Author: Thomas Sisson, MD, 2009

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Diffusion of Gases

M1 – Cardiovascular/Respiratory Sequence

Thomas Sisson, MD

Fall 2008
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 CO₂ from blood to alveoli
  – Define diffusing capacity and discuss its measurement
Airway Branching

<table>
<thead>
<tr>
<th>Structure</th>
<th>Number</th>
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<tbody>
<tr>
<td>Trachea</td>
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<tr>
<td>Main Bronchi</td>
<td>1</td>
</tr>
<tr>
<td>Lobar Bronchus</td>
<td>2</td>
</tr>
<tr>
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<td>3-4</td>
</tr>
<tr>
<td>Bronchioles</td>
<td>5-15</td>
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<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>

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.
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
Diffusion

• Driven by concentration gradients:
  – differences in partial pressure of the individual gases.
• Movement of O\textsubscript{2} and CO\textsubscript{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
Diffusion of Oxygen Across the Alveolar Wall

Pulmonary Surfactant
  ↓ Diffuses/Dissolves
Alveolar Epithelium
  ↓ Diffuses/Dissolves
Alveolar Interstitium
  ↓ Diffuses/Dissolves
Capillary Endothelium
  ↓ Diffuses/Dissolves
Plasma
  ↓ Diffuses/Dissolves
Red Blood Cell
  ↓ Binds
Hemoglobin

T. Sisson
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

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

- \( \text{O}_2 \) 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

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

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

- Carbon monoxide
- Nitrous oxide
- Oxygen

\( \text{N}_2\text{O} \) is Perfusion Limited

- \( \text{N}_2\text{O} \) is very soluble in biological tissues and diffuses rapidly.
- \( \text{PcN}_2\text{O} \) rises rapidly in the alveolar capillary
- Quickly have \( \text{PcN}_2\text{O} = \text{PAN}_2\text{O} \).
- 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 \( \text{N}_2\text{O} \).
- Increased blood flow will increase gas transfer
- Transfer of \( \text{N}_2\text{O} \) 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 P_{ACO}.
- 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

[Graph showing the transfer of oxygen with different conditions labeled as Normal, 1/4 Normal, and 1/8 Normal.]

Transfer of Oxygen

- Under normal conditions, PcO\(_2\) reaches P\(_{A\,O_2}\) 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→40
Partial pressure gradient of O$_2$ is 100→40
Fick’s Law for Diffusion

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

- \( V_{\text{gas}} \) = 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

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

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

\[
\frac{AxD}{T} = D_{LO₂}
\]

\[
\dot{V}_{O₂} = D_{LO₂} \left( P_{A O₂} - P_{C O₂} \right) = \text{ml O}_₂ / \text{min}
\]

\[
D_{LO₂} = \frac{\dot{V}_{O₂}}{(P_{A O₂} - P_{C O₂})}
\]
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

\[ DLCO = \frac{V_{CO}}{P_{A}CO - P_{c}CO} \]

\[ P_{c}CO \approx 0 \]

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
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