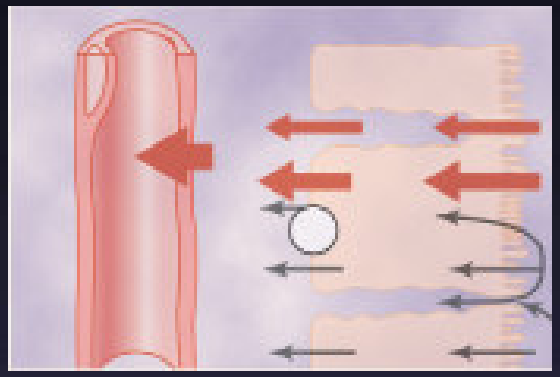
27 Urine Formation by the Kidneys: II. Tubular Processing of the Glomerular Filtrate



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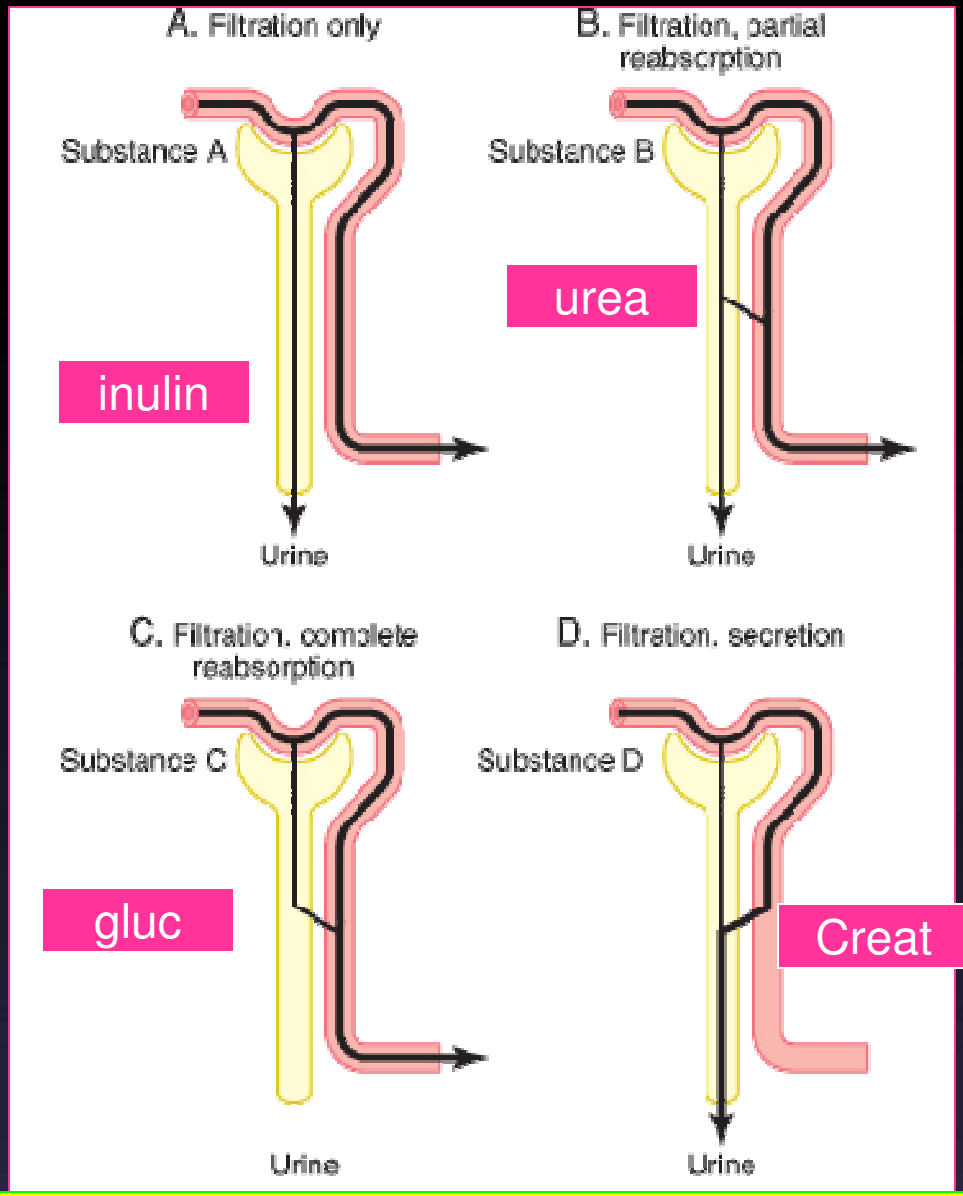
OBJECTIVES

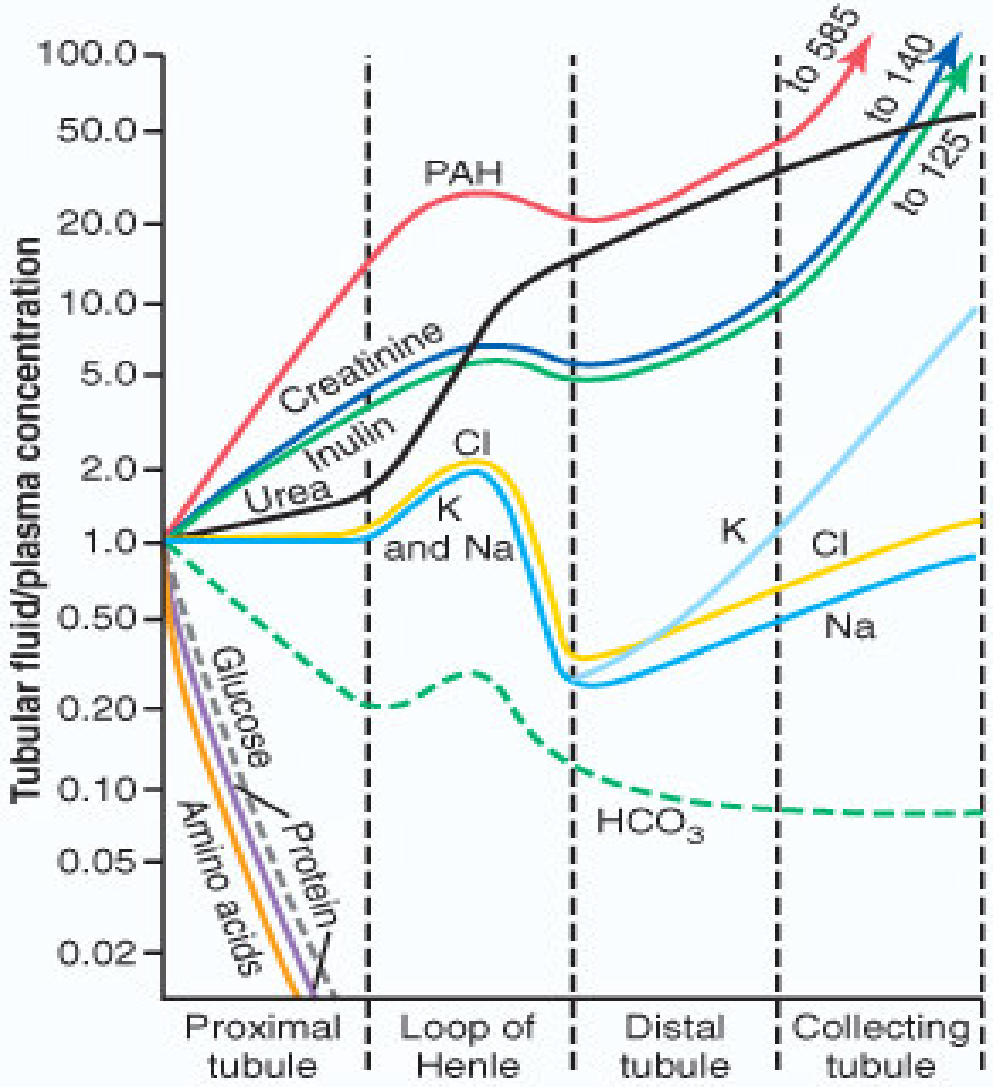
At the end of this lecture you should be able to describe:

- Absortive Characteristics of different parts of nephrons
- Transport Mechanisms operating in nephrons
- Tubular Reabsoprtion and Secretion

NEXT



Urinary Excretion Rate = Filtration Rate – Reabsorption Rate + Secretion Rate


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

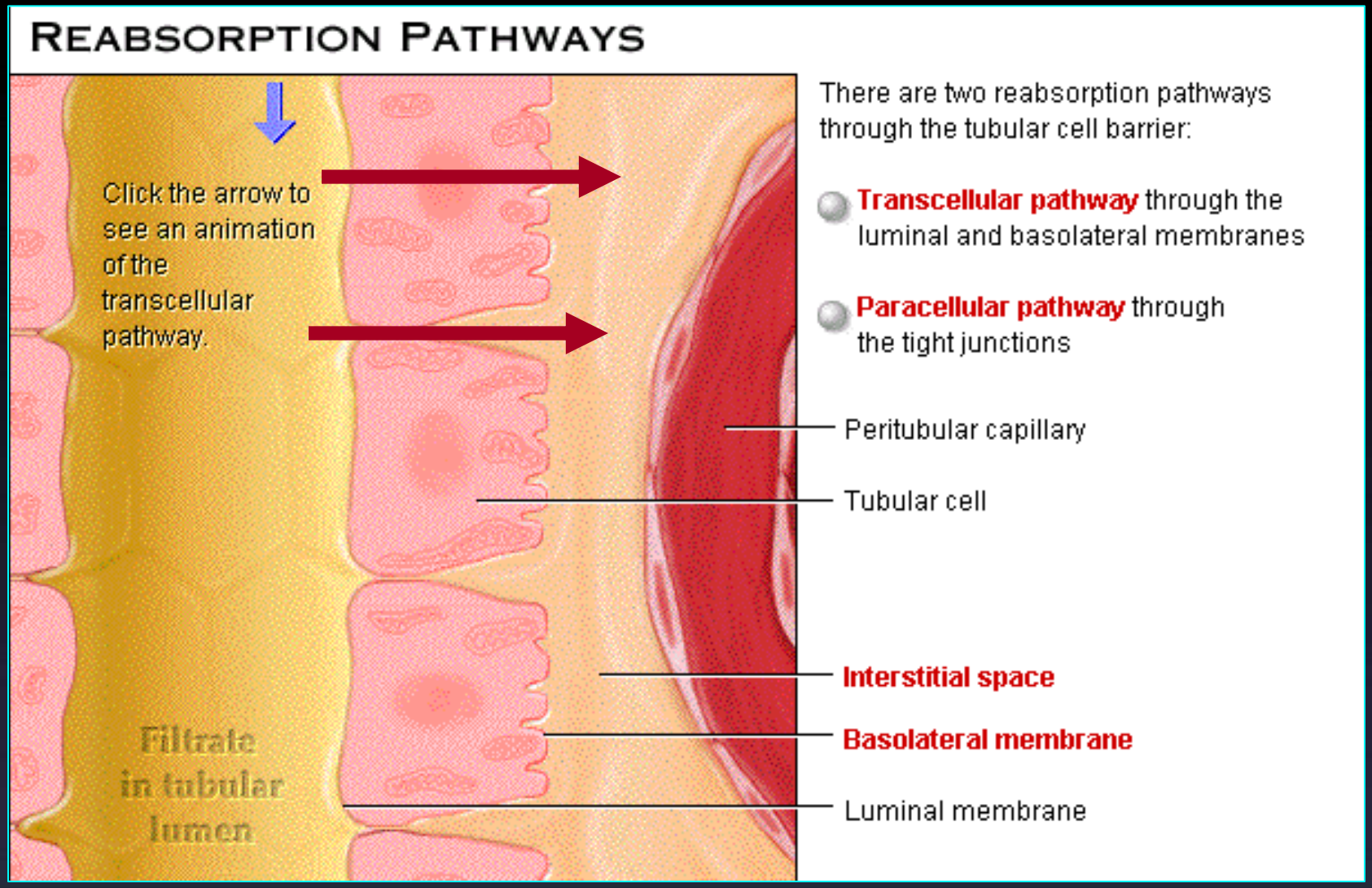
CLASSIFICATION OF TRANSPORT MECHANISMS

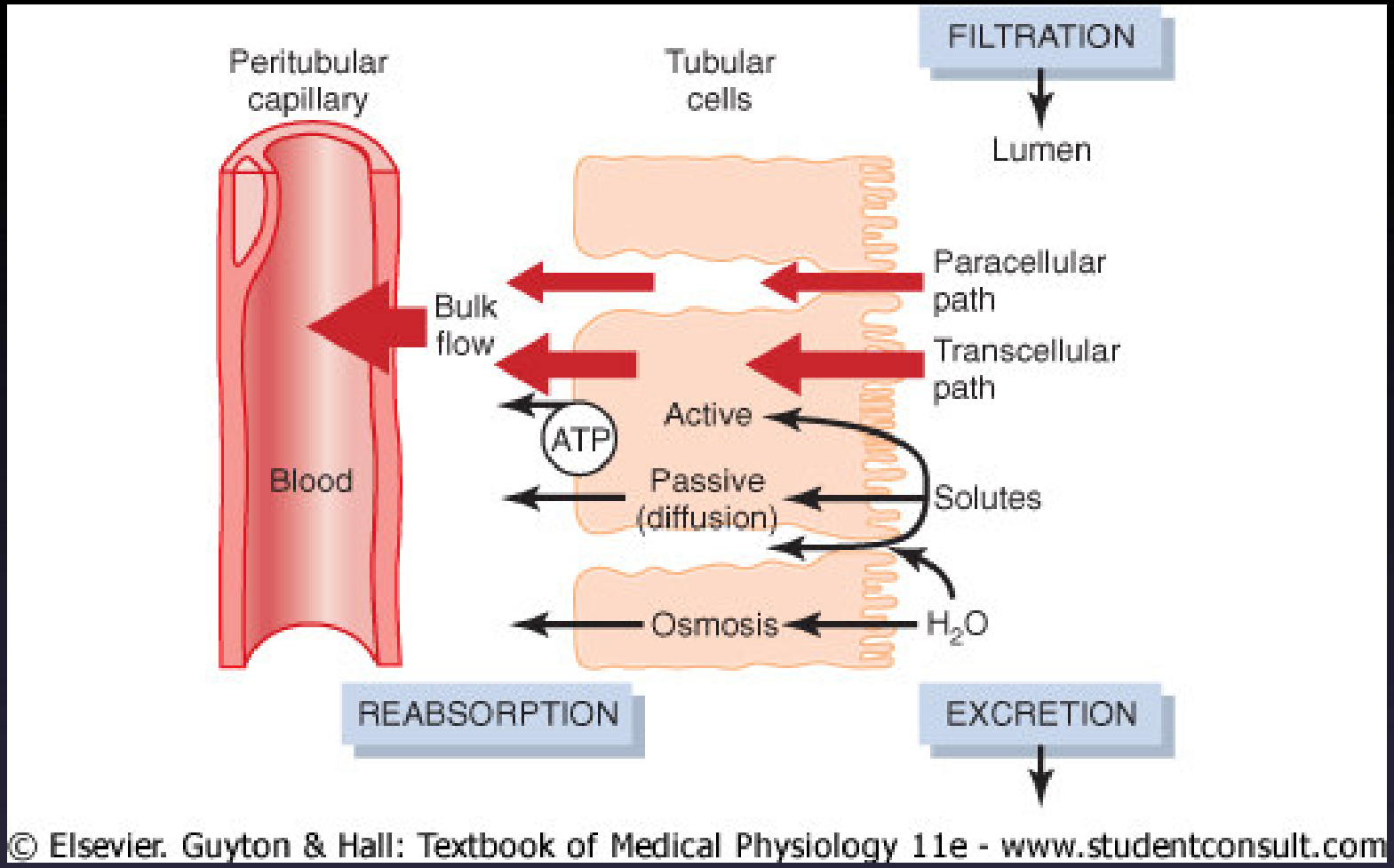
- SIMPE DIFFUSION
- FACILITATED DIFFUSION
- BULK TRANSPORT
- PRIMARY ACTIVE TRANSPORT
- SECONDARY ACTIVE TRANSPORT
- ENDOCYTOSIS
- PINOCYTOSIS

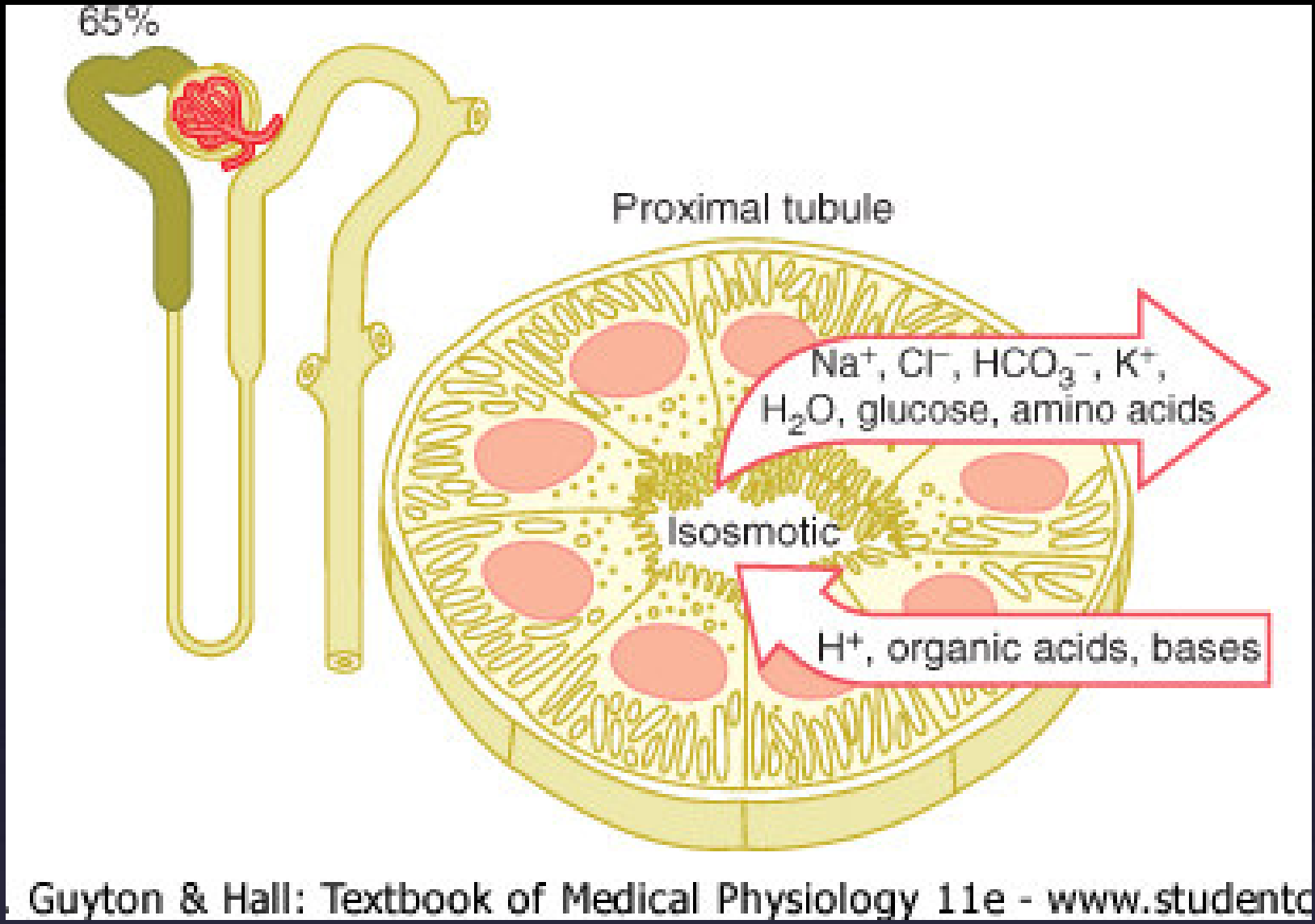
TRANPORT PATHWAYS

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

REABSORTION PATHWAYS







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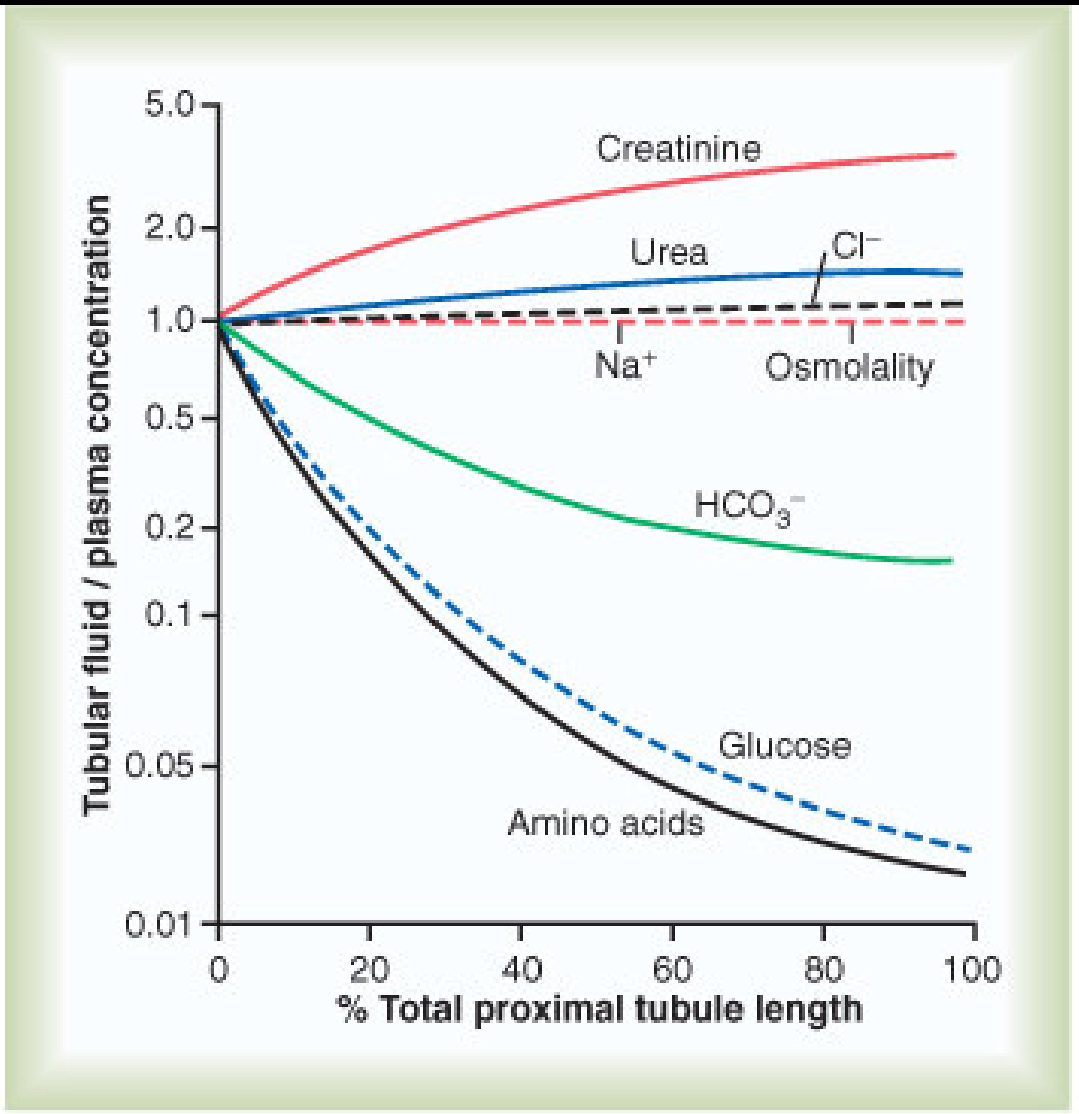
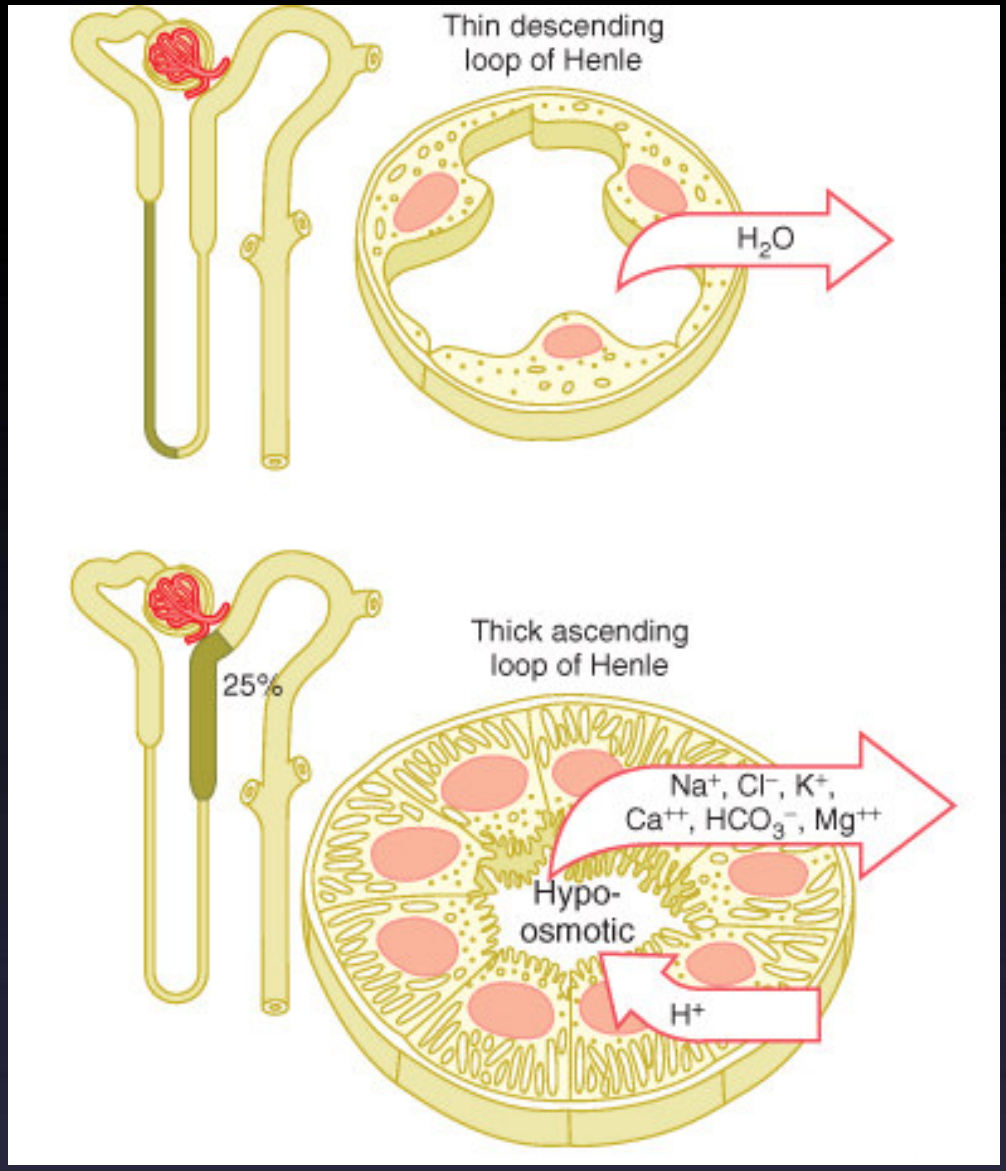
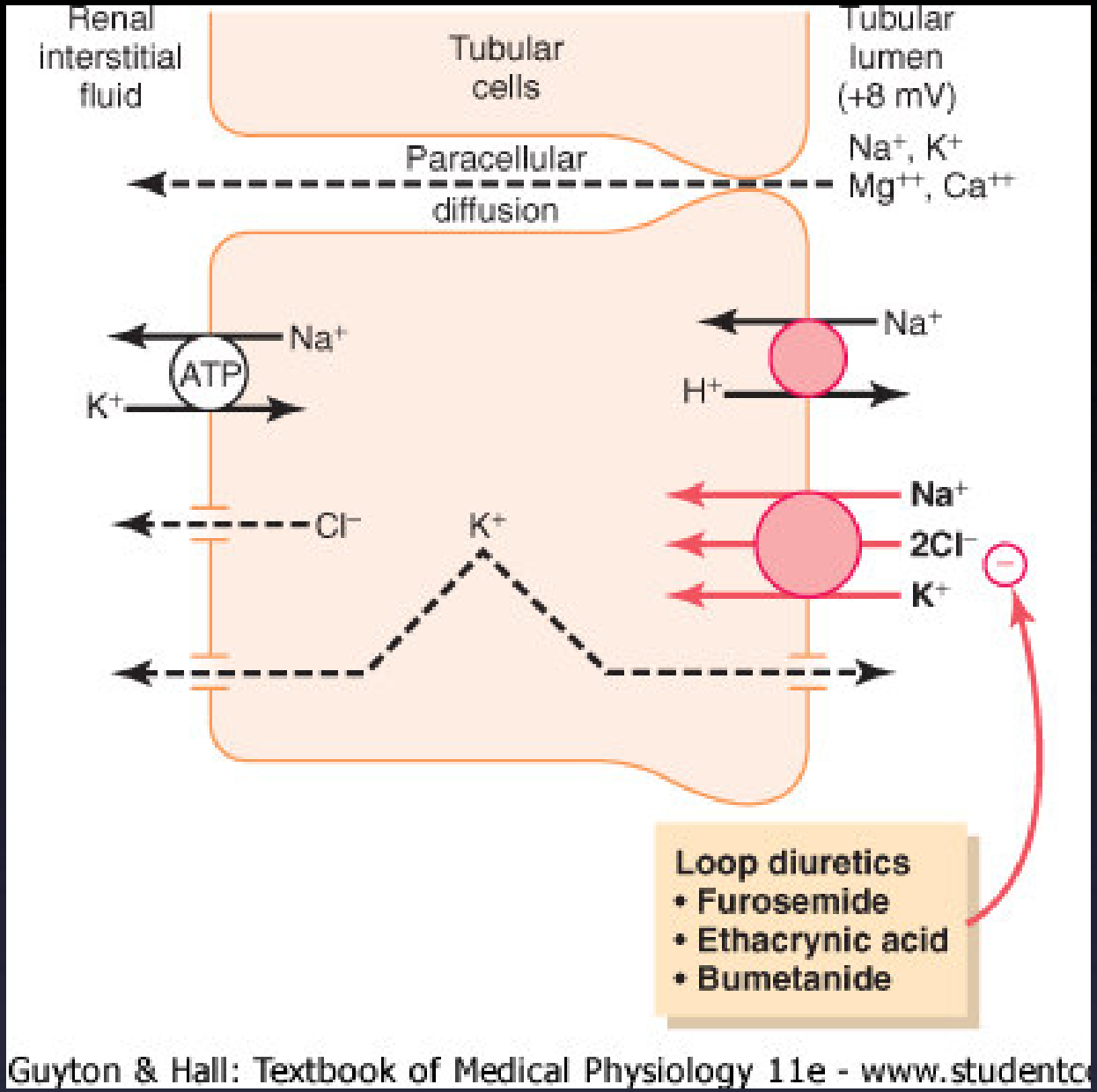



Thin descending
loop of Henle
H_2O
25%
Thick ascending
loop of Henle
Na^+, Cl^-, K^+,
Ca^{++}, HCO_3^-, Mg^{++}
Hypo-
osmotic
H^+


Renal interstitial fluid
Tubular cells
Tubular lumen (+8 mV)
Na+, K+
Mg++, Ca++
Paracellular diffusion
Na+
ATP
K+
Na+
H+
Cl−
K+
Na+
2Cl−
K+
Loop diuretics
• Furosemide
• Ethacrynic acid
• Bumetanide
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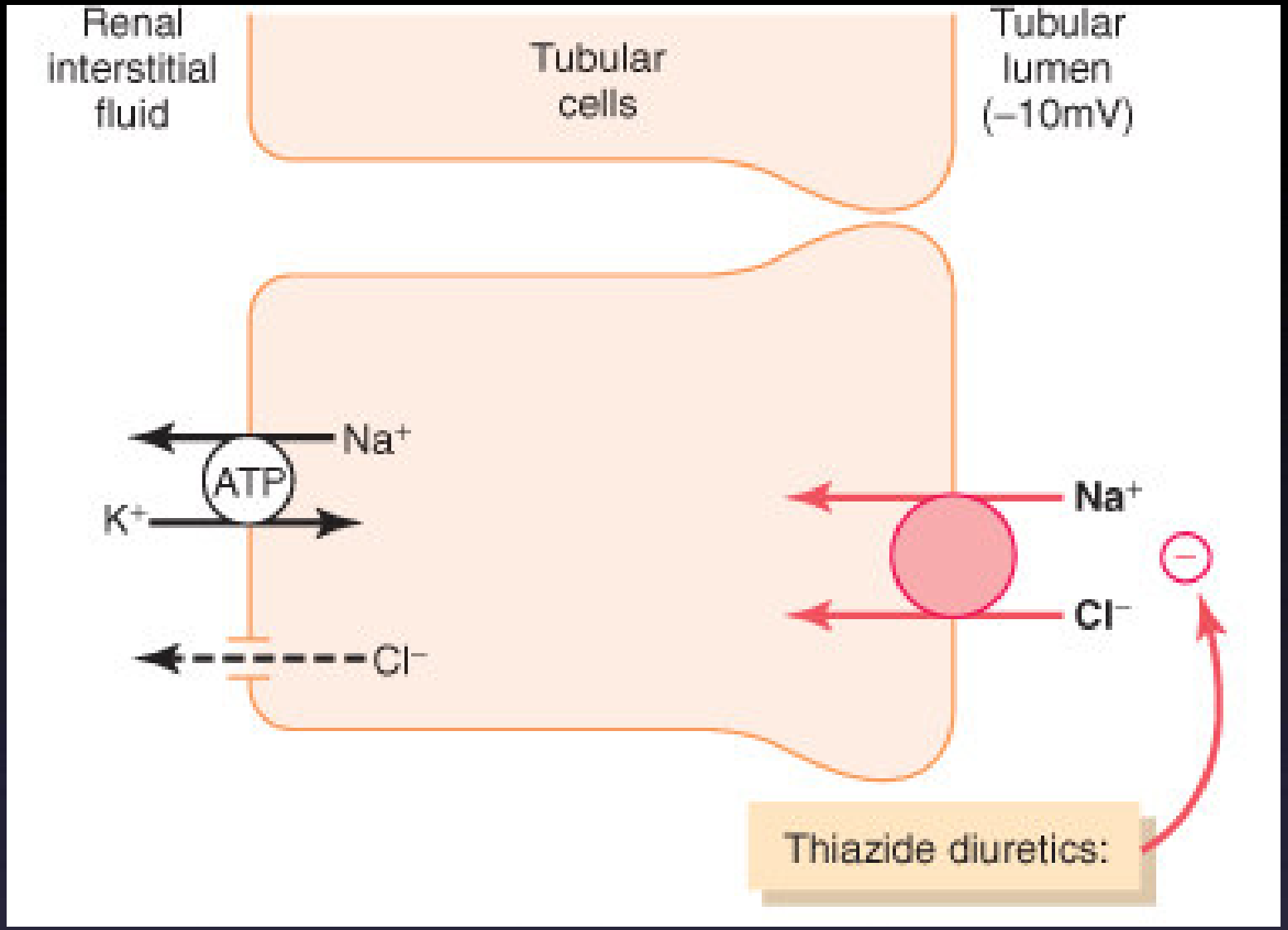
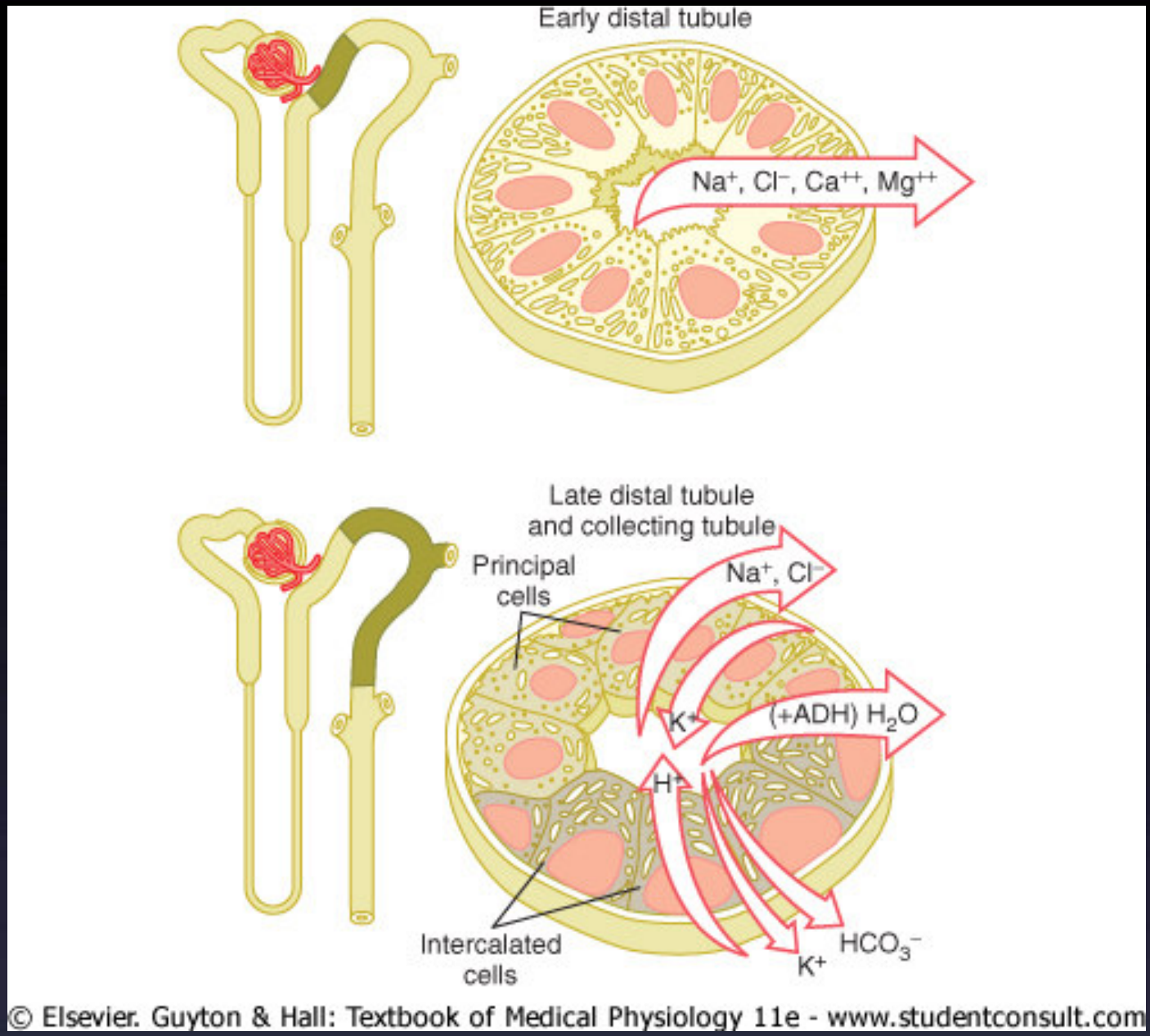
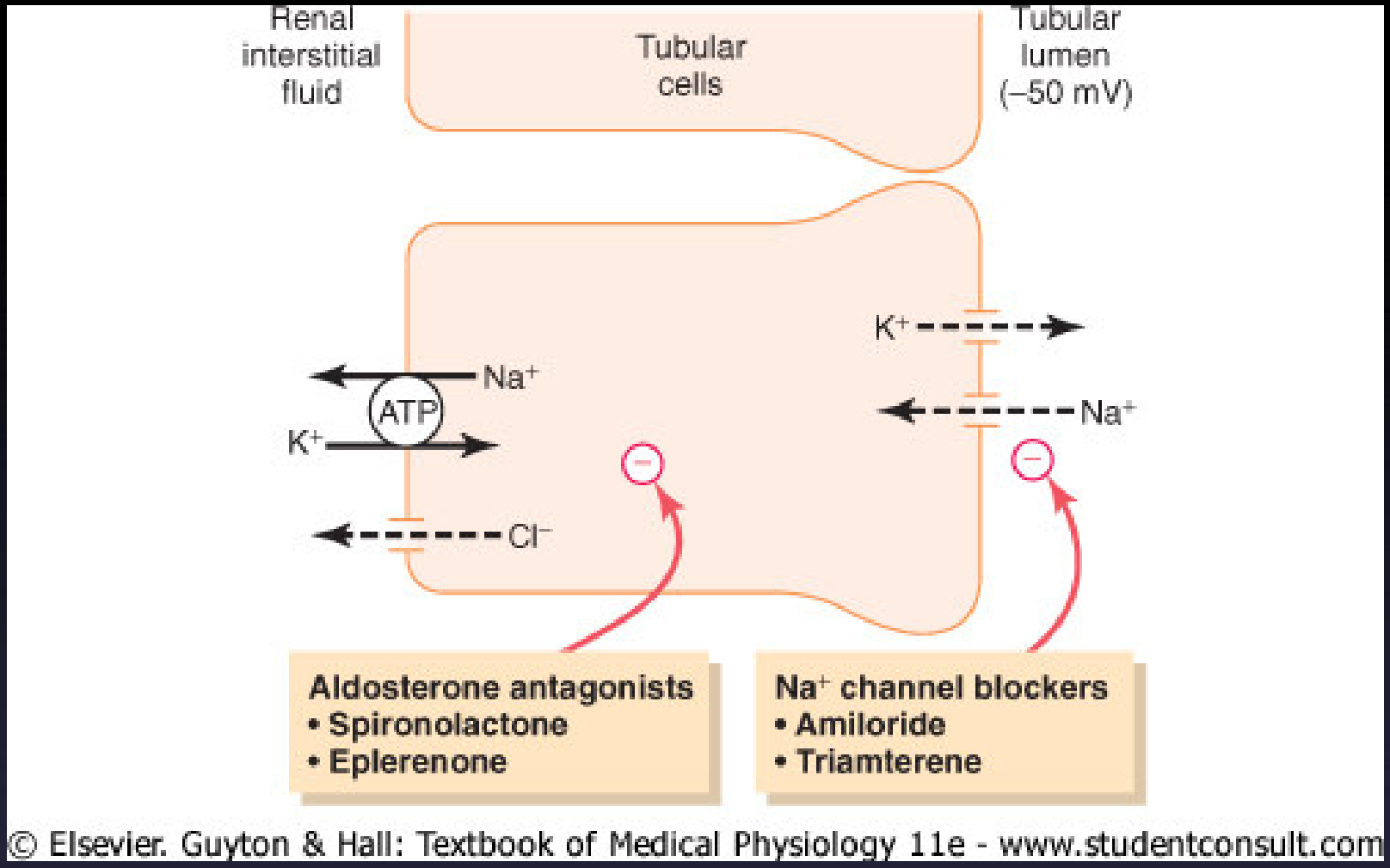
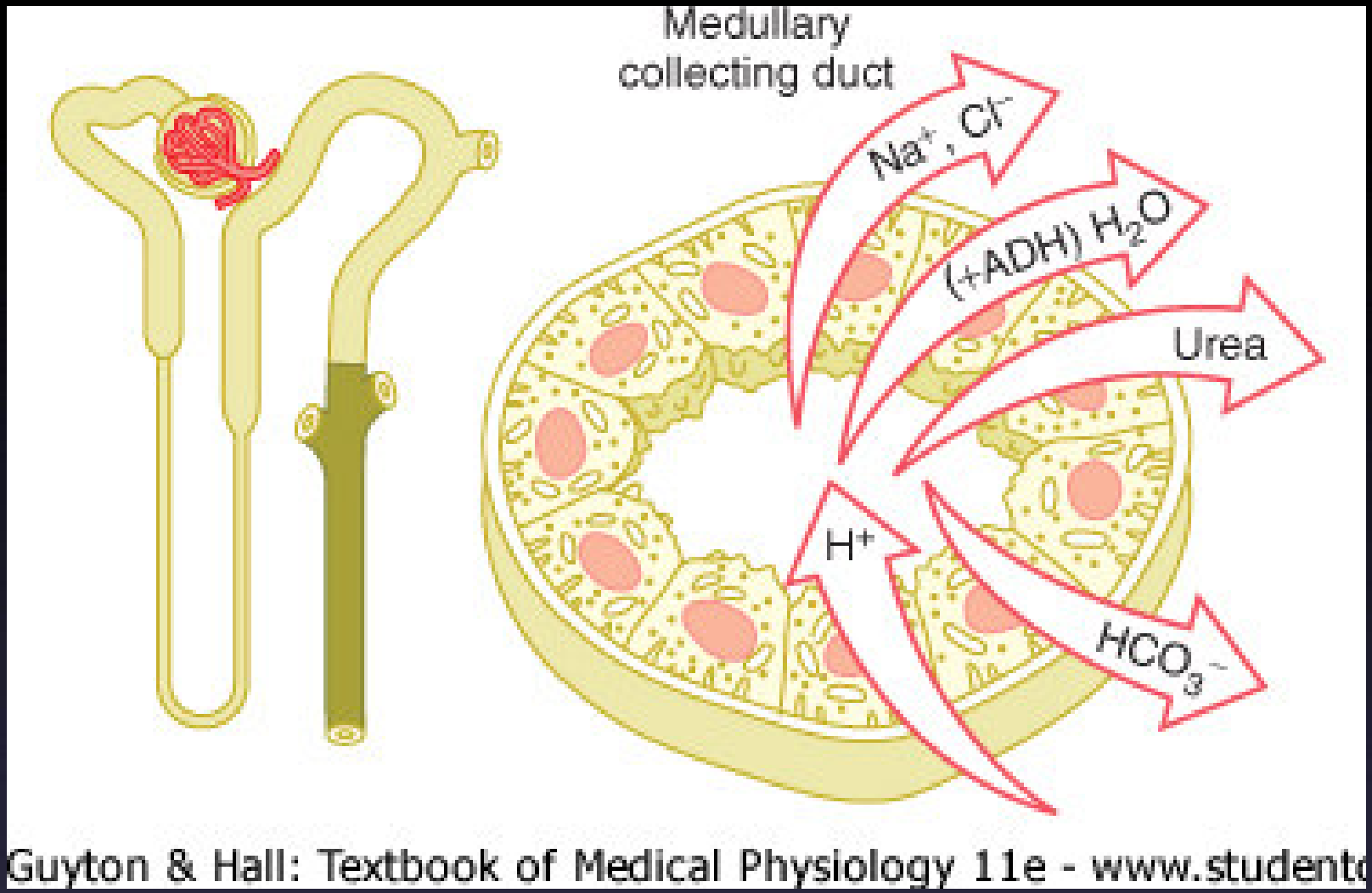

Renal interstitial fluid
Tubular cells
Tubular lumen (–10mV)
Na+
ATP
K+
Cl–
Na+
Cl–
Thiazide diuretics:







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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

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

	Amount Filtered	Amount Reabsorbed	Amount Excreted	% of 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

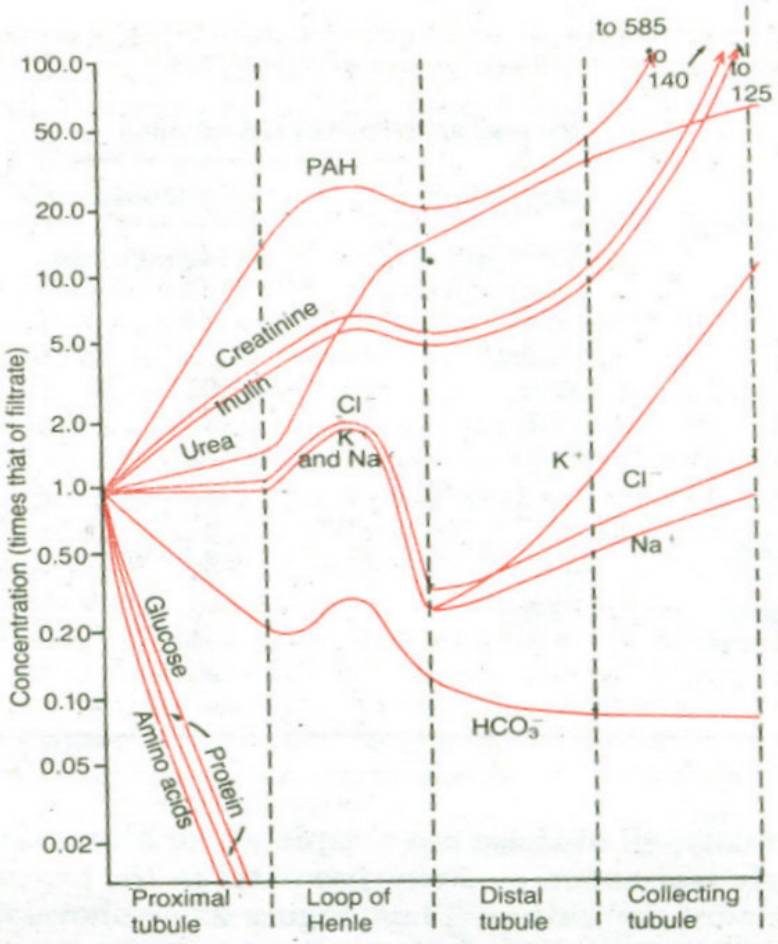


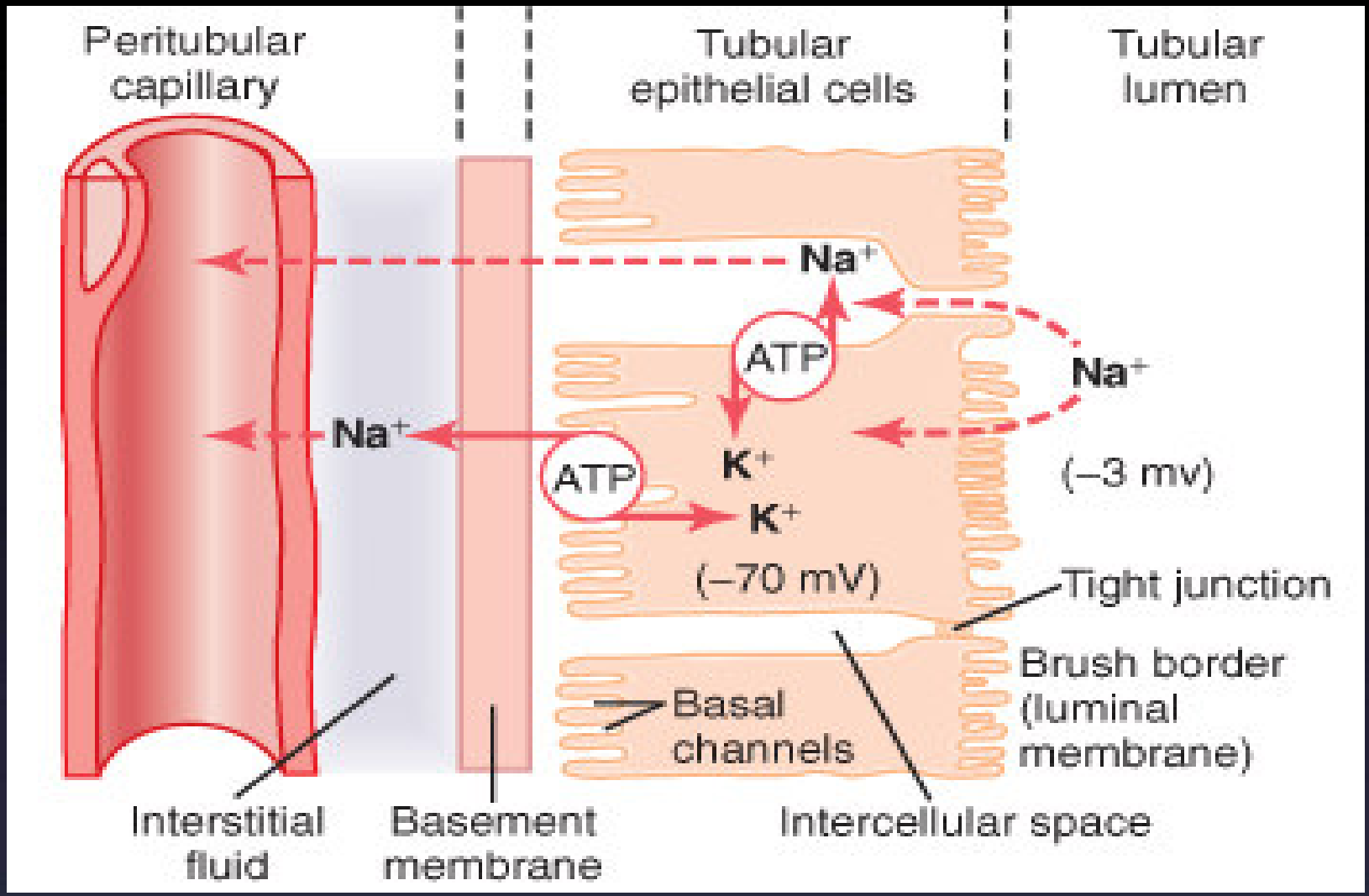
Figure 27–5. Composite figure showing average concentrations of different substances at different points in the tubular system.

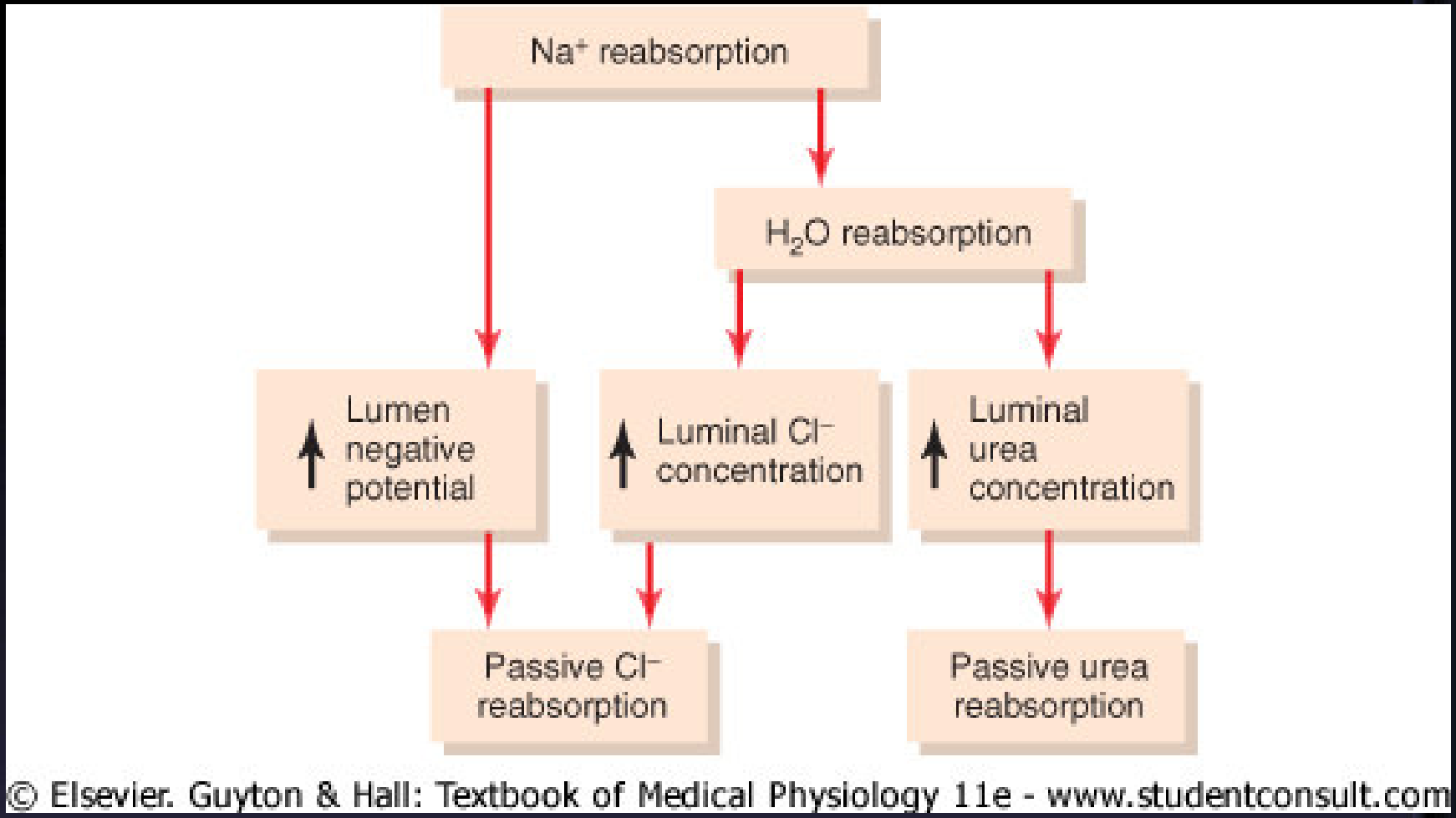
Sodium Reabsorption from tubular lumen into blood involves 3 steps:

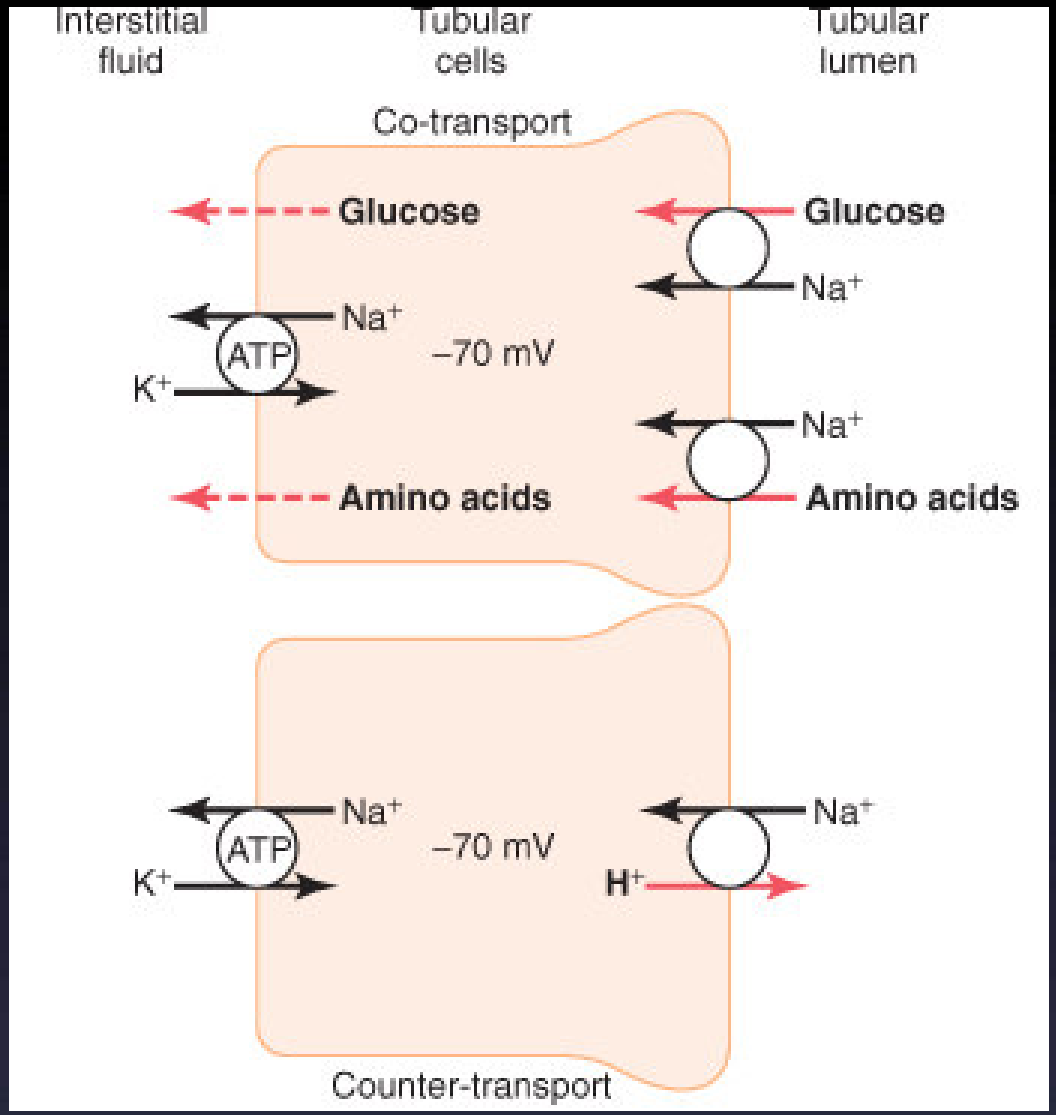
1. **Sodium diffuses across the luminal membrane into the cell down an electrochemical gradient established by the sodium-potassium ATPase pump on the basolateral side of the membrane.**
2. **Sodium is transported across the basolateral membrane against an electrochemical gradient by the sodium-potassium ATPase pump.**
3. **Sodium, water, and other substances are reabsorbed from the interstitial fluid into the peritubular capillaries by ultrafiltration, a passive process driven by the hydrostatic and colloid osmotic pressure gradients.**

SODIUM HANDLING

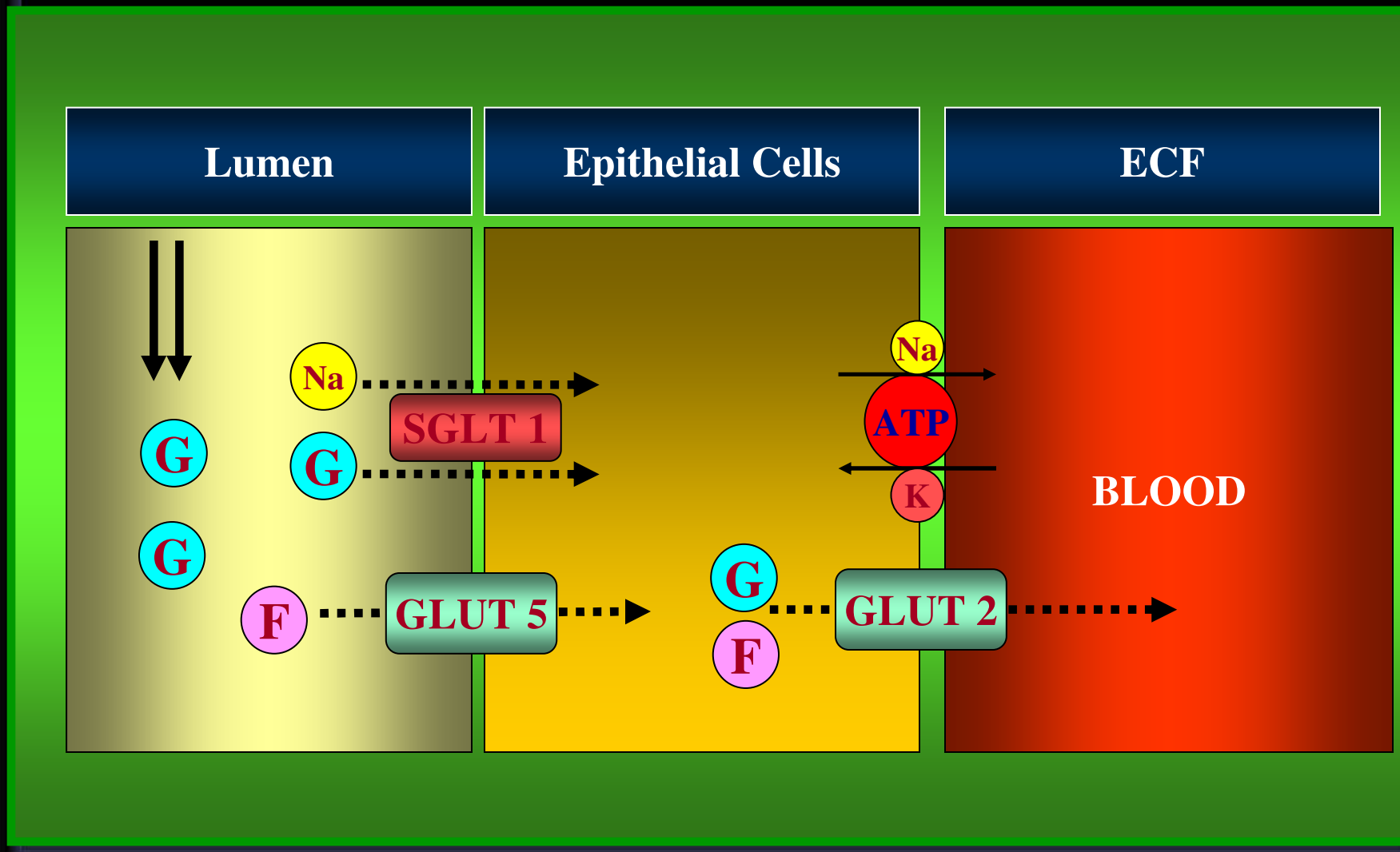
SITE	APICAL TRANSPORTER	FUNCTION
Proximal Tubule	•Na/Gluc CT •Na/Pi CT •Na/Amino Acid •Na/Lactate •Na/H Exchanger •Cl/Base Exchanger	•Na & Gluc Uptake •Na & Pi Uptake •Na & AA Uptake •Na & Lactate Uptake •Na Uptake and H Extrusion •Cl Uptake
Thick Ascending Limb	• Na, 2 Cl,, K CT •Na/H Exchanger •K Channels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


Peritubular capillary
Tubular epithelial cells
Tubular lumen
Na+
ATP
Na+
Na+
ATP
K+
K+
(–3 mv)
(–70 mV)
Tight junction
Brush border (luminal membrane)
Basal channels
Interstitial fluid
Basement membrane
Intercellular space

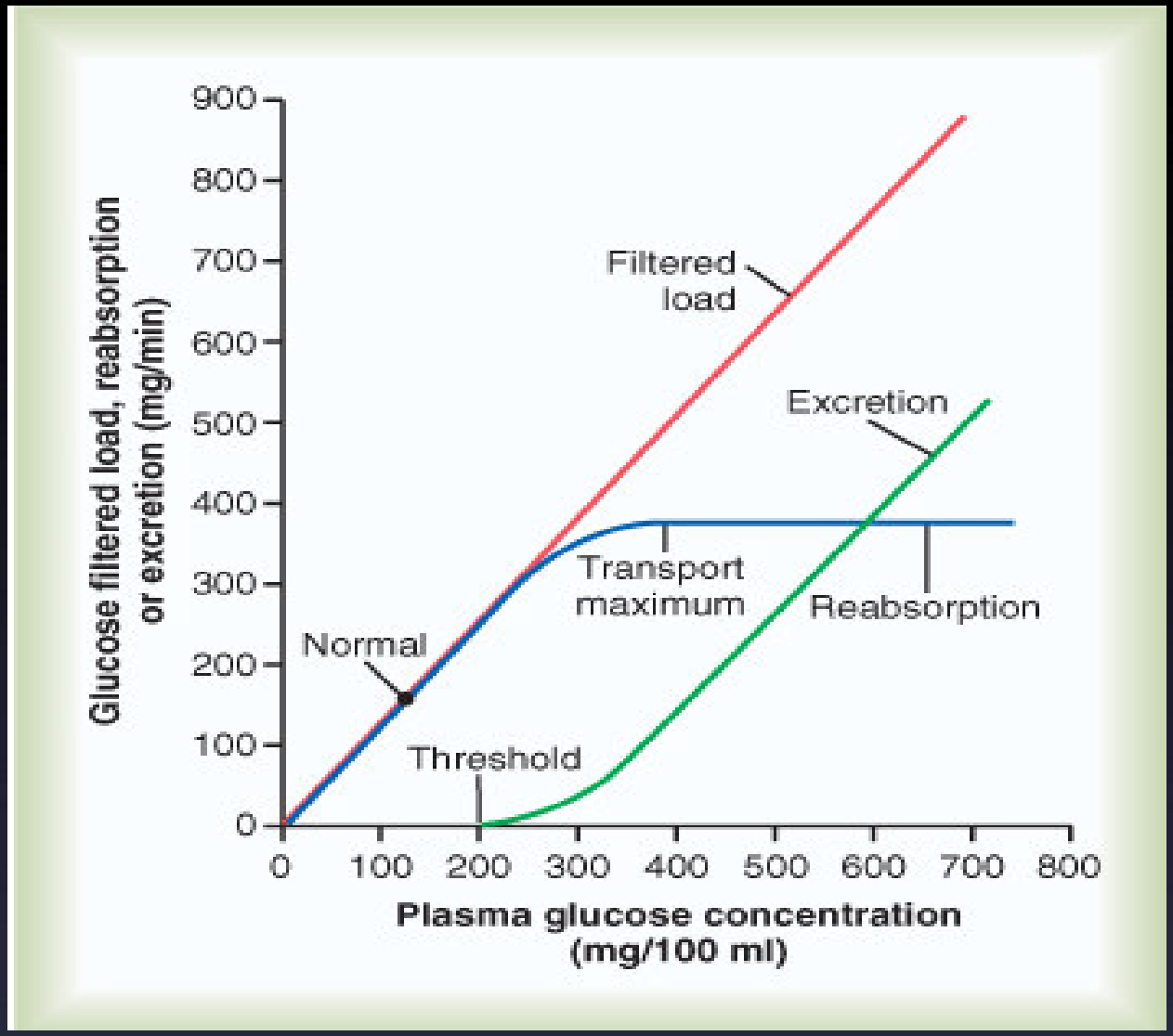



Interstitial fluid
Tubular cells
Tubular lumen
Co-transport
Glucose
Glucose
Na+
Na+
ATP
K+
–70 mV
Na+
Amino acids
Amino acids
Na+
ATP
K+
–70 mV
Na+
H+
Counter-transport

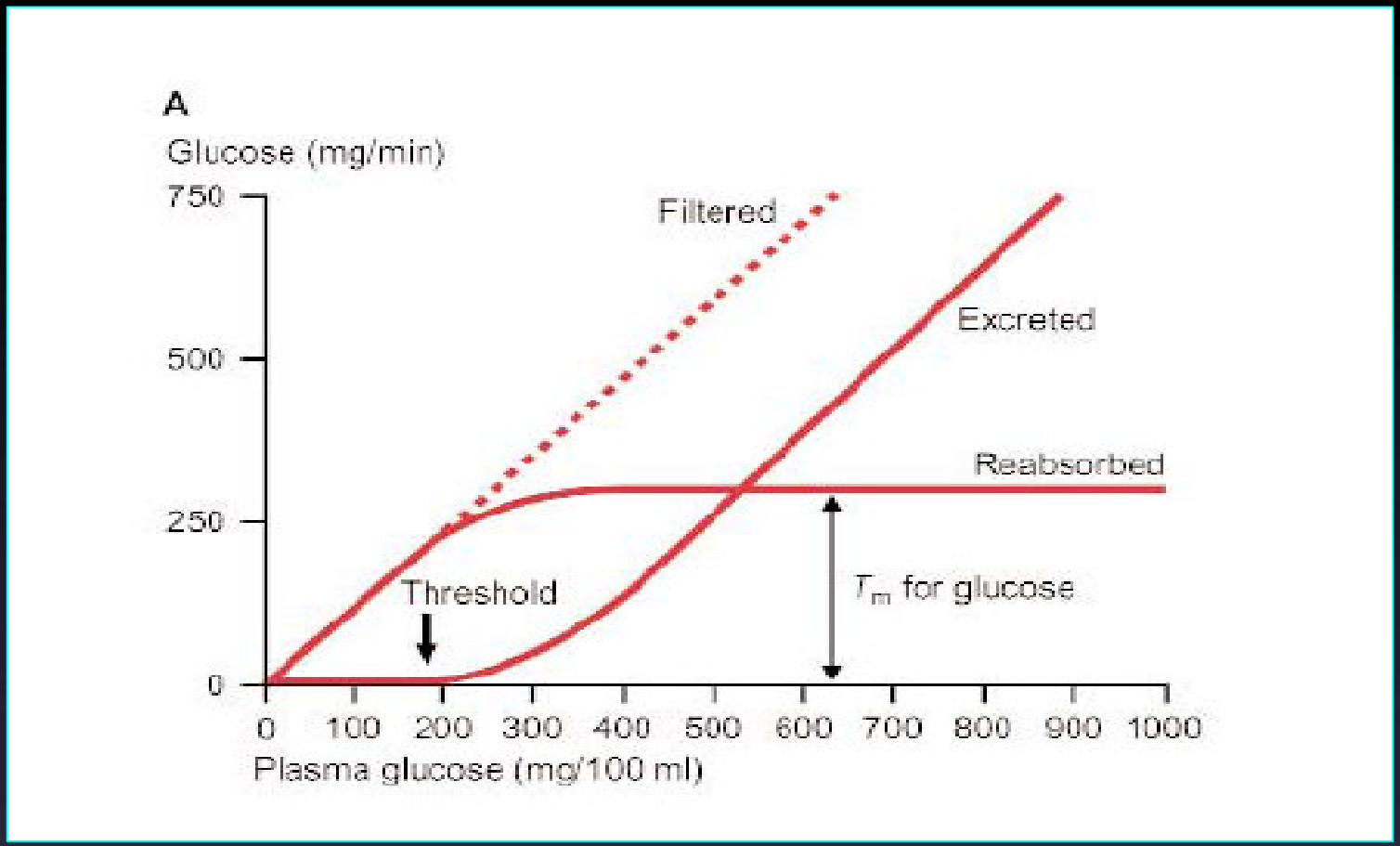
GLUCOSE REABSORPTION IN GIT



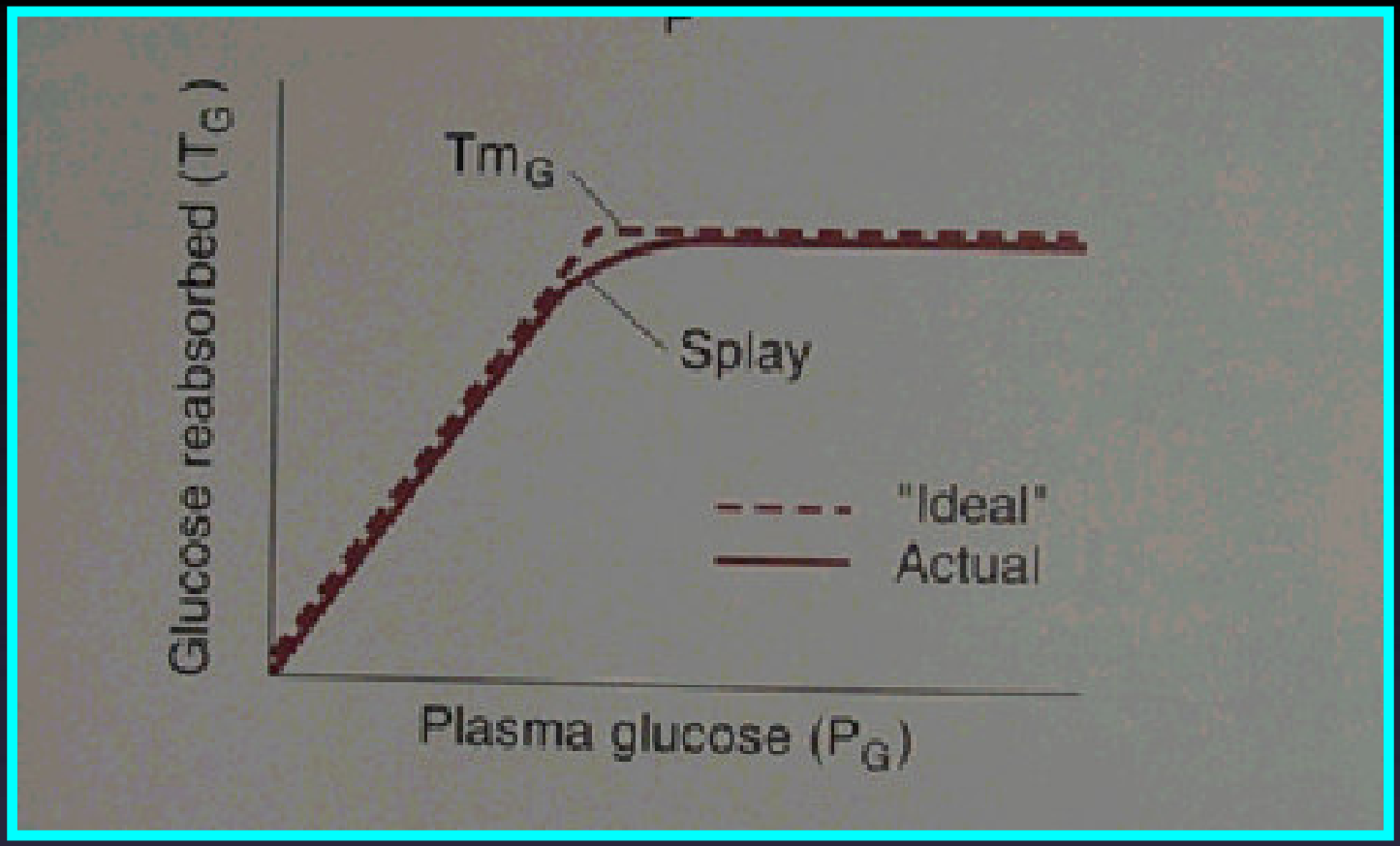
GLUCOSE REABSORPTION



GLUCOSE REABSORPTION



GLUCOSE REABSORPTION



Albumin Excretion in health and disease

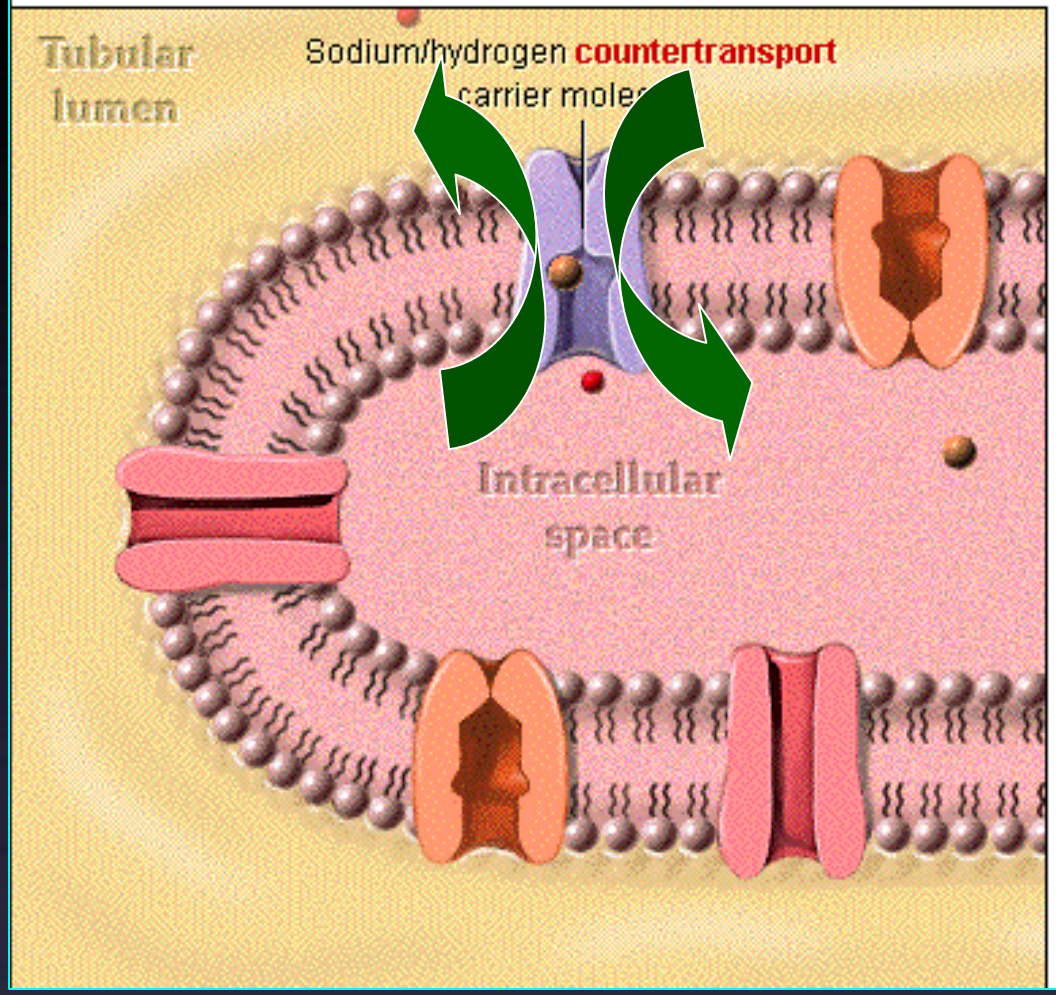
	Normal	Nephrotic syndrome
Albumin in plasma to be filtered (g)	8000	8000
Albumin actually filtered (g)	36	65
Albumin reabsorbed (g)	36	45
Albumin lost in urine (g)	0	20

HYDROGEN

- **Secreted in Proximal Tubule by Counter Transport with Na and also by H ATP ase**

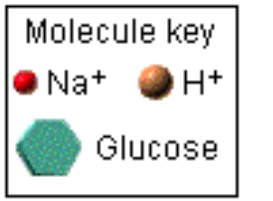
Na-H COUNTER TRANSPORT

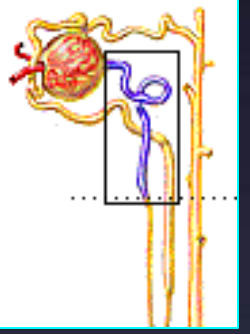
PCT Luminal Membrane Activity



Secretion of a hydrogen ion by countertransport molecule depends on the simultaneous reabsorption of a sodium ion.

Countertransport molecules can only function from the concentration **gradient** created by primary active transport pumps of basolateral membrane.





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

PHOSPHATE

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

SULPHATE

- **Like PHOSPHATE reabsorbed with Na**

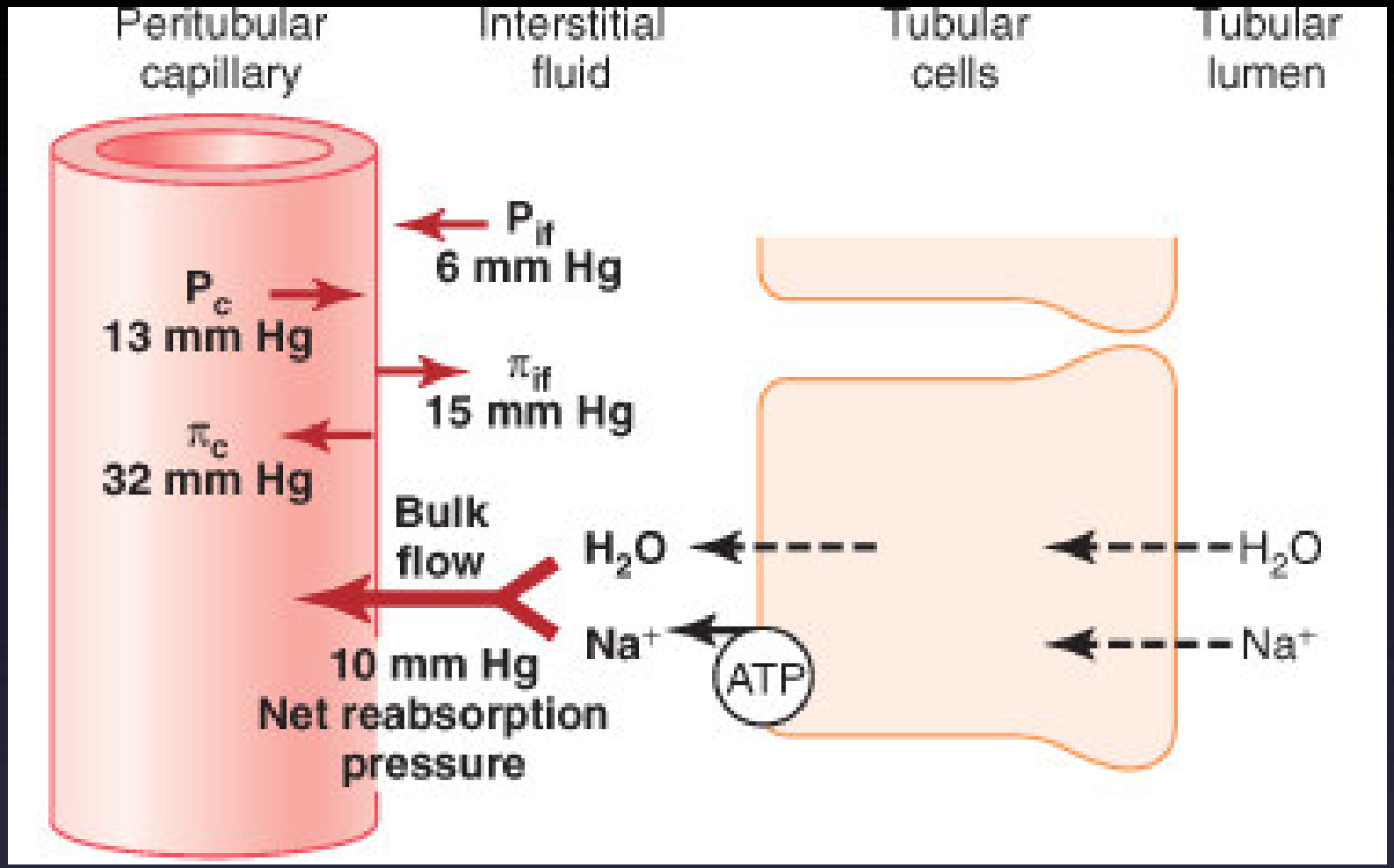
UREA

- 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 at all.

POTASSIUM

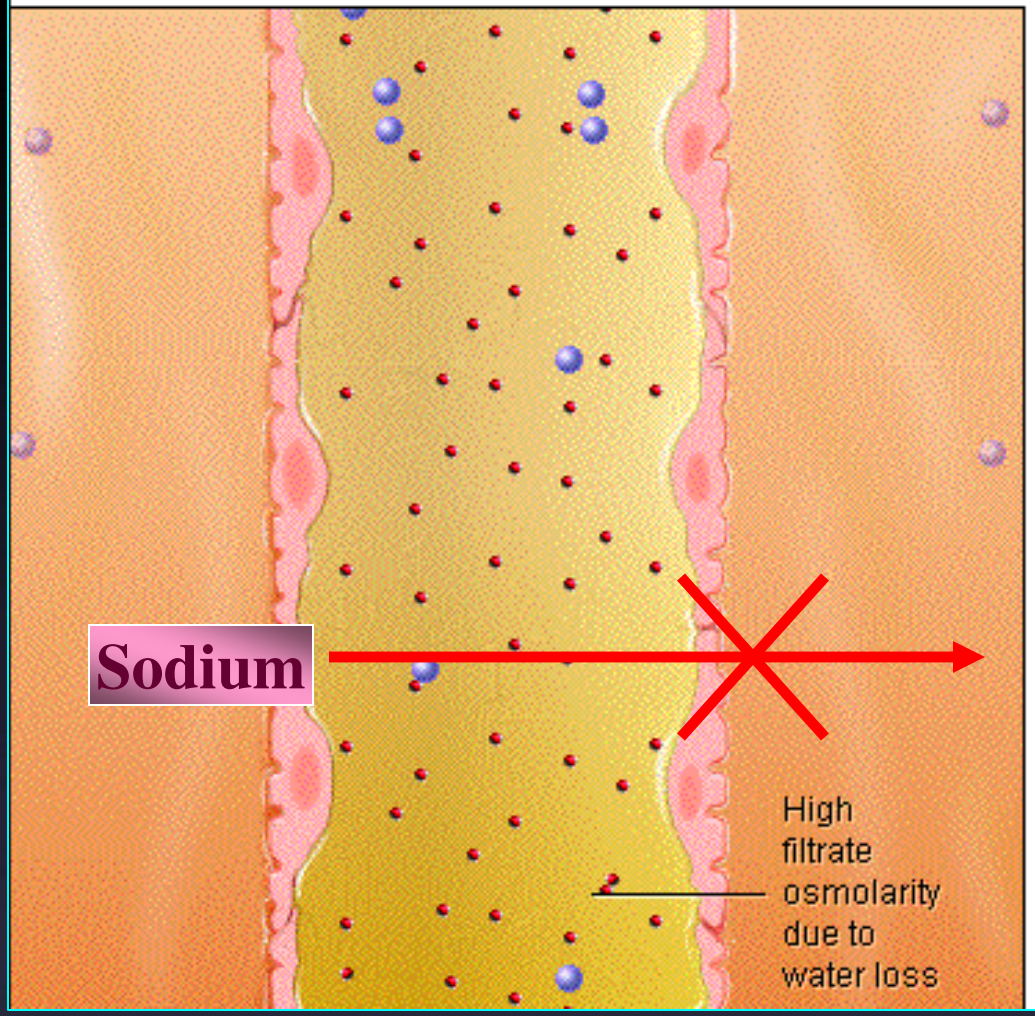
- It is both reabasorbed and secreted
- 67% of filtered load is reabsorbed by PCT
  - solvent drag
- secreted by distal tubule / collecting duct
  - correlated with dietary intake
    - 80% of filtered load appears in urine if dietary content high
    - 1% if dietary content low

Peritubular Capillary and Renal Interstitial Fluid Physical Forces



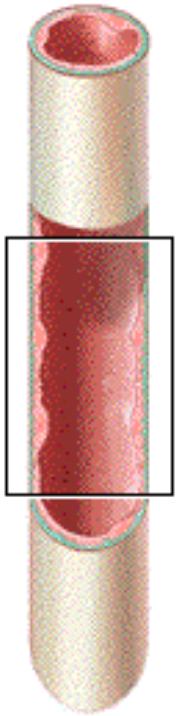
DESCENDING LIMB OF LOOP OF HENLE

Reabsorption in Thin Descending Loop of Henle



Epithelium transitions from **cuboidal epithelial cells** to **simple squamous epithelial cells**.

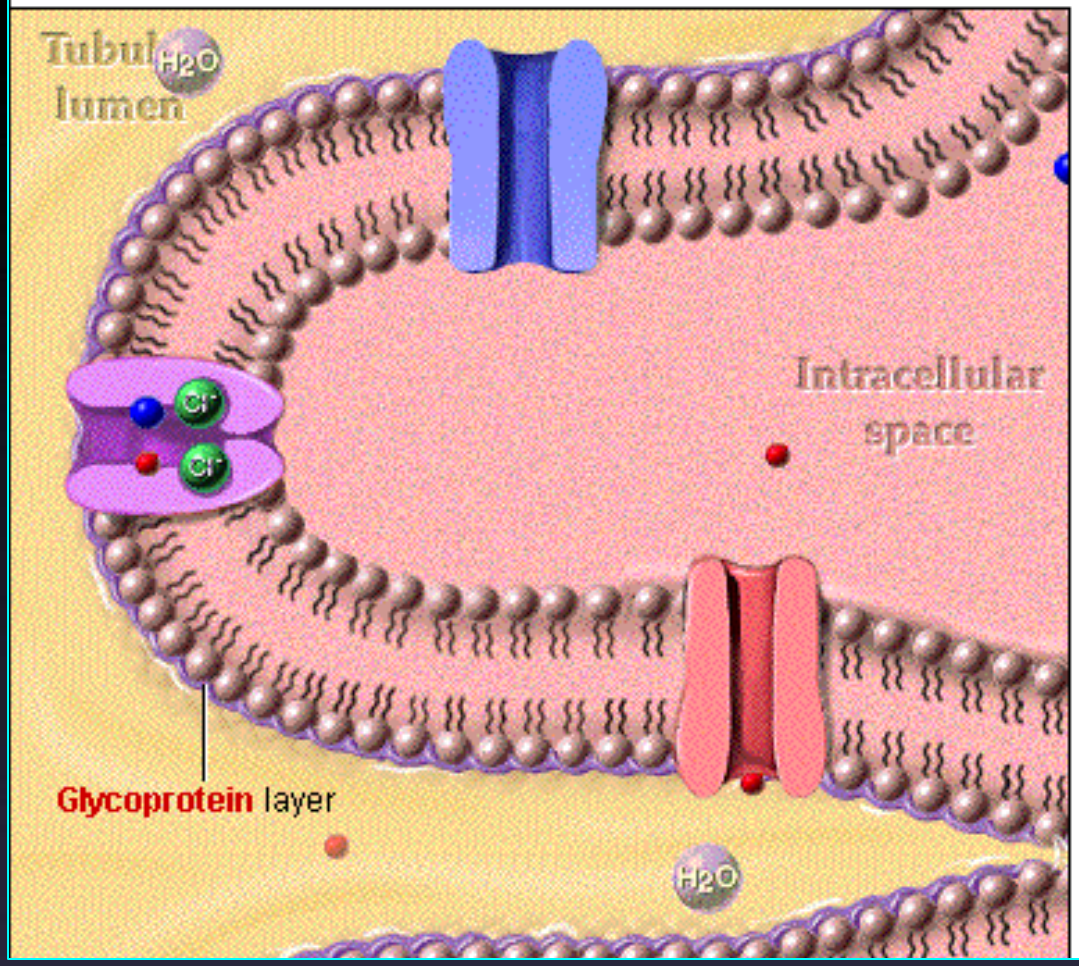
Membranes are permeable to water but not to NaCl.



Few membrane proteins serving as channels or transporter molecules.

Net result is increased osmolarity of filtrate.

Reabsorption in Ascending Loop of Henle and Early DCT: Luminal Membrane



Carrier molecule cotransports a potassium ion, two chloride ions, and a sodium ion.

Intracellular potassium concentration changes little because potassium returns to the filtrate and interstitium through its channels.

Imported chloride ions follow sodium ions to the basolateral membrane and diffuse into interstitium.