Zuur-Base Stoornissen
De Anesthesist als Peri-Operatief Geneesheer

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Co-assistenten 3-10-2012
Section III:
Preoperative Preparation and Intraoperative Management

Chapter 21:
Acid-Base Balance and Blood Gas Analysis (p. 334 - 343)
Linda L. Liu
Acid - Base Balance

- **Maintaining a physiologic pH ([H⁺]) is important**
  - Oxygen transport
  - Enzyme activity
  - Biochemical reactions
  - Cellular function
  - Organ function

- **Anesthesia and surgery affect acid-base balance**
  - Changes in ventilation
  - Hemodynamic changes
  - Intravenous fluid therapy
Topics

• Definitions
• Regulation of $[\text{H}^+]$  
  – Buffer systems  
  – Ventilatory response  
  – Renal response  
• Common acid-base disturbances  
  – Respiratory acidosis  
  – Respiratory alkalosis  
  – Metabolic acidosis  
  – Metabolic alkalosis  
• Interpretation of acid-base disturbances: practical approach
DEFINITIONS
Dissociation of Water

\[ \text{H}_2\text{O} \leftrightarrow \text{H}^+ + \text{OH}^- \]

\[ K = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]} \]

\[ K_w = [\text{H}^+][\text{OH}^-] = 10^{-14} \]

- \( K \) = dissociation constant
- \( K_w \) includes the concentration of water (which does not vary appreciably)
Acid

• Definition
  – Traditionally: a substance that can act as a proton (H⁺) donor
  – A substance that increases [H⁺] when added to a solution

• Strong acid
  – Readily and irreversibly donates H⁺
    → Increases [H⁺]

• Weak acid
  – Reversibly donates H⁺
    → Less effect on [H⁺]
Base

• **Definition**
  – Traditionally: a substance that can act as a proton (H⁺) acceptor
  – A substance that decreases [H⁺] when added to a solution

• **Strong base**
  – Avidly binds H⁺
  → Decreases [H⁺]

• **Weak base**
  – Reversibly binds H⁺
  → Less effect on [H⁺]
Acidosis and Alkalosis

The terms acidosis and alkalosis refer to a primary process and its compensatory response altering arterial pH

- **Acidosis**: a process that reduces blood pH
- **Alkalosis**: a process that increases blood pH

→ Acidosis and alkalosis can occur concomitantly
Acidemia and Alkalemia

The terms acidemia and alkalemia denote the net effect on arterial pH of primary processes and their compensatory physiologic responses

- **Acidemia**: blood pH < 7.35
- **Alkalemia**: blood pH > 7.45

→ Acidemia and alkalemia are mutually exclusive terms
Base Excess

Base excess (BE) is the amount of strong acid (BE > 0) or strong base (BE < 0) required to return 1 L of fully oxygenated blood to a pH of 7.4 (at 37°C and a PaCO₂ of 40 mmHg)

- Refers to the nonrespiratory (= metabolic) component of an acid-base disturbance
  - Normal value: -2 - 3 mmol/L
  - A positive value indicates metabolic alkalosis
  - A negative value indicates metabolic acidosis

- Graphically or electronically derived from a nomogram (Siggaard-Andersen) or algorithm
  - Utilizes plasma pH, blood PCO₂ and hemoglobin concentration
Buffer (1)

- Minimizes changes in pH by either binding or releasing $H^+$
- A buffer always consists of conjugate pairs
  - A weak acid and its conjugate base: $HA \leftrightarrow H^+ + A^-$
    - Acid (HA): protonates excess base molecules
    - Conjugate base (A$^-$): binds excess $H^+$
  - A weak base and its conjugate acid: $B + H_2O \leftrightarrow BH^+ + OH^-$
    - Base (B): binds excess $H^+$
    - Conjugate acid (BH$^+$): protonates excess base molecules
Buffer (2)

- Weak acid buffer: \( HA \rightleftharpoons H^+ + A^- \)

\[
K_a = \frac{[H^+] [A^-]}{[HA]} \quad \text{or} \quad [H^+] = \frac{K_a [HA]}{[A^-]}
\]

- The acid dissociation constant \((K_a)\) indicates the strength of an acid
Buffer (2)

- Weak acid buffer: \( \text{HA} \leftrightarrow \text{H}^+ + \text{A}^- \)

\[
K_a = \frac{[\text{H}^+] [\text{A}^-]}{[\text{HA}]} \quad \text{or} \quad [\text{H}^+] = \frac{K_a [\text{HA}]}{[\text{A}^-]}
\]

- The acid dissociation constant \((K_a)\) indicates the strength of an acid
- \(pK_a\) is the pH at which an acid is 50% dissociated
- Smaller \(pK_a\) \(\rightarrow\) stronger acid
- A buffer is most effective when \(pK_a = \text{pH}\)
Henderson-Hasselbach Equation

• The Henderson-Hasselbalch equation describes the relationship between the pH of a solution and the ratio of the concentration of a weak acid or weak base and its salt.

\[
pH = pK_a + \log \frac{[\text{Base}]}{[\text{Weak acid}]}
\]

• Bicarbonate buffer (\(H_2CO_3 / HCO_3^-\))

\[
pH = pK_a + \log \frac{[HCO_3^-]}{[H_2CO_3]}
\]

- pH is related to the ratio between \([H_2CO_3]\) and \([HCO_3^-]\)
- CO2 tension (PaCO2) may be substituted for \(H_2CO_3\)
Acidosis and Alkalosis:
Henderson-Hasselbalch Approach

- Bicarbonate-based approach
- Metabolic or respiratory acidosis or alkalosis
  - **Metabolic**: primarily affects $\text{HCO}_3^-$
  - **Respiratory**: primarily affects $\text{PaCO}_2$
- Limitations of the Henderson-Hasselbalch approach to acid-base disturbances
  - Provides an estimate of the magnitude of acid-base disturbances
  - Alterations in $\text{HCO}_3^-$ and base excess do not reflect the mechanism of acid-base disturbances
### Classification of Acid-Base Disorders (Henderson-Hasselbalch Approach)

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Primary change</th>
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<tr>
<td><strong>Respiratory</strong></td>
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Stewart Approach

- Physicochemical approach
- Plasma [HCO$_3^-$] is a dependent variable and therefore does not alter blood pH
- 3 independent variables influence the dissociation of water and the [H$^+$] $\rightarrow$ responsible for acid-base disturbances
  - Strong ion difference (SID)
  - Plasma concentration of nonvolatile weak acids ($A_{Tot}$)
  - Arterial carbon dioxide tension (PaCO$_2$)
Strong Ion Difference

\[
\text{SID} = (\text{Strong cations}) - (\text{Strong anions}) \\
= ([\text{Na}^+]+[\text{K}^+]+[\text{Ca}^{2+}]+[\text{Mg}^{2+}]) - ([\text{Cl}^-]+[\text{other strong anions}]) \\
= ([\text{Na}^+]+[\text{K}^+]) - [\text{Cl}^-]
\]

- **Normal SID** = 40 - 44 mEq/L
  - Balanced by an equal amount of buffer base (phosphate, albumin, bicarbonate)
- **Decreased SID** → decreased blood pH
  - E.g. massive volumes of NaCl 0.9%: major ions are Na\(^+\) and Cl\(^-\)
  - and SID = 0 → reduction of SID
- **Increased SID** → increased blood pH
  - E.g. gastric fluid loss: major ion is Cl\(^-\) (> strong cations)
Nonvolatile Weak Acids

• Inorganic phosphates, albumin, and other plasma proteins
  – The major practical difference with the Henderson-Hasselbalch approach is the inclusion of the serum albumin concentration
  – However, in the Henderson-Hasselbalch approach the anion gap can be corrected for albumin (hypoalbuminemia)
• Weak acids have not a great influence on the acid-base balance in healthy persons
• Hypoalbuminemia and hypophosphatemia
  → Metabolic alkalosis
• Hyperalbuminemia and hyperphosphatemia
  → Metabolic acidosis
### Classification of Acid-Base Disorders (Stewart Approach)

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<tr>
<th>Acidosis</th>
<th>Respiratory</th>
<th>Increased PaCO&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Metabolic</th>
<th>Decreased SID</th>
<th>Increased Cl&lt;sup&gt;-&lt;/sup&gt;</th>
<th>Decreased Na&lt;sup&gt;+&lt;/sup&gt;/increased free water</th>
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<td>Hyperproteinemia</td>
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REGULATION OF HYDROGEN ION CONCENTRATION
Hydrogen Ion Concentration

- Arterial blood and extracellular fluid: \([H^+] = 35 - 40 \text{ nmol/L}\)
  - Normal arterial pH = 7.35 - 7.45
  - Blood pH between 6.8 – 7.8 ([H+] between 16 and 160 nmol/L) is compatible with life

- The body has a large buffering capacity to maintain a normal [H+] despite a large amount of daily acid production
  - Daily approximately 15 000 mmol of CO\(_2\) (→ carbonic acid)
  - Daily 50 – 100 mEq of nonvolatile acid
Regulation of [H+] 

- **Buffer systems**: immediate chemical response
  - Bicarbonate buffer system
  - Hemoglobin buffer system

- **Ventilatory response**: fast response

- **Renal Response**: slow response, but nearly complete restoration of pH
  - Reabsorption of $\text{HCO}_3^-$
  - Excretion of titratable acid
  - Production of ammonia
Bicarbonate Buffer System \(^{(1)}\)

- Bicarbonate buffer: base = $\text{HCO}_3^-$
  weak acid = $\text{H}_2\text{CO}_3$
- Carbonic anhydrase (in endothelium, erythrocytes and kidneys) greatly accelerates this reaction
- Most important buffering system when combined with renal control of $\text{HCO}_3^-$ and pulmonary control of $\text{CO}_2$
- Bicarbonate buffer is effective against metabolic, but not against respiratory acid-base disturbances
Bicarbonate Buffer System (2)

\[ \text{H}^+ + \text{HCO}_3^- \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}_2\text{O} + \text{CO}_2 \]

- Henderson-Hasselbach equation for bicarbonate buffer

\[
\text{pH} = pK + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}
\]

- CO\(_2\) tension (PaCO\(_2\)) may be substituted for H\(_2\)CO\(_3\)

\[
\text{pH} = pK' + \log \frac{[\text{HCO}_3^-]}{0.3 \text{ PaCO}_2}
\]

- Solubility coefficient for CO\(_2\) = 0.03 mmol/L
- Adjusted dissociation constant pK' = 6.1
Bicarbonate Buffer System (3)

- \( \text{pK'} = 6.1 \)
  - Not close to normal arterial pH of 7.4
  - Nevertheless: bicarbonate buffer is important
- Relatively high concentrations in extracellular fluid
- Kidneys and lungs have important influences on arterial pH by altering the \( [\text{HCO}_3^-] / \text{PaCO}_2 \) ratio
  - Lungs regulate \( \text{PaCO}_2 \)
  - Kidneys regulate plasma \( [\text{HCO}_3^-] \)
- System adapts to changing acid-base conditions
Extracellular fluid

Intracellular fluid

Kidneys

Lungs

\[ \text{H}^+ + \text{HCO}_3^- \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}_2\text{O} + \text{CO}_2 \]
Bicarbonate Buffer: Simplified Equation

\[
[H^+] = 24 \times \frac{\text{PaCO}_2}{[\text{HCO}_3^-]}
\]

Clinically useful because pH can be converted to \([H^+]

- pH = 7.40: \([H^+] = 40 \text{ nEq/L}
- pH < 7.40: \([H^+]\) increases 1.25 nEq/L for each 0.01 decrease in pH
- pH > 7.40: \([H^+]\) decreases 0.8 nEq/L for each 0.01 increase in pH
Hemoglobin Buffer System (1)

- **Histidine buffer**
  - Multiple buffering sites on imidazole side chains
  - Histidine is an effective buffer from pH 5.7 – 7.7 ($pK_a$ 6.8)
- **Dependent on the HCO$_3^-$ system: a large fraction of extrapulmonary CO$_2$ is transported to the lungs as plasma HCO$_3^-$**
  - Tissues: CO$_2$ diffuses into RBC where it is eliminated as HCO$_3^-$
Figure 21-3 Hemoglobin buffering system: Carbon dioxide freely diffuses into erythrocytes, where it combines with water to form carbonic acid, which rapidly deprotonates. The protons generated are bound up by hemoglobin. The bicarbonate anions are exchanged back into plasma with chloride.
Hemoglobin Buffer System (2)

- Hb buffer depends on the HCO$_3^-$ system
  - Tissues: CO$_2$ diffuses into RBC where it is eliminated as HCO$_3^-$
  - Lungs: HCO$_3^-$ enters the RBC (in exchange for Cl$^-$) where it is converted to CO$_2$ which is released into the plasma and eliminated by the lungs.

- Oxygenated and deoxygenated hemoglobin have different affinities for H$^+$ and CO$_2$
Hemoglobin Buffer System (3)

- **Oxygenated and deoxygenated hemoglobin have different affinities for H\(^+\) and CO\(_2\)**
  - Deoxygenated Hb takes up more H\(^+\)
    - Increased HCO\(_3^-\) production
    - Facilitates removal of CO\(_2\) from tissues
  - Oxyhemoglobin favors the release of H\(^+\)
    - Increased CO\(_2\) production and elimination in the lungs
  - Physiologic pH: a small amount of CO\(_2\) is also carried as carbaminohemoglobin
- **DeoxyHb has a 3.5 x greater affinity for CO\(_2\)**
  - Venous blood carries more CO\(_2\) than arterial blood

→ **Difference in CO\(_2\) content of arterial (25.6 mmol/L) versus venous (27.7 mmol/L) plasma (Haldane effect)**
Ventilatory Response (1)

- Central chemoreceptors (medular) respond to changes in pH of CSF
  - CO₂ diffuses across the blood-brain barrier
  - [H⁺] in CSF increases → pH in CSF decreases
  - Activation of chemoreceptors
  - → Increased alveolar ventilation
- Relationship between PaCO₂ and minute ventilation: almost linear
  - Exceptions: very high PaCO₂ (carbonarcosis) and very low PaCO₂ (apneic threshold)
  - PaCO₂/ventilation response curve: wide interindividual variation
  - Generally: minute volume increases 1 - 4 L/min for every 1 mmHg increase in PaCO₂ (for PaCO₂ 40-50 mmHg)
Ventilatory Response (2)

- Peripheral chemoreceptors (bifurcation of common carotid arteries, aortic arch) are sensitive to changes in \( \text{PaO}_2 \), \( \text{PaCO}_2 \), pH, and arterial perfusion pressure
  - Most sensitive to \( \text{PaO}_2 \)
  - Glossopharyngeal nerves: communication with central respiratory centers
- There is no complete ventilatory correction
  - Pulmonary response diminishes when pH approaches 7.4
- Pulmonary response to metabolic alkalosis is generally less than pulmonary response to metabolic acidosis
Ventilatory Response (3)

- Pulmonary response to metabolic acidosis
  - Rapid response, but steady state after 12 - 24 h
  - Appropriate compensation?
    - PaCO$_2$ decreases 1 - 1.5 mmHg for each 1 mEq/L decrease in plasma [HCO$_3^-$]
    - Winter’s formula: $\text{PaCO}_2 = (1.5 \times [\text{HCO}_3^-]) + 8$
Ventilatory Response (4)

- **Pulmonary response to metabolic alkalosis**
  - Less predictable response than to metabolic acidosis
    - Progressive hypoventilation results in hypoxemia
    - Hypoxemia activates O\(_2\)-sensitive chemoreceptors stimulating ventilation
    - PaCO\(_2\) usually does not rise above 55 mmHg in response to metabolic alkalosis
  - Appropriate compensation?
    - Generalization: PaCO\(_2\) increases 0.25 - 1 mmHg for each 1 mEq/L increase in plasma [HCO\(_3\)-]
    - PaCO\(_2\) = (0.7 x [HCO\(_3\)-]) + 21
Renal Response and Metabolic Acidosis

- Slow onset (12 - 24 h)
- Maximal effect after 5 d
- Mechanisms compensating for metabolic acidosis
  1. Reabsorption of filtered \( \text{HCO}_3^- \)
  2. Excretion of titratable acids
  3. Production of ammonia
  → Generation and return of \( \text{HCO}_3^- \) into the blood stream
Figure 21-4 Three mechanisms of renal compensation during acidosis to sequester hydrogen ions and reabsorb bicarbonate: (1) reabsorption of the filtered HCO$_3^-$, (2) excretion of titratable acids, and (3) production of ammonia.
Renal Response: Reabsorption of HCO$_3^-$

HCO$_3^-$ is freely filtered at the glomerulus

- Proximal tubule
  - Reabsorbs 80-90% of filtered HCO$_3^-$
  - H$^+$ pump: linked to Na$^+$ reabsorption

- Distal tubule
  - Reabsorbs 10-20% of filtered HCO$_3^-$
  - H$^+$ pump: not necessarily linked to Na$^+$ reabsorption
  - Distal H$^+$ pump is capable of generating steep H$^+$ gradients between tubular fluid and tubular cells
    - Urinary pH can decrease as low as 4.4 (vs 7.4 in plasma)
Renal Response: Excretion of Titratable Acids

Phosphate ($H_2PO_4^-$ / $HPO_4^{2-}$) buffer: increased $H^+$ excretion

- Starts after all the $HCO_3^-$ in the tubular fluid is reclaimed
- $H^+$ combines with $HPO_4^{2-}$ and is excreted as $H_2PO_4^-$
- $H_2PO_4^- / HPO_4^{2-}$: $pK = 6.8$
  - Normally an ideal urinary buffer
  - pH 4.4: $H_2PO_4^-$ ions are no longer available for $H^+$ elimination
Renal Response: Production of Ammonia

Ammonia (NH₃/NH₄⁺) buffer: increased H⁺ elimination

- NH₃/NH₄⁺ buffer becomes important after complete reabsorption of HCO₃⁻ and after consumption of the phosphate buffer
  - More ammonia is produced during acidosis
- Excretion of NH₄⁺ in urine
  - NH₃ is produced from deamination of glutamine
  - NH₃ combines in the tubular fluid with H⁺ to form NH₄⁺
Renal Response and Metabolic Alkalosis (1)

- If necessary, the kidneys excrete large amounts of $\text{HCO}_3^-$
  - Efficient protection against metabolic alkalosis
- Metabolic alkalosis occurs only in association with
  - Sodium deficiency
    - $\text{Na}^+$ depletion increases $\text{Na}^+$ reabsorption (proximal tubule)
      - With $\text{Cl}^-$ to maintain electrical neutrality
      - $[\text{Cl}^-]$ in urine < 10 mEq/L: $\text{HCO}_3^-$ is reabsorbed
    - Increased $\text{H}^+$ secretion in exchange with $\text{Na}^+$ reabsorption favors continued $\text{HCO}_3^-$ formation (even during metabolic alkalosis)
  - Mineralocorticoid excess
Renal Response and Metabolic Alkalosis (2)

- Metabolic alkalosis occurs only in association with
  - Sodium deficiency
  - Mineralocorticoid excess
- Increased aldosterone-mediated Na$^+$ reabsorption in exchange for H$^+$ secretion in the distal tubules
  $\rightarrow$ Increased HCO$_3^-$ formation
ACID-BASE DISTURBANCES
Acid-Base Disturbances

- Acidosis or alkalosis
- Respiratory or metabolic
- Acute or chronic (compensatory response)

Mixed acid-base disorder
Acidemia: Adverse Effects (1)

• Result of balance between direct depressant effects and sympathoadrenal activation
• Mild acidemia
  – Release of catecholamines mitigate myocardial depression
  – No significant effect on systemic vascular resistance, pulmonary vascular resistance, cardiac output, or systemic O₂ delivery
• Severe acidemia
  – pH < 7.20: direct depressant effects predominate
Acidemia: Adverse Effects

- **Severe acidemia**
  - pH < 7.20: direct depressant effects predominate
  - Decreased myocardial responsiveness to catecholamines with myocardial depression and hypotension
  - Progressive hyperkalemia
    - Movement of K⁺ out of cells in exchange for extracellular H⁺
    - Plasma [K⁺] increase of 0.6 mEq/L for each 0.10 decrease in pH
  - Central nervous system effects (respiratory > metabolic acidosis)
    - Severe acute intracellular acidosis → confusion, loss of consciousness, seizures
    - Increased cerebral blood flow → increased intracranial pressure
Acidemia and Anesthesia: Risks

- Hemodynamic instability
  - Arteriolar vasodilatation and decreased cardiac output
  - Exaggerated cardiovascular depressant effects of anesthetics
  - Decreased response to vasopressors and inotropes
- Arrhythmias
- Hyperkalemia (avoid succinylcholine)
- Insulin resistance and hyperglycemia
- Acidemia may augment nondepolarizing neuromuscular blockade
- Postoperative mechanical ventilation may be necessary

In severe acidemia, consider postponing surgery until the underlying cause is treated or the patient is preoperatively optimized. However: surgery may be the treatment that is required.
Alkalemia: Adverse Effects

- **Severe alkalemia (pH > 7.6)**
  - Arteriolar vasoconstriction
    - Decreased cerebral and coronary blood flow
  - Consequences are more severe with respiratory alkalosis
    - Rapid movement of CO$_2$ across cell membranes
    - Acute hyperventilation $\rightarrow$ confusion, myoclonus, flapping tremor, depressed consciousness, seizures
  - Risk of hypokalemia
    - Movement of H$^+$ out of cells in exchange for extracellular K$^+$
Alkalemia and Anesthesia: Risks

- Coronary vasospasm and risk of myocardial ischemia
- Hypokalemia and reduced threshold for arrhythmias
- Hypocalcemia
- Reduction in CBF and risk of cerebral ischemia
  - Particularly during hypotension
- Potentiation of nondepolarizing neuromuscular blockade
- Respiratory alkalosis prolongs the duration of opioid-induced respiratory depression
  - Increased protein binding of opioids?
## Acid-Base Disorders

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<tr>
<th>Disorder</th>
<th>Primary change</th>
<th>Compensatory response</th>
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<td>Acidosis</td>
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Respiratory Acidosis

- **Primary PaCO₂ increase**

\[
\text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-
\]

- Alveolar minute ventilation is inadequate relative to CO₂ production (MV can be decreased, normal or increased)
  - Increased CO₂ production
  - Decreased CO₂ elimination
  - Increased rebreathing or absorption of CO₂
- Risk of hypoxemia
## Causes of Respiratory Acidosis

### Increased CO\(_2\) production
- Malignant hyperthermia
- Hyperthyroidism
- Sepsis
- Overfeeding

### Decreased CO\(_2\) elimination
- Intrinsic pulmonary disease (pneumonia, ARDS, fibrosis, edema)
- Upper airway obstruction (laryngospasm, foreign body, OSA)
- Lower airway obstruction (asthma, COPD)
- Chest wall restriction (obesity, scoliosis, burns)
- CNS depression (anesthetics, opioids, CNS lesions)
- Decreased skeletal muscle strength (residual effects of neuromuscular blocking drugs, myopathy, neuropathy)

### Increased CO\(_2\) rebreathing or absorption
- Exhausted soda lime
- Incompetent one-way valve
- Laparoscopic surgery (CO\(_2\)-pneumoperitoneum)

ARDS = acute respiratory distress syndrome; CNS = central nervous system; COPD = chronic obstructive pulmonary disease; OSA = obstructive sleep apnea)
Respiratory Acidosis: Compensatory Response (1)

- **[HCO₃⁻]** increase
  - Increased H⁺ secretion and HCO₃⁻ reabsorption
  - Initially [HCO₃⁻] is minimally affected
- **Limited acute (6 - 12 h) compensatory response**
  - Hb buffer
  - Exchange of extracellular H⁺ for Na⁺ and K⁺ from bone and intracellular fluid
  - Renal response to retain HCO₃⁻ is very limited acutely
  - Plasma [HCO₃⁻] increases only about 1 mEq/L for each 10 mmHg increase in PaCO₂ > 40 mmHg
Respiratory Acidosis: Compensatory Response (2)

- **Renal compensation**
  - Appreciable only after 12 – 24 hours
  - Maximal after 3 – 5 days
  - Chronic respiratory acidosis: nearly normal pH (increased PaCO₂)
  - Plasma [HCO₃⁻] increases approximately 4 mEq/L for each 10 mmHg increase in PaCO₂ > 40 mmHg
Respiratory Acidosis: Treatment (1)

• Causal treatment
  – Reduction of CO$_2$ production (in specific situations)
    • Status epilepticus: muscle paralysis
    • TPN: reduced carbohydrate intake
    • Thyroid storm: antithyroid medication
    • Malignant hyperthermia: dantrolene
  – Improving alveolar ventilation (temporary measures)
    • Bronchodilatation
    • Reversal of narcosis
    • Administration of a respiratory stimulant (doxapram)
    • Improving lung compliance (diuretics)
Respiratory Acidosis: Treatment (2)

- **Mechanical ventilation may be indicated**
  - Severe acidosis (pH < 7.2)
  - CO₂ narcosis
  - Respiratory muscle fatigue

- **Intravenous buffers are only rarely indicated**
  - Very severe acidosis (pH < 7.10 and HCO₃⁻ < 15 mEq/L)
  - NaHCO₃: transient PaCO₂ increase: \( H^+ + HCO_3^- \leftrightarrow CO_2 + H_2O \)
  - Buffers that do not increase PaCO₂: no proven benefit
Respiratory Acidosis: Treatment (3)

- Avoid overventilation in patients with chronic respiratory acidosis
  - Acute respiratory failure superimposed on chronic respiratory acidosis
  - Goal: return PaCO$_2$ to the patient’s baseline PaCO$_2$
    - PaCO$_2$ = 40 mmHg in chronic respiratory acidosis will result in metabolic alkalosis
      - Renal loss of HCO$_3^-$
      - Increased work of breathing
  - In some patients, respiratory drive is dependent on PaO$_2$
Respiratory Alkalosis

• **Primary PaCO$_2$ decrease**
  - PaCO$_2$ is decreased relative to [HCO$_3^-$] → pH increases
  - Prolonged respiratory alkalosis: central chemoreceptors reset to a lower CO$_2$ level
    • Active transport of HCO$_3^-$ out of the CSF
• **Generally, there is an inappropriate increase in alveolar ventilation relative to CO$_2$ production**
# Causes of Respiratory Alkalosis

**Increased minute ventilation**
- Hypoxia (high altitude, low FiO$_2$, severe anemia)
- Iatrogenic (mechanical ventilation)
- Anxiety and pain
- CNS disease (tumor, infection, trauma)
- Fever, sepsis
- Drugs (salicylates, progesterone, doxapram)
- Liver disease
- Pregnancy
- Restrictive lung disease
- Pulmonary embolism

**Decreased CO$_2$ production**
- Hypothermia
- Skeletal muscle paralysis

*CNS = central nervous system*
Respiratory Alkalosis: Compensatory Response

- Decreased reabsorption of $\text{HCO}_3^-$ from the renal tubules and increased urinary excretion
- Acute respiratory alkalosis
  - Plasma $[\text{HCO}_3^-]$ usually decreases 2 mEq/L for each 10 mmHg acute decrease in PaCO$_2$ below 40 mmHg
- Chronic respiratory alkalosis: variable compensatory response
  - Plasma $[\text{HCO}_3^-]$ decreases 2-5 mEq/L for each 10 mmHg decrease in PaCO$_2$ below 40 mmHg
Respiratory Alkalosis: Treatment

- Correction of the underlying disorder
- Mild alkalemia usually does not require treatment
- Severe acute respiratory alkalosis (pH > 7.60): intravenous drug therapy may be indicated
  - Hydrochloric acid
  - Arginine chloride
  - Ammonium chloride
Metabolic Acidosis

- **Primary decrease in \([\text{HCO}_3^-]\)**
- **Mechanisms**
  - Consumption of \(\text{HCO}_3^-\) by a strong nonvolatile acid
  - Renal or gastrointestinal wasting of \(\text{HCO}_3^-\)
  - Rapid dilution of extracellular fluid with a \(\text{HCO}_3^-\)-free fluid
- **Traditionally, the differential diagnosis is based on the anion gap calculation**
  - More recent: Stewart method based on the strong ion difference
- **Frequently accompanied by hyperkalemia and hyperphosphatemia**
Metabolic Acidosis: Compensatory Response

- **Decrease in PaCO₂ (hyperventilation)**
  - Starts minutes after the development of metabolic acidosis
  - Results in a near normal pH (after 12 – 24 hours)
  - PaCO₂ decreases 1.2 mmHg for 1 mEq/L decrease in [HCO₃⁻]

- **Renal compensation: generation of HCO₃⁻ and tubular secretion of H⁺ in the urine**

- **Chronic metabolic acidosis (e.g. renal failure)**
  - Buffers present in bone are used → loss of bone mass
Anion Gap (1)

• AG = Measured plasma cations – Measured plasma anions
  = ([Na$^+$] + [K$^+$]) – ([Cl$^-$] + [HCO$_3^-$])

• Electroneutrality: Sum of all anions = Sum of all cations
  ⇓
  Anion gap = Unmeasured anions – Unmeasured cations

• Normal AG = 8 – 12 mEq/L
  – Includes Ca$^{2+}$ and Mg$^{2+}$
  – Mostly anionic serum albumin: AG decreases by ~ 2.5 mEq/L for each 1 g/dL decrease in plasma albumin concentration
UMAs = strong unmeasured anions (e.g. lactate)
A⁻ = weak acids (phosphate, albumin)
Anion Gap (2)

• AG increases when the ion replacing $\text{HCO}_3^-$ is not routinely measured
  – Most common unmeasured anions: lactic acid, keto acids

• Weakness: AG may be normal in the presence of unmeasured anions
  – E.g. hypoalbuminemia and hypophosphatemia
    → Use corrected anion gap to compensate for hypoalbuminemia:
      Measured AG + 2.5 (normal – measured albumin g/dL)
  – Use of $\text{HCO}_3^-$ in the equation
    ▪ $[\text{HCO}_3^-]$ can change independently of metabolic disturbances
      (e.g. hyperventilation)
Anion Gap (3)

- AG method is a simplification of acid-base disturbances
  - Provides estimate of magnitude of acid-base disturbances
  - Alterations in H\(^+\), HCO\(_3^-\) and base excess do not help determine the mechanism of an acid-base disorder
Anion Gap: Classification of Metabolic Acidosis

- **High anion gap metabolic acidosis**
  - Acidosis is due to acid accumulation, with $\text{HCO}_3^-$ being replaced by an unmeasured anion

- **Normal anion gap metabolic acidosis**
  - Acidosis is due to gastrointestinal or renal $\text{HCO}_3^-$ losses ($\text{HCO}_3^-$ is lost with $\text{Na}^+$: no change in AG)
  - Administration of large volumes of NaCl 0.9% (> 30 mL/kg/hour)
    - Excessive $\text{Cl}^-$ administration
## Causes of Metabolic Acidosis

### Anion gap acidosis
- **M** methanol, ethylene glycol
- **U** uremia
- **L** lactic acidosis = congestive heart failure, sepsis, cyanide toxicity
- **E** ethanol
- **P** paraldehyde
- **A** aspirin, isoniazid
- **K** ketones = starvation, diabetes mellitus

### Non-anion gap acidosis
- Administration of large volumes of 0.9% NaCl
- Gastrointestinal losses (diarrhea, ileostomy, neobladder, pancreatic fistula)
- Renal losses (renal tubular acidosis)
- Drugs (acetazolamidine)
High Anion Gap Metabolic Acidosis (1)

- Metabolic acidosis and AG > 20 - 25 mEq/L
- Characteristic: increase in relatively strong nonvolatile acids
  - HA → H⁺ + A⁻
  - H⁺ consumes HCO₃⁻ to produce CO₂
    - H⁺ + HCO₃⁻ → H₂CO₃ → H₂O + CO₂
  - Anions (A⁻) accumulate and take the place of HCO₃⁻ in the extracellular fluid → increased AG (A⁻ = unmeasured anion)
- Ingestion or endogenous production of nonvolatile acids
  - Failure to excrete endogenous nonvolatile acids (renal failure)
  - Increased endogenous nonvolatile acid production
  - Ingestion of exogenous nonvolatile acids
### Causes of High Anion Gap Metabolic Acidosis

<table>
<thead>
<tr>
<th>Increased production or retention of endogenous nonvolatile acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal failure (uremic)</td>
</tr>
<tr>
<td>Ketoacidosis (diabetic, starvation)</td>
</tr>
<tr>
<td>Lactic acidosis</td>
</tr>
<tr>
<td>Mixed (nonketotic hyperosmolar coma, alcoholic)</td>
</tr>
<tr>
<td>Inborn errors of metabolism</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingestion of toxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salicylate</td>
</tr>
<tr>
<td>Methanol</td>
</tr>
<tr>
<td>Ethylene glycol</td>
</tr>
<tr>
<td>Paraldehyde</td>
</tr>
<tr>
<td>Toluene</td>
</tr>
<tr>
<td>Sulphur</td>
</tr>
</tbody>
</table>

| Rhabdomyolysis                                              |
High Anion Gap Metabolic Acidosis

- Most common causes of high AG metabolic acidosis
  - Lactic acid
    - Most common cause in hospitalized patients
    - Increased production of lactate: anaerobic metabolism
      - Hypoxemia, hypoperfusion, inability to utilize $O_2$ (cyanide)
    - Decreased utilization of lactate by the liver (and kidneys)
      - Hypoperfusion, alcoholism, liver disease
  - Ketoacidosis
  - Renal failure
  - Ingestion of toxins
High Anion Gap Metabolic Acidosis (3)

- Most common causes of high AG metabolic acidosis (2)
  - Lactic acid
  - Ketoacidosis
    - Common complication of type I diabetes mellitus
    - Occurs also with starvation, alcoholic binges
    - Free fatty acid metabolism
      - Liver: FFAs are converted to ketoacids, acetoacetic acid and \(\beta\)-hydroxybutyrate (unmeasured anions)
    - Renal failure
    - Ingestion of toxins
High Anion Gap Metabolic Acidosis

- Most common causes of high AG metabolic acidosis
  - Lactic acid
  - Ketoacidosis
  - Renal failure
    - Decreased acid excretion
    - Decreased $\text{HCO}_3^-$ reabsorption
    - High AG due to accumulation of sulphates, phosphates, urate, and hippurate
  - Ingestion of toxins
    - Acidic metabolites or triggering of lactic acidosis
    - Salicylate, methanol, ethylene glycol, paraldehyde...
Delta Ratio

Assessment of high anion gap metabolic acidosis

• **Delta ratio** = \( \Delta \text{Anion gap} / \Delta [\text{HCO}_3^-] \)
  
  = (Anion gap – 12) / (24 - [HCO_3^-])
  
  = Increase in AG / [HCO_3^-] deficit

• A delta ratio < 1 indicates a greater [HCO_3^-] deficit than would be expected by the increase in AG
  – Hyperchloremic metabolic acidosis
  – Mixed high AG and normal AG acidosis

• A delta ratio > 2 indicates a lesser [HCO_3^-] deficit than would be expected by the increase in AG
  – Metabolic acidosis with concurrent metabolic alkalosis
  – Metabolic acidosis with pre-existing compensated respiratory acidosis
<table>
<thead>
<tr>
<th>Delta Ratio</th>
<th>Assessment Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.4</td>
<td>Hyperchloremic normal AG acidosis.</td>
</tr>
<tr>
<td>0.4 – 0.8</td>
<td>Consider combined high AG and normal AG acidosis. However: DR is often &lt; 1 in acidosis with renal failure.</td>
</tr>
<tr>
<td>1 – 2</td>
<td>High AG acidosis.</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>Suggests high AG acidosis with concurrent metabolic alkalosis or with pre-existing compensated respiratory acidosis.</td>
</tr>
</tbody>
</table>

*Always correlate the delta ratio with other evidence to support the diagnosis*
Normal Anion Gap Metabolic Acidosis \(^{(1)}\)

- Normal anion gap and metabolic acidosis
- Characteristic: hyperchloremic metabolic acidosis
  - Plasma \([\text{Cl}^-]\) increase to replace lost \(\text{HCO}_3^-\)
- Causes of normal AG metabolic acidosis
  - Abnormal losses of \(\text{HCO}_3^-\)
  - Other causes
## Causes of Normal Anion Gap Metabolic Acidosis

### Increased gastrointestinal losses of $\text{HCO}_3^-$
- Diarrhea
- Anion exchange resins
- Ingestion of $\text{CaCl}_2$, $\text{MgCl}_2$
- Fistulas (pancreatic, biliary, or small bowel)
- Ureterosigmoidostomy or obstructed ileal loop

### Increased renal losses of $\text{HCO}_3^-$
- Renal tubular acidosis
- Carbonic anhydrase inhibitors
- Hypoaldosteronism

### Rapid infusion of a large amount of bicarbonate-free fluids

### Total parenteral nutrition ($\text{Cl}^-$ salts of amino acids)

### Increased intake of $\text{Cl}^-$ containing acids
- Ammonium chloride
- Lysine hydrochloride
- Arginine hydrochloride
Normal Anion Gap Metabolic Acidosis

• Abnormal losses of HCO$_3^-$: gastrointestinal or renal
  – Diarrhea
  – Pancreatic or biliary fistulae
  – Ureterosigmoidostomy
    • Colon secretes HCO$_3^-$ in exchange for Cl$^-$
    • Colon absorbs urinary ammonium (dissociates in NH$_3$ and H$^+$)
  – Renal tubular acidosis
    • Impaired H$^+$ secretion
    • Impaired HCO$_3^-$ absorption
    – Acetazolamide (Diamox©)
Normal Anion Gap Metabolic Acidosis (3)

- Other causes of normal AG metabolic acidosis
  - Rapid infusion of a bicarbonate-free fluid: e.g. normal saline
    - Fast infusion of large volumes
  - Parenteral nutrition: organic cations > organic anions
    - $\text{Cl}^-$ is commonly used as anion for the cationic amino acids
  - Excessive administration of chloride-containing acids
  - Adrenal insufficiency
Metabolic Acidosis: Treatment (1)

- Causal treatment if possible
  - Lactic acidosis
    - Restoration of adequate oxygenation and tissue perfusion with oxygen, fluid resuscitation and circulatory support
  - Diabetic ketoacidosis
    - Correction of fluid deficit
    - Insulin
    - Potassium, phosphate, magnesium
  - Methanol or ethylene glycol intoxication
    - Ethanol
Metabolic Acidosis: Treatment (2)

- NaHCO$_3$ therapy if pH < 7.1 - 7.15 (no respiratory component)
  - Therapy should always be guided using arterial blood gas measurements (goal: pH 7.2)
  - Other indications
    - pH 7.2 in case of ARDS with permissive hypercapnia
    - Acidosis and chronic renal insufficiency or renal tubular acidosis
    - Acidosis with life threatening hyperkalemia
    - Salicylate intoxication (alkalinization of urine)
Metabolic Acidosis: Treatment (3)

- **Amount of NaHCO$_3$**
  - Calculated
    - $\text{NaHCO}_3 \text{ (mEq)} = (24 - [\text{HCO}_3^-]_s) \times 0.5 \times \text{body weight (kg)}$
    - Generally 50% of the calculated dose is given initially
  - Empirically
    - A fixed dose of $\approx 1 \text{ mEq/kg}$
    - 50 – 100 mEq
- **Na$_2$CO$_3$ 8.4%**: 1000 mEq Na$^+/L$, 2000 mOsm/L
  → Side effects
Metabolic Acidosis: Treatment (4)

- **Side effects of treatment with NaHCO$_3$ 8.4%**
  - Increased production of CO$_2$
    - Intracellular acidosis and possibly electromechanical dissociation
  - Hypernatremia and hyperosmolarity
    - Hypervolemia, pulmonary edema
  - Inhibition of peripheral chemoreceptors
    - Decrease of hyperventilation, hypercapnia
  - Negative inotropic effect
    - Lactate has also a negative inotropic effect
  - Hemoglobin: increased affinity for oxygen
Metabolic Alkalosis

• **Primary increase in plasma \([\text{HCO}_3^-]\)**
  – Increased \(\text{HCO}_3^-\) reabsorption
  – \(\text{H}^+\) loss
• **Often accompanied by hypokalemia and hypophosphatemia**
• **Differential diagnosis**
  – **Chloride-sensitive metabolic alkalosis**
    • Extracellular fluid depletion
    • \(\text{NaCl}\) deficiency
    • Urinary \([\text{Cl}^-]\) < 10 - 20 mEq/L
  – **Chloride-resistant metabolic alkalosis**
    • Urinary \([\text{Cl}^-]\) > 20 mEq/L
Metabolic Alkalosis: Compensatory Response

• Decrease in PaCO$_2$ (hypoventilation)
  – PaCO$_2$ increases 0.7 mmHg for every 1 mEq/L increase in [HCO$_3^-$]
• Renal compensation by HCO$_3^-$ excretion is less efficient
Chloride-Sensitive Metabolic Alkalosis (1)

• Depletion of extracellular fluid
  → Na\(^+\) reabsorption in the renal tubules
  → There is not enough Cl\(^-\) available to accompany all reabsorbed Na\(^+\)
     → Increased H\(^+\) secretion to maintain electroneutrality
     → HCO\(_3\)\(^-\) ions that might otherwise have been excreted are reabsorbed
     → Enhanced K\(^+\) secretion
• Urinary [Cl\(^-\)] < 10 - 20 mEq/L
Chloride-Sensitive Metabolic Alkalosis

Depletion of extracellular fluid

Na⁺ reabsorption in the renal tubules

Cl⁻ absorption: insufficient to maintain electroneutrality

↑ H⁺ secretion  HCO₃⁻ absorption  ↑ K⁺ secretion

Hypokalemia
Chloride-Sensitive Metabolic Alkalosis

- **Common causes**
  - **Diuretics** (furosemide, thiazides): most common cause
    - NaCl depletion, hypokalemia
      → Mild metabolic alkalosis
  - **Loss of gastric fluid** (vomiting, nasogastric suctioning)
    - $\left[H^+\right]$: 25-100 mEq/L
    - $\left[Na^+\right]$: 40-160 mEq/L
    - $\left[K^+\right]$: 15 mEq/L
    - $\left[Cl^-\right]$: 200 mEq/L
      → Extracellular volume depletion
      → Hypokalemia
      → Marked metabolic alkalosis
Chloride-Sensitive Metabolic Alkalosis (3)

- **Other causes** (cont.)
  - Chloride diarrhea, villous adenoma
  - Posthypercapnic alkalosis: rapid normalization of PaCO$_2$ after plasma [HCO$_3$-] has risen in chronic respiratory acidosis
  - High dose sodium penicillins
  - Low chloride intake
    - Infant formula containing Na$^+$ without Cl$^-$
Chloride-Resistant Metabolic Alkalosis (1)

- Typically urinary [Cl\(^{-}\)] > 20 mEq/L
- Inappropriate increases in mineralocorticoid activity
  - Na\(^{+}\) retention and expansion of extracellular fluid volume
  - Increased H\(^{+}\) and K\(^{+}\) secretion
    - Metabolic alkalosis and hypokalemia
      - Hyperaldosteronism, primary or secondary
      - Liddle
      - Cushing
      - Licorice
      - Bartter’s syndrome
Chloride-Resistant Metabolic Alkalosis (2)

- Severe hypokalemia
- Massive blood transfusion
  - Liver converts citrate into $\text{HCO}_3^-$
- Hypercalcemia
- Milk-alkali syndrome
- Alkali therapy (renal insufficiency)
Metabolic Alkalosis: Treatment (1)

- Treatment of underlying disorder
- Chloride-sensitive metabolic alkalosis
  - Intravenous saline (NaCl)
  - Intravenous potassium (KCl) may be indicated
- Depending on the cause
  - H₂-blocker therapy (in case of excessive loss of gastric fluid)
  - Acetazolamide (edematous patients)
- Primary increase in mineralocorticoid activity
  - Aldosterone antagonist (spironolactone)
Metabolic Alkalosis: Treatment (2)

• Severe metabolic alkalosis: pH > 7.60
  – Intravenous hydrochloric acid
  – Ammonium chloride
  – Arginine hydrochloride
  – Hemodialysis
ASSESSMENT OF ACID-BASE DISORDERS
Practical Approach
1. Determine oxygenation

2. Determine pH

1. Acidemic: pH < 7.35

2. Alkalemic: pH > 7.45

3. Respiratory or metabolic

4. Respiratory acidosis: pCO₂ > 40 mmHg

5. Metabolic acidosis: [HCO₃] < 24 mEq/L

6. Respiratory alkalosis: pCO₂ < 40 mmHg

7. Metabolic alkalosis: [HCO₃] > 24 mEq/L

8. Acute or chronic

9. Anion gap

10. Gap

11. Δ Gap

12. Adequate respiratory compensation

Miller and Pardo, Basics of Anesthesia, 6th ed
Assessment of Acid-Base Disorders: Practical Approach (1)

1. Evaluate the clinical context
2. Determine pH: acidemia or alkalemia present?
   - pH < 7.35: acidemia
   - pH > 7.45: alkalemia
   - pH 7.35 – 7.45: normal or more than one acid-base disturbance
Assessment of Acid-Base Disorders: Practical Approach (2)

3. Is the primary cause of the acid-base disorder respiratory or metabolic?
   - Metabolic
     • $[\text{HCO}_3^-] < \text{ or } > 24 \text{ mEq/L}$
     • pH and $[\text{HCO}_3^-]$ change in the same direction from the normal values
   - Respiratory
     • $\text{pCO}_2 < \text{ or } > 40 \text{ mmHg}$
     • pH and PaCO$_2$ change in opposite directions from the normal values
# Acid-Base Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>pH</th>
<th>Primary change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acidosis</td>
<td>↓</td>
<td>↑ PaCO$_2$</td>
</tr>
<tr>
<td>Alkalosis</td>
<td>↑</td>
<td>↓ PaCO$_2$</td>
</tr>
<tr>
<td><strong>Metabolic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acidosis</td>
<td>↓</td>
<td>↓ HCO$_3^-$</td>
</tr>
<tr>
<td>Alkalosis</td>
<td>↑</td>
<td>↑ HCO$_3^-$</td>
</tr>
</tbody>
</table>
Assessment of Acid-Base Disorders: Practical Approach (3)

4. Determine if the compensatory response is adequate

<table>
<thead>
<tr>
<th>Disturbance</th>
<th>Compensatory Response</th>
<th>Expected change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolic acidosis</strong></td>
<td><strong>↓ PaCO₂</strong></td>
<td>1.2 mmHg decrease in PaCO₂ for every 1 mEq/L decrease in [HCO₃⁻]</td>
</tr>
<tr>
<td>(↓ [HCO₃⁻])</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Metabolic alkalosis</strong></td>
<td><strong>↑ PaCO₂</strong></td>
<td>0.7 mmHg increase in PaCO₂ for every 1 mEq/L increase in [HCO₃⁻]</td>
</tr>
<tr>
<td>(↑ [HCO₃⁻])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disturbance</td>
<td>Response</td>
<td>Expected change</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>----------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Respiratory acidosis (↑ PaCO₂)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>↑ [HCO₃⁻]</td>
<td>1 mEq/L increase in [HCO₃⁻] for every 10 mmHg increase in PaCO₂</td>
</tr>
<tr>
<td>Chronic</td>
<td>↑ [HCO₃⁻]</td>
<td>4 mEq/L increase in [HCO₃⁻] for every 10 mmHg increase in PaCO₂</td>
</tr>
<tr>
<td><strong>Respiratory alkalosis (↓ PaCO₂)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>↓ [HCO₃⁻]</td>
<td>2 mEq/L decrease in [HCO₃⁻] for every 10 mmHg decrease in PaCO₂</td>
</tr>
<tr>
<td>Chronic</td>
<td>↓ [HCO₃⁻]</td>
<td>5 mEq/L decrease in [HCO₃⁻] for every 10 mmHg decrease in PaCO₂</td>
</tr>
</tbody>
</table>
Assessment of Acid-Base Disorders: Practical Approach (4)

5. **Is it a simple or mixed acid-base disorder?**

1. In a simple acid-base disorder only one primary acid-base disturbance is present. A simple acid-base disorder is suspected if:
   - Primary and compensatory changes of \( \text{PaCO}_2 \) and \([\text{HCO}_3^-]\) occur in the same direction (↑ or ↓)
   - The measured compensatory response equals the calculated compensatory response

2. In a mixed acid-base disorder more than one acid-base disturbance is present.
Assessment of Acid-Base Disorders: Practical Approach (5)

5. **Is it a simple or mixed acid-base disorder?**

2. In a mixed acid-base disorder more than one acid-base disturbance is present. A mixed acid-base disorder is suspected if:
   - The expected compensatory response does not occur
   - The compensatory response is less than expected or too extreme
   - The pH is normal, but PaCO₂ or [HCO₃⁻] is abnormal. In a simple acid-base disorder the compensatory response never returns the pH to normal
   - PaCO₂ and [HCO₃⁻] change in opposite directions (one is elevated while the other is decreased)
   - In anion gap metabolic acidosis: the delta ratio is > 2 or < 1. This indicates that the change in [HCO₃⁻] is not proportional to the change in anion gap
<table>
<thead>
<tr>
<th><strong>Mixed metabolic disorders</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• High anion gap and normal anion gap metabolic acidosis</td>
</tr>
<tr>
<td>• High anion gap metabolic acidosis and metabolic alkalosis</td>
</tr>
<tr>
<td>• Normal anion gap metabolic acidosis and metabolic alkalosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mixed respiratory disorders</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chronic respiratory acidosis with superimposed acute respiratory acidosis</td>
</tr>
<tr>
<td>• It is impossible to have concurrent respiratory acidosis and respiratory alkalosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mixed respiratory – metabolic disorders</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chronic respiratory acidosis and high anion gap metabolic acidosis</td>
</tr>
<tr>
<td>• Chronic respiratory acidosis and metabolic alkalosis</td>
</tr>
<tr>
<td>• Respiratory alkalosis and metabolic acidosis</td>
</tr>
</tbody>
</table>
Assessment of Acid-Base Disorders: Practical Approach (6)

6. If a primary respiratory process is present determine if it is acute or chronic

<table>
<thead>
<tr>
<th>Determining whether respiratory process is acute or chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute process</strong></td>
</tr>
<tr>
<td>pH $\Delta$ 0.08 for every 10 mmHg $\Delta$ in PaCO$_2$ from 40 mmHg</td>
</tr>
<tr>
<td><strong>Chronic process</strong></td>
</tr>
<tr>
<td>pH $\Delta$ 0.03 for every 10 mmHg $\Delta$ in PaCO$_2$ from 40 mmHg</td>
</tr>
</tbody>
</table>

Miller and Pardo, Basics of Anesthesia, 6th ed
## Respiratory Acid-Base Disturbances:
### Normal Compensatory Responses

<table>
<thead>
<tr>
<th>Disturbance</th>
<th>Response</th>
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</table>
Assessment of Acid-Base Disorders: Practical Approach (7)

7. If metabolic acidosis is suspected calculate the anion gap
   - A high AG (> 20 mEq/L) indicates metabolic acidosis
   - Calculate the delta ratio to assess high AG metabolic acidosis
     • Delta ratio = $\Delta$ Anion gap / $\Delta [HCO_3^-]$
       = $(\text{Anion gap} - 12) / (24 - [HCO_3^-])$
       = Increase in AG / [HCO_3^-] deficit
     • A delta ratio < 1 indicates a greater [HCO_3^-] deficit than would be expected by the change in AG
     • A delta ratio > 2 indicates a lesser [HCO_3^-] deficit than would be expected by the change in AG
<table>
<thead>
<tr>
<th>Delta Ratio</th>
<th>Assessment Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.4</td>
<td>Hyperchloremic normal AG acidosis.</td>
</tr>
<tr>
<td>0.4 – 0.8</td>
<td>Consider combined high AG and normal AG acidosis. However: DR is often &lt; 1 in acidosis with renal failure.</td>
</tr>
<tr>
<td>1 – 2</td>
<td>High AG acidosis.</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>Suggests high AG acidosis with concurrent metabolic alkalosis or with pre-existing compensated respiratory acidosis.</td>
</tr>
</tbody>
</table>

Always correlate the delta ratio with other evidence to support the diagnosis.