

PHYSIOLOGY

BUFFER SYSTEM



Black: in male AND female slides
Red : important
Pink: in female slides only
Blue: in male slides only
Green: Notes
Gray: extra information

Editing file

Buffer

Definition

solution (a mixture of a weak acid and a weak base that are in equilibrium) that resists changes in pH upon addition of small amount of acids and bases.

To be more accurate, its either made of:

1 ■ A weak acid and its conjugated base (H_2CO_3 & $NaHCO_3^-$).

2 ■ A weak base and its conjugated acid (NH_3 & NH_4^+).

How does a buffer do its job ?

Neutralizes small additions of bases/acids —> pH remains constant. (we use buffers in laboratory tests and analysis)

If I add small amount of an acid or avbase, BUFFER solution will resist the decrease/increase in pH

Without buffer if i add acid into a solution —> pH will decrease.

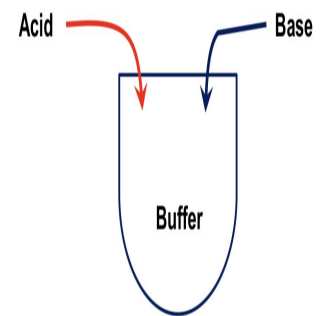
Without buffer if i add base into a solution —> pH will increase.

Comparison of changes with and without buffer:

Pure water (pH=7) + base =

With buffer solution : 7-7.5

Without buffer solution: 7-9



For better understanding check slide 4

Chemical Buffer Systems in the Body

There are 3 chemical buffers in the body:

The Bicarbonate buffer system —> (powerful extracellularly).

The phosphate buffer system —> (powerful intracellularly) and it's very good in tubular filtration (will be discussed later)

Proteins —> (powerful intracellularly).

They are the 1st line of defence against changes in pH i.e. $[H^+]$, act within seconds.

Some are more powerful extracellularly and others are more powerful intracellularly.

It depends on where is the most of their conc. in other word; if it's more abundant extracellularly it will become more powerful extracellularly.

-Buffer's power Depends on relative amount of Acid and Base in a Buffer solution.

-It is maximum when both are in equal amounts.

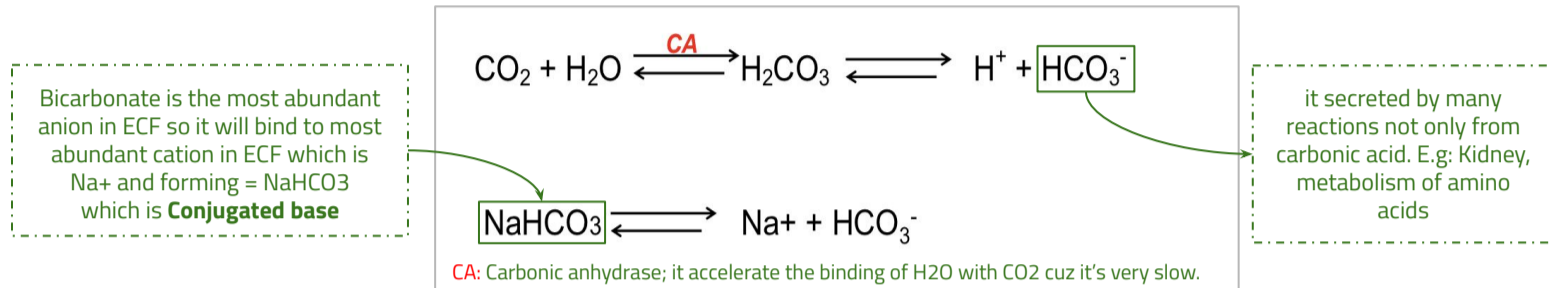
-Absolute concentration of Buffers in body fluids is also important.

-If the pH of medium is near pK of buffer system it becomes more effective.

The Bicarbonate Buffer System

Bicarbonate is the main ECF buffer system cuz it's the highest anion in ECF with chloride (as we discussed before), which is Composed of:

- A weak acid (H₂CO₃).
- Its conjugated base (NaHCO₃).



1

H₂CO₃ forms in the body by the reaction of CO₂ & H₂O

$$\text{CO}_2 + \text{H}_2\text{O} \xrightleftharpoons{\text{CA}} \text{H}_2\text{CO}_3$$

2

H₂CO₃ ionizes weakly to form small amounts of H⁺ & HCO₃⁻

$$\text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$$

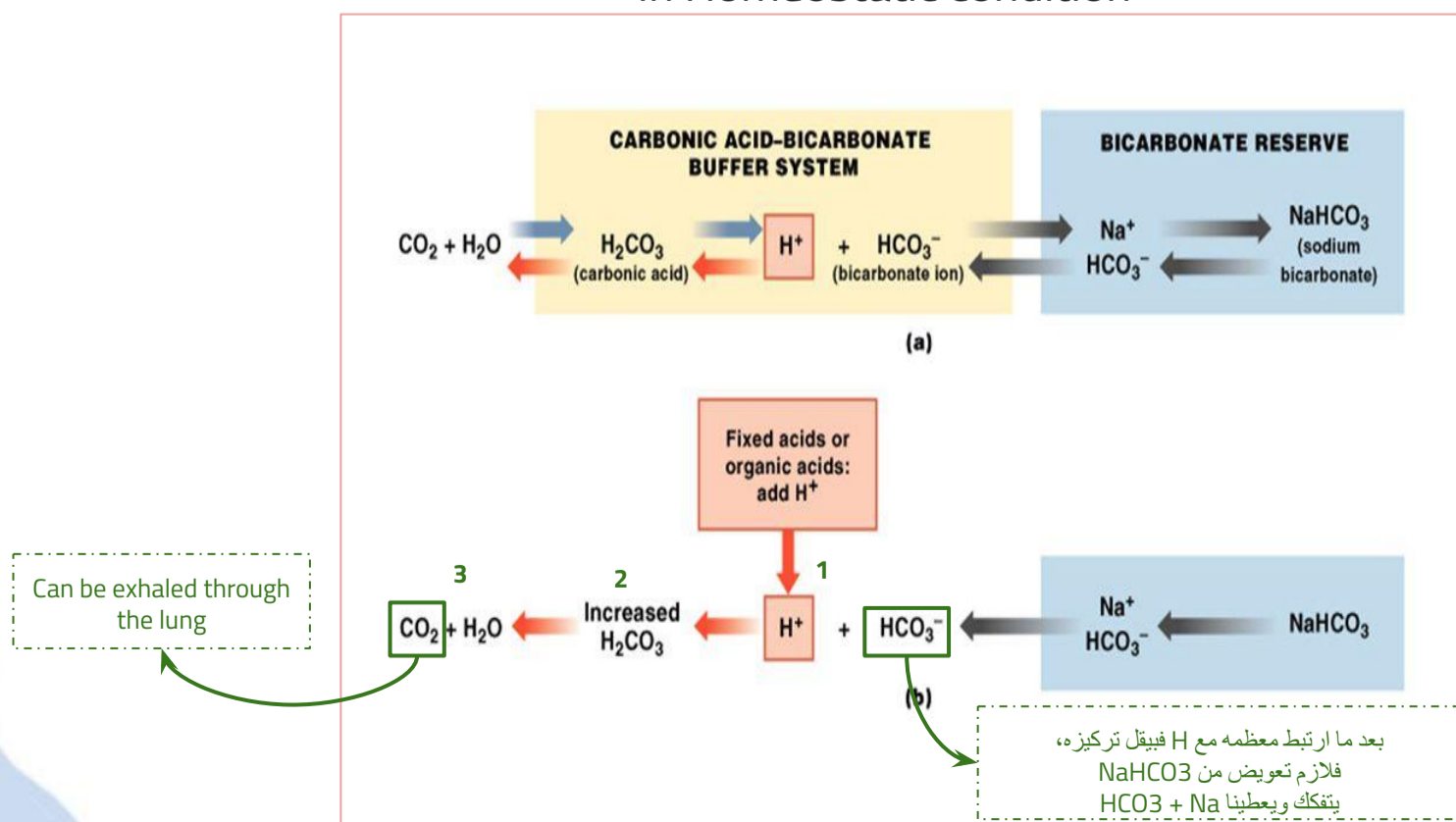
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The second component is NaHCO₃ which dissociates to form Na⁺ & HCO₃⁻

$$\text{NaHCO}_3 \rightleftharpoons \text{Na}^+ + \text{HCO}_3^-$$

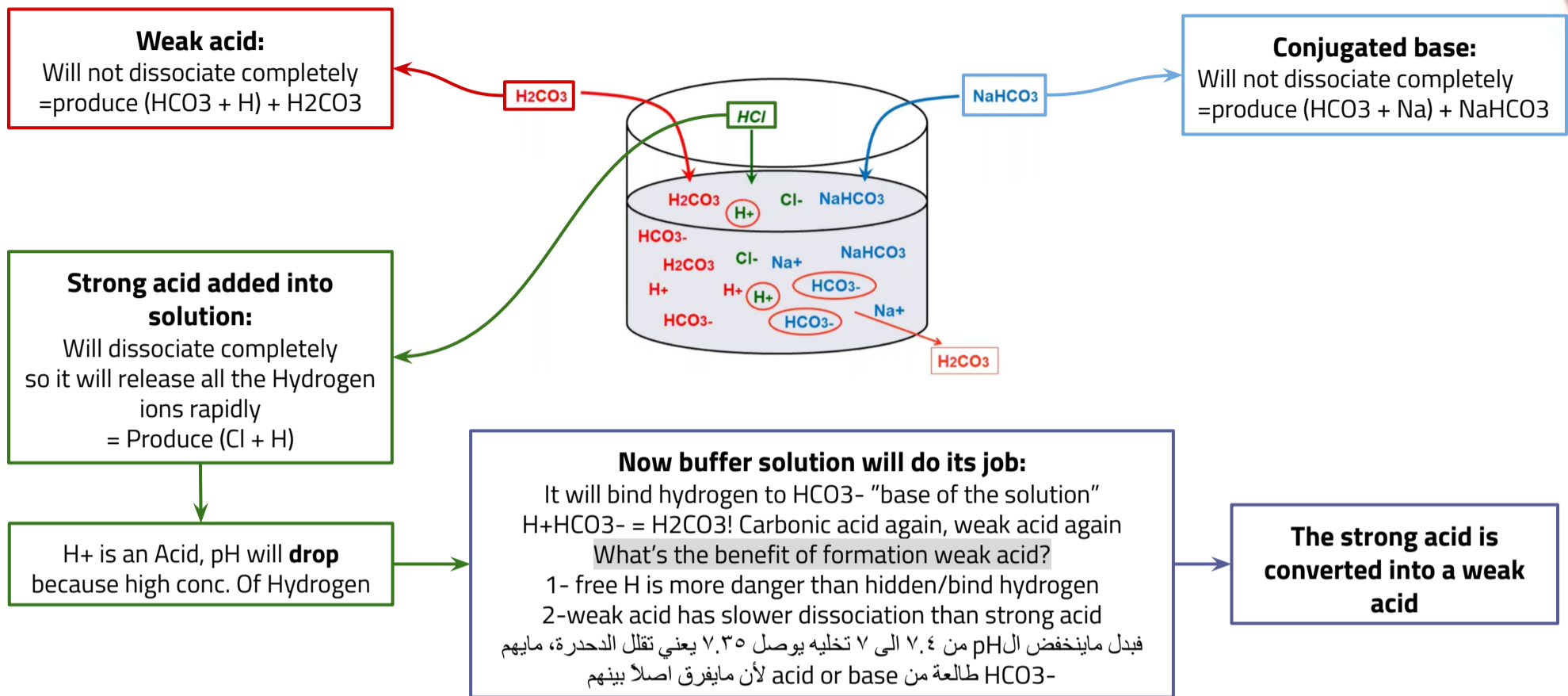
Putting it all together :

In Homeostatic condition

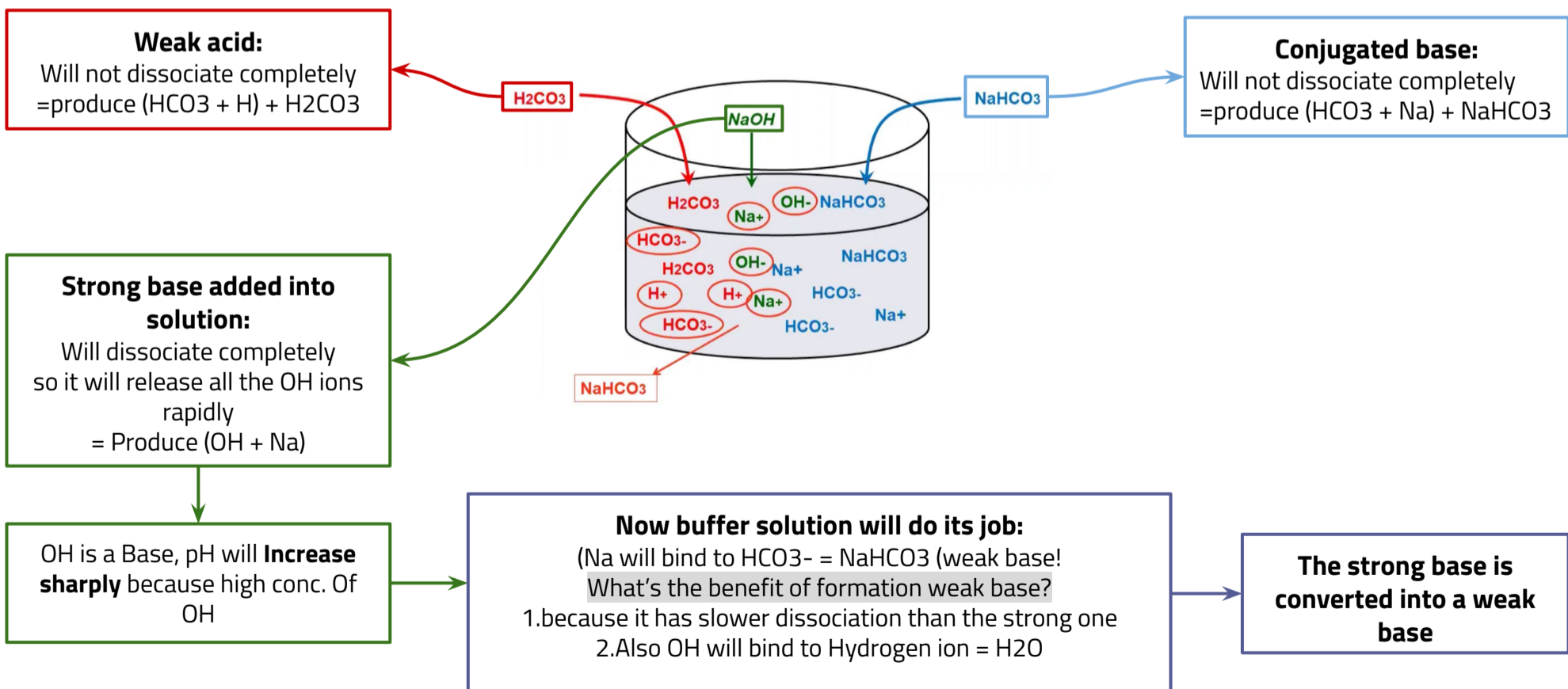


Explanation of how does a buffer do its job in different solution:

• Bicarbonate buffer solution (if we add Strong acid)



• Bicarbonate buffer solution (if we add Strong base)



Has the body now completely got rid of all excess acid (H^+) or excess base (OH^-)?

No they only got hidden, this a limitation of free ions until the lung and the kidney do their job.

The Henderson-Hasselbalch Equation (HHE)

Definition

HHE is an equation that enables the calculation of pH of a solution.

$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^- \text{ conjugated base}}{0.03 \times \text{PCO}_2 \text{ weak acid}}$$

- K = dissociation constant.
- pK = 6.1
- solubility of CO₂ = 0.03

How was HHE derived?

1



H₂CO₃ and its dissociated ions are always in equilibrium → the products of the reaction on one side of the equation are proportional to the product on the other side.

$$(1) \quad [\text{H}_2\text{CO}_3] \propto [\text{H}^+] \times [\text{HCO}_3^-]$$

- Since H₂CO₃ is a weak acid, it will not dissociate completely and the concentration of its products will depend on its dissociation constant (K)

$$(2) \quad K \times [\text{H}_2\text{CO}_3] = [\text{H}^+] \times [\text{HCO}_3^-]$$

2

Based on the (1) and (2) equations, [H⁺] can be expressed as follows:

$$[\text{H}^+] = K \times \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]}$$

- ↑ [H⁺] → ↑ [H₂CO₃] Directly proportional
- ↑ [H⁺] → ↓ [HCO₃⁻] inversely proportional

3

Because H₂CO₃ can rapidly dissociate into CO₂ and H₂O. And since CO₂ is much easier to measure it can replace H₂CO₃ in the equation:

$$[\text{H}^+] = K \times \frac{[\text{CO}_2]}{[\text{HCO}_3^-]} \quad \text{This is Henderson's equation (1908)}$$

It means that:

- ↑ [CO₂] → ↑ [H⁺]
- ↑ [HCO₃⁻] → ↓ [H⁺]

5

In 1916, Hasselbalch decided to merge Henderson's equation with Sorensen's pH scale

$$[\text{H}^+] = K \times \frac{[\text{CO}_2]}{[\text{HCO}_3^-]} \rightarrow -\log [\text{H}^+] = -\log K \times \frac{[\text{CO}_2]}{[\text{HCO}_3^-]}$$

$$-\log [\text{H}^+] = -\log K \times \frac{[\text{CO}_2]}{[\text{HCO}_3^-]} \rightarrow \text{pH} = \text{pK} + \log \frac{[\text{HCO}_3^-]}{[\text{CO}_2]}$$

This is Henderson-Hasselbalch equation

4

In 1909, Sorensen created the pH scale to express [H⁺]:

$$\text{pH} = -\log[\text{H}^+]$$

6

Since it is much easier to measure PCO₂ rather than dissolved [CO₂] and because dissolved CO₂ is proportional to PCO₂ multiplied by the solubility of CO₂ (0.03 mmol/mmHg) → [CO₂] was replaced by PCO₂ × 0.03

$$\text{pH} = \text{pK} + \log \frac{[\text{HCO}_3^-]}{0.03 \times \text{PCO}_2}$$

pH ∝ $\frac{\text{HCO}_3^- \text{ Regulated by kidney}}{\text{PCO}_2 \text{ Regulated by Lung}}$ Each element of the buffer system is regulated

It is not only the amount of base and acid that is important but the ratio between them must remain constant.

The importance of this equation (HHE):

- 1- to calculate the pH using the concentrations of bicarbonate and CO₂
- 2- pH and HCO₃⁻ Directly proportional
- 3- pH and PCO₂ inversely Proportional

The Bicarbonate Buffer System

Why is it the most important buffer system in the ECF?

1. The CO_2 component of the buffer is regulated by the **lungs**

2. The HCO_3^- component of the buffer is regulated by the **kidneys**

Ratio of $\frac{\text{HCO}_3}{\text{PCO}_2}$ is = 20:1 (important) it means we have HCO_3 more than H_3CO_3

Buffer	Composed of	Importance	Pk value
Bicarbonate	HCO_3 & H_2CO_2	In ECF / plasma	6.1
Phosphate	HPO_4^{-2} (Hydrogen phosphate) & H_2PO_4^- (dihydrogen phosphate)	In ICF / renal tubular fluid conc. in ECF is only 8 % of bicarbonate	6.8
Ammonia	NH_3 & NH_4^+	In Urine	9
Proteins (Amphoteric) <small>Proteins will bind with hydrogen, How? Proteins have COOH (carboxyl group, -ve charge) and amino group (+ve charge) So the negative (COOH) is the highest and it makes protein bind with hydrogens</small>	Prot & H Prot most proteins in our body are negative	In ICF	-
Hemoglobin (due to protein's -ve charge)	Hb & HHb The most important protein in RBCs It's a negative protein so it binds to hydrogen until lungs and kidney work	In ICF	-

NOTE: A pKa of 6.8 Makes Phosphate a Good Buffer in ECF however, its plasma conc. is low (about 1 mmol/L) unlike HCO_3^- which is 24 mmol/L

Summary of Body's Buffering Systems

- ◆ Buffer systems do not work independently in body fluids but actually work together
- ◆ Buffers do not reverse the pH change, they only limit it
- ◆ A change in the balance in one buffer system, changes the balance of the other systems
- ◆ Buffer don't correct changes in $[\text{H}^+]$ or $[\text{HCO}_3^-]$ they only limit the effect of change on body pH until their concentration is properly adjusted by either the lungs or the kidney

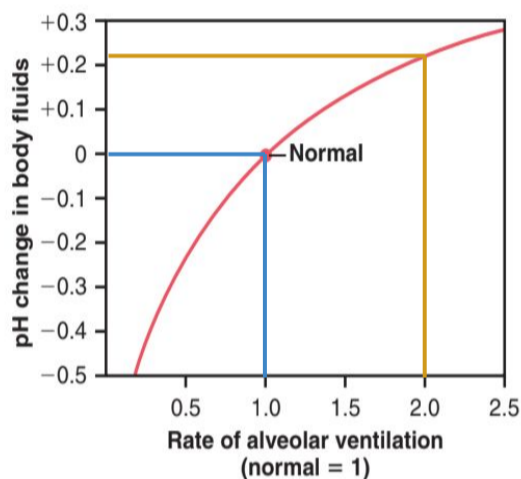
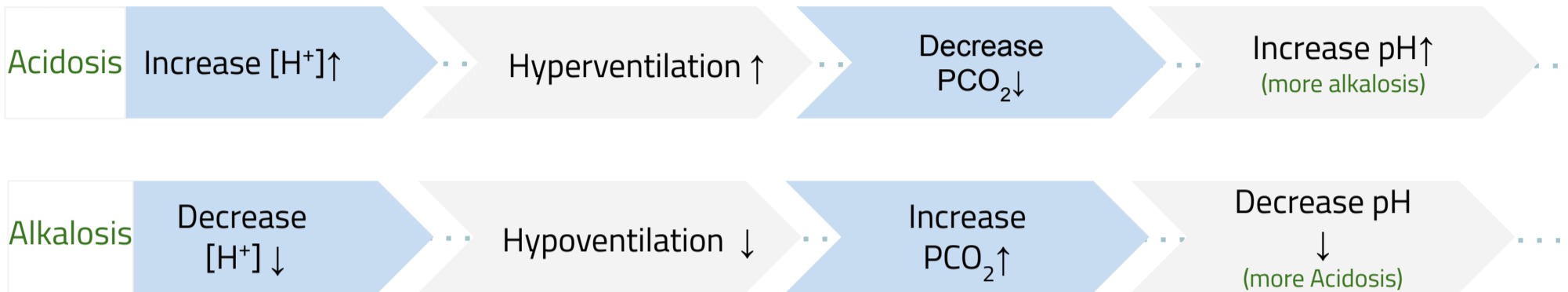
From boys slides

TABLE 25.1 Major Chemical pH Buffers in the Body

Buffer	Reaction
Extracellular fluid	
Bicarbonate/ CO_2	$\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$
Inorganic phosphate	$\text{H}_2\text{PO}_4^- \rightleftharpoons \text{H}^+ + \text{HPO}_4^{2-}$
Plasma proteins (Pr)	$\text{HPr} \rightleftharpoons \text{H}^+ + \text{Pr}^-$
Intracellular fluid	
Cell proteins (e.g., hemoglobin, Hb)	$\text{HHb} \rightleftharpoons \text{H}^+ + \text{Hb}^-$
Organic phosphates	$\text{Organic-HPO}_4^- \rightleftharpoons \text{H}^+ + \text{organic-PO}_4^{2-}$
Bicarbonate/ CO_2	$\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$
Bone	
Mineral phosphates	$\text{H}_2\text{PO}_4^- \rightleftharpoons \text{H}^+ + \text{HPO}_4^{2-}$
Mineral carbonates	$\text{HCO}_3^- \rightleftharpoons \text{H}^+ + \text{CO}_3^{2-}$

Respiratory Regulation of acid-base

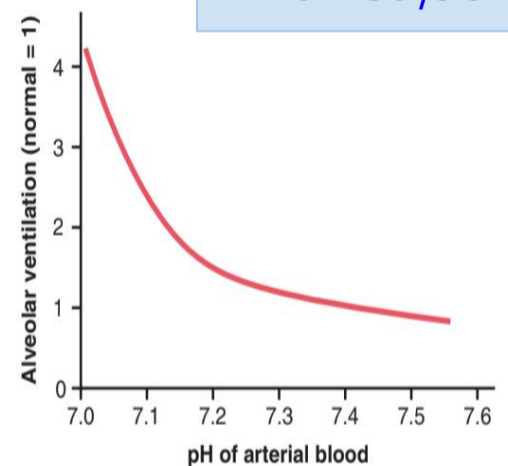
- ▶ 2nd line of defence against acid-base disturbances in the body.
- ▶ Respiratory system regulate acid - base by modulating CO₂ excretion
- ▶ works within minutes
- ▶ Normally, PCO₂ = 40 mmHg (35-45 mmHg) you have to memorize it.



doubling(Twice normal) the ventilation rate raises the pH of the extracellular fluid from 7.4 → 7.63 (+0.23)

Respiratory Regulation of Acid-Base Balance

When the alveolar ventilation increase the pH of **body fluids** increase



Effect of blood pH on rate of alveolar ventilation

When the alveolar ventilation increase the pH of **body fluids** Decrease

From boys slides

Renal Regulation of acid-base

- 1 3rd line of defence. Most powerful system that works within hours to days (slowest)
- 2 It regulates by excreting either an acidic or basic urine
- 3 The kidney secretes acidic or alkaline urine based on acid-base status

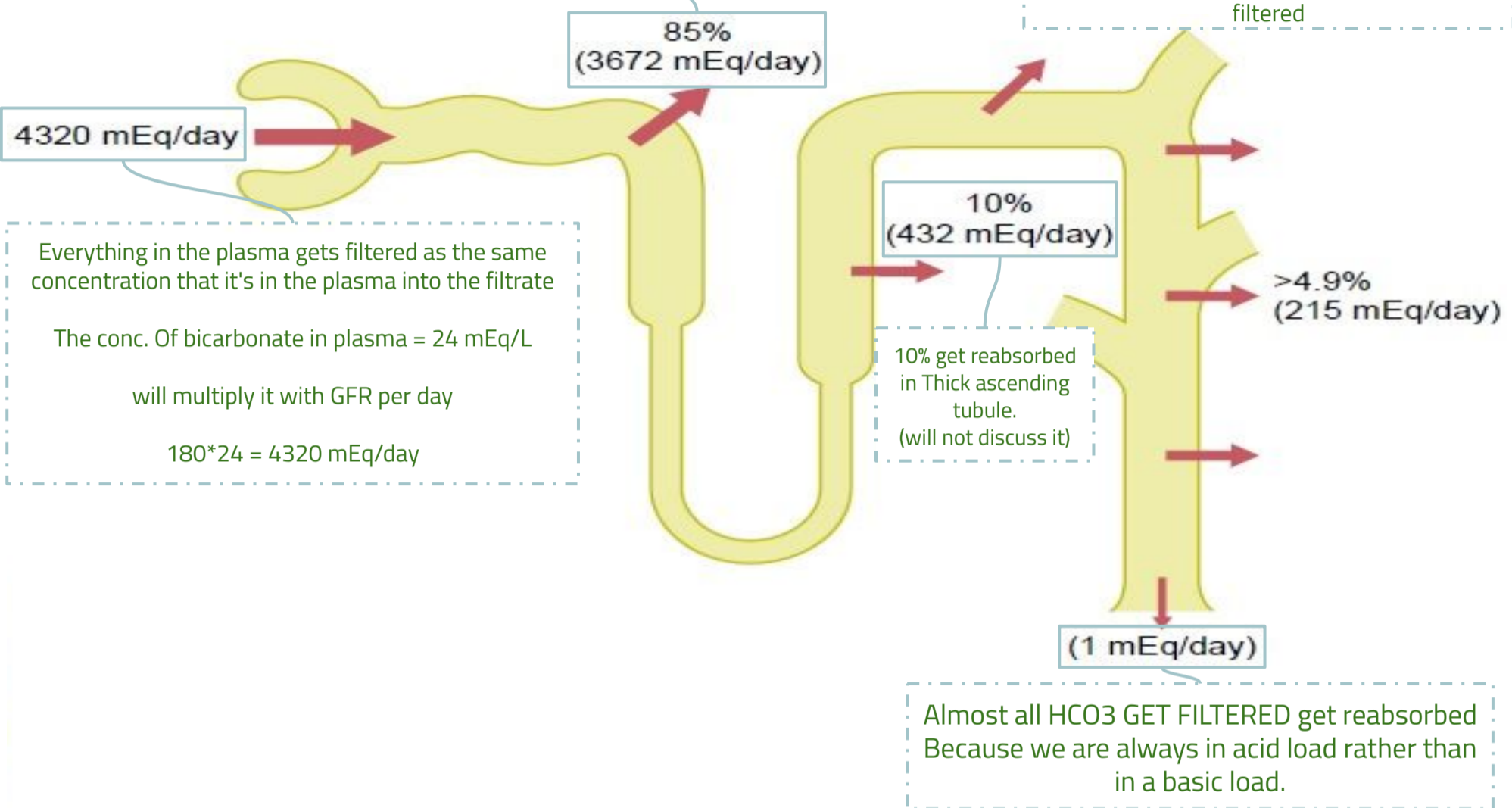
The kidney excretes acidic or alkaline urine by three process:

- ▶ Secreting H⁺
- ▶ Reabsorbing HCO₃
- ▶ Generating "new" bicarbonate ions

Overview HCO_3^- Reabsorption by the Renal Tubules

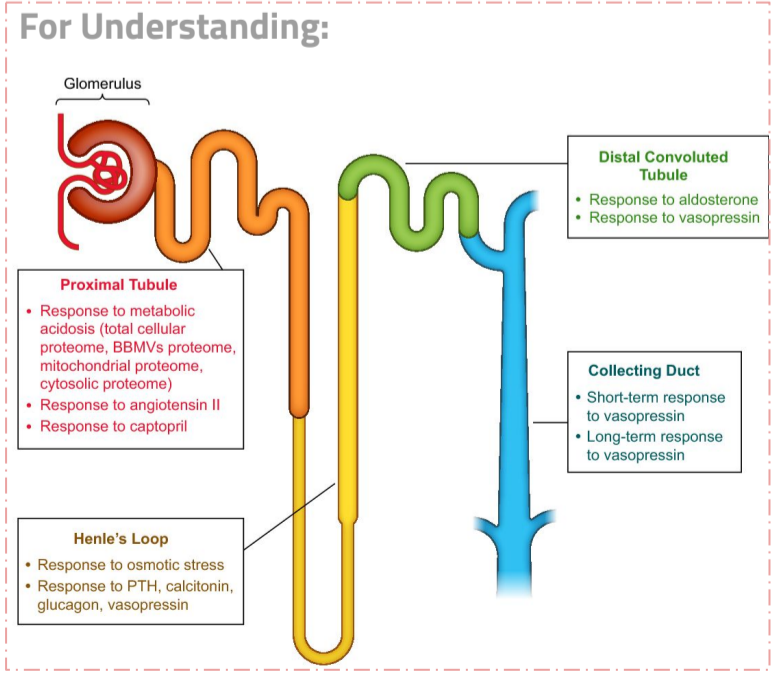
Will the body allow the 4320 of Bicarbonate to be excreted in urine in one time? No because within minutes our body will be in acid state because we excrete more base, therefore Bicarbonate have to be reabsorbed.
 In Proximal C.T 85% of HCO_3^- get reabsorbed.

Remain 10% Will be reabsorbed in distal part it will also get excreted depending on how much the body need it + the conc. of absorption. BUT usually We reabsorb 99% of bicarbonate that get filtered



the amount of bicarbonate in the body before reaching the kidney is 4320 mEq/day, the amount excreted is only 1 mEq/day. This means that 99.9% of the bicarbonate is being reabsorbed by the body in different parts of the renal tubule. around 80-90% is reabsorbed occurs in the proximal tubule.

- In PCT, LOH(A), and early DCT:
Na and H Counter Transport HCO_3^- -Buffer System
- In DCT and CT: Proton Pump
(Primary Active Transport)
- In PCT, LOH(A), and late DCT:
 PO_4 Buffer System



How is HCO_3^- reabsorbed by the tubules?

In PCT, LOH(a), and early DCT

Rich in Na and HCO_3^- and anything that can pass easily through the glomerular filtration barrier، تركيز المواد التي تقدر تخترق هالممبرين يكون فيها الفلترية نفس تركيز البلازما

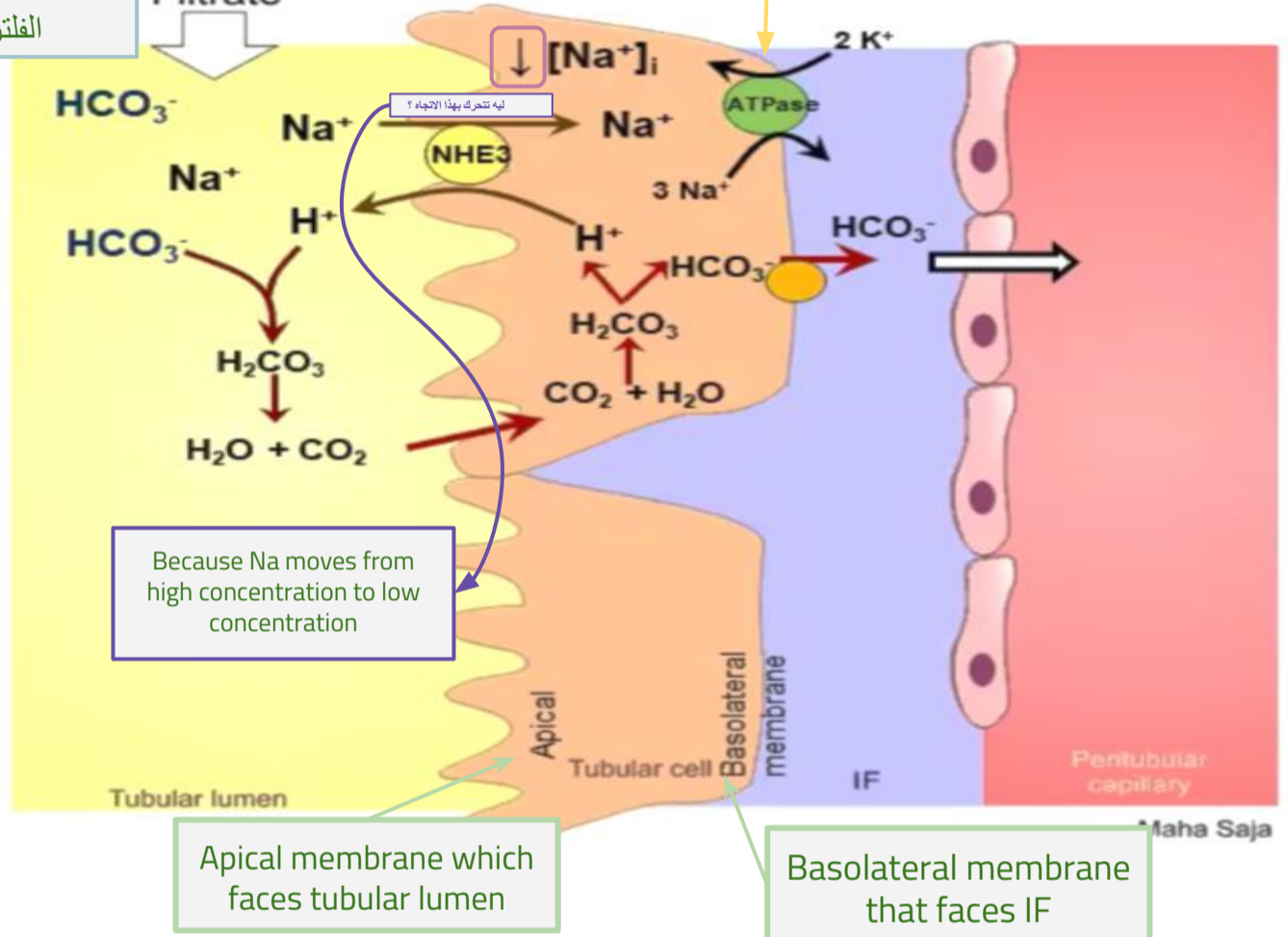
الصوديوم قليل لأن الـ pump الـ 3 Na و 2K يدخل

Na /K pump
it's the imp. one in reabsorption why? because most of ions that get reabsorbed they depend on the gradient of Na^+ which created by this pump.

Secreted H^+ binds to filtered HCO_3^- in the tubular lumen

Forming H_2CO_3 which dissociates into H_2O & CO_2

CO_2 diffuses through tubular cell membrane and react with water forming H_2CO_3 inside the cell



Explanation

1

Because Na moves from **high** concentration (in tubular filtrate) to **low** concentration (tubular cell) using a carrier molecule.
one of the carriers called sodium hydrogen exchanger
So it reabsorb Na , in exchange of Hydrogen (so it secretes hydrogen by secondary active transport).

2

Once hydrogen secreted into tubular lumen it will find HCO_3^- (Bicarbonate) they will bind together and form = H_2CO_3 (Carbonic acid).
as we know carbonic acid can dissociate specially in presence of Carbonic anhydrase enzyme.
CA enzyme is present on the surface of tubular cells so carbonic acid will dissociate into H_2O + CO_2

3

CO_2 can easily diffuse across cell membrane.
Again inside the cell CO_2 will bind to water and also inside the cell i have CA enzyme therefore Carbonic Acid (H_2CO_3) will be formed.
Again Carbonic acid will dissociate into (H^+ , HCO_3^-):
 H^+ —> will be secreted into lumen
 HCO_3^- —> will be transported into IF by carrier, then from IF to blood by bulk flow.

4

The HCO_3^- that gets into the tubular cell, it's not the same HCO_3^- that gets into the blood, not the same molecule! But for each Bicarbonate that disappears from the lumen —> there is one Bicarbonate will appear in the blood. so we consider it reabsorbed by لفة جحا 😊

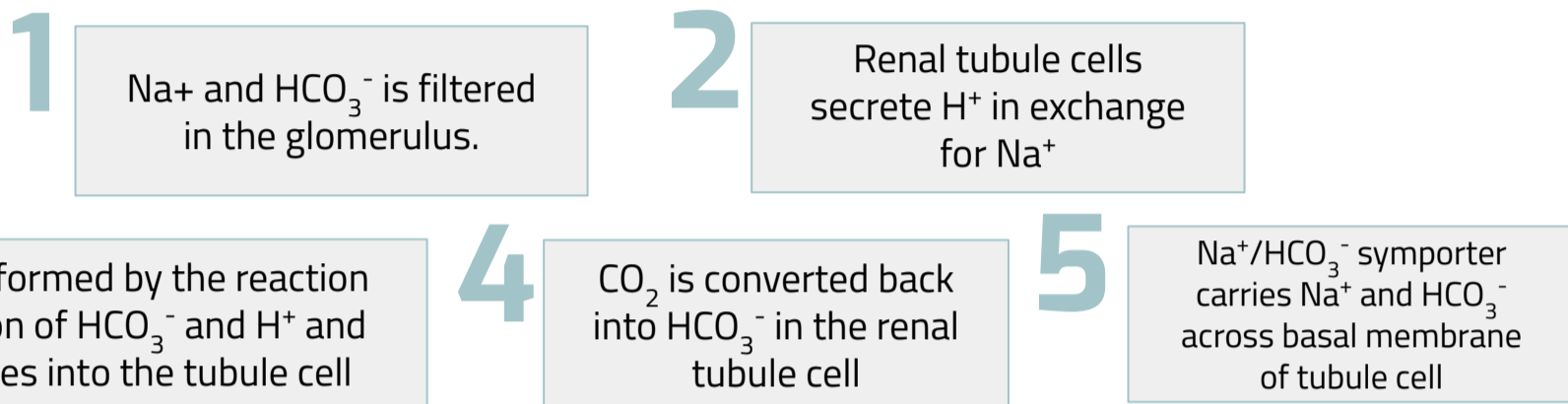
IF don't have H^+ —> Reabsorption of HCO_3^- will NOT happen. So reabsorption of bicarbonate requires secretion of hydrogen.

We are not losing hydrogen in this process.

● PCT cont...

This pattern of H^+ secretion occurs in the proximal tubule (PCT), the thick ascending segment of the loop of henle (LOH(a)), and the early distal tubule(DCT).

- ▶ The PCT reabsorbs "reclaims", 80 - 90% of the filtered HCO_3^-
- ▶ HCO_3^- reabsorption is linked to H^+ secretion. ▶ HCO_3^- is "Titrated" Against H^+ in the Tubules
- ▶ In case of no/little HCO_3^- in the lumen H^+ will bind to other buffers e.g. phosphate and ammonia resulting in the elimination of excess H^+ and generation of new HCO_3^-



● What happens at the DCT & CT?

Explanation

you should know that the amount of bicarbonate that derived here is a little amount because 85% get reabsorbed in PCT. as we know in DT there is different types of cell (principal cell, intercalated cell) here we will discuss intercalated cell and specially type a.

In the intercalated cell, there are **two pumps**:

1. H/k pump → it secretes H^+ and Reabsorbs K^+
2. Hydrogen pump → only secretes H^+

يعني مردنا بنفرز هيدروجين

If the hydrogen finds HCO_3^- in the lumen → it will bind with it and the same thing happens in PCT will happen here again.

But If the hydrogen DOESN'T find HCO_3^- in lumen → it will be excreted by binding to another buffer which is phosphate buffer but phosphate buffer doesn't have the ability to do the same cycle it was done with carbonic acid (لغة جحا) so it will excrete it in the urine.

فالحالتين كالتالي:

- 1-repeat what happens in PCT if H find HCO_3^-
- 2- get excreted in the urine.

From where we got the Hydrogen inside intercalated cell?

from H_2CO_3 dissociation which also produce HCO_3^- with the hydrogen, then HCO_3^- gets reabsorbed into blood (we consider it new bicarb) and H^+ get secreted into the lumen. (More details in slide 12)

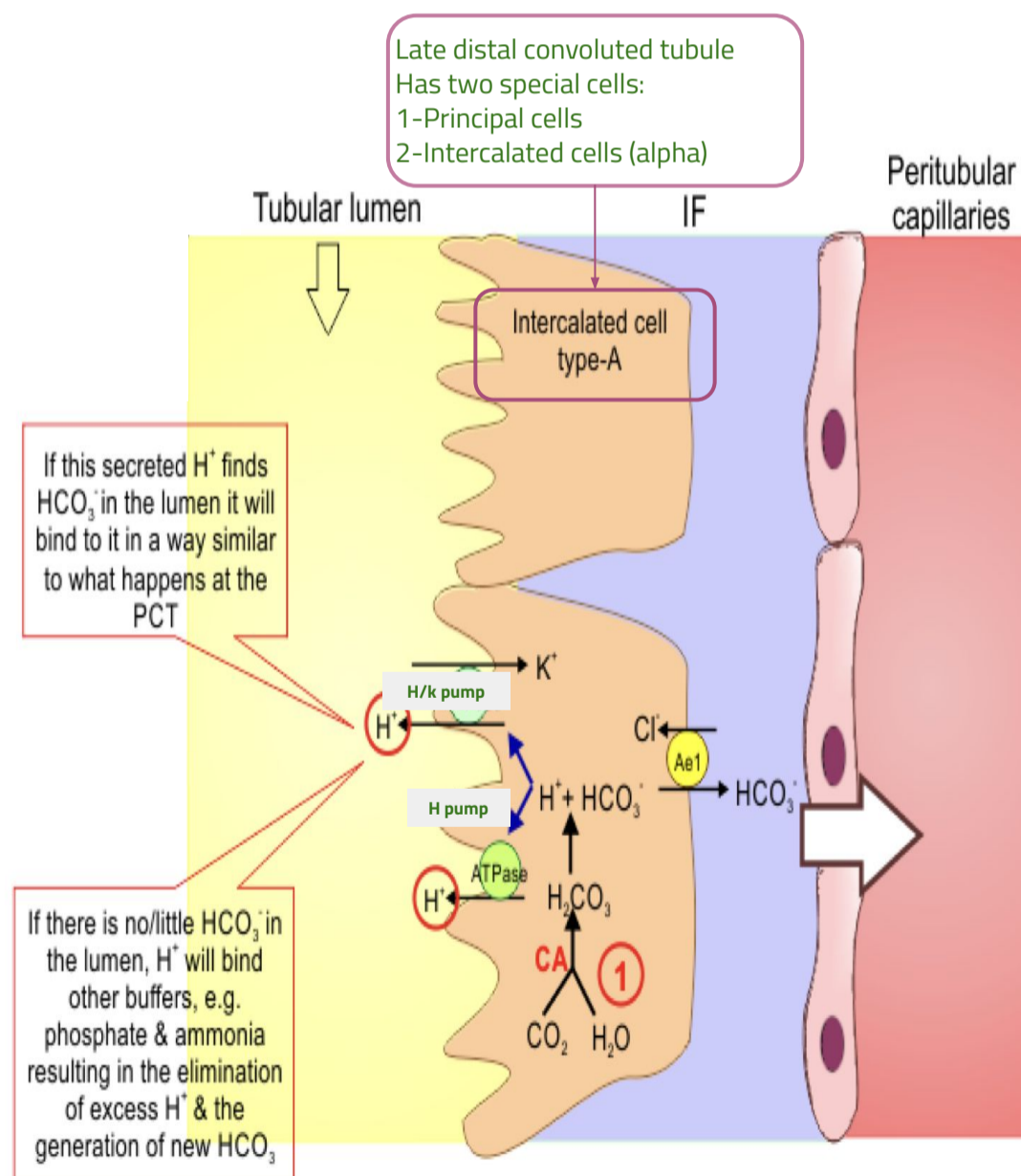
يعني هايدروجين افرز، و Bicarbonate اعيد امتصاصه

فكانه new molecules ، ليه؟ لأن ماقابله اختفاء لنفس المركب

اللي هو HCO_3^- من الجهة المقابلة اللي هي Tubule!

And this is how the **kidney** generate new HCO_3^-

العلم قميل

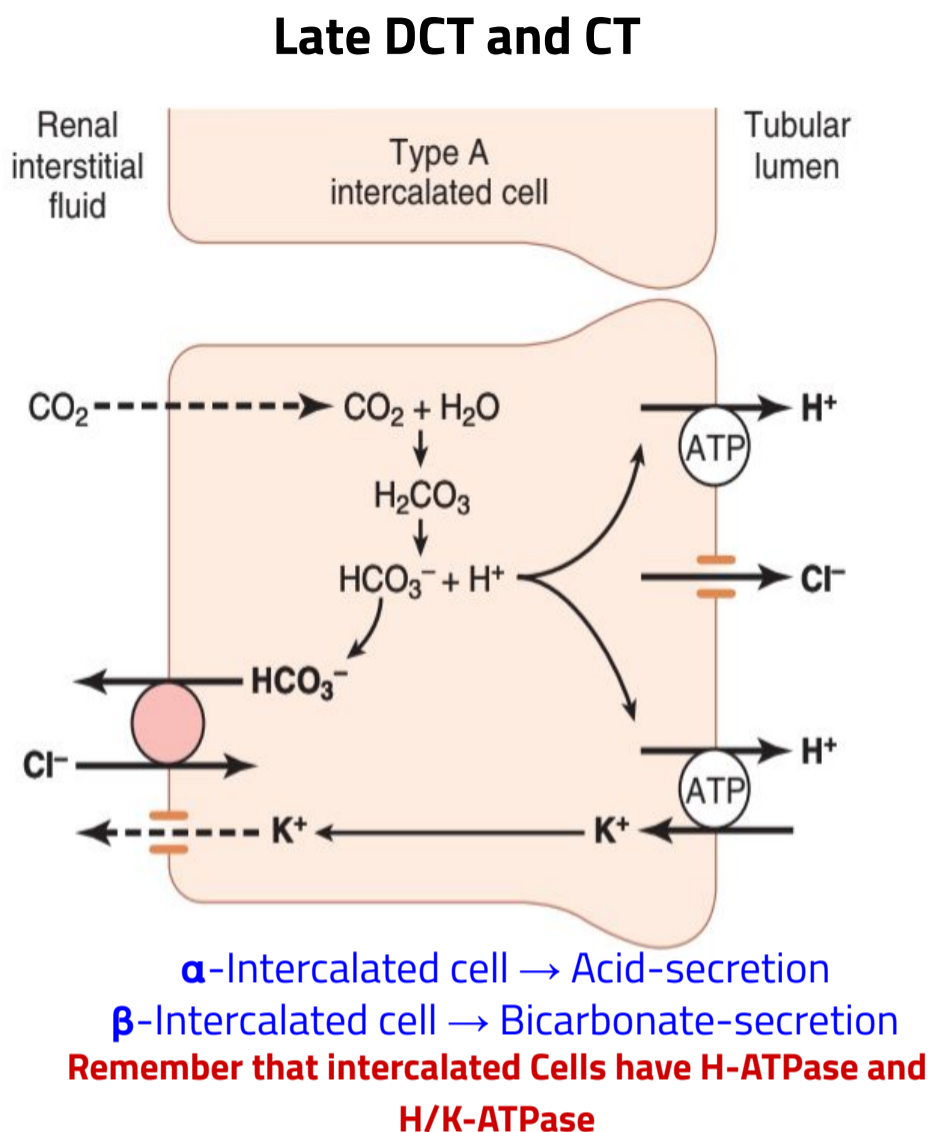


● late DCT and CT Cont...

HYDROGEN ION SECRETION

- The filtrate arriving DCT & CT is low in HCO_3^-
- The distal segments of the nephron are characterised by the presence of "intercalated cells" capable of **actively secreting H^+** through H^+ -ATPase and H^+ - K^+ ATPase present on their apical membrane (**Type-A intercalated cells**).
- Only a limited number of H^+ can be excreted in its free form in urine.
- Lowest possible urine $\text{pH} = 4.5 \rightarrow \approx 0.04 \text{ mmol/L}$ of free H^+ .

We cannot excrete urine more acidic than that because it will damage the epithelium



Non-Bicarbonate Buffers in the Tubular Lumen?

How does the kidney excrete the extra H^+ ?

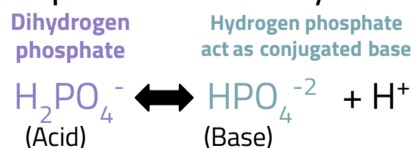
the extra H^+ secreted will need to be buffered in the tubular lumen

There are 2 main non- bicarbonate buffers in the tubular lumen

1 - Filtered

We have phosphate in ECF in the plasma, it will get filtered and will find it in Filtrate.

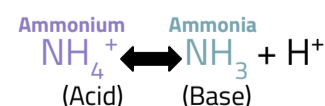
Phosphate Buffer System



2 - Synthesized

The kidney is able to synthesize ammonia, and it work as a buffer by binding H^+

Ammonia Buffer System



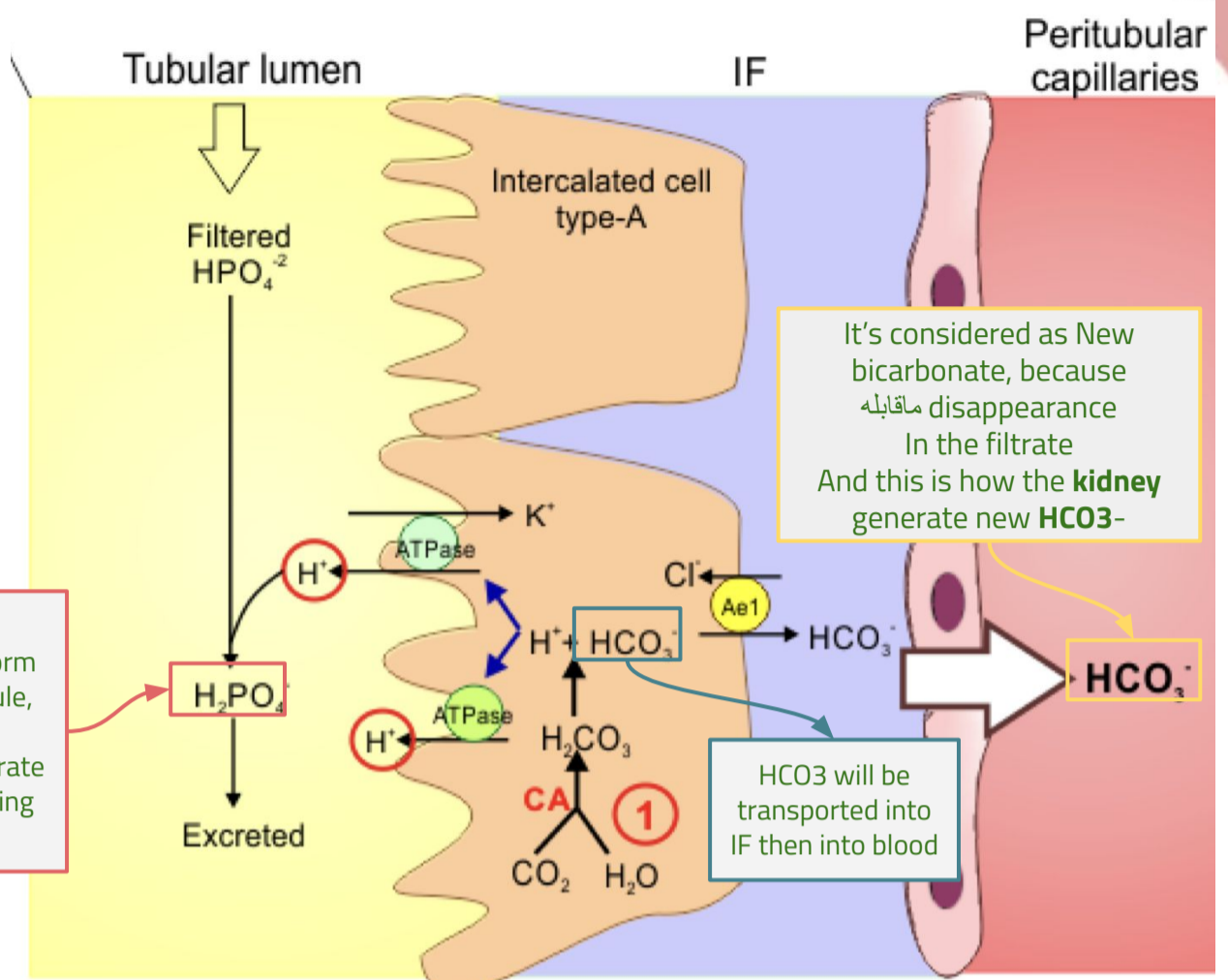
The Phosphate Buffer System

→ In DCT + collecting duct

Excretion of H⁺ and Generation of New HCO₃⁻

-Excretion of H⁺ as phosphate is capable of handling a limited amount of H⁺ and will not be enough to rid the body of its daily acid load nor if there is unusually high acid production.

H⁺ will be secreted into lumen and it will find hydrogen phosphate (HPO₄²⁻) to bind with it and form Dihydrogen phosphate which is a charged molecule, so it cannot cross the cell membrane, Therefore it gets trapped into the lumen of the filtrate and then get excreted In the urine. so now i'm losing Hydrogen as well.



It's considered as New bicarbonate, because *مقابلته* disappearance In the filtrate And this is how the **kidney** generate new HCO₃⁻

HCO₃⁻ will be transported into IF then into blood

Guyton : buffering of secreted H⁺ by filtered phosphate (NaHPO₄) → NaH₂PO₄
Note that a new HCO₃⁻ is returned to blood for each NaHPO₄ that reacts with a secreted H⁺

Same mechanism but in different picture

① CO₂ combines with water within the type A intercalate cell, forming H₂CO₃.

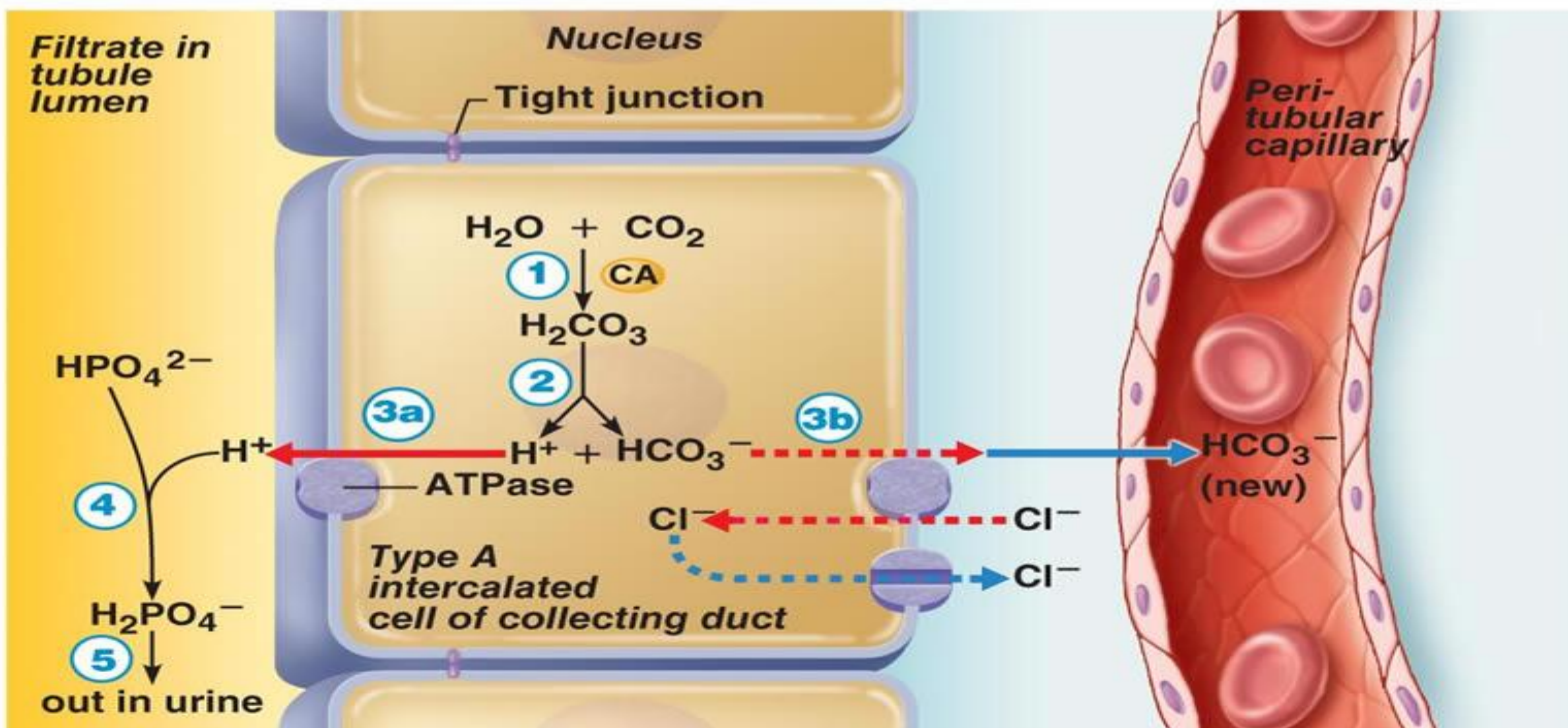
② H₂CO₃ is quickly split, forming H⁺ and bicarbonate ion (HCO₃⁻).

③a H⁺ is secreted into the filtrate by a H⁺ ATPase pump.

③b For each H⁺ secreted, a HCO₃⁻ enters the peritubular capillary blood via an antiport carrier in a HCO₃⁻-Cl⁻ exchange process.

④ Secreted H⁺ combines with HPO₄²⁻ in the tubular filtrate, forming H₂PO₄⁻.

⑤ The H₂PO₄⁻ is excreted in the urine.



→ Primary active transport
- - - Secondary active transport
→ Simple diffusion
- - - Facilitated diffusion

● Transport protein
● Ion channel
● CA Carbonic anhydrase

● The Ammonia Buffer System

انتبهوا الرسمة بياناتها عكس باقي الصفحات

Renal tubular cell, especially PCT, are capable of generating ammonium (NH_4^+) "ammoniogenesis" which is then excreted in urine carrying with it H^+ .

The rate of ammoniogenesis can be modified according to the needs of the body.

Quantitatively, the ammonia buffer system is more important than the phosphate buffer system for H^+ excretion in urine.

It is the most important system in case of acidosis.

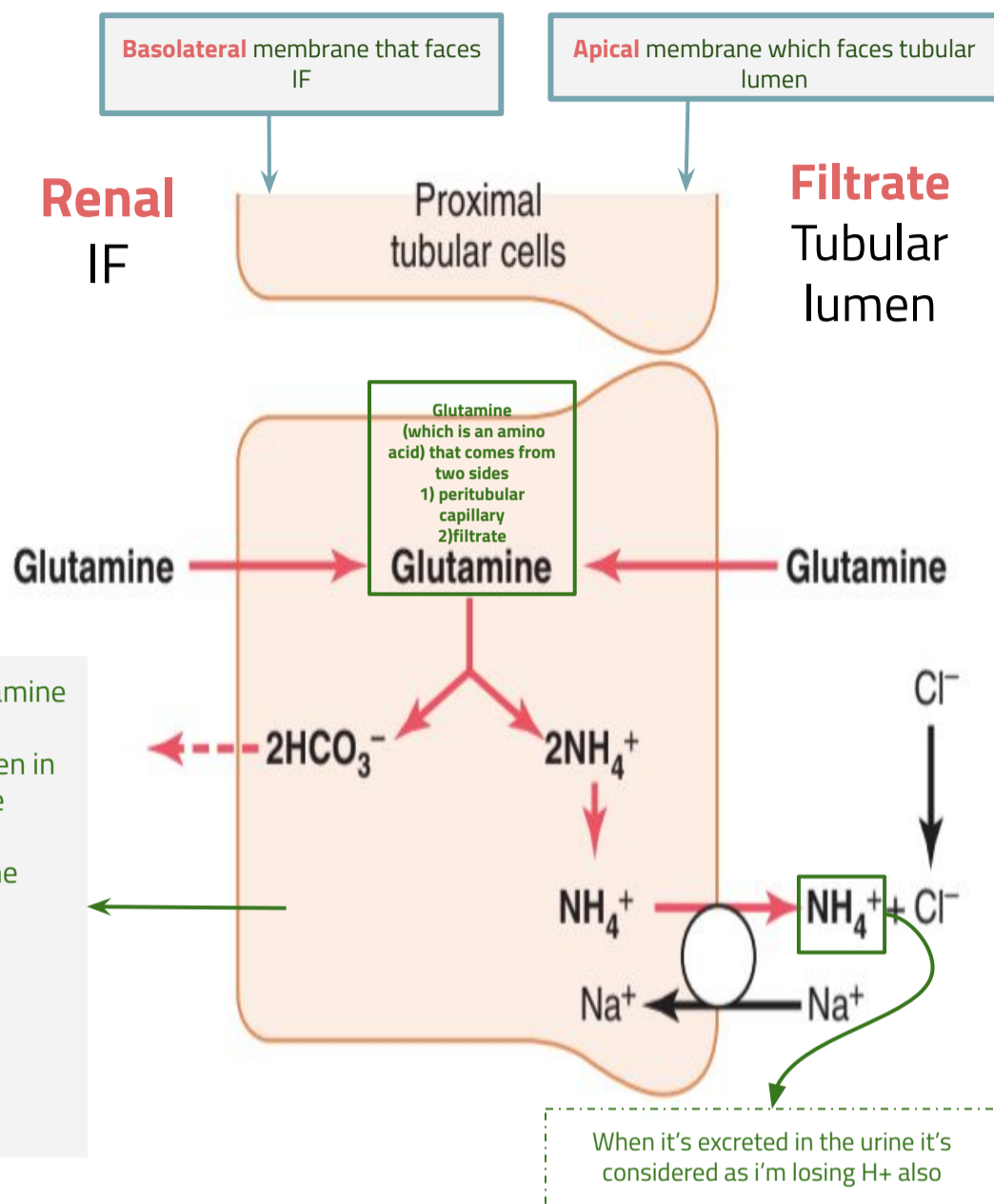
Proximal convoluted cells have the ability to degrade the glutamine into : $2\text{HCO}_3^- + 2\text{NH}_4^+$

2 ammonium molecules (2NH_4^+) get secreted into tubular lumen in exchange for Na^+ "they think this process happens by using the same carrier of hydrogen: Na/H exchanger" otherwise Two Bicarbonate (HCO_3^-) will be reabsorbed into the blood.

It's considered a **new molecules again**, because ما قابلها disappearance of HCO_3^- from the tubular lumen.

-What is the strongest buffer of these two (phosphate, ammonia) in generation new Bicarbonate?

Ammonia buffer, because it generate two HCO_3^- from one glutamine



Guyton :production and secretion of ammonium ion (NH_4^+) by proximal tubular cells. Glutamine is metabolized in the cell, yielding NH_4^+ and bicarbonate. The NH_4^+ is secreted into the lumen by a $\text{Na} - \text{NH}_4$ exchanger. For each Glutamine molecule metabolized two NH_4^+ are produced and secreted and two HCO_3^- are returned to the blood.

From boys slides

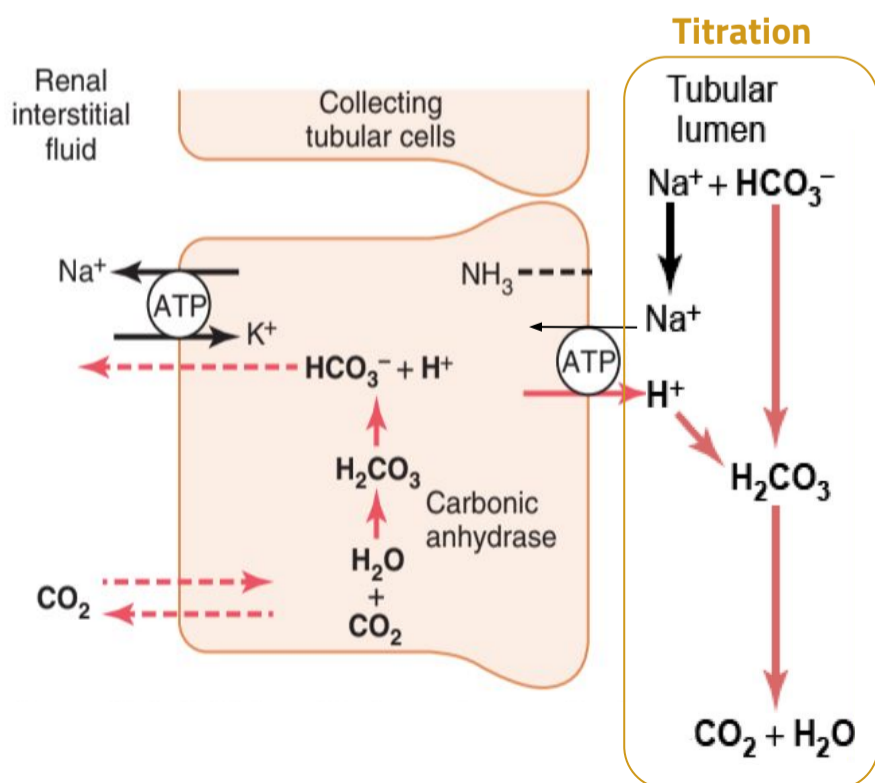
HYDROGEN ION SECRETION

Guyton :Buffering of Hydrogen ion secretion by ammonia (NH_3) in the collecting tubules. Ammonia diffuses into the tubular lumen, where it reacts with secreted H^+ to form NH_4^+ , which is then excreted. For each NH_4^+ excreted, a new HCO_3^- is formed in the tubular cells and returned to the blood.

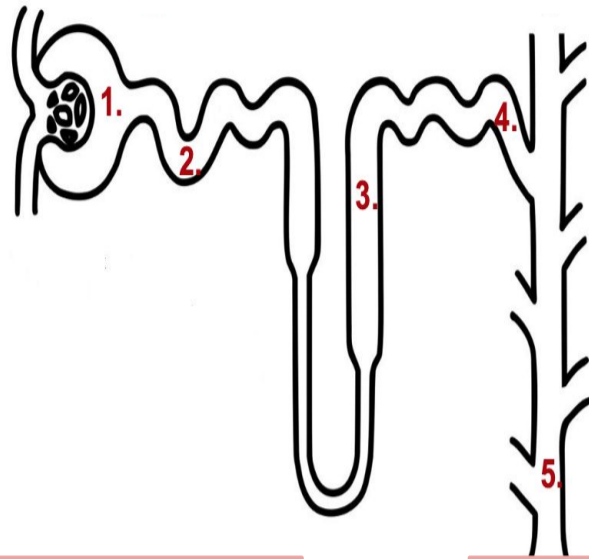
We Can Generates new HCO_3^- by two mechanisms:

- 1) When H^+ is secreted by the Intercalated cells, and it doesn't find HCO_3^- , so it starts binding to non-bicarbonate buffers such as phosphate buffer, which will lead to a newly formed HCO_3^- .
- 2) By Ammoniogenesis: due to the breakdown of Glutamine, which will give 2HCO_3^- .

HCO_3^- Is "Titrated" Against H^+ in the Tubules



The overall scheme of renal excretion of Acids & Bases



To excrete Acid:

- 1- Freely filter HCO_3^-
- 2- Reabsorb the majority of filtered HCO_3^-
- 3- Reabsorb some additional HCO_3^-
- 4- Secrete H^+ (titrate filtered bases, i.e. HPO_4^{2-}) and secrete NH_4^+
- 5- Excrete acidic urine containing NH_4^+ and H_2PO_4^-

To excrete Base:

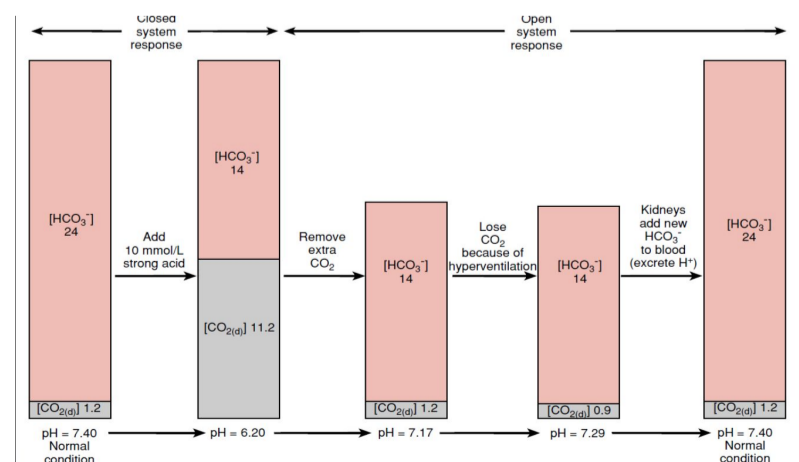
- 1- Freely filter HCO_3^-
- 2- Reabsorb the majority of filtered HCO_3^-
- 3- Reabsorb some additional HCO_3^-
- 4- Secrete some HCO_3^-
- 5- Excrete alkaline urine containing HCO_3^-

Factors Affecting H^+ Secretion and HCO_3^- Reabsorption

Increase H^+ Secretion and HCO_3^- Reabsorption	Decrease H^+ Secretion and HCO_3^- Reabsorption
$\uparrow \text{PCO}_2$	$\downarrow \text{PCO}_2$
$\uparrow \text{H}^+, \downarrow \text{HCO}_3^-$	$\downarrow \text{H}^+, \uparrow \text{HCO}_3^-$
\downarrow Extracellular fluid volume	\uparrow Extracellular fluid volume
\uparrow Angiotensin II	\downarrow Angiotensin II
\uparrow Aldosterone	\downarrow Aldosterone
Hypokalemia	Hyperkalemia

From boys slides

The $\text{HCO}_3^-/\text{CO}_2$ System. This system is remarkably effective in buffering added strong acid in the body because its open.



MCQ & SAQ

Q1: The importance of bicarbonate buffer system in

- A. ICF
- B. ECF
- C. Urine
- D. A and B

Q2: The normal values of PCO_2 are in the range

- A. 25- 35 mmHg
- B. 20- 45 mmHg
- C. 15 - 25 mmHg
- D. 35 - 45 mmHG

Q3: The CO_2 component of the buffer is regulated by

- A. Kidney
- B. Heart
- C. Lung
- D. Liver

Q4: which powerful system that works within hours to days

- A. Respiratory System
- B. Bicarbonat System
- C. Phosphate
- D. Renal System

Q5: Which of the following is capable of generating ammonium

- A. PCT
- B. DCT
- C. CT
- D. LOH

Q6: most of the reabsorption takes place in

- A. DCT
- B. PCT
- C. CT
- D. LOH

6:8
5:A
4:D
3:C
2:D
1:B
answer key:

1- How does the kidney excrete acidic or basic urine ?

2- Why is the Bicarbonat most important buffer system in the ECF?

3- How does the kidney excrete the extra H^+ ?

A1: secreting H^+ , Reabsorbing HCO_3^- , Generating "new" bicarbonate ions

A2: 1-The CO_2 component of the buffer is regulated by the lungs , 2-The HCO_3^- component of the buffer is regulated by the kidneys

A3: the extra H^+ secreted will need to be buffered in the tubular lumen, by the Phosphate Buffer System or the Ammonia Buffer System

Team Leaders

Albandari Alanazi

Abdulaziz Alsuhaime

Team Sub-Leaders

Sara Alharbi

Fahad Al-Ajmi

Organized and reviewed by:

- ❖ **Sarah alqahtani**
- ❖ **Hessah fahad**

Members:

- ❖ **Sara Alharbi**
- ❖ **Rania AlMutairi**
- ❖ **Ahmad Alkhayatt**