Acid–base disorders

Acid–base disorders are caused by disturbances in hydrogen ion (H^+) homeostasis, which is ordinarily maintained by extracellular buffering, renal regulation of hydrogen ion and bicarbonate, and ventilatory regulation of carbon dioxide (CO_2) elimination.

Notes:

- Most of the body's acid production is in the form of CO_2 and is produced from catabolism of carbohydrates, proteins and lipids.
- There are four primary types of acid–base disturbances, which can occur independently or together as a compensatory response.
- ***Metabolic acid–base disorders*** are caused by changes in plasma bicarbonate concentration (***HCO_3^-***). Metabolic acidosis is characterized by decreased HCO_3^-, and metabolic alkalosis is characterized by increased HCO_3^-.
- ***Respiratory acid–base disorders*** are caused by altered alveolar ventilation, producing changes in arterial carbon dioxide tension (***$PaCO_2$***). Respiratory acidosis is characterized by increased $PaCO_2$, whereas respiratory alkalosis is characterized by decreased $PaCO_2$.

Diagnosis:

- The primary tools for determining the cause of acid–base disorders are blood gases, serum electrolytes, medical history and clinical condition.
- Arterial blood gases are measured to determine oxygenation and acid–base status. Low pH values (<7.35) indicate acidemia, whereas high values (>7.45) indicate alkalemia.
- The $PaCO_2$ value helps determine whether there is a primary respiratory abnormality, whereas the HCO_3^- concentration helps determine whether there is a primary metabolic abnormality.

Metabolic acidosis

Metabolic acidosis is characterized by decreased pH and serum HCO_3^- concentrations, which can result from:

- Adding organic acid to extracellular fluid (e.g., lactic acid and ketoacids)
- Loss of HCO_3^- stores (e.g., in case of diarrhea)
- Accumulation of endogenous acids (e.g., phosphates and sulfates) due to impaired renal function.

Clinical presentation

- Relatively asymptomatic; major manifestations are bone demineralization with the development of rickets in children and osteomalacia and osteopenia in adults.
- Acute severe metabolic acidemia (pH <7.2) involves the cardiovascular, respiratory and central nervous systems.
- Hyperventilation is often the first sign of metabolic acidosis. Respiratory compensation may occur as Kussmaul respirations (i.e., deep, rapid respirations characteristic of diabetic ketoacidosis).

Serum anion gap determination

When a metabolic acidosis is found, the anion gap should be calculated. The anion gap represents the "unmeasured" anions in the blood, which are formed from organic acids that have dissociated in blood.

$$Serum\ anion\ gap = Na^+ - (Cl^- + HCO_3^-)$$

Some clinicians may also include the serum potassium value in the formula:

$$Serum\ anion\ gap = (Na^+ + K^+) - (Cl^- + HCO_3^-)$$

Treatment

- The primary treatment is to correct the ***underlying disorder***, for example:

Acetazolamide	treatment of salicylate poisoning
Insulin	treatment of ketoacidosis
Fomepizole	used in methanol or ethylene glycol poisoning
Activated charcoal	emergency treatment of poisoning caused by drugs and chemicals including salicylates.

Other agents:

Oral sodium bicarbonate	Oral sodium bicarbonate or other alkali preparations are used in the management of asymptomatic patients with mild to moderate acidemia with gradual correction of the acidemia over days to weeks.
i.v. sodium bicarbonate	These alkali therapy can be used to treat patients with acute severe metabolic acidosis due to hyperchloremic acidosis, but their role is controversial in patients with lactic acidosis.
Tromethamine *(THAM)*	
Potassium citrate	It is useful when the acidosis is accompanied by hypokalemia but should be used cautiously in persons with renal impairment and must be avoided in those with hyperkalemia.

Metabolic alkalosis

Metabolic alkalosis is initiated by increased pH and HCO_3^-. The most common causes of metabolic alkalosis are the use of diuretics and the external loss of gastric secretions. Metabolic alkalosis can result from:

- Loss of H^+ via the gastrointestinal tract (e.g., nasogastric suctioning, vomiting)
- Loss of H^+ from kidneys (e.g., diuretics, Cushing syndrome)
- Gain of bicarbonate (e.g., administration of bicarbonate, acetate, lactate or citrate).

Causes of metabolic alkalosis

Causes of metabolic alkalosis can be divided into:

- Chloride-responsive alkalosis (urine chloride < 20 mEq/L), include the following:
    - Loss of gastric secretions - Vomiting, NG suction
    - Loss of colonic secretions - Congenital chloridorrhea, villous adenoma
    - Thiazides and loop diuretics (after discontinuation)
    - Posthypercapnia
    - Cystic fibrosis

- Chloride-resistant alkalosis (urine chloride >20 mEq/L), which is can divided into:

Chloride-resistant alkalosis with hypertension	***Causes of chloride-resistant alkalosis without hypertension:***	***Other causes***
• *Adrenal diseases* • *Licorice, carbenoxolone* • *Chewing tobacco* • *Current use of diuretics in hypertension* • *Cushing syndrome* • *Exogenous mineralocorticoids or glucocorticoids* • *Liddle syndrome* • *Renovascular hypertension*	• *Bartter syndrome* • *Gitelman syndrome* • *Severe potassium depletion* • *Current use of thiazides and loop diuretics* • *Hypomagnesemia*	• *Alkali-loading alkalosis* • *Exogenous alkali administration - Sodium bicarbonate therapy in the presence of renal failure, metabolism of lactic acid or ketoacids* ▪ *Milk-alkali syndrome* • *Hypercalcemia* • *Intravenous penicillin* • *Hypoproteinemic alkalosis* • *Massive blood transfusion*

Clinical presentation

- Mild to moderate metabolic alkalosis: No unique signs or symptoms.
- Some patients complain of symptoms related to the underlying disorder or have a history of vomiting, gastric drainage or diuretic use.
- Severe alkalemia (pH >7.60) can be associated with cardiac arrhythmias and neuromuscular irritability.
- Metabolic alkalosis is maintained by abnormal renal function that prevents the kidneys from excreting excess bicarbonate. The respiratory response is to increase $PaCO_2$ by hypoventilation.

Treatment

- Treatment is aimed to correct factors responsible for maintaining the alkalosis.

Treatment options:

Acidic I.V. solutions	They are used to treat severe metabolic alkalosis.
	IV Hydrochloric acid (HCl), *available in preparations of 0.1 and 0.2 M*
	Ammonium chloride (NH4Cl), *available as 500-mg tablets and a 26.75% parenteral formulation for intravenous use.*
Fluid replacement	Fluid replacement is used in chloride-responsive alkalosis with volume depletion (e.g. hypertonic sodium chloride).
Diuretics	Potassium-sparing diuretics may be used to correct potassium deficiency or fluid/electrolyte imbalance. e.g. triamterene, eplerenone, spironolactone and amiloride
	Carbonic anhydrase inhibitors (e.g. acetazolamide) may be used to treat severe metabolic alkalosis in edematous states. (e.g., from CHF, COPD, or right heart failure).
ACE inhibitors	ACE inhibitors block conversion of angiotensin I to angiotensin II and prevent secretion of aldosterone from the adrenal cortex. These agents are indicated in metabolic alkalosis due to hyperaldosteronism.
Potassium supplements	Potassium supplements (e.g. potassium chloride) may be used to correct metabolic alkalosis, which is often associated with hypokalemia.
Corticosteroids	Corticosteroids are used in glucocorticoid-remediable hyperaldosteronism, metabolic alkalosis, and hypertension.
NSAIDs	NSAIDs may partially correct metabolic alkalosis in Bartter syndrome and Gitelman syndrome.

Respiratory alkalosis

- Respiratory alkalosis is characterized by a decrease in $PaCO_2$ that leads to an increase in pH.
- $PaCO_2$ decreases when ventilatory CO_2 excretion exceeds metabolic CO_2 production, usually because of hyperventilation.
- Causes include:
    - Increases in neurochemical stimulation via central or peripheral mechanisms
    - Physical increases in ventilation via voluntary or artificial means (e.g., mechanical ventilation).
- The earliest compensatory response is to chemically buffer excess bicarbonate by releasing hydrogen ions from intracellular proteins, phosphates and hemoglobin. If prolonged, the kidneys attempt to further compensate by increasing bicarbonate elimination.

Clinical presentation

- Although usually asymptomatic, respiratory alkalosis can cause adverse neuromuscular, cardiovascular and GI effects.
- Decreased cerebral blood flow can cause light-headedness, confusion, decreased intellectual functioning, syncope and seizures.
- Nausea and vomiting can occur.
- Serum electrolytes can be altered; serum chloride is usually increased; serum potassium, phosphorus and ionized calcium are usually decreased.

Treatment

- Treatment is often unnecessary because most patients have few symptoms and only mild pH alterations (i.e., pH <7.50).
- Direct measures (e.g., treatment of pain, hypovolemia, fever, infection or salicylate overdose)
- A rebreathing device (e.g., paper bag) can help control hyperventilation in patients with anxiety/***hyperventilation syndrome***.
- Correction of respiratory alkalosis associated with mechanical ventilation by:
    - Decreasing the number of mechanical breaths per minute
    - Using a capnograph and spirometer to adjust ventilator settings more precisely, or
    - Increasing dead space in the ventilator circuit.

Respiratory acidosis

Respiratory acidosis is characterized by an increase in $PaCO_2$ and a decrease in pH.

Respiratory acidosis results from:

- Disorders that restrict ventilation or increase CO_2 production
- Airway and pulmonary abnormalities
- Neuromuscular abnormalities
- Mechanical ventilator problems.

Acute respiratory acidosis is present when an abrupt failure of ventilation occurs. This failure in ventilation may result from depression of the central respiratory center by one or another of the following:

- Central nervous system disease or drug-induced respiratory depression
- Inability to ventilate adequately, due to a neuromuscular disease or paralysis (e.g., myasthenia gravis, amyotrophic lateral sclerosis [ALS], Guillain-Barré syndrome, muscular dystrophy)
- Airway obstruction, usually related to asthma or chronic obstructive pulmonary disease (COPD)

Chronic respiratory acidosis may be secondary to many disorders, including COPD. Hypoventilation in COPD involves multiple mechanisms, including the following:

- Decreased responsiveness to hypoxia and hypercapnia
- Increased ventilation-perfusion mismatch leading to increased dead space ventilation
- Decreased diaphragmatic function due to fatigue and hyperinflation
- Chronic respiratory acidosis also may be secondary to:
    - obesity hypoventilation syndrome (OHS—ie, Pickwickian syndrome)
    - neuromuscular disorders such as ALS,
    - severe restrictive ventilatory defects such as are observed in interstitial fibrosis and thoracic skeletal deformities.

<u>Clinical presentation</u>

Neuromuscular symptoms include altered mental status, abnormal behavior, seizures, stupor and coma.

Hypercapnia can produce headache, papilledema, focal paresis and abnormal reflexes.

Treatment

Patient should be provided with adequate ventilation if CO_2 excretion is acutely and severely impaired or if life-threatening hypoxia is present.

Ventilation can include:

- Maintaining a patent airway (e.g., emergency tracheostomy, bronchoscopy or intubation)
- Clearing excessive secretions
- Administering oxygen
- Mechanical ventilation.

Aggressive treatment of underlying cause, which may include:

- Administration of bronchodilators for bronchospasm

$Beta_2$ agonists	short-acting B_2A	Terbutaline, salbutamol, metaproterenol, and pirbuterol
	long-acting B_2A	arformoterol, formoterol, and salmeterol
	ultra-long-acting B_2A	vilanterol, olodaterol, and indacaterol
muscarinic receptor antagonist		ipratropium and tiotropium
Xanthine derivatives		theophylline and aminophylline

- The inhaled and systemic ***glucocorticoids*** are used to temper the inflammation in diseases associated with respiratory acidosis.
- Discontinuation of respiratory depressants such as benzodiazepine and narcotic drugs:

Benzodiazepine antagonists	Flumazenil is used in reversing the CNS-depressing effects of benzodiazepine overdoses.
Opioid antagonists	Naloxone and naltrexone can be used to reverse the effects of opiates and to improve ventilation.

- ***Bicarbonate*** administration is rarely necessary and is potentially harmful.

Chronic respiratory acidosis (e.g., COPD) is treated essentially the same as acute respiratory acidosis with a few important exceptions. Oxygen therapy should be initiated carefully and only if the PaO_2 is less than 50 mm Hg (<6.7 kPa) because the drive to breathe depends on hypoxemia rather than hypercarbia.

Mixed acid–base disorders

Failure of compensation is responsible for mixed acid–base disorders such as respiratory acidosis and metabolic acidosis, or respiratory alkalosis and metabolic alkalosis.

In contrast, excess compensation is responsible for metabolic acidosis and respiratory alkalosis, or metabolic alkalosis and respiratory acidosis.

- **Respiratory and metabolic acidosis**

Respiratory and metabolic acidosis can develop in patients with cardiorespiratory arrest, with chronic lung disease and shock, and with metabolic acidosis and respiratory failure.

It can be treated by delivering oxygen to improve hypercarbia and hypoxia. Mechanical ventilation can be needed to reduce $PaCO_2$. During initial therapy, appropriate amounts of alkali should be given to reverse the metabolic acidosis.

- **Respiratory and metabolic alkalosis**

It is the most common mixed acid–base disorder. It occurs in critically ill surgical patients with respiratory alkalosis caused by mechanical ventilation, hypoxia, sepsis, hypotension, neurologic damage, pain, or drugs; and with metabolic alkalosis caused by vomiting or nasogastric suctioning and massive blood transfusions.

Sodium and potassium chloride solutions are used to correct alkalosis. The ventilator should be readjusted and the underlying disorder causing hyperventilation should be treated.

- **Metabolic acidosis and respiratory alkalosis**

Mixed metabolic acidosis and respiratory alkalosis occur in patients with advanced liver disease, salicylate intoxication and pulmonary-renal syndromes. Treatment should be directed at the underlying cause.

- **Metabolic alkalosis and respiratory acidosis**

It can occur in patients with COPD and respiratory acidosis who are treated with salt restriction, diuretics and possibly glucocorticoids.

pH does not usually deviate significantly from normal, but treatment can be required to maintain PaO_2 and $PaCO_2$ at acceptable levels. Plasma bicarbonate can be decreased with sodium and potassium chloride therapy.