RESPIRATORY AND METABOLIC ACIDOSIS & ALKALOSIS

- Acids are hydrogen ion whereas *A base* is an ion or a molecule that can accept an H+.
- H+ regulation is essential because the activities of almost all enzyme systems in the body are influenced by H+ concentration
- Acid-Base homeostasis is concerned about the proper balancing of acid and bases, also called the pH

ACIDOSIS is the reduction in the pH due to the presence of excess H+ ions

ALKALOSIS is the decrease in the pH

Defences Against Changes in Hydrogen Ion Concentration

1. Chemical acid- base buffer system
2. Respiratory centers
3. kidneys

CHEMICAL ACID –BASE BUFFER SYSTEM

- This is the first line of defense.
- Chemical buffers include bicarbonate buffer, phosphate buffer and protein buffer
- The bicarbonate buffering system is especially key, as carbon dioxide (CO_2) can be shifted through carbonic acid (H_2CO_3) to hydrogen ions and bicarbonate (HCO_3^-)

Respiratory Regulation of Acid-Base Balance

- This is the second line of defense in acid-base disturbances
- An increase in ventilation eliminates CO2 from extracellular fluid, which, by mass action, reduces the H+ concentration.
- Conversely, decreased ventilation increases CO2, thus also increasing H+ concentration in the extracellular fluid.

- The buffering power of respiratory centers are one to two times as great as the buffering power of all the chemical buffers in the EC fluid combined

RESPIRATORY ACIDOSIS

- **Respiratory acidosis** is a medical emergency in which decreased ventilation causes increased blood carbon dioxide concentration and ultimately leads to decrease in the pH level
- During Alveolar hypoventilation there is an increase in CO2 thus leads to an increased $PaCO_2$.

Acidosis refers to disorders that lower cell/tissue pH to < 7.35
Acidemia refers to an arterial pH < 7.3

TYPES OF RESPIRATORY ACIDOSIS

ACUTE RESPIRATORY ACIDOSIS

CHRONIC RESPIRATORY ACIDOSIS

ACUTE RESPIRATORY ACIDOSIS

- $PaCO_2$ is elevated above the upper limit of the reference range (over 6.3 kPa or 45 mm Hg) with an accompanying acidemia (pH <7.36).
- occurs when an abrupt failure of ventilation occurs
- failure in ventilation may be caused by depression of the central respiratory center, inability to ventilate adequately due to neuromuscular disease, or airway obstruction related to asthma or chronic obstructive pulmonary disease (COPD) exacerbation.

CHRONIC RESPIRATORY ACIDOSIS

- Chronic respiratory acidosis may be secondary to many disorders,including COPD
- Chronic respiratory acidosis also may be secondary to Pickwickian syndrome, neuromuscular disorders, and severe restrictive ventilatory defects as observed in interstitial fibrosis and thoracic deformities.

MECHANISM

- acute respiratory acidosis, compensation occurs in 2 steps.
- The initial response is cellular buffering that occurs over minutes to hours. Cellular buffering elevates plasma bicarbonate (HCO_3^-) only slightly, approximately 1 mEq/L for each 10-mm Hg increase in $PaCO_2$.
- The second step is renal compensation that occurs over 3–5 days. With renal compensation, renal excretion of carbonic acid is increased and bicarbonate reabsorption is increased. For instance, PEPCK is upregulated in renal proximal tubule brush border cells, in order to secrete more NH_3 and thus to produce more HCO_3^-

RESPIRATORY ALKALOSIS

- **Respiratory alkalosis** is a medical condition in which increased respiration elevates the blood pH beyond the normal range (7.35-7.45) with a concurrent reduction in arterial levels of CO_2.

Alkalosis refers to disorders that elevate cellular pH to > 7.45.
Alkalemia refers to an arterial pH > 7.45.

TYPES OF RESPIRATORY ALKALOSIS

ACUTE RESPIRATORY ALKALOSIS

CHRONIC RESPIRATORY ALKALOSIS

ACUTE RESPIRATORY ALKALOSIS

- *Acute respiratory alkalosis* occurs rapidly. For every 10 mmHg drop in PCO_2 in arterial blood, there is a corresponding 2 mEq/L drop in bicarbonate ion due to acute compensation. During acute respiratory alkalosis, the person may lose consciousness where the rate of ventilation will resume to normal.

CHRONIC RESPIRATORY ALKALOSIS

- *Chronic respiratory alkalosis* is a more long-standing condition. For every 10 mmHg drop in PCO_2 in arterial blood, there is a corresponding 5 mEq/L drop in bicarbonate ion. The drop of 5 mEq/L of bicarbonate ion is a compensation effect which reduces the alkalosis effect of the drop in PCO_2 in blood. This is termed metabolic compensation.

CAUSES

- psychiatric causes
- CNS causes
- drug use: doxapram, aspirin, caffeine and coffee abuse
- moving into high altitude areas, where the low atmospheric pressure of oxygen stimulates increased ventilation
- lung disease such as pneumonia
- fever
- pregnancy
- high levels of NH_4^+ leading to brain swelling and decreased blood flow to the brain

MECHANISM

- Respiratory alkalosis generally occurs when some stimulus makes a person hyperventilate. The increased breathing produces increased alveolar respiration, expelling CO_2 from the circulation. This alters the dynamic chemical equilibrium of carbon dioxide in the circulatory system, and the system reacts according to Le Chatelier's principle. Circulating hydrogen ions and bicarbonate are shifted through the carbonic acid (H_2CO_3) intermediate to make more CO_2 via the enzyme carbonic anhydrase.

RENAL COMPENSATION

- **Renal compensation** is a mechanism by which the kidneys can regulate the plasma pH. It is slower than respiratory compensation, but has a greater ability to restore normal values.
- **In respiratory acidosis**, the kidney produces and excretes ammonium (NH_4^+) and monophosphate, generating bicarbonate in the process while clearing acid.[1]
- **In respiratory alkalosis**, less HCO_3^- is reabsorbed, thus lowering the pH.[2]

METABOLIC ACIDOSIS

- Metabolic acidosis is a condition that occurs when the body produces excessive quantities of acid or when the kidneys are not removing enough acid from the body
- If untreated it leads to ACIDEMIA
- The consequences are so serious leading to coma and death

Signs and symptoms

- Symptoms are not specific
- Symptoms may include chest pain
- , palpitations,
- headache,
- altered mental status such as severe anxiety due to hypoxia,
- decreased visual acuity,
- nausea,
- vomiting,

- abdominal pain
- altered appetite and weight gain
- muscle weakness
- bone pain and joint pain.
- Extreme acidemia leads to neurological and cardiac complications:
- **Neurological:** lethargy, stupor, coma, seizures.
- **Cardiac:** arrhythmias (ventricular tachycardia), decreased response to epinephrine; both lead to hypotension (low blood pressure).

CAUSES

- Metabolic acidosis occurs when the body produces too much acid, or when the kidneys are not removing enough acid from the body. There are several types of metabolic acidosis. The main causes are best grouped by their influence on the *anion gap*.

The **anion gap** is the difference in the measured cations and the measured anions in serum, plasma, or urine.

INCREASED ANION GAP

- lactic acidosis
- ketoacidosis
- chronic renal failure (accumulation of sulphates, phosphates, urea)
- intoxication:
  - organic acids (salicylates, ethanol, methanol, formaldehyde, ethylene glycol, paraldehyde)
  - Sulphates, metformin(Glucophage)
- massive rhabdomyolysis

NORMAL ANION GAP

- longstanding diarrhoea (bicarbonate loss)
- bicarbonate loss due to taking topiramate
- pancreatic fistula
- uretero-sigmoidostomy
- intoxication:
  - ammonium chloride
  - acetazolamide (Diamox)
  - isopropyl alcohol
- renal failure (occasionally)
- inhalant abuse
- toluene

COMPENSATION MECHANISM

- Metabolic acidosis is either due to increased generation of acid or an inability to generate sufficient bicarbonate. The body regulates the acidity of the blood by four buffering mechanisms.
- bicarbonate buffering system
- Intracellular buffering by absorption of hydrogen atoms by various molecules, including proteins, phosphates and carbonate in bone.
- Respiratory compensation
- Renal compensation

METABOLIC ALKALOSIS

- **Metabolic alkalosis** is a metabolic condition in which the pH of tissue is elevated beyond the normal range (7.35-7.45).
- This is the result of decreased hydrogen ion concentration, leading to increased bicarbonate.

CAUSES

Chloride-responsive (Urine chloride < 20 mEq/L)

Chloride-resistant (Urine chloride > 20 mEq/L)

CHLORIDE RESPONSIVE

- **Loss of hydrogen ions** - Most often occurs via two mechanisms, either vomiting or via the kidney.
  - Vomiting results in the loss of hydrochloric acid
  - Severe vomiting also causes loss of potassium (hypokalaemia) and sodium (hyponatremia). The kidneys compensate for these losses by retaining sodium in the collecting ducts at the expense of hydrogen ions (sparing sodium/potassium pumps to prevent further loss of potassium), leading to metabolic alkalosis.

- **Congenital chloride diarrhea** - rare for being a diarrhea that causes alkalosis instead of acidosis.

- **Contraction alkalosis**
- **Diuretic therapy** - loop diuretics and thiazides
- **Post hypercapnia** - Hypoventilation (decreased respiratory rate) causes hypercapnia (increased levels of CO2), which results in respiratory acidosis. Renal compensation with excess bicarbonate occurs to lessen the effect of the acidosis. Once carbon dioxide levels return to base line, the higher bicarbonate levels reveal themselves putting the patient into metabolic alkalosis.
- **Cystic Fibrosis**

CHLORIDE RESISTANT

- **Retention of bicarbonate**
- **Shift of hydrogen ions into intracellular space** - Seen in hypokalemia.
- **Alkalotic agents** - Alkalotic agents, such as bicarbonate (administrated in cases of peptic ulcer or hyperacidity) or antacids, administered in excess can lead to an alkalosis.
- **Hyperaldosteronism**

- Excess **Glycyrrhizin** consumption
- **Bartter syndrome** and **Gitelman syndrome** -
- **Liddle syndrome**
- **11β-hydroxylase deficiency** and **17α-hydroxylase deficiency** - both characterized by hypertension
- Aminoglycoside toxicity can induce a hypokalemic metabolic alkalosis via activating the calcium sensing receptor in the thick ascending limb of the nephron, inactivating the NKCC2 cotransporter, creating a Bartter's syndrome like effect.

RESPIRATORY COMPENSATION

- **Respiratory compensation** is a mechanism by which plasma pH can be altered by varying the respiratory rate. It is faster than renal compensation, but has less ability to restore normal values.
- **In metabolic acidosis**, chemoreceptors sense a deranged acid-base system, and there is increased breathing.
- **In metabolic alkalosis**, the breathing rate is decreased.


Thank you