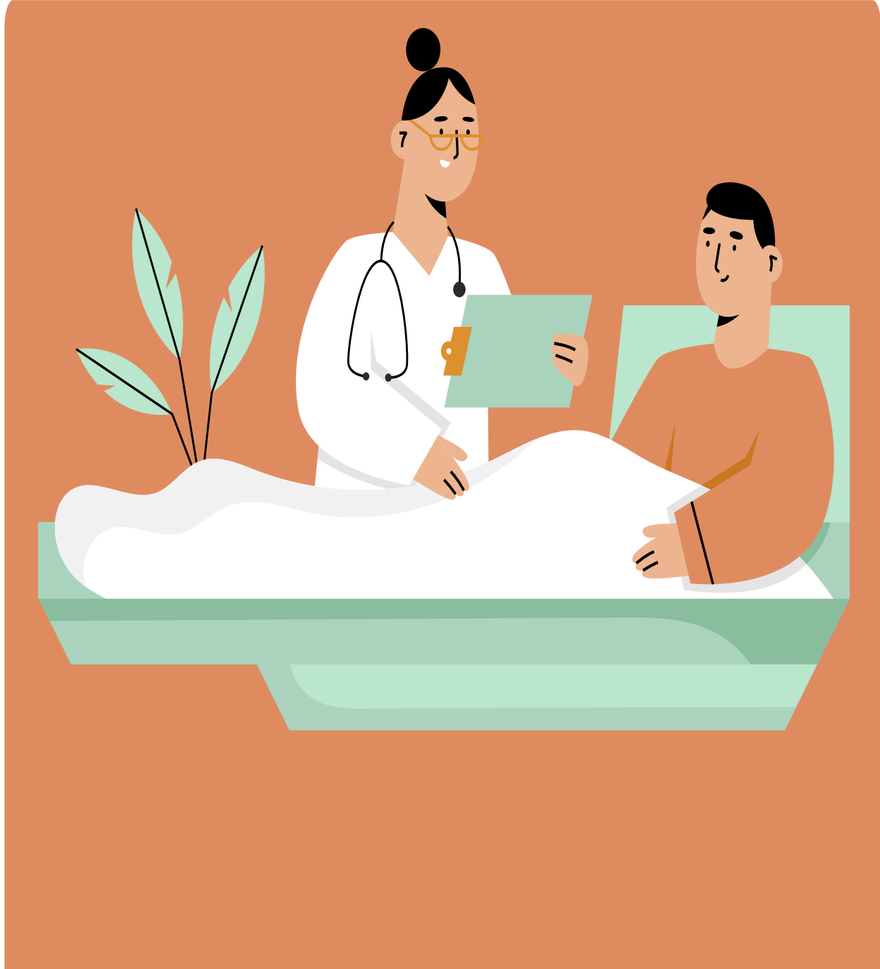
MED437
KING SAUD UNIVERSITY

SURGERY TEAM 437



Adrenal glands disorders

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Color Index:

- Important
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Editing File / Feedback

Basic review: (video 10:42)

The adrenal gland is divided into two parts; each with separate functions:

1- Adrenal medulla

2- Adrenal cortex

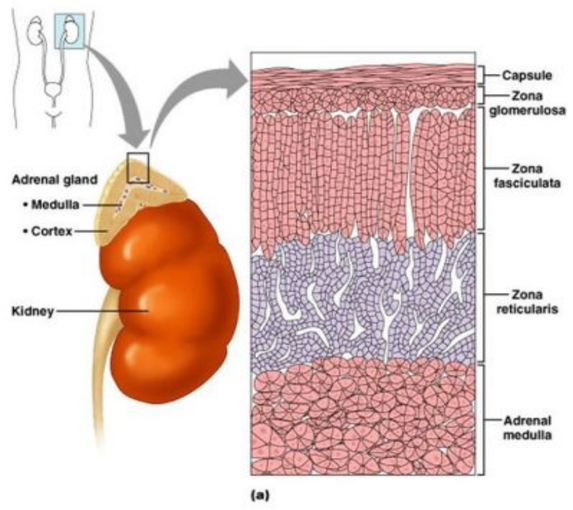
The cortex has three specific zones and each produces a specific class of steroid hormone:

A. Zona **G**lomerulosa - Mineralocorticoids (Aldosterone)

B. Zona **F**asciculata - glucocorticoids (Cortisol)

C. Zona **R**eticularis - Androgens

Remember: Salt, Sweet and Sex



What you need to know is that the hormones or secretions from the adrenal cortex can be stimulated:

- Directly by: decreased Na or increased K in the blood.
- Indirectly by: 1.hypotension or hypovolemia → kidney releases renin → angiotensin will give indirect effect.

2. by ACTH

Aldosterone (Salt): Mineralcorticoids

Function: fluid and electrolyte balance

A. Na+ retention

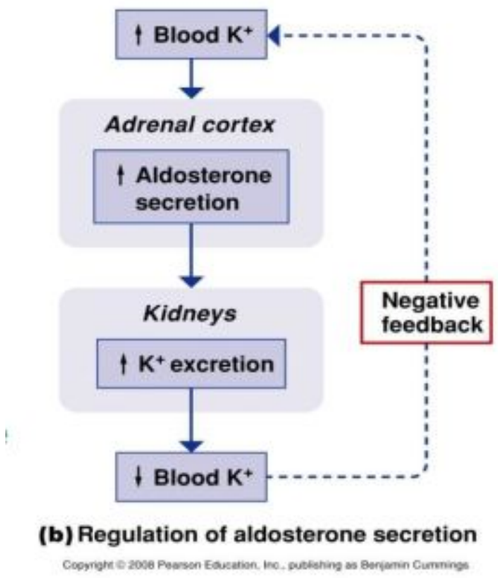
B. Water retention

C. K+ excretion serum K+ will ↓ and urine K+ will ↑)

Renin from kidneys controls adrenal cortex production of aldosterone

If your Na level is low, Aldosterone will increase

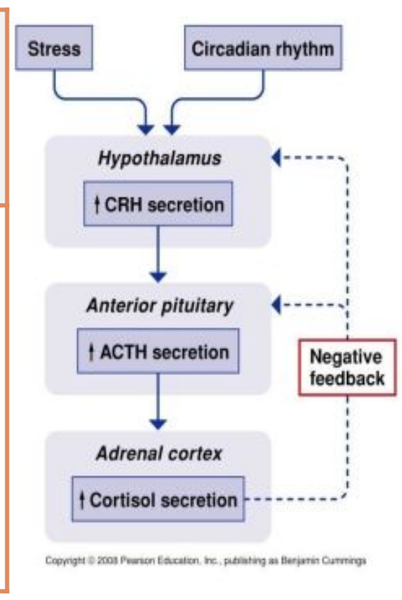
If your serum K+ level is high, Aldosterone will also increase



Cortisol (Sugar): Glucocorticoid

Function: Regulate metabolism and are critical in stress response, Stress might cause pseudo-cushing syndrome (like in exams: eating + studying = weight gain) and is responsible for control and metabolism of:

Carbohydrates	Fats	Proteins
amount of glucose **formed**, amount of glucose **released**	stimulates fatty acid, **mobilization** from adipose tissue	stimulates protein synthesis in liver, **protein breakdown in tissues**



Other functions: Decreases inflammatory and allergic response and decrease immune response, therefore prone to infection

Release of glucocorticoids is controlled by **ACTH** produced in anterior pituitary gland

Decreased levels of circulating cortisol causes **stimulation** of ACTH

Increased levels of circulating cortisol causes **decreased** release of ACTH

What type of feedback mechanism is this? Negative feedback

Also affected by:

Individual biorhythms. ACTH levels are highest 2 hours before and just after awakening (usually 5AM - 7AM). These gradually decrease the rest of the day

Stress increases cortisol production and secretion

Basic review

Androgens (Sex):

Hormones which increase male characteristics (release of testosterone)

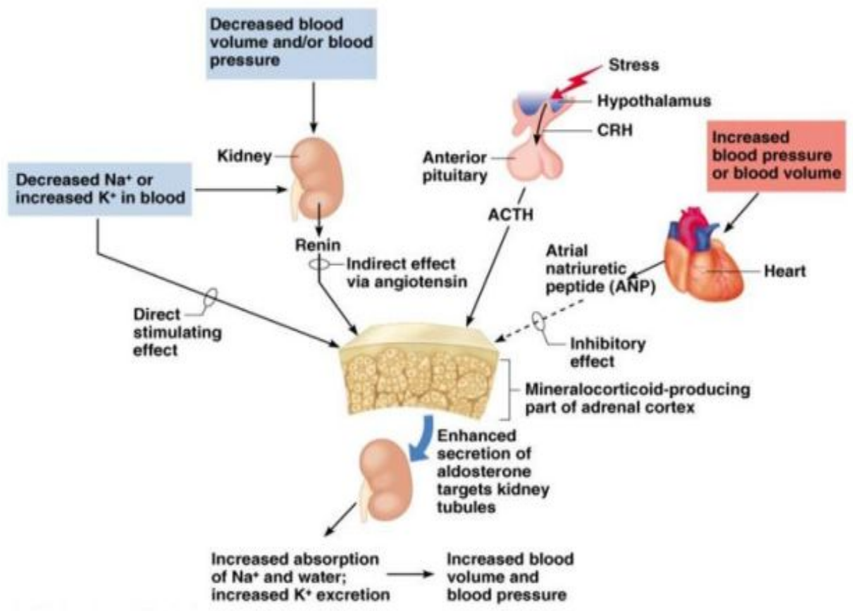
Androgen is seen more in **women** than men

Medulla:

What is released by the adrenal medulla? Catecholamines:

Epinephrine and **Norepinephrine**

These hormones are responsible for Fight or flight response



The diseases of the adrenal gland can be divided into: hypofunction, hyperfunction, & masses.

You have to understand each disease: how it presents, and how it will affect the electrolyte levels.

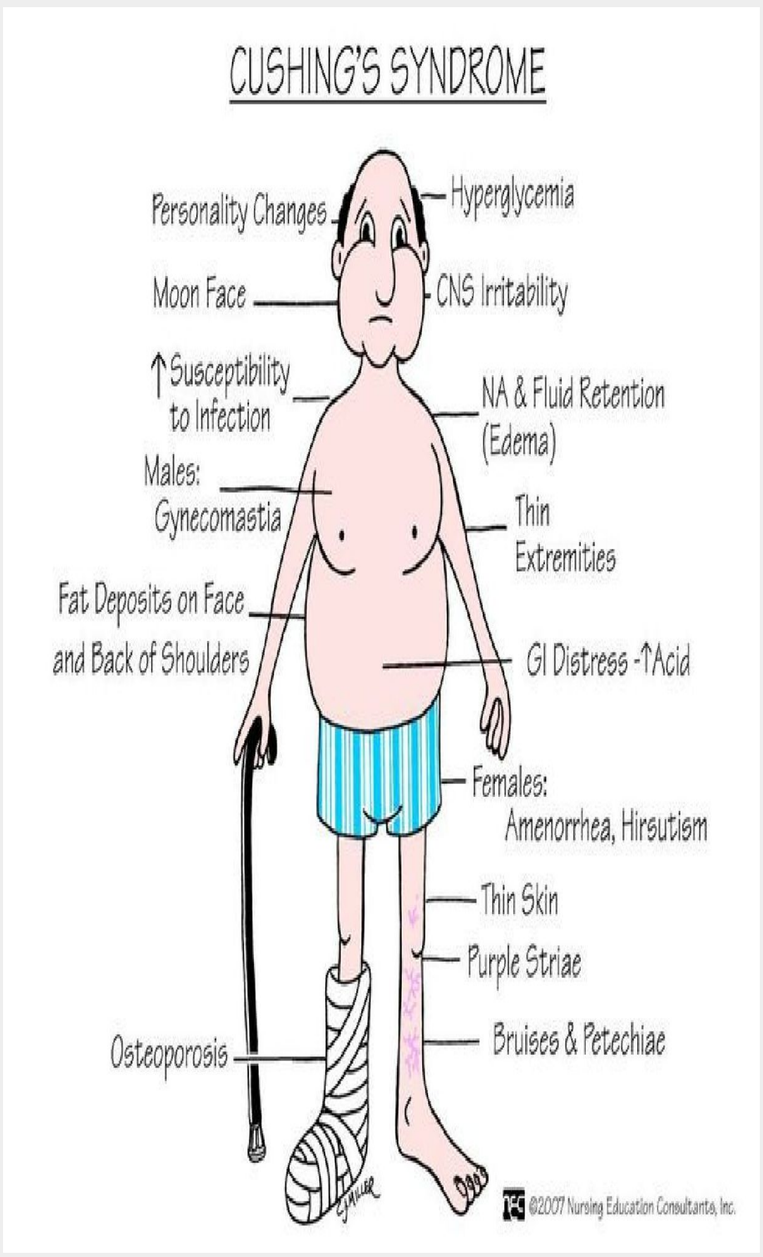
Cortex:

1. Cushing's Syndrome (video 13:42)

- Too much cortisol! Increases secretion of **cortisol** from adrenal cortex.
- 4 times more frequent in females, and usually occurs at 35-50 years of age.
- Etiology:

Primary **(20%)**	Secondary **(80%)**	Ectopic	Iatrogenic
Tumor of the adrenal cortex: • **Adenoma (more common, unilateral)** • **Carcinoma (rare, present late)**	Tumor of the anterior pituitary gland **(when the syndrome is caused by a pituitary tumor it is referred to as cushing's disease).**	ACTH secreting tumor: 1. Lung(Small cell carcinoma) 2. Pancreas 3. Thyroid	**Therapeutic steroid administration(exogenous source)** **Most common cause**

SIGNS & SYMPTOMS:



I. Cushing's original description was a "tomato head, potato body, and four matches as legs."

II. Increase protein catabolism:
- Increase muscle wasting
- Loss of collagen support (thin, fragile skin, bruises easily)
- Poor wound healing

III. Increase carbohydrate metabolism:
- Hyperglycemia → can get **diabetes** because insulin can't keep up
- Polyuria

IV. Increase fat metabolism:
- **Truncal obesity** + buffalo hump
- Moon face
- ↑ weight but ↓ strength

V. Decrease immune response:
- More prone to infection
- Decrease resistance to stress
- Death usually occurs from infection

VI. Increase androgen secretion:
- Excessive hair growth
- Acne
- Change in voice
- Receding hairline

VII. Increase mineralocorticoid activity (aldosterone) → increase sodium and water retention → elevated BP.

Investigation

(the test must be repeated at least twice to confirm the diagnosis)

- Exclude exogenous steroid use then order: 24 hr **urinary free cortisol and/or dexamethasone suppression test**. Imaging can be done → MRI (pituitary adenoma) or CT (adrenal adenoma).

IMP

1. All the following are true about cushing except? Serum and Urine Metanephrines
2. The patient presented to you with adrenal lesion, what is the most investigation you should order? Serum and Urine Metanephrines " **to exclude Pheochromocytoma** its critical to the patient because the patient might go into an adrenal crisis if you take a biopsy "

MANAGEMENT

- Most of the time you just treat the symptoms but if it failed and adrenal lesion was found then you go for surgery.
- **Adrenal adenoma: are rarely bilateral → unilateral adrenalectomy is most commonly indicated.**
- **Adrenal carcinoma: should be completely removed whenever possible +/- chemotherapy.**
- **Pituitary disease: → bilateral adrenalectomy, but at the price of lifelong steroid therapy. Pituitary irradiation or surgery avoids the side-effects of adrenalectomy, and microsurgical removal of the adenoma is now the treatment of choice.**

2.Conn's Syndrome [Video(06:11)]

- HYPERALDOSTERONISM ⟶ too much aldosterone secretion.
- Usually is caused by adrenal tumor most common in young or middle-aged women.
- What does aldosterone do? Sodium and water retention, and potassium excretion.
- Types of hyperaldosteronism:

Primary (Conn's syndrome)	Secondary
Usually due to a benign adenoma (small, single). The high circulating levels of aldosterone suppress renin secretion – a helpful biochemical diagnostic observation.	**Most commonly secondary to excessive renin secretion in chronic liver, renal or cardiac disease.**
(High aldosterone & Low renin).	(High aldosterone & High renin).

SIGNS & SYMPTOMS	1. Na and water retention (hypernatremia) ⟶ high blood pressure & visual disturbance +/- headache. 2. Decreased K+ (hypokalemia ⟶ Worsening hypokalemia, episodes of muscle weakness and nocturnal polyuria). What is the normal serum K+ level? 3.5-5 (mEq/L). 3. Usually no edema. (but if it's Secondary PT could have Edema) **They may have generalized edema but not lower limb edema** 4. **Usually present in early age**
DIAGNOSIS	1. Increased plasma aldosterone levels with low plasma renin levels (in case of primary). 2. Plasma (or serum): increased Na+ and decreased K+. 3. Increased Urinary K+ (remember serum K+ is low and urine K+ is high because of excretion!). 4. **EKG changes** (check for signs of hypokalemia ⟶ flattening of T waves, U waves).. 5. CT scan to rule out tumors
MANAGEMENT	Surgery (ADRENALECTOMY) but before the surgery you need to prep the pt and after you need to follow up (it's enough to know that you don't have to know the details).

- Note that in Case of hyperaldosterone there is NO Specific finding on physical examination to differentiate it from essential HTN, You Should Start with serum electrolyte
- **Which of the following is true in pt with Conn's Syndrome? High K+ in the urine**

Pre-op	Post-op
• Stabilize hormonally. • Correct fluid and electrolytes. • Cortisol PM before surgery, AM of surgery and during OR. • Preop: make sure serum electrolytes (Na+ & K+) are normal , no ECG changes by giving **Giving the aldosterone antagonist, Spironolactone, should ↓ blood pressure and reverse hypokalaemia**	• We observe the pt post-op and sometime we put them in the ICU (What type of problems to expect??). • IV cortisol for 24 hours. • IM cortisol 2nd day. • PO cortisol 3rd day. • Poor wound healing. • If unilateral adrenalectomy the steroids are weaned (other adrenal takes over 6-12 months)

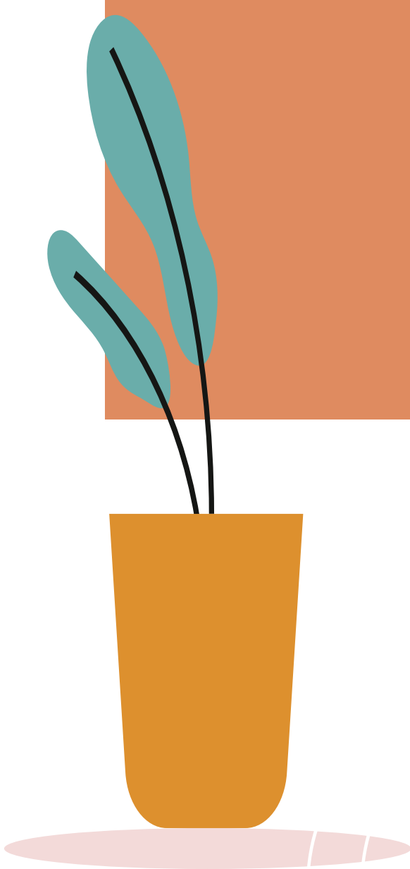
3. Addison's Disease video(16:27)

- Adrenocortical Insufficiency: Hypofunction of adrenal cortex. So which hormones will be decreased? ALL OF THEM (so the treatment is hormones replacement).
- Types of adrenocortical insufficiency:

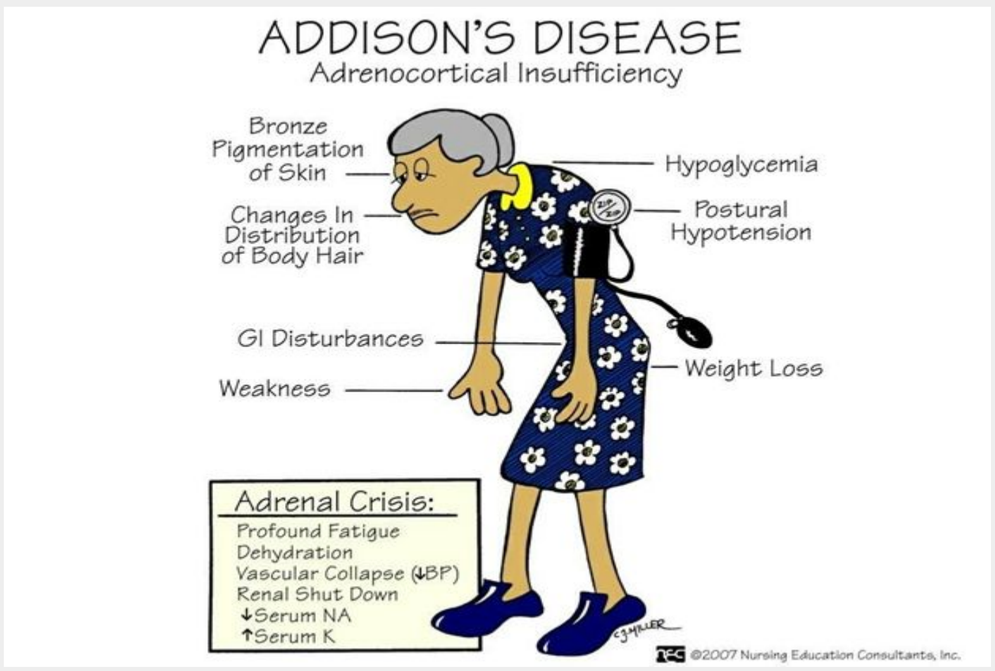
PRIMARY (ADDISON'S DISEASE)	SECONDARY
All hormones will be decreased: from all 3 cortical layers.	Only glucocorticoids will be decreased.
autoimmune , idiopathic, infection (TB) , iatrogenic	inadequate pituitary ACTH secretion.
ACTH normal or high	ACTH is low
- Hyperpigmentation - High K and low Na - Metabolic Acidosis	- No pigmentation - Normal K and normal Na or low - No metabolic Acidosis

ETIOLOGY OF ADDISON'S: not important just know the concept

- Idiopathic atrophy(Most common cause) → autoimmune condition where antibodies attack against own adrenal cortex, and 90% of tissue destroyed.
- TB/fungal infections (histoplasmosis).
- Iatrogenic causes → adrenalectomy, chemotherapy, anticoagulant tx.



SIGNS & SYMPTOMS



Most of the patients come at emergency situation

- Fluid & electrolyte imbalances:
  - Hypotension.
  - Hyponatremia.
  - Hyperkalemia (serum is high but urine is low).
  - Hypoglycemia.
- Salt craving.
- Fatigue, weight loss, anorexia; due to low cortisol.
- Changes in skin pigmentation: ↓cortisol - ↑ACTH - ↑MSH
- Muscular weakness.
- Androgens are low causing: pubic hair loss and decreased sexual drive for women. (men are not affected).
- Mental disturbances: anxiety, irritability, etc.

DIAGNOSIS:

- 24 hours urinary 17-OHCS2 and 17 KS3 is low.
- Serum cortisol is low → serum glucose is low
- Serum K is high, and Na is low .

INTERVENTION

- Lifelong hormone replacement (no need to remember the details) :
  - Primary need oral cortisone 20-25 mg in AM and 20-12 mg in PM.
  - Change dose PRN for stress.
  - Also need mineralocorticoid (florinef)
- General advice we give the patients:
  - Salt food liberally (add a lot of salt to their food helps increase their blood pressure)
  - Do not fast or omit meals.
  - Eat between meals and snack.
  - Eat high in carbs and proteins.
  - Wear medical alert bracelet.
  - Always carry a kit of 100 mg hydrocortisone IM . (stress dose)[4]
  - Keep parenteral glucocorticoids at home for injection during illness.
  - Avoid infections/stress.

COMPLICATION

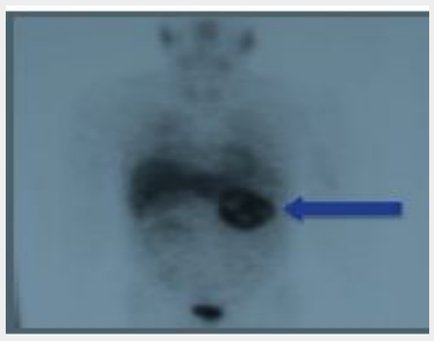
- Adrenal crisis (severe hypotension like in addison's or severe hypertension like pheochromocytoma)
- Electrolyte imbalance (hyperkalemia and hyponatremia)
- Hypoglycemia

(4) If you find them collapsed (and they have a medical bracelet saying they have addison's) look in their bag and you'll find this syringe → give it to them to stimulate their adrenal until them until they get to a hospital.

MEDULLA

1. Pheochromocytoma Video(05:46)

- Rare, benign tumor of the adrenal medulla → 10% could be malignant (Remember the rule of 10%) (5).
- Hypersecretion of? Epinephrine and norepinephrine → released sporadically .
- The median age for presentation of pheochromocytomas is 40 years .
- Associated conditions are neurofibromatosis, medullary carcinoma of the thyroid (as part of MEN type II), duodenal ulcer and renal artery stenosis.
- (5) 10% familial, 10% malignant, 10% extra-adrenal

SIGNS & SYMPTOMS	• Not specific, they may have similar presentation as conn's syndrome → headache and hypertension BUT here potassium and sodium levels are normal! So we check electrolyte to differentiate. • **Hallmark is hypertension : 200/150 or greater** (high blood pressure **not responding to treatment**) • Paroxysmal attacks "spells" provoked by bladder distension, emotional distress, exposure to cold. • Deep breathing, pounding heart (**tachycardia**), **headache** , moist cool hands and feet, visual Disturbance (Some patients may present with Nephropathy due to uncontrolled blood pressure) • **Classic triad (not found in most patients): Palpitations, Headache, Episodic diaphoresis .** • A few patients present with predominantly metabolic effects, such as those found in thyrotoxicosis.
DIAGNOSIS 	By history and examination then tests: • **Urine: 24h urine- VMA (V anillyl M andelic A cid → metabolite of epinephrine) or** urinary metanephrine . Also glycosuria is common. • Blood : Plasma catecholamines (metanephrine) . • Imaging : CT or MRI (to locate tumor), or scintigraphy (MIBG scan).
INTERVENTION	• **Surgical removal of the tumor is the treatment of choice.** • **The patient should come to operation with blood pressure and pulse rate controlled to reduce the risk of adrenal crisis! How do we do that?**

PRE-OP (admit the pt. 3 days before surgery to control HR & BP)	What to give the patient? ➔ Adrenergic blocking agents: Minipress ⟶ lower BP ➔ Beta blocking agents: Inderal ⟶ lower HR, BP & force of contraction ➔ Diet: high in vitamin, mineral,calorie, no caffeine, low salt ➔ Sedatives What to do to the patient? ➔ Monitor BP ➔ Eliminate attacks ➔ If attack ⟶ complete bed rest and head of bed 45 degrees basically we give the pt alpha blocker for 4-6 weeks before the surgery to control the HR, then we give beta blocker after the admission to control the BP.
DURING SURGERY	**Give regitine and nipride to prevent hypertensive crisis.** Make sure you have a stress dose ready because we worry about hypertension during and hypotension after the intervention. Anesthesia should have Hydralazine (for hypertension) and phenylephrine (for hypotension)
POST-OP	BP may be high initially, BUT CAN BOTTOM OUT so we prepare: - Volume expanders - Vasopressors - Hourly Input and Output - Observe for hemorrhage

2. Incidentaloma

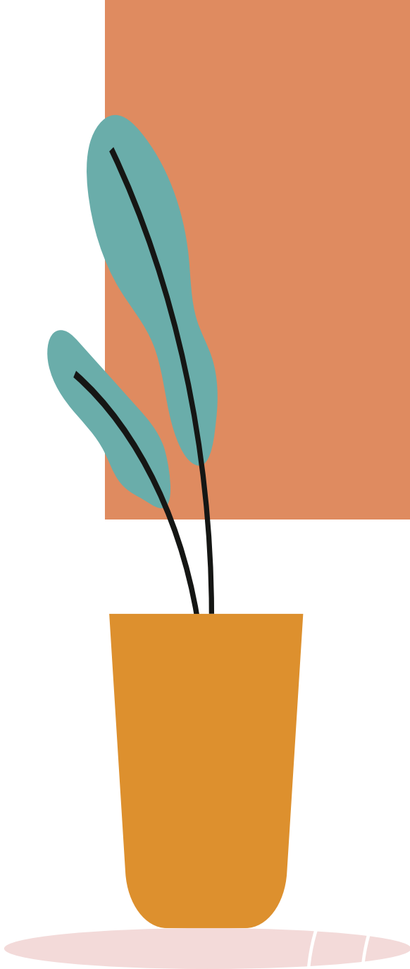
- **Mass lesion greater than 1 cm.**
- **Serendipitously (مصادفة) discovered by radiologic examinations done for other reasons such as:**
  - **Computed tomography (CT)**
  - **Magnetic resonance imaging (MRI)**
- **If you discover any mass you have to answer three questions:**
  - **Is it functioning (producing hormones) ? You have to rule out pheochromocytoma by labs.**
  - **Is it malignancy ? (may be primary tumor or metastasis* ⟶ check if they have hx of cancer)**

-Third question is what is the size of lesion?

- **the most common tumors that metastasize to the adrenal gland are renal cell carcinoma and breast cancer,**skin and small intestine cancer **(sometimes the lung will metastasize in rare cases).**

MANAGEMENT

- **First make sure it is not functioning (by history or by investigations) , then check the size.**
- **If it is more than 4 cm then take it out immediately.**
- **Less than 4 cm observe and repeat the imaging (CT or MRI) in 6 months :**
  - **No increase in size ⟶ repeat after one year and etc.. ⟶ continue to follow up the pt.**
  - **If it increased (>1 cm in 1 year) ⟶ you can take it out because you can't rule out cancer.**



Case scenarios given by the Dr. (understand them to know how to answer the exam) :

Case 1: OB / GYN patient was referred to you with 1 cm mass on the adrenal found by US (done for fibroid).
Patient has NO complaint. What is the most appropriate workup you should ask for? Is the mass functional
or not? We check labs to rule out pheochromocytoma: 24h urinary VMA, plasma and urinary metanephrines, and CT scan. If they find it to be normal→ It is most likely incidentaloma (also because pt
has no complaint). For the management see above.

Case 2: A patient diagnosed with breast cancer 10 years ago, and she is presenting with a mass on the
adrenal. → You have to rule out cancer (metastasis). So we do PET scan or biopsy to rule it out.

Case 3: A patient is referred from nephrology with headache and uncontrolled BP not responding to medications (despite being on two antihypertensives). It could be Conn's syndrome or pheochromocytoma:

- Check her electrolytes → if her serum Na and K are normal it's unlikely to be conn.
- If they did imaging and found a mass → pheochromocytoma .
- How to confirm that's pheochromocytoma? by serum and urine metanephrine level (their accuracy is around 97%)

Case 4: A patient came to the ER, she is diagnosed with HTN & is on 3 medications but her BP is still high (not responding to medication). Upon investigation, her serum K+ is low . She has been admitted to the ICU with hypokalemia 3 times before.
1- what further investigation do you want to? After history and examination, we check electrolyte (including
serum Na+ and K+) and imaging to rule out tumors.
2- what is the most likely DDx she has? Conn's syndrome

This case could come in an OSCE station asking to take a focused HX
Case 5: a 35 female referred to you with right adrenal mass.
first I have to determine is it hyper / hypo / normal function
Regardless the other usual questions these are the most important things you should ask:

1. Does she have hx of HTN ? If yes,
   A. Is it controlled. B. How many medications does she take
2. Hx of headache ?
3. Personal Hx of cancer ? especially breast, skin melanoma , small intestine, renal cell carcinoma
4. Other significant hx: medications , hx of adrenal lesions.

	Hyperfunction	Hypofunction
Aldosterone	**Conn's Syndrome** cuases: -1∘: benign adenoma -2∘:↑renin secretion in liver, renal or cardiac D. S&S: ↑Na, ↓K, HTN, no edema Dx: Plasma: ↑Na,↓K. Urinary:↑K. CT, ECG Rx: adrenalectomy	**Addison's Disease** cuases: autoimmune, infection, iatrogenic S&S: ↓BP Hypoglycemia Fatigue Anxiety ↓sexual drive for women Dx: ↓cortisol, ↓Na, ↑K Rx: hydrocortisone IM, Florinef Complication: Adrenal crisis
Cortisol	**Cushing's Syndrome** causes: -tumor,↑ACTH (1∘ or ectopic), exogenous S&S: 1-protein → muscle wasting, fragile skin 2-CHD → Hyperglycemia 3-fat →Truncal obesity, buffalo hump, Moon face 4-↓immunity → prone to infection 5-↑androgen → hair growth, Acne 6-↑BP Dx: 24-h urine cortisol level. Rx: depends on the cause	
androgen	-	
	masses	
medulla	**1-Pheochromocytoma** S&S: HTN, tachycardia, diaphoresis Dx: 24h urine VMA, MIBG scan	
	2-Incidentaloma -no hyperfunction ,<3.5 → benign -hyperfunction, >3.5 →malignancy	

Summary of electrolyte changes:

Disease	Hyper or hypo?	Findings (serum)			Other symptoms
		Na+	K+	BP	
Cushings	Hyper (cortisol)	↑	-	↑	Truncal obesity, moon face, hyperglycemia, ↓ immunity etc..
Conns	Hyper (aldosterone)	↑	↓	↑	Headache + HTN not responding to treatment + abnormal electrolytes
Addison's	Hypo (cortex)	↓	↑	↓	Fatigue, anorexia, weight loss, skin pigmentation, etc..
Pheochromocytoma	Hyper (EP & NE)	-	-	↑	High BP >200/100, headache, palpitation, diaphoresis.

Surgical Recall: (EXTRA)

What is the most common cause of Cushing's Syndrome?
Iatrogenic (i.e, prescribed prednisone)
What is the second most common cause of Cushing's Syndrome?
Cushing's disease (most common non iatrogenic cause)
What is Cushing's disease? Cushing's syndrome caused by excess production of ACTH by anterior pituitary
How can cortisol levels be indirectly measured over a short duration?
By measuring urine cortisol or the breakdown product of cortisol, 17 hydroxycorticosteroid (17-OHCS), in the urine
What is a direct test of serum cortisol?
Serum cortisol level (highest in the morning and lowest at night in healthy patients)
How are the following tumors treated:
Adrenal adenoma? Adrenalectomy (almost always unilateral)
Adrenal carcinoma? Surgical excision (only 33% of cases are operable)
Ectopic ACTH-producing tumor? Surgical excision, if feasible
Cushing's disease? transphenoidal adenectomy
What are two classic clues of Conn's syndrome? 1. Hypertension 2. Hypokalemia
What are the causes of Conn's syndrome?
Adrenal adenoma (66%), Bilateral idiopathic adrenal hyperplasia (30%), Adrenal cancer (< 1%)
What diagnostic tests should be ordered? 1. Plasma aldosterone concentration 2. Plasma renin activity
What is the treatment of the following conditions:
Adenoma Unilateral adrenalectomy (laparoscopic)
Unilateral hyperplasia Unilateral adrenalectomy (laparoscopic)
Bilateral hyperplasia Spironolactone (usually no surgery)
What are the renin levels in patients with PRIMARY hyperaldosteronism? Normal or low (key point!)
How do you remember what ADDISON's disease is? Think: ADD ison's disease = AD renal D own
What are the electrolyte findings? HYPERkalemia, hyponatremia.
Which age group is most likely affected by pheochromocytoma?
Any age (children and adults); average age is 40 to 60 years.
How can the pheochromocytoma SYMPTOMS triad be remembered?
Think of the first three letters in the word Pheochromocytoma: Palpitations, Headache and Episodic diaphoresis
What are the other common lab findings?
Hyperglycemia (epinephrine increases glucose, norepinephrine decreases insulin) Polycythemia (resulting from intravascular volume depletion).
What is the classic pheochromocytoma "rule of 10's"?
10% malignant, 10% bilateral, 10% in children, 10% multiple tumors, 10% extra-adrenal and 10% familial
What is the surgical treatment?
Tumor resection with early ligation of venous drainage (lower possibility of catecholamine release/crisis by tying off
drainage) and minimal manipulation
In the patient with pheochromocytoma, what must be ruled out? MEN type II (almost all cases are bilateral)
What is the most common cause of incidentaloma? Nonfunctioning adenoma (>75% of cases)

Quiz:

1.Which of the following statements regarding the adrenal gland are true?

A) The zona glomerulosa secretes aldosterone.
B) Cortisol is produced in the adrenal medulla.
C) Aldosterone is a corticosteroid.
D) Catecholamines are only formed in para-adrenal glands.

2.Which of the following are true in primary hyperaldosteronism?

A) Hypokalemia is not present.
B) Plasma renin activity is decreased .
C) Plasma aldosterone is increased.

3.Which tests are indicated in the diagnosis of Cushing's syndrome?

A) 24 h urinary cortisol ,9am cortisol ,Midnight cortisol
B) Serum adrenocorticotropic hormone(ACTH).
C) Dexamethasone suppression test.
D) All

4.Which of the following statements are true?

A) Patients with Cushing's are at increased risk of hospital-acquired infections.
B) Patients do not require prophylactic anticoagulation.
C) Following surgical removal of unilateral adrenal adenoma, cortisol supplementation is not necessary.
D) Nelson's syndrome is a cause of Cushing's disease.

5.A 48-year-old man presents with visual disturbance, headache and hypertension, what is the most likely diagnosis?

A) Cushing's disease.
B) Cushing's syndrome.
C) Multiple endocrine neoplasia.
D) Conn's syndrome.

6.A 36-year-old man is being investigated for resistant hypertension, what is the most likely diagnosis?

A) Cushing's disease.
B) Cushing's syndrome.
C) Multiple endocrine neoplasia.
D) Conn's syndrome.

7.Which of the following statements is false?

A) All adrenal masses need to be biopsied.
B) The likelihood of a mass being malignant increases with increasing size.
C) Nearly 80 percent of adrenal masses are non-functioning.
D) Conn's disease accounts for 1 percent of adrenal adenoma.

1.A 2.C 3.D 4.A 5.A 6.D 7.A