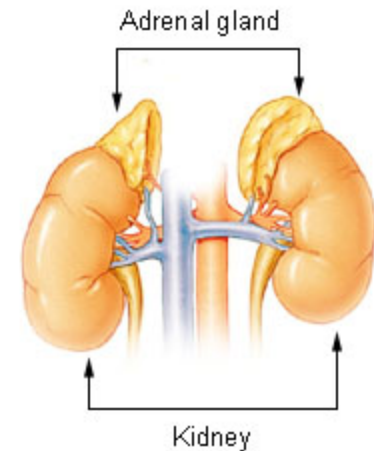


Endocrine Physiology

The Adrenal Gland 1

Dr. Khalid Alregaiey

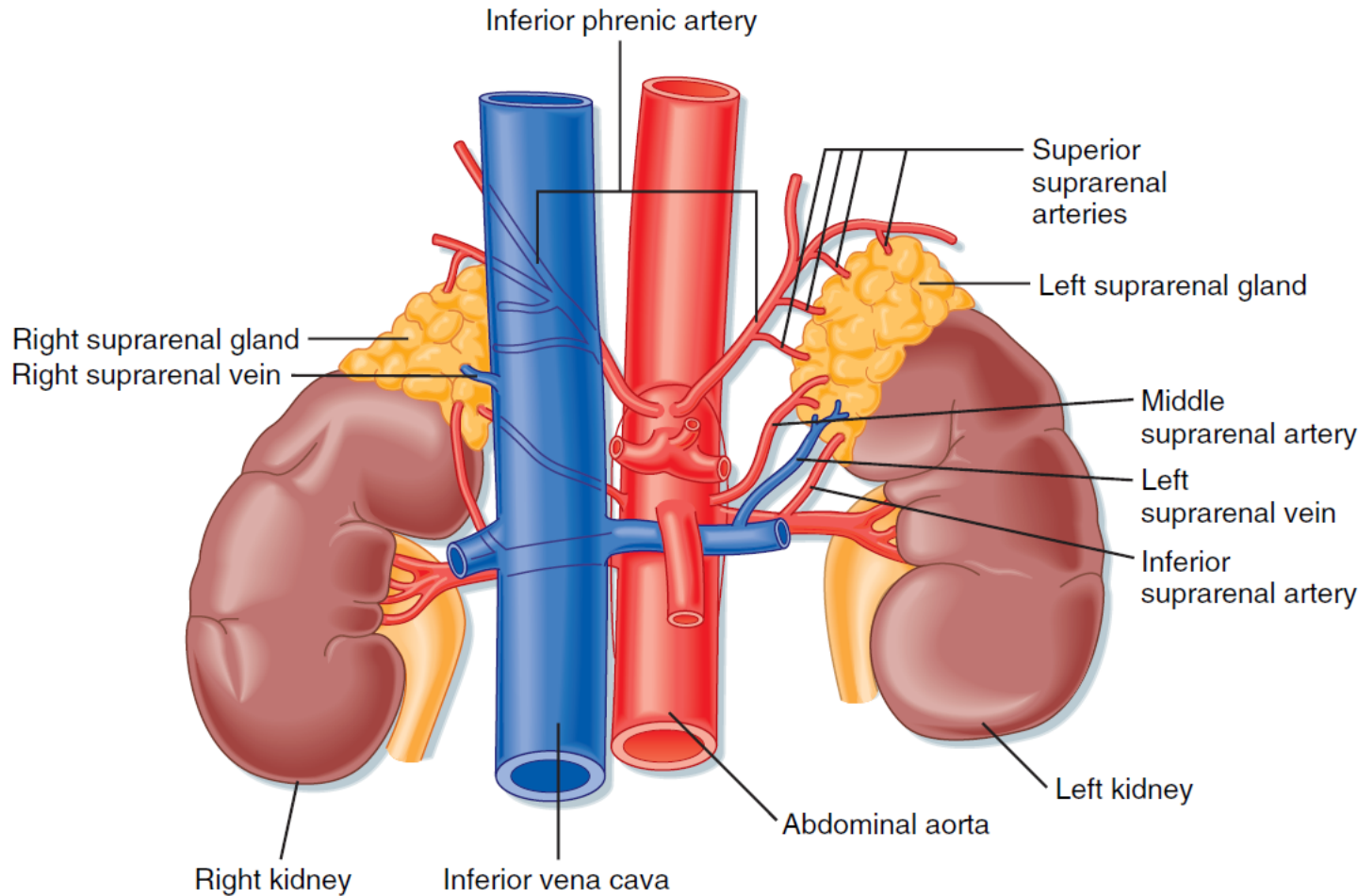
Adrenal Gland



Adrenal (Suprarenal) Glands

- Adrenal glands – paired, pyramid-shaped organs atop the kidneys
- Weigh 4-10 g.
- Structurally and functionally, they are two glands in one
 - **Adrenal cortex** (80-90%)– glandular tissue derived from embryonic mesoderm
 - **Adrenal medulla** (10-20%)– formed from neural ectoderm, can be considered a modified sympathetic ganglion

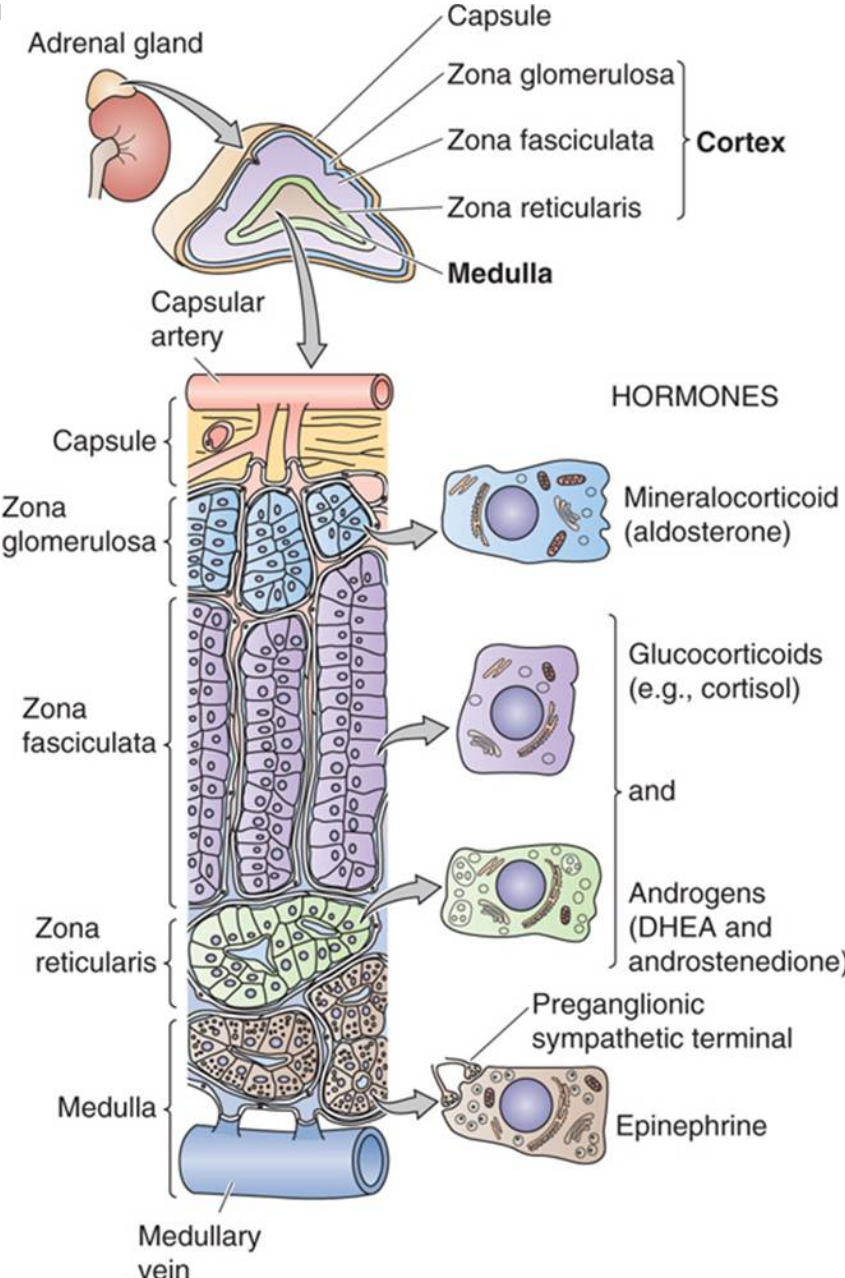
The adrenal glands sit on the superior poles of the kidneys

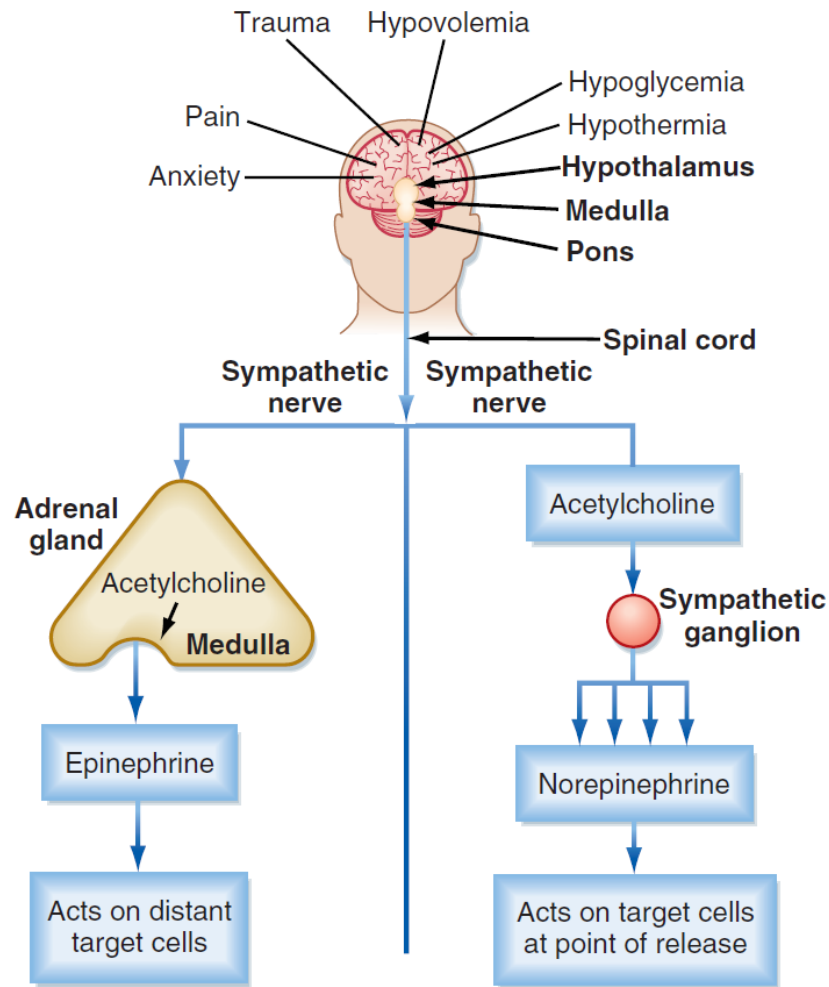


Adrenal Cortex

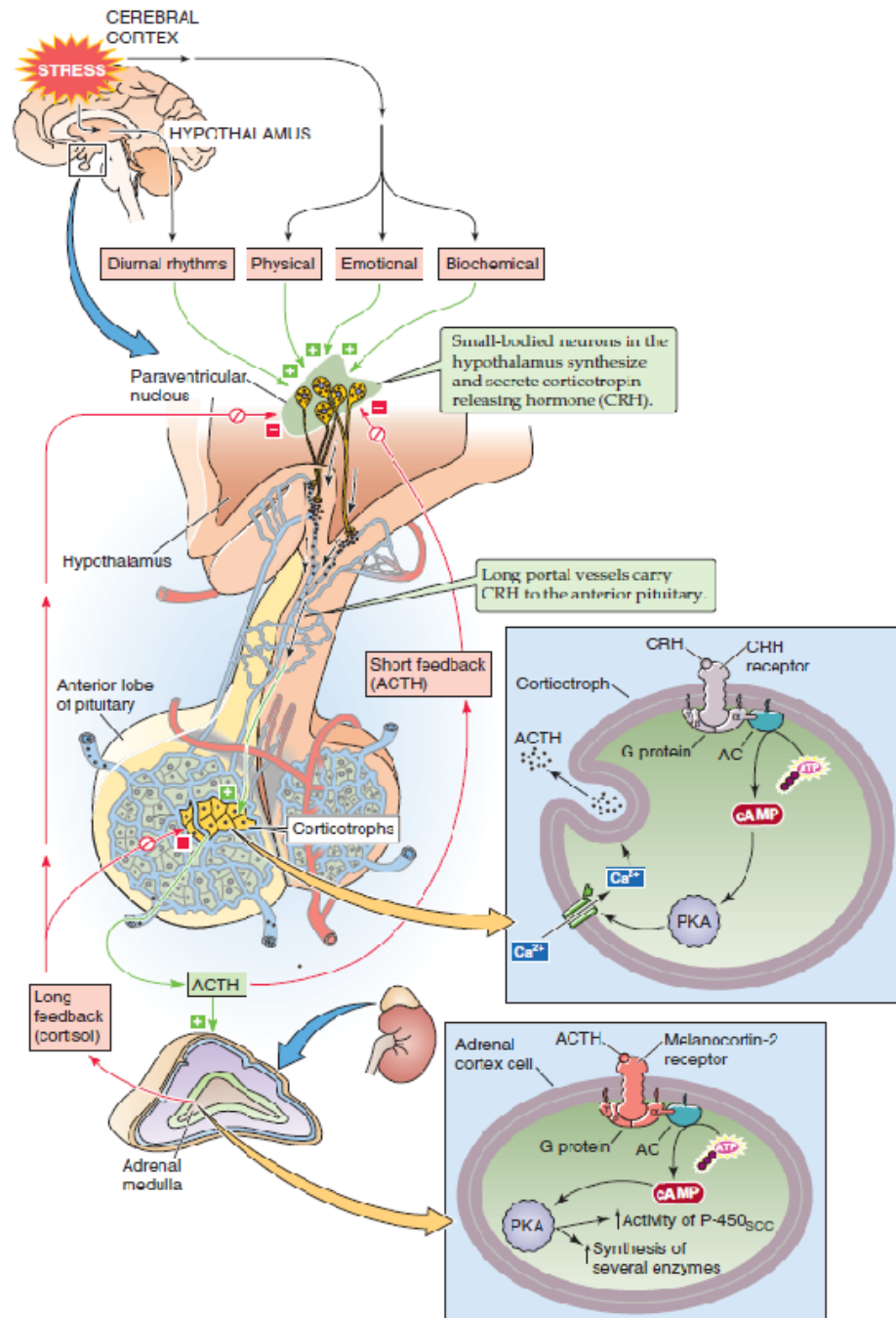
- Synthesizes and releases steroid hormones (corticosteroids)
- Different corticosteroids are produced in each of the **three layers**:
 - Zona glomerulosa (15%) – mineralocorticoids (mainly aldosterone)
 - Zona fasciculata (75%) – glucocorticoids + Androgens (mainly cortisol and corticosterone)
 - Zona reticularis (10%) – gonadocorticoids + glucocorticoids (mainly dehydroepiandrosterone DHEA)

Adrenal Cortex

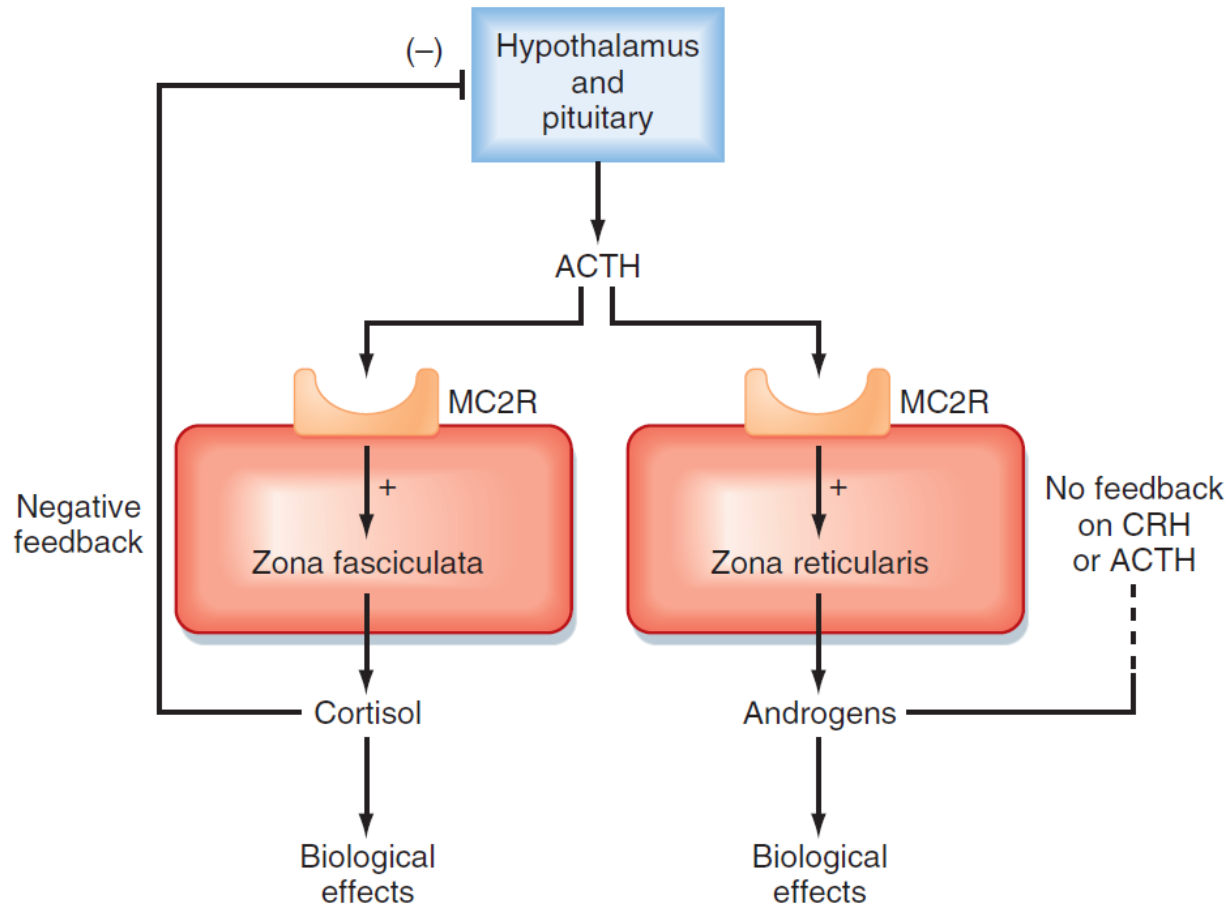




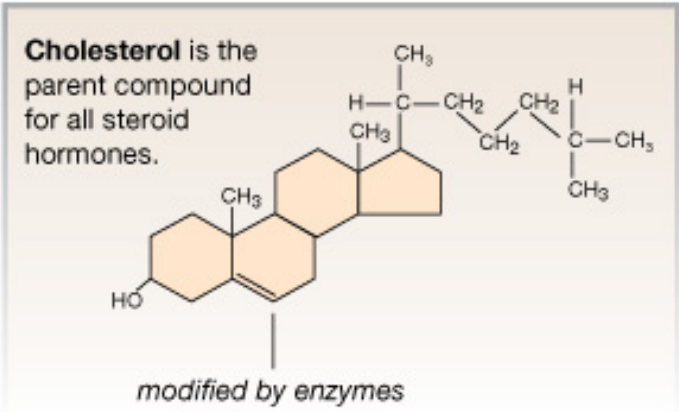
HPA Axis



Loophole in the Negative Feedback

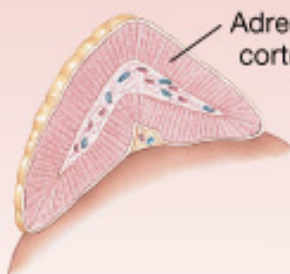


Steroid Hormones: Structure

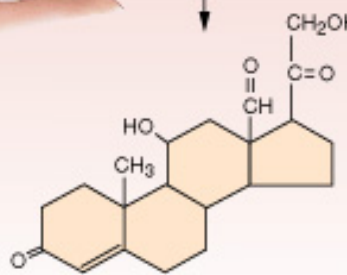


modified by enzymes to make steroid hormones such as

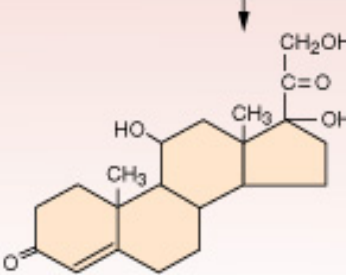
In adrenal cortex



The diagram shows a cross-section of the adrenal cortex. Two arrows point from the text 'In adrenal cortex' to the chemical structures of Aldosterone and Cortisol.




Aldosterone

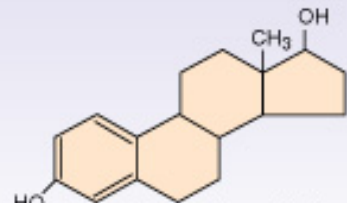


Cortisol

In ovary



The diagram shows an ovary. An arrow points from the text 'In ovary' to the chemical structure of Estradiol.



Estradiol (an estrogen)

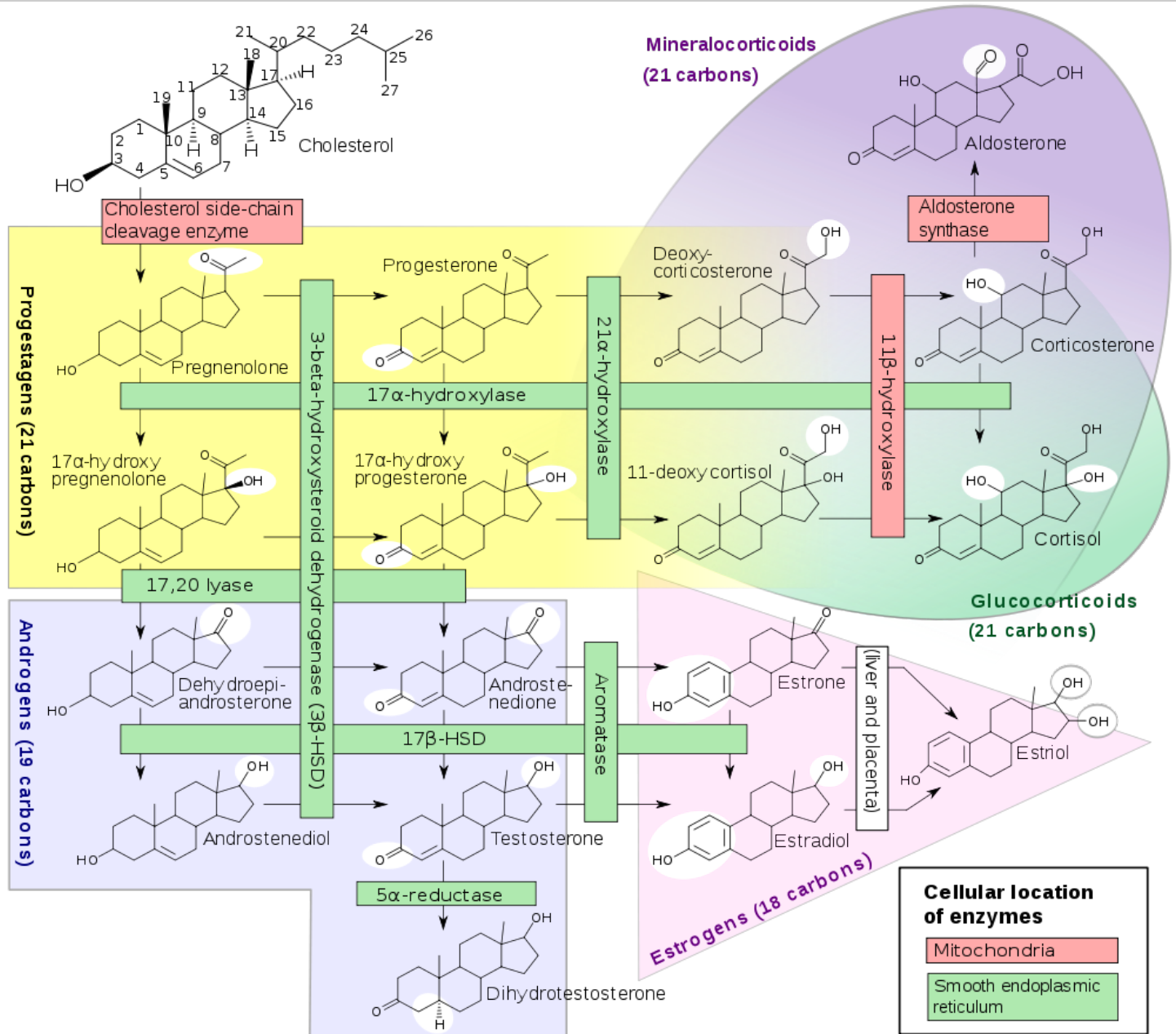
Steroid Hormones Synthesis

- Steroids are derivatives of cholesterol
- Cholesterol is from the lipid droplets in cortical cells (**cholesterol esters in LDL**)
- Removed cholesterol is replenished by cholesterol in LDL in blood or synthesized from acetate
- Steroidogenic Acute regulatory protein (**StAR protein**) transfers cholesterol to the inner membrane of the mitochondria (mutation causes accumulation of cholesterol in the cytoplasm).

Steroid Hormones Synthesis (Cont.)

- Steroid hormones are synthesized and secreted on demand (not stored)
- The first step in the synthesis of all steroid hormones is conversion of cholesterol to pregnenolone by the enzyme cholesterol dismolase (aka cholesterol side chain cleavage (SCC) enzyme)
- Newly synthesized steroid hormones are rapidly secreted from the cell
- Following secretion, all steroids bind to some extent to plasma proteins: CBG (transcortin) and albumin

Steroidogenesis



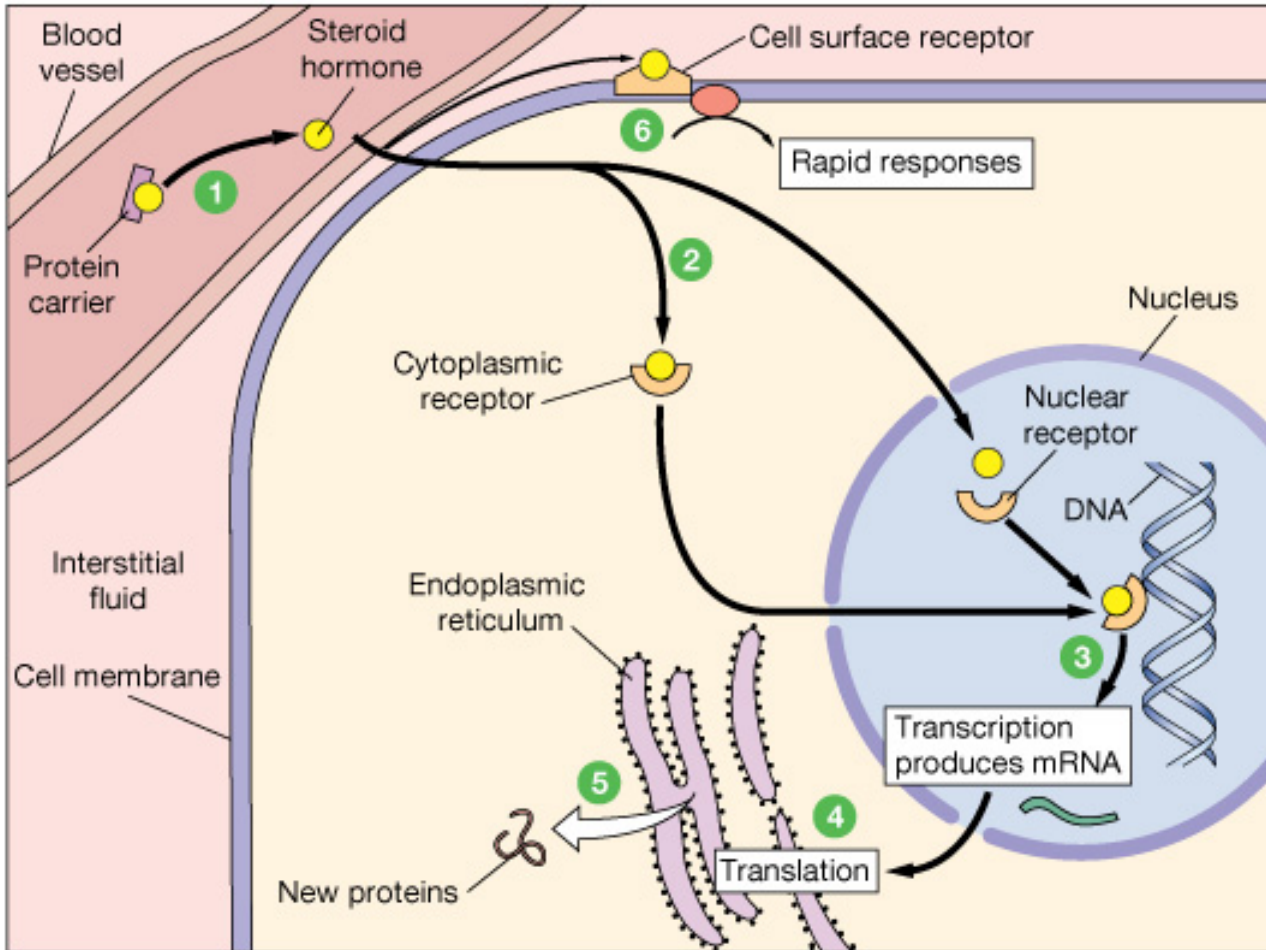
Glucocorticoids vs. Mineralocorticoids

Table 78-1 Adrenal Steroid Hormones in Adults; Synthetic Steroids and Their Relative Glucocorticoid and Mineralocorticoid Activities

Steroids	Average Plasma Concentration (free and bound, $\mu\text{g}/100\text{ ml}$)	Average Amount Secreted ($\text{mg}/24\text{ hr}$)	Glucocorticoid Activity	Mineralocorticoid Activity
Adrenal steroids				
Cortisol	12	15	1.0	1.0
Corticosterone	0.4	3	0.3	15.0
Aldosterone	0.006	0.15	0.3	3000
Deoxycorticosterone	0.006	0.2	0.2	100
Dehydroepiandrosterone	175	20	—	—
Synthetic steroids				
Cortisone	—	—	0.7	0.5
Prednisolone	—	—	4	0.8
Methylprednisone	—	—	5	—
Dexamethasone	—	—	30	—
9 α -Fluorocortisol	—	—	10	125

Glucocorticoid and mineralocorticoid activities of the steroids are relative to cortisol, with cortisol being 1.0.

Steroid Hormones: Action



- 1 Most hydrophobic steroids are bound to plasma protein carriers. Only unbound hormones can diffuse into the target cell.
- 2 Steroid hormone receptors are in the cytoplasm or nucleus.
- 3 The receptor-hormone complex binds to DNA and activates or represses one or more genes.
- 4 Activated genes create new mRNA that moves back to the cytoplasm.
- 5 Translation produces new proteins for cell processes.
- 6 Some steroid hormones also bind to membrane receptors that use second messenger systems to create rapid cellular responses.

Mineralocorticoids:

Aldosterone

Aldosterone

- A steroid hormone.
- Essential for life.
- Synthesized in zona glomerulosa
- Responsible for regulating Na^+ reabsorption in the distal tubule and the cortical collecting duct
- It also affects Na^+ reabsorption by sweat, salivary and intestinal cells.

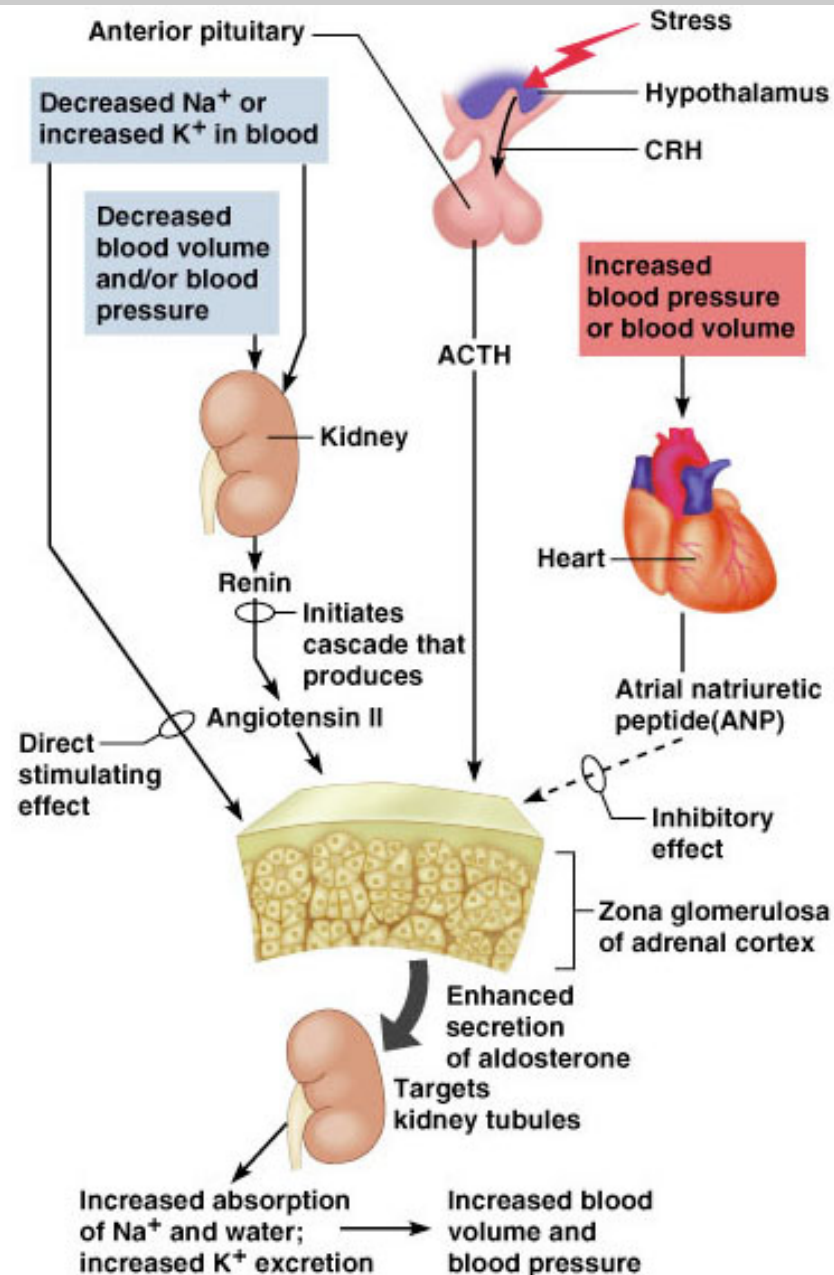
Mineralocorticoids

- Aldosterone secretion is stimulated by:
 - Decreasing blood volume or pressure (**renin-angiotensin system**) is the major stimulant
 - Rising blood levels of K^+ (**hyperkalemia**)
 - **ACTH**

The Four Mechanisms of Aldosterone Secretion

- **Renin-Angiotensin System (RAS),** hypovolemia
- **Hyperkalemia:** Plasma concentration of potassium directly influences the zona glomerulosa cells
- **ACTH** – causes small increases of aldosterone during stress
- Atrial natriuretic peptide (ANP) – inhibits activity of the zona glomerulosa and reduces aldosterone

The Four Mechanisms of Aldosterone Secretion



Transport and Metabolism of Aldosterone

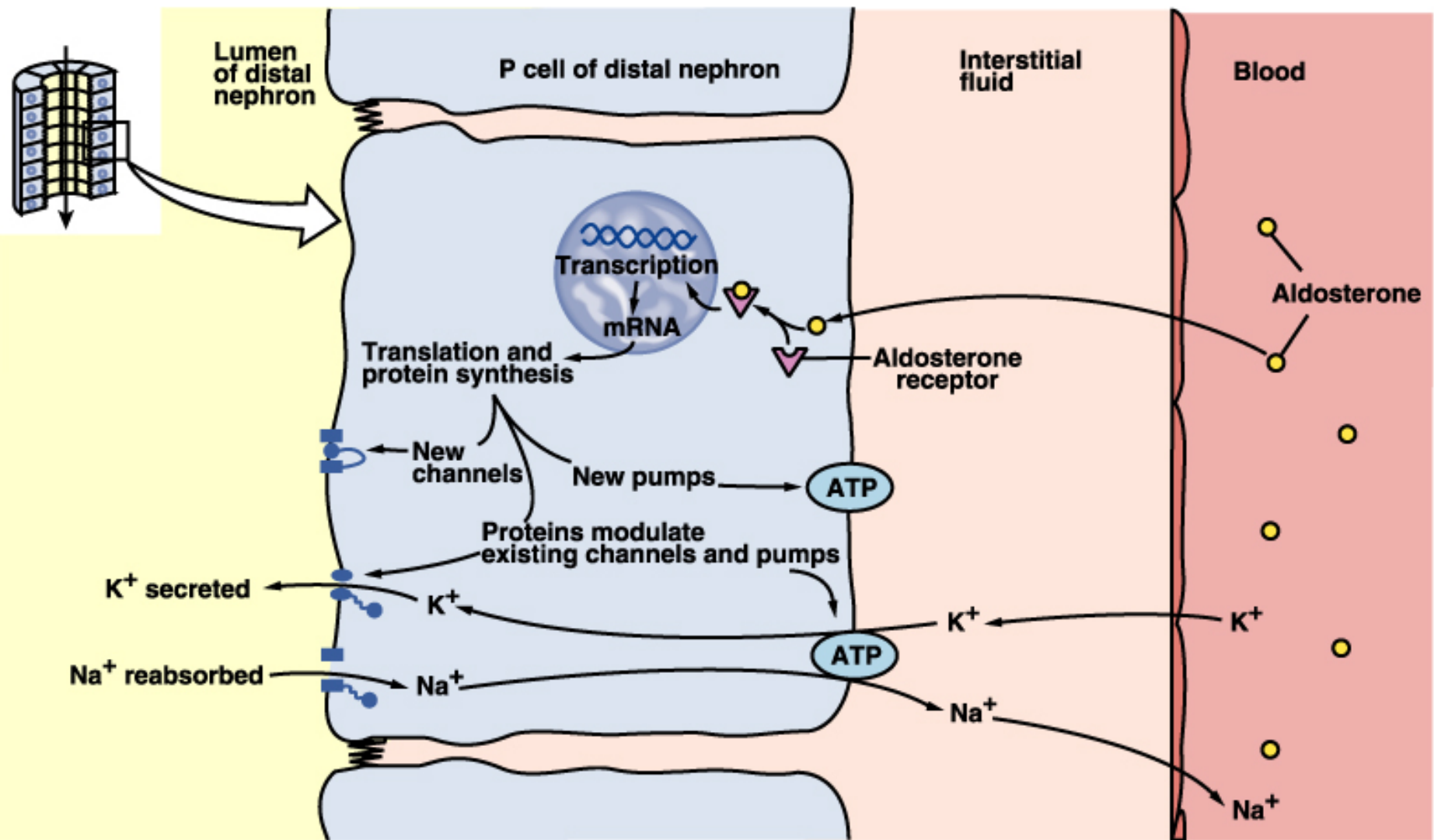
- Aldosterone binds to albumin and corticosteroid-binding protein in blood with low affinity and therefore has a biological half-life of about 20 minutes.
- Aldosterone is inactivated by the liver and conjugated to a glucuronic acid or sulfate and secreted in bile or excreted by the kidney.

Actions of Aldosterone

Binds to mineralocorticoid receptor [MR]

Stimulates sodium reabsorption by distal tubule and collecting duct of the nephron and promotes potassium and hydrogen ion excretion

- Increases transcription of Na/K pump (basolateral)
- Increases the expression of apical Na channels and Na/Cl cotransporters (NCC)
- Stimulates the secretion of K^+ into the tubular lumen
- Stimulates secretion of H^+ via the H^+ /ATPase by the intercalated cells of the cortical collecting tubule



Actions of Aldosterone

- Aldosterone increases extracellular fluid volume and arterial pressure but has only a small effect on plasma sodium concentration.

(water is also absorbed, ADH is secreted)

- Excess aldosterone not only causes loss of potassium ions from the extracellular fluid into the urine but also stimulates transport of potassium from the extracellular fluid into most cells of the body.
- Excess aldosterone increases tubular hydrogen ion secretion and causes alkalosis.

Actions of Aldosterone

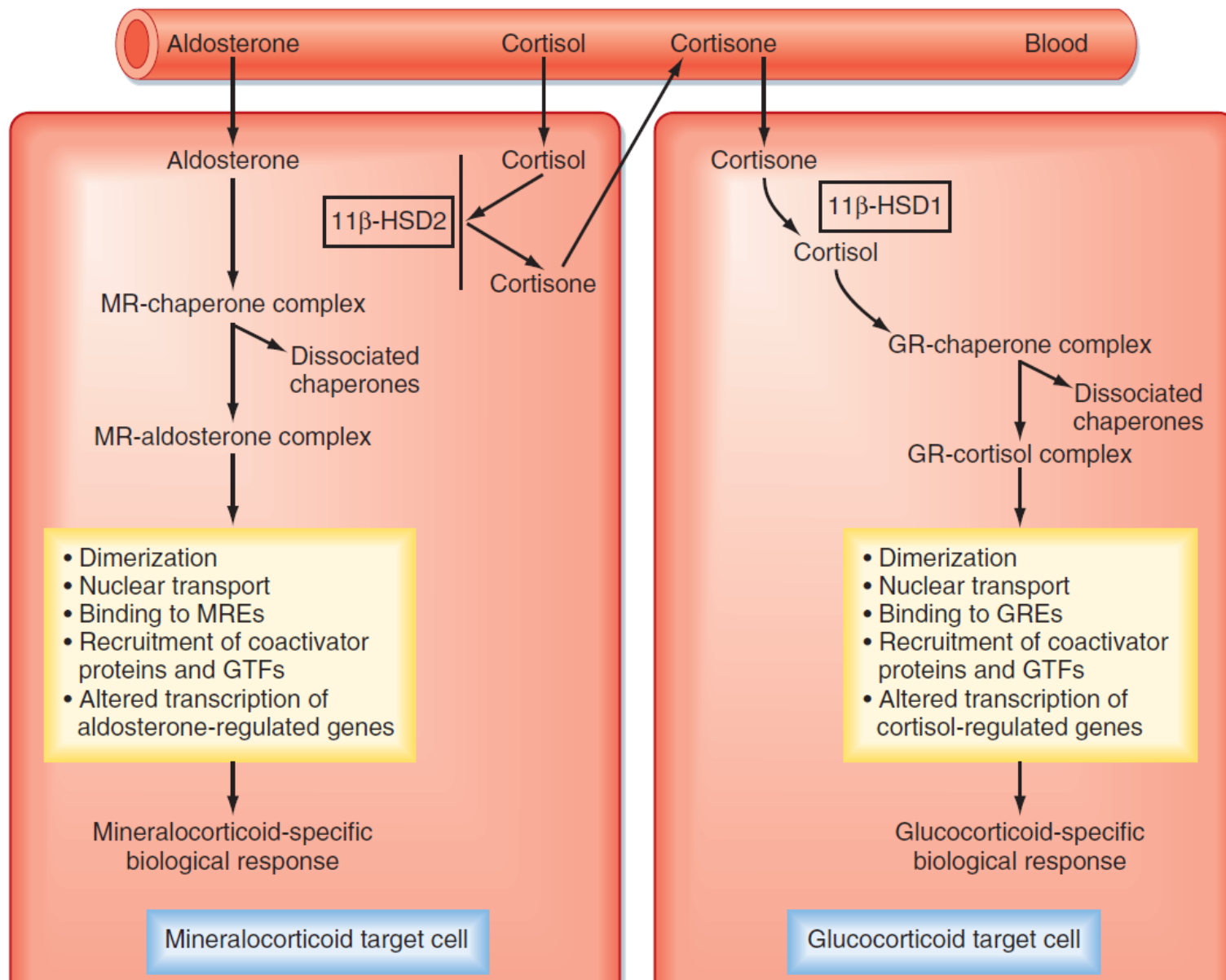
- Aldosterone has the same effects on sweat glands and salivary glands as it has on the renal tubules, reabsorption of Na^+ and Cl^- and excretion of K^+
- Aldosterone also greatly enhances sodium absorption by the intestines, especially in the colon

Aldosterone Escape

When excess amounts of aldosterone are secreted:

- The rise in arterial pressure increases kidney excretion of both sodium and water, called *pressure natriuresis* and *pressure diuresis*,

Apparent mineralocorticoid excess syndrome (AME)



Aldosterone: Role in diseases

- Complete failure to secrete aldosterone leads to death (dehydration, low blood volume).
- Hyperaldosterone states: Contribute to hypertension associated with increased blood volume.

Overproduction of aldosterone

- primary causes, ie. **Conn's syndrome**:
 - adenoma, nodular hyperplasia of zona glomerulosa
- secondary
 - left ventricular failure, cor pulmonale, cirrhosis, ascites, hyperreninism
- *Apparent mineralocorticoid excess syndrome (AME)* (cortisol binds MR)
- symptoms, signs
 - headache, hypokalemia causing muscle weakness, hypernatremia, hypervolemia, metabolic alkalosis, nocturnal polyuria, hand cramping

Overproduction of aldosterone

- treatment
 - surgical for adenoma
 - Spironolactone, a potassium-sparing diuretic that acts as an aldosterone antagonist.