- Tuberculous adrenalitis, which once accounted for as many as 90% of cases of Addison disease, has become less common with the advent of anti-tuberculosis therapy
- Disseminated infections caused by *Histoplasma capsulatum* and *Coccidioides immitis* also may result in chronic adrenocortical insufficiency.
- Patients with AIDS are at risk for the development of adrenal insufficiency from several infectious (cytomegalovirus and TB) and noninfectious (Kaposi sarcoma) .

ADDISON DISEASE

3- Metastatic neoplasms involving the adrenals:

Carcinomas of the lung and breast are the most common primary sources.

Secondary adrenocortical insufficiency

Hypothalamic- pituitary diseases including:

- Metastasis
- Infection.
- Infarction
- Irradiation

- Can be part of pan hypopituitarism.

Clinical features of adrenal insufficiency

- Clinical manifestations of adrenocortical insufficiency do not appear until at least 90% of the adrenal cortex has been compromised.

a. progressive weakness and easy fatigability .

b. Gastrointestinal disturbances are common and include anorexia, nausea, vomiting, weight loss, and diarrhea

c. In patients with **primary adrenal disease**, increased levels of ACTH precursor hormone stimulate melanocytes, with resultant ***hyperpigmentation*** of the skin and mucosal surfaces: The face, axillae, nipples, areolae, and perineum are mainly affected

Note: hyperpigmentation is not seen in patients with secondary adrenocortical insufficiency.

d. Decreased aldosterone in primary hypoadrenalism results in potassium retention and sodium loss , with consequent - *hyperkalemia, hyponatremia, volume depletion,* and *hypotension*,

- In secondary hypoadrenalism is characterized by deficient cortisol and androgen output but normal or near-normal aldosterone synthesis. This is because ACTH doesn't affects the production of aldosterone.

Adrenal medulla

- Chromaffin cells… derived from the neural crest.
- Secrete catecholamines.
- Most important disease: neoplasms.

TUMORS OF THE ADRENAL MEDULLA

Pheochromocytoma

- give rise to a surgically correctable form of hypertension.
- Pheochromocytomas usually subscribe to "rule of 10s":

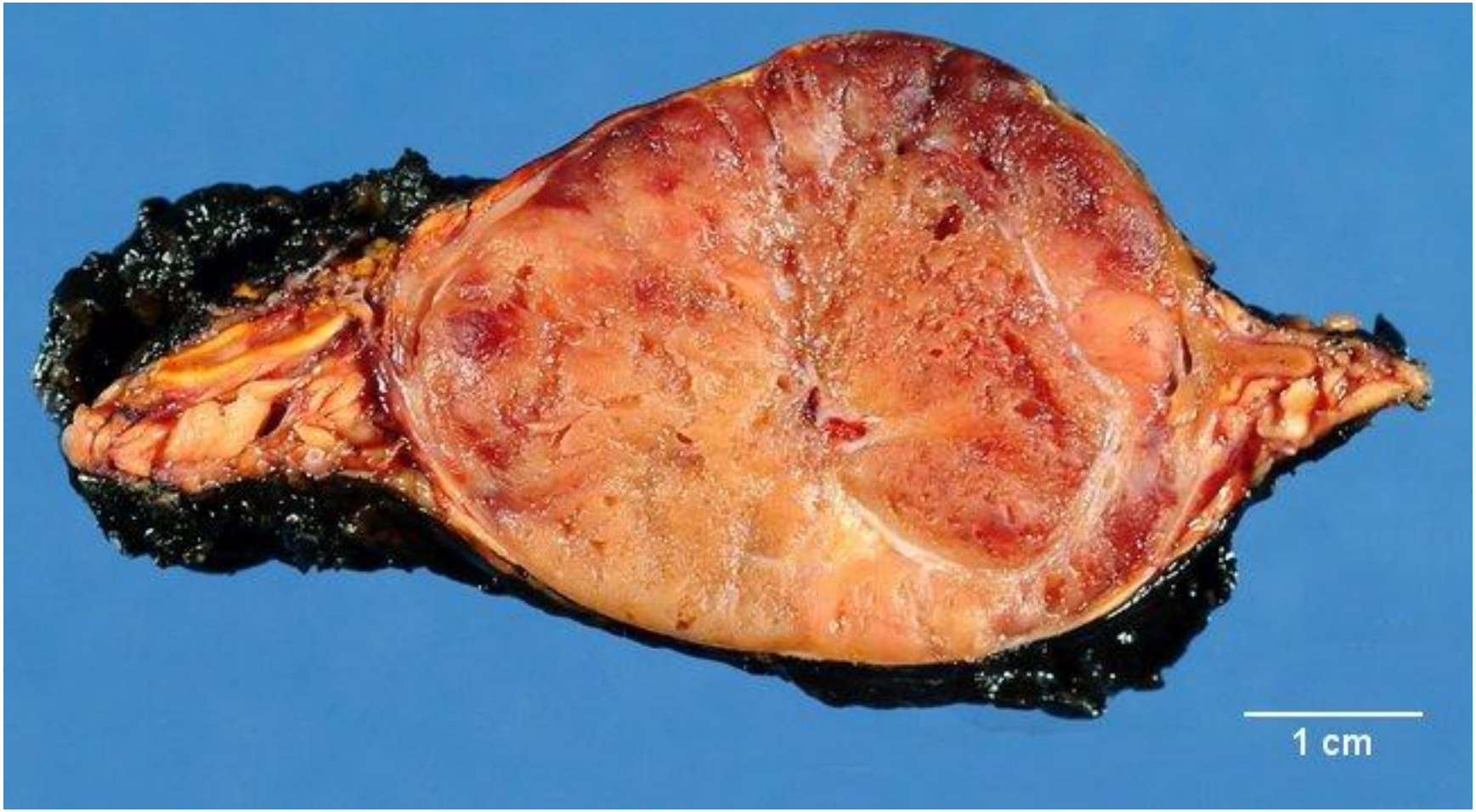
a. *10% of pheochromocytomas are extraadrenal,* called *paragangliomas,*

b. *10% of adrenal pheochromocytomas are bilateral*; this proportion may rise to 50% in cases that are associated with familial syndromes.

c. *10% of adrenal pheochromocytomas are malignant,*

d. 10% familial.. Now we think up to 25% might be familial.

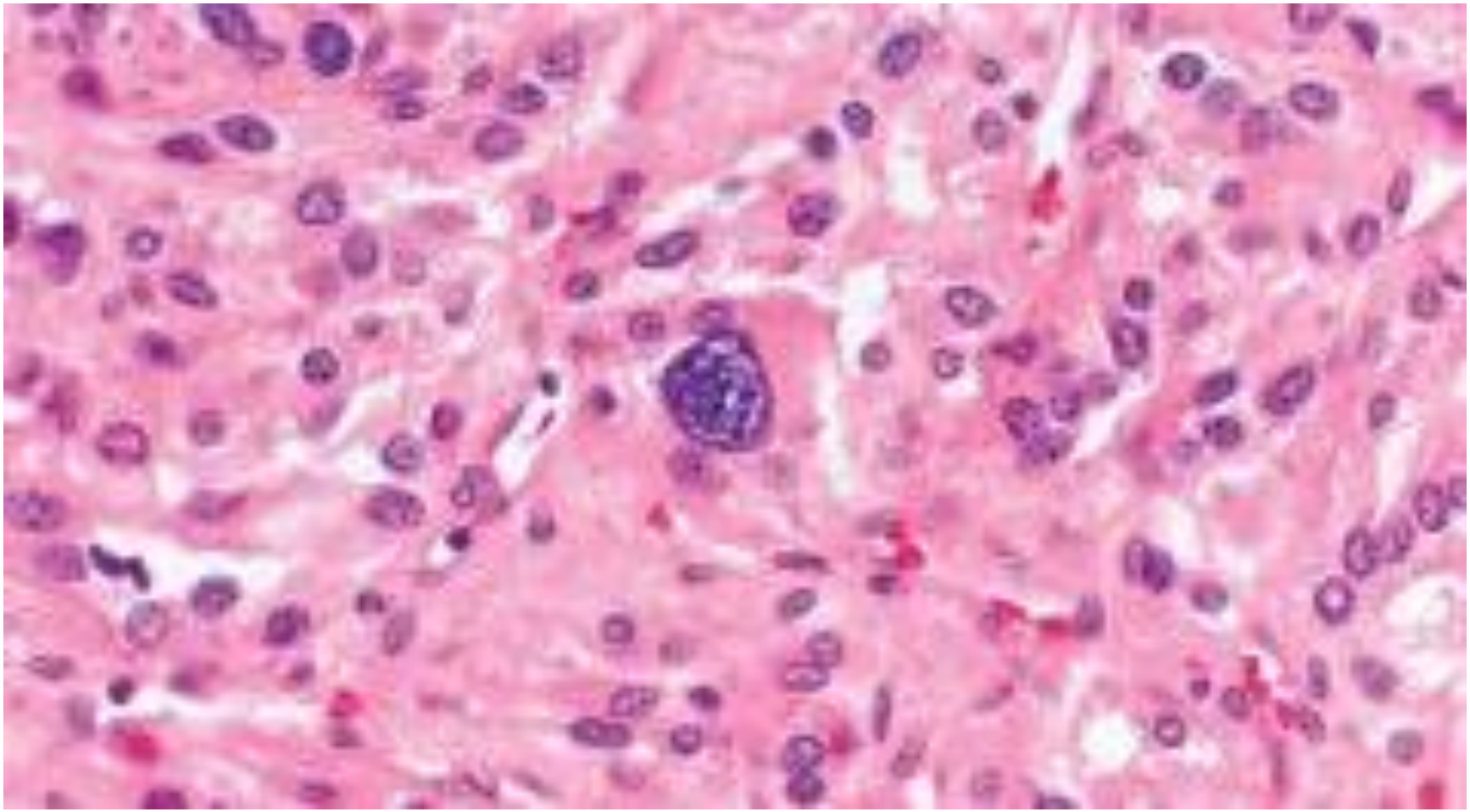
pheochromocytoma



On microscopic examination

- Are composed of polygonal to spindle-shaped chromaffin cells and their supporting cells, compartmentalized into small nests, or **Zellballen,** by a rich vascular network
- The cytoplasm has a finely granular appearance, because of the presence of granules containing catecholamines.
- The nuclei of the neoplastic cells are often pleomorphic

pheochromocytoma



Pheochromocytoma..

- The definitive diagnosis of malignancy in pheochromocytomas is based exclusively on the presence of metastases.

Clinical Features

- The predominant clinical manifestation is *hypertension*

- Sudden cardiac death may occur, probably secondary to catecholamine-induced myocardial irritability and ventricular arrhythmias.