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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

| Source: SEER Training Website (training.seer.cancer.gov) |

<table>
<thead>
<tr>
<th>Structure</th>
<th>Number</th>
</tr>
</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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<td>Segmental Bronchus</td>
<td>3-4</td>
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<td>Bronchioles</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>
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<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.

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)
• 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

Pathway of diffusion

Alveolar airspace

Source: Undetermined
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

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

- \( O_2 \) has lower MW than \( CO_2 \)
- Solubility of \( CO_2 \) is 24x that of \( O_2 \)
- \( CO_2 \) diffuses 20x more rapidly through the alveolar capillary barrier than \( O_2 \)
Diffusion Across a Membrane

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

where:
- \( D \) is the diffusion coefficient
- \( T \) is the temperature
- \( A \) is the area
- \( P_1 \) and \( P_2 \) are the partial pressures

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

**Diagram:**
- \( P_1 \)
- \( P_2 \)
- \( A = \text{Area} \)
- \( T = \text{Thickness} \)
- \( O_2 \)
- \( CO_2 \)
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$_2$O is **Perfusion Limited**

- N$_2$O is very soluble in biological tissues and diffuses rapidly.
- PcN$_2$O rises rapidly in the alveolar capillary.
- Quickly have PcN$_2$O = P$_A$N$_2$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$_2$O.
- Increased blood flow will increase gas transfer.
- Transfer of N$_2$O is **perfusion limited**.
Change in Blood Partial Pressure of Three Gases with Time in the Capillary

Carbon Monoxide isDiffusion 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

Transfer of Oxygen

• Under normal conditions, $P_{cO_2}$ reaches $P_{AO_2}$ 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?

The image shows graphs comparing the partial pressure of oxygen and carbon dioxide in blood under different conditions. The graphs illustrate the relationship between alveolar $P_{O_2}$ and the partial pressure in the blood, as well as the carbon dioxide partial pressure in the blood and alveolar $P_{CO_2}$.

- The top graph demonstrates the partial pressure of oxygen in blood under normal and reduced conditions ($\frac{1}{4}$ Normal and $\frac{1}{8}$ Normal).
- The bottom graph shows the carbon dioxide partial pressure in the blood and alveolar $P_{CO_2}$, with normal and reduced levels ($\frac{1}{4}$ Normal).

The graphs indicate how oxygen and carbon dioxide levels change over time in the capillary, with an arrow indicating the transition from entering to leaving the capillary during exercise.

Transfer of CO$_2$

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

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

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

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

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

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$_2$

\[
\frac{AxD}{T} = D_L O_2
\]

\[
\dot{V}_{O_2} = D_L O_2 \left( P_A O_2 - P_C O_2 \right) = \text{ml} \ O_2 / \text{min}
\]

\[
D_L O_2 = \frac{\dot{V}_{O_2}}{(P_A O_2 - P_C O_2)}
\]
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.

\[
\frac{1}{DL} = \frac{1}{Dm} + \frac{1}{\theta x Vc}
\]
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