Physiology
Unit 4

RESPIRATORY PHYSIOLOGY
In Physiology Today
Respiration

- **External respiration**
  - ventilation
  - gas exchange

- **Internal respiration**
  - cellular respiration
  - gas exchange

- **Respiratory Cycle**
  - Inspiration
    - Moving atmospheric air into the lungs
  - Expiration
    - Moving air out of the lungs
Lungs vs. Balloons

- A lung is similar to a balloon in that it resists stretch, tending to collapse almost totally unless held inflated by a pressure difference between its inside and outside.

- Lungs and the chest have elastic properties.
Lung Compliance

• **Compliance**
  – Elasticity
  – Tendency to recoil
  – Tendency of an elastic structure to oppose stretching or distortion
  * Resists distension

• **Surface tension**
  * Resists distension
  – **Surfactant**
    • Reduces surface tension
    • Increases compliance (makes them easier to stretch)
Airway Resistance
\[ F = \Delta P/R \]

- Same variables that affect resistance in blood vessels
  - Tube length, tube radius, friction
  - *Tube radius* most important factor
- Airway resistance is so small that small pressure differences produce large volumes of air flow
  - Average atmosphere-to-alveoli pressure difference is 1 mmHg, but 500 mL of air is moved (*tidal volume*)
  - Low pressure and low resistance
    - Pulmonary 1/10th of systemic vascular resistance
Ventilation

- Exchange of air between atmosphere and alveoli
- Atmospheric air pressure is 760 mmHg at sea level
- Air moves by bulk flow
  - $F = \frac{\Delta P}{R}$
  - $F = \frac{P_{alv} - P_{atm}}{R}$
Boyle’s Law

- Boyle’s law = \( \frac{P}{V} \)
- Pressure of a given quantity of gas is inversely proportional to volume
- An increase in the volume of the container (lungs) decreases the pressure of the gas (air)
Ventilation Mechanics

• Lung volume depends on:

1. *Transpulmonary pressure* \( (P_{tp}) \)
   - Inside to outside of the lung
   - \( P_{tp} = P_{alv} - P_{ip} \)
   - The force that keeps the lungs inflated
   - Transmural pressure
     - Across the wall

2. How compliant the lungs are
Transmural Pressures

Table 13–3 Two Important Transmural Pressures of the Respiratory System

<table>
<thead>
<tr>
<th>Transmural Pressure</th>
<th>$P_i - P_o$</th>
<th>Value at Rest</th>
<th>Explanatory Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transpulmonary ($P_{tp}$)</td>
<td>$P_{alv} - P_{ip}$</td>
<td>$0 - (-4) = 4 \text{ mmHg}$</td>
<td>Pressure difference holding lungs open (opposes inward elastic recoil of the lung)</td>
</tr>
<tr>
<td>Chest wall ($P_{cw}$)</td>
<td>$P_{ip} - P_{atm}$</td>
<td>$-4 - 0 = -4 \text{ mmHg}$</td>
<td>Pressure difference holding chest wall in (opposes outward elastic recoil of the chest wall)</td>
</tr>
</tbody>
</table>

$P_i$ is pressure inside the structure, and $P_o$ is pressure surrounding the structure.
What Keeps the Lungs Inflated?

• Elastic recoil of the lungs
  * At rest natural tendency is to **collapse**

• Lungs are held open by the positive $P_{tp}$
  – At rest exactly opposes elastic recoil
    • Collapsing force of the lungs is 4 mmHg
    • Intrapleural pressure is -4 mmHg

• Elastic recoil of the chest
  * At rest natural tendency is to **expand**
Pneumothorax

- A pierce in the chest wall allows atmospheric air to rush in causing $P_{ip}$ to go from -4 mmHg to 0 mmHg
- Transpulmonary pressure acting to hold the lungs open is eliminated
- Lung collapses
- Chest wall expands
Inspiration/Expiration

- In order for air to move into the lungs, the pressure in the lungs must drop below atmospheric pressure
  \[ P_{\text{atm}} > P_{\text{alv}} \]

- In order for air to move out of the lungs, the pressure in the lungs must exceed atmospheric pressure
  \[ P_{\text{alv}} > P_{\text{atm}} \]
The Respiratory Cycle
Partial Pressure of Gases

• *Dalton’s Law*
  – Pressure of each gas is independent of the pressure of other gases
  – Pressure of the gas is directly proportional to its concentration
  – Individual gas pressures in air is termed the partial pressure of a gas
  – Atmospheric air 760 mmHg at sea level
    • Air is 78% nitrogen
      – \(0.78 \times 760\) mmHg = 593 mmHg
      – \(P_{N2} = 593\) mmHg
    • Air is 21% oxygen
      – \(0.21 \times 760\) mmHg = 159 mmHg
      – \(P_{O2} = 159\) mmHg
  – Altitude and Temperature also affect pressure
Partial Pressure of O$_2$ and CO$_2$ in Blood

Table 13-7  Normal Gas Pressure

<table>
<thead>
<tr>
<th></th>
<th>Venous Blood</th>
<th>Arterial Blood</th>
<th>Alveoli</th>
<th>Atmosphere</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{O_2}$</td>
<td>40 mmHg</td>
<td>100 mmHg*</td>
<td>105 mmHg*</td>
<td>160 mmHg</td>
</tr>
<tr>
<td>$P_{CO_2}$</td>
<td>46 mmHg</td>
<td>40 mmHg</td>
<td>40 mmHg</td>
<td>0.3 mmHg</td>
</tr>
</tbody>
</table>

*The reason that the arterial $P_{O_2}$ and alveolar $P_{O_2}$ are not exactly the same is described later in this chapter.
Transport of O₂ in the Blood

• 1 Liter of blood contains 200 mL of oxygen
  – Dissolved in plasma
  – Bound to hemoglobin (Hb)

• Solubility of O₂ is relatively low
  – Only 3 mL of O₂ can dissolve in 1 L of blood at arterial PₐO₂ of 100 mmHg (2%)  
  – Remaining 197 mL of oxygen bound Hb (98%)
Transport of $O_2$ in the Blood

- **Hemoglobin**
  - Heme, globin
  - 280 million Hb per RBC x 4 = >1 billion molecules of oxygen per RBC

- **States of Hb**
  - Hb
    - deoxyhemoglobin
  - $O_2 + Hb \rightleftharpoons HbO_2$
    - Oxyhemoglobin

- **Oxygen carrying-capacity of blood – a percent**
  - Amount of $HbO_2$ is 80% of total Hb, the sample is 80% saturated
Oxygen-Hemoglobin Dissociation Curve

- **Sigmoid curve**
  - Each Hb molecule has 4 sub-units
  - Binding cooperativity
    - Binding of first O\textsubscript{2} increases the affinity for O\textsubscript{2} at remaining three heme units

- **Significance of the shape of the curve**
  - Steep slope between 20-60 mmHg
    - Increased unloading
  - Plateau
    - At 60 mmHg, 90% saturation
    - Oxygen reserve
Shifts in the Oxygen-Hemoglobin Dissociation Curve

- Other factors influence the degree of Hb saturation
  - 2,3-diphosphoglycerate (DPG)
  - Temperature
  - pH
  - PCO2

- A shift to the right decreases the affinity of Hb for O$_2$
  - increased unloading in the tissues

- A shift to the left increases the affinity of Hb for O$_2$
  - increased loading in the lungs
Hb Saturation
Effects of DPG Concentration

- 2,3-diphosphoglycerate (DPG)
  - Always produced by RBCs
  - Increase in DPG causes a shift to the right

- RBCs increase production of DPG when there is a decrease in $P_{O_2}$
  - Higher altitude
  - Anemia
  - Transfer from maternal blood to fetal Hb

- Increased unloading in the tissues to maintain $O_2$ delivery
**Hb Saturation**

**Effects of Temperature**

- Higher temperature in tissue capillary blood than in arterial blood
- The more metabolically active the tissue is, the higher the temperature will be
- Increased unloading in the tissue
  - Provides more metabolically active cells with more $O_2$

$P_{O_2}$ (mmHg)

Hemoglobin saturation (%)
Hb Saturation
Effects of pH

- Higher \([H^+]\) in tissue capillary blood than in arterial blood
  - Elevated \(P_{CO_2}\)
  - Metabolically produced acids such as lactic acid
- The more metabolically active the tissue is, the greater the \([H^+]\)
  - Lower pH
  - Higher acidity
- Increased unloading in the tissue
  - Provides more metabolically active cells with more \(O_2\)
Transport of CO$_2$ in Blood

- 200 mL CO$_2$/min produced by metabolism
- 10% dissolved in plasma
- 30% as carbaminohemoglobin (HbCO$_2$)
  - CO$_2$ + Hb $\rightleftharpoons$ HbCO$_2$
- 60% as bicarbonate (HCO$_3^-$)
  - CO$_2$ + H$_2$O $\rightleftharpoons$ H$_2$CO$_3$ $\rightleftharpoons$ HCO$_3^-$ + H$^+$
  - *Carbonic anhydrase*
  - Present in RBCs
Chloride Shift
Tissue Level

- **Bicarbonate reaction** shifts to the right...WHY??
  - \( \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+ \)

- **Steps:**
  - \( \text{CO}_2 \) diffuses out of the tissue cells into the blood
  - \( \text{CO}_2 \) moved into the red blood cells
  - \( \text{CO}_2 \) combines with \( \text{H}_2\text{O} \) to produce \( \text{H}_2\text{CO}_3 \)
    - Carbonic anhydrase makes this reaction fast
  - \( \text{H}_2\text{CO}_3 \) dissociates producing \( \text{H}^+ + \text{HCO}_3^- \)
  - \( \text{H}^+ \) buffered by hemoglobin, facilitating the offloading of \( \text{O}_2 \)
    - Forms HHb
  - \( \text{Cl}^- \) moves into the RBC in exchange for \( \text{HCO}_3^- \) moving into plasma
  - **Bohr effect**
    - Increased oxygen unloading in tissues
    - Enhanced transport of \( \text{CO}_2 \)
Chloride Shift
Tissue Level

(a) Oxygen release and carbon dioxide pickup at the tissues

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Reverse Chloride Shift
Pulmonary Capillaries

• Equation shifts to the left.....WHY??
  – $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+$

• Steps:
  – Hb oxygenated
  – Hb decrease in affinity for $\text{H}^+$
  – Reverse chloride shift as $\text{Cl}^-$ moves into plasma and $\text{HCO}_3^-$ moves into the RBC
  – $\text{H}_2\text{CO}_3$ dissociates to $\text{CO}_2 + \text{H}_2\text{O}$
  – $\text{CO}_2$ expired out

• Remember:
  – $\text{H}^+$ is buffered by Hb in RBC
  – $\text{HCO}_3^-$ goes into the plasma and buffers incoming $\text{H}^+$
Reverse Chloride Shift
Pulmonary Capillaries

(b) Oxygen pickup and carbon dioxide release in the lungs

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Respiratory Control Centers
Rhythmical Breathing

• Medulla oblongata
  – *Respiratory Rhythmicity Center*
    • Controls the diaphragm and intercostals

• Pons
  – *Apneustic Center*
    • Terminates inspiration
  – *Pneumotaxic Center*
    – Modulates activity of apneustic center
    – Smoothes the transition from inspiration to expiration
      • Cyclic inhibition

• Pulmonary stretch receptors
  – Cut off signal for inspiration to allow expiration to occur
Control of Ventilation

Monitoring $P_{O_2}$, $P_{CO_2}$, $H^+$

- Respiratory rate and tidal volume can be altered
- Peripheral chemoreceptors
  - *Aortic and Carotid bodies*
  - Provides afferent input to the medulla via the Vagus Nerve
  - Sensitive to $P_{O_2}$
- Central chemoreceptors
  - In the Medulla
  - Highly sensitive to $P_{CO_2}$
Control of Ventilation

Monitoring $P_{O_2}$, $P_{CO_2}$, $H^+$

• Peripheral chemoreceptors
  – Aortic and Carotid Bodies
  – Sensitive to:
    • Decreased $P_{O_2}$ (hypoxia)
    • Increased $H^+$ due to the build up of other acids (metabolic acidosis)
    • Increased $H^+$ due to $CO_2$ retention (respiratory acidosis)

• Central chemoreceptors
  – Medulla
  – Sensitive to
    • Increased $H^+$ in brain extracellular fluid (CSF)
      – $CO_2$ crosses blood brain barrier to stimulate receptors
Protective Reflexes

- Pulmonary irritant reflexes
  - Reflex constriction to prevent particulates from entering lungs
  - Receptors located between airway epithelial cells
  - Cough reflex
  - Sneeze reflex
  - Cessation of breathing reflex
    - Triggered when noxious agents are inhaled
    - Chronic smoking causes loss of this reflex