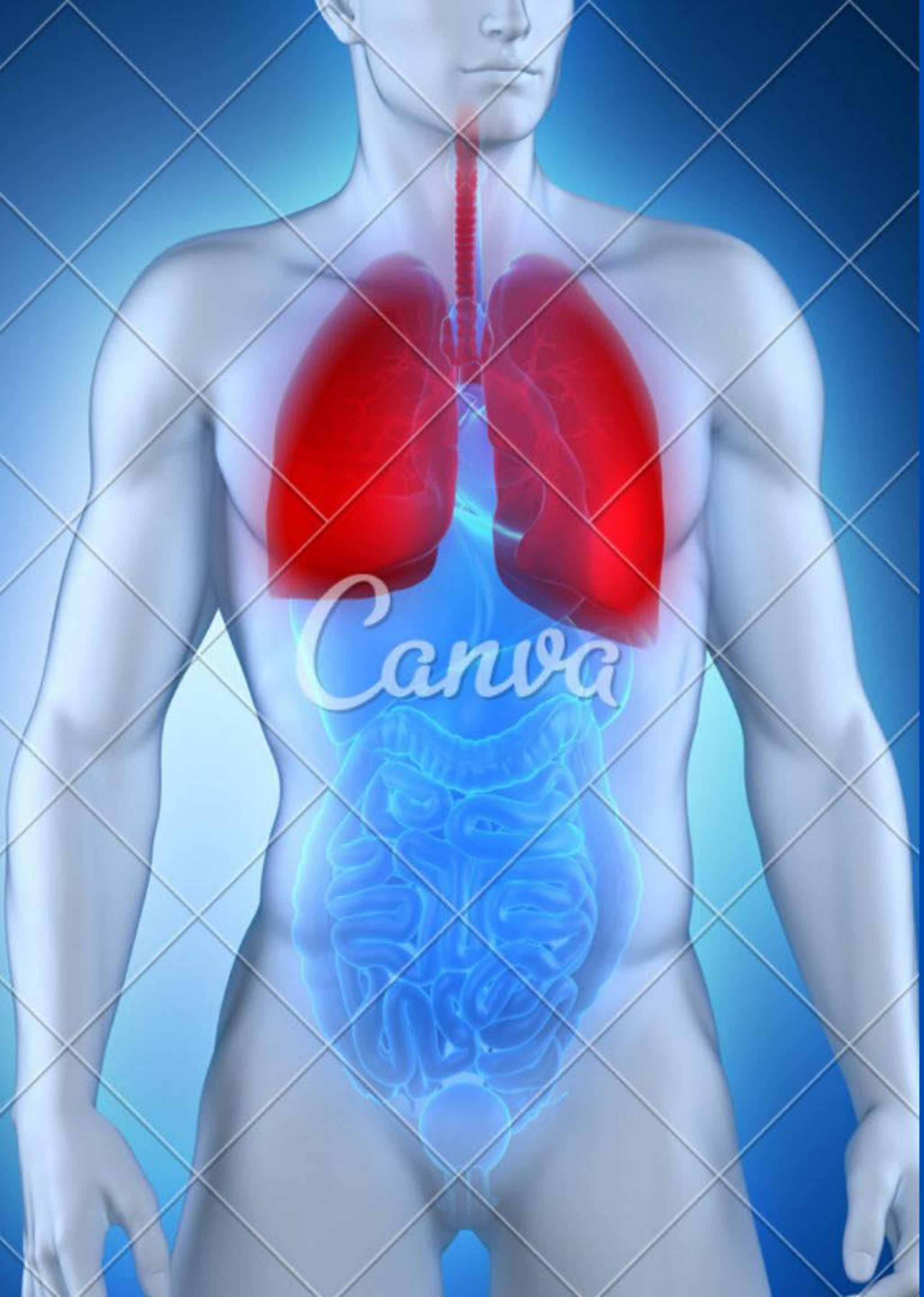


PASSION ACADEMIC TEAM

YU - MEDICINE

Sheet#

Lec. Date : 13-2-2020

Lec. Title : Acid-base balance

Written By :

If you come by any mistake , please kindly report it to shaghafbatch@gmail.com

RESPIRATORY SYSTEM

Acid-Base Balance

DR. MAZHAR AL ZO'UBI| RS-BIOCHEMISTRY

SOURCE: TEXTBOOK OF BIOCHEMISTRY FOR MEDICAL STUDENTS, CHAPTER 29: P 390-406

- According to the acid_base balance ,the function of respiratory system is to correct PH value.
- We gonna be attention on certain thinds which are → acidosis and alkalosis
- Acidosis→ increase H+ , decrease PH
- Alkalosis→ decrease H+ , increase PH
- ABG (arterial blood gas) : is one of the test we do to know these balances.

- In general we say acidosis and alkalosis but actually they have subtypes:
- Respiratory or metabolic acidosis.
- Respiratory or metabolic alkalosis.

Note that: our bodies don’t produce bases. So the metabolic alkalosis is due to hyperexecretion of hydrogen ions or depletion of acids.

- The PH value in our bodies is controlled by respiratory and renal system.

Definitions

Acids			Bases		
HA	$\rightleftharpoons$	$H^+ + A^-$	$NH_3 + H^+$	$\rightleftharpoons$	NH^+_4
HCl	$\rightleftharpoons$	$H^+ + Cl^-$	$HCO_3^- + H^+$	$\rightleftharpoons$	H_2CO_3
H_2CO_3	$\rightleftharpoons$	$H^+ + HCO_3^-$			

HCl	$\longrightarrow$	$H^+ + Cl^-$	(Complete)
H_2CO_3	$\rightleftharpoons$	$H^+ + HCO_3^-$	(Partial)

BUFFERS

Buffers are solutions which can resist changes in pH when acid or alkali is added

- In general we have two types of acids :
- Weak acids→ depend on the concentrations of dissociation and undissociation form.
- Strong acids→ which completely dissociated (ionized) in aqueous solutions.
- In the equation of H2CO3 (in previous slide) , both dissociated and undissociated form are found in order to H+(it determine how much H+ we have) → more acids, more H+

Table 29.1. Relation between hydrogen ions, hydroxyl ions and pH of aqueous solutions. Ionic product of water = $[H^+][OH^-] = 10^{-14}$

$[OH^-]$ mol/liter	$[H^+]$ mol/liter	log $[H^+]$	$-\log[H^+]$ =pH	pOH	Inference
1×10^{-13}	1×10^{-1}	–1	1	13	Strong acid
1×10^{-10}	1×10^{-4}	–4	4	10	Acid
1×10^{-7}	1×10^{-7}	–7	7	7	Neutral
1×10^{-4}	1×10^{-10}	–10	10	4	Alkali
1×10^{-1}	1×10^{-13}	–13	13	1	Strong alkali

Box 29.1. Terms Explained

Term	Definition and explanations
pH	Negative logarithm of hydrogen ion concentration. Normal value 7.4 (range 7.38 -7.42)
Acids	Proton donors; pH <7
Bases	Proton acceptors; pH > 7
Strong acids	Acids which ionize completely; e.g. HCl
Weak acids	Acids which ionize incompletely e.g. H_2CO_3
pK value	pH at which the acid is half ionized; Salt : Acid = 1 : 1
Alkali reserve	Bicarbonate available to neutralize acids; Normal 24 mmol/L (range 22-26 mmol/L)
Buffers	Solutions minimise changes in pH

EFFECTIVE RANGE OF A BUFFER

The effective range of a buffer is **1 pH unit higher or lower than pKa**

ACID-BASE BALANCE

Acidosis

If the pH is below 7.38, it is called acidosis.

Life is threatened when the pH is lowered below 7.25.

Acidosis leads to CNS depression and coma.

Death occurs when pH is below 7.0.

Alkalosis

When the pH is more than 7.42, it is alkalosis.

It is very dangerous if pH is increased above 7.55.

**Simply the *buffer system* is a solution that minimize the change of PH.

Box. 29.2. Mechanisms of Regulation of pH

First line of defense	**:**	**Blood buffers**
Second line of defense	**:**	**Respiratory regulation**
Third line of defense	**:**	**Renal regulation**

The most sensitive mechanism

As example→ if you have vomiting , you will wildly loss of H+ so the mechanism will be changed to the second or third one.

Predominant sources

*we mentioned previously that our bodies don't produce bases , so we have two choices:

1- ↑ produce of H+ → acidosis

2- ↑excretion of H+ → alkalosis

❑Our cells release between 50 and 100 mmol of H^+(النسبة الي بنتجها الجسم اصلا)

❑But the H^+ ion concentration maintained 40 nmol/L (pH 7.4)

وهاي النسبة ال لازم تكون موجودة بالجسم فقط (في فرق كبير بينهم لهيك لازم نطلع كتير هيدروجين)❑

- CO_2 (majority) →from the cellular respiration.
- Lactate
- Acetoacetate (keto-acids). (see the next slide ☺.
- During conversion of amino nitrogen to urea in the liver. → they will produce NH4+.
- Sulphydryl groups of some amino acids to sulphate. → cysteine and methionine.

* Acetoacetate (keto-acids).
It Occur in two situations :
1-pathological : like diabetes….
In diabetes the body can not consume glucose so it will shift to the lipids consumption → with consuming the lipids (especially fatty acids) , this breaking of fatty acids will produce acetyl CoA which will accumulates to form keton bodies which will go to the blood , this is toxic to our bodies (although it will be used from some tissues as brain.
2-physiological : starvation.

Protons are produced by metabolism

1. From carbon dioxide

Tissue metabolism of glucose, fatty acids and amino acids generates CO_2 which reacts with water in the presence of **carbonic anhydrase** to form carbonic acid which dissociates to produce bicarbonate and a proton. **This reaction means that carbon dioxide can be thought of as a weak acid**

$$CO_2 + H_2O \xrightarrow{\text{carbonic anhydrase}} H_2CO_3 \longrightarrow HCO_3^- + H^+$$

carbon dioxide + water → carbonic acid → bicarbonate + proton

2. Anaerobic glucose metabolism, ketogenesis and catabolism of methionine and cysteine produce protons

(i) The process of anaerobic glycolysis to form lactate produces protons

$$\text{glucose} \longrightarrow \text{lactate}^- + H^+$$

(ii) Similarly, protons are formed during the production of acetoacetate and β-hydroxybutyrate from fatty acids

(iii) **methionine** $\longrightarrow H_2SO_4 \longrightarrow SO_4^{2-} + 2\,H^+$

(iv) **cysteine** $\longrightarrow H_2SO_4 \longrightarrow SO_4^{2-} + 2\,H^+$

Buffer Systems

ICF	ECF	Erythrocytes
Phosphate & Proteins	**Bicarbonate & Phosphate**	**Hb & Phosphate**

1.ICF:

A-Phosphate: very effective buffer system. It's able to buffer until 3 PH values (because it has 3 H).

B. Protein: have amino acids, each one have side chain, especially acidic amino acids, they are controlling PH value.

Albumin: proteins in blood, they are doing a lot of functions; transporting, osmotic pressure as well as PH control.

Question…!

The histidine which has PK equal to 6.1, is the best buffer system in hemoglobin to control the PH of blood, which is 7.4,,, How?!

Answer…

The free histidine (unconjugated), has PK equal to 6.1, but when it's a part of protein, the PK will change to a higher value to be closer to 7.4.

Bicarbonate Buffer System

- The **normal bicarbonate level of plasma is 24 mM**
- The **normal pCO** of **arterial** blood is **40 mmHg.**
- The **normal carbonic acid** concentration in blood is **1.2 mM.**

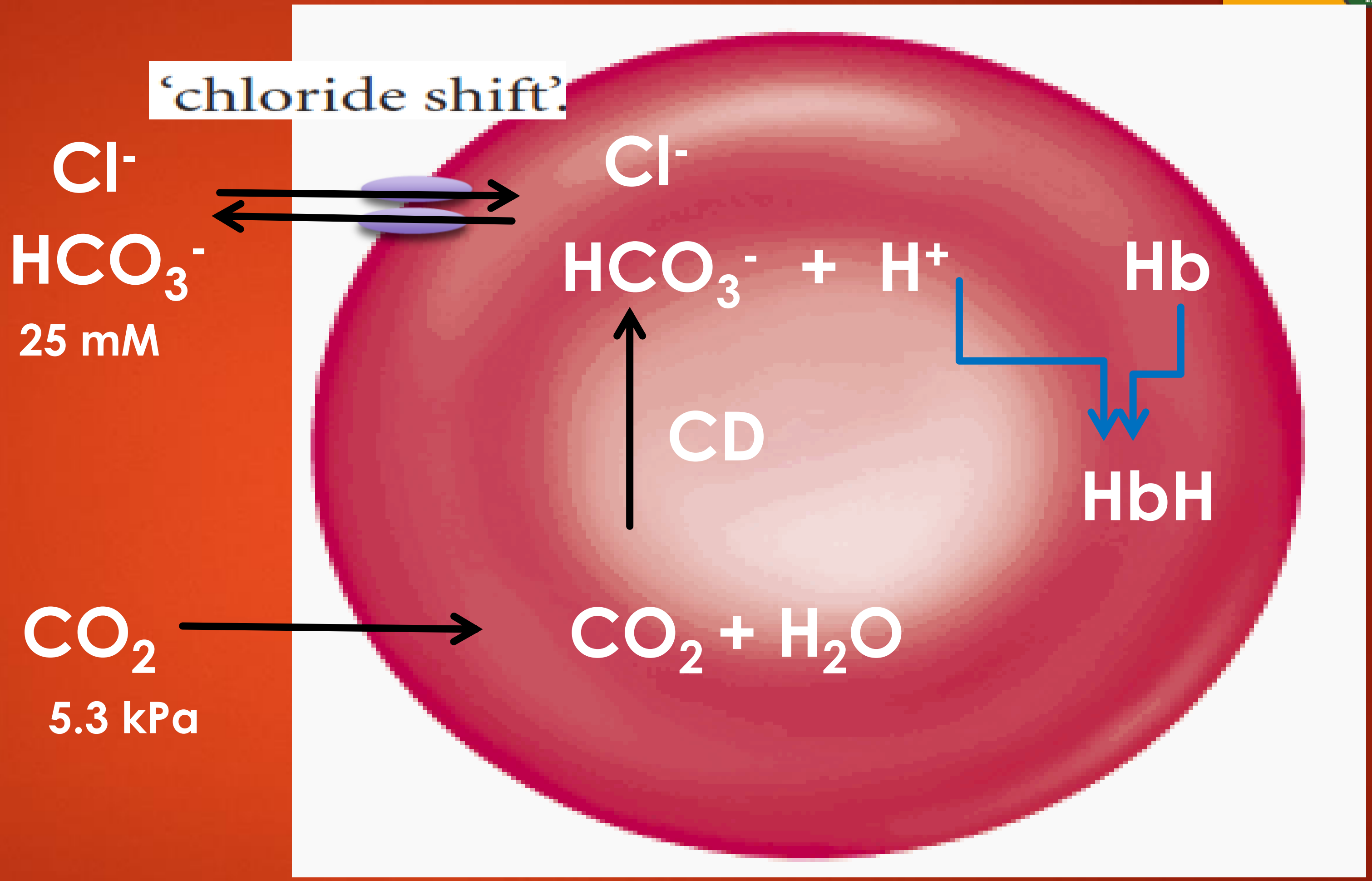
The ratio of bicarbonate to the carbon dioxide is20:1
It should be this value to have PH value equal to 7.4

$$pH = pKa + \log \frac{[HCO_3^-]}{[H_2CO_3]}$$

$$7.4 = 6.1 + \log \frac{24}{1.2}$$

$$= 6.1 + \log 20 = 6.1 + 1.3$$

Bicarbonate generation by erythrocytes

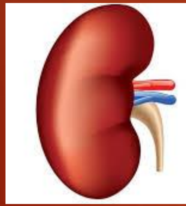


CD: carbon dehydrase enzyme. (which is found in RBCs)

Bicarbonate

- ***<u>The erythrocytes and renal tubular cells generate HCO_3^-</u>***

✓Erythrocyte mechanism makes fine adjustments



✓kidneys play the major role in maintaining HCO_3^- generation and H^+ elimination

Phosphate Buffer System ($H_2PO_4^-$)

- Mainly an **intracellular buffer**

$$pH\ (7.4) = pKa\ (6.8) + \log \frac{[salt]}{[acid]}$$

$$\text{or } 0.6 = \log \frac{[salt]}{[acid]}$$

Relative capacity of buffer systems

In the body:

- 52% buffer activity is in tissue cells.
- 6% in RBCs.
- Rest 42% is by extracellular buffers.
  - 40% buffering action is by bicarbonate system;
  - 1% by proteins
  - 1% by phosphate buffer

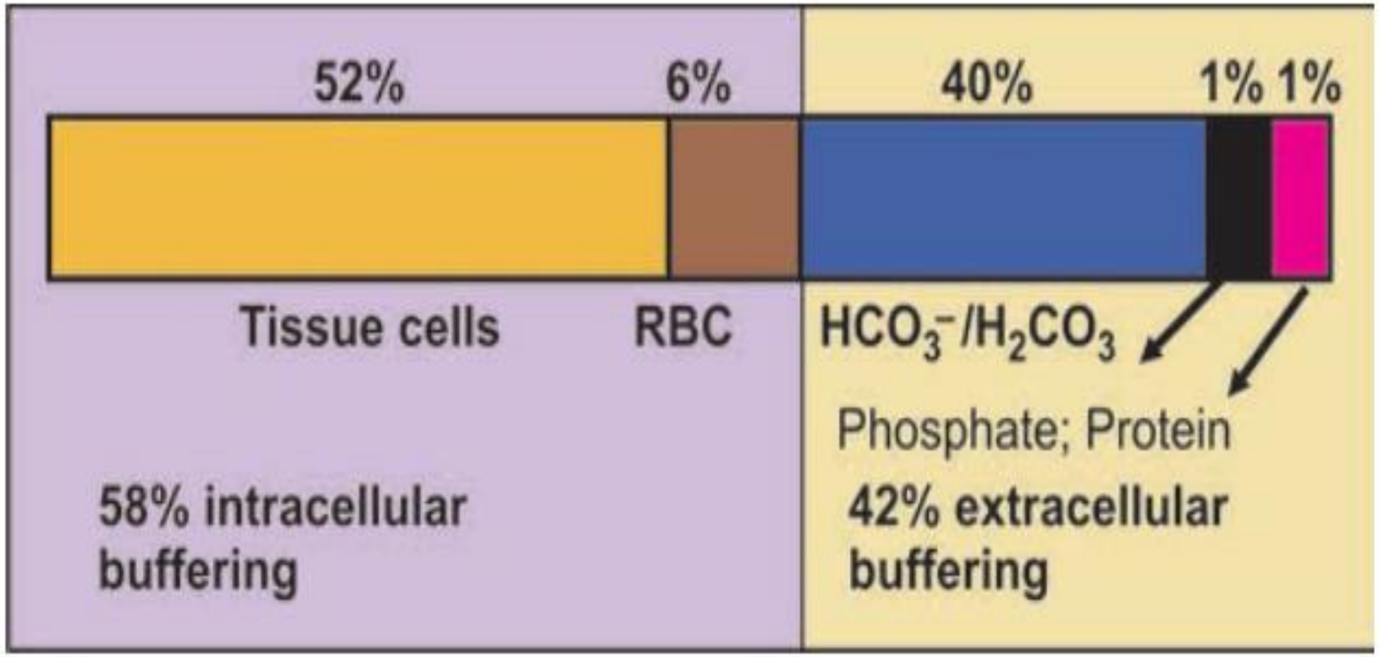


Fig. 29.1. Intracellular buffers play a significant role to combat acid load of the body

*If there is no response to any line of buffering, we should go to drugs that decrease the acidity in stomach (it's work as alkaline to solute condition).

* We are controlling our PH by 2 major systems; cells and extra cellular components, (which with each other, make 100% of buffer system).

CO_2 is an essential component of the extracellular buffering system.

Healthy function of the **kidneys** and the **lungs** is required for normal acid–base homeostasis

RESPIRATORY REGULATION OF pH

- **The Second Line of Defense**
  - The chemoreceptors in the respiratory center are sensitive to changes in the pH of blood.
  - When there is an **acidosis**, the respiratory rate is increased (**hyperventilation).**
  - **Immediate response not prolonged** →in compare with renal system.

- The respiratory system do either hyper or hypo ventilation.
- In order to reduce the ventilation process what's happens in our bodies?
- the concentration of CO_2 and PH value have sensors in aorta (carotid) , they are making sensation in your body, so we do hypo or hyper ventilation
- If you have hyper alkalosis, !?
- voluntary hyper ventilation (breathing in a bag) ; to respire the CO_2 again.

- **Action of Hemoglobin**
  - At acidosis (Tissues)

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3$$

$$H_2CO_3 \longrightarrow HCO_3^{-} + H^{+}$$

$$H^{+} + Hb^{-} \longrightarrow HHb$$

  - Lung side

$$HHb + O_2 \longrightarrow HbO_2 + H^{+}$$

$$HCO_3^{--} + H^{+} \longrightarrow H_2CO_3$$

$$H_2CO_3 \longrightarrow H_2O + CO_2$$

The activity of the carbonic anhydrase (also called carbonate dehydratase) increases in acidosis.