430 SURGERY TEAM

DISEASES OF THE ADRENALS

MAYSOON ALHAIZAN

MOHAMMED ALRASHEED

Green: Doctor's notes & explanation during the lecture.
Blue: Further explanation & team's notes.
Red: important notes.

ADRENAL GLANDS

HISTORY

1563: Anatomy
1855: Addison described clinical features of the syndrome named after him (Addisonial crisis)
1912: Cushing described hypercortisolism
1934: The role of adrenal tumors in hypercortisolism understood
1955: Pheochromocytoma was first described by Frankel
2003:The first robotic adrenalectomy

EMBRYOLOGY

Paired gland

- **Cortex (coelomic epithelium)**

Zonaglomerulosa→Mineralocorticoids
Zonafasciculate→Glucocorticoids
Zonareticularis→Sex hormones

- **Medulla (ectoderm: neural crest)**

ECTOPIC TISSUES:

Very small and are of negligible importance, unless they grow bigger

Cortical ectopic tissue → abdominal
Medullary ectopic tissue → anywhere (chest, abdomen, pelvis)
That's why pheochromocytoma maybe thoracic in origin

ANATOMY

- The adrenals cannot be palpated normally, if it was palpable it's most likely cancer.
- **What is clipped in surgeries (adrenalectomy)is the veins**! Any tear may cause severe hemorrhage ..
- The adrenal vein returns the blood from the medullary venous plexus and receives branch from the cortex. It emerges from the hilum and on the **right side** and opens into the inferior vena cava, and on the **left side** into the renal vein.
- That's why the **right side** is shorter (more prone to bleed), while the **left side** is longer.
- When sampling the right adrenal we take from **Right adrenal vein** and for left adrenal we take from **Left renal vein**.

PHYSIOLOGY

- **Adrenal cortex:**

1. Aldosterone (Aldosterone promotes sodium reabsorption and potassium excretion by the renal tubular epithelial cells of the collecting and distal tubules. As sodium is reabsorbed, water follows passively, leading to an increase in the extracellular fluid volume with little change in the plasma sodium concentration.)

2.Cortisol (1.Cortisol stimulates gluconeogenesis in the liver results is an increase in serum glucose and increased glycogen stores in the liver. 2.Cortisol decreases protein stores in the body, except in the liver, by inhibiting protein synthesis and stimulating catabolism of muscle protein. 3. Cortisol has anti-inflammatory effects, blocking the early stages of inflammation by stabilizing lysosomal membranes, preventing excessive release of proteolytic enzymes, decreasing capillary permeability and, consequently, edema, and decreasing chemotaxis of leukocytes. In addition, it induces rapid resolution of inflammation that is already in progress.)

3.Sexsteroids(play a role in early development of the male sex organs in childhood, and they have an important role in women during pubarche.)

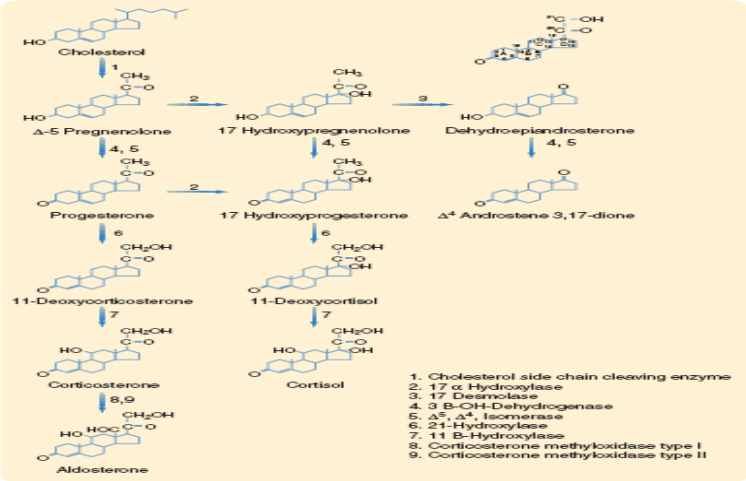
- **Adrenal medulla:**

1. Adrenaline (80%)
2. Noradrenaline (20%)

When performing adrenalectomy → Carefully remove all tissues around adrenal, without touching the gland, to prevent laceration or rupture of the gland which may cause huge secretion especially in pheochromocytoma which may cause severe hypertension .
also when pheochromocytoma is suspected we never do Fine Needle Aspiration (FNA) it will cause Hypertensive crisis with cardiac arrhythmia which will lead to cardiac arrest.

HORMONAL PATHWAY

The precursor for all hormones is cholesterol, a specific enzyme converts it to the appropriate hormone in each step and it is the limiting step, it differs from one hormone to another..



ADRENAL IMAGING

1. CT scan: benign and malignant? Gold standard imaging!

- **Benign**

- Intensity similar to liver(this indicates benign lesion)
- Low attenuation
- Homogeneous
- Smooth border
- Smooth contour No invasion of vascular structures.
- < 4 cm in greatest dimension (the first criteria to be checked and then the others, size should be less than 4)

- **Malignant**

- High attenuation (>30 HU)
- Heterogeneous
- Irregular borders
- Local/ vascular invasion
- Lymphadenopathy
- Metastases.
- Large size (>6cm) (black size 6cm-12cm →malignant .. remove it ,
  black size 2cm - 4cm → cyst)

2. MRI expensive
3. Nuclear scan function
4. PET scan

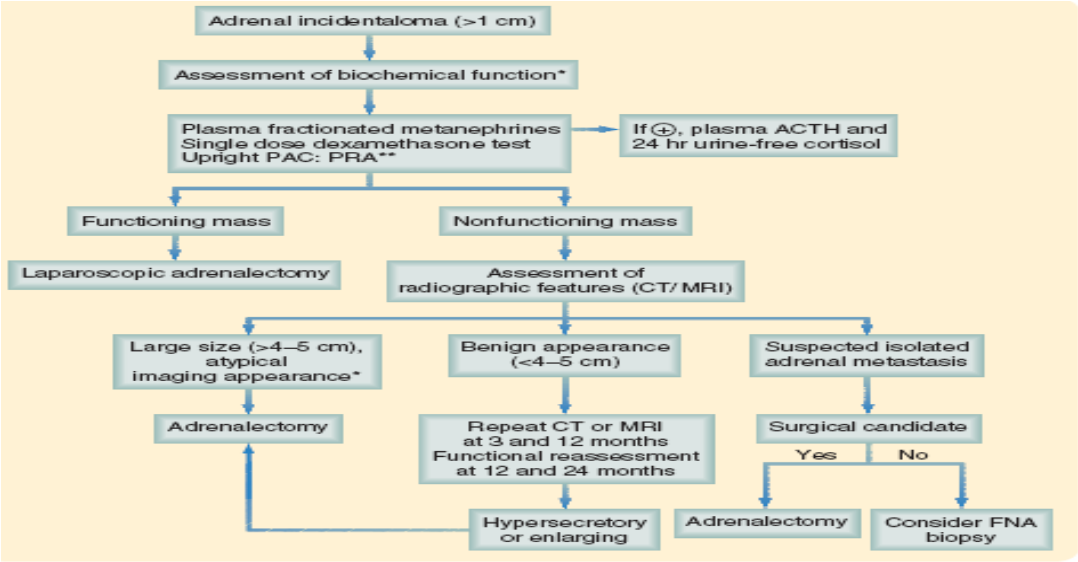
INCIDENTALOMA most common ! As the name suggests it is found accidentally.

- Found in 1-4 % of CT scans
- Increases with age
- Small nonfunctioning adrenal tumors
- Some withsubclinical secretions of hormones.
- Adrenocortical carcinoma
- Metastases

- Nonfunctioning adenoma 82%(small)
- Subclinical Cushing 5%
- Pheochromocytoma 5%
- Adrenocortical cancer 5%
- Metastatic carcinoma 2%
- Conn's 1%

* Then we assess the gland's function → Plasma fraction metanephrines single dose dexamethasone test upright PAC
Any functioning tumor →**Surgical removal**! But we never remove **bilateral tumors.**

CLINICAL PATHWAY

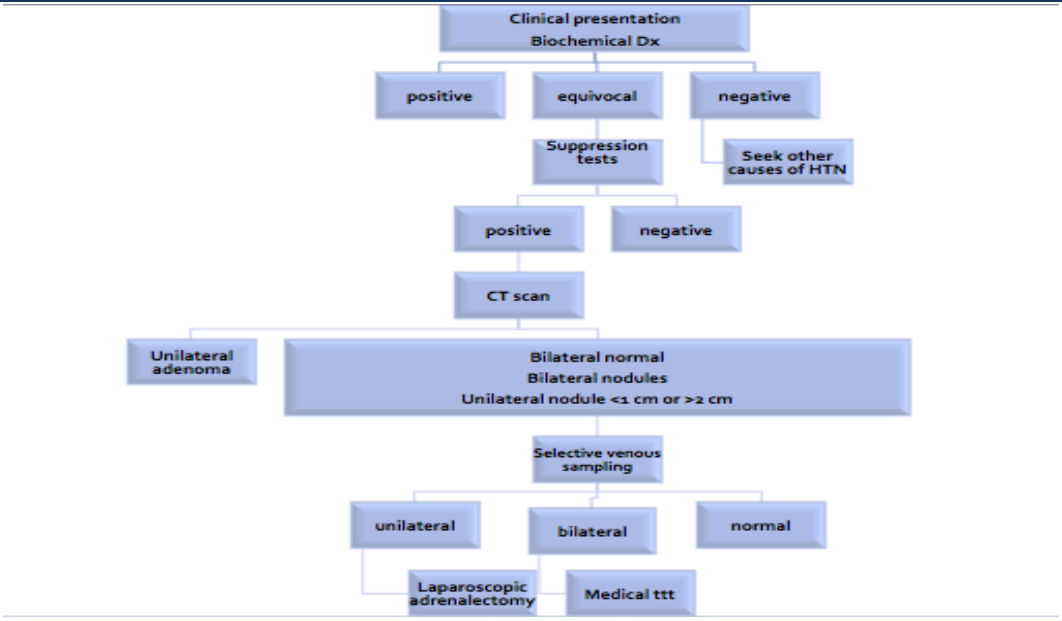


If functioning mass → Surgery.

If non-functioning mass → CT scan
CT may show:

- **Benign appearance (< 4 cm) you repeat the scan after 3-12 months.**
- **If it secretes or has a malignant appearance we perform surgery.**

Handled based on the Size and function.



DISEASES OF THE ADRENALS

1) HYPERALDOSTERONISM

Causes:

- **Primary** hypertension + metabolic alkalosis + with or without hypokalemia → primary hyperaldosteronism

- Adenoma (Most common)
- Idiopathic bilateral adrenal hyperplasia.
- Unilateral adrenal hyperplasia.
- Adrenocortical carcinoma.
- Familial (rare)

- **Secondary to** any decrease in renal perfusion → Causes secondary hyperaldosteronism

- Renal artery stenosis
- CHF
- Liver cirrhosis
- Pregnancy

Pathophysiology of high aldosterone:

Hypernatremia + hypokalemia→ water retention → ECF volume expansion & HTN Hypokalemia →muscle weakness Acid excretion → metabolic alkalosis

PRIMARY HYPERALDOSTERONISM

Age 30-50 years (middle age group)
Female > male, 2:1 (in all endocrine diseases and cancers, females are more prone. **Except** in cortical carcinoma males are more prone)
Prevalence 5-13%

- hypertension with or without hypokalemia
- Weakness, polyuria, paresthesias, tetany, cramps
- Metabolicalkalosis, relative hypernatremia
- Elevated aldosterone secretion and suppressed plasmarenin activity

Not all symptoms may appear .. these are collected symptoms

- **DIAGNOSIS**
- **Screening tests:** as outpatients
  1. PAC (ng/dl) / PRA (ng/ml) >20 PAC: Plasma aldosterone concentration PRA: Plasma renin activity
  2. Plasma aldosterone>15ng/dl

- **Confirmatory tests:** memorize the screening tests, confirmatory is not important.

1. Sodium suppression test
2. Urinary aldosterone excretion >14ug/24hr

- **TREATMENT AND PROGNOSIS**

Pre-operative preparation:

- **Spironolactone**: Competitive aldosterone antagonist :
- Promotes K retention (K+ sparing diuretic)
- Reduces extracellular volume
- Reactivates the renin-angiotensin-aldosterone system
- **Amiloride**: not as common as spironolactone
- **K+ sparing diuretics**

Surgery:

- Laparoscopic adrenalectomy
- Open surgery

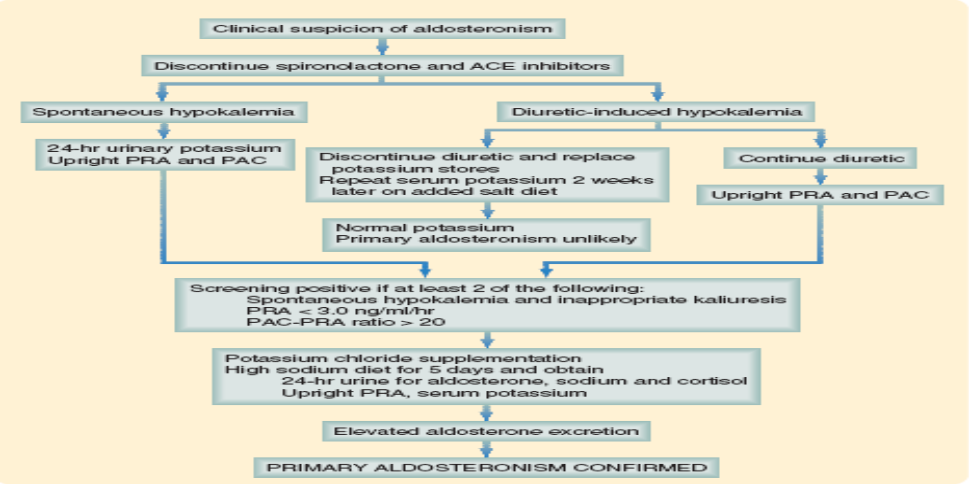
Medical treatment:

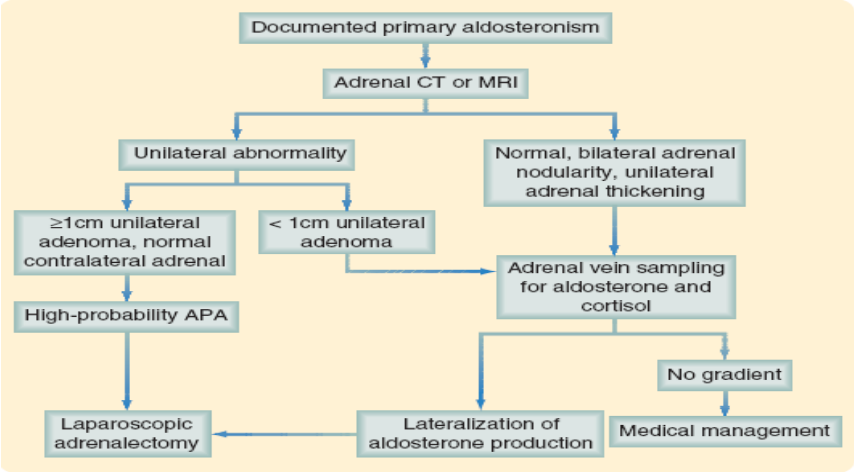
- Unfitpatients.
- Bilateralald.

- **PROGNOSIS**

- 1/3 persistent hypertension patients should know that 1/3 of patient won't be cured from hypertension
- K levels will be restored
- Usually after treatment they get back to their normal lives with no complaints of HTN.

- **CLINICAL PATHWAY**





2) PHEOCHROMOCYTOMA

If pheochromocytoma is suspected we don't treat as an out-patient
Patient could die due to a crisis.

EPIDEMIOLOGY:

- Less than < 0.1% of patients with hypertension
- Not common.
- 5% of tumors discovered incidentally on CT scan (less than 4-5 cm but functioning)
- Most occur sporadically (no genetic predisposition)
- Associated with familial syndromes, such as:
- Multiple endocrine neoplasia type2 (MEN2A) 40%
- MEN 2B
- Reckling hausen disease (Neurofibromatosis type I)
- Von Hippel-Lindau disease
- 90% of patients with pheochromocytoma are hypertensive (Once you diagnose the patient for the first time with HTN you HAVE to perform an US to the abdomen)
- Hypertension is less common in children
- In children, 50% of patients have multiple (bilateral) or extra-adrenal tumors

SYMPTOMS AND SIGNS pass urine → collapse

- Clinical findings are variable
- Episodic or sustained hypertension
- **Triad** of **palpitation, headache, and diaphoresis**
- Anxiety, tremors and weight loss
- Dizziness, nausea, and vomiting
- Abdominal discomfort, constipation, diarrhea
- Visual blurring
- Tachycardia, postural hypotension
- Hypertensive retinopathy (in short period of HTN history, few years only!)

ESSENTIAL FEATURES

- **Episodic headache**, excessive **sweating**, **palpitations**, and **visual blurring**
- **Hypertension**, frequently sustained, with or without paroxysms
- Postural tachycardia and hypotension
- Elevated urinary catecholamines or their metabolites, hyper-metabolism, hyperglycemia

- **Rule of 10s:**

10% **familial**
10% **malignant**
10% **bilateral**
10% **multiple tumors**
10% **extra-adrenal**

EXTRA-ADRENAL

Very **RARE**
Abdomen (75%) most common
Bladder (10%)
Chest (10%)
Pelvis (2%)
Head and neck (3%)

LABORATORY FINDINGS

- Hyperglycemia
- Elevated plasma metanephrines
- Elevated 24-hour urine metanephrines and
- free catecholamines
- **Elevated urinary vanillyl mandelicacid**(VMA)
- Elevated plasma catecholamines

IMAGING

Adrenal mass seen on CT or MRI
Characteristic bright appearance on T2-weighted MRI
Asymmetric uptake on MIBG nuclear scan
Particularly useful for extra-adrenal, multiple, or malignant pheochromocytomas
Not useful for sporadic biochemical syndrome with unilateral mass

DIAGNOSTIC CONSIDERATIONS

* **Avoid arteriography** or fine-needle aspiration as they can precipitate a hypertensive crisis
Early recognition during **pregnancy** is important because if left untreated, half of fetuses and nearly half of the mothers will die.
Patients with pheochromocytoma usually die of high Blood pressure, as the adrenal gland itself is very sensitive if it were to be touched in surgery there will be a surge of secretions, which leads to a severe increase in blood pressure leading to a BP of 250 leading to intracranial hemorrhage!

RULE OUT

- Other causes of hypertension
- Hyperthyroidism
- Anxiety disorder
- Carcinoid syndrome

WORK-UP

- History and physical exam
- Suspect pheochromocytoma based on symptoms
- CT, MRI, or other scans
- Plasma and urine studies (metanephrines, catecholamines, VMA)
- Begin treatment with a-blockers
- Possible MIBG scan
- Operative excision of tumor

WHEN TO ADMIT

HYPERTENSIVE CRISIS (can develop multisystem organ failure, mimicking severe sepsis)

TREATMENT AND MANEGEMENT

- **MEDICAL**

α-Adrenergic blocking agents should be started (AT LEAST 2 weeks before the surgery) as soon as the biochemical diagnosis is established to restore blood volume, to prevent a severe crisis, and to allow recovery from the cardiomyopathy

- **SURGICAL**

Indications:

All pheochromocytoma should be excised

Contraindications to surgery:

Metastatic disease

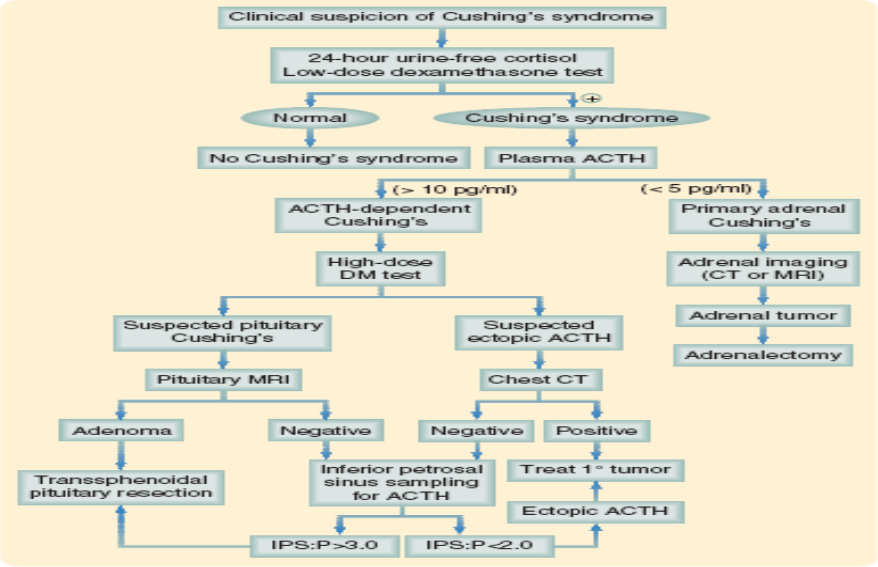
Inadequate medical preparation (α-blockage) , without proper **α**-blockade surgery is contraindicated.

3) CUSHING'S DISEASE VS. SYNDROME

CUSHING DISEASE --> Secondary to pituitary adenoma

CUSHING SYNDROME --> Secondary to anything else

CLINICAL PATHWAY



4) ADRENOCORTICAL CARCINOMA: Very rare

ESSENTIAL FEATURE

Variety of clinical symptoms through excess production of adrenal hormones

Complete surgical removal of the primary lesion and any respectable metastatic sites has been the mainstay of treatment.

EPIDEMIOLOGY

- These tumors are rare; 1—2 cases per million persons in the United States
- Less than 0.05% of newly diagnosed cancers per year
- Bimodal occurrence, with tumors developing in Children< 5 years of age and in adults in their fifth through seventh decade of life
- Male: female ratio is 2:1 as we said the only endocrine disease or cancer which is more common in males, with functional tumors being more common in women
- **Left adrenal** involved slightly more often than the right (53% vs. 47%); bilateral tumors are rare (2%)
- 50—60% of patients have symptoms related to hypersecretion of hormones (most Commonly Cushing's syndrome and virilization)
- Feminizing and purely aldosterone-secreting carcinomas are rare
- 50% of patients have metastases at the time of diagnosis
- It is very difficult to diagnose, because the symptoms appear when it is too late (Just like pancreatic cancer)

SYMPTOMS AND SIGNS

- Symptoms of specific hormone excess (cortisol excess, virilization, feminization, moon face)
- Palpable abdominal mass
- Abdominal pain
- Fatigue, weight loss, fever, hematuria

LAB FINDINGS:

- All laboratory abnormalities depend on hormonal status of tumor
- Elevated urinary free cortisol or steroid precursors
- Loss of normal circadian rhythm for serum cortisol
- Low serum adrenocorticotropic hormone (ACTH)
- Abnormal dexamethasone suppression test
- Elevated serum testosterone, estradiol, or aldosterone levels

IMAGING

- Evaluation of adrenal glands with CT or MRI (adrenocortical carcinomas are typically iso-dense to liver on T1-weighted MRI, and hyper-dense relative to liver on T2-weighted MRI images)
- **MRI** more accurately gauges the extent of any intracaval tumor **thrombus**

Right sided surgeries are always more difficult the left sided ones. Right tumors go to the IVC creating big thrombi and that makes the surgery more difficult. (Restrict part of IVC→ remove the thrombus → anastomose it again)
All tissues involved should be removed, such as part of kidney or part of liver or maybe lymph nodes.

CONSIDERATIONS

Mean diameter of adrenal carcinoma at diagnosis is 12 cm
(black size 6cm to 12cm → malignant .. remove it , black size 2cm to 4cm → cyst)
Radiographic evaluation of suspected metastatic sites for purposes of staging should be undertaken prior to thought of any surgery.

RULE OUT

Pheochromocytoma

DOCTOR'S SUMMARY:

- Any functioning tumor or disease should be removed unless the patient is unfit or it's bilateral go with medical treatment.
- Any non functional, small in size we follow up.
- In surgeries they clip "ligate" the adrenal vein not the artery, they are usually very small branches and very fragile .

Best of luck