

# 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

**Team Members:** شروق الصومالي, محمد اليوسف, أشواق الماجد, عبدالعزيز السفاعي, نوره الشبيب

**Team Leader:** Faris Nafisah :) :(

**Revised By:** Yara Aldigi and Basel almeflh

**Resources:** 435 team + Davidson + kumar + Recall questions step up to medicine.

- [Editing file](#)
- [Feedback](#)

## Basic Review of Adrenal Gland (go through)

### Anatomy:

#### Adult adrenal gland :

- The glands weigh 8-10gm.
- Location: in the retroperitoneum above or medial to the upper poles of the kidneys.
- Surrounded by a fibrous capsule.
- The yellowish outer cortex comprises 90% of adrenal weight.
- The inner medulla comprises 10% of adrenal weight.

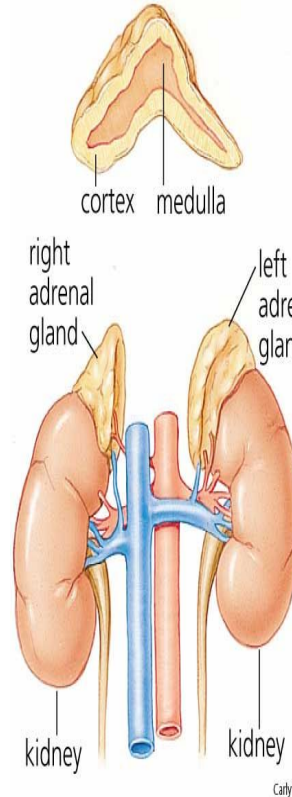
### Physiology:

#### The outer cortex has three zones:

- Zona Glomerulosa: Produce mineralocorticosteroids like aldosterone.<sup>1</sup>
- Zona Fasciculata: Produce glucocorticosteroids like cortisol and corticosterone.
- Zona Reticularis: Produce adrenal androgens.
- **The zona fasciculata and reticularis are regulated by ACTH, excess or deficiency of this hormone alters the structure and function of both zones i.e. both zones atrophy when ACTH is deficient and when ACTH is present in excess, hyperplasia and hypertrophy of these zones occur.**
- The synthesis of aldosterone is primarily regulated by the renin-angiotensin system and by potassium.
- The zona fasciculata and reticularis produce cortisol, androgens and small amounts of estrogens and they do not contain the enzymatic system necessary for production of aldosterone.

#### The inner medulla:

- Composed of chromaffin cells that produce catecholamines like epinephrine (adrenaline), norepinephrine (noradrenaline) and dopamine. Activates sympathetic fibers and increases (BP, HR, blood sugar)



This is an easy way to memorise it GFR & 3S

Salt	Glomerulosa
Sugar	Fasciculata
Sex	Reticularis

Aldosterone acts on salt & secreted from G  
Cortisol acts on sugar & secreted from F  
Androgen is a sex hormone & secreted from R

### Hormonal Functions

#### Mineralocorticoids: (mainly by Aldosterone)

- Maintain intravascular volume by: Increase reabsorption of Na<sup>+</sup> and water
- Regulatory control: angiotensin II, K<sup>+</sup> Na<sup>+</sup>

<sup>1</sup> The zona glomerulosa produces aldosterone and lacks 17-hydroxylase activity and cannot synthesize cortisol and androgens.



### Glucocorticosteroids:

- Lipolysis will increase blood sugar
- Regulatory control: ACTH
- Stimulation of gluconeogenesis by the liver.
- “Insulin antagonistic hormones are: Cortisol, adrenaline, glucagon, and growth hormone”
- Protein Catabolic effect in all body cells except of the liver.
- Protein Anabolic effect in the liver:
  - 1- Enhanced liver proteins.
  - 2- Increased plasma proteins.
- Immunity impairment: Decrease production of eosinophils, lymphocytes, T cells and antibodies production.
- Enhancing catecholamine activity (by upregulation of alpha1 receptors (they are found in blood vessels, therefore HTN may develop)
- Cortisol has mineralocorticoid effect, but is not as potent as aldosterone.

### Androgens:

- Zona Reticularis is the main source of androgen in humans but it is important in the disorders(e.g CAH)
- Regulatory control: ACTH
- Not important in adult men, encourage bone growth, muscle growth, and blood formation in children and women.

### Catecholamines:

Increase cardiac activity, blood pressure, glycogen breakdown, blood glucose level; release of lipids by adipose tissue (lipolysis).

### Biochemistry

don't memorise the enzymes just understand the pathways

- All adrenal cortex hormones originate from Cholesterol
- All adrenal medulla hormones originate from the amino acid Tyrosine
- Cortisol and the adrenal androgens circulate while bound to plasma proteins.
- The plasma half life of cortisol (70-90 min) is determined by the extent of plasma binding and by the rate of metabolic inactivation.
- The hormone after secretion binds to plasma proteins upon entering the circulation.
- Cortisol binds mainly to CBG (cortisol binding globulin) or transcortin =75% and to a lesser extent to albumin=15% (total cortisol is affected by protein binding)
- About 10% of circulating cortisol is free and it is the biologically active cortisol that is regulated by ACTH
- Androgens except for testosterone bind weakly to albumin. However, testosterone binds extensively to a specific globulin - sex hormone binding globulin (SHBG).

CBG increases in:	CBG decreases in:
<ul style="list-style-type: none"> <li>• Pregnancy</li> <li>• Oral contraceptive users</li> <li>• Hyperthyroidism</li> <li>• D.M.</li> <li>• Certain hematological disorders</li> <li>• Genetic familial condition</li> </ul>	<ul style="list-style-type: none"> <li>• Familial deficiency states</li> <li>• Hypothyroidism</li> <li>• Protein deficiency states</li> <li>• Severe liver disease</li> <li>• Nephrotic syndrome</li> </ul>

## Regulation of secretion:

### Circadian Rhythm

Regulates both the magnitude and the number of CRH and ACTH secretory episodes. Cortisol secretion is low in the late evening and high in the early morning.

#### which can be changed by:

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>• Changes in Sleep pattern</li> <li>• Light-dark exposure</li> <li>• Feeding times</li> <li>• Psychological stress</li> <li>• CNS and pituitary disorders</li> </ul> | <ul style="list-style-type: none"> <li>• Cushing syndrome</li> <li>• Liver disease</li> <li>• Chronic renal failure</li> <li>• Alcoholism</li> <li>• Certain Drugs e.g. cyproheptadine</li> </ul> |
|---|---|

“The peak of cortisol is in the morning (That’s why the measurement of cortisol is done in the morning). It’s low at night.”

### Stress:

e.g. surgery and hypoglycemia. It causes ACTH and cortisol to be secreted within minutes of the onset of stress and this is mediated by increased CRH secretion. This is abolished by prior high dose glucocorticoid administration and in Cushing’s syndrome.

### Feedback inhibition:

Glucocorticoids act on both the pituitary and hypothalamus to inhibit CRH and ACTH production and thus further synthesis of glucocorticoids.

## Adrenal Disorders:

Function	Structural
Hypersecretion / Hyposecretion <b>Primary and Secondary</b>	Adenoma • Hyperplasia • Bilateral vs unilateral • Adrenal vs extra-adrenal

## Adrenocortical Insufficiency

### ★ Primary adrenocortical insufficiency (Addison disease):

**Will destruct all 3 layers of the cortex**

- **low aldosterone: hypotension, electrolyte imbalance (hyponatremia, hyperkalemia)**
- **low cortisol: hypoglycemia, hypotension (HYPERPIGMENTATION= with primary hypofunction)**
- **low androgens:** بشكل عام نقصه ماله قيمة

### Major Causes:

1. **Autoimmune** “idiopathic” (80%) and Tuberculosis (20%). (autoimmune dx comes in association with other autoimmune diseases)
2. Rare Causes "any infiltrative lesion can destroy the adrenal":  
 “Adrenal hemorrhage and infarction, Fungal infections, Metastatic and lymphomatous replacement, Sarcoidosis, Amyloidosis, Hemochromatosis, Radiation therapy, Surgical adrenalectomy, Enzyme inhibitors e.g. metyrapone, Cytotoxic drugs e.g. mitotane, Congenital diseases e.g. enzyme defects and Hypoplasia”
  - 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
  - Idiopathic Addison's disease is frequently accompanied by other glandular failure disorders and also with a higher incidence of other immunological and autoimmune endocrine disorders e.g. hyperthyroidism, hypothyroidism, hashimoto, anemia and gonadal failure.
  - One or more of these disorders is usually present in 40-53% of patients with idiopathic addison’s disease.
  - Addison’s disease is more common in women 2.6:1. It is usually diagnosed in the 3rd to 5th decade.

### Pathophysiology:

- Gradual adrenocortical destruction causes decrease in adrenal reserve with normal basal steroid secretion in the initial phase, but with failure to respond to stress. With further loss of cortical tissue, even basal secretion of mineralocorticoids and glucocorticoids become deficient leading to the manifestation of chronic adrenocortical insufficiency when more than 90% of both adrenal cortices are destroyed. (after the loss of 90% > symptoms start to appear)
- Acute crises can be precipitated by stresses of surgery, trauma or infection which require increased corticosteroid secretion.
- About 25% of cases present with a crises or an impending one at the time of diagnosis

## Clinical features:

- The chief symptoms of chronic primary adrenocortical insufficiency are **hyper-pigmentation**
- It is due to secondary increase in ACTH, BLPH and MSH because of decrease **negative feedback inhibition**. (it is indirectly caused by increase in ACTH, **MSH** is the cause of the pigmentation which have the same origin of ACTH so “it not caused by ACTH” ) “Hyperpigmentation occurs because melanocyte stimulating hormone (MSH) and (ACTH) share the same precursor molecule which is Proopiomelanocortin (POMC).”
- Generalized hyperpigmentation of skin & mucous membranes is the earliest manifestations (the **classical physical finding**). The hyperpigmentation is increased in sun exposed areas and accentuated at pressure areas (knuckles, toes, elbows, knees), and is associated with black or dark brown freckles. It can also be seen in other areas: palmar creases, nail beds, nipples, areola, perivaginal, perianal mucosa & scars that formed after onset of ACTH become hyperpigmented.

## Other Symptoms:

Symptom	Percent
Weakness, fatigue, anorexia, weight loss	100%
<b>Hyperpigmentation</b>	92%
Hypotension	88%
G.I. disturbances	56%
Salt craving	19%
Postural symptoms	12%

- Salt craving<sup>2</sup>
- **Postural symptoms, Muscular or joint pains, and Amenorrhoea<sup>34</sup>.**

## Signs:

- weight loss.
- loss of body hair “axillary and pubic hair” (secondary to deficient adrenal androgens secretion)
- **Hypotension:** present in about 90% of patients and causes **orthostatic symptoms**. (may cause syncope and in severe cases shock) Think about AI, if not respond to IVF and initial management  
significant postural hypotension: drop > 20/10
- The most important 2 hormones that control the blood pressure are cortisol and aldosterone

<sup>2</sup> Salt craving occurs because of sodium wasting secondary to mineralocorticoid deficiency, can lead to dehydration, hyponatremia, hyperkalemia and acidosis.

<sup>3</sup> common and can be due to weight loss and chronic illness or associated ovarian failure

<sup>4</sup> "considered fifth vital sign for a woman"

### Laboratory findings:

- Electrolytes disturbances:
  - Hyponatremia and Hyperkalemia (classical in primary adrenal insufficiency)
  - Mild to moderate Hypercalcemia.
- Azotemia and increased serum creatinine (due to volume depletion and dehydration)
- might be:
  - Normocytic Anemia<sup>5</sup>
  - Eosinophilia
  - Neutropenia
  - Relative lymphocytosis
- Mild acidosis frequently present
- Severe hypoglycemia (uncommon in adults, but can be provoked by fasting, fever, infection or nausea and vomiting)
  
- Abdominal radiograph reveal adrenal calcification in half of the patients with tuberculous adrenalitis and in some patients with other invasive or hemorrhagic causes of adrenal insufficiency.

★ **Secondary/Tertiary adrenocortical insufficiency:** "mujammami didn't discuss it in details but female's doc did"

**Causes:** Female slides

- ACTH deficiency (most commonly due to exogenous glucocorticoid administration)
- Pituitary/Hypothalamic tumors are the most common causes of naturally occurring pituitary ACTH hyposecretion.

**Causes:** Male slides

Pan hypopituitarism (congenital / acquired): • Tumors, surgery, radiation therapy • Hypothalamic / pituitary disorders	Surgical removal of ACTH-producing adenoma of the pituitary gland (Cushing's disease)	Withdrawal from glucocorticoid therapy
Isolated ACTH deficiency	Infant born to steroid-treated mother	Inadequate glucocorticoid replacement

<sup>5</sup> thyroxine and cortisol are important in erythropoiesis, so decrease in any one of them will lead to anemia

## Pathophysiology:

ACTH deficiency is the primary event, This leads to:

- 1- Decreased Cortisol & Androgen secretion.
- 2- **Aldosterone secretion remains normal. "it has RAAS"**

- in early stages, Basal ACTH & cortisol levels may be normal but: ACTH reserve is impaired and the response of ACTH & cortisol to stress is subnormal.
- With chronicity there is atrophy of zona fasciculata and reticularis and therefore basal cortisol secretion is decreased.
- At this stage, the pituitary adrenal axis is impaired (i.e. Decreased ACTH responsiveness to stress & decreased adrenal responsiveness to stimulation with exogenous ACTH) so When these patients develop a serious illness or undergo trauma, they cannot release an appropriate amount of cortisol because of chronic suppression of CRH and ACTH by the exogenous steroids. Therefore, symptoms of adrenal insufficiency result.

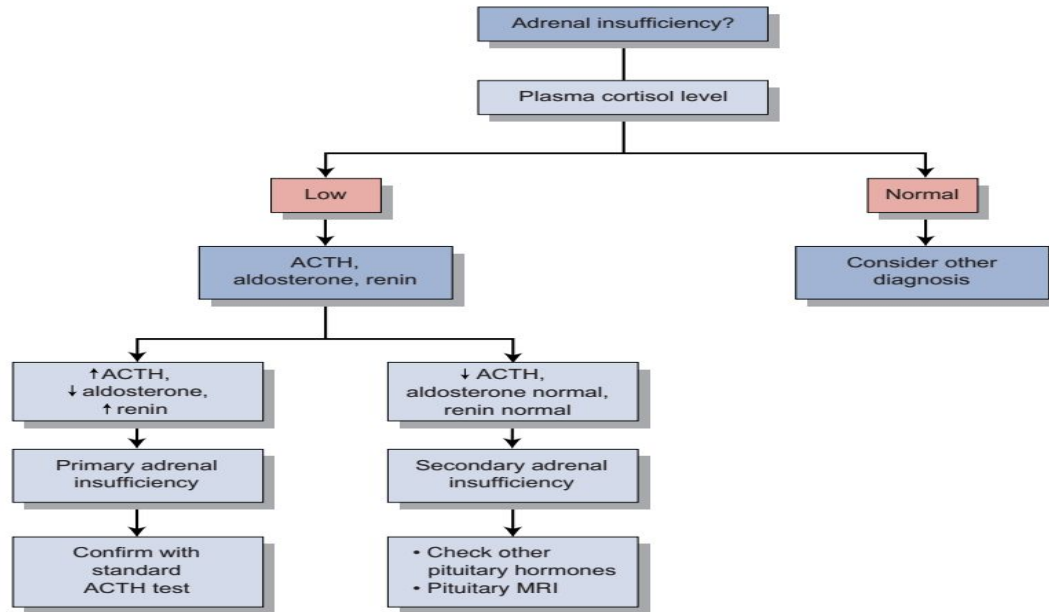
## Clinical features:-

- The clinical features may be non-specific initially unless an acute crisis occurs in an undiagnosed patient.
- **No hyper-pigmentation!** because of deficient ACTH and BLPH and the mineralocorticoid secretion is usually normal. Otherwise the symptoms may be similar to primary electrolyte abnormalities are usually absent
  - **Hyponatremia** may occur because of water retention and inability to excrete a water load **with no hyperkalaemia.**
  - Hypoglycemia is occasionally the presenting feature.
  - hypotension is usually not present except in acute presentations.

## \*Diagnosis of primary and secondary adrenocortical insufficiency:

Diagnosis of primary and secondary adrenocortical insufficiency (should be in a stepwise):		
1	Measure Plasma cortisol level:	<ul style="list-style-type: none"> <li>✓ <u>if it is Normal</u> → consider other diagnoses.</li> <li>✓ <u>if it is Low</u> → Adrenal problem → go to the next step.</li> <li>✓ If borderline result : proceed for confirmatory test "ACTH stimulating test"</li> </ul>
2	Measure ACTH, renin & aldosterone level:	<ul style="list-style-type: none"> <li>✓ <u>If ACTH is low, aldosterone and renin are normal</u> → <b>secondary</b> adrenal insufficiency → check other pituitary hormones and perform pituitary MRI.</li> <li>✓ <u>If ACTH is high, aldosterone is low and renin is high</u> → <b>primary</b> adrenal insufficiency → confirm with ACTH stimulation test.</li> </ul>
3	Rapid ACTH stimulation test:	<ul style="list-style-type: none"> <li>✓ ►Note: it's a <b>DEFINITIVE</b> test to diagnose primary adrenal insufficiency.</li> </ul> <p><b>Procedure:</b></p> <ul style="list-style-type: none"> <li>○ After a baseline cortisol sample is obtained (in the morning)</li> <li>○ "Dr: If very low "zero" in the morning it's diagnostic.</li> <li>○ → a synthetic ACTH called <b>Tetracosactrin</b> is given in a dose of 0.25mg IM Or IV → and additional cortisol samples are obtained at 30 and 60 min following the injection.</li> </ul> <p><b>Results interpretation:</b></p> <ul style="list-style-type: none"> <li>✓ <u>Failure to increase cortisol</u> → confirm <b>Primary adrenal insufficiency.</b></li> <li>✓ <u>Increase in cortisol</u> → confirm <b>Secondary adrenal insufficiency</b></li> </ul>





<b>Important</b>	<b>primary</b>	<b>secondary</b>
<b>ACTH</b>	high	low
<b>cortisol</b>	low	low
<b>androgen</b>	low high in CAH	low
<b>aldosterone</b>	low	normal N.B: <b>RAS</b>
<b>K</b>	high	normal or high
<b>Na</b>	low	low or normal
<b>glucose</b>	low	low
<b>Hb</b>	normal or low	low

**No indications to do imaging unless clinically indicated such as:**

- Patient on anticoagulation
- Malignancy with metastasis
- Or other infiltrative diseases



## Treatment of primary and secondary adrenocortical insufficiency:

### • IVF: dextrose and salt for:

- Rehydration and to restore intravascular volume
- Electrolytes replacement

### If primary:

- replace both Glucocorticoids (cortisol): **hydrocortisone** - 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

## ★ Congenital Adrenal Hyperplasia :

- Classic congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder
- Non-classic CAH is less severe and affects 1 in 500-1000 individuals  
90-95% of cases are caused by deficiency of 21-hydroxylase, which catalyses the synthesis of cortisol and aldosterone from cholesterol
- Failure to thrive

Note :  
the cause of virilization is that the precursor of cortisol & aldosterone build up & shunted toward androgen synthesis

## clinical presentation:

Clinical severity depends on degree of 21-hydroxylase deficiency

- **Classical CAH:**
  - Simple Virilizing: Ambiguous genitalia in females
  - Salt Wasting: Dehydration (and shock), vomiting and diarrhoea. If untreated can prove fatal
- **Non-classical CAH:**
  - Milder than classical CAH
  - Androgen excess can cause precocious puberty in either sex
  - Males are often undiagnosed/asymptomatic

## 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 (hydroxyprogesterone)
  - High androgens especially testosterone level
  - Low Aldosterone ( in salt losing types only)

## Treatment:

- Hydrocortisone:
  - 10-20 mg/m<sup>2</sup>/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
- Glucocorticoids which suppress ACTH, are used to reduce the levels of adrenal sex steroids in the blood
- Individuals with salt wasting CAH also require mineralocorticoids and sodium chloride supplements
- Growth monitoring to detect over and under treatment
- Dexamethasone can be used to prevent/reduce prenatal virilisation. Side effects for the mother include weight gain, irritability and oedema
- Medical Alert : bracelet

## ★ Acute adrenal crisis : "mujammami didn't discussed it in details but female's doc did"

A state of acute adrenocortical insufficiency occurring in patients with Addison's disease who are exposed to the stress of infection, trauma, surgery or dehydration which require increased corticosteroid secretions. (it's life threatening)

About 25% of cases present with crisis or an impending one at the time of diagnosis.

## Clinical Features:

- Hypotension and shock
- Dehydration and volume depletion
- Weakness, apathy, and depressed mentation
- Hypoglycemia
- Fever
- Nausea, vomiting, anorexia
- Abdominal Pain

- Shock and coma may rapidly lead to death in untreated patients.

## Treatment of acute adrenal crisis:

- It should be started as soon as possible once diagnosis is suspected.
- Parenteral cortisol is commonly used and it has sufficient mineralocorticoid activity so additional treatment is not required.
- The dose is 100 mg every 6 hrs, and the dose is gradually tapered when condition is stable.
- Maintenance therapy with oral cortisol with or without a mineralocorticoid is then given.
- Intravenous fluids including glucose and saline are required to correct volume depletion, hypotension and hypoglycemia as well as the acidosis and hyperkalemia but the shock may not respond to vasopressors unless glucocorticoids are administered.
- Adrenal crisis can be prevented in an already diagnosed patient by proper education on dosage of drugs during illness.
- The patient should be informed about life-long therapy and the need to increase the dose of steroids during illness (it should be at least doubled for minor illnesses) and if symptoms continue, a physician should be called. If oral therapy cannot be taken because of vomiting or diarrhoea, then medical assistance should be sought for parenteral therapy

## Adrenal Cortical Hyperfunction

### ★ **Hypercortisolism**

#### **Causes:**

##### **1- Iatrogenic: (exogenous)**

Chronic glucocorticoid excess whatever the cause leads to a constellation of symptoms and physical features known as Cushing's syndrome.

i.e. secondary to chronic steroid ingestion (**the most common cause**).

## 2- ACTH dependent: (endogenous)

- Cushing’s disease (excessive pituitary ACTH secretion, commonly secondary to pituitary adenoma, Women to men ratio is 8:1 and the age of diagnosis is usually between 20-40 yrs.).
- Ectopic ACTH syndrome (non-pituitary tumors secrete biologically active ACTH, It is most commonly seen with oat-cell carcinoma of the lung (50% of the cases) but other tumors, e.g. pancreatic cell tumors, carcinoid tumors, etc can cause it. **(It is more common in men,** female to male ratio is 1:3 with the peak incidence at the age of 40-60 years)

“70% of the cases is due to pituitary adenoma. In ACTH dependant, the cause is pituitary until proven otherwise”

- Ectopic CRH secretion, it is very rare

## 3-ACTH independent: (endogenous)

Glucocorticoid producing adrenal adenomas and carcinomas arise spontaneously and they are autonomous and not under pituitary hypothalamic control.

- Adrenal adenoma
- Adrenal carcinoma

## Clinical features: [img](#) “details here only in females slides”

<p><b>1- Obesity</b></p> <ul style="list-style-type: none"> <li>● <b>The most common manifestation</b> and is classically <b>central obesity</b> affecting mainly the face (moon faced) with a plethoric appearance , neck, trunk (prominent supraclavicular and dorsal cervical fat pads), and abdomen with relative sparing of the extremities.</li> </ul>	<p><b>2- Skin changes</b></p> <ul style="list-style-type: none"> <li>● Thinning of the skin (because of atrophy of the epidermis and underlying connective tissue support) and facial plethora.</li> <li>● <b>Red to Purple striae</b> are due to loss of connective tissue support as well as easy bruising.</li> <li>● <b>Hyperpigmentations</b> are common in ectopic ACTH secreting tumor.</li> <li>● Minor wound heal slowly and they have frequent mucocutaneous fungal infections.</li> </ul>
<p><b>3- Hirsutism</b></p> <ul style="list-style-type: none"> <li>● Facial hirsutism<sup>6</sup> is the most common, but it can occur anywhere in the body.</li> <li>● It is due to the hypersecretion of adrenal androgens.</li> <li>● Acne, seborrhea and muscularization may accompany the hirsutism.</li> <li>● Virilism is rare and occur in adrenal carcinoma.</li> </ul>	<p><b>4- Hypertension:</b></p> <ul style="list-style-type: none"> <li>● It is a classical feature in Cushing’s syndrome</li> <li>● Its complication contribute greatly to the morbidity and mortality of the disease.</li> </ul>
<p><b>5-Gonadal Dysfunction:</b></p> <ul style="list-style-type: none"> <li>● This is very common as a result of elevated androgens and cortisol, e.g. amenorrhoea, infertility, decreased libido.</li> </ul>	<p><b>6- Psychological Disturbances:</b></p> <ul style="list-style-type: none"> <li>● Symptoms range from mild irritability to anxiety, depression, poor memory and concentration, euphoria, mania, and sleep disorders.</li> <li>● Severe depression, psychosis, hallucinations, and paranoia can occur.</li> </ul>

<sup>6</sup> Hirsutism and Virilism are only seen in ACTH dependant form

<p><b>7- Muscle Weaknes/wastings:</b></p> <ul style="list-style-type: none"> <li>Commonly proximal and more prominent in the lower limbs.</li> </ul>	<p><b>8- Osteoporosis:</b></p> <ul style="list-style-type: none"> <li>Osteoporosis is a common complication presenting with back pain, and pathological fractures can occur in severe cases.</li> </ul>
<p><b>9- Thirst and Polyuria:</b></p> <ul style="list-style-type: none"> <li>occur secondary to development of diabetes mellitus but asymptomatic glucose intolerance is much more common.</li> </ul>	<p><b>10- Renal Calculi</b></p> <ul style="list-style-type: none"> <li>Renal colic occurs secondary to hypercalcuria and may occasionally be a presenting complaint.</li> </ul>

### Laboratory findings:

- High normal hemoglobin and hematocrit
- Lymphocytopenia
- Depressed eosinophils count
- Hypokalemic alkalosis (may occur in the setting of ectopic ACTH production -> mineralocorticoid like activity of cortisol)<sup>7</sup>
- Hyperinsulinism and abnormal glucose tolerance test while some have fasting hyperglycemia or clinical diabetes mellitus .(As a result of high glucose level in the blood)



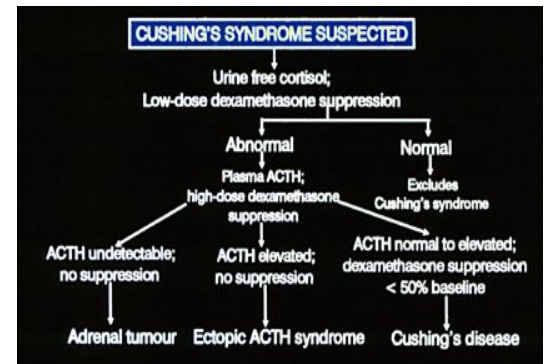
### Diagnosis of Cushing's syndrome<sup>8</sup>

The diagnostic tests can be divided into screening and confirmatory tests. explains the diagnostic approach Efhm - Biochemical tests of cushing's syndrome

#### Helpful diagram

In Cushing's disease, ACTH is normal or modestly elevated while in the ectopic syndrome, it is markedly elevated. In adrenal tumors, ACTH is undetectable.

- The 24- hour urinary free cortisol:** is an excellent method for diagnosis of Cushing's syndrome and in differentiating it from other forms of hypercortisolism, e.g. obesity, Values greater than four times the normal range are rare except in Cushing's syndrome.
- Dexamethasone Suppression Tests:** Establish the presence of a Cushing's syndrome regardless of the cause. It assesses feedback inhibition of the hypothalamic pituitary adrenal axis which is abnormal in Cushing's syndrome.



<sup>7</sup> may occur in the setting of ectopic ACTH production.

<sup>8</sup> There is hypersecretion of cortisol which is random and episodic with loss of normal circadian rhythm, therefore plasma cortisol ( and ACTH in the ACTH dependent types) remain elevated throughout the day

low dose	high dose
<p><b>A.OVERNIGHT 1 MG DEXAMETHASONE SUPPRESSION TEST:</b>            A screening test .            If the test is positive (<b>the serum cortisol is higher than 5</b>) in the absence of conditions causing false positive results. e.g. alcoholism, depression, and drugs, then the diagnosis should be confirmed by other tests.            (normal response: DXM &gt; ↓ CRH &gt; ↓ ACTH &gt; ↓ cortisol)</p>	<p><b>A.OVERNIGHT HIGH DOSE DEXAMETHASONE SUPPRESSION TEST:</b>            A simple fast test – The AM cortisol after 8 mg of Dexamethasone given the night before should reduce to less than 50% of the baseline value.</p>
<p><b>B.TWO-DAY LOW DOSE TEST:</b>            Dexamethasone 0.5 mg is given every 6 hours for two days. Plasma cortisol level should suppress after the last dose</p>	<p><b>B.TWO-DAY HIGH DOSE TEST:</b>            Dexamethasone 2 mg every 6 hours is given for two days Serum and urine cortisol should suppress to less than 50% the baseline values.</p>

^ Dr just said:

- 1) at night: cortisol “midnight salivary or blood”
- 2) 24-hour urinary free cortisol
- 3) overnight dexamethasone suppression test in the morning: normally should be suppressed
- 4) to know the cause: plasma ACTH levels

- **Midnight salivary cortisol:** Normally low cortisol level (remember the circadian rhythm)
  - If these tests are normal > think of other diagnoses.
  - If the diagnosis of cushing’s syndrome is confirmed (by using 2 of these 3 tests) > go to the confirmatory test to determine the exact cause.

**2- Confirmatory test: the goal is to tell the site of the lesion.**

- Plasma ACTH level.
- High-dose dexamethasone suppression test. (HDDST)
- CRH stimulation test.
- Imaging studies.
- bilateral inferior petrosal sinus sampling(BIPSS) It is invasive so we try not to use unless we need to.

**Radiological:**

- CT scanning will help in localizing pituitary and adrenal tumors and in some instances, ectopic ACTH production.
- Small tumors may be difficult to detect and selective venous sampling may be needed. In some cases, more detailed isotope scanning and arteriography or venography may be needed.



### We start with plasma ACTH:

- If low ( $< 1.1$  pmol/L on more than two occasions)  $>$  it is either adrenal tumor or adrenal hyperplasia  $>$  perform adrenal imaging. (If there is no adrenal lesion on imaging think of exogenous steroid use)
- If high  $>$  we should determine the source by performing high DST test and CRH stimulation test “If ACTH is high then it’s either from pituitary or ectopic tumor **BUT** always think about the pituitary (remember 70% of cases is due to pituitary adenoma).”

In summary, In ACTH dependant it’s caused by the pituitary gland unless you rule it out with all three tests above  $\Rightarrow$  Only then look for ectopic tumors and do chest and abdominal CT.

Think about ectopic lung cancer if you see signs of malignancy (like a very thin patient) with extremely high levels of ACTH”.

### Treatment of Cushing’s syndrome

- **Cushing’s Disease – Hypercortisolism has a lot of complications and can be fatal if left untreated.**
- **Treatment is directed at control of ACTH hypersecretion by the pituitary and available methods include:**

#### 1- Cushing’s disease:

- Microsurgery
- Radiotherapy
- Pharmacological inhibition of ACTH secretion

#### 2- Ectopic ACTH:

- Therapy is directed at removal of the tumour which is only successful in the benign tumours
- otherwise drugs that block steroid synthesis can be used, e.g. Metyrapone and mitotane with steroid replacement if necessary.

#### 3- Adrenal Tumors:

Adenomas are successfully treated by adrenalectomy while this treatment for carcinoma is usually unsuccessful and medical therapy can control hypercortisolism in these patients.

#### Drugs:

- Mitotane: acts by inhibiting cortisol synthesis through inhibiting the P450 enzyme responsible for 11B hydroxylation.
- Metyrapone: also blocks cortisol synthesis by inhibiting 11B hydroxylase action and also the cholesterol side-chain cleavage.
- Ketoconazole “anti-fungal”: a potent inhibition of the P450 enzymes with a principle effect on the 17-20 lyase enzymes but it also inhibits 11B hydroxylase, 18 hydroxylase and cholesterol side-chain cleavage. + Aminoglutethimide. and RU486 (Mifepristone)



## Primary hyperaldosteronism “conn’s syndrome”

- The principle mineralocorticoid hormone is aldosterone. It is produced in the zona glomerulosa exclusively and is **primarily controlled by the renin-angiotensin system**
- Other regulators include:
  1. **Potassium level**
  2. ACTH (without ACTH RAAS will take over and aldosterone won't be affected)
  3. Neural Components of the adrenergic and dopamenergic systems.
- There is increased production of aldosterone by abnormal zona glomerulosa tissue (adenoma or hyperplasia) that will increase the activity of the  $\text{Na}^+\text{K}^+$  pumps in the cortical collecting tubules which leads to :
  - Increased sodium retention
  - Expansion of the extracellular fluid volume
  - Increased total body sodium content that leads to suppression of renin production.
  - Potassium depletion occur decreasing the total body and plasma concentration of potassium and producing alkalosis.
  - With moderate potassium depletion. There is decreased carbohydrate tolerance and resistance to antidiuretic hormone.
- Because aldosterone biosynthesis is intensified, the entire biosynthetic pathway becomes activated and precursors like DOC corticosterone and 18-hydroxycorticosterone are present in increased amount in person with an aldosterone producing tumour.
- There is no abnormalities in cortisol production, plasma cortisol levels or cortisol metabolism.

### Causes:

- **Aldosterone producing adenoma (APA):** usually unilateral, of the glomerulosa cells of the adrenal cortex (Conn's syndrome).
- Bilateral adrenal hyperplasia; idiopathic AH
- Indeterminate hyperaldosteronism
- Dexamethasone suppressible hyperaldosteronism
- Adrenocortical carcinoma: rare

**Clinical features:** Patient usually come to medical attention because of symptoms of hypokalemia or detection of previously unsuspected hypertension. The clinical picture may mimic CAH from of 11  $\alpha$ -hydroxylase deficiency

1- Non-specific There are no characteristic symptoms and often nonspecific complaints, e.g. tiredness, lethargy, weakness, nocturia and symptoms of potassium depletion.

2- Salt and water retention **Hypertension is the most common clinical feature** (can range from borderline to severe hypertensive levels, Accelerated/malignant hypertension is rare and postural fall in blood pressure without reflex tachycardia is observed in severe potassium depletion because of blunting of the baroreceptors.) Retinopathy is mild with hemorrhages being rare.

3- Hypokalemia and alkalosis: Positive chvostek's sign and trousseau sign may suggest alkalosis with severe potassium depletion. The ECG shows signs of modest LVH and potassium depletion (low K levels cause metabolic alkalosis which will shift ca to protein binding this is called pseudohypocalcemia)

**If potassium depletion is severe with alkalosis there is:** increased thirst and polyuria and maybe parasthesia. Headache is a frequent complaint. Blood pressure can range from borderline to severe hypertensive levels.

### Laboratory findings:

- Potassium depletion<sup>9</sup>(episodic weakness, Paresthesias, transient paralysis, tetany, nephropathy with polyuria and polydipsia)
- **Metabolic alkalosis**
- High serum sodium in the presence of reduced haematocrit value (due to increased extracellular fluid and plasma volume from sodium retention)
- There is also failure to concentrate urine.
- Abnormal glucose tolerance
- All features of potassium depletion.
- high Cl, high Aldosterone

### Diagnosis of primary hyperaldosteronism:

(When a patient presents to you with hypertension, hypokalemia and is not taking diuretics then suspect primary hyperaldosteronism)

---

<sup>9</sup> Diuretics should be stopped three weeks prior to potassium measurement.

- If hypokalemia is documented, the next step is:
  - to assess the **renin angiotensin system** by doing a **random plasma renin** activity level:
    - if normal or high in the absence of diuretics therapy → then primary aldosteronism is very unlikely
    - if it is suppressed → then primary aldosteronism is a likely diagnosis.
  - **Aldosterone measurement:** both plasma and urinary aldosterone measurement should be performed while the patient is taking a high salt diet with sodium chloride supplementation.
    - Assessment of aldosterone production can be best done by:
      - measurement of urinary aldosterone excretion over 24 hour period and it is superior to plasma aldosterone measurement in detecting abnormal production of aldosterone but cannot discriminate between adenoma and hyperplasia.
      - While the plasma levels can differentiate between the two conditions in most cases.

#### Screening test:

#### Ratio of the plasma aldosterone level to plasma renin [the best initial test]

If the Ratio is high (High aldosterone & Low renin) > Primary, do confirmatory test.

If the Ratio is Low (High aldosterone & High renin) > Secondary, look for secondary causes.

#### confirmatory test:

##### A-Saline infusion test:

infusion of saline will decrease aldosterone level in normal patients but not in those with primary aldosteronism.

if aldosterone level is <8.5 ng/dL after saline infusion, primary aldosteronism may be ruled out.

##### B-Oral Salt (sodium) loading:

The patient is given a high salt for 3 days. Serum and urine electrolytes ,aldosterone, and creatinine are measured on the third day. High urine aldosterone in the setting of high urine sodium confirms the diagnosis

##### C- Captopril test

##### D- Fludrocortisone suppression test

- Localization of Adenoma/Carcinoma:
  - **Scanning:**
    - using i.v. Administered  $^{131}$ I-iodocholesterol locates tumour in 80% of the cases depending on the size of the tumour.
    - NP59 scan is another scan which consumes less time.
    - CT scanning is also useful with less radiation hazard.
    - Other methods include adrenal venography, adrenal vein catheterization and bilateral sampling of blood for aldosterone measurements.



- **adrenal venous sampling for aldosterone levels**

- To diagnose the cause of primary aldosteronism we use adrenal venous sampling for aldosterone levels<sup>10</sup>.
  - High level of aldosterone on one side indicates an adenoma.
  - High levels on both sides indicate bilateral hyperplasia.
- Renin–aldosterone stimulation test — Recumbency or upright positions are assumed, followed by measurement of serum aldosterone.

- **Imaging tests:**

A-CT scan and MRI of adrenals: may demonstrate adenoma or hyperplasia.

B-Iodocholesterol scanning: functional approach to differentiate between adenoma and hyperplasia.

C- Arteriography\ Venography.

## **Treatment of primary hyperaldosteronism:**

- In aldosterone producing adenoma, unilateral adrenalectomy is recommended ( provided there is adequate potassium replacement and adequate extracellular volume expansion with adequate control of BP before surgery all of which can be achieved by spironolactone<sup>11</sup> with or without other medications which should be given for some time before surgery)
- The surgical cure of hypertension, associated with adenoma, is excellent as it is reported to be curative over 50% in many series with reduction of hypertension in the remainder.
- In hyperplasia, antihypertensive medication should be given as surgery will not ameliorate the hypertension.
- Adenoma → Surgical resection
- Adrenal hyperplasia → Spironolactone.

---

<sup>10</sup> it is a sample of the venous blood draining the adrenal, and it is the most accurate test to confirm “**unilateral adenoma**”

<sup>11</sup> Mineralocorticoid receptor antagonist

## pheochromocytoma

- Pheochromocytoma is a tumor that arises from (medulla) the chromaffin cells which produce catecholamines.
- They release epinephrine or norepinephrine (or both) and in some cases, dopamine into the circulation causing hypertension as well as other signs and symptoms.
- Only 0.1% of hypertensive patients have pheochromocytoma but recognition is important because it can be fatal during delivery or surgery if unrecognized and not properly treated.
- It may occur as a heritable disorder either alone or in combination with other endocrine tumours, e.g. MEN type IIA: pheochromocytoma, hyperparathyroidism, pituitary adenoma and medullary thyroid carcinoma or MEN Type IIB: pheochromocytoma with mucosal neuroma
  - **Follows the rule of 10**
    - 10% bilateral , 10% are multiple
    - 10% Familial , 10% occur children
    - 10% Malignant
    - 10% Extra adrenal: the Common extra adrenal sites and near the kidneys and the organ of Zuckerkandl. They can also occur in the posterior mediastinal region.

### Clinical features:

- Most patients have symptoms that vary in intensity and are perceived to be mainly episodic or paroxysmal by about half the patients.
- 50% are silent. ( NO symptoms)
- Most patients with persistent hypertension also have superimposed paroxysms and only few patients are entirely free of symptoms and hypertension between attacks and give no evidence of catecholamine excess during these intervals.
- **Severe Hypertension** (due to vasoconstriction by catecholamines)
- Headache
- Sweating <sup>12</sup>
- Forceful heartbeat with or without tachycardia
- Anxiety or fear of impending death
- Tremor
- Fatigue or exhaustion
- Nausea and vomiting, constipation and weight loss

The most important symptoms are  
**5Ps**  
**P**aroxysmal  
**P**ain(headache)  
**P**ressure(HTN)  
**P**alpitation  
**P**erspiration(sweating)

<sup>12</sup> The decreased heat loss and increased metabolism cause a rise in temperature and flushing and leads to reflex sweating which may be profuse and usually follows the cardiovascular effects

- Abdominal or chest pain
- Visual disturbance
- Hyperglycemia<sup>13</sup>
- cold hands and feet

**Attacks are usually precipitated by activities that compress the tumour, e.g changes in position, exercise lifting, defecation or eating and by emotional distress or anxiety.**

### **Other cause of increased sympathetic activity must be thought of:**

- Angina due to coronary vasospasm
  - Severe anxiety state
  - Hypertension
  - Hypertensive crises associated with (Paraplegia, Tabesansalis Lead ,poisoning and acute porphyria)
  - Menopausal hot flushes
  - Thyrotoxicosis, etc.
  - In the attack the symptoms resemble those produced by injection of epinephrine or norepinephrine.
- 
- The attacks in pheochromocytoma in those patients with paroxysmal symptoms occur several times a week or oftener and last 15 minutes or less but they may occur at intervals of months or as often as 25 times a day and may last minutes to days. With time the attacks usually increase in frequency but do not change much in character.
  - Hypertension is usually present and characteristically there is wide fluctuations and an episode of marked hypertension might be followed by hypotension and shock.
  - The blood pressure typically does not respond to commonly used antihypertensive medications.
  - Chronic constriction of the arterial and venous beds leads to reduction in plasma volume and the inability to further constrict the bed upon arising causes the postural hypotension that is characteristically observed.
  - A mass is felt in the neck or abdomen and palpation may produce a typical paroxysm.
  - Patients with persistent symptoms and hypertension may develop hypertensive retinopathy or nephropathy as well as the other sequelae of hypertension.
  - CVA, CCF and MI are all observed. A significant number were found to have myocarditis post partum.

Ganglioneuromas and neuroblastomas can produce catecholamines with dopamine being the major product leading to a similar picture resembling pheochromocytoma

### **Diagnosis:**

The diagnosis of pheochromocytoma should be considered in the following patients:

- a. Patients with **paroxysmal symptoms**
- b. Children with hypertension

---

<sup>13</sup> The increased glycolysis and alpha receptor-mediated inhibition of insulin release causes an increase in blood sugar levels

- c. Adults with severe hypertension not responding to therapy (3 drugs or more).
- d. Hypertensive patients with diabetes or hyper-metabolism.
- e. Hypertensive patients with symptoms resembling the symptom complex described above or can be evoked by exercise, position changes .. ect. or certain antihypertensive medications.
- f. Patients who become severely hypertensive or go into shock during anesthesia, surgery or obstetric delivery.
- g. Patients who have disorders sometimes associated with pheochromocytoma, e.g. neurofibromatosis, mucosal adenomas, medullary carcinoma of thyroid or those who have first degree relatives who have pheochromocytomas or other manifestations of MEN

”In general: Young patients < 40 with 3 anti-hypertension medications, accelerated hypertension, or resistant hypertension => Suspect secondary hypertension => **Rule out pheochromocytoma, cushing's syndrome, and hyperaldosteronism.**”

### Laboratory Diagnostic Tests :

- In patients with continuous hypertension or symptoms, levels of plasma or urinary catecholamines and their metabolites are usually clearly increased
- the difficulty arises in patients having brief and infrequent paroxysms with symptom-free intervals and in such cases, sampling of blood or urine should be done during a carefully observed episode to confirm the diagnosis.
- Analysis of blood samples obtained for venous drainage can be of great value in locating small tumours in unusual locations.

	COMPOUND	INTERFERING SUBSTANCES
Blood /Urine	Metanephrin - Normetanephrin	Increased by catecholamines, MAOI and others
Urine	Vanilly Mandelic Acid (VMA)	Increased by catecholamines and food that contain vanillin or L-dopa. Decreased by Clofibrile and MAOI
Blood/Urine	Catecholamines	
Urine	Epinephrine- Norepinephrine- Dopamine	May be increased with highly fluorescent compounds, e.g. tetracycline, quinidine as well as food and drugs containing catecholamines, e.g. bananas and other drugs, e.g. methyldopa, ethanol

- **Radiological Diagnostic Tests:**
  - Imaging of the adrenal glands with CT or MRI is done only after biochemical testing.
  - once the diagnosis has been established, the tumor must be located prior to surgical removal.
  - CT scan gives better results than sonography or other radiological tests.
  - **MRI** is evolving as very specific and excellent technique for detecting pheochromocytomas.



- MIBG scanning: if (Paraganglioma • Young • large size • or malignant features), can detect even the smallest tumour but not all pheochromocytomas produce detectable images and other tumours e.g. neuroblastoma give positive images.
- Genetic Tests: N.B: 30-40% of Pheochromocytoma and Paraganglioma Have positive genetic test.( not 10% )

### Treatment:

- Treatment is directed toward:
  - Reduction of symptoms
  - Lowering of BP
  - Amelioration of paroxysms
- **Therapy with alpha adrenergic antagonists** should be instituted. Such treatment will allow expansion of the vascular bed and plasma volume.
- **Alpha blocker: because the blood pressure is due to vasoconstriction not due to high intravascular volume, volume is depleted)** Agents commonly used include phentolamine and phenoxybenzamine, small doses of propranolol maybe required for marked tachycardia or arrhythmia prior or during surgery.
- Patients should be fully, prepared medically prior to surgery to avoid intra and post operative complications. Once the tumor is removed, the blood pressure usually falls and i.v. fluids and / or blood might be needed to restore circulatory volume.
- Persistence of high BP after surgery should alert physician to look for other causes, e.g. renal vascular hypertension.  
our problem is the the volume is low! we have to give them salt. Only case where we give salt in hypertension.
- Salt loading: Oral NaCl: 3 days Or IVF 0.9% saline 1-2 days before surgery
  - **Surgical tumour resection** with early ligation of venous drainage is the **treatment of choice**. Ligation lowers the possibility of catecholamine release/crisis by tying off drainage.
  - $\alpha$ -blockade (typically phenoxybenzamine or phentolamine) for 10 to 14 days prior to surgery as well as  $\beta$ -blockade (i.e., propranolol) for 2 to 3 days prior to surgery. The  $\alpha$ -blockade is used to control BP, and the  $\beta$ -blockade is used to decrease tachycardia. Ca-blockers can be used
  - Laparoscopic adrenalectomy can be safely performed for most small to medium-sized pheochromocytomas.

“In pheochromocytoma the vessels are constricted which causes hypertension (due to catecholamines) and there is low intravascular volume.

So, if surgery is done it will cause hypertensive crisis (Because the patient is hypertensive and there is stress from the surgery).

To prevent that, **PRIOR TO SURGERY**  $\alpha$  and  $\beta$  blockers must be taken\* + Salts and fluids\*\*.



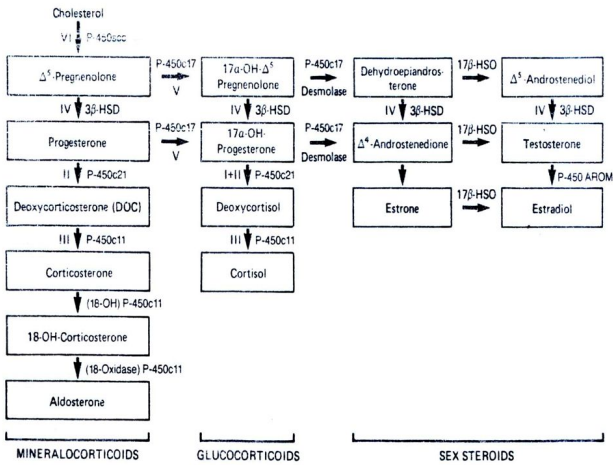
\*Give  $\alpha$  blockers **FIRST** then  $\beta$  blockers. (why? because vasoconstriction is mainly by  $\alpha$  receptors which are located at the blood vessels, so If  $\beta$  receptors are blocked first  $\Rightarrow$  more catecholamine acting on  $\alpha$  receptors  $\Rightarrow$  more vasoconstriction).

\*\* Salts and fluids are given to prevent the sudden drop in pressure that will happen if  $\alpha$  blockers are given (there is low volume and vasodilation from the blockers).

Once the tumor is removed, the blood pressure usually falls and i.v. fluids and / or blood might be needed to restore circulatory volume. Persistence of high BP after surgery should alert physician to look for other causes, e.g. renal vascular hypertension.

- think of secondary hypertension if:
  - young <40y/o
  - on 3 antihypertensives
  - resistant hypertension “doesn’t respond to medications”
  - accelerated hypertension
- any adrenal mass “adrenal incidentaloma”:
  - rule out: cushing, pheochromocytoma
- if also has high blood pressure: rule out hyperaldosteronism

**helpful pictures :->**





## Summary

<b>Adrenal Disorders</b>	
<u>Hypofunction</u>	
<b>Primary adrenal insufficiency (Addison disease)</b>	<b>Secondary adrenal insufficiency</b>
<p><b>Causes:</b> Autoimmune (most common), TB</p> <p><b>Clinical features:</b></p> <ul style="list-style-type: none"> <li>• hypotension</li> <li>• <b>Hyperpigmentation</b> (only in primary !!!), due to MSH not ACTH.</li> </ul> <p>weakness, fatigue, N/V, Hypoglycemia...</p>	<p><b>Causes:</b> Panhypopituitarism withdrawal from glucocorticoid therapy surgical removal of pituitary glands</p> <p><b>Pathophysiology:</b> ACTH deficiency this leads to:</p> <ol style="list-style-type: none"> <li>1- Decreased Cortisol &amp; Androgen secretion.</li> <li>2- <b>Aldosterone secretion remains normal.</b></li> </ol>
<p><b>Biochemical:</b></p> <ol style="list-style-type: none"> <li>1. Measure Plasma cortisol level:</li> <li>2. Measure ACTH, renin &amp; aldosterone level</li> <li>3. ACTH stimulation test (<b>definitive diagnosis!</b>)               <ul style="list-style-type: none"> <li>• Failure to increase cortisol → Primary adrenal insufficiency.</li> <li>• Increase in cortisol → Secondary adrenal insufficiency</li> </ul> </li> </ol>	
<p><b>Treatment: Replace both:</b></p> <ul style="list-style-type: none"> <li>• glucocorticoids (<b>Hydrocortisone</b>)</li> <li>• Mineralocorticoids (<b>Fludrocortisone</b>)</li> </ul>	<p><b>Treatment:</b></p> <ul style="list-style-type: none"> <li>• <b>Replace</b> glucocorticoids (<b>Hydrocortisone</b>) <b>Only.</b></li> </ul>
<b>Congenital Adrenal Hyperplasia</b>	
<p><b>Caused by: 21-OH deficiency.</b></p> <p><b>Clinical feature:</b></p> <ul style="list-style-type: none"> <li>• Ambiguous genitalia in female</li> <li>• Dehydration &amp; shock</li> </ul> <p><b>Management:</b></p> <ul style="list-style-type: none"> <li>• glucocorticoids (<b>Hydrocortisone</b>)</li> <li>• Mineralocorticoids (<b>Fludrocortisone</b>)</li> <li>• Surgery (for female)</li> </ul>	<p><b>Diagnosis</b></p> <ul style="list-style-type: none"> <li>• Electrolytes imbalance (hyponatremia, hyperkalemia, hypoglycemia)</li> <li>• High 17- OHP</li> <li>• High androgens</li> </ul>



Hyperfunction

Hyperfunction	
Hypercortisolism ( <b>Cushing Syndrome</b> )	Hyperaldosteronism ( <b>Conn's syndrome</b> )
<p><b>Causes:</b></p> <ul style="list-style-type: none"> <li>· <b>ACTH dependent:</b> pituitary tumor (<b>Cushing's disease</b>) or Ectopic.</li> <li>· <b>ACTH independent:</b> iatrogenic or Adrenal tumor</li> </ul> <p><b>Clinical features:</b></p> <ul style="list-style-type: none"> <li>-Moon face                      - purple striae</li> <li>-Truncal obesity                - osteoporosis</li> </ul>	<p><b>Causes:</b></p> <ul style="list-style-type: none"> <li>· Adenoma</li> <li>· hyperplasia</li> </ul> <p><b>Clinical features:</b></p> <ul style="list-style-type: none"> <li>· Secondary HTN</li> <li>· High Na, low K, high Cl</li> <li>· Alkalosis</li> <li>· Positive chvostek's sign and trousseau sign</li> </ul>
<p><b>Biochemical:</b></p> <ul style="list-style-type: none"> <li>· 24 h urine free cortisol level (high)</li> <li>· 1 mg DST (no suppression)</li> <li>· Midnight salivary cortisol (High)</li> <li>· ACTH measurement to know the cause</li> </ul>	<p><b>Biochemical:</b></p> <p><b>Initial (screening) test:</b> Aldosterone\ Renin ratio</p> <p><b>Confirmatory test:</b></p> <ul style="list-style-type: none"> <li>• Saline infusion test</li> </ul> <p><b>Imaging tests:</b> CT</p>
<p><b>Treatment:</b></p> <ul style="list-style-type: none"> <li>· Surgical</li> </ul>	<p><b>Treatment:</b></p> <ul style="list-style-type: none"> <li>· Adenoma = surgical resection</li> <li>· hyperplasia = spironolactone</li> </ul>
Pheochromocytoma	
<p><b>Caused by:</b></p> <p>Tumor of adrenal medulla produces catecholamines</p> <p><b>Clinical feature:</b></p> <ul style="list-style-type: none"> <li>· Secondary HTN</li> <li>· Episodic (spells): sweating, palpitation, headache</li> </ul> <p><b>Diagnosis</b></p> <ul style="list-style-type: none"> <li>· 24 hr urine collection of Metanephrines</li> <li>· Plasma Metanephrines</li> </ul>	<p><b>Management:</b></p> <ol style="list-style-type: none"> <li>1. <math>\alpha</math>-blocker then B-Blocker (10-14 days before operation)</li> <li>2. Oral NaCl: 3 days before surgery</li> <li>3. Surgical removal (<b>definitive diagnosis</b>)</li> </ol>

## Questions

1-which one of the following statement is correct :

- A-The zona glomerulosa secrete Aldosterone
- B-The zona fasciculata secret Glucocorticoid
- C-The zona reticularis secrete Androgen
- D-All of the above

2-All cortex hormone are originated from :

- A- Tyrosine
- B-Testosteron
- C-Cholesterol
- D-Cortisol

3-In addison disease which on of the following hormone is missed:

- A-Androgen
- B-Glucocorticoid
- C-Aldosterone
- D-all of the three hormon are missed

4-what is the most important clinical feature that addison patient present with:

- A-Hypotension
- B-Shock
- C-Hypertension
- D-Bleeding

5- What is the cause of hyperpigmentation in primary addison disease:

- A-Stimulating of thyroid stimulating hormone TSH
- B-Stimulation of melanocyte stimulating hormone MSH
- C-Stimulation of ACTH
- D-none of the following

6-what is the steroid replacement in case of primary addison disease:

- A-Cortisol + aldosterone
- B-Cortisol only
- C-No need for replacement
- D-give insulin

7-A 55-year-old patient presents with chronic cough. In addition to the cough, the patient has gained weight recently with development of a "buffalo hump" and Cushingoid features. A chest x-ray film demonstrates a mass involving the central area of the chest. Bronchoscopy is performed, and it proves possible to biopsy the tumor during the procedure. Which of the following is the most likely diagnosis?

- (A) Adenocarcinoma
- (B) Bronchoalveolar carcinoma
- (C) Large cell carcinoma
- (D) Small cell carcinoma

8-A 27-year-old woman comes to her physician because of weakness, weight loss, and amenorrhea for 6 months. Her blood pressure is 100/65 mm Hg. On examination, increased skin pigmentation is seen, especially around the nipples and over the knees, elbows, and knuckles. Laboratory analysis shows:

- ◀ Sodium 125 mEq/L
- ◀ Potassium 6.3 mEq/L
- ◀ Chloride 100 mEq/L
- ◀ Calcium 10 mEq/L

Complete blood count shows mild lymphocytosis with eosinophilia. Low plasma levels of cortisol and high levels of ACTH are detected on a blood sample drawn at 8 am. Which of the following is the most common cause of this disease?

- (A) Adrenoleukodystrophy
- (B) Autoimmune destruction
- (C) Bilateral adrenal hemorrhage
- (D) Fungal infection

9-64-year-old man presents to the emergency department after a motor vehicle crash and receives a CT of the abdomen that shows a finding of a unilateral mass in the left adrenal gland. He is unharmed from the accident, feels well, and has never smoked. His blood pressure is 155/90 mm Hg, deep tendon reflexes are 3/4, and muscle strength is 4/5. Laboratory studies show:

- ◀ Na<sup>+</sup>: 150 mEq/L
- ◀ K<sup>+</sup>: 3.0 mEq/L
- ◀ Cl<sup>-</sup>: 105 mEq/L
- ◀ HCO<sub>3</sub><sup>-</sup>: 36 mEq/L

Plasma renin activity is also decreased. Which of the following is most likely to be increased?

- (A) Aldosterone
- (B) Anion gap
- (C) Carcinoembryonic antigen
- (D) Prostate-specific antigen

Answer:

1-D , 2-C , 3-D , 4-A , 5-B , 6-A , 7-D , 8-B , 9-A