M1 - Cardiovascular / Respiratory, Fall 2007

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Diffusion of Gases

Thomas Sisson, M.D.
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>Source: SEER Training Website (training.seer.cancer.gov)</th>
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<table>
<thead>
<tr>
<th>Structure</th>
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</thead>
<tbody>
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<tr>
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<td>Resp. Bronchioles</td>
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<tr>
<td>Alveolar Ducts</td>
<td>20-22</td>
</tr>
<tr>
<td>Alveolas Sacs</td>
<td>23</td>
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</table>
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

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 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**
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

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

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

\( \dot{V}_{\text{gas}} \) is the rate of gas flow, \( A \) is the area, \( D \) is the diffusion coefficient, \( P_1 \) and \( P_2 \) are the partial pressures, and \( T \) is the temperature.

\( D \) is proportional to the solubility per square root of molecular weight.
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

N\textsubscript{2}O is **Perfusion Limited**

- N\textsubscript{2}O is very soluble in biological tissues and diffuses rapidly.
- P\textsubscript{c}N\textsubscript{2}O rises rapidly in the alveolar capillary.
- Quickly have P\textsubscript{c}N\textsubscript{2}O = P\textsubscript{A}N\textsubscript{2}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 N\textsubscript{2}O.
- Increased blood flow will increase gas transfer.
- Transfer of N\textsubscript{2}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

• Under normal conditions, PcO₂ reaches PAO₂ 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 \( \text{O}_2 \).
Transfer of $\text{CO}_2$

- Is transfer of $\text{CO}_2$ diffusion or perfusion limited?

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

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

- \( V_{gas} \): 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 $DLO_2$

\[
\frac{AxD}{T} = DLO_2
\]

\[
\dot{V}_{O_2} = DLO_2 \left( P_{A_2O_2} - P_{C_2O_2} \right) = \text{ml O}_2 / \text{min}
\]

$DLO_2 = \frac{\dot{V}_{O_2}}{(P_{A_2O_2} - P_{C_2O_2})}$
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.

\[ \frac{1}{DL} = \frac{1}{Dm} + \frac{1}{\theta_x V_c} \]
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