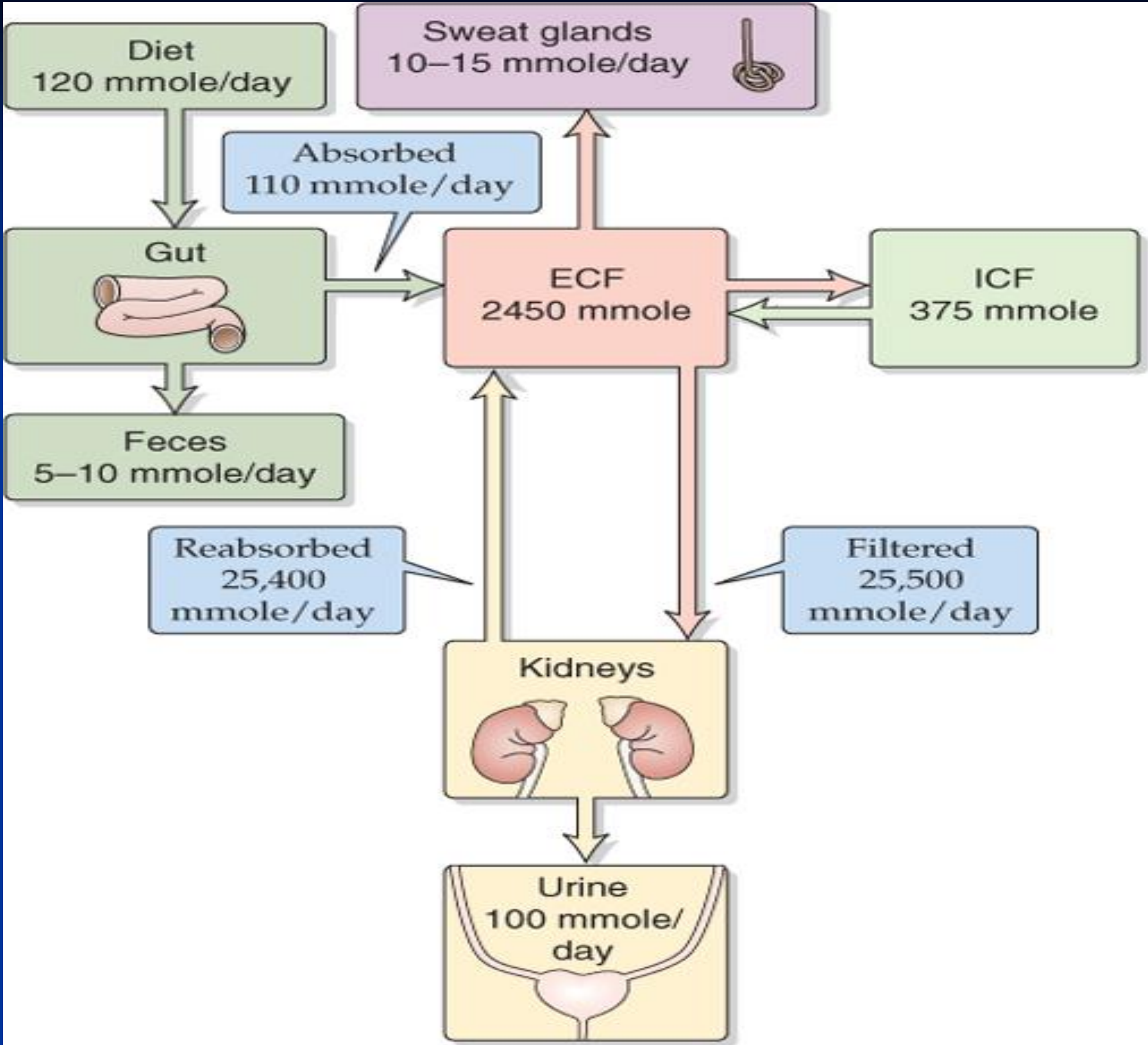
Sodium Homeostasis

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

1. normal extracellular volume dynamics
2. excitability of certain tissues
3. cotransport and countertransport
4. countercurrent mechanism
5. concentration of urine
6. Sodium accounts for a significant portion of plasma osmolarity. The latter can be estimated by multiplying plasma sodium concentration times 2.1.

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. 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.



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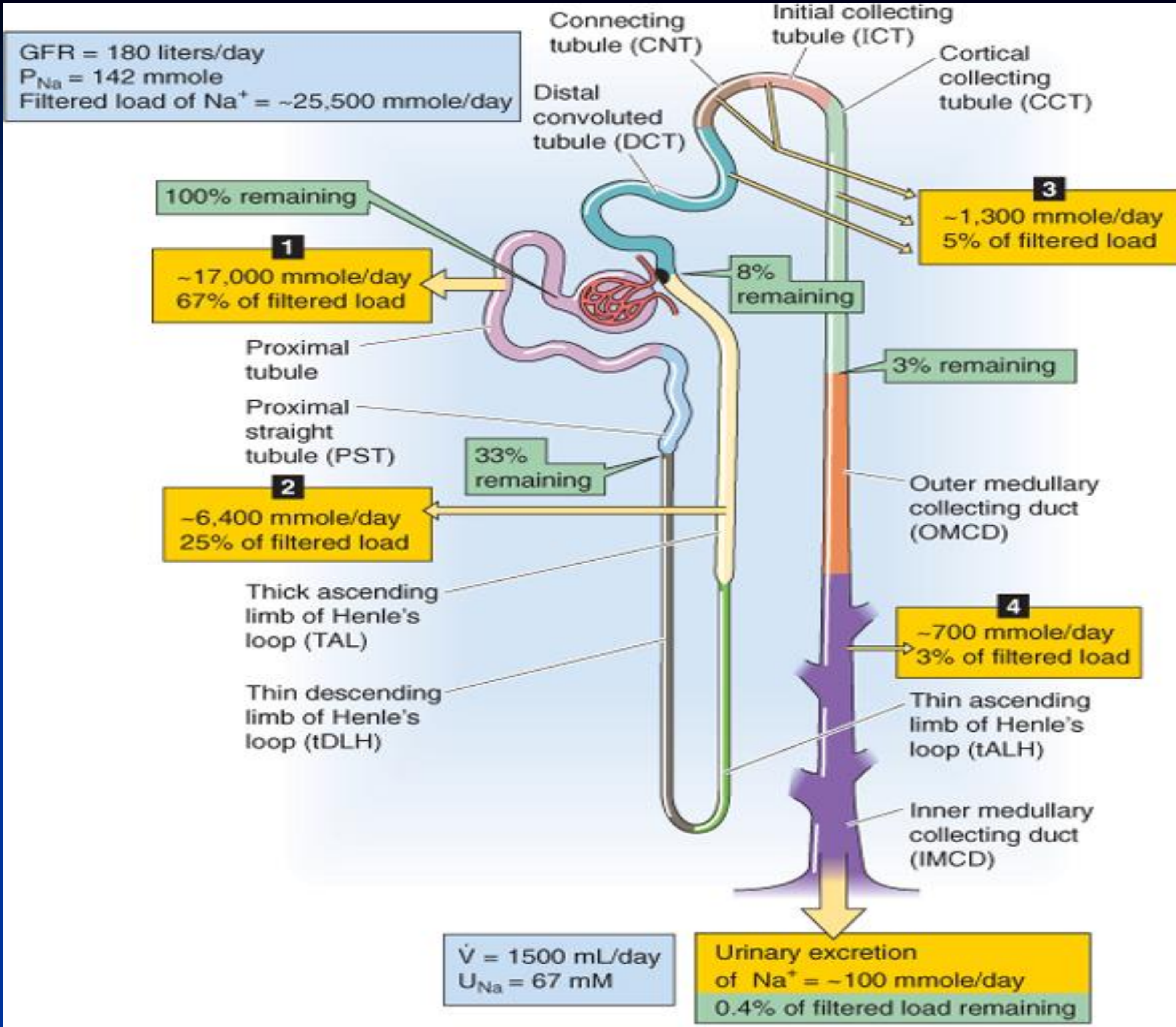

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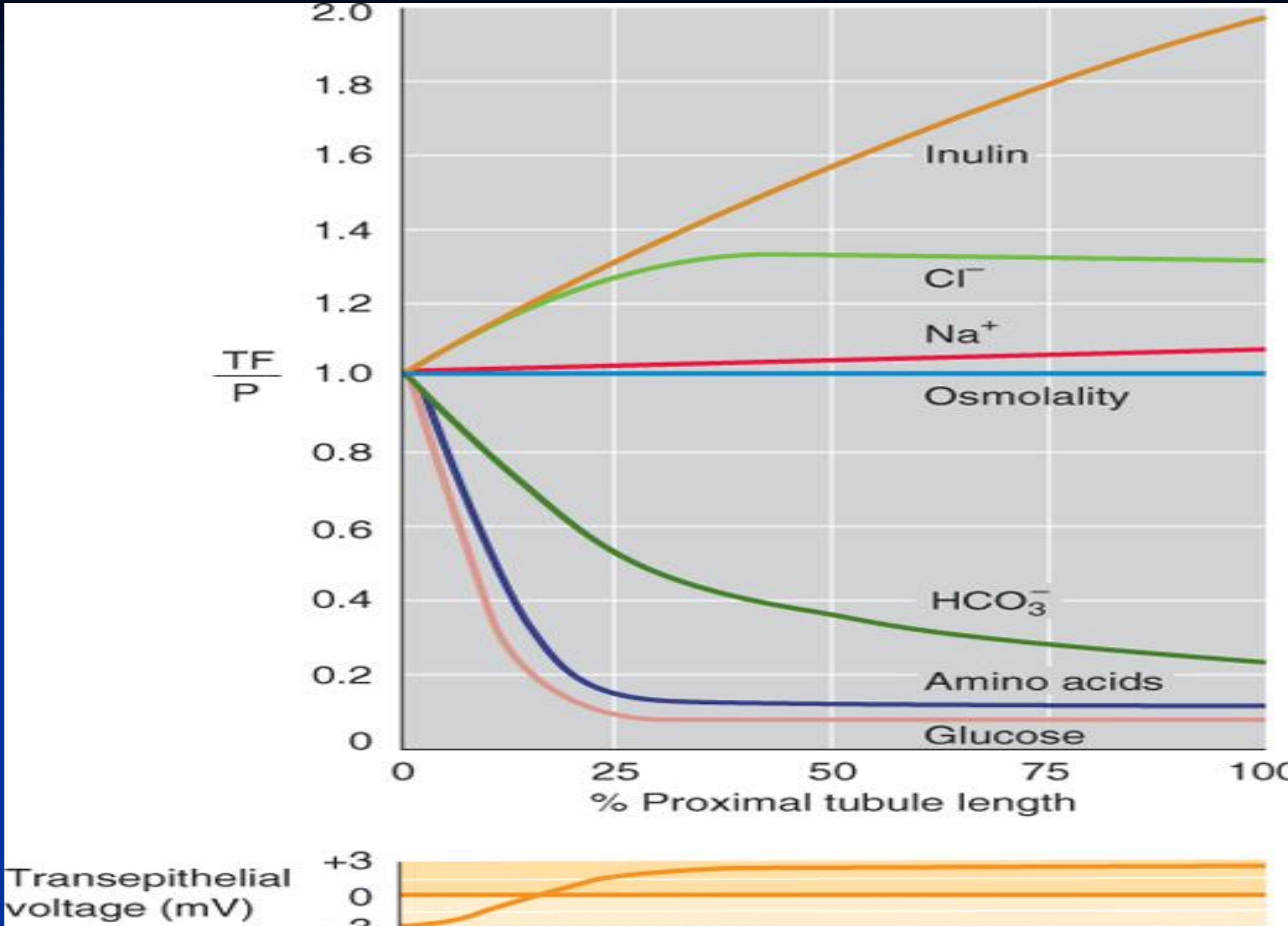
Na Clearence

- 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
- 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,
2. Aldosterone,
3. Atrial natriuretic peptide.



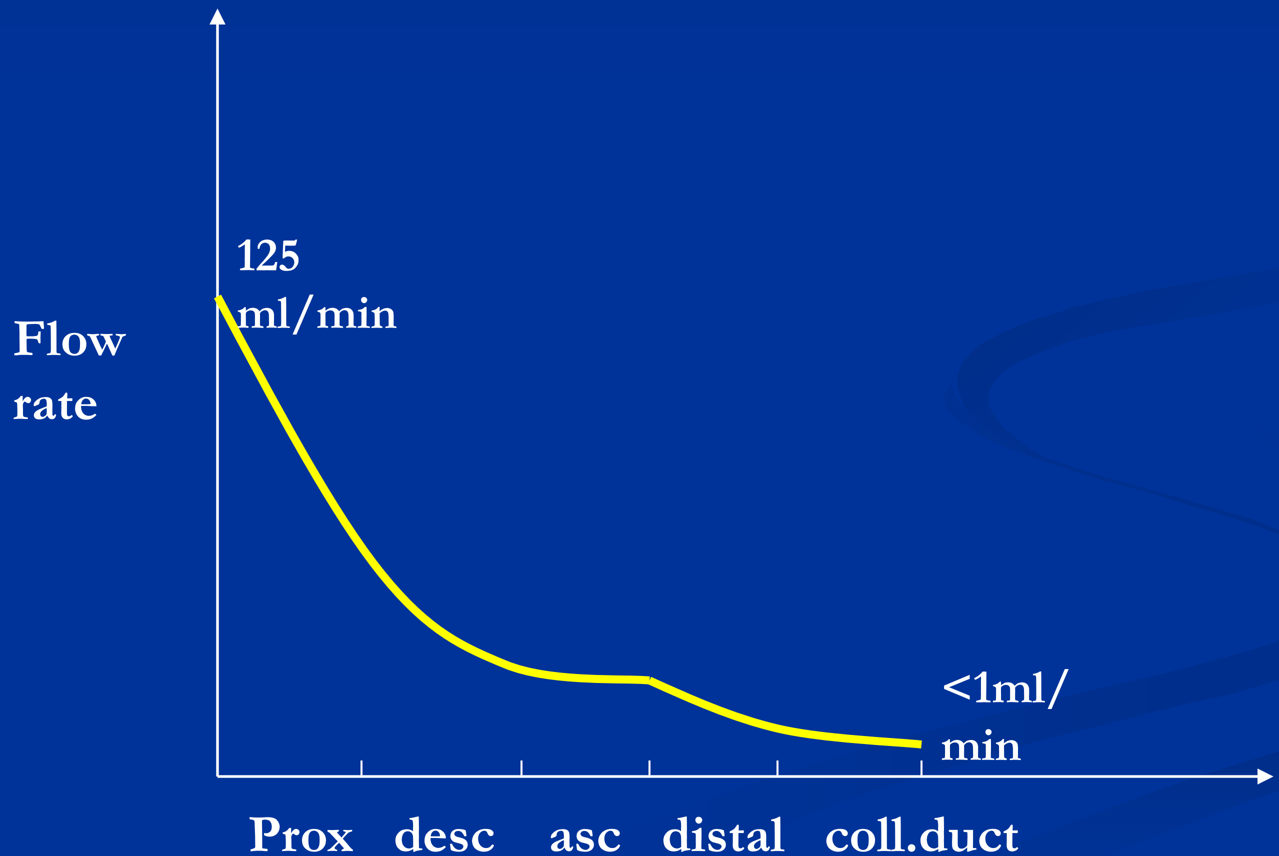
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
TF/P
Inulin
Cl⁻
Na⁺
Osmolality
HCO₃⁻
Amino acids
Glucose
0
25
50
75
100
% Proximal tubule length
Transepithelial voltage (mV)
+3
0
−3

Na^+ & H_2O reabsorption occurs as the following :

Segment	Na^+%	H_2O%
Proximal tubule	65%	65%
Descend (Henle)	-	15%
Ascending (Henle	25%	-
Distal tubule	5%	10%
Collecting duct	4%	9%

$$C_{Na+} = U_{Na+} / P_{Na+}] \times V$$

$$= 100/140 \times 1 = < 1\ ml/min$$



- about the curve :

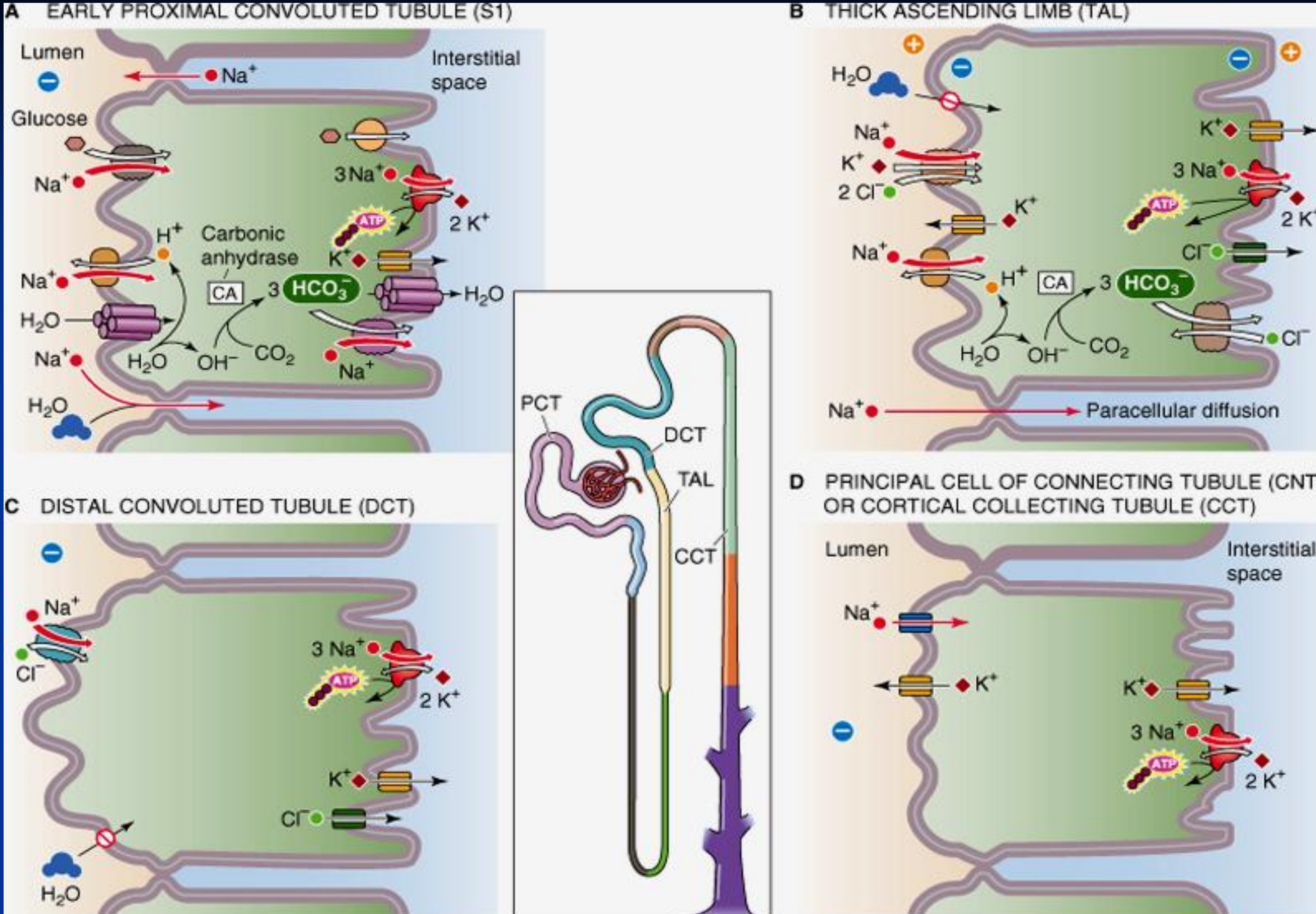
1. the decrement in the flow rate (F.R) throughout the kidney tubules .
2. F.R remains relatively constant at the level of the ascending limb of Henle .

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

1) Through filtration or

2) Reabsorption

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



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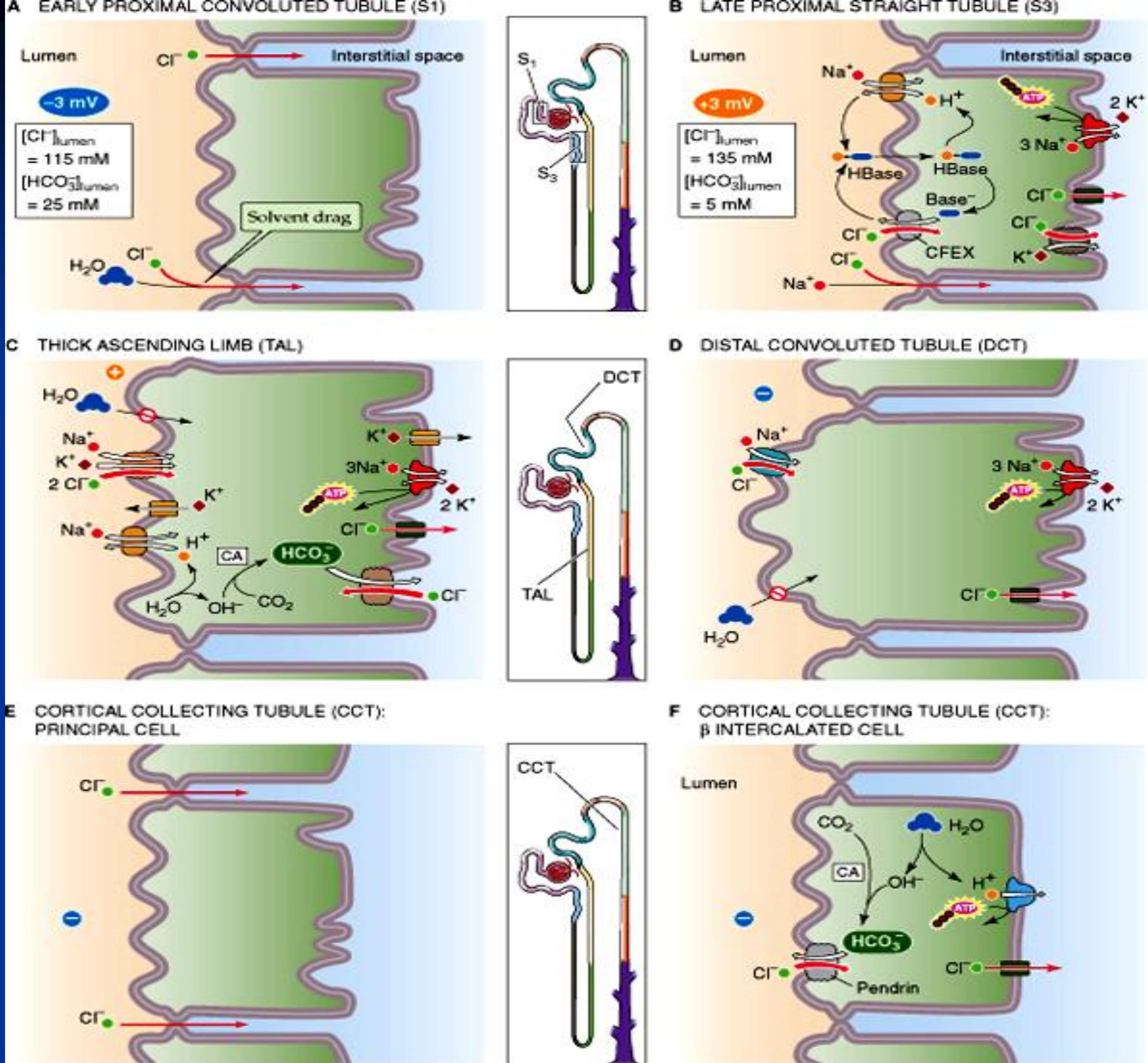
A-Reabsorption in proximal tubules

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

1. transcellular → channels (T-max)
2. paracellular → tight junction

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



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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+ with glucose 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 , ↓ osmolarity in the lumen.

Clinical point

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

   Indicated in pulmonary edema & hypertension.

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

- Those 2 diuretics are called [k+_ wasting diuretics]
-

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): works on principal cells by decreasing K+ secretion → Hypokalemia. aldactone diuretics are called [K+ sparing diuretics] or [aldosterone antagonists].
- 2. **Osmotic diuretics** , (ex: Mannitol) is a glomerular marker & has an osmotic effect i.e. it's not reabsorbed so it drives H2O with it , used in brain edema .

Control of Na^{++}

- when Na+ intake ↑ → ↑ GFR by : -
  ↑ ECV
  ↑ BP
  ↓ peritubular π
- when ECV ↑ → ↓ π peritubular capillary due to dilution → ↓ Reabsorption.

Control of Na^{++}

- How does the body control ↑ Na+ intake ?

1. Altering GFR
2. Altering Reabsorption

- **1-Altering GFR:**
- When Na^{+} intake ↑↑↑ , Glomerulotubular feedback is not working for unknown reason → ↑ Na Excretion.
- ↑ Na intake → ↑ pressure → ↑ filtration & this is called (**Pressure Natriuresis**)

Control of Na

2-Altering reabsorption:

- Macula densa suppresses " Angiotensin II " →

1. ↓ reabsorption from Proximal
2. ↓ aldosterone → ↓ reabsorption from distal

- Aldosterone is autoregulated.
  Ex. ↑ Na+ → ↓ aldosterone (by itself).
- ANP (Atrial Natriuretic Peptide) increases due to ↑ atrial pressure →
  1. Aff. Arterial dilatation.
  2. inhibit adrenal cortex → ↓ aldosterone

K+ - Reabsorption

- $[K^+]$ plasma = 4 mEq.

Too small as compared to $[Na^+]$ plasma= 140mEq.

- K-balance :

- K intake=100 mEq/day

-K excretion=100 mEq/day→

(92-95) by kidneys the rest is removed by other routes

- Renal Failure→ huperkalemia

Renal Failure does not cause hypernatrimea because when Na increases H_2O increases too thus Na+ remains relatively constant or slightly decreased.

K+ - Reabsorption

- K contributes to RMP so
- ↑ k → hyperpolarization and cardiac arrest
- ↓ k → increased exitability and arrhythmia.

$$C_{k+} = \frac{60\ mEq/L}{4\ mEq} * 1\ ml/min$$

$= 15\ ml/min$

Which is much more than C_{Na+}

Calcium		Increase Reabsorption	Decrease Reabsorption
Proximal	65%	Volume Contraction	Volume Expansion
TAL	25%	PTH, Clacitonin	Furosemide
DCT	8%	PTH VitD AVP (ADH) Alkalosis Thiazide	Phosphate depletion
Coll Ducts	1%	Amiloride	