Physiology Team 434

# 9&10 .Basics of Acid Base & Buffer Systems

Color index

- Important
- Extra Information
- CLASS NOTES

Physiology Team 434
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# Contents



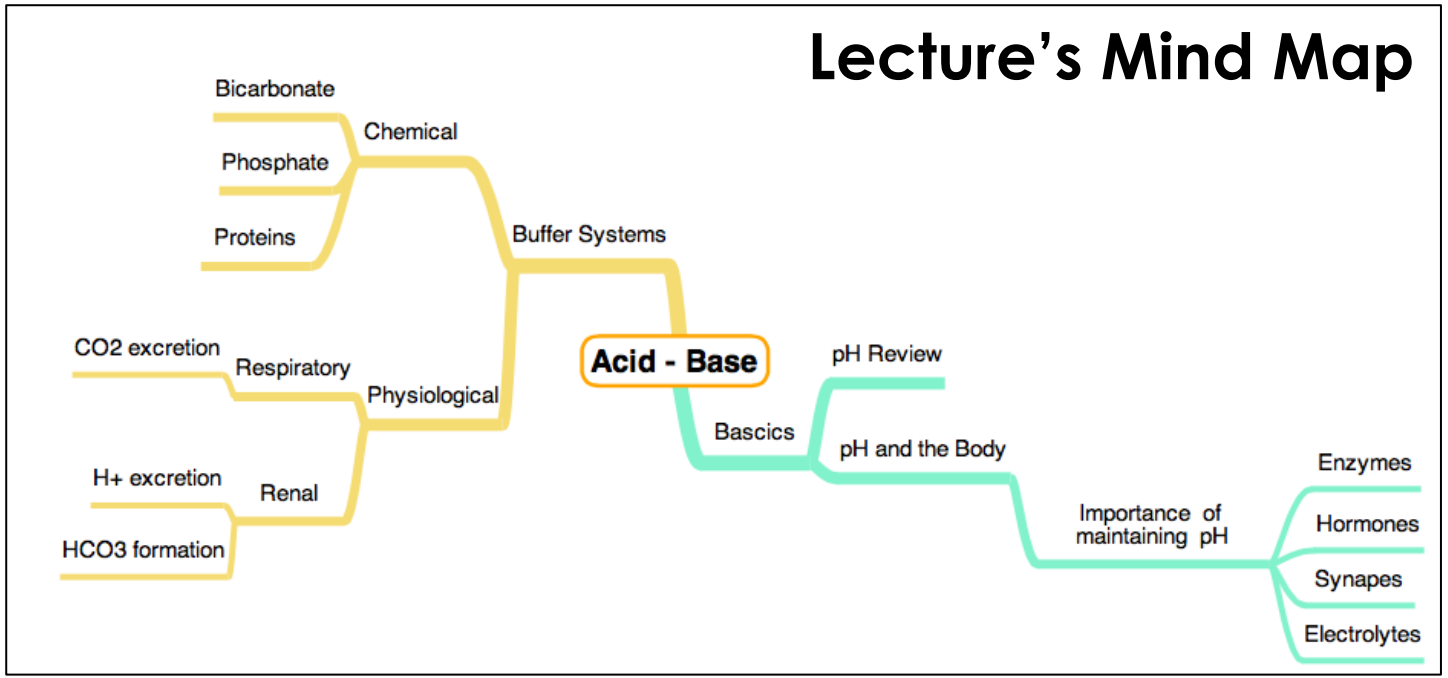
**Recommended Video!**

Not much related but it gives a great concept on buffers

**Please check out this link before viewing the file to know if there are any additions/changes or corrections. The same link will be used for all of our work Physiology Edit**

# Introduction

Acid-base balance in concerned with maintaining a **normal hydrogen ion concentration in body fluids**. This balance is achieved by utilization of **buffers** in extracellular fluid, by respiratory mechanisms that excrete carbon dioxide, and by renal mechanisms that reabsorb bicarbonate and secrete hydrogen ions



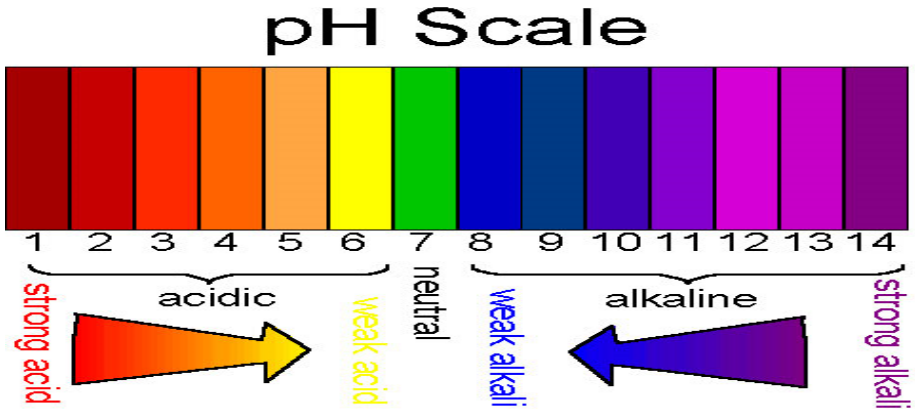
# pH Review

**What does pH means?**

pH (always written little p, big H) of a substance is an indication of how many hydrogen ions it forms in a certain volume of water. There's no absolute agreement on what "pH" actually stands for, but most people define it as something like "power of hydrogen" or "potential of hydrogen."

- pH = - log $[H^+]$
- $H^+$ is really a proton
- Range is from 0 – 14 *THIS IS THE RANGE* اللي على وجه الأرض *NOT IN OUR BODIES!*
- If $[H^+]$ is high, the solution is acidic pH < 7
- If $[H^+]$ is low, the solution is basic or alkaline pH > 7
- Acids are $H^+$ donors.
- Bases are $H^+$ acceptors, or give up $OH^-$ in solution

| Acids & Bases Can Be | |
|---|---|
| **Strong** | **Weak** |
| Dissociate **completely** in solution. | Dissociate **only partially** in solution. |
| **Examples** | |
| HCl *(ACID)* , NaOH *(BASE)* | Lactic acid, Carbonic acid |



# The Body & pH

- ✧ Homeostasis of pH is tightly controlled
- ✧ Extracellular fluid pH= 7.4
- ✧ Arterial Blood pH= 7.35 – 7.45 *(OUR NORMAL RANGE)*
- ✧ **Venous blood is more acidic than arterial?**

Because it contains more CO2 than arterial blood.

- < 6.8 or > 8.0 death occurs
- Acidosis : below 7.35
- Alkalosis : above 7.45

**1:** Enzymes are proteins. Each enzyme have a specific proteins structure to function ➔ The free H+ have the capability to bind to the proteins of an enzyme and changes their configuration therefore denaturing them.

**2:** The synapses (nerves junctions) of the nerves is dependent on the pH so it may increase or decrease the transmission of signals between nerves if it was in under acidic affect the transmission will decrease and the person may get into coma.

## Why is it important to maintain pH of blood within normal range?

- Most enzymes function only with narrow pH ranges [1]
- Acid-base balance can affect electrolytes ($Na^+$, $K^+$, Cl, $Ca^{++-}$)
- pH affect hormones.
- To maintain normal function of synapses[2]

# The Body & pH cont.

## The Body Produces More Acids Than Bases

### Sources of acids threats:

1. **Acids taken in with food.** FOOD CONTAINING FATS SO THIS IS FATTY ACIDS , PROTEINS DIET WHICH IS AMINO ACIDS

1. **Acids produced by metabolism of lipids and proteins**

THE METABOLISM OF THEM CAUSES ACIDS TO BE PRODUCED BUT THAT DOESNT MEAN THAT THEY ARE STRONG ACIDS. AMINO ACIDS BEHAVE AS ACIDS WHEN IN AN ACIDIC SOLUTION AND VISE VERSA...

**3. Cellular metabolism produces $CO_2$.**

$$CO_2 + H_20 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

CARBONIC ACID COULD DISSOCIATE TO EITHER WATER AND CARBON DIOXIDE OR BICARBONATE AND HYDROGEN

KEY:

**$CO_2$ =** Carbon Dioxide
**$H_2O$ =** Water
**$H_2CO_3$ =** Carbonic Acid
**$H^+$ =** Hydrogen ion
**$HCO_3^-$ =** Bicarbonate

# Buffer Systems

- THE BODY DEFENSE HAS A LIMIT BECAUSE IF IT WAS PERFECT THEN THERE WON'T BE DISEASES!
- THE BUFFER SYSTEM BUFFERS THE CHANGE THAT OCCURS IN THE MEDIUM

## Body Defence Against Changes in pH

**First Line**

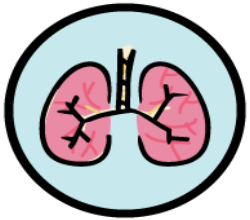
**Chemical Buffer System**

- Bicarbonate Buffer System
- Phosphate Buffer System
- Proteins Buffer System

**Second Line**

**Physiological Buffer System**

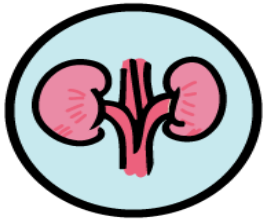
Respiratory Mechanism
EXCRETE $CO_2$



**Third Line**

**Physiological Buffer System**

Renal Mechanism
EXCRETE H Ions



# Chemical Buffer Systems

| | Bicarbonate Buffer | Phosphate Buffer | Proteins Buffer |
|---|---|---|---|
| **Location** | It is the most abundant and acts both extracellular and intracellular. | Major intracellular buffer as its concentration is high intracellularly and tubular fluid | Abundant buffers especially intracellular |
| **The Main Elements** | •Sodium Bicarbonate ($NaHCO_3$)<br>• weak (acid carbonic acid ($H_2CO_3$). *CARBONIC ACID IS ALSO CALLED CARBON DIOXIDE* | •$H_2PO_4^-$ (acid)<br>•$HPO_4^{2-}$ (base) | • **Hemoglobin,** work in RBC<br>• **Plasma proteins.**<br>• **Intracellular proteins**. |
| **Notes** | ✧ **The two elements are regulated as:**<br>▪ $CO_2$ by the lungs,<br>▪ HCO3- by the kidney.<br><br>✧ Its concentration in blood = **27mEq/L** and is called Alkali Reserve. الاحتياطي القلوي<br><br>✧ Maintain a **20:1** ratio :<br>**$HCO_3^-$ : $H_2CO_3$**<br>*BECAUSE THE BODY PRODUCES A LOT OF ACIDS SO I NEED TO GIVE A LOT OF BASE IN ORDER TO MAINTAIN A BALANCE* | ✧ It is an important buffer in renal tubules.<br>**why?**<br><br>o Becomes concentrated in the tubular fluid, so become powerful.<br>2. its pKa = 6.8, which close to the pH in the tubular fluid of the distal nephron. | |

# Chemical Buffer Systems cont.

THE EQUATIONS ARE NOT FOR MEMORIZING!

## ✧ Bicarbonate Buffer:

- We must have acid and base to react with each others:

**HCl** (strong acid) + $NaHCO_3$ ↔ **$H_2CO_3$**(weak acid) + NaCl

**NaOH** (strong base) + $H_2CO_3$ ↔ **$NaHCO_3$**(weak base) + $H_2O$

**The main goal of chemical buffer systems is to convert strong acids and bases into weak acids and bases to maintain blood pH**

## ✧ Phosphate Buffer:

$H^+ + HPO_4^{2-}$ (base) ↔ $H_2PO_4^-$ ( **Mono**hydrogenphosphate = **BASE** "hydrogen acceptor" )

$OH^- + H_2PO_4^-$ (acid) ↔ $H_2O + HPO_4^{2-}$ ( **Di**hydrogenphosphate = **ACID** "Donner" )

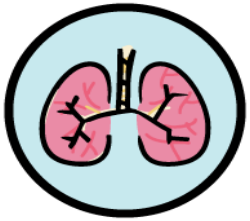
## ✧ Protein Buffer:

For example: hemoglobin in RBC

Carboxyl group gives H+ (decrease PH) , Amino group accept H+ (increase PH)

# Physiological Buffer Systems

## Respiratory Mechanism



**Powerful,**
but only works with volatile[1] acids

Body pH can be adjusted by **changing rate and depth of breathing.**

**Respiratory System**
**The Lungs**

**Exhalation** of carbon dioxide.

**Hyperventilation**
Wash out excess $CO_2$.

**Hypoventilation**
Retain $CO_2$.

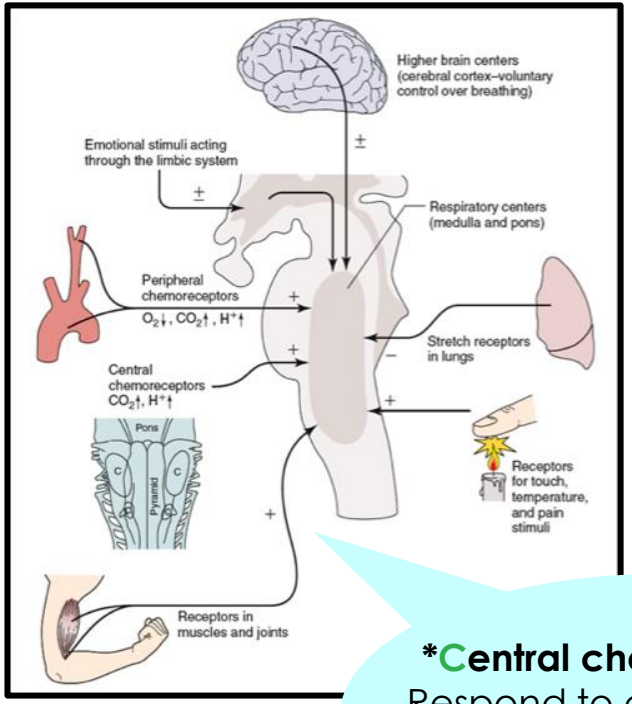
Does**NOT** affect **fixed acids** like lactic acid

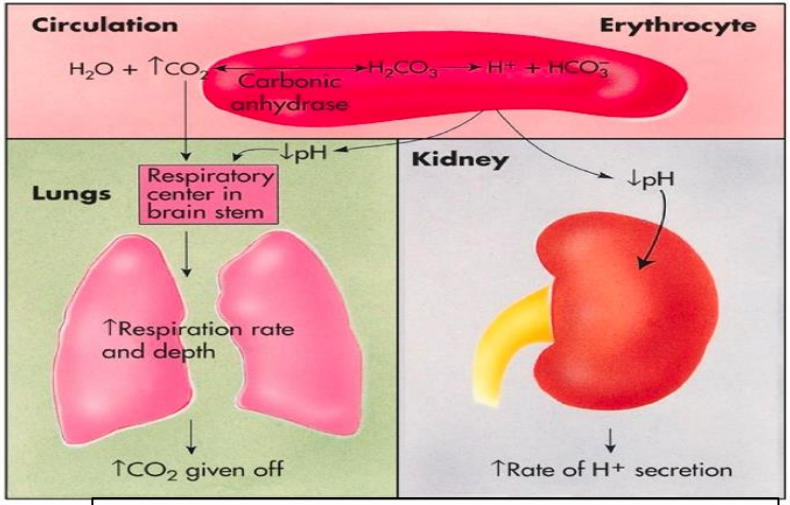
This process is controlled by **chemoreceptors.**

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

1: (of a substance) easily evaporated at normal temperatures.

# Respiratory Mechanism




**Why?**

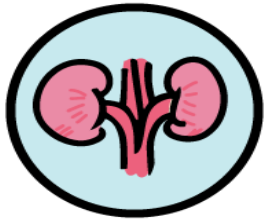
HYDROGEN IONS CANT CROSS BBB SO ONLY THE PERIPHERAL CHEMORECEPTORS WILL SENSE THEIR CHANGES

***Central chemoreceptors:** Respond to changes in **$CO_2$**
***PeripHeral chemoreceptors** respond to changes in **H+**

The carbonic acid in the RBC is gonna give the $CO_2$ and water to the lungs, and from the other side the carbonic acid will give H and $HCO_3$ to the kidney so it will excrete the hydrogen in the urine and reabsorbed the $HCO_3$.

# Physiological Buffer Systems

## Renal Mechanism

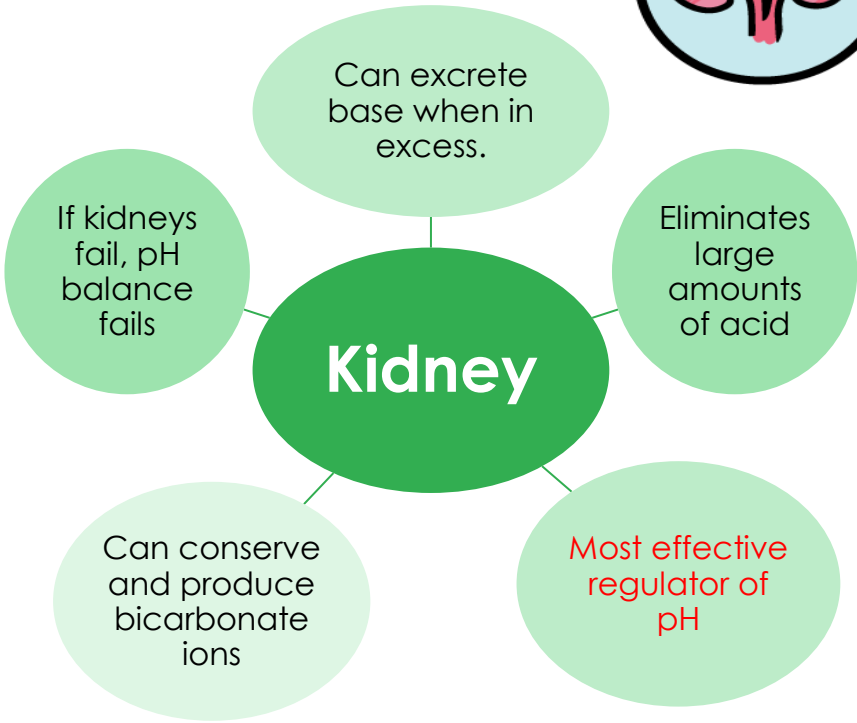


How the kidney regulates blood pH?

1- Reabsorption of filtered bicarbonate.

2- Generation of new bicarbonate.

3- Excretion of H+ and urine acidification as low as pH of urine =5.0.



# Physiological Buffer Systems

## Renal Mechanism cont.

**For the kidney to continue excretion of acidic urine, the excreted H+ has to be buffered by two buffer systems in the renal tubules:**

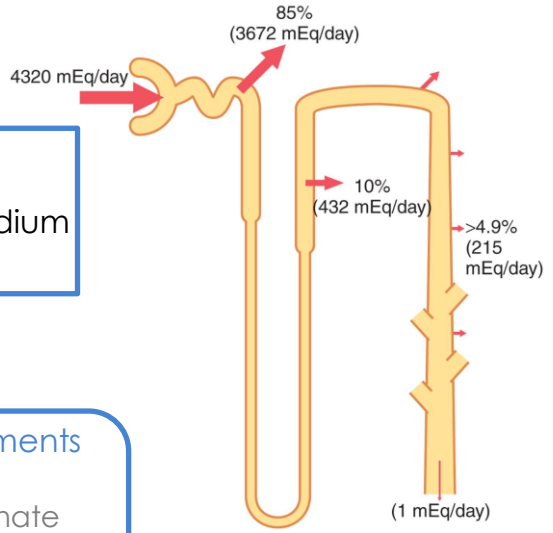
THE AMMONIA IS MANUFACTURED AND SYNTHESIZED IN THE KIDNEY

### A. Ammonia

Which binds the secreted H+ and forms ammonium to finally binds CL to give ammonium-CL which is excreted in urine.

### B. Phosphate buffer:

Which binds H+ and gives sodium di-hydrogen phosphate.




Reabsorption of Bicarbonate in different segments of the nephron

The percentages of the filtered load of bicarbonate absorbed by the various tubular segments are shown as well as the number of milliequivalents reabsorbed per day under normal conditions.

# Renal Mechanism cont.

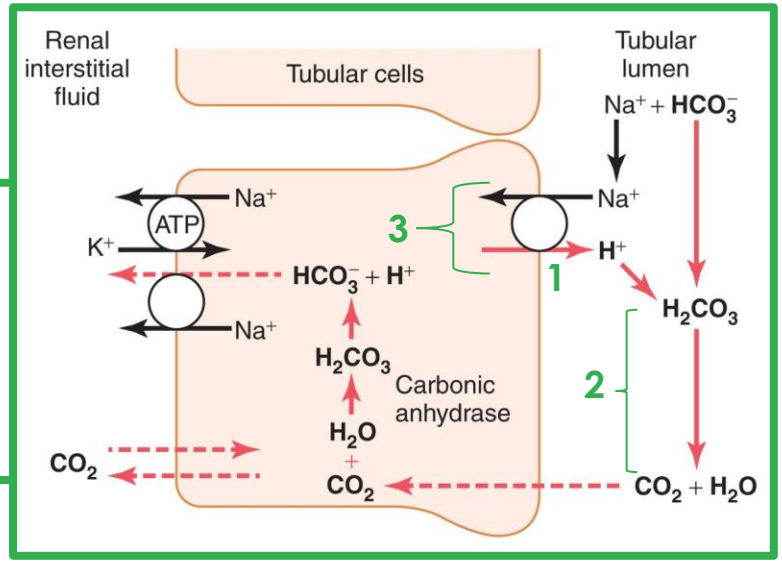
## in Proximal Convoluted Tubules, Thick Ascending & Early Distal Tubules

**Cellular mechanisms for**

1 -Active secretion of hydrogen ions into the renal tubules

2 -Tubular reabsorption of bicarbonate by combination with Hydrogen ions to form carbonic acid , which dissociates to form $CO_2 + H_2O$

3- Na ion reabsorption in exchange for the hydrogen ions secreted.




- For each secreted H+ one molecule of $HCO_3$- is reabsorbed back to the blood.
- Energy for H+ transport against concentration gradient, **is derived from Na+ gradient developed by Na-K pump.**
- >90% of bicarbonate reabsorbed in this way
- The reabsorption of $HCO_3$- in this segment does not lead to net secretion of H+ because the secreted H+ binds with the filtered $HCO_3$-
- The secreted H+ in this segment does not lead to a significant drop in tubular pH.
  - The transport of $HCO_3$- at the basolateral membrane is facilitated by:
    1. Na-$HCO_3$- cotransport. 2. Cl- $HCO_3$- exchange

# Renal Mechanism cont.

## Generation of New $HCO_3$- and Secretion of H+ :

## Intercalated cells of distal & Collecting tubules

- This rids the body of 80 mEq of H+ per day which comes from the metabolism.
- Most of this H+ is secreted in combination with urinary buffers; phosphate & ammonia.

**1.** H+ is secreted by primary active transport (H+ ATPase). The energy required comes from the breakdown of ATP at the luminal border.

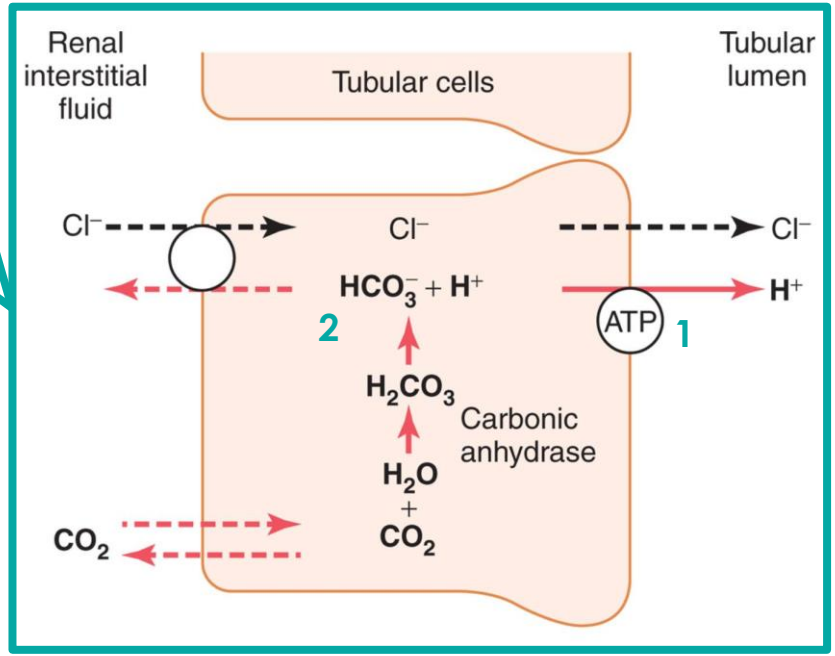
- This secretion can decrease pH of tubular fluid to 4.5, which is the lowest pH achieved in normal kidney. It is responsible for urine acidity.

**2.** For each H+ molecule secreted in this segment one $HCO_3$- molecule is formed and reabsorbed.

THIS IS THE SYNTHESIS OF BICARBONATE

**Where the actual H+ Secretion Occur**

Primary Active H+ secretion **(H+ATPase)** by the distal tubule & collecting tubules



# Renal Mechanism cont.

## Generation of New $HCO_3$- and Secretion of H+ : H+ Buffering By Ammonia & Phosphate

- **When H+ is secreted in excess of $HCO_3$-,**
only small part of H+ can be excreted in the ionic form (H+)in urine.
- The lower limit of tubular fluid pH that allows H+ secretion is 4.5.

OTHERWISE THE TUBULES WILLL ALL BE BURNED

- To continue secretion of H+, the excess H+ has to be buffered (phosphate & ammonia).

At the same time new molecules of $HCO_3$- will be formed and pass into the blood.

SO, when there is excess H+ in the extracellular fluid, the kidney:
1. Absorb all filtered $HCO_3$-
2. Secrete excess H+
3. Generate new $HCO_3$-

# Renal Mechanism cont.

THIS HAPPENS IN THE PROXIMAL TUBULES CUASE I HAVE MORE PHOSPHATE THERE.

## Phosphate Buffer

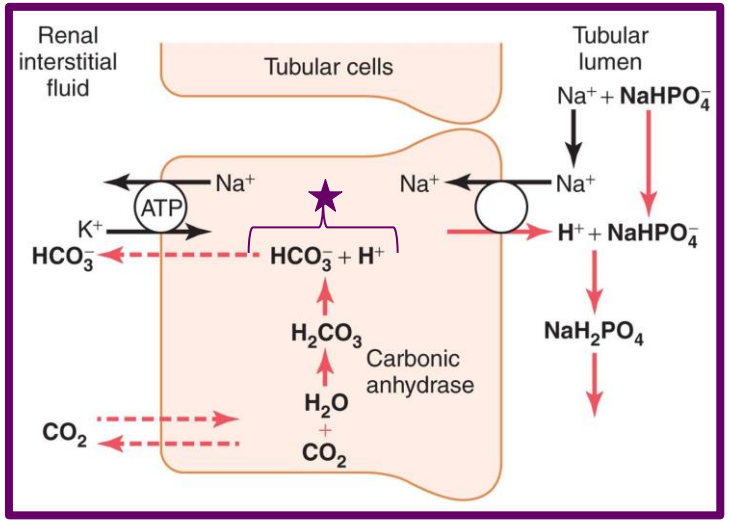
**Phosphate works well in tubular fluid for many reasons:**

1. Concentrated in tubular fluid due to $H_2O$ and low permeability to phosphate.

2. pH of tubular fluid close to pKa of phosphate.

★**$HCO_3$- formed by this mechanism represent a net gain not replacement of filtered molecule.**

Buffering of H+ by phosphate. Secretion of H+ results in de-novo[1] formation of one molecule of HCO-3




1: a new.

# Renal Mechanism cont.

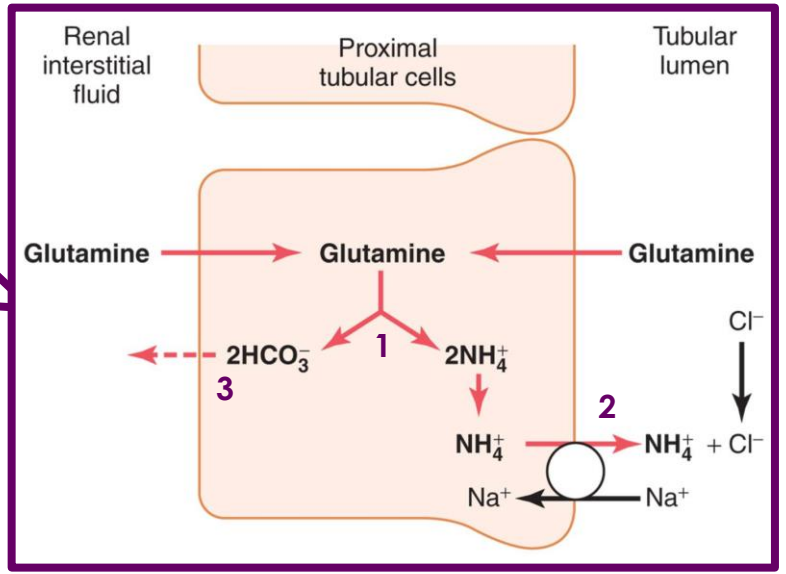
## Formation & Secretion of Ammonium ($NH_4$+)

**1.** Glutamine is present in the tubular cells and it gets metabolized into 2 bicarbonate and $2NH_3$ and those $2NH_3$ will bind to hydrogen and form $NH_4$

**2.** $NH_4$ will be secreted to bind with chloride and be excreted later on in urine.

**3.** The new 2 bicarbonate that has been formed will go back to blood.

THIS HAPPENS IN THE PROXIMAL TUBULES




Ammonia = $NH_3$
Ammonium $NH_4$+

# Renal Mechanism cont.

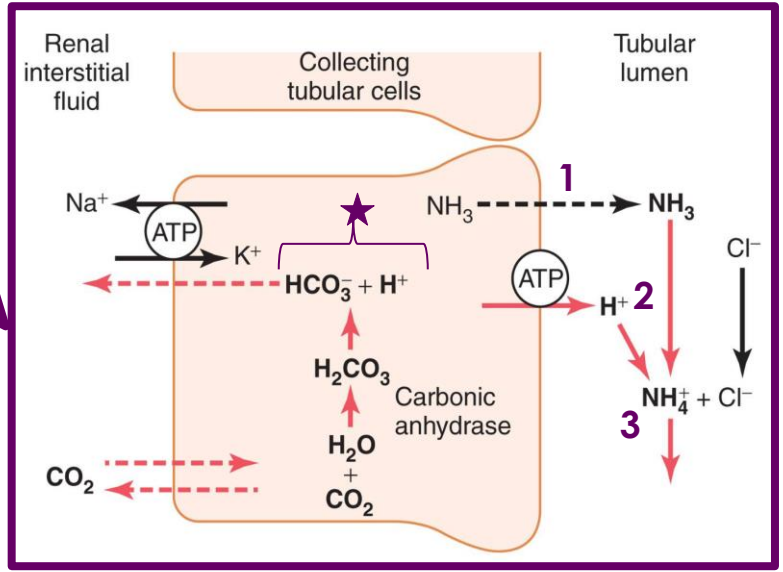
## Buffering of H+ Secretion By Ammonia ($NH_3$)

THIS HAPPENS IN COLLECTING TUBULES

Here ammonia will catch the H+ outside the cell.

1. $NH_3$ freely diffuses into the lumen from cells
2. Associate with H+ that has been secreted in the lumen to form $NH_4$+
3. Which is trapped in the lumen and excreted.

★**Again, the loss of a $H^+$ from the cell creates de-novo synthesis of a $HCO_3^-$ molecule to be reabsorbed.**




Ammonia = $NH_3$
Ammonium $NH_4$+

## ACID BASE MNEMONIC (ROME)

**R** Respiratory

**O** Opposite

pH ↑ $PCO_2$ ↓ Alkalosis

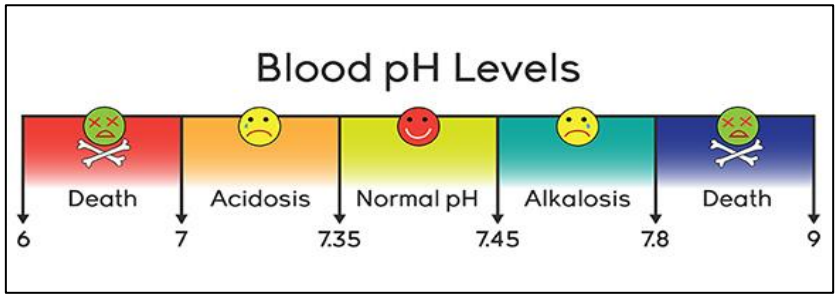
pH ↓ $PCO_2$ ↑ Acidosis

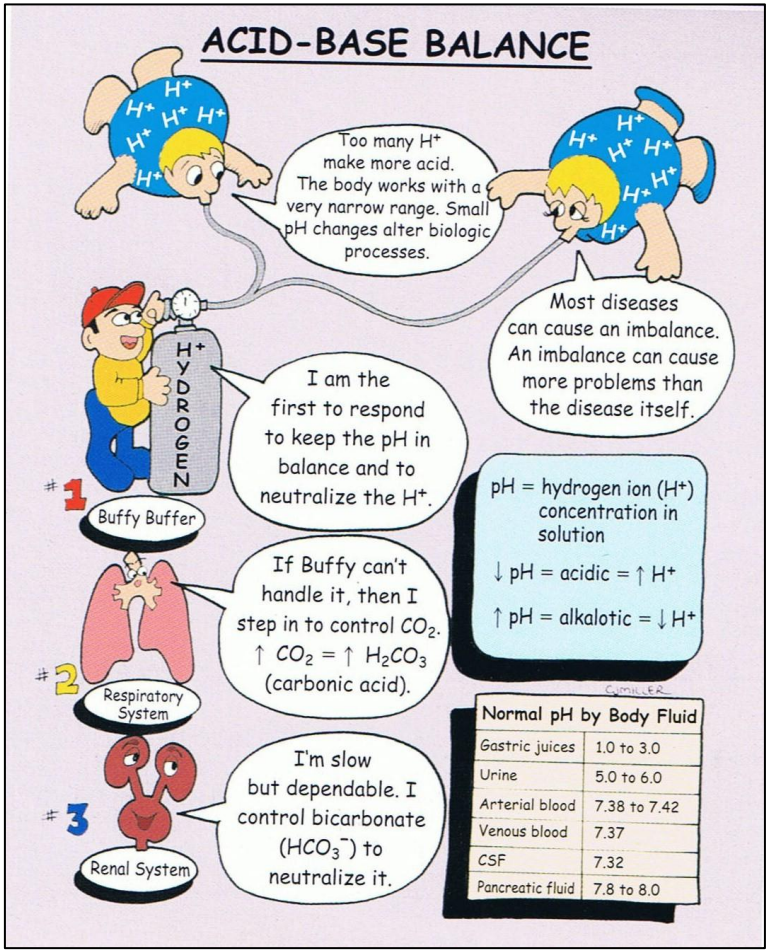
**M** Metabolic

**E** Equal

pH ↑ $HCO_3$ ↑ Alkalosis

pH ↓ $HCO_3$ ↓ Acidosis

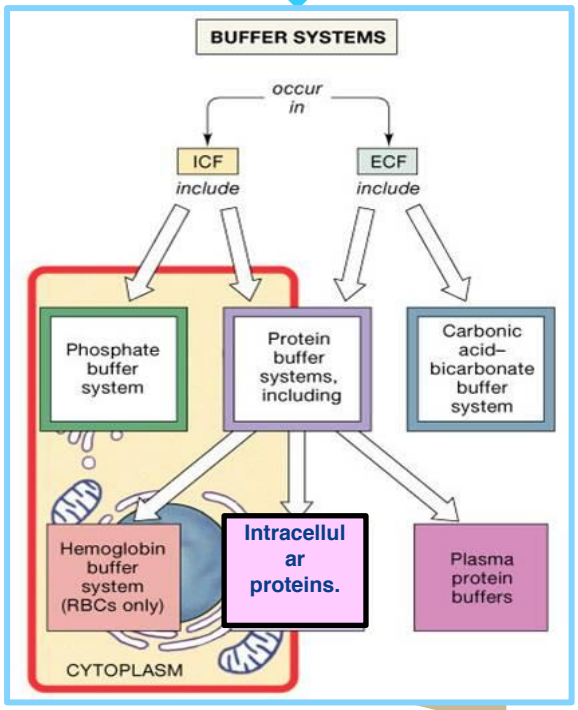



Summary

## Body defense against changes in pH:

### First line of defense against PH shift (Chemical buffer system):




### Second& Third line of defense against PH shift ( Physiological buffers):

**Respiratory mechanism:** (Co2 excretion)

- Powerful, but only works with **volatile acids($CO_2$)**
- Doesn't affect **fixed acids** like lactic acid
- -Body pH can be adjusted by changing rate and depth of breathing.

**Renal mechanism:** (H+ excretion)

**Three main processes:**

- Reabsorption of filtered bicarbonate.
- Generation of new bicarbonate.
- Excretion of H+ and urine acidification.

**- For the kidney to continue excretion of acidic urine, the excreted H+ has to be buffered by two buffer systems in the renal tubules:**

Ammonia

Phosphate buffer:

| Bicarbonate Buffer: | Phosphate Buffer: | Protein Buffer: |
|---|---|---|
| - It acts both **extracellular** and **intracellular**.<br>- It is the most **abundant**.<br>- **Most** important extracellular buffer: the two components are regulated as: **CO2** by the lungs, **HCO3-** by the kidney. | **Major** intracellular buffer and important buffer in **renal tubules**. | **Abundant** buffers especially **intracellular** |

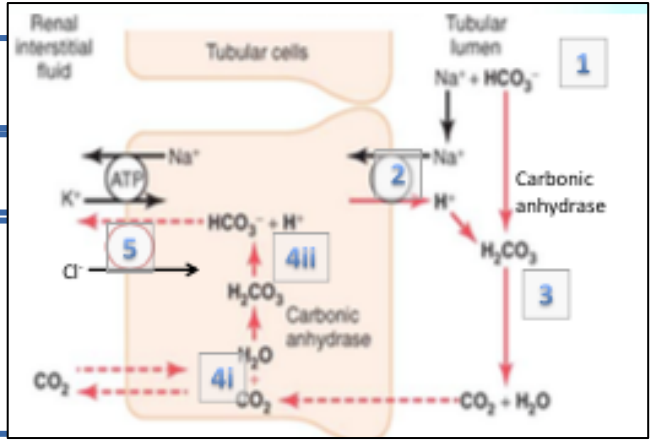
Summary

# -Secretion of H+ and Reabsorption of $HCO_3$-

**Keep in mind that for each HCO3- reabsorption, a H+ must be secreted.**

Occurs in all tubule Except: descending and ascending loop of Henle.

- The reabsorption of HCO3- in this segment of the nephron (PCT & diluting segment) does **not** lead to **net secretion** of H+ because the secreted H+ binds with the filtered HCO3-
- Also the secreted H+ in this segment **does not lead to a significant drop in tubular pH.**

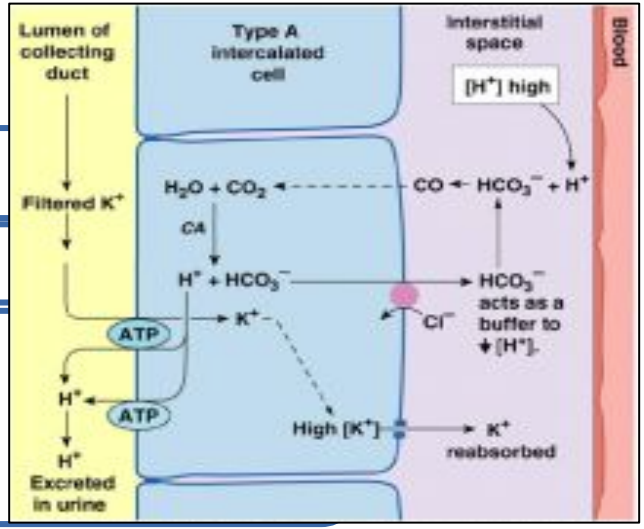



# - Primary Active H+ secretion (H + ATPase)

**For each H+ molecule secreted in this segment one HCO3- molecule is formed and reabsorbed.**

**- Occurs in the intercalated cells of distal & collecting tubules.**

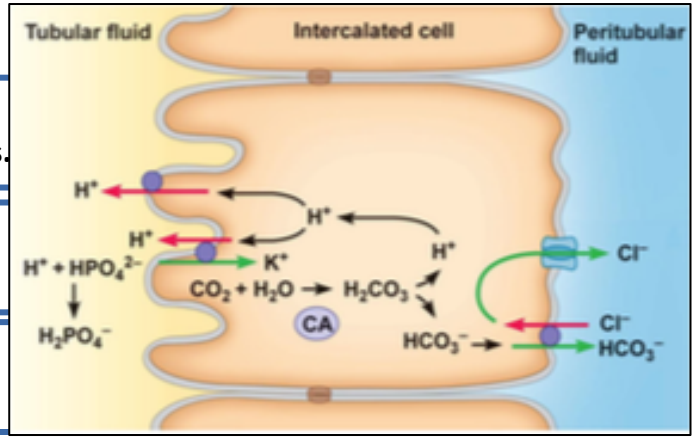
- **Most of this H+ is secreted in combination with urinary buffers; phosphate & ammonia**
- **This secretion can decrease pH of tubular fluid to 4.5, which is the lowest pH achieved in normal kidney. It is responsible for urine acidity.**




Summary

- **Generation of new HCO3- :H+**

**buffering by ammonia & phosphate(Why?)**




Because H+ reduced tubular pH 4.5. This is the lower limit that can be achieved in normal kidneys. Further decrease will cause tubular acidosis.

**What is the most important buffer of renal tubules?**

Ammonia because excreted two H+ and formation two $HCO_3$-

**When there is excess H+ in the extracellular fluid, the kidney:**

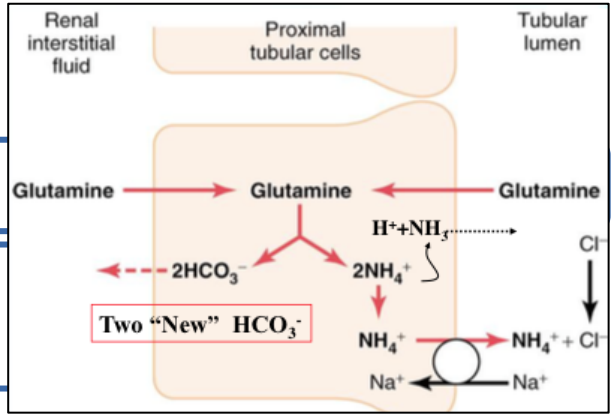
1. Absorb all filtered HCO3-
2. Secrete excess H+
3. Generate new HCO3-

## Ammonia (NH3)

(Generation of new HCO3- and secretion of H+: )

Production and secretion of NH4+ and HCO3- by proximal, thick loop of Henle and distal tubules.

Acidosis → metabolize of glutamine into Two NH3 (ammonia) and Two HCO3 → Two H+ will bind with two NH3 to form two NH4 (ammonium) → Secreted of NH4 to tubules → NH4 bind with Cl to form ammonium chloride → excreted with urine

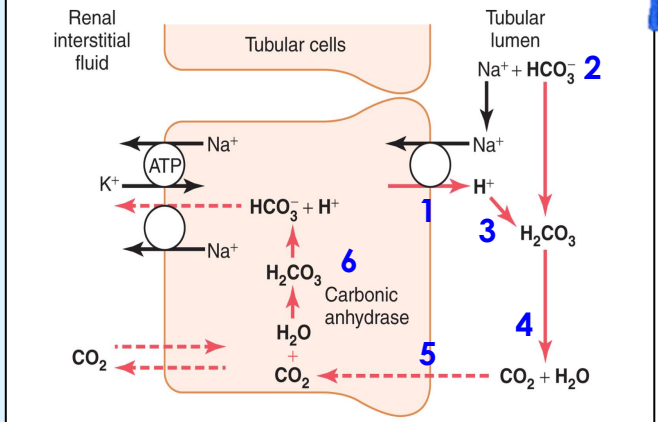



Summary

# STORY TIME

## Reabsorption of filtered $HCO_3$ ( In PCT, Thick ascending & Early DCT )

**1.** Hydrogen ion will be secreted by sodium hydrogen antiporter
-this hydrogen wont cause the pH of the tubular fluid to be acidic
عشان على طول راح يمسك بال bicarbonate.
**2.** The filtrated bicarbonate should be reabsorbed.
**3.** راح تمسك بال secreted hydrogen
**4.** وتحولها ل $CO_2$ and water
**5.** That will easy go inside the cells and then inside the cells
**6.** it will find carbonic anhydrase that will turn it to bicarbonate and hydrogen.

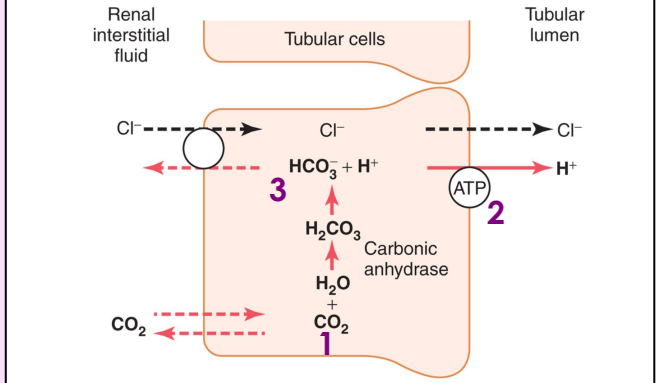



## Primary Active H+ secretion ( In interclated cells of distal tubule & collecting tubules)

**1.** $CO_2$ is present by cell metabolism, and this is used to secrete 1 new bicarbonate and 1 new hydrogen that is going to be secreted.

**2.** This secreted hydrogen here is responsible for acidification of urine, وطلعت بقوة عشان ماراح يقابلها bicarbonate
فمارضت تطلع إلا يوم عطيناها فلوس.. ATP

**3.** New bicarbonate formed!!



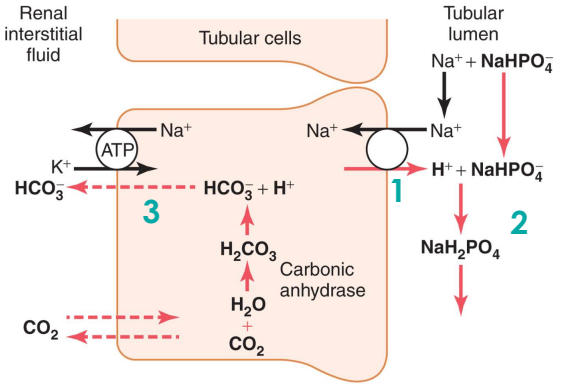

Summary

# STORY TIME

## Buffering of H+ Secretion By Filtered Phosphate ($NaHPO_4$)

It's kind of the same story as when the H+ was pumped, but the different this time, that the H+ is present in large amount! and we need this H+ to be secreted and never coming back! It needs to be buffered!! in this case $NaHPO_4$ is the hero that is gonna catch the H+ and sacrifice himself with her in the urine..

1. H+ is secreted in exchange with Na.
2. The $NaHPO_4$ Found her and caught her then he was converted to $NaH_2PO_4$
3. New bicarbonate formed!!




## Production and Secretion of Ammonium ($NH_4$) (in PCT)

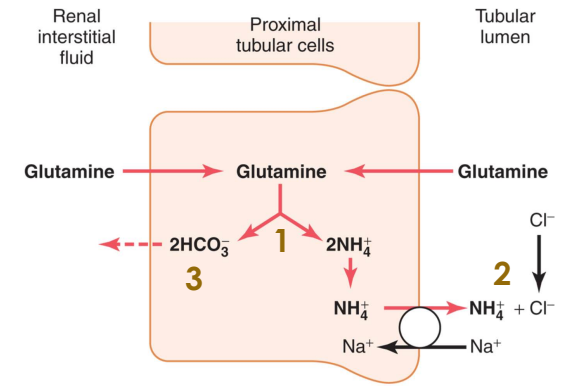
القصة هنا، انو في Glutamine.

1. Once this Glutamine is metabolized to 2 bicarbonate and 2 $NH_4$

في الحقيقة $NH_4$ ماراح تطلع على طول راح يسبقها $NH_3$ وهي المسؤولة انها تمسك الهيدروجينة وبعدين راح تصير $NH_4$

2. This $NH_4$ will be secreted.. but it will find Cl in the lumen, They'll bind and be secreted in the urine together with the H+ happily!

3. Remember the 2 new bicarbonate that has been formed!




Summary

# STORY TIME

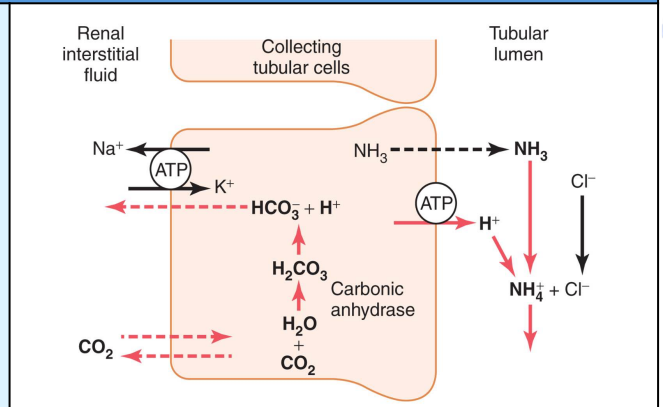
## Buffering of H+ Secretion By Ammonia ($NH_3$) (in Collecting Tubules)

Glutamine نفس سالفة

بس هذه المرة ماراح يمسك الهيدروجينية جوا الخلية ويطلع فيها، راح يطلع ويمسكها من برا.

Meaning

1. $NH_3$ freely diffuses into the lumen from cells
2. Will find the H+ that has been pumped from that ATPase in they'll to form $NH_4$+
3. Which will then find its Cl bound with it and excrete in urine happily... ever after.




# THE END

HOPE THAT WAS HELPFUL!

I KNOW YOU WILL MISS OUR STORIES....I KNOW WILL DO...

Summary

**1- Which one of the following is NOT a chemical buffer?**
A. Bicarbonate buffer system
B. Respiratory mechanism
C. Protein buffer system

**2- The concentration of bicarbonate in blood is:**
A. 27 mEq/L
B. 23 mEq/L
C. 37 mEq/L

**3- Major intracellular buffer is:**
A.Bicarbonate
B. Protein
C. Phosphate

**4- The lowest PH achieved in normal kidney is:**
A. 4.5
B. 6.8
C. 7.4

**5- Which one of the following is the best buffer in the renal tubule and tubular fluid?**
A. Ammonia
B. Phosphate
C. Bicarbonate

**6- The major source for production of ammonium within the proximal tubular cells is:**
A. Valine
B. Glutamine
C. Tyrosine

**7- What is the correct sequence of events?**
A. Conversion of $H_2CO_3$ to $CO_2$ and $H_2O$
B. Conversion of $HCO_3$ to H+ and $CO_3$
C. Conversion of $H_2O$ to $CO_2$ and H+
D. None of the above

**8- Which is the best indicator of H+ excreted in urine?**
A. Urine pH
B. Filtered load of $HPO_4$
C. Filtered load of $NH_3$
D. Both A and B

**9- Which condition has the highest excretion of $NH_4$?**
A. Diabetic ketoacidosis
B. Chronic renal failure
C. Vomiting
D. None of the above

1.B
2.A
3.C
4.A
5.B
6.B
7.A
8.B
9.A

MCQs

**1- What are the buffer systems in the renal tubules that buffer the excreted H+?**
*Ammonia *Phosphate

**2- List the three things that the kidney will do when there is excess H+ in the extracellular fluid?**
*Absorb all filtered HCO3-
*Secrete excess H+
*Generate new HCO3-

**3- Why is it important to maintain pH of blood within normal range? Mention 2.**
*Prevent denaturing of enzymes
*Maintain normal function of synapses

**4- Mention 2 of the sources that makes our body produce more acids?**
*Acids taken with foods (such as proteins)
*Cellular metabolism produces $CO_2$.

**5- Why the phosphate buffer is important in renal tubules?**
*Becomes concentrated in the tubular fluid, so become powerful
*Its pKa = 6.8, which close to the pH in the tubular fluid of the distal nephron

**6- How the kidney regulates blood pH?**
By Reabsorption of filtered bicarbonate, Generation of new bicarbonate and Excretion of H+ .

THANK YOU FOR CHECKING OUR WORK!

# BEST OF LUCK

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