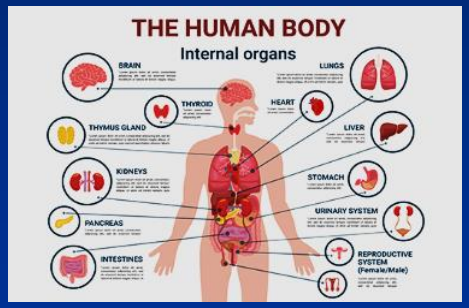
10. Acid-Base balance.



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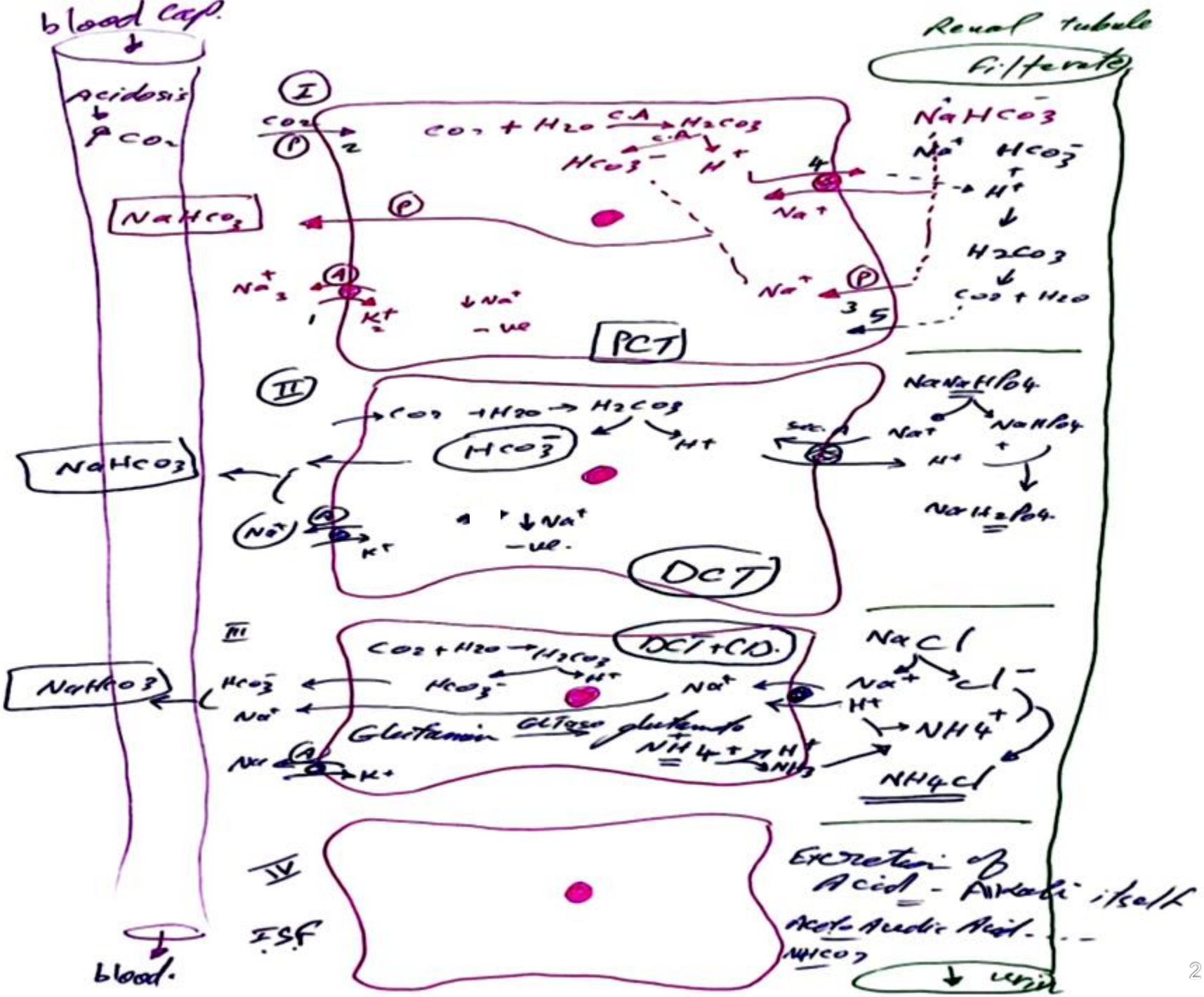

blood cap.
Renal tubule
Filtrate
Acidosis
PCO2
I
CO2
CO2 + H2O CA H2CO3
HCO3⁻ H+
NaHCO3
Na+ HCO3⁻
H+
H2CO3
CO2 + H2O
Na+
K+
↓Na+
-ve
PCT
II
CO2 + H2O → H2CO3
HCO3⁻
H+
NaNaHPO4
NaH2PO4
DCT
III
DCT+CD.
CO2 + H2O → H2CO3
HCO3⁻
H+
Na+
NaCl
Cl⁻
Glutamine
Glutaminase
glutamate
NH4+
NH4Cl
IV
ISF
blood.
Excretion of
Acid - Alkali
Acetoacetic Acid
NH4CO3
urine

III. Renal Handling of Hydrogen & Bicarbonate

Bicarbonate HCO_3^- is the normal alkali reserve in the body which must be kept constant at a concentration of 26-28 mEq/litre at arterial P_{CO2}= 40mmHg.

Renal handling of HCO_3^-:

-In the PCT

More than 99% of HCO_3^- is reabsorbed by the kidney especially in PCT.

This reabsorption is affected by the acid base balance:

Alkalosis → increase excretion of HCO_3^- & urine becomes alkaline (normal urine is acidic PH=6)

Acidosis → complete HCO_3^- reabsorption.

Renal tubules are poorly-permeable to HCO_3^-. However, ***it is reabsorbed in the form of CO_2*** (highly permeable)

Mechanism

-Step 1(intracellular): CO_2 of blood & of tubular fluid diffuses into cells of PCT → CO_2 bind with H_2O in presence of Carbonic Anhydrase, CA enzyme → H_2CO_3 → ***ionized forming*** HCO_3^- + H^+.

-Step 2: ***H^+ is secreted*** to the lumen in ***exchange with*** Na^+ (from filtered $NaHCO_3$) by secondary active transport (Na^+/H^+ counter-transport) & then Na^+ diffuses to blood.

-Step 3 (intra-luminal)**:** Secreted H^+ combine with the **filtered** HCO_3^- by the help of CA enzyme in the brush luminal border of the PCT cells → H_2CO_3 → H_2O & CO_2 (which diffuses into the tubular cells again).

-Step 4:Formed HCO_3^- inside the cell moves passively through basal border to interstitium → bind Na^+ → $NaHCO_3$.

In late DCT & collecting ducts:

-In the intercalated cells of DCT & collecting duct, H^+ secretion mechanisms is either dependent on Na^+ (***formation of acid phosphate***) or independent of Na^+ (***formation of ammonia***).

Formation of acid phosphate:

Step 1: In tubular cells CO_2 enters from blood inside the cell to $CO_2 + H_2O +$ CA $\rightarrow H_2CO_3 \rightarrow \mathbf{H_+} + \mathbf{HCO_3^-}$.

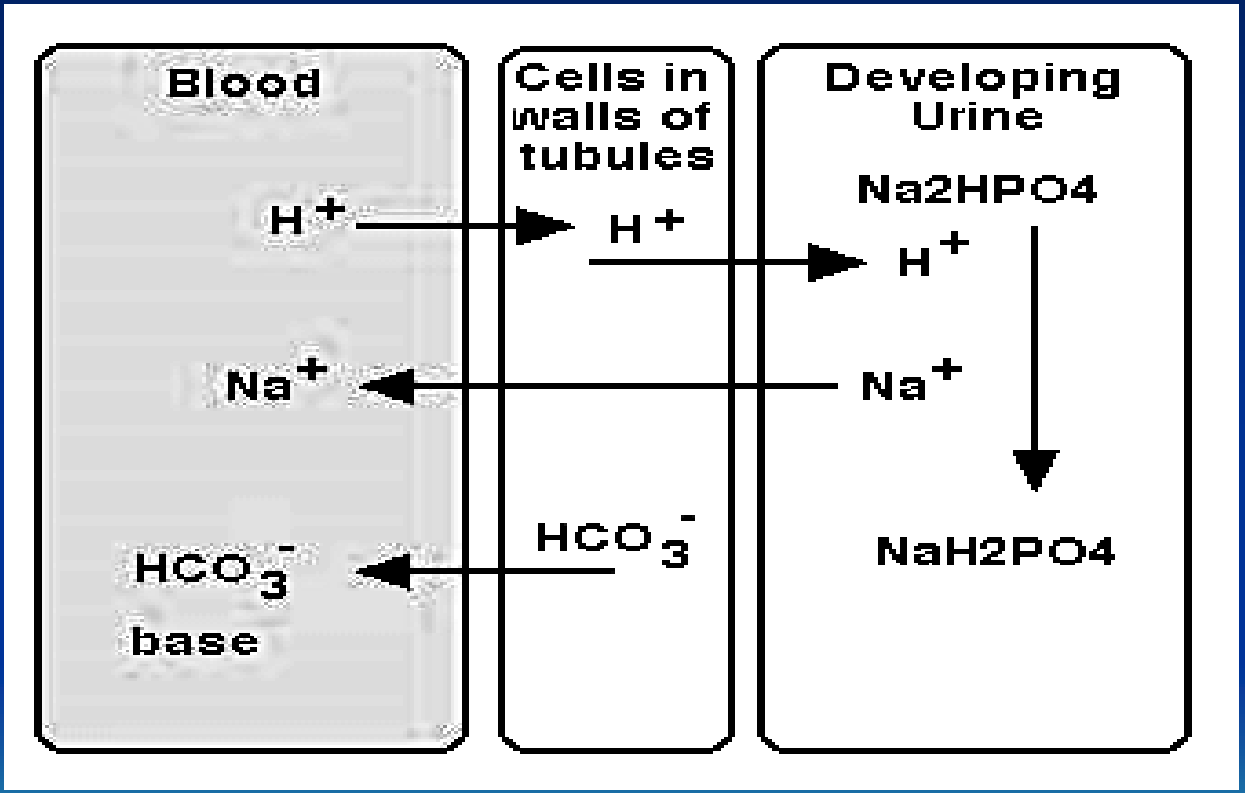
Step 2: H^+ is secreted to the lumen in ***exchange with Na***$^+$ (from filtered $\mathbf{Na_2HPO_4}$) by ***secondary active transport*** (Na^+/H^+ counter-transport) at the luminal border.

Then Na^+ actively transported by to interstitial fluid by Na^+/K^+ counter-transport through the basal membrane then to blood.

Step 3: In the lumen: $H^+ + \mathbf{Na_2\ HPO_4}$ (dibasic phosphate, alkaline) $\rightarrow Na^+ + NaH_2PO_4$ (monobasic phosphate, acid).

Step 4: HCO_3^- formed inside the cell moves passively to interstitial fluid where bind with actively pumped Na^+ to form $\mathbf{NaHCO_3}$ (alkaline tide) in blood.

Steps of acid phosphate formation



b- Ammonium salts formation in the proximal & distal tubules:

Steps:

1- Metabolic reactions in the renal tubular cells produce NH_4^+

Glutamine + glutaminase → glutamate + ammonium (NH_4^+).

Glutamic dehydrogenase ↓

Alpha-ketoglutarate + more NH_4^+

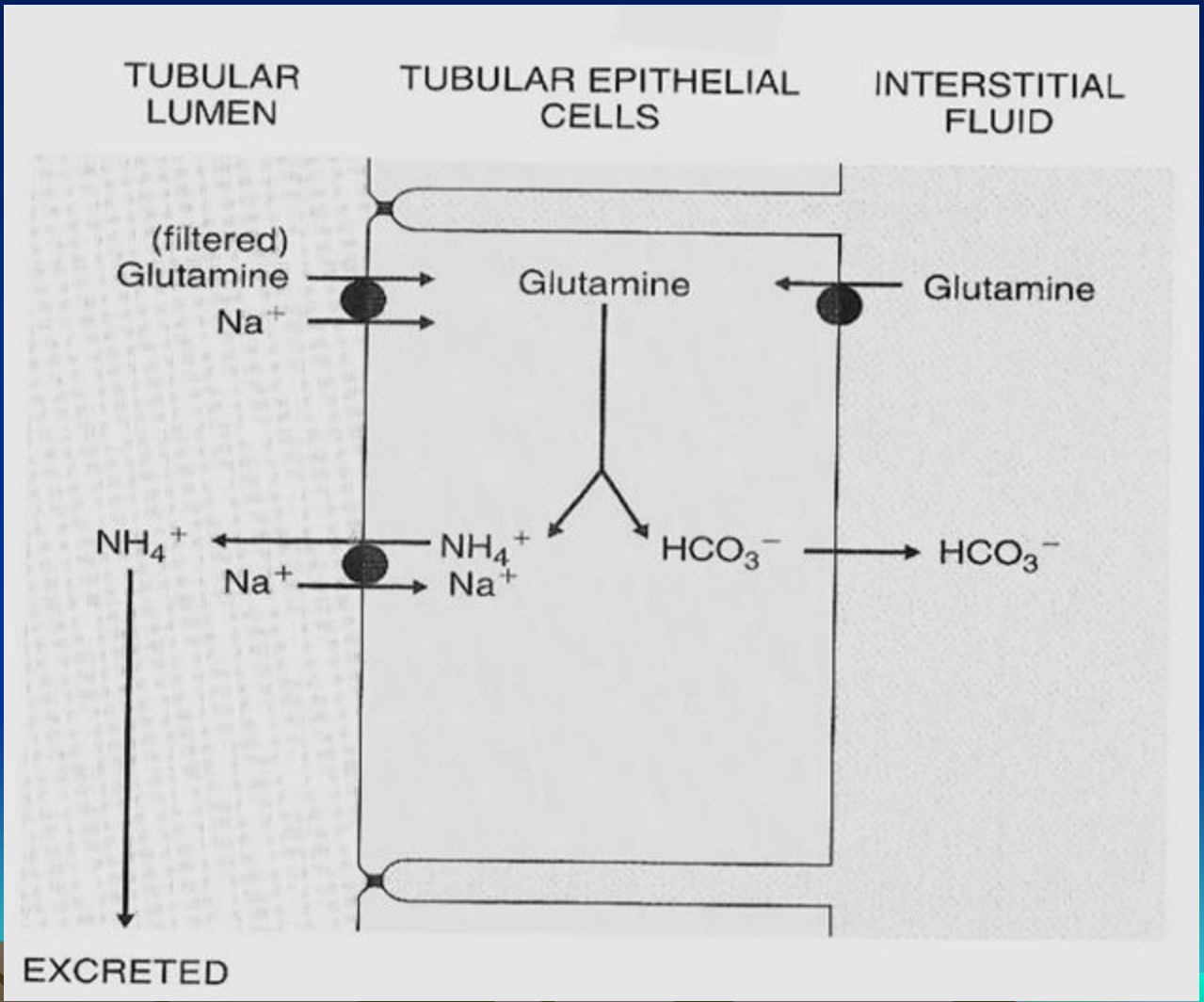
2-Alpha-ketoglutarate utilizes 2H+ freeing 2 HCO3- And NH4+is in equilibrium with NH3 (ammonia) + H+

3-H+ is secreted to the **lumen** by active proton (ATP-driven) pump present on the intercalated cells .However, ammonia (not ammonium) diffuse rapidly (non ionic diffusion), because it is lipid soluble, into tubular fluid (if urine is acidic)or diffuse to blood (if urine is alkaline).

4-In the lumen: Ammonia (NH3) + H+ (secreted) reconstructed to ammonium (NH4+) which is trapped in the lumen and not re-diffused to blood (ammonia trapped mechanism). It is estimated that about 40mEq of H+ ion combines with NH3 are excreted/day.

⟹5-Then ammonium (lipid insoluble) combine with any anion (A-) either Cl- of NaCL to form ⟹Na+ cation and NH4Cl ammonium chloride salt or Phosphate group(of Na H2PO4 to form Na+ cation and ammonium phosphate salt (NH4H2PO4). Both NH4Cl and NH4H2PO4 are excreted in urine. However, Na+ is reabsorbed to blood to give NaHCO3 .so for each H+ ion excreted also one NaHCO3 is added to blood giving alkaline tide.

6-The amount of ammonium salts excreted in urine depends on activity of glutaminase enzyme & H+ secretion that increased in cases of chronic acidosis.


TUBULAR LUMEN
TUBULAR EPITHELIAL CELLS
INTERSTITIAL FLUID
(filtered) Glutamine
Na+
Glutamine
Glutamine
NH4+
Na+
NH4+
Na+
HCO3−
HCO3−
EXCRETED

Thank You