MINERALOCORTICOIDS

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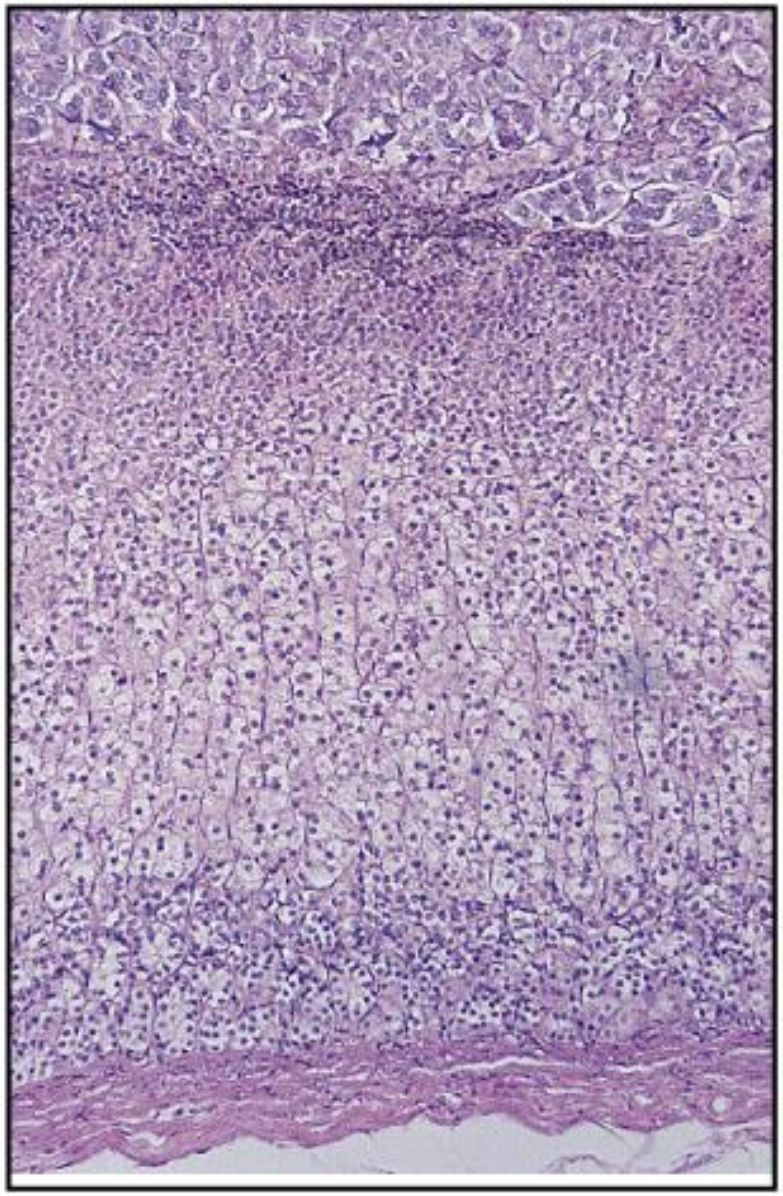
gion of adrenal gland



Adrenal medulla

Zona reticularis

Adrenal cortex

Zona fasciculata

Zona glomerulosa

Capsule

Secretes

Catecholamines

Sex hormones

Glucocorticoids

Aldosterone

Hormones of Adrenal gland

- **Cortex: (Secretes steroid hormones)**
  - Glucocorticoids.
  - **Mineralocorticoids.**
  - Androgens.
- **Medulla (Amino acid secretions)**
  - Catecholamines

Mineralocorticoids:

Aldosterone

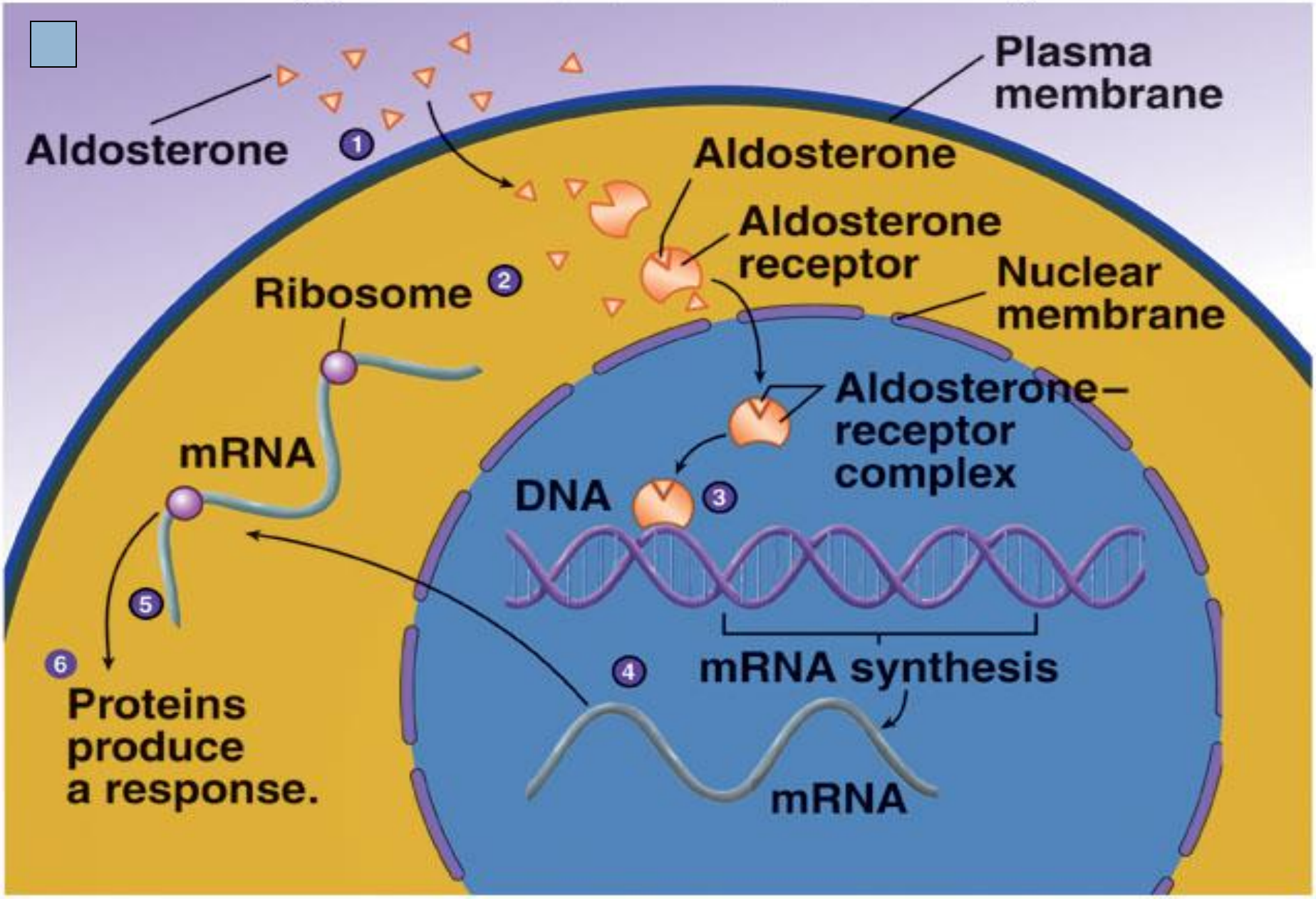
- A steroid hormone.
- Essential for life.
- Responsible for regulating Na^+ reabsorption in the distal tubule and the cortical collecting duct
- Target cells are called “principal (P) cell”.

- It also affects Na+ reabsorption by sweat, salivary and intestinal cells. Stimulates synthesis of more Na/K-ATPase pumps.
- Much of secreted aldosterone is converted in the liver to tetrahydroglucuroind derivative.

Aldosterone, cont……

- Aldosterone exerts the 90% of the mineralocorticoid activity.
- Cortisol also have mineralocorticoid activity, but only 1/400th that of aldosterone.

- Secreted by Zona glomerulosa.



Aldosterone action

- Maintains extracellular fluid volume by conserving body sodium. Aldosterone stimulates sodium & potassium transport in sweat glands, salivary glands, & intestinal epithelial cells.

Aldosterone action

- Aldosterone stimulates the active secretion of potassium from the distal tubular cell into the urine.
- Hence aldosterone is critical for disposal of daily dietary potassium load at normal plasma potassium concentrations.
- Stimulates secretion of H+ by the kidney.

Regulation of aldosterone secretion

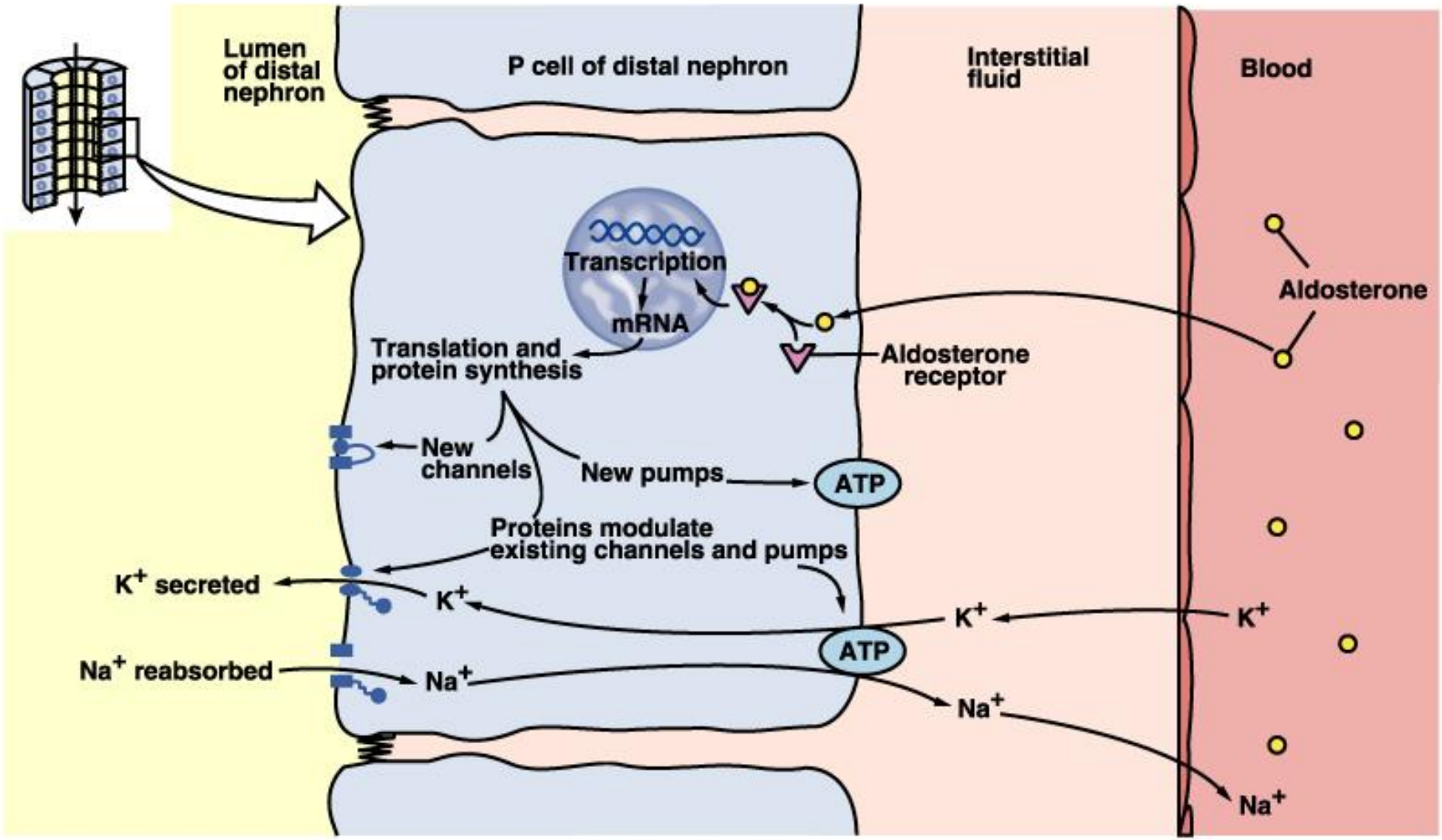
- Direct stimulators of release:

  High plsama potassium level

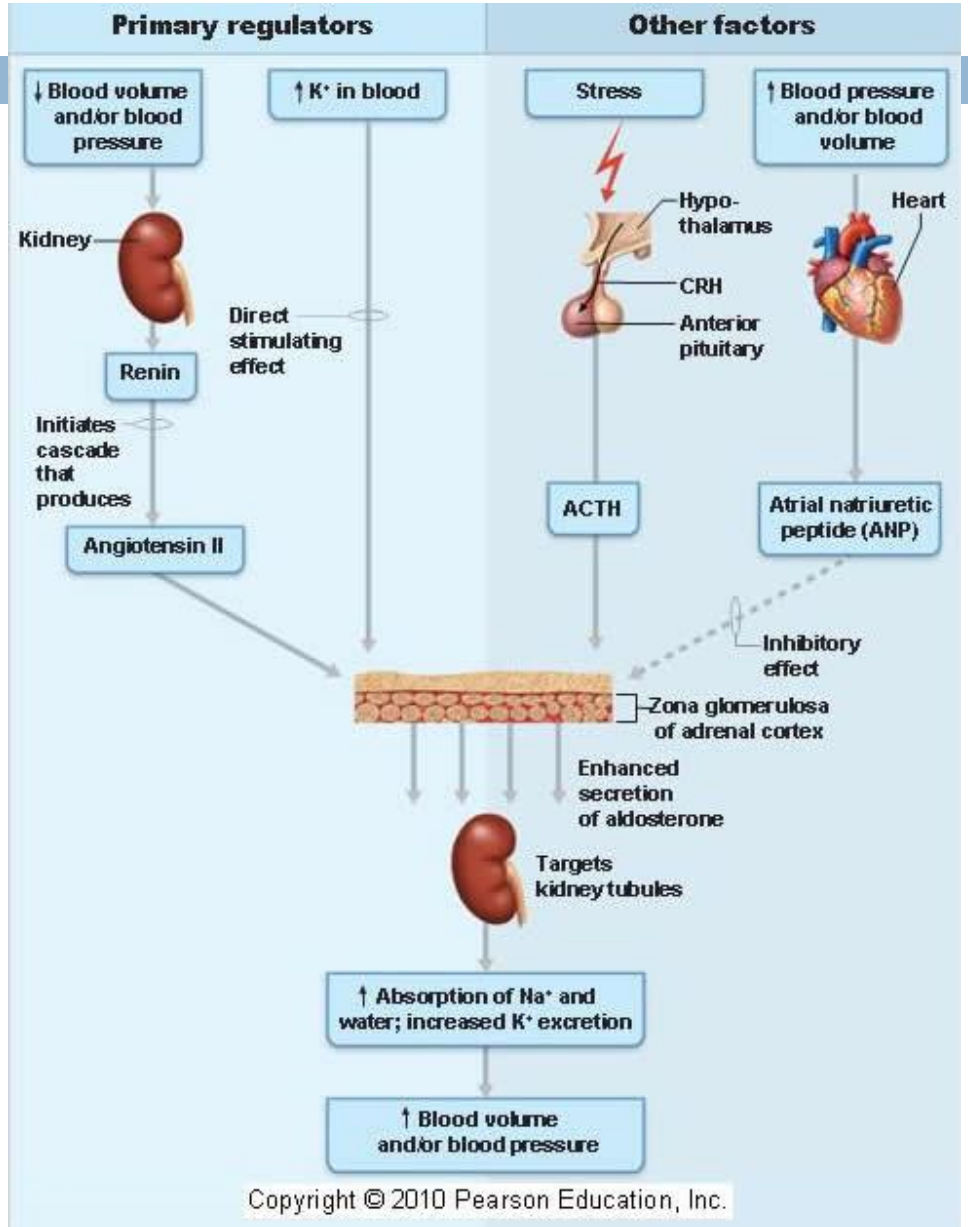
  ACTH

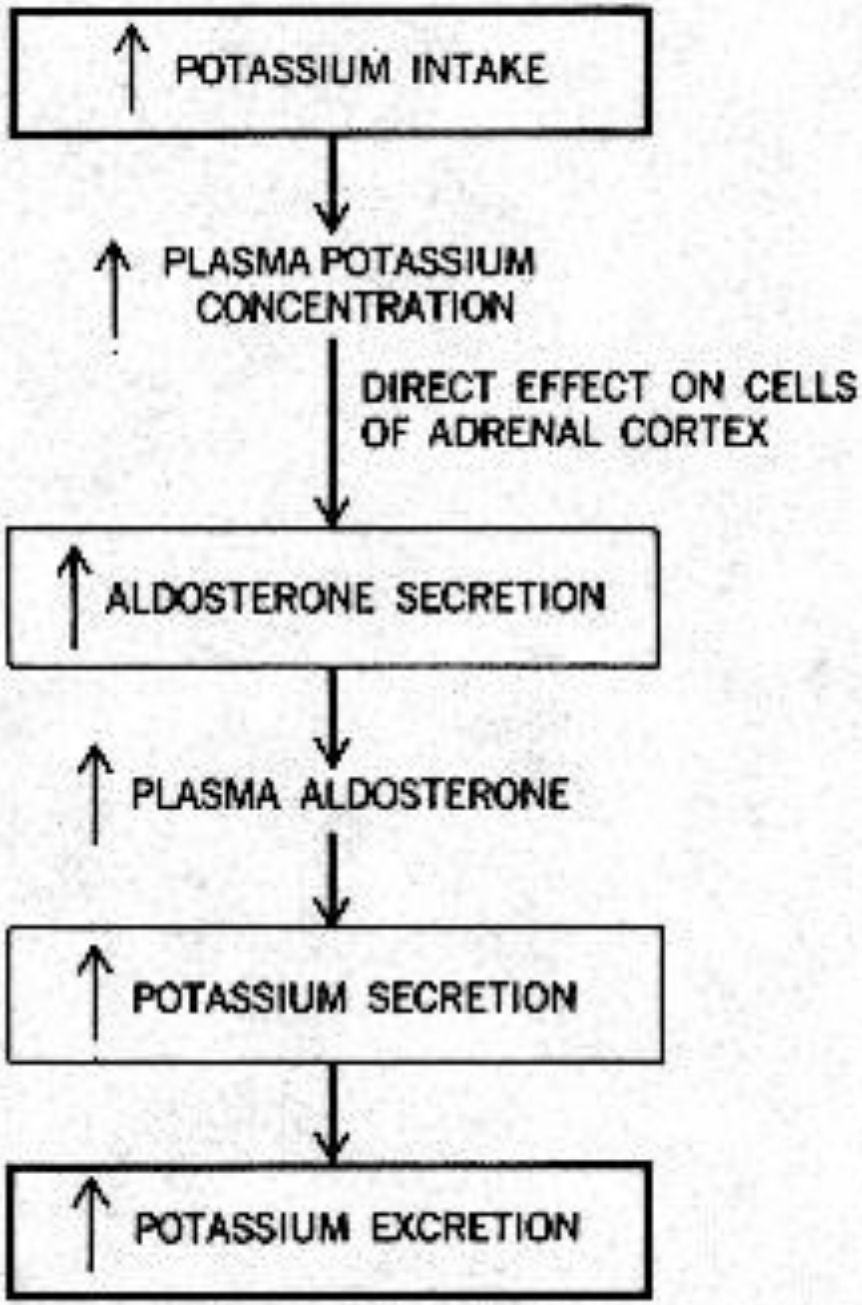
- Indirect stimulators of release:

  Ang II (RAAS): this system is activated by renal ischemia and low Na+ conc. At macula densa.


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+

Regulation of Aldosterone secretion





Pathway by which an increased potassium intake induces greater potassium excretion mediated by aldosterone

Potassium stimulates aldosterone synthesis by depolarizing *zona glomerulosa* cell membranes

Role of ACTH in Aldosterone synthesis/release

- ACTH also stimulates aldosterone synthesis.
- However the ACTH stimulation is more transient than the other stimuli and is diminished within several days.

- Aldosterone levels fluctuate diurnally—highest concentration being at 8 AM, lowest at 11 PM, in parallel to cortisol rhythms.

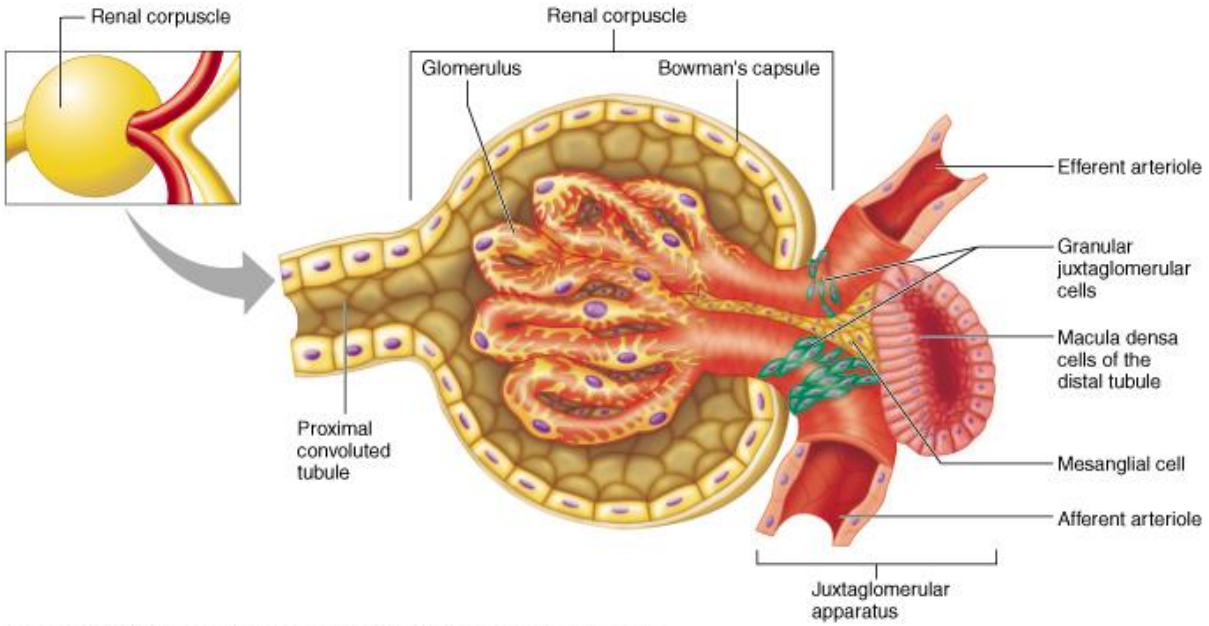
Juxtaglomerular apparatus (JGA)

JGA

A specialized collection of two cell types:

- Macula densa cells
- Juxtaglomerular cells

located at the juncture of the afferent and efferent arterioles with a portion of the distal convoluted tubule of the nephron of the kidney



JGA

- **Macula densa cells –**
  - Specialized **chemoreceptor** cells in the wall of the distal convoluted tubule
  - respond to changes in solute concentration (especially sodium levels) in the tubular fluid.
  - Information is conveyed to the juxtaglomerular cells which will adjust their output of renin accordingly.

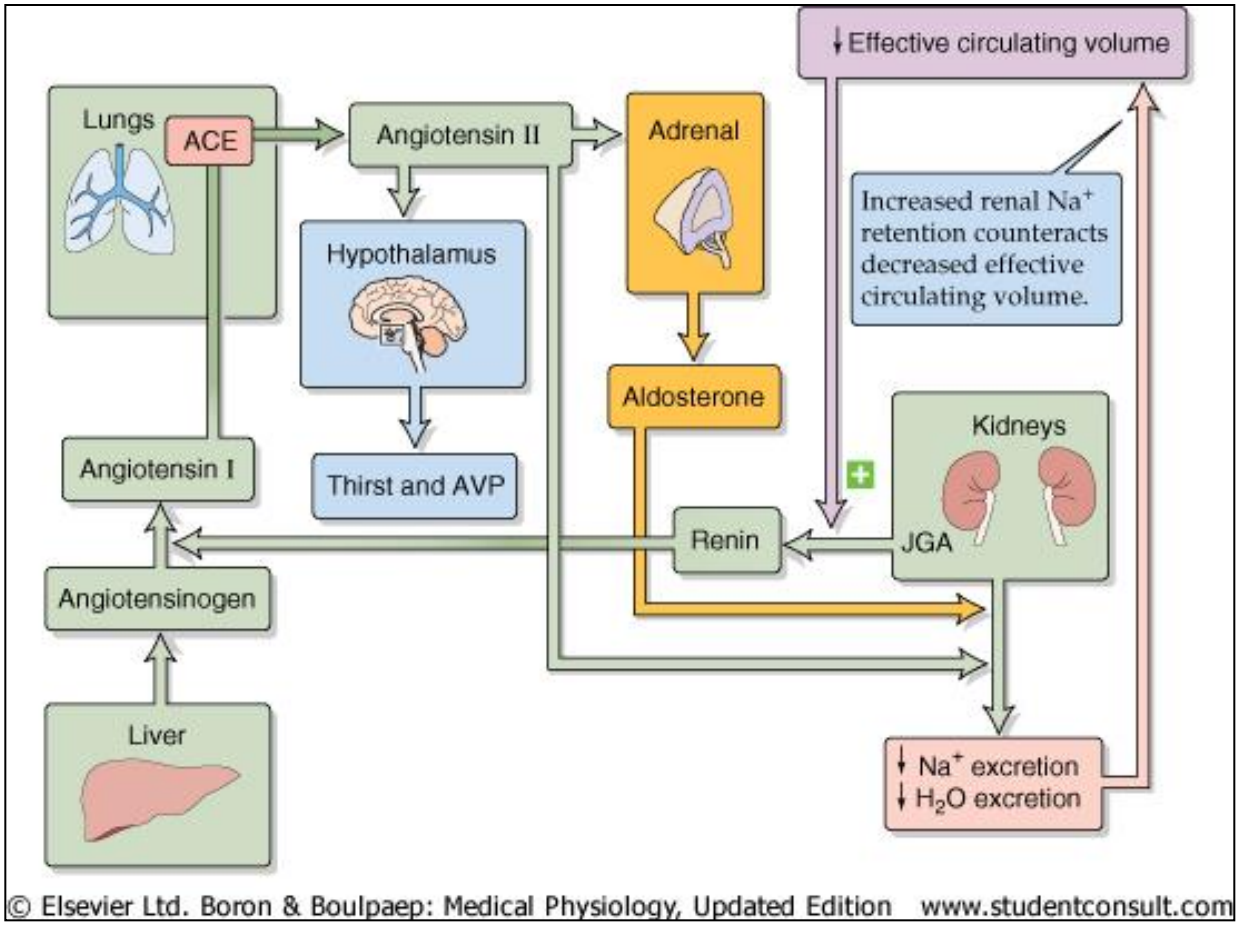
- **Juxtaglomerular cells**
  - Specialized smooth muscle cells which act as **mechanoreceptors** which stretch in response to increases in the blood pressure of the afferent arteriole
  - synthesize and secrete the enzyme renin

Renin-angiotensin-aldosterone axis

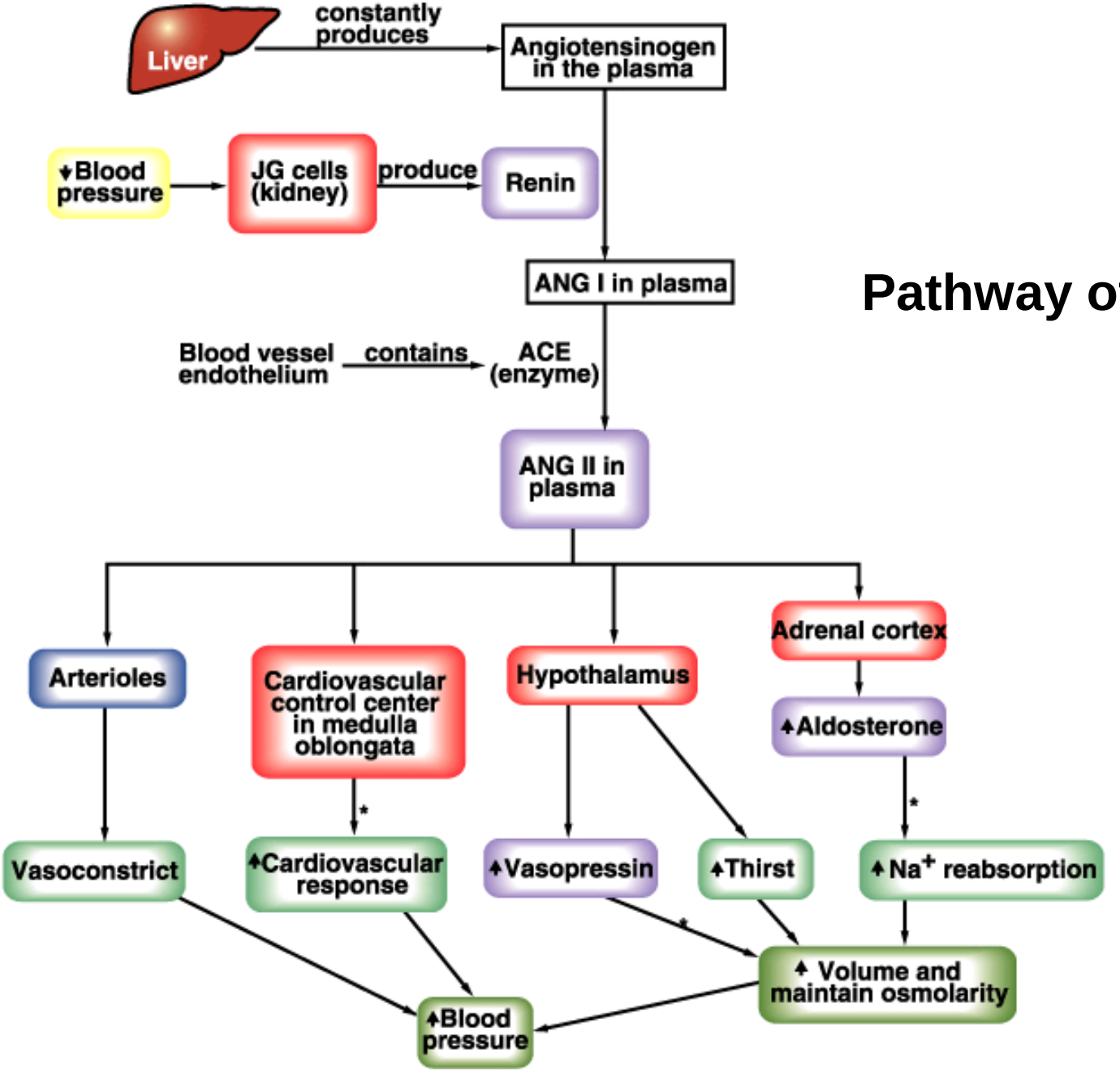
Principal factor controlling Ang II levels is renin release.

Decreased circulating volume stimulates renin release via:

- Decreased BP (symp effects on JGA).
- Decreased [NaCl] at macula densa ("NaCl sensor")
- - Decreased renal perfusion pressure ("renal" baroreceptor)



Pathway of RAAS



Role of AngII in Aldosterone synthesis

- **Angiotensin II** acts on the *zona glomerulosa* to stimulate aldosterone synthesis.
- Angiotensin II acts via increased intracellular cAMP to stimulate aldosterone synthesis.

Adrenal insufficiency

- **Addison's Disease**

- Inadequate amounts of adrenocortical hormones due to bilateral destruction of adrenal cortices.
- Causes;
- Autoimmunity.
- TB
- Radiation.
- Malignancy.

Mineralocorticoid Deficiency

- Lack of aldosterone:
  - Increased loss of sodium, chloride, water
  - Decrease ECF volume
  - Hyperkalemia
  - Mild acidosis
  - Plasma sodium decreases and may lead to circulatory collapse. Decrease cardiac output – shock - death within 4 days to a 2 weeks if not treated.

Hyperaldosteronism

Hyperaldosteronism can be caused by:

- Primary overproduction of aldosterone in conditions such as Conn's syndrome.

Clinical Features of Primary Aldosteronism

- Hypertension.
- Hypokalemia
- Nocturnal polyuria & polydipsia
- Increased tubular (intercalated cells) hydrogen ion secretion, with resultant mild alkalosis.
- Neuromuscular manifestations
  - weakness, paresthesia
  - intermittent paralysis

Tests Confirming the Diagnosis of Primary Aldosteronism

- Plasma supine aldosterone at 0800h > 15 ng/dl
- Urinary aldosterone metabolites
  - 18-Monoglucuronide > 20 ug/24h
  - Tetrahydroaldosterone > 65 ug/24h
- NaCl infusion/ suppression test -- PA > 10 ng/dl