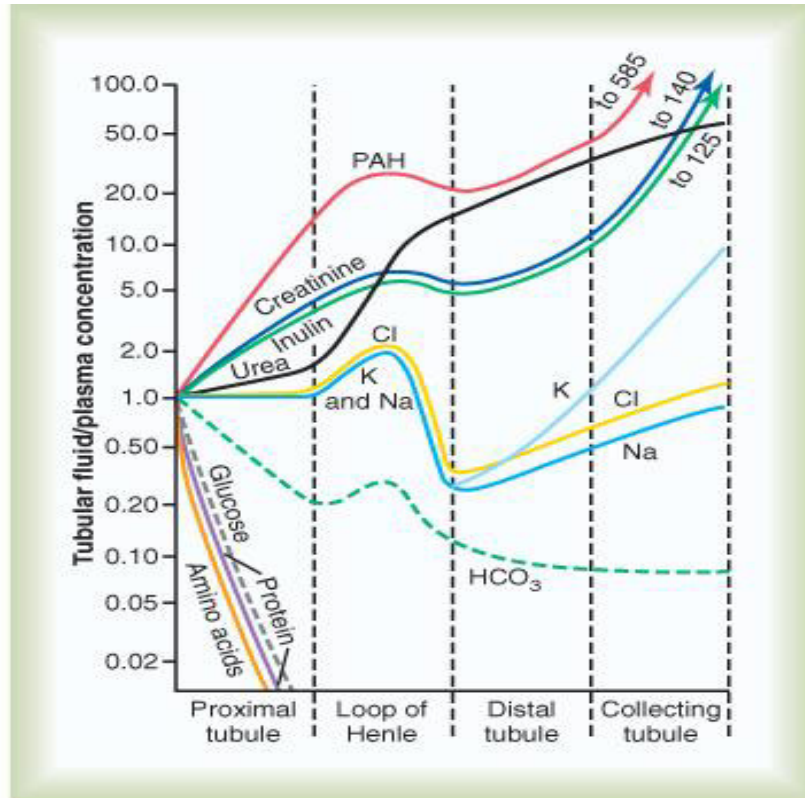


Sodium and potassium Homeostasis

Note: I rearranged a lot of information to make this sheet as easy as possible.

“[TF]/[P] curve”



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In this curve we see that all substance start with concentration of 1 mg (100%):

- 1) Glucose + Amino acids: will become zero before the end of proximal tubules.
- 2) Inulin: increases 3 times by the end of the proximal tubules, clearance reach 125ml/min.
- 3) Creatinine: slightly more than inulin, clearance reaches 140ml/min.
- 4) PAH : the highest one ,clearance can reach 585ml/min .
- 5) Sodium (Na⁺) + potassium (k⁺) + chloride (cl⁻): straight line , then one third of it will be reabsorbed at the end the clearance become less than 1 ml/min .



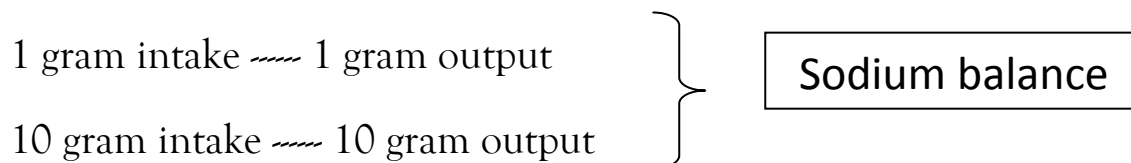
Sodium Homeostasis:

Sodium is necessary for :

- 1) Sodium is the major cation in the plasma, so Sodium accounts for a significant portion of plasma osmolarity. The osmolarity can be estimated by multiplying plasma sodium concentration times 2.1 (in plasma concentration of cation = concentration of anion).
- 2) Determine the normal extracellular volume dynamics (too much sodium means ECF expansion, too little sodium means ECF contraction)
- 3) Increase excitability of membranes (depolarization) like in the heart and skeletal muscles.
- 4) Important in secondary active transport:
 - A) co transport (glucose and amino acid)
 - B) counter transport (sodium exchange for hydrogen ; cell secrete hydrogen and absorb sodium or sodium exchange for potassium) .
- 5) Important in the ability of the kidney to make concentrated urine (important in kidney function test in renal failure)

Note : The last function of kidney will return to normal after renal failure it's to make concentrated urine .

Sodium intake per day must be equal to sodium output per day to maintain **sodium balance** , if sodium intake increase we will have positive balance ; more sodium more fluid and this lead to hypervolemia which increase risk for edema .





Normally

Hint : mmol = mEq

sodium intake = 120-155 mmol /day

sodium output = 120-155 mmol /day ; 150mmol excreted is by urine and 5mmol by other routes like sweating .

SO, The kidney is a major organ in sodium homeostasis.

1) How much is the filtered load of the sodium ?

Answer : GFR= 180 l/day >>>>125ml/day .

Sodium concentration in plasma = 140mM >>>> 140mEq/L

Filtered load = GFR*[Na⁺]Filtered load = 180 l/day *140 mM
=25200mM2) How much is excreted? 150mM (which equals the daily intake of Na⁺)

150/25200 *100% = 0.6 % of sodium will be excreted per day

3) How much is reabsorbed? 25050 mM

25050/25200 *100%= 99.4% of sodium will be reabsorbed per day

4) In which part of the nephron the sodium will be reabsorbed ?

Segment	Na ⁺ %	H ₂ O%
Proximal tubule	65%	65%
Descend (Henle)	-	15%
Ascending (Henle)	25%	-
Distal tubule	5%	10%
Collecting duct	4%	9%



****65% in the proximal tubules (2\3 of sodium):**

exchange with hydrogen (counter transport)

with glucose and amino acid (co transport)

These 2\3 are fixed whether we have too much or too little sodium.

****0% in the descending "it's not permeable to sodium" why ?**

Because as we go down in the medulla the osmolarity will increase, so the loop will reabsorb water more than sodium .

The concentration of sodium will increase here because it's not reabsorbed .

Note :

Short loop of henle, osmolarity will reach maximally 900 .

Long loop of henle " juxtamedullary" , osmolarity will reach maximally 1400(at the tip) ; more chance to reabsorb water .

****25% in the thick ascending by co transport ($\text{Na}^+ \text{--} \text{K}^+ \text{--} 2\text{Cl}^-$) from inside to outside, and this segment it's impermeable to water .**

SO , the more we are ascending in the loop, water remains and the sodium is removed , the tubular fluid become diluted (osmolarity =100) , so the fluid will reach collecting duct **hypoosmolar** , then if the ADH present the collecting duct will remove water to the interstitium (allowing water to be reabsorbed) therefore making concentrated urine , but if the ADH is absent, we will have diluted urine (osmolarity =65)

Explanation: as we go down in the medulla the loop will reabsorb more water but when we ascend up toward cortex the loop will reabsorb more sodium.

****5% in the distal tubules under the effect of aldosterone (reabsorb sodium by exchange with potassium) . The most important part in determining sodium homeostasis .**

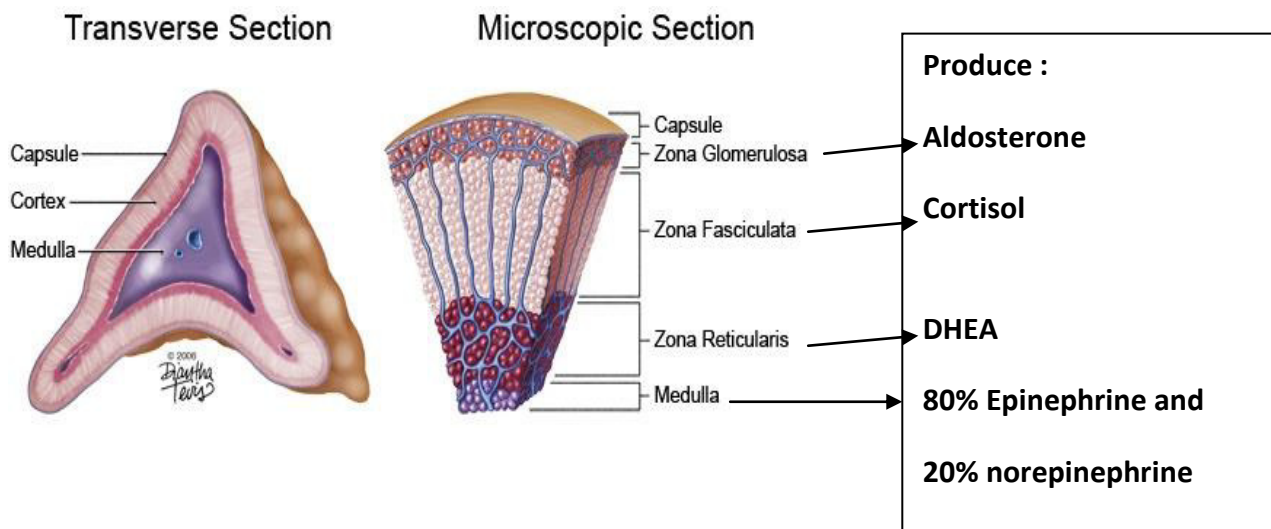


Clinical note :

Conn's disease

These three layers of adrenals are abbreviated in GFR (Glomerulosa, Fasciculata, Reticularis)

Tumor in the adrenal cortex (micro tumor (very small) can't be detected by CT scan)



So, the zona Glomerulosa will secrete too much aldosterone; means too much sodium and water will be reabsorbed; and this means hypervolemia which lead to high blood pressure (hypertension).

Clinical note : In each hypertension patient, you definitely should measure his blood potassium too, because we reabsorb sodium in exchange for potassium (secrete K^+) so he will be having hypokalemia. And when you find this hypernatremia associated with hypokalemia you should rule out Conn's disease (a tumor in adrenal cortex).

**4% reabsorbed in the collecting duct.

less than 1% is excreted.

Question : If we have too much aldosterone which part of the nephron will absorb most of the sodium ??

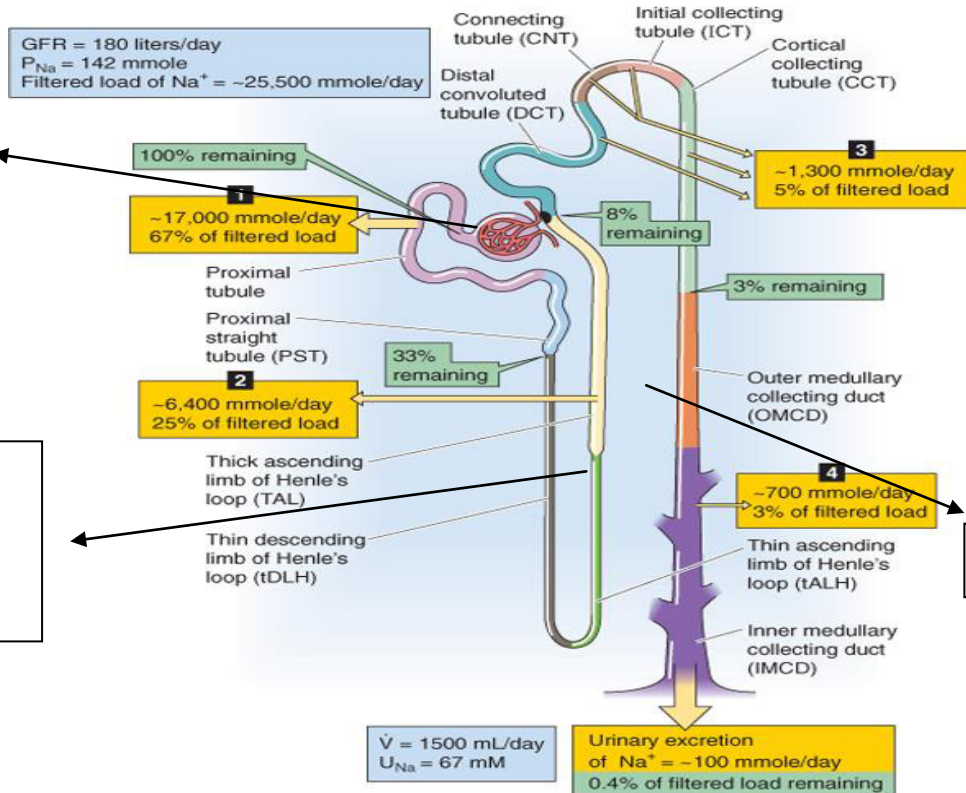


Answer: Still proximal tubules will absorb most of sodium(2\3) even with high aldosterone .

1)Intravascular : separated from interstitial by capillary membrane .

2)Interstitial : separated from intracellular by cell membrane .

3)Intracellular



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These 3 compartment (1+2+3) differ in everything (Na^+ , K^+ , Cl^- ,.....), except osmolarity it's the same in the 3 (300mM) .

** Why the osmolarity is the same ?? Because water easily moves through the membrane , so any change in osmolarity the water will move and equilibrate the osmolarity between the three compartments .



Control of Na⁺

**when Na⁺ intake increases → GFR increases by :-

1) Increase ECV

2) Increase BP

3) Decrease peritubular π " oncotic pressure " ,, (when ECV increase → π peritubular capillary decrease due to dilution → decrease Reabsorption)

When Na⁺ intake increases, Glomerulotubular feedback is not working for unknown reason → increase Na Excretion.

Na intake increase → increase pressure → increase filtration, increase Na Excretion & this is called **pressure diuresis or natriuresis** .

Factors affect sodium homeostasis

1) GFR (more GFR more Na⁺ excretion)

2) Aldosterone (HIGH Na⁺; inhibition of aldosterone; inhibition of reabsorption, LOW; more aldosterone)

3) Atrial natriuretic peptide or hormone "ANP or ANH" (more Na⁺>>> expansion of ECV>>> stimulate the release of ANH from the right atrium >>> decrease sodium reabsorption. (the only hormone will decrease sodium reabsorption)



Diuretics

There are three types of diuretics :

1) **loop diuretics** :: they work at the early thick ascending ; inhibit $\text{Na}^+ \text{--} \text{K}^+ \text{--} 2\text{Cl}^-$ reabsorption , the Na^+ will attract water we end up with excrete a lot of water and Na^+ , the urine output will be 4,5, ..L, Example : lasix (potent loop diuretics) .

2) **Thiazide/Chlorothiazide** (moderate diuretic) acts on distal convoluted tubule DCT inhibiting Na/Cl reabsorption (less sodium reabsorbed here so it has moderate) .

***The problem with these diuretics (1+2) that they are **potassium wasting** "the potassium will appear in the urine; end up with hypokalemia ; which is dangerous and affect the heart " .

3) **potassium sparing diuretics or aldosterone antagonists** :: **Spironolactone** (aldactone): works on principal cells by decreasing K^+ secretion → correct Hypokalemia , used in : patients with very high sensitivity to hypokalemia ,like in liver cirrhosis, hypertension .

4) **Osmotic diuretics**:: (ex: Mannitol) is a glomerular marker & has an osmotic effect i.e. it's not reabsorbed so it drives H_2O with it , used in:

1) brain edema.

2) patients with high glucose (hyperglycemia) in the blood " diabetes" , some of it will be reabsorbed and some of it will be excreted , glucose by osmotic effect it will trap water with it and the patients end up with polyuria followed by (العطش polydipsia .)



Potassium homeostasis

Resting membran potential has high conductance for K⁺ more than Na⁺ and Ca⁺⁺ ; means that resting membrane potential is close to K⁺ equilibrium potential .

$$K^+ \text{ equilibrium potential} = -61 \cdot \log \left\{ \frac{K^+ \text{ in}}{K^+ \text{ out}} \right\}$$

$$= -61 \cdot \log 150 \backslash 4$$

$$= -61 \cdot \log 35$$

$$= -61 \cdot 1.5$$

$$= -91.5 \text{ mV}$$

K⁺ mainly inside the cells .

Different cells have different RMP; for example Ventricular Cardiac cells have RMP = -90 so we conclude that K⁺ is the only ion which determines it's RMP ,but other cells have RMP= -70 ,How these cells differ ?? They differ in one aspect which is fast sodium channels are close and active at -90 " fast response action potential ",fast sodium channels are close and inactive at -70 "slow response action potential " .

Note :

The cell is surrounded by a lot of ions , each ion will try to stay in equilibrium .

Equilibrium : no force acting on the ion to push it in or out .

Equilibrium : RMP= ion equilibrium potential " this is determined by the one with higher permeability "

If we increase K⁺ out "hyperkalemia >>> renal failure " ::

$$K^+ \text{ equilibrium potential} = -61 \cdot \log \left\{ \frac{K^+ \text{ in}}{K^+ \text{ out}} \right\}$$

$$= -61 \cdot \log 150 \backslash 8$$

$$= -61 \cdot 1.27$$



= -77.47 "less negative"

Less negative it's going to affect the channels which are voltage sensitive channels, and this results in change of excitability in heart or skeletal muscles, end up with muscle weakness.

Potassium balance:

K^+ intake = K^+ output

K^+ intake = 100mEq /day

K^+ output = 100mEq /day >>>> 95mEq by kidney, 5mEq by other routes.

SO, The kidney is a major organ in potassium homeostasis.

How much is potassium filtered load / day??

Filtered load = $GFR \times \{K^+ \text{ in plasma}\}$

= 180L/day * 4mmol/L

= 720mmol/day

How much is excreted by kidney?? 95mEq

To summarize all information in this sheet you can go back to BRS book (pages 158 -166) , don't forget to solve review test " the doctor loves them :P " .

Thank you ☺