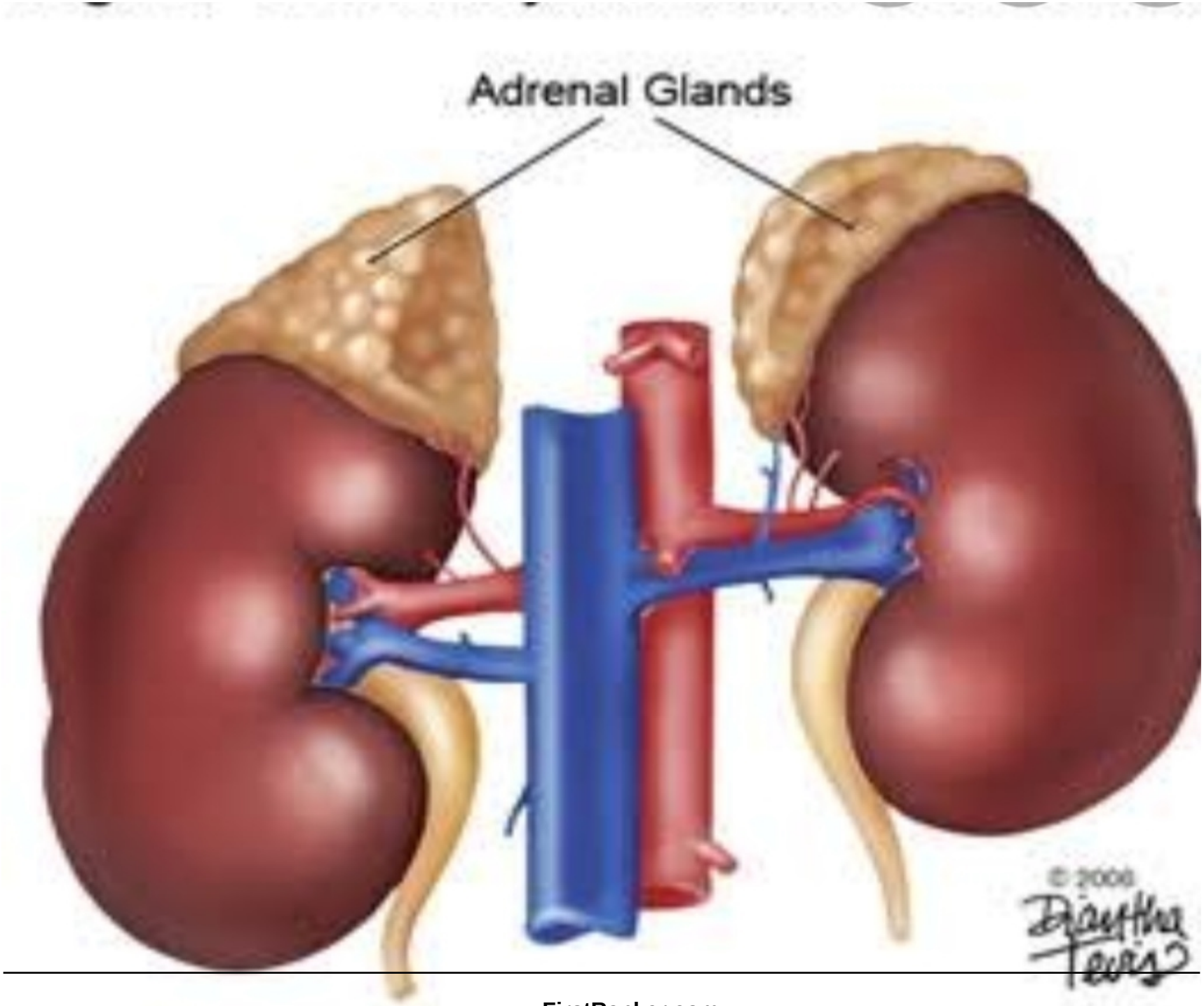
ADRENAL CORTEX

Anatomy of Adrenal gland

- The 2 adrenal gland wt. about 4gm lies at the superior pole of the two kidney.
- Each gland composed **of two** distinct parts , the adrenal medulla, and the adrenal cortex.
- **Adrenal medulla** secretes → **Catecholamines** and Adrenal **cortex** → steroid hormones.
- Blood supply by superior, middle and inferior adrenal arteries



Histology and Develpoment

- The adrenal cortex in adult comprises 3 distinct zone:
    - Zona glomerulosa(outermost), 15%
    - Zona fasciculata(middle zone),50%
    - Zona reticularis(innermost zone),7%
- The adrenocortical cells contains abundant lipids, especially in outer portion of zona fasci culata.

Section of Adrenal gland showing medulla & zones of cortex

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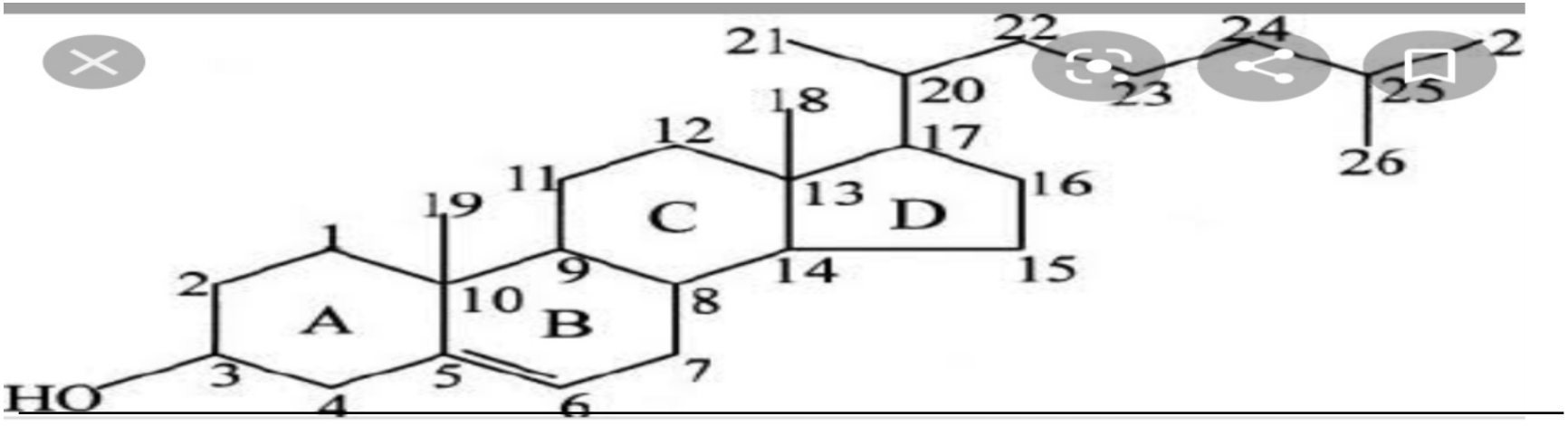
- Fetal **adrenal gland** begins developing **3-4 wks** of gestation
  - **At 6-8wks** ,there is rapid enlargement of adrenal gland.
  - **Cells of cortex differentiate** to form 'fetal zone' and an outer layer called definitive zone
  - **Fetal zone** is capable of synthesizing steroids at 8-10 wks.
  - **At birth** : Fetal **cortex, 80%** of the gland **with 20% true cortex.**
- Within **1 months after birth**: fetal cortex 50% and adrenal medulla increases in size.
- ACTH regulates growth and development of adrenal gland

Adrenal cortex

- Secretes two major hormones :mineralocorticoids and glucocorticoids, and small amounts of sex steroids especially androgenic hormones.

Structure of Adrenocortical hormones

- The hormones of adrenal cortex are <u>derivatives of cholesterol</u>.
- Contains Cyclopentanoperhydre phenanthrene nucleus like cholesterol, bile acid ,vit.D, ovarian and testicular steroid



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- Gonadal and adrenocortical steroids are of 3 types: C21,C19,C18 steroids
- The adrenal cortex secretes primarily C21 &C19 steroids.
- C19 steroids have keto group at position 17 ,so called 17-ketosteroid,they have androgenic activity.
- C21 steroid have hydroxyl group at position 17 in addition to side chain , hence called 17-hydroxysteroid.have both moneralocorticoid and glucocorticoid activity.

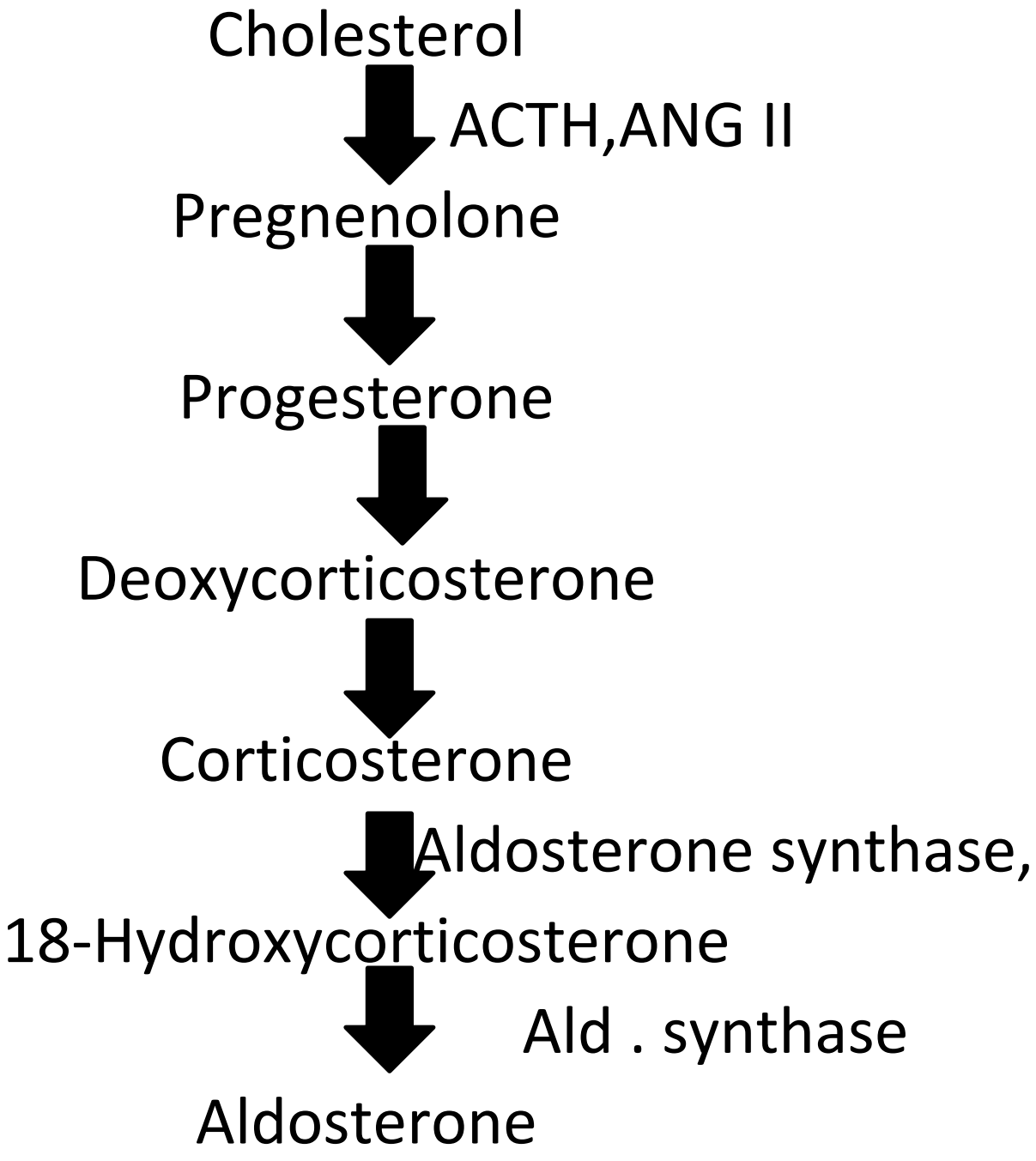
Basic structure of adrenocortical and gonadal hormone

Steroid Biosynthesis

- The precursor of all steroids is cholesterol.
- Some is synthesized, but most are taken up from LDL in the circulation.
- LDL receptors are especially abundant in adrenocortial cells.
- ACTH facilitates cortisol synthesis by activating enzyme cholesterol ester hydrolase.

Synthesis of mineralocorticoids

- Mineralocorticoids are formed in zona glomerulosa of adrenal cortex.
- The conversion of cholesterol to pregnenolone is stimulated **by ACTH** and **angiotensin II**.
- Aldosterone synthesis is limited to this zone b'coz **aldosterone synthase** is found only in cells of zona glomerulosa.
- Zona glomerulosa lacks enzyme **17α-hydroxylase**, hence glucocorticoids and sex steroid are not formed here.



Function of mineralocorticoid- Aldosterone

- Aldosterone is **very potent** and accounts for about 90% of mineralocorticoid activity.
- Deoxycorticosterone is 1/30 as potent as aldosterone ,but very small quantity secreted..
- Aldosterone increases renal tubular reabsorbtion of Na+ and secretion of K+ especially in the principal cells (P cells)of collecting tubules, and lesser extent in DT and collecting ducts.

Functions of aldosterone

- Aldosterone is very essential for life.
- It maintains the **osmolarity** and volume of **ECF**.
- Main function of aldosterone are:
  - ➢ Reabsorbtion of Na+ from renal tubules
  - ➢ Excretion of K+ and through renal tubules
  - ➢ **Secretion of H+** into renal tubules.
  - ➢ Also ↑es Na+ reabsorbtion from **sweat , Saliva , and contents of colon.**

MOA Of Aldosterone

- Like other steroids. Aldosterone binds to cytoplasmic receptor.

- HR complex moves to nucleus.

- Transcription of mRNA.

- ↑ production of proteins that alter cell functions.

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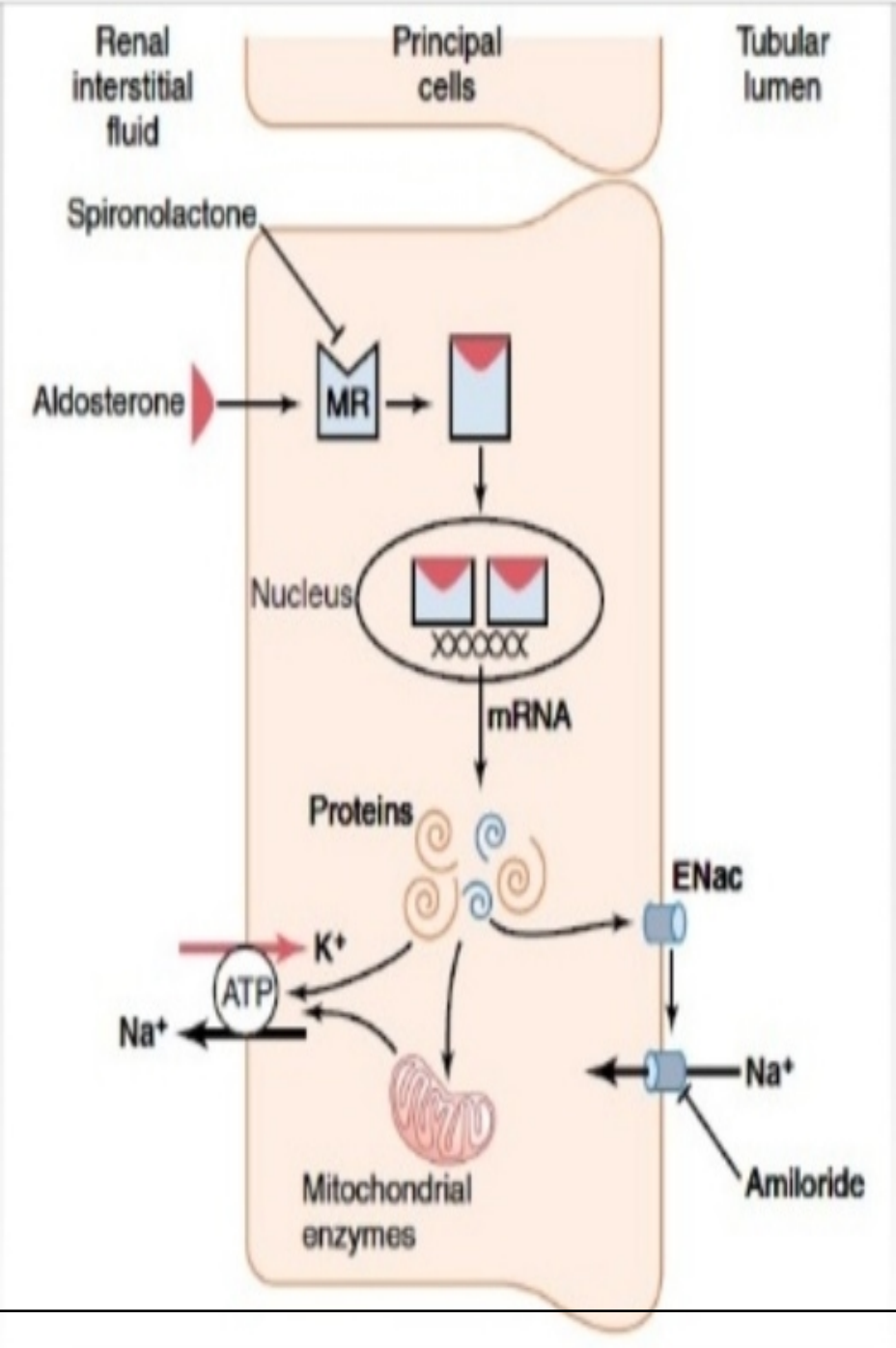
Aldosterone stimulated proteins leads to:

Genomic actions like

- ↑es activity of ENaCs (epithelial Na+ channels),a **rapid action**.
- **Slower effect** is that it increases the synthesis of ENaCs , by ↑ing the mRNA activity for synthesis of proteins.
- **↑es insertion of these channels** on cell membrane.

➢ Gene activated by aldostrone is sgk gene ,a serine-threonine protein kinase.



- **Non-Genomic Actions**: mediated by IP3
  - Nongenomic actions occurs rapidly.
  - It ↑es activity of Na+K+exchangers,which

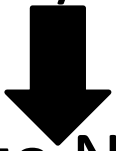
Increases intracellular accumulation of Na+

What is Aldosterone escape phenomenon ?

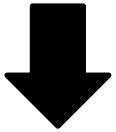
- When there is **aldosterone excessive secretion** the **ECF expands** due to Na+ and water retention **, but** when the ECF expansion passes a certain point ,**Na+ excretion** is usually ↑ed inspite of continued action of mineralocorticoids on renal tubules.

Mechanism

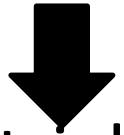
- Mineralocorticoid/aldosterone excess.



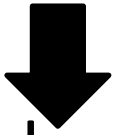
- ECF expansion(due to Na+ & water retension).



- BP rises leading to distention of atria.



- Secretion of ANP(atrial natriuretic peptide).



- ANP causes profound natriuresis and diuresis.

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- ECF returns back to normal.

➢ Due to this phenomenon **edema is not produced** by mineralocorticoids **in normal individual** and in patients of hyperaldosteronism.

Regulation of Aldosterone Secretion

- Aldosterone secretion is regulated mainly by 3 important stimuli:

1. ACTH
2. Angiotensin II
3. Plasma K+ conc.

RAAS system

RAAS system

- Angiotensinogen

↓ Renin(JGA)

Angiotensin

↓ ACE(lungs)

Angiotensin II

↓ Adrenal cortex

Aldosterone

↓

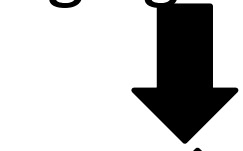
Na+ and water retention, ↑es ECF volume

ACTH

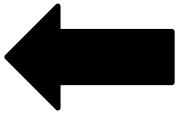
- Cells of zona glomerulosa have ACTH receptors.
- ACTH mediates aldosterone secretion by cAMP& Protein kinase.
- **Effect of ACTH on aldosterone** secretion is **temporary** , aldosterone secretion declines even if ACTH secretion is elevated ,**due to decrease renin secretion.**

Plasma K+ Conc.

- Plasma K+ level need increase only 1meq/L to stimulate aldosterone secretion.
- Like angiotensin II, K+ stimulates the conversion of cholesterol → pregnenolone ,& deoxycortecosterone→aldosterone.
- ↑ ECF K+ → Activate voltage gated Ca channel



↑ cytosolic Ca



↑ aldosterone secretion

Dysfunction Of Aldosterone

- Hypersecretion → Primary
- Hypersecretion → Secondary

Primary Hyperaldosteronism

- The cause of excess aldosterone secretion is due to adrenal disease : Adrenal adenoma
  - Adrenal hyperplasia
  - Adrenal carcinoma

Conn's Syndrome

- Major cause of primary hyperaldosteronism.
- Occurs due to the tumor(adenoma) of zona glomerulosa of adrenal cortex.
- Clinical features: Hypertension
  - Muscle weakness
  - Polyuria
  - Edema is absent
  - Hypokalemia
  - Hypernatremia
  - Low renin level
  - Metabolic alkalosis

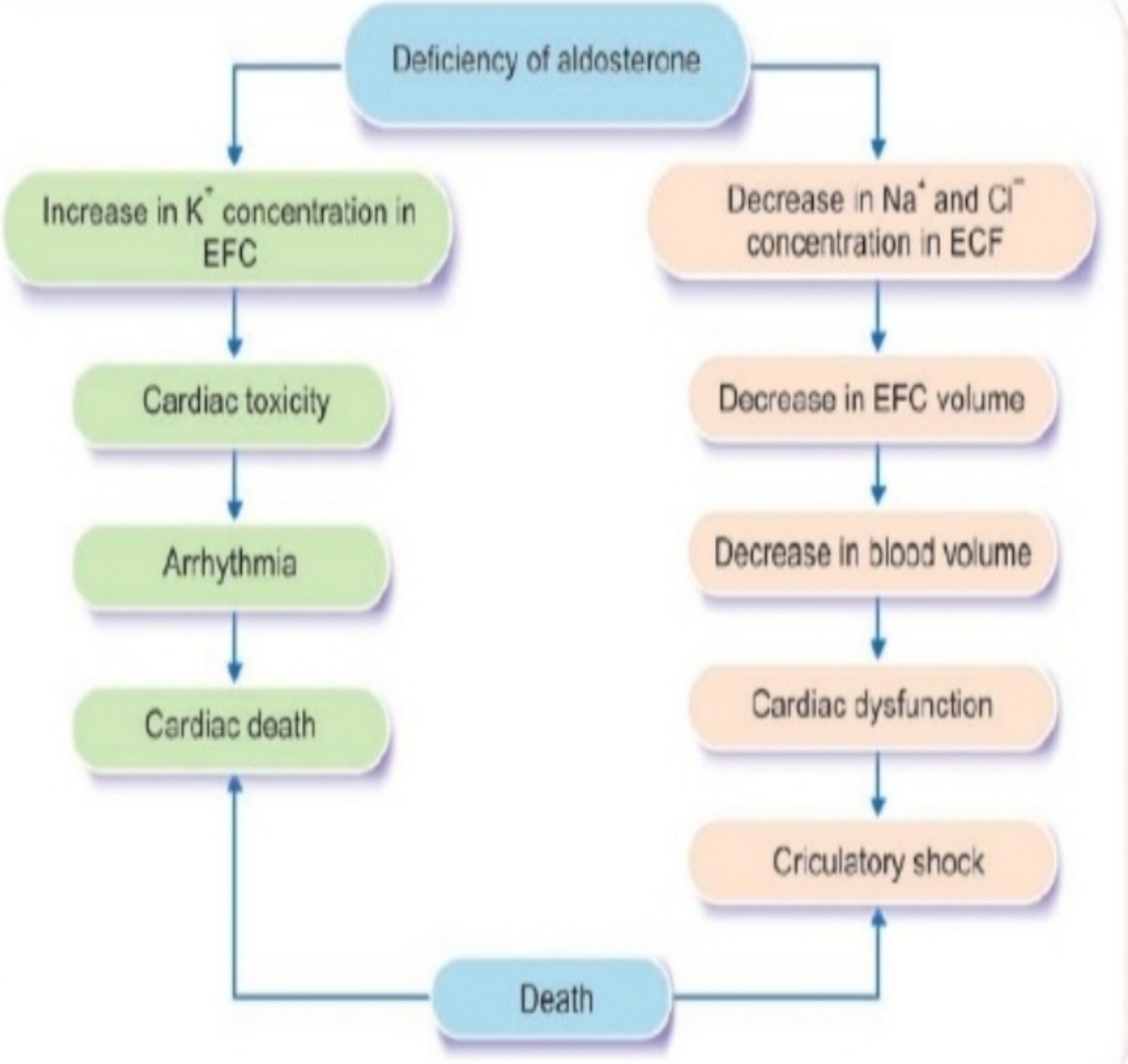
Secondary Hyperaldosteronism

- ↑ed aldosterone secretion is due to activation of RAAS .
- Occurs in cirrhosis, heart failure, nephrosis, renin secreting tumor.
- ↑ renin in plasma.
- Edema is a usual feature.

Hyposecretion of Aldosterone

Addison's disease/Primary Adrenal Insufficiency

- Occurs due to autoimmune inflammation of adrenal gland, tuberculosis.
- Deficiency of mineralocorticoids occurs.Leading to hyponatremia , hyperkalemia, ↓ECF, metabolic acidosis, ↓cardiac output,↓BP.
- Also there is glucocorticoid deficiency, so patient is unable to maintain blood glucose conc.



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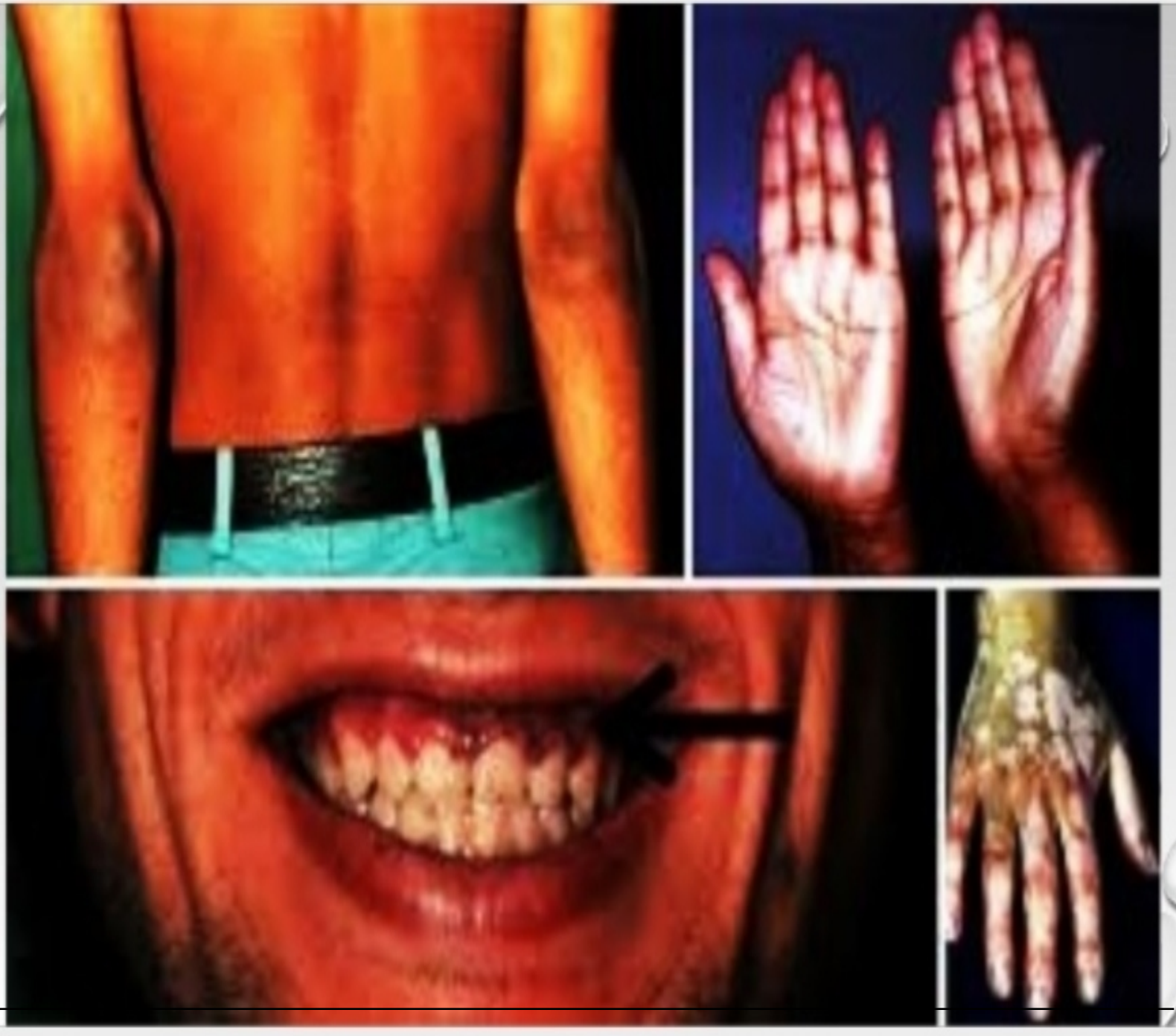
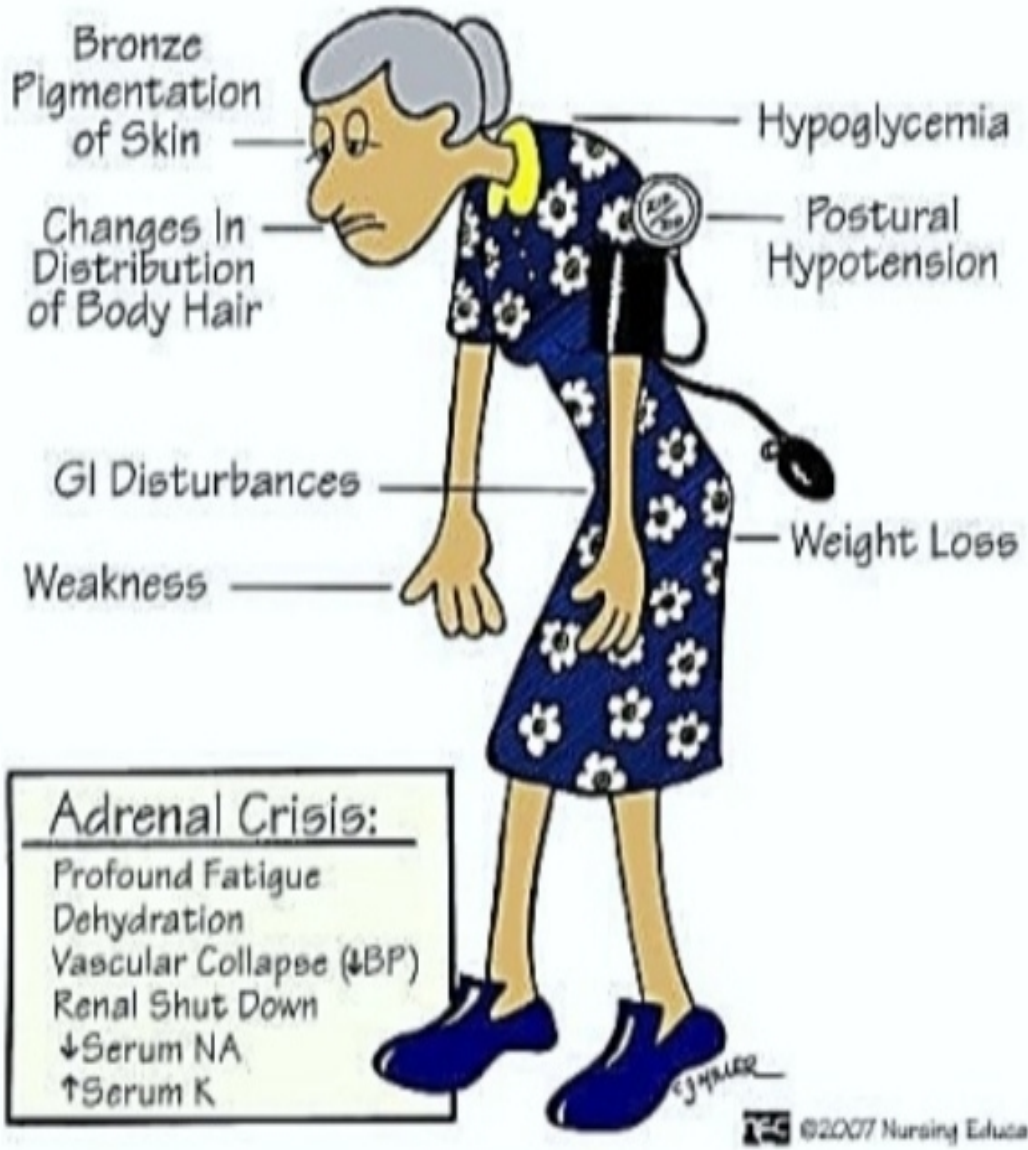
- Circulating ACTH levels are elevated, leading to melanin deposition , so there is pigmentation of palm creases, lips ,gums etc.
- Untreated patient may die in 4days-2wks.
- Treatment: Mineralocorticoid & Glucocorticoids replacement.

➢ Addisonian Crisis : Glucocorticoid level does not ↑ during stress in addison's disease patients e.g.; trauma, surgery etc leading to severe debility.



ADDISON'S DISEASE



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- **Secondary adrenal insufficiency**: caused by pituitary disease and decrease ACTH secretion.
- **Tertiary adrenal insufficiency** : caused by hypothalamic disorders disrupting CRH release.
- Pseudohypoaldosteronism : produced when there is resistence to action of aldosteronism.