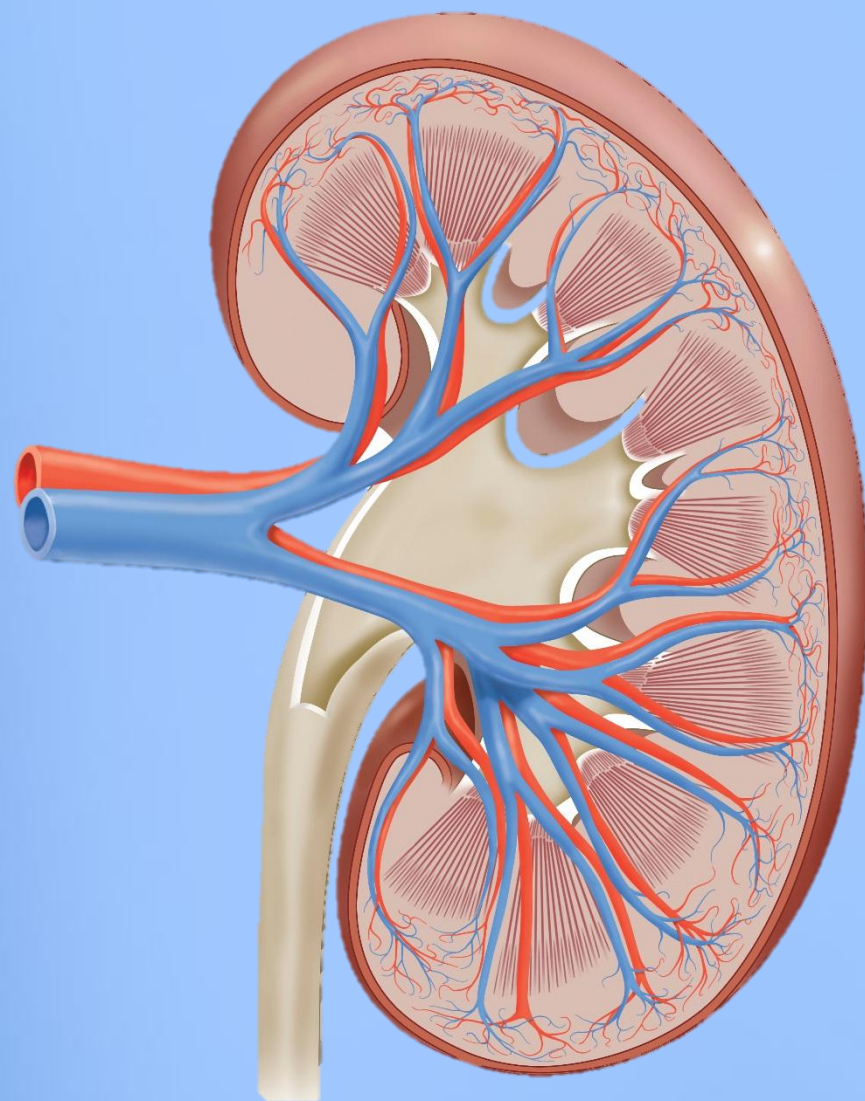


9&10

BASICS OF ACID BASE BALANCE & BUFFER SYSTEMS



Renal Block

Objectives

Basics of Acid-base balance:

- Define: acid and base.
- Explain what is meant by strong and weak acids and bases
- List and identify the names/formulas for the common strong acids and strong bases.
- To explain the role of Henderson-Hasselbalch equation in acid-base regulation

Buffer systems:

- To define buffer system and discuss the role of blood buffers and to explain their relevant roles in the body
- To describe the role of kidneys in the regulation of acid-base balance
- To describe the role of lungs in the regulation of acid-base balance

Basics of Acid Base Balance

Overview of pH

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What pH represent?

H⁺ concentration in the blood

What is the normal range of pH?

- in general: 0-14
- in the blood: 7.35-7.45
- Extracellular fluid (ECF): 7.4

What is the type of blood sample should be taken to measure pH and Why?

Arterial blood sample (not venous), because it represents the actual contents of blood such as Oxygen, nutrients.. Etc.

Does pH in the body change?

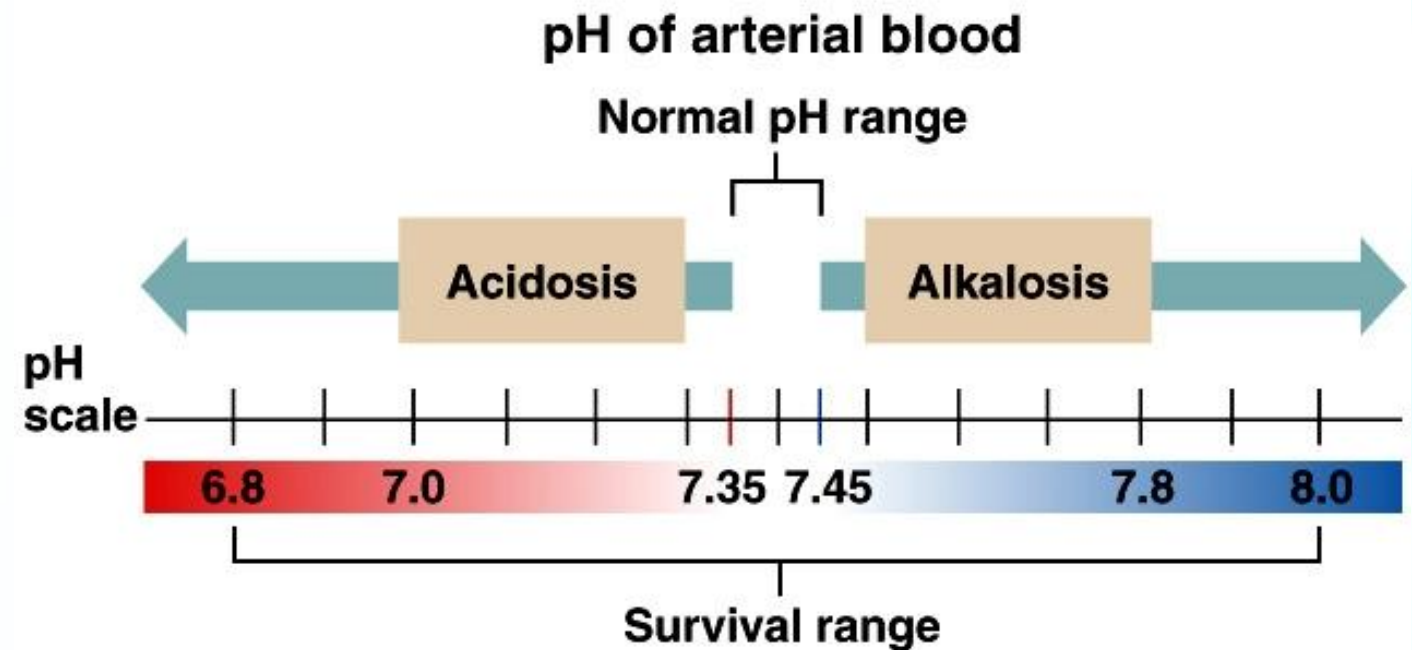
Yes, like exercise body will add some hydrogen to blood through lactic acid and change pH.

How can we calculate the pH?

pH= 1/H⁺ concentration log

OR

pH= - log [H⁺]



What is the survival range of pH in the blood?

Between 6.8 and 8. More or less will lead to death

When we said it is acidosis or alkalosis?

-pH less than 7.35 (acidosis)

-pH more than 7.45 (alkalosis)

Acids and Bases

What acids and bases?

- Acids are **H⁺ donors**
- Bases are **H⁺ acceptors**

Why acids more than bases in our bodies?

1. Food that contain **proteins** and **lipids** are rich in acids

2. The end cellular metabolism in mitochondria produced **CO₂** which **source of H⁺** from the following reaction:



Why venous blood is more acidic than arterial?

Because it has higher **CO₂ concentration** than arterial blood

Why pH tightly regulated and small changes in pH is a serious condition?

- Most enzymes work only in specific pH (change in pH → enzymes become inactive)
- Change in pH cause disturbance in electrolytes - Can affect some hormones
- Acidosis** can cause depression of synaptic ending and lead to coma such as a patient with **diabetes ketoacidosis and Hypercalcaemia**
- Alkalosis** can cause **convulsion**, **muscle twitching**, **tetany** and **hypocalcemia**

Strong and weak acids and bases

- **Strong acid** = **HCL** (complete dissociation)
- **Weak acid** = **Lactic acid, CO₂, H₂CO₃** “Carbonic acid” (Partial dissociation)
- **Strong base** = **NaOH** (complete dissociation)
- **Weak base** = **NaHCO₃, HCO₃** (Partial dissociation)

Buffer systems

Systems that regulate pH

-Chemical buffer system: (first line)

Buffer system (**immediately**)

-Physiological buffer system: (second line)

1. Respiratory system (**from minutes to hours**)

2. Renal system (**from hours to days**) **The most effective regulator of pH**

The component of chemical buffer system

1. Bicarbonate buffer (intracellular and **extracellular**)
2. Phosphate buffer (intracellular and **renal tubule fluid**)
3. Protein buffer (**the most important intracellular**)

What is the goal of chemical buffer systems?

Convert **strong acids and bases to weak acids and bases** to maintain blood pH

The most important feature of chemical buffers

pH of buffer must be the same or very close to the pH of sites that buffer work in. to observe the changes in pH.

First line of defense against pH shift

Chemical buffer system

Bicarbonate buffer system

Phosphate buffer system

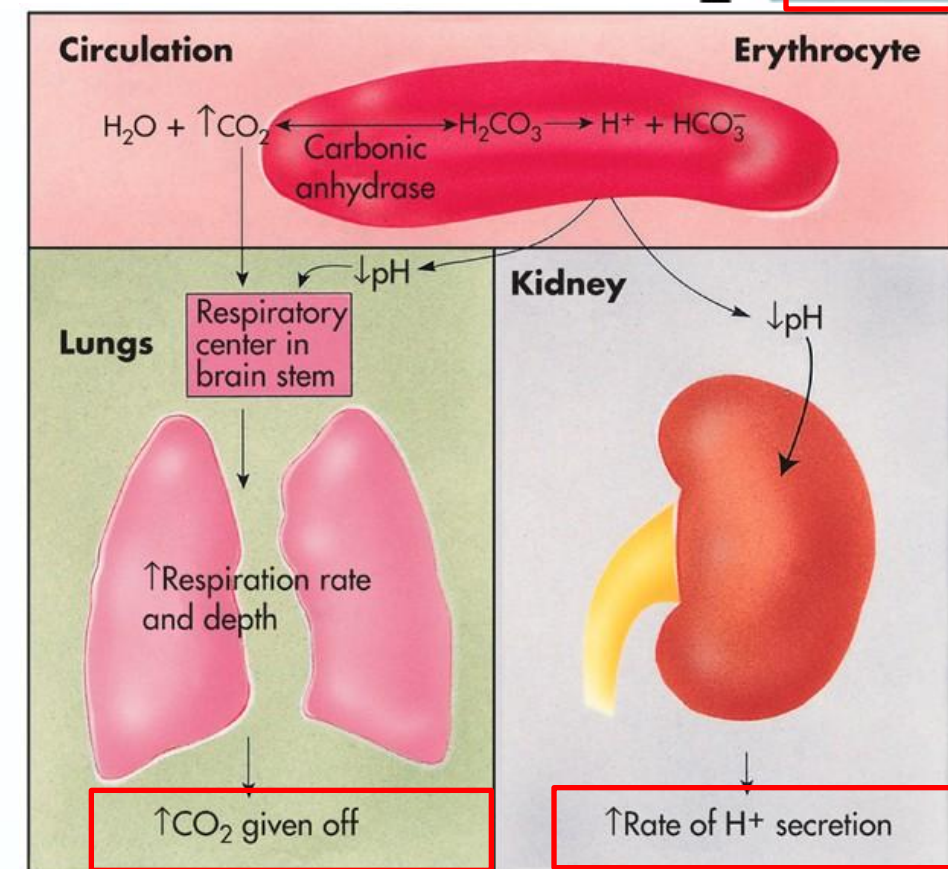
Protein buffer system

Second line of defense against pH shift

Physiological buffers

Respiratory mechanism
(CO₂ excretion)

Renal mechanism
(H⁺ excretion)



• Bicarbonate buffer

What are the components of bicarbonate buffer system?

-**Sodium bicarbonate:** NaHCO_3 regulated by kidney

-**Carbonic acid:** H_2CO_3 regulated by lungs through equation:



Why it is the most important extracellular buffer system?

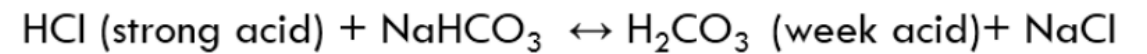
Because it regulated by kidney and lungs

What is the concentration of HCO_3^- in the blood and what it is called?

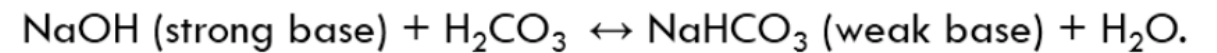
Its concentration in blood equals = 27mEq/L and is called alkali reserve.

How bicarbonate buffer work?

We must have acid and base to react with each other. Then:



OR



How can we calculate blood pH through bicarbonate buffer?

By **Handerson-Hasselbalch equation:**

$$\text{pH} = 6.1 + \log \frac{\text{HCO}_3^-}{0.03 \times \text{PCO}_2}$$

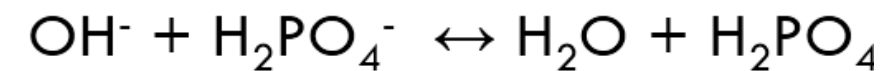
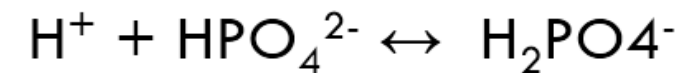
Note that 6.1 represent pH of the buffer not the blood

• Phosphate buffer

What are the components of bicarbonate buffer system?

-Hydrophosphate: HPO_4 which bind to H^+ to Increase pH

-Dihydrophosphate: H_2PO_4 which bind to OH^- to Decrease pH



Why it is the most important kidney or renal tubules buffer system?

Because it has pH that so close to the pH of fluid in the tubules

pH of phosphate is around 5 (acidosis) because of that it works inside the cell

• Proteins buffer

-Hemoglobin:

Carboxyl group gives H^+ “Decrease pH”

Amino group accept H^+ “Increase pH”

-Plasma proteins

-Intracellular proteins (the most important intracellular buffer)

the most important intracellular buffer as follow
1) Intracellular proteins buffer
2) Phosphate buffer
3) Bicarbonate buffer

Respiratory mechanism

What are the components of system?

The only component regulated here is **CO₂ (carbon dioxide)** which is **volatile acids**. It cannot deal with **fixed acids** such lactic acids that accumulate in skeletal muscles. **(Fixed acids is regulated by kidneys)**

What is the general mechanism?

pH can be adjusted by changing **RATE** and **DEPTH** of breathing.

Patient with acidosis → Hyperventilation → wash out CO₂ → increase pH

Patient with alkalosis → Hypoventilation → retain CO₂ → Decrease pH

What happened if a healthy person has FAST hyperventilation?

He will stop ventilation after 15 seconds because amount of CO₂ reduced and **chemoreceptors** in the brain will observe this reduction. Therefore, it will inhibit ventilation.

What happened if a healthy person has chronic hyperventilation?

Patient with **Anorexia** will develop alkalosis due to reduction in CO₂.

Renal mechanism

What is the normal secretion of H^+ and reabsorption of HCO_3 per day?

Secretion H^+ = 4400 mEq/day

Filtration HCO_3 = 4320 mEq/day

So, the 80 that remains must be titers by ammonia and phosphate buffer systems

What is the general mechanism?

Secretion of H^+ :

1. Sodium/ H^+ counter transport (PCT, Thick ascending loop and early DCT)
2. H^+ pump (Late DCT and collecting ducts) “phosphate buffer”
3. Secretion of H^+ with ammonia “ammonia buffer”

Reabsorption of HCO_3 :

1. Reabsorption of 99% of filtered HCO_3 (PCT, Thick ascending loop and early DCT)
2. Generate a new one HCO_3 by intercalated cells (Late DCT and collecting ducts) “phosphate buffer”
3. Generate new two HCO_3 from glutamine “ammonia buffer”

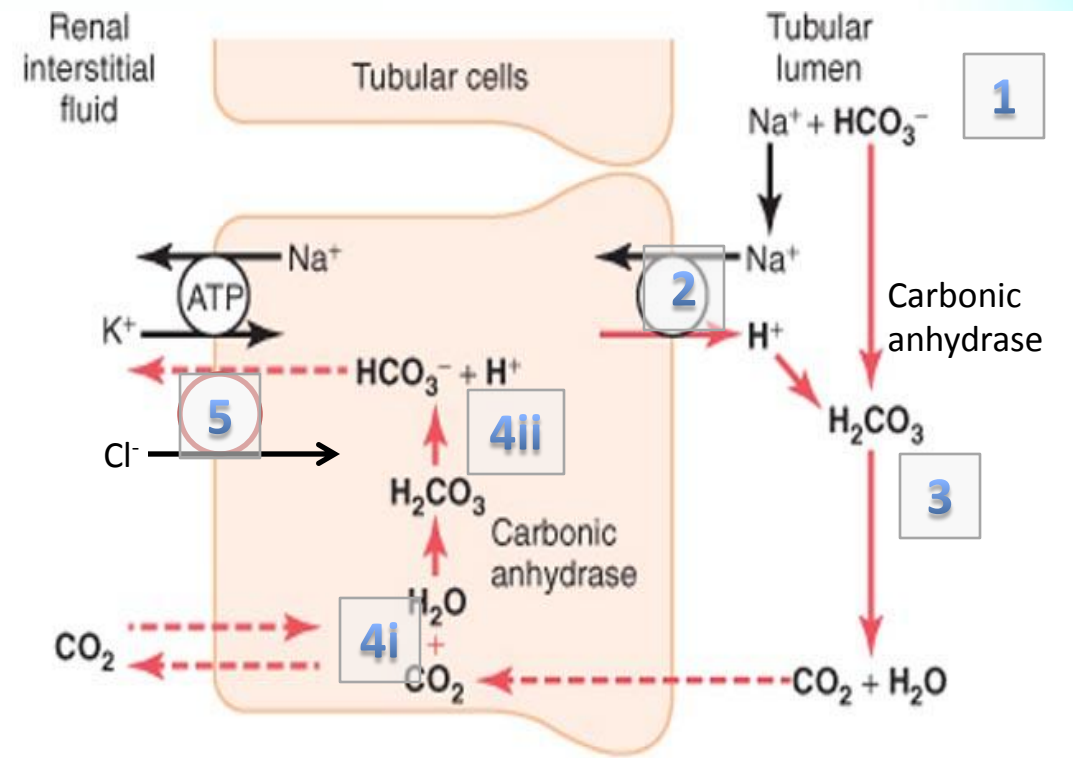
SECRETION OF H⁺ AND REABSORPTION OF HCO₃⁻

H⁺ secretion and HCO₃⁻ reabsorption occur in all parts of tubules EXCEPT:

1- descending and

2- thin ascending loop of Henle.

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



- Carbonic anhydrase is an enzyme that combines HCO₃⁻ with H⁺ to make H₂CO₂. And dissociates H₂CO₃ to H⁺ and HCO₃⁻
- Carbonic anhydrase inhibitors will create alkaline urine > body won't be able to excrete H⁺ and reabsorbed H₂CO₃. (Will be discussed in 1st pharmacology lecture)
- **In renal failure the body won't be able to do this function, which result of acidosis.**

**In circulation : reabsorption of HCO₃⁻ by counter – transport with Cl.
In the tubules lumen : reabsorption of HCO₃⁻ by counter – transport with Na.**

1

Bicarbonate is filtered in glomeruli

2

tubules secrete H⁺ by Na-H Counter-transport (secondary active transport)

3

H⁺ is combined with HCO₃⁻ to form Carbonic acid which is converted to Co₂ + H₂O by carbonic anhydrase

4

CO₂ diffuses into the cell passively and
i- combines again with H₂O by carbonic anhydrase to form carbonic acid which
ii- dissociates to H⁺ and HCO₃⁻

5

H⁺ is excreted into the lumen (step 1) and HCO₃⁻ backs into the circulation by counter-transport with Cl.

HOW THE KIDNEY DOES SYNTHESIS A NEW BIOCARBONATE?

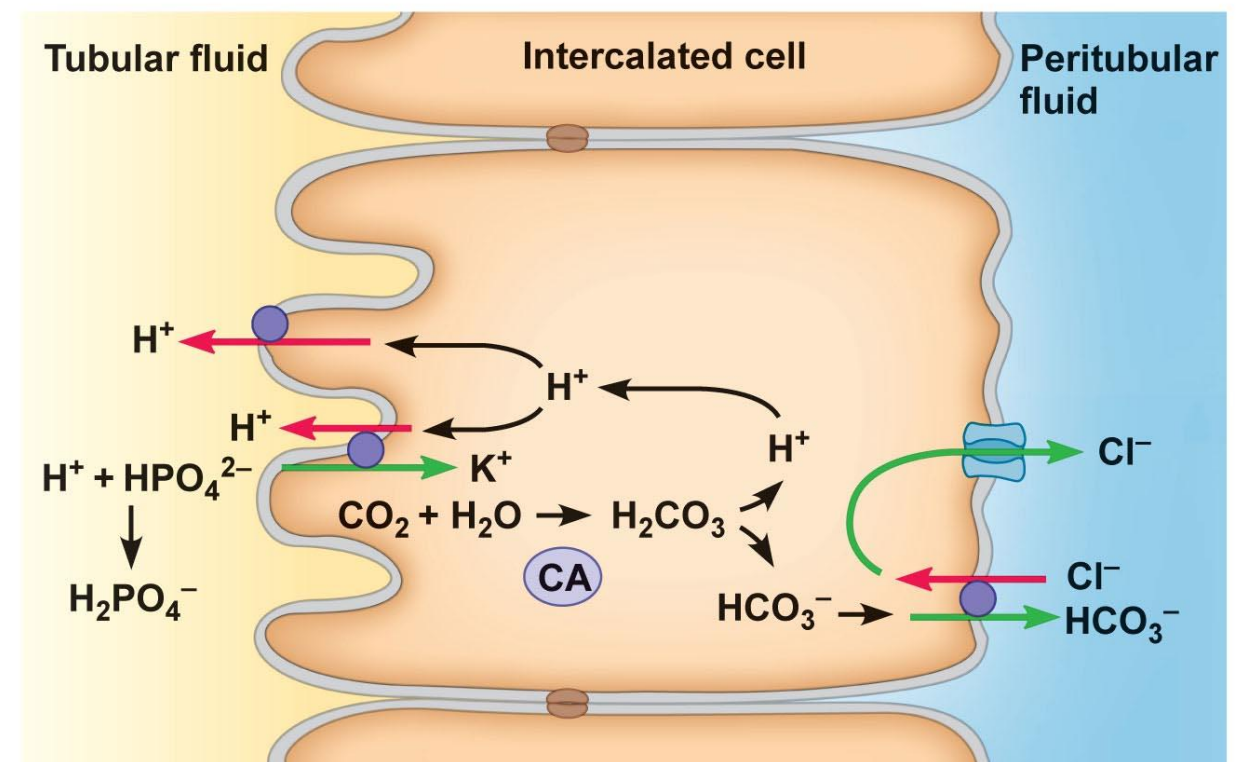
Why there is a buffer system for tubules by ammonia and phosphate?

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 or phosphate?

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

- No filtrated Bicarbonate in tubules
- CO_2 binds to H_2O to form H_2CO_3
- H_2CO_3 dissociates to bicarbonate and H^+
- Bicarbonate is secreted back to blood as “new bicarbonate synthesized by metabolism”
- H^+ is pumped into the tubular fluid. And it will bind to monohydrate phosphate (buffer of tubules)



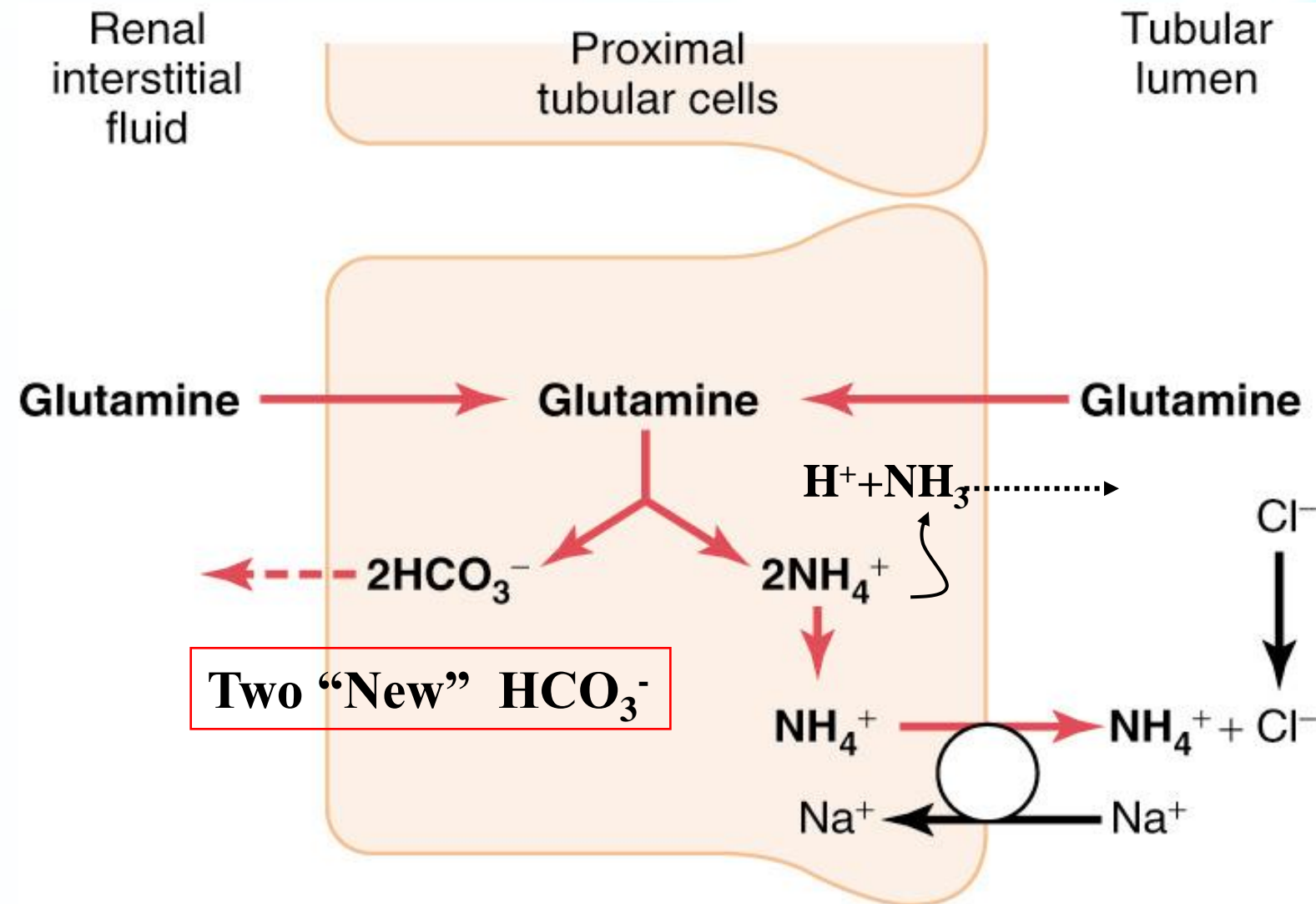
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Ammonia

Ammonia buffers H^+ and form Ammonium

Acidosis \rightarrow metabolize of glutamine into **Two NH_3** (ammonia) and **Two HCO_3^-** \rightarrow Two H^+ will bind with **two NH_3** to form **two NH_4^+** (ammonium) \rightarrow Secreted of NH_4^+ to tubules \rightarrow NH_4^+ bind with Cl^- to form ammonium chloride \rightarrow excreted with urine

PRODUCTION AND SECRETION OF NH_4^+ AND HCO_3^- BY PROXIMAL, THICK LOOP OF HENLE, AND DISTAL TUBULES



MCQS

1-What pH represent?

- A-CO₂ concentration
- B-HCO₃ concentration
- C-H⁺ concentration
- D-OH⁻ concentration

2-Which of the following is a strong base?

- A-HCl
- B- NaOH
- C-HCO₃
- D-H₂CO₃

3-A patient with acidosis. He may develop:

- A-Coma
- B-Convulsion
- C-Tetany
- D-muscle twitching

4-Venous blood is more acidic than arterial blood due to:

- A-CO₂ concentration
- B-HCO₃ concentration
- C-H⁺ concentration
- D-OH⁻ concentration

5- Which of the following is a protein buffer:

- A-Albumin
- B-Myosin
- C-Actin
- D-Hemoglobin

6-generation of new HCO₃ take place in:

- A- PCT
- B- DCT
- C- Collecting ducts
- D- Intercalate cells

7-Which of the following is a part of mechanism of phosphate buffer?

- A- generation of two HCO₃
- B- generation of two HPO₄
- C- generation of one HCO₃
- D- generation of one HPO₄

8-Ammonia will excreted in the urine as:

- A-Ammonium
- B-Ammonia
- C-Ammonium phosphate
- D-Ammonium chloride

Ans: 1-C, 2-B, 3-A, 4-A, 5-D, 6-D, 7-C, 8-D,