REVISITON :
Renal physiology & Acid-Base balane

Nephron : is the structural and functional unit in kidney .

Has two type :

I. Cortical nephrons : glomerular in outer cortex , short loop of henle(thin segment) , about 85% .

II. Jaxtamedullary nephron : glomerular in deep cortex , long loop of henle (thin segm-ent) , about 15% , has a vasa recta .

Composed of :

1. Renal corpuscle , consist of :

a. Glomerular : group of capillaries whi-ch is along the Afferent arterioles .

b. Bowman's capsule : cup-shaped , cove-ring the glomerular , type of cell is sim-ple sequamous epithelium .

2. Proximal convoluted tubule (PCT) : has length about 15 mm , simple long coboidal cell (with micrivilli to increase the surface area) , numerous mitochondria (provide ATP for Ac-tive transport) .

3. Loop of henle : U-shaped , **consist of :**

a. Thin part (descending limb and lower part of ascending limb) : flat cells , 2-14 mm .

b. Thick part (ascending limb" remain part") : cubiodal cells , 12 mm .

4.Distal convoluted tubule (DCT) : simple low cuboidal cells(fewer microvilli),

divided into :

a. 1st half called diluting segment .

b. 2nd half called late DT .

5. Collecting duct : about 20mm , collecting urine .

 # Blood supply of the kidney

renal artery → segmental artery → inter lobar artery → arcuate artery → inter lobular artery → afferent arterioles→glomerular capillaries→efferent arterioles.

Function of kidney:

- **preserving blood volume** (low → ↑ water reabs-orbtion , high → ↑ urine secretion) .
- **preserving ion concentration** Na ,K,Ca and P).
- **Acid-base balance :** by excreation of H^+ or absorbing bicarbonate .
- **sectetory function :** as : renin , erythropoietin and active form of vit. D .

Function of angiotensin II :

- raises blood supply to kidney (↑blood pressure) .
- stimulates the **adrenal cortex** to secrete (Aldos-terone) hormone → 1) Na-water reabsorption , 2) K-H excretion .

Jaxtaglomerular apparatus :

- The point where efferent & afferent arterioles meet with a part of the distal convoluted tubule .
- This specific part of the kidney "**changes**" and adapts to different situations , it has :

1. a type of cells called "**Macula densa cell**" (in distal convoluted tubule) .
2. special cells "**JG cells**" that has *renin enzyme* (in wall of afferent arteriole) .

* NOTE : Macula densa → it's measures and senses the Na ions concentration in the filtrate .

*** Renin enzyme** : it's secreted from the wall of the afferent arteriole that's in contact with (**JGA**) or close to distal convoluted tubule specifically .

* **Angiotensinogen :** it's a hormone secreted from the **liver** .

Angiotensinogen $\xrightarrow{\text{renin}}$ Angiotensin I $\xrightarrow{\text{ACE}}$ Angiotensin II ⟶ Aldosterone .

Don't forget to review **GLOMERULAR MEMBRANE and DONNAN EFFECT** !!!

Characters of Glomerular membrane :

1. **High permeability .**
2. **High degree of selectivity ;** the cause of it is :
   a. The size of pores (8nm) .
   b. The strong –ve charge of protein that lining in pores .

Urine formation :

1) **Glomerular filtration** → the filtrate passes though distal , proximal convoluted tubules and loop of henle .
2) **Reabsorption** → (mainly for water , sodium and good nutrients).
3) **secretion** → the molecules that escaped from filtration are gonna be secreted from peri-tubular capillaries to renal tubules "*tubular secretion*" .

*** Glomerular filtration rate (GFR) :** fluid that are filtered by all the nephrons in both kidneys per minute.

Filtration force :

a. Glomerular capillary hydrostatic pressure :
- Has a +ve pressure value = 60 mmHg .

b. Osmotic pressure of plasma protein :
- Has a –ve pressure value = -32 mmHg .

c. Bowman's capsule hydrostatic pressure :
- Has a –ve pressure value = -18 mmHg .

d. Bowman's capsule osmotic pressure :
- Has a +ve pressure value = ZERO .

→ The NET filtration force = 10 mmHg .

Factor affecting glomerular filtration :

I.Glomerular capillary pressure :

a) Renal blood flow (GFR) :

↑RBF → ↑GBR → ↑glomerular capillary pressure

b) Diameter of Afferent arteriole :

To rise the glomerular capillary pressure the Afferent arteriole is dilated (vasodilatation) ↑ diameter (dilatation) → ↑ GBR → ↑ glomerular capillary pressure → ↑GFR .

c) Diameter of Efferent arteriole :

To raise the glomerular capillary pressure the Efferent arteriole is constricted (vasoconstriction) ↓ diameter (constriction) → ↑ GBR → ↑ glomerlular capillary pressure → ↑ GFR .

d) Sympathetic stimulation :

mild and moderate → no effect .

Severe → Constriction of afferent arteriole → ↓ GFR →↓glomerular capillary pressure→↓ GFR.

e) Arterial blood pressure (ABP) :

Changes in ABP within the **physiological range** (80 -180 mm Hg) has a little effect on renal blood flow or GFR due to *autoregulation mechanism* . **Autoregulation** is a mechanism by which RBF and GFR are maintained at a nearly constant rate inspite of changes in ABP within the physiological range , has two mechanism :

1. Tubuloglomerular feedback mechanism :

↓GFR→ So , the kidney starts to reabsorb Na , Cl (in the ascending limb of loop of Henle) to raise blood volume , when the filtrate reaches distal convoluted tubule , Macula densa cell (which have osmoreceptor to sense Na , Cl concentration in filtrate) will indicate the loss of Na ,Cl ions which have been reabsorbed . this leads to :- stimulating Juxtaglomerular cells to secrete the renin which ends with the formation of **angiotensin II** causing vasoconstriction of Efferent arterioles → ↑ GFR .

2. Myogenic mechanism:

if the blood supply is high → the Afferent arteriole will be stretched →smooth muscle contraction of Afferent arteriole stopping (inhabiting) the high blood pressure to reach the delicate glomerular capillary casing injuries .

II.Osmotic pressure of proteins in Bowman's capsule :

When increased → ↑ GFR , and vice versa .

III.Osmotic pressure of plasma proteins:

↓ Osmotic pressure of plasma protein (as: hypoproteinemia → ↑ GFR , and vice versa .

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*Renal handling of sodium ions :

I. PCT :

((**Generally, Reabsorption** of : I) ~67% of Na^+ and water, K^+ & Ca^{+2} , Most of HCO_3^- . II) All filtered glucose and A.As in early PCT .

Secretion of : organic acids and bases, catecholamine and some drugs)) .

NOW in details :

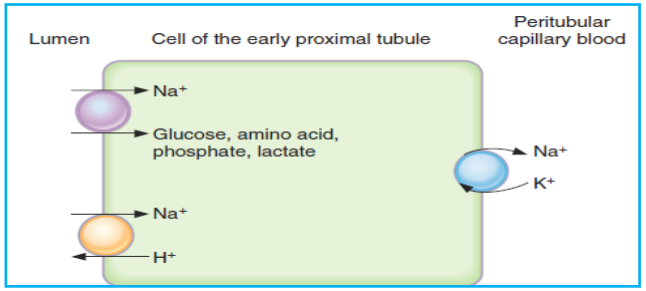
a. 1st half : First half (7 mm)

Apical border of the cell → Na^+ is diffused down electrical gradient . (Na^+ transport passively in 2ry active transport with Glucose, A.As, and H^+).

Basolateral border → Na^+-K^+ pump (3 Na^+ to outside cell , 2K to inside cell → "provide –ve charge inside → activation 2ry active transport".

- **In ACIDOSIS:** to get rid of these hydrogen ions → Na^+-H^+ counter transport is activated and H^+ ions are released with urine .
- **In ALKALOSIS:** we need to preserve H^+ ions, and $HCO3^-$ is released with urine , (Na^+-H^+ counter transport is not activated) .

b. 2st half : Na^+ and Cl^- are reabsorbed via co-transport → at this point , all previously absorbed substances (glucose , amino acid ….) are totally transferred to the blood .

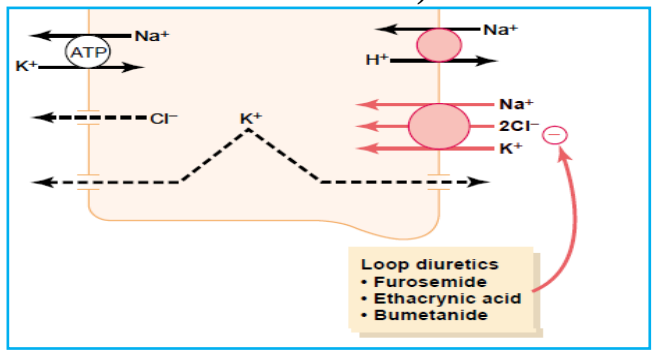


II. Loop of henle :

a – ***Thin*** *segment* of the **ascending** limb, Na^+ reabsorbed passively occur after Cl^- reabsorption along the paracellular route . It is a passive tran-sport .

b – ***Thick*** *segment* of the **ascending** limb, Na^+ reabsorption across the luminal membrane is mediated primarily by (Na^+ - $2Cl^-$ - P^+) co-transporter .

(**generally** , reabsorption of : ~27% Na^+ and 20% of ~K^+ and ~27% of Ca^{+2}) .

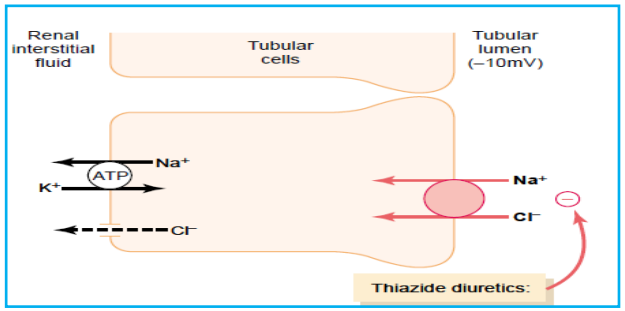


NOTE: Descending limb of loop of Helen → filtrate passes rapidly , no solute reabsorption , But this segment is freely permeable to water(it cell has aquaporins 1"protein"), so large amount of water(~10%) is reabsorbed .

III. DCT and collecting duct :

1. Early distal tubule

- Reabsorbs NaCl by a Na^+–Cl^- co-transporter.
- Is **impermeable to water** , as is the thick ascending limb.



2. Late distal convoluted tubule AND cortical collecting duct :

- Have two type of cells:

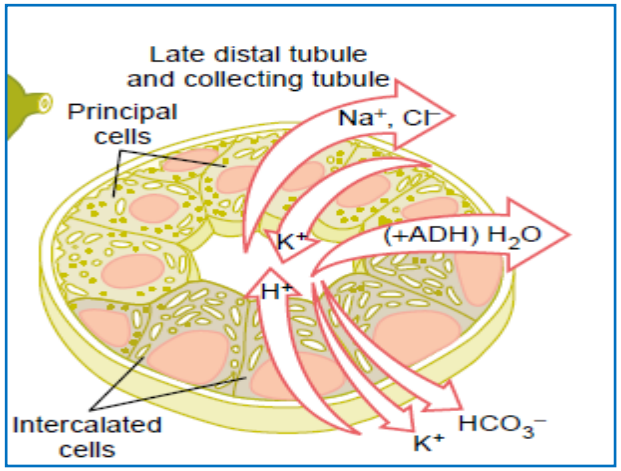
(1) *Principal cells :*

■ reabsorb Na^+ and H_2O , secrete K^+, Aldosterone increases Na^+ reabsorption and increases K^+ secretion**.**

(2) *a-Intercalated cells :* (tow types)

■ regulation H^+ and HCO_3^- .

((we will describe them in Acid-Base balance))



3. Medullary collecting duct :

-it's permeable to urea .

NOTE : Collecting duct has a receptor for ADH hormone , which is help in urine concentration .

↑ ADH → bind to receptor → secrete aquaporins 2 which ↑ the expressure → ↑ formation aquaporins 1 in DCT → water reabsorption .

Obligatory water reabsorption :

It's equal to 65% of water amount that reabsorbed in PCT .

Then according to **hydrated** :

a. If the person well hydrated → ↓ ADH → *diluted urine* . (especially in winter) .

b. If the person well dehydrated → ↑ ADH → *concentration urine* " hyperosmolar urine " . (especially in summer)

How the kidney concentration urine ?

***** in **vasa recta** blood circulate slow motion and low pressure .

This stimulus to concentrate urine by secrete ADH → open aquaporins channel → ↑ water reabsorption .

N.B : water reabsorbed also need **hyperosmotic** in medullary interstitial , which produce from ascending limb of loop of henle .

For concentration urine we need **three factor** :

1) **Counter current multiplier →**

Caused by loop of henle of jaxtamedullary nephron (U-shape) → hyperosmotic in interstitial → water reabsorbed from collecting duct & DCT to Medullary interstitial .

2) **Counter current exchange →**

Vasa recta responsible for hyperosmolarity in Medullary interstitial which act as loop of henle.

3) **Urea cycle →**

Urea has a small coefficient but high osmotic active .

- If water reabsorbed in Medullary collecting duct urea will follow it (*solvent drag*) .
- Urea hanging in Medullary interstitial → make hyperosmolarity active secrete to thin ascending limb of loop of henle and so on .

Note : not all urea will reabsorbed !!

Acid-Base balance :

pH of blood → concentration of H^+, has a normal value = 7.4.

- Source of H^+ :

a. Diet → Protein diet .

b. Intermediary Metabolism →

1) Volatile acids → Carbonic acid .

2) Fixed acids → Lactic acid & Ketoacids .

Defensive mechanism against changes in [H^+]:

There are 3 mechanism …

I- Buffer system - Rapid Mechanism (takes minutes) :

Note: The most effective **extracellular** buffer system is bicarbonate system , while the most important **intracellular** buffer systems are phosphates and proteins systems.

a. Bicarbonate buffer system :

* This system accounts **for 65 % of buffering capacity i**n plasma and **40 % of buffering action in the whole body.**

* Bicarbonate is regulated by the **kidney** (Metabolic component) , while Carbonic acid is under **respiratory regulation** (Respiratory component).

N.B: We use the concentration of Co2 instead of H2Co3 because it is easy to assay and it is a mirror of H2Co3 because when H2Co3 concentration increases the concentration of Co2 increase. So we can use Co2 instead of H2Co3.

B-Phosphate buffer system:

- intracellular buffer and tubular fluid buffer
- Its two elements are:

Phosphoric acid (H_2PO_4) & Phosphate salt.

- It is an *effective buffer system* because its concentration is high intracellular and in tubular fluid.

C-Protein buffer system:

- It is a *powerful system* because of its high concentration in intracellular fluid and in plasma.
- Amino acids can act as an acid (Proteinic acid) and or alkali (Na proteinate) .
- In RBCs Hb is a powerful buffer.

Note: Phosphate buffer system and protein buffer system neutralize with H+ as it inside the cell, as if any H+ exit the cell it will be neutralized by bicarbonate system.

II- Respiration regulation - Intermediate mechanism (takes hours) :

$$H_2CO_3 \leftrightarrow H_2O + CO_2$$

- **In acidosis** → ↑ H_2CO_3 → ↑ CO_2 in the blood → stimulate R.C → ↑ rate of respiration and elimination of the excess CO_2 leading to decreased acid in the blood and so correcting acidosis.

- **In alkalosis** (the reverse occurs) i.e. decreased level of H_2CO_3 leads to decreased CO_2 concentration and inhibit R.C leading to CO_2 retention in the blood and increased H_2CO_3 so correcting alkalosis.

III- Renal Regulation - Slow mechanism (takes days) :

- Renal compensation in acid base disturbances takes place through Excretion or absorption of H^+ and HCO_3^- This occur in two ways:

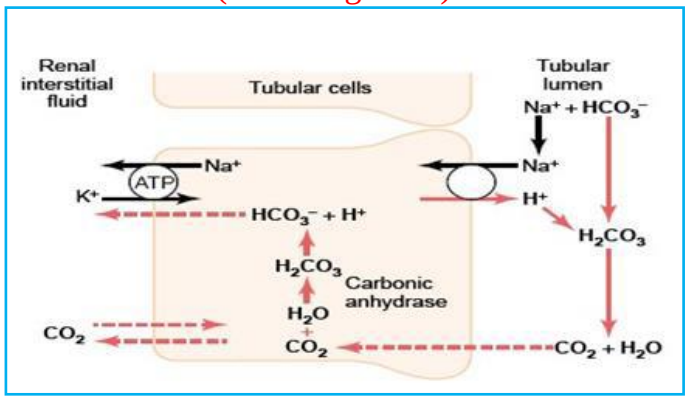
1-Directly by retaining or excreting H^+, 2-Indirect by changing Reabsorption or excretion of H_2CO_3 buffer.

In PCT :

- ***H^+ secretion and HCO_3^- Reabsorption*** .
- The proximal tubule is responsible for Reabsorption of most of the $HCO3^-$.
- **Mechanism:**

Net result: Filtered Na^+ and $HCO3^-$ are reabsorbed H^+ is secreted.

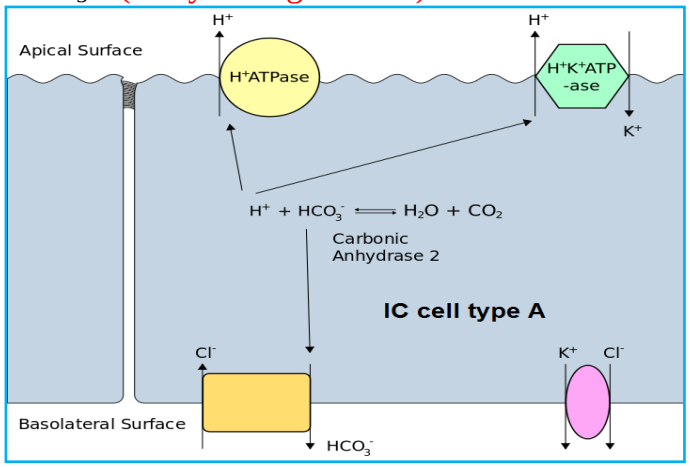
- **Mechanism:** (in the figure!!!) …



In DCT & colleting duct :

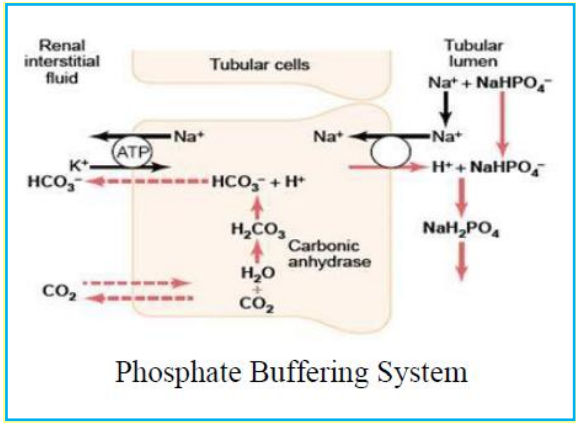
Has two type of **intercalated cells** which characterized by high concentration of **carbonic anhydrase** in their cytoplasm .

In acidosis, type (A) → secrete H^+ and reabsorb HCO_3^- . (study the figure well)

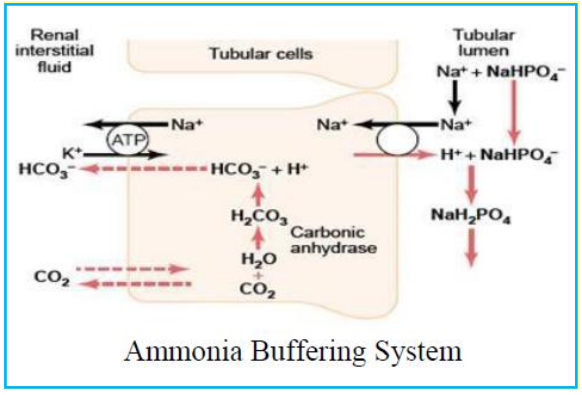


In acidosis, The kidney secretes H^+ into the lumen of both proximal and distal tubules using direct (distal) and indirect (proximal) active transport If H^+ is secreted rapidly by this mechanism in the tubular fluid its concentration is increased and tubular pH drops rapidly to (4.5) leading to stoppage of H^+ secretion.

So, for H^+ secretion to continue more and more in acidosis it must be carried and transported by Ammonia and phosphate ions to become in non-ionized state i.e. ammonia and phosphate ions in urine act as urinary buffers trapping H^+ and allowing more H^+ to be secreted.

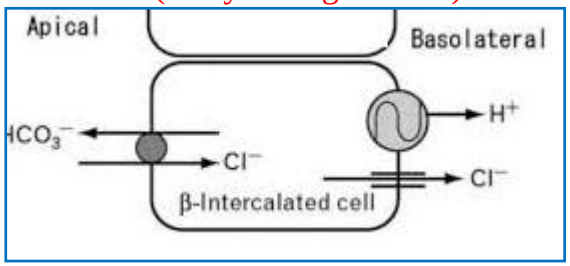


Phosphate Buffering System



Ammonia Buffering System

In alkalosis, type (B) → secrete HCO_3^- and reabsorb H^+ . . (study the figure well)



In alkalosis, the kidney reverses the process described above by secreting HCO_3^- into the lumen, and absorbing H^+ in an effort to bring pH back into normal range.

H_+ are reabsorbed into extracellular fluid on basolateral border by H_+ ATPase and H_+ - K_+ ATPase

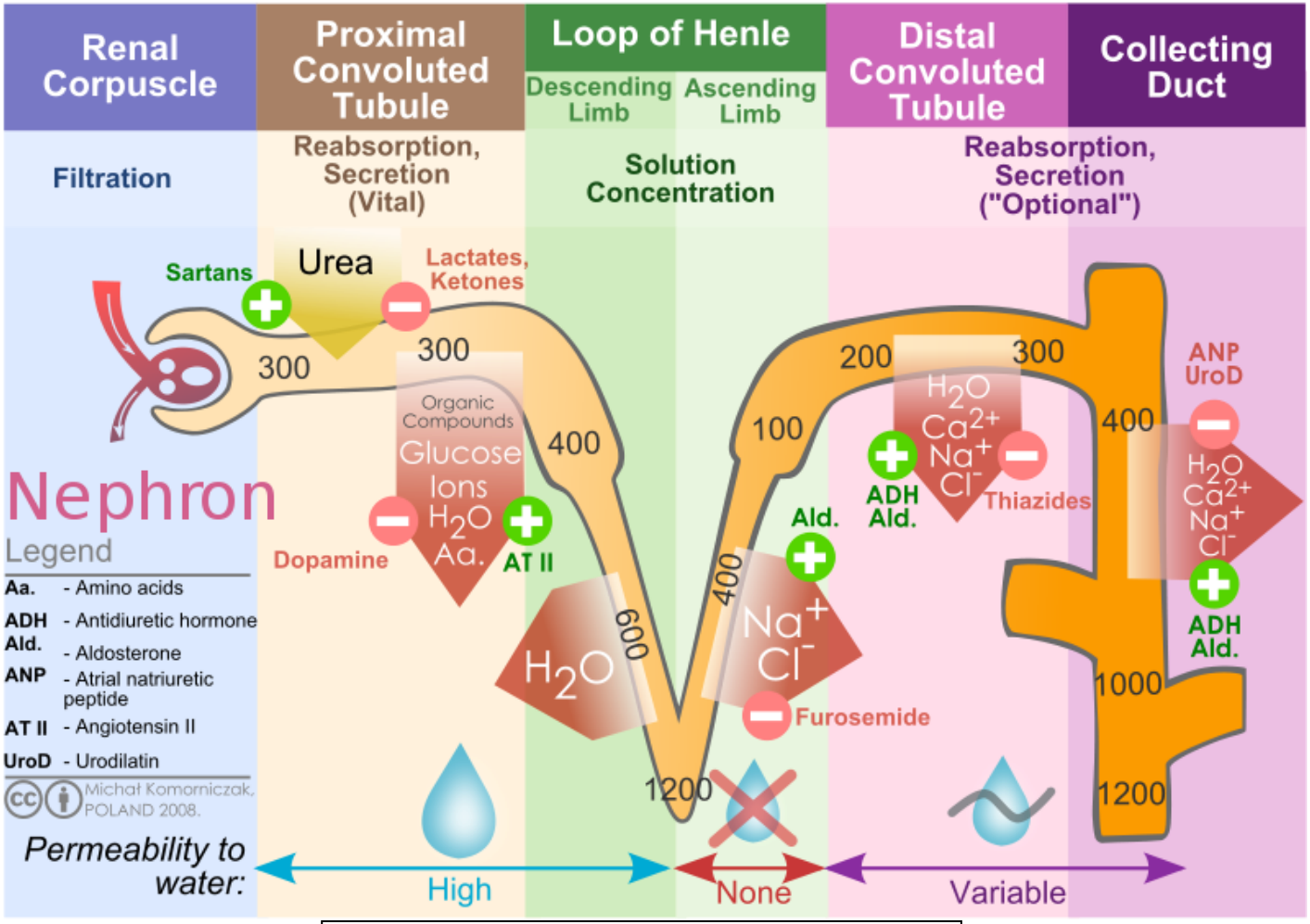
The H^+-K^+ ATPase of the distal nephron provides link between H^+ and K^+ creates an increase in K^+ excretion and **hypokalemia**, while in acidosis the kidney secretes H^+ into urine and reabsorbs K^+ leading to **hyperkalemia**.

Role of the liver in regulation of Acid – base balance:

1.Transform ammonia to urea (Neutral) .
2.Transformation of Lactic acid (produced during exercise) to glycogen .
3.In alkalosis: (glucose → lactic acid) .
4. In alkalosis : it ↑ ketone bodies.

Disturbances of acid –base balance

❖ The 3 compensatory mechanisms Buffer, Ventilation and Renal excretion Keep the plasma PH at its normal value 7.4, but under some conditions the production or loss of H+ and HCO3 is so extreme that compensatory mechanisms fail to maintain PH homeostasis.



JUST study what we need from this figure !!

إعداد : منذر القطاونة
#لجنة_التبييض
#لجنة_الطب_والجراحة