Module G: Oxygen Transport

Topics to Cover
- Oxygen Transport
- Oxygen Dissociation Curve
- Oxygen Transport Studies
- Tissue Hypoxia
- Cyanosis
- Polycythemia

Oxygen Transport
- Oxygen is carried from the lungs to the tissues in two different fashions:
  - Oxygen Dissolved in the blood plasma (PO₂)
  - Oxygen Combined with Hemoglobin (SO₂)

Dissolved Oxygen
- As oxygen diffuses across the A-C membrane, it dissolves into the plasma and remains in that fashion until it reaches the tissue.
- Expressed as a partial pressure - PO₂
  - Normal arterial level = 80-100 mm hg
  - Normal venous level = 35 – 45 mm hg
- The quantity of oxygen dissolves is a function of Henry's law.
  - At 37°C 0.003 ml of oxygen will dissolve in 100 ml of blood. (Henry’s Law)
  - At 100 mm hg PaO₂, the amount of dissolved oxygen is 0.3 ml O₂/100 ml blood (0.3 vol%).

Combined Oxygen
- Dissolved oxygen is inadequate for metabolic needs.
- Need a substance which will bind to oxygen and carry it, BUT will release it when needed.
- Voila! Hemoglobin!
  - Miracle #2...As we’ll see later, hemoglobin also carries carbon dioxide and is a key buffer of [H⁺].
Hemoglobin
- Each RBC contains approximately 280 million molecules of hemoglobin
- Adult Hemoglobin (Hb A) consists of
  - 4 Heme Groups – Primarily iron in the Fe^{+2} (ferrous) state.
  - 4 Globulin – 4 amino acid chains (2 \( \alpha \) & 2 \( \beta \))
- One heme group binds with one of the amino acid chains and oxygen binds with the iron in the heme group in a reversible way.
  \[ O_2 + Fe^{+2} \rightleftharpoons FeO_2 \] (Oxyhemoglobin)

Hemoglobin & the RBC
- “Normal” hemoglobin level
  - 15 g/dl (men) & 13-14 g/dl (women) - Malley
  - 15 ± 1.5 g/dl (men) & 13.5 ± 1.5 g/dl (women) – Egan
  - 15 ± 2 (men) & 14 ± 2 (women) - Easy
  - Why do women have less?
- The hemoglobin molecule resides in the erythrocyte and is responsible for giving the blood its red color.
- Hundreds of hemoglobin variants.
  - Normal: A, A2, F
  - Abnormal: S, H
- The affinity of hemoglobin for oxygen increases with each oxygen molecule attached
  - “All or Nothing”

Oxygen Saturation
- Saturation = Sites Filled
  Total Sites Available
- Example:
  - 80 sites filled = 80% saturation
  100 sites available
- Oxygen Saturation only talks about how much hemoglobin is saturated, NOT how much hemoglobin is present.
Combined Oxygen
- Each gram of Hemoglobin combines with 1.34 mL of oxygen.
  - \( O_2 \) bound to Hb = 1.34 mL \( O_2 \) x 15 g Hb
    = 20.1 vol% \( O_2 \)

Quantity of Oxygen Bound to Hemoglobin
- Not all hemoglobin molecules are bound with oxygen.
  - Normal saturation
    - Arterial (\( S_{aO2} \)) – 97%
    - Venous (\( S_{vO2} \)) – 75%
  - Some “desaturated” hemoglobin exists because of normal physiologic shunts:
    - Mixing of poorly saturated venous blood with arterial blood
    - Thebesian, bronchial, and pleural veins
    - Intrapulmonary shunts (perfused alveoli that are not ventilated)
      - 20.1 vol% \( O_2 \) x 0.97 = 19.5 vol% \( O_2 \)
  - Hemoglobin not bound with oxygen is called reduced hemoglobin.

Oxygen Content
- The total amount of oxygen in 100 mL of blood is the sum of the dissolved oxygen & the oxygen bound to hemoglobin.
  - Arterial Content
    - \( C_{aO2} = (Hb \times 1.34 \times S_{aO2}) + (PaO_2 \times 0.003) \)
  - Venous Content
    - \( C_{vO2} = (Hb \times 1.34 \times S_{vO2}) + (P_{vO2} \times 0.003) \)
  - Capillary Content
    - \( C_{cO2} = (Hb \times 1.34 \times S_{cO2}) + (P_{cO2} \times 0.003) \)
      - \( S_{cO2} \) = Ideal Saturation = 100%
      - \( P_{cO2} \) = Ideal Partial Pressure = \( P_{A02} \)

Oxygen Dissociation Curve
- The relationship between the partial pressure of oxygen and the saturation of oxygen is not linear.
  - 2 lines

Steep Portion of Curve
- “Dissociation Portion” of curve.
- Between 10 and 60 mm Hg.
- Small increases in \( P_{O2} \) yield large increases in \( S_{O2} \).
- At the tissue capillary, blood comes in contact with reduced tissue \( P_{O2} \) and oxygen diffuses from the capillary to the tissue. As the \( P_{O2} \) falls, oxygen bound to the hemoglobin (\( S_{O2} \)) is released.

Flat Portion of Curve
- “Association Portion” of curve.
- Greater than 60 mm Hg.
- Large increases in \( P_{O2} \) yield small increases in \( S_{O2} \).
- At the pulmonary capillary, blood comes in contact with increased alveolar \( P_{O2} \) and oxygen diffuses from the alveolus to the capillary. As the \( P_{O2} \) rises, oxygen binds with the hemoglobin (increasing \( S_{O2} \)).
- Very little rise in oxygen saturation above 100 mm Hg of \( P_{A02} \).
Key Points to Remember

- The amount of oxygen that is saturated on the hemoglobin (SO₂) is dependent on the amount dissolved (PO₂).
- Between a PaO₂ of 60 and 100 mm Hg, the curve is flat.
  - This means that small changes in PaO₂ can occur without a big drop in saturation and oxygen content.
- At the tissues, where the PO₂ is about 40 mm Hg, the curve is steep.
  - This means that small changes in PO₂ will result in a large amount of oxygen being unloaded.

Rules of Thumb of the Oxyhemoglobin Curve

<table>
<thead>
<tr>
<th>PO₂</th>
<th>SO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>50</td>
</tr>
<tr>
<td>40</td>
<td>75</td>
</tr>
<tr>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>250</td>
<td>100</td>
</tr>
</tbody>
</table>

- The degree to which oxygen is attracted to hemoglobin can be assessed by evaluating at what PO₂ there is a 50% SO₂ (P₅₀).
- Normal P₅₀ value is 27 mm Hg
- As P₅₀ increases/decreases, we say the “curve has shifted”.
  - P₅₀ less than 27: Shift to the left.
  - P₅₀ greater than 27: Shift to the right.

Leftward Shift of the OHDC

- Left Shift.
  - Increased oxygen affinity for hemoglobin.
  - This is the expected shift at the lungs (Left-Lungs).
  - For any given PO₂, SO₂ will be higher.
  - Decreasing P₅₀
  - LOW THINGS CAUSE A LEFT SHIFT
    - ↓H⁺ concentration (↑pH, alkalosis)
    - ↓Temperature (Hypothermia)
    - ↓Carbon Dioxide (PCO₂, Hypocarbia)
    - ↓2,3 DPG

Rightward Shift of the OHDC

- Right Shift.
  - Decreased oxygen affinity for hemoglobin.
  - This is the expected shift at the tissues.
  - For any given PO₂, SO₂ will be lower.
  - Increasing P₅₀
  - ELEVATED THINGS CAUSE A RIGHT SHIFT (Up-Right)
    - ↑H⁺ concentration (↓pH, acidosis)
    - ↑Temperature (Hyperthermia)
    - ↑Carbon Dioxide (PCO₂, Hypercarbia)
    - ↑2,3 DPG
2,3 DPG
- 2,3 DPG is an organic phosphate normally found in the RBC that has a tendency to bind with Hemoglobin and thereby decrease the affinity of Hemoglobin for oxygen.
- It promotes a rightward shift and enhances oxygen unloading at the tissues. This shift is longer in duration than that due to \([\text{H}^+]\), \(\text{PCO}_2\) or temperature.
- A doubling of DPG will result in a 10 torr increase in \(P_{50}\).

2,3 DPG
- The levels increase with
  - Cellular hypoxia.
  - Anemia
  - Hypoxemia secondary to COPD
  - Congenital Heart Disease
  - Ascent to high altitudes
- The levels decrease with
  - Septic Shock
  - Acidemia
  - Stored blood
    - No DPG after 2 weeks of storage.

Oxygen Transport
- The volume of oxygen leaving the left ventricle each minute.
  - \(\text{CaO}_2 \times \text{CO} \times 10 = 20 \text{ mL O}_2 \times 5 \text{ L/min} \times 10\)
  - Make sure to convert CO to L/min!
  - Normal value is 1,000 mL \(\text{O}_2\) / min
- Decreased oxygen delivery occurs when there is:
  - A decreased blood oxygenation
  - Decreased hemoglobin concentration
  - Decreased cardiac output.

Bohr Effect
- The effect of \(\text{CO}_2\) on the OHDC is known as the Bohr Effect.
  - \((\text{OH} – \text{Bohr})\)
  - High \(\text{PCO}_2\) levels and low pH decrease affinity of hemoglobin for oxygen (a rightward shift).
  - This occurs at the tissues where a high level of \(\text{PCO}_2\) and acidemia contribute to the unloading of oxygen.

Arterial-Venous Oxygen Content Difference
- \(\text{C(a - v)O}_2\)
- \(\text{CaO}_2 – \text{C v O}_2\)
- The venous blood is "mixed venous" blood obtained from the pulmonary artery via a pulmonary artery catheter.
  - Normal \(\text{CaO}_2\): 20 vol%
  - Normal \(\text{C v O}_2\): 15 vol%
  - Normal \(\text{CaO}_2 – \text{C v O}_2\): 5 vol%
- Decreased with:
  - Increased CO
  - Certain Poisons
  - Hypothermia
Oxygen Extraction Ratio

- Def: The amount of oxygen extracted by the peripheral tissues divided by the amount of oxygen delivered to the peripheral cells.
- aka: Oxygen coefficient ratio & Oxygen utilization ratio
- $O_2$ER = ($CaO_2 - C \cdot O_2$)/$CaO_2$
- Normal is 25%
- Increased with:
  - Decreased CO
  - Increased VO_2
  - Exercise
  - Seizures
  - Shivering
  - Hyperthermia
  - Anemia
  - Low PaO_2
- Decreased with:
  - Increased Cardiac Output
  - Skeletal Muscle Relaxation
  - Peripheral Shunting
  - Certain Poisons
  - Hypothermia
  - Increased Hemoglobin
  - Increased PaO_2

Pulmonary Shunting

- PERFUSION WITHOUT VENTILATION.
- Pulmonary shunt is that portion of the cardiac output that enters the left side of the heart without coming in contact with an alveolus.
  - “True” Shunt – No contact
    - Anatomic shunts (Thebesian, Pleural, Bronchial)
    - Cardiac anomalies
  - “Shunt-Like” (Relative) Shunt
    - Some ventilation, but not enough to allow for complete equilibration between alveolar gas and perfusion.
- Shunts are refractory to oxygen therapy.
  - Delivery of oxygen therapy will NOT help (at least to the expected degree).

Venous Admixture

- The mixing of oxygenated blood with “contaminated” deoxygenated blood resulting in a reduction in:
  - $PaO_2$
  - $SaO_2$

Alveolar-arterial Gradient

- $PAO_2 - PaO_2$
- More on this in today’s 1060 class.

Shunt Equation

- So just how much blood is shunted?
- $Q_T = (CcO_2 - CaO_2) / (CcO_2 - C\cdot O_2)$
- Where $CcO_2 = (Hb \times 1.34) + (PAO_2 \times .003)$
- You will need
  - $PBARO$ – Barometric Pressure
  - $PaO_2$ – Arterial Partial Pressure of Oxygen
  - $PaCO_2$ – Arterial Partial Pressure of Carbon Dioxide
  - $P \cdot O_2$ – Venous Partial Pressure of Oxygen
  - $Hb$ – Hemoglobin concentration
  - $PAO_2$ – Alveolar Partial Pressure of Oxygen
  - $FiO_2$ – Fractional Concentration of Inspired Oxygen

Shunt Equation Example

You obtain the following data on you patient. What is the percent shunt present?

1. pH: 7.25  $PaCO_2$: 28 torr  $PaO_2$: 68 torr  $SaO_2$: 91%
2. PB: 749  $P \cdot O_2$: 38 torr  $S \cdot O_2$: 72%  Hb: 13 gm%
3. $FiO_2$: .90
4. Steps:
   - Calculate $CaO_2$
   - Calculate $C \cdot O_2$
   - Calculate $PaO_2$
   - Calculate $PaCO_2$
   - Calculate $CcO_2$
   - Plug in numbers & solve!
Shunt – Clinical Significance

- Normal Shunt: 3 to 5%
- Shunts above 15% are associated with significant hypoxemia.

Tissue Hypoxia

- Hypoxemia: Reduced oxygen in blood (PaO₂).
- Hypoxia: Reduced oxygen at the tissue.
- Four types:
  - Hypoxic (Hypoxemic) Hypoxia
  - Anemic Hypoxia
  - Circulatory Hypoxia
  - Histotoxic Hypoxia

Hypoxic Hypoxia

- Tissues have inadequate oxygen levels because there is inadequate levels in the blood (reduced PaO₂).
- Rule out causes of hypoxemia
  - Low Alveolar Oxygen (reduced PaO₂)
  - Altitude
  - Hypoventilation (increased PaCO₂)
  - Breathing of gas mixtures less than 21%
  - Diffusion Impairment
  - Intrapulmonary Shunt
  - Ventilation/Perfusion Mismatch

Anemic Hypoxia

- Tissues have inadequate oxygen levels secondary to reduced oxygen carrying capacity.
- No hypoxemia!
- Caused by
  - Reduced Hemoglobin
  - Defective Hemoglobin
    - Carboxyhemoglobin
    - Methemoglobin
    - Sulfahemoglobin
    - Sickle Cell Anemia (HbS)

Carboxyhemoglobin

- Carbon Monoxide has 245 times the affinity for hemoglobin as oxygen.
- Causes a leftward shift (increased affinity of Oxygen)
- Normal level is less than 3%
- 10% is common with smokers.
- Toxic at 20%; Lethal at 50%.
- Suspect incomplete combustion if level is elevated.
  - Furnace, space heater
- Treatment is 100% oxygen
  - Reduces half-life of HbCO from 5 hours to 20 minutes.
  - Hyperbaric treatment remains controversial.
Methemoglobin
- A normal variant of adult hemoglobin.
- Ferrous to Ferric (loses an electron, Fe\(^{+3}\))
- Normal levels are less than 1%.
- Usually associated with excessive nitrate ingestion.
  - Amyl Nitrate
  - Nitroglycerine
  - Topical anesthetics
- Treatment with methylene blue

Sulfhemoglobin
- Sulfhemoglobin results from the union of hemoglobin with medications such as sulfonamides (antibiotics including Bactrim & Septra).
- The resultant form of hemoglobin is unable to transport oxygen, and is untreatable.
- The only treatment is to wait until the affected red blood cells are destroyed as part of their normal life cycle.

Hemoglobin S
- Hemoglobin S is an abnormal variant of Hemoglobin A where one of the 146 amino acids in the beta chain is altered.
- Inherited disorder from both parents.
  - 1% of African Americans.
- Recurrent painful episodes (Crisis) occur as sickled cells become obstructed.
- Typical “anemic” symptoms.
- Can lead to infections and stroke.

Circulatory Hypoxia
- Tissues have inadequate oxygen levels secondary to reduced oxygen delivery.
- Most significant cause is reduced cardiac output or blood pressure abnormalities.

Histotoxic Hypoxia
- Tissues have inadequate oxygen levels secondary to inability of tissue to use oxygen for metabolism.
- Cyanide poisoning.

Cyanosis
- A clinical condition manifested by a bluish discoloration of the mucous membranes or nail beds.
  - Peripheral vs. Central
  - Present when 5 g/dl of hemoglobin is desaturated.
  - This usually correlates with a SaO\(_2\) below 85%.
  - ANEMIC PATIENTS WILL NEVER BE CYANOTIC!
Polycythemia

- Response to chronic hypoxemia is the release of erythropoietin and stimulation of the bone marrow to produce more RBC and hemoglobin.
- Increased hemoglobin allows for greater carrying capacity BUT also results in increased viscosity of the blood.
- Increased viscosity increases work of the heart.

Fetal Hemoglobin (HbF)

- Fetal hemoglobin (hemoglobin F) is the main hemoglobin that transports oxygen around the body of the developing baby during the last 7 months of pregnancy.
- It has a greater affinity for oxygen than Hemoglobin A ($P_{50}$ of 20 mm Hg).
- At about 30 weeks gestation, the fetus begins to make increasing amounts of hemoglobin A.
- Hemoglobin F does not turn into hemoglobin A.
- As they grow babies automatically turn off the production of hemoglobin F (usually complete by one year). Failure to stop Hemoglobin F production is found in certain beta thalassemias. Possible link to SIDS.