Adrenal disorders

Objectives:

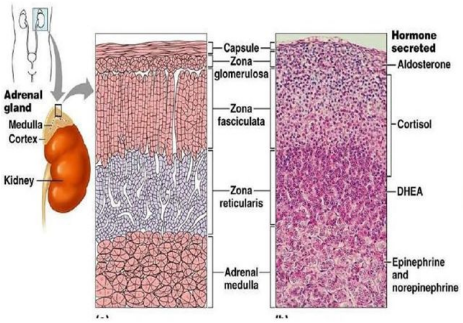
- **Understand anatomy, physiology and biochemistry of adrenal glands**
- **Understand clinical approach and management of adrenal disorders:**
  - **Function: hyper and hypo-secretion**
  - **Structure**

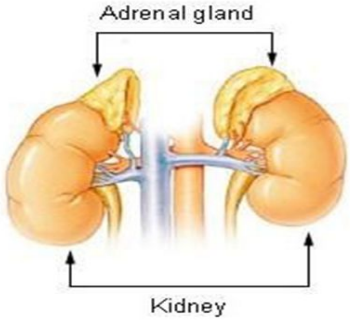
The work was done by: فارس نفيسه, امال الشيبي

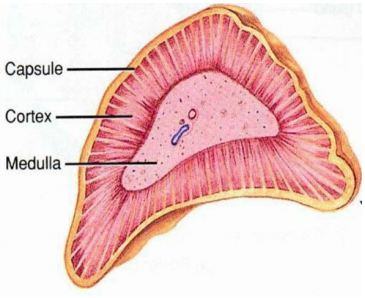
Resources: Dr mujammami slides + notes

- Editing file
- Feedback

Adrenal gland overview







ZONA	Hormone	Effect	Regulatory control
Glomerulosa	**S**alt: Mineralocorticoids (aldosterone).	**Kidney:** Maintain intravascular volume by increase reabsorption of Na+ and water & potassium excretion. ***Important for blood pressure and electrolytes.**	• **RAAS: angiotensin II** • **K+ and Na+** • **ACTH** (mild effect) ***If we took ACTH, aldosterone won't be affected, RAAS will take over.**
Fasciculata	**S**weet: Glucocorticoids (cortisol)	Lipolysis Increase blood sugar	**ACTH**
Reticularis	**S**ex: Androgens	It is the main source of androgen in human But it is important in the disorders	**ACTH**

*cortisol follows circadian rhythm 'highest in morning lowest at sleep time'

Q: Someone had an accident and found bleeding, do you think aldosterone will be affected? NO

Medulla:

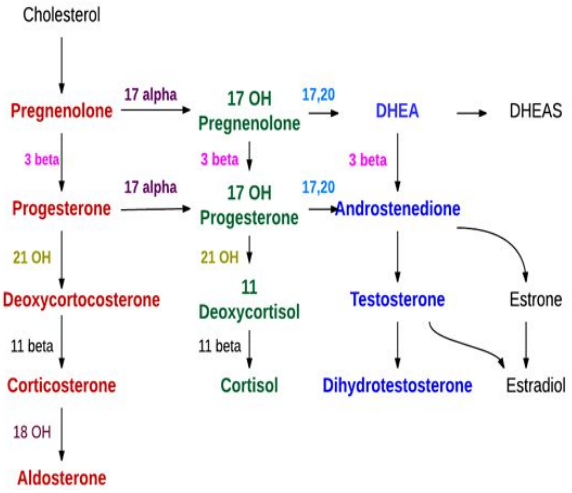
Catecholamines (Epinephrine, Norepinephrine, Dopamine): Most of the time **activate sympathetic** fibers and increase (BP, HR, blood sugar)

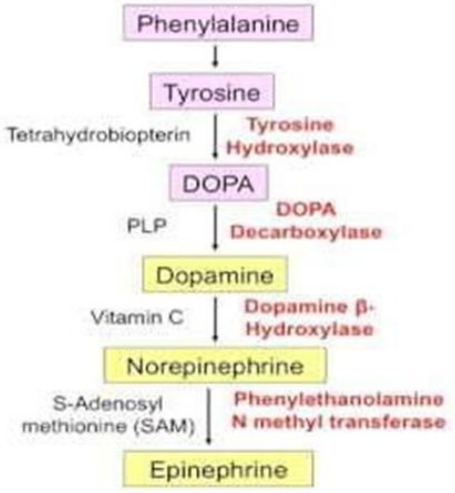
But could present with activations of parasympathetic as pathologic disorders

Biochemistry:

All adrenal cortex hormones are originating from Cholesterol

All adrenal medulla hormones are originating from amino acid Tyrosine





Adrenal disorders could be:-

Functional: Hypersecretion vs Hyposecretion, Primary vs Secondary.

- Adrenal Hypofunction:
    1. **Adrenal Insufficiency**
    2. **Congenital Adrenal Hyperplasia (CAH)**
- Adrenal cortical Hyperfunction:
    1. **Hypercortisolism: Cushing syndrome**
    2. **Hyperaldosteronism**

Structural:

- Adenoma
- Hyperplasia
- Bilateral vs unilateral
- Adrenal vs extra-adrenal

Evaluation of adrenal disorders:

C: clinical (history and examination)

- Function (oversecretion or hyposecretion)
- Structural (headache, visual symptoms)

B: biochemical

- Screen test
- Confirmatory test

A: anatomical

- CT or MRI adrenal (adenoma, hyperplasia, uni or bilateral, adrenal or extra-adrenal, benign or malignant).

Then Treatment.

1. Adrenal Insufficiency

1. **Primary Adrenal Insufficiency: Destruction of adrenal cortex (3 layers)**. It's **also called Addison's disease** regardless of the cause weather it's due to autoimmune or other causes. TB was the commonest cause. Now, autoimmune: the most common cause. Often positive adrenal antibodies.

   Could be: an isolated problem, or associated with other autoimmune diseases:

   - Type I (APECED): affects children: Adrenal insufficiency, hypoparathyroidism, pernicious anaemia, chronic candidiasis, chronic active hepatitis, and hair loss)
   - Type II "Schmidt's syndrome" usually affects young adults : hypothyroidism, adrenal insufficiency and diabetes mellitus, vitiligo. (won't ask about the types I, II...)

   ★ **Causes:** (won't ask about the causes)

   - Idiopathic atrophy (autoimmune)
     - Isolated or part of polyglandular disease (type 1 or type 2).
   - Infection (TB, fungal: Histoplasmosis, CMV HIV, Syphilis, ..etc)
   - Infiltration (lymphoma, Hemochromatosis, Amyloidosis, Sarcoidosis, malignancy)
   - Iatrogenic
     - Surgical removal
     - Anticoagulation and hemorrhage
   - Medications (ketoconazole, rifampin, phenytoin, Phenobarbital, Mitotane, Metyrapone, Aminoglutethimide)
   - Hereditary
     - (Congenital adrenal hyperplasia,adrenal unresponsiveness to ACTH, adrenoleukodystrophy, adrenomyeloneuropathy, Refsum disease, Wolman disease)
   - Miscellaneous:
     - Triple A syndrome = Allgrove syndrome
     - Adrenal hemorrhage

2. **Secondary/ Tertiary adrenal insufficiency:**
   - **Pan**hypopituitarism (congenital/ acquired): Tumor, surgery, radiation therapy, hypothalamic, pituitary disorders.
   - Isolated ACTH deficiency
   - withdrawal from glucocorticoid therapy
   - Inadequate glucocorticoid replacement
   - Infant born to steroid treated mother
   - **Surgical removal** of ACTH-producing adenoma of the pituitary gland (cushing syndrome)

   *In secondary and tertiary AI, aldosterone will be NORMAL!!

★ Clinical manifestations:

- Weakness, tiredness, fatigue, Nausea, Vomiting, Constipation, Abdominal pain, Diarrhea, weight loss, Hyperpigmentation, fasting hypoglycemia.
- **Hypotension**, Shock and death (If the patient presented with hypotension Think about AI if not respond to IV fluid and initial management)
- Decreased axillary and pubic hair
- Hyperpigmentation: **only in Primary adrenal insufficiency** due to melanocyte stimulating hormone (MSH) from pro-opiomelanocortin (POMC) Not ACTH. Clinically when cortisone is low > ACTH & CRH is high > stimulate melanocyte releasing hormone > hyperpigmentation.

***Postural hypotension when there is drop more than 20/10 when changing position**

★ Biochemical: doctor focused on the first 4

	Primary	Secondary
ACTH	**High**	**Low**
cortisol	**Low**	**low**
Androgen	**low** **high in CAH**	**low**
Aldosterone	**Low**	**Normal ''RAS''**
K+	High	normal/high
Na+	low	Normal/low
Glucose	low	low
Hb	normal or low	low

★ Investigations: Adrenal insufficiency is a clinical and biochemical diagnosis.

1. Measure AM cortisol:
   - If high: Rule out
   - If very low: diagnosis
   - If borderline result : proceed for confirmatory test

***remember in endocrine: anything high suppress and anything low stimulate**

2. Measure ACTH (ACTH stimulation test): to differentiate primary or secondary (to confirm)
3. No indications to do imaging unless clinically indicated such as:
   - Patient on anticoagulation
   - Malignancy with metastasis
   - other infiltrative disease

★ Treatment:

- IVF: dextrose and salt for rehydration and to restore intravascular volume, Electrolytes replacement.
- **Steroid replacement**
  - **If primary:**

    replace both Glucocorticoids (cortisol): hydrocortisone and Mineralocorticoids (aldosterone): Fludrocortisone

  - **If secondary:**

    Replace Glucocorticoids (cortisol): hydrocortisone only

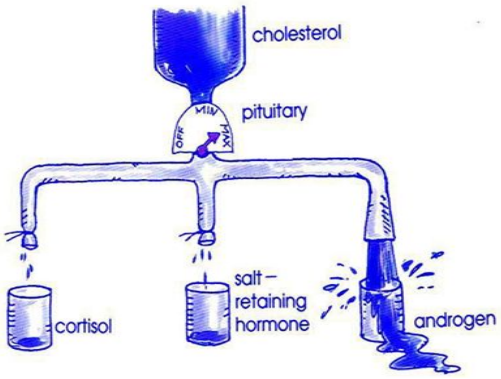
NB: hydrocortisone has some Mineralocorticoids activity, so if you use hydrocortisone in high IV dose, stop Fludrocortisone

2. Congenital Adrenal Hyperplasia (CAH)

90–95% of CAH cases are caused by 21- OHD

★ Clinical Findings:

- Ambiguous genitalia (Female)
- Failure to thrive
- Dehydration & Shock (usually male)
- Salt-loss presentations with electrolytes imbalance:
  - Hyponatremia
  - Hyperkalaemia
  - Hypoglycemia
- Hyperpigmentation



★ Diagnosis:

- Clinical: History and examination (B.P)
- Biochemical:
  - Serum electrolytes & glucose:
    - Low Na & high K
    - Fasting hypoglycemia
    - Elevated serum urea due to associated dehydration
- Elevated plasma Renin & ACTH levels
- **Low Cortisol**
- High 17 – OHP
- High androgens especially testosterone level
- Low Aldosterone (in salt losing types only)

★ Treatment:

- Hydrocortisone:
  - 10-20 mg/m2/day divided into three doses
  - Adult usually 10-5-5 mg
  - Fludrocortisone 0.05 - 0.2 mg/day
- During adrenal crisis intravenous hydrocortisone 50-100 mg Q 6-8hrs
- IVF D5 0.9% saline
- During fever or sickness 2-3 fold increment in hydrocortisone dose
- In vomiting or diarrhea, parental therapy is indicated
- Medical Alert: bracelet
- Surgery if genitalia is affected

Hypercortisolism: Cushing syndrome

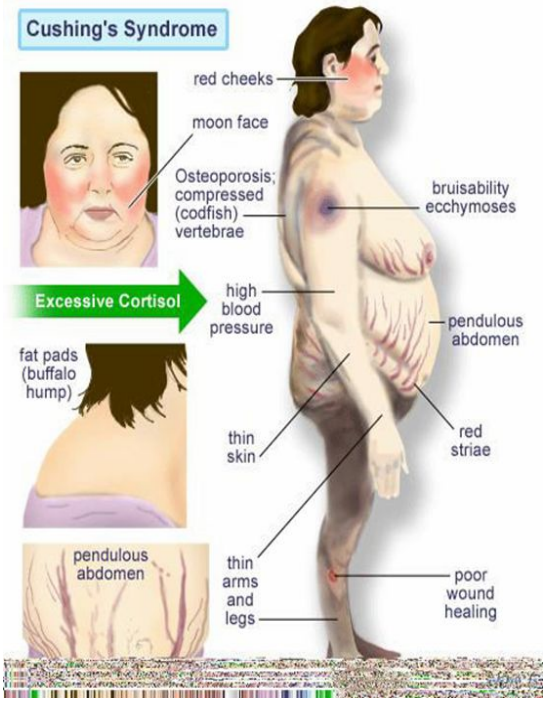
First described by Cushing in 1932

A constellation of clinical abnormalities due to chronic exposure to excesses of cortisol

- ACTH dependent: **pituitary** (cushing disease) or ectopic
- ACTH independent (Iatrogenic (most common), adrenal adenoma or carcinoma)

★ Clinical findings:

- rounded "moon" facies with a plethoric appearance
- truncal obesity with prominent supraclavicular and dorsal cervical fat pads "buffalo hump"
- distal extremities and fingers are slender
- Muscle wasting and weakness, proximal weakness
- The skin is thin and atrophic, with poor wound healing and **easy bruising.** Purple striae may appear on the abdomen.
- Hypertension
- renal calculi
- osteoporosis
- DM, Obesity
- Hirsutism, Acne
- Depression
- **Fractures**
- Recurrent infections due to cortisol effect.
- OSA, so be careful during sedation prior to surgery



★ Investigations:

- High cortisol, high ACTH (ACTH dependent) and low if (non-ACTH dependent)
- 24hrs for UFC (Urine cortisol)
- 1MG DST (dexamethasone)
- Midnight salivary cortisol
- if ACTH: high > MRI pituitary
- If ACTH: low > history then CT adrenals

★ Treatment: **Surgical (1st line if cushing disease) or medical based on the etiology.**

Hyperaldosteronism: Conn's syndrome

★ Primary hyperaldosteronism

- Adenoma, usually unilateral, of the glomerulosa cells of the adrenal cortex
- rarely, adrenal carcinoma
- Hyperplasia
- The clinical picture may mimic CAH from of 11 α-hydroxylase deficiency

★ Clinical signs:

- Secondary HTN
- High Na, high Cl, high Aldosterone
- Alkalosis
- Low K (episodic weakness, Paresthesias, transient paralysis, tetany, nephropathy with polyuria and polydipsia)

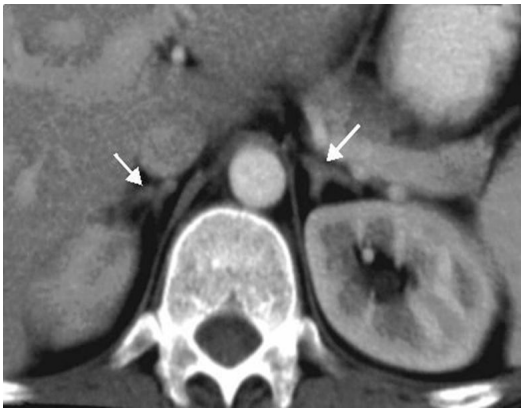
★ Investigations:

Screening test:

- aldosterone /renin ratio
  - If high: do confirmatory test
  - If low: look for secondary causes

Confirmatory test:

- Saline infusion test
- Oral salt loading test
- Captopril test
- Fludrocortisone suppression test



★ Treatment:

- Adrenal adenoma: Surgery
- Adrenal hyperplasia: Spironolactone.

Pheochromocytoma

- Adrenal medulla: sympathetic nervous system
- 50% are silent. (NO symptoms)
- Isolated or part of MEN type II A or MEN type II B

★ Clinical findings:

- Think of **Secondary causes of HTN** if a pt presented with HTN with these features:
  - Young age < 40
  - pt on 3 anti-HTN medications
  - Resistant HTN
  - Accelerated HTN
- **Episodic (spells):** sweating, palpitation, headache

❖ Any adrenal mass in image: **adrenal incidentaloma**

- **You should R/O:**
  - Pheochromocytoma
  - Cushing
  - If there's HTN, you should R/O hyperaldosteronism also

★ Investigations:

- 24 hr urine collection of **Metanephrines (2X)**
- Plasma Metanephrines. *someone came to you with a mass spotted incidentally, we request metanephrine/cortisol. we don't order aldosterone unless he has HTN.
- Make sure about medications that affect the result of the test (false positive)
- CT scan = MRI
- MIBG: if
  - Paraganglioma, Young, large size, or malignant features
- Genetic Tests: 30-40% of Pheochromocytoma and Paraganglioma Have positive genetic test.

★ Treatment:

- Control HTN: α-blocker then B-Blocker (10-14 days before operation) Ca-blockers: can be used
- Salt loading: Oral NaCl: 3 days, or IVF 0.9% saline 1-2 days before surgery
- **Surgery**

The end...