

## Physiology Practical - Acid-base balance \*

**Definition** - all the processes inside the body which keep H<sup>+</sup> concentration within normal values. It is a result of the hydroelectrolytic balance and a sum of mechanisms involved in blood gas homeostasis.

One can express blood acidity by:

- H<sup>+</sup> concentration - which is 35- 45 mmol/l
- Hydrogen activity, as pH, which is 7,38- 7,42

$\text{pH} = -\log [\text{H}^+]$

Normal pH is maintained inside our body through 2 types of mechanisms:

1. Buffer systems, composed of a weak acid and its salt with a powerful base, which have two origins: plasmatic and cellular (erythrocyte).

They guard **against sudden shifts** in acidity and alkalinity. The pH buffer systems are combinations of the body's naturally occurring weak acids and weak bases. These weak acids and bases exist in balance under normal pH conditions. The pH buffer systems work chemically to minimize changes in the pH of a solution by adjusting the proportion of acid and base. The most important pH buffer system in the blood involves carbonic acid (a weak acid formed from the carbon dioxide dissolved in blood) and bicarbonate ions (the corresponding weak base).

They may also be classified as:

- Extracellular: bicarbonate system, phosphate system and protein system
- Intracellular: bicarbonate system, phosphate system and histidine system

### Plasmatic buffer systems:

Examples:

- H<sub>2</sub>CO<sub>3</sub>/ NaHCO<sub>3</sub>
- NaH<sub>2</sub>PO<sub>4</sub>/ Na<sub>2</sub>HPO<sub>4</sub>
- Free protein/ sodium bound to proteins

### Intracellular systems:

- Erythrocyte systems: HHb/ KHb; HbHO<sub>2</sub>/ KHbO<sub>2</sub>; KH<sub>2</sub>PO<sub>4</sub>/K<sub>2</sub>HPO<sub>4</sub>

2. Biological mechanisms- in which lungs and kidneys play a major role

- Lungs role in acid-base balance: ventilation is a major process contributing to the equilibrium of plasma pH; it permanently adapts to pCO<sub>2</sub> variations. CO<sub>2</sub> passes the blood-brain barrier and it hydrates, forming H<sub>2</sub>CO<sub>3</sub>, which rapidly dissociates in H<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>. H<sup>+</sup> stimulates central receptors, regulating the depth and frequency of ventilation. This system corrects plasma pH in 1- 15 minutes.
- Kidneys role in acid base balance: the major mechanism is elimination of H<sup>+</sup> through urine by active secretion, while recovering HCO<sub>3</sub><sup>-</sup> from the urine. This system works slowly, in 1-3 days.

### Acid base equilibrium parameters are:

- a. Extracellular pH (plasmatic pH)= 7.38- 7.42  
< 7.38= acidosis  
>7.42= alkalosis

Physiological variations:

- Age: newborn babies and children have a pH closer to the superior limit of the interval (7.42)- this favors anabolic processes (growth), while older people have more acidic pH do the catabolic processes
- Digestion phases:
  - o gastric digestion, there is a more basic pH (elimination of H<sup>+</sup> in the gastric secretions)
  - o intestinal digestion, the pH is more acid (HCO<sub>3</sub><sup>-</sup> in the intestinal secretions)
- circadian rhythm – in the morning and at night- more acidic pH - CO<sub>2</sub> accumulation during sleep
- altitude- more basic pH-physiological alkalosis- low pO<sub>2</sub> causes hyperventilation and low CO<sub>2</sub>.

The classical description of acid- base balance is based on Henderson- Hasselbach equation:

$$\text{pH} = \text{pKa} + \log \frac{[\text{base}]}{[\text{acid}]}$$

pKa is the ionizing constant or dissociation constant of the acid from the buffer system. For bicarbonate buffer system, the value of pKa= 6.1.

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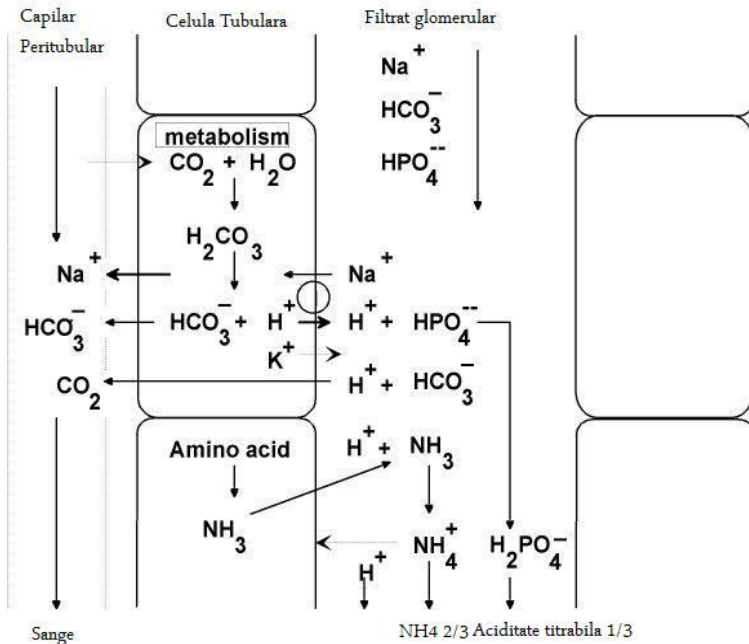
- b.  $p\text{CO}_2 = 38 - 42$  mmHg - pressure of carbon dioxide in arterial blood
- c. Alkaline reserve= actual bicarbonate= 21- 24 mEq/l= content of  $\text{HCO}_3^-$  in patients' blood at actual  $p\text{CO}_2$ ; it represents the metabolic component of the buffer system, and it is usually modified by kidneys.
- d. Standard bicarbonate=  $[\text{HCO}_3^-]$  in standard conditions: standard  $p\text{aCO}_2$  and complete Hb oxygenation (thus eliminating the influence of the lungs on blood base concentration). Normal values= 21-27 mEq/l; high  $[\text{HCO}_3^-]$  means metabolic alkalosis and low  $[\text{HCO}_3^-]$  means metabolic acidosis.  
 $[\text{HCO}_3^-]/[\text{H}_2\text{CO}_3] = 20/1$
- e. Total buffer bases - the sum of all buffer anions in the blood, capable to accept protons (bicarbonate, phosphate, proteins, hemoglobin). Normal values= 45- 50 mEq/l.
- f. Excess bases - the amount of acid or bases which could reestablish the acid-base balance within 1 liter of blood at  $p\text{CO}_2$  of 40 mmHg. Negative in metabolic acidosis and positive in metabolic alkalosis. Normal value= +2.5  $\rightarrow$  -2.5 mmol/l.
- g. Intracellular pH, mean value = 6.9, change with cellular activity and extracellular pH, small differences in different cell types.
- h. Total concentration of  $\text{CO}_2$  - the sum of the actual bicarbonate concentration and carbonic acid concentration in the arterial blood =  $p\text{CO}_2 * 0.03$ . Normal values = 24- 28 mmol/l.
- i. Anionic gap- the difference between cations and anions which are normally determined in the plasma.  
 $\text{AG} = (\text{Na}^+ + \text{K}^+) - [(\text{Cl}^-) + (\text{HCO}_3^-)]$ ; normal value =  $16 \pm 2$  mmol/l.  
 $\text{AG} = (\text{Na}^+) - [(\text{Cl}^-) + (\text{HCO}_3^-)]$ ; normal value=  $12 \pm 4$  mmol/l.  
 Corrected AG in case of low albumin level:  $\text{AG corrected} = \text{AG} + 0,25 \times (\text{normal albumin} - \text{measured albumin})$

#### Acid-base abnormalities:

1. Respiratory acidosis - increase of  $p\text{CO}_2$  over 40 mmHg in respiratory diseases associated with hypoventilation, results in accumulation of  $\text{H}_2\text{CO}_3$  and decreased blood pH. Compensation - kidneys increase of  $\text{HCO}_3^-$  production and reabsorption, and  $\text{H}^+$  excretion.  
 Causes:
  - Alveolar hypoventilation
    - o CNS depression (meds, trauma)
    - o Myopathic diseases
    - o Restrictive pulmonary disease
    - o Obstructive pulmonary disease
  - High  $\text{CO}_2$  production- thyrotoxicosis, malignant hyperthermia, convulsions
2. Respiratory alkalosis - decrease of  $p\text{CO}_2$  due to hyperventilation is followed by increased pH. Compensation- kidneys decreased  $\text{H}^+$  secretion and increased  $\text{HCO}_3^-$  excretion.  
 Causes:
  - Peripheral stimulation (hypoxemia, anemia, altitude)
  - Central stimulation (pain, anxiety, meds)
  - Metabolic encephalopathy (hepatic cirrhosis)
3. Metabolic acidosis - decrease in  $[\text{HCO}_3^-]$  due to excess utilization of acid buffering (lactic acid in physical exercise, ketonemia in diabetes), followed by plasma pH decrease. Compensation may be:
  - a. Renal- increased  $\text{HCO}_3^-$  reabsorption and  $\text{H}^+$  and  $\text{NH}_4^+$  excretion
  - b. Respiratory- hyperventilation
4. Metabolic alkalosis- increased  $[\text{HCO}_3^-]$ , followed by increased arterial blood pH. Compensation:
  - a. Renal- decreased  $\text{HCO}_3^-$  reabsorption
  - b. Respiratory- hypoventilation
 Causes:
  - Digestive loss (gastric acid), renal loss (diuretics), primary hyperaldosteronism,

## Practical part

Due to cellular metabolism, acids will be formed: volatile (eliminated through respiration) and non-volatile (renal elimination). So, kidneys maintain acid base balance by eliminating non-volatile acids and  $\text{HCO}_3^-$ -reabsorption. Acids are eliminated in urine in two forms: titrated acidity (1/3) and  $\text{NH}_4^+$  (2/3)



### Titration determination

It is represented by acids in urine, with  $\text{pKa} < 7.4$  (acid phosphate, uric acid, creatinin, betahydroxibutiric acid). Normal value = 20- 50 mEq/l.

Method: bring urine pH to 7.4 by adding NaOH

- Pour 25 ml of urine in a Berzelius glass + 1 ml phenolphthalein
- Pour NaOH drop by drop with pipette, until urine turns pink (when this achieved, pH is 7.4)
- Calculate titratable acidity using formula:

$$M_1 \times V_1/n_1 = M_2 \times V_2/n_2$$

$M_1$  = molarity of NaOH solution

$V_1$  = volume of NaOH solution used

$n_1$  = no of  $\text{HO}^-$  / mol of NaOH = 1

$M_2$  = urine molarity

$V_2$  = urine volume- 25 ml

$n_2$  = no of  $\text{H}^+$  mols titrated by  $\text{HO}^-$  = 1

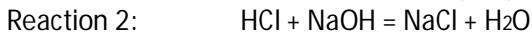
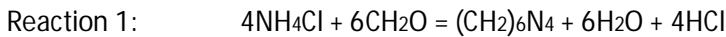
### Ammonium ion ( $\text{NH}_4^+$ ) dosing in urine

Ammonium salts in urine react with formic aldehyde, forming an equivalent quantity of acid which is titrated in the presence of phenolphthalein, with a NaOH solution of known concentration.

Method:

- 25 ml urine + 1 drop of phenolphthalein
- Titrator with NaOH 20mM/l until turns pink (this step is used to neutralize free acidity in urine)
- Add 10 ml of neutral formic aldehyde solution 10% (decolorates by adding formol because of acid forming due to ammonium salts decomposing)
- Titrate acidity with NaOH 20mM/l until turns pale pink and note down the volume used for this titration

Calculus:



No of mM of NaOH is equal with no of mM of HCl in urine.

$$M_1 \times V_1/n_1 = M_2 \times V_2/n_2$$

$M_1$  = molarity of NaOH solution

$V_1$  = volume of NaOH solution used

$n_1$  = no of  $\text{HO}^-$  / mol of NaOH = 1

$M_2$  = urine molarity

$V_2$  = urine volume- 25 ml

$n_2$  = no. of  $\text{H}^+$  mols titrated by  $\text{HO}^-$  = 1

### Acid base disorder example:

pH = 7,15

$\text{PaCO}_2$  = 28 mmHg

$\text{PaO}_2$  = 80 mmHg

$\text{HCO}_3$  = 5 mmol/l

BE = -21 mmol/l

Oxygen saturation  $\text{SaO}_2$  = 90 %

Na = 138 mmol/l

Cl = 105 mmol/l

1. pH evaluation- < 7.38- acidosis
2. Respiratory or metabolic?  
Low bicarbonate= metabolic acidosis
3. Compensation degree  
 $\text{pCO}_2$ = 28 mmHg (low value) - there is a degree of respiratory compensation= partially respiratory compensated metabolic acidosis
4. Anionic gap calculus:  
 $\text{AG} = (\text{Na}^+) - [(\text{Cl}^-) + (\text{HCO}_3^-)] = 138 - 105 - 5 = 18$   
High AG
5. Causes?  
Intoxications  
Lactic acidosis  
Rhabdomyolysis  
Renal insufficiency  
Diabetic ketoacidosis