Al-Mustaqbal University
College of Pharmacy
5th Stage
Applied therapeutics I
Lecture: 2

ACID–BASE DISORDERS

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ACID–BASE DISORDERS

- Acid–base disorders are caused by **disturbances in hydrogen ion** homeostasis, which is **ordinarily maintained** by:

1. Extracellular **buffering**
2. **Renal regulation** of hydrogen ion and bicarbonate excretion
3. **Ventilatory regulation** of CO2 elimination

GENERAL PRINCIPLES

- **Buffering refers** to the **ability** of a solution to **resist** change in pH after the **addition** of a strong acid or base.
- The body's **principal** extracellular buffer system is the **carbonic acid/bicarbonate** (H_2CO3/HCO_3^-) system.
- Most of the **body's acid production** is in the form of **CO_2** and is produced from the **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.

GENERAL PRINCIPLES

- **Metabolic** acid–base disorders are caused by changes in plasma **bicarbonate** concentration.
- **Metabolic acidosis** is characterized by **decreased HCO3**, and **metabolic alkalosis** is characterized by **increased HCO3**.
- **Respiratory** acid–base disorders are caused by altered alveolar **ventilation**, producing changes in arterial CO2tension (**PaCO2**).
- **Respiratory acidosis** is characterized by **increased PaCO2**, whereas **respiratory alkalosis** is characterized by **decreased PaCO2**.

DIAGNOSIS

- Blood gases, serum electrolytes, medical history, and clinical condition are the **primary tools** for determining the **cause** of acid–base disorders and for designing **therapy**.
- Arterial blood gases (**ABGs**) are measured to determine oxygenation and acid-base status.
- **Low pH values** (<7.35) indicate **acidemia**, whereas **high values** (>7.45) indicate **alkalemia**.
- The **PaCO2** value **helps** determine whether there is a **primary respiratory** abnormality, whereas the **HCO3** concentration **helps** determine whether there is a **primary metabolic** abnormality.

TABLE 73-1 Normal Blood Gas Values

	Arterial Blood	Mixed Venous Blood
pH	7.40 (7.35–7.45)	7.38 (7.33–7.43)
PO_2	80–100 mm Hg (10.6–13.3 kPa)	35–40 mm Hg (4.7–5.3 kPa)
SaO_2	95% (0.95)	70–75% (0.70–0.75)
PCO_2	35–45 mm Hg (4.7–6.0 kPa)	45–51 mm Hg (6.0–6.8 kPa)
HCO_3^-	22–26 mEq/L (mmol/L)	24–28 mEq/L (mmol/L)

HCO_3^-, bicarbonate; PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; SaO_2, saturation of arterial oxygen.

TABLE 73-2 Steps in Acid–Base Diagnosis

1. Obtain ABGs and electrolytes simultaneously
2. Compare [HCO_3^-] on ABG and electrolytes to verify accuracy
3. Calculate SAG
4. Is acidemia (pH <7.35) or alkalemia (pH >7.45) present?
5. Is the primary abnormality respiratory (alteration in $PaCO_2$) or metabolic (alteration in HCO_3)?
6. Estimate compensatory response (Table 73-3)
7. Compare change in [Cl^-] with change in [Na^+]

ABG, arterial blood gases; [Cl^-], chloride ion concentration; [HCO_3^-], bicarbonate concentration; [Na^+], sodium ion concentration; $PaCO_2$, partial pressure of carbon dioxide from arterial blood; SAG, serum anion gap.

Metabolic Acidosis

PATHOPHYSIOLOGY

- Metabolic acidosis is characterized by a **decrease in pH** as a result of a primary **decrease in serum HCO3** concentration, which can result from:

1. The **buffering of an exogenous acid** (consumption of HCO3)
2. **Accumulation of an organic acid** because of a metabolic disturbance (eg, lactic acid and ketoacids)
3. **Loss of bicarbonate-rich body fluids** (eg, diarrhea, biliary drainage, or pancreatic fistula)
4. Progressive **accumulation of endogenous acids** secondary to impaired kidney function (eg, phosphates and sulfates)
5. Rapid **administration of non-alkali-containing IV fluids** can cause dilutional acidosis

PATHOPHYSIOLOGY

- **Serum anion gap (SAG)** can be used to infer whether an **organic** or **mineral** acidosis is present.
- SAG is calculated as follows:

$$\mathrm{SAG} = [Na^{+}] - [Cl^{-}] - [HCO^{-}]$$

- The **normal anion gap** is approximately 9 mEq/L (mmol/L), with a range of **3–11** mEq/L (mmol/L).
- SAG is a **relative** rather **than an absolute** indication of the cause of metabolic acidosis.

CLINICAL PRESENTATION

- **Chronic** metabolic acidosis is 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** (ie, deep, rapid respirations characteristic of diabetic ketoacidosis).
- The compensatory response for metabolic acidosis is **to increase CO2 excretion** by **increasing the respiratory rate**.

TREATMENT

- The **primary** treatment is to **correct the underlying** disorder.
- **Additional** treatment depends on the severity and onset of acidosis.
- **Manage** asymptomatic patients with **mild** to **moderate** acidemia (HCO_3 12–20 mEq/L [mmol/L]; pH 7.2–7.4) **with gradual correction** of the acidemia over days to weeks **using oral sodium bicarbonate** or other **alkali preparations**.

  - The dose of bicarbonate can be calculated as follows:

$$\text{Loading dose (mEq or mmol/L)} = (V_d\ HCO_3^- \times \text{body weight}) \times (\text{desired } [HCO_3^-] - \text{current } [HCO_3^-]),$$

where $V_d\ HCO_3^-$ is the volume of distribution of HCO_3^- (0.5 L/kg).

TREATMENT

- **Intravenous** alkali therapy can be used to treat patients with **acute severe metabolic acidosis**.
- Therapeutic options include **sodium bicarbonate** and historically, **tromethamine**, which is no longer available in the United States.
- Sodium bicarbonate is recommended to raise arterial pH to 7.2.
- If IV sodium bicarbonate is administered, the **goal is to increase, not normalize, pH to 7.2 and HCO_3 to 8–10 mEq/L (mmol/L).**

Metabolic Alkalosis

PATHOPHYSIOLOGY

- Metabolic alkalosis is initiated by **increased pH and HCO_3**, which can result from:

1. **Loss of hydrogen ions** via the **GIT** (eg, nasogastric suctioning, vomiting) or **kidneys** (eg, diuretics, Cushing syndrome)
2. **Gain of bicarbonate** (eg, administration of bicarbonate, acetate, lactate, or citrate).

- Metabolic alkalosis is **maintained by abnormal renal function** that **prevents** the kidneys from **excreting excess bicarbonate**.

CLINICAL PRESENTATION

- **No unique signs or symptoms** are associated with **mild** to **moderate** metabolic alkalosis.
- **Some** patients complain of **symptoms** related to the **underlying disorder** (eg, muscle weakness with hypokalemia or postural dizziness with volume depletion) 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**.
- The **compensatory** response to metabolic alkalosis is **respiratory**, manifested as **hypoventilation** which **increases PaCO2**.

TREATMENT

- **Treatment** is aimed at **correcting** the factor(s) responsible for maintaining the alkalosis and depends on whether the disorder is sodium chloride **responsive** or **resistant**.

Respiratory Alkalosis

PATHOPHYSIOLOGY

- 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:

1. **Increases** in **neurochemical stimulation** via central or peripheral mechanisms,
2. **Physical increases in ventilation** via voluntary or artificial means (eg, mechanical ventilation).

CLINICAL PRESENTATION

- **Although usually asymptomatic**, respiratory alkalosis **can cause** adverse neuromuscular, cardiovascular, and GI effects.
- Light-headedness, confusion, decreased intellectual functioning, syncope, and seizures can be caused by **decreased cerebral blood flow**.
- **Nausea** and **vomiting** can occur, probably due to **cerebral hypoxia**.
- **Cardiac arrhythmias** can occur in **severe** respiratory alkalosis.

CLINICAL PRESENTATION

- **Serum electrolytes** can be altered; serum **chloride** is usually **increased**; serum **potassium**, **phosphorus**, and ionized **calcium** are usually **decreased**.
- The **initial compensatory** response is to chemically buffer **excess bicarbonate** by **releasing H^+ ions** from intracellular proteins, phosphates, and hemoglobin.
- If **prolonged** (>6 hours), the **kidneys** attempt to further **compensate** by **increasing bicarbonate elimination**.

TREATMENT

- Treatment is often **unnecessary** because most patients have **few symptoms** and only **mild pH alterations** (ie, pH not exceeding 7.50).
- **Direct measures** (eg, treatment of pain, hypovolemia, fever, infection, or salicylate overdose) can be **effective**.
- A **rebreathing device** (eg, paper bag) can help **control hyperventilation** in patients with anxiety/hyperventilation syndrome.
- **Correct 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

PATHOPHYSIOLOGY

- Respiratory acidosis is characterized by an **increase in PaCO2** and a **decrease in pH**.
- Respiratory acidosis **results from** disorders that:

1. Disorders that restrict ventilation or increase CO2 production
2. Airway and pulmonary abnormalities
3. Neuromuscular abnormalities
4. Mechanical ventilator problems

CLINICAL PRESENTATION

- **Neuromuscular symptoms** include altered mental status, abnormal behavior, seizures, stupor, and coma.
- **Hypercapnia** can **mimic** a **stroke or CNS tumor** by producing headache, papilledema, focal paresis, and abnormal reflexes.
- **CNS symptoms** are caused by increased cerebral blood flow and are **variable**, **depending** in part on the **acuity of onset**.
- The **initial compensatory response** to acute respiratory acidosis is **chemical buffering**.
- If **prolonged** (>12–24 hours), **proximal tubular HCO3 reabsorption**, **ammoniagenesis**, and distal tubular **H+ secretion** are enhanced, **resulting** in an increase in serum HCO3 concentration that raises pH to normal.

TREATMENT

- Provide **adequate ventilation** if CO2 excretion is **acutely** and **severely impaired** (PaCO2 >80 mm Hg [>10.6 kPa]) or if **life-threatening hypoxia** is present (arterial oxygen tension [PaO2] <40 mm Hg [<5.3 kPa]).
- **Ventilation** can include **maintaining** a patent airway (eg, emergency tracheostomy, bronchoscopy, or intubation), **clearing** excessive secretions, **administering** oxygen, and **providing** mechanical ventilation.
- **Treat underlying cause** aggressively (eg, administration of **bronchodilators** for bronchospasm; narcotic or benzodiazepine **antagonists** to reverse effect of these agents on the respiratory center).

TREATMENT

- **Bicarbonate** administration is **rarely** necessary and is potentially harmful.
- **Chronic** respiratory acidosis (eg, chronic obstructive pulmonary disease [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 **PaO2 is less than 50 mm Hg** (6.7 kPa) **because** the drive to breathe depends on **hypoxemia** rather than **hypercarbia**.

EVALUATION OF THERAPEUTIC OUTCOMES

- **Monitor patients closely** because acid–base disorders can be serious and even life-threatening.
- **ABGs** are the **primary tools** for the evaluation of therapeutic outcomes.

THANK YOU FOR YOUR ATTENTION