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PEARLS OF LABORATORY MEDICINE

Acid-Base Disorders

Brenda Suh-Lailam, PhD, D(ABCC), FAC

*Ann & Robert H. Lurie Children's Hospital of Chicago,
Northwestern University Feinberg School of Medicine*

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Acid-Base Homeostasis

1. Bicarbonate buffer system – Major buffer system
2. Plasma protein buffer system
3. Hemoglobin buffer system

Bicarbonate Buffer System

$$H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2(gas) + H_2O$$

Metabolic component

Respiratory component

- ↑pCO_2 and↓HCO_3^- → shift to left →↑H^+ → ↓pH → Acidosis
- ↓pCO_2 and↑HCO_3^- → shift to right →↓H^+ →↑pH → Alkalosis

Henderson-Hasselbalch Equation

$$\mathrm{pH} = \mathrm{p}K_a' + \log\frac{\mathrm{HCO_3^-}}{0.0307 \times \mathrm{pCO_2}}$$

- $\mathrm{p}K_a'$ = pH at which the concentration of protonated and unprotonated species are equal
- 0.0307 = Solubility coefficient of carbon dioxide

- Knowing 3 of 4 variables allows for calculation of the 4th variable
  - $\mathrm{p}K_a'$ is a constant (6.4)
  - pH and $\mathrm{pCO_2}$ are measured during blood gas analysis
  - $\mathrm{HCO_3^-}$ can be determined

Acid-Base Disorders

- Metabolic disorders
  - Metabolic acidosis
  - Metabolic alkalosis
- Respiratory disorders
  - Respiratory acidosis
  - Respiratory alkalosis

Metabolic Acidosis

Disorder results when there are decreases in bicarbonate and buffering capacity is reduced.

Causes:

- Excessive production of organic acids
  - Acetoacetic acid and B-hydroxybutyric acid – diabetic ketoacidosis
  - Lactic acid – lactic acidosis
- Reduced acid excretion
  - Renal failure
  - Renal tubular acidosis
- Excessive loss of bicarbonate
  - Decreased renal retention
  - Diarrhea
  - Drainage from biliary, pancreatic, or intestinal fistula

Anion Gap (AG) in Metabolic Acidosis

$$AG = [Na^{+} + K^{+}] - [Cl^{-} + HCO_3^{-}]$$

Formula without potassium:

$$AG = [Na^{+}] - [Cl^{-} + HCO_3^{-}]$$

- Useful in assessing causes of metabolic acidosis
  - Addition of acid
    - Electroneutrality maintained by retention of conjugate base
    - Anion gap = increased
  - Removal of base
    - Loss in stool or urine
    - Electroneutrality maintained by retention of chloride
    - Anion gap = normal

Metabolic Acidosis

High Anion Gap	Normal Anion Gap
Methanol **U**remia **D**iabetic ketoacidosis/ alcoholic acidosis/ starvation **P**araldehyde **I**soniazid **L**actic acidosis **E**thylene glycol **S**alicylate	Gastrointestinal fluid loss • Severe diarrhea • Pancreatitis • Intestinal fistula Renal tubular acidosis Chloride excess from administration of chloride-containing fluids (saline, HCL, NH_4CL)

Metabolic Alkalosis

Disorder results from an increase in bicarbonate

Causes:

- Addition of excess base
    - Excess administration of Na bicarbonate
    - Ingestion of bicarbonate-producing salts
        - E.g. antacids
- Loss of acid-rich fluids
        - Vomiting
        - Nasogastric suctioning
        - Prolonged use of diuretics that ↑H^+ loss
- Decreased elimination of bases

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Respiratory Acidosis

Disorder results from an increase in pCO_2

Causes:

- Decreased elimination of CO_2
  - Direct depression of the respiratory center
    - Drugs: Narcotics, barbiturates
    - CNS trauma, tumors, degenerative disorders
    - CNS infections: encephalitis, meningitis
    - Primary central hypoventilation
  - Disruption of CO_2 elimination by lungs
    - Chronic obstructive pulmonary disease (most common)
    - Severe pulmonary fibrosis
    - Status asthmaticus (severe)
  - Other (e.g. extreme obesity)

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Respiratory Alkalosis

Disorder results from a decrease in pCO_2

Causes:

- Excessive elimination of CO_2 by lungs
    - Increase in rate and/or depth of breathing
        - ○ Hypoxia
        - ○ Drugs: salicylate, progesterone
        - ○ Gram-negative septicemia
        - ○ Fever
        - ○ Pulmonary emboli
        - ○ Pneumonia

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Compensation in acid-base disorders

- Goal: Normalize pH
- Alteration of factor not initially disturbed
  - If metabolic component is primarily affected, respiratory component is altered
    - Response is rapid and max compensation is achieved in 12-24 hrs
  - If respiratory component is primarily affected, metabolic component is altered
    - Response is slow and max compensation is achieved in 3-4 days

Compensatory Mechanisms

- Metabolic acidosis
  - Hyperventilation → ↑CO_2 elimination → ↑pH
- Metabolic alkalosis
  - Hypoventilation → ↑CO_2 retention → ↓pH
- Respiratory acidosis
  - ↑ Excretion of H^+ by kidneys
  - ↑ Reclamation of HCO_3^- by kidneys

→ ↑pH

- Respiratory alkalosis
  - ↑ Excretion of HCO_3^- by kidneys
  - ↑ Reclamation of H^+ by kidneys

→ ↓pH

Case 1

- A 13-year-old girl was brought to the emergency room after being found in her room. She was minimally responsive and had the following laboratory results:

		Results	Reference Interval (RI)
pH		7.10	7.35-7.45
pCO_2	(mmHg)	29	35-45
HCO_3^-	(mmol/L)	9	22-26
Na^+	(mmol/L)	144	134-146
Cl^-	(mmol/L)	103	98-108

What is the acid-base disorder in this patient?

Case 1

- A 13-year-old girl was brought to the emergency room after being found in her room. She was minimally responsive and had the following laboratory results:

		Results	Reference Interval (RI)
pH		7.10↓	7.35-7.45
pCO_2	(mmHg)	29↓	35-45
HCO_3^-	(mmol/L)	9↓	22-26
Na+	(mmol/L)	135	134-146
Cl-	(mmol/L)	103	98-108
AG = 135 – (103 + 9) = 23			12 ± 2

- What is the acid-base disorder in this patient?
  - Metabolic acidosis
  - High AG – Ethylene glycol poisoning

Assessing Adequacy of Compensation

Acid-base Disorder	Primary Change	Compensatory Response	Formula for Calculating Expected Change in Compensation
Metabolic acidosis	↓HCO_3^-	↓pCO_2	$\Delta pCO_2 = 1.2 (\Delta HCO_3^-) \pm 2$
Metabolic alkalosis	↑HCO_3^-	↑pCO_2	$\Delta pCO_2 = 0.7 (\Delta HCO_3^-) \pm 5$
Respiratory Acidosis - Acute	↑pCO_2	↑HCO_3^-	$\Delta HCO_3^- = 0.07 (\Delta pCO_2) \pm 1.5$
Respiratory Acidosis - Chronic	↑pCO_2	↑HCO_3^-	$\Delta HCO_3^- (\uparrow) = 0.4 (\Delta pCO_2) \pm 3$
Respiratory Alkalosis - Acute	↓pCO_2	↓HCO_3^-	$\Delta HCO_3^- (\downarrow) = 0.2 (\Delta pCO_2) \pm 2.5$
Respiratory Alkalosis - Chronic	↓pCO_2	↓HCO_3^-	$\Delta HCO_3^- (\downarrow) = 0.5 (\Delta pCO_2) \pm 2.5$

ΔpCO_2 and ΔHCO_3^- = Difference between measured and normal results

Case 2

- A 6-year-old boy with acute, severe diarrhea presented to the emergency room with the following laboratory results:

		Results	**Reference Interval (RI)**
pH		7.29	7.35-7.45
pCO_2	(mmHg)	30	35-45
HCO_3^-	(mmol/L)	15	22-26
Na^+	(mmol/L)	132	134-146
Cl^-	(mmol/L)	103	98-108

How would you describe the acid-base disorder in this patient?

Case 2

- A 6-year-old boy with acute, severe diarrhea presented to the emergency room with the following laboratory results:

		Results	Reference Interval (Optimal)
pH		7.29 ↓	7.35-7.45 (7.40)
pCO_2	(mmHg)	30↓	35-45 (40)
HCO_3^-	(mmol/L)	15↓	22-26 (24)
Na^+	(mmol/L)	132	134-146
Cl^-	(mmol/L)	103	98-108
AG = 132 – (103 + 15) = 14			12 ± 2

- How would you describe the acid-base disorder in this patient?
  - Normal anion gap metabolic acidosis with compensatory respiratory alkalosis
  - Expected compensation:
    - $\Delta pCO_2 = 1.2\ (24-15) = 10.8 \pm 2$
    - Expected $pCO_2 = 40 - 10.8 = 29.2 \pm 2$
  - Compensation is maximal; because pCO_2 should be 29.2 ± 2 and it is 30

Summary: Evaluation of Acid-Base Disorders

Evaluate the pH

- Normal (pH = RI)
- Acidemia (pH < RI)
- Alkalemia (pH > RI)

Determine the primary disorder

- Metabolic acidosis
- Respiratory acidosis
- Metabolic alkalosis
- Respiratory alkalosis

Compute the anion gap

Anion gap is useful in identifying cause of metabolic acidosis

Assess adequacy of compensation

If compensation is present, carbon dioxide and bicarbonate change in the same direction

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