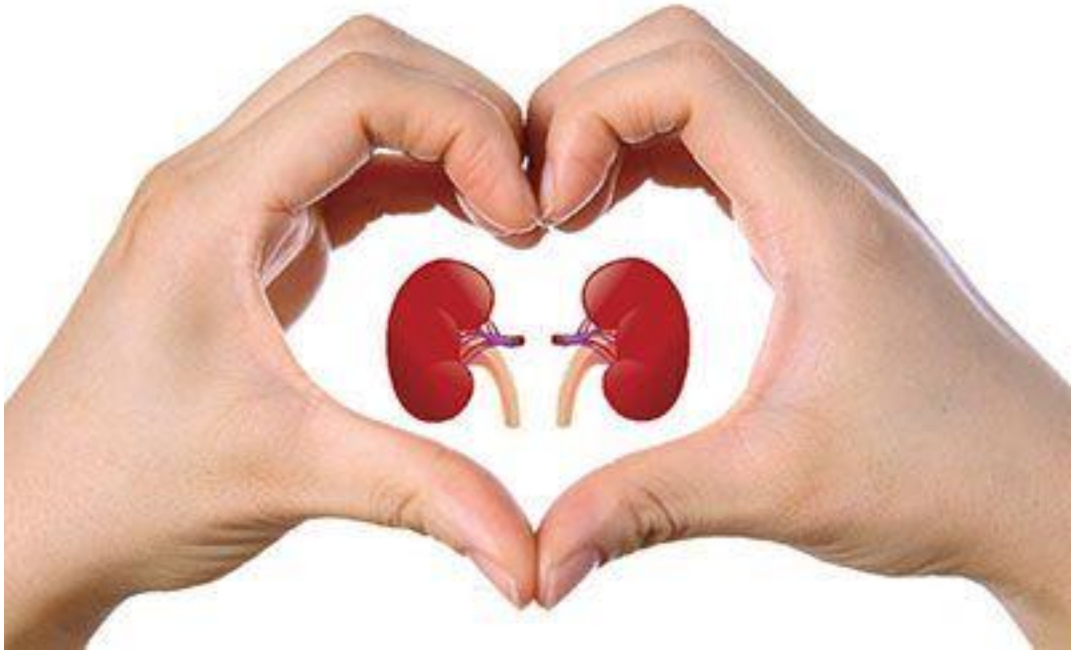
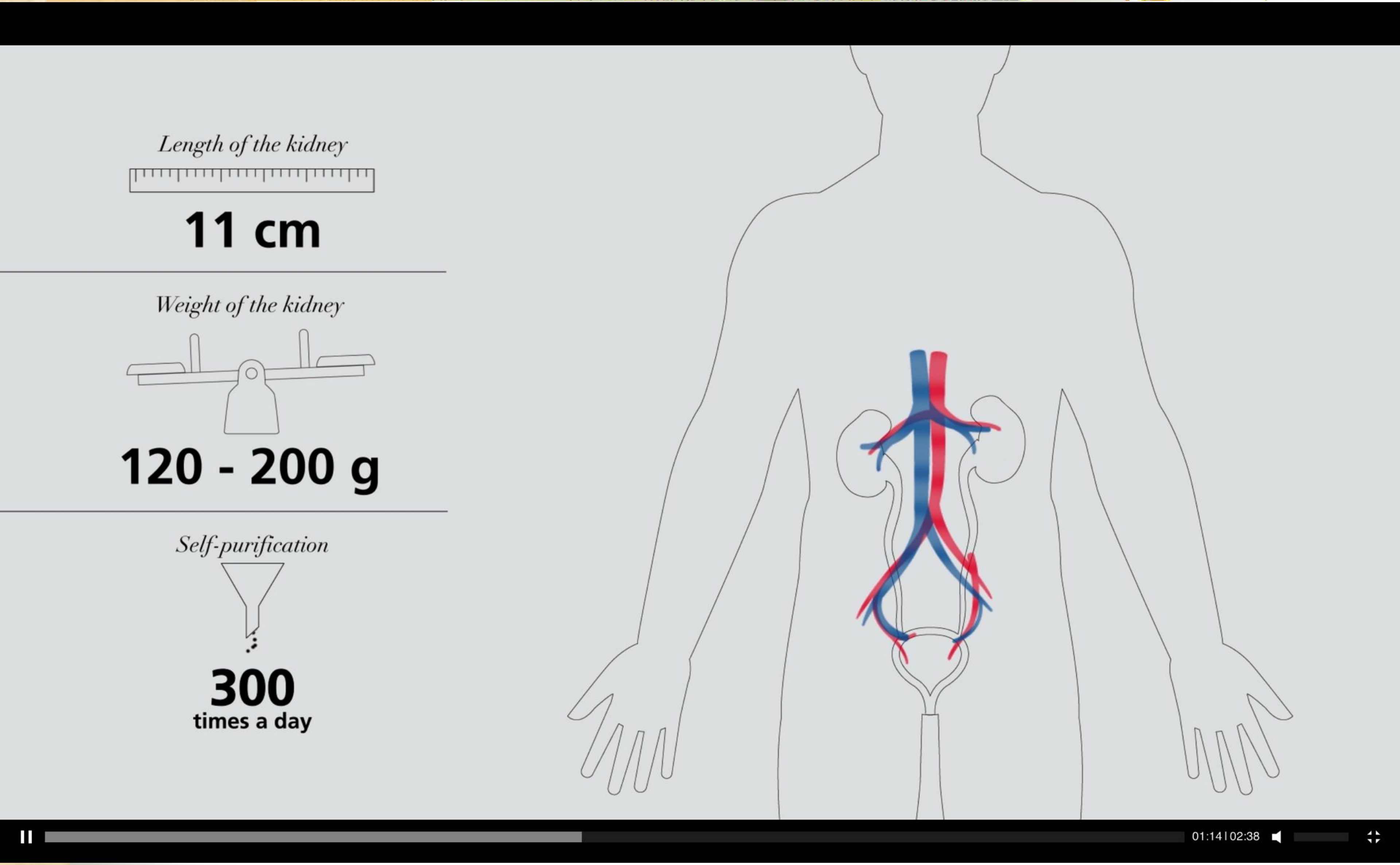
Physiology of kidneys



Dr mirhosseini

Assistant Professor of Nephrology


Length of the kidney
11 cm
Weight of the kidney
120 - 200 g
Self-purification
300
times a day
01:14 | 02:38

Major Functions of the Kidneys

1. Regulation of:
   - body fluid osmolality and volume
   - electrolyte balance
   - acid-base balance
   - blood pressure

2. Excretion of
   - metabolic products
   - foreign substances (pesticides, chemicals etc.)
   - excess substance (water, etc)

3. Secretion of
   - erythropoitin
   - 1,25-dihydroxy vitamin D_3 (vitamin D activation)
   - renin
   - prostaglandin

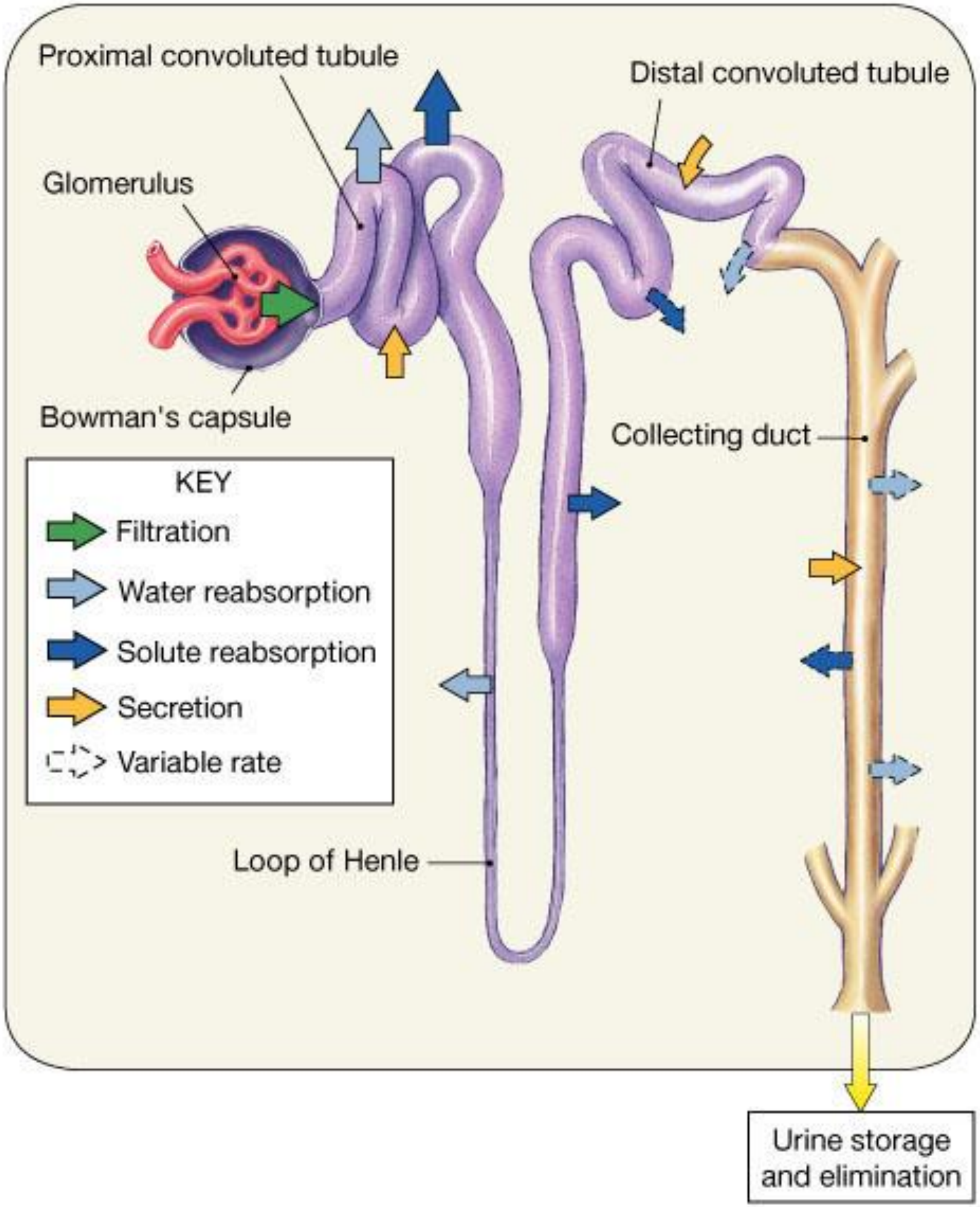
Nephron and Collecting Duct

Nephron: The functional unit of the kidney

Each kidney is made up of about 1 million nephrons

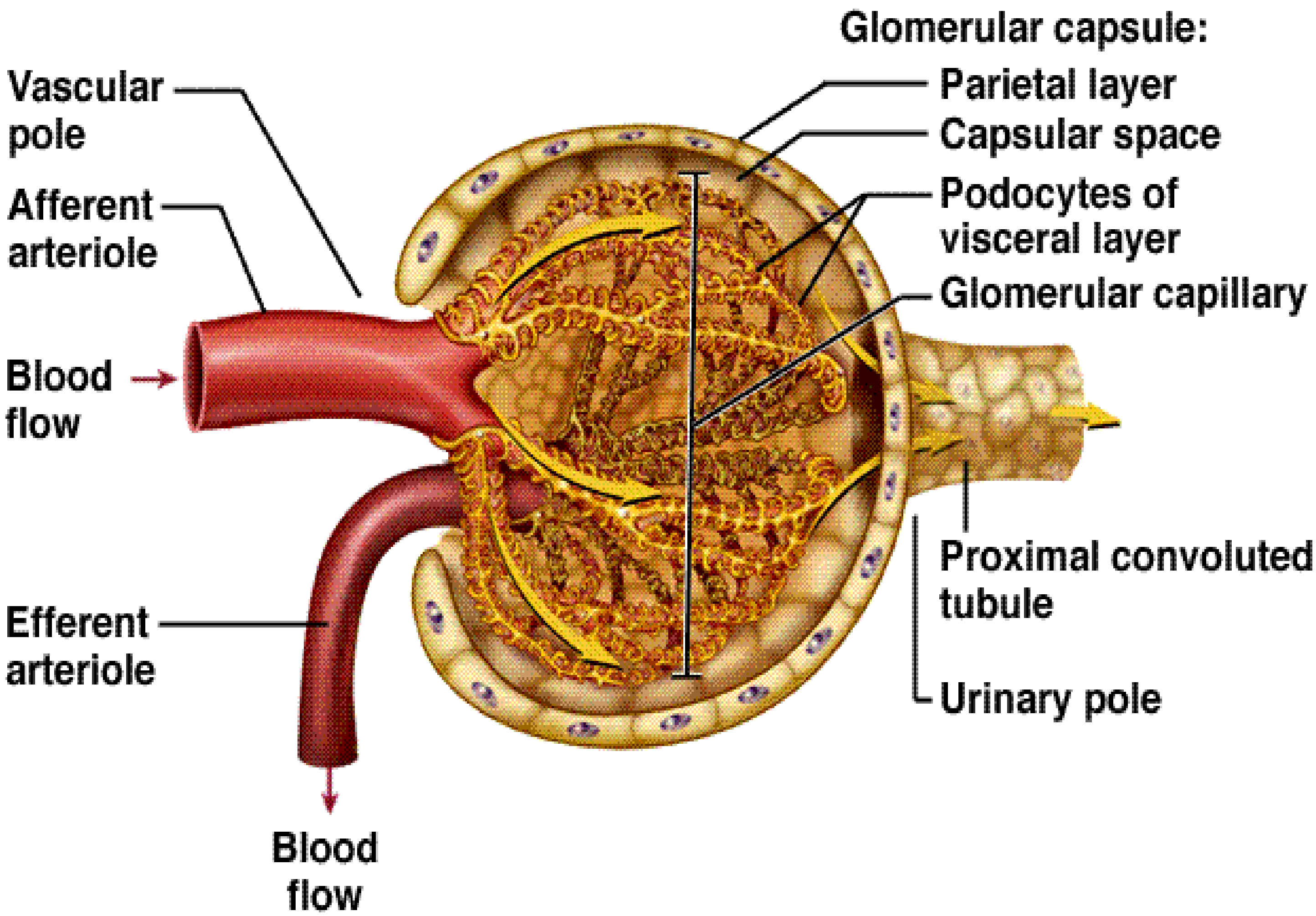
Each nephrons has two major components:

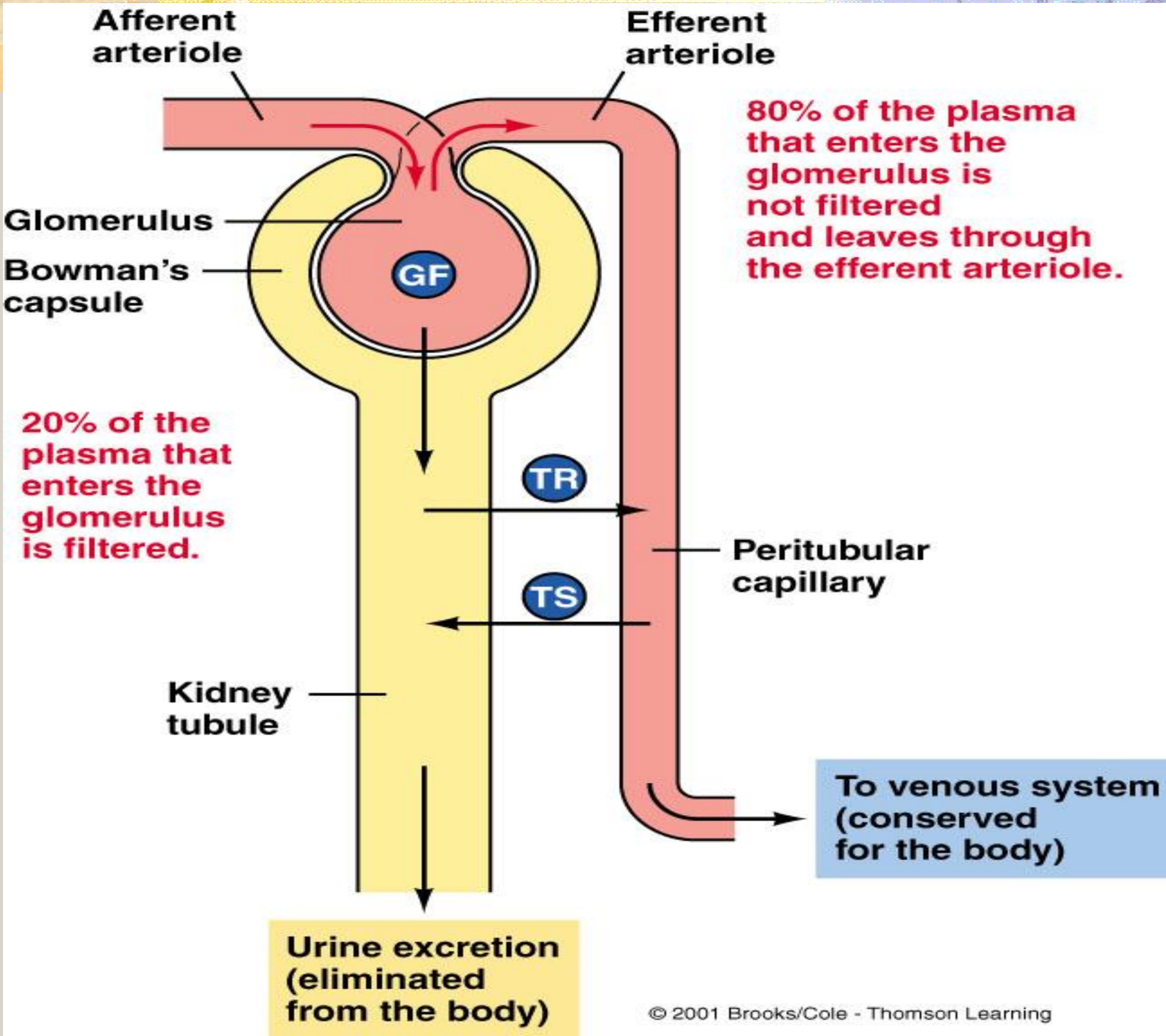
1) A glomerulus
2) A long tube



Renal tubules and collecting duct

The Renal Corpuscle




Afferent arteriole
Efferent arteriole
80% of the plasma that enters the glomerulus is not filtered and leaves through the efferent arteriole.
Glomerulus
Bowman's capsule
GF
20% of the plasma that enters the glomerulus is filtered.
TR
TS
Peritubular capillary
Kidney tubule
To venous system (conserved for the body)
Urine excretion (eliminated from the body)

Determinants and Regulation of Glomerular Filtration

- Renal blood flow normally drains approximately 20% of the cardiac output, or 1000 mL/min
- The hydrostatic pressure gradient across the glomerular capillary wall is the primary driving force for glomerular filtration

Glomerular Filtration

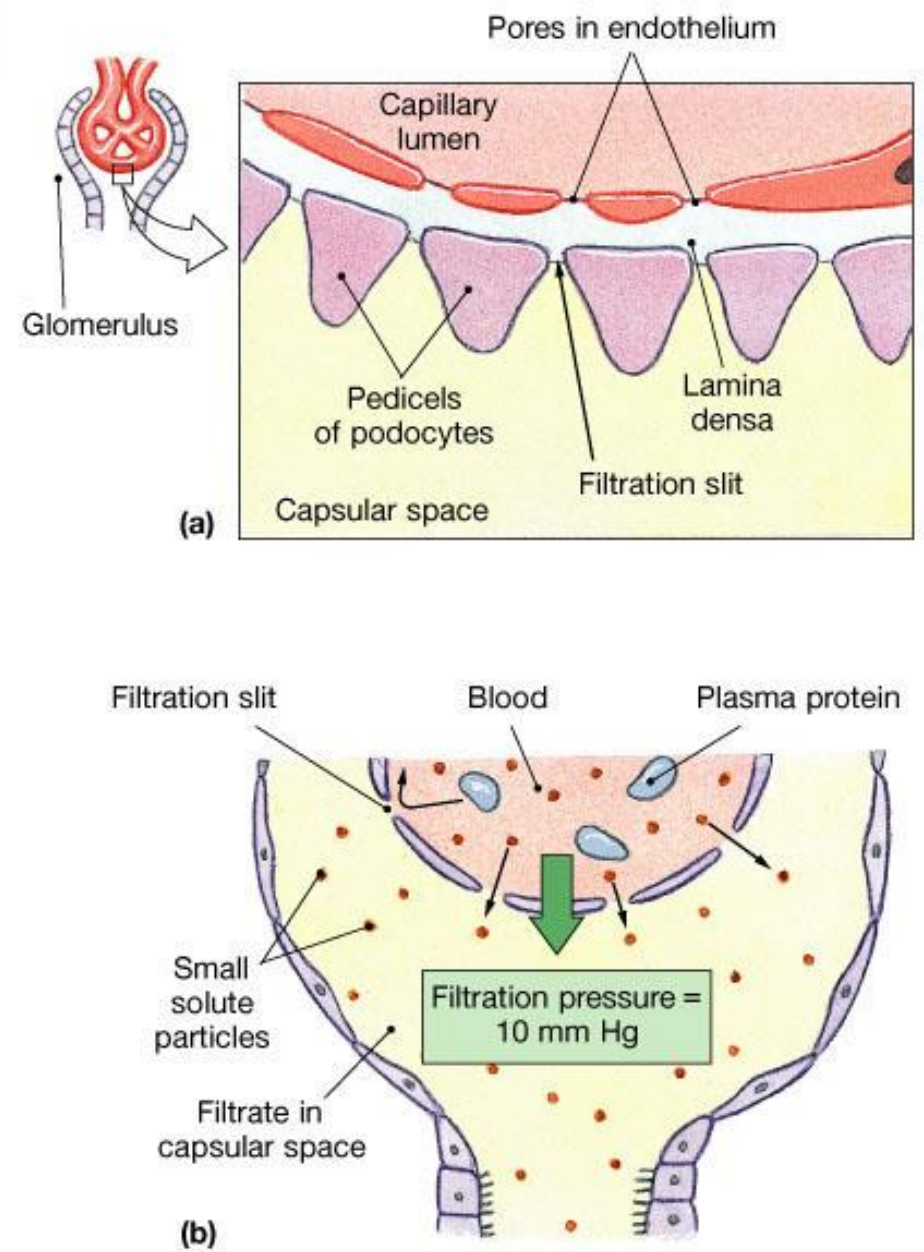
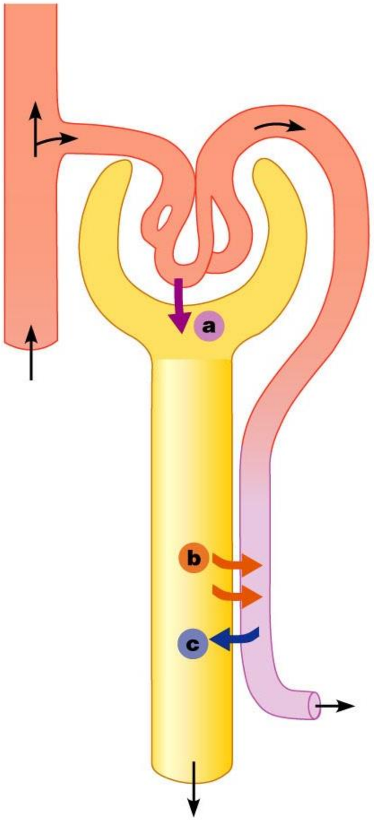


Figure 26.10a, b

Production of urine

- Glomerular filtration: 180 litres / day
- Tubular reabsorption: 178.5 litre
- Tubular secretion

- Urine: 1.5 litres/day

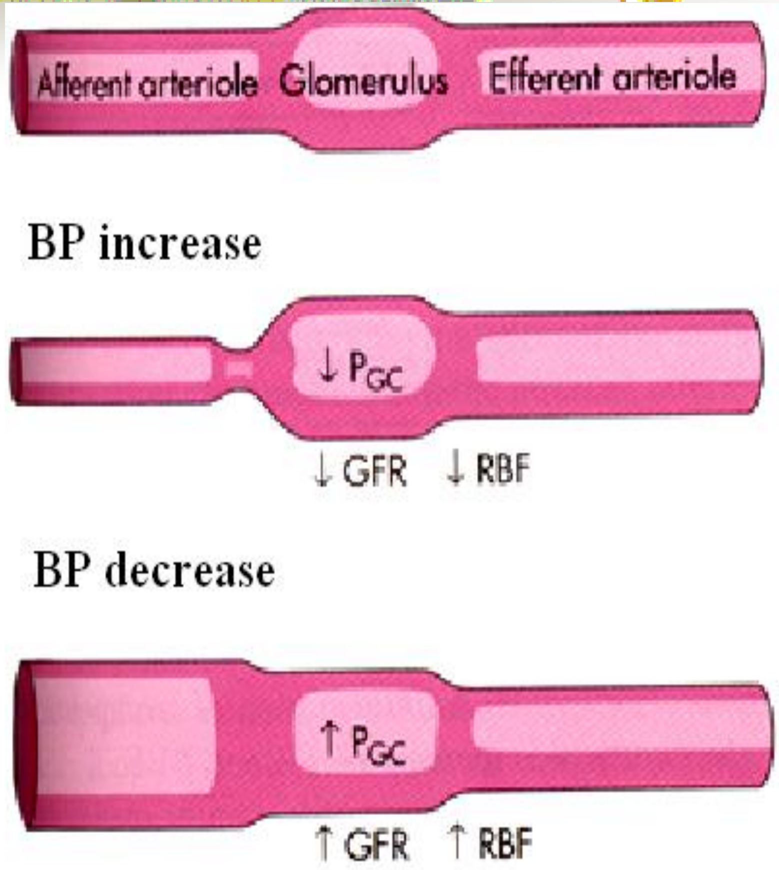


- three major factors that modulate either afferent or efferent arteriolar tone:
  - autonomous vasoreactive (myogenic) reflex in the afferent arteriole
  - *tubuloglomerular feedback*
  - angiotensin II–mediated vasoconstriction of the efferent arteriole

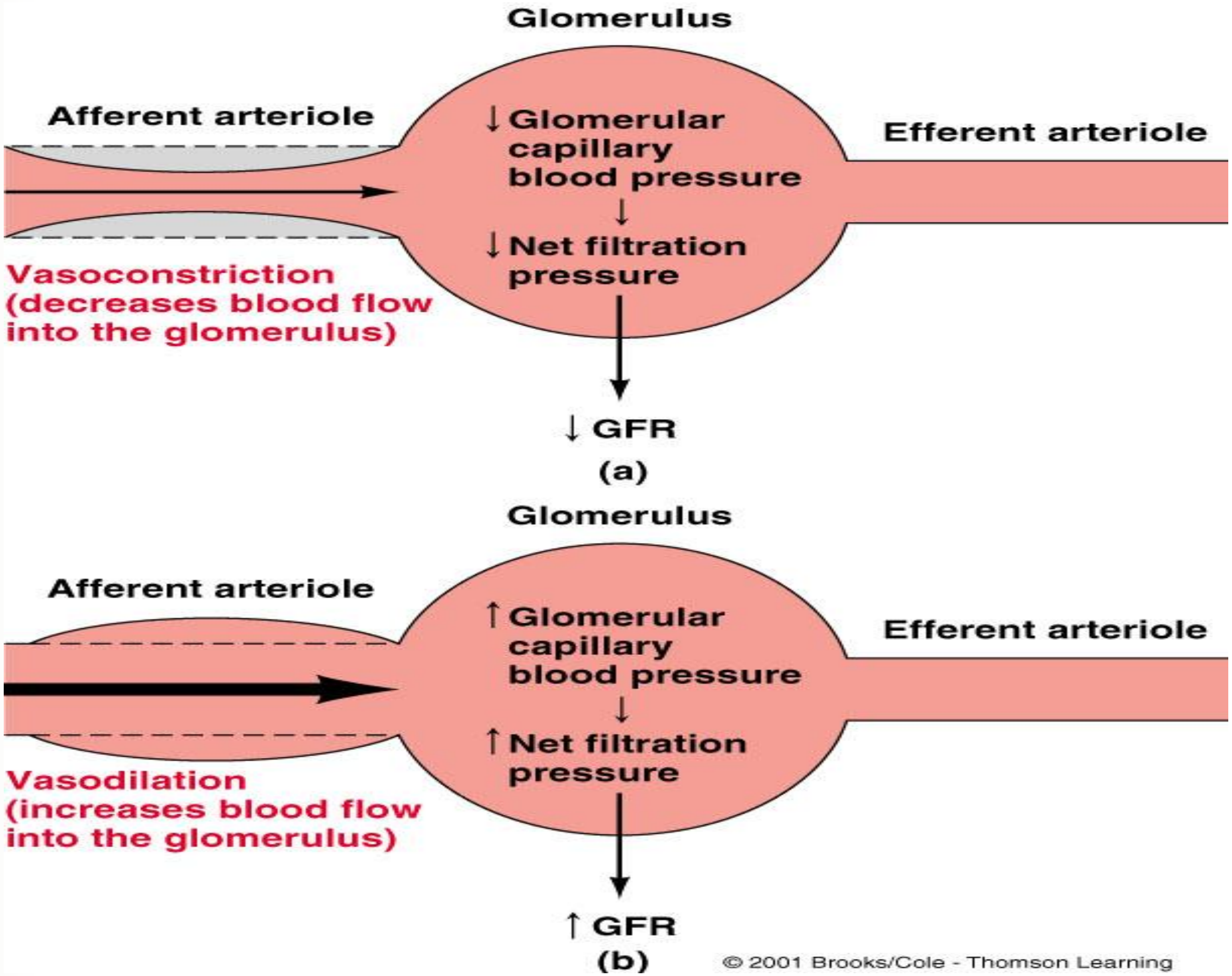
autonomous vasoreactive (myogenic) reflex

- first line of defense against fluctuations in renal blood flow
- This phenomenon helps protect the glomerular capillary from sudden changes in systolic pressure

Myogenic Mechanism of the autoregulation



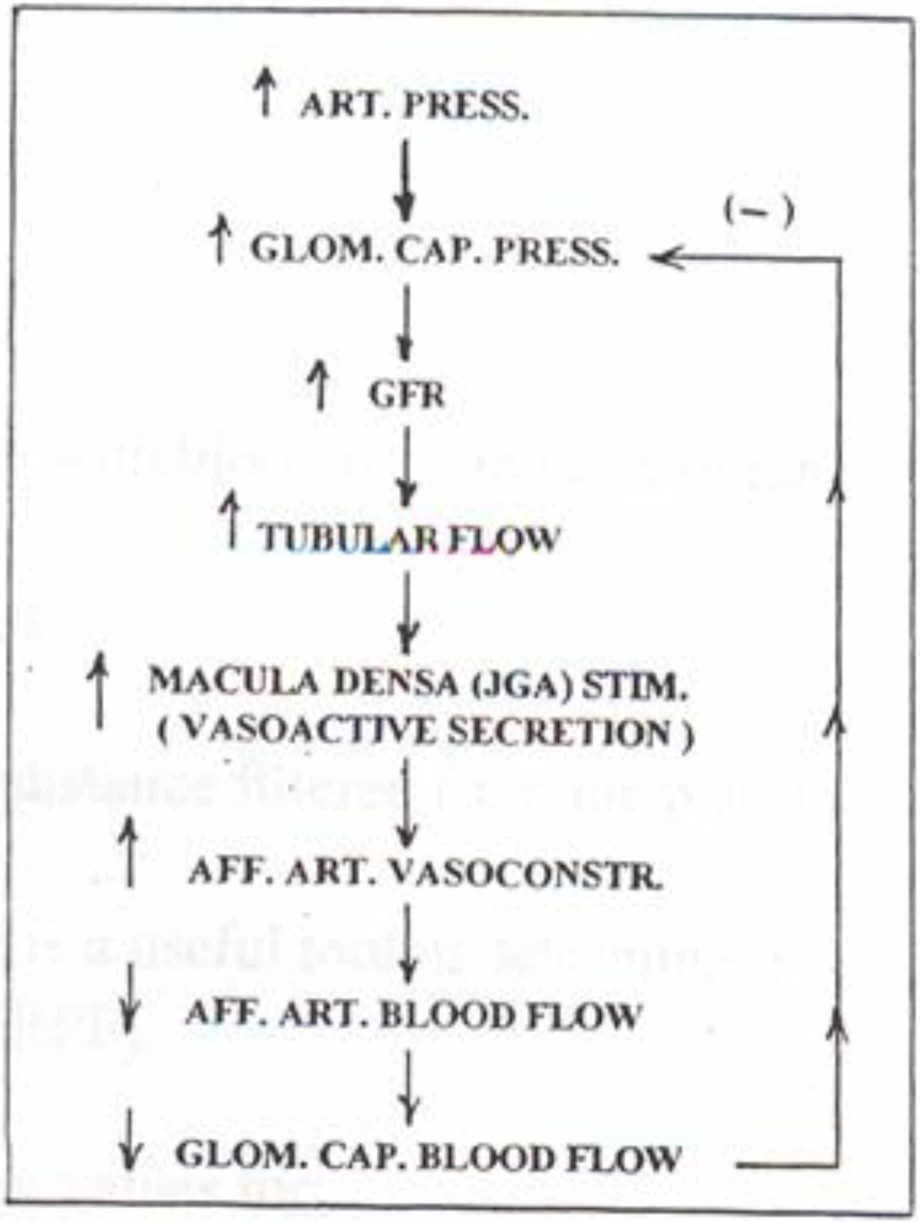
Regulation of Filtration Pressure

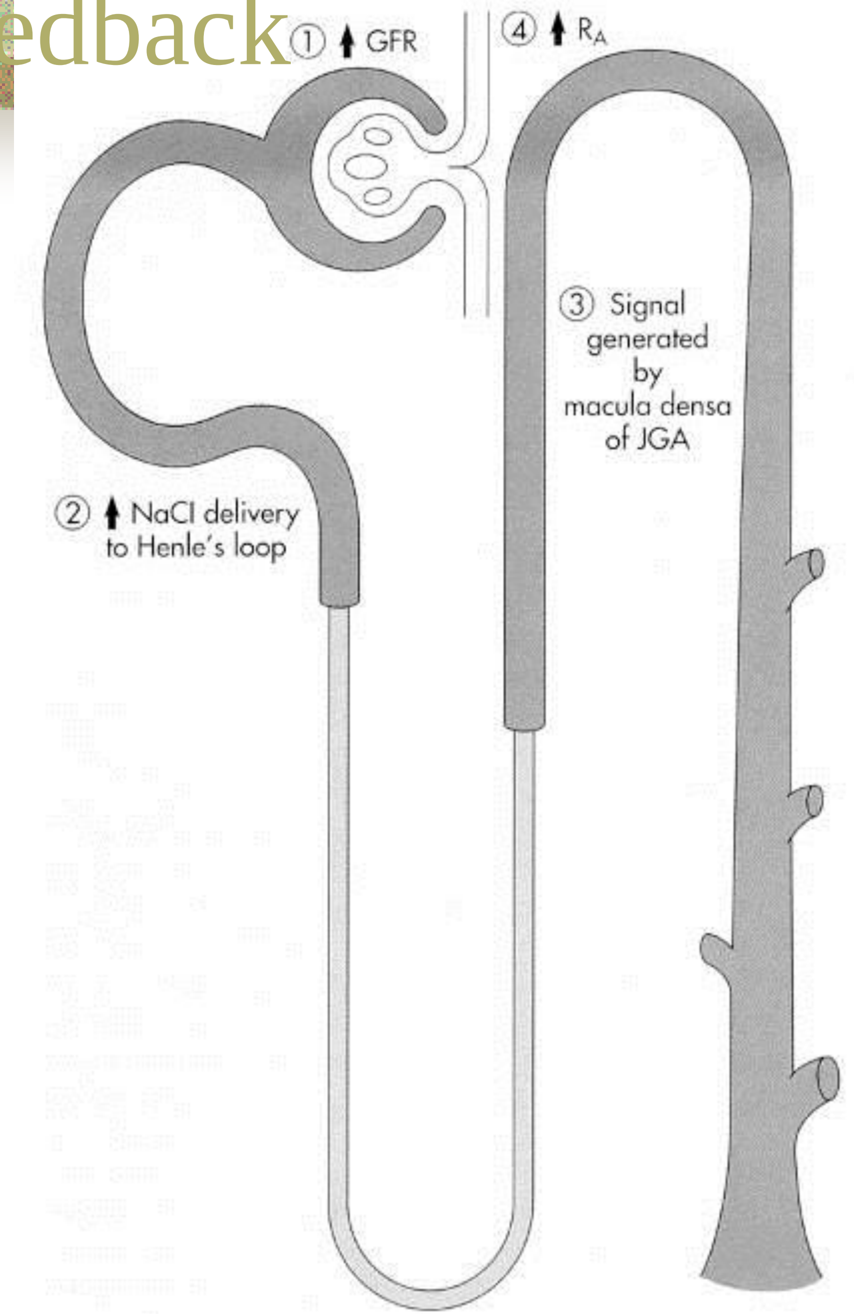


Tubuloglomerular feedback

- mediated by specialized cells in the thick ascending limb of the loop of Henle called the *macula densa*
- act as sensors of solute concentration and tubular flow rate

2) Tubuloglomerular feedback



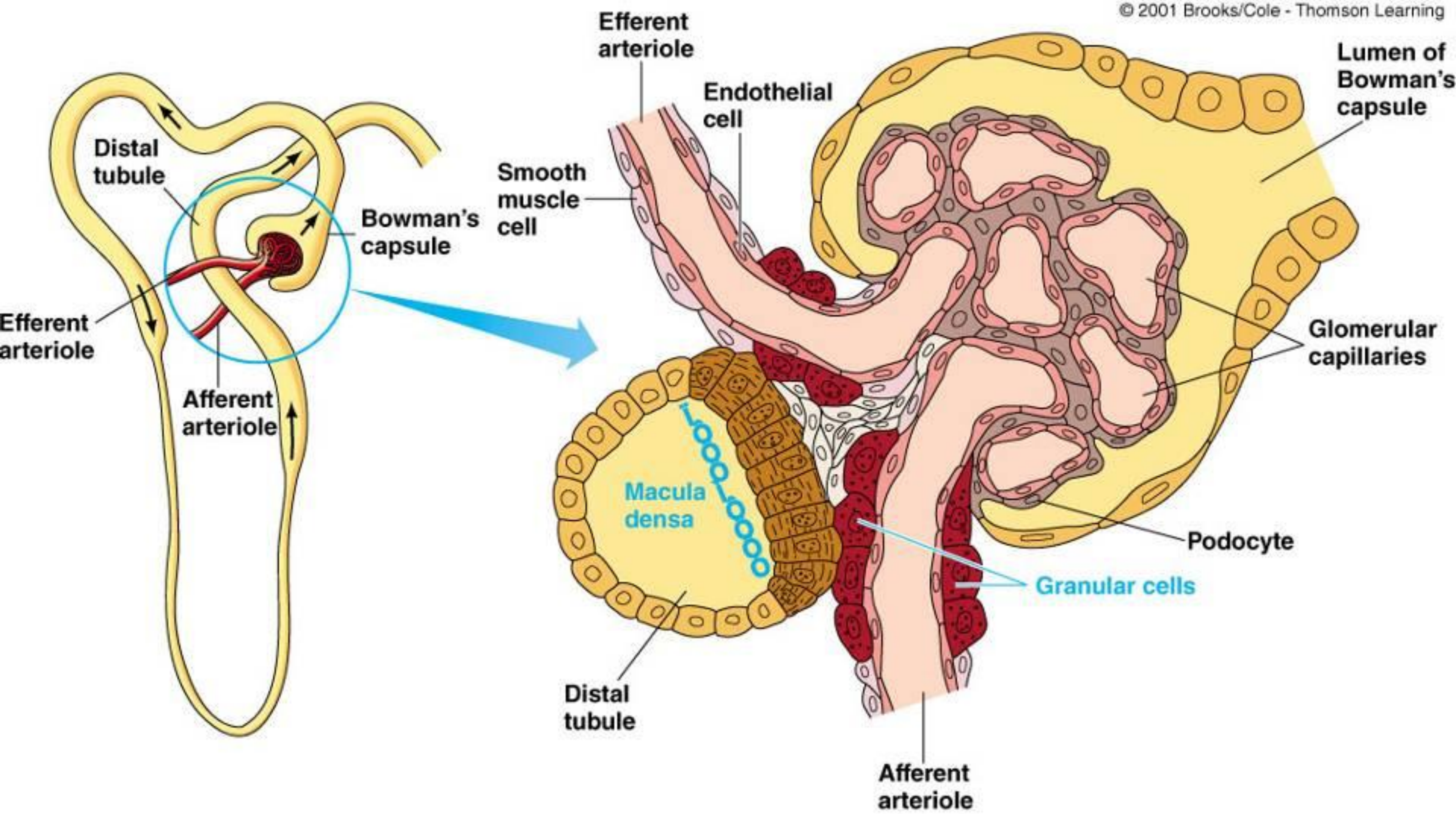


angiotensin II–mediated vasoconstriction

- During states of reduced renal blood flow, renin is released from granular cells within the wall of the afferent arteriole near the macula densa in a region called the juxtaglomerular apparatus

2. The juxtaglomerular apparatus

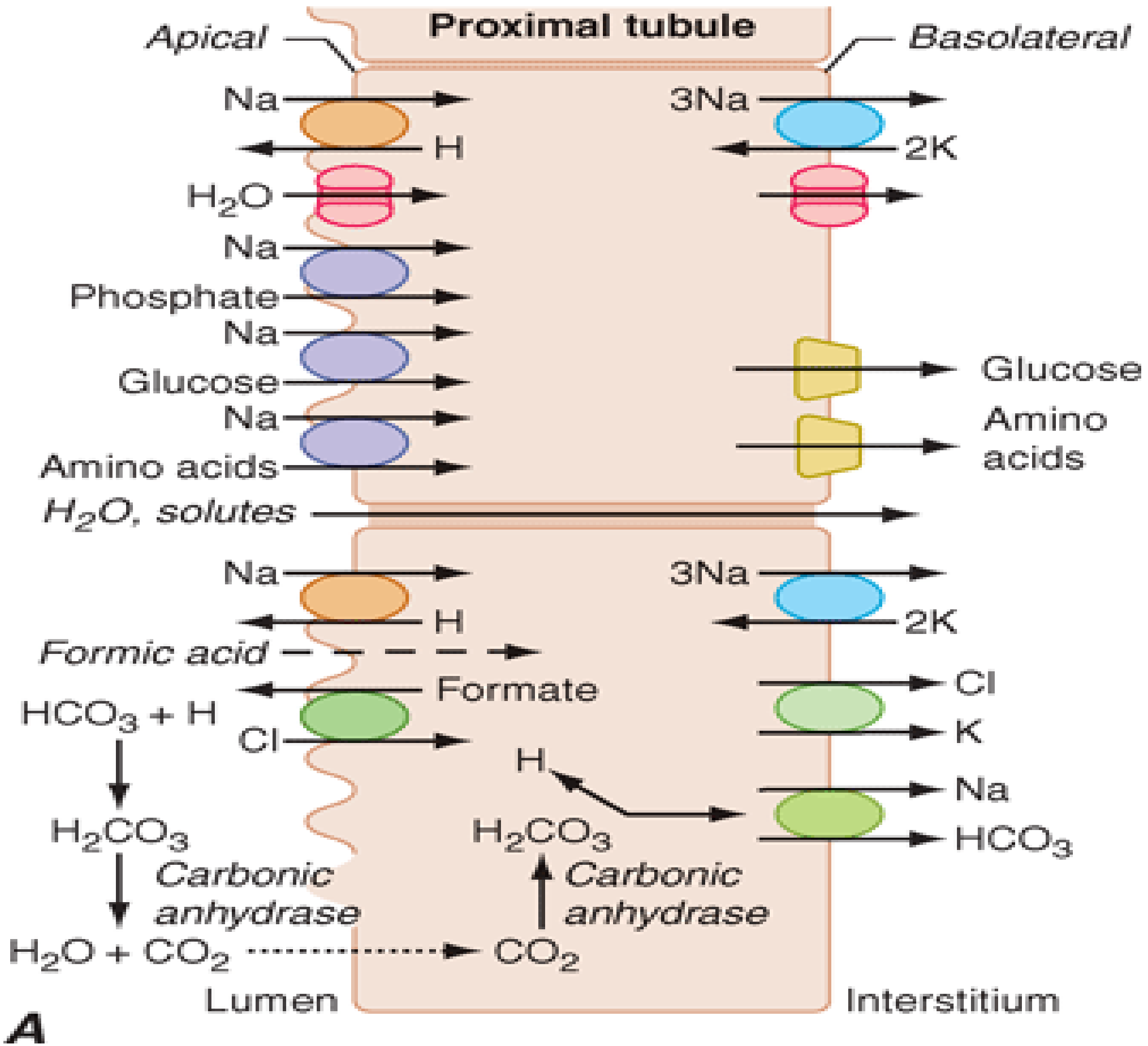
Including macula densa, extraglumerular mesangial cells, and juxtaglomerular (granular cells) cells



Segmental Nephron Functions

Proximal Tubule

- reabsorbing ~60% of filtered NaCl and water
- ~90% of filtered bicarbonate and most critical nutrients such as glucose and amino acids
- Bulk fluid reabsorption by the proximal tubule is driven by high oncotic pressure and low hydrostatic pressure within the peritubular capillaries



Proximal tubule
Apical
Basolateral
Na
H
3Na
2K
H_2O
Na
Phosphate
Na
Glucose
Na
Amino acids
Glucose
Amino acids
H_2O, solutes
Na
H
3Na
2K
Formic acid
Formate
Cl
K
HCO_3 + H
Cl
H
Na
HCO_3
H_2CO_3
H_2CO_3
Carbonic anhydrase
Carbonic anhydrase
$H_2O + CO_2$
CO_2
Lumen
Interstitium
A

Cellular transport by the proximal tubule

- coupled to the Na^+ concentration gradient established by the activity of a basolateral Na^+/K^+-ATPase
- such as Na^+-glucose and Na^+-phosphate cotransporters
- water reabsorption by constitutively active water channels (aquaporin-1) present on both apical and basolateral membranes

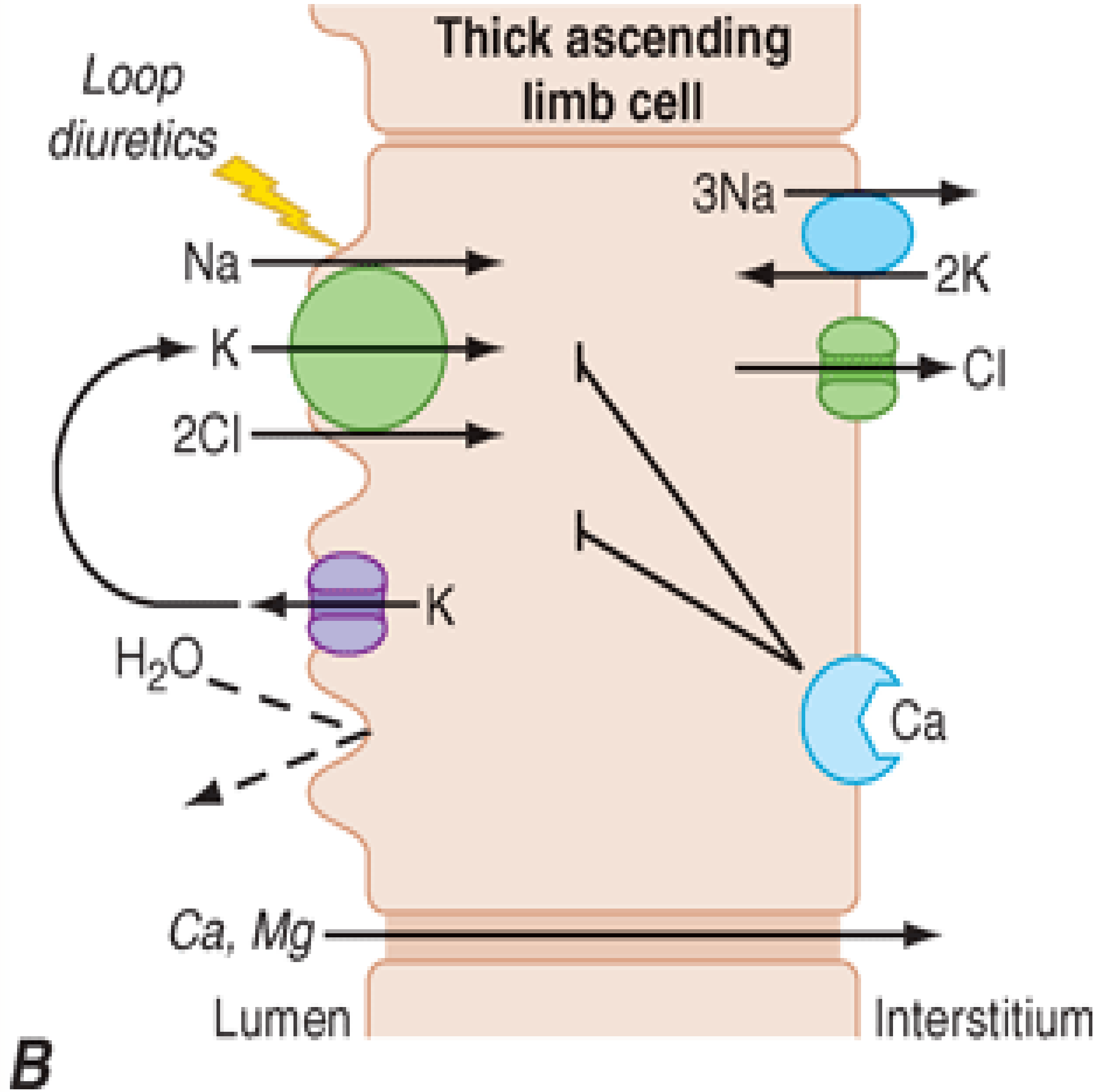
Loop of Henle

- The loop of Henle consists of three major segments:
  - Descending thin limb
  - Ascending thin limb
  - Ascending thick limb

(based on cellular morphology and anatomic location)

- Approximately 15–25% of filtered NaCl is reabsorbed in the loop of Henle (mainly by the thick ascending limb)
- important role in urinary concentration by contributing to the generation of a hypertonic medullary interstitium in a process called *countercurrent multiplication*

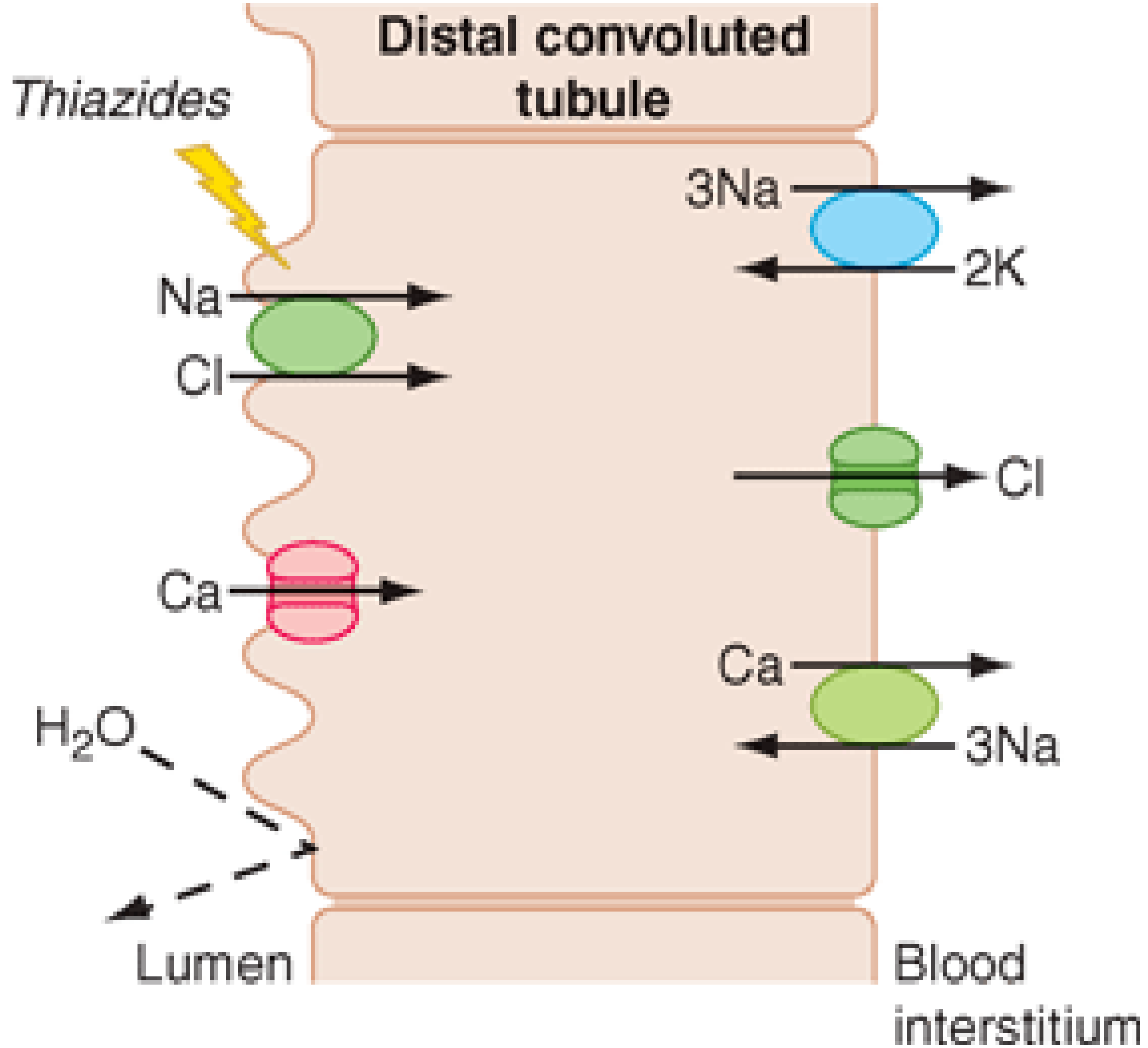
- Descending thin limb
  - Highly water permeable
- Ascending limb
  - water permeability is negligible
- Ascending thick limb
  - $Na^+/K^+/2Cl^-$ cotransporter



Thick ascending limb cell
Loop diuretics
Na
K
2Cl
K
H_2O
3Na
2K
Cl
Ca
Ca, Mg
Lumen
Interstitium
B

Distal Convoluted Tubule

- reabsorbs ~5% of the filtered NaCl
- little water permeability
- Apical Ca^{2+}-selective channels (TRPV5) and basolateral Na^{+}/Ca^{2+} exchange mediate calcium reabsorption
- Ca^{2+} reabsorption is inversely related to Na^{+} reabsorption and is stimulated by parathyroid hormone


Distal convoluted tubule
Thiazides
Na
Cl
Ca
H2O
Lumen
3Na
2K
Cl
Ca
3Na
Blood interstitium

Collecting Duct

- The two major divisions:

  - cortical collecting duct

  - inner medullary collecting duct
- contribute to reabsorbing ~4–5% of filtered Na^+
- hormonal regulation of salt and water balance

Collecting Duct

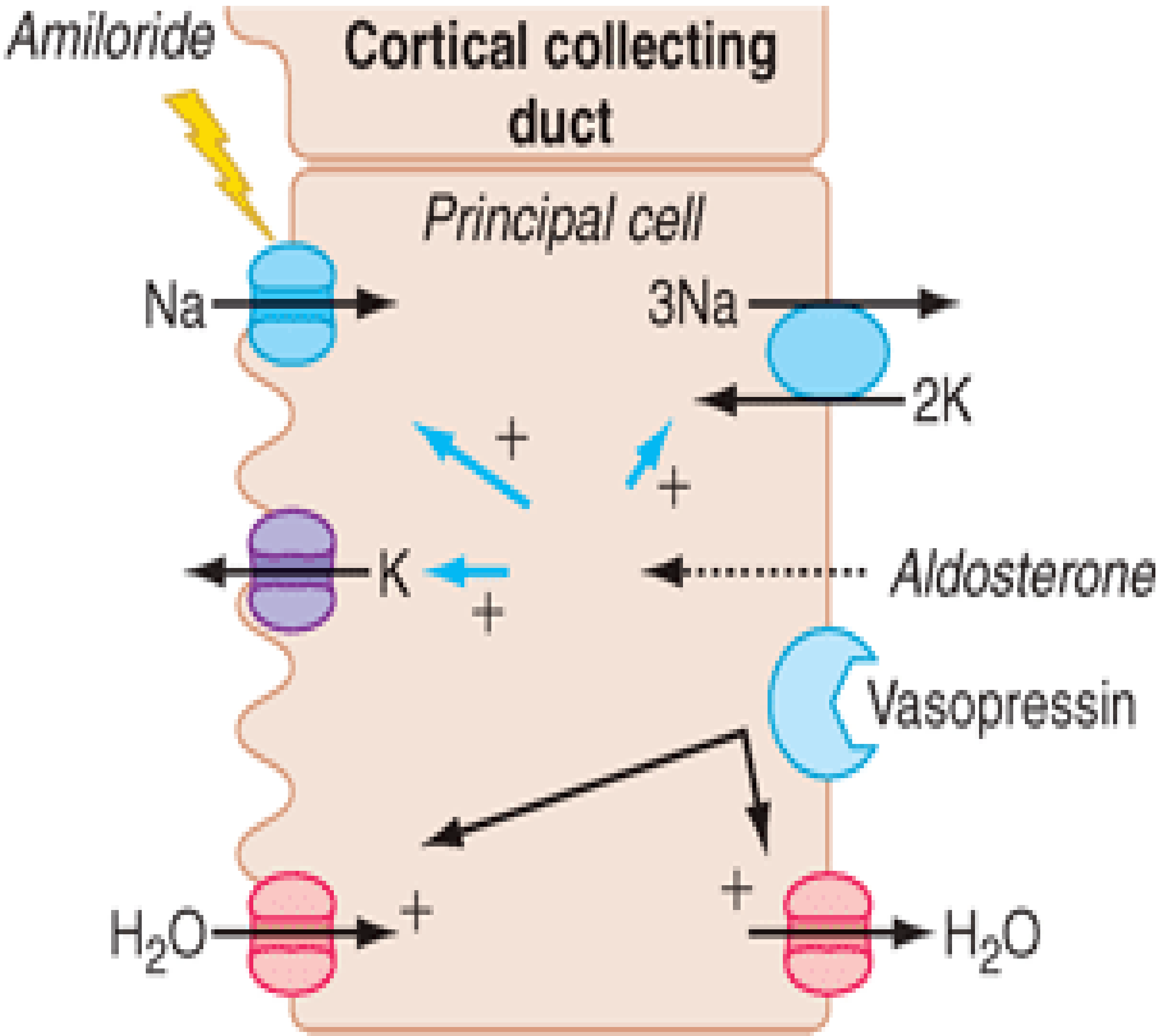
- two cell types:
  - Principal cells
  - type A and B intercalated cells

Principal cells

- main water, Na^+-reabsorbing, and K^+-secreting cells
- the site of action of aldosterone, K^+-sparing diuretics, and mineralocorticoid receptor antagonists such as spironolactone

Principal cells

- passive apical Na^+ entry occurs through the amiloride-sensitive, epithelial Na^+ channel (ENaC) with basolateral exit via the Na^+/K^+-ATPase
- This Na^+ reabsorptive process is tightly regulated by aldosterone


Amiloride
Cortical collecting duct
Principal cell
Na
3Na
2K
K
Aldosterone
Vasopressin
H2O
H2O

HORMONAL REGULATION OF SODIUM AND WATER BALANCE

Water Balance

- Normal tonicity (~280 mosmol/L) is rigorously defended by :

  - osmoregulatory mechanisms that control water balance to protect tissues from inadvertent *dehydration* (cell shrinkage) or *water intoxication* (cell swelling)

- Any reduction in total body water, which raises the Na^+ concentration, triggers :

  - a brisk sense of thirst
  - conservation of water by decreasing renal water excretion mediated by release of vasopressin from the posterior pituitary

- The kidneys play a vital role in maintaining water balance through the regulation of renal water excretion
- aquaporin 1 is constitutively active in all water-permeable segments of the proximal and distal tubules
- vasopressin-regulated aquaporins 2, 3, and 4 in the inner medullary collecting duct promote rapid water permeability

Sodium Balance

- Under normal conditions, volume is regulated by :

- sodium balance

- balance between daily Na^+ intake and excretion

- If Na^+ intake exceeds Na^+ excretion (positive Na^+ balance)

  - an increase in blood volume will trigger a proportional increase in urinary Na^+ excretion

- when Na^+ intake is less than urinary excretion (negative Na^+ balance):

  - blood volume will decrease and trigger enhanced renal Na^+ reabsorption, leading to decreased urinary Na^+ excretion

renin-angiotensin-aldosterone system

- Renin is synthesized and secreted by granular cells in the wall of the afferent arteriole
- Renin and ACE activity eventually produce angiotensin II

Angiotensin II

- Stimulation of proximal tubular Na^+/H^+ exchange
- stimulating aldosterone secretion

Aldosterone

- Aldosterone is synthesized and secreted by granulosa cells in the adrenal cortex
- It binds to cytoplasmic mineralocorticoid receptors in the collecting duct principal cells that :

  - increase activity of ENaC, apical membrane K^+ channel, and basolateral Na^+/K^+-ATPase


THANK
YOU