Renal Transport Process

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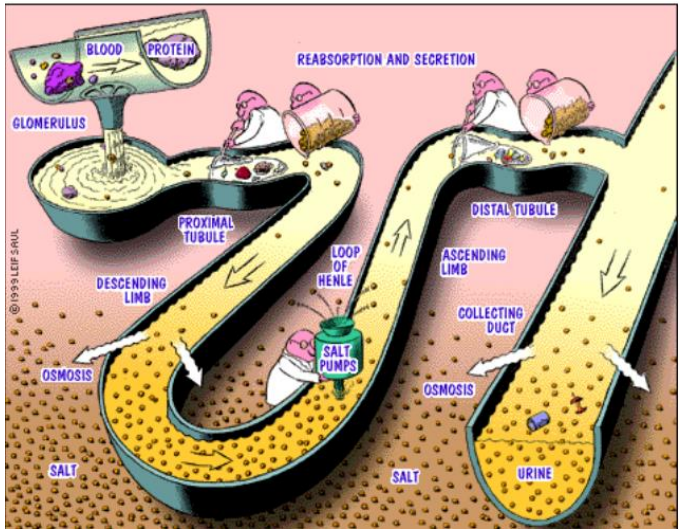


Learning Objectives:

- Define tubular reabsorption, tubular secretion, transcellular and paracellular transport.
- Identify and describe mechanisms of tubular transport
- Describe tubular reabsorption of sodium and water
- Revise tubulo-glomerular feedback and describe its physiological importance
- Identify and describe mechanism involved in Glucose reabsorption
- Study glucose titration curve in terms of renal threshold, tubular transport maximum, splay, excretion and filtration
- Identify the tubular site and describe how Amino Acids, HCO_3^-, PO_4^- and Urea are reabsorbed

Renal Threshold

- When the plasma concentration of the substance is beyond it $\Rightarrow$ the substance begins to appear in urine.
- At this level $\Rightarrow$ the filtered load exceeds the absorptive capacity of the tubules.
- Substances of high threshold: glucose, amino acids & vitamins.
- Substances of medium threshold: K+ & urea.
- Substances of low threshold: phosphate & uric acid.
- Substances of no threshold: creatinine, mannitol & inulin.

Tubular transport maximum

- **Definition:**

  It is the maximal amount of a substance (in mg) which can be transported (reabsorbed or secreted) by tubular cells/min.

Tubular Transport Maximum

- Many substances are reabsorbed by carrier mediated transport systems e.g. glucose, amino acids, organic acids, sulphate and phosphate ions.

- Carriers have a maximum transport capacity (T_m) which is due to **saturation** of the carriers. If T_m is exceeded, then the excess substrate enters the urine.

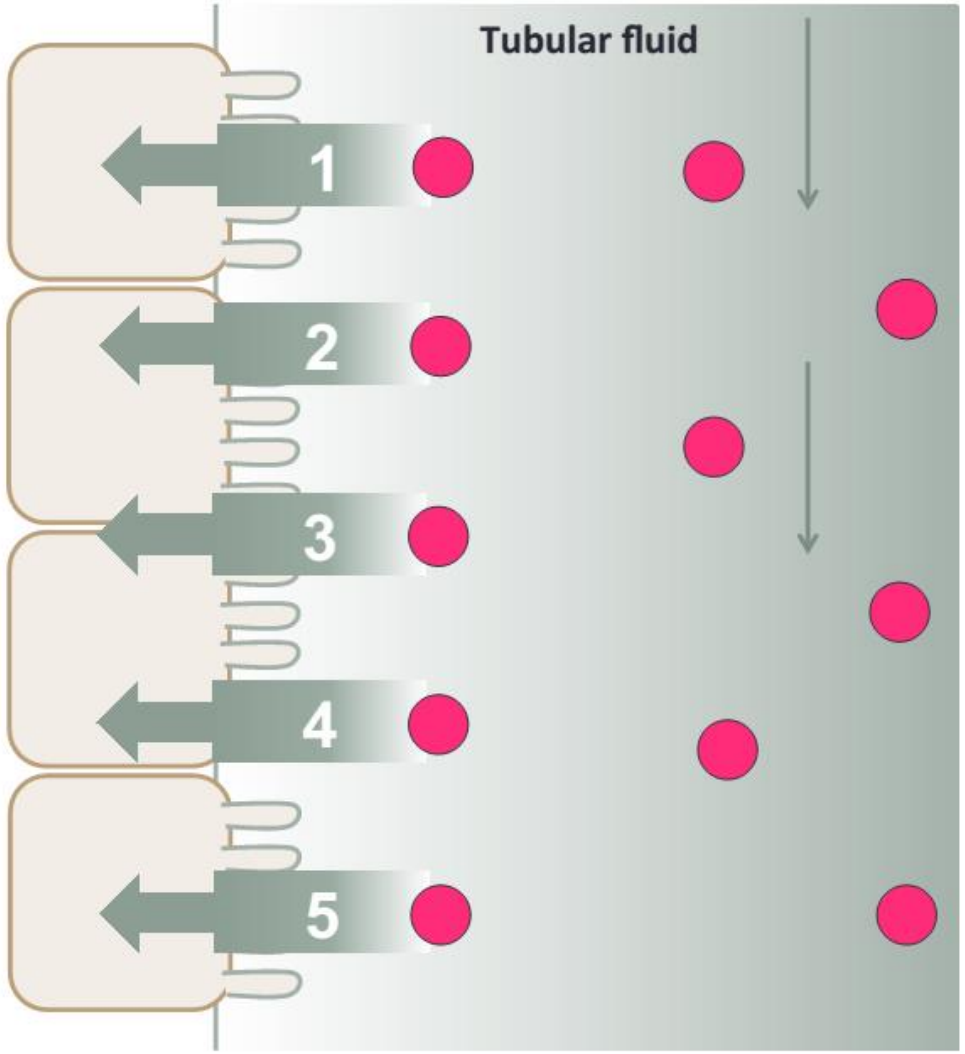
- Glucose is **freely filtered**, so whatever its [plasma] that will be filtered.

= solute

= transporter

5 solute molecules/min

Transport maximum is reached when carriers are saturated.

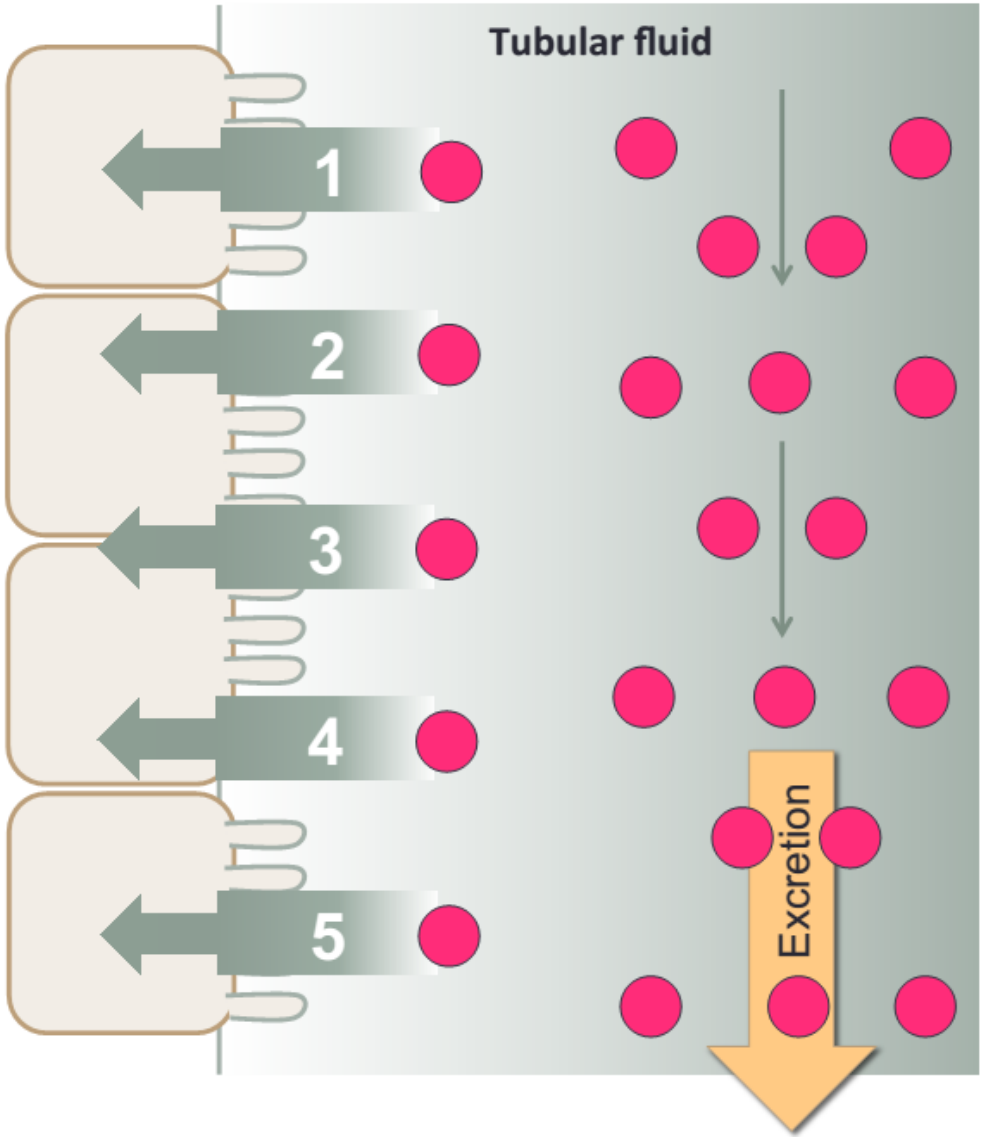


= solute

= transporter

5 solute molecules/min

Saturation is reached,
Maximum speed, T_m

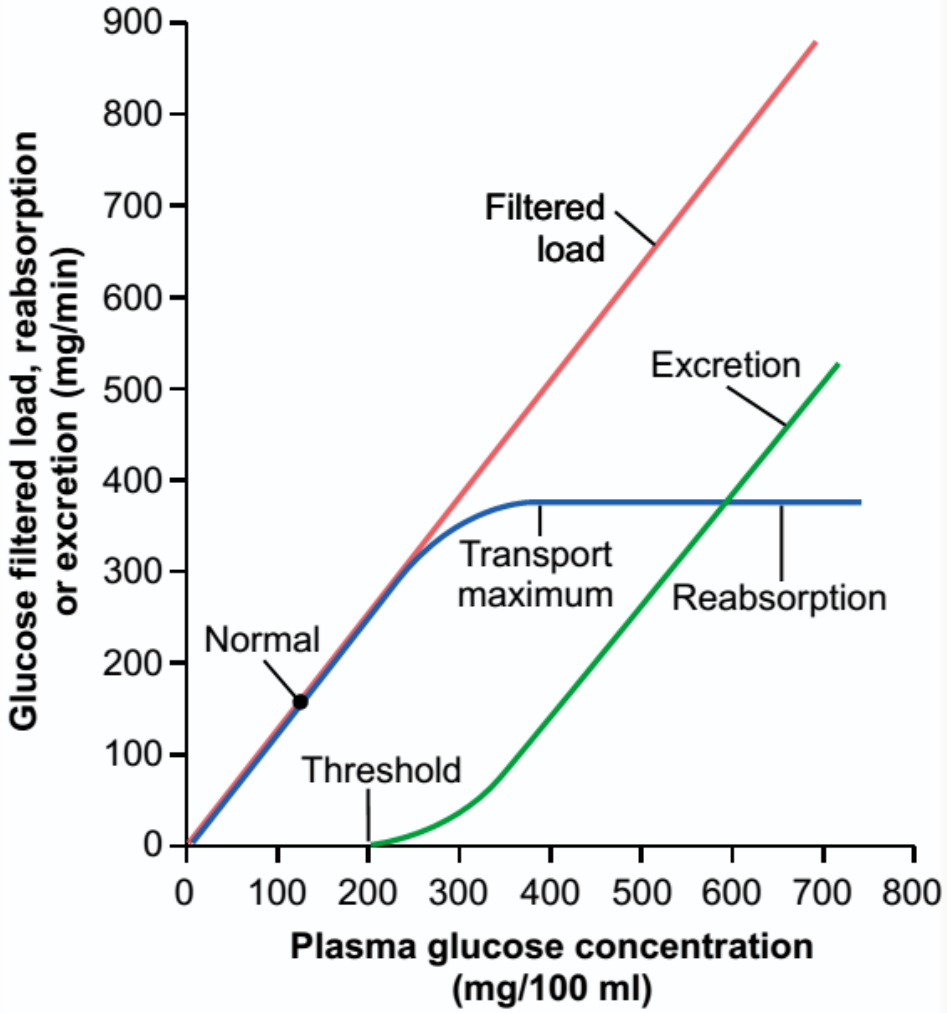


Tubular Transport Maximum

- In man for plasma glucose up to 180 mg/dl, all will be **reabsorbed**. Beyond this level of plasma [glucose], it appears in the urine = Renal plasma threshold for glucose.
- (If plasma [glucose] = 275 mg/dl, 275 mg/dl will be filtered, 180mg/dl reabsorbed and 90 mg/dl excreted.)
- Kidney does NOT regulate [glucose], (insulin and glucagon). Normal [glucose] of 90 mg/dl, so T_m is set way above any possible level of (non-diabetic) [glucose] at 360 mg/dl. Thus, ensure that all this valuable nutrient is normally reabsorbed. The appearance of glucose in the urine of diabetic patients = glycosuria, is due to failure of insulin, NOT, the kidney.

Transport Maximum (T_m):
Once the transport maximum is reached for all nephrons, further increases in tubular load are not reabsorbed, but are then excreted.

Threshold is the plasma concentration at which tubular load just exceeds the transport maximum (T_m) for reabsorption, where below threshold all solute molecules are reabsorbed, and above threshold, some solutes are not



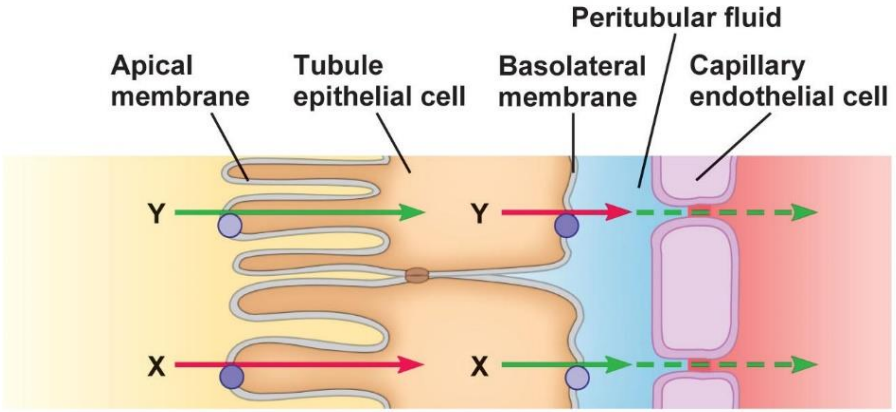
Tubular Transport Maximum

- For amino acids, T_m also very high $\rightarrow$ no urinary excretion occurs.

- However, kidney does regulate some substances by means of the T_m mechanism, eg sulphate and phosphate ions. This is because T_m is set at a level whereby the normal [plasma] causes saturation so any $\uparrow$ above the normal level will be excreted, therefore achieving its plasma regulation. (Also subject to PTH regulation for phosphate, PTH $\downarrow$ reabsorption).

Tubular Reabsorption

- Transported substances move through three membranes
  - Luminal and basolateral membranes of tubule cells
  - Endothelium of peritubular capillaries
- Ca^{2+}, Mg^{2+}, K^{+}, and some Na^{+} can be reabsorbed via **paracellular** pathways.



(a) Active solute reabsorption

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Tubular Reabsorption

All **organic nutrients** are reabsorbed

Water and ion reabsorption is **hormonally controlled**

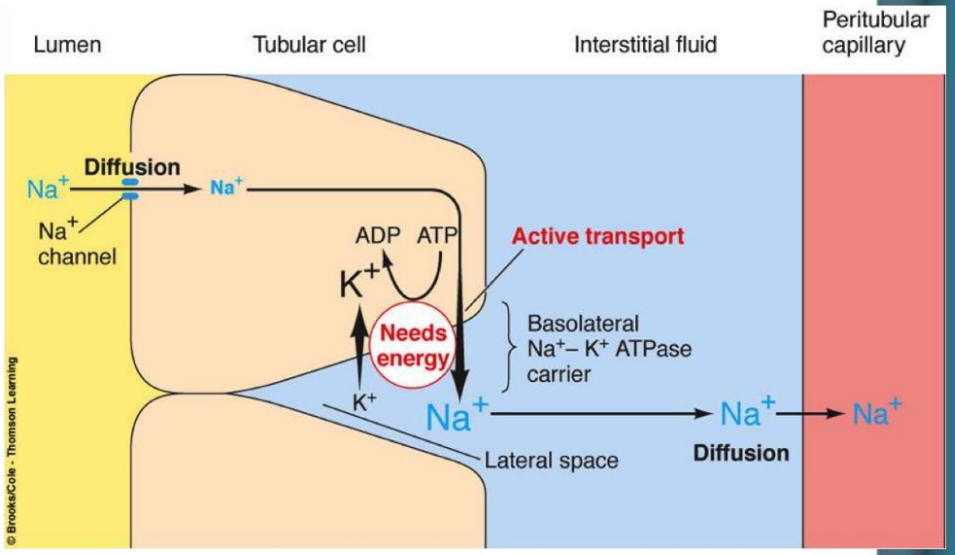
Reabsorption may be an **active** (requiring ATP) or **passive** process

Filtration, Excretion, and Reabsorption of Water, Electrolyte, and Solute by the Kidneys

Substance	Measure	Filtered*	Excreted	Reabsorbed	% Filtered Load Reabsorbed
Water	L/day	180	1.5	178.5	99.2
Na^+	mEq/day	25,200	150	25,050	99.4
K^+	mEq/day	720	100	620	86.1
Ca^{++}	mEq/day	540	10	530	98.2
HCO_3^-	mEq/day	4320	2	4318	99.9+
Cl^-	mEq/day	18,000	150	17,850	99.2
Glucose	mmol/day	800	0	800	100.0
Urea	g/day	56	28	28	50.0

Sodium Reabsorption: Primary Active Transport

- Sodium reabsorption is almost always by active transport
- Na^+ enters the tubule cells at the luminal membrane
- Is actively transported out of the tubules by a **Na^+-K^+ ATPase** pump



Water & Solute handling

- One of the main functions of nephron

  - 25,000 mEq/day Na+
  - 179 L/day water

  } Reabsorped daily by renal tubules

- Other important solutes are linked either directly or indirectly to reabsorption of Na^+.

Mechanisms of tubular absorption & secretion

- Passive:

  Diffusion

  facilitated diffusion

  } Down chemical, electrical gradient

- Active transport

  endocytosis

  } Against chemical, electrical gradient, need energy

Proximal convoluted tubule
Na+ Reabsorption

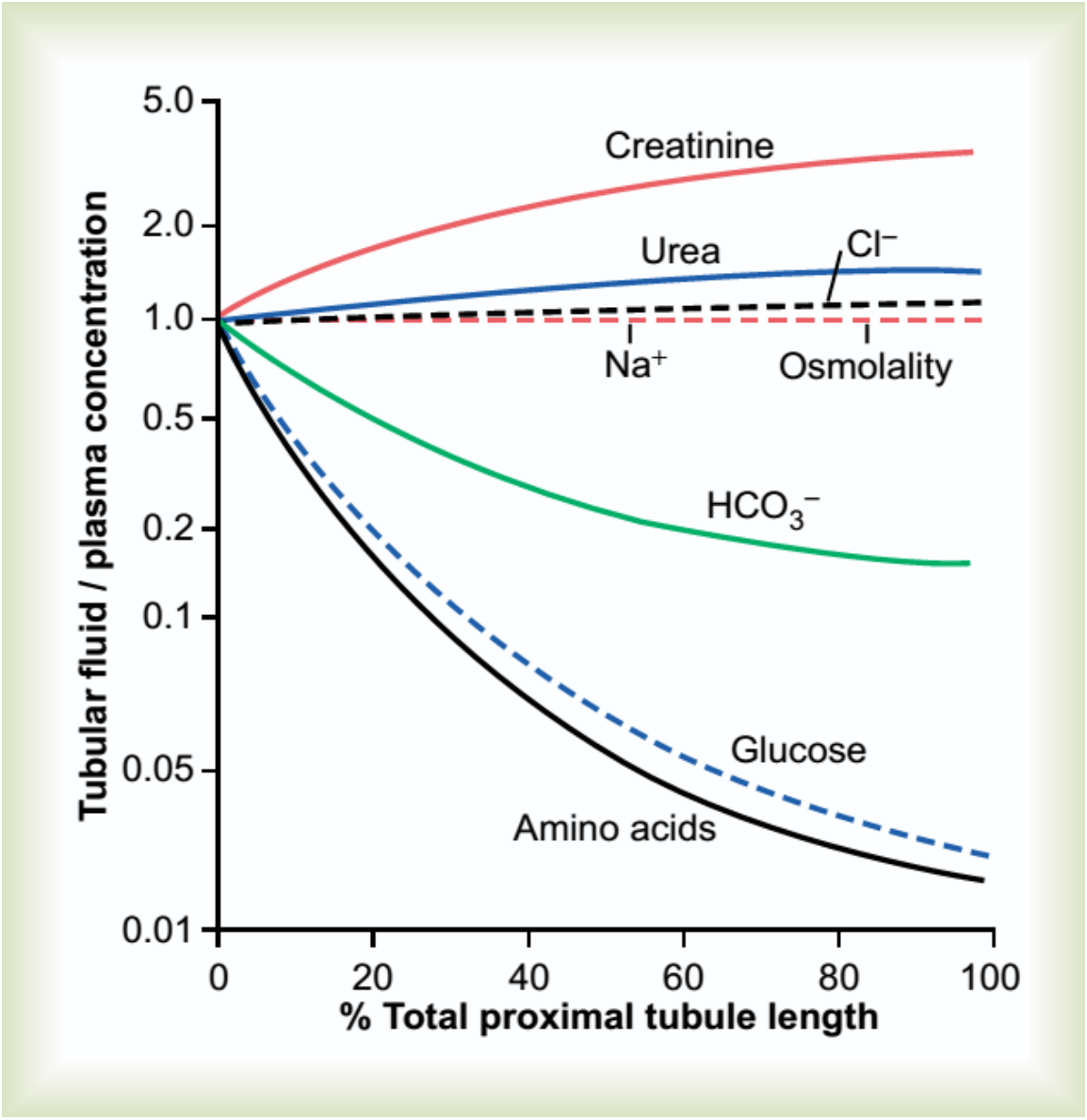
- Leaky epithelium permeable to ions & water
- ~ 70 % of Na+, Cl-, K+, water absorbed passively (follows Na+)

- **Na+ Reabsorption (transcellular):**

Early PCT Na+ absorbed:

1) exchanged with H+,
   but HCO3- reabsorbed
2) with organic substances
   glucose, amino acids, lactate, Pi

} Na^+/K^+-ATPase important


Tubular fluid / plasma concentration
5.0
2.0
1.0
0.5
0.2
0.1
0.05
0.01
0
20
40
60
80
100
% Total proximal tubule length
Creatinine
Urea
Cl⁻
Na⁺
Osmolality
HCO3⁻
Glucose
Amino acids

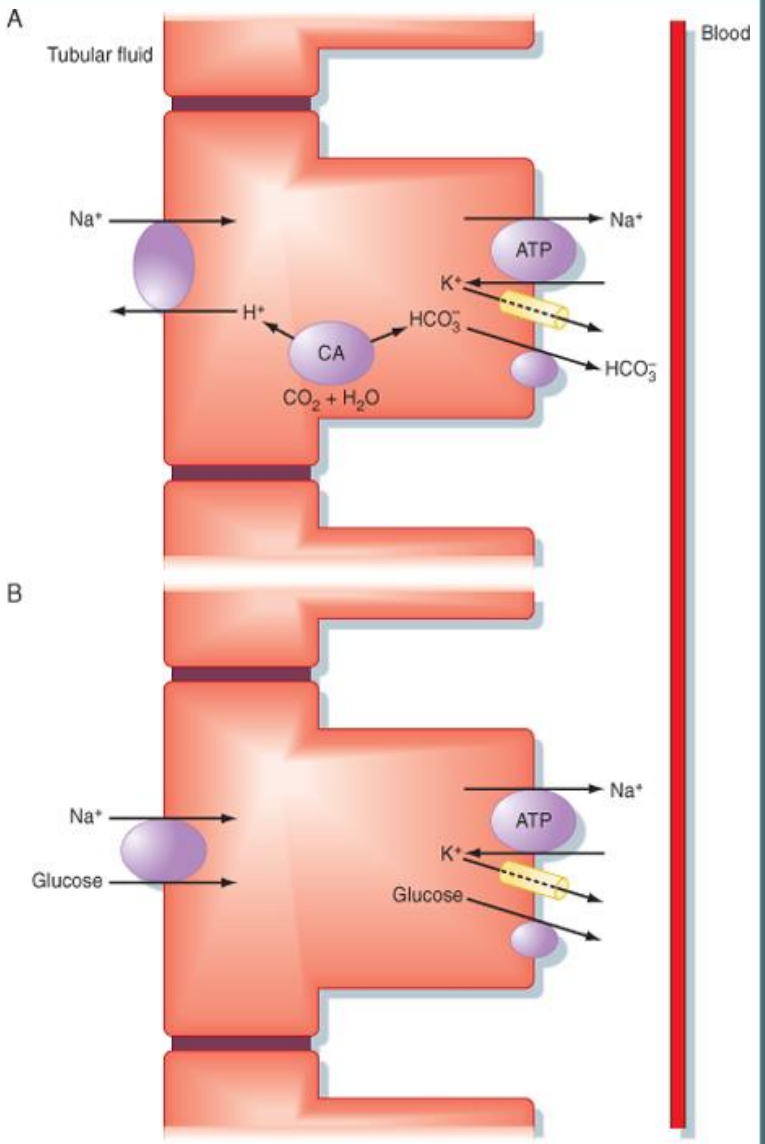
PCT
Na+ Reabsorption

a) NHE takes up Na^+ for H^+

- Causes reabsorption of HCO3-

b) Symporters:

- Na^+-glucose
- Na^+-amino acid
- Na^+-Pi
- Na^+-lactate



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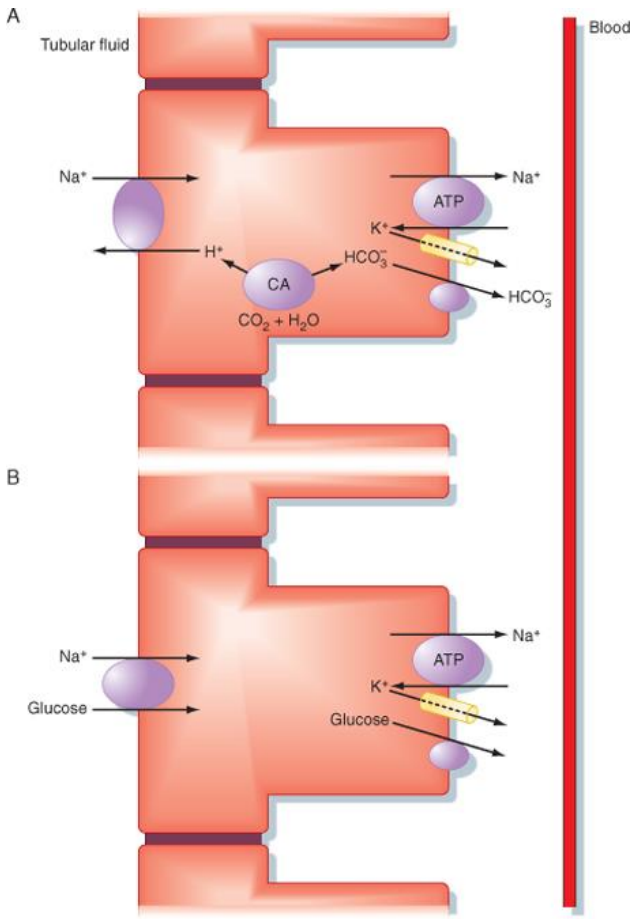
Glucose Reabsorption

- From tubular lumen to tubular cell: ***Sodium co-transporter (Carrier-mediated secondary active transport***). Uphill transport of glucose driven by electro-chemical gradient of sodium, which is maintained by Na-K pump presents in basolateral cell membrane.

- From tubular cell to peritubular capillary: ***Facilitated diffusion*** (***Carrier-mediated passive transport***)



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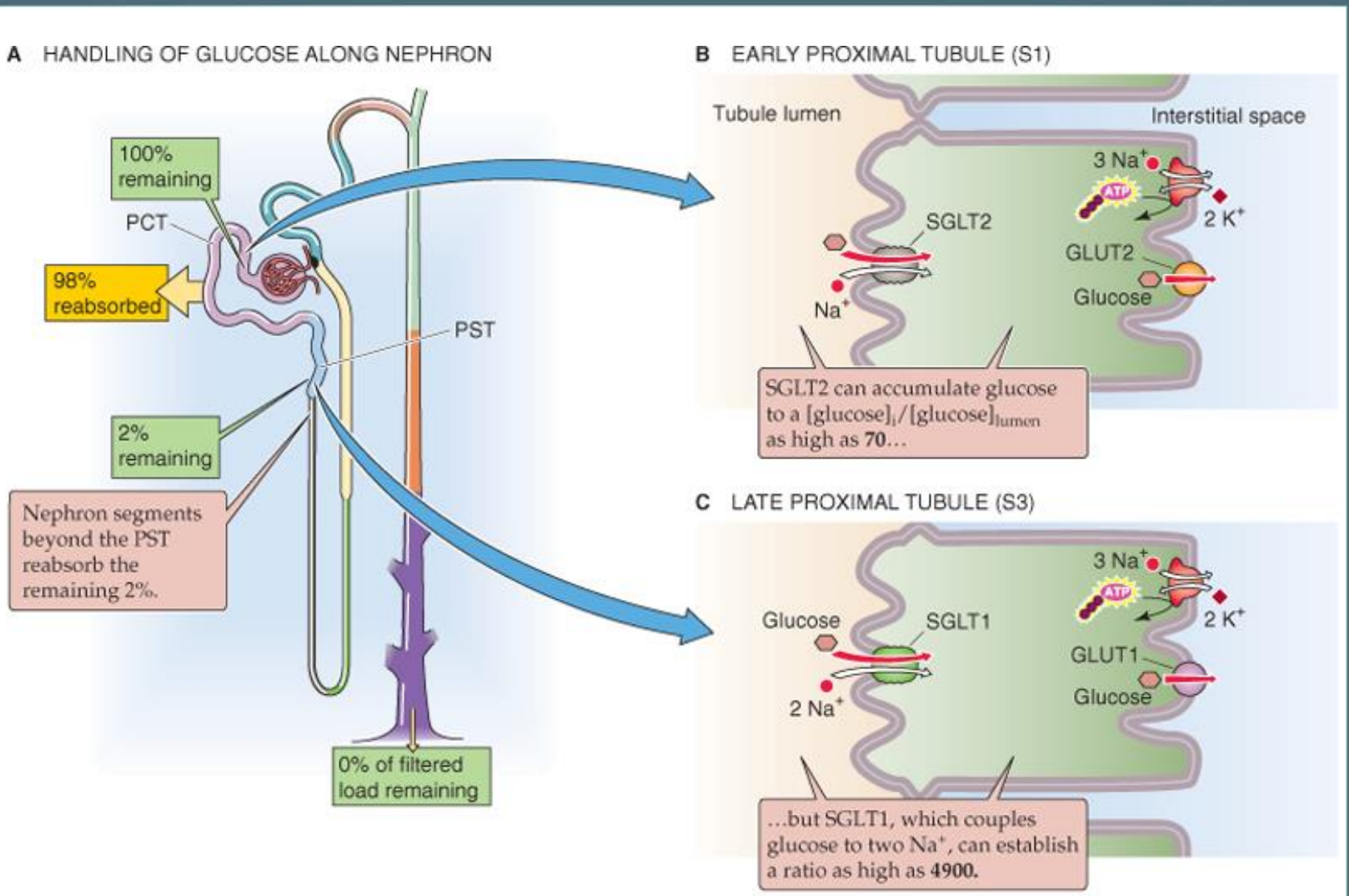

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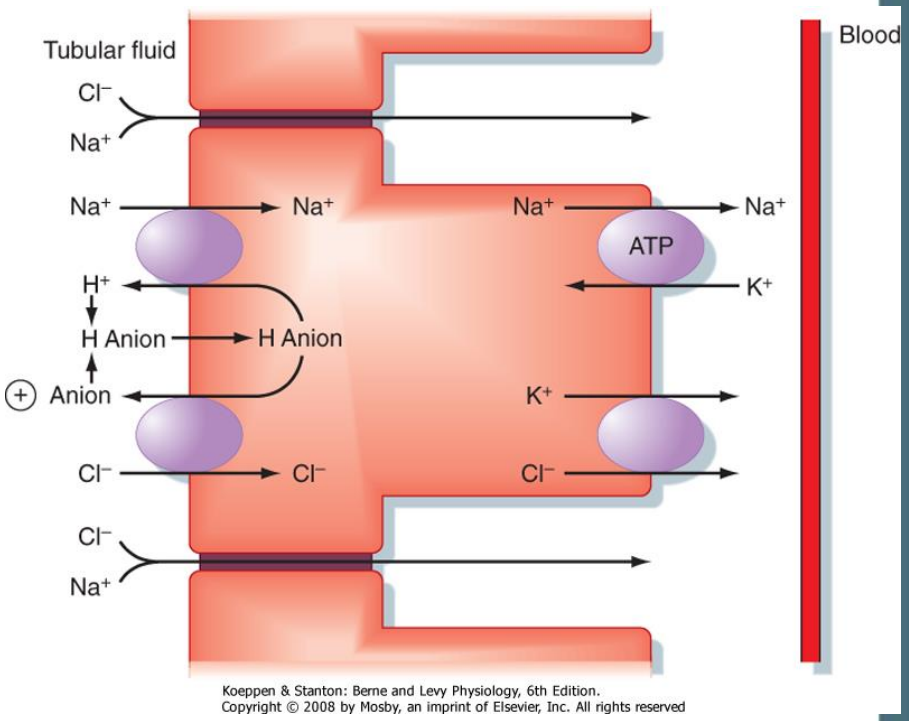
PCT
Na+ Reabsorption

- **Late PCT** Na+ Reabsorbed mainly with Cl-
- Why ? due to different transport mechanisms in late PCT, lack of organic molecules

a) Transcellular: Na+ entry using NHE & 1 or 2 Cl^--anion antiporters



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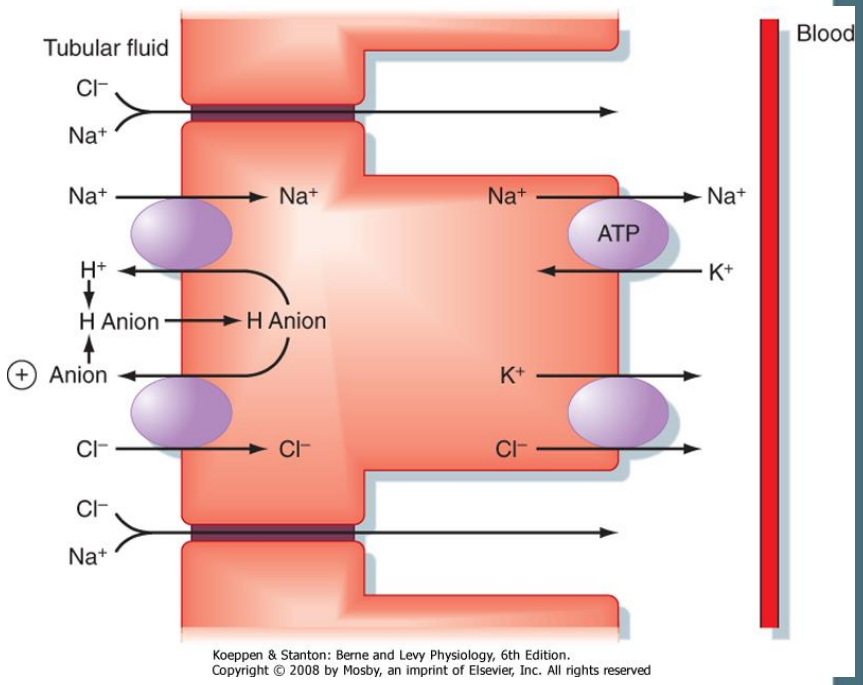
PCT
Na+ Reabsorption

b) Paracellular (passive diffusion) With Cl-

- driven by high [Cl-] in tubule
- 140mEq/L in the tubule lumen and 105 mEq/L in interstitium.
- This conc. gradient favors diffusion of Cl- from the tubular lumen a cross the tight junction into the lateral intercellular space.



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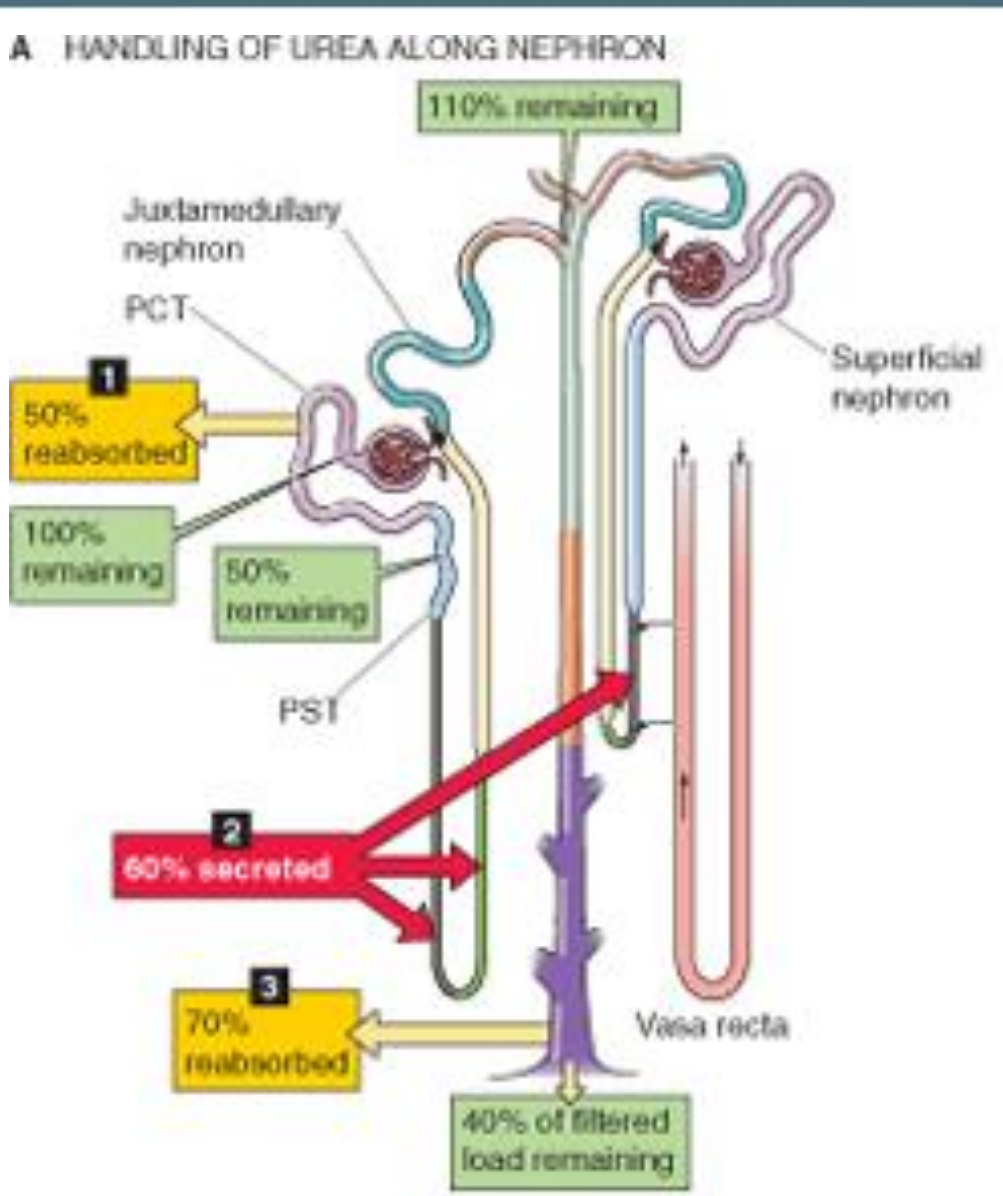
Urea Reabsorption

- Normal plasma level of urea 2.5-6.5 mM/L (15-39 mg/100ml)

Mechanism of urea reabsorption:

- About **40-70%** of filtered load of urea is reabsorped in:
  - Second half of PCT.
  - Medullary CT and CD (ADH dependent)
- Due to water reabsorption in the first half of PCT, the conc. of urea is increased in the second half and urea is reabsorbed by simple diffusion (downhill)

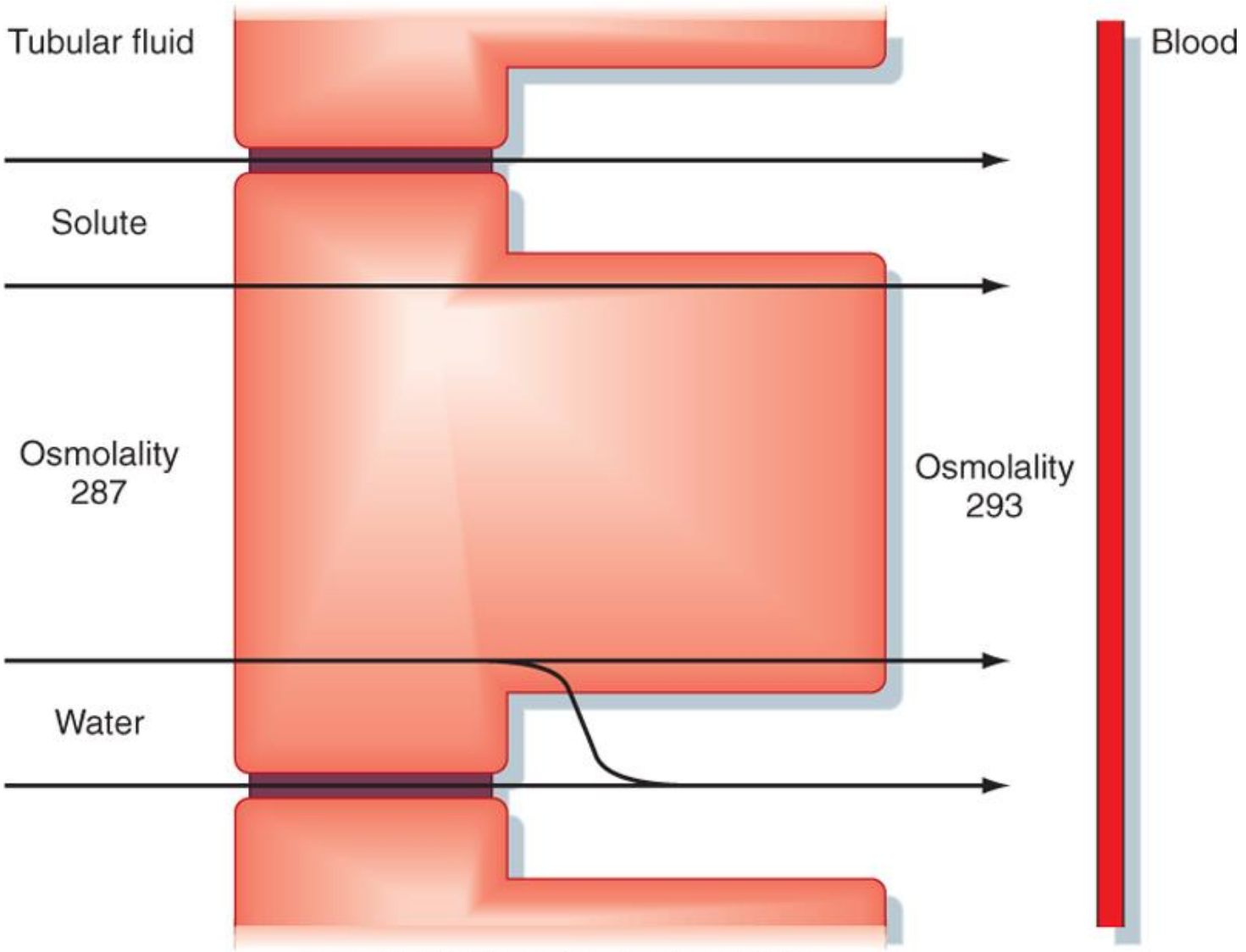

A HANDLING OF UREA ALONG NEPHRON
110% remaining
Juxtamedullary nephron
PCT
Superficial nephron
1
50% reabsorbed
100% remaining
50% remaining
PST
2
60% secreted
3
70% reabsorbed
Vasa recta
40% of filtered load remaining

Water reabsorption

- PCT cells permeable to water
- PCT Reabsorbs 67% of filtered water.
- Transtubular Passive (osmosis), due to osmotic active substances that are absorbed e.g. **Na+**, glucose, HCO3-, Cl-

  $\Rightarrow$ $\downarrow$ tubule osmolality

  $\uparrow$ intracellular space osmolality



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Water reabsorption

- Solvent drag: K+, Ca2+, carried with water & hence reabsorbed
- The accumulation of fluid and solutes within the lateral intercellular space increases hydrostatic pressure in this compartment
- The increased hydrostatic pressure forces fluid and solutes into the capillaries. Thus, water reabsorption follows solutes.
- The proximal tubule reabsorption is isosmotic

Protein reabsorption

- Peptide hormones, small proteins & amino acids reabsorbed in PCT
- Undergo Endocytosis into PCT, either intact or after being partially degraded by enzymes.
- Once protein inside the cell, enzyme digest them into amino acids, which leave the cell to blood.
- Has a maximum capacity

  - too much protein filtered = proteinuria

Organic ion/cation secretion

- **Endogenous compounds:**
  - End products of metabolism
  - Bile salts
  - Creatinine
  - Catecholamines (adrenaline, noradrenailne)

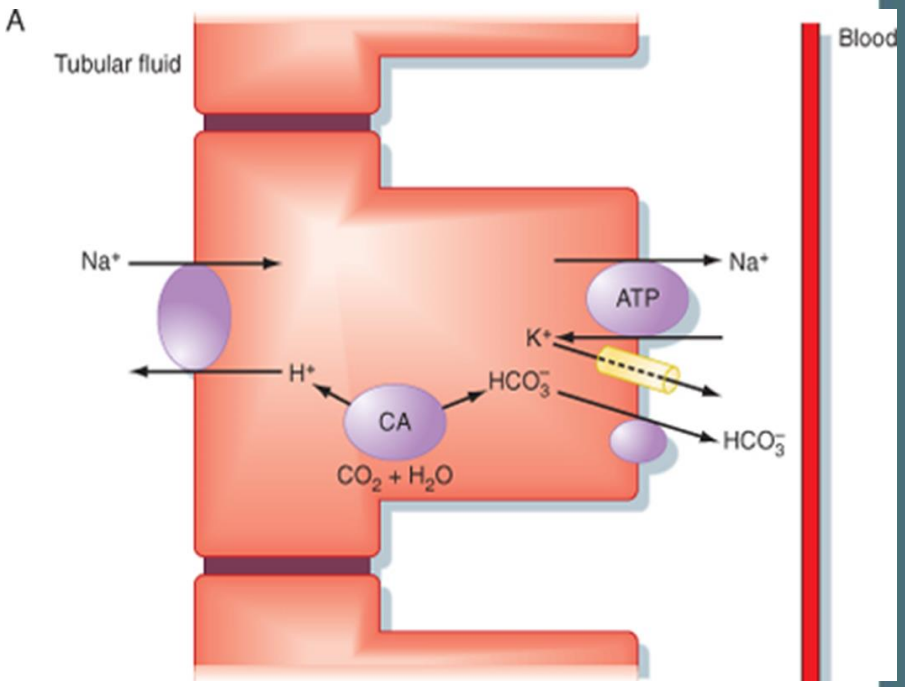
- **Exogenous compounds:**
  - Penicillin
  - NSAIDs (e.g. ibuprofen)
  - Morphine

HCO_3^- reabsorption

- The renal tubules are poorly-permeable to HCO_3^-. However, it is still reabsorbed but in the form of CO_2 (to which the tubules are very highly permeable).

This occurs through the following steps:

1. H^+ is formed inside the cells then secreted in the tubular fluid.
2. H^+ combines with HCO_3^- in the tubular fluid forming H_2CO_3.



HCO_3^- reabsorption

3. By activity of the **carbonic anhydrase enzyme (C.A.)** in the tubular cells, H_2CO_3 dissociates into CO_2 & H_2O.

4. CO_2 diffuses into the cells where it combines with H_2O (by activity of an intracellular C.A.), forming H_2CO_3 which dissociates into HCO_3^- & H^+.

5. HCO_3^- passively diffuses into the interstitial fluid (then to the blood) while H^+ is secreted into the tubular fluid to help more reabsorption of HCO_3^-.

HCO_3^- reabsorption

- Factors affecting **HCO_3^-** reabsorption:

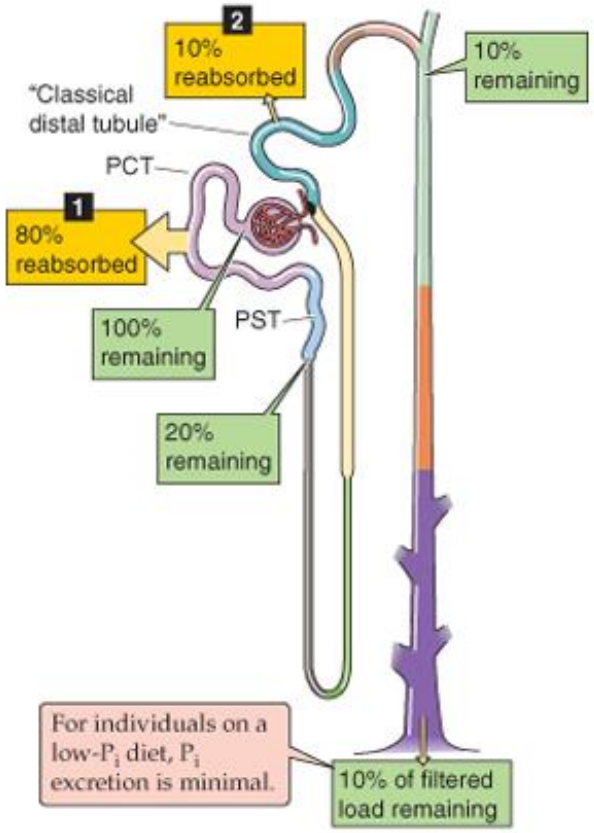
1. Arterial Pco_2
2. Plasma[K^+]
3. Plasma Aldosterone.
4. Plasma [cl^-]

References

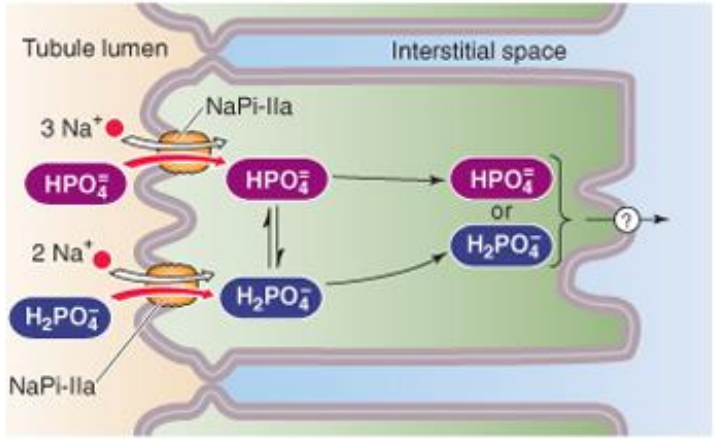
- Guyton and Hall Textbook of physiology
  - Chapter 27


Thanks

A HANDLING OF PHOSPHATE ALONG NEPHRON



B PROXIMAL TUBULE



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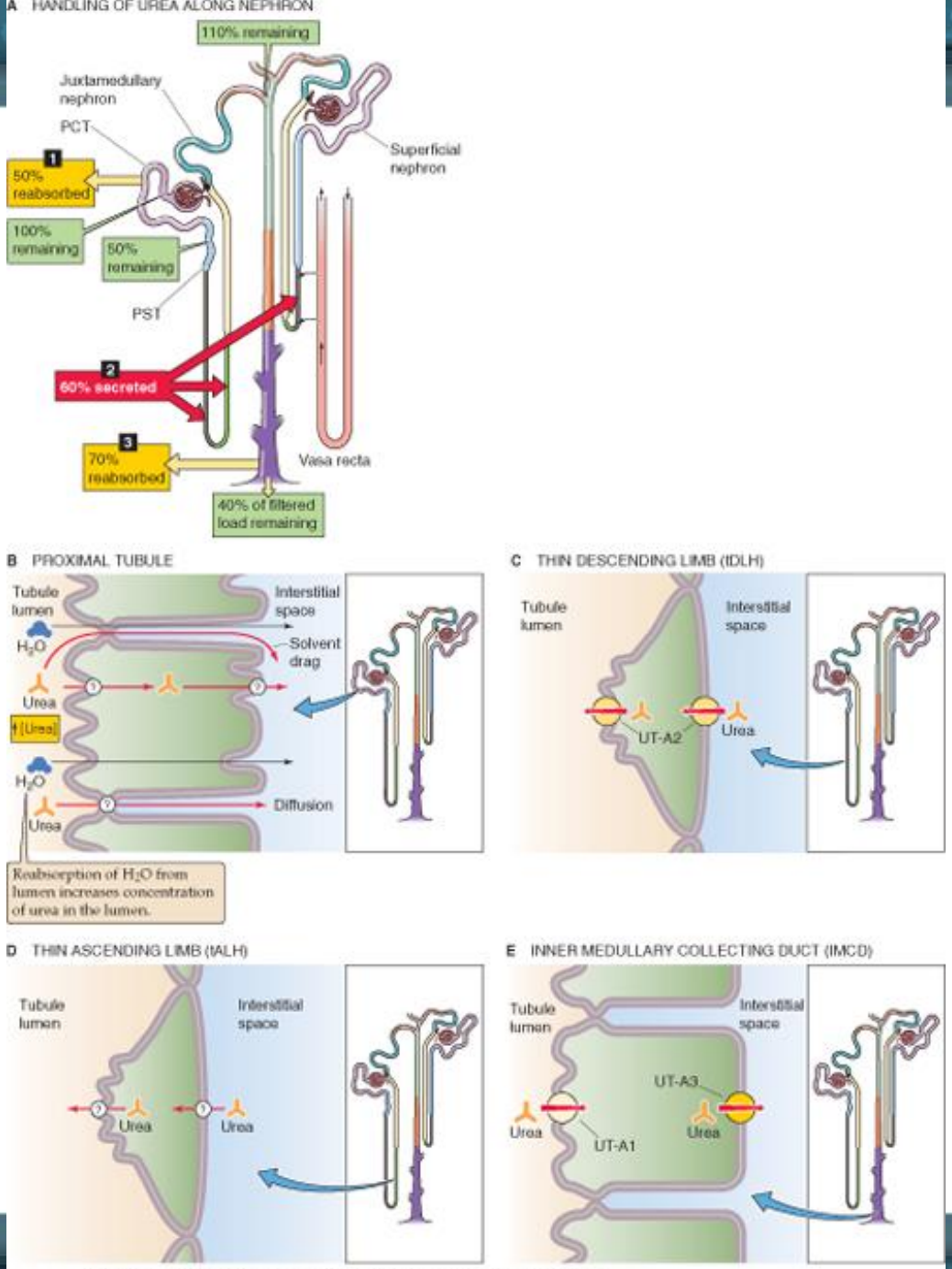

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