REGULATION OF EXTRACELLULAR FLUID VOLUME AND OSMOLALITY

Blood Osmolality (mOsm/L) equals:

$2[Na^+]$ (mEq/L) + 0.055[Glucose] (mg/dL) + 0.36[BUN] (mg/dL)

Chapter 28
pages 348 – 364

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OBJECTIVES

At the end of this lecture you should be able to:

- Identify and describe the role of the Sensors and Effectors in the renal regulation of body fluid volume & osmolality
- describe the role of the kidney in regulation of body fluid volume & osmolality
- Understand the role of ADH in the reabsorption of water and urea
- Identify the site and describe the influence of aldosterone on reabsorption of Na^+ in the late distal tubules.

Renal regulation of ECF Volume & Osmolality

Is a reflex mechanism in which variables reflecting **total body sodium** and **ECV** are monitored by appropriate sensors

Regulation of ECF volume =
Regulation of body Na^+ =
Regulation BP

Thus, regulation of Na^+ is also dependent upon baroreceptors.

Renal Regulation of ECV

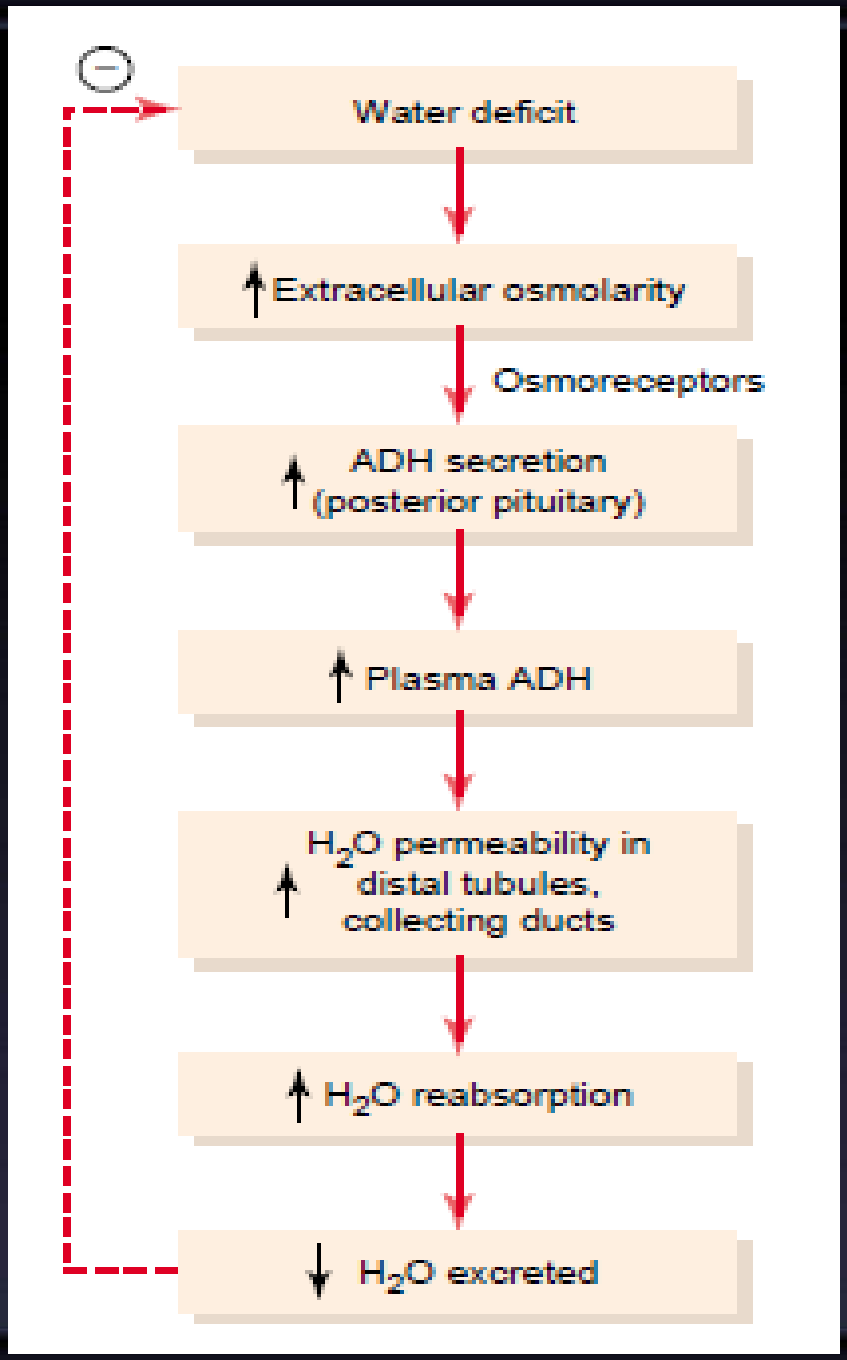
- **Sensor**
  - Carotid sinus
  - Volume receptors (large vein, atria, intrarenal artery)
- **Effectors**
  - Rennin/angiotensin, aldosterone
  - Renal sympathetic nerve
  - ANF
  - ADH
- **Affecting**
  - Urinary Na excretion

Renal regulation of blood osmolality

- **Sensors**
  - Hypothalamic osmoreceptors
- **Effectors**
  - ADH
  - thirst
- **Affecting**
  - Urine osmolaity
  - Water intake

Osmoreceptor ADH Feedback System

1. INCREASED OSMOLALITY
2. DECREASED ARTERIAL PRESSURE
3. DECREASED BLOOD VOLUME



FACTORS AFFECTING ADH

Increase ADH	Decrease ADH
↑ Osmolarity	↓ Osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure

Renal Sympathetic

↓ ECV → ↑ renal sympathetic activity → stimulate Na absorption by direct tubular effect mediated through α-receptors on renal tubules (mainly PCT) to correct for low ECV

High Osmolality

Low ECF Volume

decreases 15 to 25 percent or more

Osmoreceptors

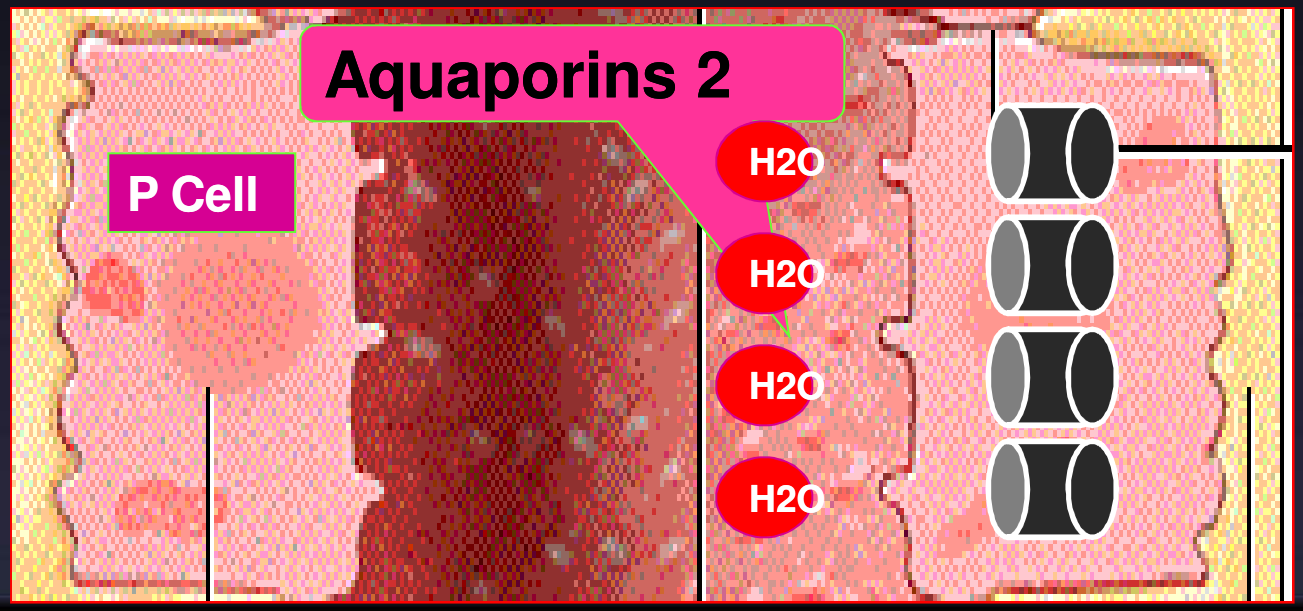
Lat Hypothalamus

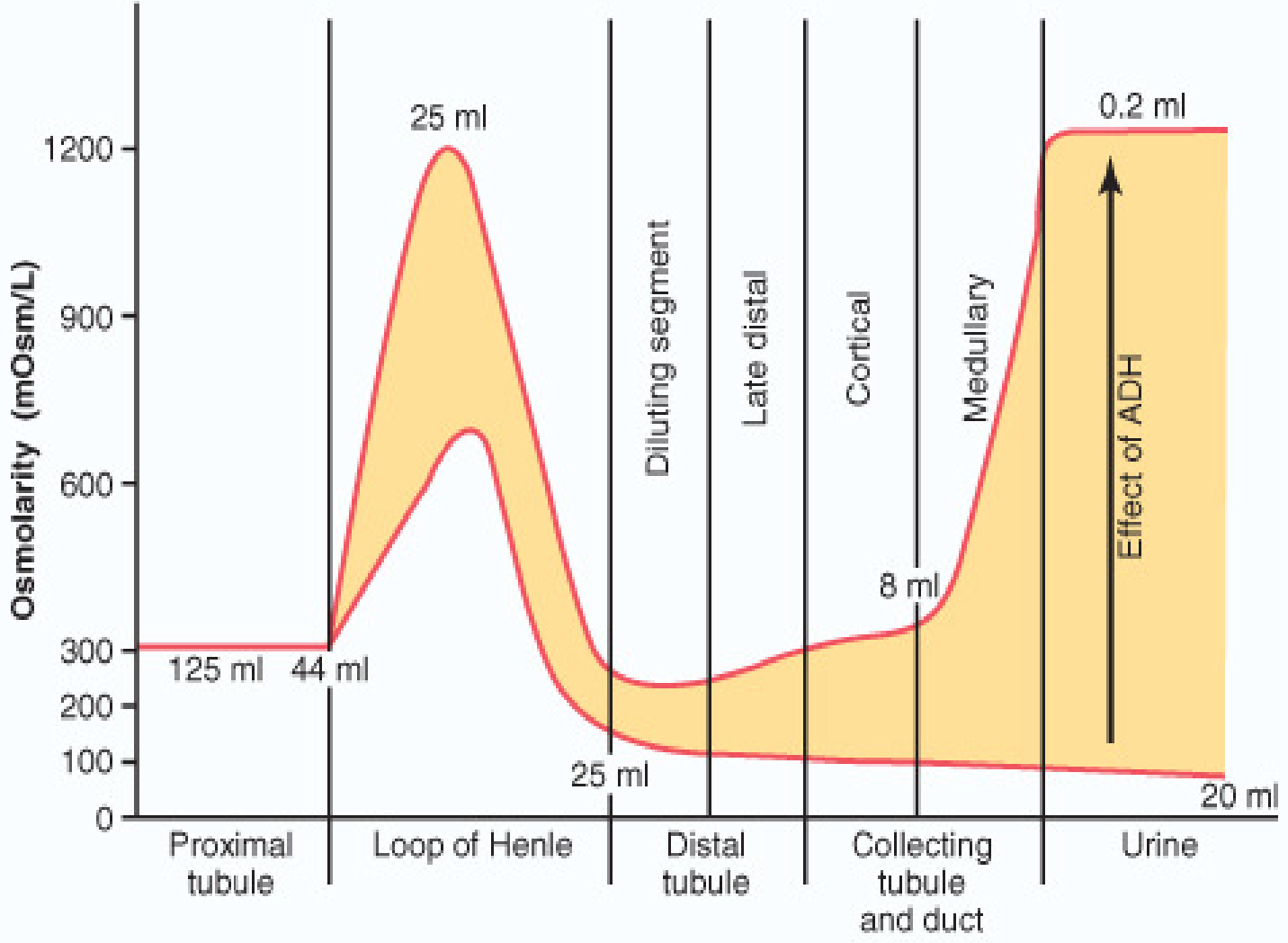
(Stimulate Thirst)

Low Pressure Receptors

Atria Aortic Carotid Pulmonary

↑ADH




Osmolarity (mOsm/L)
1200
900
600
300
200
100
0
125 ml
44 ml
25 ml
25 ml
8 ml
0.2 ml
20 ml
Diluting segment
Late distal
Cortical
Medullary
Effect of ADH
Proximal tubule
Loop of Henle
Distal tubule
Collecting tubule and duct
Urine

Thirst

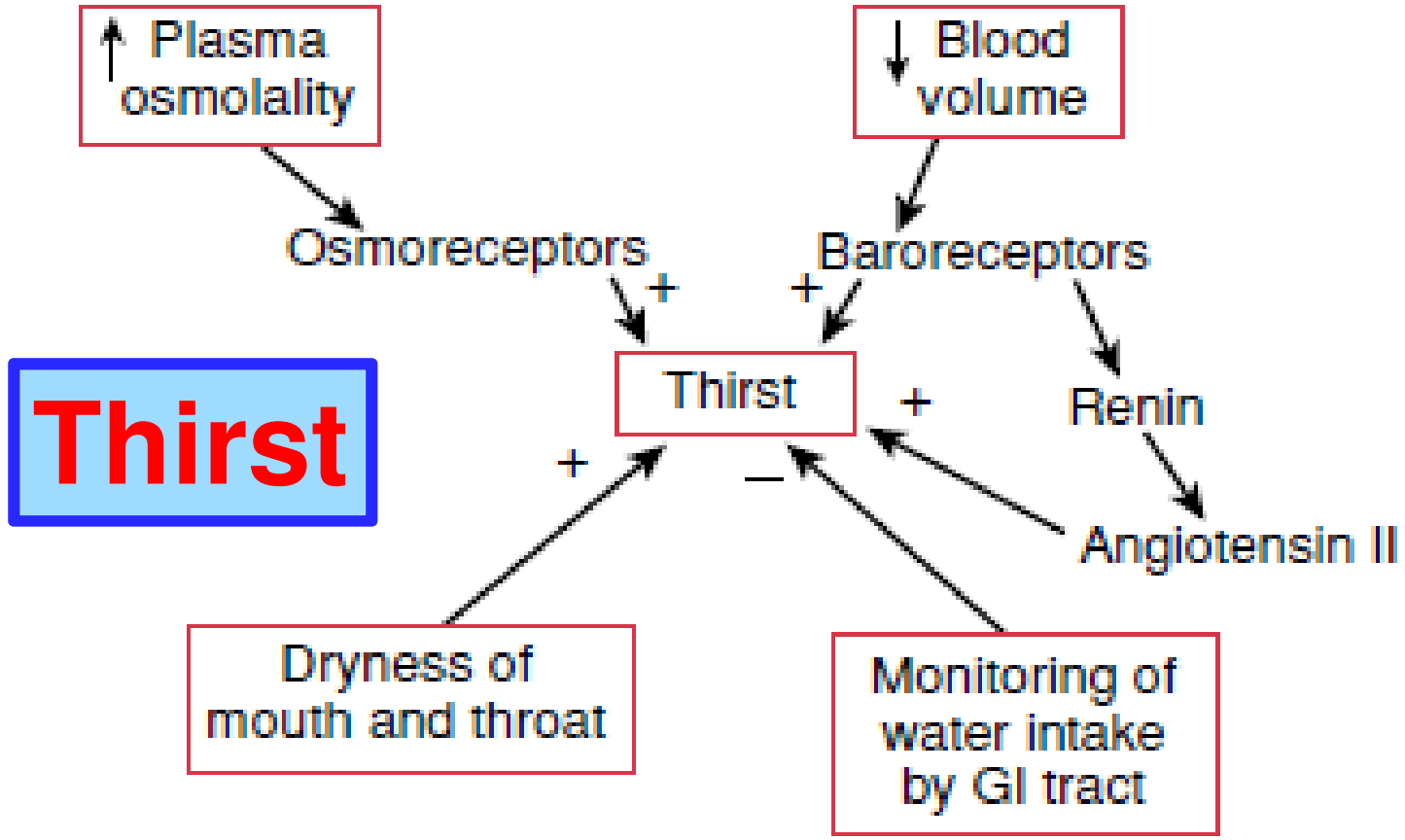
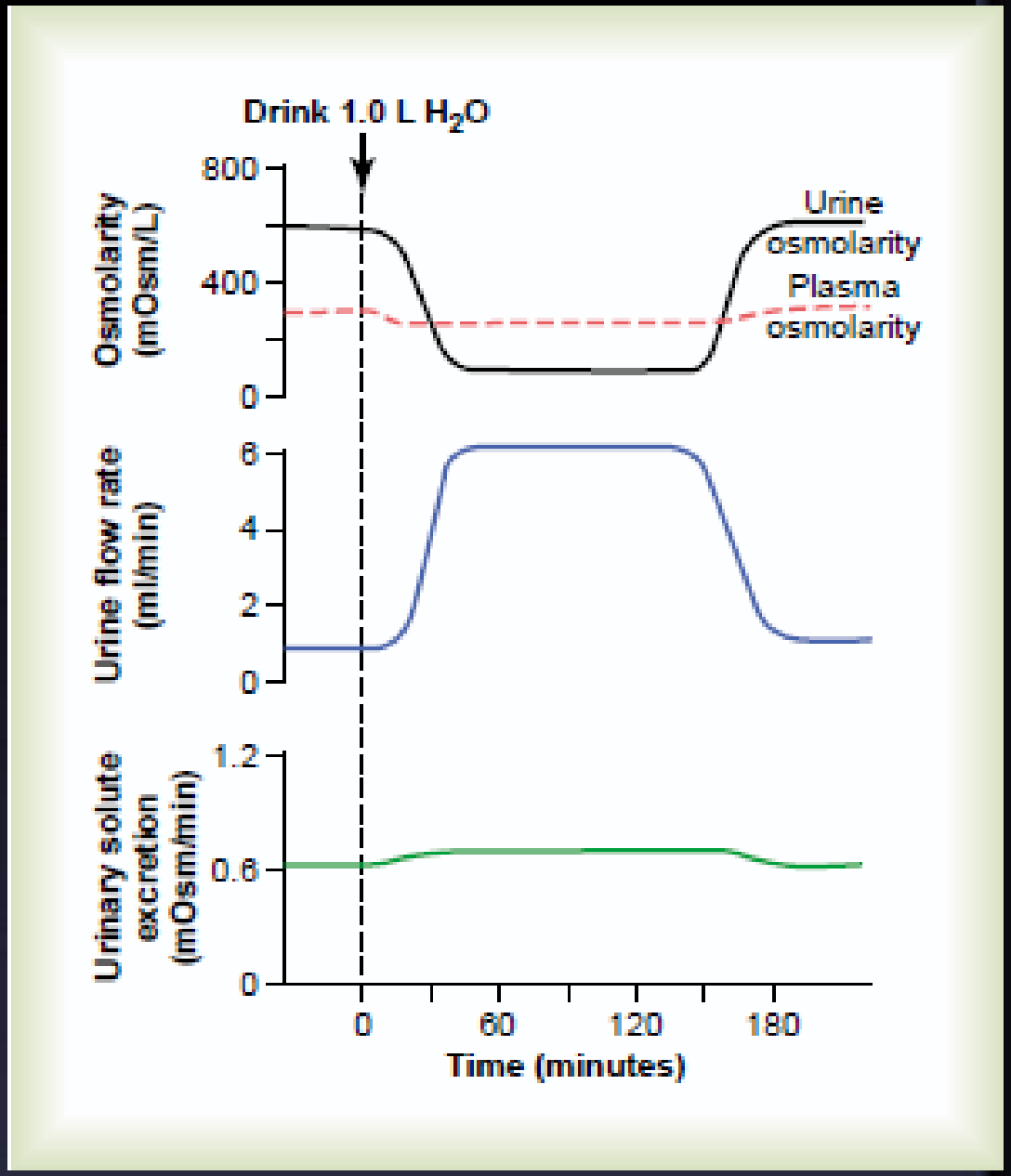


FIGURE 24.7 **Factors affecting the thirst sensation.** A plus sign indicates stimulation of thirst, the minus sign indicates an inhibitory influence.

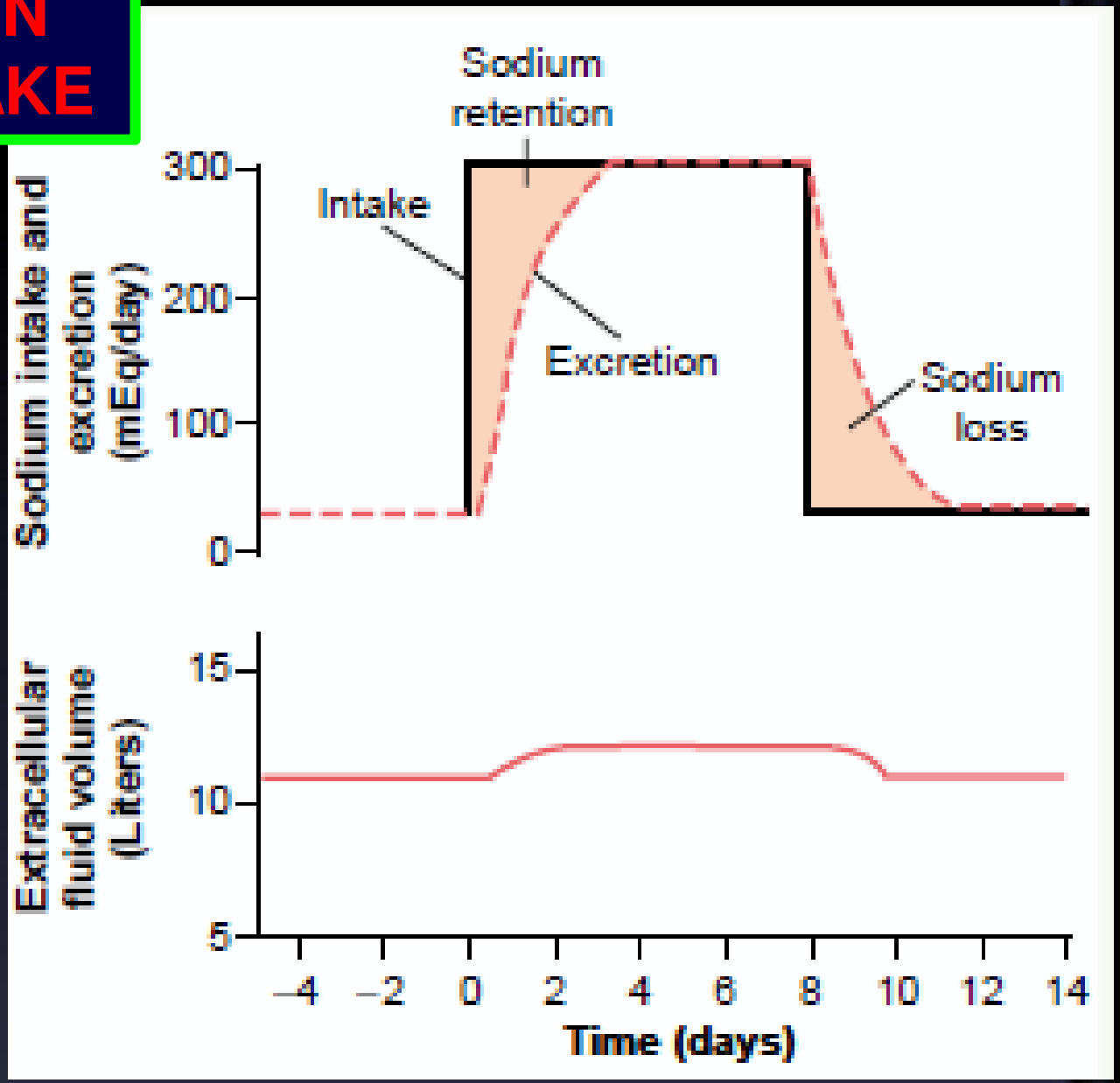
Role of Thirst in Controlling Extracellular Fluid Osmolarity and Sodium Concentration

Increase Thirst	Decrease Thirst
↑ Osmolarity	↓ Osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
↑ Angiotensin	↓ Angiotensin II
Dryness of mouth	Gastric distention

INCREASE IN WATER INTAKE



INCREASE IN SODIUM INTAKE



ATRIAL NATRIURETIC PEPTIDE (ANP)

- INCREASE GLOMERULAR FILTRATION
- INHIBIT Na^+ REABSORPTION.
- INCREASE IN CAPILLARY PERMEABILITY LEADING TO EXTRAVASATION OF FLUID AND A DECLINE IN BLOOD PRESSURE.
- RELAX VASCULAR SMOOTH MUSCLE IN ARTERIOLES AND VENULES
- INHIBIT RENIN SECRETION & ALDOSTERONE

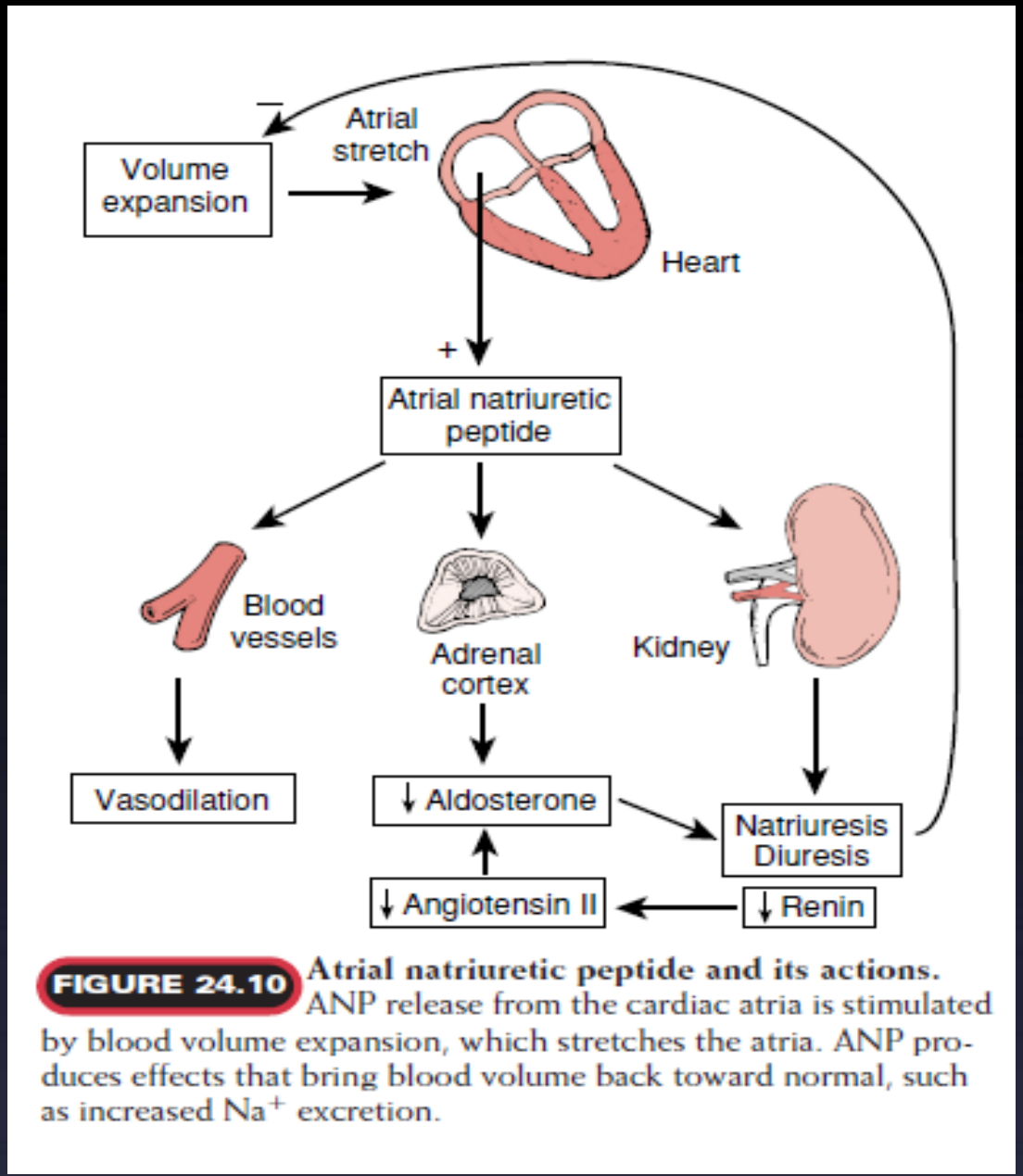
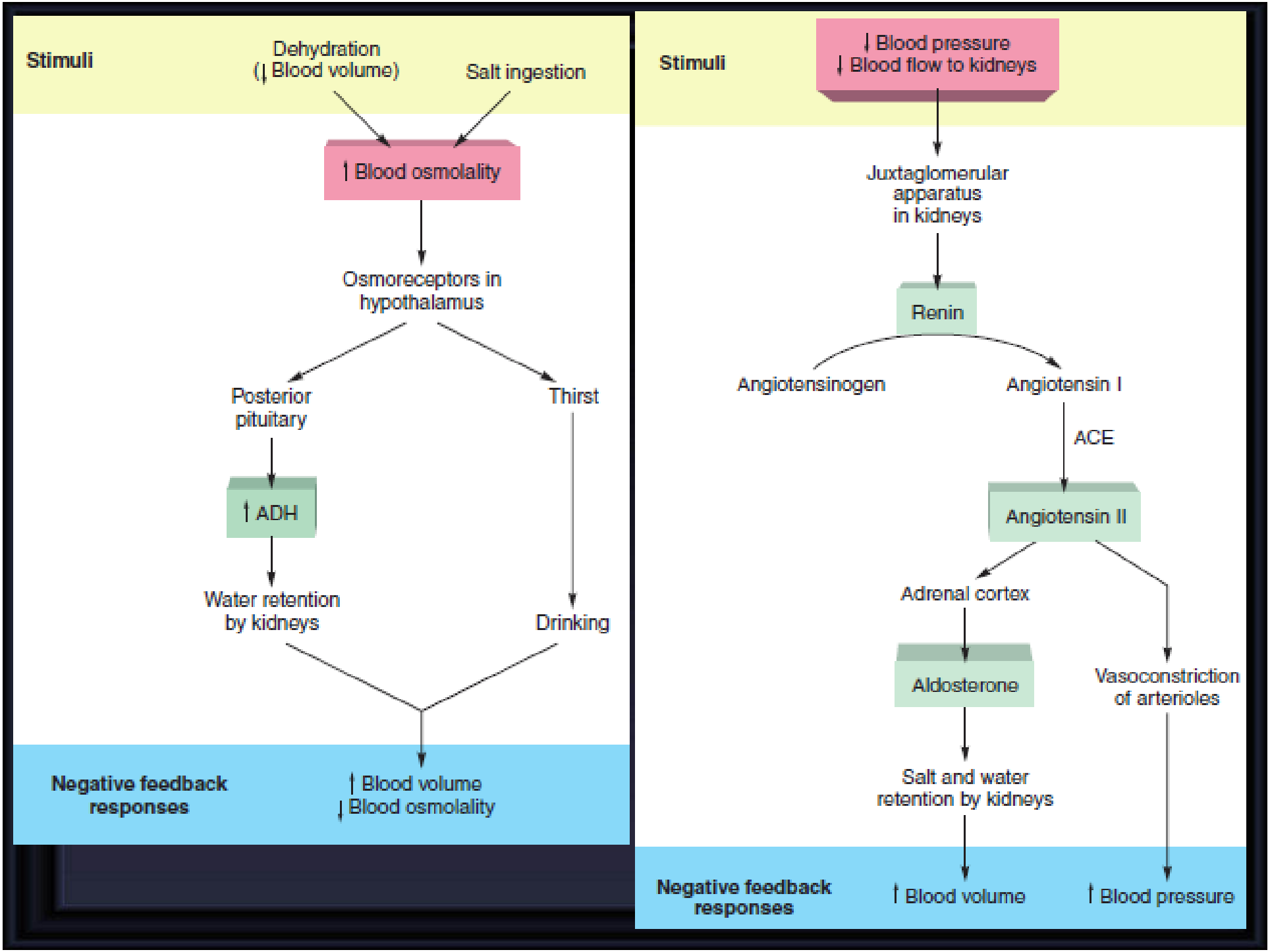
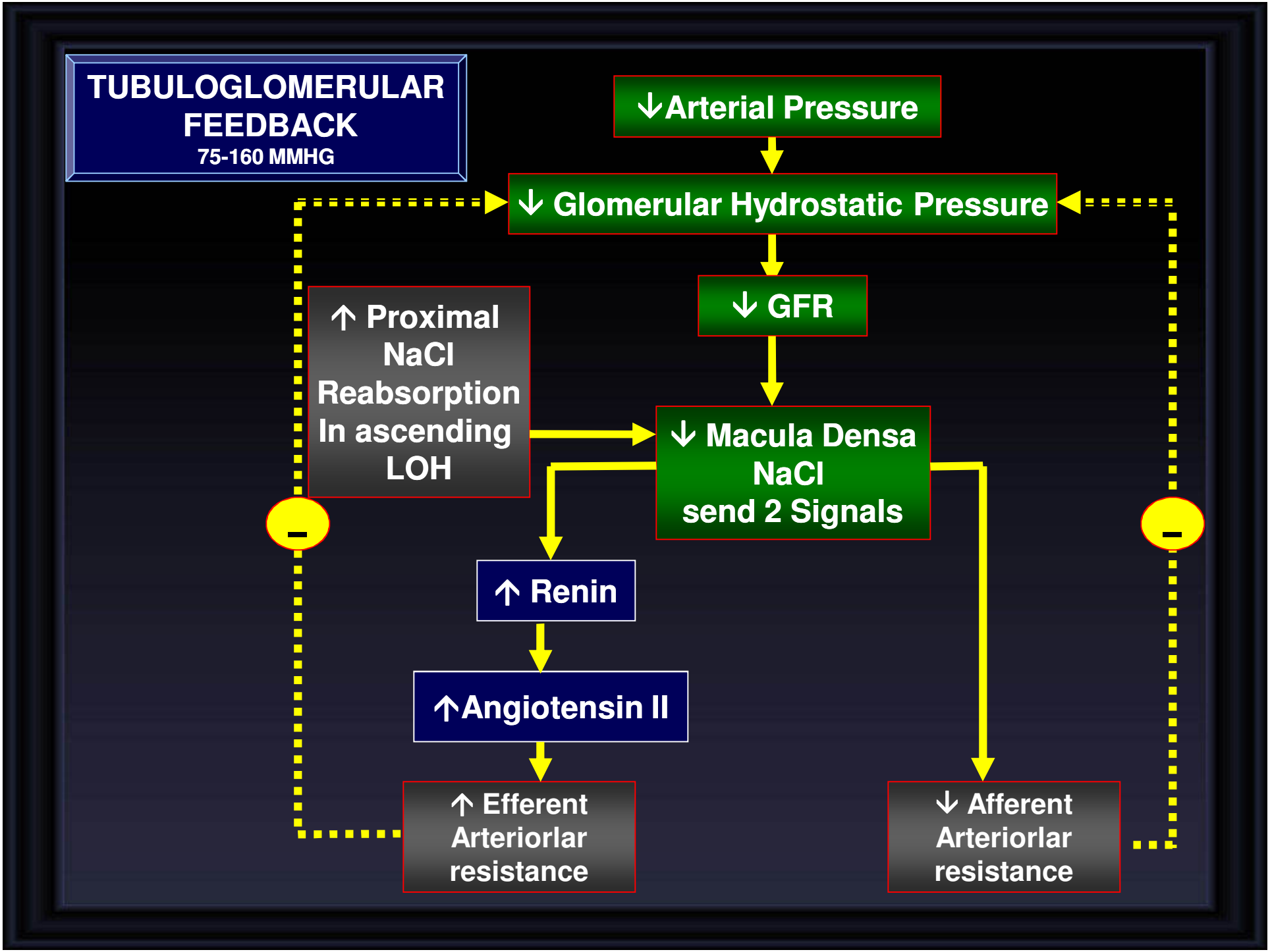


FIGURE 24.10 **Atrial natriuretic peptide and its actions.** ANP release from the cardiac atria is stimulated by blood volume expansion, which stretches the atria. ANP produces effects that bring blood volume back toward normal, such as increased Na^+ excretion.


Stimuli
Dehydration
(↓ Blood volume)
Salt ingestion
↑ Blood osmolality
Osmoreceptors in
hypothalamus
Posterior
pituitary
Thirst
↑ ADH
Water retention
by kidneys
Drinking
Negative feedback
responses
↑ Blood volume
↓ Blood osmolality
Stimuli
↓ Blood pressure
↓ Blood flow to kidneys
Juxtaglomerular
apparatus
in kidneys
Renin
Angiotensinogen
Angiotensin I
ACE
Angiotensin II
Adrenal cortex
Aldosterone
Vasoconstriction
of arterioles
Salt and water
retention by kidneys
Negative feedback
responses
↑ Blood volume
↑ Blood pressure

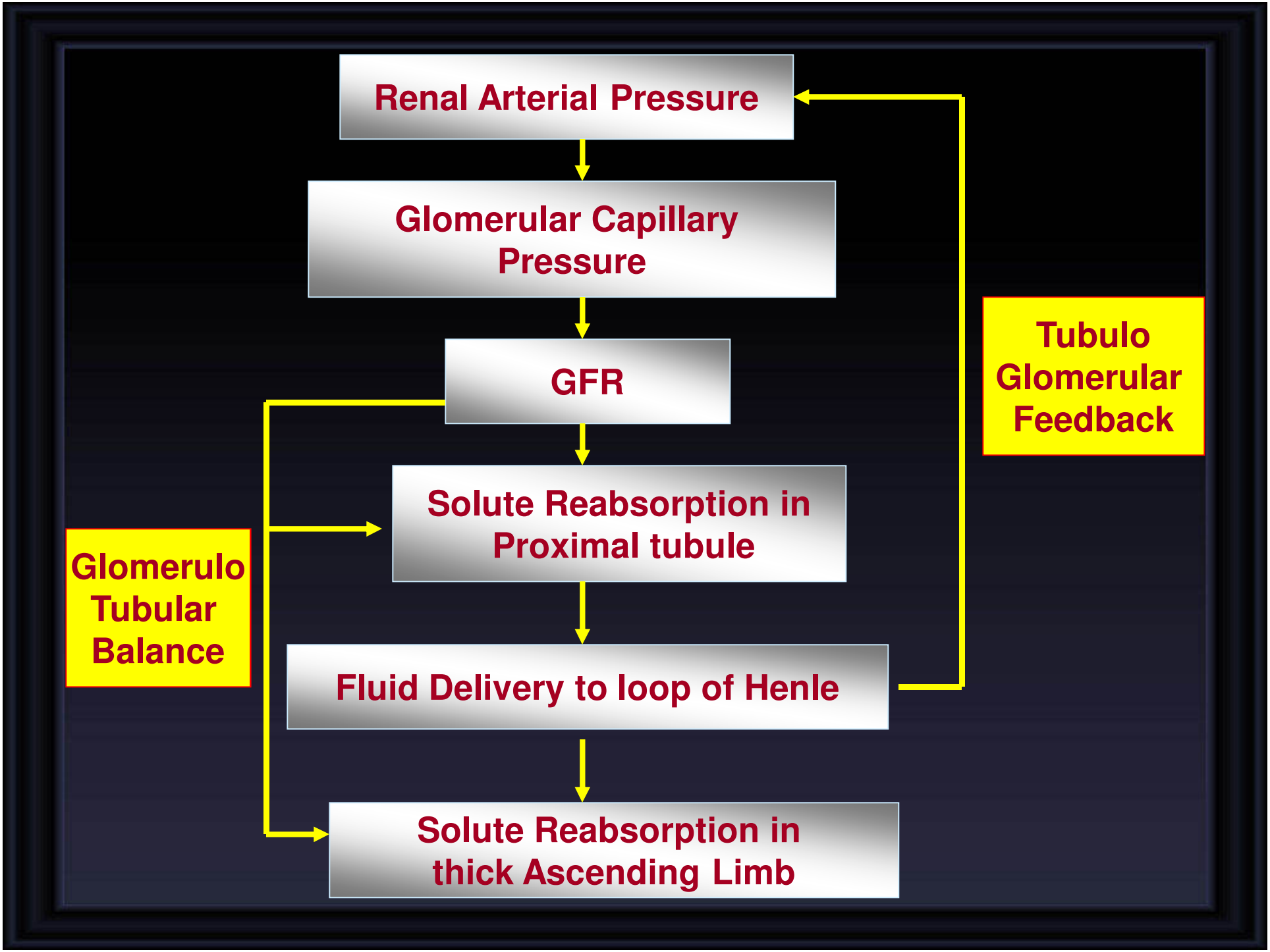
TUBULOGLOMERULAR FEEDBACK


TUBULOGLOMERULAR FEEDBACK
75-160 MMHG
↓Arterial Pressure
↓ Glomerular Hydrostatic Pressure
↓ GFR
↑ Proximal NaCl Reabsorption In ascending LOH
↓ Macula Densa NaCl send 2 Signals
↑ Renin
↑Angiotensin II
↑ Efferent Arteriorlar resistance
↓ Afferent Arteriorlar resistance

GLOMERULOTUBULAR BALANCE

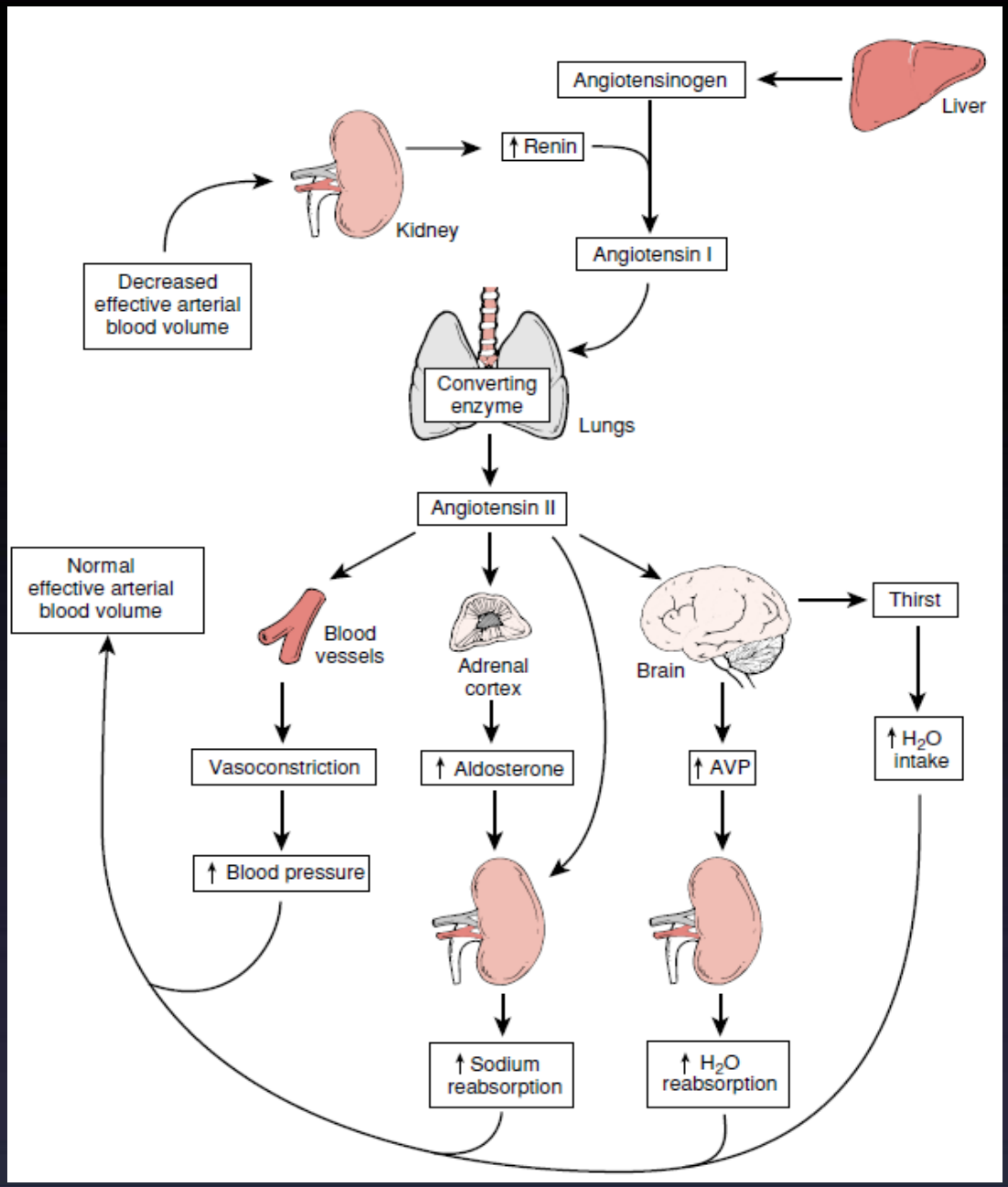
An increase in GFR causes an increase in the reabsorption of solutes to keep the percentage of the solute reabsorbed constant

When the GFR is high, there is a relatively large increase in the oncotic pressure of the plasma leaving the glomeruli via the efferent arterioles and hence in their capillary branches This increases the reabsorption of Na+ from the tubule


Renal Arterial Pressure
Glomerular Capillary Pressure
GFR
Solute Reabsorption in Proximal tubule
Fluid Delivery to loop of Henle
Solute Reabsorption in thick Ascending Limb
Tubulo Glomerular Feedback
Glomerulo Tubular Balance

SODIUM HANDLING

SITE	APICAL TRANSPORTER	FUNCTION
Proximal Tubule	•Na/Gluc CT •Na/Pi CT •Na/Amino Acid •Na/Lactate •Na/H Exchanger •Cl/Base Exchanger	•Na & Gluc Uptake •Na & Pi Uptake •Na & AA Uptake •Na & Lactate Uptake •Na Uptake and H Extrusion •Cl Uptake
Thick Ascending Limb	• Na, 2 Cl,, K CT •Na/H Exchanger •K Channels	•Na, 2 Cl,, K Uptake •Na Uptake and H Extrusion •K Extrusion
EarlyDCT	NaCl CT	Na & Cl Uptake
Late DCTCollecting Duct	Na Channel (ENaC)	Na Uptake


Angiotensinogen
Liver
↑ Renin
Kidney
Decreased effective arterial blood volume
Angiotensin I
Converting enzyme
Lungs
Angiotensin II
Normal effective arterial blood volume
Blood vessels
Adrenal cortex
Brain
Thirst
Vasoconstriction
↑ Aldosterone
↑ AVP
↑ H_2O intake
↑ Blood pressure
↑ Sodium reabsorption
↑ H_2O reabsorption

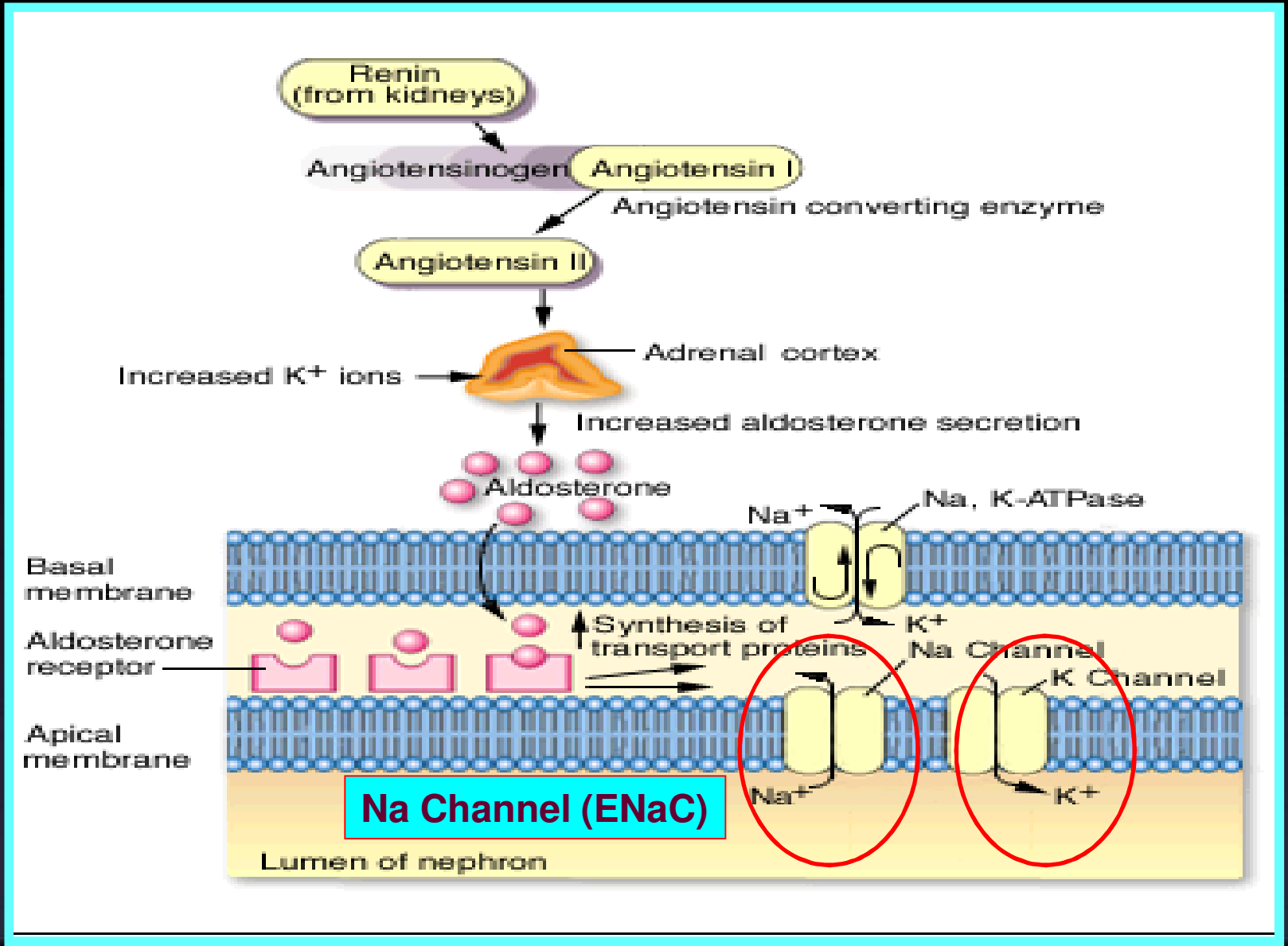
ALDOSTERONE EFFECTS

Renal tubules

Aldosterone acts on collecting duct principal cells

(1)increase the Na permeability of the luminal plasma membrane
(2)increase the number and activity of basolateral plasma membrane Na/K-ATPase pumps
(3)increase the luminal plasma membrane K permeability,
(4)increase cell metabolism.
All of these changes result in increased K secretion.

Effect Of Aldosterone On Cortical Collecting Duct



Factors Affecting Aldosterone Secretion

Stimulatory agents
Angiotensin II
Adrenocorticotropic hormone
High potassium
Sodium deficiency
Inhibitory agents
Atrial natriuretic hormone
High sodium concentration
Potassium deficiency

Regulation of Aldosterone Secretion