Adrenal cortex (continue)

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Aldosterone

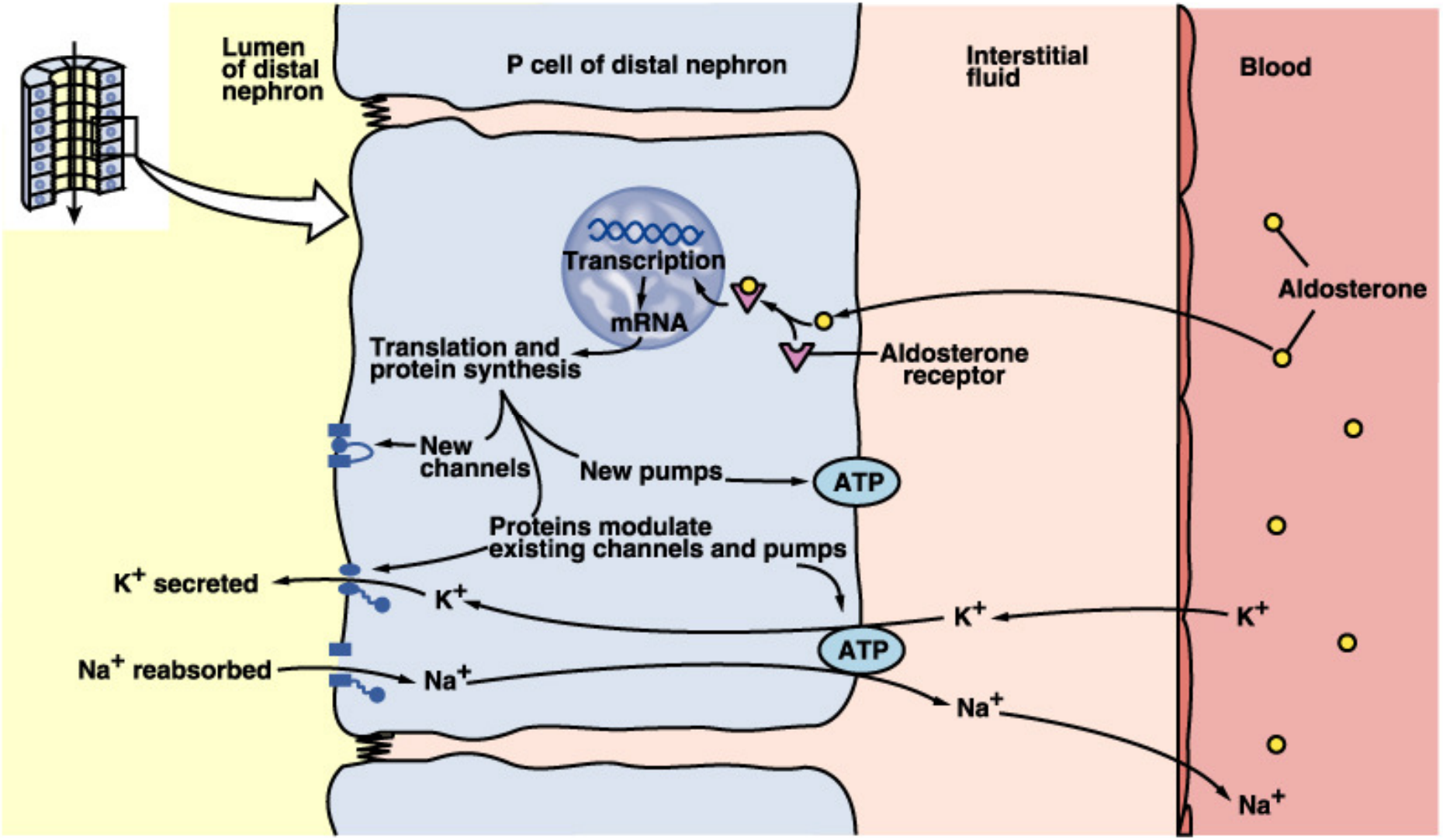
- a steroid hormone

- essential for life (acute)

- responsible for regulating Na^+ reabsorption in the **distal tubule** and the **collecting duct**

- target cells are called "**principal (P) cell**"

- stimulates synthesis of **more Na+/K+ ATPase pumps**


Lumen of distal nephron
P cell of distal nephron
Interstitial fluid
Blood
Transcription
mRNA
Translation and protein synthesis
Aldosterone receptor
Aldosterone
New channels
New pumps
ATP
Proteins modulate existing channels and pumps
K+ secreted
K+
K+
K+
ATP
Na+ reabsorbed
Na+
Na+
Na+

Functions of Aldosterone

- Aldosterone plays a major role in mineral and water balance:
  -increases sodium reabsorption in distal tubules and collecting ducts of the kidney

  -as **sodium is actively reabsorbed**, also get **passive absorption of water by osmosis**

  -also get excretion of **potassium (active and passive)** and **protons(H+)**
  - result: **increased retention of sodium and of water and excretion of K+ and H+**

- Aldosterone also increases sodium reabsorption in sweat glands.

Regulation of Aldosterone Release

- direct stimulators of release

  - increased extracellular K^+
  - decreased osmolarity

- indirect stimulators of release through renin angiotensin system (RAS)

  - decreased blood pressure
  - decreased renal blood flow

Mechanism of Aldosterone Action

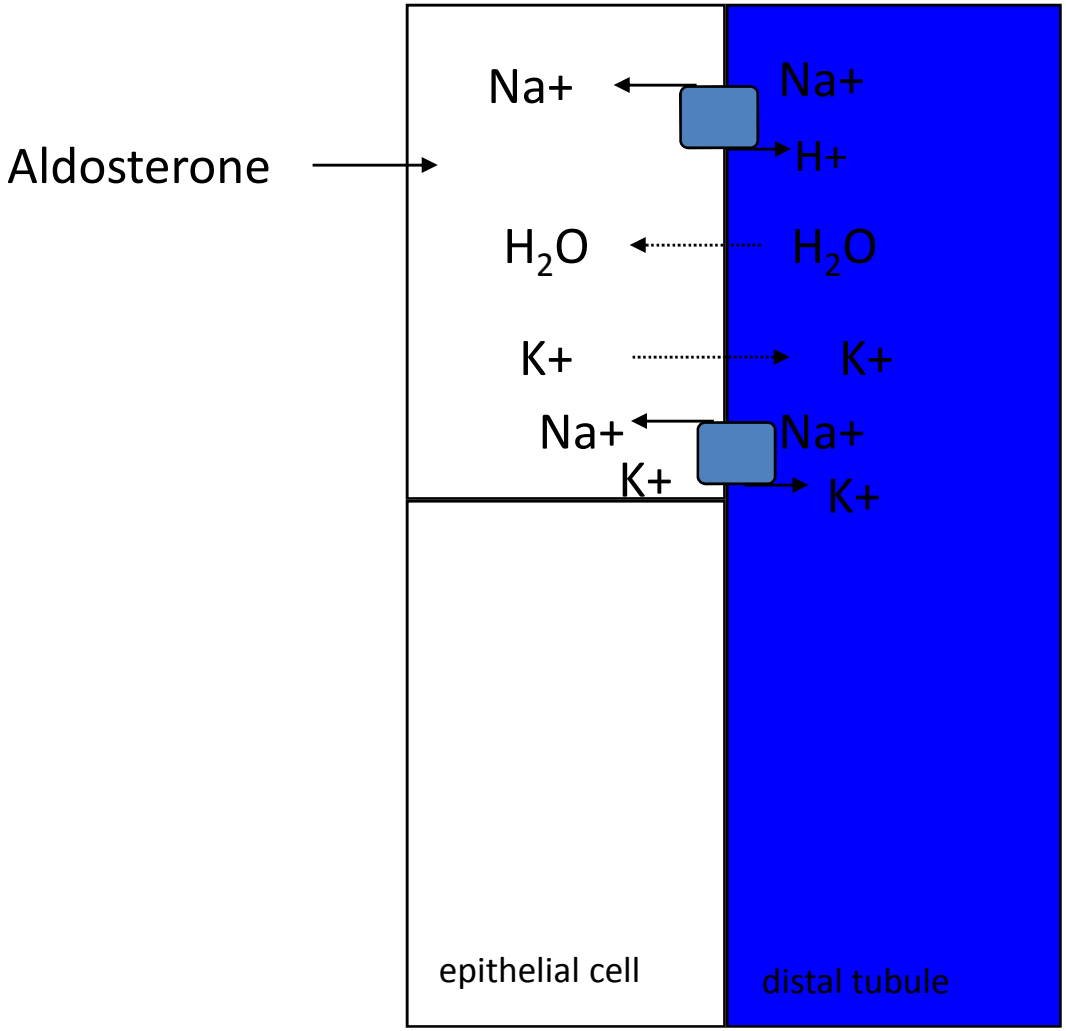
- Aldosterone acts through the **intracellular mineralocorticoid receptor.**
- Binding of hormone to the receptor results in **expression of gene** products that influence the rate of sodium transport from urine back into the kidney.
- **These target genes result in:**

  - increased availability of ATP to drive active transport

  - increased synthesis of sodium transporters

  - increased permeability of the membrane to sodium, so that sodium is reabsorbed by diffusion

Influence of Aldosterone on Sodium and Water Reabsorption, and Potassium Excretion



Regulation of Aldosterone Production

- The main stimulator of aldosterone production is **angiotensin II**, not ACTH.

- ACTH *does* have a trophic (stimulatory) effect on the zona glomerulosa, preventing atrophy.

The Renin-Angiotensin System

- **The juxtaglomerular cells (JG)** of the kidney **release renin** in response to:
- decreased blood pressure,
- decreased sodium levels,
- or sympathetic stimulation.

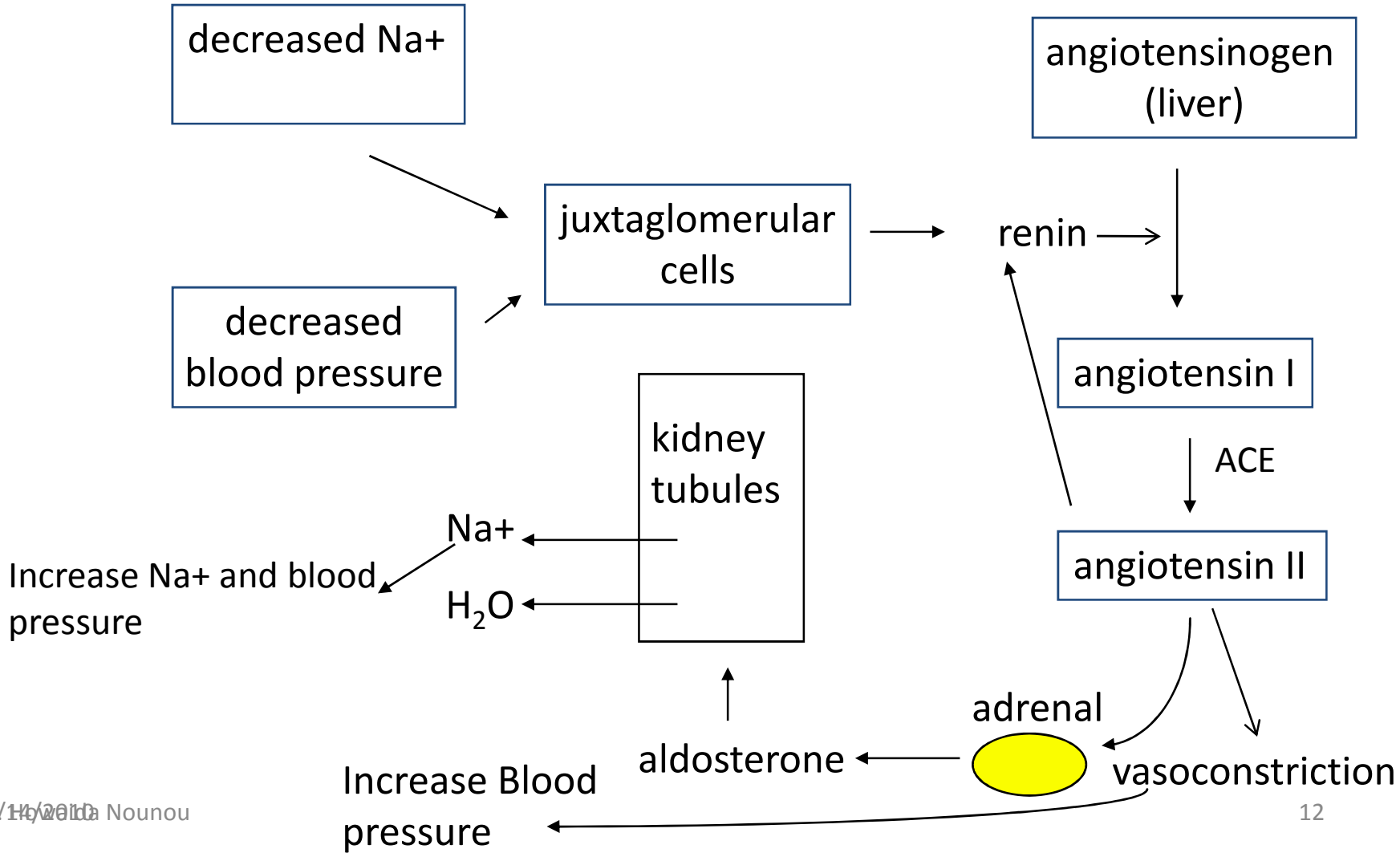
Factors that affect renin release

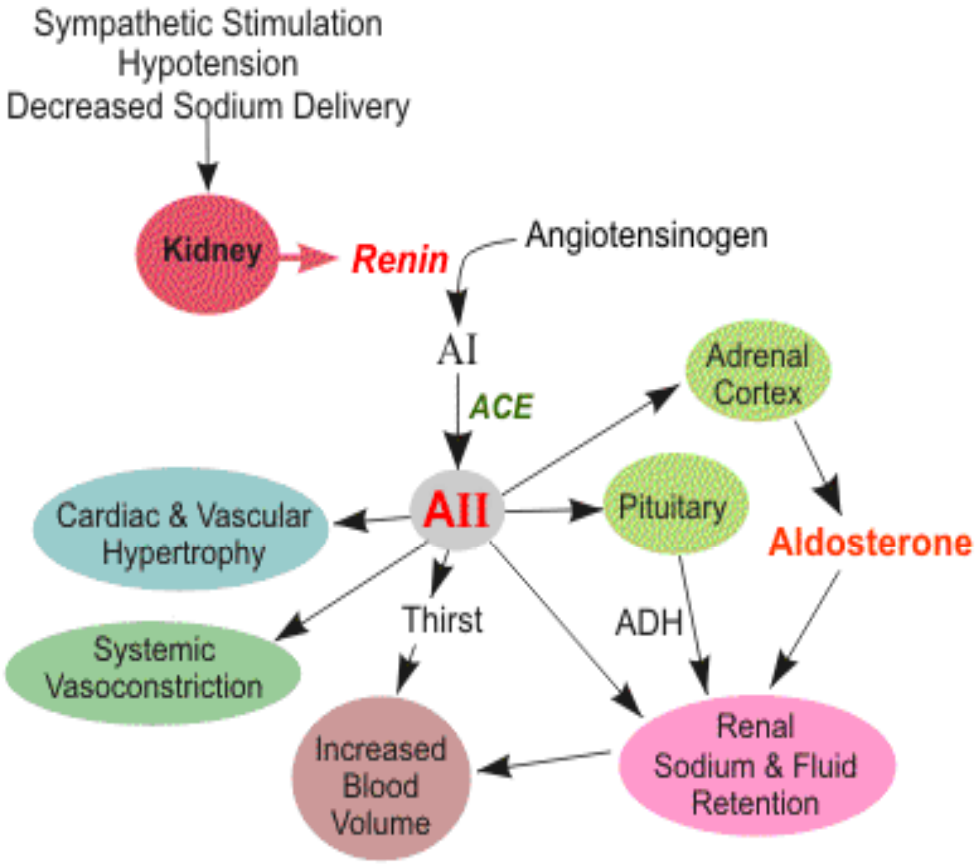
Stimulators	inhibitors
Decreased blood pressure	Increased blood pressure
Change from supine to erect posture (decreased blood pressure)	Change from erect to supine posture (Increased blood pressure)
Salt depletion (decreased sodium levels)	Salt loading
Prostaglandins	Prostaglandin inhibitors
sympathetic stimulation	Potassium
	Angiotensin II

The Renin-Angiotensin System

- **Renin** converts **angiotensinogen** (from the liver) into **angiotensin I (Ang I)**
- **Angiotensin I** (Ang I)is converted to **angiotensin II** (Ang II) in a number of places in the body by **angiotensin converting enzyme(ACE)**. (ie, lungs, endothelial cells, placenta)
- **Angiotensin II (Ang II)acts** on adrenal cells to **stimulate aldosterone release**, and is itself a **vasoconstrictor** (increases blood pressure)

The Renin-Angiotensin System




Sympathetic Stimulation
Hypotension
Decreased Sodium Delivery
Kidney
Renin
Angiotensinogen
AI
ACE
Adrenal Cortex
Cardiac & Vascular Hypertrophy
AII
Pituitary
Aldosterone
Thirst
ADH
Systemic Vasoconstriction
Increased Blood Volume
Renal Sodium & Fluid Retention

Transport and Metabolism of Aldosterone

- There is no specific aldosterone carrier protein
- As a result, most aldosterone is biologically available.
- The circulating half life of aldosterone is very short.
- Aldosterone is metabolized in the liver, conjugated with glucoronide and excreted in the urine

Role of Atrial Natriuretic Factor (ANF)

- **ANF** is produced by atria of the heart, and production is increased **by increased blood pressure**.
- ANF **inhibits aldosterone production** (to inhibit resorption of water) (blocks actions of angiotensin II).

Net result: decreased water volume, decreased blood pressure.

Androgenic hormones

- **DHEA – dehydroepiandrosterone**
- **androstendione**
- **testosterone**
  - testosterone is a precursor of estradiol
- **effects:**
  - anabolic
  - development of the secondary sexual signs
  - distribution of hair
  - voice
  - sexual behavior

Adrenal Androgens

- Produced in the **zona reticularis**.
- **Production is stimulated by ACTH.**
- Main product: **androstenedione**
- **In females**, adrenal androgens may play roles in

  - development of axillary and pubic hair

  - sexual behavior

(**In men**, androgens from the testis serve these functions)

- Adrenal androgens may also be peripherally converted (in adipose tissue, for example) into testosterone and estrone.

Adrenal Cortex Dysfunctions

Hypoadrenalism – **Addison's Disease**(primary adrenal insufficiency) atrophy of adrenal cortex.

- adrenal cortex produces inadequate amounts of hormones
- caused by autoimmunity against cortices 80%
- also caused by tuberculosis, drugs, cancer
- plasma **sodium decreases and may lead to circulatory collapse**

Secondary adrenal insufficiency:

Due **deficiency** of **ACTH**.

Similar metabolic syndrome to the primary without hyper pigmentation.

Mineralocorticoid Deficiency

- **Lack of aldosterone**:
  - Loss of sodium, chloride and water in urine , hypotension.
  - Decrease ECF volume
  - Hyperkalemia (increased potassium levels in blood)
  - Mild acidosis (increased proton levels in blood)
  - Shock - death within 4 days to a 2 weeks if not treated

Glucocorticoid Deficiency

- **Loss of cortisol**
- depressed gluconeogenesis
- reduced fat and protein metabolism
- high level of ACTH **- pigmentation**

  – decrease of energy mobilization result in weak muscle even when glucose and other nutrients are available – cortisol is needed for metabolic function

Melanin Pigmentation

- Characteristic of Addison's disease is uneven **distribution of melanin deposition** in thin skin eg. Mucous membranes, lips, thin skin of the nipples.
- Loss of feedback inhibition of hypothalamus and anterior pituitary results **in increased ACTH and POMC products including MSH** leading to **hyperpigmentation**.

Treatment

- If untreated, could lead to death with a few days.
- Treatment – **small quantities of mineralocorticoids and glucocorticoids daily**.

Conn's Disease

- **Primary hyperaldosteronism**
- Caused by adrenal tumor
- Main symptom**: hypertension** (up to 15% of clinical hypertension)

Conn's Disease

- **Features:**
- Hypokalemia (Increase excretion of potassium causes decease potassium level in blood).
- Damage of the kidney.
- Na+ retention (increase sodium level in blood) (hypernatermia).
- Alkalosis (increase excretion of protons).
- Hypertension.
- Plasma RAS are suppressed (decrease renin and Angiotensin II)

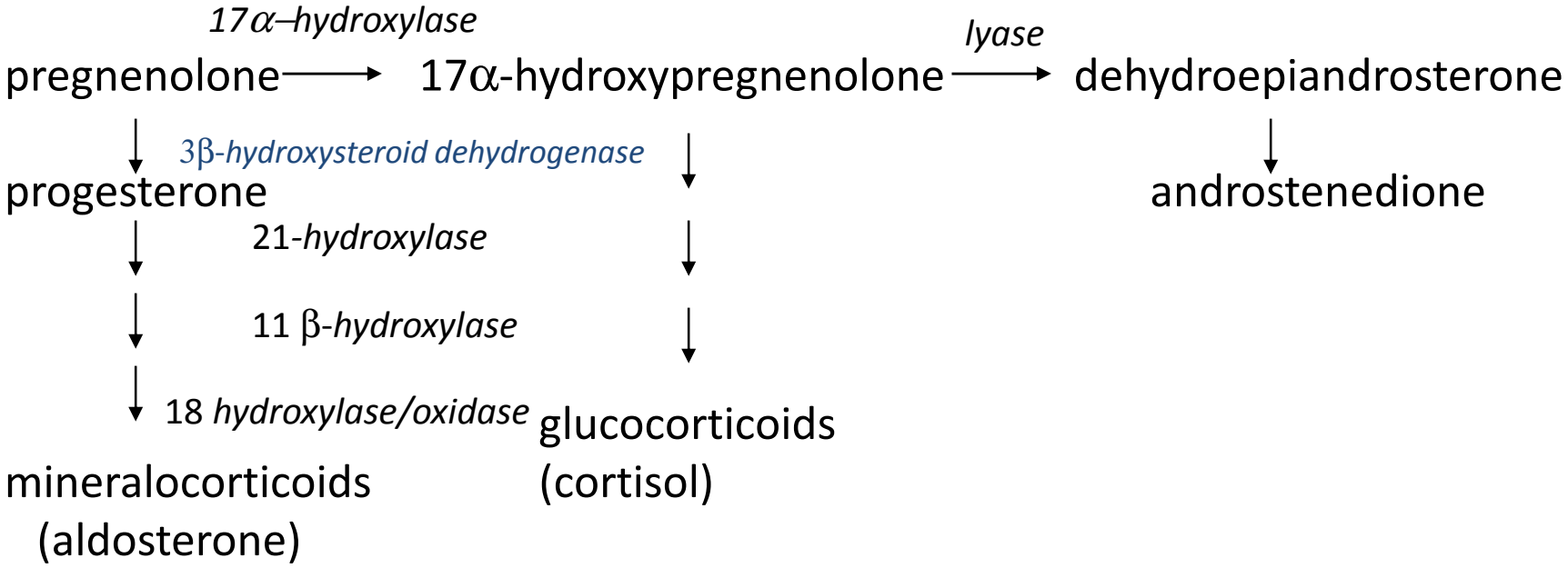
Secondary hyperaldosteronism

- Due **liver or kidney** dysfunction.
- Increase aldosterone.
- **Kidney**: Increase renin & ACE ⟶ increase Ang II
- **Liver**: abnormal increase amount of angiotensinogen.
- Like the primary form except **for elevated renin & Ang II levels.**

Congenital Adrenal Hyperplasia

-Deficiency in 3β-HSD blocks cortisol formation, leading to increased ACTH (less negative feedback)

- Result: Increased formation of DHEA (aderanl androgen).



Congenital Adrenal Hyperplasia (CAH)

in childhood in girls and in adulthood in women

✓Increase body growth.

✓virilization (Masculinizing effect) , growth of beard, deeper voice, masculine distribution of hair.

✓Big external genitalia.

in adulthood in men – non-visible