Learning Objectives:
- Explain the physiology and pathophysiology of carbon dioxide exchange and acid-base balance.
- Determine the ventilatory and acid-base status from blood-gas values.

CO2 Transportation and Regulation
- Produced with H2O as product of glucose metabolism
- Excreted by ventilation

CO2 Production & Excretion
- Increased metabolism

CO2 Production & Excretion
- Increased ventilation
CO2 Transport

Mechanisms
- dissolved in plasma (PCO2 x .03)
- converted to HCO3-
  - greatest amount of CO2
  - requires carbonic anhydrase (CA) as catalyst

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

CO2 Abnormalities

- Increased- hypoventilation
  - depressed ventilation
    - ventilatory fatigue
    - depressant drugs; e.g., anesthetics
    - neuromuscular dysfunction

- Decreased- hyperventilation
  - neurogenic hyperventilation
    - increased intracranial pressure (ICP)
    - anxiety
  - hypoxemia
  - compensation for metabolic acidemia

CO2 Transport

Mechanisms
- combined with hemoglobin
  - greatest amount of exchanged CO2
  - CO2-Hb dissociation increased by increased O2- Haldane shift

CO2 Abnormalities

- Increased- hypoventilation
  - depressed ventilation
  - ventilatory fatigue
  - depressant drugs
  - neuromuscular dysfunction
  - increased dead space ventilation
    - emphysema - loss of alveolar capillaries
    - tachypnea - decreased tidal volume
  - massive pulmonary embolism

CO2 Abnormalities

- Decreased- hyperventilation
  - neurogenic hyperventilation
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CO2 Abnormalities

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    - emphysema - loss of alveolar capillaries
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  - massive pulmonary embolism
**CO₂ Abnormalities**
- Increased CO₂ production
  - increased metabolism
  - fever
  - shivering - recovery from hypothermia
  - seizures - may also cause hypoventilation

**CO₂ Abnormalities**
- Increased CO₂
  - excessive glucose intake; e.g., IV fluids
  - compensation for metabolic alkalemia

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**Regulators of Acid-Base Balance**
- Buffers
  - first to act
  - no pH change until they are depleted
  - HCO₃⁻ is the most important one
  - Hemoglobin - second most important

**Regulators of Acid-Base Balance**
- Buffers
- Ventilation
- Renal function

**Regulators of Acid-Base Balance**
- Ventilation
  - responds almost immediately to pH change
  - excretes/retains CO₂ volatile acid
Regulators of Acid-Base Balance

Kidney
- requires time to respond
- excretes/retains HCO3- or H+
  (fixed base, acid)

Acid-Base Balance

Parameters used to interpret
- pH- normal = 7.40
- PCO2- normal = 40
- HCO3- normal = 24

Base change- also known as base excess
- defined- the quantity of base, in mEq/L required to normalize the pH, with PCO2 adjusted to 40
  - normal value = 0 (zero)
  - estimate by subtracting normal HCO3 (24) from measured HCO3
  - used to calculate dosage of bicarbonate to treat acidemia

Depends on maintaining 20:1 ratio of base:acid (Henderson-Hasselbalch equation)

\[ \text{pH} = \text{pKa} + \log \left( \frac{\text{Base}}{\text{Acid}} \right) \]

FYI - click to see calculation of pH, using the H-H equation

http://www.cod.edu/people/faculty/fullerd/ProbHTMBuffer/GIFs/B-10HHCalculation.html

Respiratory acidemia

- hypoventilation- addition of volatile acid- CO2
  - acute, uncompensated
Compensated respiratory acidemia
- chronic hypoventilation
- renal retention of HCO3
- occurs over hours- days
- rarely fully compensated

Respiratory acidemia
- Management
  - increase alveolar ventilation - caution with chronic hypercapnea
    - rapid reversal is hazardous - alkalemia
    - complete reversal will delay ventilator weaning
  - if ventilation cannot be increased; e.g., for permissive hypercapnea-
    Tromethamine (THAM)

Metabolic acidemia
- Fixed acid excess OR
- Base deficiency
- pH does not change until buffers are neutralized
- Ventilation compensates immediately, unless compromised or controlled
- Associated with hyperkalemia

Metabolic acidemia
- Causes:
  - diabetes - ketones
  - renal failure
    - non-production of HCO3-
    - failure to excrete acid anions
  - hepatic failure - failure to catabolize lactic acid

Metabolic acidemia
- Causes:
  - diarrhea - HCO3- loss
  - ingestion of acid
  - congenital metabolic disease; e.g., maple syrup urine disease (MSUD)

Metabolic acidemia
- Causes:
  - tissue hypoxia- lactic acidemia
    - severe hypoxemia
    - shock; e.g., septic shock
    - nucleoside analogues (HIV meds)
    - diagnosed with serum lactate measurement

FYI - Link to article on MSUD

FYI - Link to article on lactic acidemia and nucleoside analogues
**Metabolic acidemia**
- Anion gap = [(Na+) - (Cl--- + HCO3)]
- Normal = [(140) - (100 + 24)] = 16
- So what?? - If the source of acidemia is unclear, the anion gap can narrow the choices.

FYI - Link to more information on anion gap

**Metabolic acidemia**
- Elevated anion gap acidemia causes
  - Methanol, metformin (diabetic agent)
  - Uremia
  - Diabetic ketoacidosis
  - Paraldehyde - rarely used
  - Iron, isoniazid, inhalants (abuse)
  - Lactic acid
  - Ethylene glycol, ethanol (alcoholic ketoacidosis)
  - Salicylates, solvents, starvation

**Metabolic acidemia**
- Non-anionic gap acidemia sources
  - Gastrointestinal HCO3- loss - diarrhea
  - renal failure - renal tubular acidosis
  - hyperalimentation
  - post-hypocapnea; e.g., normal postnatal maternal condition

FYI - click for more information on renal acidosis
http://www.anaesthesiamcq.com/AcidBaseBook/ab8_3.php

**Uncompensated metabolic acidemia**
- Negative base change- estimated = (19 - 24) = -5 mEq/L

**Partly compensated metabolic acidemia**
- full compensation is rare

**Metabolic acidemia- management**
- do not treat pH ≥ 7.20
- treat underlying cause
  - insulin - ketoacid
  - restore oxygenation
  - restore perfusion
  - restore hemoglobin
  - dialysis - renal failure
  - withdraw any causative agents
- buffer therapy (later)
**Respiratory alkalemia**
- acute, uncompensated
- hyperventilation

**Metabolic alkalemia - base excess**
- Causes
  - administration of HCO3
  - vomiting, nasogastric suctioning
  - diuretic therapy

FYI - Link to article on metabolic alkalemia

**Respiratory alkalemia**
- chronic hyperventilation - common in late pregnancy
- renal compensation - excrete HCO3
- management - treat underlying cause

**Metabolic alkalemia - base excess**
- causes
  - administration of HCO3
  - vomiting, nasogastric suctioning
  - diuretic therapy
- consequences
  - hypokalemia - tachydysrhythmias
  - leftward shift in HbO2 curve - aggravates hypoxia

**Metabolic alkalemia**
- acute, uncompensated

**Metabolic alkalemia**
- partly compensated
- hypoventilation to retain CO2
- results in base excess - estimated = (31 - 24) = 7
**Metabolic alkalemia**

- Management
  - Treat underlying cause
  - Acetazolamide (Diamox)
    - For pH = 7.48 and HCO3- = 28 mmol/l
    - Single dose - 500 mg

FYI - Link to article on acetazolamide and alkalemia
http://ccforum.com/content/10/1/R14

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**Arterial vs. venous samples**

- Mixed venous samples
  - Superior to arterial samples in determining
    - Acid-base status, especially during resuscitation
    - Lactate levels
  - Sites
    - Pulmonary artery
    - Central veins
    - Peripheral vein - emergency

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**Acid-Base Balance Algorithm**

<table>
<thead>
<tr>
<th>Acidemia or Alkalemia? Check pH</th>
<th>pH &lt; 7.40 = acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary Source Check PCO2</td>
</tr>
<tr>
<td>PCO2 &gt; 40 ==&gt; respiratory</td>
<td></td>
</tr>
</tbody>
</table>

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<tr>
<td>PCO2 &gt; 40 ==&gt; respiratory</td>
<td>Compensation? Check HCO3 and PCO2</td>
</tr>
<tr>
<td>HCO3 &gt; 24 ==&gt; compensated</td>
<td>HCO3 = 24 ==&gt; uncompensated</td>
</tr>
<tr>
<td>Base deficit ==&gt; combined</td>
<td></td>
</tr>
</tbody>
</table>

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**Arterial vs. venous samples**

- Mixed venous normal values

<p>| | |</p>
<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.36</td>
</tr>
<tr>
<td>PCO2</td>
<td>44</td>
</tr>
<tr>
<td>HCO3-</td>
<td>28</td>
</tr>
<tr>
<td>lactate</td>
<td>1 mmol/L</td>
</tr>
</tbody>
</table>
Acidemia or Alkalemia? Check pH

pH < 7.40 = acid
Primary Source Check PCO2
PCO2 < 40 ==> metabolic

Acidemia or Alkalemia? Check pH

pH > 7.40 = alkalemia
Primary Source Check PCO2
PCO2 < 40 ==> respiratory

Acidemia or Alkalemia? Check pH

pH > 7.40 = alkalemia
Primary Source Check PCO2
PCO2 < 40 ==> respiratory
Compensation? Check HCO3 and PCO2
HCO3 < 24 ==> compensated
HCO3 > 24 ==> combined

Acidemia or Alkalemia? Check pH

pH > 7.40 = alkalemia
Primary Source Check PCO2
PCO2 < 40 ==> metabolic
Compensation? Check HCO3 and PCO2
PCO2 > 40 ==> compensated
Interpretation Practice

Interpret these values: pH = 7.48, PCO2 = 32, HCO3 = 24

**Acidemia or Alkalemia?**
- **Check pH**
  - pH > 7.40 = alkalemia

**Primary Source**
- Check PCO2
  - PCO2 < 40 ==> respiratory

**Compensation?**
- Check HCO3 and PCO2
  - HCO3 < 24 ==> compensated

**Ans.: acute (uncompensated) respiratory alkalemia**

Interpret these values: pH = 7.30, PCO2 = 28, HCO3 = 19

**Acidemia or Alkalemia?**
- **Check pH**
  - pH < 7.40 = acid

**Primary Source**
- Check PCO2
  - PCO2 < 40 ==> metabolic

**Compensation?**
- Check PCO2
  - PCO2 < 40 ==> compensated

**Ans.: Partly compensated metabolic acidemia**

Interpret these values: pH = 7.36, PCO2 = 54, HCO3 = 28

**Acidemia or Alkalemia?**
- **Check pH**
  - pH < 7.40 = acid

**Primary Source**
- Check PCO2
  - PCO2 > 40 ==> respiratory

**Compensation?**
- Check HCO3 and PCO2
  - HCO3 < 24 ==> compensated

**Ans.: Partly compensated metabolic acidemia**

Interpret these values: pH = 7.48, PCO2 = 32, HCO3 = 24

**Acidemia or Alkalemia?**
- **Check pH**
  - pH > 7.40 = alkalemia

**Primary Source**
- Check PCO2
  - PCO2 < 40 ==> respiratory

**Compensation?**
- Check HCO3 and PCO2
  - HCO3 < 24 ==> compensated

**Ans.: acute (uncompensated) respiratory alkalemia**
Acidemia or Alkalemia?
Check pH

- pH < 7.40 = acid
- PCO2 > 40 ==> respiratory
- HCO3 > 24 ==> compensated

Primary Source
Check PCO2 Compensation?
Check HCO3 and PCO2

Ans.: Compensated respiratory acidemia

Buffer Therapy

- Purpose - to reverse acid-base imbalance, usually acidemia
- NaHCO3 - action - provides HCO3- ==> [H+1 + [HCO3-] ==> H20 + C02 ==> depends on ventilation to excrete C02

NaHCO3 - complications
- Respiratory acidemia if C02 not excreted
- Metabolic alkalemia (overdose)
- Hypernatremia
- Cerebral edema

NaHCO3 - contraindications
- pH > 7.20
- severe hypernatremia

NaHCO3
- administration titrated with blood pH
- Formula for dosage

\[ \text{HCO}_3^- \text{(mEq)} = \text{kg} \times (15 - \text{observed HCO}_3^-) \times 0.5 \]
Carbicarb
- Mixture of NaHCO3 and NaCO3
- Buffers without net generation of CO2
- No human trials have been conducted

Buffer therapy
- Tris-hydroxymethyl aminomethane-
  Tromethamine (THAM) - reverses acidemia without excretion of CO2
  - Action- organic proton acceptor (eats H+)

Buffer
- THAM™
  - Indications
    - metabolic acidemia with hypernatremia
    - acidemia in conjunction with limitations in ventilation-
      permissive hypercapnia

Buffer
- THAM™
  - Complications
    - apnea
    - hypoglycemia
    - hypokalemia
    - alkalemia
    - tissue necrosis from infiltration

Buffer
- THAM™
  - Dosage- ml’s of THAM of 0.3M solution = body wt in kg X base deficit in MEq/l

Buffer
- Trometamol (Tribonat™)
  - Currently used in Europe
  - Ingredients
    - NaHCO3
    - THAM
    - acetate
    - PO4

FYI - click to download article on lactic acidemia management (includes carbicarb)
http://jasn.asnjournals.org/cgi/reprint/12/suppl_1/S15

FYI - Link to article on THAM and permissive hypercapnea
http://ccforum.com/content/pdf/cc2918.pdf
Buffer

- Tribonat - advantages
  - minimal effect on PCO2
  - minimal overcorrection risk
  - less Na than NaHCO3
  - no tissue irritability

O2-induced hypercapnia

- COPD patients who are CO2 retainers
- During exacerbations
- Underlying causes:
  - VQ mismatch - increased VDA
  - Haldane effect - increased release of CO2 from Hb
- Maintain SPO2 < 92%

Summary & Review

- CO2 transport and balance
  - balance - production vs. excretion
  - transport forms and mechanisms
  - causes of abnormal PCO2

Summary & Review

- Acid-base balance
  - regulators
  - parameters and normal values
  - abnormalities
    - values
    - causes
    - management
  - acid-base algorithm

Summary & Review

- Buffer therapy
  - NaHCO3 - metabolic acidemia
  - Carbicarb
  - THAM - metabolic and respiratory acidemia
  - Trometamol (Tribonat (TM))
    - best of both
    - not available in USA

END
REFERENCES


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