بسم ألله الرحمن الرحيم

Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Fluid, Electrolyte, and Acid-Base Balance

Part-2- Acid-Base Balance

2st Medical and Biochemistry (BIQC-101) Lecture

by

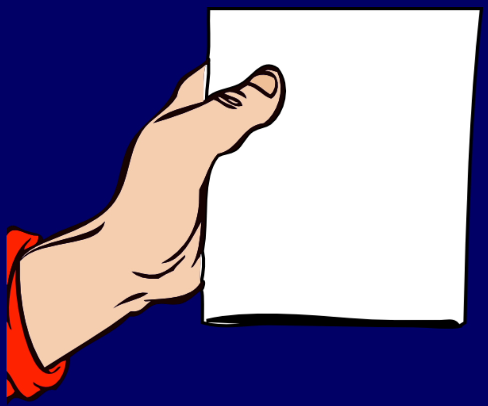
Prof. Dr. Salih Mahdi Salman

Acid-Base Balance

Learning Objective

1. Defines acids, bases.
2. Know the natural acids and bases ratio of the body.
3. Recognize the types of acid and base.
4. List the source of acids and bases of the body.
5. Study the systems responsible for maintenance of the acid-base balance.
6. Explain the role of buffer systems in regulating the pH of the intracellular fluid and the extracellular fluid.
7. Discuss acid base disorders
8. Analysis of Acid-Base Imbalances Report

List of Content



Introduction

- Maintaining of stable anion and cation concentrations in blood plasma is denoted as **isoionia**.
- Maintaining of constant proton (H^+) concentration is **isohydria**.
- Plasma and extracellular space concentrations of the protons are held in very **narrow physiologic range**.
- There is 40 nmol/l of protons in the arterial blood physiologically. (nmol/l↔mol/L 1 mol/L = 1000000000 nmol/l)
- pH is used for express concentration of the protons:

$$pH = -\log c(H^+)$$

- pH could be easily calculated as follows:

$$pH = -\log 40 \times 10^{-9} \text{ mol/l}$$

$$pH = 7.4$$

- Physiologic range of the pH **is (7.36-7.44).**

- Venous pH and pH of interstitial fluid is about 7.35.
- There is quite variable and lower pH value intracellular, it is about 7.0 ($[H^+]$ = 100 nmol/l).
- Intracellular pH compared to arterial pH gives difference 0.4
- This corresponds to fact that there is 2.5 fold difference between intracellular and arterial H^+ concentration.
- This concentration gradient drives the movement of H^+ from cells to blood.
- Extensive deviations of pH value can cause serious consequences. For example

1. Change of protein structure (i.e. enzymes)
2. Membranes permeability
3. Electrolyte distribution.

Acid-base Sources

- Source of acids in the body is chiefly metabolism , source of bases is predominantly nutrient.
- The mean sources of acid is presented by:-

1. Metabolic activities produce acids.
2. Aerobic respiration produce CO_2 which converted to carbonic acid by the reaction with water in presences of carbohydrase enzyme.

$$CO_2 + H_2O \xrightarrow{\text{carbohydrase}} H_2CO_3$$

3. Gluconeogenesis (transforms non-carbohydrate substrates such as lactate, amino acids, and glycerol into glucose).
4. Anaerobic glycolysis (the transformation of glucose to lactate) in muscles and erythrocytes

$$\text{Glucose} \rightarrow 2\ CH_3CHOHCOO^- + 2\ H^+$$

5. Ketogenesis – production of ketone bodies

$$\text{Fatty acids} \rightarrow \text{ketone bodies} + n\ H^+$$

6. Lipolysis

$$TAG \rightarrow 3\ FA + \text{glycerol} + 3\ H^+$$

6. Ureagenesis

$$CO_2 + 2\ NH^+_4 \rightarrow \text{urea} + H_2O + 2\ H^+$$

Type of Acid Found in the Body

1. Volatile acids or respiratory acids can leave body by external respiration (carbonic acid)
2. Non-volatile acids (metabolic acids) remain in body fluids until kidney excretion categorized to:-

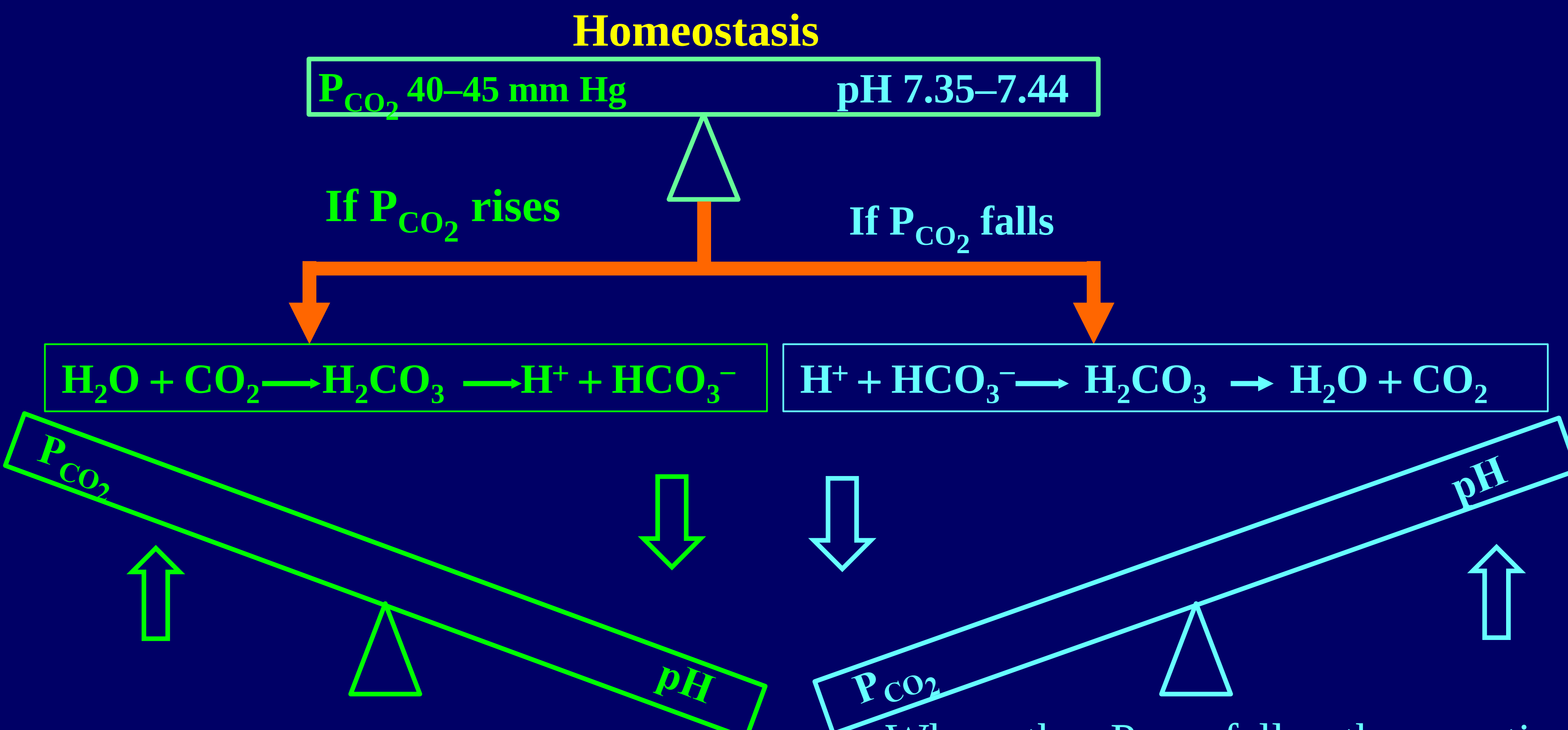
1) Organic acid: including: lactic acid , fatty acids. ,ketone bodies (acetoacetic acid, β-hydroxybutyric acid).
2) Inorganic acids: including sulphuric acid , hydrochloric acid and phosphoric acid

Acid-base Homeostasis

- Physiologic range of the pH is **(7.36-7.44).**
- Acid-base balance (Homeostasis) mean H^+ production = H^+ loss.
- Value of pH higher than 7.44 in arteries is denoted as alkalemia, pH lower than 7.36 is acidemia.
- Acidemia is more common due to acid-producing metabolic activities.
- Extensive deviations of pH value can cause serious consequences. For example

1. Change of protein structure (i.e. enzymes)
2. Membranes permeability
3. Electrolyte distribution.

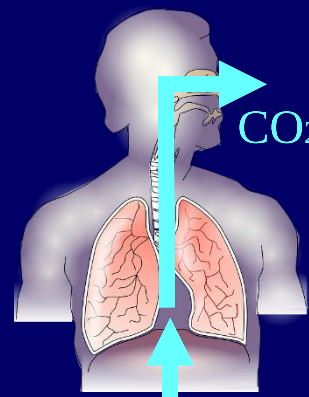
Acid-base Homeostasis



When carbon dioxide levels rise, more carbonic acid forms, additional hydrogen ions and bicarbonate ions are released, and the pH goes down.

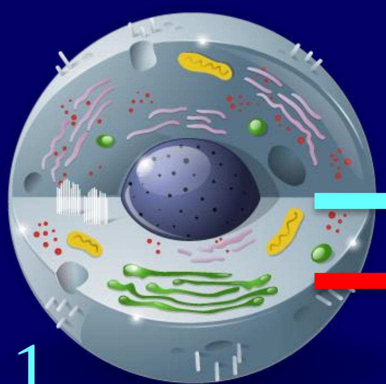
When the P_{CO_2} falls, the reaction runs in reverse, and carbonic acid dissociates into carbon dioxide and water. This removes H^+ ions from solution and increases the pH.

Four Factors Involved in the Maintenance of Acid-Base Homeostasis



2 **The respiratory system** plays a key role by eliminating carbon dioxide.

3 **The kidneys** play a major role by secreting hydrogen ions into the urine and generating buffers that enter the bloodstream. The rate of excretion rises and falls as needed to maintain normal plasma pH. As a result, the normal pH of urine varies widely but averages 6.0—slightly acidic.

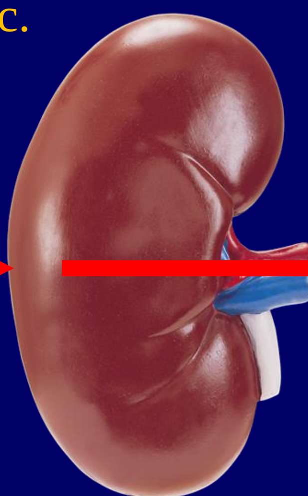


CO_2

H+

Normal plasma pH (7.35–7.44)

H+



1 **Active tissues**

Continuously generate carbon dioxide, which in solution forms carbonic acid. Additional acids, such as lactic acid, are produced in the course of normal metabolic operations.

Buffer Systems

4 **Buffer systems** can temporarily store H^+ and thereby provide short-term pH stability

Buffer Systems

Buffer: Substance that opposes changes to pH by removing or adding H^+ generally consists of:

1. Weak acid (HY)
2. Anion released by its dissociation (Y^-)

$HY \rightarrow H^+ + Y^-$ and $H^+ + Y^- \rightarrow HY$

- The major body buffer systems. all can only temporarily affect pH (H^+ not eliminated):

1. **Chemical buffer system**
   1) Phosphate buffer system ($Na_2HPO_4^{2-}$/ $NaH_2PO_4^-$)
   2) Carbonic acid–bicarbonate (HCO_3^- / CO_2) (HCO_3^- / H_2CO_3)
   3) Protein buffer categorized to:
      a) Amino acids buffer
      b) Hemoglobin buffer (Hb / $Hb\text{-}H^+$)
2. **Physiological Buffer systems**
   a) Respiratory System
   b) Renal System

Classification of Buffer Systems

Buffer Systems occur in:

- **Intracellular fluid (ICF)**
  - **Phosphate Buffer System**: Has an important role in buffering the pH of the ICF and of urine
  - **Protein Buffer Systems**: Contribute to the regulation of pH in the ECF and ICF; Interact extensively with the other two buffer systems
    - **Hemoglobin buffer system (RBCs only)**
    - **Amino acid buffers (All proteins)**
    - **Plasma protein buffers**
- **Extracellular fluid (ECF)**
  - **Carbonic Acid/Bicarbonate Buffer System**: Is most important in the ECF

Buffer	Plasma	Erythrocytes	Together
HCO_3^- / CO_2	35 %	18 %	53 %
Hb / Hb-H^+	–	35 %	35 %
Plasma proteins	7 %	–	7 %
Inorganic phosphate	1 %	1 %	2 %
Organic phosphate	–	3 %	3 %
Total	43 %	57 %	100 %

1. **Phosphate buffer system:** Buffers pH of ICF and urine. $HCl + Na_2HPO_4^{2-} \rightarrow NaH_2PO_4^- + NaCl$

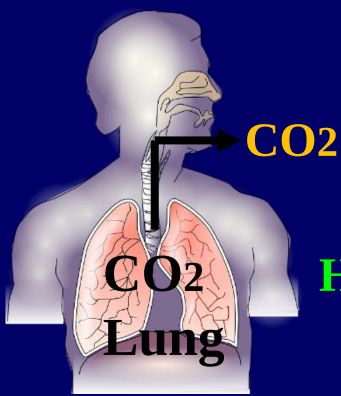
(strong acid) + (weak base) → (weak acid) + (salt)

$NaOH + NaH_2PO_4^- \rightarrow Na_2HPO_4^{2-} + H_2O$

(strong base) + (weak acid) → (weak base) + (water)

2. Carbonic acid–bicarbonate buffer system

Bicarbonate reserve : body fluids contain a large reserve of **HCO_3^-** , primarily in the form of dissolved molecules of the weak base sodium bicarbonate ($NaHCO_3$). This readily available supply of **HCO_3^-** is known as the **bicarbonate reserve**.



Carbonic Acid/ Bicarbonate Buffer System

$H_2O + CO_2 \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^- \leftarrow HCO_3^- + Na^+ \leftarrow NaHCO_3$

H_2CO_3 **(carbonic acid)**; HCO_3^- **(bicarbonate ion)**; $NaHCO_3$ (sodium bicarbonate)

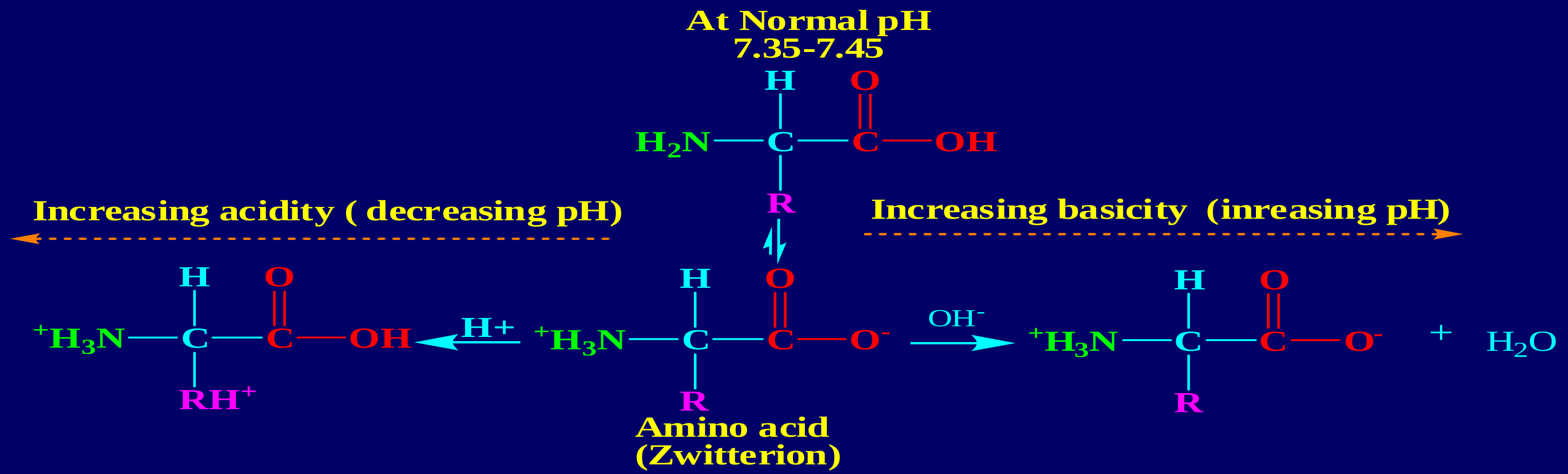
Start → **Addition of H^+ from metabolic activity**

The primary function of the carbonic acid–bicarbonate buffer system is to protect against the effects of the organic and fixed acids generated through metabolic activity. In effect, it takes the H^+ released by these acids and generates carbonic acid that dissociates into water and carbon dioxide, which can easily be eliminated at the lungs.

3. Protein buffer Systems

1. Amino acid buffers : (in ICF and ECF)

At the normal pH of body fluids (7.35– 7.44), the carboxyl groups of most amino acids have released their hydrogen ions.



If pH drops, the carboxylate ion (COO^-) and the amino group ($-NH_2$) of a free amino acid can act as weak bases and accept additional hydrogen ions, forming a carboxyl group (-COOH) and an amino ion ($-NH_3^+$), respectively. Many amino acids have acid or basic side chains (R-groups) such s (His, Lys, Arg, Glu, Asp) can also accept hydrogen ions, forming RH^+ .

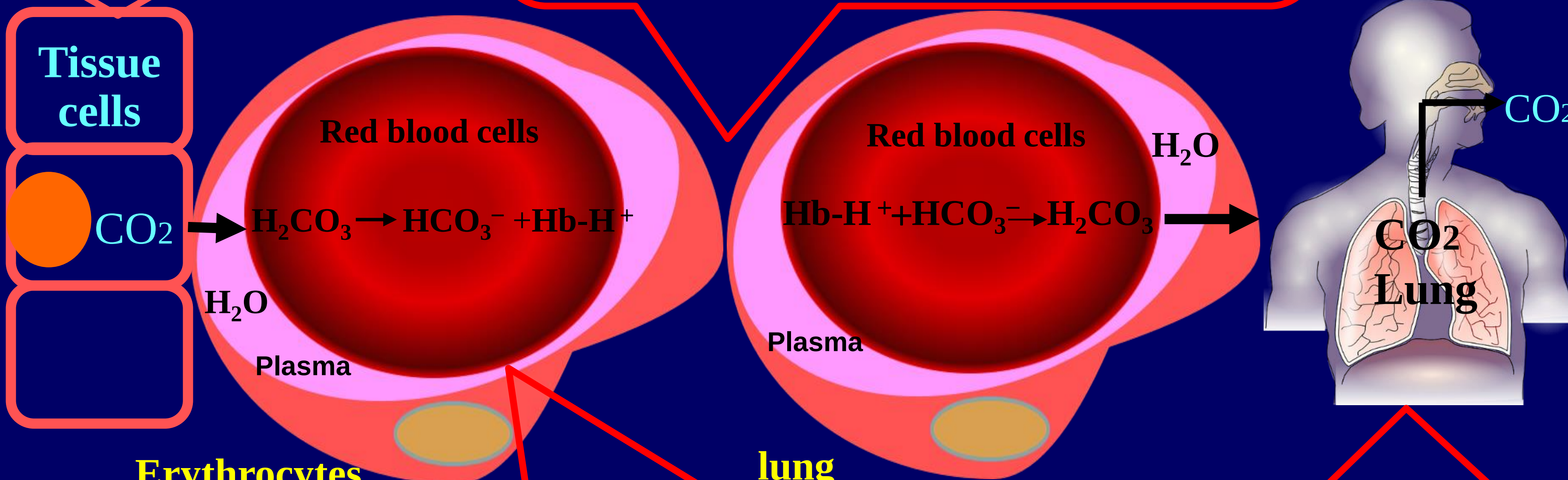
2. Hemoglobin buffer system

- Only intracellular system with immediate effects.
- CO_2 produced in working tissue diffuses to erythrocytes. In red blood cell CO_2 either:-
  1. Binds to hemoglobin to carbaminohemoglobin.
  2. Reacts with water using carbonic anhydrase (CA, carbonate dehydratase) to form carbonic acid. $CO_2 + H_2O \leftrightarrow H_2CO_3$
- Produced carbonic acid dissociates: $H_2CO_3 \leftrightarrow HCO_3^- + H^+$
- Generated protons are buffered (Hb-H^+) by deoxygenated hemoglobin and transport to the lung.
- In **lung** HCO_3^- is dissociates to CO_2 using enzyme CA. CO_2 is exhaled.
- Reaction $HCO_3^- \rightarrow CO_2 + H_2O$ demands H^+. Protons for this process are taken from buffered (Hb-H^+) hemoglobin which affinity to H^+ has lowered just when it arrived to lung where is high pO_2 and hemoglobin become oxygenated. Reaction catalyzed by carboanhydrase : $HCO_3^- + H^+ \rightarrow CO_2 + H_2O$

1. CO_2 produced in working tissue diffuses to erythrocytes

3. Produced carbonic acid dissociates: $H_2CO_3 \leftrightarrow HCO_3^- + H^+$ Generated protons are buffered (Hb-H^+) by deoxygenated hemoglobin and transport to the lung.

Released with exhalation



2. In red blood cell CO_2 either:-
    1. Binds to hemoglobin to carbaminohemoglobin.
    2. Reacts with water using carbonic anhydrase (CA, carbonate dehydratase) to form carbonic acid.

4. Reaction $HCO_3^- \rightarrow CO_2 + H_2O$ demands H^+. Protons for this process are taken from hemoglobin

Basic disturbances in the acid-base balance

1. **Metabolic acid-base disorders:** Production or loss of excessive amounts of Non-volatile acids organic acids, carbonic acid–bicarbonate system works to counter , categorized to:-
   1. Metabolic acidosis
   2. Metabolic alkalosis
2. **Respiratory acid-base disorders.** Imbalance of CO_2 generation and elimination .Must be corrected by depth and rate of respiration changes categorized to:-
   1. Respiratory acidosis
   2. Respiratory alkalosis

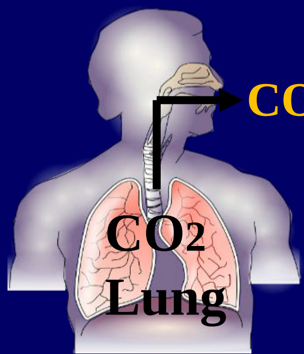
- **Compensation:** is process when organism tries to maintain almost normal pH. Metabolic disturbances are compensated by respiratory system and respiratory disturbances are compensated by metabolic components.
- **Correction:** is solving the acid-base problem in the spot where it started. Metabolic disorder is corrected by another component of the metabolic component of acid-base balance.

Metabolic Acidosis (Bicarbonate deficit below 22 mEq/L)

Develops when large numbers of H^+ are released **by organic or fixed acid**

Accommodated by: **Respiratory response** : Increased respiratory rate lowers PCO_2. and **Renal response** : H^+ secreted into urine , HCO_3^- reabsorbed into ECF

Start → **Addition of H^+**



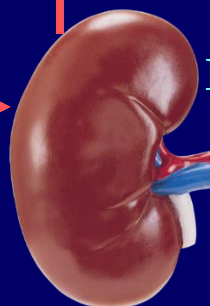
1.Carbonic Acid/ Bicarbonate Buffer System

$H_2O + CO_2 \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^- \leftarrow HCO_3^- + Na^+ \leftarrow NaHCO_3$

(carbonic acid) (bicarbonate ion) (sodium bicarbonate)

Bicarbonate Reserve

Generation of HCO_3^-



Secretion of H^+

3. Respiratory Response to Acidosis

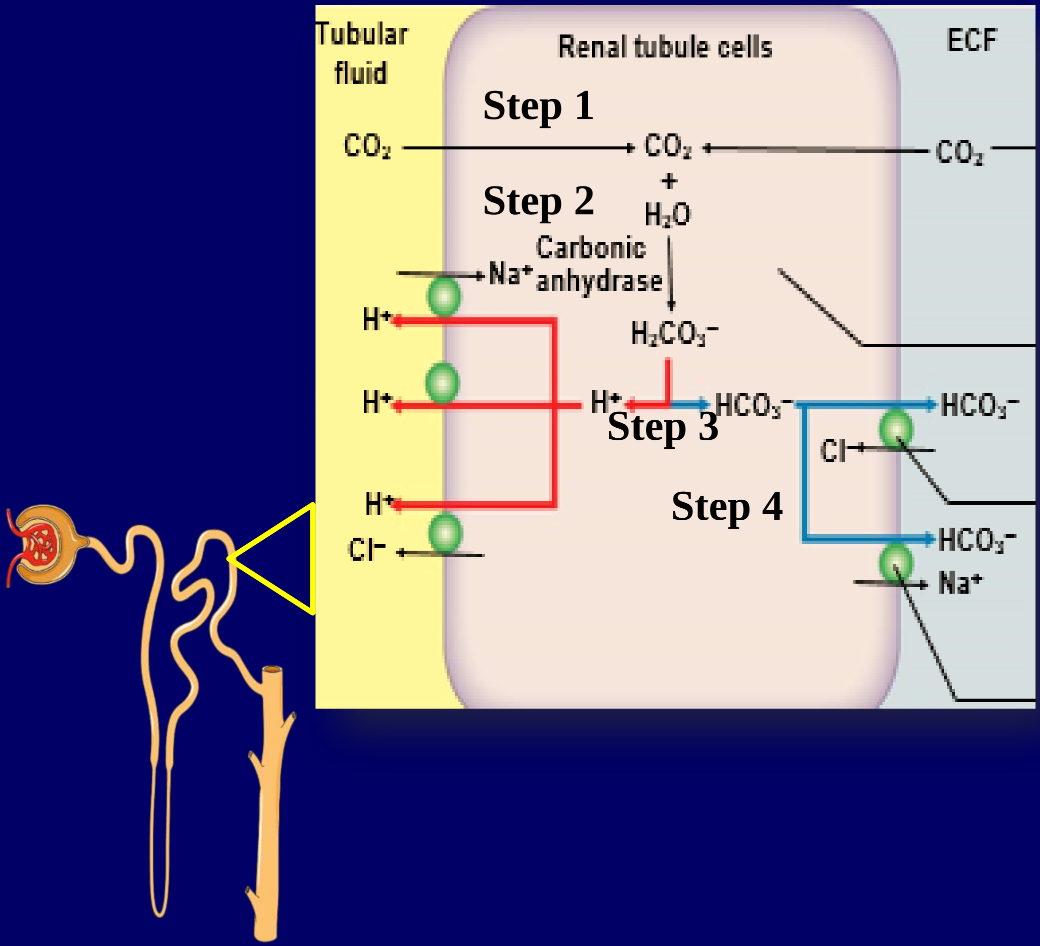
Increased respiratory rate lowers P_{CO_2}, effectively converting carbonic acid molecules to water. (Compensation)

4. Other buffer systems absorb H^+

2. Renal Response to Acidosis

Kidney tubules respond by: (1) Secreting H^+ ions (2) Removing CO_2, and (3) Reabsorbing HCO_3^- to help replenish the bicarbonate reserve. (Correction)

The Activity of Renal Tubule Cells in CO_2 Removal and HCO_3^- Production

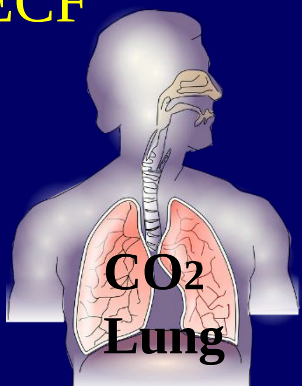


Steps in CO2 removal and HCO_3^- production:-

1. CO2 generated by the tubule cell is added to the CO2 diffusing into the cell from the urine and from the ECF.
2. Carbonic anhydrase converts CO2 and water to carbonic acid, which then dissociates.
3. The chloride ions exchanged for bicarbonate ions are excreted in the tubular fluid.
4. Bicarbonate ions and sodium ions are transported into the ECF, adding to the bicarbonate reserve.

Metabolic Alkalosis (Bicarbonate excess greater than 26 mEq/L)

Develops when large number of H^+ are removed from body fluids. Accommodated by respiratory and renal system: Respiratory responses decreased respiratory rate raises PCO_2 while renal system : HCO_3^- secreted into urine (in exchange for Cl^-) H^+ actively reabsorbed into ECF



Start → **Remove H^+**

1. Carbonic Acid/ Bicarbonate Buffer System

$H_2O + CO_2 \rightarrow H_2CO_3 \leftarrow H^+ + HCO_3^- \rightarrow HCO_3^- + Na^+ \rightarrow NaHCO_3$

(carbonic acid) (bicarbonate ion) (sodium bicarbonate)

Bicarbonate Reserve

3. Respiratory Response to Alkalosis

Decreased respiratory rate elevates P_{CO_2}, effectively converting CO_2 molecules to carbonic acid.

Other buffer systems release H^+

Generation of H^+

Kidney

Secretion of HCO_3^-

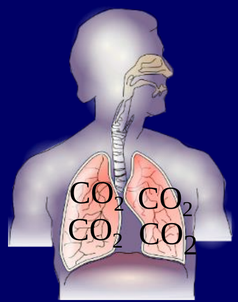
2. Renal Response to Alkalosis: Kidney tubules respond by conserving H^+ ions and secreting HCO_3^-.

Respiratory acidosis (pCO_2 above 45 mm Hg (hypercapnia))

CO_2 generation outpaces rate of CO_2 elimination at lungs shifts bicarbonate buffer system toward generating more carbonic acid.

$$H_2O + CO_2 \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$$ (HCO_3^- to bicarbonate reserve)

1. Respiratory (increased respiratory rate) 2. Renal (H^+ secreted and HCO_3^- reabsorbed) 3. Proteins (bind free H^+).



Carbonic Acid/ Bicarbonate Buffer System

$$H_2O + CO_2 \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^- \rightarrow HCO_3^- + Na^+ \rightleftarrows NaHCO_3$$

H_2CO_3 (carbonic acid); HCO_3^- (bicarbonate ion); $NaHCO_3$ sodium bicarbonate

(HCO_3^- to bicarbonate reserve

1. When respiratory activity does not keep pace with the rate of CO_2 generation, plasma P_{CO_2} increases. This upsets the equilibrium and drives the reaction to the right, generating additional H_2CO_3, which releases H^+ and lowers plasma pH .
2. As bicarbonate ions and hydrogen ions are released through the dissociation of carbonic acid, the excess bicarbonate ions become part of the bicarbonate reserve.
3. To limit the pH effects of respiratory acidosis, the excess H^+ must either be tied up by other buffer systems or excreted at the kidneys. The underlying problem, however, cannot be eliminated without an increase in the respiratory rate.

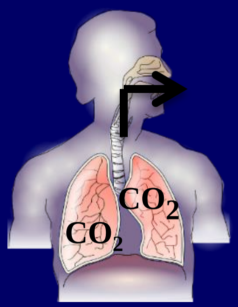
Respiratory alkalosis (pCO_2 less than 35 mm Hg (hypocapnea))

CO_2 elimination at lungs outpaces CO_2 generation rate , shifts bicarbonate buffer system toward generating more carbonic acid

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

H^+ removed as CO_2 exhaled and water formed

Respiratory (decreased respiratory rate), Renal (HCO_3^- secreted and H^+ reabsorbed), Proteins (release free H^+)



Carbonic Acid/ Bicarbonate Buffer System

$$H_2O + CO_2 \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^- \leftarrow HCO_3^- + Na^+ \rightleftarrows NaHCO_3$$

(carbonic acid) (bicarbonate ion) sodium bicarbonate

If respiratory activity exceeds the rate of CO_2 generation, plasma P_{CO_2} decline, and this disturbs the equilibrium and drives the reactions to the left, removing H^+ and elevating plasma pH.

As bicarbonate ions and hydrogen ions are removed in the formation of carbonic acid, the bicarbonate ions but not the hydrogen ions are replaced by the bicarbonate reserve.

Analysis of Acid-Base Imbalances Report

1. Note whether the pH is low (acidosis) or high (alkalosis)
2. Decide which value, is outside the normal range and could be the cause of the problem pCO_2 (If the cause is a change in pCO_2, the problem is respiratory or HCO_3^- (If the cause is HCO_3^- the problem is metabolic).
3. Look at the value that doesn't correspond to the observed pH change whether its inside (If it is inside the normal range, there is no compensation occurring). or outside(If it is outside the normal range, the body is partially compensating for the problem) the normal range.

Practice Problem 1

A patient is in intensive care because he suffered a severe myocardial infarction 3 days ago. The lab reports the following values from an arterial blood sample:

ABG's: pH 7.31 PCO_2 55 mm Hg HCO_3^- 28 mEq/L

ANSWER:

Normal values for ABG's:

pH 7.31 (7.35 - 7.44) = low acidosis

PCO_2 55 (35 - 45) = High respiratory

HCO_3^- 28 (24 - 28) = normal no compensation

The final diagnosis is Respiratory acidosis without compensation

Practice Problem 2

ABG's: pH 7.48 PCO_2 25 mm Hg HCO3- 28 mEq/L

pH 7.84 (7.35 - 7.44) = high alkalosis

PCO_2 25 (35 - 45) = low respiratory alkalosis

HCO_3 28 (24 – 28) = normal no compensation


thank you!