M1 - Cardiovascular / Respiratory, Fall 2007

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Diffusion of Gases

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Objectives

• To understand the diffusion of gases in the lung
  – Define diffusion and contrast with bulk flow
  – State Fick’s law for diffusion
  – Distinguish between diffusion limitation and perfusion limitation
  – Describe the diffusion of oxygen from the alveoli into the blood
  – Describe the diffusion of CO$_2$ from blood to alveoli
  – Define diffusing capacity and discuss its measurement
Airway Branching

<table>
<thead>
<tr>
<th>Structure</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>Trachea</td>
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<tr>
<td>Main Bronchi</td>
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<tr>
<td>Lobar Bronchus</td>
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<tr>
<td>Segmental Bronchus</td>
<td>3-4</td>
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<tr>
<td>Bronchioles</td>
<td>5-15</td>
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<td>Terminal Bronchioles</td>
<td>16</td>
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<tr>
<td>Resp. Bronchioles</td>
<td>17-19</td>
</tr>
<tr>
<td>Alveolar Ducts</td>
<td>20-22</td>
</tr>
<tr>
<td>Alveolas Sacs</td>
<td>23</td>
</tr>
</tbody>
</table>

Source: SEER Training Website (training.seer.cancer.gov)
Bulk Flow vs. Diffusion

• The cross sectional area increases with airway generation.

• Large volume/time, with decreasing velocity at any point.
  – Imagine a fast flowing river reaching a delta.

• The velocity of gas during inspiration becomes tiny at the level of the respiratory bronchiole- at this level diffusion becomes the chief mode of gas movement.

Source: Undetermined
Gas Movement due to Diffusion

- Diffusion - movement of gas due to molecular motion, rather than flow.
  - Akin to the spread of a scent in a room, rather than wind.
  - Random motion leads to distribution of gas molecules in alveolus.
Gas Movement due to Diffusion

(1) [Diagram showing initial distribution of gas molecules]

(2) [Diagram showing movement of gas molecules due to diffusion]

(3) [Diagram showing the equilibrium state of gas molecules]

Source: Jkrieger (wikimedia.org)
Diffusion

• Driven by concentration gradients:
  – differences in partial pressure of the individual gases.

• Movement of $O_2$ and $CO_2$ between the level of the respiratory bronchiole and that of the alveolar space depends only on diffusion.

• The distances are small, so diffusion here is fast.
Diffusion of Gas Through the Alveolar Wall

- Alveolar airspace
- Pathway of diffusion

Source: Undetermined
Diffusion of Oxygen Across the Alveolar Wall

Pulmonary Surfactant

\[ \downarrow \text{Diffuses/Dissolves} \]

Alveolar Epithelium

\[ \downarrow \text{Diffuses/Dissolves} \]

Alveolar Interstitium

\[ \downarrow \text{Diffuses/Dissolves} \]

Capillary Endothelium

\[ \downarrow \text{Diffuses/Dissolves} \]

Plasma

\[ \downarrow \text{Diffuses/Dissolves} \]

Red Blood Cell

\[ \downarrow \text{Binds} \]

Hemoglobin
Fick’s Law for Diffusion

\[ V_{\text{gas}} = \frac{A \times D \times (P_1 - P_2)}{T} \]

- \( V_{\text{gas}} \) = volume of gas diffusing through the tissue barrier per time, in ml/min
- \( A \) = surface area available for diffusion
- \( D \) = diffusion coefficient of the gas (diffusivity)
- \( T \) = thickness of the barrier
- \( P_1 - P_2 \) = partial pressure difference of the gas
**Diffusivity**

\[ D \equiv \text{Solubility}/\sqrt{\text{MW}} \]

- \( \text{O}_2 \) has lower MW than \( \text{CO}_2 \)
- Solubility of \( \text{CO}_2 \) is 24x that of \( \text{O}_2 \)
- \( \text{CO}_2 \) diffuses 20x more rapidly through the alveolar capillary barrier than \( \text{O}_2 \)
Diffusion Across a Membrane

\[ \dot{V}_{gas} = \frac{A \cdot D(P_1 - P_2)}{T} \]

\[ D \propto \frac{\text{Solubility}}{\sqrt{MW}} \]

\[ A = \text{Area} \]

\[ T = \text{Thickness} \]
Limitations of Gas Transfer

• **Diffusion Coefficient.**
  – Different gases behave differently.

• **Surface Area and Thickness** of the alveolar wall.

• **Partial Pressure Gradient** across the alveolar wall for each individual gas.
  – Depends on both alveolar and mixed venous partial pressure (start of capillary).
Change in Blood Partial Pressure of Three Gases with Time in the Capillary

N₂O is Perfusion Limited

- N₂O is very soluble in biological tissues and diffuses rapidly.
- PcN₂O rises rapidly in the alveolar capillary
- Quickly have PcN₂O = PA N₂O.
- Because there is no pressure gradient, no diffusion occurs after about 0.1 sec.
- Fresh blood entering the capillary has not yet equilibrated and can still take up N₂O.
- Increased blood flow will increase gas transfer
- Transfer of N₂O is perfusion limited.
Change in Blood Partial Pressure of Three Gases with Time in the Capillary

Carbon Monoxide is **Diffusion Limited**

- Blood PCO rises very slowly because CO is bound to Hgb, with very little dissolved.
- Capillary PcCO does not approach PA CO.
- Partial pressure gradient is maintained throughout the time the blood is in the capillary.
  - Diffusion continues throughout this time.
- Transfer of CO is limited by diffusivity, surface area, and thickness of the wall.
Transfer of Oxygen

Transfer of Oxygen

- Under normal conditions, \( \text{PcO}_2 \) reaches \( \text{PAO}_2 \) about 1/3 of the distance through the capillary.

- Therefore under normal conditions transfer is perfusion limited.

- With exercise, the time blood spends in the capillary is reduced- no longer perfusion but diffusion limitation.

- In the setting of thickened alveolar wall, transfer is reduced.
  - With severely disturbed diffusion, there is limitation even at rest
Transfer of Oxygen is Limited at Low Alveolar $O_2$
Transfer of CO$_2$

- Is transfer of CO$_2$ diffusion or perfusion limited?

Transfer of CO$_2$

Why is the transfer of CO$_2$ so similar to that of O$_2$?

$$V_{\text{gas}} = \frac{A \times D \times (P_1 - P_2)}{T}$$

Diffusivity of CO$_2$ is $20x >$ than that of O$_2$

Partial pressure gradient of CO$_2$ is $45 \rightarrow 40$

Partial pressure gradient of O$_2$ is $100 \rightarrow 40$
Fick’s Law for Diffusion

\[ V_{gas} = \frac{(AxD)}{T} x (P_1 - P_2) \]

- \( V_{gas} \) = volume of gas diffusing through the tissue barrier per time, in ml/min
- \( A \) = surface area available for diffusion
- \( D \) = diffusion coefficient of the gas (diffusivity)
- \( T \) = thickness of the barrier
- \( P_1 - P_2 \) = partial pressure difference of the gas

\( (AxD)/T = \text{diffusing capacity of the lung (DL)} \)
Diffusing Capacity

\[
\frac{(AxD)}{T} = \frac{\dot{V}_{gas}}{(P_{1x} - P_{2x})} = D_{Lx}
\]

Source: Undetermined
Measuring Diffusing Capacity

• Inhale mixture containing known concentration of tracer gas.

• Allow diffusion from alveolus into blood.

• Measure concentration of tracer in exhaled gas.

• Calculate rate of removal of tracer gas by diffusion into blood and the partial pressure gradient from alveolus into blood.

• Choice of gas:
  – Readily available.
  – Easily measured.
  – Diffusion limited.
  – No arterial partial pressure.
We Could Use DLO₂

\[
\frac{Ax D}{T} = D_{LO₂}
\]

\[
\dot{V}_O₂ = D_{LO₂} \left( P_{A O₂} - P_{C O₂} \right) = \text{ml O₂/min}
\]

\[
D_{LO₂} \quad = \quad \frac{\dot{V}_O₂}{\left( P_{A O₂} - P_{C O₂} \right)}
\]

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Carbon Monoxide is an Ideal Gas for Measuring Diffusing Capacity

- CO binds avidly to hemoglobin.
- While CO content of the blood rises, the PCO in blood rises very slowly.
- The gradient of partial pressures from alveolus to blood remains almost constant during test
Carbon Monoxide Measurement of Diffusing Capacity

\[ DLCO = \frac{\dot{V}_{CO}}{P_{ACO} - P_{cCO}} \]

\[ P_{cCO} \approx 0 \]

Normal DLCO = 20-30 ml/min/mmHg
DLCO Has Two Components

Diffusion across the alveolar membrane.

Reaction with hemoglobin.

\[
\frac{1}{DL} = \frac{1}{Dm} + \frac{1}{\theta x Vc}
\]
Conditions that Impact Diffusion Capacity for CO.

\[ DLCO = \frac{AxD}{T} \]

- Decreased Surface Area.
  - Destruction of Alveolar Wall
- Increased Barrier Thickness.
- Anemia.
How would the Following Change the Diffusion Capacity of the Lungs?

- Changing from supine to upright
- Exercise
- Anemia
- Valsalva maneuver
- Low cardiac output due to hemorrhage
- Emphysema
- Pulmonary fibrosis