



Pharmacology of corticosteroids I

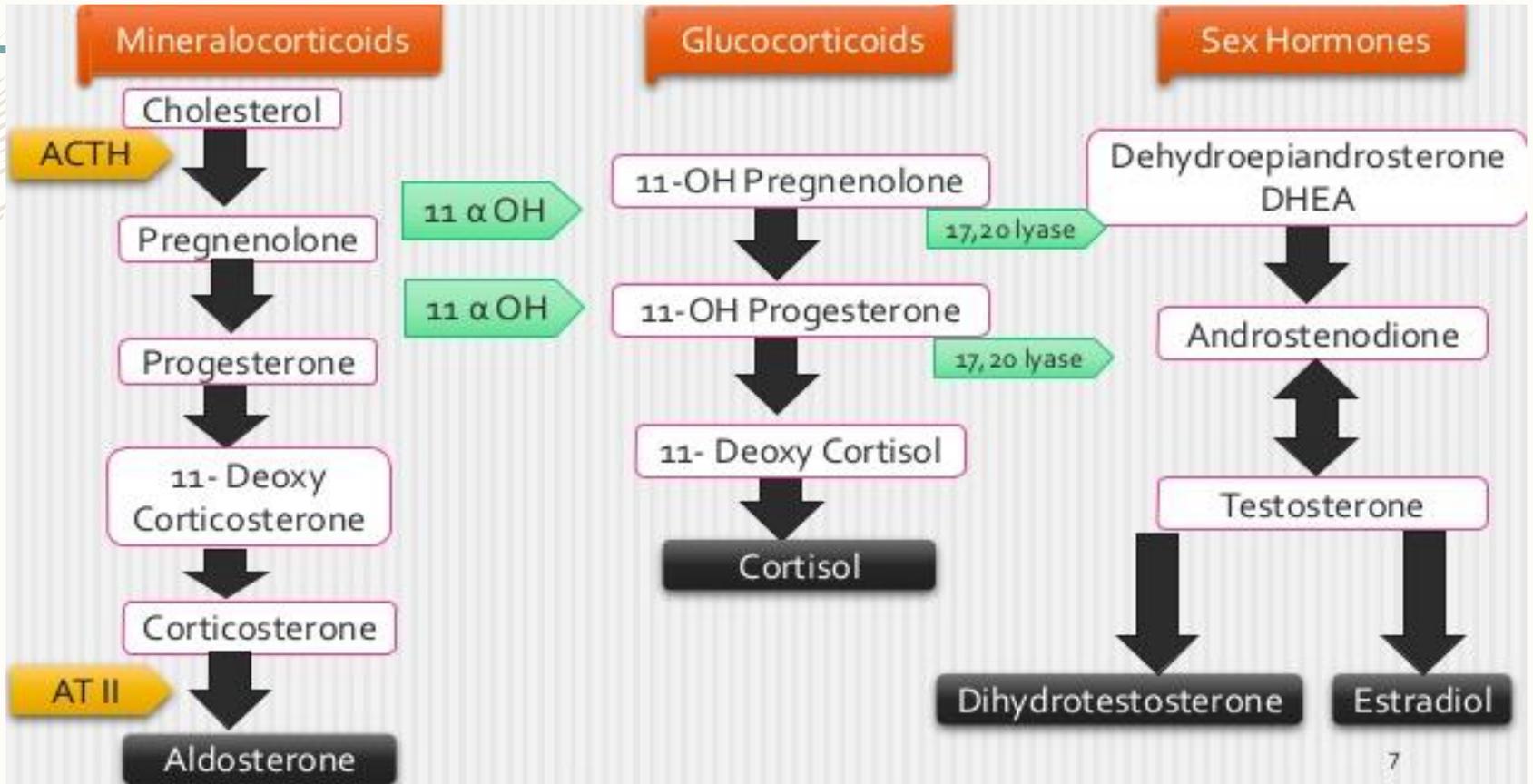
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Synthesis of corticosteroids



Corticosteroids



- Corticosteroids are steroid hormones produced by the adrenal cortex. They consist of two groups:
- 1- Glucocorticoids
- 2- Mineralocorticoids
- 3- Sex hormones

1- Glucocorticoids

They have important effects on intermediary metabolism, catabolism, immune responses, growth & inflammation.

2- Mineralocorticoids

They have salt-retaining activity which regulate Na & K reabsorption in the collecting tubules of the kidney.

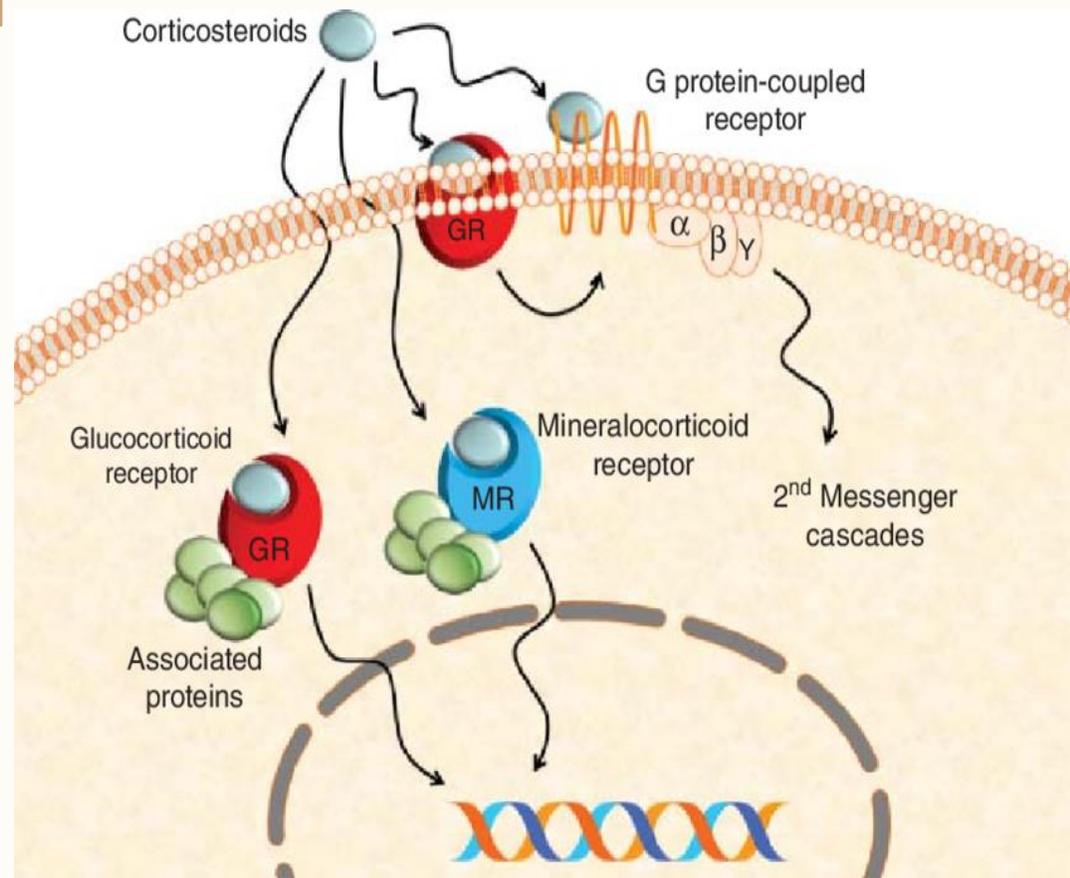
Mechanism of action of corticosteroids

Corticosteroid is present in the blood bound to the corticosteroid binding globulin (CBG) and enters the cell as the free molecule.

The intracellular receptor is bound to the stabilizing proteins. When the complex binds a molecule of steroid, the proteins are **released**.

The resulting mRNA is coding **production of protein that brings about the final hormone response.**

The Steroid – receptor complex enters the nucleus and binds to the **corticosteroid response element (CRE)** on the gene, and regulates gene transcription.



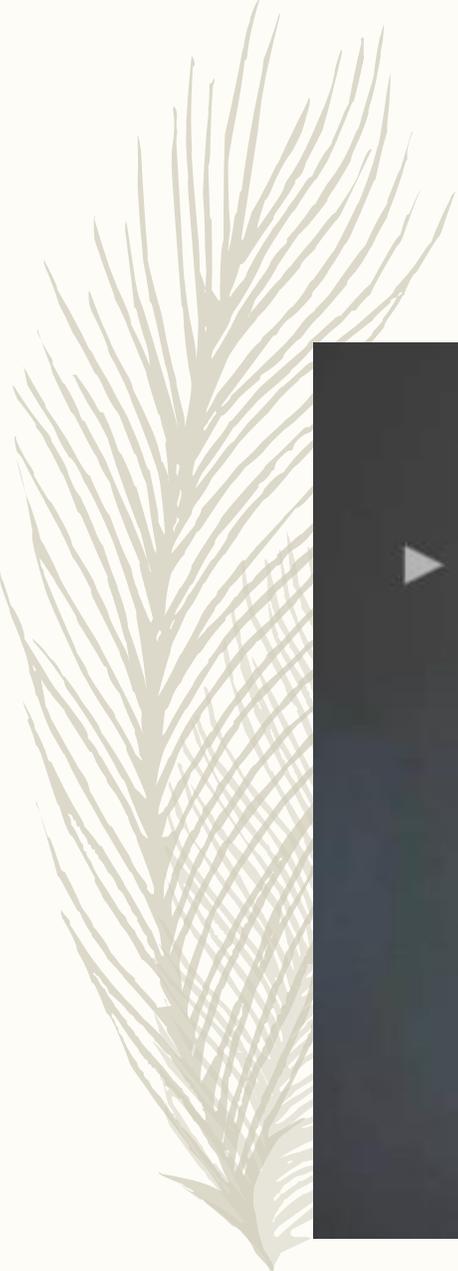
Mineralo-corticoids

- ▶ Mineralo-corticoids are the corticosteroids that act on the minerals (electrolytes), particularly **sodium and potassium**.
- ▶ Mineralocorticoids are:
 1. **Aldosterone**
 2. **11-deoxycorticosterone**



- ▶ **Source Of Secretion**

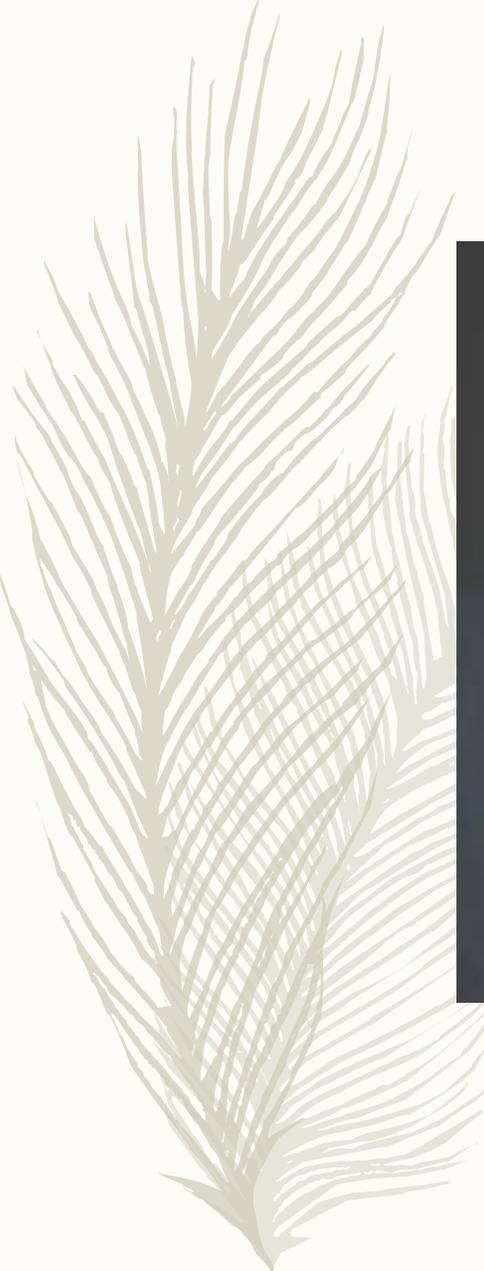
- ▶ Secreted by **zona glomerulosa** of adrenal cortex.



– Half life: 20 min.

▶ **Functions Of Mineralocorticoids**

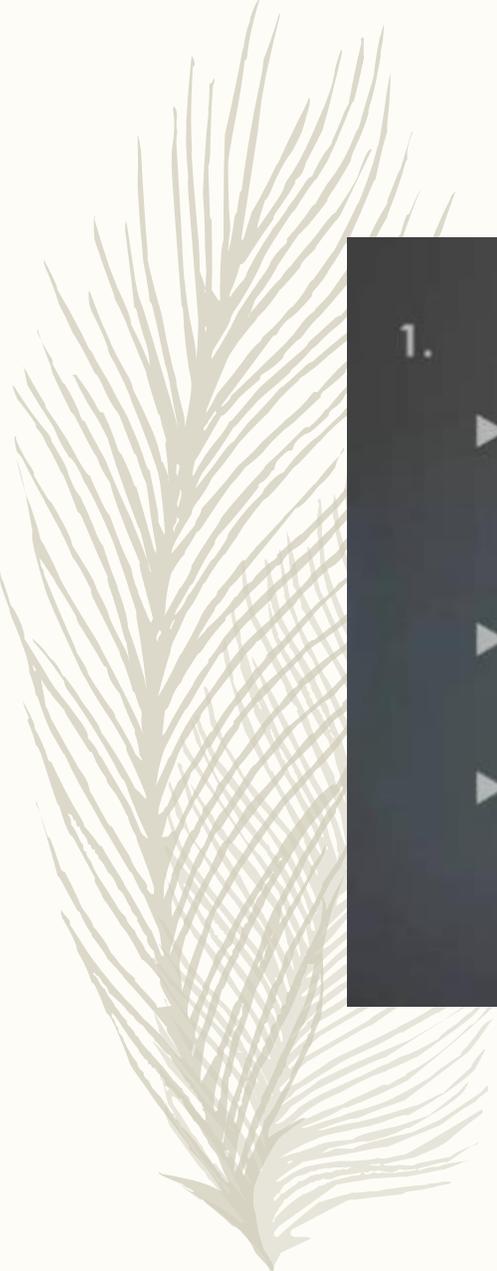
- ▶ **90%** of mineralocorticoid activity is provided by aldosterone
- ▶ It is very essential for life and it maintains the osmolarity and volume of ECF.
- ▶ It is usually called life-saving hormone because, its absence causes death within 3 days to 2 weeks.

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- ▶ Aldosterone has three important functions.
 - ▶ It increases:
 1. **Reabsorption of sodium from renal tubules**
 2. **Excretion of potassium through renal tubules**
 3. **Secretion of hydrogen into renal tubules.**



► **Functions of Aldosterone:**

1. **On Sodium Ions**
2. **On Extracellular Fluid Volume**
3. **On Blood Pressure**
4. **On Potassium Ions**
5. **On Hydrogen Ion Concentration**
6. **On Sweat Glands and Salivary Glands**
7. **On Intestine**



1. On Sodium Ions

- ▶ Acts on the distal convoluted tubule and the collecting duct and increases the reabsorption of sodium.
- ▶ During hypersecretion of aldosterone, the loss of sodium through urine is only few milligram per day.
- ▶ But during hyposecretion of aldosterone, the loss of sodium through urine increases (**hypernatruria**) up to about 20 g/day.

2. **On Extracellular Fluid Volume**

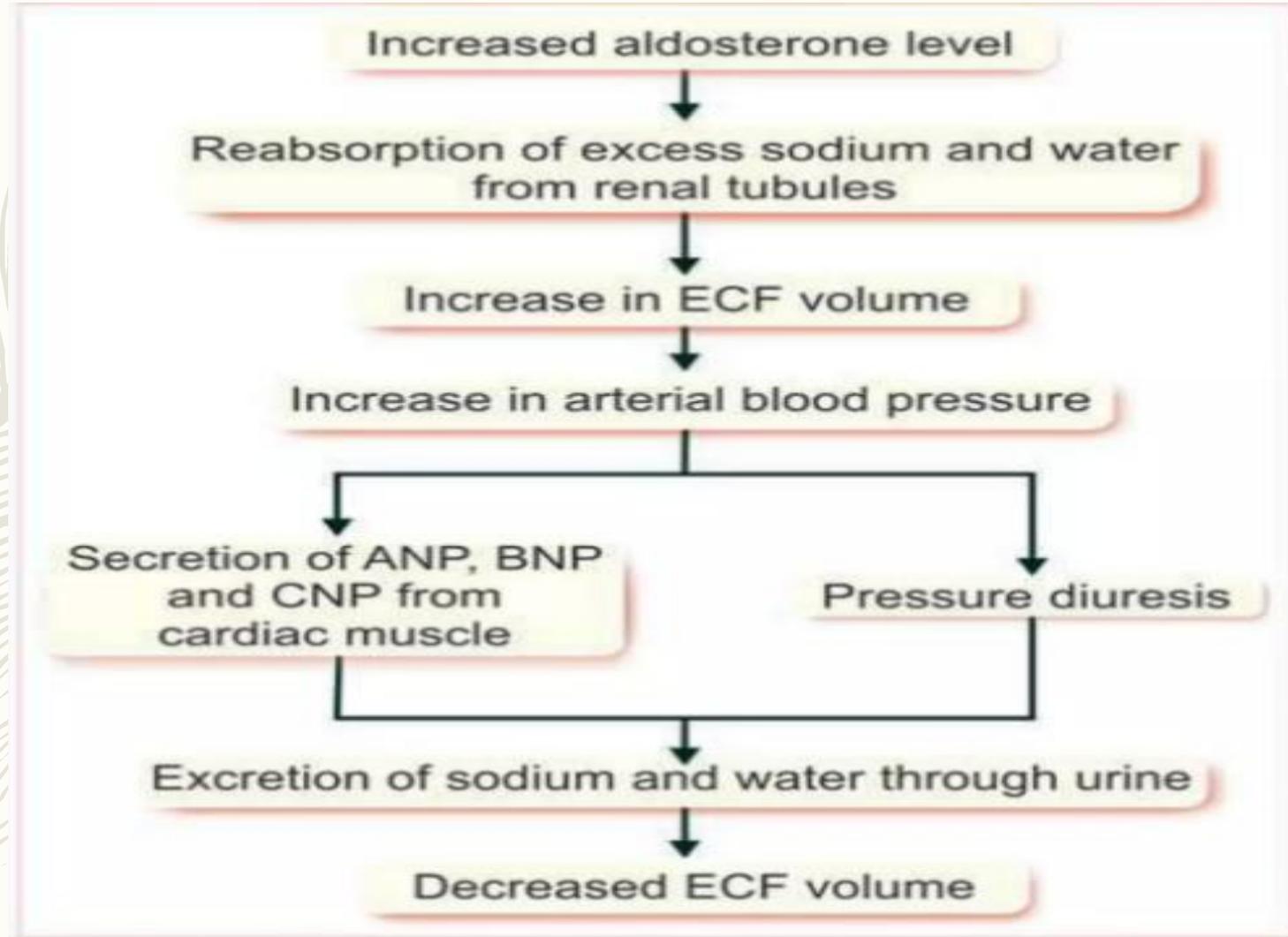
- ▶ When sodium ions are reabsorbed from the renal tubules, simultaneously water is also reabsorbed.
- ▶ Water reabsorption is almost equal to sodium reabsorption; so the net result is the increase in ECF volume.
- ▶ Even though aldosterone increases the sodium reabsorption from renal tubules, the concentration of sodium in the body does not increase very much because water is also reabsorbed simultaneously.

3. **On Blood Pressure**

- ▶ Increase in ECF volume and the blood volume finally leads to increase in blood pressure.



Aldosterone escape phenomenon



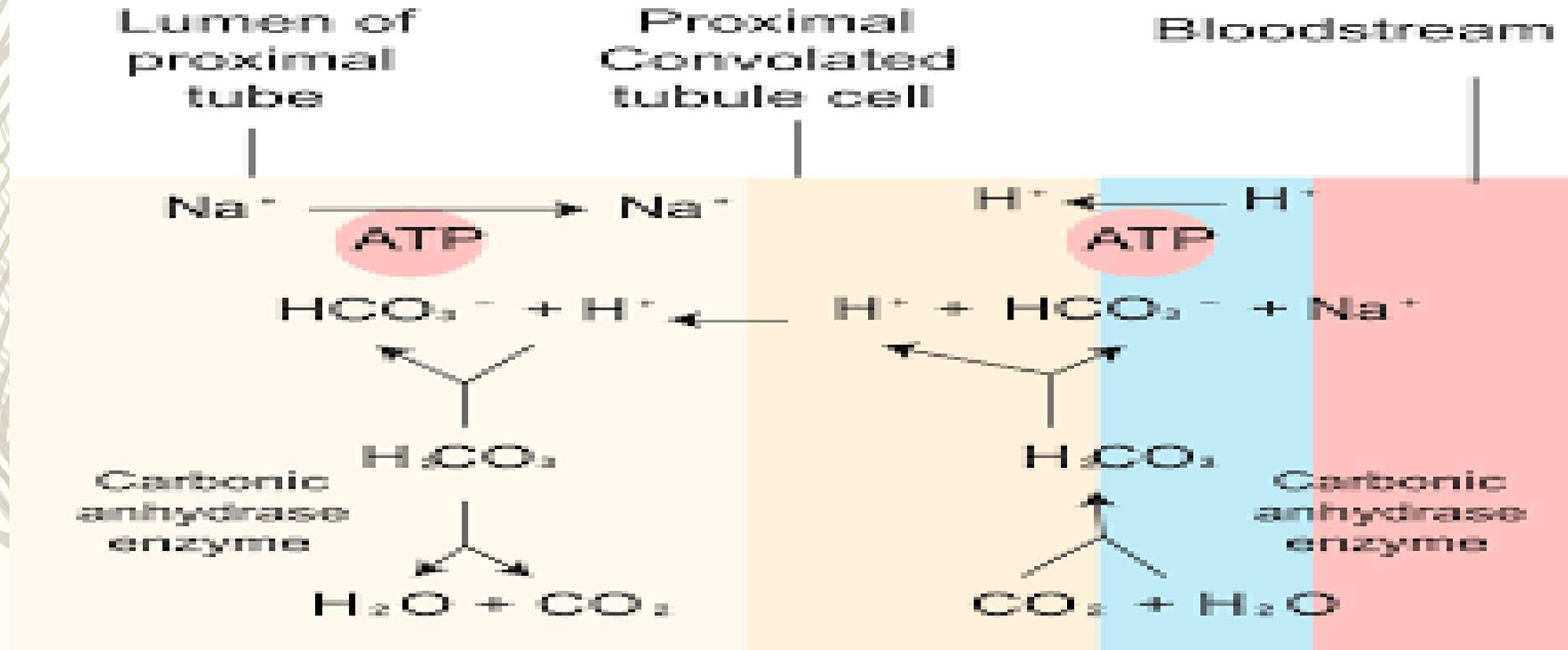
4. **On Potassium Ions**

- ▶ It increases the potassium excretion through the renal tubules.
- ▶ When aldosterone is deficient, the potassium ion concentration in ECF increases leading to hyperkalemia.
- ▶ Hyperkalemia results in serious cardiac toxicity, with weak contractions of heart and development of arrhythmia.
- ▶ In very severe conditions, it may cause cardiac death.

- ▶ When aldosterone secretion increases, it leads to hypokalemia and muscular weakness.

5. On Hydrogen Ion Concentration

- ▶ While increasing the sodium reabsorption from renal tubules, aldosterone causes tubular secretion of hydrogen ions.
- ▶ To some extent, secretion of hydrogen ions is in exchange for sodium ions.
- ▶ It obviously reduces the hydrogen ion concentration in the ECF.





6. **On Sweat Glands and Salivary Glands**

- ▶ It has similar effect on sweat glands and salivary glands as it shows on renal tubules.
- ▶ Sodium is reabsorbed from sweat glands under the influence of aldosterone, thus the loss of sodium from the body is prevented.
- ▶ Same effect is shown on saliva also.
- ▶ Thus, aldosterone helps in the conservation of sodium in the body.



7. **On Intestine**

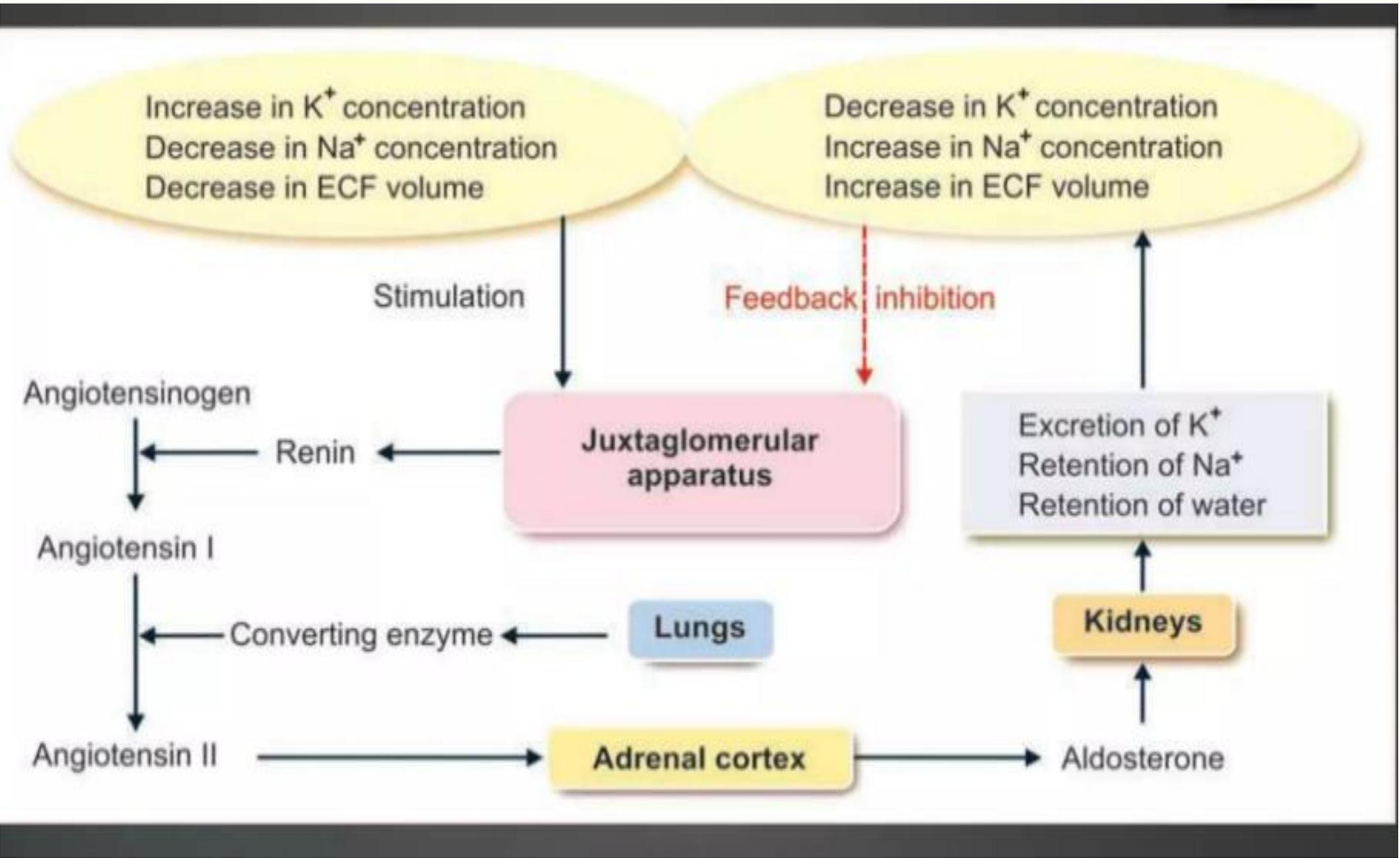
- ▶ It increases sodium absorption from the intestine, especially from colon and prevents loss of sodium through feces.
- ▶ Aldosterone deficiency leads to diarrhea, with loss of sodium and water.

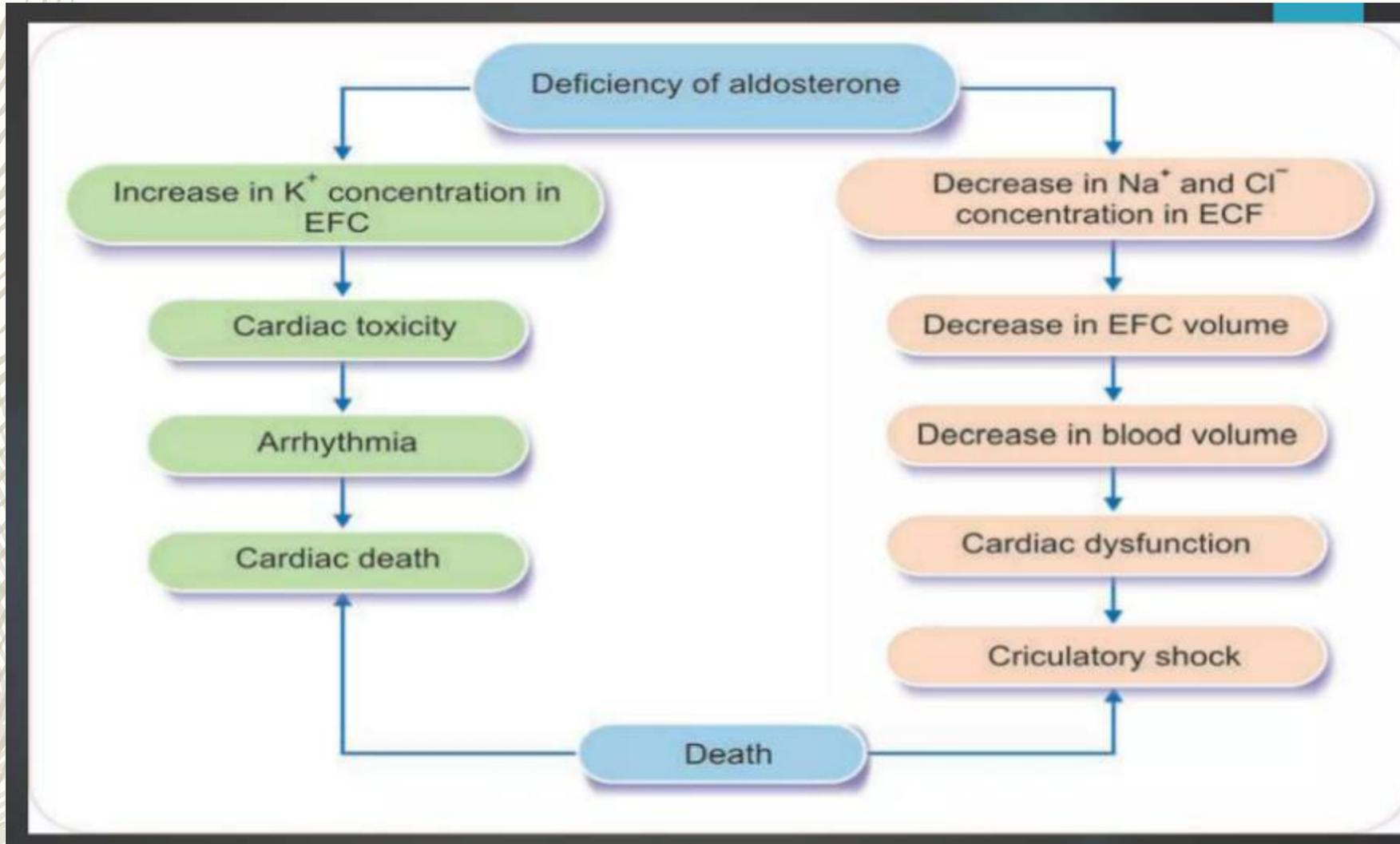


▶ Regulation Of Secretion

▶ Regulated by four important factors which are given below in the order of their potency:

1. Increase in potassium ion (K^+) concentration in ECF
2. Decrease in sodium ion (Na^+) concentration in ECF
3. Decrease in ECF volume
4. Adrenocorticotrophic hormone (ACTH).





Aldosterone (e.g. Fludrocortisone)

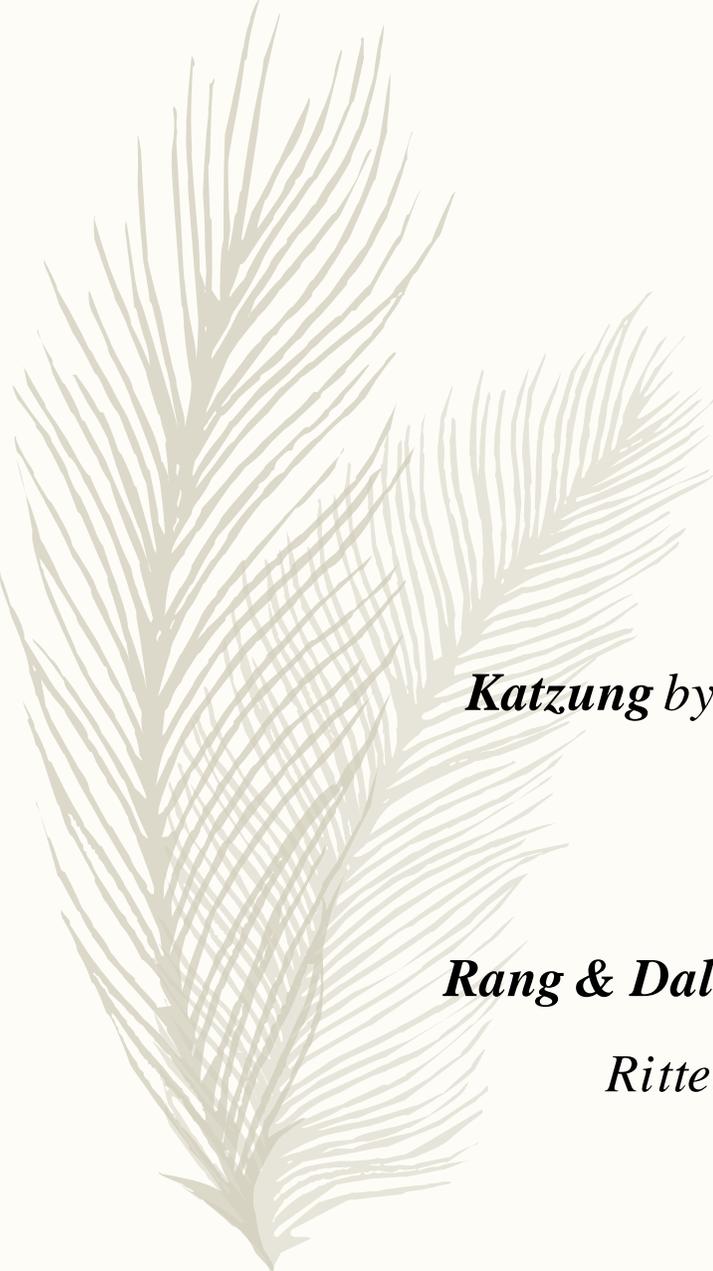
Notes

- Aldosterone has short half life & little glucocorticoid activity

- **Fludrocortisone**: it is a mineralocorticoid has a long duration of action and significant glucocorticoid activity compared to aldosterone

Uses

Fludrocortisone is favored for replacement therapy after adrenalectomy & in other conditions in which mineralocorticoid therapy is needed. **And can be given to hypotensive people to maintain normal Na and water levels.**



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THANK YOU