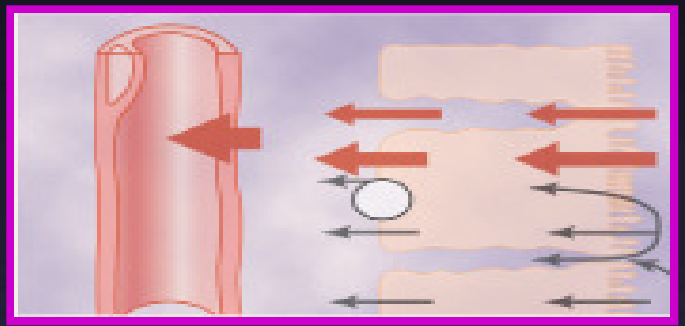
Urine Formation by the Kidneys

Tubular Processing of the Glomerular Filtrate

TUBULAR REABSORPTION AND SECRETION



Chapter 27
pages 327 – 347

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OBJECTIVES

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

- Absorptive Characteristics of different parts of nephrons
- Define and describe tubular reabsorption and tubular secretion mechanisms
- Describe tubular reabsorption of sodium and water
- Identify and describe mechanism involved in Glucose, Amino Acids and Urea reabsorption
- Study glucose titration curve in terms of renal threshold, tubular transport maximum, splay, excretion and filtration
- Describe Urea transport into and out of the renal tubules

Characteristics

Volume		1 – 2 liters (quarts) per day (influenced by many factors)
Color		Yellow or Amber (varies with concentration and diet)
Turbidity		Transparent when fresh (becomes cloudy)
Odor		Aromatic (becomes ammonia-like)
pH		Averages 6.0 (ranges between 4.6 and 8.0)
Specific Gravity		1.001 – 1.035 (denser than water)

Organic Solutes

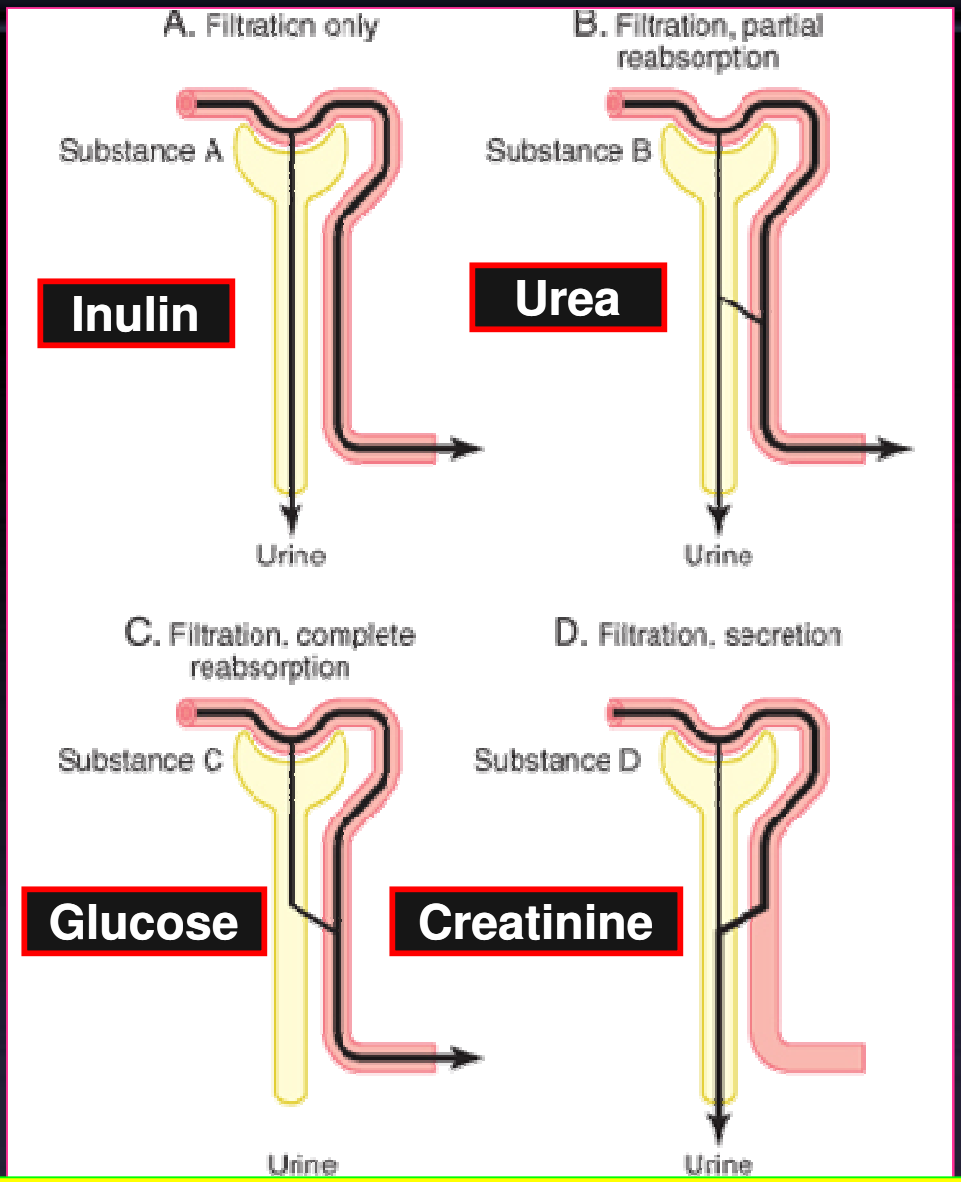
Nitrogenous Wastes	Urea; Creatinine; Uric Acid
Hippuric Acid	Derived from Benzoic Acid
Indican	Derived from Indole
Ketone Bodies	Derived from Triglycerides

Inorganic Solutes

Cations	Sodium; Potassium; Ammonium; Magnesium; Calcium
Anions	Chloride; Sulfate; Phosphates

URINE COMPOSITION

pH	freshly voided urine is usually acidic (around pH 6), range=4.8 and 7.5
Colour	Bright Yellow & transparent
Specific Gravity	1.001 to 1.035
Volume	1-2 L per day
Albumin	20 µg of albumin per minute (30 mg in 24 hours)
Glucose	None



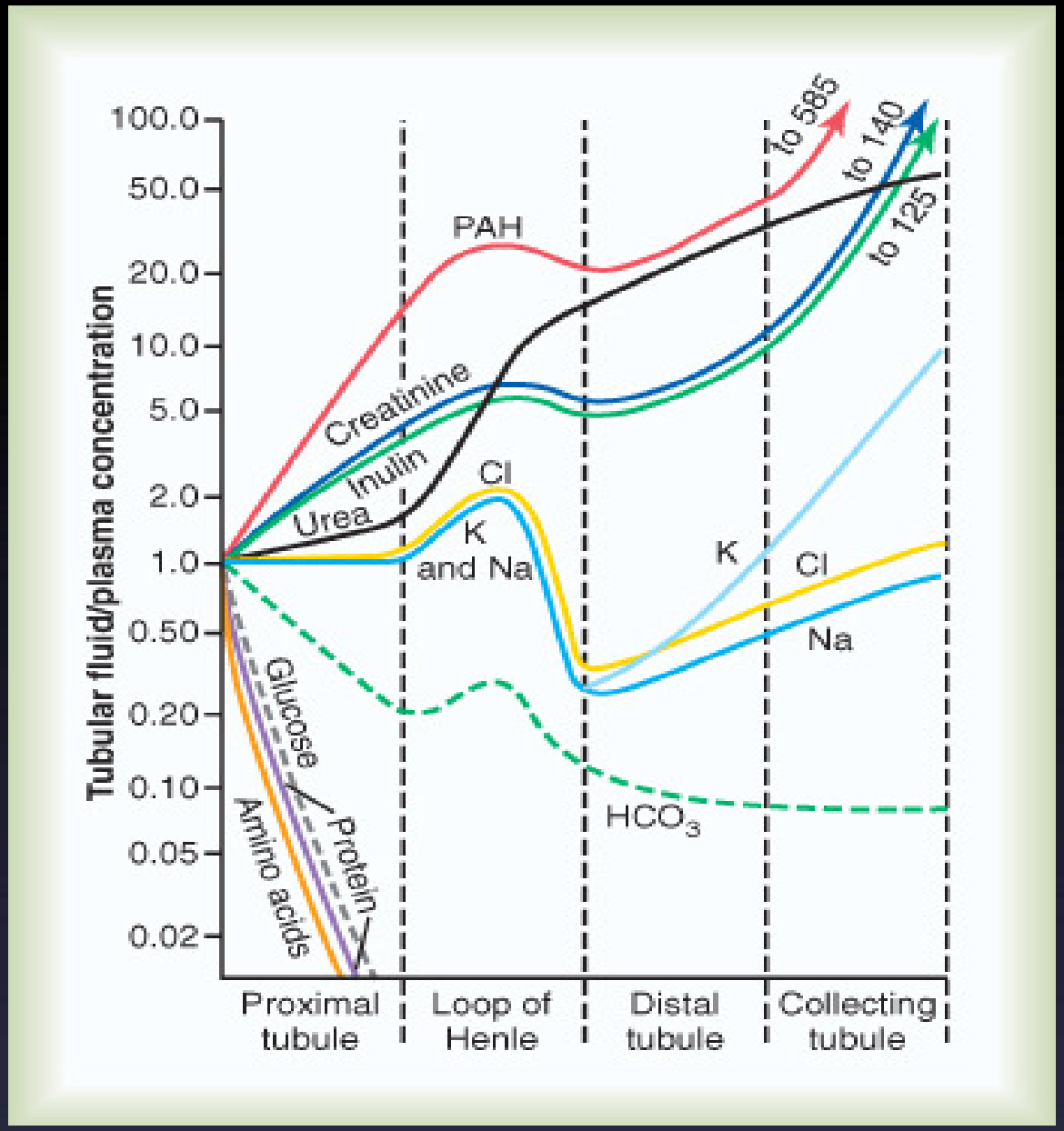
Urinary Excretion Rate =

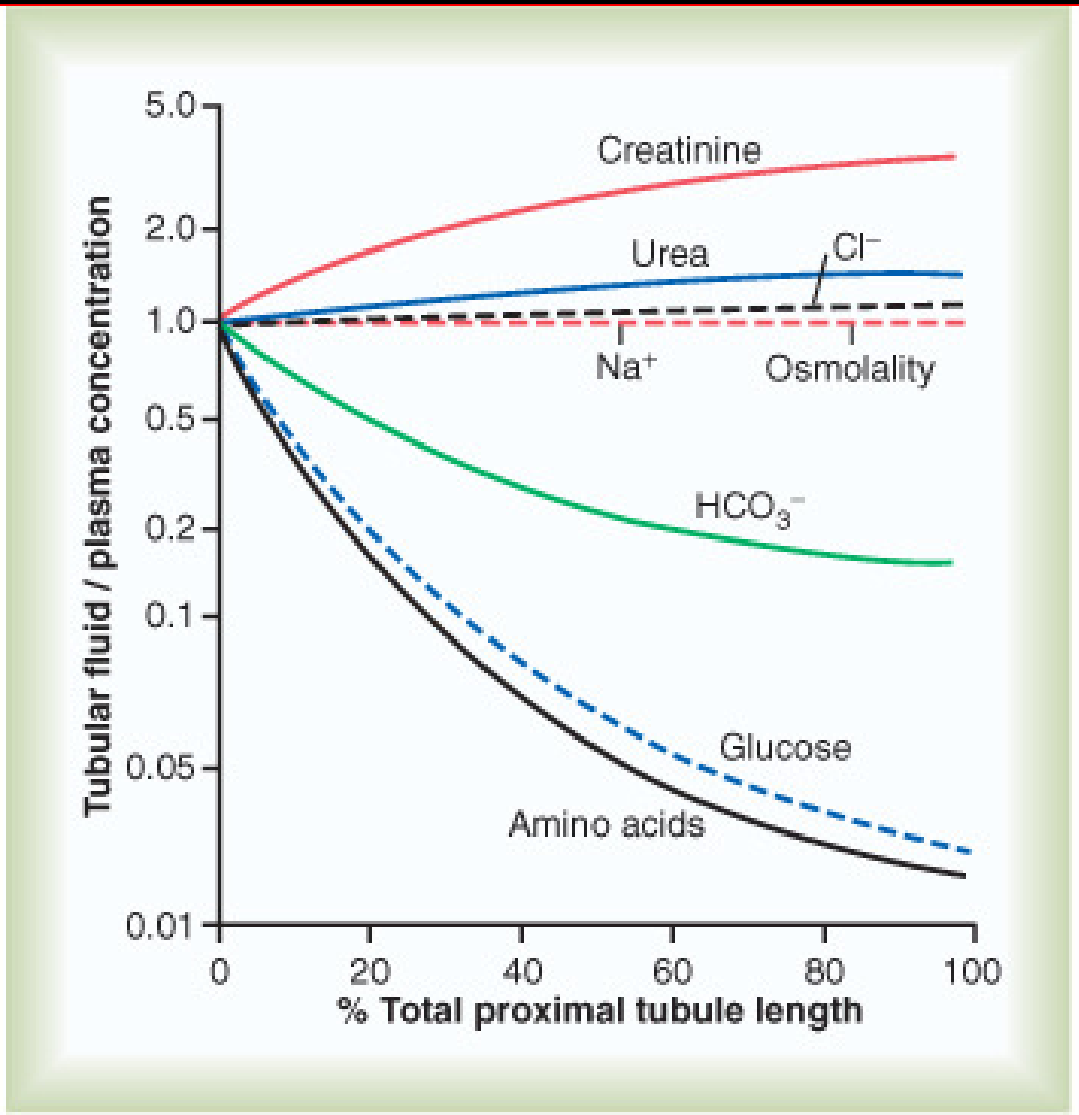
Filtration Rate – Reabsorption Rate + Secretion Rate

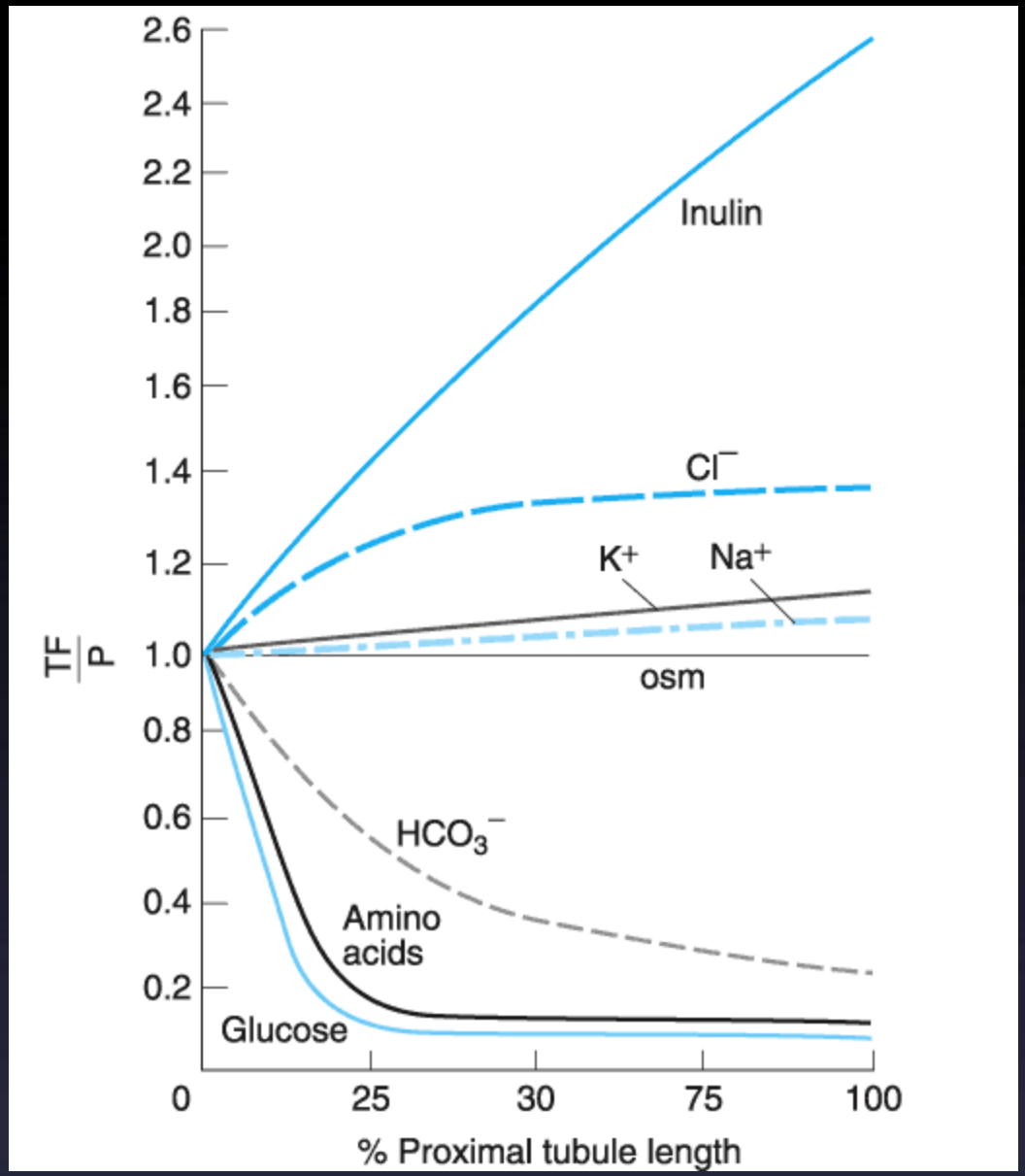
PROCESSES OF GLOMERULAR FILTRATION TUBULAR REABSORPTION AND SECRETION

SUBSTANCES	Amount Filtered	Amount Reabsorbed	Amount Excreted	% Filtered Load Reabsorbed
Glucose (g/day)	180	180	0	100
Bicarbonate (mEq/day)	4,320	4,318	2	>99.9
Sodium (mEq/day)	25,560	25,410	150	99.4
Chloride (mEq/day)	19,440	19,260	180	99.1
Potassium (mEq/day)	756	664	92	87.8
Urea (g/day)	46.8	23.4	23.4	50
Creatinine (g/day)	1.8	0	1.8	0

Changes in Average Concentration of Different Substances at Different Points in Tubular System Relative to Glomerular Filtrate


Tubular fluid/plasma concentration
100.0
50.0
20.0
10.0
5.0
2.0
1.0
0.50
0.20
0.10
0.05
0.02
PAH
Creatinine
Inulin
Urea
Cl
K
and Na
Glucose
Amino acids
Protein
HCO_3
to 585
to 140
to 125
K
Cl
Na
Proximal tubule
Loop of Henle
Distal tubule
Collecting tubule




2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
TF/P
Inulin
Cl⁻
K⁺
Na⁺
osm
HCO3⁻
Amino acids
Glucose
0
25
30
75
100
% Proximal tubule length

CLASSIFICATION OF TRANSPORT MECHANISMS

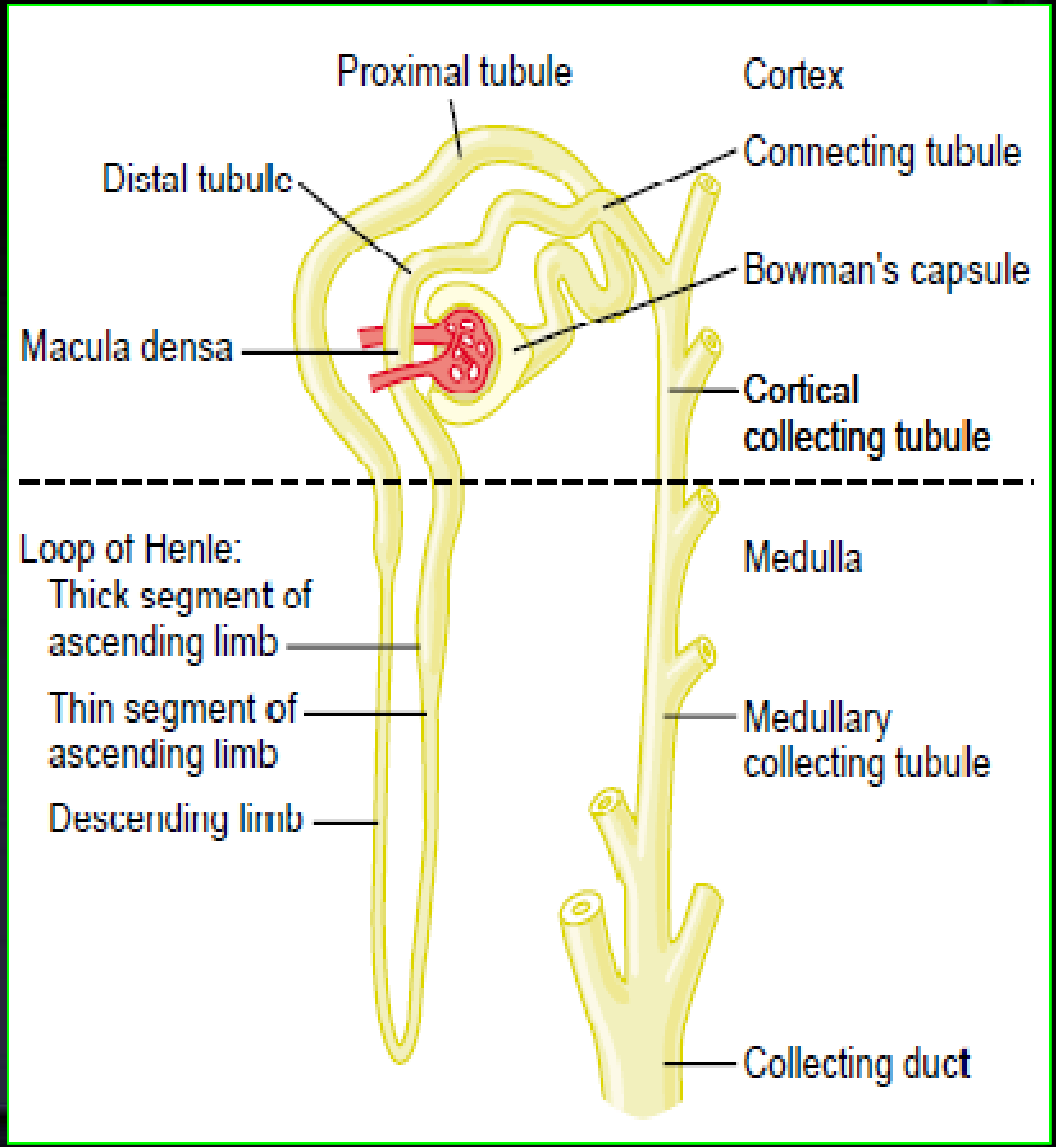
- SIMPE DIFFUSION
- FACILITATED DIFFUSION
- PRIMARY ACTIVE TRANSPORT
- SECONDARY ACTIVE TRANSPORT
- PINOCYTOSIS
- BULK FLOW

PRIMARY ACTIVE TRANSPORTERS

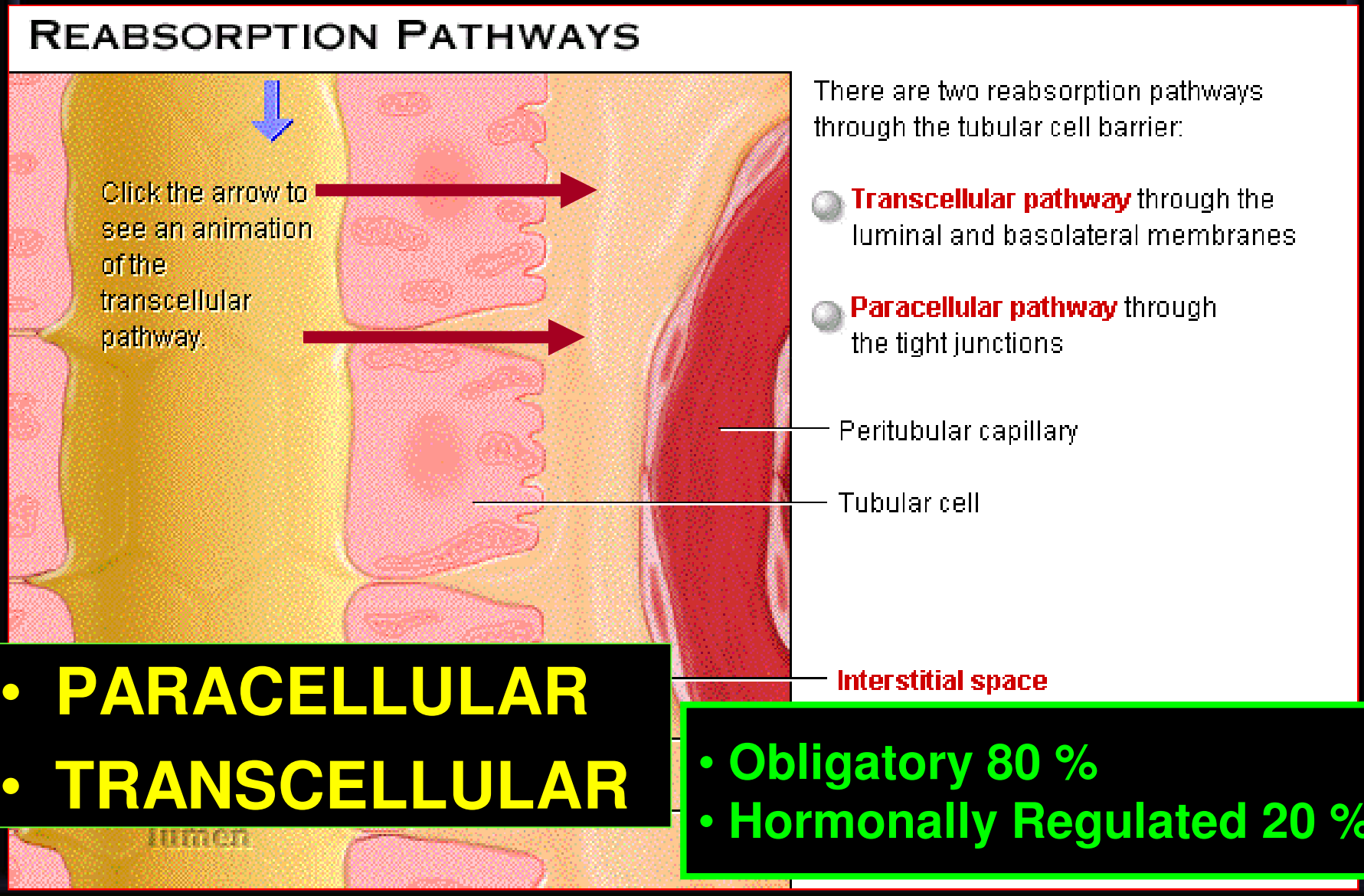
- Sodium-potassium ATPpase
- Hydrogen ATPpase
- Hydrogen-potassium ATPpase
- Calcium ATPpase.

PARTS OF NEPHRON

- Proximal Convoluted Tubule
- Loop of Henle
- Distal Convoluted Tubule
- Collecting Tubule
- Collecting Duct



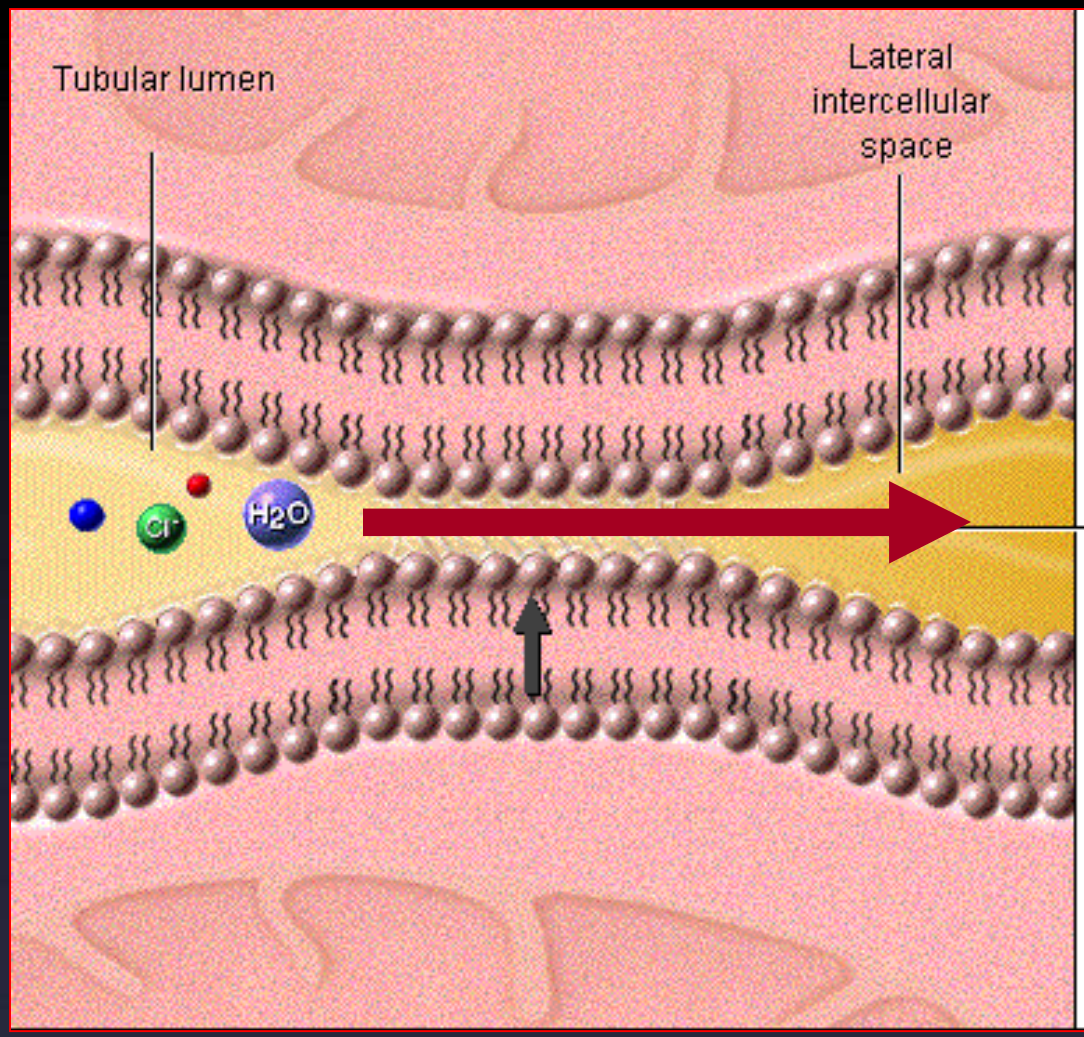
REABSORTION PATHWAYS



- **PARACELLULAR**
- **TRANSCELLULAR**

- **Obligatory 80 %**
- **Hormonally Regulated 20 %**

PCT PARACELLULAR PATHWAY



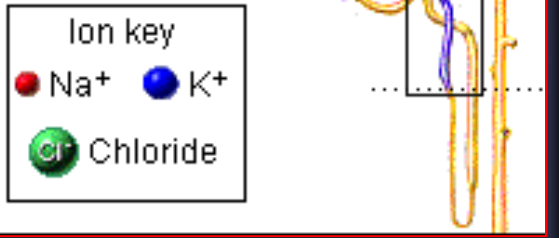
The tight junctions of the PCT are not as tight as their name implies.

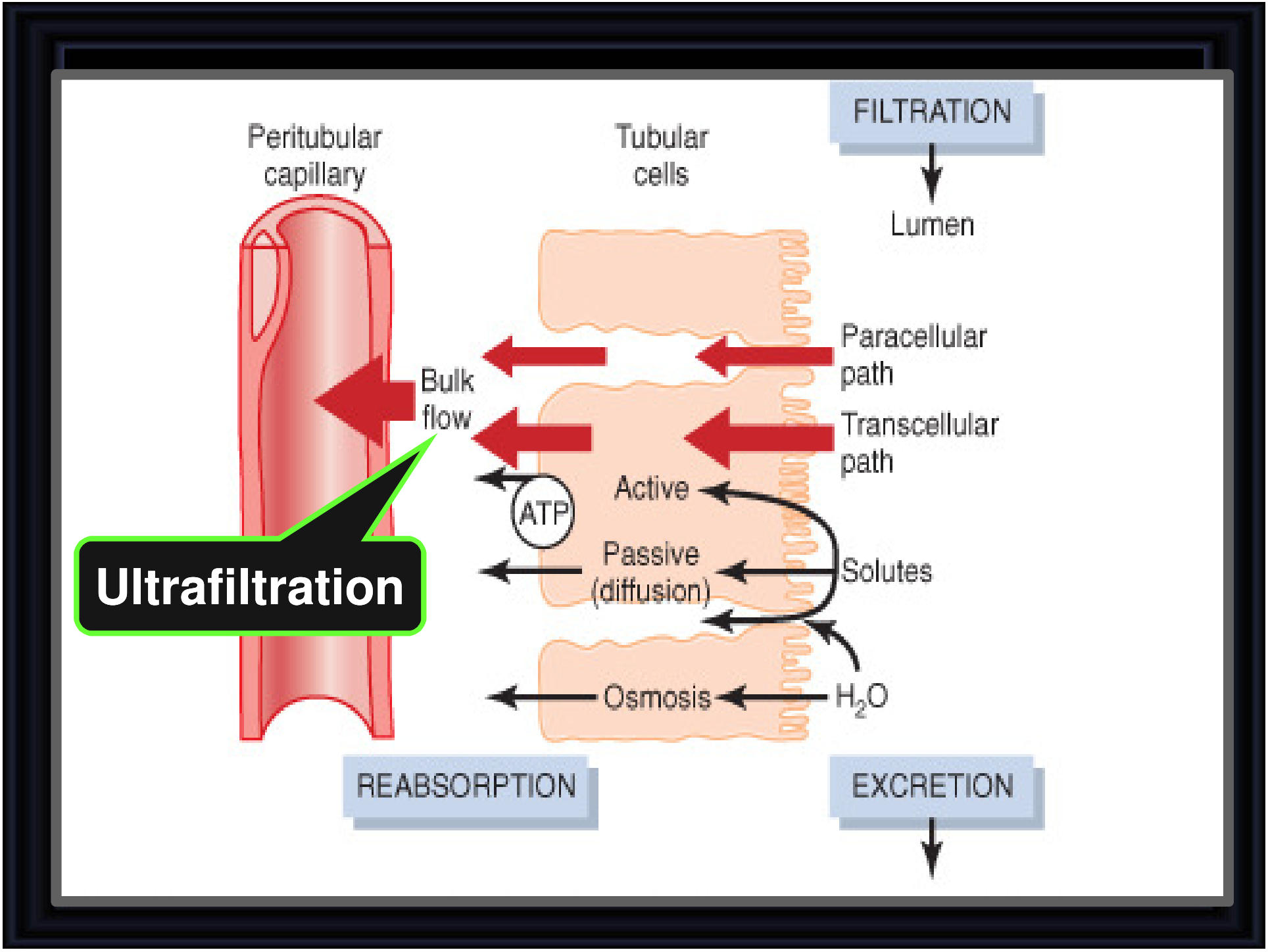
In the PCT, water diffuses through the tight junction down its concentration **gradient**.

Sodium, chloride, and potassium may also follow in a process called **solvent drag**.

Tight junction

Click the enlarged tight junction to see this activity.




FILTRATION
Peritubular capillary
Tubular cells
Lumen
Paracellular path
Bulk flow
Transcellular path
ATP
Active
Passive (diffusion)
Solutes
Osmosis
H_2O
REABSORPTION
EXCRETION
Ultrafiltration

REABSORPTION OF WATER IN DIFFERENT SEGMENTS OF TUBULES

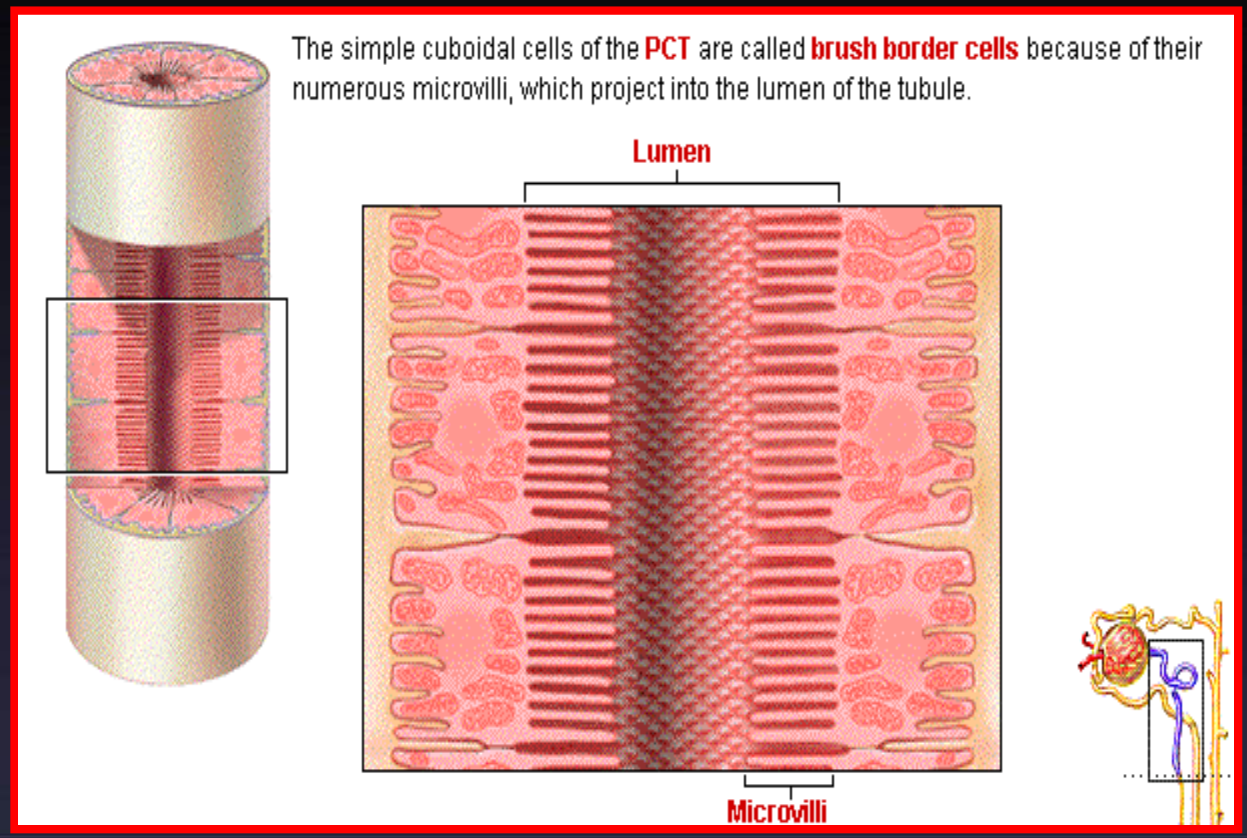
PART OF NEPHRON	PERCENTAGE REABSORBED
Proximal tubules	65
Loop of Henle	15
Distal tubules	10
Collecting ducts	9.3
Passing into urine	**0.7**

REABSORPTION OF WATER IN DIFFERENT SEGMENTS OF TUBULES

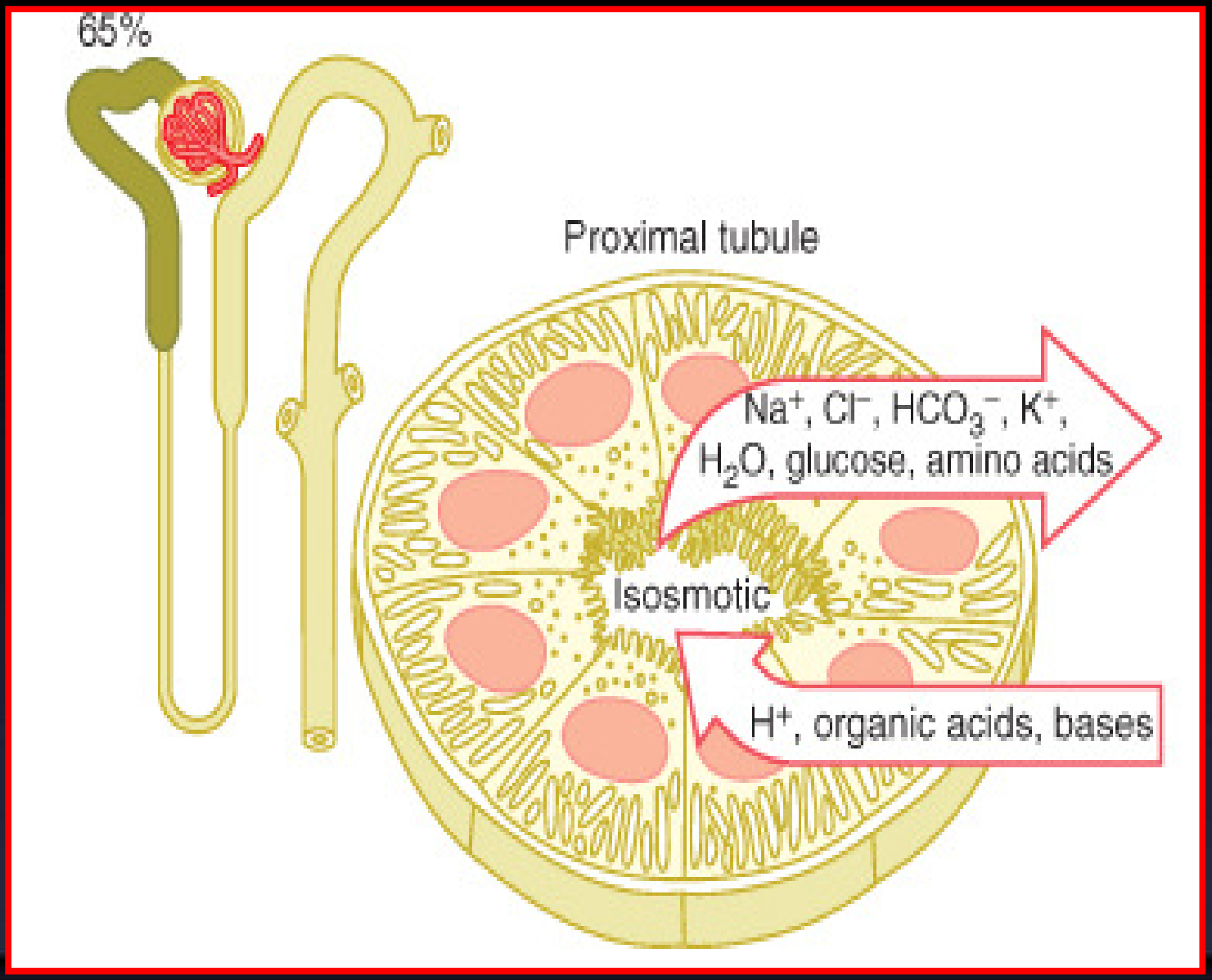
PART OF NEPHRON	AMOUNT REABSORBED
Glomerular Filtrate	125
Flowing into the loops of Henle	45
Flowing into the distal tubules	25
Flowing into the collecting tubules	12
Flowing into the urine	1

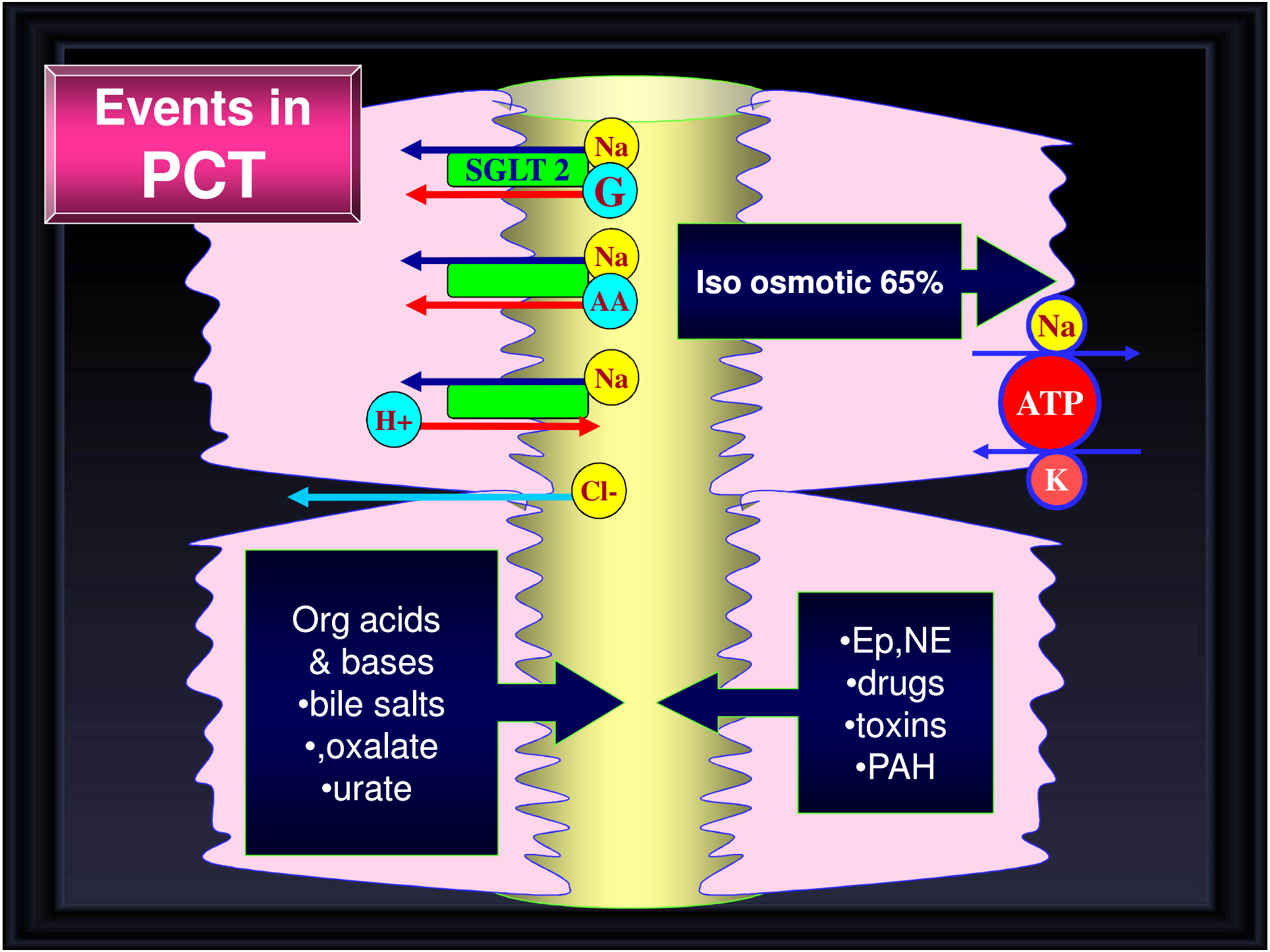
PROXIMAL CONVOLUTED TUBULE

- **Many mitochondria**
- **Brush border** multiplies the surface area about 20-fold.
- **Tight junctions**
- **Lateral intercellular spaces.**



PROXIMAL CONVOLUTED TUBULE




Events in PCT
SGLT 2
Na
G
Na
AA
Na
H+
Cl-
Iso osmotic 65%
Na
ATP
K
Org acids & bases
•bile salts
•,oxalate
•urate
•Ep,NE
•drugs
•toxins
•PAH

Events in PCT

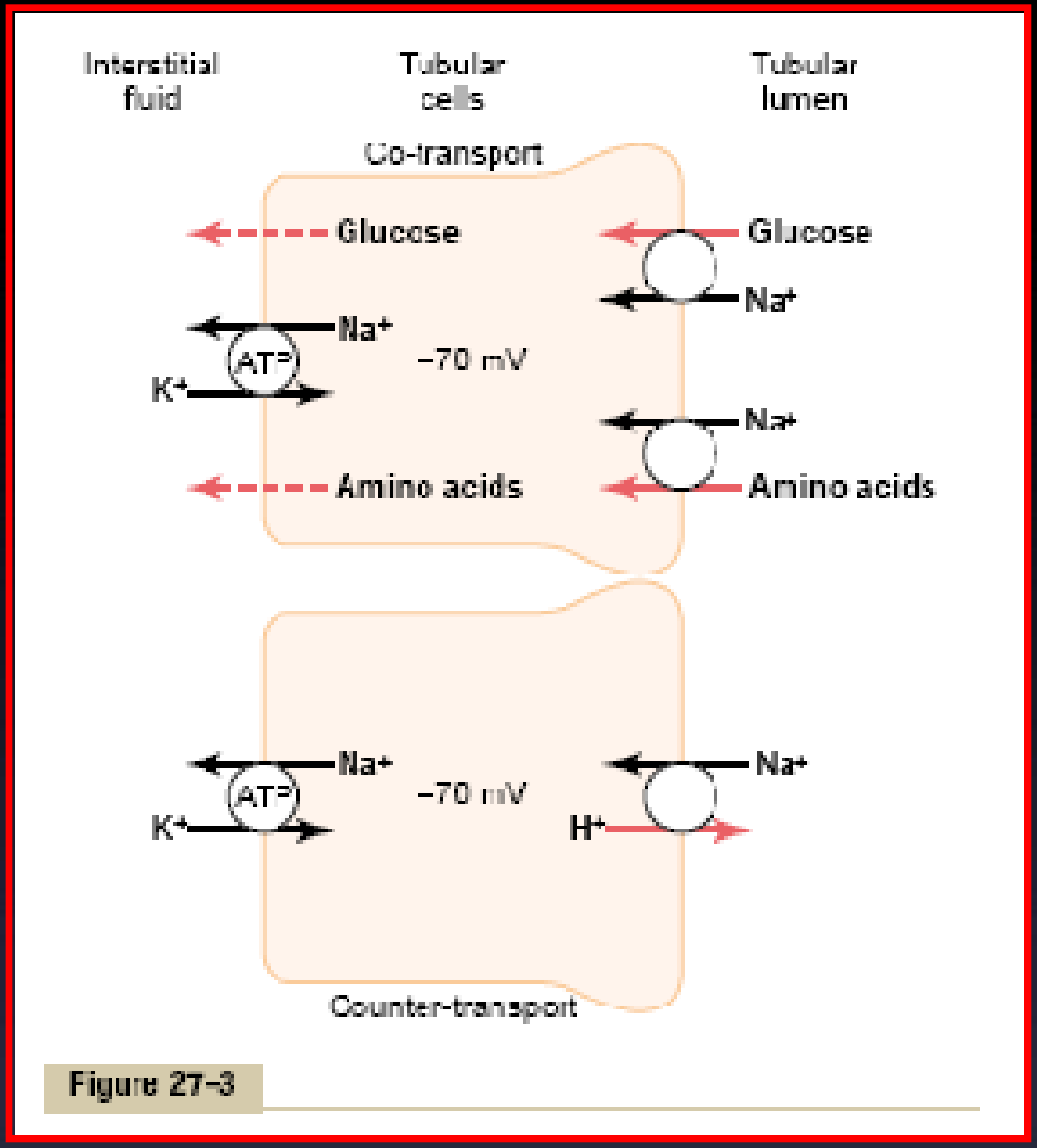
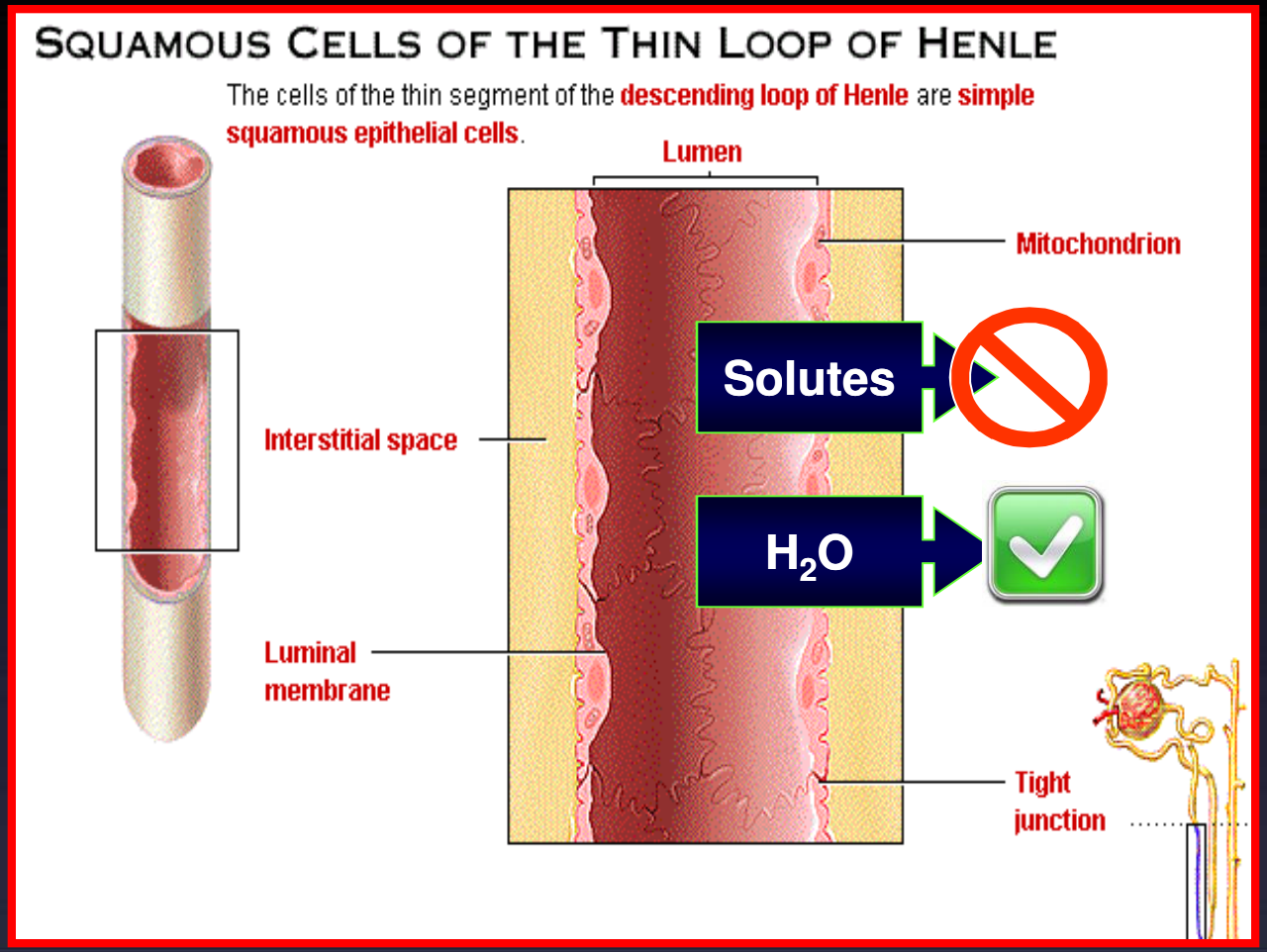


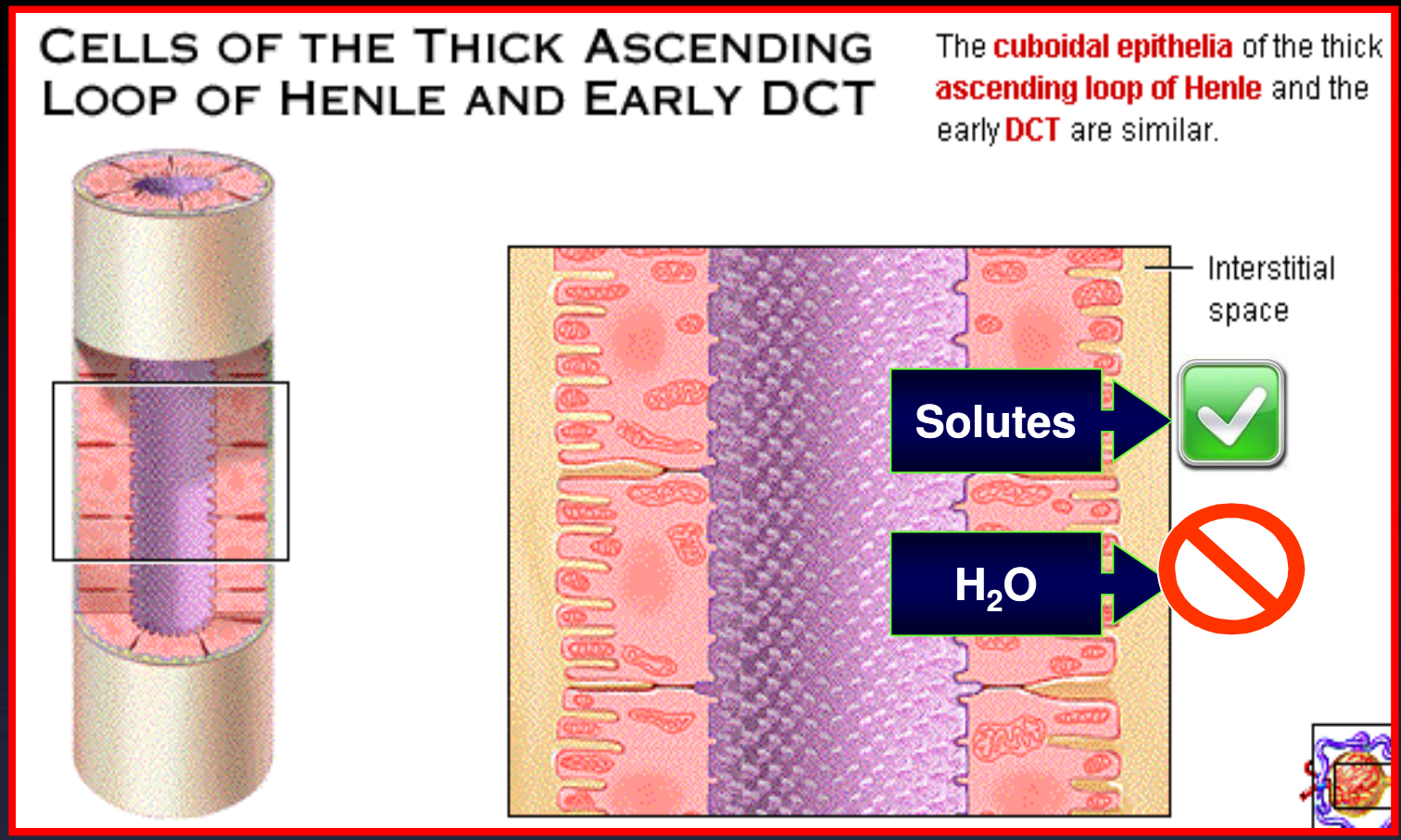
Figure 27–3

DESCENDING LIMB OF LOOP OF HENLE

- Few mitochondria
- Flattened with few microvilli

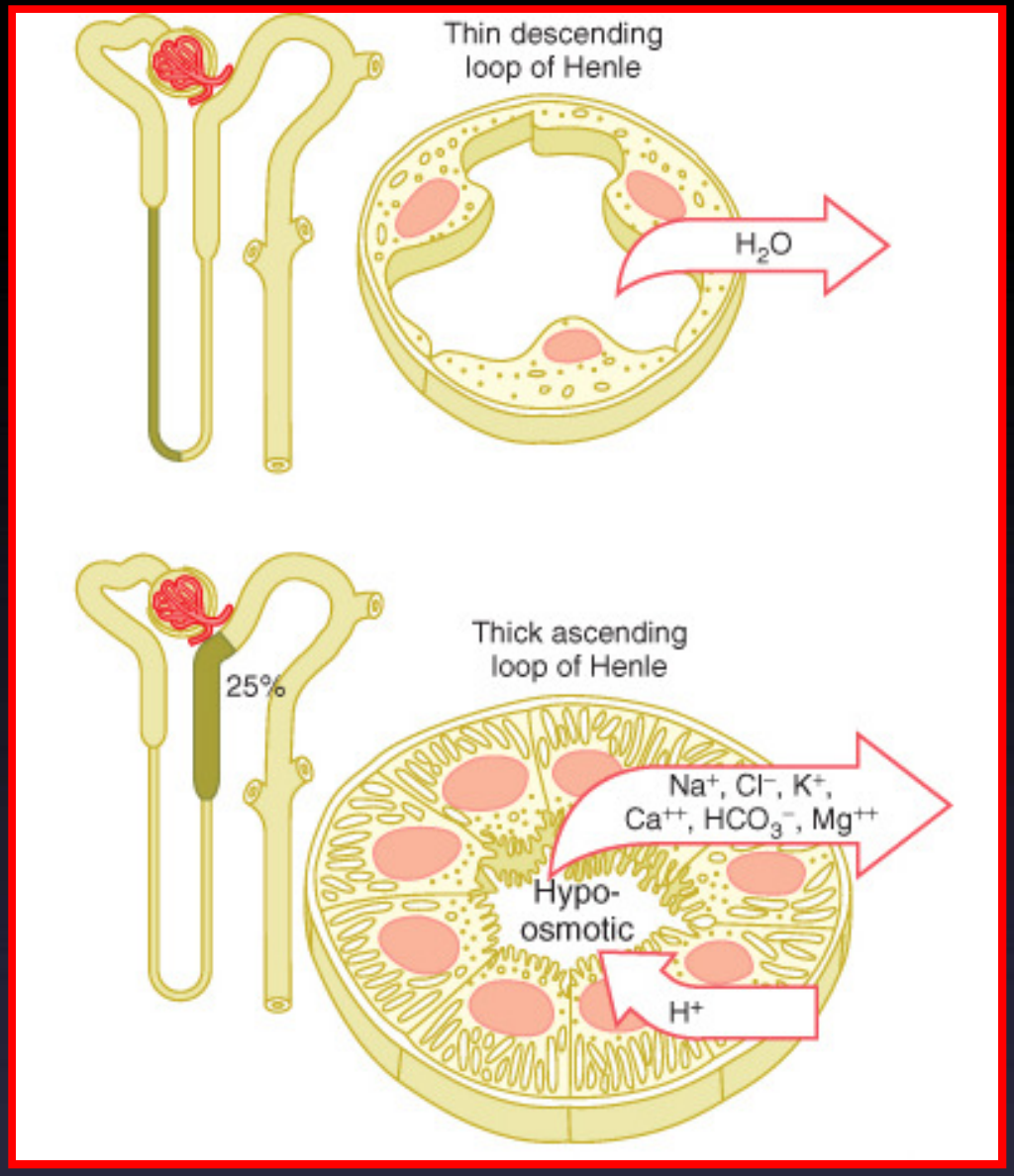


THICK ASCENDING LOOP OF HENLE AND EARLY DCT

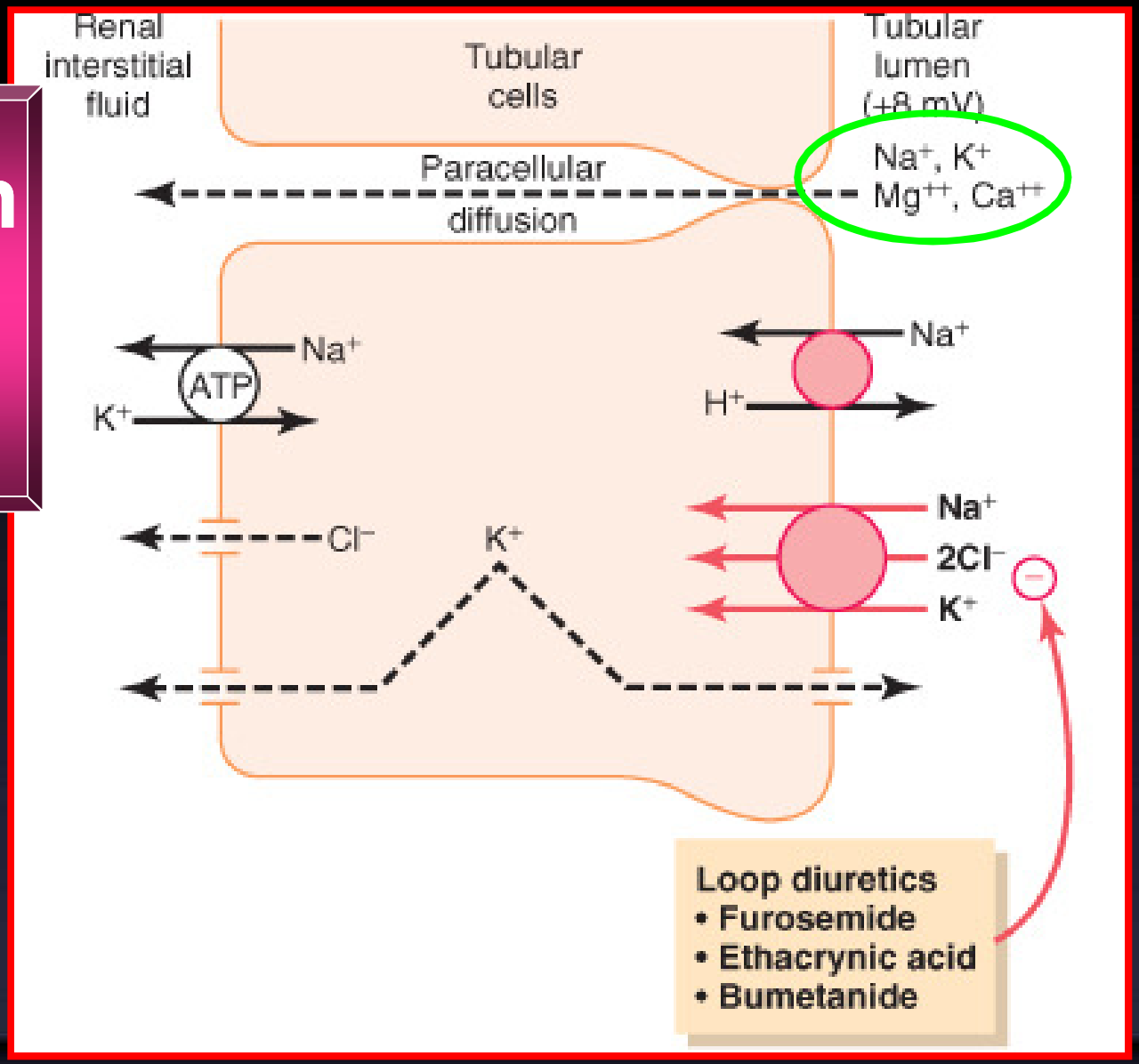


Many mitochondria and microvilli, but fewer than in the proximal tubule

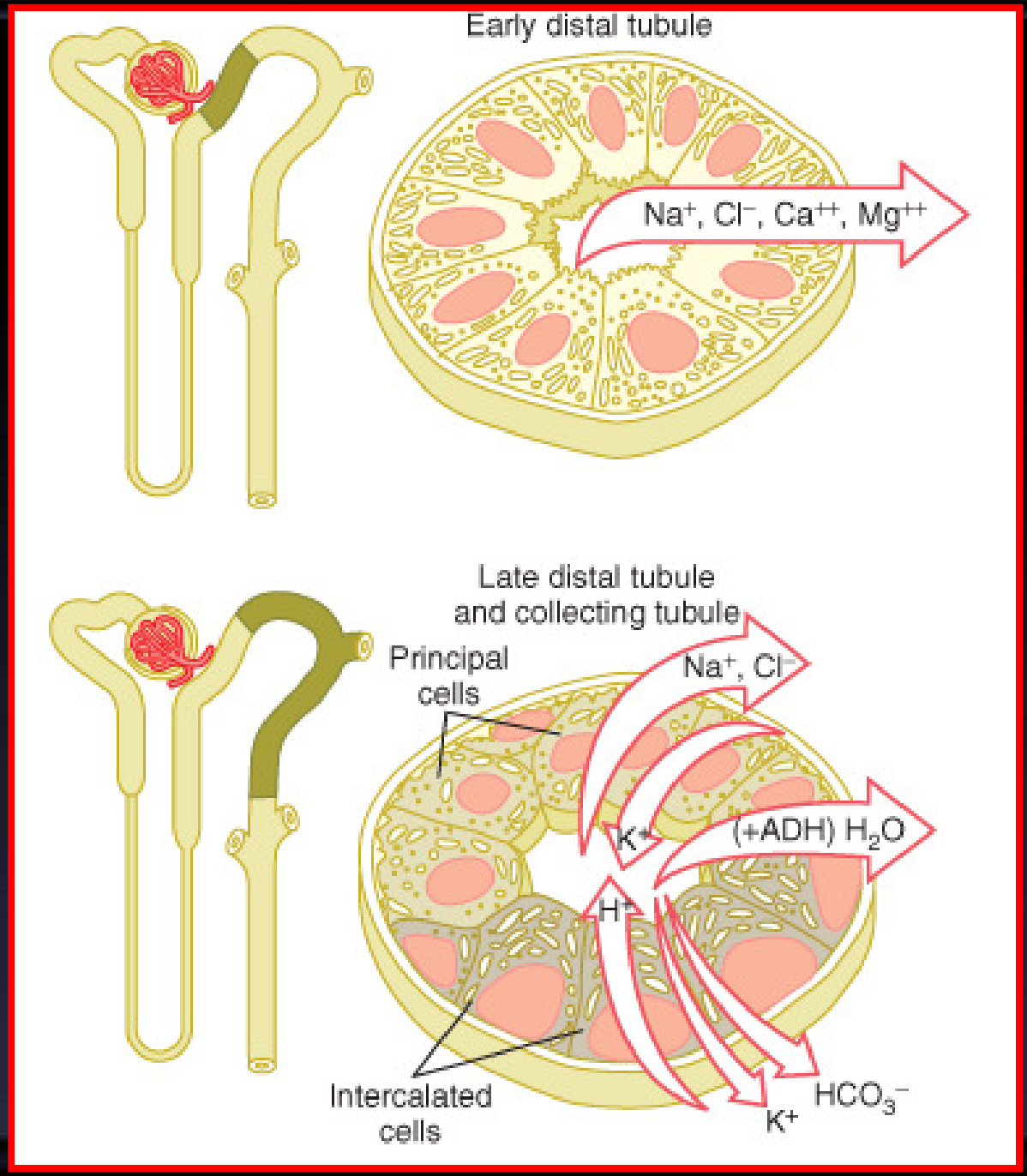
Events in LOH

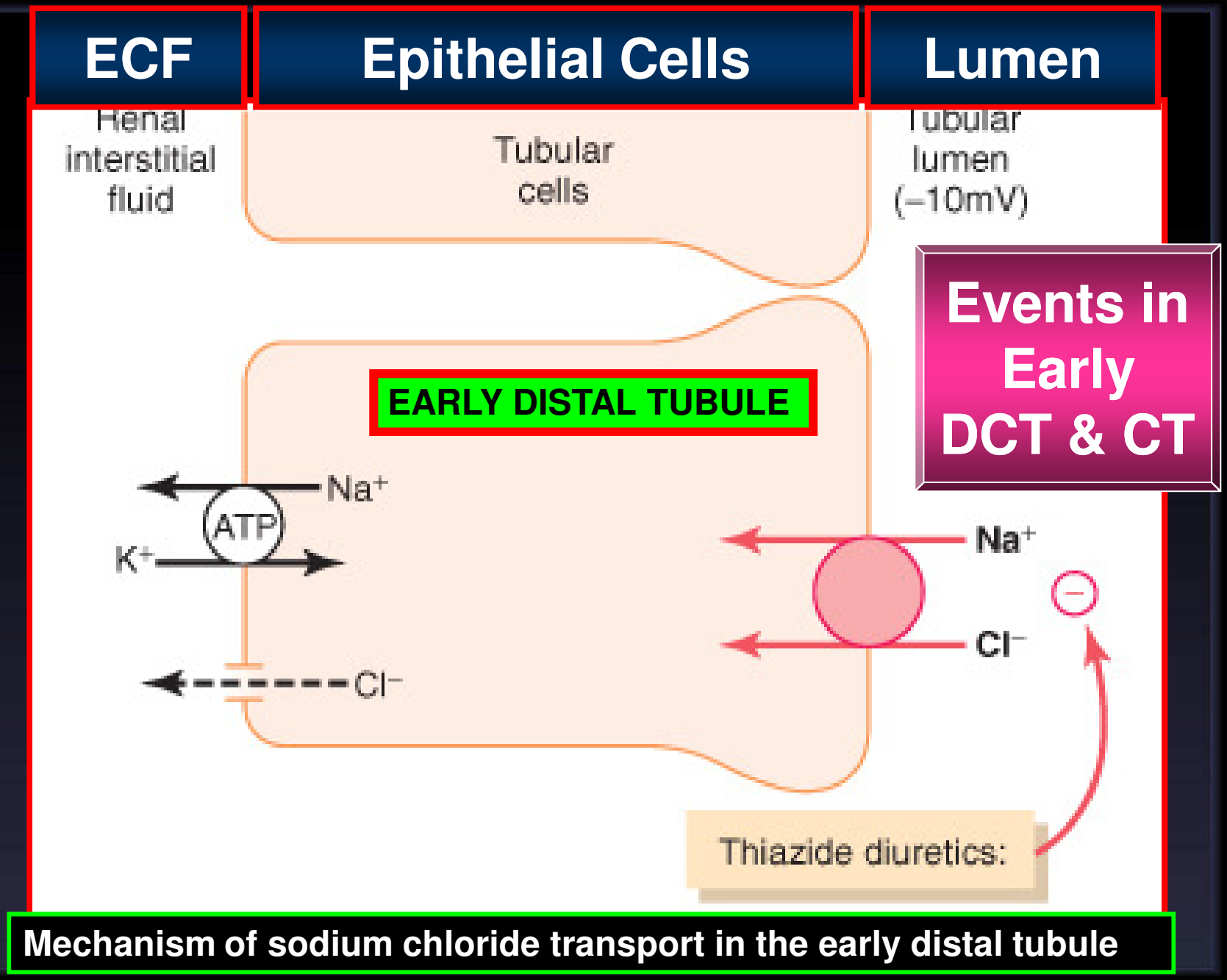


Events in Thick ALOH



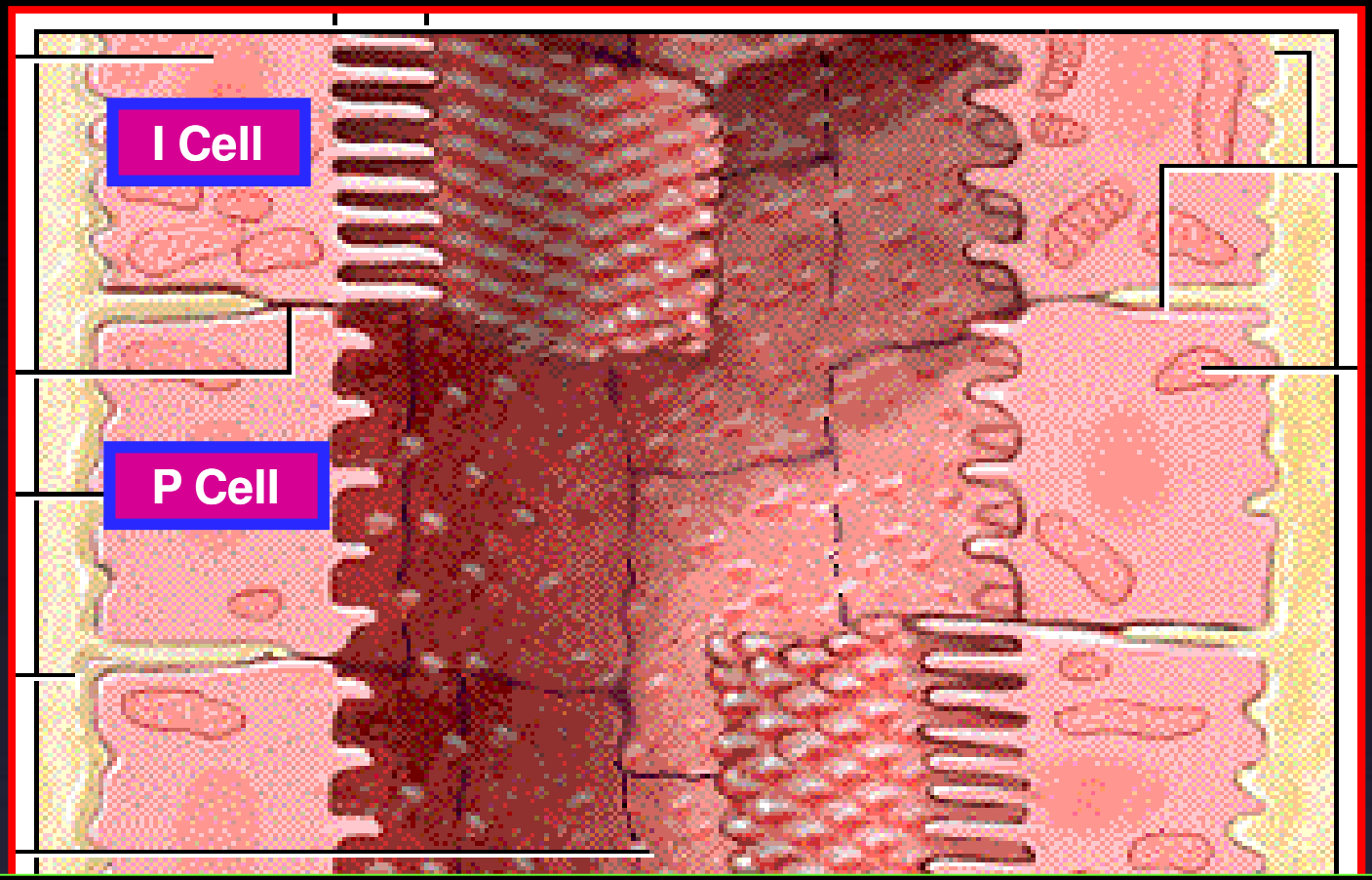
Events in DCT





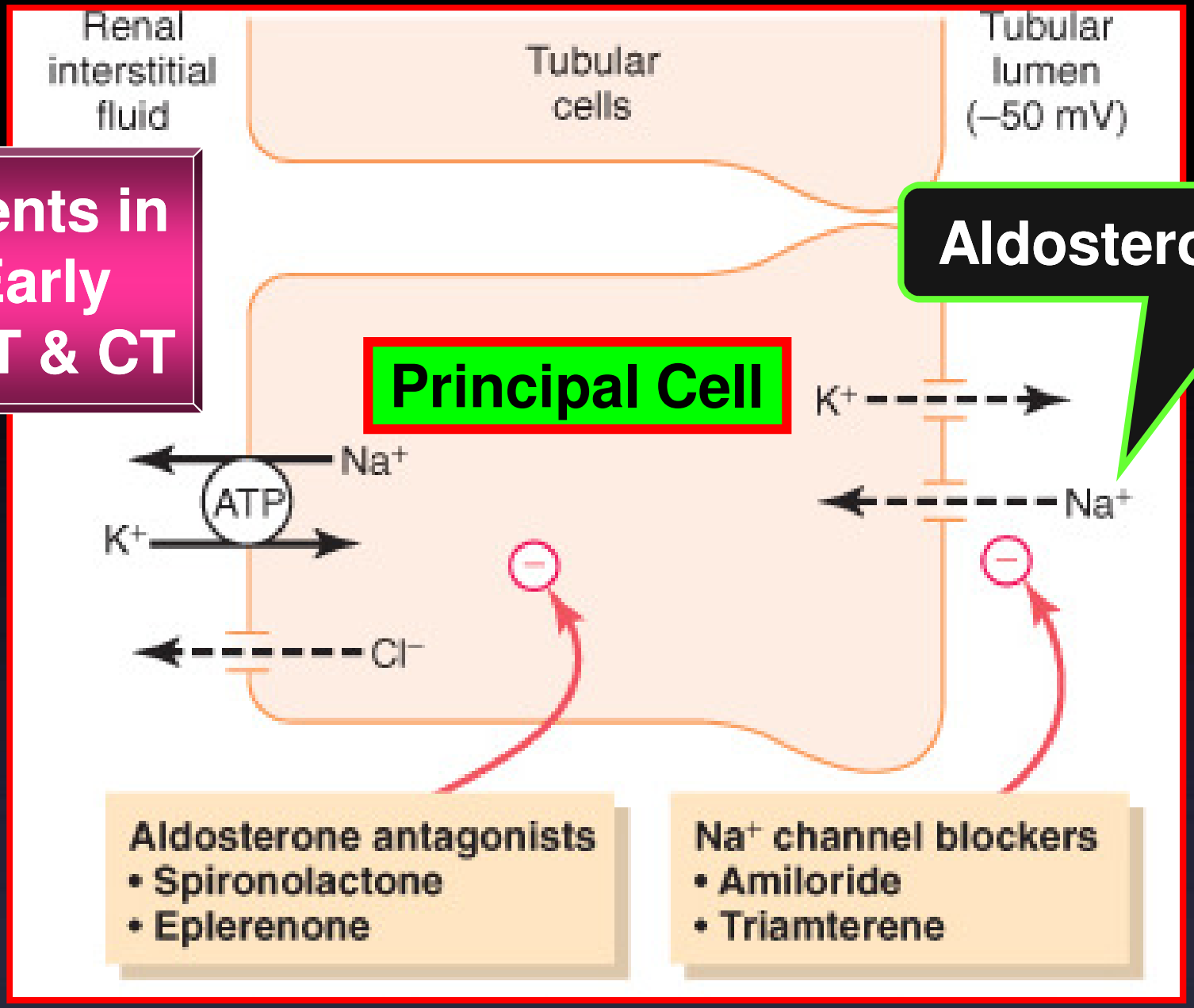
Mechanism of sodium chloride transport in the early distal tubule

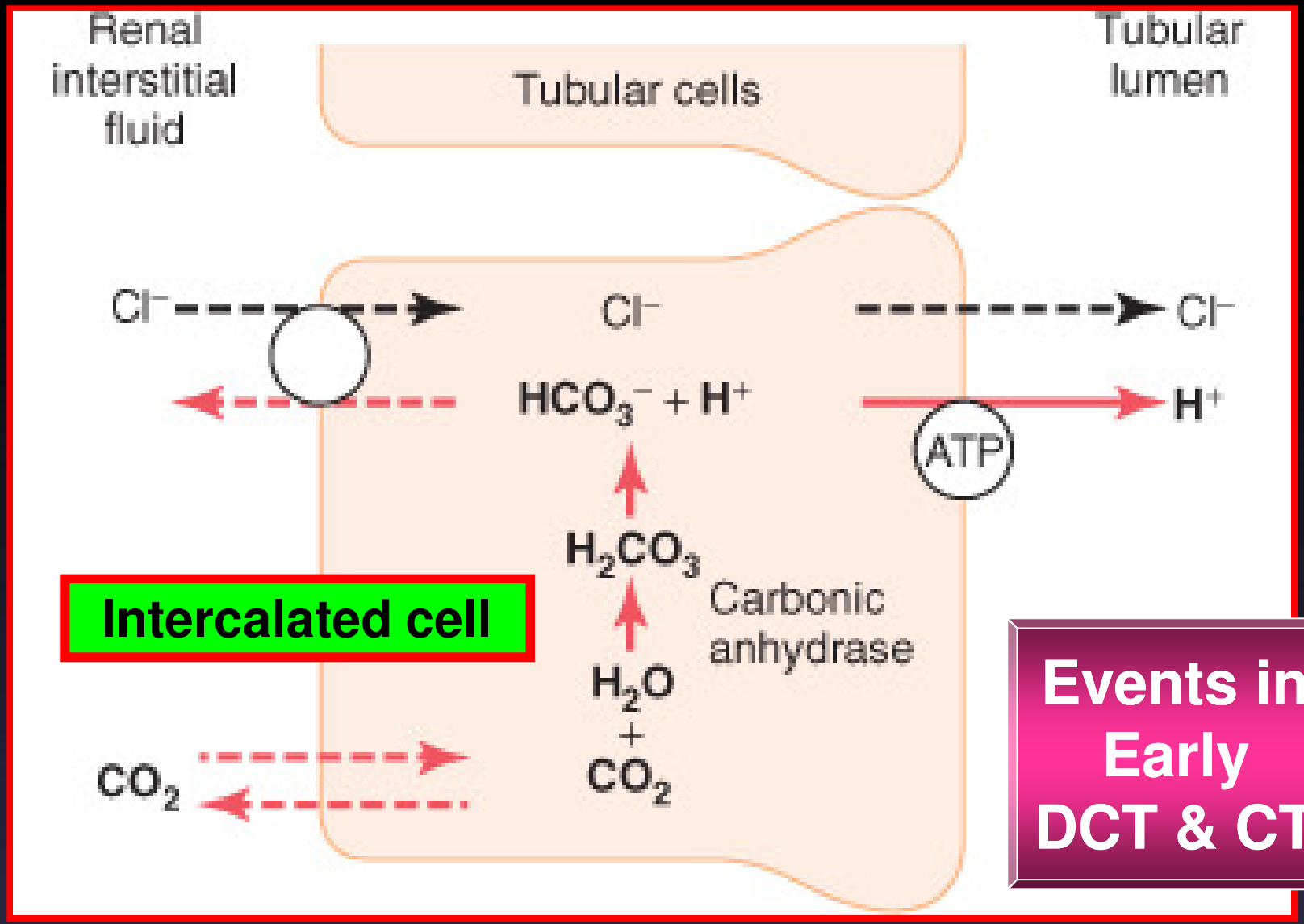
LATE DCT AND CORTICAL COLLECTING TUBULE



- Mitochondria and microvilli decrease
- Principal Cells (Na Abs and ADH related Water abs)
- Intercalated Cells (Acid Sec and HCO_3 Transport)

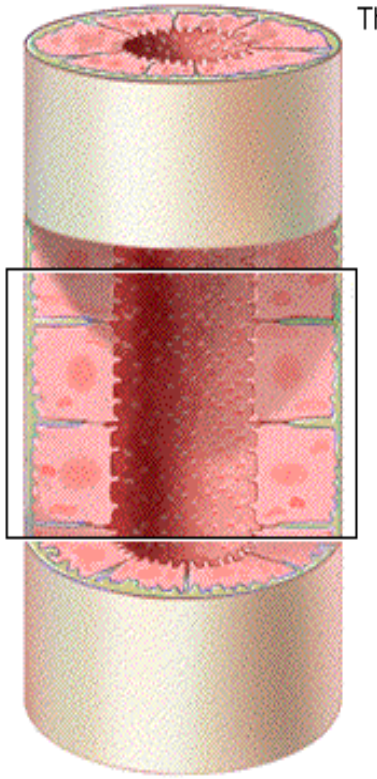
Events in Early DCT & CT



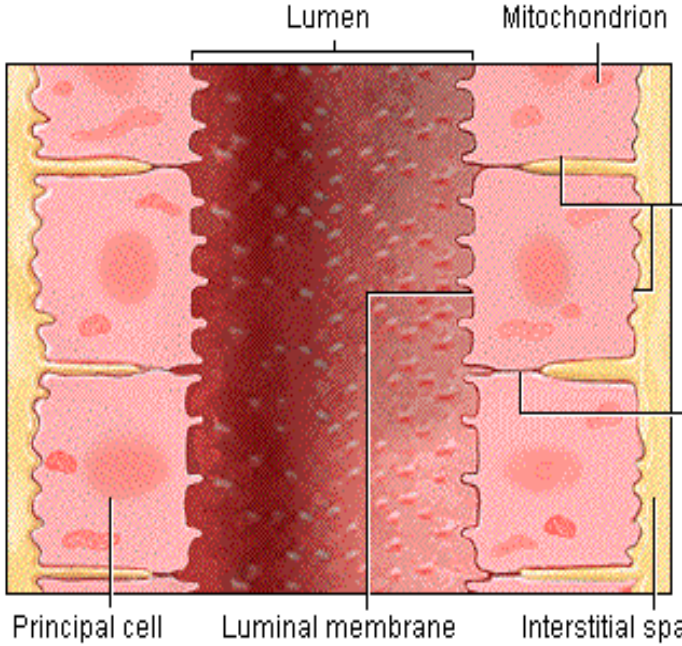

Renal interstitial fluid
Tubular cells
Tubular lumen
Cl⁻
Cl⁻
Cl⁻
HCO3⁻ + H+
H+
ATP
H2CO3
Carbonic anhydrase
H2O
+
CO2
CO2
Intercalated cell
Events in Early DCT & CT

MEDULLARY COLLECTING DUCT

CELLS OF THE MEDULLARY COLLECTING DUCT



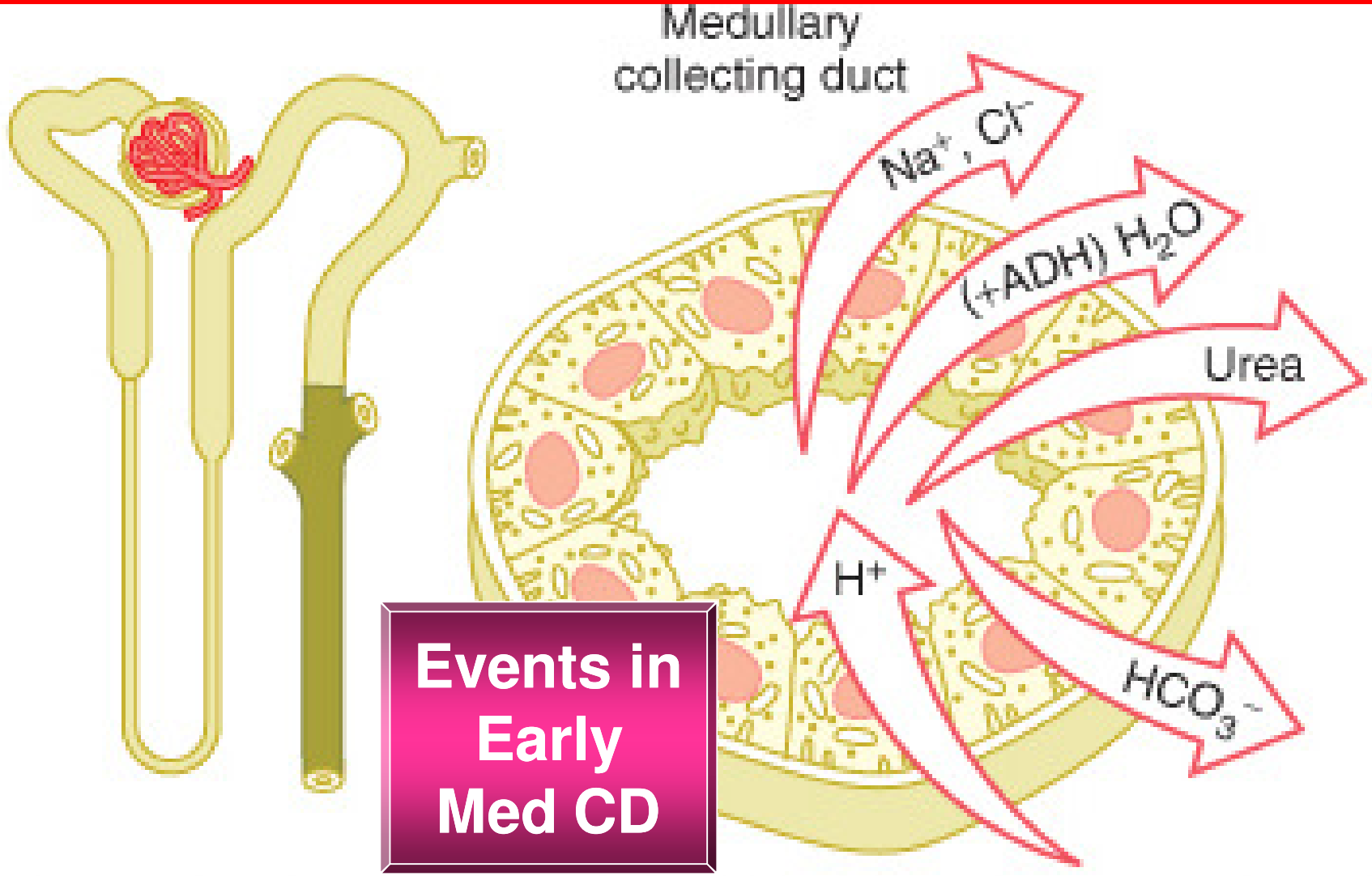
The **medullary collecting duct** is composed mainly of **principal cells**.



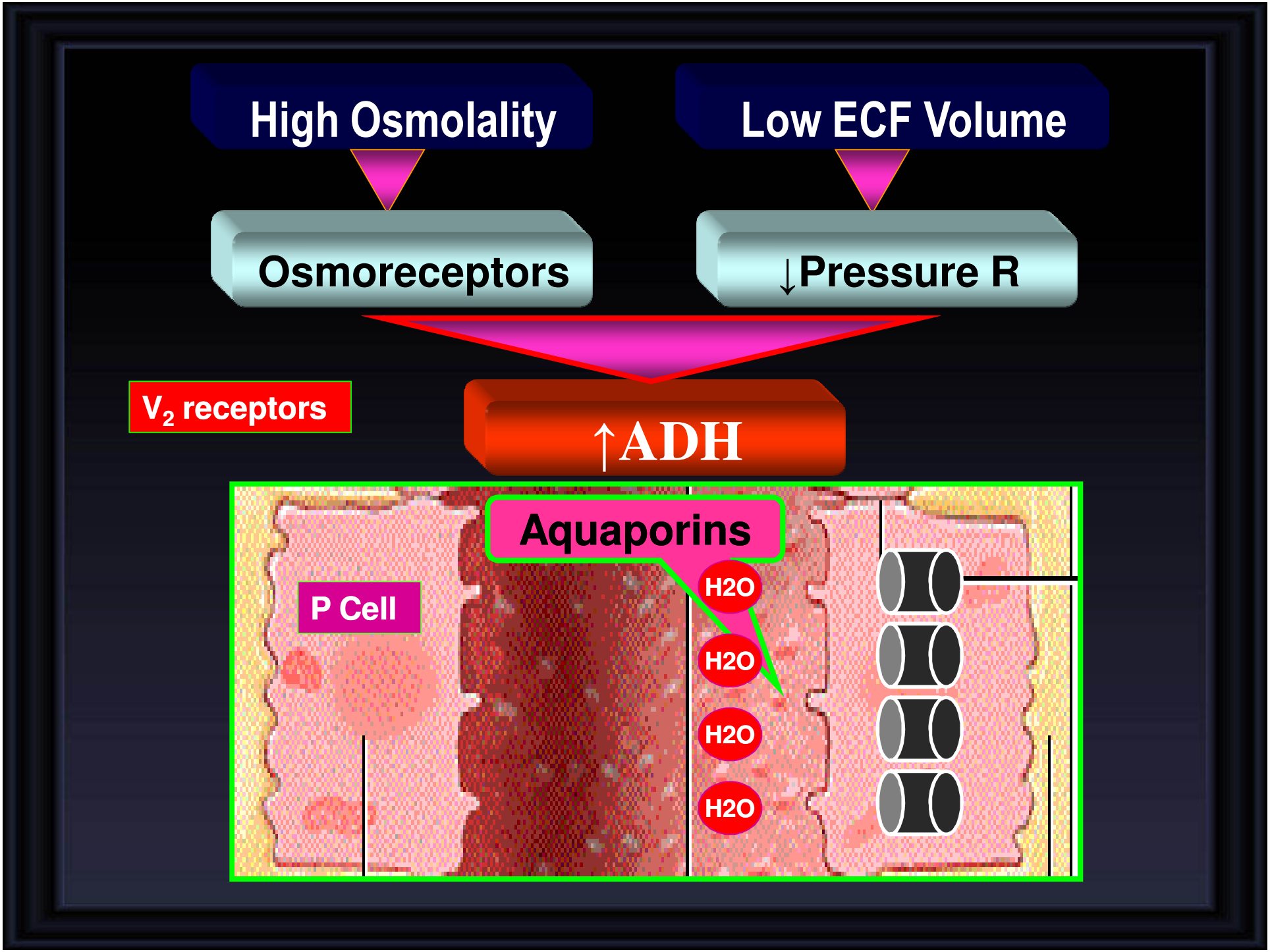
Key feature: hormonally regulated permeability to water and **urea**

Click the forward arrow to see photomicrographs.

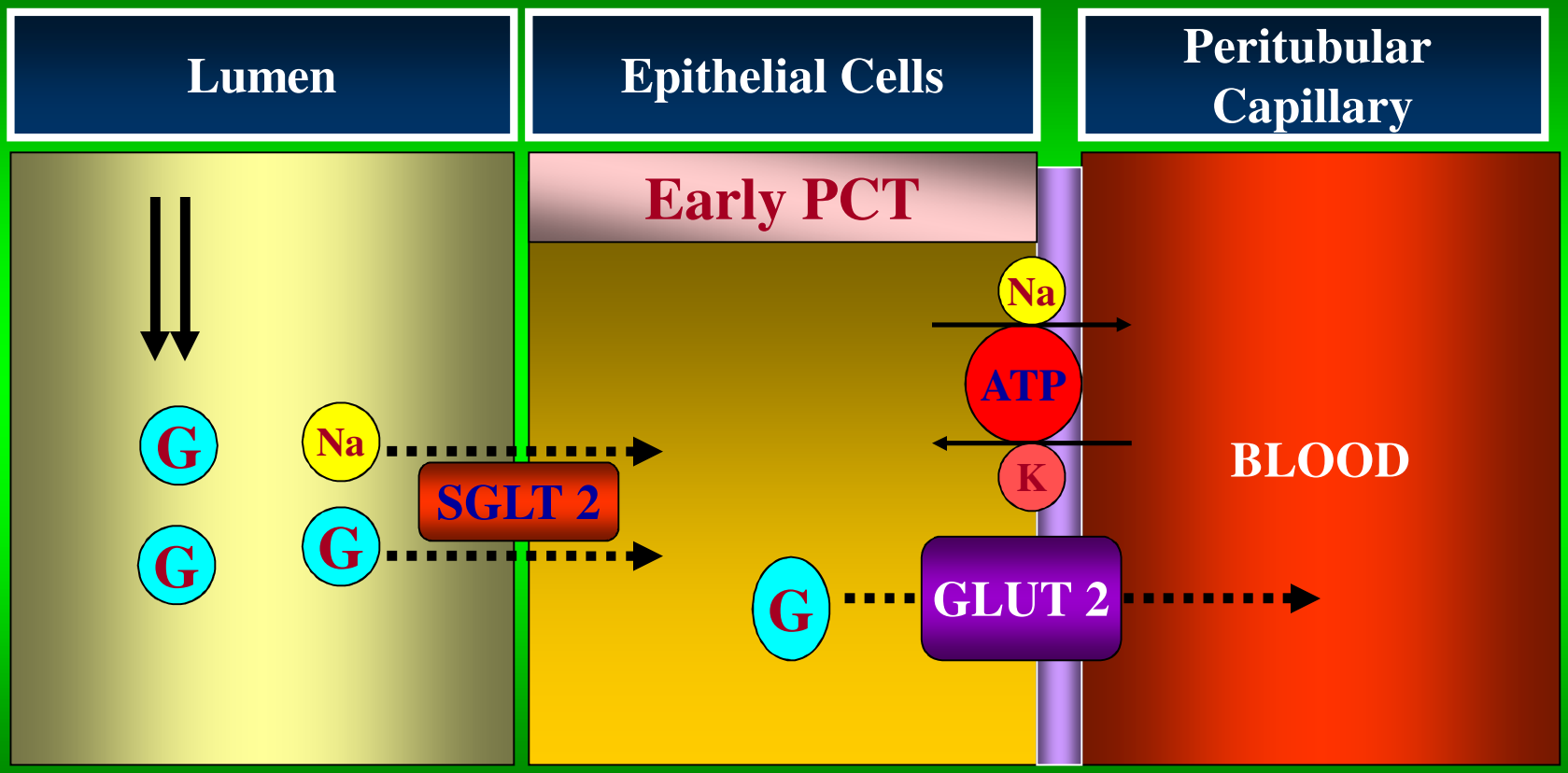
MEDULLARY COLLECTING DUCT



Events in Early Med CD

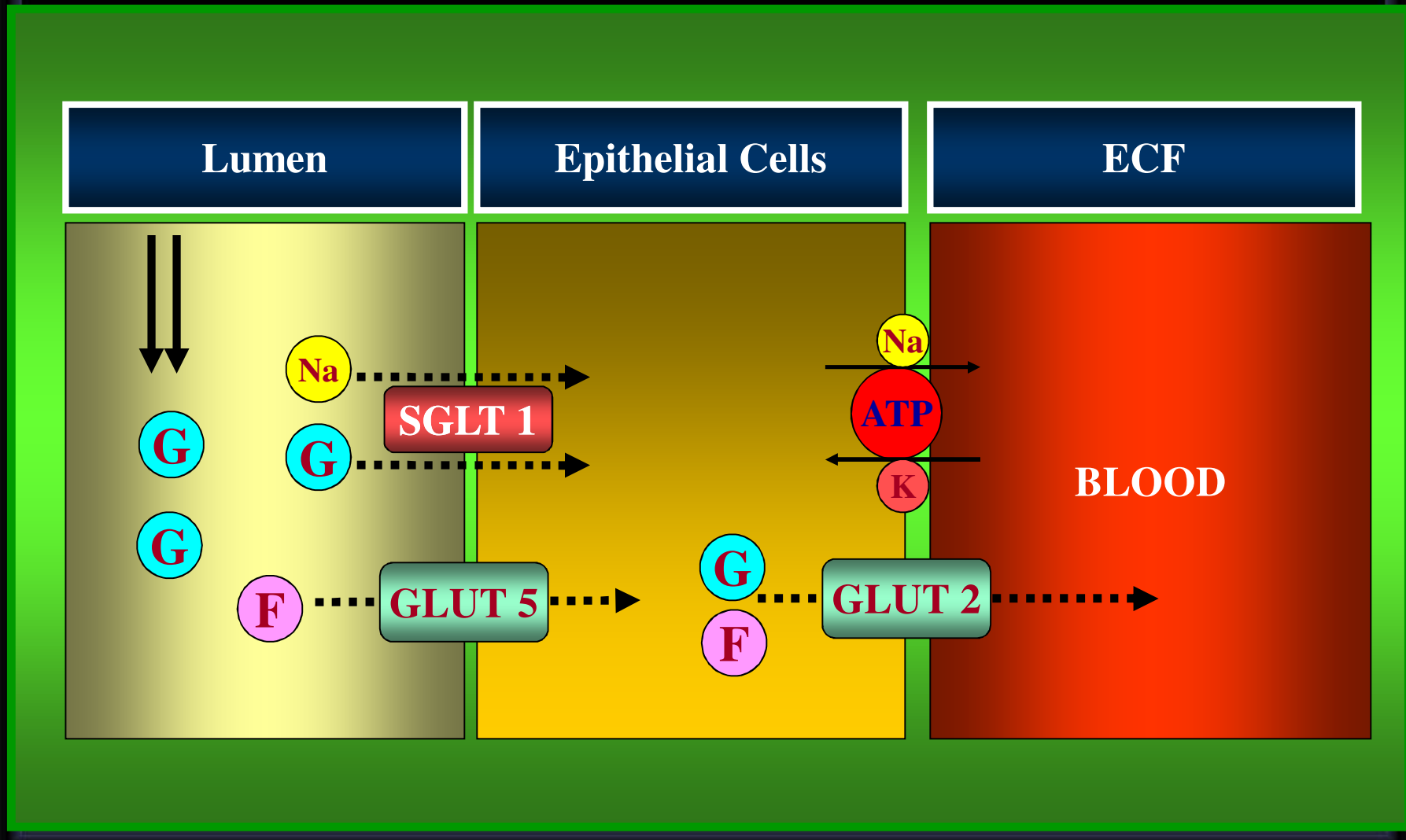

High Osmolality
Low ECF Volume
Osmoreceptors
↓Pressure R
V2 receptors
↑ADH
Aquaporins
P Cell
H2O
H2O
H2O
H2O

GLUCOSE REABSORPTION IN NEPHRON



Tm for Glucose is 375 mg/min

GLUCOSE REABSORPTION IN GIT

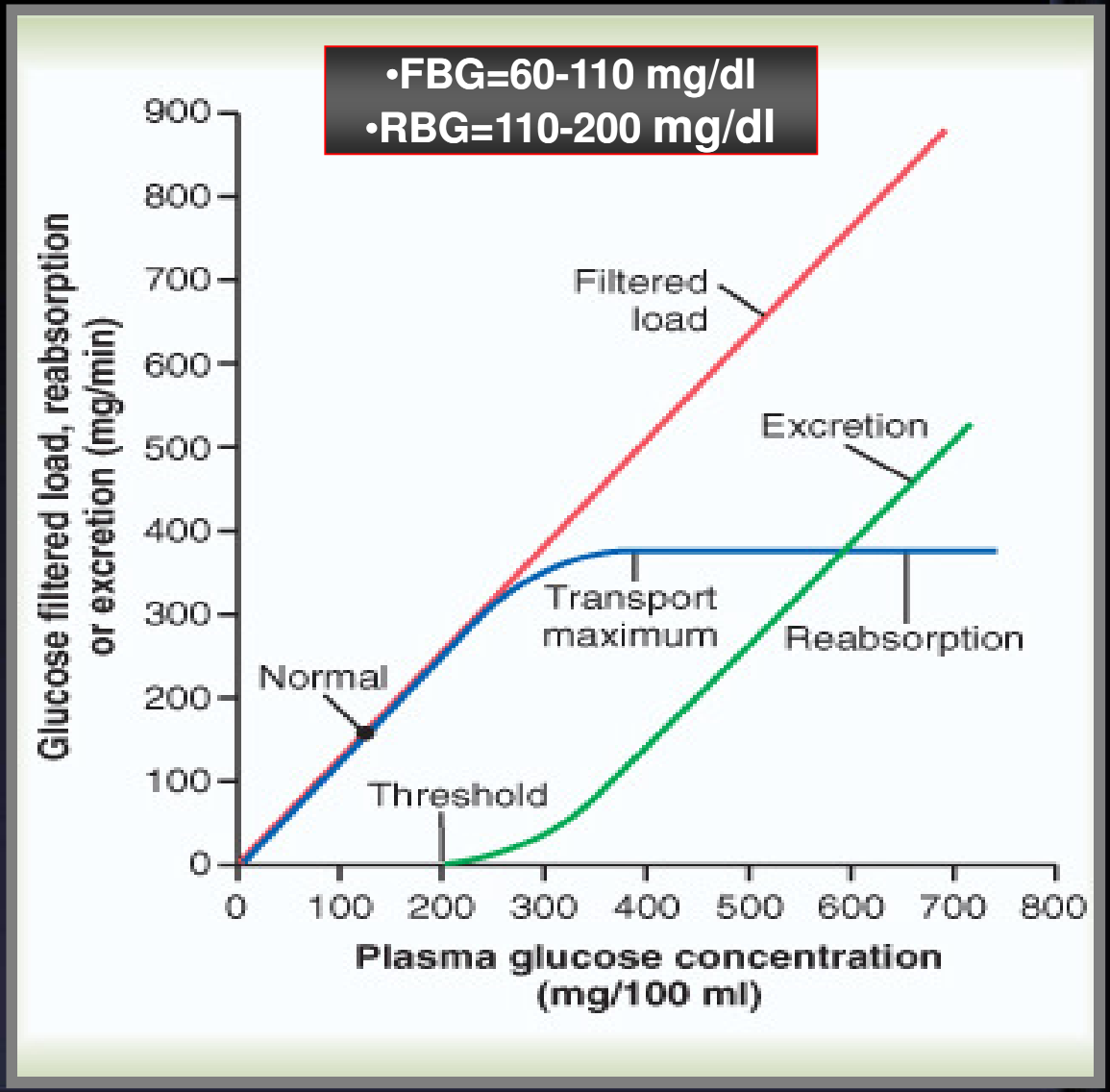


GLUCOSE REABSORPTION

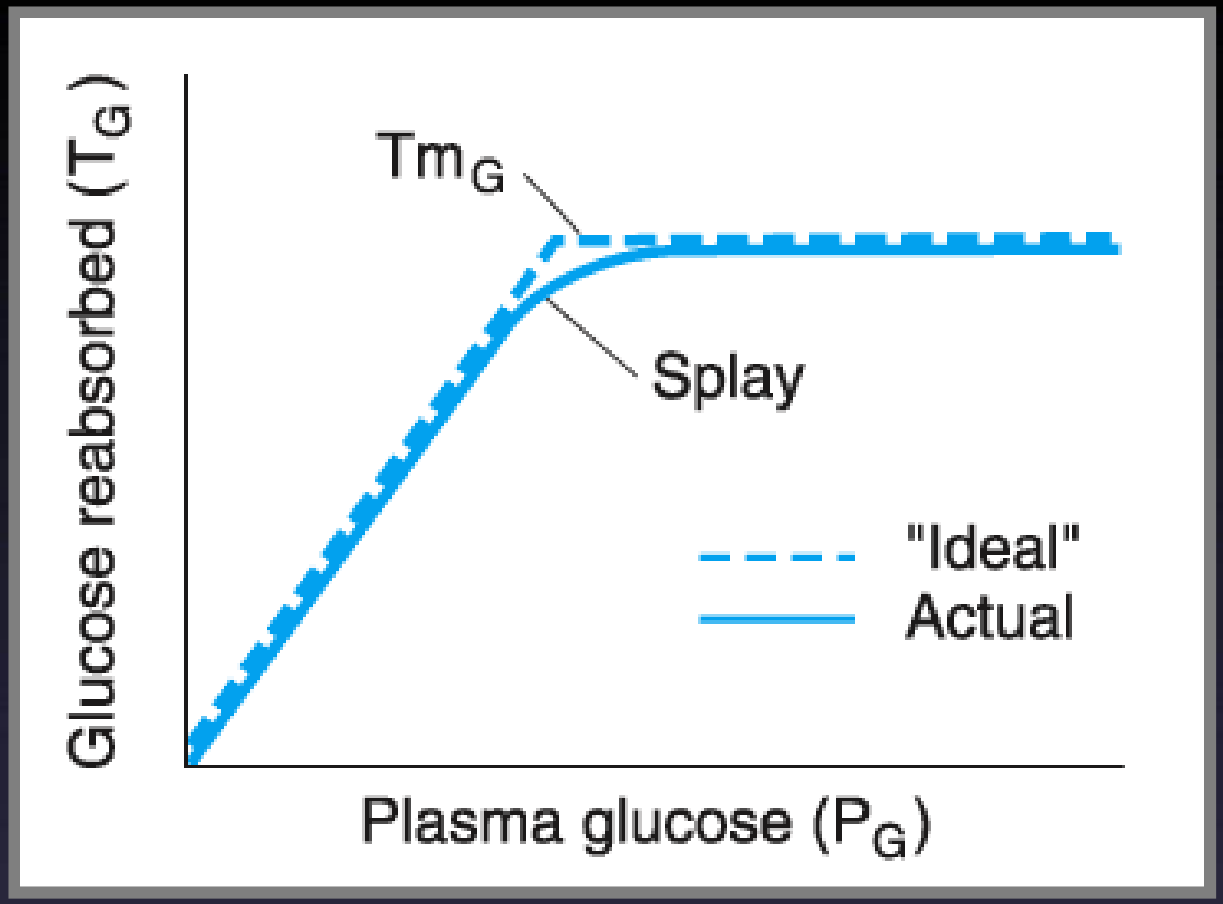
Tmax
375 mg/min

Filtered Load
125 mg/min
(GFRxPlasmaGlu)

Renal Threshold
200mg/dl



GLUCOSE REABSORPTION



Albumin Excretion in health and disease

	Normal	Nephrotic syndrome
Albumin in plasma to be filtered (g)	8000	8000
Albumin actually filtered (g)	36	65
Albumin reabsorbed (g)	36	45
Albumin lost in urine (g)	0	20

TUBULAR TRANSPORT MAXIMUM

The Maximum limit/rate at which a solute can be transported across the tubular cells of kidneys is called TUBULAR TRANSPORT MAXIMUM

Tm for Glucose is 375 mg/min

TUBULAR TRANSPORT MAXIMUM FOR DIFFERENT SUBSTANCES

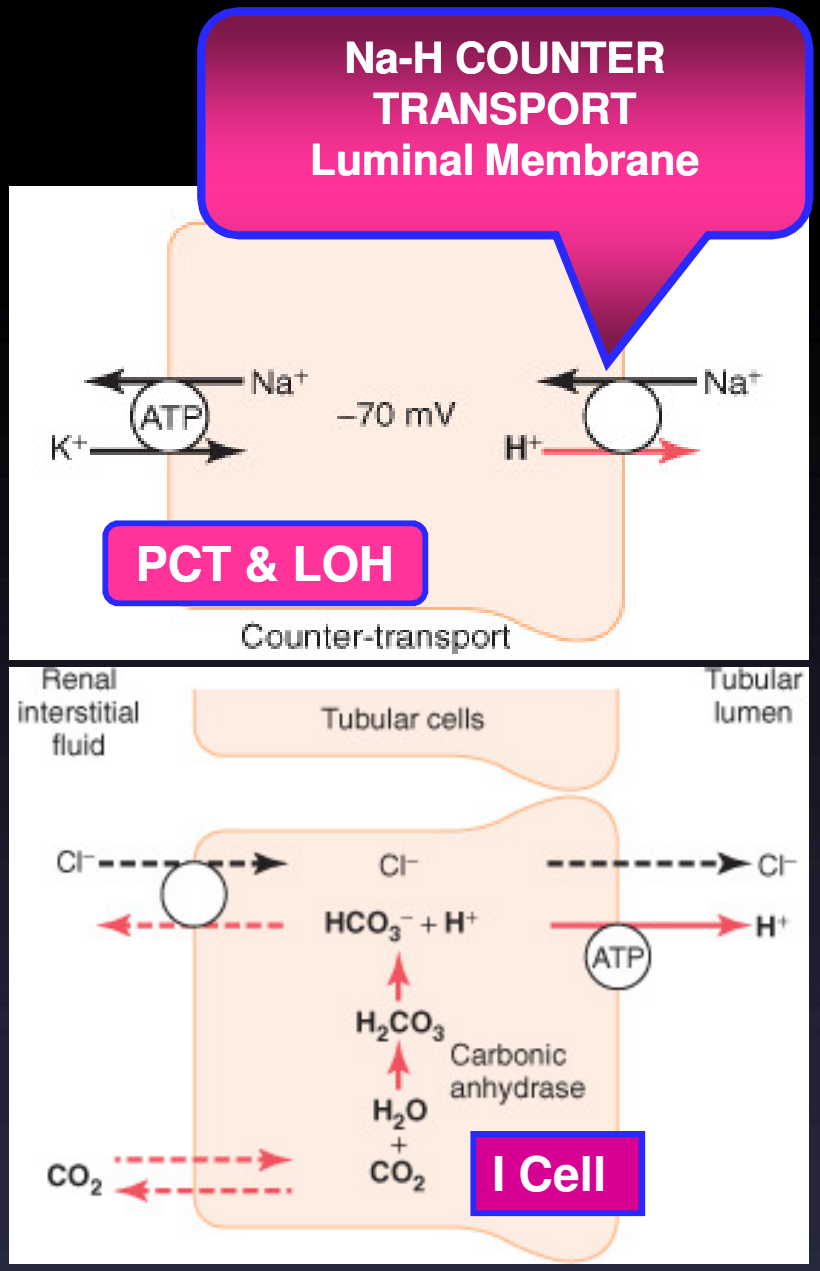
SUBSTANCE	Tm
Glucose	375 mg/min
Phosphate	0.1 mM/min
Sulfate	0.06 mM/min
Amino Acids	1.5 mM/min
Urate	15 mg/min
Plasma Protein	30 mg/min
Hemoglobin	1 mg/min
Lactate	75 mg/min
Acetoacetate	variable

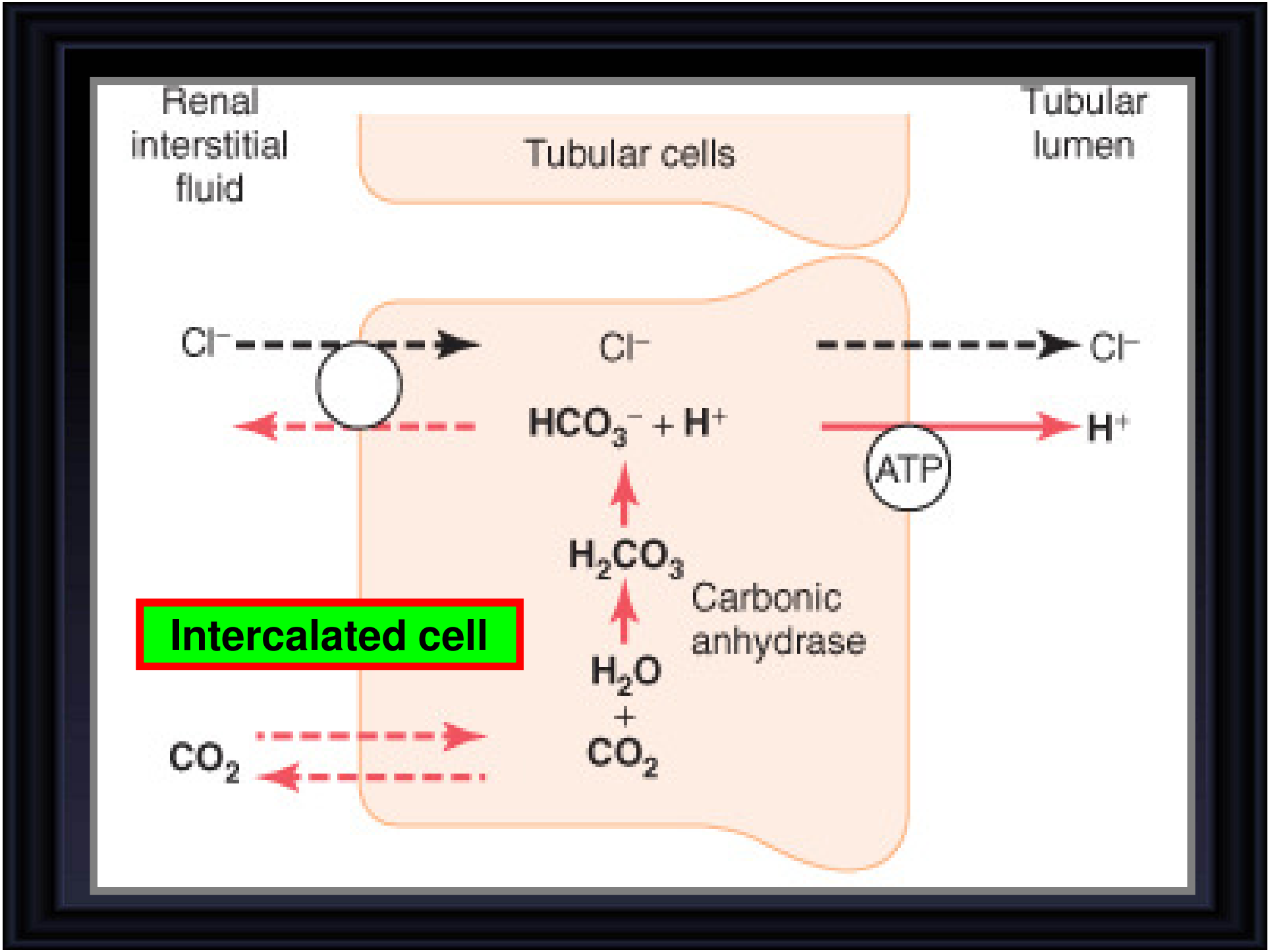
Transport Maximums for Substances That Are Actively Secreted

Substance	Transport Maximum
Creatinine	16 mg/min
Para-aminohippuric acid	80 mg/min

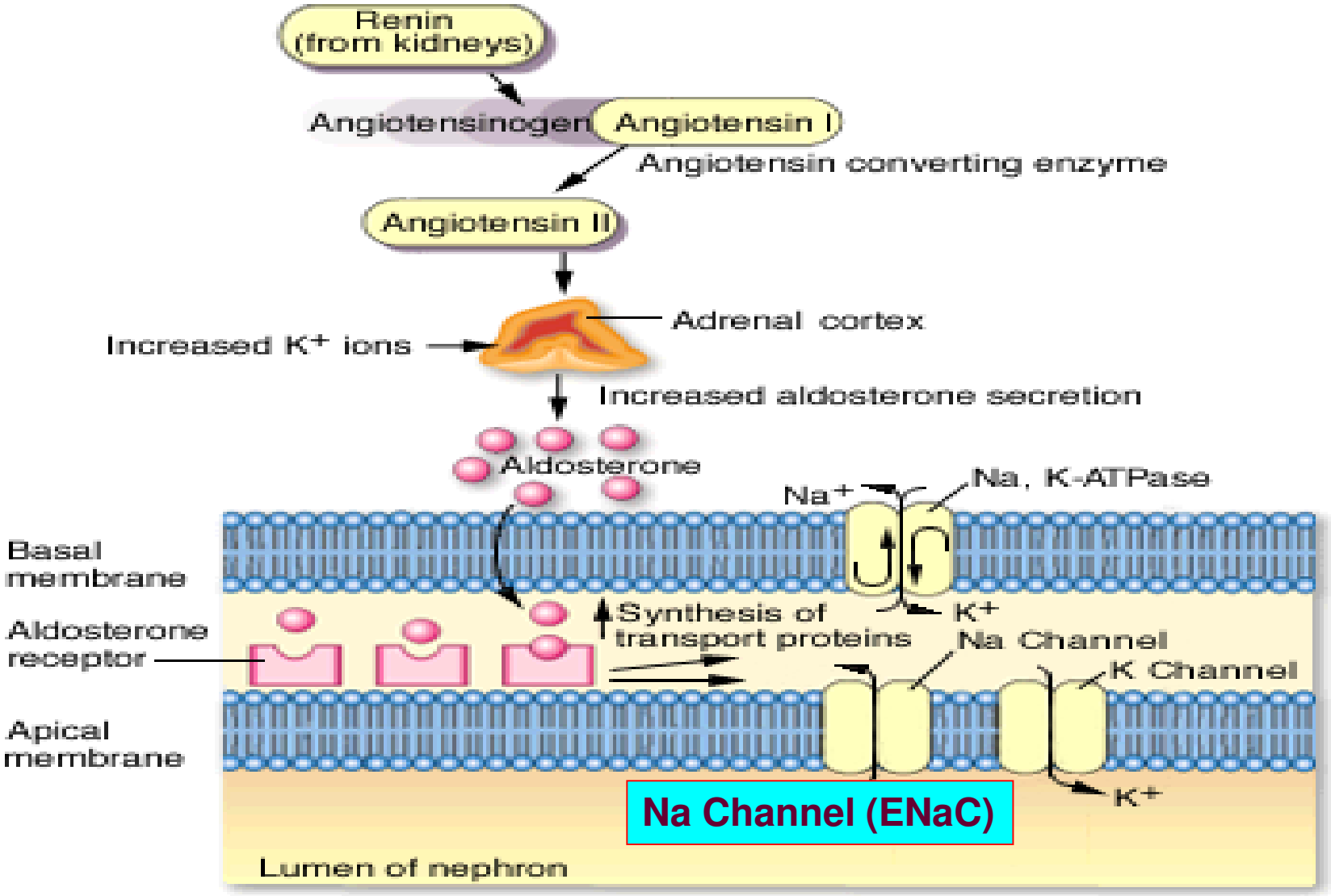
HYDROGEN

- Secreted in Proximal Tubule and Thick ascending LOH by Counter Transport with Na
- Secreted in DCT by H^+ ATP ase

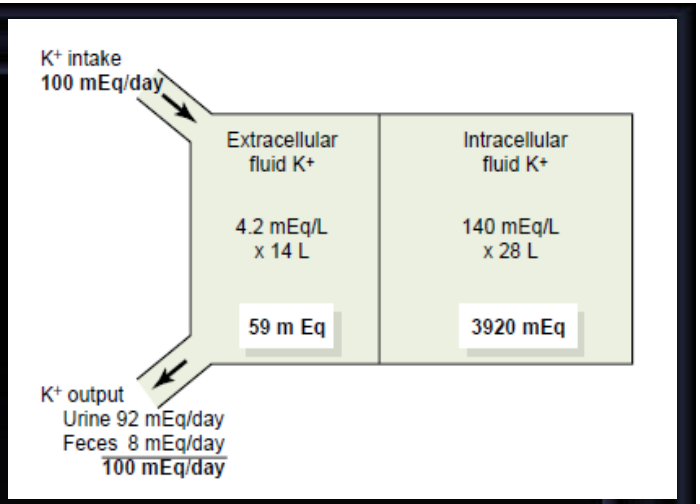



Renal interstitial fluid
Tubular cells
Tubular lumen
Cl⁻
Cl⁻
Cl⁻
HCO3⁻ + H+
H+
ATP
H2CO3
Carbonic anhydrase
Intercalated cell
H2O
+
CO2
CO2

Effect Of Aldosterone On Cortical Collecting Duct



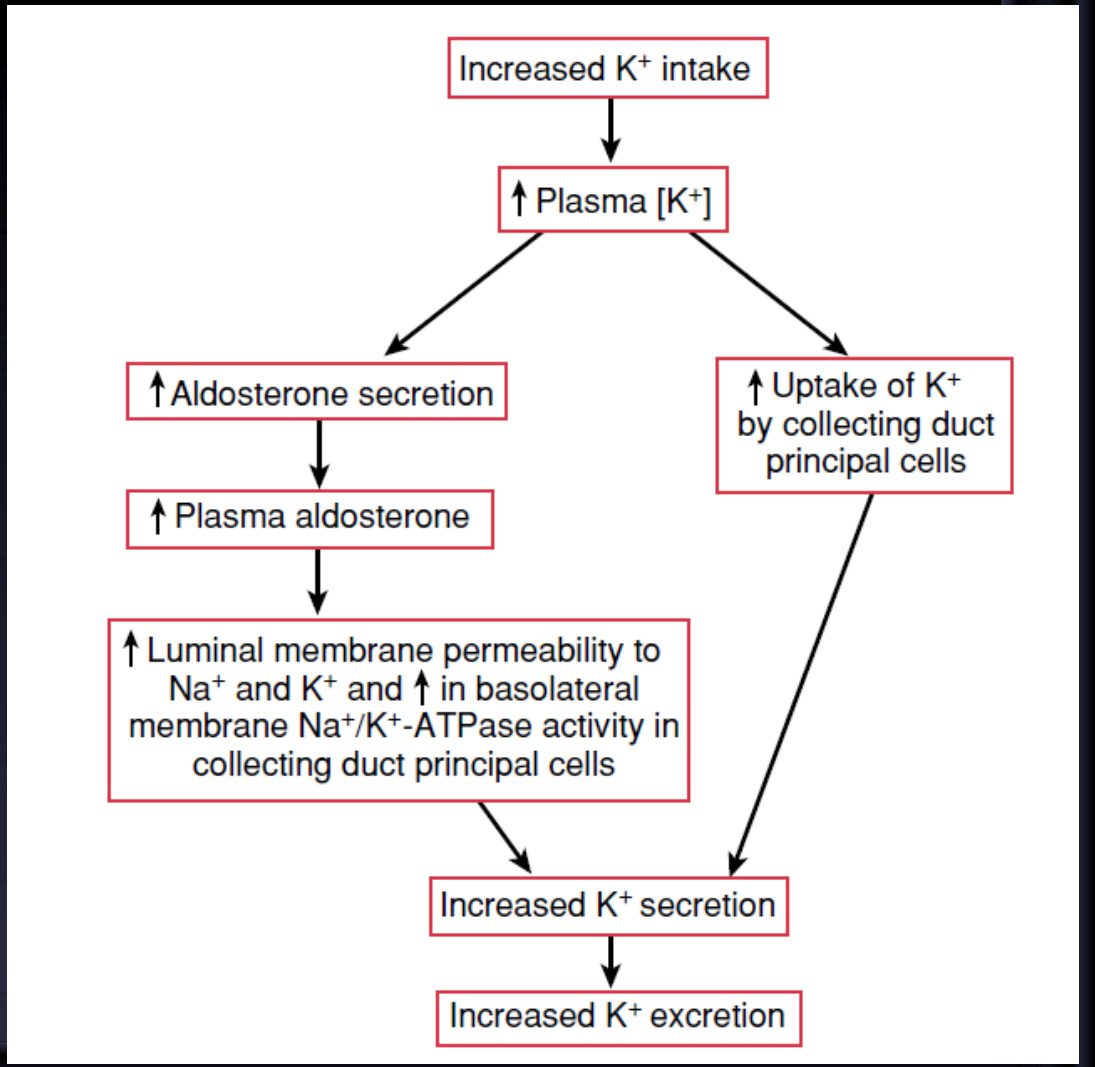
POTASSIUM



- Both reabsorbed and secreted
- 67% is reabsorbed by PCT(solvent drag)
- Secreted by Thick Asc LOH, early distal tubule / collecting tubule
  - correlated with dietary intake
    - 80% of filtered load appears in urine if dietary content high
    - 1% if dietary content low
- Excretion is controlled by Aldosterone

EFFECT OF INCREASED DIETARY K INTAKE ON K EXCRETION

K directly stimulates aldosterone secretion and leads to an increase in cell [K] in collecting duct principal cells. Both of these lead to enhanced secretion and, hence, excretion, of K.



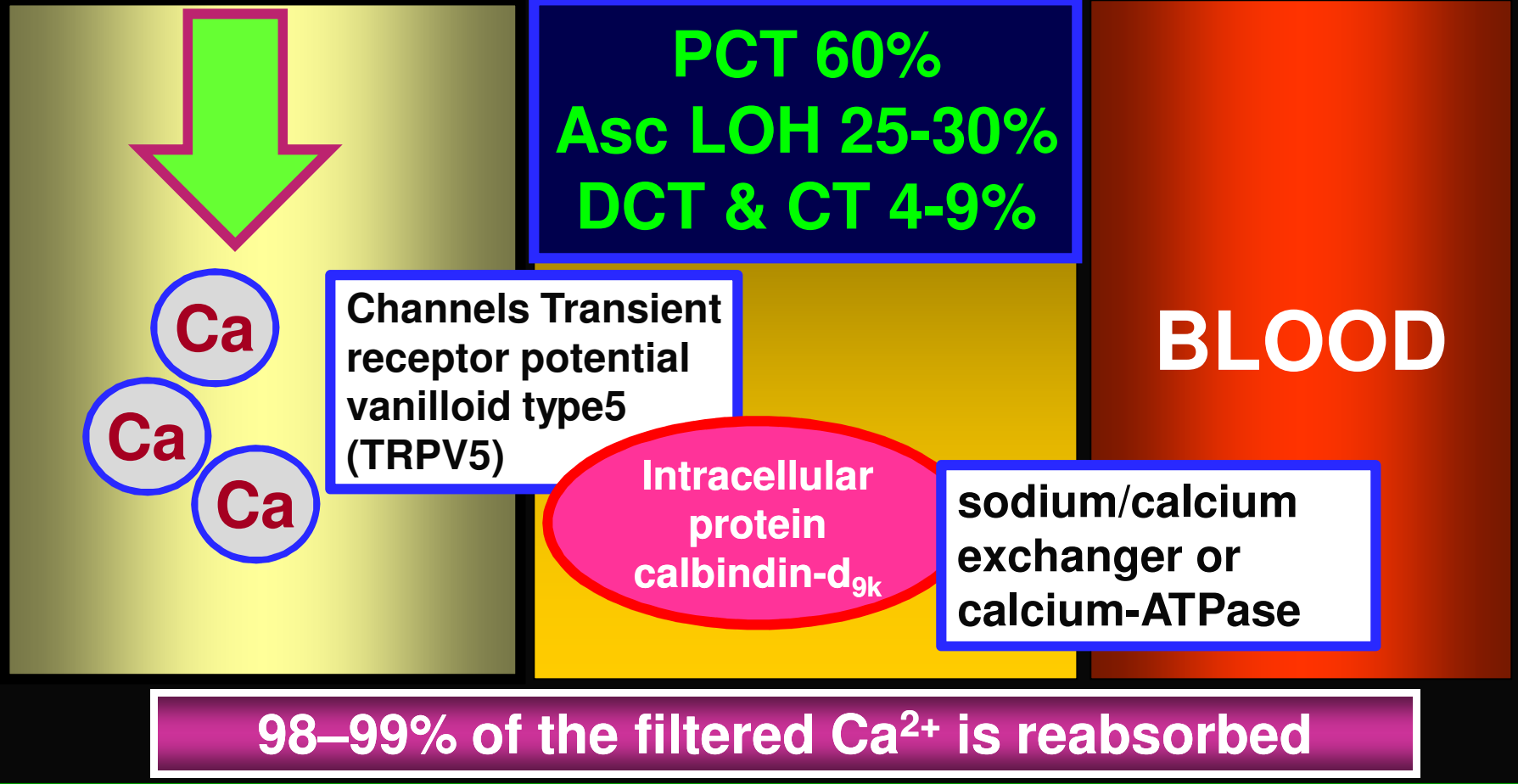
UREA

- Plasma concentration is 2.5 – 7.5 mmol/L
- 50 % is reabsorbed in PCT passively with water
- It is the only waste to be reabsorbed
- Creatinine and Phenol are not reabsorbed.

CALCIUM

- Ionized Calcium is freely filtered and reabsorbed in PCT
- It moves into tubular cells passively (downhill)
- It moves out of the cell by Ca/Na Counter Transport or Actively by Ca ATP ase Mechanism
- Its reabsorption is Hormonally controlled

CALCIUM REABSORPTION IN NEPHRON



98–99% of the filtered Ca^{2+} is reabsorbed

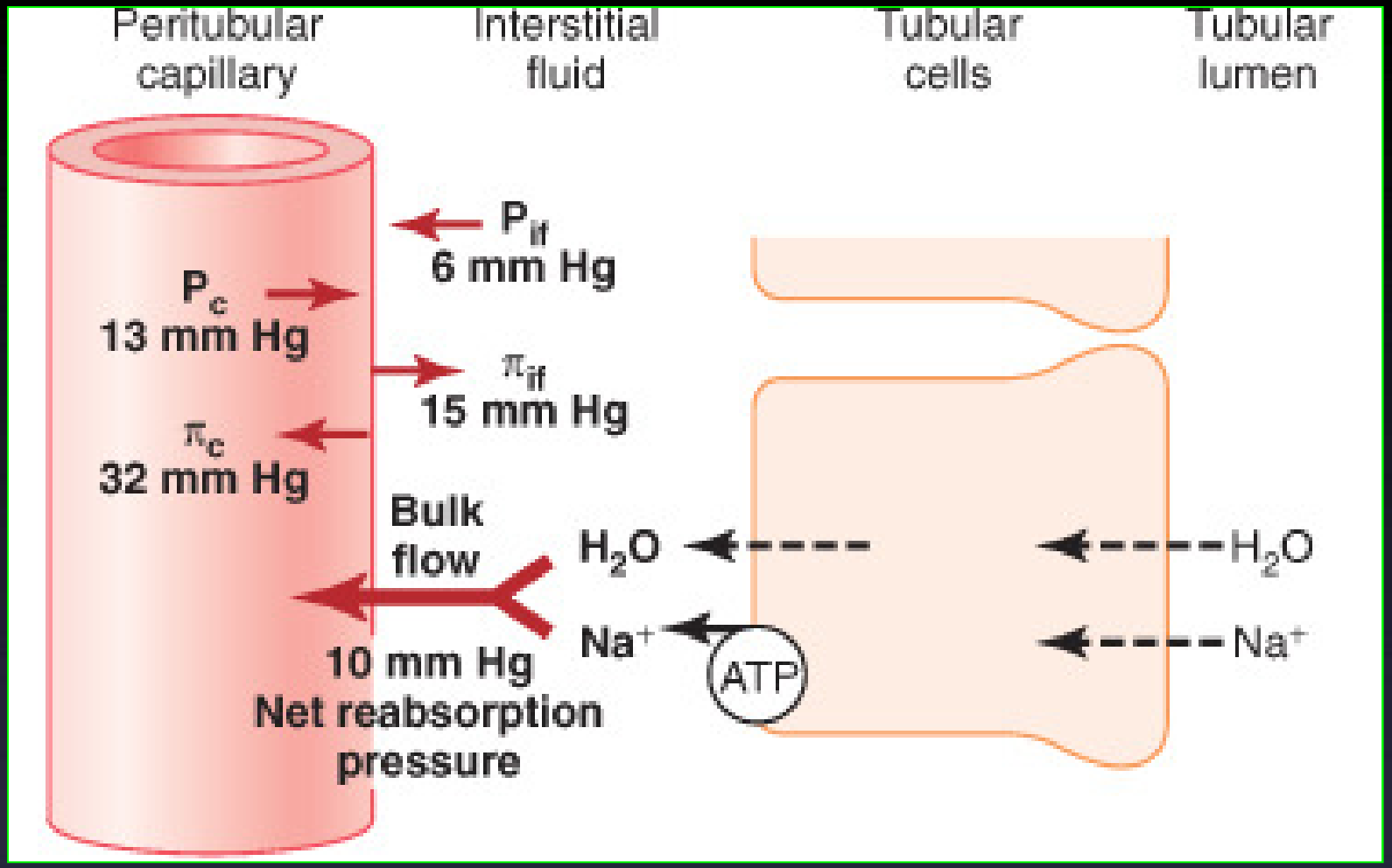
PHOSPHATE

- It is reabsorbed by cotransport with Na in PCT in luminal border (Na/Pi)
- Its reabsorption is Hormonally controlled
- It is increased by Vit D and decreased by Parathyroid Hormone

SULPHATE

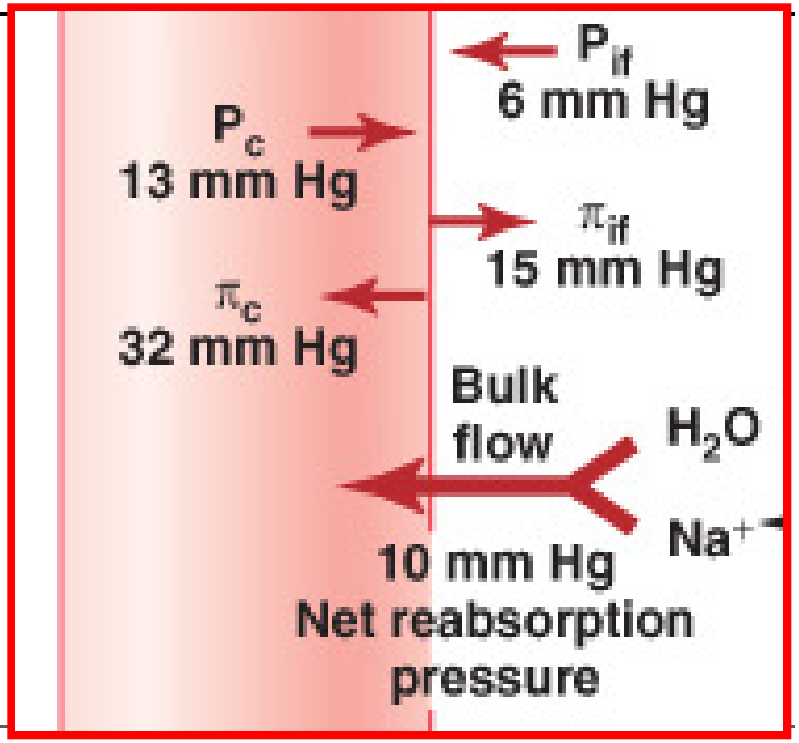
- Like PHOSPHATE reabsorbed with Na

PERITUBULAR CAPILLARY AND RENAL INTERSTITIAL FLUID PHYSICAL FORCES



Factors That Can Influence Peritubular Capillary Reabsorption

- ↑ P_c → ↓ Reabsorption
  - ↓ R_A → ↑ P_c
  - ↓ R_E → ↑ P_c
  - ↑ Arterial Pressure → ↑ P_c
- ↑ π_c → ↑ Reabsorption
  - ↑ π_A → ↑ π_c
  - ↑ FF → ↑ π_c
- ↑ K_f → ↑ Reabsorption



P_c, peritubular capillary hydrostatic pressure; R_A and R_E, afferent and efferent arteriolar resistances, respectively; π_c, peritubular capillary colloid osmotic pressure; π_A, arterial plasma colloid osmotic pressure; FF, filtration fraction; K_f, peritubular capillary filtration coefficient.

Table 27–3

Hormones That Regulate Tubular Reabsorption

Hormone	Site of Action	Effects
Aldosterone	Collecting tubule and duct	↑ NaCl, H_2O reabsorption, ↑ K^+ secretion
Angiotensin II	Proximal tubule, thick ascending loop of Henle/distal tubule, collecting tubule	↑ NaCl, H_2O reabsorption, ↑ H^+ secretion
Antidiuretic hormone	Distal tubule/collecting tubule and duct	↑ H_2O reabsorption
Atrial natriuretic peptide	Distal tubule/collecting tubule and duct	↓ NaCl reabsorption
Parathyroid hormone	Proximal tubule, thick ascending loop of Henle/distal tubule	↓ PO_4^{---} reabsorption, ↑ Ca^{++} reabsorption