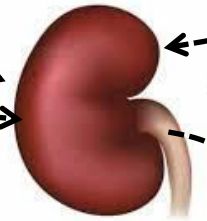
Regulation of aldosterone secretion

1)↑ Blood K^+

↓Blood volume
↓ and/or pressure

3) ↓Blood Na^+

Stimulation of β receptors



Angiotensinogen

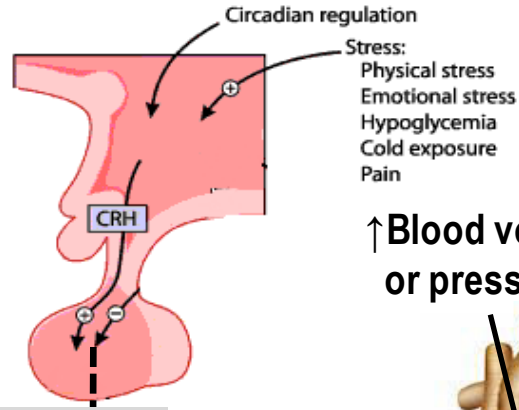
↓ Renin

Angiotensin I

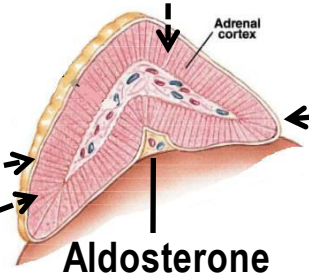
↓ ACE

2) Angiotensin II

Direct stimulatory effect

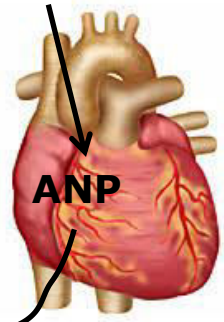


4) ACTH

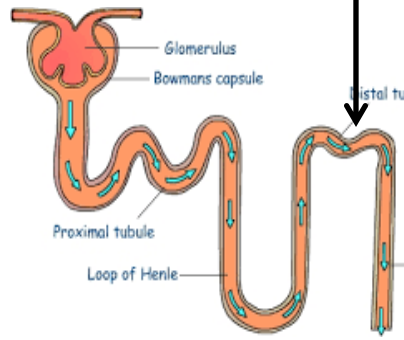


Aldosterone

↑Blood volume or pressure



Direct inhibitory effect



↑Na^+ & H_2O reabsorption
↑K^+ excretion

↑Blood volume & pressure

Regulation of aldosterone secretion

- **ECF K^+** (1meq/L ↑ in K^+ in ECF → ↑ aldosterone secretion)
  - ↑Secretion (depolarization of zona glomerulosa cells)
  - ↑Synthesis
- **Renin-angiotensin aldosterone system:** renin secretion increas by:
  - ↓ Renal blood flow (hemorrhage, renal artery stenosis)
  - ↓ Na^+ in ECF
  - Sympathetic stimulation (β receptors)
- **Quantity of body sodium**
  - Macula densa: (↓Na^+ → macula densa→ ↑renin)
  - Renin angiotensin system: (↓Na^+ → ↓ECF &↓CO → ↑renin)
- **ACTH**
  - Doesn't affect basal level
  - ↑Aldosterone in stress

Disorders of adrenocortical secretion

Hyposecretion	Hypersecretion
1) Chronic adrenal insufficiency ▪ Primary(Addison's disease) ▪ Secondary ▪ Tertiary	1) Hyperaldosteronism ▪ Primary aldosteronism ▪ Secondary aldosteronism ▪ Glucocorticoid remediable aldosteronism
2) Acute (Addisonian crisis)	2) Cushing syndrome ▪ ACTH dependent ▪ ACTH independent

Primary aldosteronism (Conn's syndrome)

- **Cause:** Tumor or hyperplasia of zona glomerulosa
- **Effects:**

1) Sodium retention → hypertension
   - No or slight edema due to aldosterone escape (↑ANP)

2) Hypokalemia
   - Muscle weakness (hyperpolarization)
   - ↓ Glucose tolerance (↓ insulin secretion)

3) ↓ H^+ → metabolic alkalosis

Secondary aldosteronism

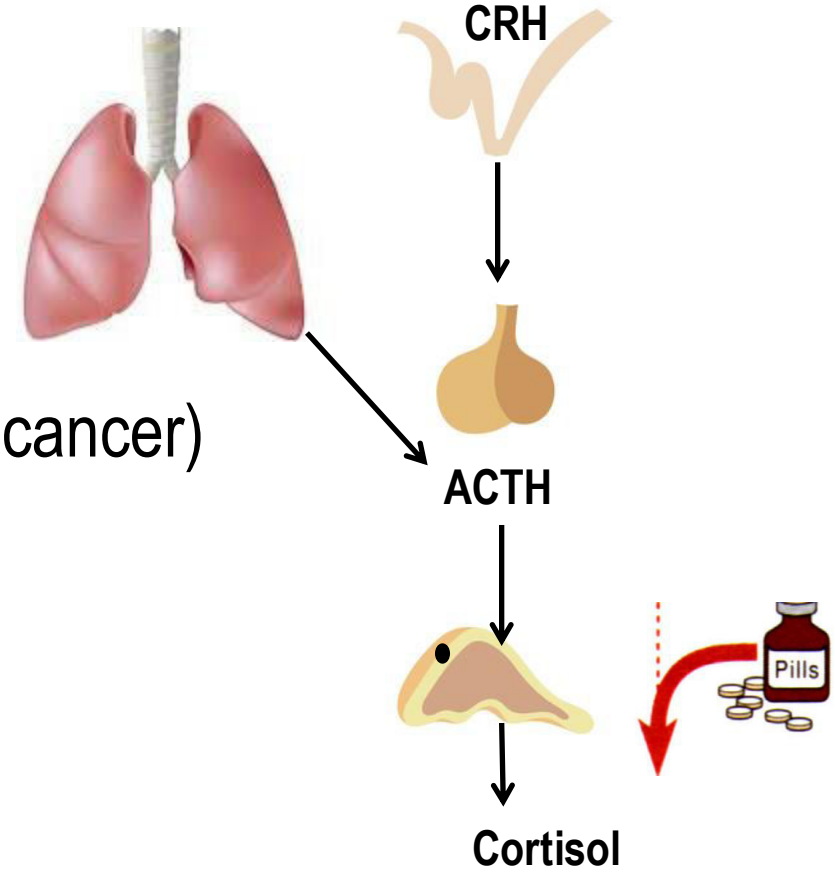
- **Cause**
  - Kidney (nephrosis)→ ↑renin
  - Heart (failure)→ renal ischemia → ↑renin
  - Liver (cirrhosis) → ↑renin (↓inactivation of renin)

Effects: Same as Conn's syndrome but massive edema

Glucocorticoid remediable aldosteronism

- **Cause:**
  - Autosomal dominant
  - Zona glomerulosa extremely sensitive to ACTH
- **Treatment:**
  - Glucocorticoid $\rightarrow\downarrow$ ACTH

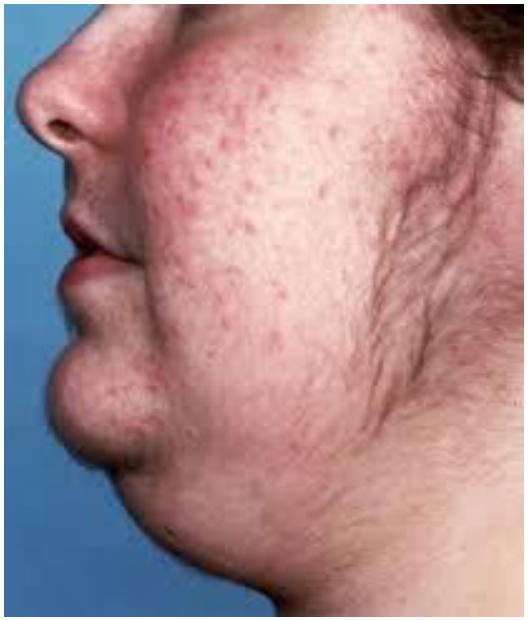
Cushing's syndrome



- **Cause**
  1) ACTH dependent
     - Hypothalamus (↑CRH)
     - Pituitary (↑ACTH)
     - Ectopic ACTH secretion (lung cancer)
  2) ACTH independent
     - Adrenal adenoma
     - Iatrogenic (drug)
- **Effects:**
  1) Glucocorticoid effect
     - CHO →Hyperglycemia
     - Fat → moon face, truncal obesity, buffalo hump
     - Protein → thin skin, purpule striae, muscle weakness, osteoporosis, ↓ immunity
     - CNS → insomnia, euphoria, ↑ appetite

2) Mineralocorticoid effect

- ↑Na^+ →Hypertension
- ↓K^+ → hypokalemia

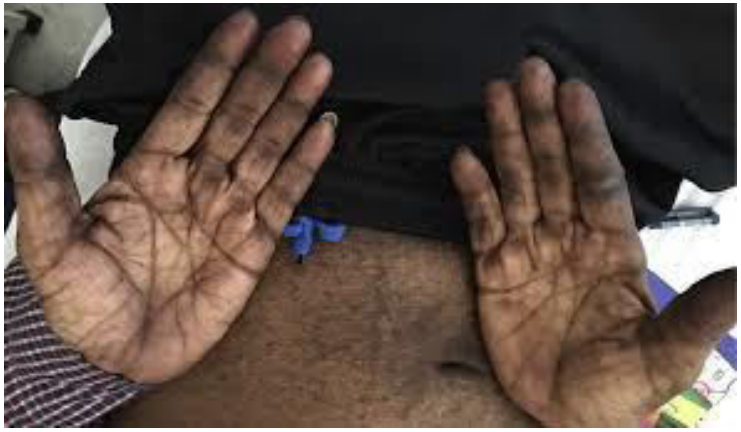


3)↑Androgens

- Masculinizing effect
- Hirsutism (face) & acne

4)↑ACTH

- Pigmentation (ACTH has MSH activity)



Hyposecretion

- **Cause**
  1) Primary adrenal insufficiency (autoimmune, TB, tumor) **(sever)**
  2) Secondary adrenal insufficiency (pituitary) **most common** **(mild)**
  3) Tertiary adrenal insufficiency (hypothalamus) **(mild)**

1) Addison's disease (primary adrenal insufficiency)

- **Effects:**

1) ↓ Mineralocorticoid deficiency
   - ↓Na^+ → hypotension, eventually shock
   - Hyperkalemia and acidosis (metabolic)
2) Glucocorticoid deficiency
   - CHO → hypoglycemia (fasting causing fatal hypoglycemia)
   - Fat & protein →↓ energy mobilization (↓ FA and AA)→ sever muscle weakness, ↓resistance to stress (stress → death)
3) ↑ ACTH → pigmentation (gum, skin crease)

2) Secondary adrenal insufficiency (pituitary: ↓ACTH)

3) Tertiary adrenal insufficiency (hypothalamus: ↓ CRH)

⊙ **Effects of secondary and tertiary adrenal insufficiency**

- Similar to primary adrenal insufficiency but milder & no pigmentation
  - ☞ Milder: no mineralocorticoid deficiency
  - ☞ No pigmentation: low ACTH

Addisonian crisis

1) Caused by different stresses in Addison's disease patients → shock and death
2) Exogenous glucocorticoids → ↓ ACTH → Adrenal cortex atrophy → abrupt stoppage of glucocorticoid → shock