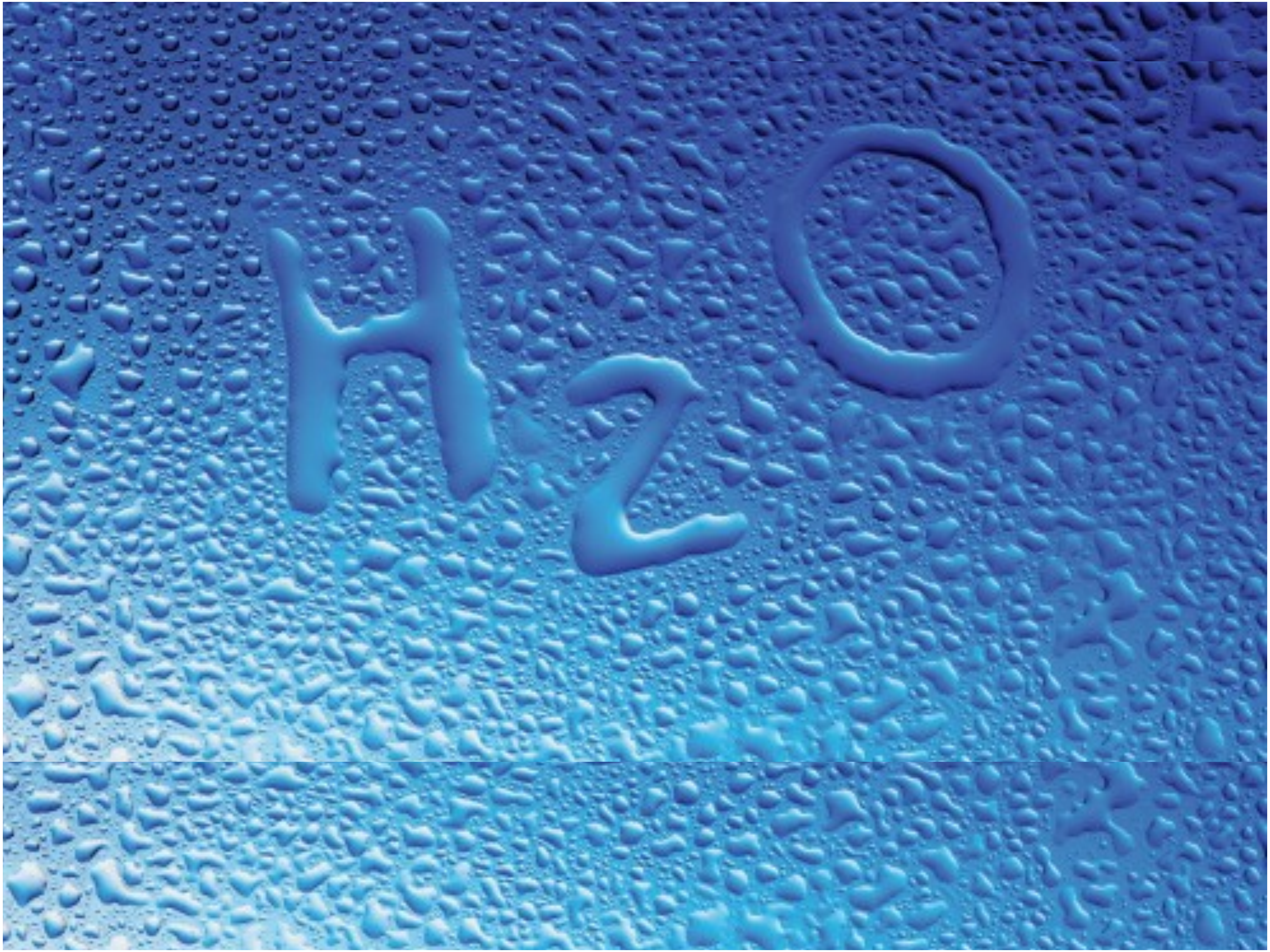
Acid-Base Balance

Filiz Bakar Ateş, Assoc.Prof.


H2O

pH

- pH IS THE NEGATIVE LOG OF THE HYDROGEN ION CONCENTRATION !!!

- The term **pH** was introduced in 1909 by Sörensen, who defined pH as the negative log of the hydrogen ion concentration:

$pH = -\log [H^+]$

- This definition, while not rigorous, suffices for many biochemical purposes.

- To calculate the pH of a solution:

$pH + pOH = 14$

pH

To solve the problem by this approach:

1. Calculate hydrogen ion concentration [H+].
2. Calculate the base 10 logarithm of [H+].
3. pH is the negative of the value found in step 2.

- For example, for pure water at 25° C,

$pH = -\log[H^+] = -\log 10^{-7} = -(-7) = 7.0$

Acid-Base

- **Acid**

Any compound which forms H+ ions in solution (proton donors)

eg. Carbonic acid releases H+ ions

- **Base**

Any compound which combines with H+ ions in solution (proton acceptors)

eg: bicarbonate (HCO_3^-) accepts H+ ions

pH

- Intracellular and extracellular pH is usually in balance
- H^+ concentration of normal blood is 40 nmol/L
- Negative logarithm of this value is pH 7.40

Inverse relation between H^+ concentration and pH !

- $[H^+]$ ↑ ➔ pH ↓
- $[H^+]$ ↓ ➔ pH ↑

Acid-Base Balance

- Normal pH: 7.35-7.45
- a continuous blood pH below 7.0 and above 7.8 is fatal

ACIDS

- Volatile Acids
  - ✓ Produced by oxidative metabolism of Ch, Fat, Protein
  - ✓ Average 15.000-20.000 mmol CO_2/day
  - ✓ Excreted through lungs as CO_2 gas

ACIDS

- **Fixed Acids**

✓ These acids don't leave solution, once produced they remain in body fluids until eliminated by kidneys.

Eg: Sulfuric acid, phosphoric acid, organic acids

✓ They are most important acids in the body

✓ They are generated during catabolism of

- Aminoacids (oxidation of sulfhydryl groups of cystine, methionine)
- Phospholipids (hydrolysis)
- Nucleic acids

ACID-BASE BALANCE

- The , acid-base balance is supplied by some mechanisms in living organisms:

A. Buffer systems,

B. Compensation

A. Buffer Systems

- First line of defence
- Most common chemical buffer groups are;

1) *Carbonic acid/Bicarbonate buffers*
2) *Phosphate buffers*
3) *Protein buffers*
4) *Hemoglobin buffers*

1. *Carbonic acid/Bicarbonate Buffer System*

- **Most body cells constantly generate CO_2**
- **Most CO_2 is converted to Carbonic acid, which dissociates into H^+ and a bicarbonate ion**
- Normal HCO_3^- / H_2CO_3 ratio is 20/1
- Increased acid: $H^+ + HCO_3^- \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$
- Increased base: $OH^- + H_2CO_3 \rightarrow HCO_3^- + H_2O$

reactions occur and thus the pH of extracellular fluid is kept constant.

2. Phosphate buffer system

- Consist of anion $H_2PO_4^-$ (a weak acid, pKa-6.8)
- Works like the carbonic acid-bicarbonate buffer system.
- is important in buffering pH of intracellular fluid
- Normally HPO_4^{2-} / $H_2PO_4^-$ ratio is 7/1
- increased acid: $H^+ + HPO_4^{2-} \rightarrow H_2PO_4^-$
- increased base : $OH^- + H_2PO_4^- \rightarrow HPO_4^{2} + H_2O$

3. Acid protein/Proteinate buffer system

- Important buffer system of tissue cells
- Increased acid: H^+ + Proteinate → Acid protein
- Increased base: OH^- + Acid protein → Proteinate + H_2O

4. Hemoglobin Buffer System

- CO_2 diffuses across RBC membrane
  - ✓ No transport mechanism required
- *As carbonic acid dissociates*
  - ✓ *Bicarbonate ions diffuse into plasma*
  - ✓ *In exchange for chloride ions (chloride schift)*

4. Hemoglobin Buffer System

- *Hydrogen ions are buffered by nemoglobin molecules*
- *is the only intracellular buffer system with an immediate effect on ECF pH*
- *Hepls prevent major changes in pH when plasma P_{CO2} is rising or falling*

B. Respiratory Acid-Base Control Mechanisms

- When chemical buffers alone can not prevent changes in blood pH, the respiratory system is the **second line** of defence against changes.
- ✓ Eliminate or retain CO_2
- ✓ Change in pH are rapid
- ✓ Occurs within minutes

C. Renal Acid-Base Control Mechanisms

- The kidneys are the third line of defence against wide changes in body fluid pH.
- ✓ movement of bicarbonate
- ✓ retention / excretion of acids
- ✓ generating additional buffers
- Long-term regulator of Acid-Base balance
- May take hours to days for correction

a) HCO_3^- reabsorbtion

- Role of kidneys is preservation of body's bicarbonate stores
- Accomplished by:

-Reabsorption of 99.9% of filtered bicarbonate

-Regeneration of titrated bicarbonate by excretion of

- Titratable acidity (mainly phosphate)
- Ammonium salts

$$H_2O + CO_2 \xleftrightarrow{CA} H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

Factors affecting renal bicarbonate reabsorbtion

- Filtered load of bicarbonate
- Prolonged changes in pCO2
- Extracellular fluid volume
- Plasma chloride concentration
- Plasma potassium concentration
- Hormones (e.g. mineralocorticoids, glucocorticoids)

- If secreted H^+ ions combine with filtered bicarbonate, bicarbonate is reabsorbed
- If secreted H^+ ions combine with phosphate aor ammonia, net acid excretion and generation of new bicarbonate occur

Metabolic Acidosis: Primary Bicarbonate Deficiency

- **Metabolic acidosis** occurs when the blood is too acidic (pH below 7.35) due to too little bicarbonate, a condition called primary bicarbonate deficiency.
- At the normal pH of 7.40, the ratio of bicarbonate to carbonic acid buffer is 20:1.
- If a person's blood pH drops below 7.35, then he or she is in metabolic acidosis.
- The most common cause of metabolic acidosis is the presence of organic acids or excessive ketones in the blood.

ANION GAP CONCEPT

- To know if Metabolic Acidosis due to
- ✓ Loss of bicarbonate
- ✓ Accumulation of non-volatile acids
- Provides an index of the relative conc of plasma anions other than chloride,bicarbonate
- [serum Na^+ - (serum Cl^- + serum HCO_3^-)]
- Unmeasured anions – unmeasured cations
- 8 – 16 mEq/L (5 – 11,with newer techniques)
- Mostly represent ALBUMIN

Metabolic Alkalosis: Primary Bicarbonate Excess

- **Metabolic alkalosis** is the opposite of metabolic acidosis.
- It occurs when the blood is too alkaline (pH above 7.45) due to too much bicarbonate (called primary bicarbonate excess).

Respiratory Acidosis: Primary Carbonic Acid/CO2 Excess

- **Respiratory acidosis** occurs when the blood is overly acidic due to an excess of carbonic acid, resulting from too much CO_2 in the blood.
- Respiratory acidosis can result from anything that interferes with respiration, such as pneumonia, emphysema, or congestive heart failure.

Respiratory Alkalosis: Primary Carbonic Acid/CO2 Deficiency

- **Respiratory alkalosis** occurs when the blood is overly alkaline due to a deficiency in carbonic acid and CO_2 levels in the blood.
- This condition usually occurs when too much CO_2 is exhaled from the lungs, as occurs in hyperventilation, which is breathing that is deeper or more frequent than normal.
- An elevated respiratory rate leading to hyperventilation can be due to extreme emotional upset or fear, fever, infections, hypoxia, or abnormally high levels of catecholamines, such as epinephrine and norepinephrine.

Compensation Mechanisms

- Various compensatory mechanisms exist to maintain blood pH within a narrow range, including buffers, respiration, and renal mechanisms.
- Although compensatory mechanisms usually work very well, when one of these mechanisms is not working properly (like kidney failure or respiratory disease), they have their limits.
- If the pH and bicarbonate to carbonic acid ratio are changed too drastically, the body may not be able to compensate.
- Moreover, extreme changes in pH can denature proteins.
- Extensive damage to proteins in this way can result in disruption of normal metabolic processes, serious tissue damage, and ultimately death.

Respiratory Compensation

- Respiratory compensation for metabolic acidosis increases the respiratory rate to drive off CO_2 and readjust the bicarbonate to carbonic acid ratio to the 20:1 level.
- This adjustment can occur within minutes.
- Respiratory compensation for metabolic alkalosis is not as adept as its compensation for acidosis.
- The normal response of the respiratory system to elevated pH is to increase the amount of CO_2 in the blood by decreasing the respiratory rate to conserve CO_2.
- There is a limit to the decrease in respiration, however, that the body can tolerate.
- Hence, the respiratory route is less efficient at compensating for metabolic alkalosis than for acidosis.

Metabolic Compensation

- Metabolic and renal compensation for respiratory diseases that can create acidosis revolves around the conservation of bicarbonate ions.
- In cases of respiratory acidosis, the kidney increases the conservation of bicarbonate and secretion of H^+ through the exchange mechanism discussed earlier. These processes increase the concentration of bicarbonate in the blood, reestablishing the proper relative concentrations of bicarbonate and carbonic acid.
- In cases of respiratory alkalosis, the kidneys decrease the production of bicarbonate and reabsorb H^+ from the tubular fluid.
- These processes can be limited by the exchange of potassium by the renal cells, which use a K^+-H^+ exchange mechanism (antiporter).

Diagnosing Acidosis and Alkalosis

- Lab tests for pH, CO2 partial pressure (pCO2),and $HCO3^{-}$ can identify acidosis and alkalosis, indicating whether the imbalance is respiratory or metabolic, and the extent to which compensatory mechanisms are working.
- The blood pH value indicates whether the blood is in acidosis, the normal range, or alkalosis.
- The pCO2 and total $HCO3^{-}$ values aid in determining whether the condition is metabolic or respiratory, and whether the patient has been able to compensate for the problem.
- Metabolic acid-base imbalances typically result from kidney disease, and the respiratory system usually responds to compensate.

References

- Lippincott's Biochemistry, 5th Edition
- Harper's Illustrated Biochemistry, 28th Edition