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

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?
P 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:
   
   \[ \text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \]

Why venous blood is more acidic than arterial?

Because it has higher CO₂ concentration than arterial blood

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)

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

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Buffer systems
**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.
Bicarbonate buffer

What are the components of bicarbonate buffer system?
- **Sodium bicarbonate**: NaHCO₃ regulated by kidney
- **Carbonic acid**: H₂CO₃ regulated by lungs through equation:
  \[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \]

Why it is the most important extracellular buffer system?
Because it regulated by kidney and lungs

What is the concentration of HCO₃ 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:

\[ \text{HCl (strong acid)} + \text{NaHCO}_3 \leftrightarrow \text{H}_2\text{CO}_3 \text{ (week acid)} + \text{NaCl} \]

**OR**

\[ \text{NaOH (strong base)} + \text{H}_2\text{CO}_3 \leftrightarrow \text{NaHCO}_3 \text{ (weak base)} + \text{H}_2\text{O}. \]

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: $\text{HPO}_4^{2-}$ which bind to H+ to Increase pH
- Dihydrophosphate: $\text{H}_2\text{PO}_4^-$ 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

$\text{H}^+ + \text{HPO}_4^{2-} \leftrightarrow \text{H}_2\text{PO}_4^-$

$\text{OH}^- + \text{H}_2\text{PO}_4^- \leftrightarrow \text{H}_2\text{O} + \text{H}_2\text{PO}_4$  

**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 HCO3 per day?

*Secretion H+ = 4400 mEq/day*
*Filtration HCO3 = 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 HCO3:**
1. Reabsorption of 99% of filtered HCO3 (*PCT, Thick ascending loop and early DCT*)
2. Generate a **new one HCO3** by *intercalated cells* (*Late DCT and collecting ducts*) “phosphate buffer”
3. Generate **new two HCO3** from glutamine “ammonia buffer”
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.

**Bicarbonate is filtered in glomeruli**

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

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

3. **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-**

4. **H+ is combined with HCO3- to form Carbonic acid which is converted to Co2 + H2O by carbonic anhydrase**

5. **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.
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 HCO3

- No filtrated Bicarbonate in tubules
- CO2 binds to H2O to form H2CO3
- H2CO3 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)
Ammonia buffers H+ and form Ammonium

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
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,