5

BIOCHEMISTRY

faculty of medicine - JU2017

☒ Sheet ☐ Slides

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Buffers in human body: -

Enzymes and proteins are active and stable only at a certain pH, so we must maintain the pH of active enzymes in our body (blood, cells, etc.).

- In our blood, the pH should range between **(7.35-7.45)**, any pH out of this range is a pathological condition.
- In our cells the pH should be **6.9 - 7.4** (wider range).
- In lysosomes the optimal pH for protein/sugar degradation is around 5.5

For this reason, we have a lot of buffers that can be used to help our body to maintain its appropriate pH, the following are some examples:

Remember:

A buffer is a molecule that can donate or accept H+ when the pH is disturbed

1- Carbonic acid/bicarbonate system (major in ECF (blood)).

2- Dihydrogen phosphate/monohydrogen phosphate system (in cells)

→ **Notice**: the pH in our cells is around 7.4 and the buffering capacity for monophosphate buffer is (6.2-8.2), therefore it is an excellent buffer.

Also, ATP, glucose-6-phosphate, diphosphoglycerates (RBC) can act as buffers inside cells.

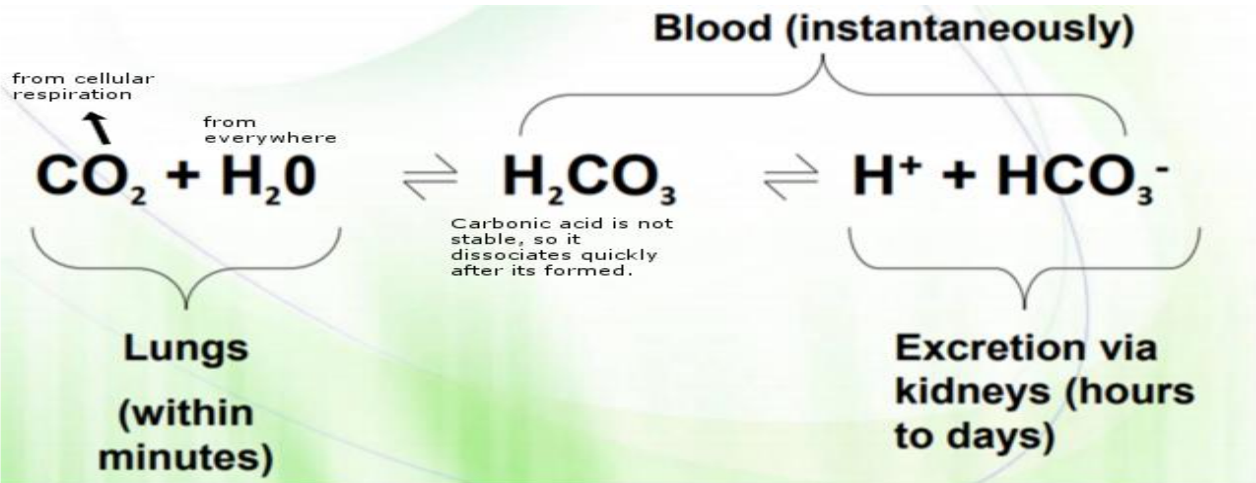
3-Proteins: Proteins are very important buffers because they consist of amino acids which can donate or accept H^+.

Examples of proteins:

A- Hemoglobin in blood which exists in very large quantities.

B- Other proteins in blood and cells.

Bicarbonate buffer:



↑ This equation is totally balanced by two major organ systems: **LUNGS AND KIDNEYS.**

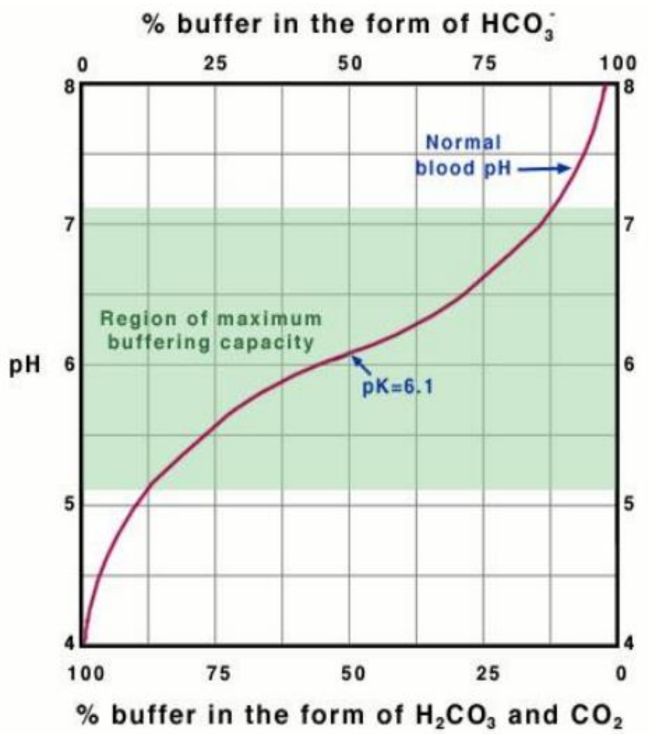
It can also be represented in two separate equations →

$$CO_2(d) + H_2O \xrightleftharpoons{K_h} H_2CO_3$$
$$H_2CO_3 \xrightleftharpoons{K_a} H^+ + HCO_3^-$$

NOTICE (in the picture):

The pka of bicarbonate buffer is 6.1 so the capacity ranges between (5.1-7.1), but the blood pH is 7.4!!!

The best explanation for this is that the range (5.1-7.1) is only true for a closed system (no interaction with the surroundings) like in a tube.



Carbonic acid/ bicarbonate pair is important for many reasons:

1- It is in an open system (continually interacts and exchanges with the environment), your body can control rate of breathing to maintain pH (unconsciously).

2- Bicarbonate is present in a relatively high concentration in the ECF (24mmol/L) (can be controlled easily) (20 to 1 ratio with carbonic acid).

3- The components of the buffer system are effectively under physiological control: the CO_2 by the lungs, and the bicarbonate by the kidneys.

So, the buffer acts as a first line defense against pH change, the kidneys are the second line of defense and lungs are the third.

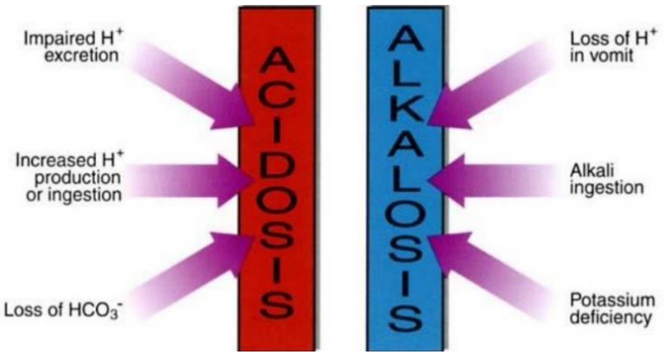
Pathological conditions:

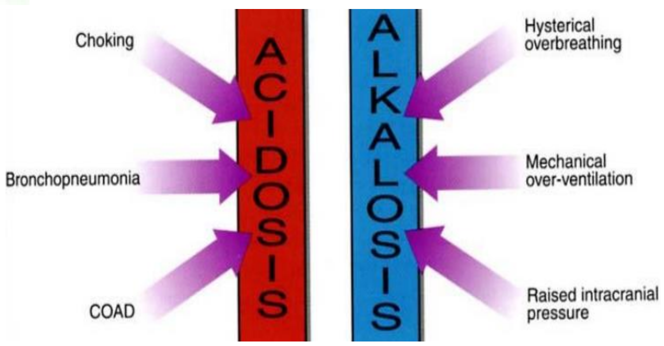
There are two abnormal conditions that results from pH change, these conditions can be either metabolic or respiratory conditions, depending on the affected organ.

	1- Acidosis (pH<7.35)		2- Alkalosis (pH>7.45)	
TYPES	Metabolic (defective kidneys)	Respiratory (defective lungs)	Metabolic	Respiratory
CAUSES	1-Production of ketone bodies (starvation): Diabetic people or in Ramadan the body is full of ketone bodies **which are acidic**, organs use them as a source of energy, they are produced from fatty acids). 2- low secretion of bicarbonate 3- when you take a lot of aspirin	Pulmonary (asthma;emphysema) Happens when CO_2 is accumulated in the body=> more H_2CO_3=> more H^+ => less pH	1-Administration of salts or bases. 2-High secretion of bicarbonate from kidneys	**Hyperventilation (anxiety)** The Panic Attack (afraid of something) causes Vertigo because you can't control your breathing, the body automatically controls the rate of breathing (coma), the best solution is to breath is a bag to increase the CO_2 %.
Processes	Low HCO_3^- => more acid dissociates=> more H^+=> less pH	Difficulties in breathing =>CO_2 accumulates in the body=> more H_2CO_3=> more H^+ => less pH	High HCO_3^-=> more CO_2=> less H^+ => high pH	hyperventilating (low CO2)=> decrease in H+=> high pH

***Remember the main equation ***

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



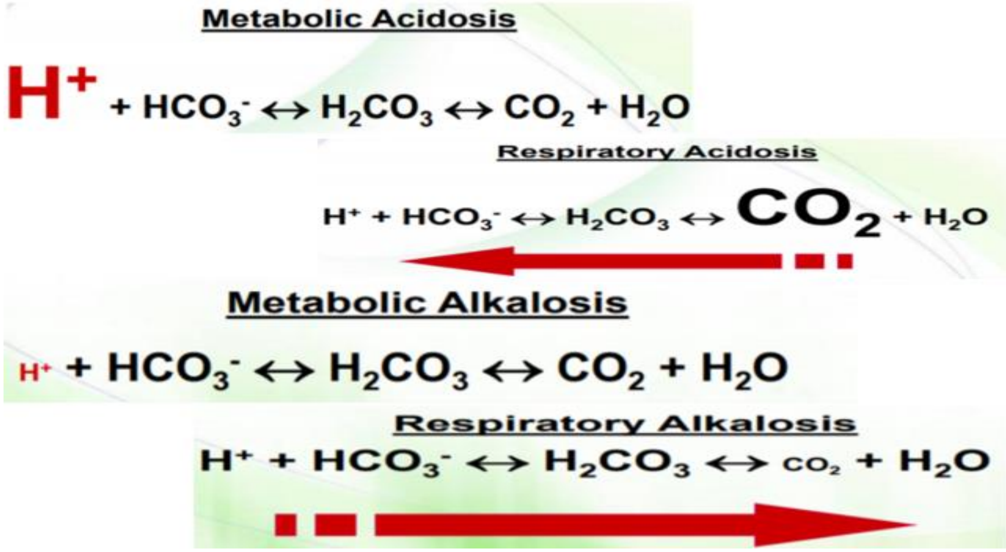


↑↑ Metabolic disorders

↑↑ Respiratory disorders

Memorize only the main cases from above, but it's better to know them all.

Processes from slides:



Compensation:

The body always tries to return the pH to its normal range.

The compensation is either respiratory or metabolic.

Problem	Metabolic	Respiratory
compensation	Respiratory	metabolic

This makes sense, because if the problem is in the kidney (metabolic), the kidney can't repair itself, so the compensation is done by the lungs (respiratory) and vice versa.

NOTICE: in the equation, the only two things that can be controlled are HCO3$^-$ (by the kidneys) and CO_2 (by the lungs).

Acid-Base Disorder	Primary Change	Compensatory Change
Respiratory acidosis	pCO_2 up	HCO_3^- up
Respiratory alkalosis	pCO_2 down	HCO_3^- down
Metabolic acidosis	HCO_3^- down	PCO_2 down
Metabolic alkalosis	HCO_3^- up	PCO_2 up

$$H^+(aq) + HCO_3^-(aq) \rightleftharpoons H_2CO_3(aq) \rightleftharpoons H_2O(l) + CO_2(g)$$

All the arrows in this sheet depend on this equation

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

		Problem (respiratory)		Compensate (metabolic)	
Case	Cause	CO2	Reaction	HCO3-	Reaction
1	Hypoventilation (hold your breath)	↑	→	↑	←
2	Hyperventilation (breath quickly)	↓	←	↓	→

	Problem(metabolic)		Compensate(respiratory)		solution
case	HCO3-	Reaction	CO2	Reaction	
3	↓	→	↓	←	Breath fast
4	↑	←	↑	→	Hold your breath

Compensation can be divided into full compensation and a partial one.

We measure the pH, the concentration of CO_2 and HCO_3^-

- if the concentrations of both, CO_2 and HCO_3^- are abnormal this means that the compensation has been completed.
- Now if the pH is normal, the compensation is full.
- If the pH is abnormal, the compensation is partial.

Full compensation

(study the picture first)

For further understanding:

1- when abnormal **(high)** concentrations of both CO_2 and HCO_3^- are present, there are two cases that are possible (the pH value determines the real cause):

	pH	pCO_2	HCO_3^-
Resp. acidosis	Normal But<7.40	↑	↑
Resp. alkalosis	Normal but>7.40	↓	↓
Met. Acidosis	Normal but<7.40	↓	↓
Met. alkalosis	Normal but>7.40	↑	↑

- High CO_2 is the primary problem, and high HCO_3- is caused due to compensation (case 1 in picture)
  This called <u>respiratory acidosis</u>.
- High HCO_3- is the primary problem and high CO_2 is caused due to compensation (case 4 in picture)
  This is called <u>metabolic alkalosis</u>.

2- When abnormal **(low)** concentrations of both CO2 and HCO3- are present, there are two cases that are possible (the pH value also determines the real cause):

- Low CO_2 is the primary problem and low HCO_3- is caused due to compensation. (case 2 in picture)
  This called respiratory alkalosis.
- Low HCO_3- is the primary problem and low CO_2 is caused due to compensation (case 3 in picture)
  This called metabolic acidosis.

Partial compensation:

	pH	pCO_2	HCO_3^-
Res.Acidosis	↓	↑	↑
Res.Alkalosis	↑	↓	↓
Met. Acidosis	↓	↓	↓
Met.Alkalosis	↑	↑	↑

The 4 cases are the same as full compensation, the difference is the pH value, here it is abnormal (below 7.35 or above 7.45).

Check your grasp of the previous concepts:

1) If the pH was high and the CO_2 was low but the HCO_3- was normal, what is the condition?
   - The pH is high ----> alkalosis
   - CO2 is high ----> problem is respiratory
   - HCO3- is normal ---> there is no compensation yet.
2) Mohammed Tariq used to live at sea level, but for some circumstances he moved to the mountains, would he suffer alkaloses or acidosis?
   - Since he will suffer hyperventilation (no enough O_2), it would be alkaloses.

In the end: You just have to focus on the main equation and know the main concept of equilibrium, concentrations, cases and disorders.

Useful links:

https://www.youtube.com/watch?v=ArmELNEfXs0 => Bicarbonate Buffer System and pH Imbalances
https://www.youtube.com/watch?v=lpBAEaBKusw => examples

GOOD LUCK!