Chapter 11

Gas Exchange and Transport
Objectives

- Describe how oxygen and carbon dioxide move between the atmosphere and tissues.

- Identify what determines alveolar oxygen and carbon dioxide pressures.

- Calculate the alveolar partial pressure of oxygen (\(PAO_2\)) at any given barometric pressure and \(FIO_2\).

- State the effect that normal regional variations in ventilation and perfusion have on gas exchange.
Objectives (cont.)

- Describe how to compute total oxygen contents for arterial blood.

- State the factors that cause the arteriovenous oxygen content difference to change.

- Identify the factors that affect oxygen loading and unloading from hemoglobin.

- Describe how carbon dioxide is carried in the blood.
Objectives (cont.)

- Describe how oxygen and carbon dioxide transport are interrelated.

- Describe the factors that impair oxygen delivery to the tissues and how to distinguish among them.

- State the factors that impair carbon dioxide removal.
Introduction

Respiration is the process of moving oxygen to tissues for aerobic metabolism and removal of carbon dioxide

- Involves gas exchange at the lungs and tissues
  - \( O_2 \) from atmosphere to tissues for aerobic metabolism
  - Removal for \( CO_2 \) from tissues to atmosphere
Diffusion

● Whole-body diffusion gradients
  - Gas moves across system by simple diffusion
  - Oxygen cascade moves from PO$_2$ of 159 mm Hg in atmosphere to the intracellular PO$_2$ of ~5 mm Hg
  - CO$_2$ gradient is the reverse from an intracellular CO$_2$ ~60 mm Hg to the atmosphere where it is <1 mm Hg

● Determinants of alveolar CO$_2$
  - PACO$_2$ = (\(\dot{V}_{CO_2} \times 0.863\))/\(V_A\)
  - PACO$_2$ will increase with \(\uparrow \dot{V}_{CO_2}\) or \(\downarrow V_A\)
Diffusion (cont.)

- Alveolar oxygen tensions ($PAO_2$)
  - $PIO_2$ is the primary determinant.
  - In lungs it is diluted by water vapor and $CO_2$.
  - Alveolar air equation accounts for all these factors:

$$PAO_2 = FIO_2 \times (P_B - 47) - (PACO_2/0.8)$$

- Dalton’s law of partial pressures accounts for first part of the formula; the second relates to the rate at which $CO_2$ enters the lung compared to oxygen exiting.
  - This ratio is normally 0.8.
Diffusion (cont.)

- Changes in alveolar gas partial tensions
  - $O_2$, $CO_2$, $H_2O$, and $N_2$ normally comprise alveolar gas.
    - $N_2$ is inert but occupies space and exerts pressure.
    - $PAN_2$ is determined by Dalton’s law.

$$PAN_2 = P_B - (PAO_2 + PACO_2 + PH_2O)$$

- The only changes seen will be in $O_2$ and $CO_2$.
  - Constant $FIO_2$, $PAO_2$ varies inversely with $PACO_2$.
  - Prime determinant of $PACO_2$ is $V_A$. 
Diffusion: Mechanisms

- Diffusion occurs along pressure gradients

- Barriers to diffusion
  - A/C membrane has three main barriers.
    - Alveolar epithelium
    - Interstitial space and its structures
    - Capillary endothelium
  - RBC membrane

- Fick’s law: The greater the surface area, diffusion constant, and pressure gradient, the more diffusion will occur.
Diffusion (cont.)

- **Pulmonary diffusion gradients**
  - Diffusion occurs along pressure gradients.
  - **Time limits to diffusion:**
    - Pulmonary blood is normally exposed to alveolar gas for 0.75 second, during exercise may fall 0.25 second
    - Normally equilibration occurs in 0.25 second
    - With a diffusion limitation or blood exposure time of less then 0.25 second there may be inadequate time for equilibration
Diffusion (cont.)
Normal Variations From Ideal Gas Exchange

- $\text{PaO}_2$ normally 5 – 10 mm Hg less than $\text{PAO}_2$ due to the presence of anatomic shunts

- Anatomic shunts
  - Two right-to-left anatomic shunts exist.
    - Bronchial venous drainage
    - Thebesian venous drainage
    - These drain poorly oxygenated blood into arterial circulation which lowers the $\text{CaO}_2$

- Regional inequalities in $\dot{V}/\dot{Q}$
  - Changes in either $\dot{V}$ or $\dot{Q}$ affect gas tensions.
Normal Variations From Ideal Gas Exchange (cont.)

- **V/Q ratio and regional differences**
  - An ideal ratio is 1, where V/Q is in perfect balance
  - In reality the lungs don’t function at the ideal level
    - High V/Q ratio at apices >1 V/Q (~3.3)
      - P\(_{\text{AO2}}\) (132 mm Hg), P\(_{\text{ACO2}}\) (32 mm Hg)
    - Low V/Q ratio at bases <1.0 (~0.66)
      - Blood flow is ~20 times higher at bases
      - Ventilation is greater at bases but not 20×
      - P\(_{\text{AO2}}\) (89 mm Hg), P\(_{\text{ACO2}}\) (42 mm Hg)

- See Table 11-1.
Oxygen Transport

- Transported in two forms: dissolved and bound

- Physically dissolved in plasma
  - Gaseous oxygen enters blood and dissolves.
  - Henry’s law allows calculation of amount dissolved.
    - Dissolved $\text{O}_2$ (ml/dl) = $\text{PO}_2 \times 0.003$

- Chemically bound to hemoglobin (Hb)
  - Each gram of Hb can bind 1.34 ml of oxygen.
  - $\text{[Hb g]} \times 1.34 \text{ ml } \text{O}_2$ provides capacity.
  - 70 times more $\text{O}_2$ transported bound than dissolved
Oxygen Transport (cont.)

- Hemoglobin saturation
  - Saturation is percentage of Hb that is carrying oxygen compared to total Hb
    - \( \text{SaO}_2 = \frac{[\text{HbO}_2/\text{total Hb}]}{\times 100} \)
    - Normal \( \text{SaO}_2 \) is 95% to 100%

- \( \text{HbO}_2 \) dissociation curve
  - The relationship between \( \text{PaO}_2 \) and \( \text{SaO}_2 \) is S-shaped.
  - Flat portion occurs with \( \text{SaO}_2 > 90\% \)
    - Facilitates \( \text{O}_2 \) loading at lungs even with low \( \text{PaO}_2 \)
  - Steep portion (\( \text{SaO}_2 < 90\% \)) occurs in capillaries
    - facilitates \( \text{O}_2 \) unloading at tissues
Oxygen Transport (cont.)
Oxygen Transport (cont.)

- Total oxygen content of blood
  - Combination of dissolved and bound to Hb
  - \( \text{CaO}_2 = (0.003 \times \text{PaO}_2) + (\text{Hb} \times 1.34 \times \text{SaO}_2) \)
  - Normal is 16–20 ml/dl

- Normal arteriovenous difference (~5 ml/dl)
Oxygen Transport (cont.)

<table>
<thead>
<tr>
<th>Oxygen Content</th>
<th>Arterial $O_2$ (ml/dl)</th>
<th>Venous $O_2$ (ml/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined $O_2 (1.34 \times 15 \times SO_2)$</td>
<td>19.5</td>
<td>14.7</td>
</tr>
<tr>
<td>Dissolved $O_2 (PO_2 \times 0.003)$</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Total $O_2$ content</td>
<td>19.8</td>
<td>14.8</td>
</tr>
</tbody>
</table>

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**Oxygen Transport (cont.)**

- **Fick equation**
  - $C(a - \bar{v})O_2$ indicates tissue oxygen extraction in proportion to blood flow (per 100 ml of blood)
  - Combined with total oxygen consumption ($\dot{V}O_2$) allows the calculation of cardiac output ($\dot{Q}_t$)
    \[
    \dot{Q}_t = \frac{\dot{V}O_2}{[C(a - \bar{v})O_2 \times 10]}
    \]
  - Normal adult $\dot{Q}_t$ is 4–8 L/min.
  - $\dot{V}O_2$ constant, changes in $C(a - \bar{v})O_2$ are due to changes in $\dot{Q}_t$; i.e. ↑$C(a - \bar{v})O_2$ signifies ↓$\dot{Q}_t$
Factors affecting oxygen loading and unloading

- Besides the shape of the HbO$_2$ curve, many factors affect O$_2$ loading and unloading.

- **pH (Bohr effect)**
  - Describes the affect pH has on Hb affinity for O$_2$
  - pH alters the position of HbO$_2$ curve.
    - Low pH shifts curve to right, high pH shifts to left.
  - Enhances oxygen transport
    - At tissue pH is ~7.37 shift right, more O$_2$ unloaded
    - Lungs pH ~7.4 shifts back left, enhancing O$_2$ loading
Oxygen Transport (cont.)

- **Body temperature (T) and HbO$_2$ curve**
  - Changes in T alter the position of the HbO$_2$ curve.
    - Decreased T shifts the curve left.
    - Increased T shifts the curve right.
    - T is directly related to metabolic rate.
      - When T is higher, the right shift facilitates more oxygen unloading to meet metabolic demands.
      - With lower metabolic demands, curve shifts left as not as much oxygen is required.

- See Figure 11-10.
Oxygen Transport (cont.)

- 2,3-Diphosphoglycerate (DPG) and the HbO$_2$ curve
  - Found in quantity in RBCs, it stabilizes deoxygenated Hb, decreasing oxygen’s affinity for Hb
    - Without 2,3-DPG Hb affinity is so great that O$_2$ cannot unload
  - $\uparrow$2,3-DPG shifts curve to right, promoting O$_2$ unloading
  - $\downarrow$2,3-DPG shifts curve to left, promoting loading
    - Stored blood loses 2,3-DPG, large transfusions can significantly impair tissue oxygenation
Oxygen Transport (cont.)

Abnormal hemoglobins

- **HbS (sickle cell):** fragile leads to hemolysis and thrombi.
  - Acute chest syndrome most common cause of death

- **Methemoglobin (metHb):** abnormal iron (Fe$^{3+}$) cannot bind with oxygen and alters HbO$_2$ affinity (left shift)
  - Commonly caused by NO, nitroglycerin, lidocaine

- **Carboxyhemoglobin (HbCO):** Hb binds CO, which has 200 times greater Hb affinity than O$_2$.
  - Displaces O$_2$ and shifts curve left
    - That O$_2$ which is bound cannot unload (left shift)
  - Treat with hyperbaric therapy
Oxygen Transport (cont.)

- Measurement of Hb affinity for oxygen

![Graph showing the relationship between oxygen saturation and PO2](image)

(Modified from Lane EE, Walker JF: Clinical arterial blood gas analysis. St Louis, 1987, Mosby.)
Carbon Dioxide Transport

Transport mechanisms

- Dissolved in blood: ~8% as high solubility coefficient

- Combined with protein: ~12% binds with amino groups on plasma proteins and Hb

- Ionized as bicarbonate: ~80% is transported as $\text{HCO}_3^-$ due to hydrolysis reaction
  - Majority of hydrolysis occurs in RBCs as they contain carbonic anhydrase which serves as a catalyst
  - $\text{HCO}_3^-$ diffuses out of RBCs in exchange for $\text{Cl}^-$, called the *chloride shift* or *hamburger phenomenon*. 
Carbon Dioxide Transport (cont.)

- CO₂ dissociation curve
  - Relationship between PaCO₂ and CaCO₂
  - HbO₂ affects this relationship
    - The Haldane effect describes this relationship
    - As HbO₂ increases, CaCO₂ decreases
      - Facilitates CO₂ unloading at lungs
    - At tissues, HbO₂ decreases and facilitates a higher CaCO₂ for transport to the lungs
  - See Figure 11-14.
Abnormalities of Gas Exchange and Transport

Impaired oxygen delivery ($DO_2$)

- $DO_2 = CaO_2 \times Q_t$
- When $DO_2$ is inadequate, tissue hypoxia ensues.

- Hypoxemia: Defined as an abnormally low PaO$_2$
  - Most common cause is V/Q mismatch
    - Because of shape HbO$_2$ curve, areas of high V/Q cannot compensate for areas of low V/Q, so ↓PaO$_2$
      - See Figure 11-16.
  - Other causes: hypoventilation, diffusion defect, shunting, and a low P$_{IO_2}$ (altitude)
Abnormalities of Gas Exchange and Transport (cont.)

Impaired DO₂ due to Hb deficiencies

- Majority of O₂ is carried bound to Hb, for CaO₂ to be adequate there must be enough normal Hb
  - If Hb is low, although the PaO₂ and SaO₂ are normal, the CaO₂ will be low.
  - Absolute low Hb is caused by anemia
  - Relative deficiency may be due to COHb or metHb.
Abnormalities of Gas Exchange and Transport (cont.)
Abnormalities of Gas Exchange and Transport (cont.)

Reduction in blood flow (shock or ischemia)

- Hypoxia can occur with a normal \( \text{CaO}_2 \) if \( Q_t \) is low
  - May be due to
    - Shock
      - Results in widespread hypoxia
      - Limited ability to compensate
        - Prolonged shock becomes irreversible
    - Ischemia
      - Local reductions in blood flow that may result in hypoxia and tissue death, i.e., myocardial infarction and stroke
Abnormalities of Gas Exchange and Transport (cont.)

**Dysoxia**

- $\text{DO}_2$ is normal but cells undergo hypoxia.
- Cells are unable to adequately utilize oxygen
  - Cyanide poisoning prevents cellular use of $\text{O}_2$.
  - In very sick individuals (sepsis, ARDS), oxygen debt may occur at normal levels of $\text{DO}_2$.
    - If oxygen uptake increases with increased $\text{DO}_2$, then $\text{DO}_2$ was inadequate.
    - Demonstrates a low $\text{VO}_2/\text{DO}_2$ (extraction ratio), thus dysoxia.
Abnormalities of Gas Exchange and Transport (cont.)

Impaired CO$_2$ removal

- Disorders that decreases $\dot{V}_A$ relative to metabolic need
  - Inadequate $\dot{V}_E$
    - Usually result of $\downarrow V_T$, $\downarrow f$ rare (drug overdose)
  - Increased $V_D/V_T$
    - Caused by rapid shallow breathing or high $\dot{V}/Q$
  - $\dot{V}/Q$ imbalance
    - Typically, CO$_2$ does not rise; instead, increase $\dot{V}_E$.
    - If patient is unable to $\uparrow \dot{V}_E$, then hypercarbia with acidosis occurs.
      - Seen in severe chronic disorders, i.e., COPD