

THE ADRENAL GLAND (cortex)

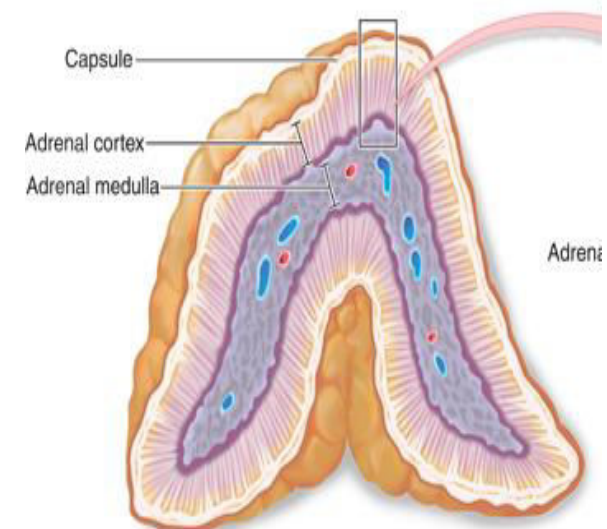
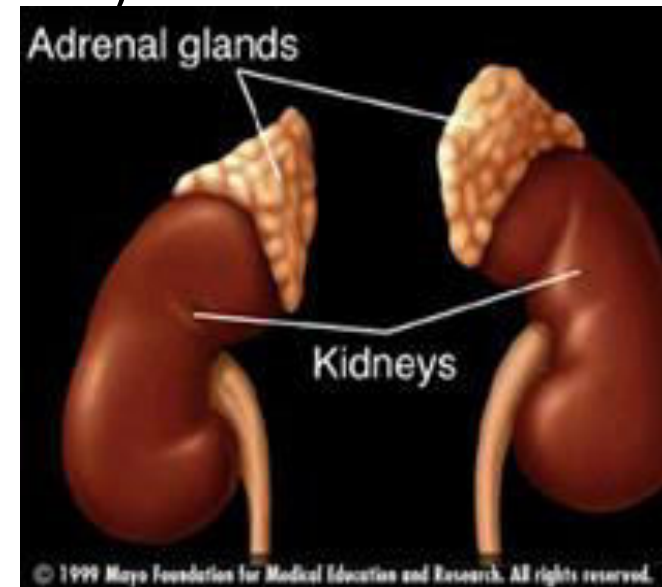
Objectives

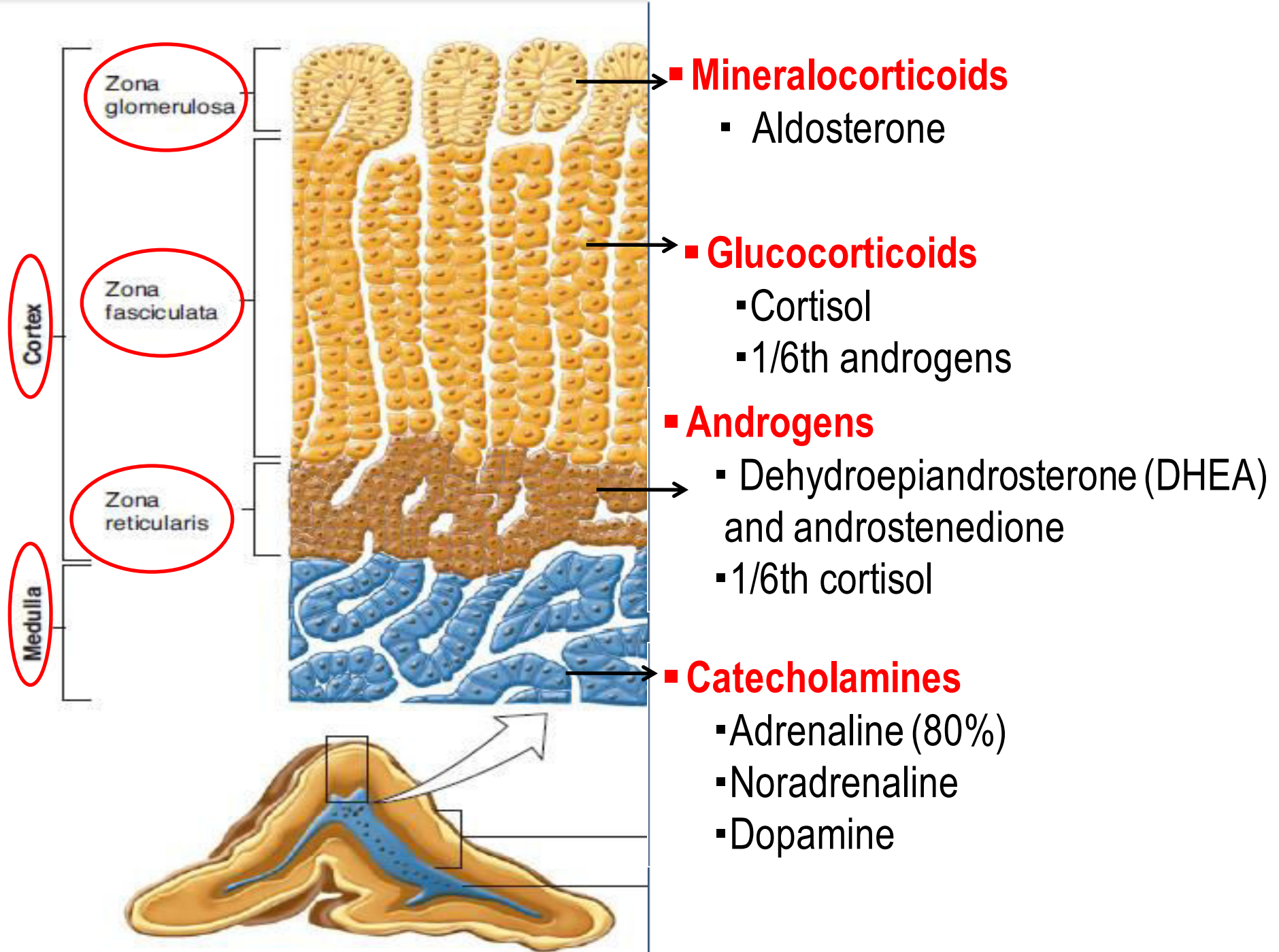
- ⦿ The steps of adrenocortical hormone synthesis.
- ⦿ Transport, metabolism and mechanism of action of adrenocortical hormones.
- ⦿ The actions of adrenocortical hormones and the mechanisms regulating their secretion.
- ⦿ Features of excess and deficiency of adrenocortical hormone secretion.

THE ADRENAL GLANDS

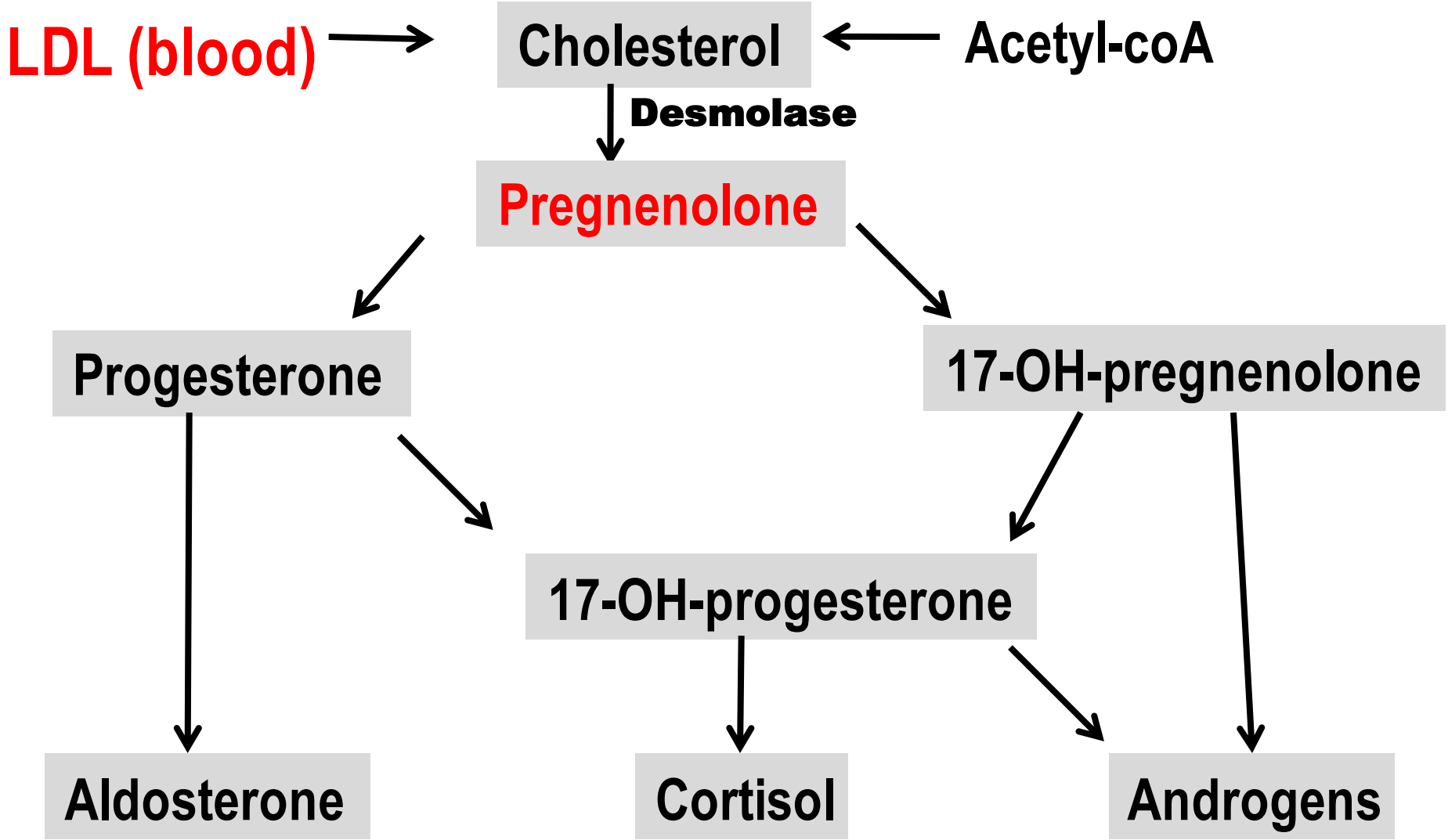
(essential for life-stress gland)

- Location: at top of the kidneys (suprarenal gland)
- Weight \approx 4 gm
- Structurally and functionally \rightarrow 2 glands:
 - Adrenal cortex (72%)
 - Secrete corticosteroids
 - Essential for the life
 - Adrenal medulla (28%)
 - Secrete catecholamines
 - Not essential for the life
 - Modified sympathetic ganglion





SYNTHESIS OF ADRENOCORTICAL HORMONES



Transport and fate of adrenal hormones

Transport

◎ Cortisol

- Bound to plasma proteins (inactive) (90%)
 - CBG (Corticosteroid binding globulin) transcortin (75%) synthesis in liver stimulated by estrogen:
 - ☞ ↑ **CBG** (pregnancy) → ↑ bound → ↓ free → ↑ ACTH → ↑ cortisol secretion → normal free (↑ **total**)
 - ☞ ↓ **CBG** (liver disease) → ↓ bound → ↑ free → ↓ ACTH → ↓ cortisol secretion → normal free (↓ **total**)
 - Albumin (15%)
 - Free (active) (10%):

◎ Aldosterone: 60% bound to CBG and albumin

Metabolism

◎ In liver by conjugation with glucuronides.

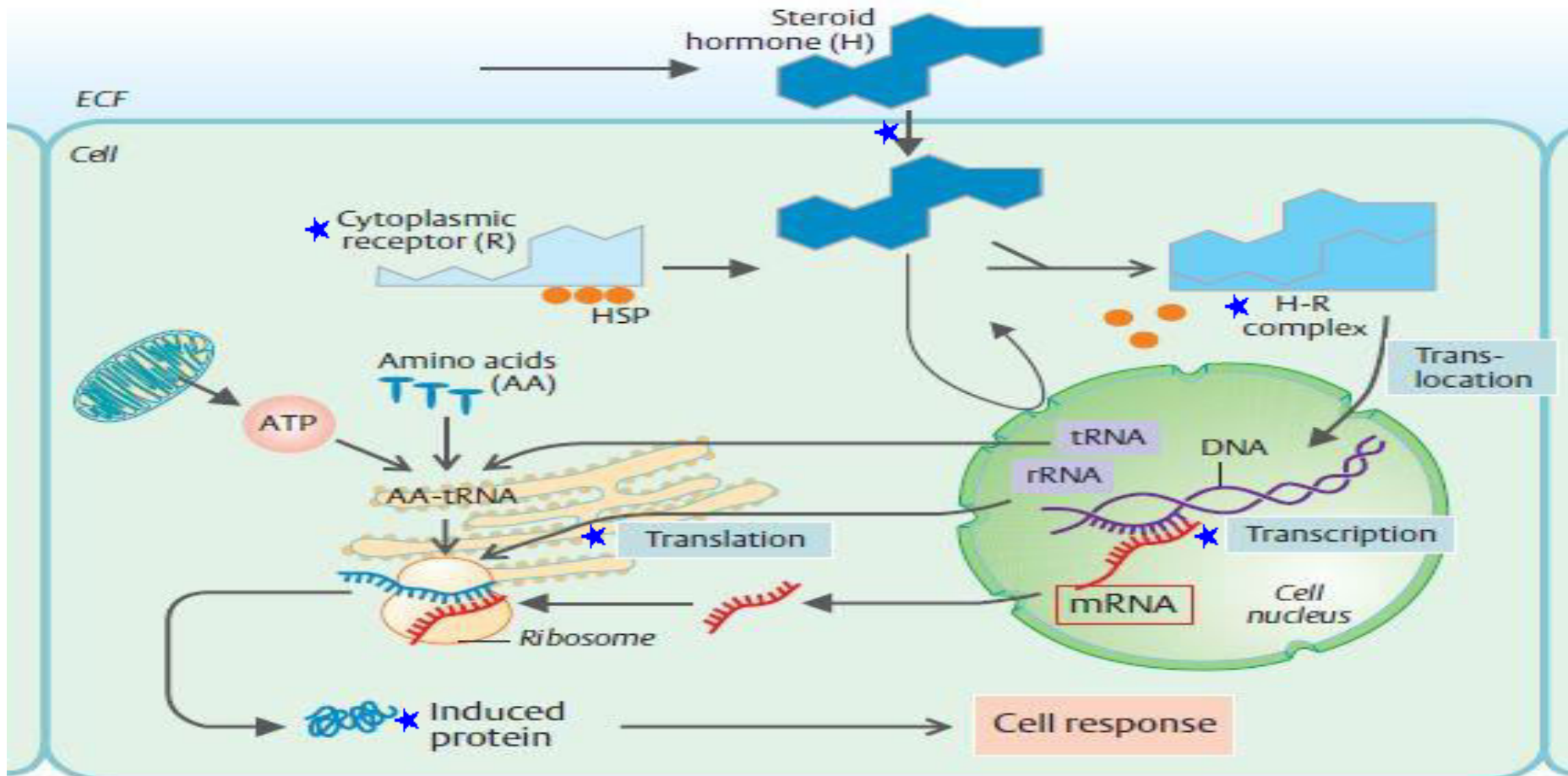
Excretion

◎ 75% in urine and 25% in bile then in the feces.

GLUCOCORTICOIDS

- **Cortisol:** very potent, 95% of all glucocorticoid activity
- Corticosterone: less potent, 4% of glucocorticoid activity
- Cortisone, prednisolone, dexamethasone (synthetic)

Mechanism of action



Effects of glucocorticoids

Permissive action (low level is needed)

- Gluconeogenesis by glucagon
- Lipolysis by catecholamine and GH
- Vasoconstriction by catecholamine and angiotensin II

Physiological action (normal level)

1) Metabolism

→ A.CHO (diabetogenic)

- Gluconeogenesis (↑ gluconeogenic enzymes)
 - ↑ Extra-hepatic protein catabolism
 - ↑ Hepatic uptake of AA
- ↓ Glucose utilization by muscle and adipose tissue
 - ↓ Affinity to insulin receptors
 - ↓ Mobility of glucose transporters
 - ↓ Phosphorylation

B. Protein (extra-hepatic catabolism)

- Protein catabolism in bone, muscle and skin
- ↓ AA transport into muscle and adipose tissue
- ↑ AA transport into the liver → Gluconeogenesis

C. Fat (lipolysis and ketogenic)

- ↑ Activity of lipase

2) Stress (Anti-stress)

- ↑ Glucose and FA → Energy
- Pressor effect (permissive)

3) Appetite

- ↑ Appetite (↑ neuropeptide)
- ↓ Appetite (↑ leptin)

4) CVS (maintenance of normal arterial blood pressure)

- ++ Inotropic effect ($\uparrow\beta$ receptors $\uparrow\text{Na}^+\text{-K}^+\text{ATPase}$)
- \downarrow Vasodilatation (\downarrow PG)
- Maintain blood volume (\downarrow vascular permeability)

5) Blood cells

- \uparrow RBC, \uparrow platelets, \uparrow neutrophils (\downarrow function)
- \downarrow Eosinophils, basophils & lymphocytes

6) CNS

- Modulate behavior & mood of individuals (euphoria)
- \downarrow REM sleep, \uparrow awake time

7) Other effects

- Slight mineralocorticoid effect
- Maturation of surfactant
- \uparrow Gastric HCl

Pharmacological action (high level)

1) On bone (osteoporosis)

- ↓ Bone formation (↓ osteoblast, ↓ collagen, anti-vitamin D)
- ↑ Bone resorption

2) On CT

- ↓ Collagene synthesis
- ↓ Fibroblast

3) Anti-inflammatory

- Stabilizes lysosomes, inhibits phospholipase A₂

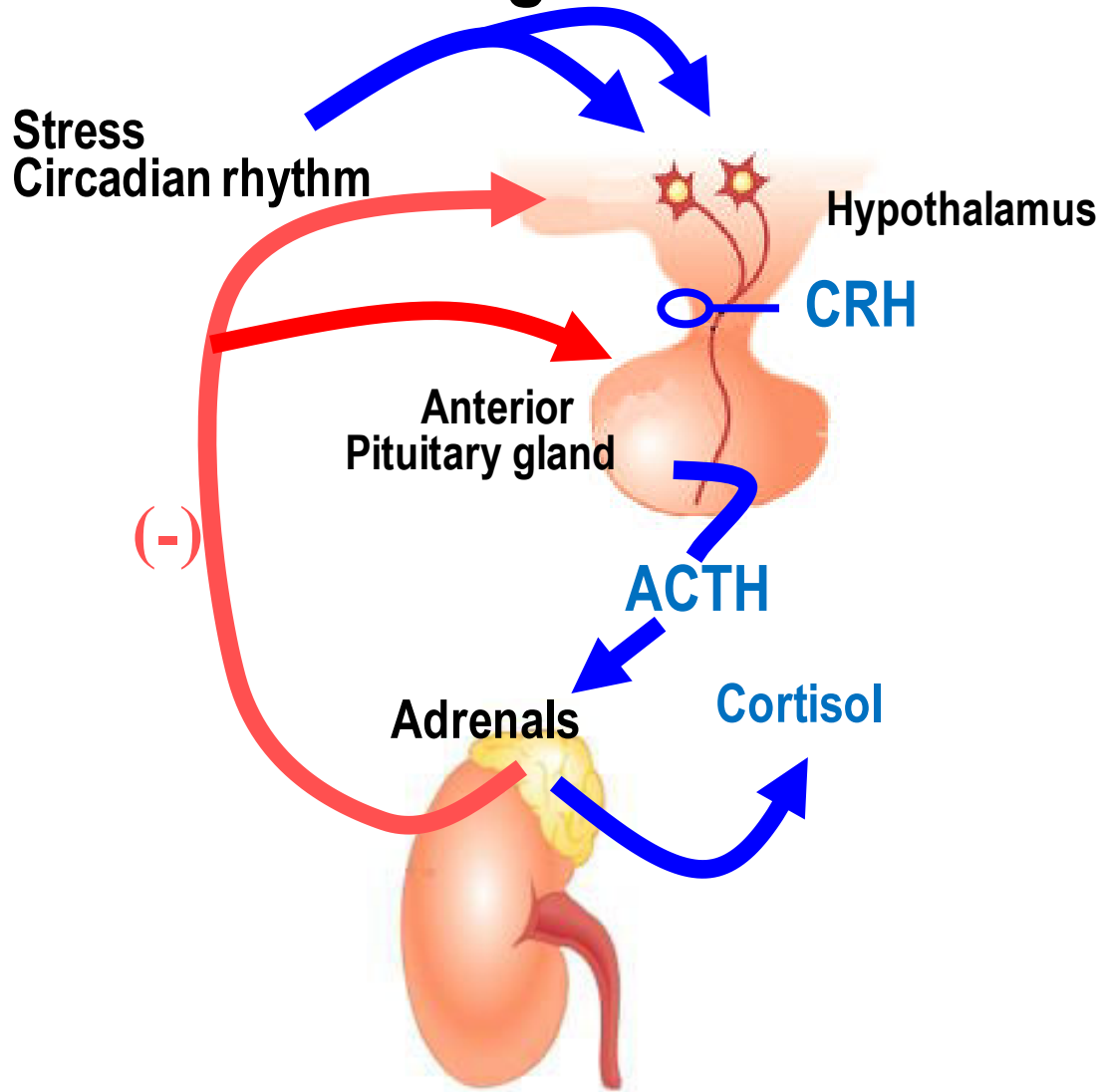
4) Antiallergic

- ↓ Histamine release

5) Immunity and lymphoid tissue

- ↓ Cellular immunity (↓ T lymphocytes)
- ↓ Humoral immunity (↓ Ig)

Regulation of cortisol secretion



- 75% of daily production of cortisol occurs between 4 AM and 10 AM

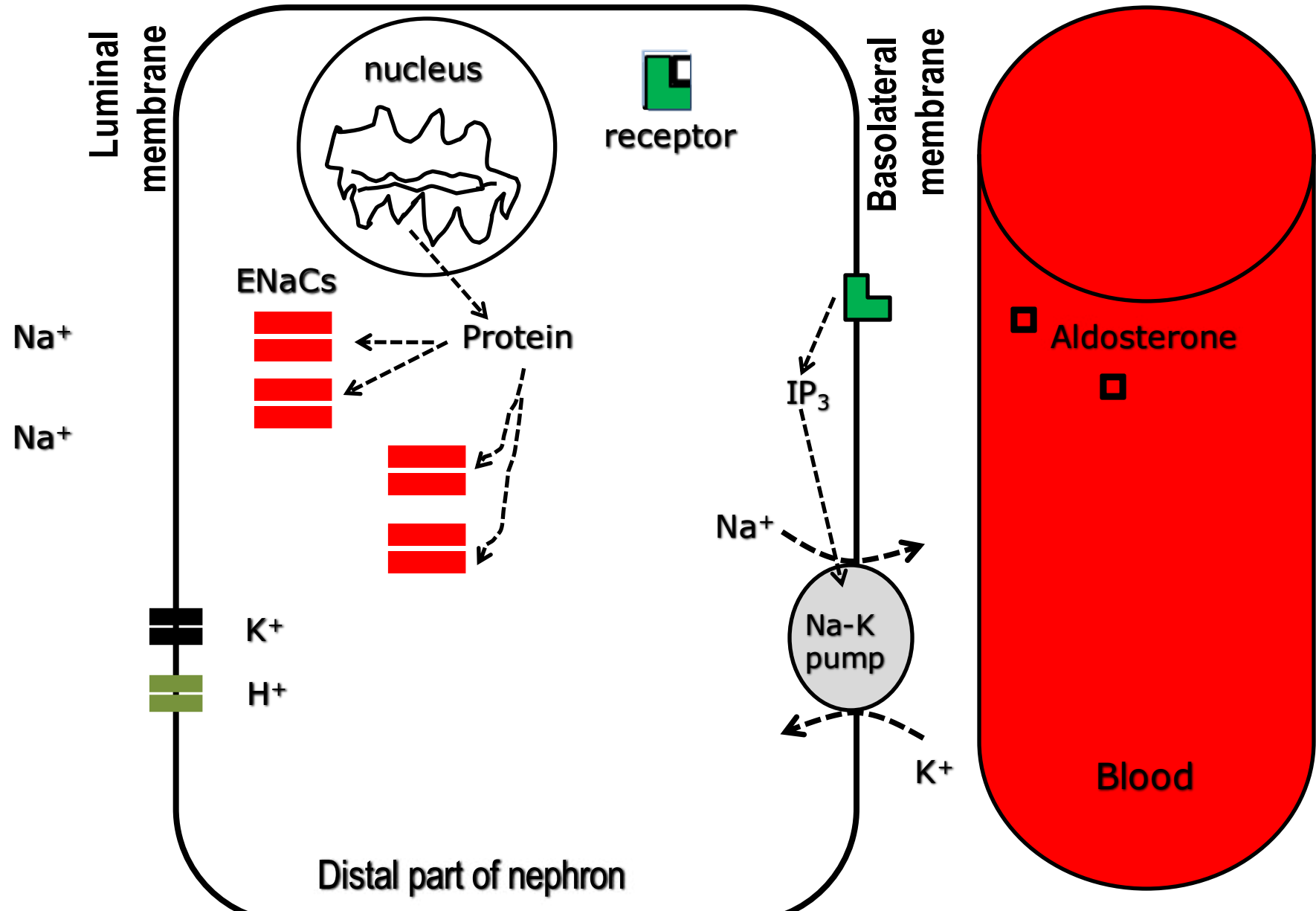
THE MINERALOCORTICOIDS

- **Aldosterone:** very potent, 90% of mineralocorticoid activity
- Deoxycorticosterone: less potent, 1/15th aldosterone potency
- Corticosterone, cortisol, cortisone: slight activity

Aldosterone



MECHANISMS OF ALDOSTERONE ACTION



Actions of aldosterone

On kidney

Distal parts of nephron (DCT, collecting tubule and collecting duct)

- Luminal membrane: \uparrow Na⁺ reabsorption (epithelial sodium channels-ENaCs) in exchange with K⁺ or H⁺
- Baso-lateral membrane (\uparrow Na⁺-K⁺ATPase)

On colon (distal colon)

- \uparrow Na⁺ reabsorption

On glands (sweat glands and salivary glands)

- \uparrow Na⁺ reabsorption