

# Adrenal disorders

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MD 5<sup>th</sup> year

# Overview

- Hypercortisolism (↑ cortisol)
- Adrenal insufficiency (↓ cortisol)
- Hyperaldosteronism (↑ aldosterone)
- Pheochromocytoma (↑ catecholamines)

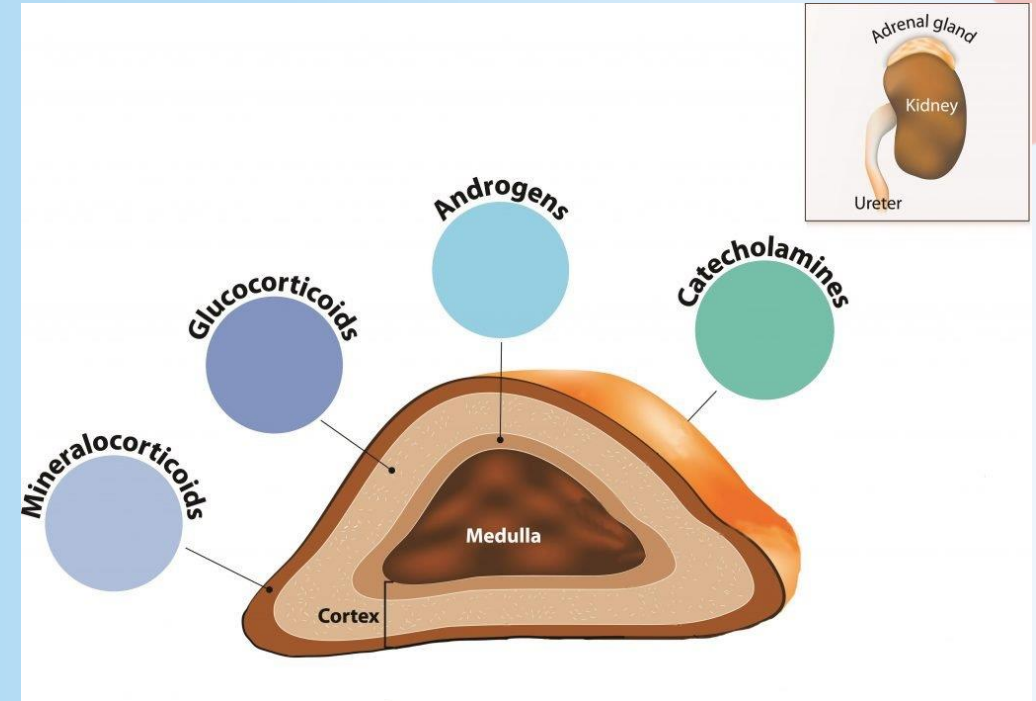
# Quick recap of adrenal function

Adrenal cortex → steroid hormones

- **Glucocorticoids (cortisol)**
  - Increase blood **glucose**, suppresses immune function, maintains BP
- **Mineralocorticoids (aldosterone)**
  - Regulate Na<sup>+</sup>, K<sup>+</sup> and fluid balance
- **Androgens (DHEA)**
  - Precursors for sex hormones

Adrenal medulla → catecholamines

- Epinephrine
- Norepinephrine
- Dopamine



# Hypercortisolism/ Cushing's syndrome

# Cushings syndrome vs Cushings disease

- Cushings disease = excess cortisol due to pituitary tumor
- Cushings syndrome = excess cortisol
- **D**isease → **d**umb pitutary
- **S**yndrome → **s**omething else



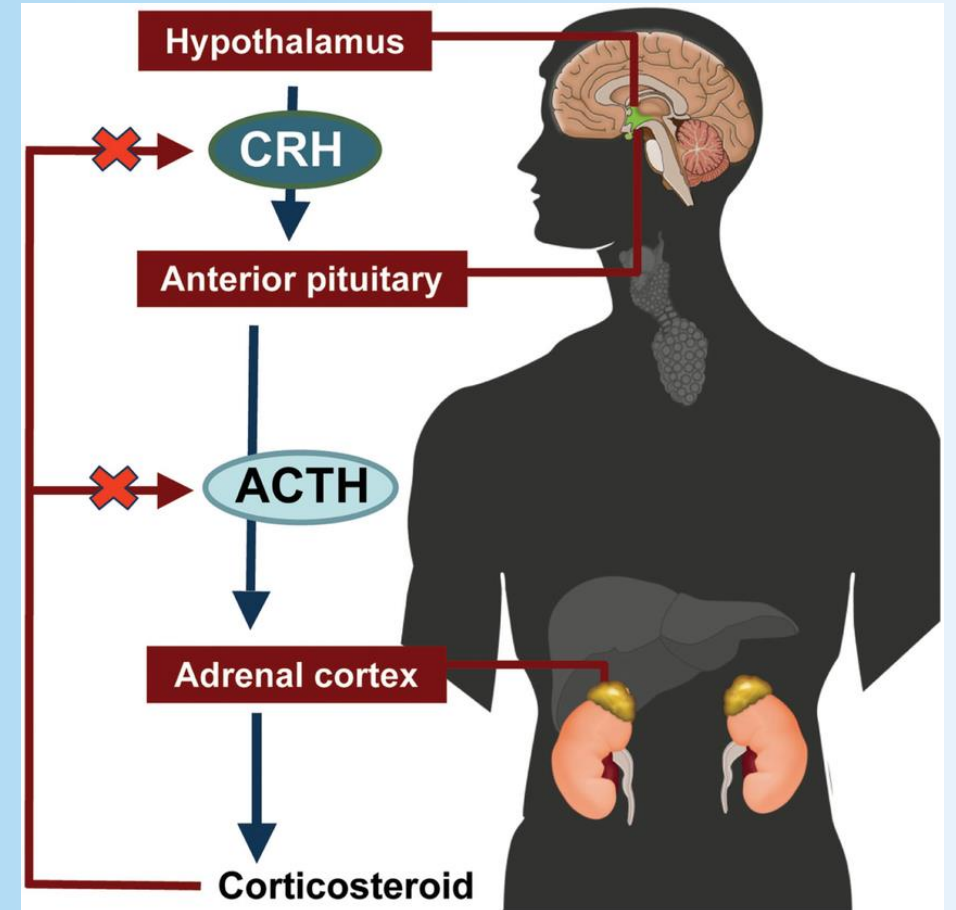
# Pituitary adrenal axis

CRH from hypothalamus

ACTH from ant. pituitary gland

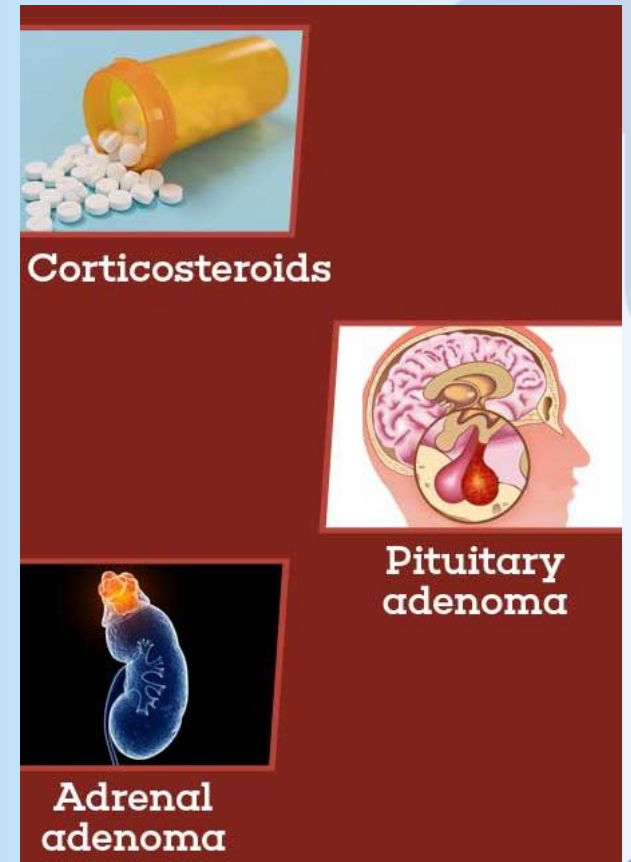
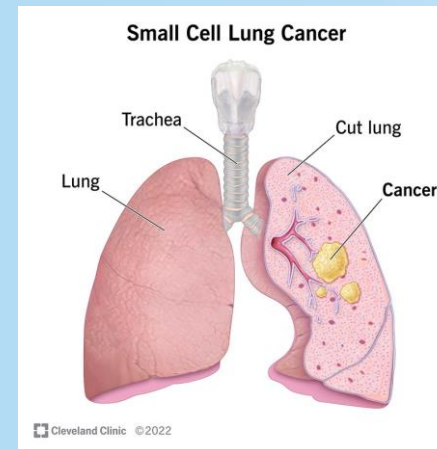
Cortisol from adrenal gland

Cortisol causes NEGATIVE feedback loop



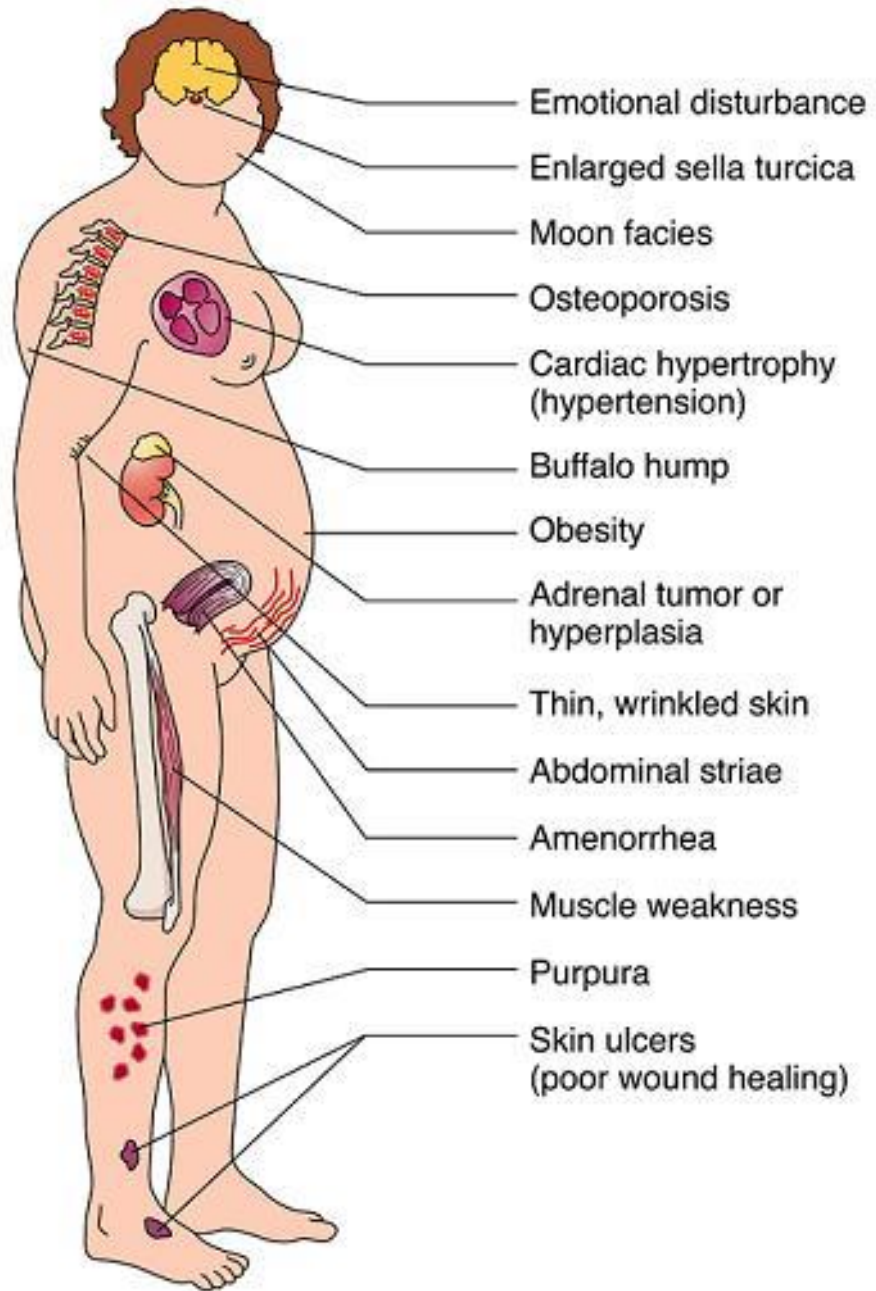
# Causes of adrenal hypercortisolism

- Most common - exogenous glucocorticoids!
    - Normal adrenal glands
  - Overproduction of ACTH from pituitary gland (**Cushings disease**)
    - **Cushing syndrome** = prolonged excess cortisol
  - ACTH from ectopic tumor
    - Small cell lung cancer most common
  - Cortisol by adrenal adenoma
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- **C** - cushing disease
  - **A** - adrenal tumor
  - **P** - paraneoplastic syndrome
  - **E** - exogenous steroids

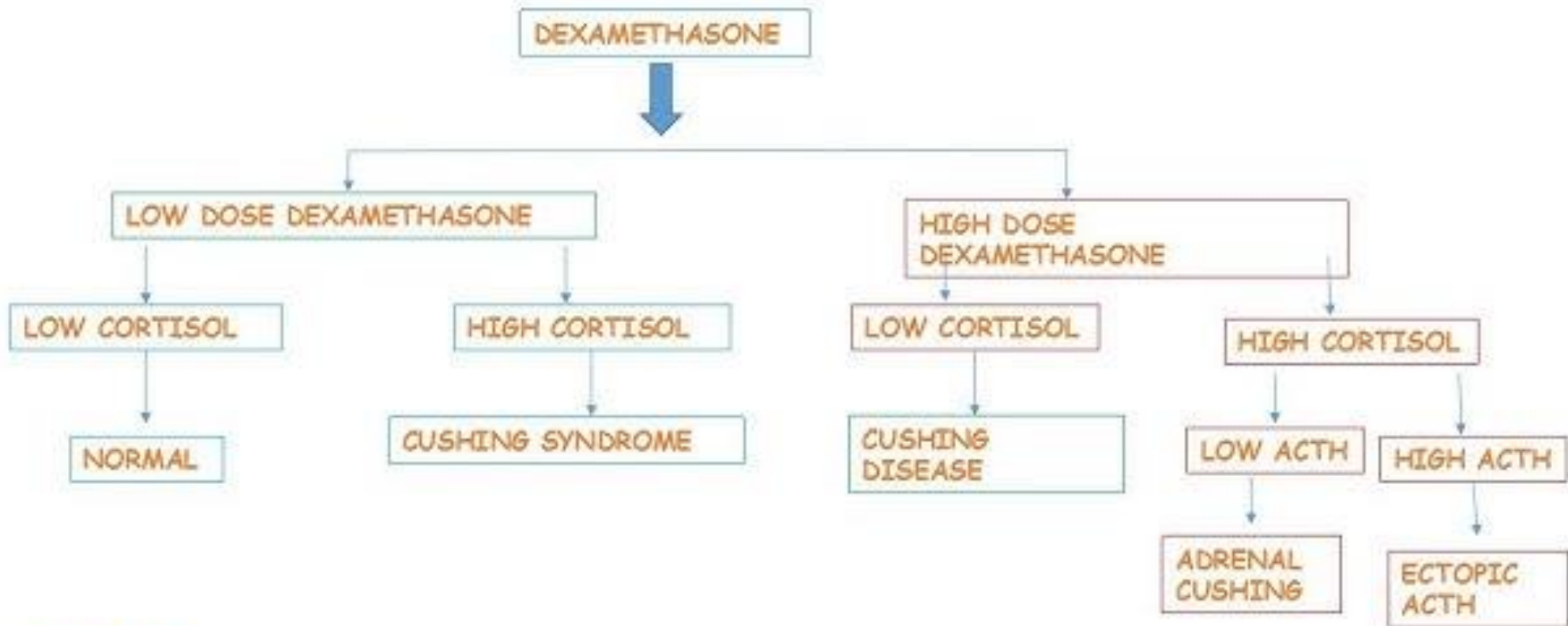


Major effect of excess cortisol	How?
Immunosuppression	↓ T cells and B cells in plasma, ↓ histamine, ↓ eosinophils and blocks neutrophils
Hyperglycemia	↑ Liver production of glucose, cells become more resistant to insulin → ↑ risk of DM
Hypertension	Important in maintaining normal blood pressure
Fat deposition	Destruction of fat cells → ↑ total cholesterol and triglycerides + stimulates fat deposition in face, around trunk and upper back
Muscle, bone and skin changes	Muscle atrophy → thin arms and legs Skin stretches → rapid fat deposition + thin skin Bad for bones → inhibits osteoblasts → hypercalcemia
Reproductive effect	↓ LH and FSH <b>Woman</b> = irregular menses or absence of menstruation <b>Men</b> = low testosterone and low sperm count

- ↑ *Sodium* + ↓ Potassium



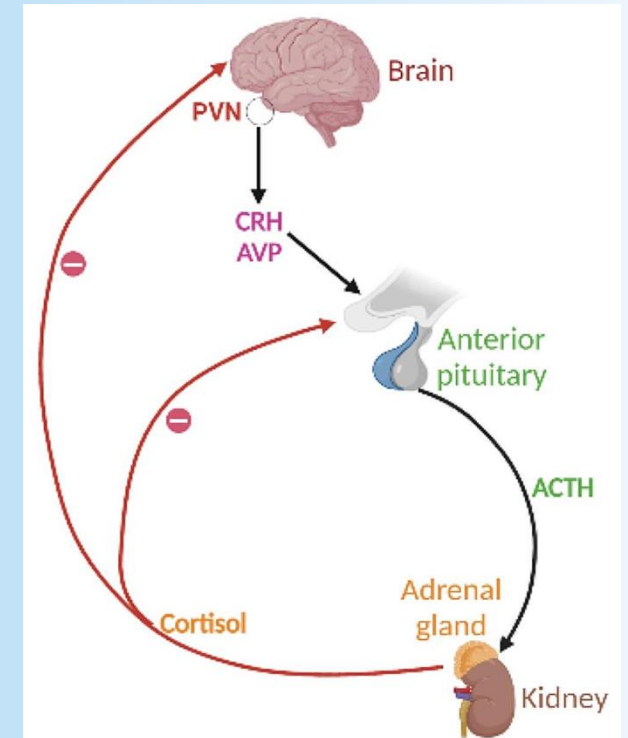
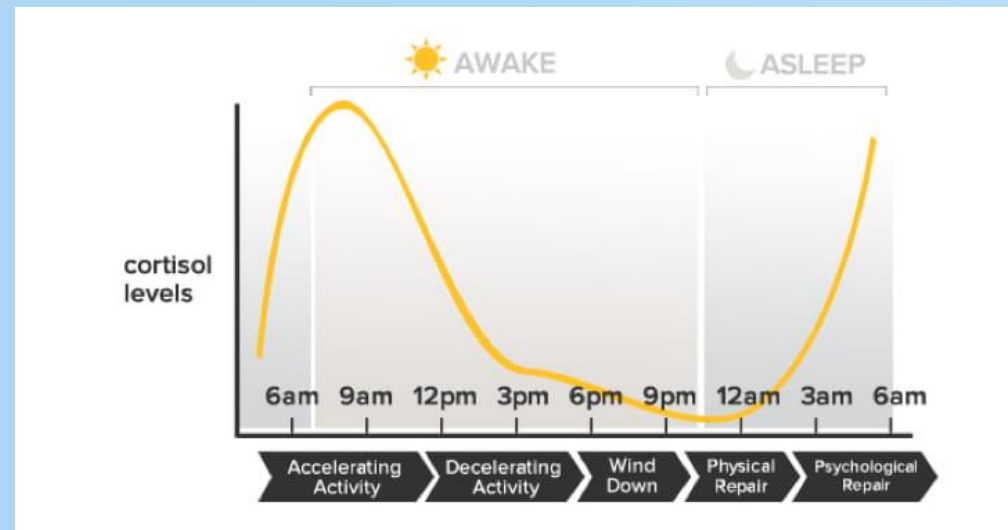
# Dexamethasone Suppression Test



# Diagnosing Cushings

## step 1 - confirm hypercortisolism

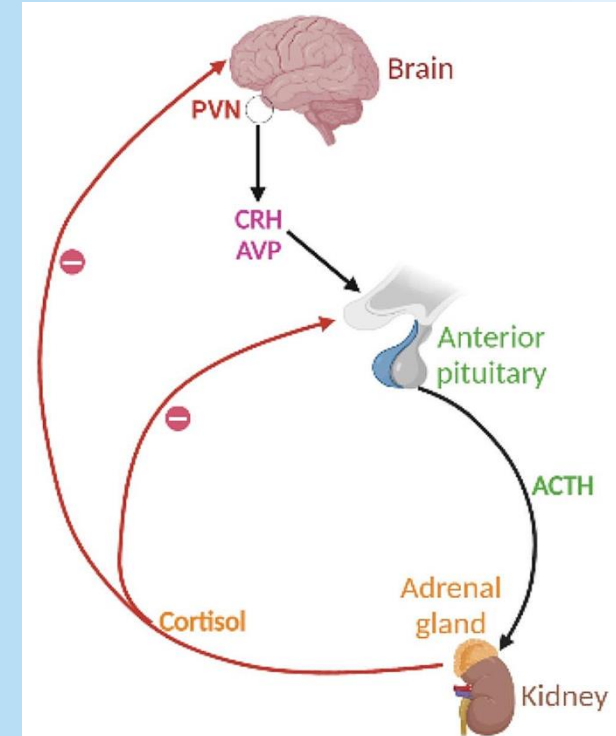
- 24 hour urinary cortisol excretion test
- Late night salivary/serum cortisol
- Low dose (1 mg) dexamethasone at bed time
- Person w/o Cushing → low cortisol in the morning
- Person w Cushing → high cortisol in the morning



# Diagnosing Cushing

## step 2 - determine the cause

- Low plasma ACTH → ACTH independent (adrenal adenoma)
- Normal/ high plasma ACTH → ACTH dependent (Cushings disease or ectopic adenoma)

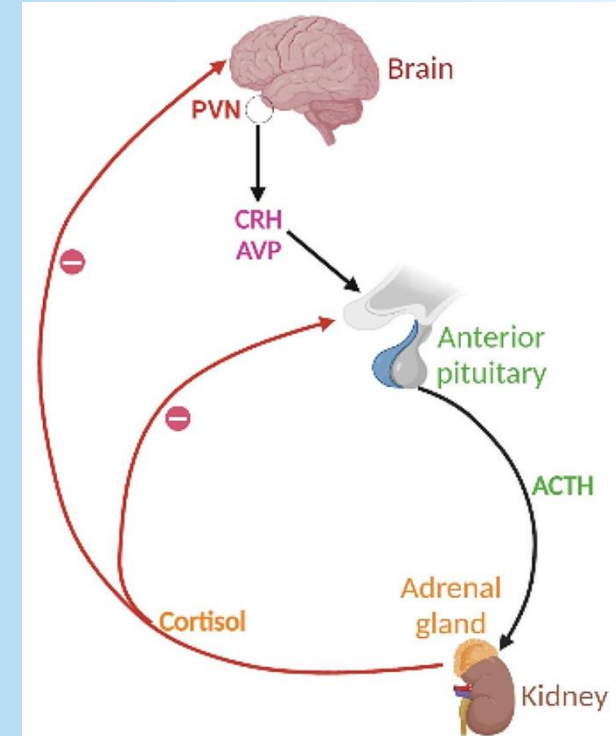


# Diagnosing Cushing

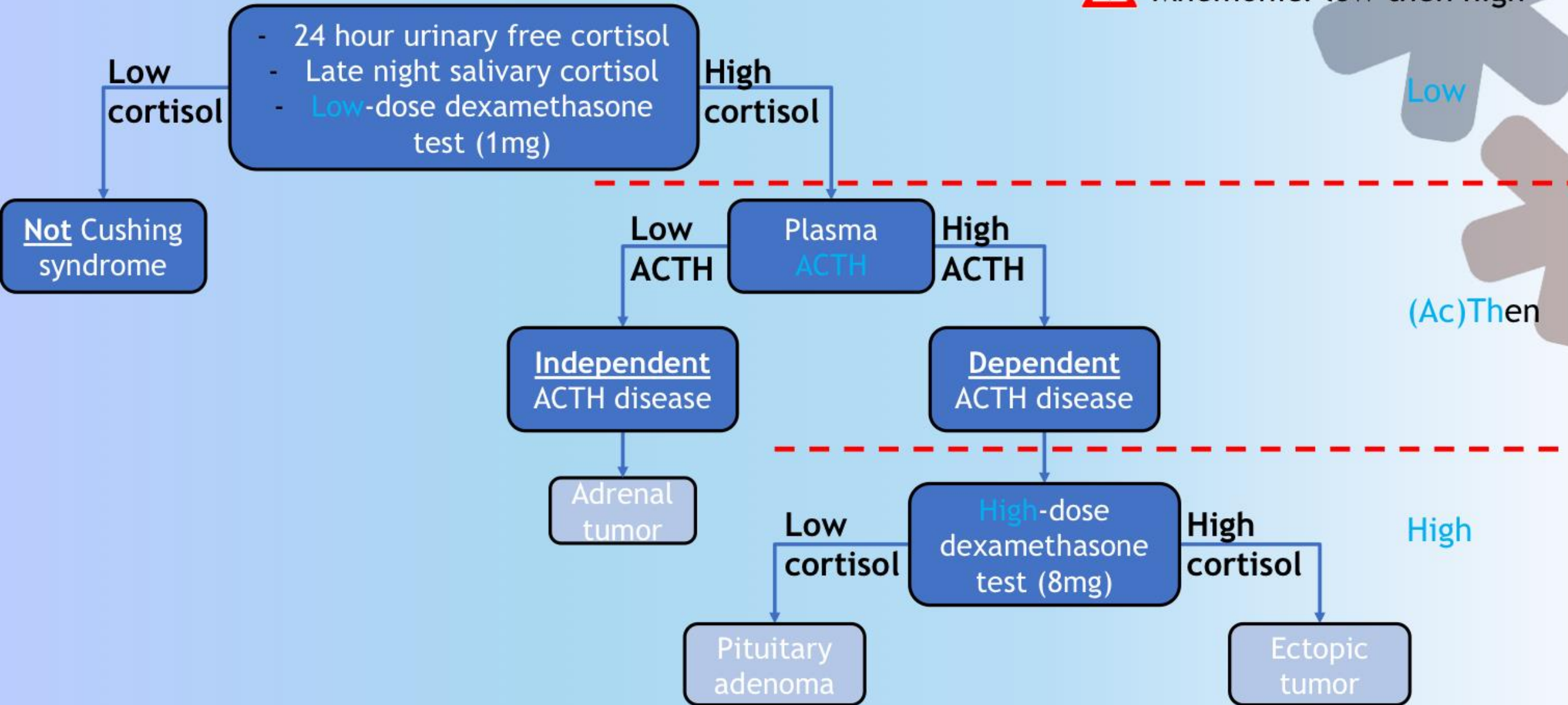
## step 3 - localize the source

high dose dexamethasone test

- Give high dose (8 mg) at bedtime
- Low cortisol = pituitary adenoma
- High cortisol = ectopic tumor



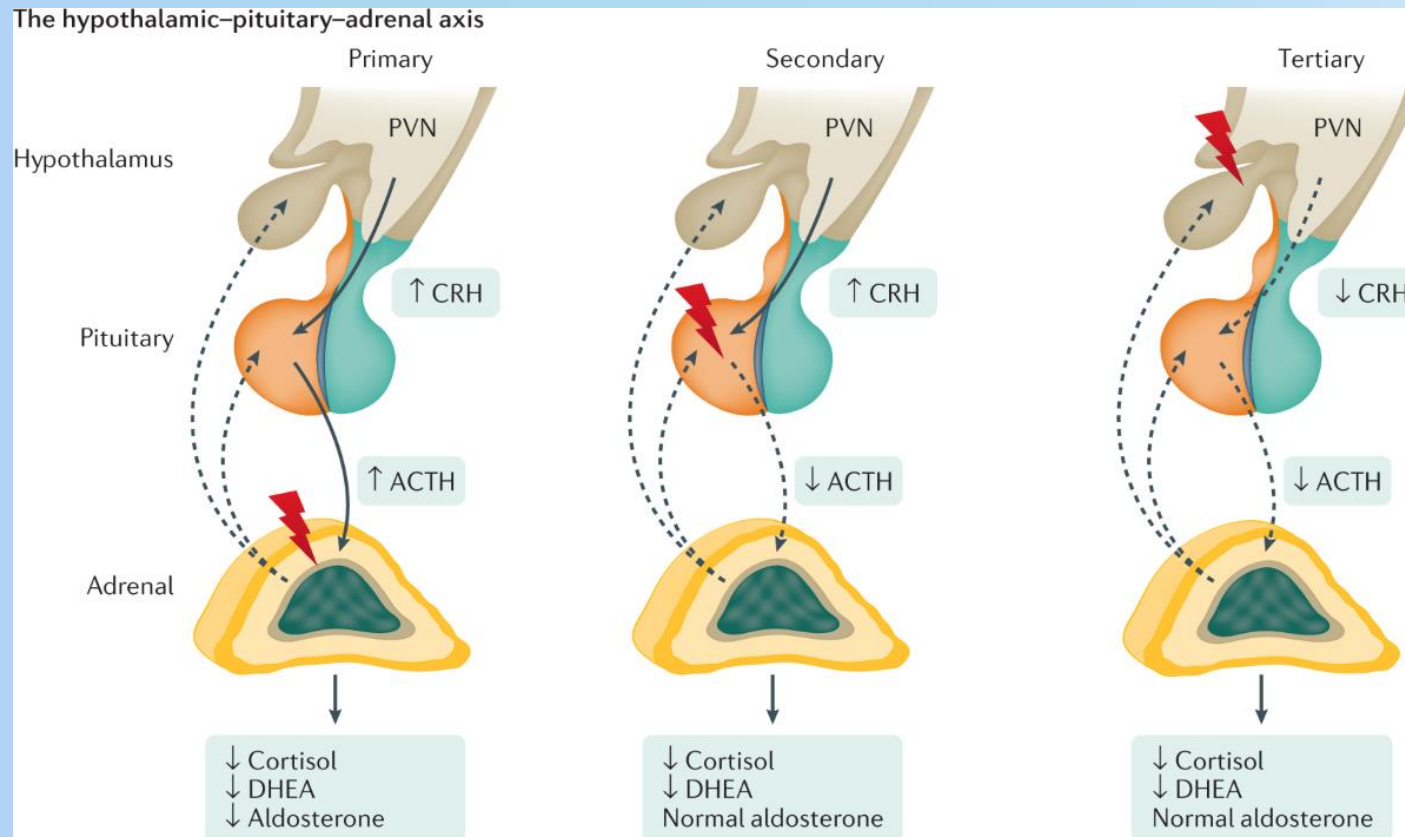
⚠ Mnemonic: low then high



# Adrenal insufficiency

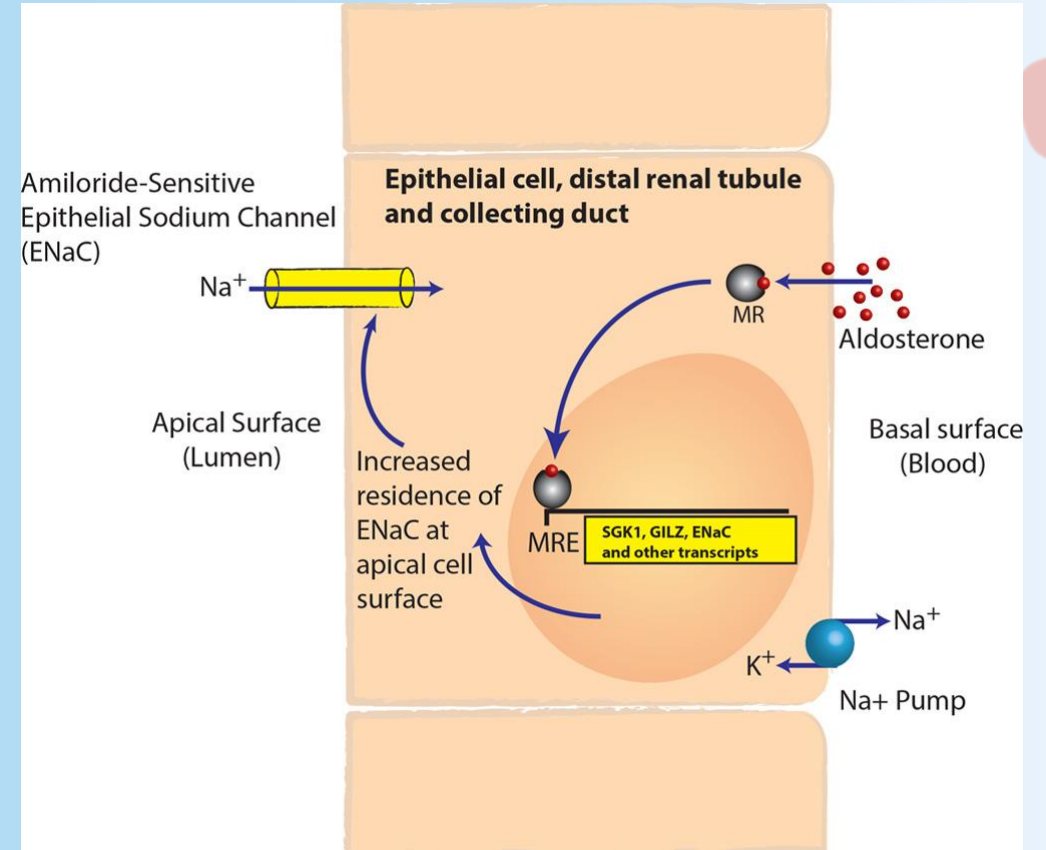
# Adrenal insufficiency

- Loss of adrenal hormones
- ALL FORMS = loss of cortisol



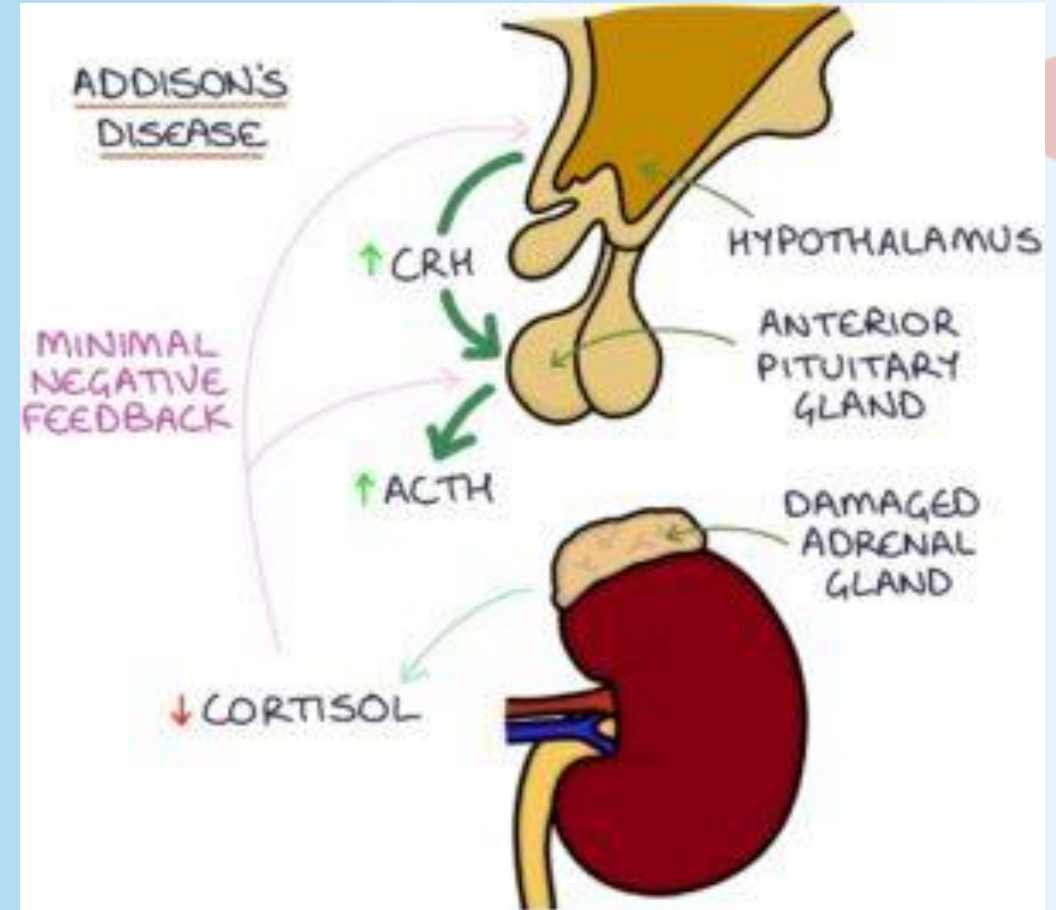
# Aldosterone

- Produced in response to low BP (RAAS)
- Increase  $\text{Na}^+$  in blood
- Decrease  $\text{K}^+$  and  $\text{H}^+$  in blood
- Increase BP



# Primary adrenal insufficiency (PAI)

- Addison disease
- Destruction of adrenal gland → loss of ALL adrenal hormones
- Symptoms
  - Salt craving
  - Hyponatremia
  - Hyperkalemia
  - Metabolic acidosis (H<sup>+</sup>)
  - Hyperpigmentation → ACTH stimulate MSH



Glucocorticoid deficiency	How?
Hypotension	Cortisol maintains blood pressure → therefore ↓cortisol = hypotension
Hypoglycemia	Cortisol normally provide glucose to the body → therefore ↓cortisol = hypoglycemia
N/V + abdominal pain	
Adrenal crisis	Acute onset of life-threatening shock due to the lack of cortisol.

# Causes of PAI

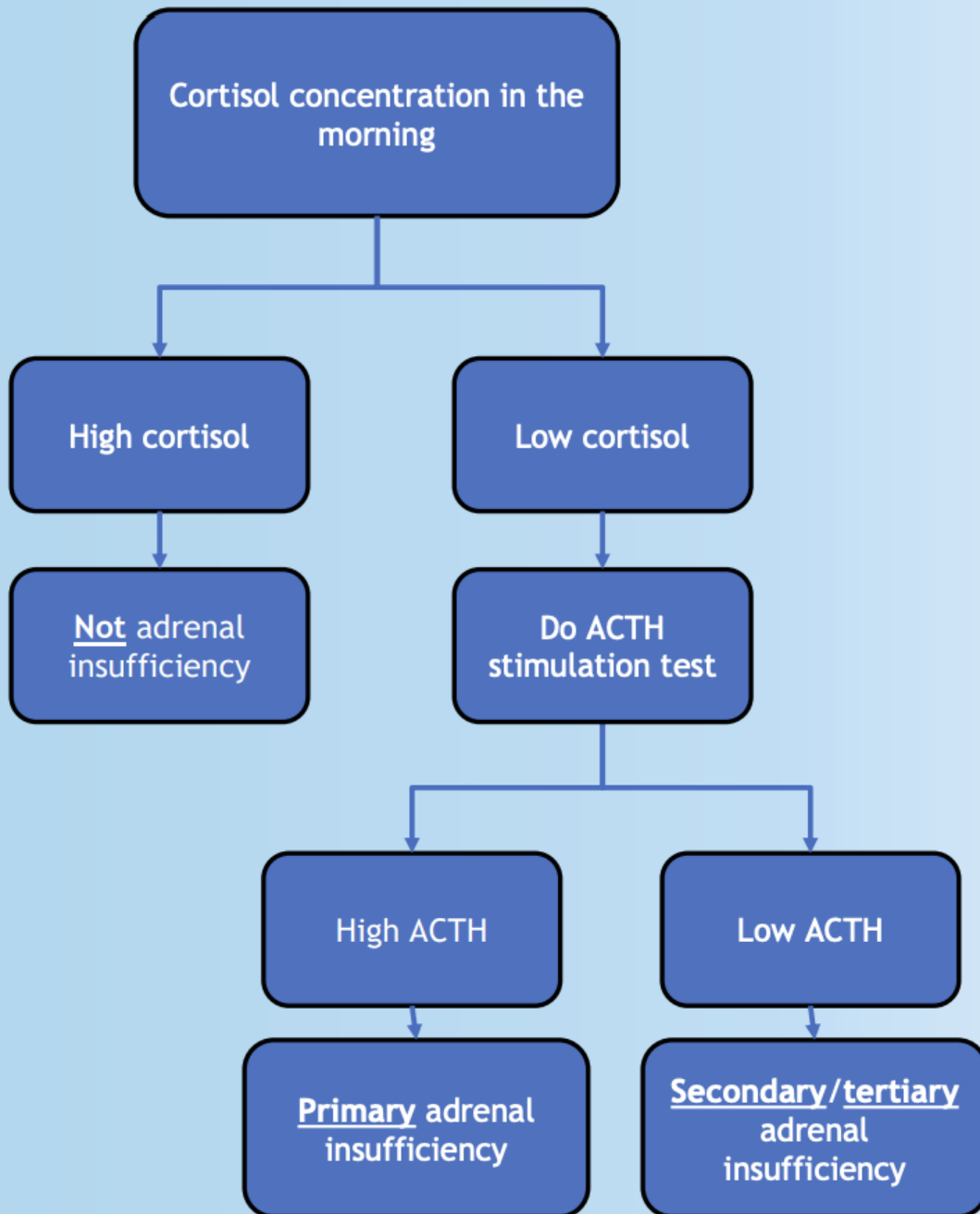
- Autoimmune adrenalitis
  - Most common - JFK
  - Autoimmune destruction by autoantibodies against 21-hydroxylase enzyme
- Infectious adrenalitis
- Hemorrhagic infarction
  - Bleeding into adrenal glands
  - Usually caused by sepsis (Waterhouse-Friedrichsen syndrome)
- Metastatic cancer
  - Rare



# Secondary and tertiary adrenal insufficiency

- Secondary: ACTH
- Tertiary: CRH
- Loss of **cortisol** and sometimes **androgens** (not aldosterone def.!!)
- Can be due to ACTH def. from patients taking chronic glucocorticosteroid therapy
- Hypotension → vasodilation
- NO hyperpigmentation (low ACTH)
- NO hyperkalemia

	Primary (Addison)	Secondary/ Tertiary
ACTH	↑	↓
Cortisol	↓	↓
Aldosterone	↓	Normal
Hyperkalemia	Yes	No
Hypotension	Severe	Mild



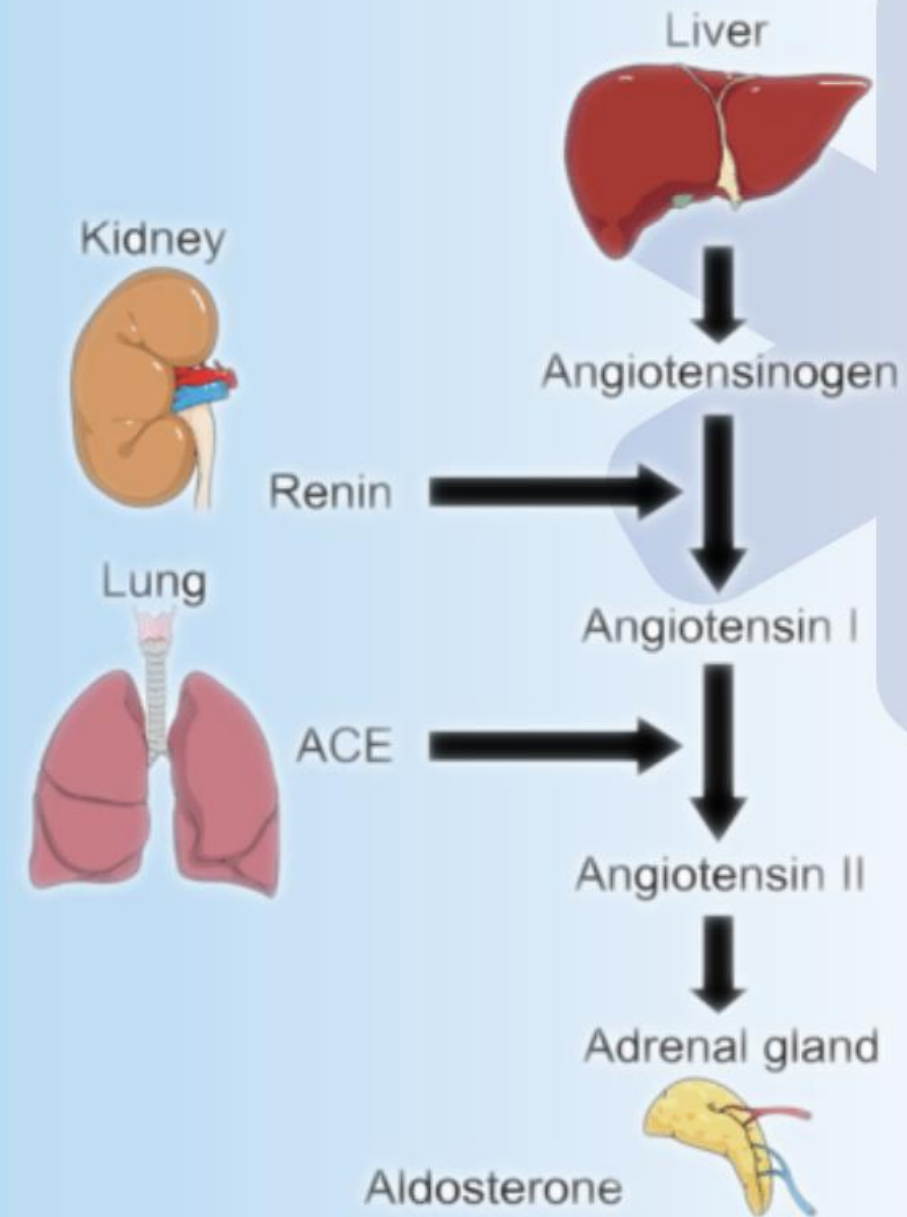
# Diagnosis

Can also do a CRH stimulation test to distinguish secondary and tertiary

# Hyperaldosteronism

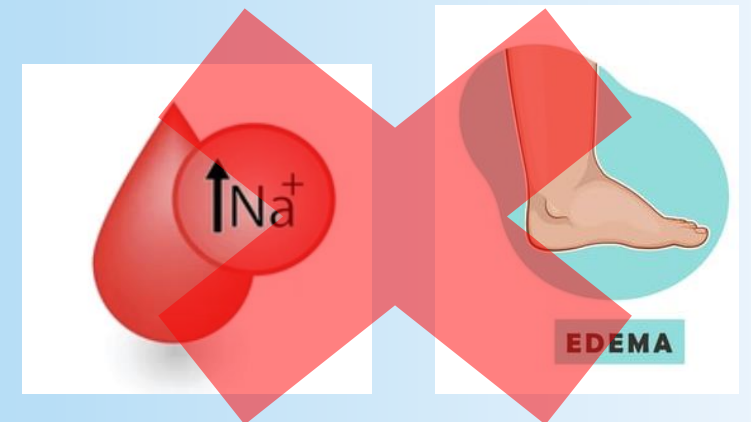
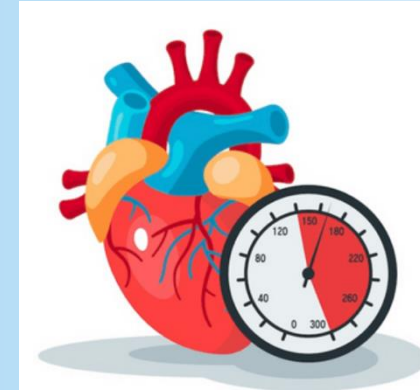
# Hyperaldosteronism

- Excess secretion of aldosterone from adrenal gland
- **Primary hyperaldosteronism** (in adrenals)
- ↑ Aldosterone, ↓ Renin
  - Can be caused by:
    - **Adrenal adenoma** (Conn's syndrome) = small portion of the gland overproduce aldosterone
    - **Bilateral idiopathic adrenal hyperplasia** = the glands enlarge and produce too much aldosterone
    - Adrenal carcinoma - rare
- **Secondary hyperaldosteronism** (overactive RAAS)
- ↑ Aldosterone, ↑ Renin
  - Can be caused by:
    - Renal artery stenosis
    - CHF



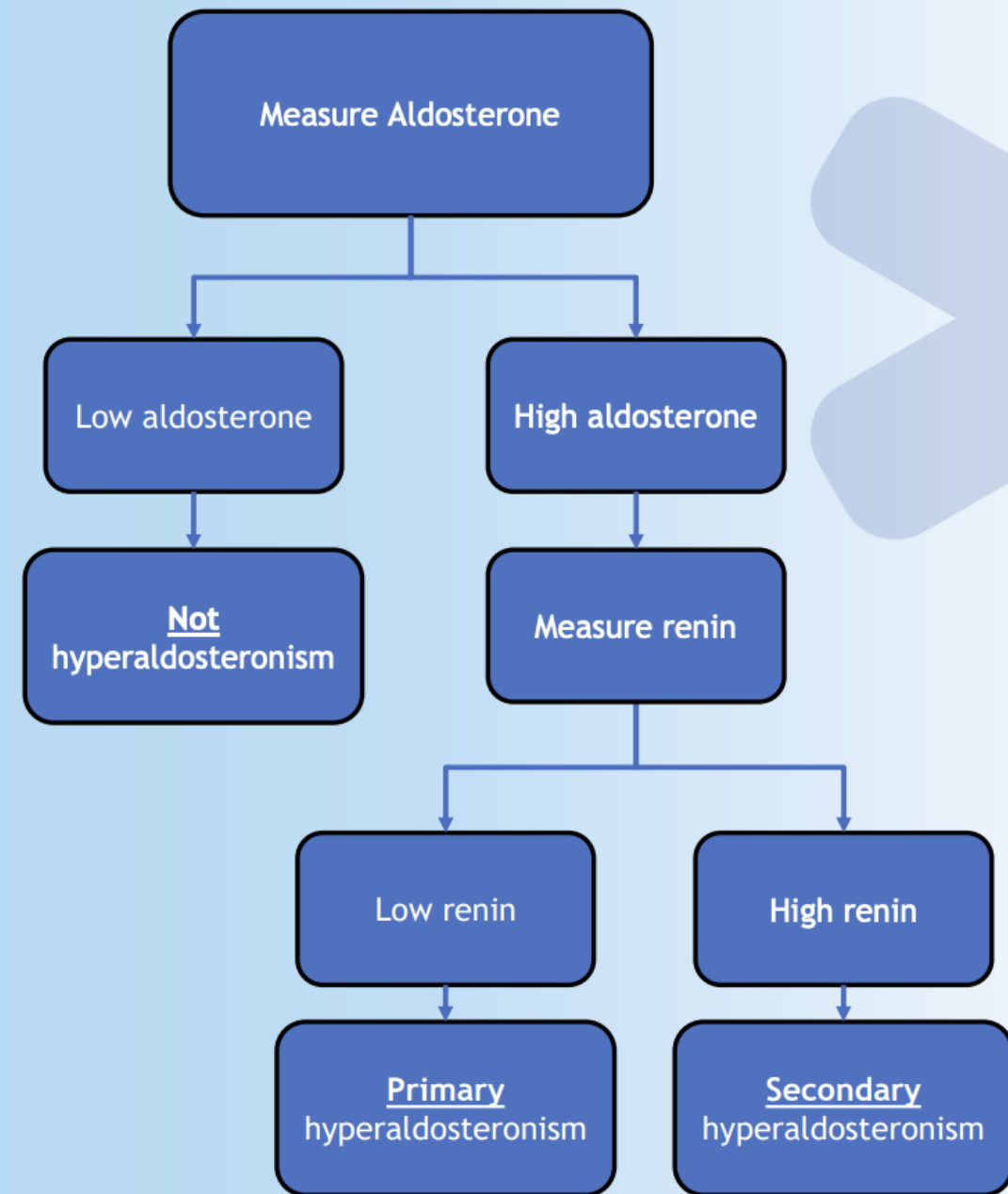
# Clinical features

- **Aldosterone** = functions at the collecting duct of the nephrones
  - $\text{Na}^+$  increase  $\rightarrow$   $\text{H}_2\text{O}$  follows  $\rightarrow$  **hypertension**
    - Resistant to hypertension medication
  - $\text{K}^+$  decrease  $\rightarrow$  **hypokalemia**
  - $\text{H}^+$  decrease  $\rightarrow$  **metabolic alkalosis**
- **Aldosterone escape phenomenon** = reduce edema and hypernatremia
  - ANP released by heart  $\rightarrow$  promotes natriuresis
  - Not seen in secondary hyperaldosteronism



# Diagnosis

- Typical patient = HTN and hypokalemia not responding to HTN meds.
- Two blood tests:
  - Plasma renin activity (PRA)
  - Plasma aldosterone concentration (PAC)
- Take the ratio ( $PAC/PRA=ARR$ )
  - If high = primary hyperaldosteronism
  - If low or normal = secondary hyperaldosteronism



# Pheochromocytoma

# Pheochromocytoma

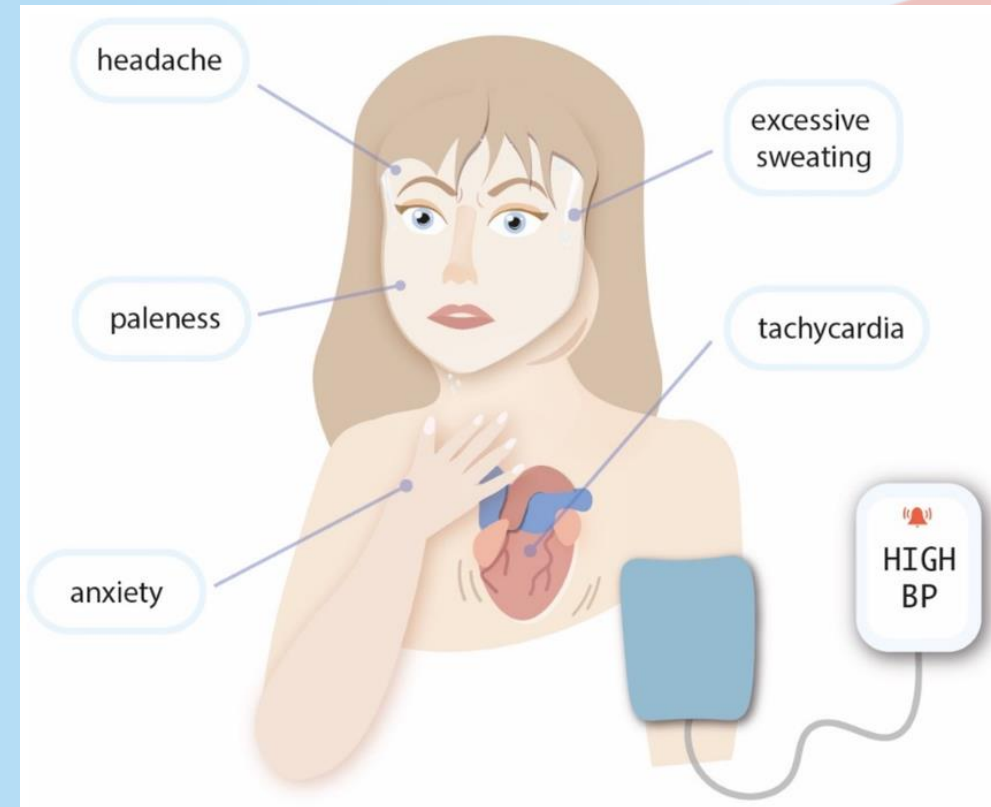
- Tumor in adrenal medulla producing catecholamines
  - Epinephrine
  - Norepinephrine
  - (Dopamine)
- Tumor secreting epinephrine= episodic HTN
- Tumor secreting norepinephrine= less often HTN, often hyperglycemia and glycosuria

## Rule of 10%

- 10%** are multiple
- 10%** are malignant
- 10%** are adrenal bilateral
- 10%** are extra-adrenal
- 10%** are familial
- 10%** are in children

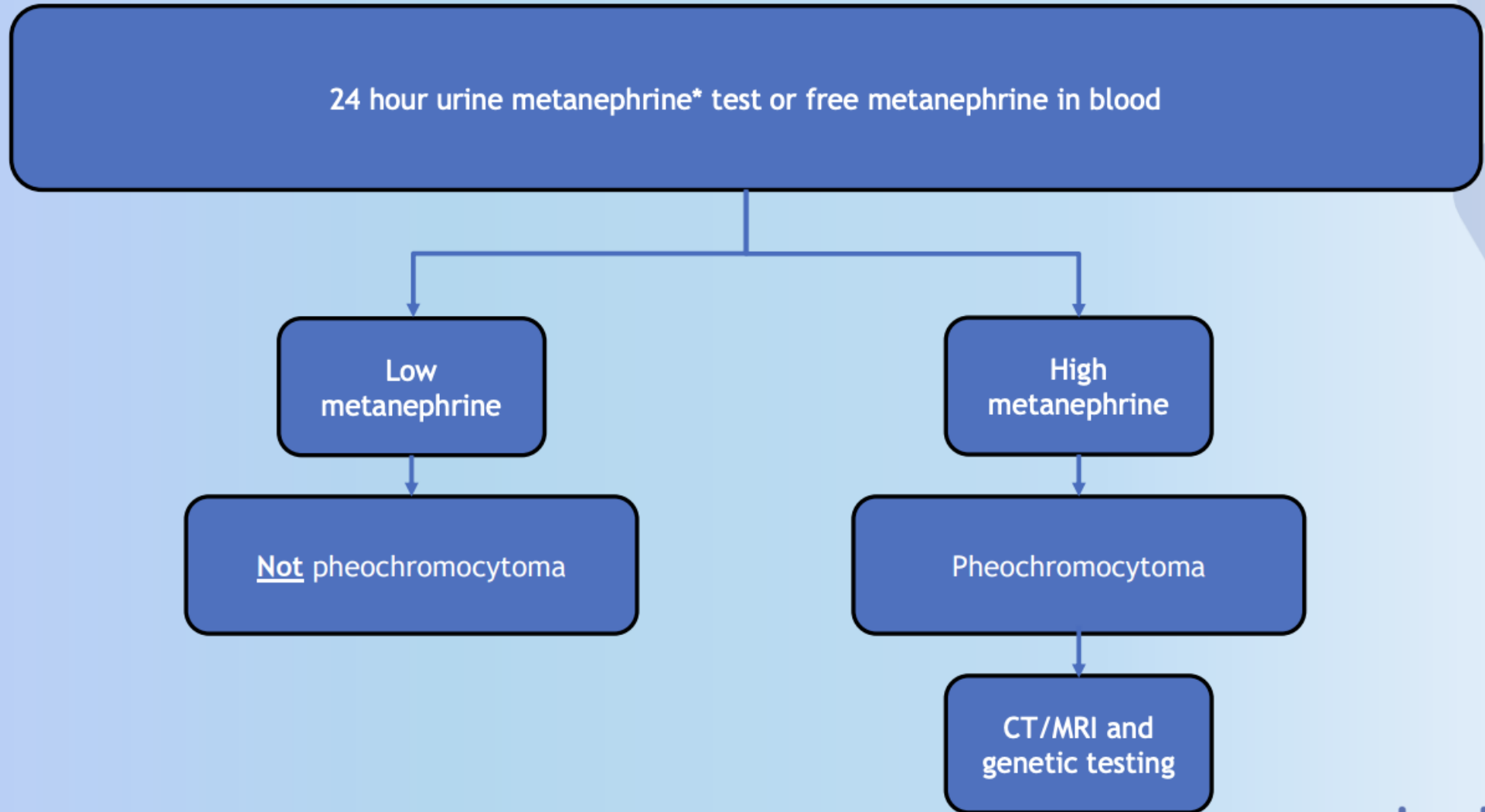
# Clinical features

- Norepinephrine and epinephrine activates **adrenergic receptors**
- $\alpha_1$  = causes HTN (vasoconstriction)
- $\beta_1$  = causes an increase in HR
- $\beta_2$  = causes bronchodilation
- +  $\uparrow$ Glucose,  $\uparrow$ fat metabolism
- Symptoms are fluctuating in tumors
- The classic triad (**PHE**): **P**alpitations, **H**eadache, **E**pisodic sweating



\*Metanephrine = breakdown product of catecholamine

# Diagnosis



THANK YOU!

Good luck on your exam!