Adrenal gland

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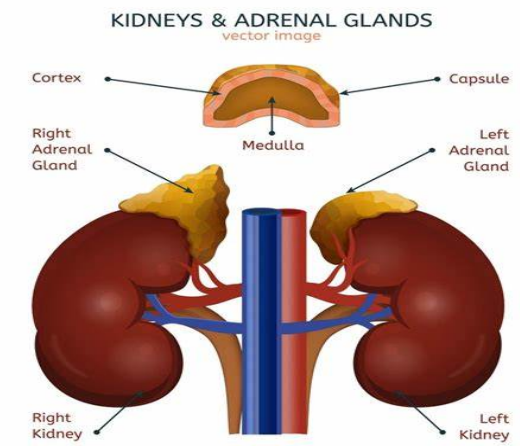
Anatomy

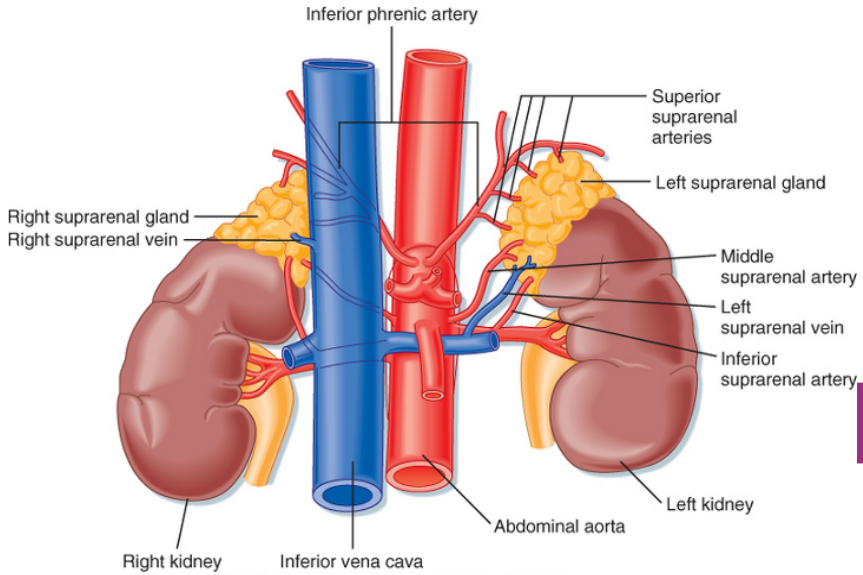
- The adrenal glands are a paired endocrine organs situated at anteromedial surface of the kidneys near the superior poles; both the gland and kidneys are **retroperitoneal**.
- The **weight** of a normal adrenal gland is **4-8 g** and measures 4 x 3 x 1 cm.
- It is larger in women than in men.
- The two glands differ in shape, **the left gland** is semilunar in form and more flattened and may extend on the medial surface of the kidney, while **the right gland** is more triangular and lies higher on the kidney.
- The adrenal glands are composed of two distant parts, with differing functions and embryonic origins
  - **Adrenal cortex**: derived from **mesoderm**
  - **Adrenal medulla**: derived from the **neural crest**



Vascular Supply

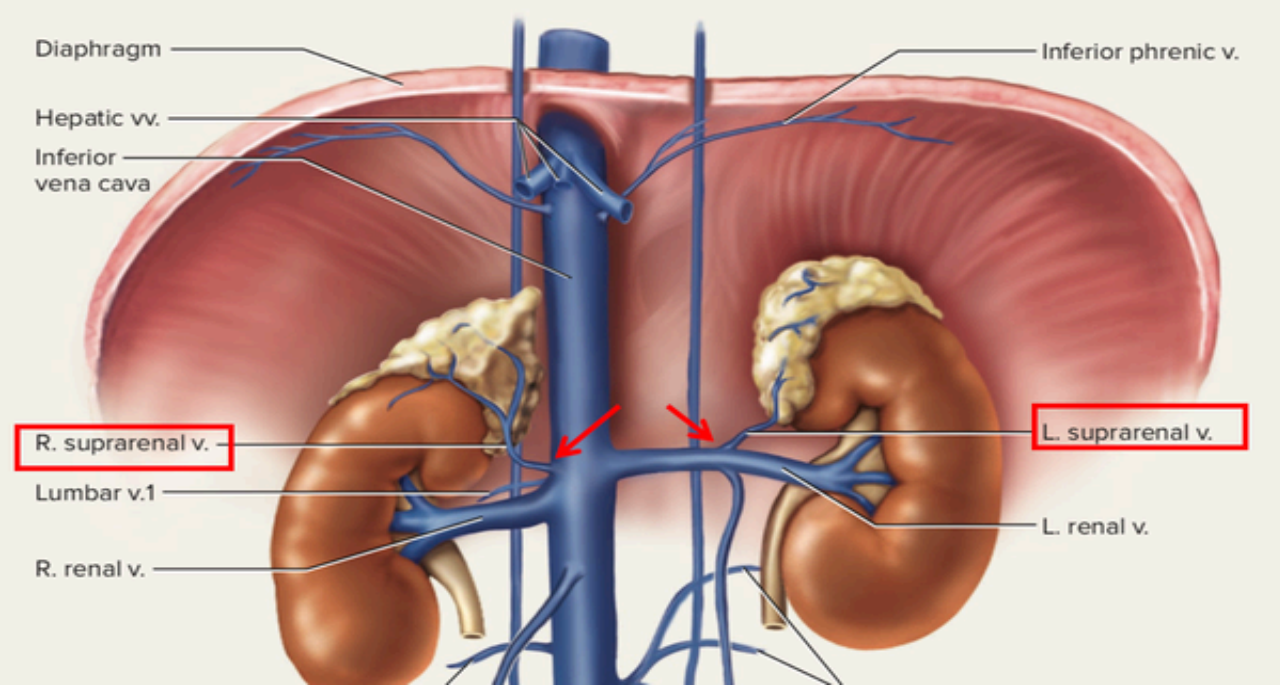
Arterial blood supply :

- Superior suprarenal artery which arise from the inferior phrenic artery.
- Medial suprarenal artery which arise from the abdominal aorta.
- Inferior suprarenal artery which arise from the renal artery.



Venous drainage

- Right suprarenal vein into the inferior cava vein .
- Left suprarenal vein into the left renal vein.



Lymphatics and innervation

Lymph drainage

- Left aortic lymph nodes
- Right caval lymph nodes

Innervation

- The adrenal glands are innervated by the **coeliac plexus and greater splanchnic nerves**.
- **Sympathetic** innervation to the **adrenal medulla** is via myelinated pre-synaptic fibers, mainly from the T10 to L1 spinal cord segments.

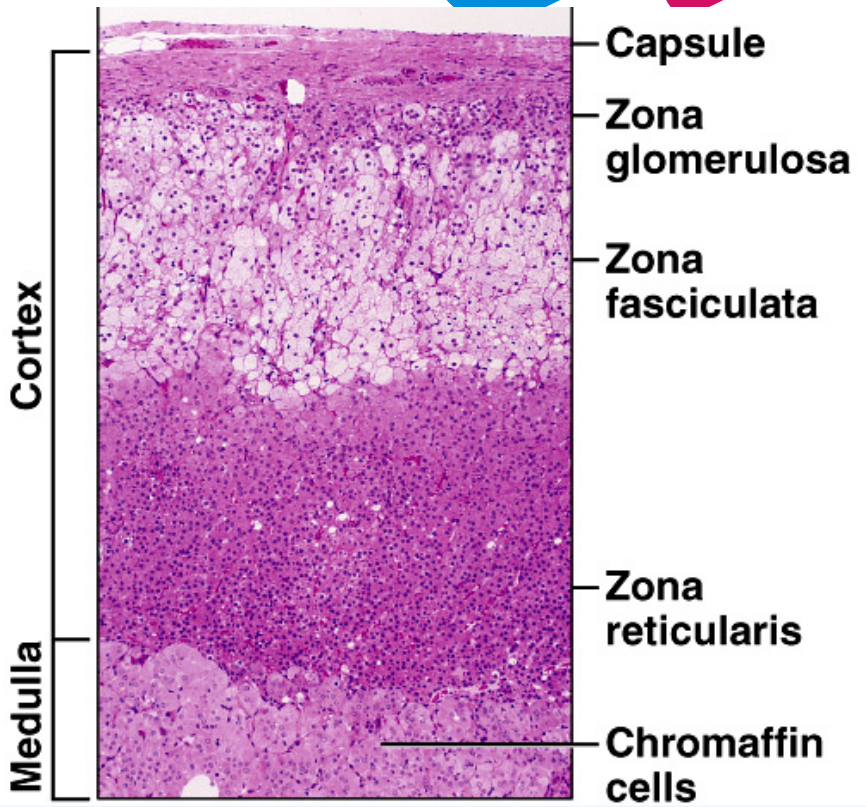
Histology

ADRENAL CORTEX

1) Zona glomerulosa: secretes the Aldosterone.
2) Zona fasciculata: secretes glucocorticoids (cortisol).
3) Zona reticularis: secrete androgenic steroid.

ADRENAL MEDULLA

- its cells are called **chromaffin cells**
- secrete the catecholamines: Adrenaline (epinephrine), Noradrenaline (norepinephrine) and dopamine.



PHYSIOLOGY OF THE ADRENAL CORTEX

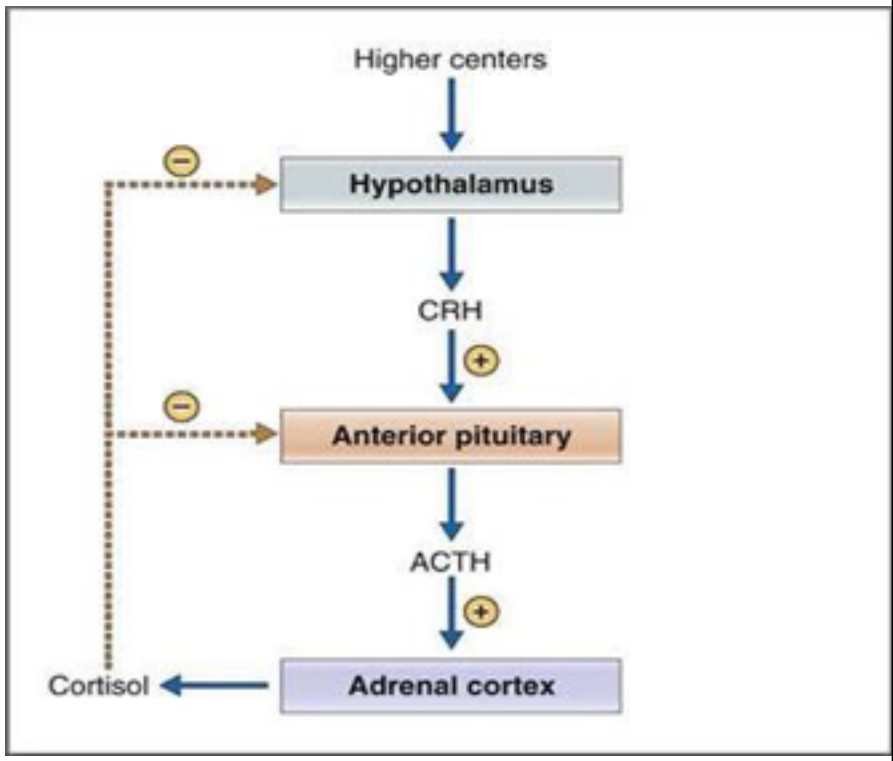
- The zona glomerulosa cells produce the hormone aldosterone. Aldosterone increases the blood pressure by promoting sodium and water retention in the kidneys. It also promotes potassium loss at the same site.

- The two well-known stimulators of aldosterone secretion are **angiotensin II** (released by activation of the renin-angiotensin system after hyponatremia or hypovolemia) and an **increase in the level of serum potassium** (hyperkalemia).

PHYSIOLOGY OF THE ADRENAL CORTEX cont..

- Cells of the **zona fasciculata** and **zona reticularis** synthesize cortisol and the adrenal androgens.

- Cortisol secretion is regulated by **adrenocorticotrophic hormone** (ACTH), which is produced by the anterior pituitary gland. The hypothalamus controls ACTH secretion by secreting corticotropin-releasing hormone (CRH). The cortisol level inhibits the release of CRH and ACTH via a closed-loop system



Cushing's syndrome

(Hypercortisolism : Excessive cortisol production)

Safaa Matar

Etiology of Cushing's syndrome

A) **Exogenous (**Iatrogenically by Excessive or prolonged administration of cortisol-like drugs (steroid)**)**

B) **Endogenous**

1) ACTH dependent :

- Pituitary Adenoma (Cushing disease)
- Ectopic ACTH secretion tumors (small cell lung cancer)

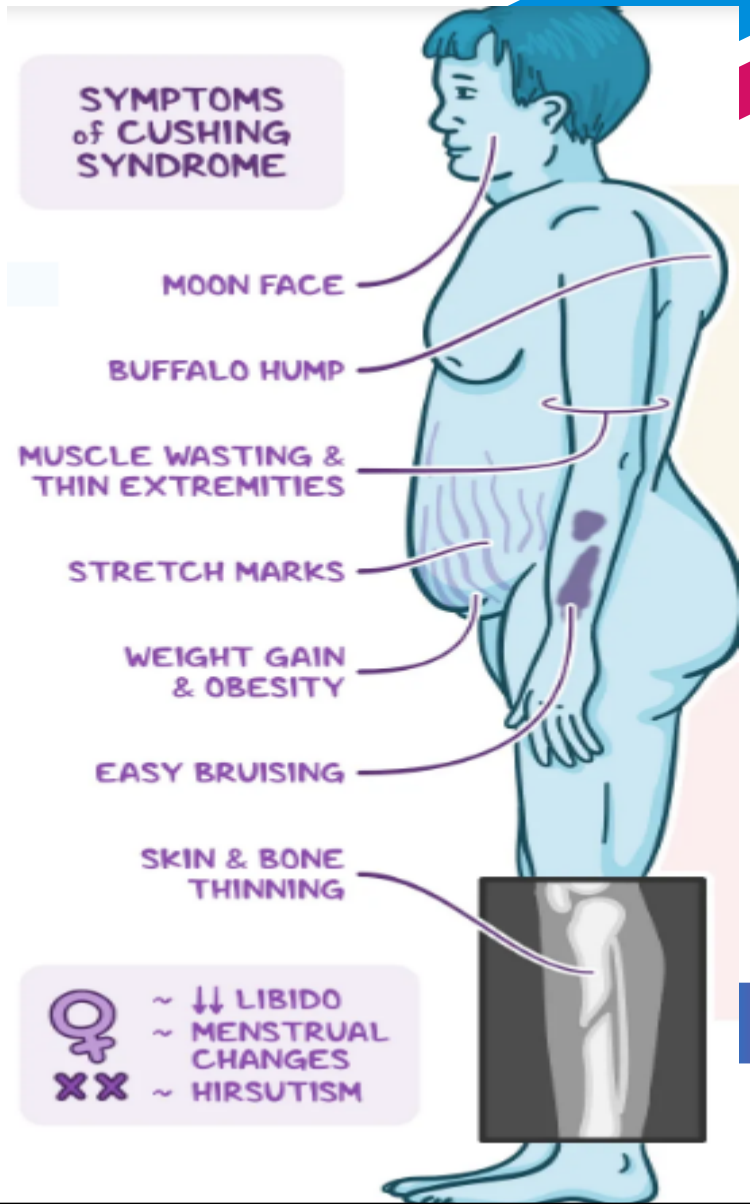
2) ACTH independent :

- Adrenocortical Adenoma
- Adrenocortical Carcinoma
- Bilateral Hyperplasia

Clinical features of Cushing's syndrome

Clinical features of Cushing's syndrome

- Weight gain/central obesity
- Diabetes
- Hirsutism
- Hypertension
- Skin changes (abdominal striae, facial plethora, ecchymosis, acne)
- Muscle weakness
- Menstrual irregularity/impotence
- Depression/mania
- Osteoporosis
- Hypokalaemia



Diagnosis

1) 24_hr urine cortisol level (is raised).
2) Low dose dexamethasone suppression test.
3) Serum ACTH levels.
4) MRI / CT scan

Diagnosis

- Serum ACTH levels (to discriminate ACTH-dependent from ACTH-independent disease).
- Patients with elevated ACTH levels **(ACTH-dependent):**

  - **MRI** of the pituitary gland must be performed

    - If pituitary MRI +ve → **Pituitary adenoma**

    - If pituitary MRI –ve → a CT scan of the chest and abdomen is warranted to detect an **ectopic ACTH producing tumor** .

- Patients with suppressed ACTH levels **(ACTH-independent):**

  - Abdominal CT or MRI scan is performed to assess the adrenal glands .

Treatment

1) Exogenous Cushing's syndrome

- Lowering dose of glucocorticoids

2) Endogenous Cushing's syndrome

- if surgery is possible:
  - ACTH-dependent
  - ACTH-producing pituitary adenoma are treated by trans-sphenoidal resection or radiotherapy.

Treatment

- If an ectopic ACTH source is localized, **resection** will correct hypercortisolism.

- **ACTH-independent:**

- A unilateral adenoma → adrenalectomy .
- A Bilateral adenoma → bilateral adrenalectomy is the primary treatment.

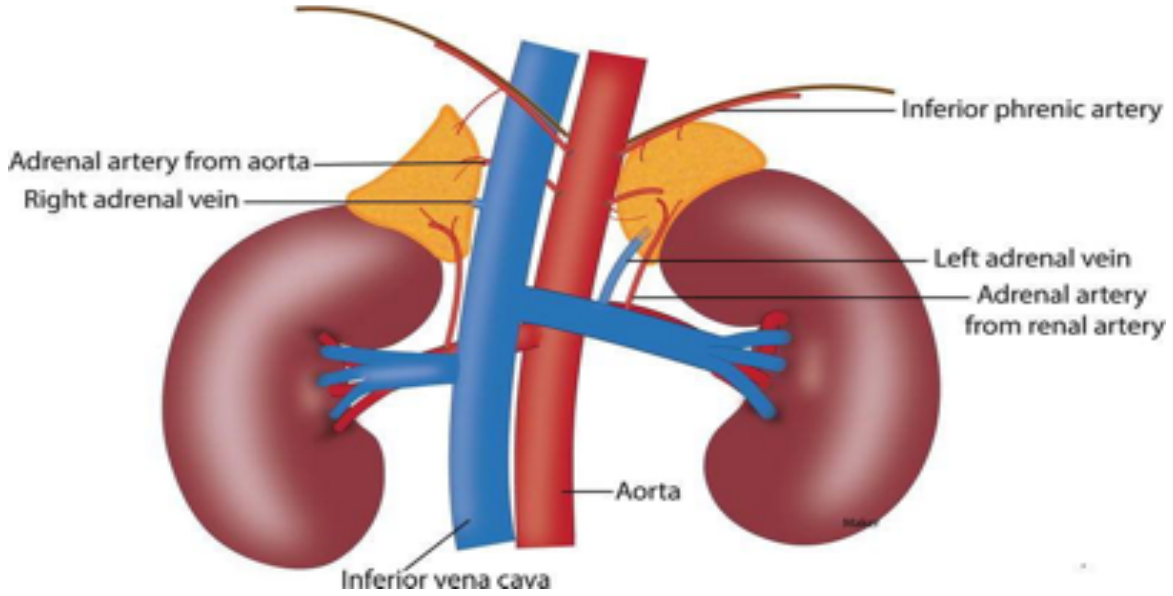
If surgery is not possible: Medical therapy with metyrapone or ketoconazole (drugs that reduce steroid synthesis and secretion) can be used

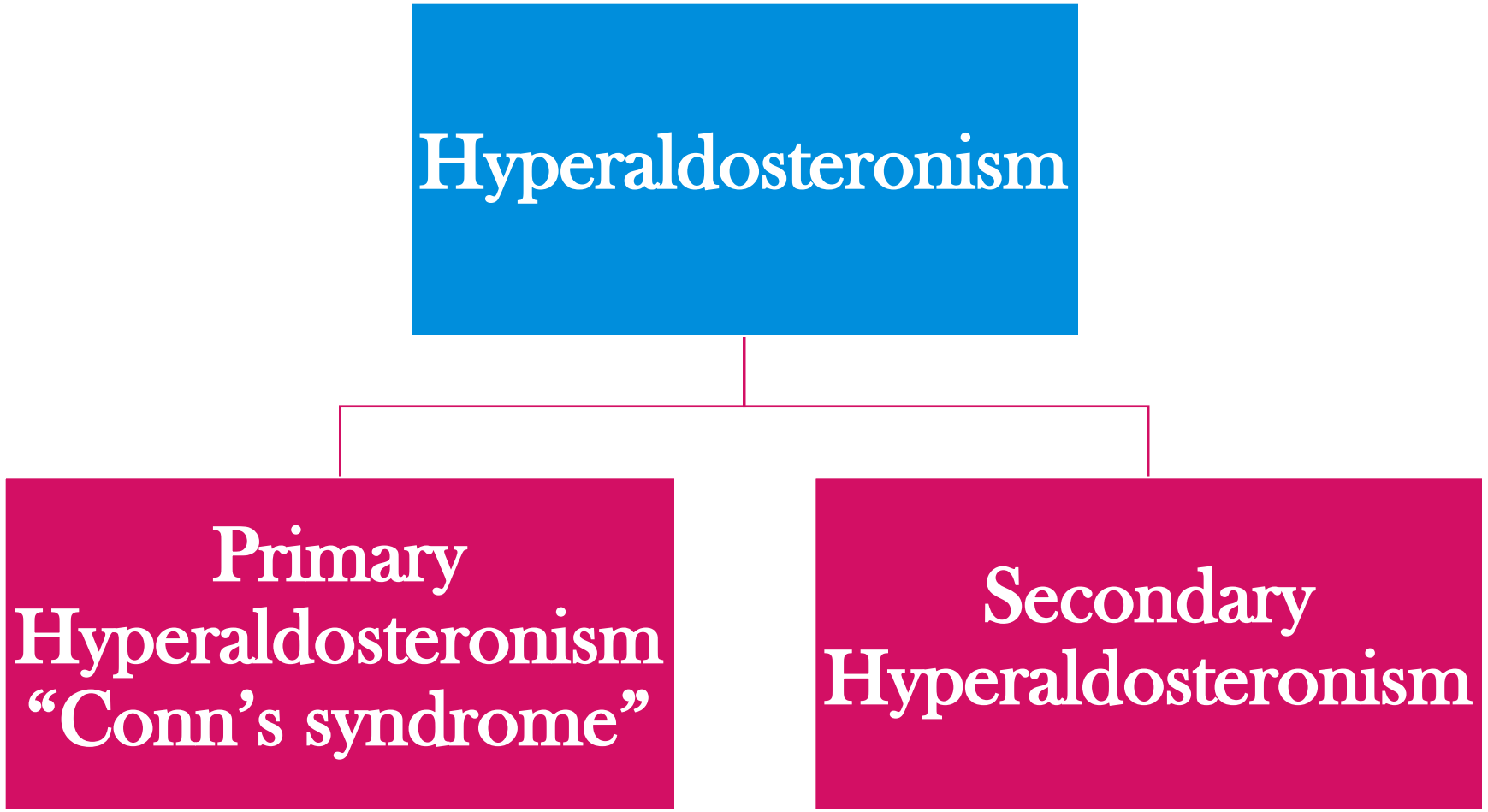
Hyperaldosteronism

Done by :
Kareem Al-Sinnawi

Definition

Hyperaldosteronism is a disease caused by Excessive levels of aldosterone which causes sodium retention and potassium excretion with resultant hypertension and hypokalemia.

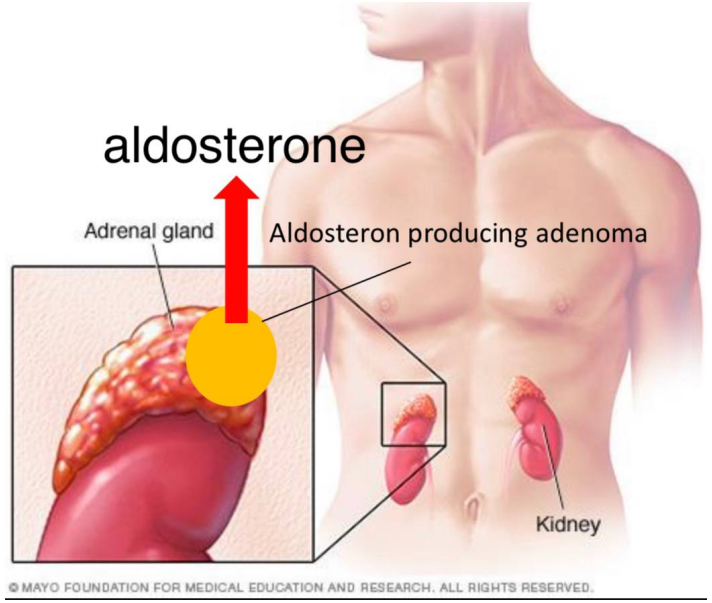



Hyperaldosteronism
Primary Hyperaldosteronism "Conn's syndrome"
Secondary Hyperaldosteronism

Primary hyperaldosteronisms (Conn syndrome)

- Caused by a problem within the adrenal glands
- The main causes are :
    1- **Tumor** (adenoma) the most common; 80% of the cases.
    2- **Primary Adrenocortical hyperplasia**.15% of the cases.
    3- **Carcinoma**.

Conn syndrome occurs most frequently in middle adult life, and is more common in females than males (2:1)



Secondary Hyperaldosteronism

- In which aldosterone release occurs in response to activation of the rennin-angiotensin system, and it's characterized by increased levels of plasma rennin and is encountered in conditions associated with:-
  1. **Decreased renal perfusion** (renal artery stenosis)
  2. **Arterial hypovolemia and edema** (congestive heart failure, cirrhosis, nephritic syndrome)
  3. **Pregnancy** (caused by estrogen-induced increases in plasma renin)

As we said, The most common cause of Hyperaldosteronsim is **aldosterone-secreting adenoma**, and mostly it's a benign adenoma causing hypertension and Hypokalemia.

We know that hypertension mainly occurs in elderly and people with atherosclerosis, So if a 30-year-old patient comes to you with hypertension you should look for possible primary cause of this hypertension.

5-18% of these patients (Young and Hypertensive) are due to **Hyperaldosteronism, making it the leading cause for secondary Hypertension**

Pathophysiology and clinical presentation

❖ Pathophysiology:-

Aldosterone Functions:-

- ✓ Promotes sodium absorption and secretion.
- ✓ Promotes water retention.
- ✓ Increase potassium secretion.

❖ Clinical presentations:-

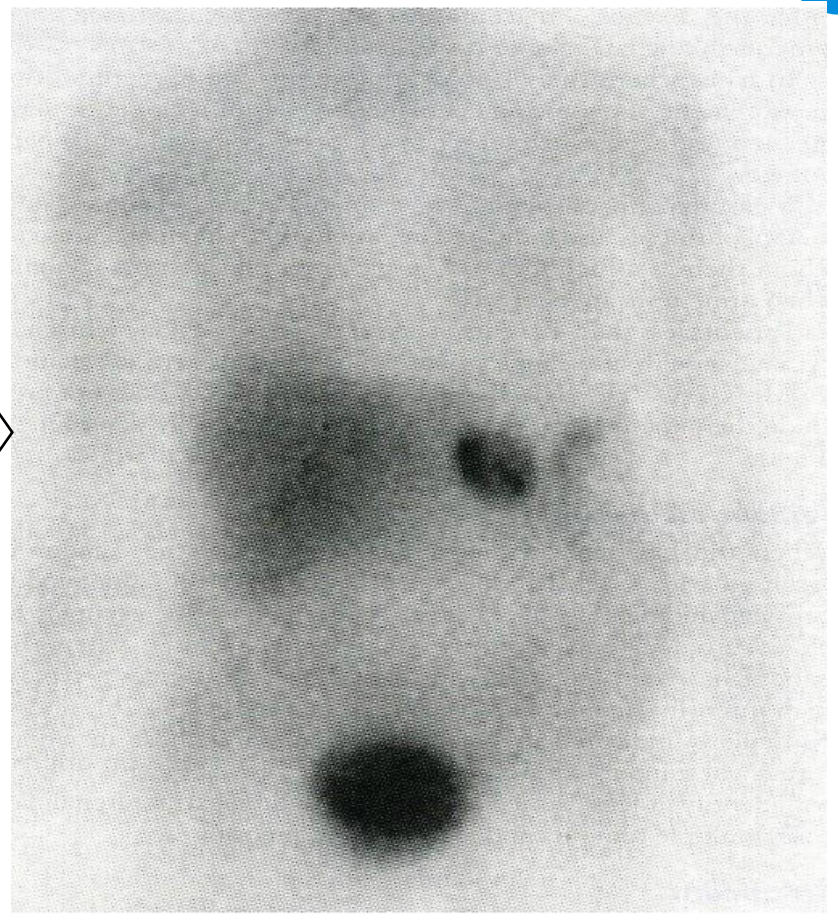
- Moderate to severe hypertension.
- Hypokalemia.
- Hypernatremia.
- Muscle weakness.
- Malaise.
- Polyurea.
- polydypsia.

Investigations

- **Blood** : Hypokalemia
- **Plasma** aldosterone and you will find it persistently high.
- **Urine** : Increase urinary potassium
- **Imaging for diagnosis:**
  - ✓ US.
  - ✓ CT.
  - ✓ MRI.
  - ✓ Iodo-cholestrol isotope scan, to see where is the site of hyperfuctioning.

Isotope scan for adrenal adenoma

This patient is having **Conn`s syndrome due to adenoma**. This patient was given isotope scan and we can clearly see the side which there is hyperfunctioning, the left side, also some of this isotope will go to the urinary bladder and some will go the reticuloendothelial system" the liver contains the largest RES", so we can see the liver and urinary bladder.



Treatment

- Conn`s disease is not a killing disease, usually the hypertension is mild and usually if you give the patient **spironolactone** (potassium sparing diuretics), he will improve; But because of the improvement in the surgical technique such as laparoscope, you can go and remove the adenoma with minimal incidence of mortality.
- Also by **Adrenalectomy**; if the cause was adenoma, then we do unilateral adrenalectomy (laparoscopic), if the cause was unilateral hyperplasia, then we do unilateral adrenalectomy (laparoscopic).

Incidentaloma

Disorders of the adrenal cortex

Raghad Amr

Definition and incidence

- **Incidentaloma:** is an adrenal mass, detected incidentally by imaging studies conducted for other reasons, not known previously to have been present or causing symptoms.
- The **prevalence of adrenal masses in autopsy** studies ranges from **1.4 to 8.7 per cent** and increases with age.
- Incidentalomas may be detected on imaging studies in 1% of patients.
- **More than 75% of masses are non-functioning adenomas**. but Cushing's adenomas, phaeochromocytomas, metastases, adrenocortical carcinomas and Conn's tumors may be present .

Tumour	Prevalence (%)
Non-functioning adenoma	78
Cushing's adenoma	7
Adrenocortical carcinoma	4
Phaeochromocytoma	4
Myelolipoma	2
Cyst	2
Metastases	2
Conn's adenoma	1

Diagnosis

- When an incidentaloma is identified, a **complete history and clinical examination are required**.
- The main goal is to *exclude* a **functioning** or a **malignant** adrenal tumor.
- A **biochemical work-up for hormone excess** is needed and sometimes **additional imaging studies** are also required.

Hormonal evaluation

- Morning and midnight **plasma cortisol** measurements.
- 1-mg overnight **dexamethasone suppression test**
- 24-hour **urinary cortisol excretion**

→ To exclude Cushing

- 12 or 24-hour **urinary excretion of metanephrines** or **plasma free metanephrines**

→ To exclude pheochromocytoma

- Serum **potassium, plasma aldosterone and plasma renin** activity
- Serum **DHEAS**, **testosterone or 17-hydroxyestradiol** (virilising or feminising tumour).

Further investigations

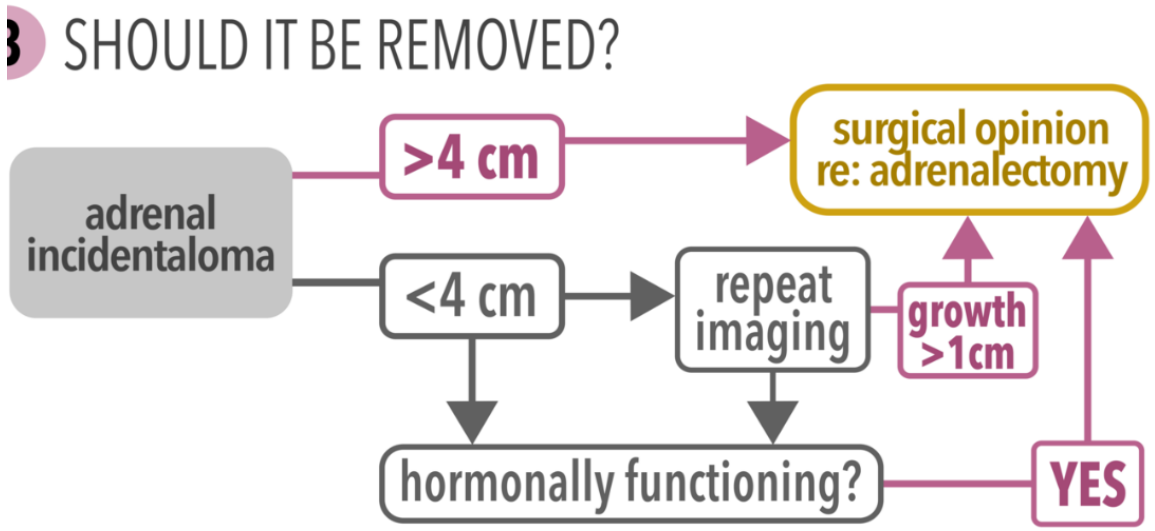
- **Imaging studies** that are done for diagnosis of incidentaloma: Computed tomography (***CT***) or magnetic resonance imaging (***MRI***) should be performed in all patients with adrenal masses.
- The likelihood of an adrenal mass being an adrenocortical carcinoma increases with the size of the mass (25 per cent >4 cm).

- **Biopsy**: only indication is to confirm adrenal metastasis from a distant primary site (Never biopsy until pheochromocytoma is biochemically excluded)
- Adrenal metastases are likely in patients with a history of cancer elsewhere

Treatment

- Any non-functioning adrenal **tumor greater than 4 cm** in diameter and **smaller tumors that increase in size** over time should undergo surgical resection.

- Non-functioning tumours **smaller than 4 cm** should be **followed-up after 6, 12 and 24 months by imaging (MRI) and hormonal evaluation.**



Adrenocortical carcinoma

Ibraheem Alkhawaldeh

Introduction and epidemiology

- **Adrenocortical carcinomas** (ACs) are uncommon malignancies that can have protean clinical manifestations (variable presentations).
- A majority of cases are metastatic at the time of diagnosis, with the most common sites of spread being the local periadrenal tissue, lymph nodes, lungs, liver, and bone.

- Adrenocortical carcinoma is a rare malignancy with an incidence of population per year and **a1–2 cases per 1 000 000** riable but generally poor prognosis.
- A slight **female** predominance is observed (**1.5:1**).
- The age distribution is **bimodal** with a first peak in **childhood** and a second between the **fourth and fifth decades**

Pathology

- **Criteria for malignancy are:**
- **Preoperatively**

    1. tumor size and Hounsfield units, Urine metabolomics

- **Post operatively**

    2. presence of necrosis or hemorrhage

    3. microscopic features such as capsular or vascular invasion (Weiss ,Helsinki histopathological criteria)

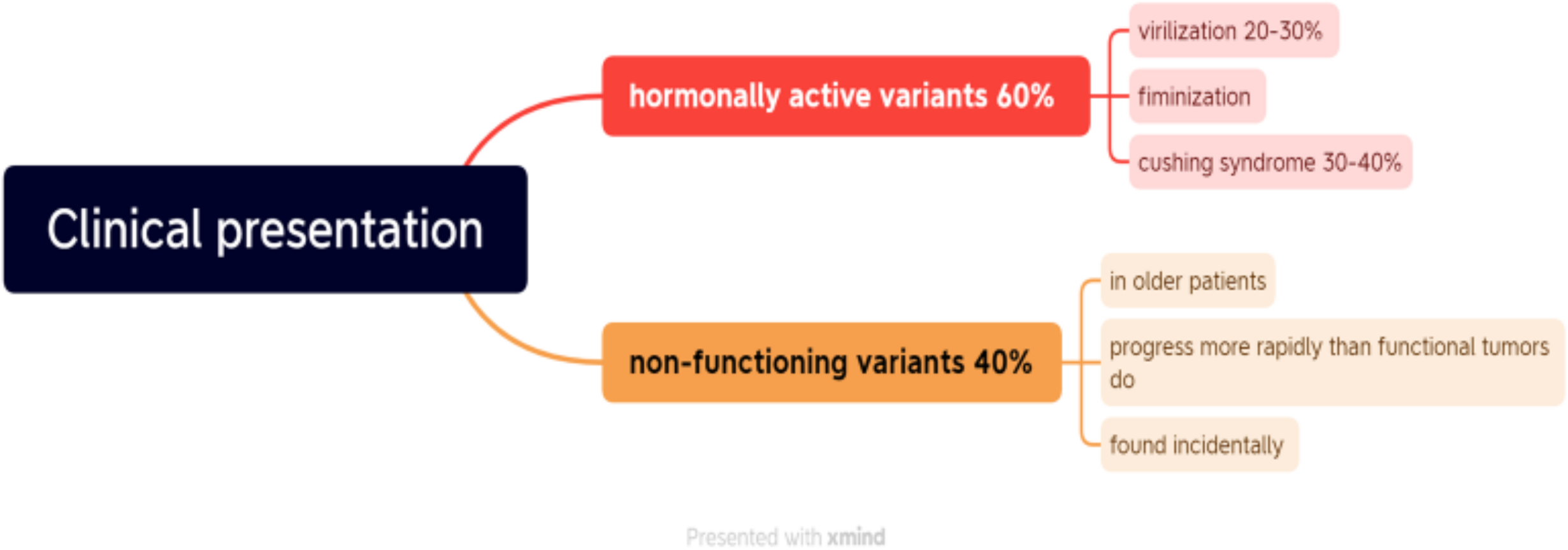
- Emerging pre-operative noninvasive markers :
    - Methylome
    - Liquid biopsy
    - Markers ,ex igf2 with ki67 index

Clinical Characteristics

Functional Breakdown of Adrenal Cortical Carcinomas

Nonfunctional	21%-50%
Functional	50%-79%
Cushing syndrome	33%-53%
Cushing syndrome + virilization	20%-24%
Virilization alone	10%-20%
Feminization	6%-10%
Hyperaldosteronism	2.5%-5%

most common hormone secreted by adrenal cortical carcinoma is cortisol


Clinical presentation
hormonally active variants 60%
virilization 20-30%
fiminization
cushing syndrome 30-40%
non-functioning variants 40%
in older patients
progress more rapidly than functional tumors do
found incidentally
Presented with xmind

1. Nonfunctioning variants

- These hormonally silent tumors account for approximately **40%** of patients with AC.
- Nonfunctional variants of AC tend to be more common in **older patients** and appear to **progress more rapidly** than functional tumors do.
- In some cases they are found **incidentally** (incedentaloma).

- Typically present with any of the following:

- Abdominal pain and tenderness
- Fever
- Weight loss
- Back pain
- Abdominal fullness

2. Hormonally active variants

- The hormonally active variants of AC constitute approximately **60**% of cases.
- Approximately 30-40% of adult patients with these present with the typical features of Cushing syndrome, while 20-30% present with virilization syndromes.
- **Signs of Cushing syndrome** include a round face, a double chin, buffalo-hump fat distribution, generalized obesity, failure of growth velocity, and hypertension.

Virilization

- Finding in **males** include: premature puberty with enlargement of the penis and scrotum, pubic hair, acne, and deepening voice.

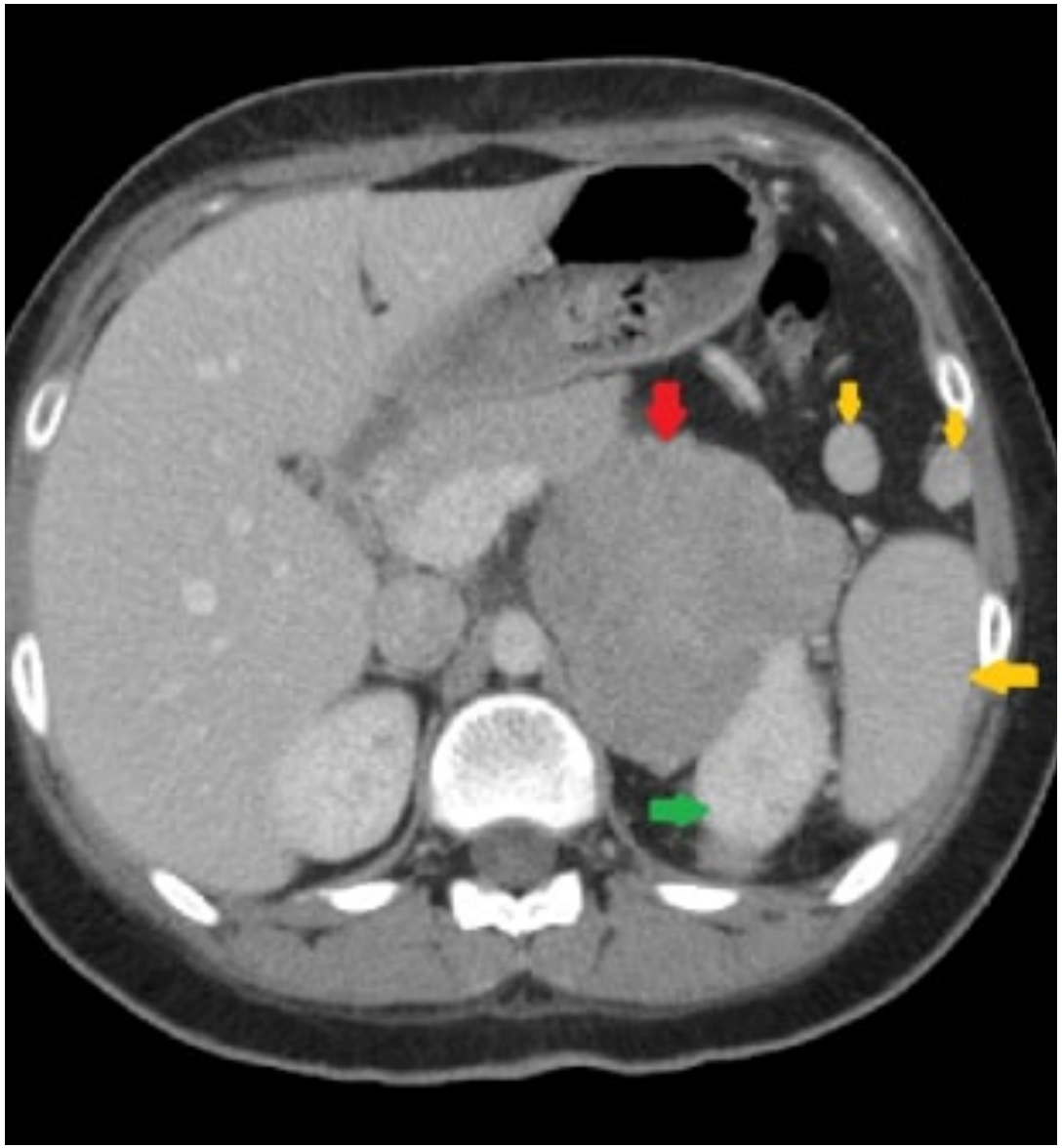
- Finding in **females** include: premature appearance of pubic and axillary hair, clitoral hypertrophy, acne, deepening voice, premature increase in growth velocity, lack of appropriate breast development, and lack of menarche.

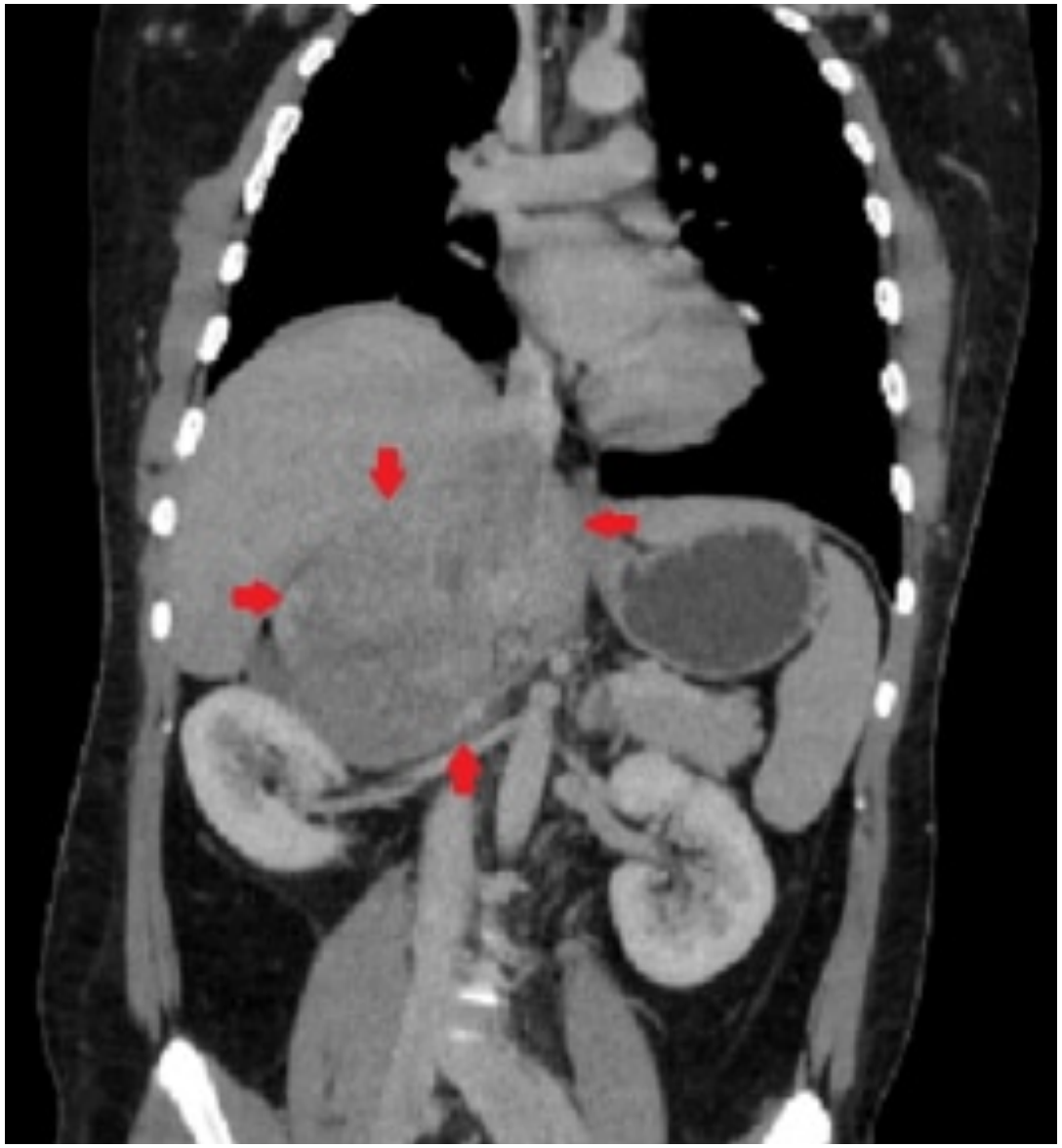
Feminization

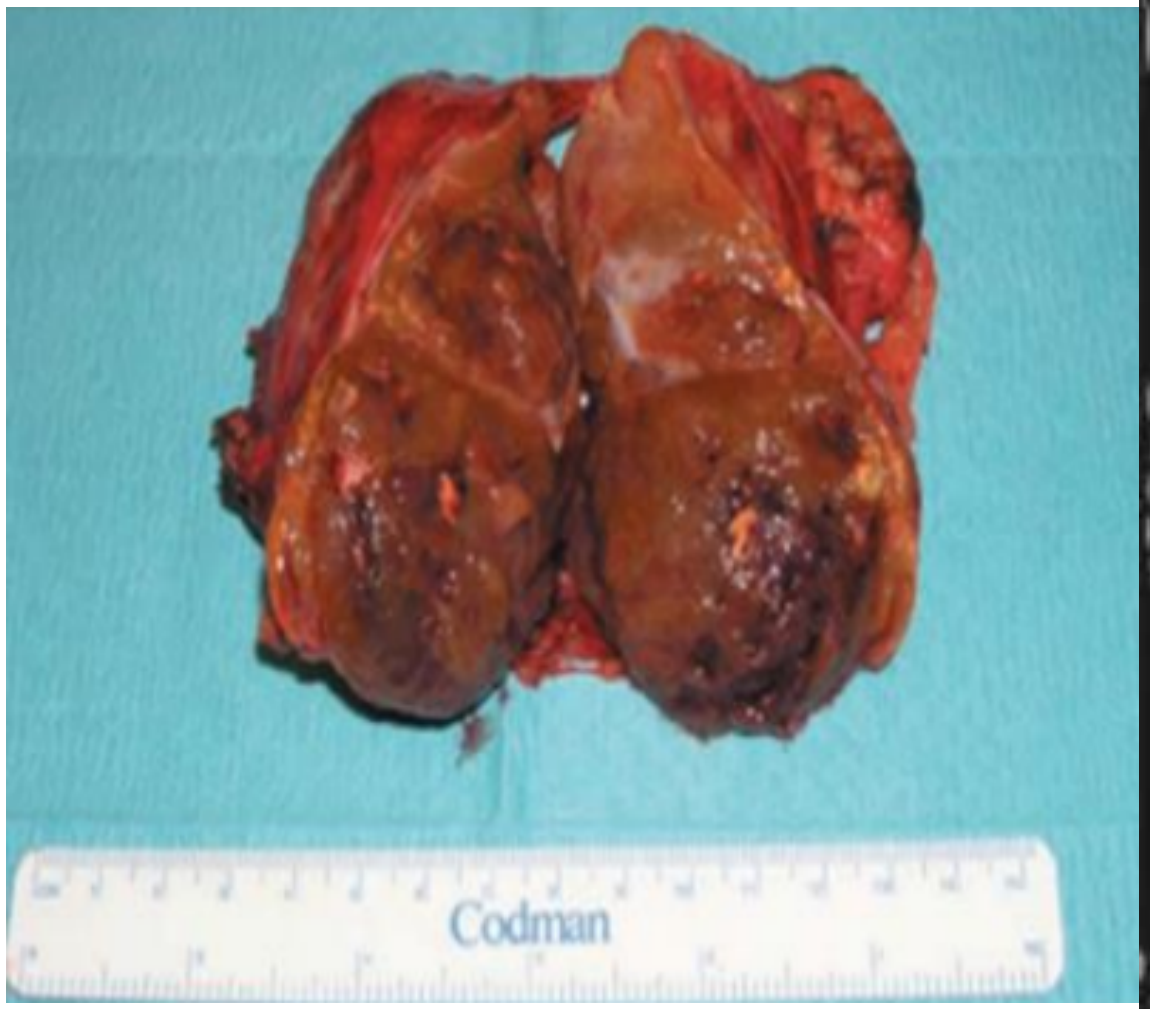
- In rare cases, feminization may occur. Findings in male patients include gynecomastia and hypertension. Findings in female patients include precocious sexual development and hypertension

- **Common radiographic characteristic of ACC on CT imaging include**
  - the presence of irregular borders,
  - irregular enhancement,
  - calcifications
  - Necrotic areas with cystic degeneration.
- Evaluation of spread/mets
  - IVC, Adjacent organs, Liver ,lungs, Bones

- The diagnostic work-up should include measurements of **DHEAS, cortisol and catecholamines to exclude phaeochromocytoma** and a **dexamethasone suppression test**.
- **MRI and CT** are equally effective in imaging adrenocortical carcinoma



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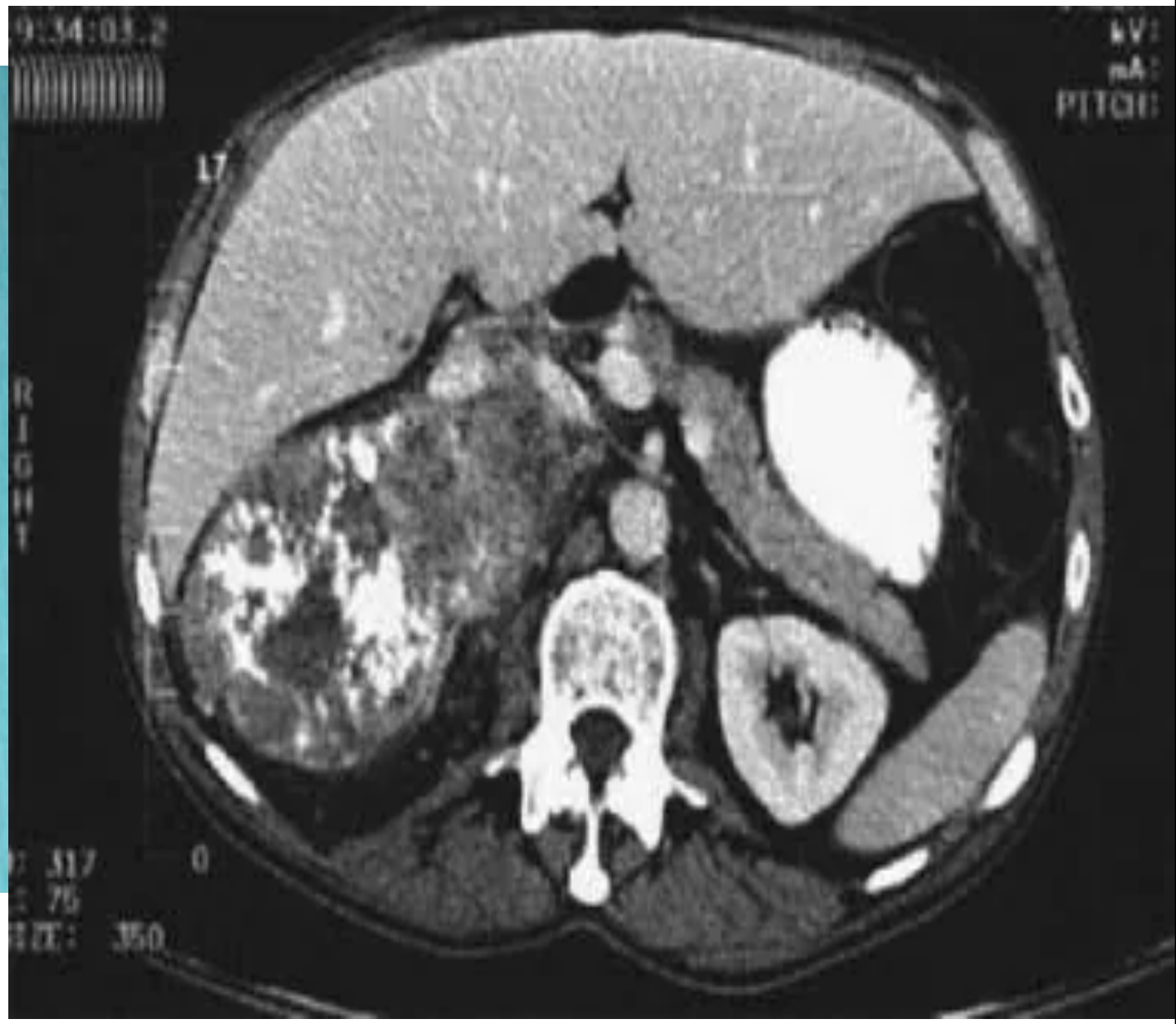
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Adrenal cancer TNM staging

Stage	Description
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤5 cm in greatest dimension limited to the adrenals
T2	Tumor >5 cm in greatest dimension, limited to the adrenals
T3	Tumor of any size with local invasion, but not invading adjacent organs
T4	Tumor of any size with invasion of adjacent organs

Regional Lymph Nodes (N)

Stage	Description
NX	Regional lymph node cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

Distant Metastasis (M)

Stage	Description
M0	No distant metastasis
M1	Distant metastasis

Anatomic Stage/Prognostic Groups

Stage	T	N	M
I	T1	N0	M0
II	T2	N0	M0
III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
IV	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
	Any T	Any N	M1

A new study showed staging system that incorporates the patient's age better and predicts 5-year survival among patients with stages I/II ACC. Consideration should be given to include age in staging for ACC, because it may better inform providers about treatment and prognosis.[4]

Treatment

- Complete tumor resection is associated with favorable survival and should be attempted whenever possible.
- In order to prevent tumor spillage and implantation metastases, the capsule must not be damaged.
- **En bloc resection** with removal of locally involved organs is often required.
- In case of metastatic adrenal carcinoma:
- **Cystoreductive removal** of the primary tumor **and debulking metastatectomy** (alleviate tumor side effects).
- Patients can be treated postoperatively with **mitotane** (adjuvant chemotherapy). Adjuvant radiotherapy may reduce the rate of local recurrence.
- **Radiation** has a **limited role**, but it remain the treatment of choice in **bone and CNS metastasis**, and it **decreases local recurrence rate following complete resection** .

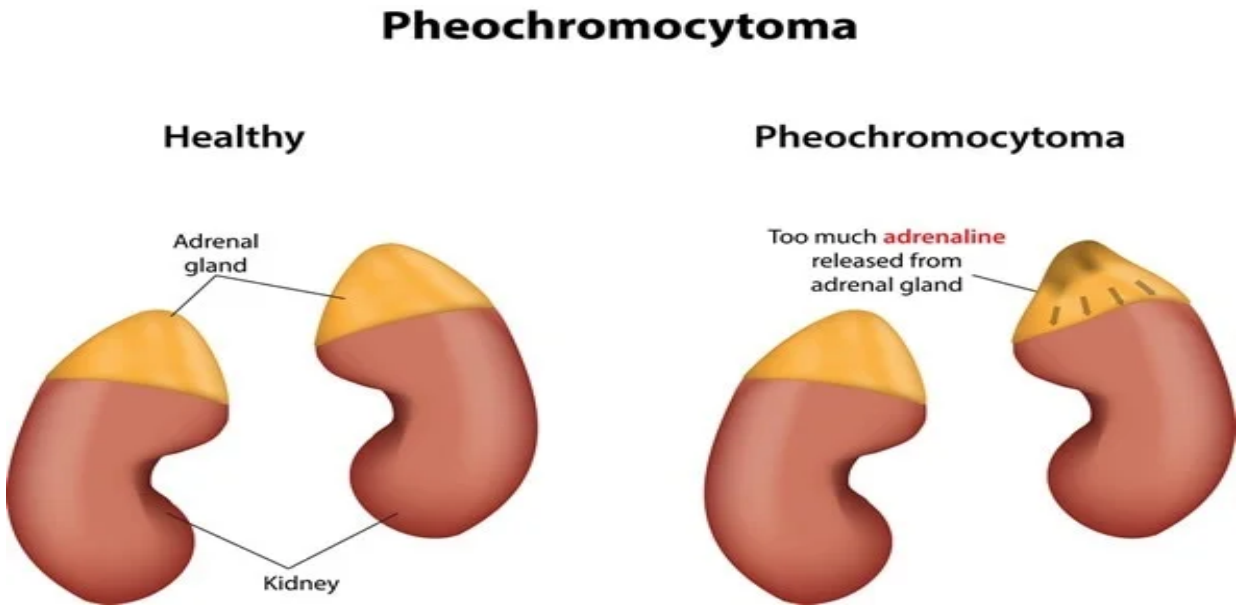
Follow up

- Follow-up should include CT examination of the chest, abdomen, and pelvis every 3 months for the first 2 years.
- In patients with evidence of functional tumors, measurement of the initially elevated hormones postoperatively may help to reveal early disease recurrence despite negative radiographic studies.

Prognosis

- **Overall 5-year survival in adrenal cortical carcinomas** is poor, ranging from 20% to 47%.

Pheochromocytoma



Rana Aqaileh

Definition and causes

- **Pheochromocytoma** :is a rare, benign tumor of the adrenal *medulla* that arise from chromaffin cells (secreting catecholamine).
- *Causes:*
  - Most of the cases are **sporadic**
  - **multiple endocrine neoplasia (MEN)** including **type 2A and type 2B (RET mutation** /protoncogen)
  - **Von Hippel-Lindan disease (VHL mutation)**/tumor suppressor gene
  - **Neurofibromatomosis type 1 (NF1 mutation)**/tumor suppressor gene

Pathophysiology

- Under **normal** conditions, the medulla releases **norepinephrine and epinephrine** (fight or flight response) as a response to stress.

- In such disease, there will be **increase in catecholamines(E,NE)** → smooth muscle **contraction** → and increase in **peripheral vascular resistance leading to** ***HYPERTENSION***

- Notes: the prevalence of pheochromocytoma in patients with hypertension is 0.1–0.6 per cent with an overall prevalence.
- **Due to the variation in catecholamine secretion,** hypertension is considered *EPISODIC in adults*

Pathophysiology

- Type of receptor Action

I. A1 **Vasoconstriction** and smooth muscle contraction

II. B1 Increase CO,HR

III. B2 Smooth muscle relaxation (Respiratory)

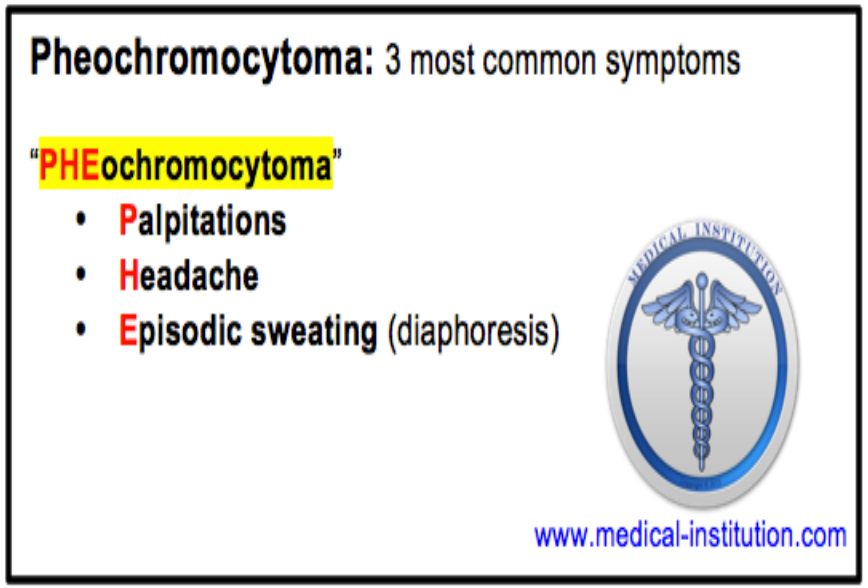
The 10 percent tumor of the rule 10

- 10% extraadrenal
- 10% bilateral
- 10% Familial
- 10% children
- 10% malignant
- 10% associated with MEN
- 10% present with a stroke

Signs and symptoms

The classic triad

1. Episodic pounding headache
2. Palpitations and tachycardia
3. Diaphoresis (increase sweating)



TRIGGERS of symptoms

Stress ,exertions ,anesthesia and certain drugs like TCA

Signs and symptoms

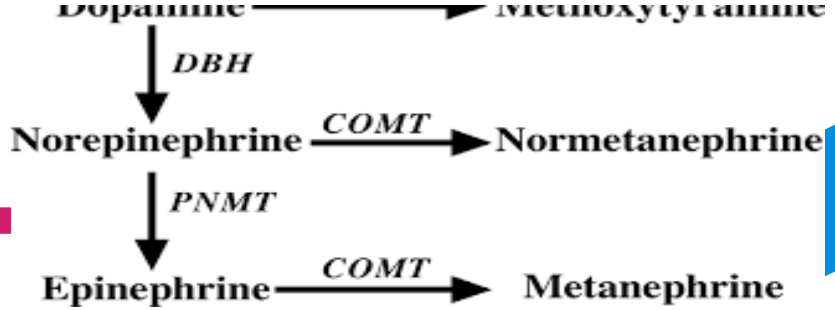
- Less common symptoms

a. Wight loss
b. Constipation
c. Polyuria and polydipsia
d. Papilledema
e. Hyperglycemia and insulin resistance

Investigations

- 24-hour **urine** samples for catecholamines and their metabolites
- **Plasma metanephrine** levels
- **Urinary** metanephrines are highly sensitive & specific, whereas **VMA** measurements are slightly less in so > False positive VMA tests may result from ingestion of caffeine, raw fruits, or medications like methyldopa.
- Fractionated **urinary** catecholamines also are very sensitive but less specific for pheochromocytomas.

Diagnosis



- **Biochemical tests**

- .the determination of adrenaline and noradrenaline breakdown products, **metanephrine and normetanephrine level**, in ***a 12- or 24-hour urine collection***. Levels that exceed the normal range (meta 24-96 mcg/24h and normeta 75-375 mcg/24h) by 4–40 times will be found in affected patients .

- •Determination of ***plasma-free metanephrine levels*** also has a high sensitivity .

- •Biochemical tests should be performed at least twice.

- 2. **The localization of pheochromocytoma** : MRI is preferred because contrast media used for CT scans can provoke paroxysms

Treatment

Surgical Resection

• **Preoperative** alpha-adrenergic blockade, THEN beta-adrenergic blockade•

Alpha-adrenergic blockade

10_14 days before surgery•

Phenoxybenzamine

• Daily BP monitoring

• High Sodium Diet (>5g/day) - 2nd-3rd day of alpha blockade

• Long-term alpha-adrenergic blockadeOH

• Prazosin, terazosin, doxazosin•

IV Phentolamine

Beta-adrenergic blockade

• Propanolol (1st day), switch to long-acting

Pheochromocytoma in pregnancy

- With mother and unborn child are threatened by hypertensive crisis ** during delivery.

❖ In the first and second trimesters, the patient should be scheduled for **laparoscopic adrenalectomy** after adequate **α-blockade**; the risk of a miscarriage during surgery is high.

❖ In the third trimester, elective **Caesarean** with consecutive **adrenalectomy** should be performed.

❖ The maternal mortality rate is 50 per cent when a pheochromocytoma remains undiagnosed.

Malignant pheochromocytoma

- Approximately 10 per cent of pheochromocytoma are malignant. This rate is higher in extra-adrenal tumors (paragangliomas).

- Treatment: **Surgical** excision is the only chance for cure.

Summary

- A pheochromocytoma is a catecholamine-secreting tumor that typically develops in the adrenal medulla

- *. Pheochromocytomas are usually benign (~ 90% of cases) but may also be malignant. Classic clinical features are due to excess sympathetic nervous system stimulation and involve episodic blood pressure crises with paroxysmal headaches, diaphoresis, heart palpitations, and pallor.*

- *However, pheochromocytomas may also be asymptomatic or manifest with persistent hypertension.*

- Elevated catecholamine metabolites in the plasma or urine confirm the diagnosis, while imaging studies in patients with positive biochemistry are used to determine the location of the tumor. Surgical resection is the treatment of choice but is only carried out once alpha-adrenergic blockade with phenoxybenzamine has become effective