Sodium Homeostasis

- **Sodium is an electrolyte of major importance in the human body. It is necessary for :**

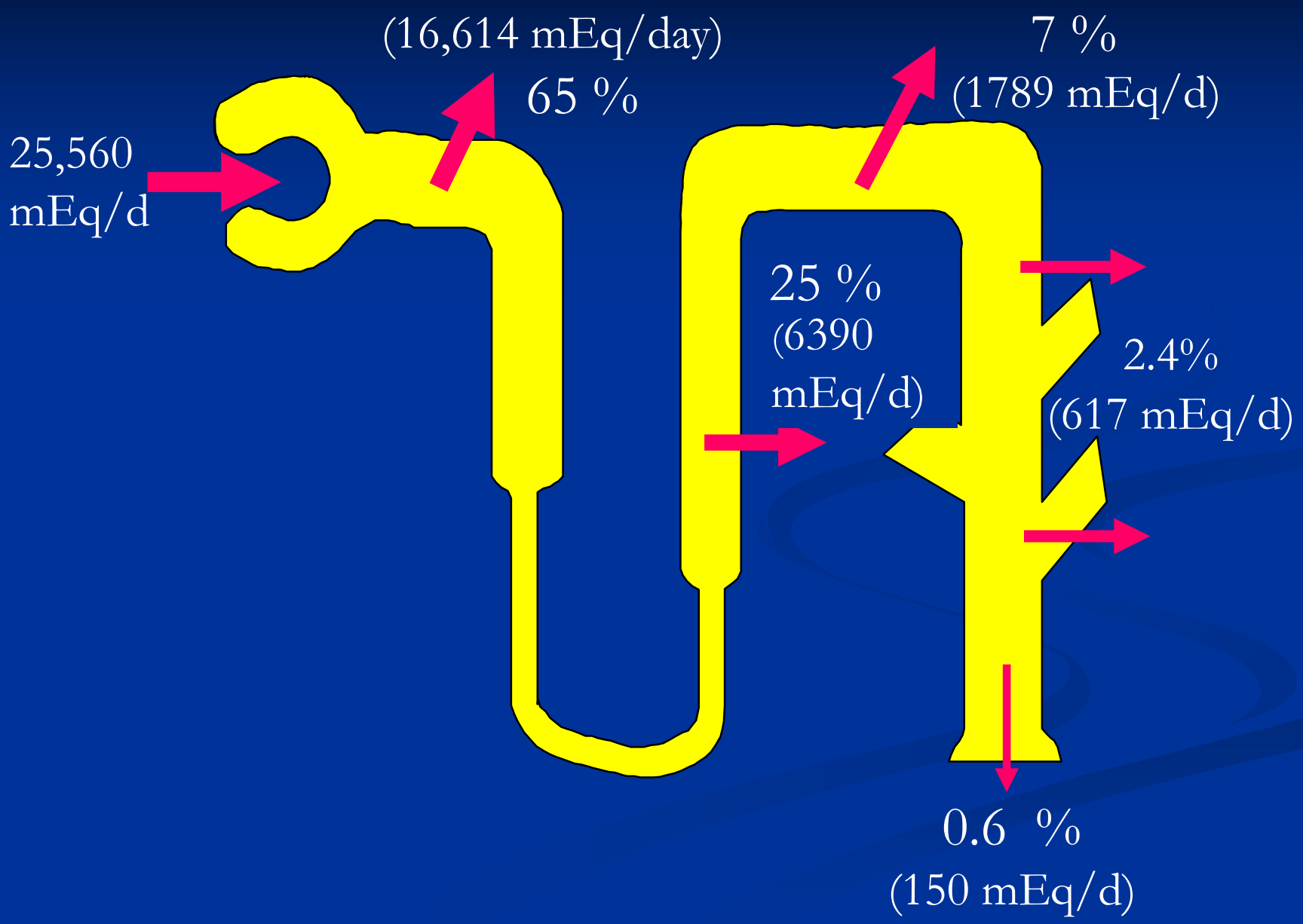
1. **normal extracellular volume dynamics**

- ↓ Na in ECF → volume contraction. ↑ Na in ECF → edema.

1. **excitability of certain tissues**
2. **cotransport and counter transport…glucose, a.a, H^+**
3. **concentration of urine in thick ascending**
4. **Sodium accounts for a significant portion of plasma osmolarity. The latter can be estimated by multiplying plasma sodium concentration times 2.1.**

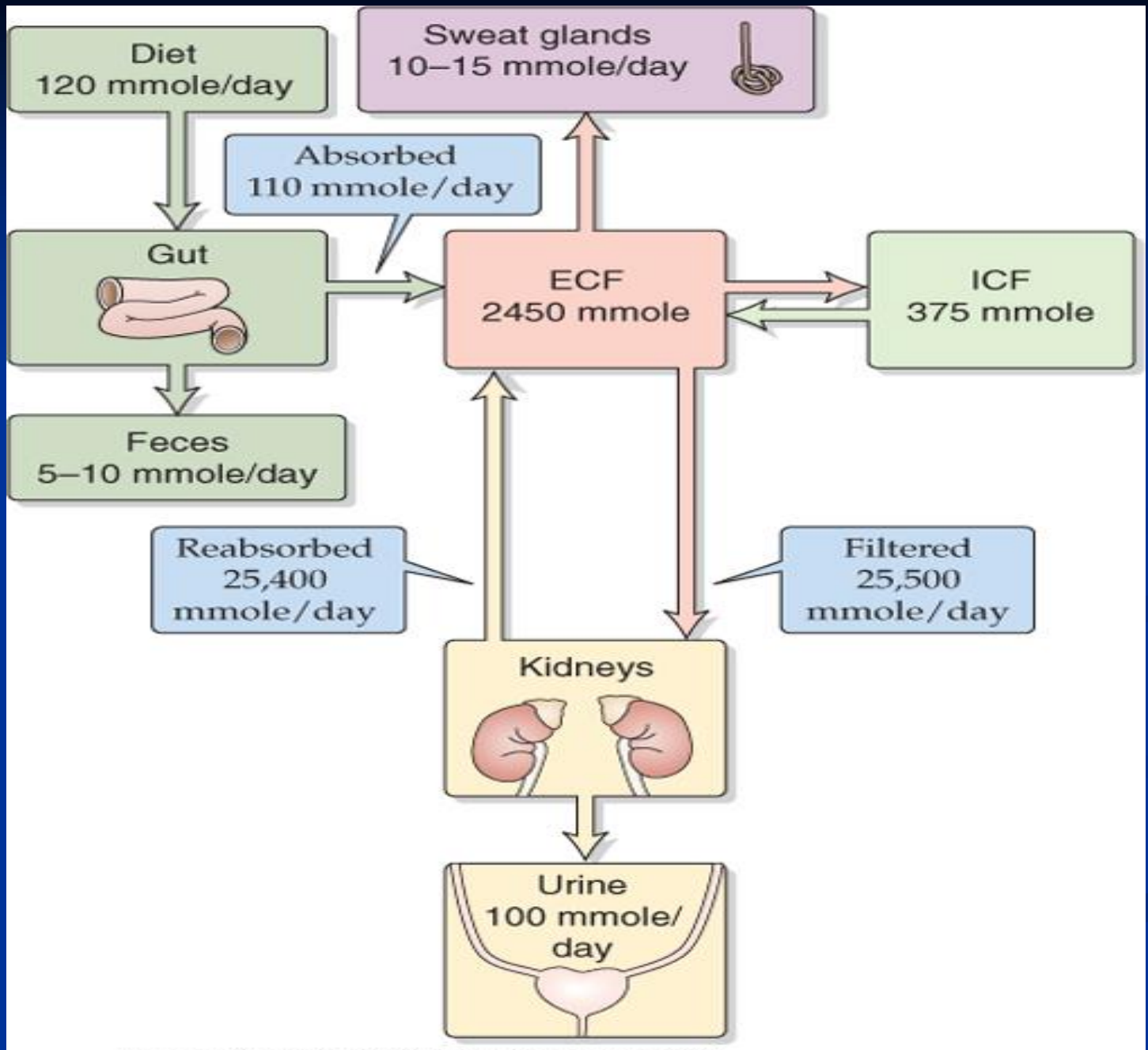
Most of the primary active transport in the entire tubular system is to transport Na^+

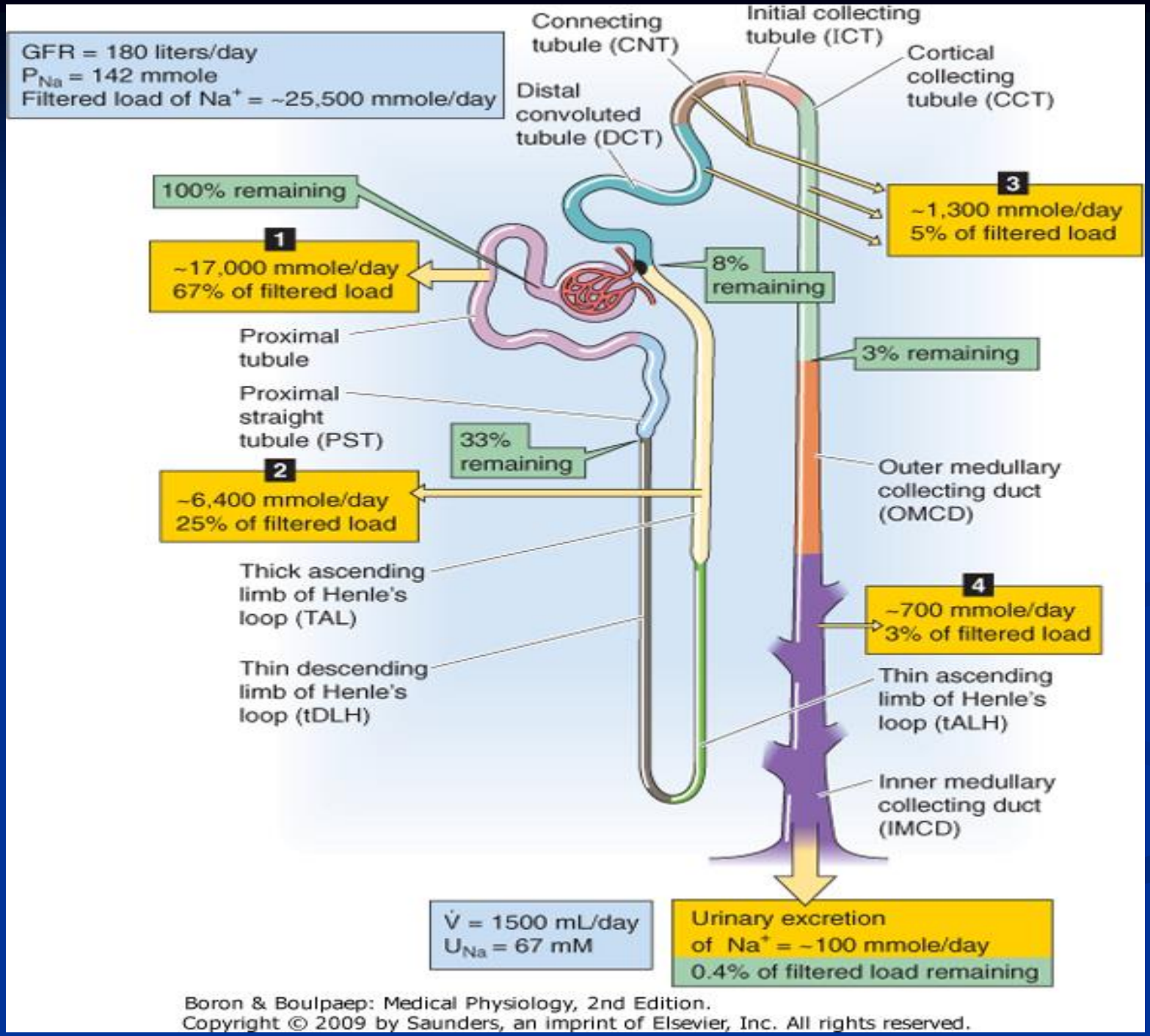
Normal Renal Tubular Na^+ Reabsorption



Sodium Homeostasis

- Sodium balance is achieved when intake and output equal each other.
- Sodium intake is about 120-155 mmol/d in the average American diet (≈ 4 gm). Logically, the daily output would be 120-155mmol/d as well.
- The kidney accounts for 115-150 mmol of this output. Hence, the kidney is a major organ in sodium homeostasis.





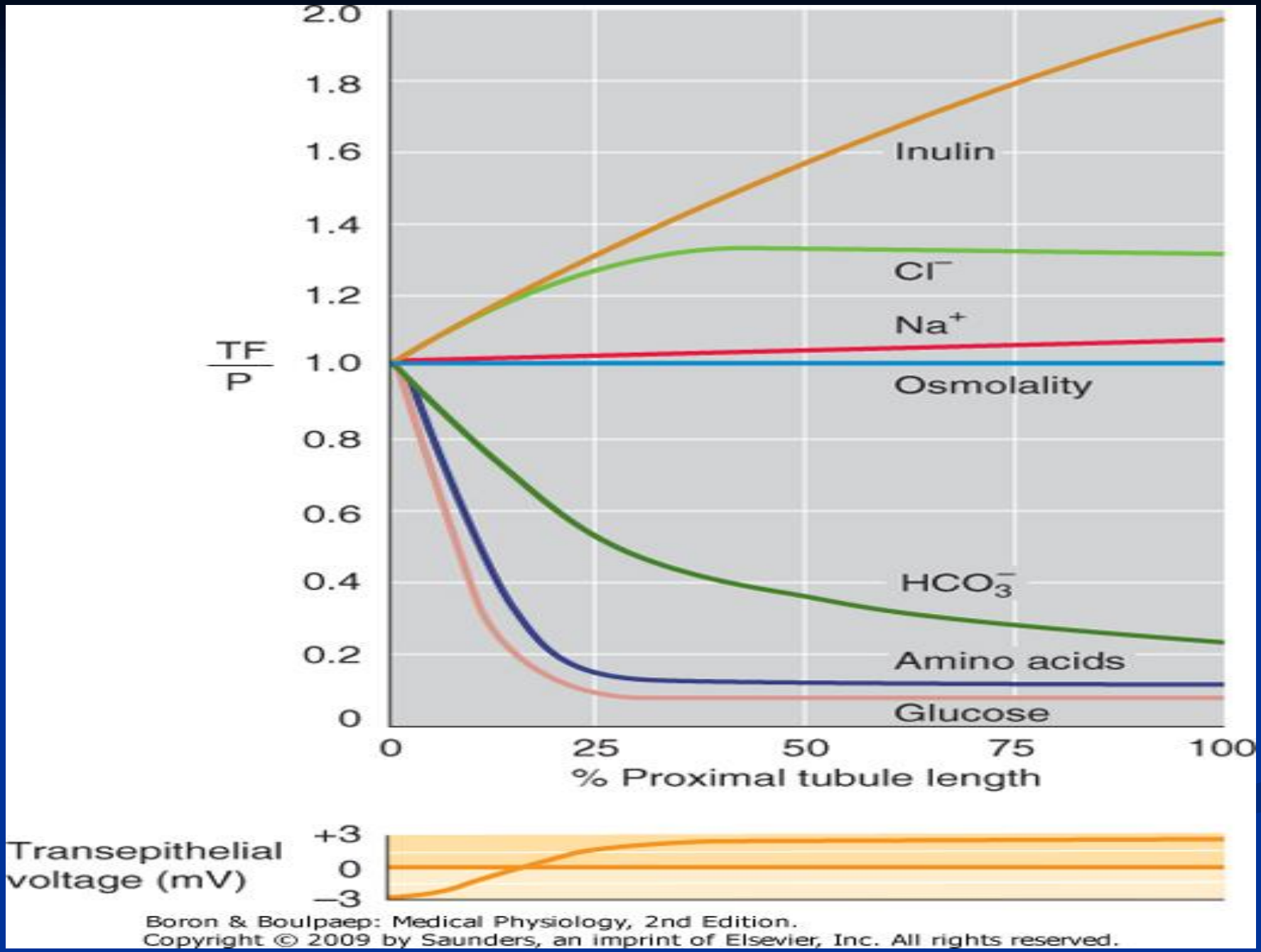
Na^+ Clearence

- Sodium clearance can be calculated as follows:
- U_{Na+} = 150mmol/d ÷ 1.5l/d urine per day = 100mmol/l
- $C_{Na+} = (U_{Na+} / P_{Na+}) * V = (100 / 145) * 1 = 0.69$ml/min
- Notice that the value is less than 1 ml/min, which indicates that sodium is mostly reabsorbed.
- Sodium reabsorption is rather extensive. In order to appreciate this, let's do the math.
- Amount of sodium filtered per day = 180l/d * 140mM = 25200mEq…sometimes you are facing with slightly different numbers…don't worry.
- Amount of sodium excreted by the kidney = 150 mM
- Percent reabsorbed = 25050 / 25200 = 99.4%

sodium homeostasis

- **Three factors are principally involved in sodium homeostasis:**

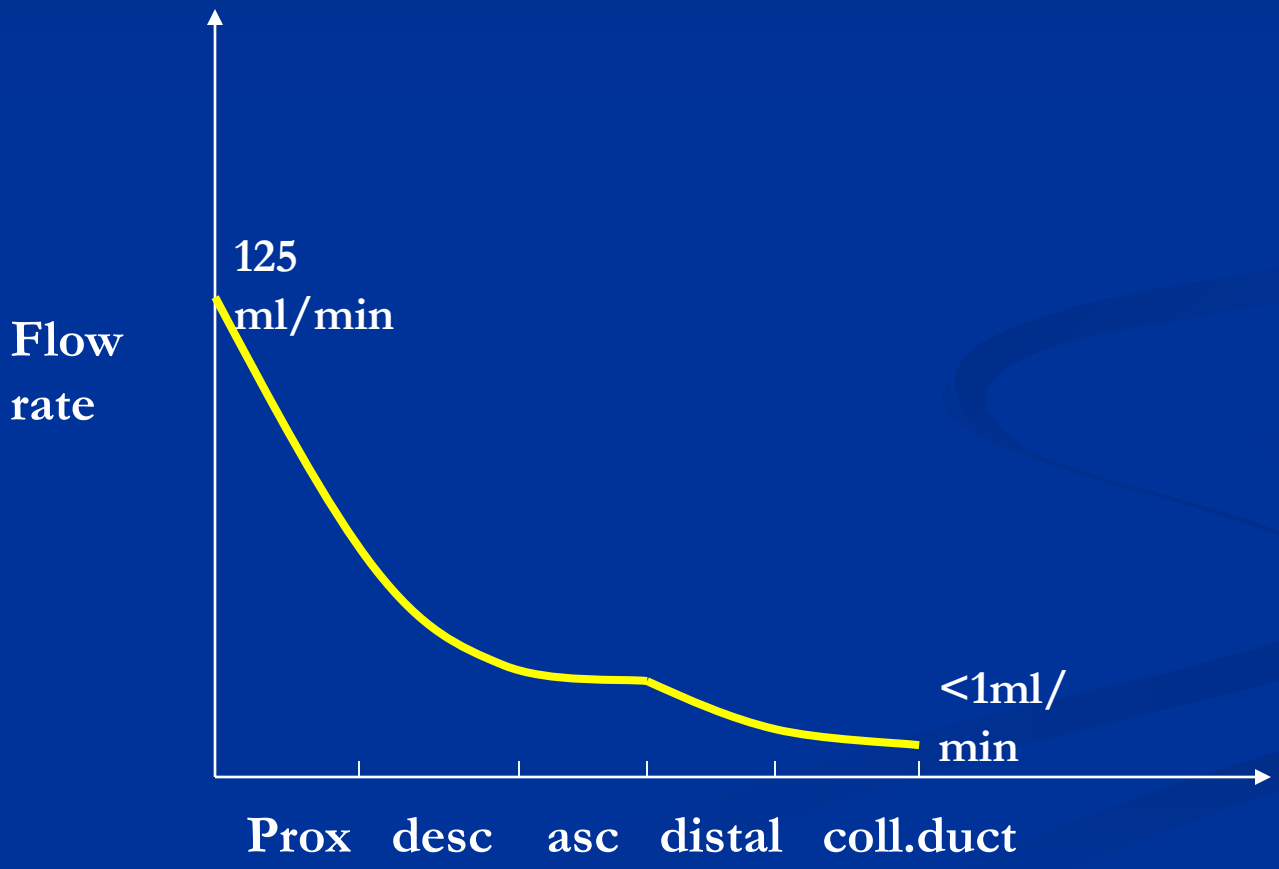
1. **GFR (1st factor)**
2. **Aldosterone (2nd factor)**
3. **Atrial natriuretic peptide (3rd factor)**



Na^+ & H_2O reabsorption occurs as the following :

Segment	Na^+%	H_2O%
Proximal tubule	65%	65%
Descend (Henle)	-	15%
Ascending (Henle	25%	-
Distal tubule	7%	10%
Collecting duct	2.4%	9%

$$C_{Na+} = [U_{Na+} / P_{Na+}] \times V$$
$$= 100/140 \times 1 = < 1 \text{ ml/min}$$



- about the curve :

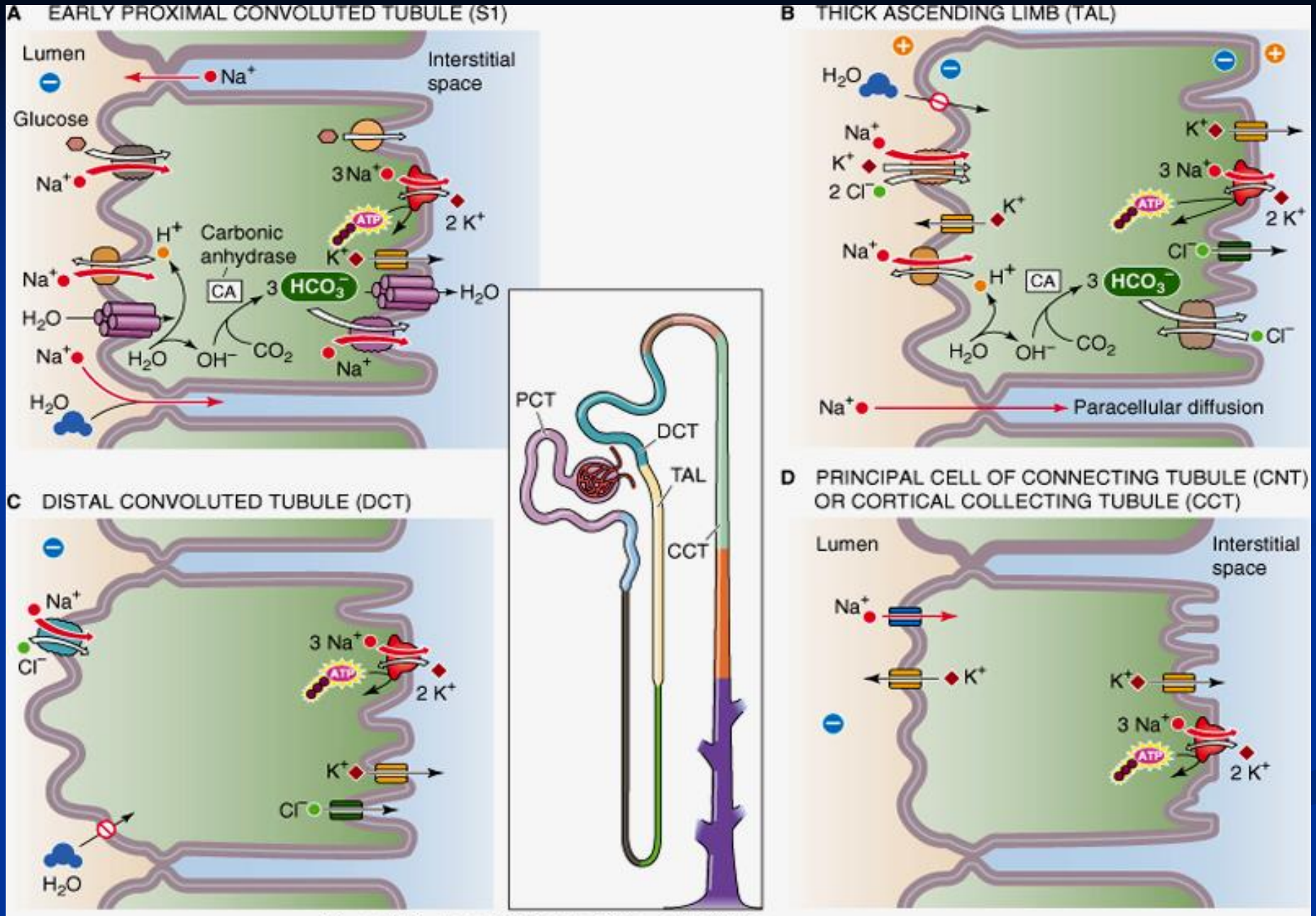
1. the decrement in the flow rate (F.R) throughout the kidney tubules .
2. F.R remains relatively constant at the level of the ascending limb of Henle .

- There are 2 ways to handle Na^+ in the kidney :

1) Through filtration (↑or↓) or

2) Reabsorption (↑or↓)

- Example: when Na^+ intake is increased:
- → ↑Na^+ filtered → ↑reabsorption in the proximal… This is called " glomerulotubular balance " to ensure that a constant fraction is reabsorbed (≈ 2/3) → this occurs in the proximal tubules
- In distal tubule Na^+ reabsorption is decreased.

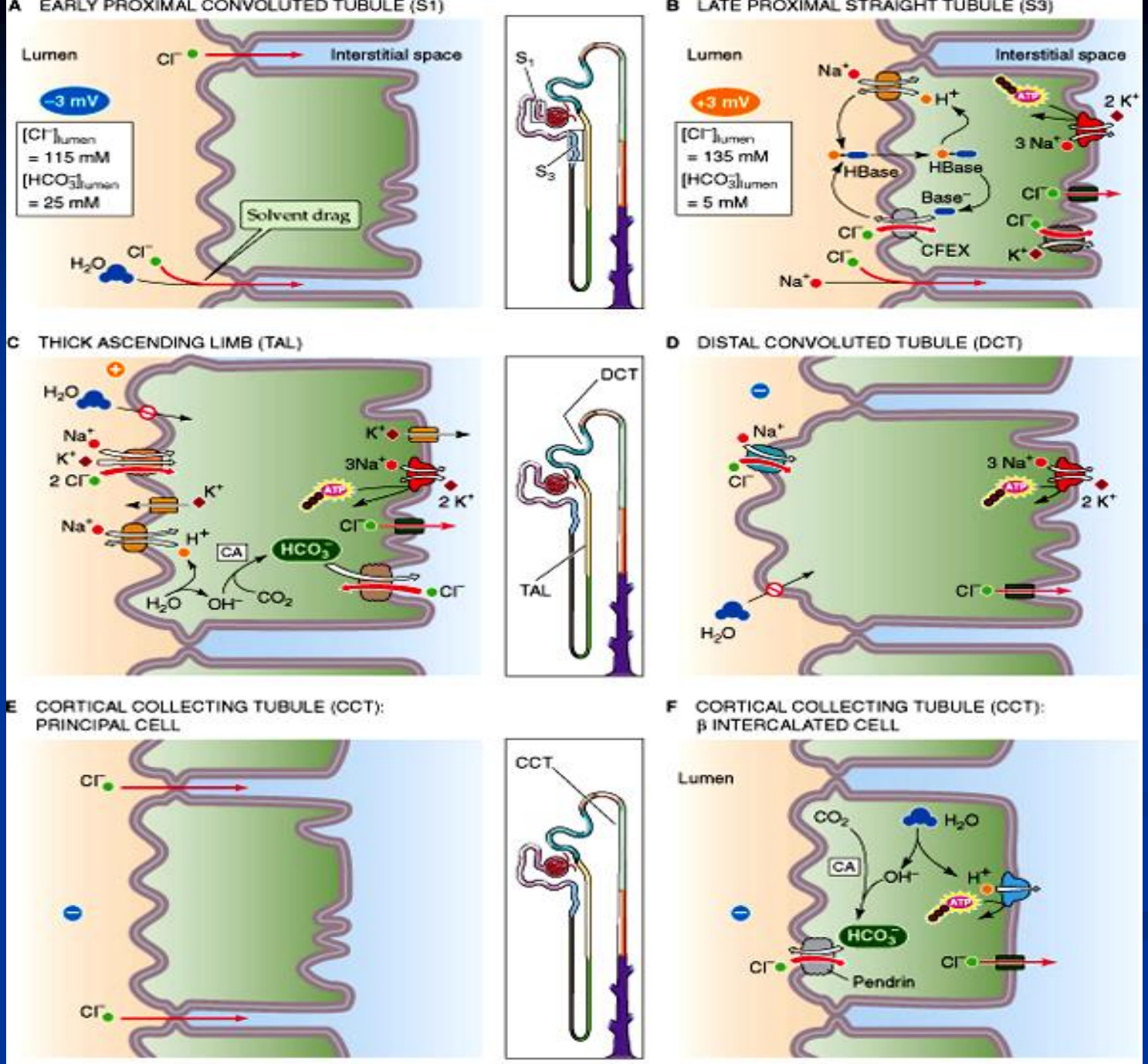


A-Reabsorption at proximal tubules

- There are 2 ways for Na^+ transport through the cells:

1. transcellular → channels (T-max)…passive at the apical side and active at the basolateral side
2. Paracellular pathway → through the tight junctions which are not that tight

- in the early proximal tubules, tight junctions are not so tight → paracellular route (+ transcellular route), so transport is NOT T-max dependent → it is gradient/time dependent .
- ↑[Na+] or ↑ time in TF stays in prox. tubules → more chance to be reabsorbed.
- In more distal parts of the nephron , the tight junctions are tighter → T-max dependent transport can be exhibited.



A-Reabsorption in proximal tubules

- In the early part of the proximal tubule , Na^+ & H_2O are reabsorbed with glucose & amino acids by "cotransport process".
- $[Na+]_{out}$ = 140 mEq
- $[Na+]_{in}$ = 14 mEq
- So Na^+ moves down gradient from the luminal side to the cell, while it is pumped actively through the basolateral membrane (anti-gradient) .

A-Reabsorption in proximal tubules

- In the late proximal tubule , Na^+ is reabsorbed with Cl^- , because in the early prox.tub. , removal of large amounts of Na^+ creates negativity inside the lumen. so to get back to normal , Cl^- is reabsorbed. Na^+ follows Cl^-.

- **<u>B. Reabsorption in descending limb of Henle</u>** (no reabsorption).
- **<u>C. Reabsorption in the Ascending limb of Henle.</u>**

  reabsorption involves (Na^{+}-K^{+}-$2Cl^{-}$) co-transporter **without** H_2O , this is called [single effect] → ↑ osmolarity in the interstitium and ↓ osmolarity in the TF (diluting segment…bcs TF become diluted)

Clinical point

1. Furesamide (Lasix): a potent loop diuretic acts on the thick ascending limb of Henle TAL where it inhibits Na-2Cl-K → ↑ Na^+ and water Excretion.

Lasix is used to treat pulmonary edema

2. Thiazide/Chlorothiazide (moderate diuretic) acts on distal convoluted tubule DCT inhibiting Na/Cl reabsorption

- Those 2 diuretics are called [potassium-wasting diuretics]…they induce hypokalemia
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Reabsorption of Na^+

- **D. Reabsorption in late distal tubules & cortical collecting duct.**
- Reaborption of Na^+ & secretion of K^+ occur through the principal cells.

Clinical point

- 1. **Spironolactone** (aldactone): is aldosterone antagonist: it decreases Na^+ reabsorption and works on principal cells by decreasing K^+ secretion → aldactone diuretics are called [K^+ sparing diuretics].
- 2. **Osmotic diuretics** , (ex: Mannitol): Theoretically can be considered as glomerular marker & has an osmotic effect i.e. it's not reabsorbed so it drives H_2O with it , used in brain edema .

Control of Na^+

- when Na^+ intake is increased → increase in GFR through increasing ECV and BP.

When ECV increases → π in peritubular capillary decreases due to dilution

Control of Na^+

- How does the body control increase in Na^+ intake ?

1. Altering GFR
2. Altering Reabsorption

- **1-Altering GFR:**
- When Na^+ intake increases → Glomerulotubular feedback does not work for unknown reason →increase Na^+ Excretion.
- increase Na^+ intake → increase Pa → increase GFR (**Pressure Natriuresis**)

Control of Na

2-Altering reabsorption:

When Na^+ intake increases the RFC is shifted to the left to ensure increase Na^+ excretion. This shift means less production of AII, which results in less Na^+ reabsorption and thus increase its excretion. In addition less AII means less aldosterone and less Na^+ reabsorption.

- **Aldosterone is also autoregulated….means whenever [Na^+] in plasma increases, Aldosterone production decreases**
- **ANP (Atrial Natriuretic Peptide) increases due to increase atrial pressure resulting in two things:**

  1. Afferent Arterial dilatation → increase GFR →increase Na excertion

  2. inhibit adrenal cortex → decrease aldosterone production.

Diuretics

- They are actually 7 groups each work on a specific cell and with a different mechanism.
- some of these groups are used for specific indications like carbonic anhydrase inhibitors which is used in glaucoma
- hypokalemia is a serious complication of loop diuretics and thiazide
- I will leave this slide to pharmacology lecture

Diuretics

Class	Mechanism	Site of Action
Osmo-diuretics	Mannitol	
loop diuretics like furosemide, ethacrynic acid and bometanide	inhibit Na-K-2Cl cotransport. Most powerful available. They increase *Ca^{++} and *Mg^{++} elimination	At thick ascending
**Thiazide	Inhibit Na-Cl cotransport.: increase Ca^{++} reabsorption …can be used in hypercalciuria	At distal
Acetazolamide (Diamox)	C.A inhibitors	Proximal..used for glucoma
***Spironolactone	Inhibit Na^{+} reabsorption	At principal cells
Na^{+} channel blockers such as Amiloride and triamterene	Because they inhibit Na^{+} reabsorption, they also inhibit K^{+} secretion. Therefore, they are also K+ sparing.	