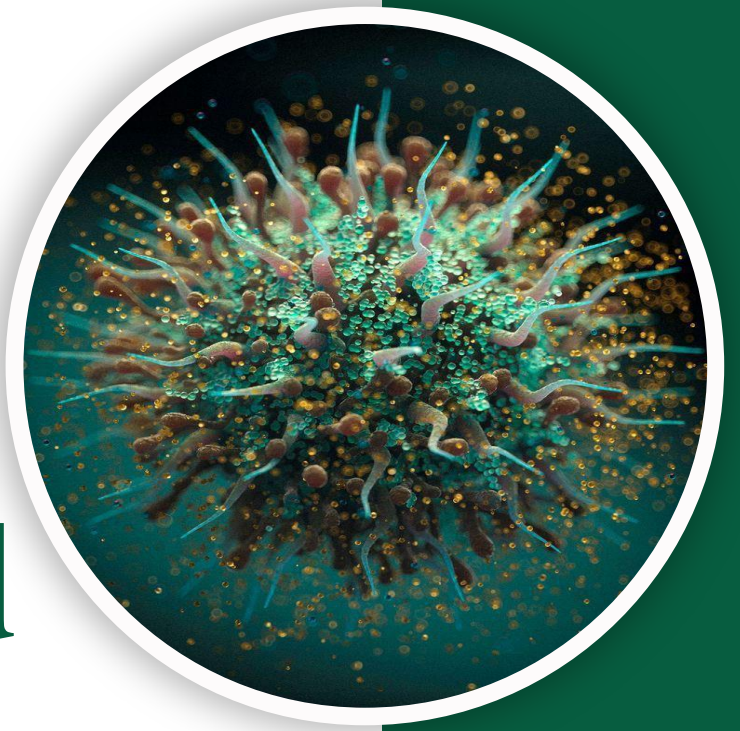
بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Endocrine Pathology | FINAL 2

Diseases of The Adrenal Gland



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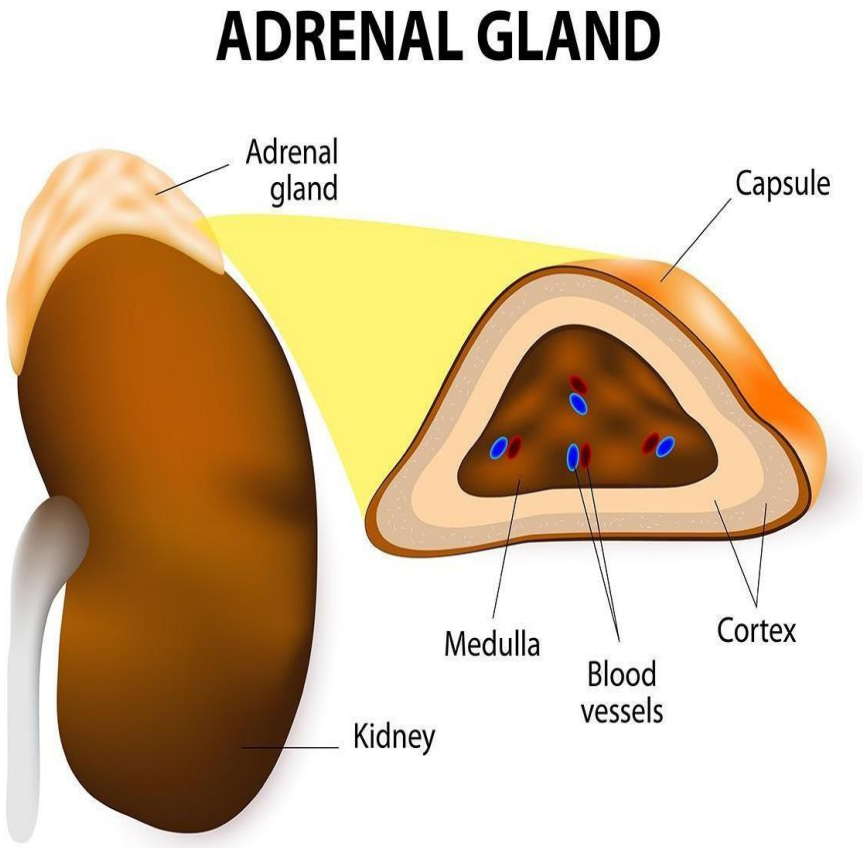
Endocrine system
Adrenal gland

Heyam Awad

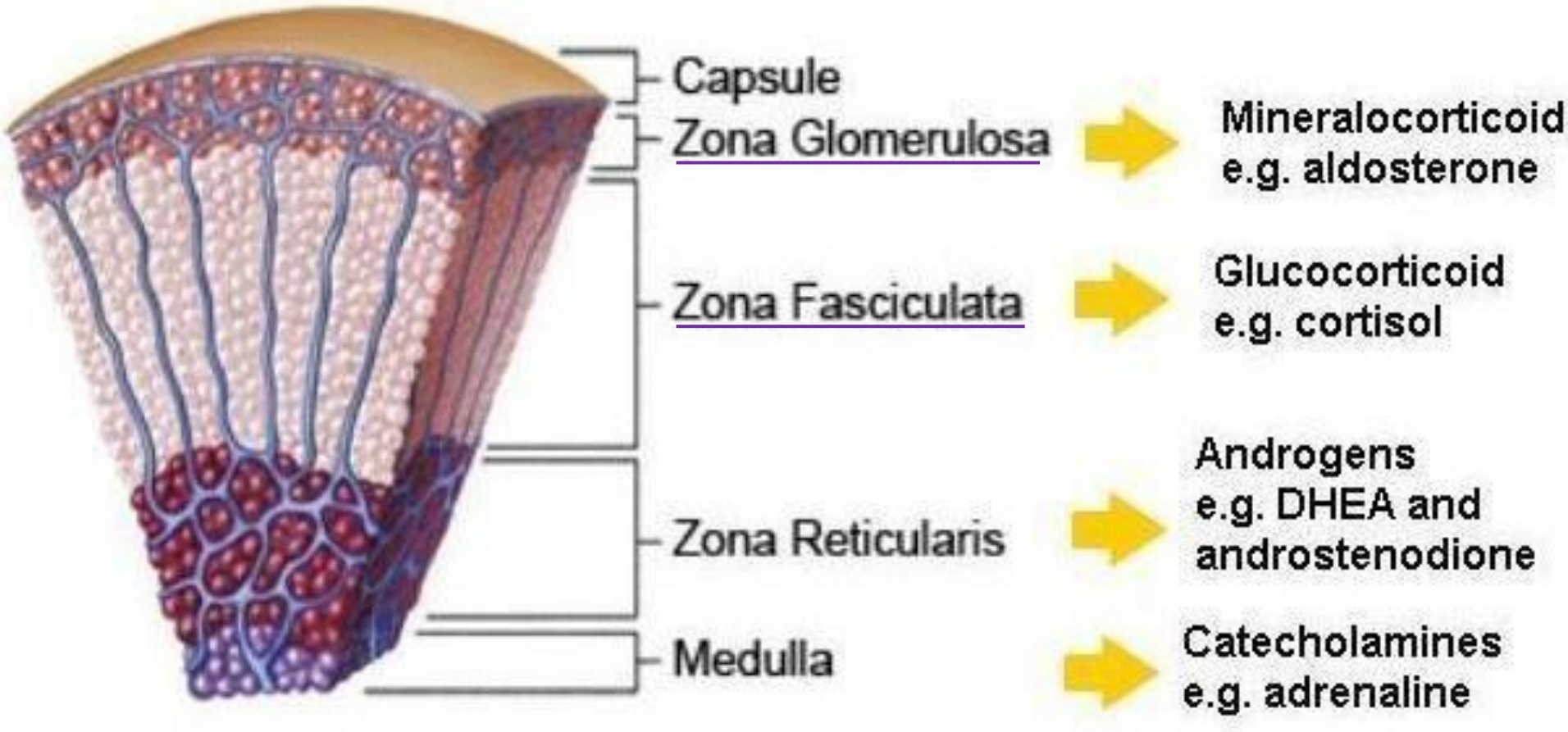
MD, FRCPath

Adrenal gland

الغدة
الكظرية



Adrenal gland



We will focus on zona glomerulosa and zona fasciculata in this system.
Zona reticularis is to be covered in the urogenital system (UGS).

- **Zona fasciculata + Zona reticularis** are regulated by the pituitary gland through **ACTH**.
- Zona **glomerulosa** is **not regulated by the pituitary gland** and has no significant relationship with pituitary ACTH. It's regulation is mainly through the **RAAS**.

➢ THEREFORE: causes of hypoaldosteronism/hyperaldosteronism can be different from causes of hypercortisolism/hypercortisolism.

Sometimes the same condition can affect both, but they don't necessarily occur together because their regulatory mechanisms are different.

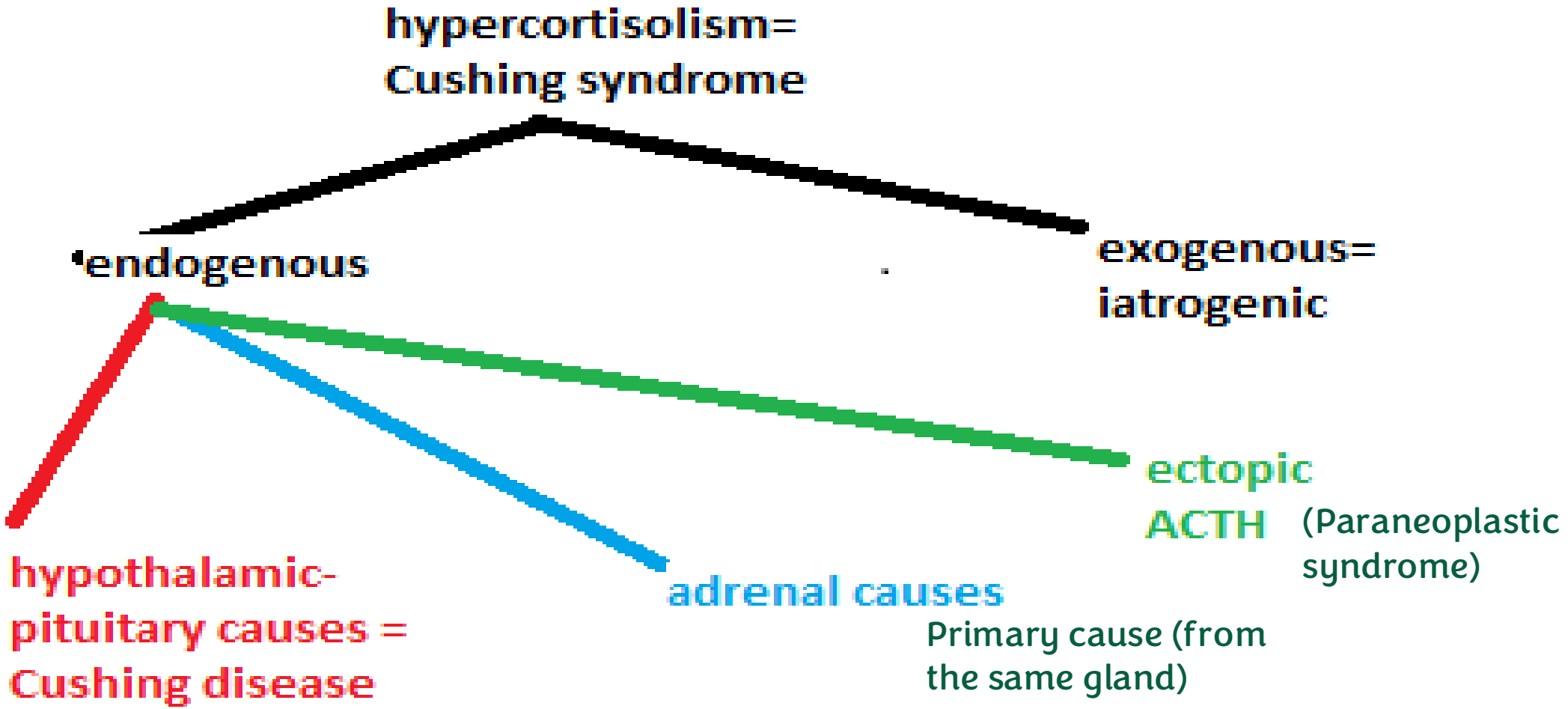
- If the problem is **secondary** and originates from the **pituitary grand**, the effect is mainly on **cortisol and adrenal androgens**(Zona fasciculata + Zona reticularis), while aldosterone secretion may remain normal.
- If the problem is in the RAAS, aldosterone secretion is affected, while cortisol secretion is not directly affected.

Adrenal cortex: same old story: mass effect and hormonal abnormalities.

- Hyperadrenalism:
  - Hypercortisolism
  - Hyperaldosteronism
  - Adrenogenital syndromes (will not be discussed)
- Hypoadrenalism:
  - Acute adrenal insufficiency
  - Chronic adrenal insufficiency (Addison disease)
  - Secondary adrenal insufficiency
- Masses = Neoplasms or hyperplasia
  - Adenoma
  - Carcinoma

In adrenal hyperfunction, two key hormones are involved – cortisol and aldosterone. Cortisol secretion is regulated via the hypothalamic-pituitary-adrenocortical axis, whereas aldosterone secretion is controlled by the renin-angiotensin-aldosterone system (RAAS). Due to these distinct regulatory pathways, hypercortisolism does not necessarily imply concurrent hyperaldosteronism, and vice versa.

Hypercortisolism



Cushing's syndrome refers to any condition causing excess cortisol levels, regardless of origin. Cushing's disease specifically denotes hypercortisolism secondary to a pituitary hyperfunction (mostly adenoma), in which elevated ACTH drives increased cortisol secretion.

Hypercortisolism (Cushing Syndrome)

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

- Endogenous causes

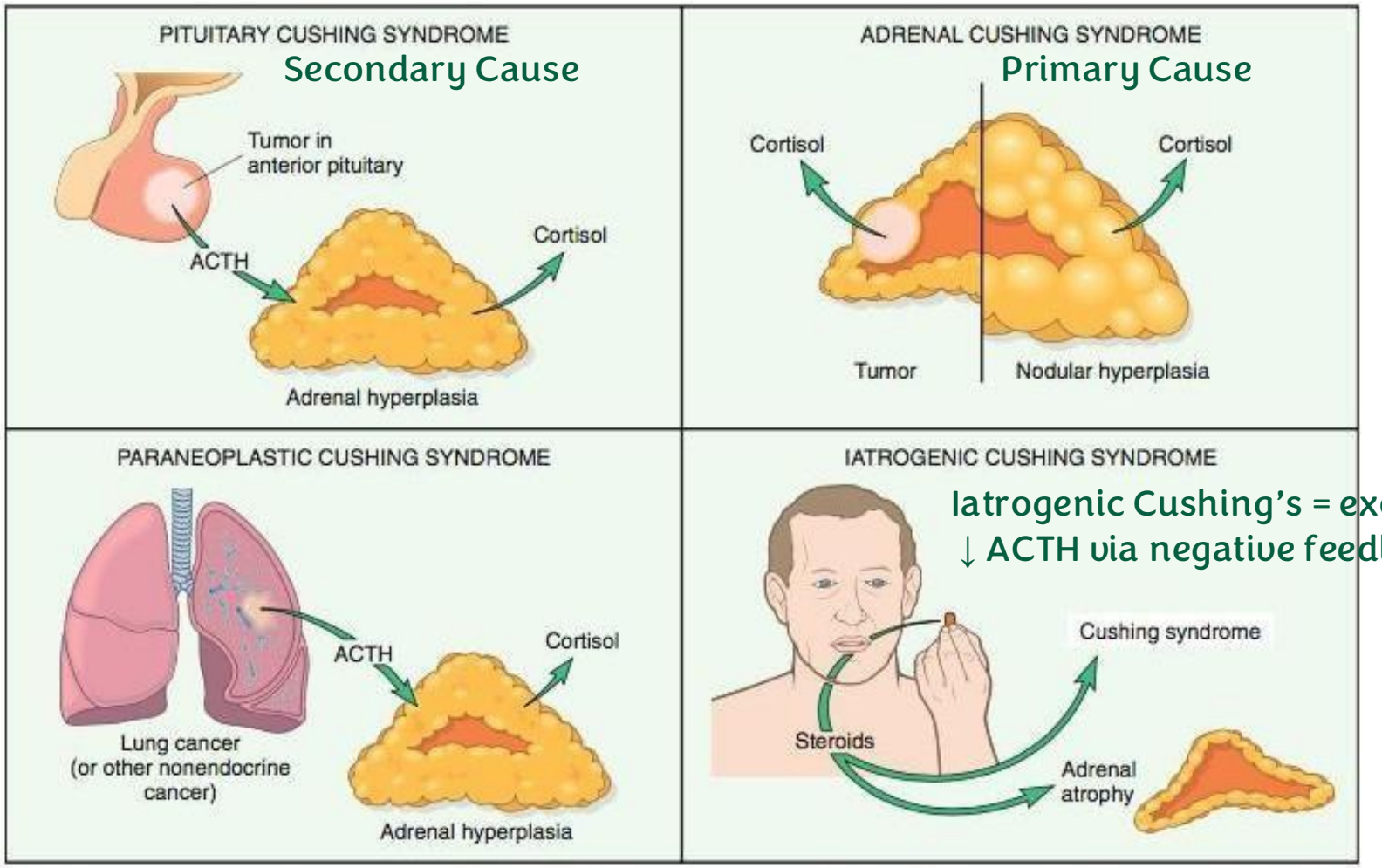
A. Hypothalamic-pituitary diseases causing hypersecretion of ACTH (Cushing disease), causing secondary adrenal hypertrophy and hyperplasia.

B. Primary adrenal hyperplasia and neoplasms

C. Secretion of ectopic ACTH by nonpituitary tumors; most common example is SCC of the lung.

SCC = small-cell carcinoma

Cushing syndrome

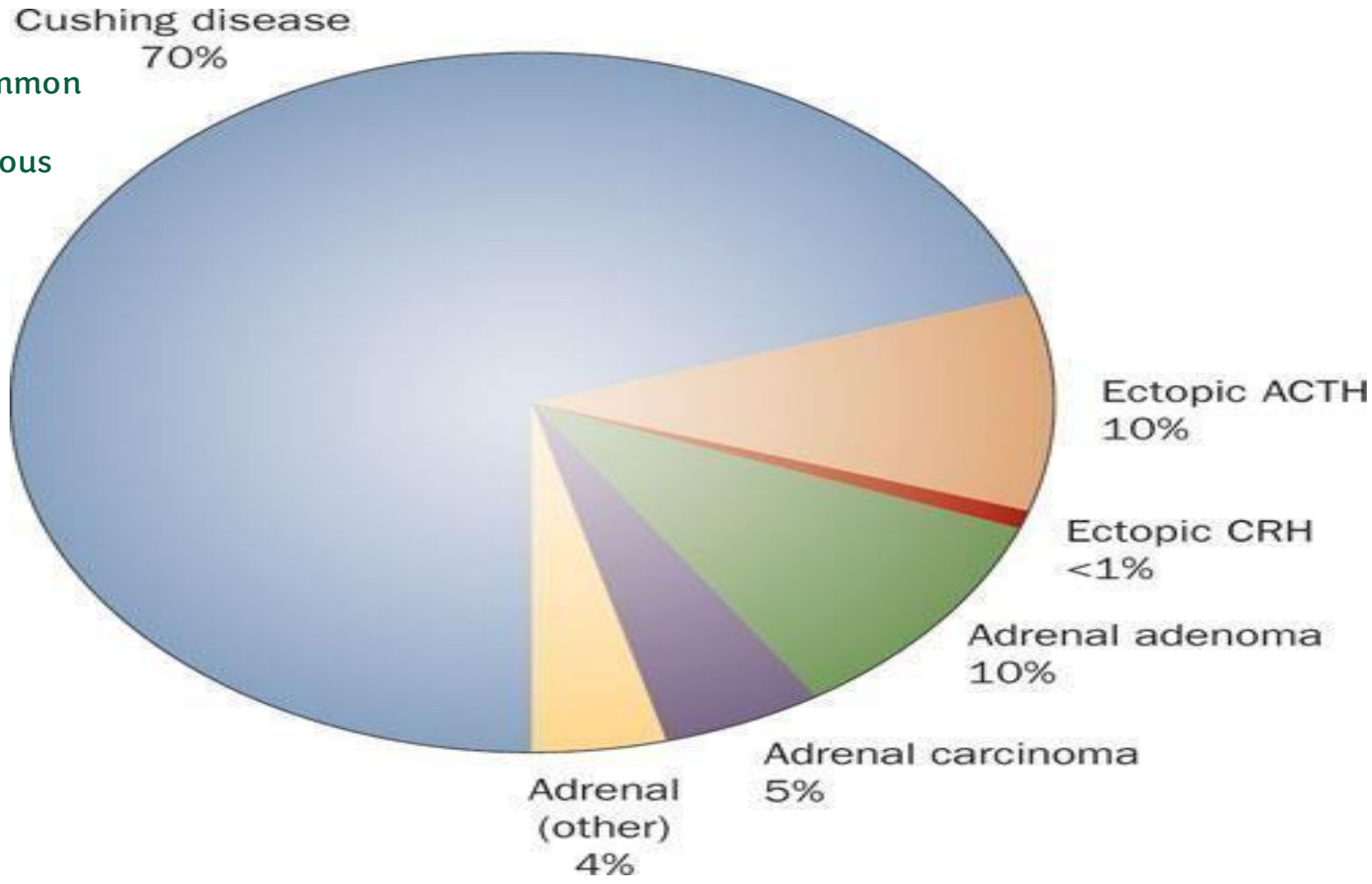


Iatrogenic Cushing's = exogenous cortisol → ↓ ACTH via negative feedback → adrenal atrophy.

ig. 20.34 Schematic representation of the various forms of Cushing syndrome: The three endogenous forms, as well as the more common exogenous atrogenic) form. *ACTH*, Adrenocorticotropic hormone.

Causes of endogenous Cushing syndrome

Most common from the endogenous



Iatrogenic Cushing: effect on the adrenals

- We give patients glucocorticoids(steroids) because of their unti-inflammatory effects.
- However, prolonged **exogenous** glucocorticoid therapy can cause iatrogenic Cushing syndrome, the **most common overall cause of the cushing syndrome.**

- In patients in whom the syndrome results from exogenous glucocorticoids, suppression of endogenous ACTH results in bilateral cortical atrophy, the mechanism is negative feedback from the exogenous glucocorticoids –> ↓ ACTH secretion , due to a lack of stimulation of the zona fasciculata and zona reticularis by ACTH.

The atrophy particularly affects the ACTH-dependent zones.

- ✓ When we give exogenous glucocorticoids (steroids) in high doses, specially for a long period, the increased cortisol level causes negative feedback on the pituitary.
- ✓ The pituitary senses that there is sufficient cortisol –> ↓ ACTH secretion.
- ✓ ↓ ACTH –> ↓ stimulation of the adrenal cortex –> adrenal cortical trophy.

This is specially important with large doses for a long period of time.

IMPORTANT CLINICAL POINT : ***stopping steroids:***

- ➢ **Exogenous steroids should not be stopped suddenly** after prolonged high dose therapy.
- ➢ Steroids should be tapered gradually (the dose is decreased step-by-step).
- ➢ Gradual Tapering gives the pituitary time to resume ACTH secrection.
- ➢ Its also gives the adrenal cortex time to recover and resume normal cortisol production.
- ➢ Sudden withdrawal can therefore result in acute adrenal insufficiency.

HYPOTHALAMIC- PITUITARY CAUSES
CUSHING DISEASE

- 70% of cases of spontaneous, endogenous Cushing syndrome are due to Cushing disease.
- **When the cause of hypercortisolism is a pituitary disease with increased ACTH, it is specifically called Cushing disease.**
- Occurs most frequently during young adulthood (the 20s and 30s)
- mainly affecting women.

CUSHING DISEASE

Secondary Cushing syndrome occurs when the problem is in the pituitary gland, causing increased ACTH secretion.

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

(Pituitary adenoma → ↑ ACTH → stimulation of the adrenal cortex → adrenal hyperplasia + hypertrophy → ↑ cortisol production.

- 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

Rarely, pituitary carcinoma.

Diffuse hyperplasia

Diffuse hyperplasia is found in patients with ACTH- dependent Cushing syndrome. ↑ ACTH from the pituitary →continuous stimulation of both adrenal glands →bilateral diffuse cortical hyperplasia.
The adrenal glands may become enlarged and heavier.
This is a secondary adrenal response to increased ACTH, rather than a primary adrenal disease.

- Both glands are enlarged, either subtly or markedly, each weighing up to 30 g.
- The yellow color of diffusely hyperplastic glands derives from the presence of lipid-rich cells, which appear vacuolated under the microscope.

DIFFUSE CORTICAL HYPERPLASIA

- Hyperplasia+ hypertrophy of the adrenal cortex.
- It is called **diffuse** adrenal hyperplasia because the **whole adrenal cortex is affected.**
- There is no nodularity, the enlargement is diffuse.
- Both adrenal glands are affected.
- This is seen in ACTH dependent Cushing syndrome
    - Medulla isn't affected.

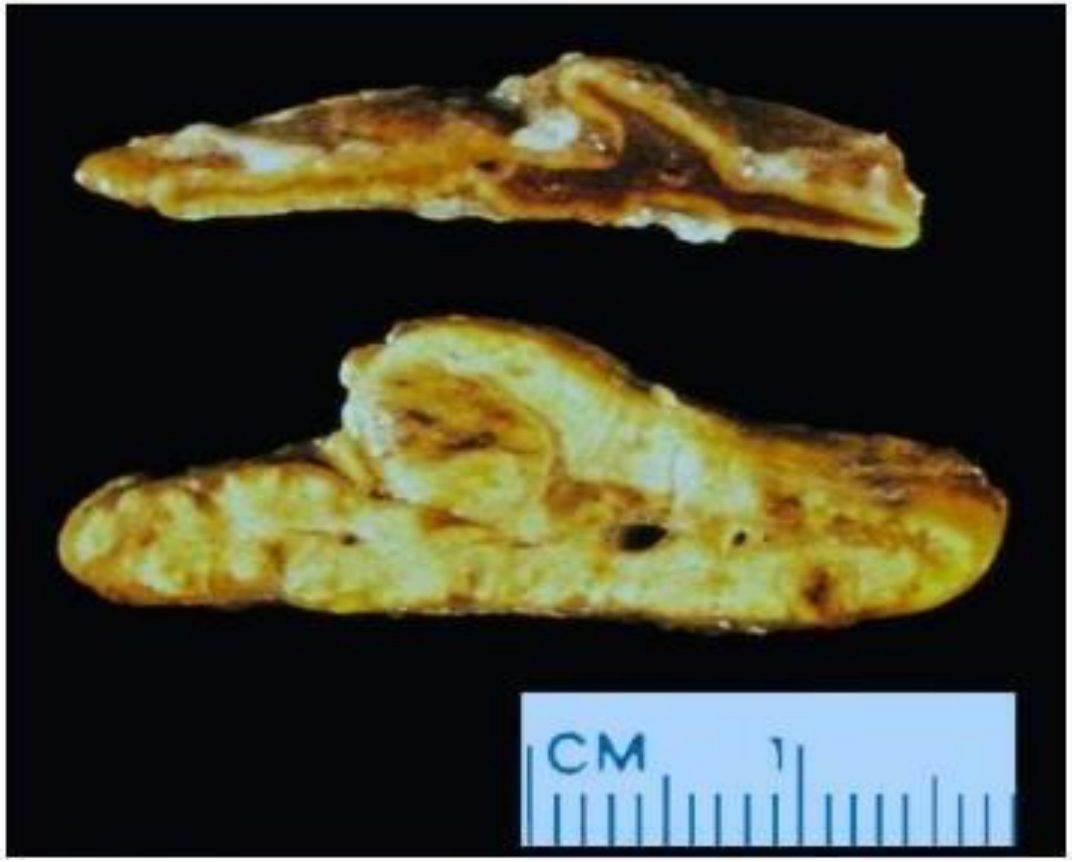


Fig. 20.35 Diffuse hyperplasia of the adrenal gland *(bottom)* contrasted with a normal adrenal gland *(top)*. In a cross-section, the adrenal cortex is yellow and thickened, and a subtle nodularity is evident. The abnormal gland was from a patient with ACTH-dependent Cushing syndrome, in whom both adrenal glands were diffusely hyperplastic. *ACTH*, Adrenocorticotropic

PRIMARY ADRENAL HYPERPLASIA AND NEOPLASMS

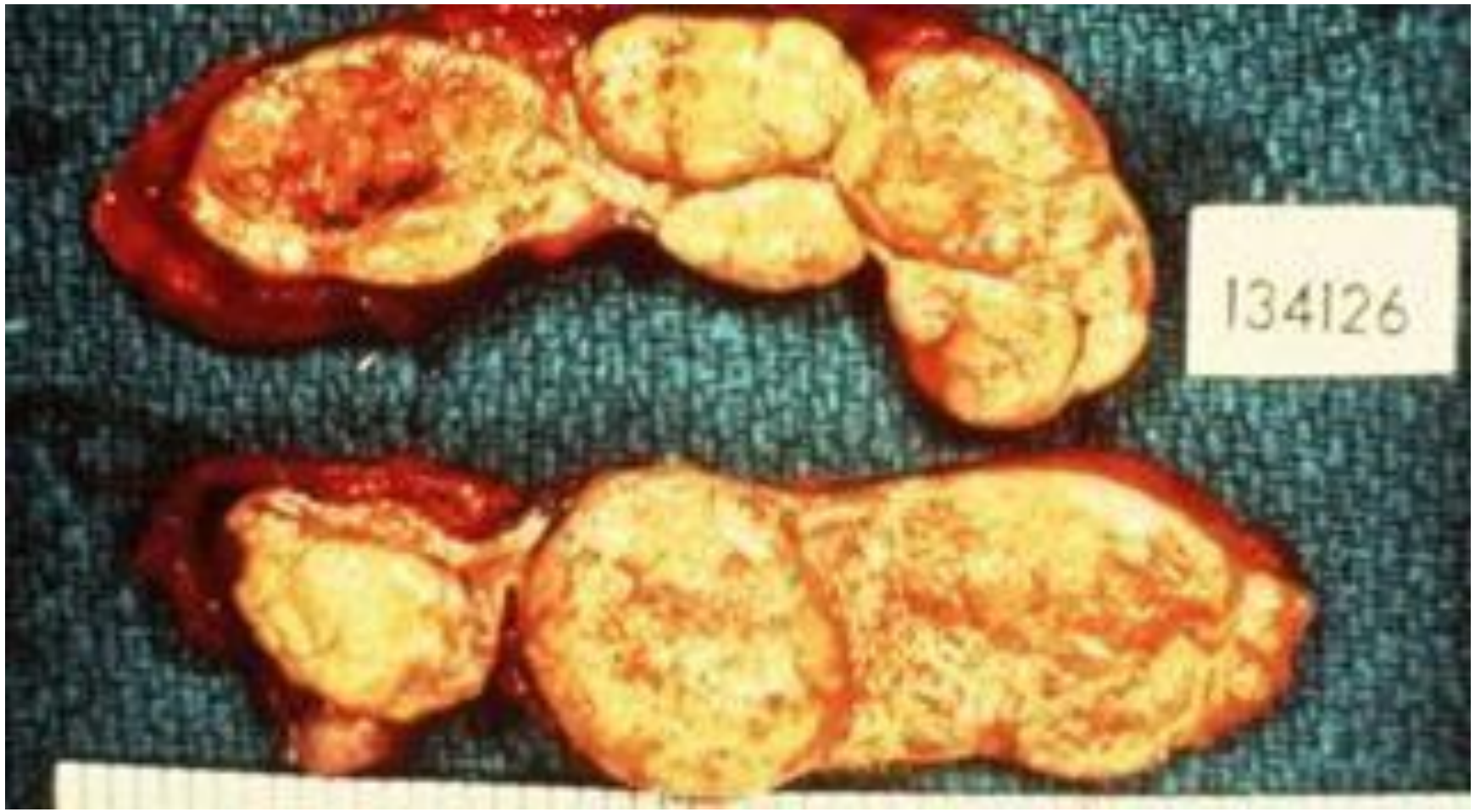
- 10% to 20% of cases of endogenous Cushing syndrome are due to primary diseases in the adrenal gland.
- *This is called ACTH-independent Cushing syndrome,* because of the low serum levels of ACTH
- It is caused by adrenal adenoma or carcinoma.
- Can also be caused by primary hyperplasia but this is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

Primary adrenal hyperplasia

- In primary cortical hyperplasia, the cortex is replaced almost entirely by macronodules or 1- to 3-mm micronodules.

In adrenal hyperfunction, the cause may be primary or secondary. **Primary** causes originate within the adrenal gland itself, most often as **nodular cortical hyperplasia**, which is usually **unilateral** but may occasionally be bilateral. Secondary causes arise from excessive pituitary ACTH secretion, as in Cushing's disease, leading to persistent stimulation of both adrenal glands. This results in **bilateral diffuse** cortical hyperplasia. Secondary hyperplasia occurs because both glands are driven to overproduce cortisol, whereas nodular cortical hyperplasia is typically limited to one gland, though bilateral involvement is possible

Nodular cortical hyperplasia



Primary Adrenocortical Neoplasms

- Are more common in women in their 30s to 50s.
- ✓ Adrenocortical adenomas: Are yellow tumors surrounded by thin capsules, and most weigh less than 30 g
- ✓ Carcinomas tend to be nonencapsulated masses , exceeding 200 to 300 g in weight

Size is an indicate indication of whether the tumour is more likely to be benign or malignant.
However, size in only an indication, not definitive proof of malignancy.
Definitive evidence of malignancy is invasion or metastasis.

Adrenocortical Adenoma

How to differentiate between hyperplasia from adenoma?
Hyperplasia: there are several nodules. The whole adrenal gland is enlarged .Hyperplasia is a pathologic disease process; it is not neoplastic.
Adenoma: usually one single nodule. The remaining adrenal gland is relatively normal.

Normal adrenal gland

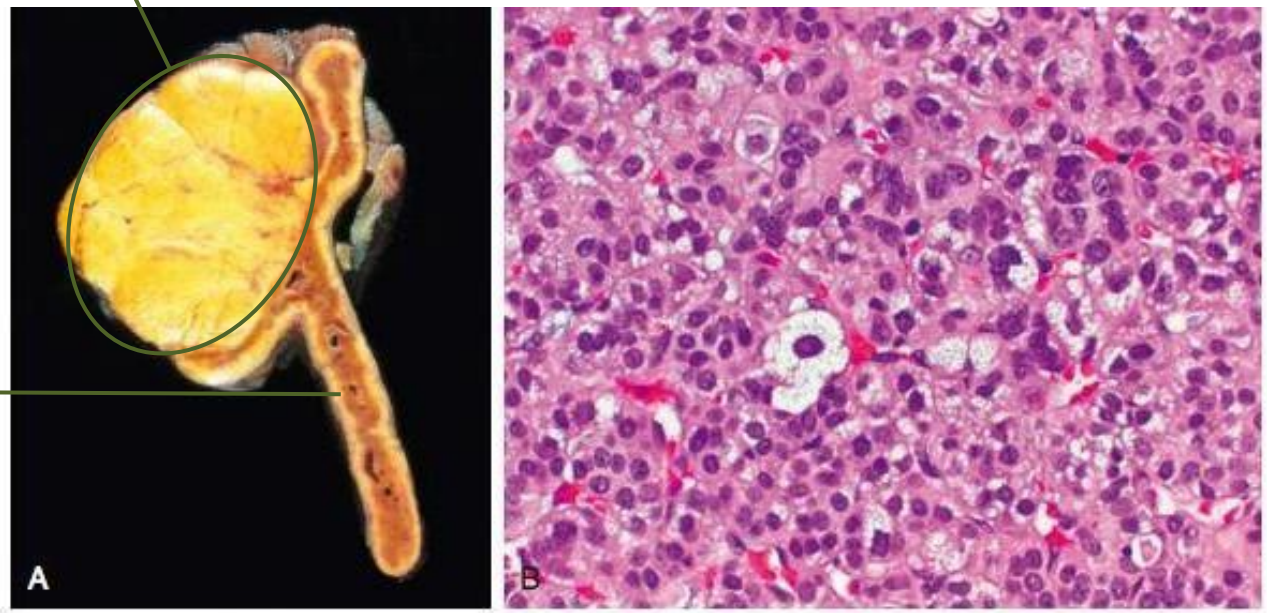


Fig. 20.37 Adrenocortical adenoma. (A) The adenoma is distinguished from nodular hyperplasia by its solitary, circumscribed nature. The functional status of an adrenocortical adenoma cannot be predicted from its gross or microscopic appearance. (B) Histologic features of an adrenal cortical adenoma. The neoplastic cells are vacuolated because of the presence of intracytoplasmic lipid. There is mild nuclear pleomorphism. Mitotic activity and necrosis are not seen.

An adrenal adenoma is well-circumscribed, soft lision. Under the microscope, the cells may have a monotonous appearance (cells look relatively similar to each other). Endocrine atypia may be present, but atypia doesn't necessarily mean malignancy.

ECTOPIC ACTH BY NONPITUITARY TUMORS

- mostly caused by small cell carcinoma of the lung, which will cause the adrenal gland to undergo bilateral hyperplasia due to elevated ACTH.

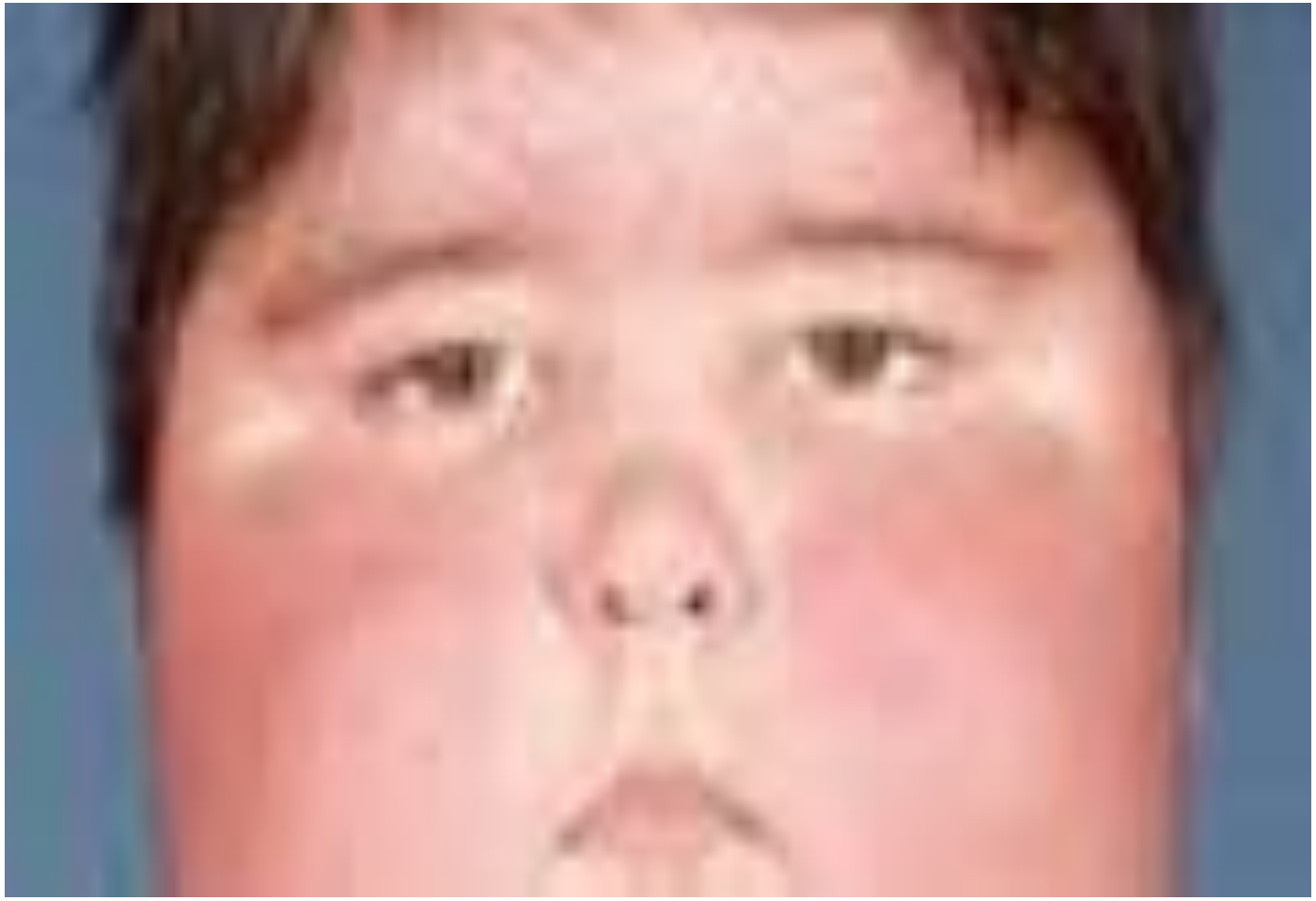
Small cell carcinoma of the lung → ectopic production of ACTH → ↑ ACTH→ bilateral adrenal hyperplasia → ↑ cortisol.

Ectopic ACTH production is considered a paraneoplastic syndrome.

CLINICAL MANIFESTATIONS OF CUSHING SYNDROME

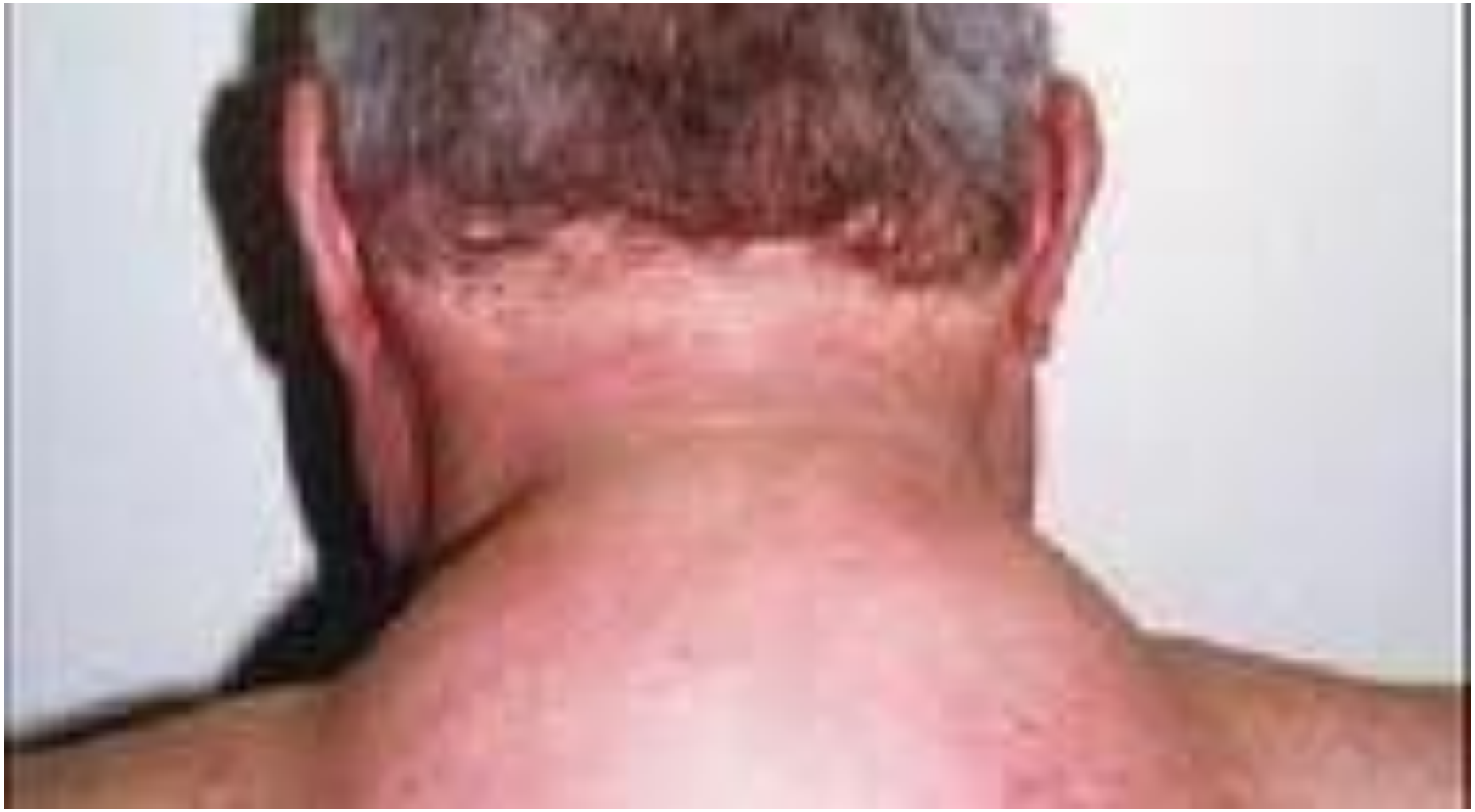
- Hypertension and weight gain
- Truncal (central) obesity, "moon facies," accumulation of fat in the posterior neck and back ("buffalo hump").
- **Effect of glucose:** Glucocorticoids induce gluconeogenesis with resultant *hyperglycemia* (diabetes), *glucosuria,* and *polydipsia.*
- The catabolic effects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

Moon face



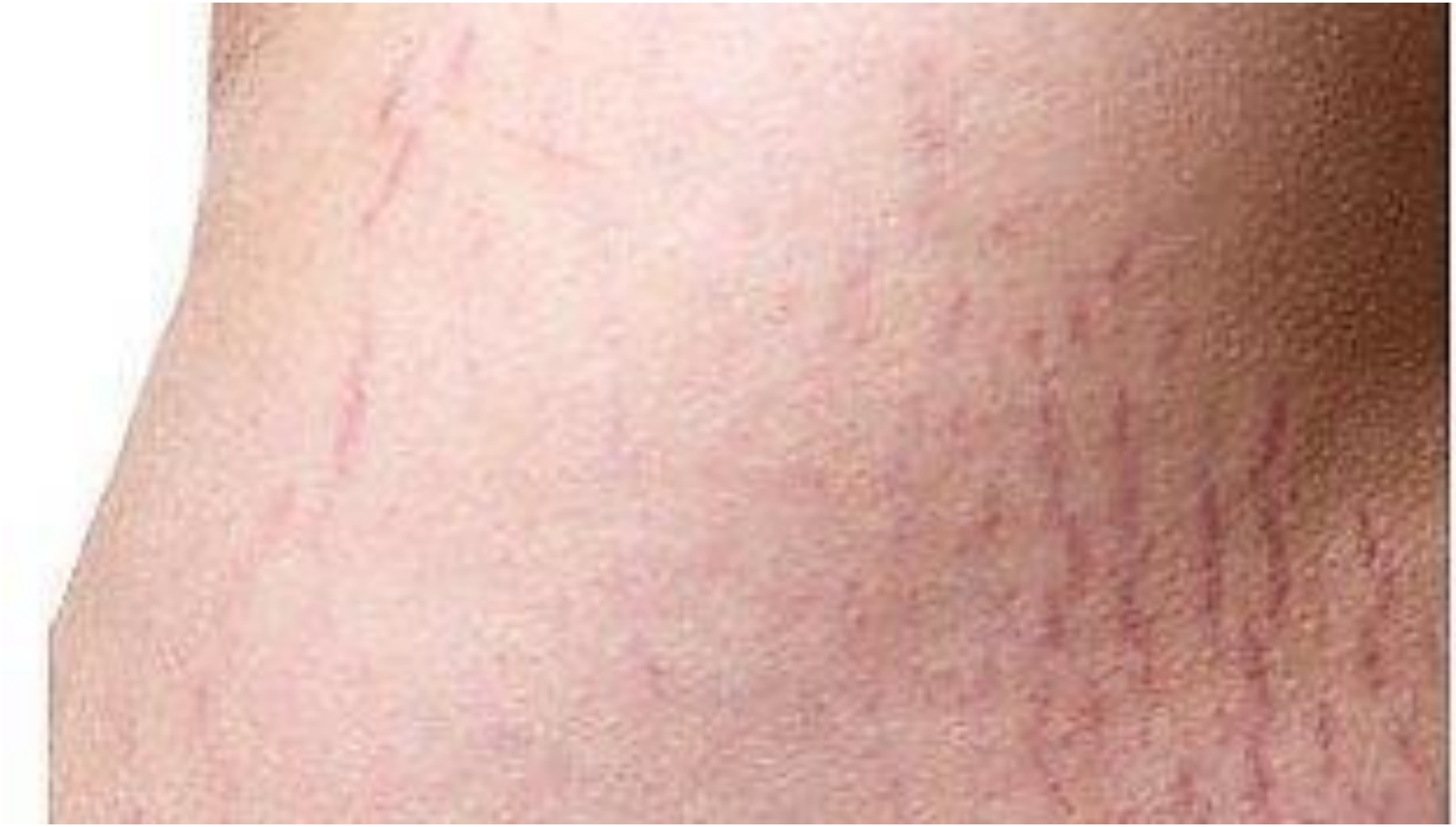
Rounded face due to redistribution of fat in Cushing syndrome.
A naturally round face does not necessarily indicate Cushing syndrome.
To recognize a pathological change, compare the patient's current appearance with previous photographs (e.g.,2-5 years earlier) and look for a new, obvious change in facial appearance.

Buffalo hump



Buffalo

Stria



May occur after pregnancy or rapid weight loss.
They can also occur in Cushing syndrome due to catabolic effect of glucocorticoids on protein, including collagen.

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.

The RAAS (from Dr. Yanal [MID]):

- The renin-angiotensin-aldosterone system (RAAS) is very important in regulating blood pressure.
  - Renin enzyme is produced from the kidney in response to decreased renal perfusion, such as in severe bleeding that decreases the cardiac output and thus the renal perfusion, which is normally about 1250 ml/min.
  - The liver produces angiotensinogen (14 aa), which is cleaved by the action of renin into angiotensin 1 (10 aa), an inert peptide.
  - Angiotensin I is converted in the lungs by the action of angiotensin converting enzyme (ACE) into angiotensin II (8 aa), an active peptide.
  - In the zona glomerulosa, angiotensin II acts via GPCR/cAMP/PKA to activate enzymes responsible for aldosterone synthesis.
  - **Aldosterone in turn increases Na^+, which drags water from the lumen toward the circulation, increasing blood volume and thus blood pressure.**

RAAS

The **renin-angiotensin-aldosterone system (RAAS)** regulates aldosterone secretion and contributes to the regulation of blood pressure.

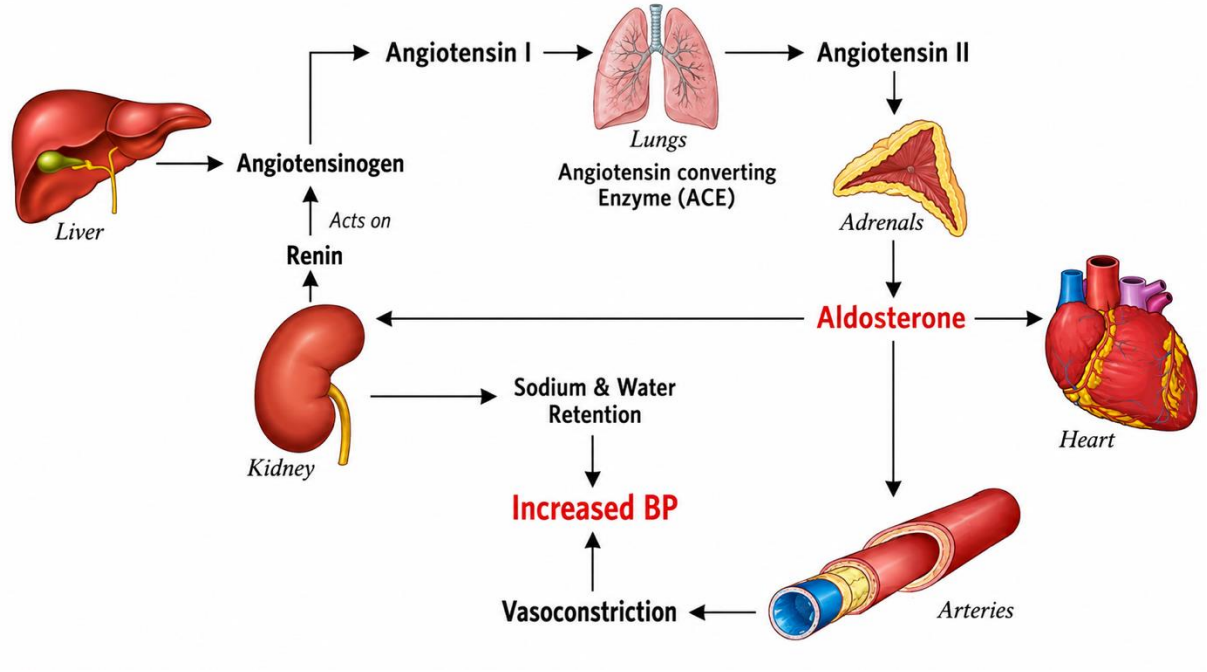
The pathway occurs as follows:

Liver → Angiotensinogen → Renin → Angiotensin I → ACE → Angiotensin II → Adrenal gland → Aldosterone

·The **liver** produces **angiotensinogen**.

·**Renin**, released from the **kidney**, acts on angiotensinogen to produce **angiotensin I**.

·**Angiotensin-converting enzyme (ACE)**, mainly associated with the pulmonary circulation, converts **angiotensin I → angiotensin II**.



- **Angiotensin II** has two important effects:
- It acts directly on the **arteries**, causing **vasoconstriction → ↑ blood pressure**.
- It acts directly on the **adrenal gland**, stimulating the secretion of **aldosterone**.
- **Aldosterone** acts on the **kidney**, promoting **Na^+ and water retention → ↑ blood volume → ↑ blood pressure**.

Therefore:

Angiotensin II → vasoconstriction + ↑ aldosterone → ↑ blood pressure

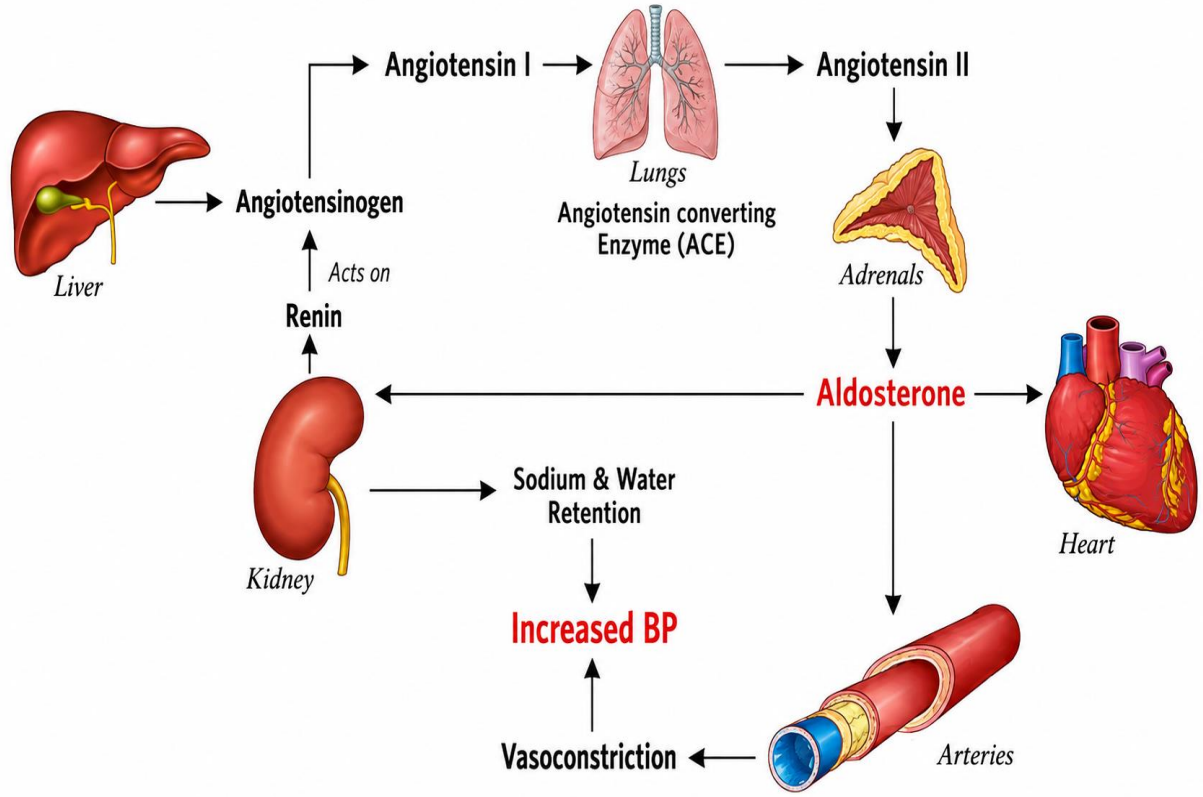
Aldosterone, regulated by the renin–angiotensin system, promotes **sodium and water retention**. Together with the vasoconstrictor effect of angiotensin II, these effects contribute to **increased blood pressure**, which is the **main clinical feature of hyperaldosteronism**.

The increase in aldosterone may occur because of:

↑ Renin → secondary hyperaldosteronism

OR

Primary disease of the adrenal gland → primary hyperaldosteronism



ACE Inhibitors

ACE inhibitors are among the medications used in the management of hypertension.

They block the conversion of:

Angiotensin I → Angiotensin II

Therefore, blocking this pathway results in:

↓ Angiotensin II → ↓ vasoconstriction + ↓ stimulation of aldosterone secretion → ↓ Na^+ and water retention → ↓ blood pressure

Thus, ACE inhibitors interfere with the RAAS and help **regulate blood pressure in hypertension**

HYPERALDOSTERONISM

Primary hyperaldosteronism:

- **autonomous** overproduction of aldosterone (tumor for example) 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

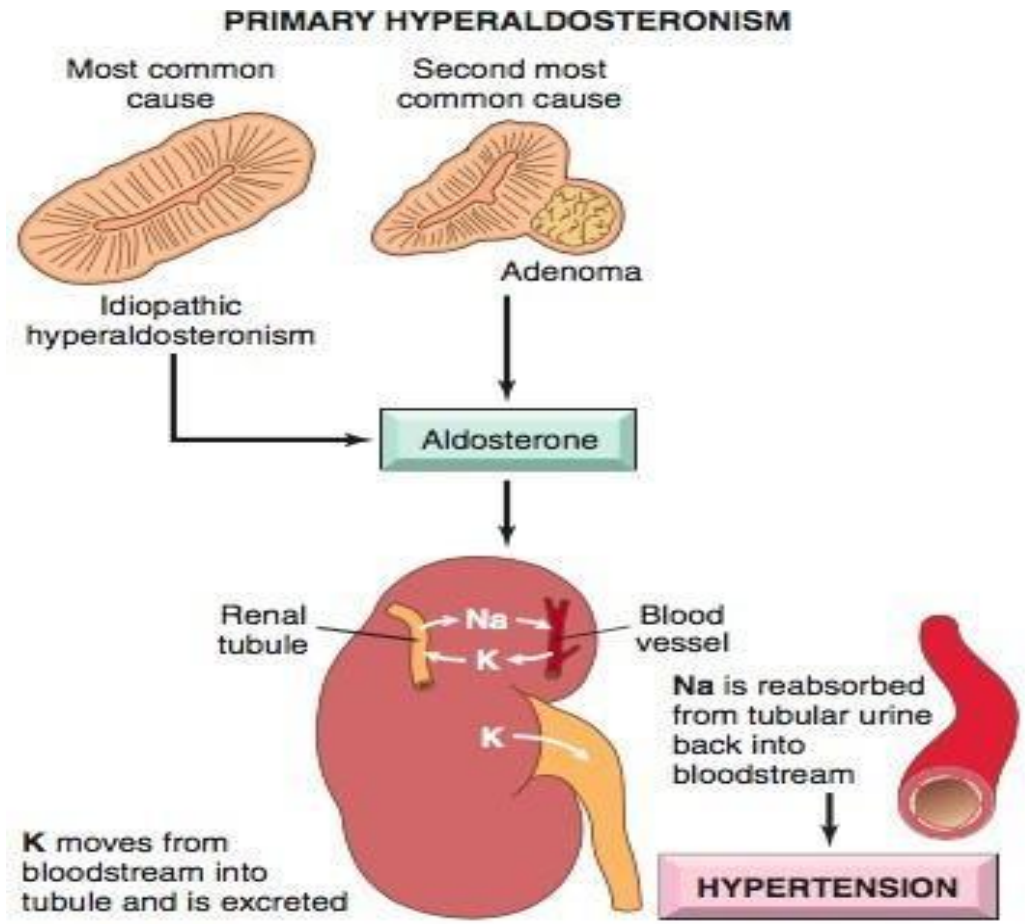


Fig. 20.39 The major causes of primary hyperaldosteronism and its principal effects on the kidney.

CAUSES OF SECONDARY HYPERALDOSTERONISM

- Decreased renal perfusion(renal artery stenosis)
- Arterial hypovolemia and edema e.g heart failure
- Pregnancy (caused by estrogen-induced increases in plasma renin substrate

Further explanation about the causes of 2 hyperaldosteronism

Secondary hyperaldosteronism as mentioned that it means there is an increase in renin, which subsequently increases aldosterone secretion.

Causes of increased renin

1. Hypotension / low blood volume

One of the major stimuli for renin secretion is **low blood pressure or low blood volume (hypovolemia)**. When renal perfusion decreases, the kidney increases renin secretion in an attempt to restore blood volume and blood pressure.

↓ Blood volume / ↓ renal perfusion → ↑ Renin → ↑ Angiotensin II → ↑ Aldosterone → Na^+ and water retention

This mechanism can occur in conditions associated with reduced effective circulating volume, such as **heart failure** and **liver cirrhosis**.

2. Pregnancy – Physiological

Pregnancy is another situation associated with increased aldosterone. This is considered **physiological**, as expansion of blood volume is required during pregnancy.

3. Renal Artery Stenosis – Most Important

The **renal artery supplies blood to the kidney**. If renal artery stenosis occurs, blood flow to the affected kidney decreases. Even if the patient's systemic blood pressure or blood volume is normal, **the kidney perceives decreased perfusion as low blood pressure**.

Therefore:

Renal artery stenosis → ↓ renal perfusion → ↑ renin → ↑ angiotensin II → ↑ aldosterone → secondary hyperaldosteronism

The increased aldosterone can contribute to **hypertension**.

Therefore, **renal artery stenosis is an important cause of secondary hyperaldosteronism and secondary hypertension.**

Primary vs. Secondary Hypertension

It is important to distinguish between **primary and secondary hypertension**.

Primary (essential) hypertension is generally **idiopathic and multifactorial**, particularly in older patients. There is no single identifiable cause that can simply be removed. Therefore, treatment is generally long-term, and its main purpose is to **control blood pressure**.

In contrast, some cases of hypertension have an **identifiable and potentially treatable underlying cause**. This is particularly important in **young patients with hypertension**.

If a young patient presents with hypertension, we should therefore **look for potentially treatable causes before assuming that lifelong antihypertensive therapy is required**.

For example:

Renal artery stenosis → treat the underlying renovascular problem → blood pressure may improve substantially.

Another important treatable cause is **pheochromocytoma**.

Pheochromocytoma is a tumor of the adrenal medulla that can cause hypertension.(mentioned later)

Therefore, when pheochromocytoma is responsible for a patient's hypertension, treating/removing the tumor can potentially resolve the underlying cause of hypertension.

Pheochromocytoma can be evaluated using appropriate imaging, including **MRI**.

In a **young patient with hypertension**, two important potentially treatable causes emphasized here are:

1. Renal artery stenosis

2. Pheochromocytoma

Renal artery stenosis is evaluated by **vascular imaging** to determine whether the renal artery is narrowed.

Common non-invasive methods include:

- **Duplex Doppler ultrasonography, CT angiography (CTA), MR angiography (MRA)**

Renal angiography can provide definitive assessment when necessary.

Hypertension is strongly related to **renal function and fluid regulation**. For this reason, **nephrology**—the medical specialty concerned with kidney diseases—has an important role in the evaluation and management of hypertension, particularly when a renal cause is suspected.

Medical students + continuous stress → hypertension loading...

So,the doctor's advice:

"Run away while you still can, before all this stress gives you hypertension."

PRIMARY HYPERALDOSTERONISM

- *Bilateral idiopathic hyperaldosteronism,*

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

- *Adrenocortical neoplasm,* adenoma, cortisol secreting(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*

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

⚠ Important: Distinguish Adrenocortical Adenomas

Not all adrenal cortical adenomas are the same. Always identify which hormone the adenoma secretes.

- **Cortisol-producing adrenocortical adenoma → ↑ Cortisol → Cushing syndrome**
- **Aldosterone-producing adrenocortical adenoma → ↑ Aldosterone → Primary hyperaldosteronism (Conn syndrome)**

Therefore:

Cortisol-producing adenoma ≠ Aldosterone-producing adenoma

Cushing syndrome ≠ Primary hyperaldosteronism (Conn syndrome)

Neoplastic VS Hyperplasic

In the adrenal gland, primary causes of hormone excess include:

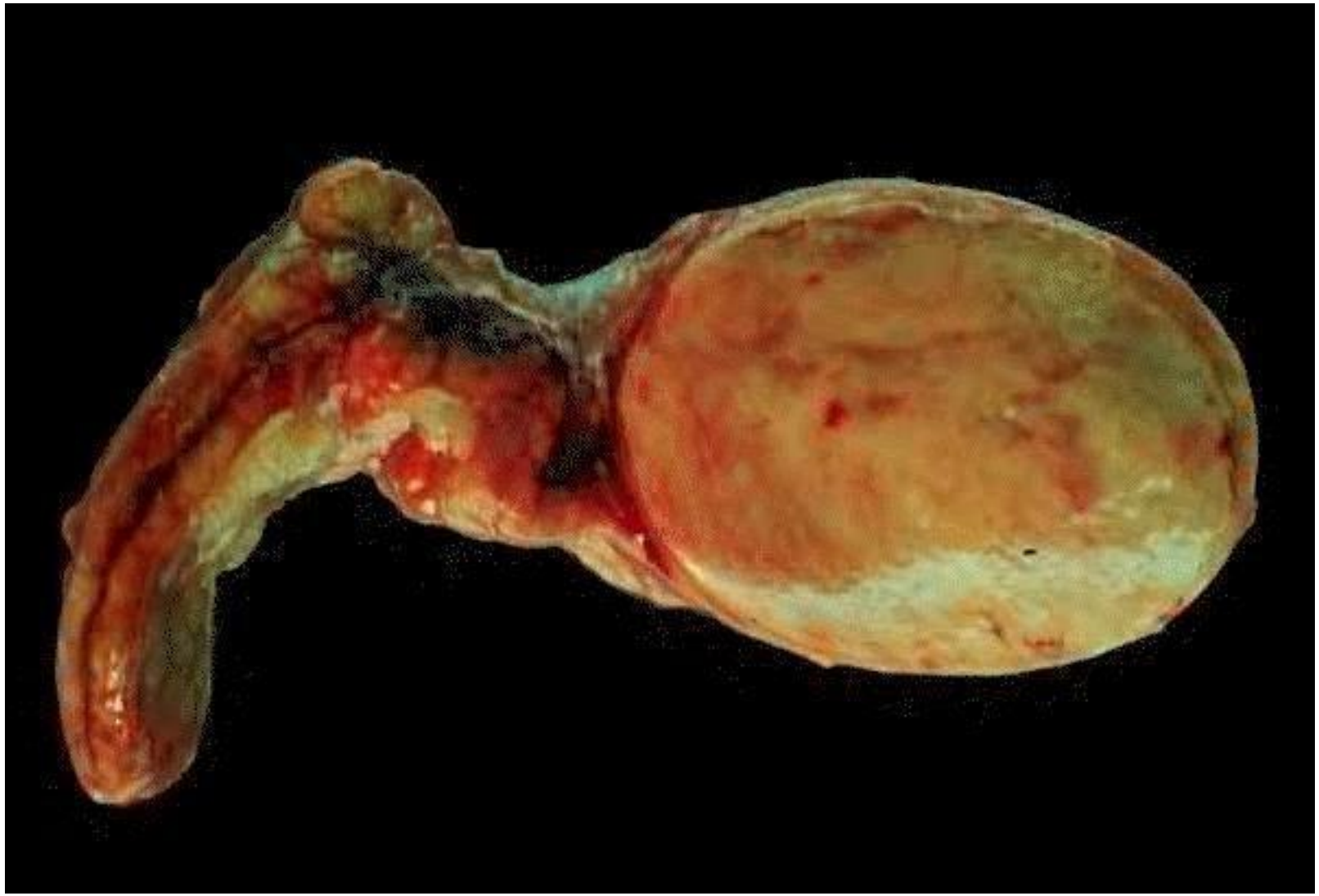
(1) **Adenomas and carcinomas**, both of which are typically monoclonal, arising from a single cell and usually producing excess of one hormone—such as cortisol or aldosterone—resulting in cortisol **or** aldosterone adenomas.

(2) **Nodular hyperplasia**, which can involve multiple nodules and may cause overproduction of one hormone or both cortisol and aldosterone simultaneously. Additionally, adrenal adenomas can be nonfunctional, while carcinomas are usually nonfunctional, though functional carcinomas also occur.

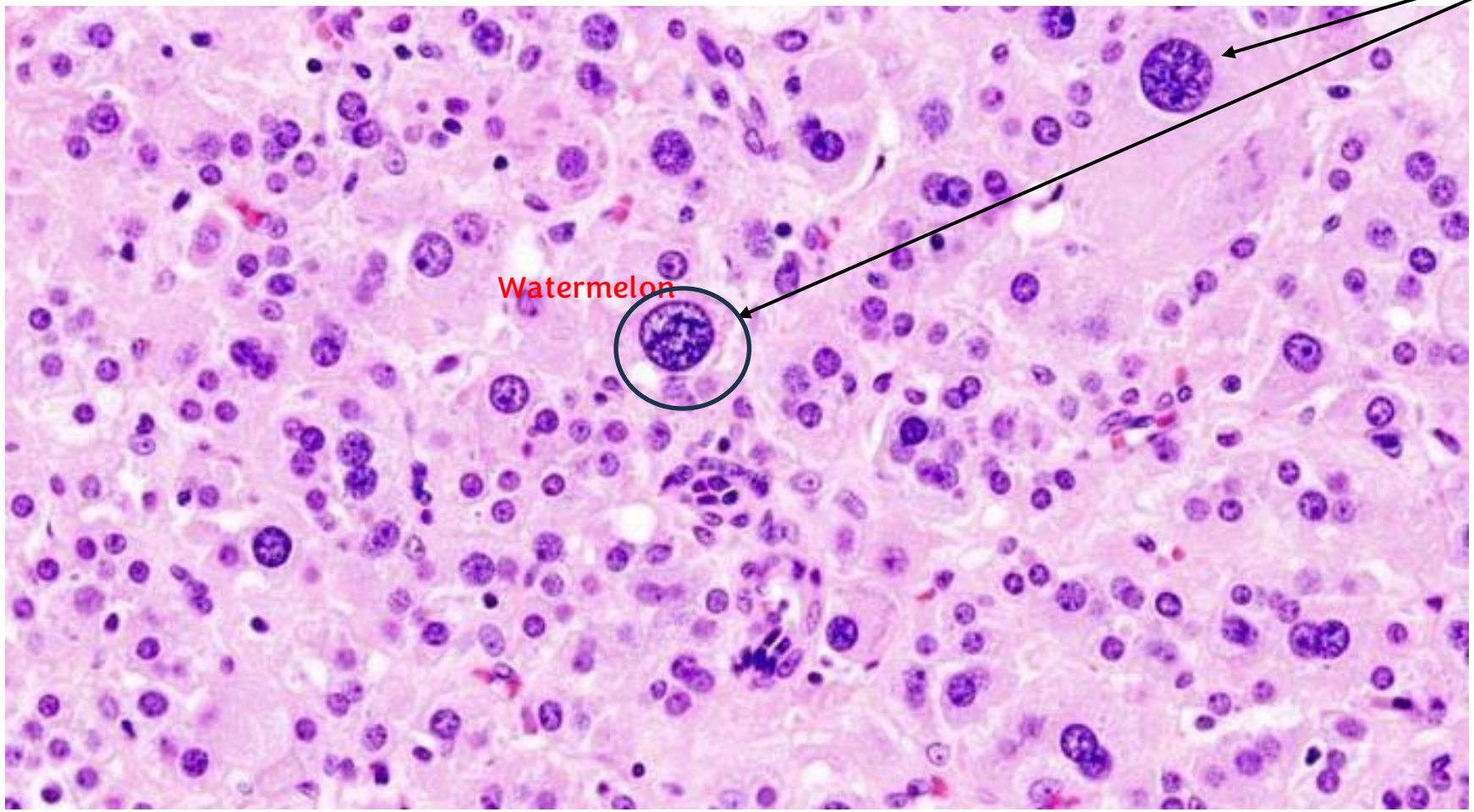
Features of adrenocortical adenoma

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

Adrenocortical adenoma



Adrenocortical adenoma/ note the endocrine atypia



having all the features of malignancy but not malignant

CLINICAL FEATURES OF HYPERALDOSTERONISM

The clinical hallmark is hypertension

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

Adrenal insufficiency

- = Decreased hormonal production from the adrenal **(Hyposecretion)**
- Divided into three types

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

Primary insufficiency

Acute Adrenocortical Insufficiency :

Sudden cessation of glandular function, resulting in complete loss of hormone secretion.

Occurs in the following situations:

- Crisis in patients with chronic adrenocortical insufficiency precipitated by physiological stress(surgery, trauma...)
- In patients maintained on exogenous corticosteroids .. Sudden withdrawal, or stress
- Massive adrenal hemorrhage. The most important

A. In a patient with chronic adrenal insufficiency, any stressor that increases corticosteroid demand can precipitate an acute adrenal crisis, representing **acute-on-chronic insufficiency.** Therefore, a patient with chronic adrenocortical insufficiency who requires surgery should receive **steroids before surgery** to prevent a crisis

B. **Iatrogenic corticosteroid** therapy suppresses ACTH through negative feedback, causing adrenal cortical atrophy. Sudden cessation may trigger acute adrenal insufficiency, so **gradual tapering** is essential to allow adrenal recovery and prevent a crisis.

Massive adrenal hemorrhage

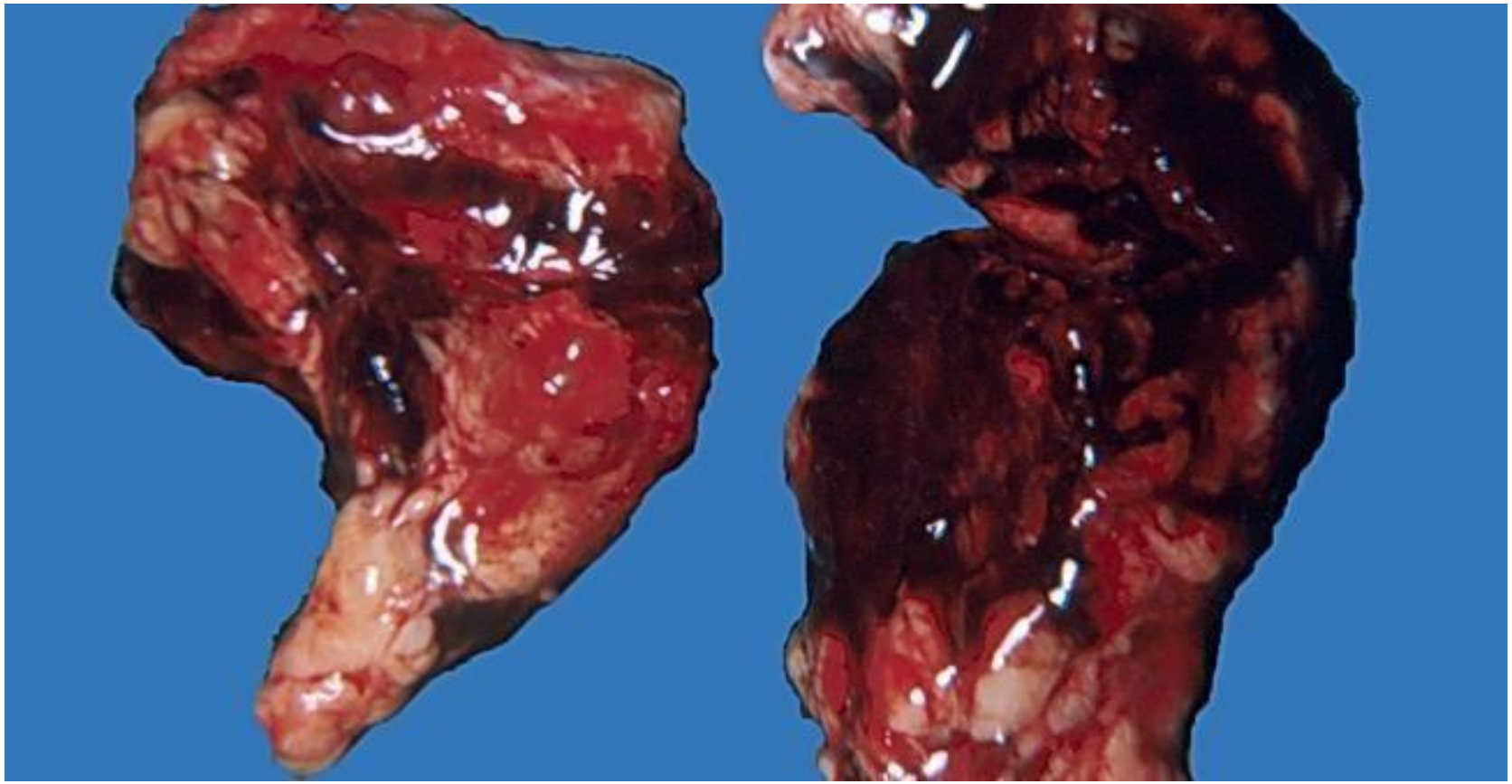
May destroy enough of the adrenal cortex to cause acute adrenocortical insufficiency.

- This condition may occur:

1. In patients maintained on anticoagulant therapy as a side effect but not a must
2. Patients suffering from sepsis: a condition known as the Waterhouse-Friderichsen syndrome

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

Massive adrenal hemorrhage



Loss of 80–90% of adrenal tissue, exceeding the normal functional reserve, as in massive adrenal hemorrhage, results in adrenal insufficiency.

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

- Uncommon disorder resulting from **gradual** **progressive destruction** of the adrenal cortex.
- Causes:

❑ Autoimmune adrenalitis.(most common)

❑ Infections

❑ Metastatic tumors

ADDISON DISEASE

1. *Autoimmune adrenalitis*

Some endocrinologists consider only autoimmune adrenalitis as Addison's disease, while others consider it a subtype (as we do).

- 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 (slowly 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, affects blood vessels and is related to herpesvirus-8) .

ADDISON DISEASE

3- *Metastatic neoplasms* involving the adrenals:

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

Remember, adrenal insufficiency requires massive gland destruction, typically 80–90% loss of tissue. Even in metastatic disease—most often from lung cancer—this degree of destruction is necessary before insufficiency develops.

Secondary adrenocortical insufficiency

- Hypothalamic- pituitary diseases **(Hypopituitarism)** including:
- ❑ Metastasis
- ❑ Infection.
- ❑ Infarction
- ❑ Irradiation
- Can be part of pan hypopituitarism.

Hypopituitarism causes decreased ACTH secretion, resulting in reduced cortisol secretion from the adrenal cortex and, consequently, secondary adrenocortical insufficiency. Aldosterone remains relatively preserved, because it is mainly regulated by the RAAS rather than ACTH.

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 because there is no increase in ACTH (POMC MSH + ACTH).

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 (most of them are adenomas).

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 (***outside the adrenal)** , called *paragangliomas,* **catecholamine-producing cells**. Cells similar to those of the adrenal medulla are also present at other locations in the body and can give rise to tumors with similar effects.

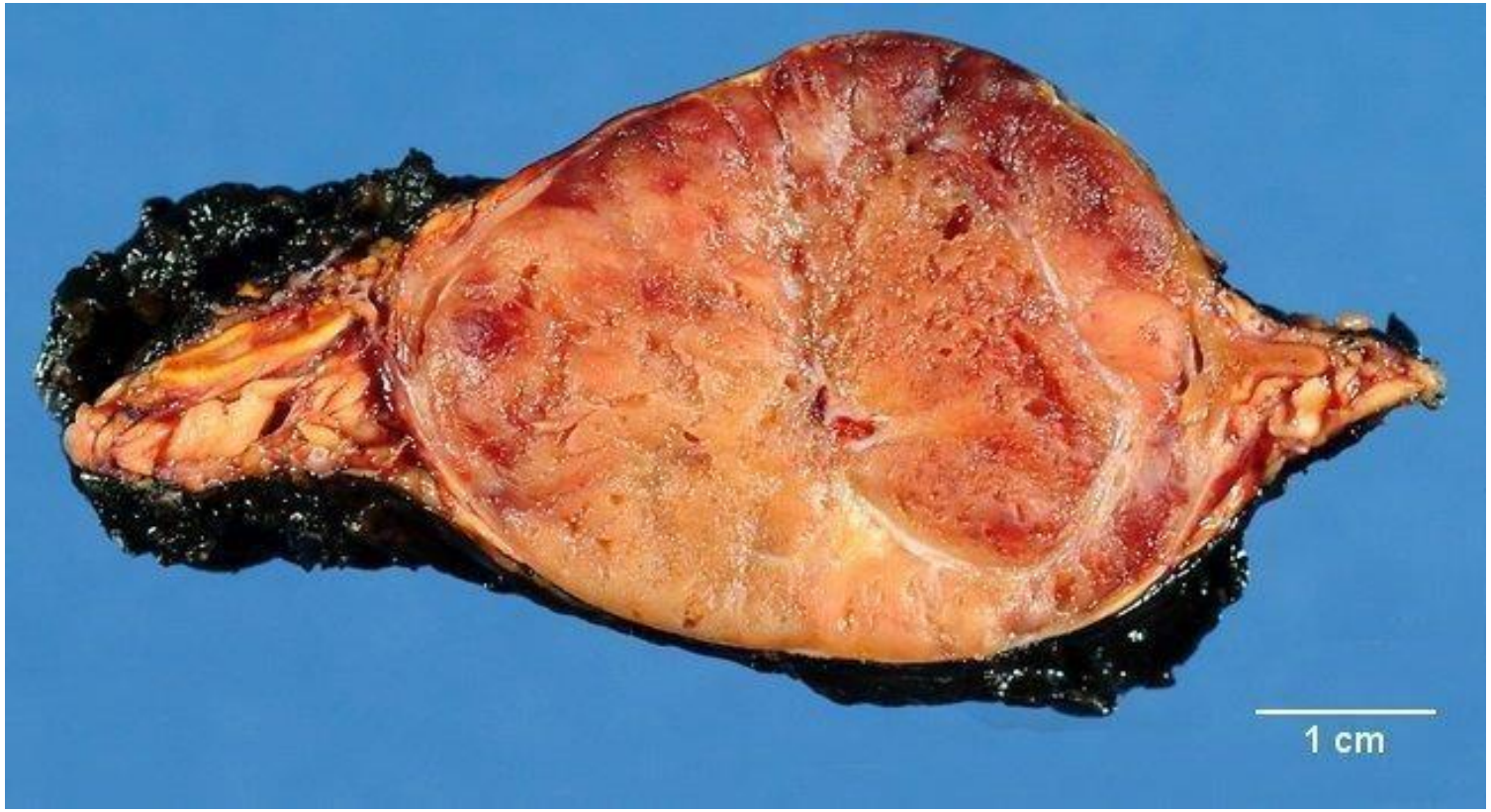
b. *10% of adrenal pheochromocytomas are bilateral(both glands)*; this proportion may rise to 50% in cases that are associated with familial syndromes.

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

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

Pheochromocytoma

- ✓ Encapsulated
- ✓ well-circumscribed
- ✓ Atypia may be seen



Pheochromocytoma

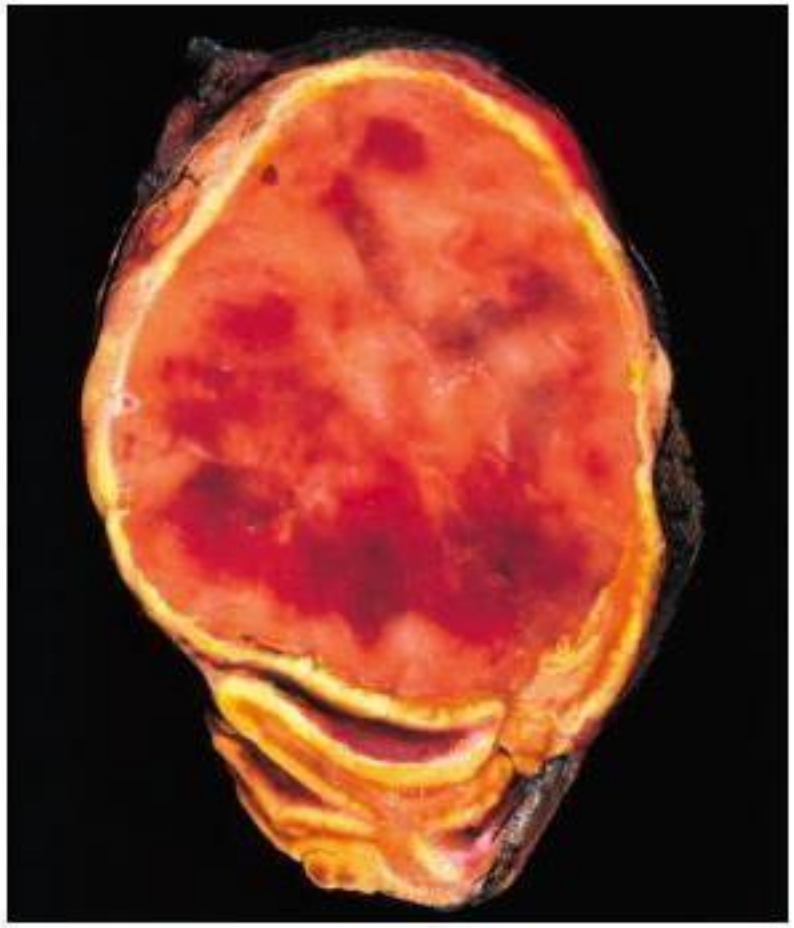
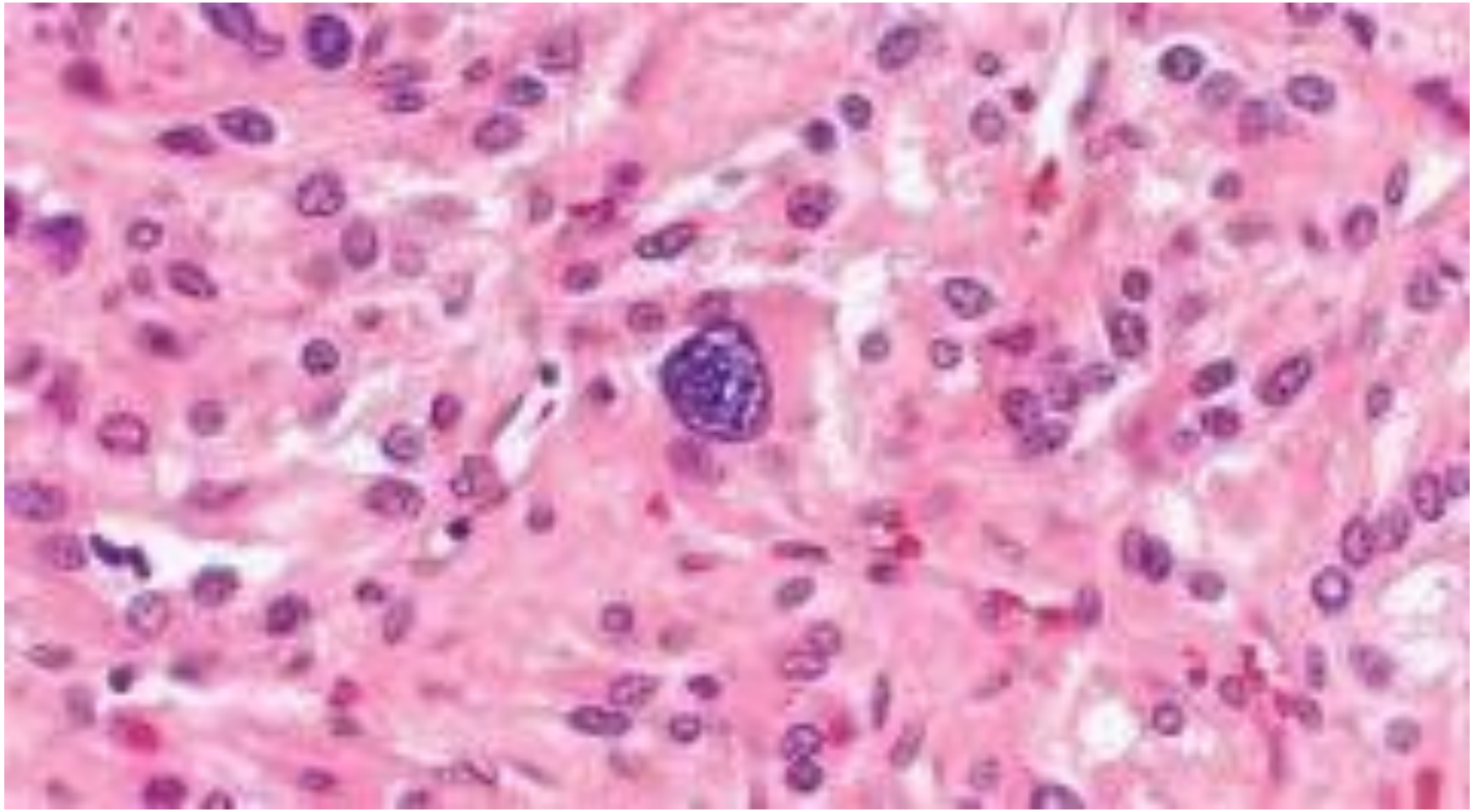


Fig. 20.44 Pheochromocytoma. The tumor is enclosed within an attenuated cortex and demonstrates areas of hemorrhage. The comma-shaped residual adrenal gland is seen *(lower portion)*.

Pheochromocytoma



Pheochromocytoma

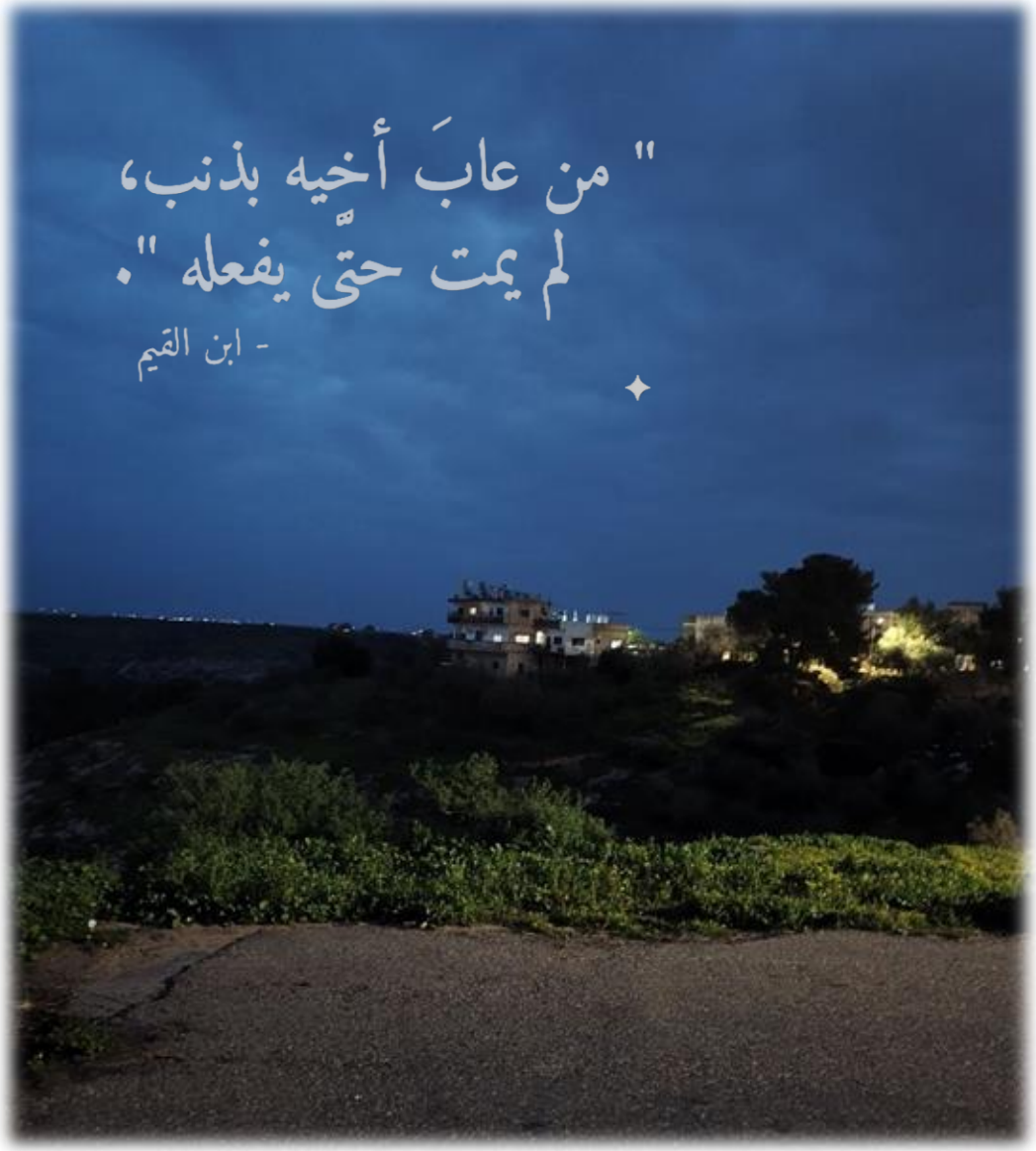
- The definitive diagnosis of malignancy (10%) in pheochromocytomas is based exclusively on the presence of metastases.

Clinical Features

- The predominant clinical manifestation is ***Hypertension*** *(considered a cause of secondary hypertension especially in young people in their 20-30s)*

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

رسالة من الفريق العلمي:



في ممرات هذه الحياة، نلتقي بأشخاصٍ كثر، لكلٍّ منهم تفاصيله، ظروفه، ومعاركه الخفية التي لا نعلم عنها شيئاً. كلنا بشر، مجبولون على الخطأ والنسيان، ولا أحد منا يملك صكّاً بالكمال أو العصمة.

تأملتُ يوماً قول الإمام ابن القيم: "مَن عابَ أخاهُ بذَنبٍ، لَم يَمُتْ حتّى يَفعَلَه"، فاستوقفتني هذه الكلمات عميقاً، فهي تذكيرٌ رقيق وهام بأن القلوب بين أصبعين من أصابع الرحمن يقلبها كيف يشاء، وأن من أُصيب اليوم بزلّة، قد يعافيه الله ويبتلي من عابه وسخر منه.

لذا، ما أجمل أن نجعل من أنفسنا ملاذاً آمناً للآخرين بالستر والرحمة، فبدلاً من تتبع العثرات أو إطلاق الأحكام، نلجأ للدعاء بالهداية والصلاح ونحمد الله على العافية، وننشغل بإصلاح أنفسنا ففي عيوبنا ما يكفينا لنداويه، وفي طموحاتنا ما يشغلنا لنبنيه، مستبدلين كلمات النقد الجارحة بكلمات طيبة ترمم القلوب وتترك أثراً جميلاً لا يُمحى...

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			