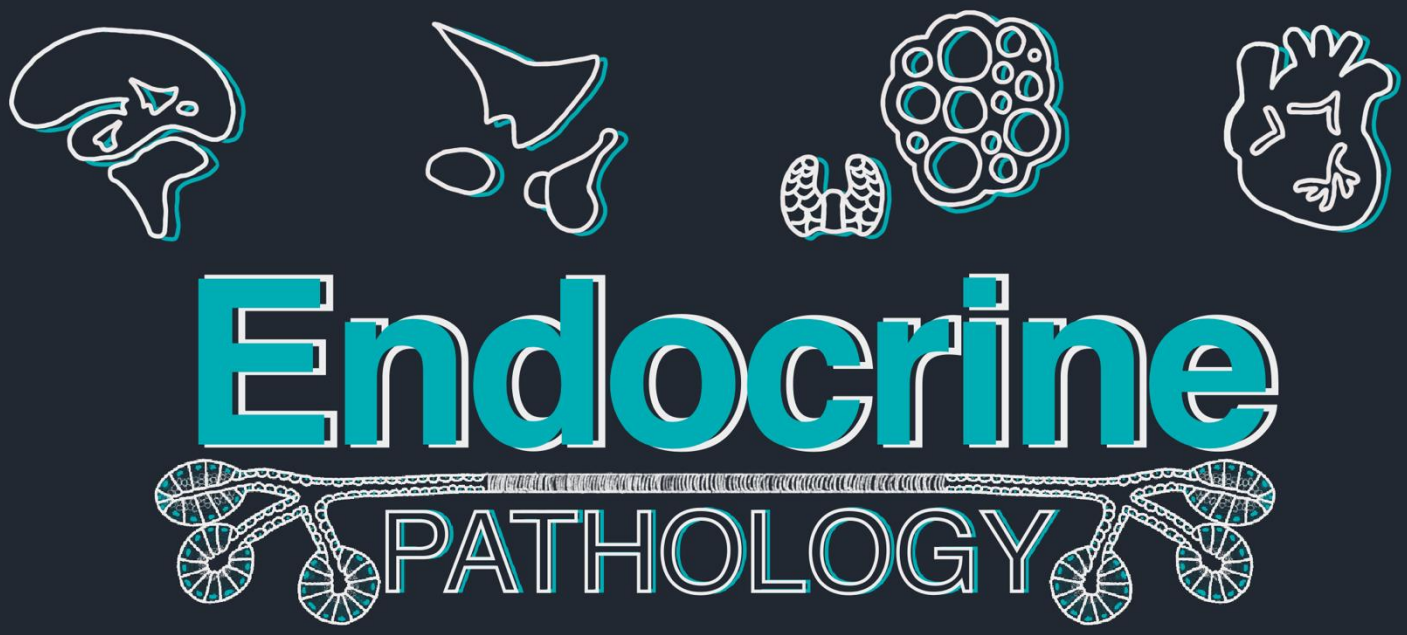
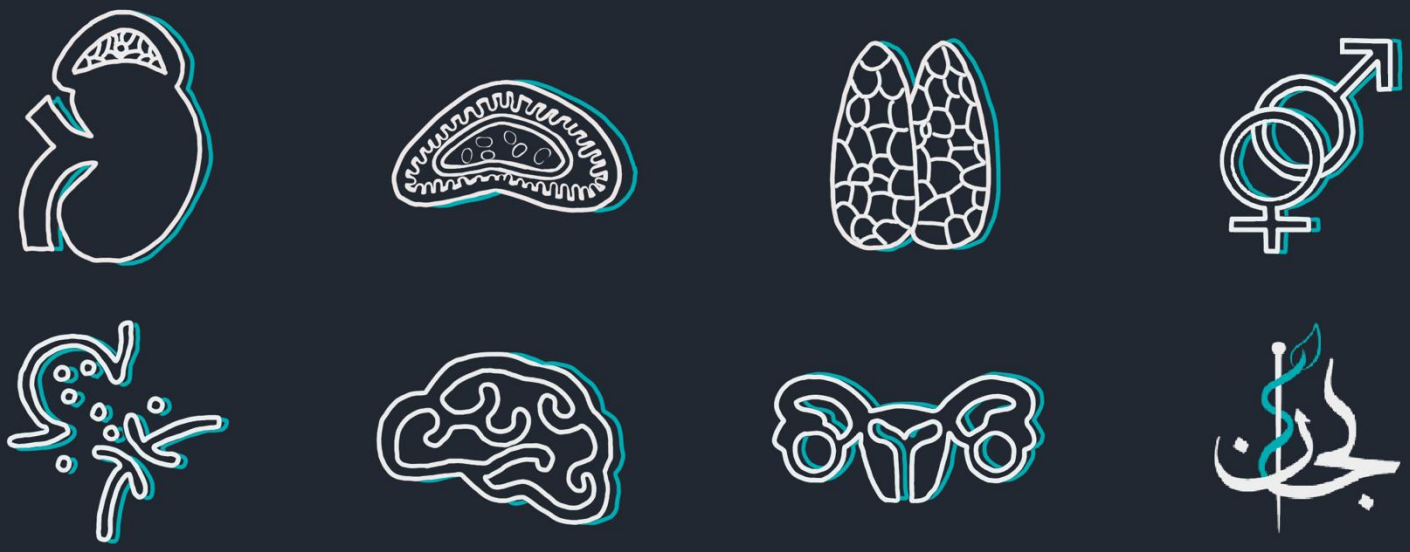


Endocrine PATHOLOGY



Title: Sheet 8 – Adrenal Gland 2

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Recap:

Aldosterone

- What is aldosterone? It is a cholesterol-derived hormone that Is essential for life, produced by the adrenal cortex (to be specific zona glomerulosa).
- This hormone is part of bigger system which is The **renin–angiotensin–aldosterone system** (**RAAS**).
- But what is the **renin–angiotensin–aldosterone system** (**RAAS**)? It is a hormone system that is involved in the **regulation of the plasma sodium concentration** and **arterial blood pressure**.

Aldosterone-related diseases

HYPERALDOSTERONISM: divided into two sub-types :

❖ **Primary hyperaldosteronism** (problem in the adrenal gland itself)
- ✓ Autonomous overproduction of aldosterone with secondary suppression of renin-angiotensin system and decreased plasma renin activity.
- ✓ **Note : low renin concentration in blood due to feedback inhibition by increased blood volume** (done by high level aldosterone and angiotensin 2).

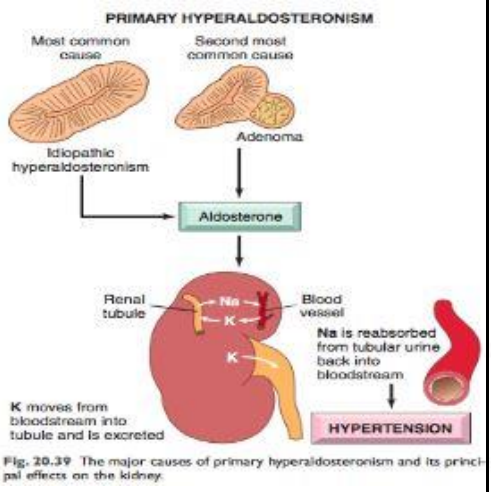


Fig. 20.39 The major causes of primary hyperaldosteronism and its principal effects on the kidney.

❖ **Secondary hyperaldosteronism**:
- ✓ Aldosterone release occurs in response to activation of renin-angiotensin system characterized by increased levels of plasma renin.
- ✓ CAUSES:

  a. Decreased renal perfusion (renal artery stenosis "Stenosis: narrowing of capillaries"), how? Renin is secreted by kidney when blood volume decreases. In renal artery stenosis, a decrease in blood perfusion toward kidney happens (there are sensors in kidney that measure any difference in blood pressure), leading to activation of renin secretion (to raise blood pressure that is already normal) which increases the level of aldosterone (additional note).

  b. Arterial hypovolemia and edema e.g. heart failure

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

NOW let's start our lecture

PRIMARY HYPERALDOSTERONISM: (0:05)

❖ Causes:

1. Bilateral idiopathic hyperaldosteronism

- Idiopathic: have unknown reason. Bilateral: affects both adrenal glands
- bilateral nodular hyperplasia of adrenals = increase in aldosterone-secreting cells.
- the most common underlying cause (60% of cases) لانه اغلب الحالات بتصير بدون سبب معروف

2. Adrenocortical neoplasms

- 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***.

3. Rarely, Familial hyperaldosteronism

- May result from a genetic defect that leads to overactivity of the *aldosterone synthase* gene, *CYP11B2.*

❖ Features of aldosterone producing adrenocortical adenoma (1:25)


Figure 1: Adrenocortical adenoma

- Solitary
- Encapsulated
- Well circumscribed
- Histology: can show endocrine atypia
- May contain spironolactone bodies if treated with spironolactone.
- **Endocrine atypia**: polymorphism of cells , variation in size and shape of cells, hyperchromasia and mitotic activity.

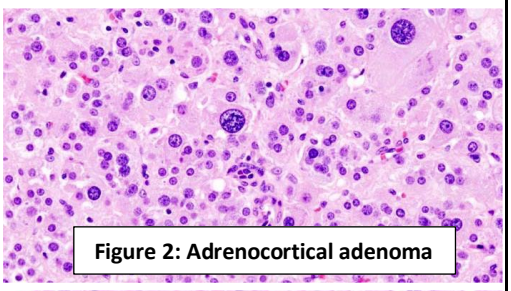


Figure 2: Adrenocortical adenoma

- **Figure 2: Adrenocortical adenoma**. Note the endocrine atypia. We don't depend on endocrine atypia for diagnosis of malignancy, we depend on other features such as presence of metastasis (Endocrine atypia might be present in all tumor of endocrine cells)
- **Figure 3: Spironolactone bodies**. Aldosterone producing adenomas contain **eosinophilic, laminated cytoplasmic inclusions=spironolactone bodies** which appear after treatment with spironolactone (an aldosterone antagonist)

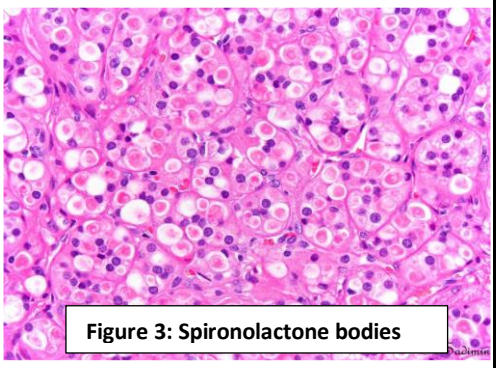


Figure 3: Spironolactone bodies

❖ Clinical Features of Hyperaldosteronism (4:27)

- The clinical hallmark is **hypertension**
- Hyperaldosteronism may be the most common cause of **secondary hypertension**
- **Hypokalemia** results from renal potassium wasting

Adrenal insufficiency (hypofunction) (4:54)

- Decreased hormonal production from the adrenal
- Divided into three types
  1. Acute insufficiency 2. Chronic insufficiency (Addison disease) 3. Secondary insufficiency

1. Acute Adrenocortical Insufficiency (AAI): (5:28)

Occurs in the following situations:

A. **Crisis in patients with chronic adrenocortical insufficiency precipitated by stress**
   - chronic adrenocortical insufficiency is characterized **by atrophy of both adrenal glands** leading to **deficiency in production of cortisol**. Patients who encounter **any form of stress** (infection, trauma) **need more cortisol**, and with absence of cortisol, they will develop AAI.

B. **In patients maintained on exogenous corticosteroids and Sudden withdrawal, or stress happen**
   - exogenous cortisol will cause decreased ACTH stimulation on the adrenal glands leading to atrophy of both glands and inability to produce cortisol.

C. **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 Hemophilus influenzae
- ✓ Underlying cause involves endotoxin-induced vascular injury.

Figure 3:Massive adrenal hemorrhage

2. Primary chronic adrenocortical insufficiency (Addison disease): (9:25)

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

A. Autoimmune adrenalitis. (10:30)

- Accounts for 60% to 70% of Addison disease cases and it 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

B. Infections: Tuberculosis and Fungal infections. (11:15)

- **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 Coccidiodes immitis*** may also 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

C. Metastatic tumors involving the adrenals: (12:18)

- The adrenals are a fairly common site for metastases in patients with disseminated carcinomas, which sometimes destroy sufficient adrenal cortex to produce a degree of adrenal insufficiency
- Carcinomas of the **lung** and **breast** are the most common **primary sources**.

3. Secondary adrenocortical insufficiency (12:46)

- Any lesion in the hypothalamus or pituitary that disturbs their parenchyma and reduce the output of ACTH, will cause it.
- The causes are similar to the causes of hypopituitarism.
- Hypothalamic-pituitary diseases including:
  - ✓ **Metastasis diseases** to the pituitary or hypothalamus, most commonly from lung carcinoma or breast carcinoma.
  - ✓ **Infection** might destroy pituitary gland and hypothalamus and causing **Secondary adrenocortical insufficiency**
  - ✓ **Infarction or ischemic necrosis** of the pituitary, it causes **hypopituitarism** and **secondary adrenocortical insufficiency**

- ✓ **Irradiation** causes fibrosis for the anterior parenchyma. This will lead to hypopituitarism and will increase the susceptibility to **Secondary adrenocortical insufficiency.**

❖ Clinical features of adrenal insufficiency: (14:07)

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

- progressive weakness and easy fatigability
- Gastrointestinal disturbances are common and include anorexia, nausea, vomiting, weight loss, and diarrhea.
- In patients with **primary adrenal disease**, increased levels of ACTH precursor hormone stimulates melanocytes, with resultant **hyperpigmentation** of the skin and mucosal surfaces: more common in the face, axillae, nipples, areolae, and perineum are mainly affected
- Note: **hyperpigmentation is not seen in patients with secondary adrenocortical insufficiency**. Why?? (think).
- 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 affect the production of aldosterone**.

All what we talked about previously was about the **adrenal cortex** in most. But now we will talk about the **adrenal medulla.**

Adrenal medulla (17:09)

- The adrenal medulla is embryologically, functionally, and structurally distinct from the adrenal cortex.
- It is populated by **chromaffin cells** derived from **the neural crest**.
- Secrete **catecholamines**.
- Most important disease: **neoplasms**.

TUMORS OF THE ADRENAL MEDULLA: (17:35)

Pheochromocytoma

- What does it mean? (additional info.) Pheo= dark, chromo= color, cytoma= cell tumor. From the name, cells darken when forming a tumor.
- **It is neoplasm composed of chromaffin cells that synthesize and release catecholamines and, in some cases, other peptide hormones.**
- Gives rise to a surgically correctable form of hypertension.
- Pheochromocytomas usually subscribe to "rule of 10s":
  - ✓ 10% of pheochromocytomas are extra-adrenal ,called **paragangliomas**, one of sites is neck
  - ✓ 10% of adrenal pheochromocytomas are bilateral; this proportion may rise to 50% in cases that are associated with familial syndromes.
  - ✓ 10% of adrenal pheochromocytomas are malignant
  - ✓ 10% familial… Now we think up to 25% might be familial.

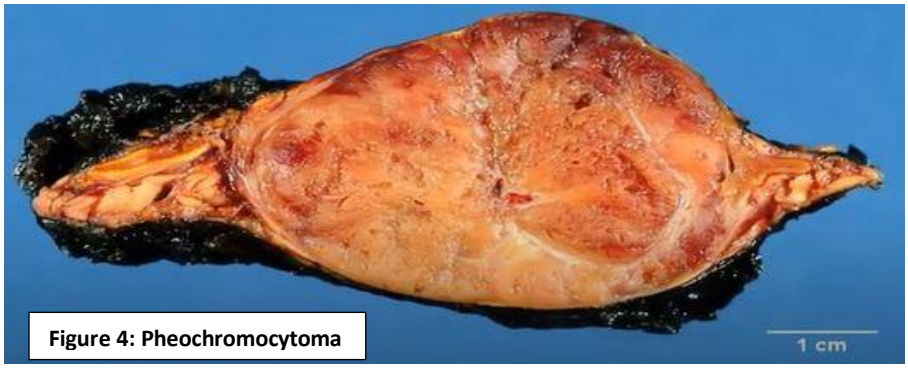
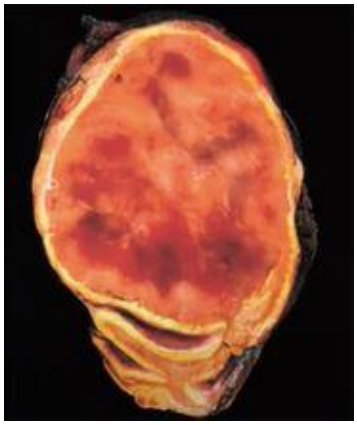
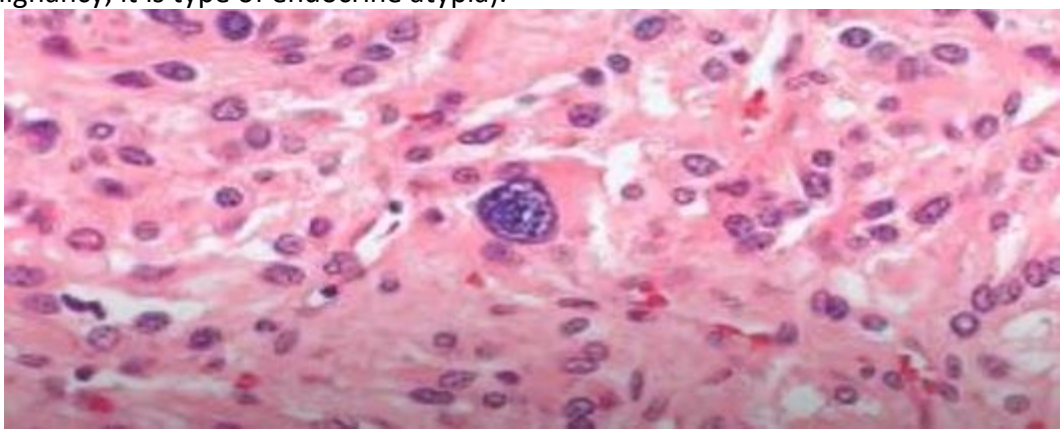


Figure 4: Pheochromocytoma



❖ On microscopic examination (19:47)

- Are composed of polygonal to spindle-shaped chromaffin cells (sustentacular cells) and their supporting cells compartmentalized into small nests, or **Zellballen**, by a rich vascular network
- The cytoplasm has a finely **granular eosinophilic** in appearance, because of the presence of granules containing **catecholamines**.
- The nuclei of the neoplastic cells are often **pleomorphic** (pleomorphic here doesn't indicate malignancy, it is type of endocrine atypia).



❖ Diagnosis: (21:19)

- The definitive diagnosis of malignancy in pheochromocytomas is based exclusively on the **presence of metastases**.
- We don't depend on cytological features in diagnosis of **Pheochromocytoma,** because cytological features are part of endocrine atypia**.**

❖ Clinical Features: (21:38)

- The predominant clinical manifestation is **hypertension (surgically correctable).**
- some patients may develop **sudden cardiac death**, probably secondary to catecholamine-induced myocardial irritability, and **ventricular arrhythmias**.
- Actually, these clinical manifestations make sense and are all connected. Why? (think) it is due to high irregular secretion of catecholamines done by this tumor. Remember, this tumor affects **chromaffin cells.**