ADRENAL DISORDERS

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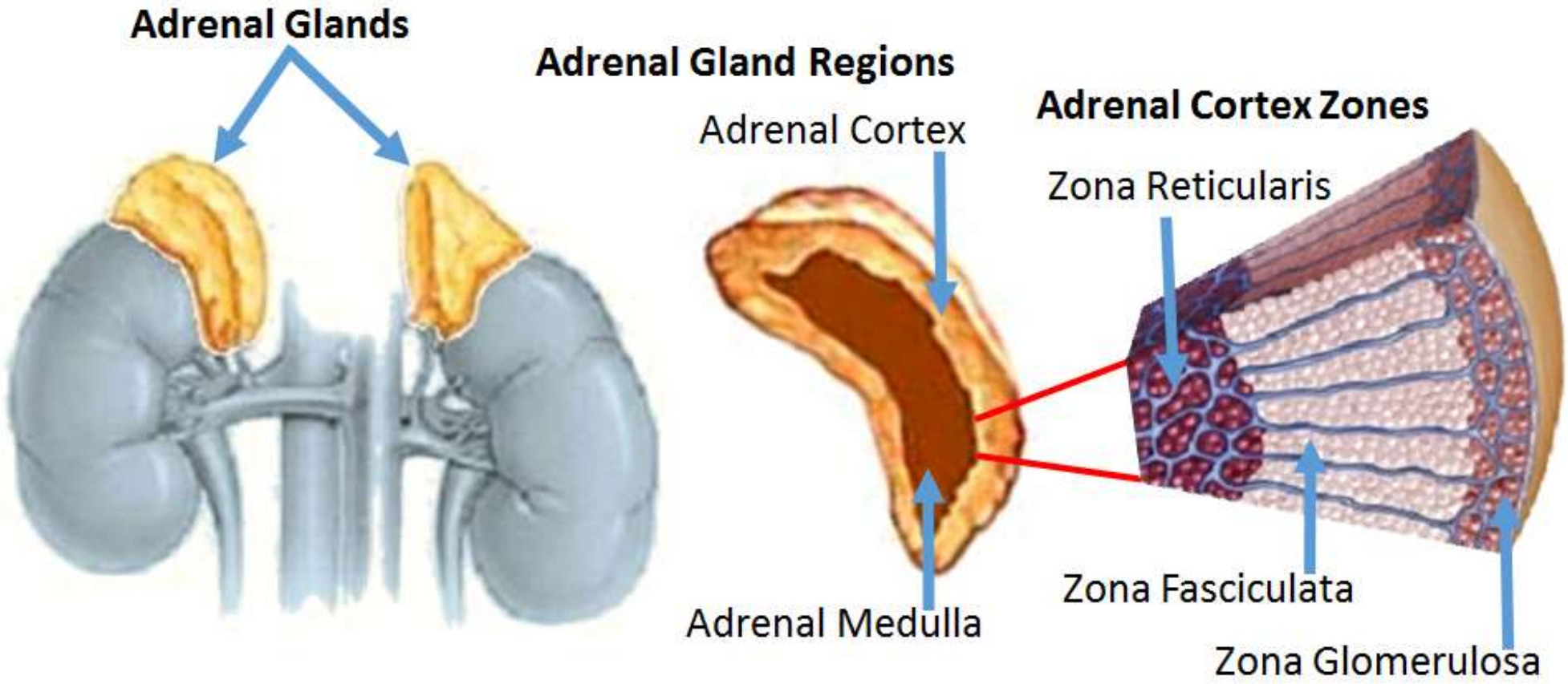
Adrenal anatomy and physiology

Done by : Yazeed Mouawia

Adrenal Glands



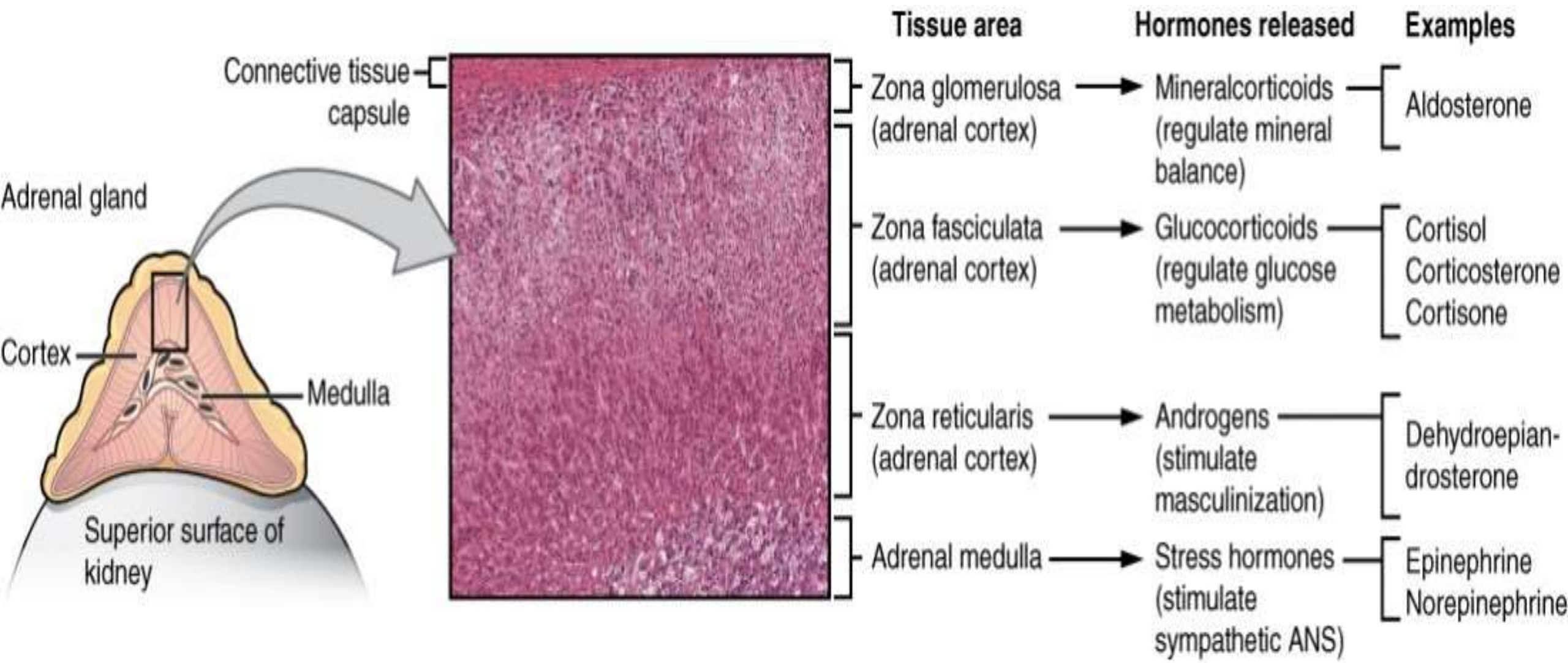
Supra renal gland —> located at the superior surface of both kidneys.

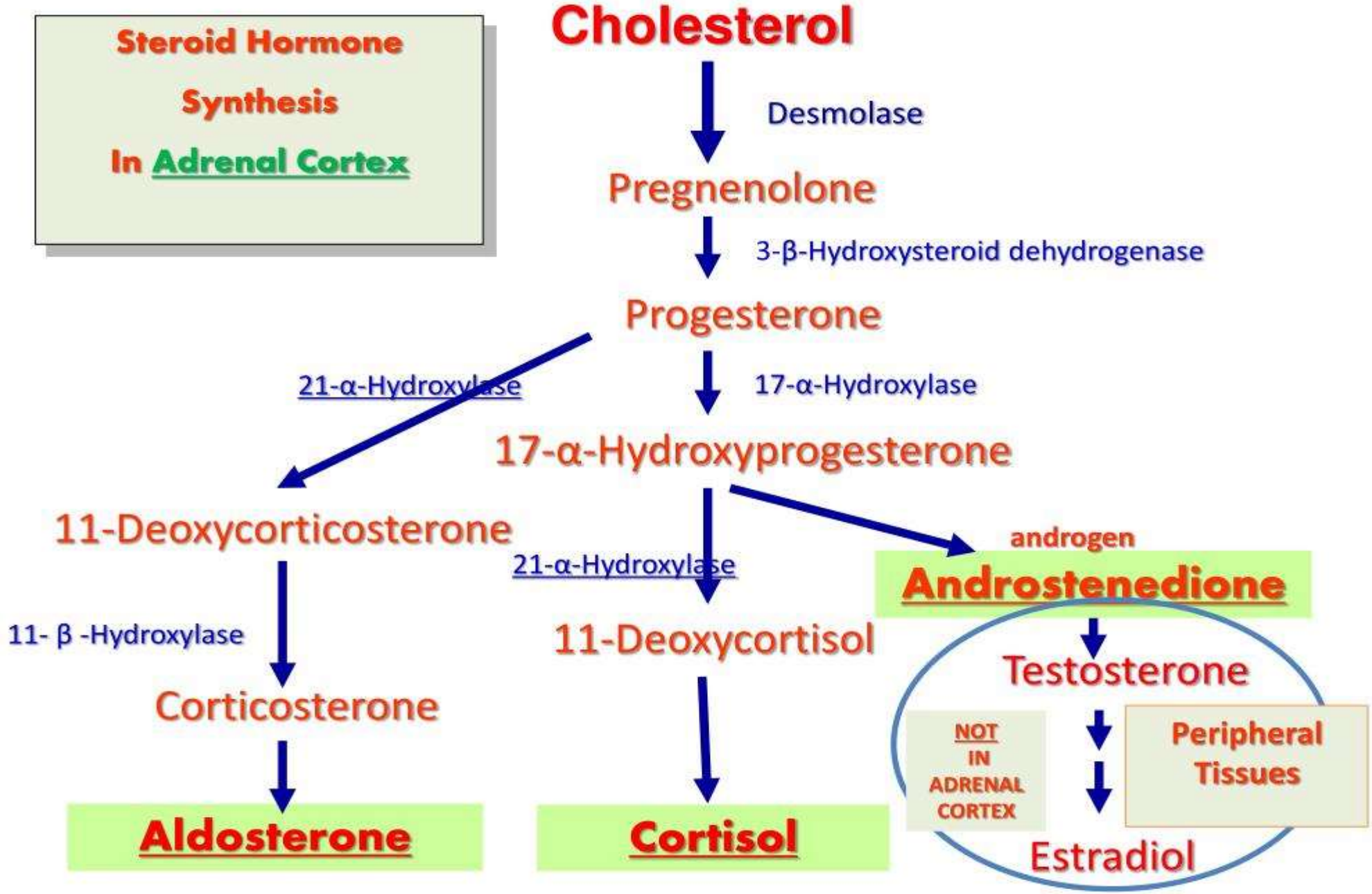
Has three layers (From outermost to innermost) :

1- connective tissue capsule.

2-cortex: consisting of : 1-zona Glomerulosa
2-zona Fasciculata
3-zona Reticularis

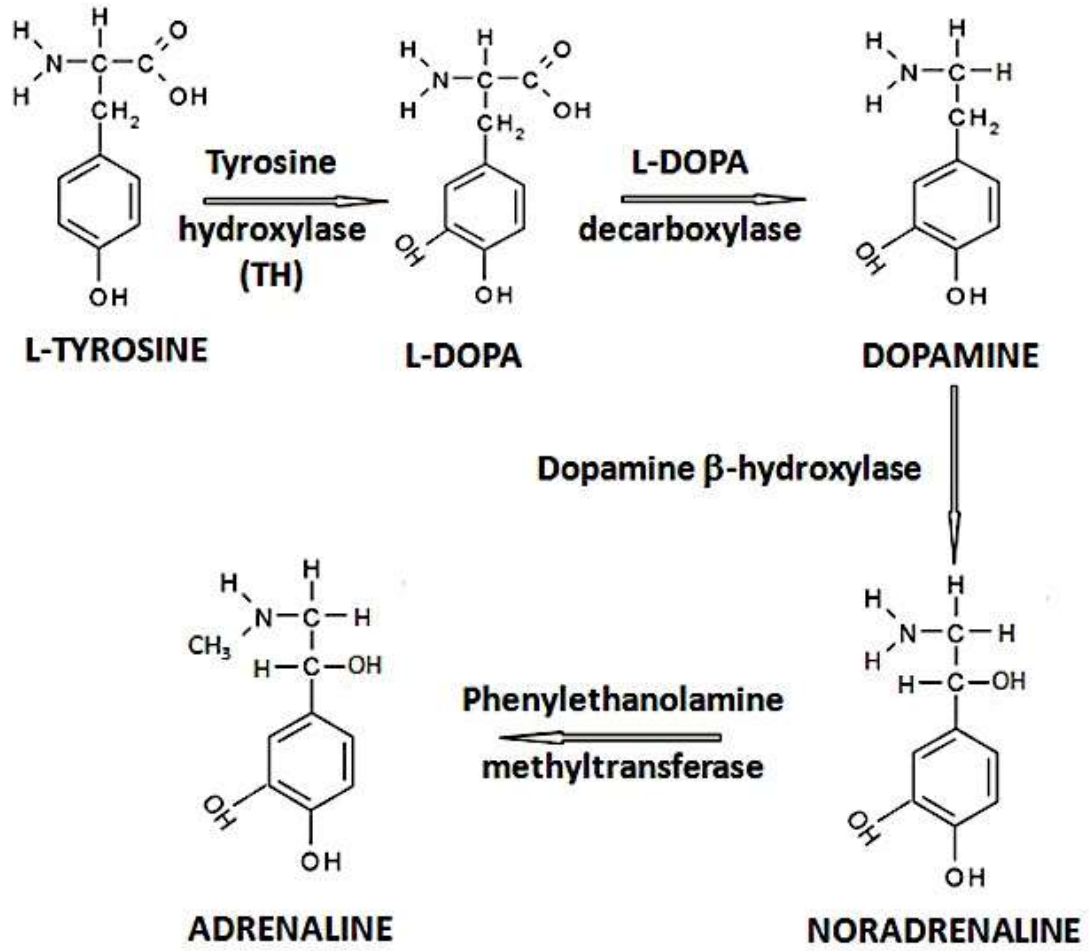
3-medulla, which contain the blood vessels.


Connective tissue capsule
Adrenal gland
Cortex
Medulla
Superior surface of kidney
Tissue area
Hormones released
Examples
Zona glomerulosa (adrenal cortex)
Mineralcorticoids (regulate mineral balance)
Aldosterone
Zona fasciculata (adrenal cortex)
Glucocorticoids (regulate glucose metabolism)
Cortisol
Corticosterone
Cortisone
Zona reticularis (adrenal cortex)
Androgens (stimulate masculinization)
Dehydroepian-drosterone
Adrenal medulla
Stress hormones (stimulate sympathetic ANS)
Epinephrine
Norepinephrine

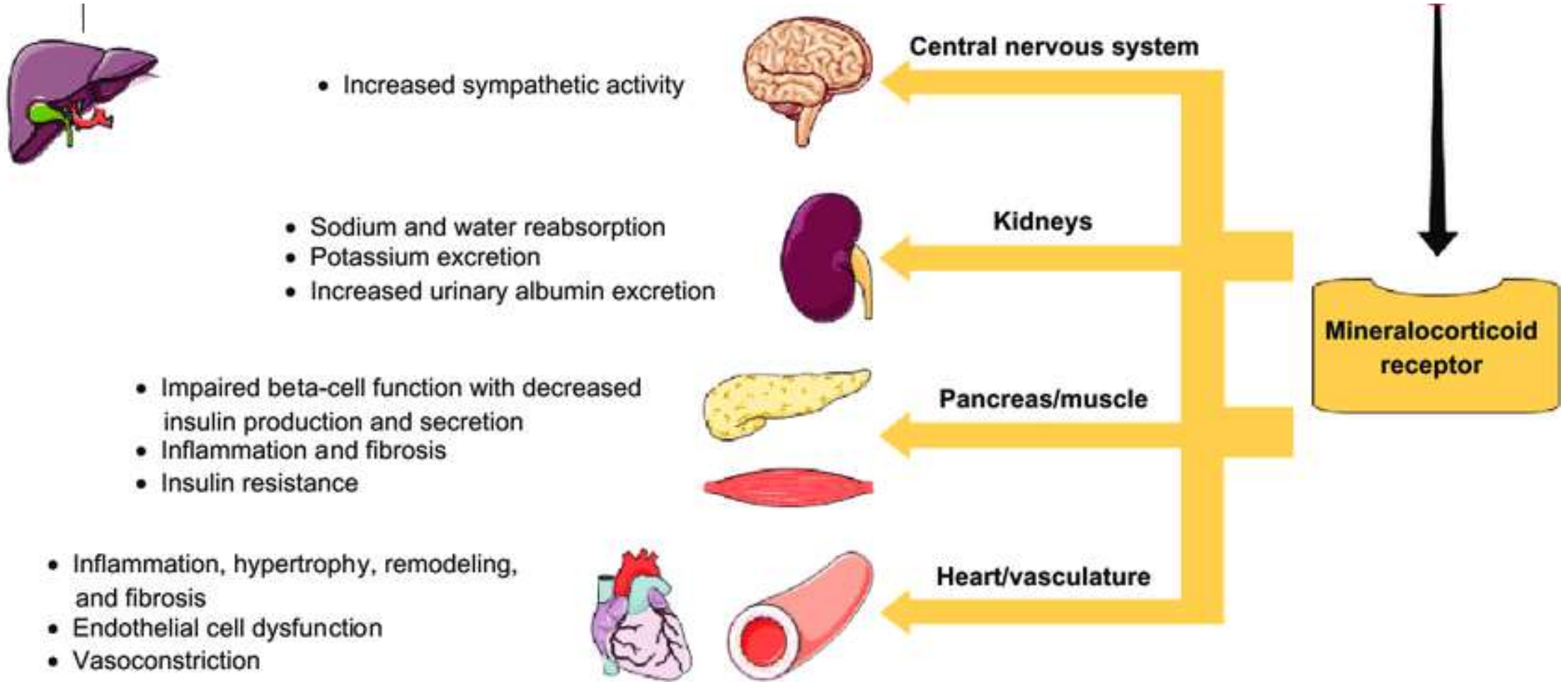

Steroid Hormone
Synthesis
In Adrenal Cortex
Cholesterol
Desmolase
Pregnenolone
3-β-Hydroxysteroid dehydrogenase
Progesterone
21-α-Hydroxylase
17-α-Hydroxylase
17-α-Hydroxyprogesterone
11-Deoxycorticosterone
21-α-Hydroxylase
androgen
Androstenedione
11- β -Hydroxylase
11-Deoxycortisol
Testosterone
Corticosterone
NOT IN ADRENAL CORTEX
Peripheral Tissues
Aldosterone
Cortisol
Estradiol

Catecholamines Synthesis :

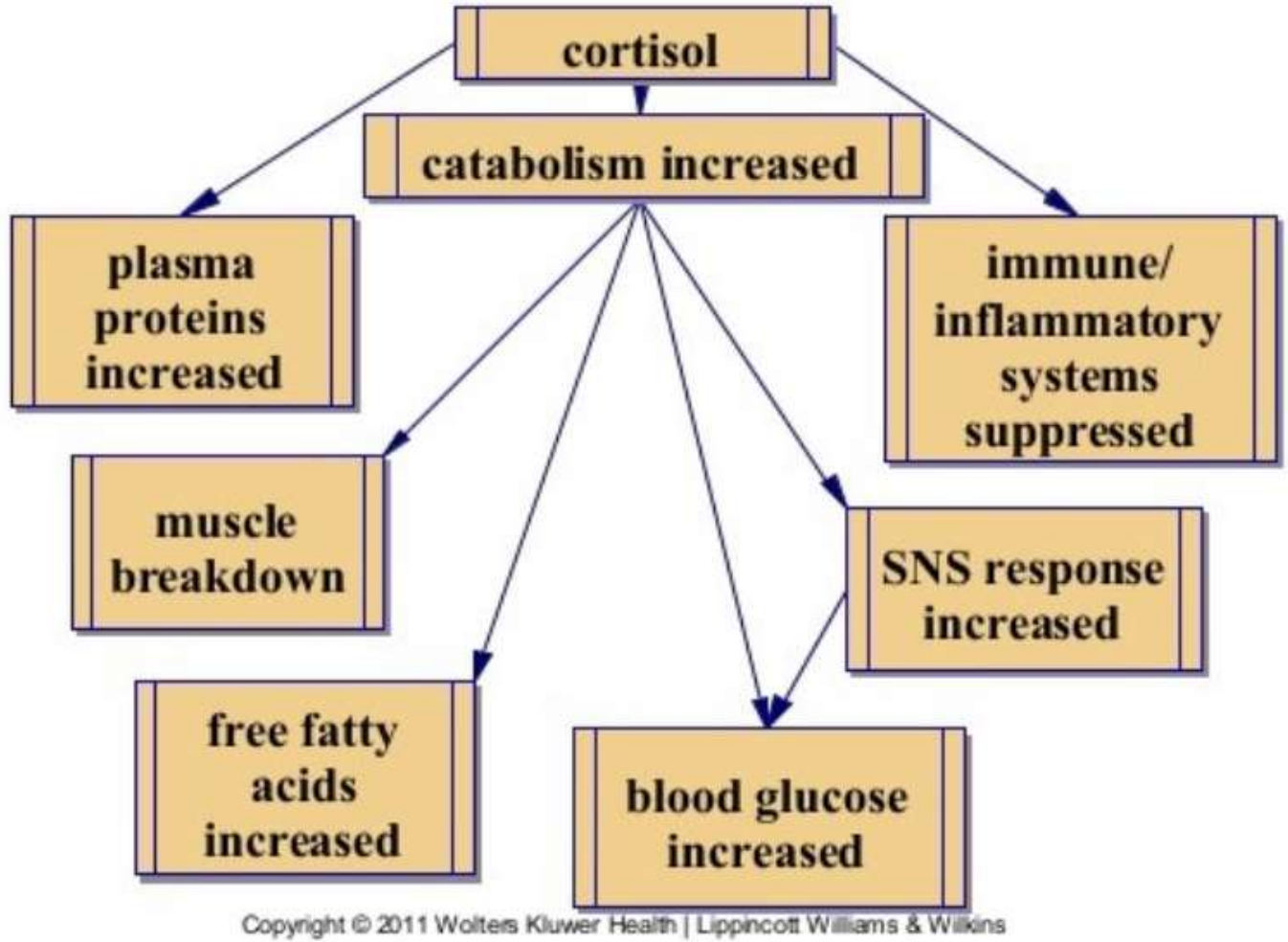
Figure 1



Mineralocorticoid effect :



Actions of Cortisol



Androgen effect :

Functions of Androgen:

- Development of the male
  i. Testes formation
  ii. Early regulation
- Spermatogenesis
- Inhibition of fat deposition
- Muscle mass (Androgens promote the enlargement of skeletal muscle cells)
- Brain (Circulating levels of androgens can influence human behavior because some neurons are sensitive to steroid hormones)

Catecholamine (stress hormones)effects :

The “fight or flight” response of the sympathetic nervous system is a direct result of the multisystem action of catecholamines.
1-regulate blood pressure by contracting the smooth muscle in the vasculature.

2-The musculoskeletal actions of catecholamines include enhanced contractility of cardiac muscle , contraction of the pupillary dilator , and relaxation of smooth muscle in the gastrointestinal tract, urinary tract, and bronchioles .

3-modulate metabolism to increase blood glucose levels by stimulating glycogenolysis in the liver , increased glucagon secretion , decrease insulin secretion from the pancreas and decrease lipolysis in adipose tissue.

4-inhibits release of mediators from mast cells and basophils in type I hypersensitivity reactions.

Cushing’s syndrome

Ahmad Al-Julani

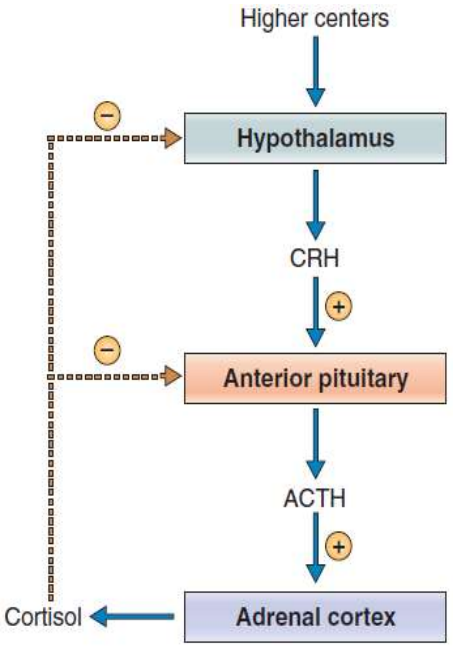
Cushing's syndrome

❖Clinical state induced by chronic cortisol excess to any cause

- Ineffective HPA axis feedback mechanisms
- results in Loss of normal circadian cortisol levels

  normally highest upon waking up ↑↑ AM blood sugar and lipid levels

  and lowest at the evening



❑Can be divided into two categories :

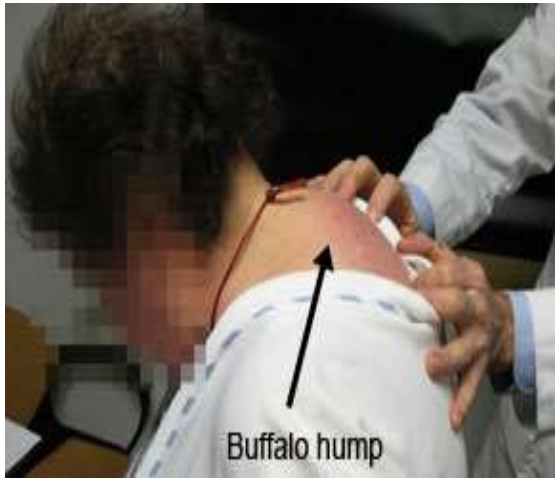
I. ACTH dependent → ↑ACTH → + ↑cortisol

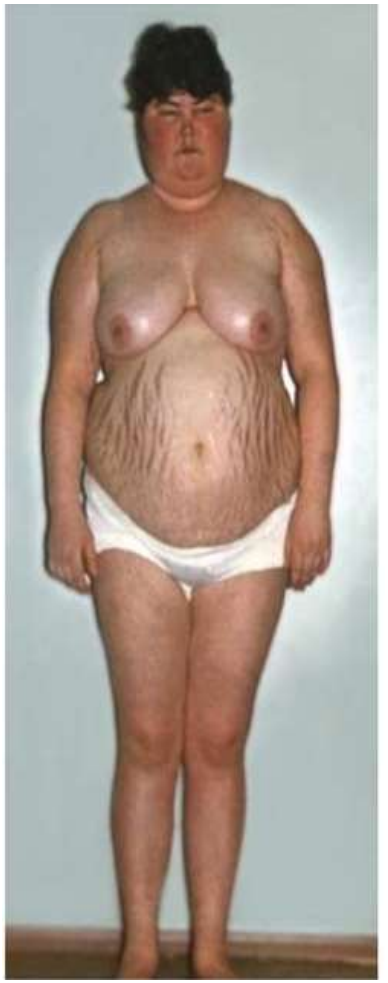
II. ACTH independent → ↑cortisol with ↓ACTH due to (-) feedback inhibition

CLINICAL MANIFESTATIONS

- Weight gain and Central obesity
- moon face
- Buffalo hump
- Supraclavicular fat pads
- Facial plethora
- purple stria
- Easily bruising
- Poor skin healing
- muscle wasting
- Osteoporosis
- Hypertension
- Hypokalemia and metabolic alkalosis
- Hyperglycemia
- diabetes
- Gonadal dysfunction(irregular menses , hirsutism ,and erectile dysfunction)
- Recurrent infections
- Depression , insomnia, psychosis

- hyperphagia, fat redistribution and promotion of adipocyte differentiation
- impaired collagen synthesis -> fragile skin
- Inhibition of fibroblasts and keratinocytes migration
- catabolic effect
- up-regulating α1-adrenergic receptors + ↑↑ cortisol exerts effect on MR
- promotion of gluconeogenesis and insulin resistance "diabetogenic effect"
- immunosuppression





ACTH dependent causes

Cushing's disease

- Common cause of Cushing's syndrome (70%)
- ACTH-secreting pituitary adenoma →adrenal hyperplasia leads to ↑cortisol
- The endogenous ↑ in cortisol doesn't effectively suppress the tumor corticotrophs but could be suppressed if injected with a high dose ↑receptors set-point
- rarely present with hyperpigmentation (secreted ACTH is inadequate)
- Excess ACTH stimulates production of adrenal androgens, females can present with virilization (hirsutism and acne).

Ectopic ACTH secreting tumor

- Constitutes 15% of all causes
- ACTH-secreting tumor outside the pituitary gland →adrenal hyperplasia leads to ↑↑cortisol ,mostly small cell lung carcinomas and carcinoid tumors .
- Tumor cells lack GR thus an absent (-) feedback inhibition → no response with high dose injected dexamethasone
- Mostly presents with hyperpigmentation(↑↑ACTH -> ↑ α-MSH) and weight loss -> could lack the typical signs of Cushing's syndrome

ACTH independent causes

- **Iatrogenic(exogenous)**

➢The most common and is due to prolonged glucocorticoid therapy

➢Continuous exogenous cortisol leads to ↓ACTH

- **Adrenal adenoma/carcinoma/hyperplasia(15%)**

➢Autonomous production of cortisol of the adrenals -> high cortisol/low ACTH

➢No suppression with high dose dexamethasone

Pseudo-Cushing’s syndrome (PCS)

- A condition that mimics true Cushing's syndrome and could present with similar cushingoid signs and symptoms with elevated serum cortisol.

➢ physiologic overactivity of the hypothalamic–pituitary–adrenal axis due to :

❖ Psychological stress

❖ Obesity , diabetes

❖ Depression

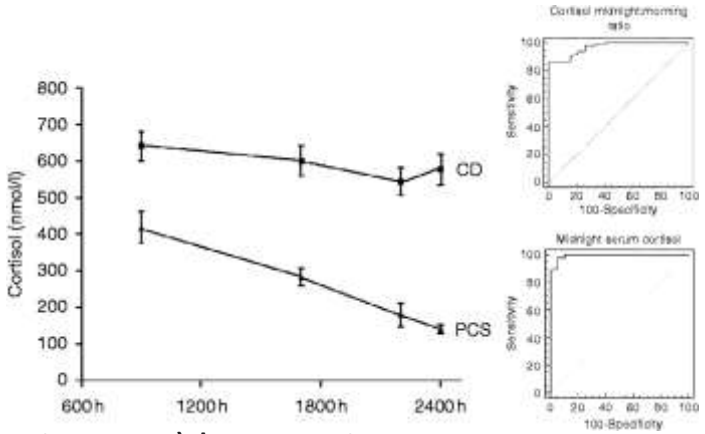
❖ Alcoholism

➢ Treatment of these underlying conditions resolves this syndrome

➢ ↑CRH->↑ACTH->↑cortisol

➢ How to distinguish it from true Cushing's syndrome?

- ➢ Usually there’s the preservation of the circadian cortisol level
- ➢ Detectable alcohol in the blood in case of alcoholism
- ➢ Injecting low-dose dexamethasone inhibits cortisol levels as normal
- ➢ IV Desmopressin increases ACTH levels significantly in Cushing's syndrome(hyperresponsiveness) but not in PCS



Diagnosis of Cushing's syndrome

- The diagnosis of Cushing's is a two-step process:
- 1. establish whether the patient has Cushing's syndrome
- Repeat testing is required
  - Low dose dexamethasone(1mg) suppression test
  - 24H urine free cortisol
  - Late night salivary cortisol level(assess circadian cortisol levels)
- 2. define its cause
  - High dose dexamethasone(8mg)
  - Serum ACTH

Establishing Cushing's syndrome

1- the 24-hour urinary free cortisol level

An excellent screening test values greater than four times of the normal are rare except in Cushing syndrome

2- low dose dexamethasone test

Give the patient 1 mg of dexamethasone at 11 pm. Measure the serum cortisol level at 8 am.

If the serum cortisol is **<50 nmol/l** , Cushing syndrome can be excluded (this test is very sensitive).

If the serum cortisol is **>50 nmol/l** (and often >100nmol/l), the patient has Cushing syndrome.

Establishing the Cause

- Once the diagnosis of Cushing's syndrome is done ↑**cortisol** , we need to know the category of Cushing's syndrome
- Measuring Serum ACTH measuring is the key!

➢ ↓**ACTH**(which means ACTH-independent) is most likely an autonomous adrenal tumor exerting (-) feedback on the pituitary inhibiting its secretion

- ↑**ACTH** (which means ACTH-dependent) is most likely 1-Cushing's disease or 2-ectopic ACTH-secreting tumor
- To further differentiate between the ACTH-dependent types(↑ACTH, ↑cortisol) we have two tests

I. High dose dexamethasone -> a decrease of more than 50% in cortisol level yields Cushing's disease (ACTH-secreting pituitary adenoma being suppressed)

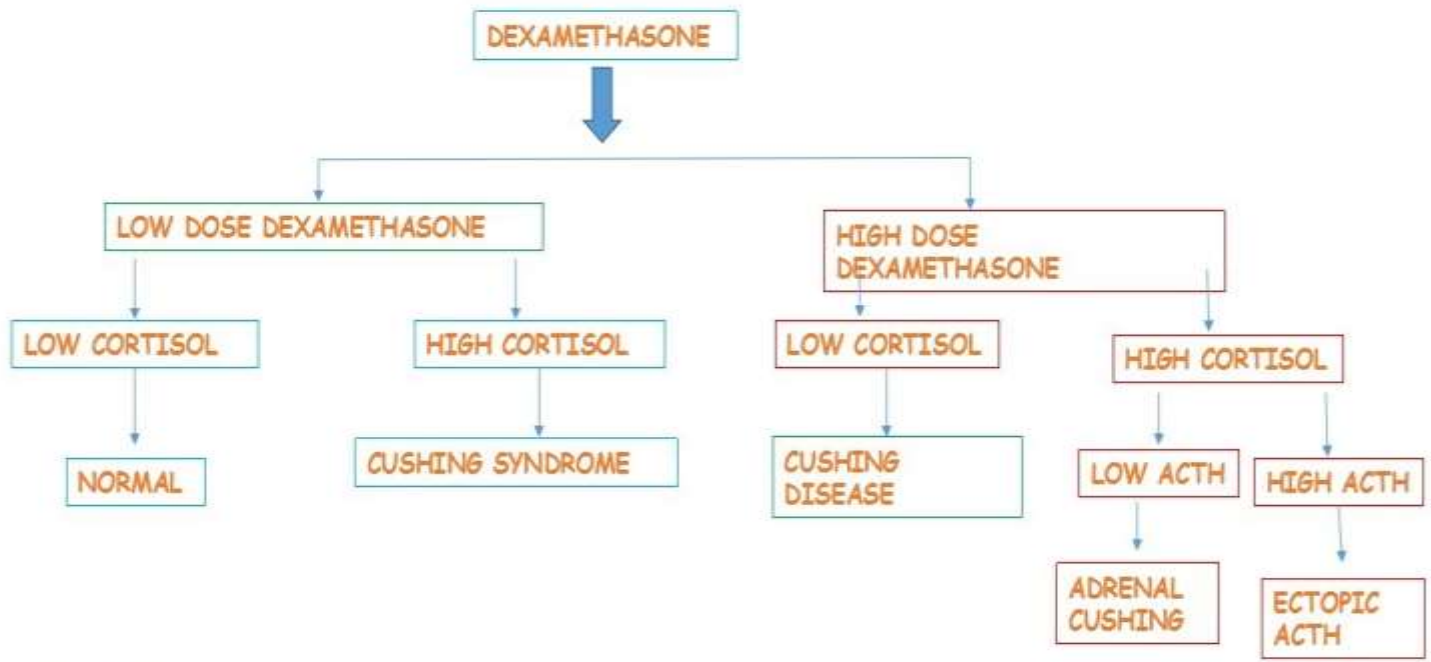
II. No change in cortisol level ->ectopic ACTH-secreting tumor

- CRH stimulation test
- Increase in ACTH/cortisol →Cushing's disease
- no change → ectopic or adrenal

AM Cortisol After Dexamethasone

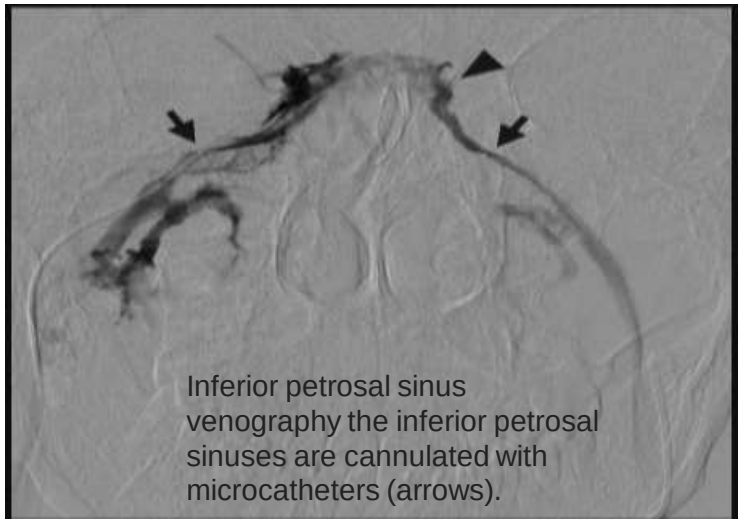
	Low Dose	High Dose
Normal	↓	↓
Pituitary Adenoma	--	↓
ACTH Tumor	--	--

ACTH-Dependent Causes (High ACTH)	ACTH-Independent Causes (Low ACTH)
Cushing's disease Ectopic ACTH	Steroid therapy Adrenal adenoma



Imaging studies

- **CT scan**
- Adrenal glands → adrenal tumors
- Chest abdomen pelvis → ectopic cause
- **Mri**
- Pituitary gland → Cushing's disease
- **bilateral inferior petrosal sinus sampling (BIPSS)**


Inferior petrosal sinus venography the inferior petrosal sinuses are cannulated with microcatheters (arrows).

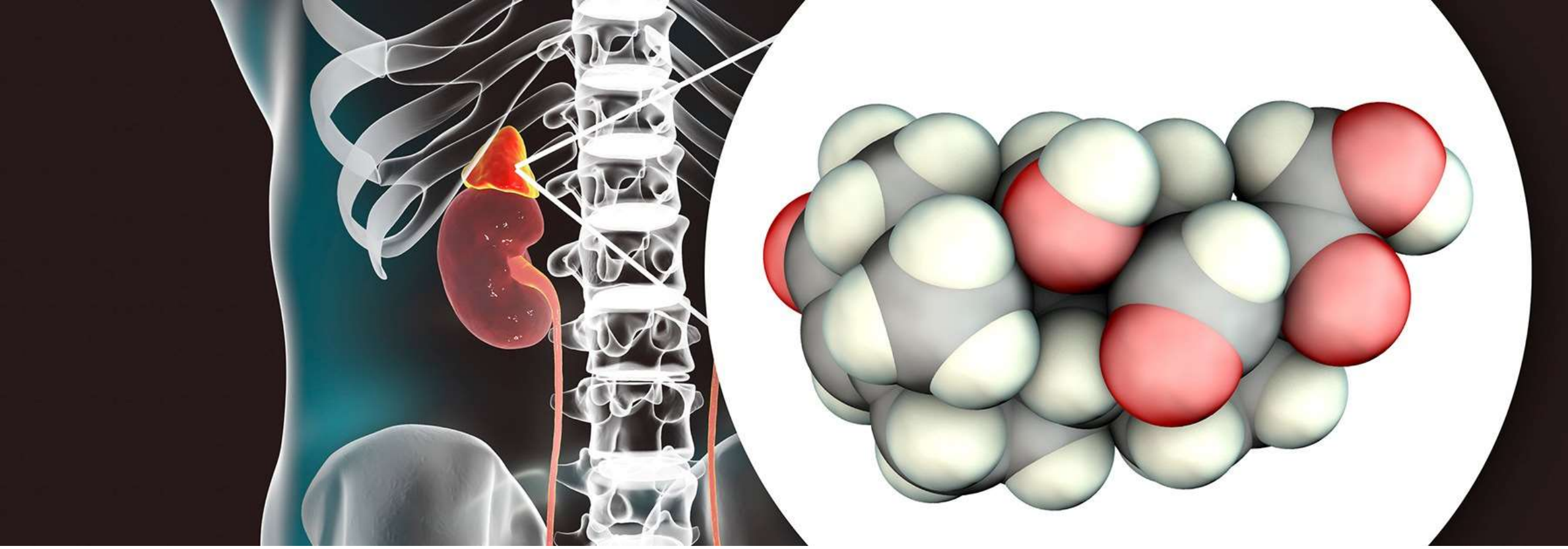
- ❑ invasive and elaborate but established procedure in distinguishing Cushing's disease (CD) from ectopic (ACTH) in case of inconclusive studies, with sensitivity and specificity reaching 100%.
- ❑ inferior petrosal sinuses receive drainage from the pituitary gland without mixture of blood from other sources
- ❑ if the patient has pituitary Cushing's, the ACTH levels in the IPS are high compared to an ACTH drawn in the periphery. In contrast, in ectopic Cushing's, the ACTH in the IPS and the periphery should be equivalent because the tumor is located elsewhere
- ❑ CRH could be used to increase the sensitivity →↑ACTH in CD and no response in ectopic ACTH

Treatment

- Iatrogenic: Tapering of glucocorticoids
- Cushing's disease: surgical resection of adenoma
- Adrenal tumor: surgical resection is effective in adenomas but rarely effective in carcinomas , radiotherapy required
- Ectopic ACTH secretion : surgical resection
- Ketoconazole , metyrapone and fluconazole can be used when surgery is contraindicated -> ↓ cortisol synthesis

Prognosis

- Untreated severe Cushing's syndrome has a 50% 5-year mortality.
- Treated patients have **good prognosis** but with remaining long-lasting effects to varying degrees (hypertension,dyslipidemia,atherosclerosis,osteoporosis,myopathy,obesity)



Hyperaldosteronism

By Hossam Al-Noaimi

Mineralocorticoids Overview

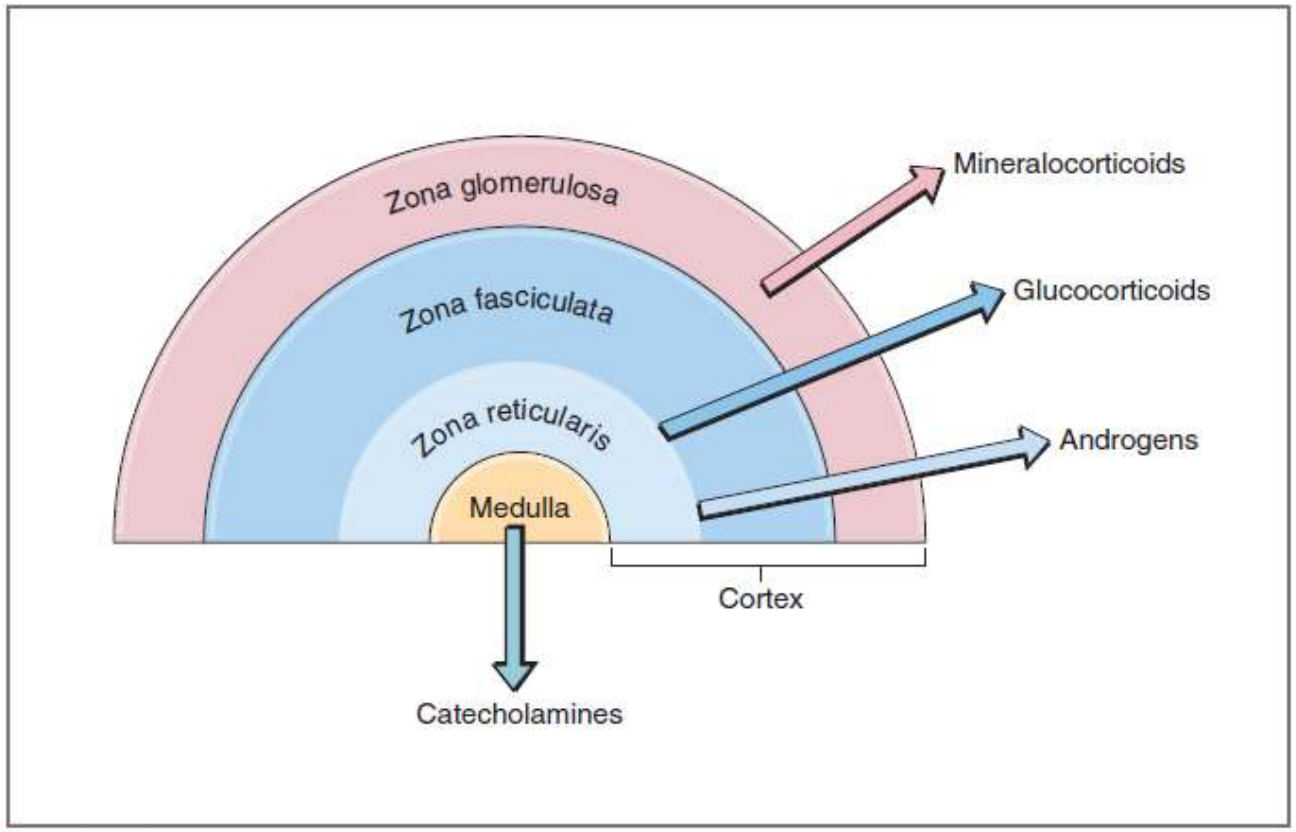


Fig. 9.21 Secretions of the adrenal medulla and adrenal cortex. The zonae fasciculata and reticularis secrete glucocorticoids and androgens; the zona glomerulosa secretes mineralocorticoids.

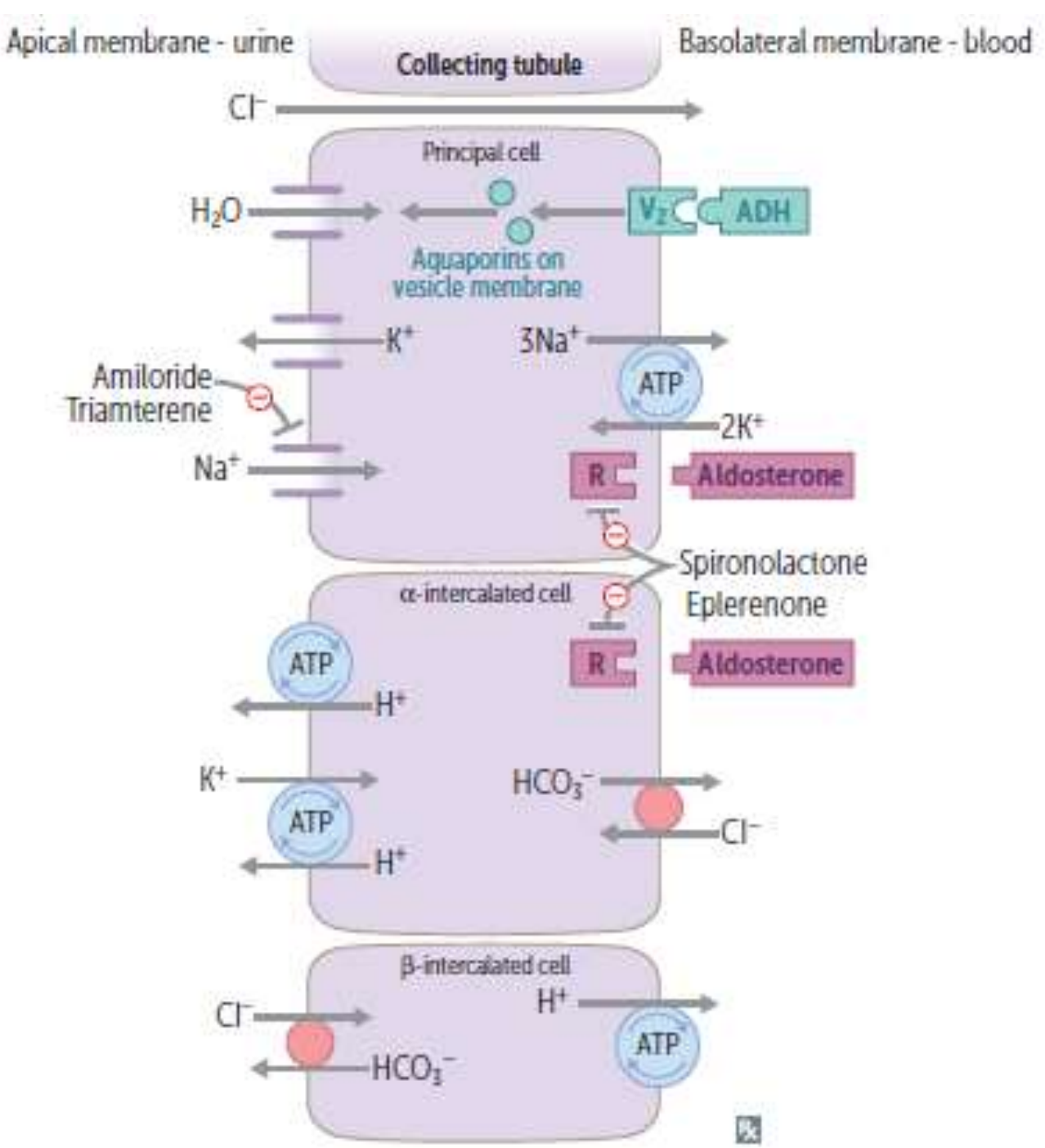
- **The main mineralocorticoid is Aldosterone**

Mineralocorticoids Overview

How do mineralocorticoid(aldosterone) **work**?

In the cell's cytoplasm, the hormone binds to its receptor forming a mineralocorticoid-receptor complex, this complex is then transferred to the nucleus, where it binds to mineralocorticoid response elements(MREs), which directs the synthesis of specific messenger RNAs (mRNAs). These mRNAs then direct the synthesis of new proteins that are involved in Na+ reabsorption by the principal cells in the collecting ducts of the kidney. The aldosterone-induced proteins include the **epithelial Na+ channel** (ENaC), the Na+/K+ ATPase(pump).

Mineralocorticoids Overview



Mineralocorticoids Overview

Aldosterone increases the following:

1- The number Na+/K+ pumps.

2- The synthesis of more epithelial Na+ channels, which increases Na+ entry into the cell and provides more Na+ to the Na+/K+ ATPase.

3- Conductance of K+ through the apical membrane into the lumen.

As more Na+ is being reabsorbed from the lumen into the blood, lumen negativity increases, which acts as a driving force for K+ to leave the cell into the lumen.

Also, because the negativity in the lumen increases, H+ ATPase in the a-intercalated cell increases in activity leading to H+ excretion. BUT this creates more negativity in the cell itself, so HCO_3^- must leave the cell into the blood to compensate for the increased negativity, so the activity HCO_3^-/Cl^- increases to keep the overall balance of charges stable.

Net Result:

Na+ retention/ increased ECV

K+ excretion

H+ secretion/ metabolic alkalosis

Mineralocorticoids Overview

Triggers for aldosterone secretion:

1- Renin-angiotensin system

2- Hyperkalemia

3- ACTH(minor trigger)

Mineralocorticoids Overview

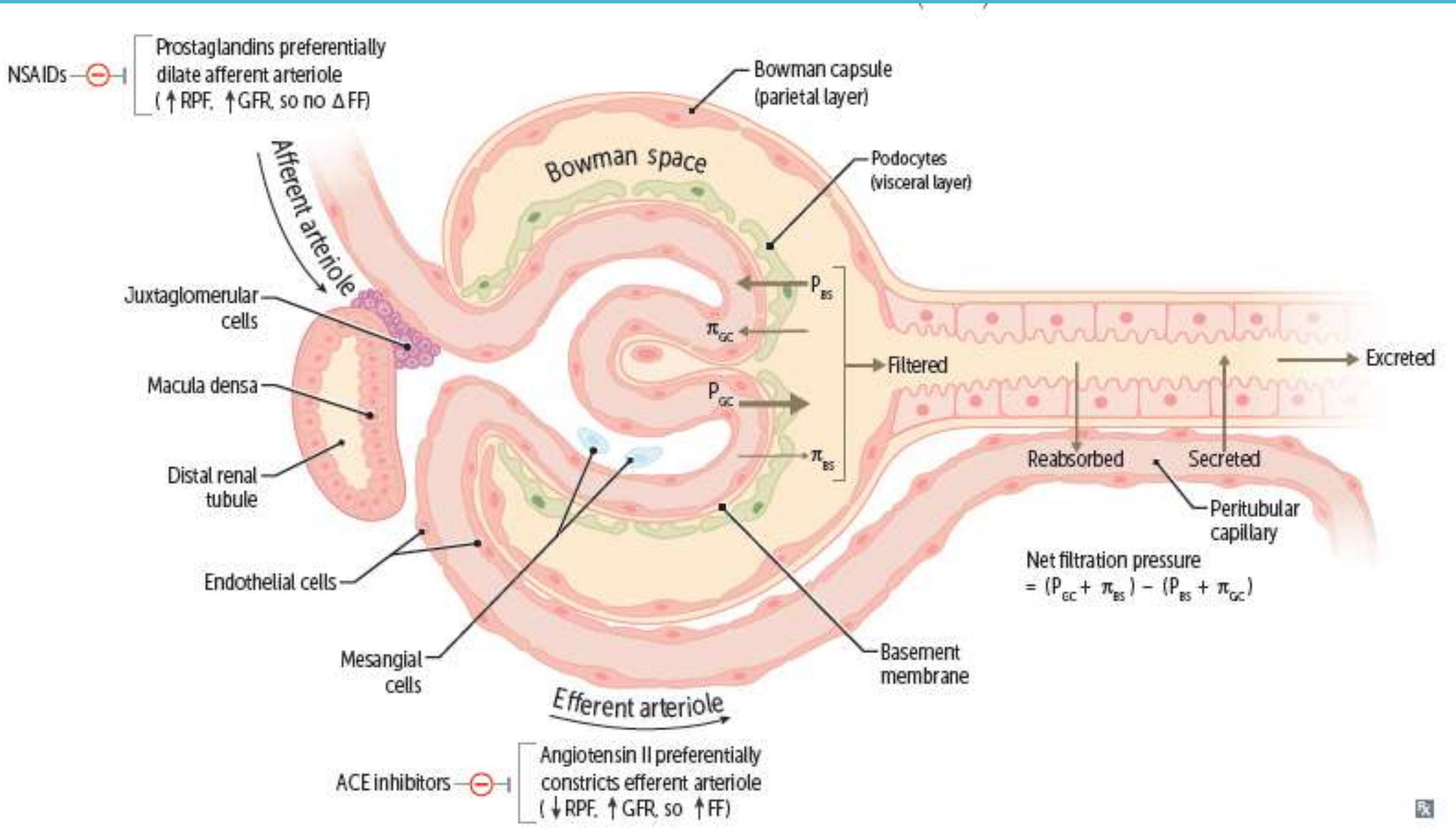
Review: Renin is released by the healthy kidney from the juxtaglomerular apparatus in response to at least 3 independent factors:

I) **Decreased** blood **volume**, as measured by the juxtaglomerular cells. These are specialized vascular smooth muscle cells in the afferent arteriole.

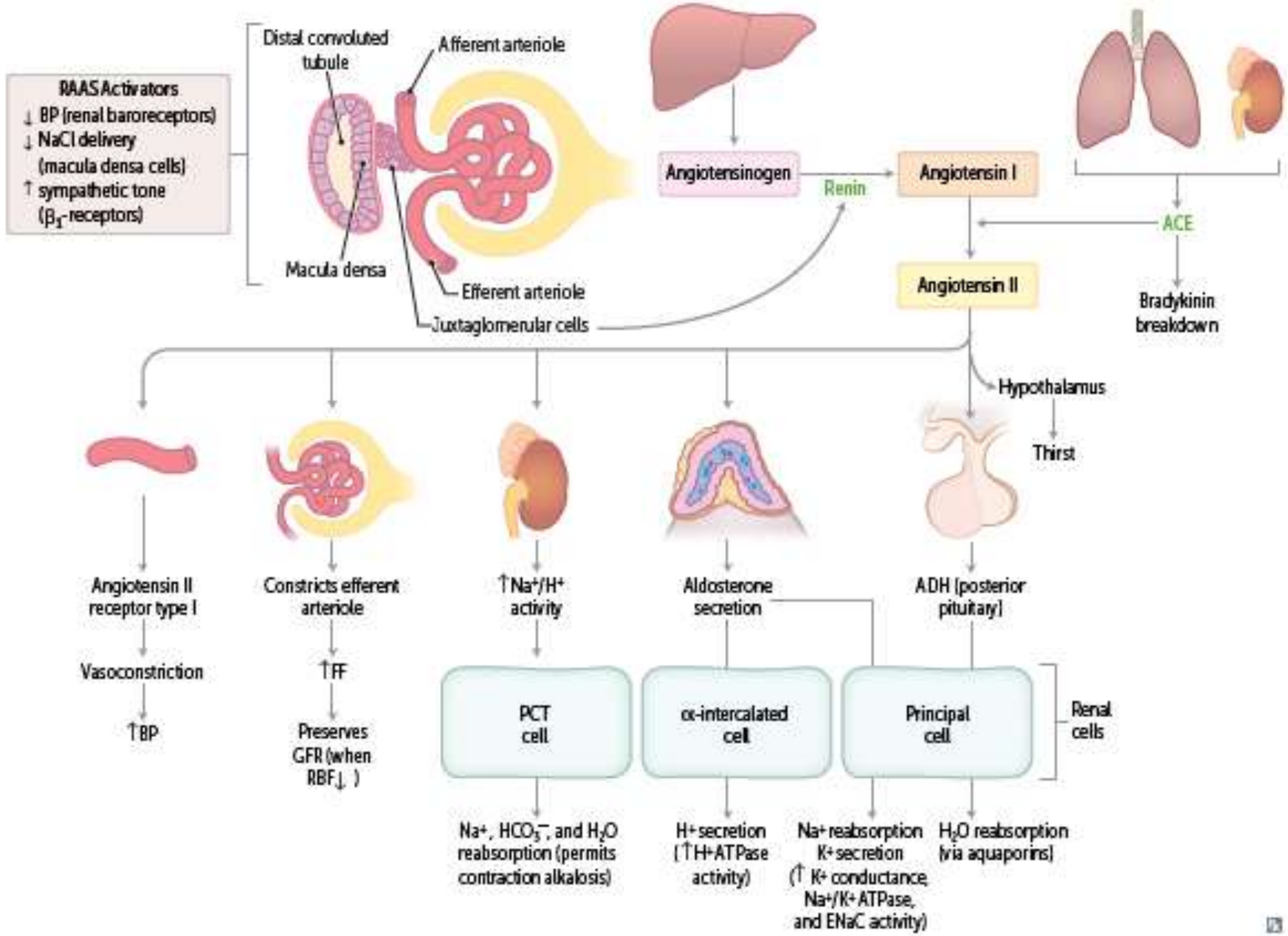
2) Elevated levels of filtered **sodium**, as measured by the efferent macula densa cells in the DCT.

3) **Sympathetic** nervous system stimulation(B1 receptors).

Function of Renin: it converts angiotensinogen to angiotensin I, which is then converted to angiotensin II by ACE-mainly in the lungs. Angiotensin II has pressor effects and stimulates aldosterone release from the zona glomerulosa in the adrenal glands.


NSAIDs
Prostaglandins preferentially dilate afferent arteriole
(↑RPF, ↑GFR, so no ΔFF)
Bowman capsule (parietal layer)
Bowman space
Podocytes (visceral layer)
Afferent arteriole
Juxtaglomerular cells
Macula densa
Distal renal tubule
Endothelial cells
Mesangial cells
P_{BS}
π_{GC}
P_{GC}
π_{BS}
Filtered
Excreted
Reabsorbed
Secreted
Peritubular capillary
Net filtration pressure
$= (P_{GC} + \pi_{BS}) - (P_{BS} + \pi_{GC})$
Basement membrane
Efferent arteriole
ACE inhibitors
Angiotensin II preferentially constricts efferent arteriole
(↓RPF, ↑GFR, so ↑FF)

Renin-angiotensin-aldosterone system



Hyperaldosteronism

Hyperaldosteronism is a syndrome associated with hypersecretion of aldosterone.

Hyperaldosteronism can be divided into the following:

-Primary aldosteronism: in which the stimulus for the excessive aldosterone production is *within* the adrenal gland independent on the RAAS

-Secondary aldosteronism: in which the stimulus is *extra-adrenal*

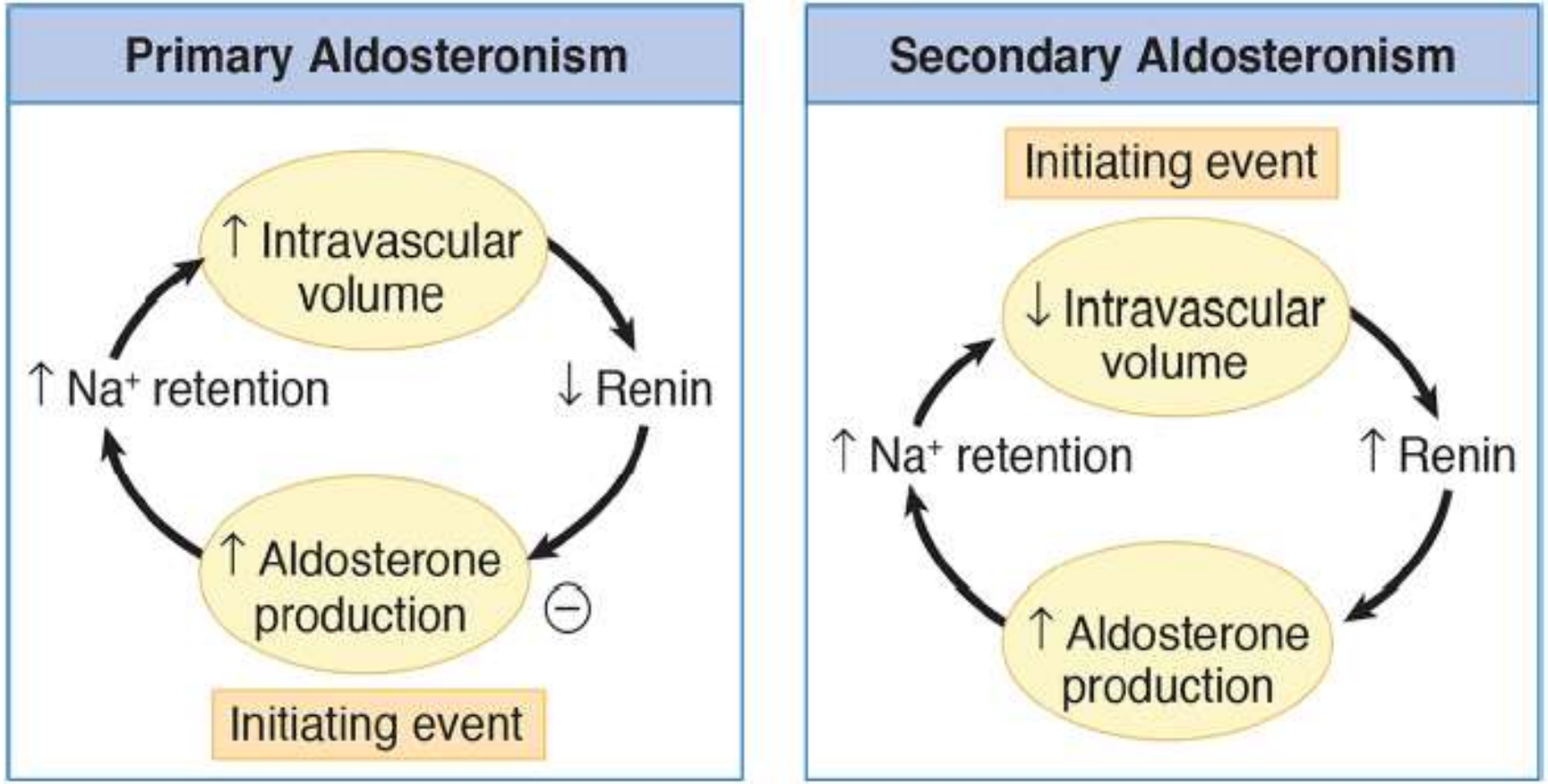
A. General Characteristics:

a. Sodium retention causes ECF volume expansion and HTN.

b. Potassium loss results in hypokalemia.

c. Excess aldosterone also increases the secretion of hydrogen ions into the lumen of the medullary collecting tubules resulting in metabolic alkalosis

Hyperaldosteronism



Hyperaldosteronism

18.46 Causes of mineralocorticoid excess

With renin high and aldosterone high (secondary hyperaldosteronism)

- Inadequate renal perfusion (diuretic therapy, cardiac failure, liver failure, nephrotic syndrome, renal artery stenosis)
- Renin-secreting renal tumour (very rare)

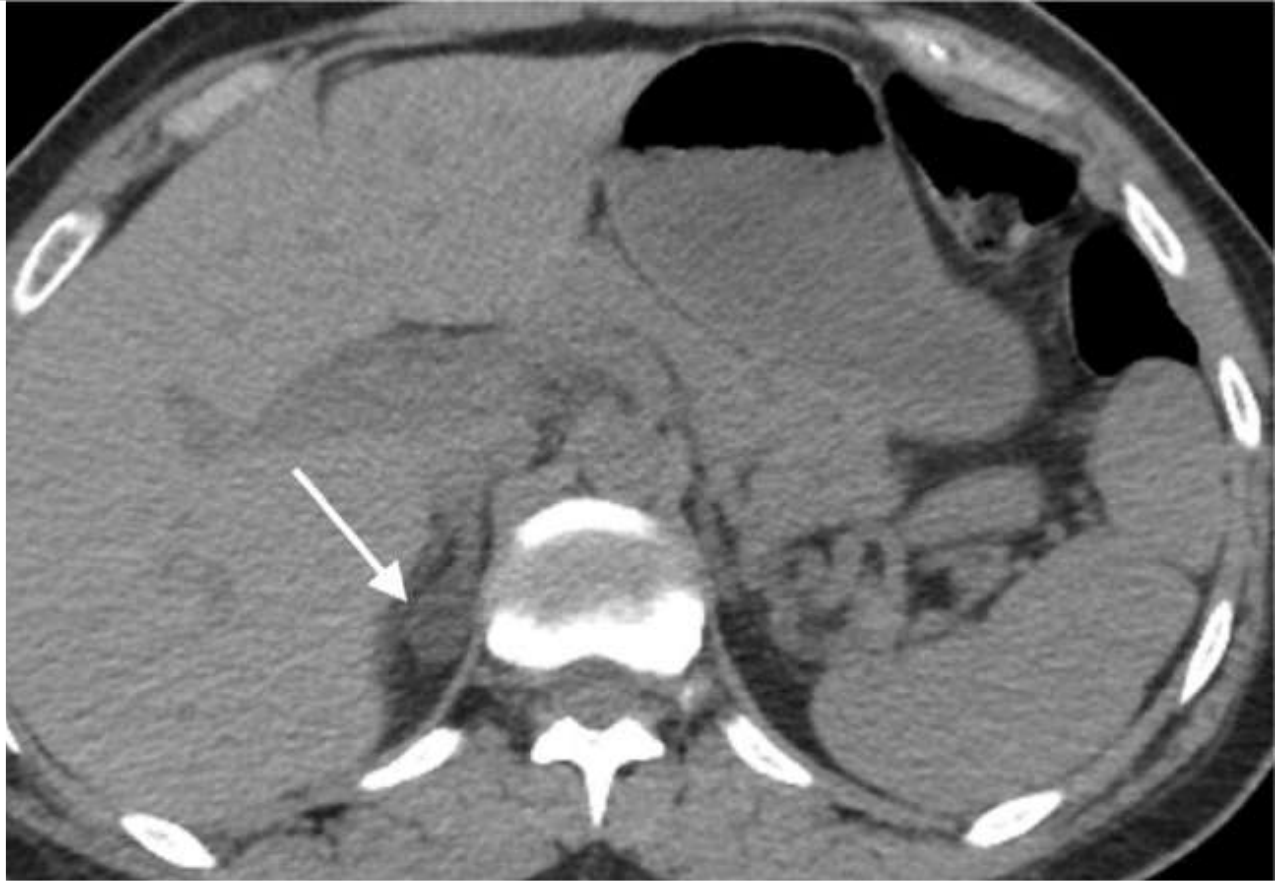
With renin low and aldosterone high (primary hyperaldosteronism)

- Adrenal adenoma secreting aldosterone (Conn's syndrome)
- Idiopathic bilateral adrenal hyperplasia
- Glucocorticoid-suppressible hyperaldosteronism (rare)

With renin low and aldosterone low (non-aldosterone-dependent activation of mineralocorticoid pathway)

- Ectopic ACTH syndrome
- Liquorice misuse (inhibition of 11β-HSD2)
- Liddle's syndrome
- 11-deoxycorticosterone-secreting adrenal tumour
- Rare forms of congenital adrenal hyperplasia and 11β-HSD2 deficiency

(11β-HSD2 = 11β-hydroxysteroid dehydrogenase type 2; ACTH = adrenocorticotrophic hormone)



Conn syndrome (Adrenal Adenoma)

Hyperaldosteronism

Clinical Features:

1. Hypertension (most common clinical feature)(**due to Na+ retention**)
2. Headache, fatigue
3. Muscle weakness (even paralysis), Polydipsia, polyuria (**excessive K+ excretion leads to decreased Na+ reabsorption**)
4. Muscle cramps and, in severe cases, can cause tetany (**due to metabolic alkalosis**)
5. **Absence of peripheral edema (aldosterone escape)**
6. Maybe asymptomatic

D. Diagnosis:

1. Screening for (primary vs secondary)
2. Confirm primary Dx by **NaCl challenge**

Hyperaldosteronism

For the screening test: Ratio of the plasma *aldosterone* level to plasma *renin*.

Primary disease shows inappropriately elevated aldosterone and decreased plasma renin; if ratio of aldosterone: renin is more than 30, Think adrenal disease **(tumor or hyperplasia).**

Secondary disease: both aldosterone and renin are elevated, with a ratio usually < I 0. Think kidney disease (**renovascular or renal tumor).**

Hyperaldosteronism

For definitive diagnosis, one of the two tests is usually performed.

a. Saline infusion test

Infusion of saline will decrease aldosterone levels in normal patients but not in those with primary aldosteronism.

If aldosterone levels are <8.5 ng/dL after saline infusion, primary aldosteronism may be ruled out.

b. Oral sodium loading

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

So, no suppression of aldosterone levels suggests adrenal disease

Hyperaldosteronism

Note : It is important to distinguish adenoma from hyperplasia because hypertension associated with hyperplasia is **not** benefited by bilateral adrenalectomy, whereas hypertension associated with adenoma is usually improved/cured by removal of the adenoma.

3. To diagnose **the cause:**

A- of primary aldosteronism:

a. Adrenal venous sampling for aldosterone levels—A high level of aldosterone on one side indicates an adenoma. High levels on both sides indicate bilateral hyperplasia.

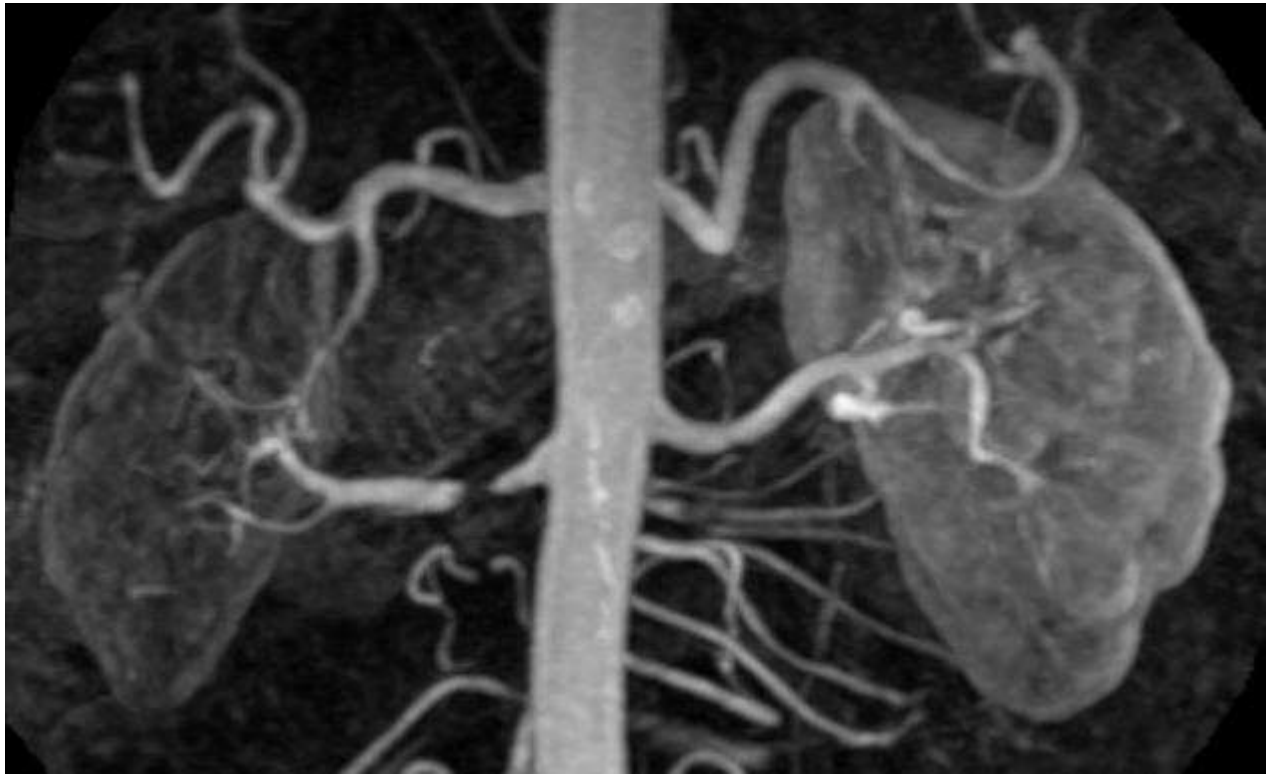
b. Imaging tests

CT scan/MRI of adrenals: may demonstrate adenoma or hyperplasia.

Hyperaldosteronism

B- of secondary aldosteronism:

Go straight to renal angiography ----renovasular (stenosis) vs renal tumor(secreting)



Hyperaldosteronism

Treatment:

1. For **adenoma:**

Surgical resection (adrenalectomy) is often curative.
Spironolactone for symptomatic treatment before surgery.

2. For **bilateral hyperplasia**:

a. Spironolactone inhibits the action of aldosterone.

b. Surgery **is not** indicated.

ADRENAL INCUFICIENCY

Done by : AHMAD AL-ZAWAHREH

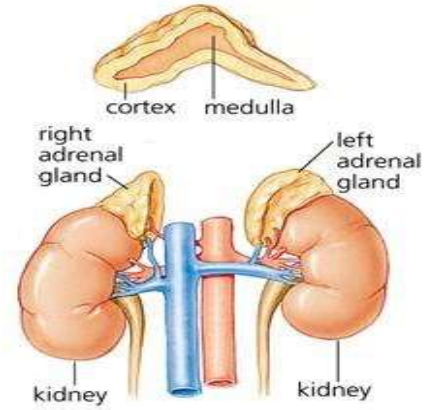
Adrenal insufficiency

- Loss of adrenal function
- Loss of one or more adrenal hormones

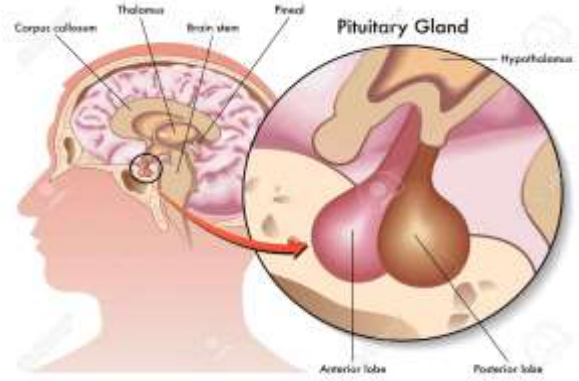
- Glucocorticoids: cortisol
- Mineralocorticoids: aldosterone
- Androgens: dehydroepiandrosterone (DHEA)

TYPES

There are three major types of adrenal insufficiency



- **Primary adrenal insufficiency** :
  - is due to impairment of adrenal glands. (Addison's disease)
  - Loss of cortisol, aldosterone and androgens
- **Secondary adrenal insufficiency** :
  - is caused by impairment of pituitary glands
  - Loss of ACTH from pituitary (secondary)
  - Loss of cortisol only



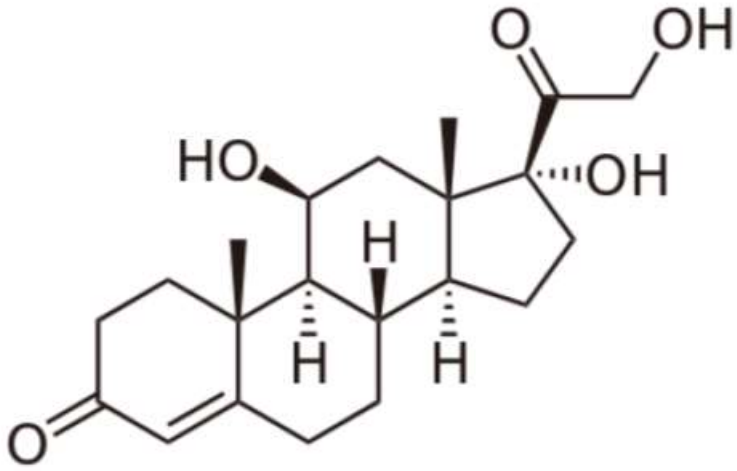
- **Tertiary adrenal insufficiency** :
  - is due to hypothalamic disease and decrease in corticotropin releasing Hermon (CRH)
  - Loss of cortisol only

Glucocorticoid Deficiency Clinical Features

- Fatigue
- Weight loss
- Gastrointestinal symptoms
  Usually nausea
  Sometimes vomiting, abdominal pain or diarrhea

- Hypoglycemia—Cortisol is a gluconeogenic hormone.

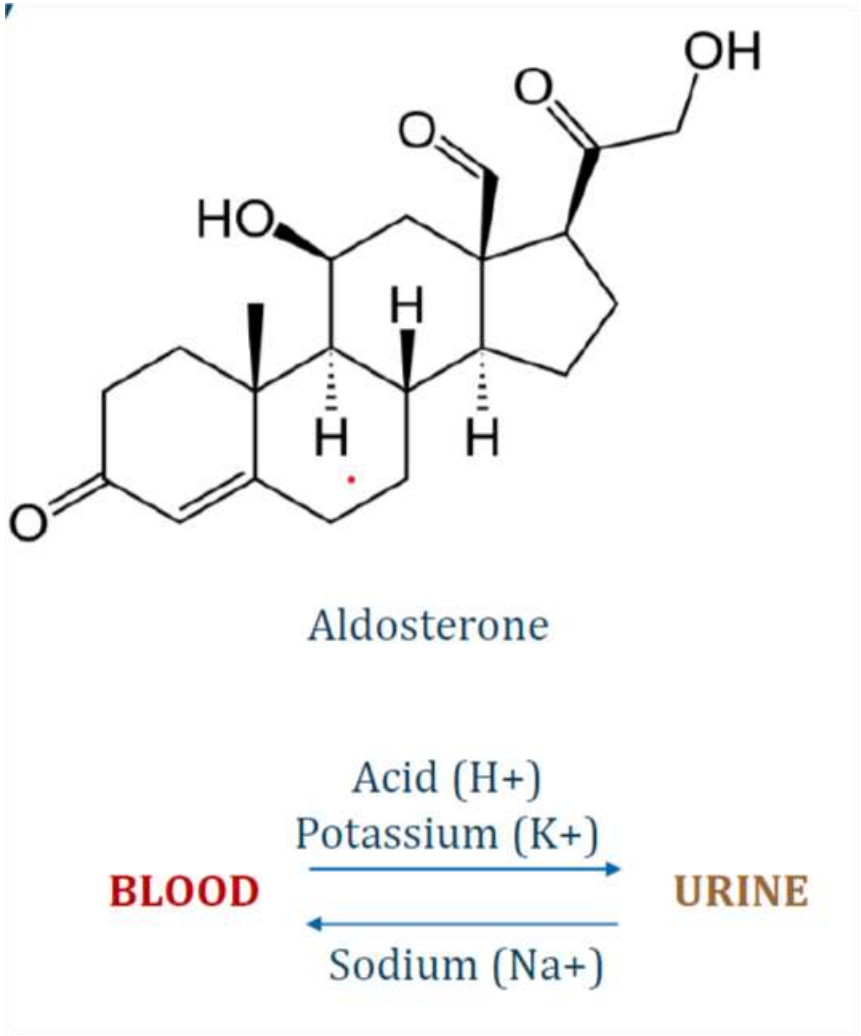
- Hypotension +/ syncope
  Cortisol maintains vascular tone
  Often orthostatic hypotension
- Muscle and joint pain
- Hyponatremia (↑ ADH release)



Cortisol

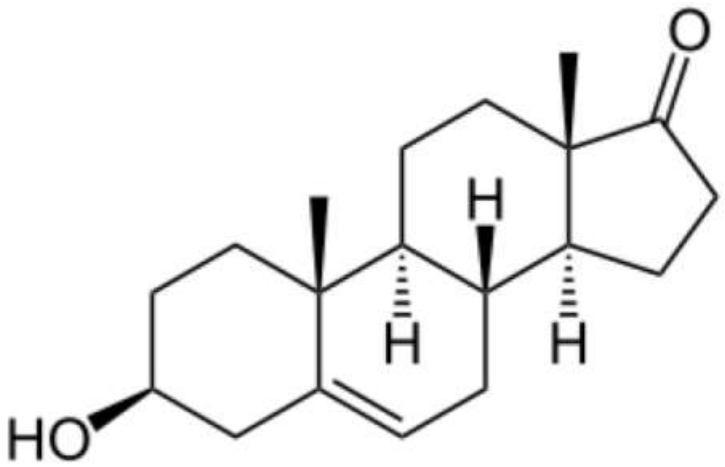
Mineralocorticoid Deficiency Clinical Features

- Hypovolemia
  "Salt wasting " patient may crave salty foods
  Loss of sodium and water in urine
  May lead to hypovolemic shock
- Hyponatremia
  High ADH from hypovolemia
  Retention of free water
- Hyperkalemia
  Decreased urinary potassium
- Metabolic acidosis
  Decreased urinary acid excretion



Androgen Deficiency Clinical Features

- No significant impact in males (testes)
- Decreased axillary and pubic hair in females

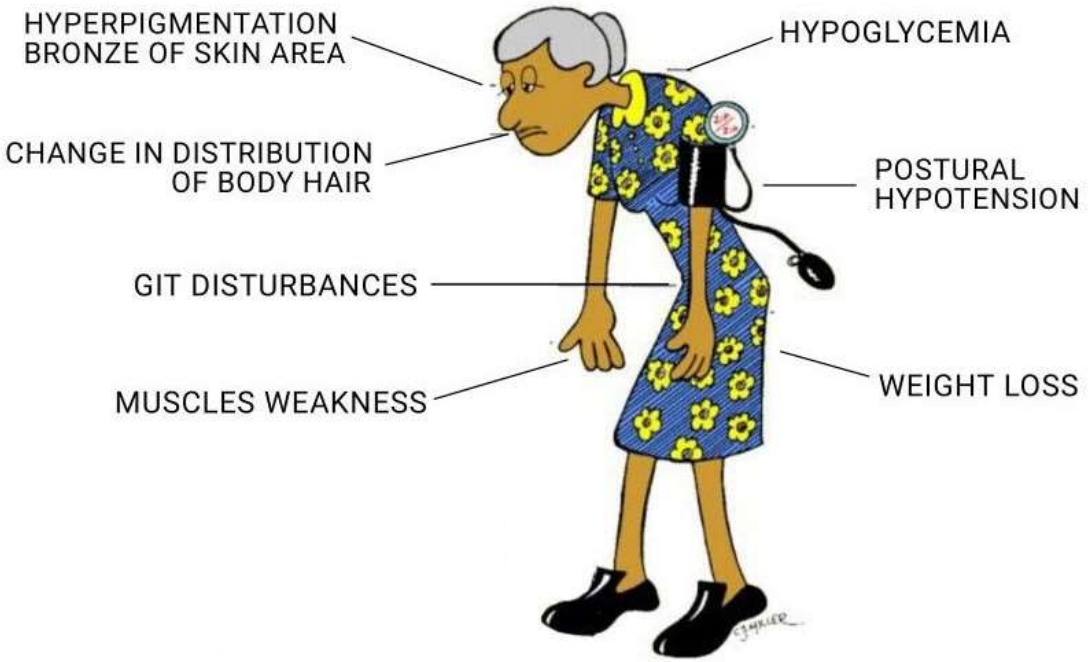


Dehydroepiandrosterone
(DHEA)

Primary Adrenal Insufficiency

Clinical feature:

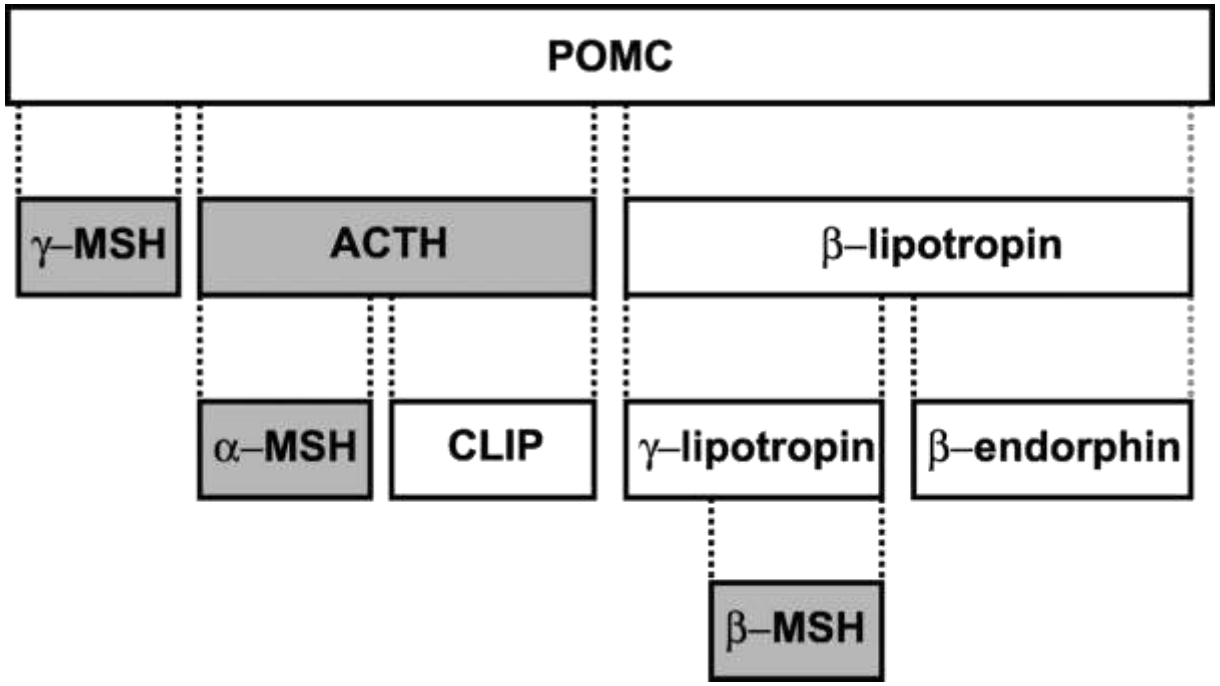
- Fatigue
- Weight loss
- Nausea, vomiting and abdominal pain
- Muscle and joint pain
- Postural hypotension
- Salt craving
- Hyponatremia
- Hyperkalemia
- Eosinophilia

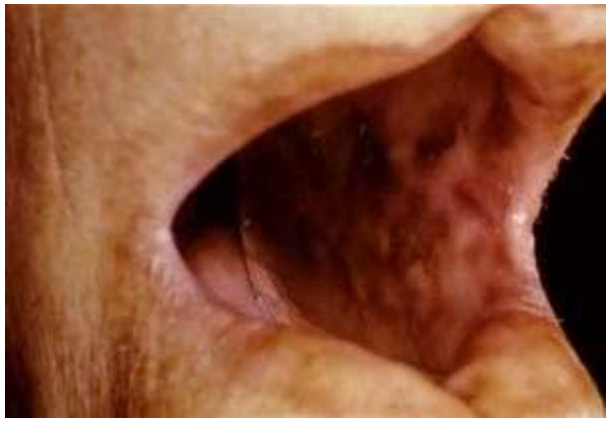


Skin hyper pigmentation

- ACTH is high in primary adrenal insufficiency
- ↑ melanocyte stimulating hormone (MSH)
- Common precursor in pituitary with ACTH
- Proopiomelanocortin (POMC)
- ↑ ACTH →↑ MSH →↑ melanin synthesis
- Most obvious in sun exposed areas

  Face, neck, backs of hands
- May also occur on mucous membranes





High ACTH---NO glucocorticoids and Mineralocorticoids

Primary Adrenal Insufficiency

causes

a. **Idiopathic** (thought to be autoimmune disease) is the most common type in the industrialized world.

b. Infectious diseases—these include tuberculosis (most common cause worldwide) and fungal infections. Causes also include cytomegalovirus, cryptococcus, toxoplasmosis, and pneumocystis.

c. Iatrogenic—for example, a bilateral adrenalectomy.

d. Metastatic disease—from lung or breast cancer.

Central Adrenal Insufficiency
clinical feature

- Weakness and fatigue
- Muscle and joint pain
- Weight loss
- Nausea, vomiting and abdominal pain

- Hypotension (less prominent)
  Decreased vascular tone only
  No loss of mineralocorticoids
- Hyponatremia (but less common)
  Intact mineralocorticoids

- No skin hyperpigmentation (low ACTH)

Central Adrenal Insufficiency

causes

- Secondary adrenal insufficiency:

a. Patients on long-term steroid therapy—This is the most common cause of secondary adrenal insufficiency today. 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.

b. Hypopituitarism (rare)—due to a variety of insults.(no ACTH)

NO ACTH---NO glucocorticoids.

- Tertiary adrenal insufficiency—hypothalamic disease.(no CRH)

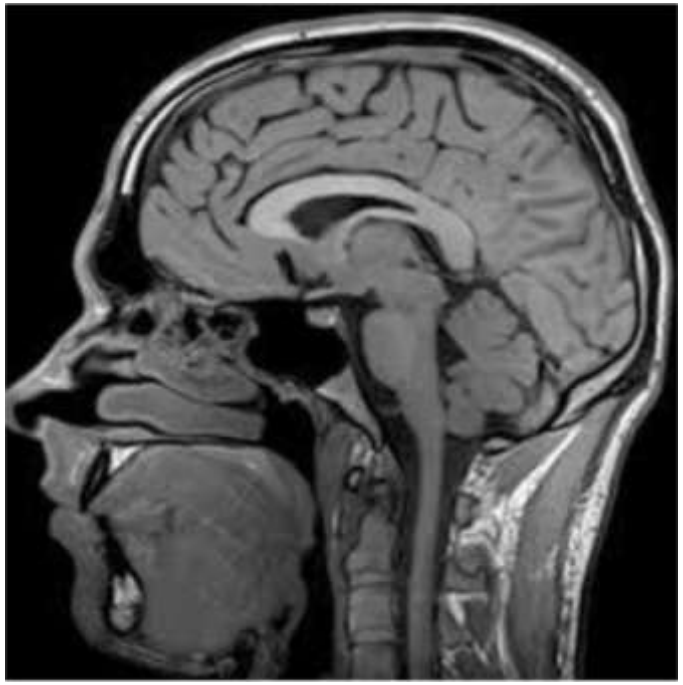
NO CRH ---NO ACTH---NO glucocorticoids

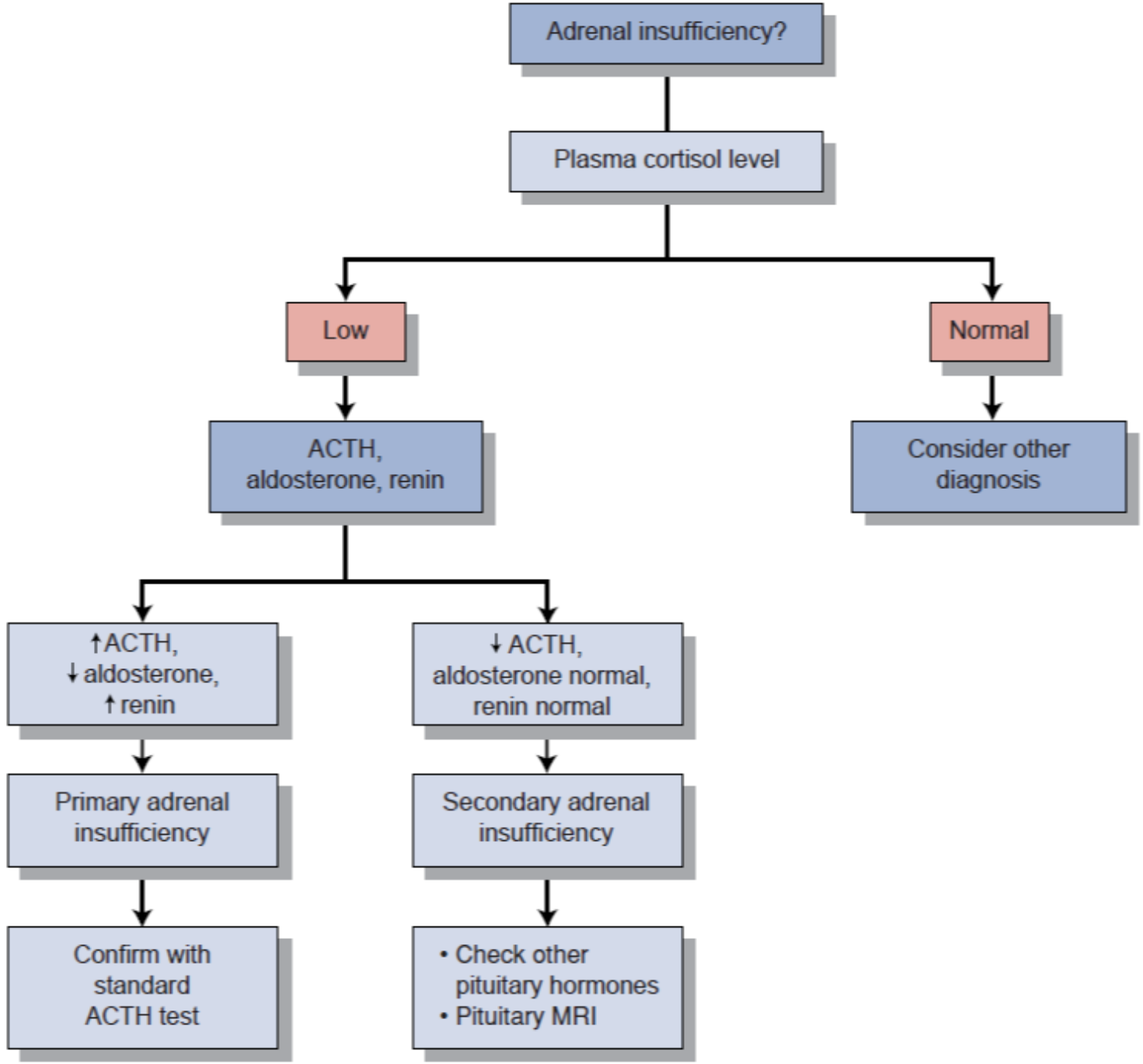
Diagnosis

- Morning cortisol
  Cortisol concentration higher in early morning
  Low value at this time suggests adrenal insufficiency

- Plasma ACTH
  Low cortisol + high ACTH = primary disease
  Low cortisol + low ACTH = central disease

- Head MRI
- CRH stimulation test
  Differentiates 2 from 3
  No cortisol rise after CRH: 2 ∘ (pituitary failure)
  Cortisol rise after CRH: 3 ∘ (hypothalamic failure)




Adrenal insufficiency?
Plasma cortisol level
Low
Normal
ACTH, aldosterone, renin
Consider other diagnosis
↑ACTH, ↓aldosterone, ↑renin
↓ACTH, aldosterone normal, renin normal
Primary adrenal insufficiency
Secondary adrenal insufficiency
Confirm with standard ACTH test
• Check other pituitary hormones
• Pituitary MRI

Cosyntropin Stimulation Test

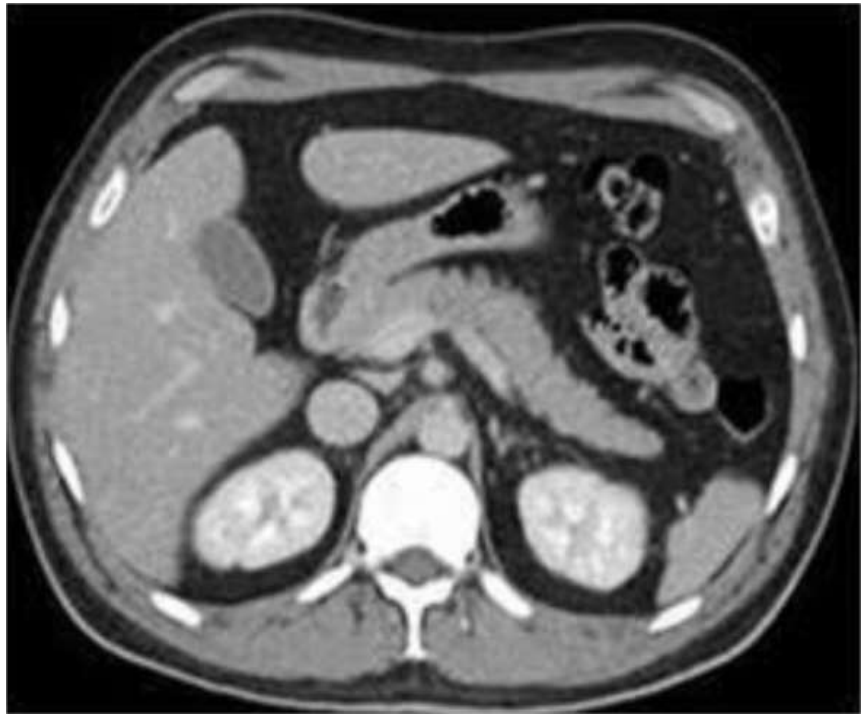
- Cosyntropin: synthetic ACTH

This is a definitive test for primary adrenal insufficiency; give an IV infusion of synthetic ACTH, and measure plasma cortisol at the end of the infusion.

- Normal response: rise in serum cortisol
  Measured after 30 or 60 minutes
  Should peak at ≥ 18 to 20 mg/dL
- In primary adrenal insufficiency, cortisol does not increase sufficiently.
- In secondary adrenal insufficiency, cortisol fails to respond to ACTH infusion, as in primary adrenal insufficiency (the adrenals are not used to being stimulated, so they do not respond right away). However, if the test is repeated for 4 or 5 days, the adrenals eventually respond normally.

• Determination of cause

- **Cause may be evident from history and exam**
  Tuberculosis, HIV or meningococcemia
- **Antibodies against 21 hydroxylase**
  Autoimmune adrenalitis
- **CT abdomen**
  Infection, hemorrhage or malignancy
- **CT directed fine needle aspiration**
  Infection or malignancy



TREATMENT

- Primary adrenal insufficiency: daily oral glucocorticoid (hydrocortisone or prednisone) and daily fludrocortisone (mineralocorticoid).

- Secondary adrenal insufficiency: same as in primary adrenal insufficiency, except that mineralocorticoid replacement is not necessary.

Adrenal Crisis

- An acute and severely symptomatic stage of adrenal insufficiency that can include severe hypotension and cardiovascular collapse, abdominal pain (can mimic an acute abdomen), acute renal failure, and death.
- Any stress (e.g., trauma, infection, surgery) can precipitate an adrenal crisis.
- Can be fatal if untreated.
- Treat with IV hydrocortisone, IV fluids (several liters of normal saline with 5% dextrose), and a search for the underlying condition that precipitated the crisis.

20.48 Management of adrenal crisis

Correct volume depletion

- IV saline as required to normalise blood pressure and pulse
- In severe hyponatraemia (< 125 mmol/L) avoid increases of plasma Na > 10 mmol/L/day to prevent pontine demyelination (p. 437)
- Fludrocortisone is not required during the acute phase of treatment

Replace glucocorticoids

- IV hydrocortisone succinate 100 mg stat, and 100 mg 4 times daily for first 12–24 hours
- Continue parenteral hydrocortisone (50–100 mg IM 4 times daily) until patient is well enough for reliable oral therapy

Correct other metabolic abnormalities

- Acute hypoglycaemia: IV 10% glucose
- Hyperkalaemia: should respond to volume replacement but occasionally requires specific therapy (see Box 16.17, p. 443)

Identify and treat underlying cause

- Consider acute precipitant, such as infection
- Consider adrenal or pituitary pathology (see Box 20.45)

PHEOCHROMOCYTOMA

Done by Rahaf ALshorman

- A rare,idiopathic usually benign neuro-endocrine tumors, that arises from the chromaffin cells of the sympathetic nervous system.
- May secrete catecholamines and responsible for 0.1% of HNT.
- Similar to paraganglioma.

Role of 10%

- 10% are extra-adrenal.(e.g. organ of zukerkandl at inferior mesenteric artery roof or bladder wall).
- 10% are malignant.
- 10% occur in children.
- 10% bilateral or multiple.
- 10% are not associated with HTN.
- 10% are familial (in association with one of several familial syndromes MEN 2A,MEN 2B,VON HIPPEL-LINDAU disease).

Clinical findings:

Symptoms are paroxysmal in >50 of patient (during crises)

1- episodic pounding headache, flushing.

2-palpitations, tachycardia, sweating, nausea and vomiting.

3-anxiety, tremor, weight loss.

4-40% have blood pressure elevation only during attaks.

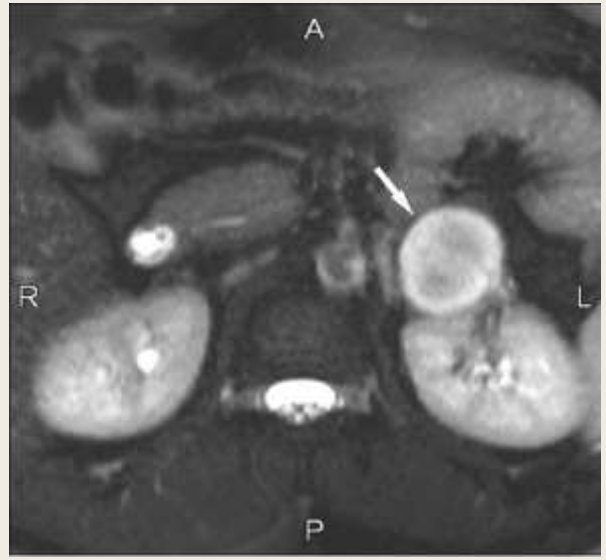
5-hyperglycemia in 1\3 of patients

6-orthostatic hypotension

7-chest, abdomen pain

Diagnosis:

- Established by demonstrating increased in amount of caticholamines or its metabolites (metanephrines, most sensitive and specific) in 24 urine collection.
- Clonidine-suppression test is used when the above test is equivocal. Clonidine should suppress epinephrine levels. Failure to suppress is highly suggestive of pheochromocytoma.
- The tumor is confirmed by CT or MRI scan. MIBG (metaiodobenzylguanidine) screening is used when pheochromocytoma is not found on CT with positive biochemical tests.



- There is ahigh false positive rate because concentrations are high in stressed patients (during acute illness, sever pain, smoking).
- Smoking can increase plasma free metanephrines. Thus, patient must not smoking at least 4 hours before the test.
- Genetic testing in people with a family history of pheochromocytoma or paraganglioma.

Treatment:

- The most important step is controlling blood pressure by using alpha-adrenergic blocking agents (phentolamine, phenoxybenzamine).
- Pre-operative beta-blocker should be added to prevent hypertension crises.
- **No other hypertensive drugs should be used before adequate control of blood pressure is accomplished with alpha blockade.**
- Curative surgical removal of pheochromocytoma is only preformed when after stabilization of blood pressure.
- Post operative hypotension might occur and require volume expansion and occasionally norepinephrine.

Congenital adrenal hyperplasia

Done by Yousef khreasat

Congenital adrenal hyperplasia

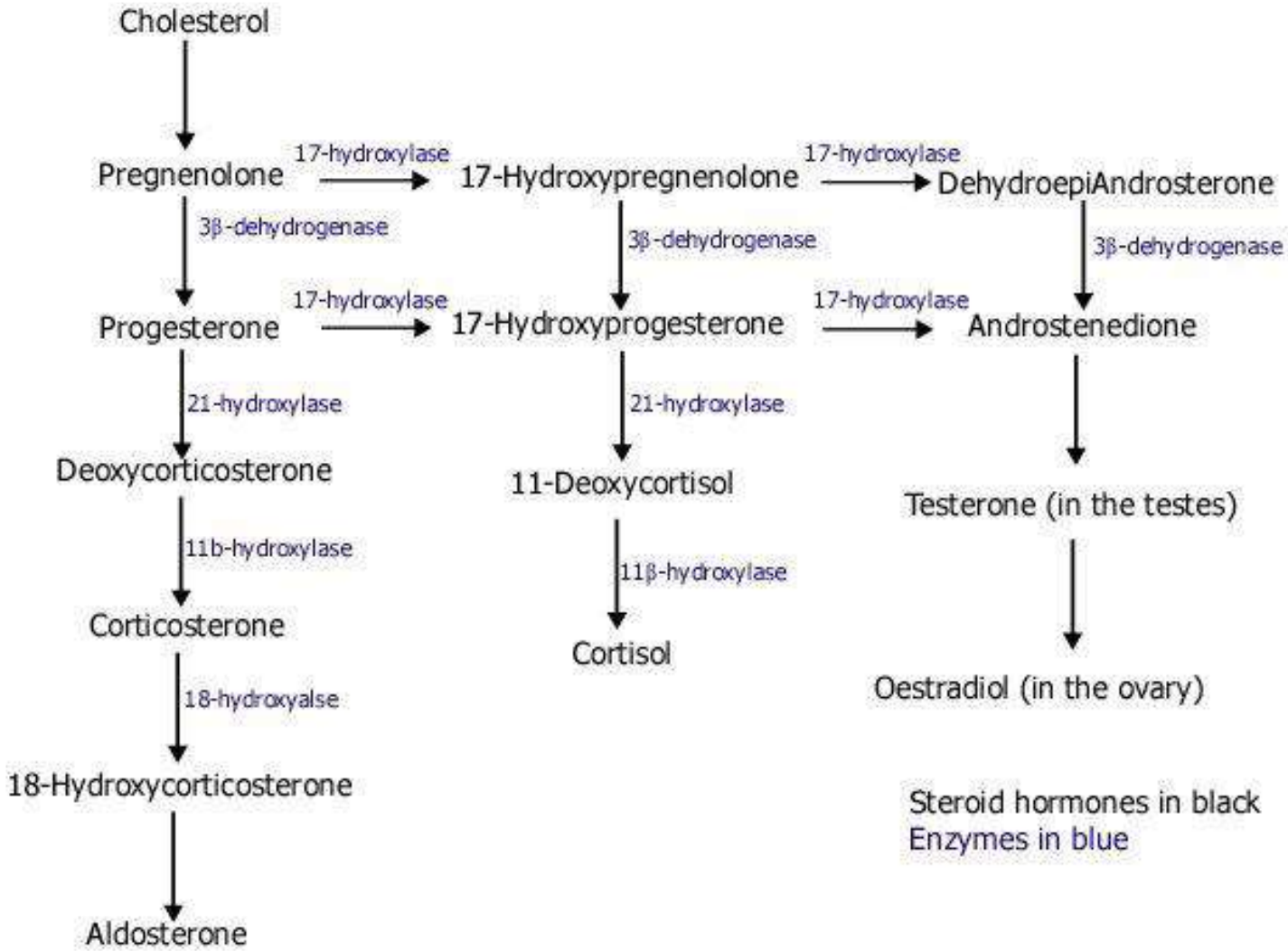
- CAH is the most common adrenal disorder of infancy and childhood.
- Autosomal recessive disease
- Inherited defects in enzymes of the cortisol biosynthetic pathway result in insufficiency of hormones downstream of the block, with impaired negative feedback and increased ACTH, that results in adrenal hyperplasia and increase in androgen production.

Common Enzymatic defects:

- 95% of enzymatic defects cases have C-21 hydroxylase deficiency , which is associated with reduction in aldosterone in 1/3 of patients and increase in androgen. (Adrenal virilization)

- C-11 hydroxylase deficiency; the mineralocorticoid manifestations can be **Biphasic** ! In early infancy, despite having excessive mineralocorticoid hormones, patients presents with relative salt-wasting, this is because some infants have inefficient salt conservation as well as immature aldosterone production. Later in life, there is better ability to hold onto salt. (develops typical C-11 deficiency sym.)

- C-17 hydroxylase deficiency resulting increased production of 11-deoxycorticosterone. Characterized by hypogonadism, hypokalemia, and hypertension.


Cholesterol
Pregnenolone
17-hydroxylase
17-Hydroxypregnenolone
17-hydroxylase
DehydroepiAndrosterone
3β-dehydrogenase
3β-dehydrogenase
3β-dehydrogenase
Progesterone
17-hydroxylase
17-Hydroxyprogesterone
17-hydroxylase
Androstenedione
21-hydroxylase
21-hydroxylase
Deoxycorticosterone
11-Deoxycortisol
Testerone (in the testes)
11b-hydroxylase
11β-hydroxylase
Corticosterone
Cortisol
Oestradiol (in the ovary)
18-hydroxyalse
18-Hydroxycorticosterone
Aldosterone
Steroid hormones in black
Enzymes in blue

Clinical Findings:

Virilization features:

- A. Female infants: ambiguous external genitalia.
- B. Male infants: macrogenitosomia
- C. Male postnatally: precocious puberty

Salt wasting form (very severe):

- A. Emesis, dehydration, hypotension, shock.
- B. Hyponatremia and hyperkalemia due to lack of aldosterone.
- C. Hypoglycemia due to lack of cortisol

Diagnosis

- CAH should be considered in all infants exhibiting failure to thrive, especially those with episode of acute adrenal insufficiency, salt wasting, or hypertension.

- Increased serum 17 OH-progesterone levels in 21-hydroxylase deficiency, it can be routinely measured in a heel prick sample from all infants in the first week of life leading to early diagnosis.

- In siblings of affected children antenatal genetic diagnosis can be made.

Management:

1- Medically: Use cortisol and mineralocorticoid; this shuts off excess ACTH secretion.

2- Surgically: Correction of female genital abnormalities.

References :

- STEP-UP TO MEDICINE
- Davidson’s Principles and Practice of Medicine
- Up-to-date
- Board and beyond videos
- Pathoma

Thank you