Respiratory System

Part 2: Respiratory Physiology

Respiration

• Exchange of gases between air and body cells

• Three steps
  1. Ventilation
  2. External respiration
  3. Internal respiration

Ventilation

• Pulmonary ventilation consists of two phases
  1. Inspiration: gases flow into the lungs
  2. Expiration: gases exit the lungs

• Relies on pressure gradients
  — Atmosphere and alveoli

• Negative pressure breathing
  — Thoracic pressures
  — Atmospheric pressure

Boyle’s Law

• The relationship between the pressure and volume of a fixed quantity of gas in a closed container

• Pressure ($P$) varies inversely with volume ($V$):

$$P_1 V_1 = P_2 V_2$$

While one increases the other decreases

Ventilation

• Intrapleural pressure is subatmospheric
  — Inward elastic recoil of lung tissue
  — Outward elastic recoil of chest wall

Resting lung volume

• Atmospheric pressure ($P_{atm}$)
  — Pressure exerted by the air surrounding the body
  — 760 mm Hg at sea level

• Thoracic pressures are described relative to $P_{atm}$
  — Negative respiratory pressure is less than $P_{atm}$
  — Positive respiratory pressure is greater than $P_{atm}$
Ventilation

- Intrapulmonary (intra-alveolar) pressure ($P_{\text{pul}}$)
  - Pressure in the alveoli
  - Fluctuates with breathing
  - Always eventually equalizes with $P_{\text{atm}}$

Ventilation

- Negative $P_{\text{ip}}$ is caused by opposing forces
  - Two inward forces promote lung collapse
    - Elastic recoil of lungs decreases lung size
    - Surface tension of alveolar fluid reduces alveolar size
  - One outward force tends to enlarge the lungs
    - Elasticity of the chest wall pulls the thorax outward

Pulmonary Ventilation

- Inspiration and expiration
- Mechanical processes that depend on volume changes in the thoracic cavity
  - Volume changes $\rightarrow$ pressure changes
  - Pressure changes $\rightarrow$ pressure gradient $\rightarrow$ gases flow to equalize pressure

Inspiration

- An active process
  - Inspiratory muscles contract
    - Thoracic volume increases
    - Lungs are stretched and intrapulmonary volume increases
      - Intrapulmonary pressure drops
      - Air flows into the lungs, down its pressure gradient
        $P_{\text{pul}} = P_{\text{atm}}$
Expire

- Quiet expiration is normally a passive process
  - Inspiratory muscles relax
    - Thoracic cavity volume decreases
    - Elastic lungs recoil and intrapulmonary volume decreases
      - $P_{pl}$ increases
    - Air flows out of the lungs down its pressure gradient until $P_{pl} = 0$

Air Flow

- Physical factors influencing efficiency of air flow
  - Inspiratory muscles overcome three factors that hinder air passage and pulmonary ventilation
    1. Airway resistance
    2. Alveolar surface tension
    3. Lung compliance

NOTE: Study guide, Respiratory pg 10
6b. Friction is inversely proportional to airway diameter
Air Flow

- Bronchoconstriction
  - Smooth muscle contracts
  - Reduced air flow

Lung Compliance

- Measure of lung’s ability to stretch and expand
- Diminished by
  - Nonelastic scar tissue (fibrosis)
  - Reduced production of surfactant
  - Decreased flexibility of the thoracic cage
- Emphysema/COPD is associated with increased compliance
  - Due to diminished elastic recoil – patient has no trouble filling lungs with air, but great effort is required for exhalation

Gas Laws

- Dalton’s Law of Partial Pressure
  - Describes how a gas behaves when it is part of a mixture
    - Partial pressure = pressure exerted by a single gas in the mixture = proportional to the percentage of gas in a mixture
    - Total pressure exerted by a mixture of gases is the sum of the pressures exerted by each gas

- Fick’s Law of Diffusion
  - Gives the rate of diffusion for a given gas across a membrane
    - CO₂ has a high diffusion coefficient and diffuses 20 times more rapidly across a membrane than O₂

\[
V = \frac{A (P_1 - P_2) D}{T}
\]
- \(A\) = membrane surface area
- \(P_1 - P_2\) = difference in partial pressures
- \(D\) = diffusion coefficient
- \(T\) = thickness of membrane

Gas Laws

- Dalton’s Law of Partial Pressure
  - Example:
    - Air contains 20.9% O₂
    - Atmospheric Pressure = 760 mmHg
    - \(P_{O₂}\) = partial pressure of oxygen in the atmosphere

\[
0.209 \times 760 \, \text{mmHg} = 160 \, \text{mmHg}
\]

Gas Laws

- Diseases related to gas diffusion
  - Pulmonary edema
  - COPD

Gas Laws

- COPD
Gas Exchange

- External respiration
  - Pulmonary gas exchange
- Internal respiration
  - Gas exchange between blood capillaries and tissues

External Respiration

- Exchange of O$_2$ and CO$_2$ across the respiratory membrane
  - Between lung and blood

Thought Question

- Can you think of some factors that might influence the exchange of gases between the lungs and the blood? Hint: remember Fick’s Law?

External Respiration

- Respiratory membrane
  - Site of gas exchange between lung and blood
- Not actually a membrane, but a collection of associated structures
  - Membrane of lung epithelium
  - Pulmonary capillary membrane
  - Surfactant
  - Connective tissue

External Respiration

- Partial pressure gradient for O$_2$ in the lungs is steep
  - Venous blood pO$_2$ = 40 mm Hg
  - Alveolar pO$_2$ = 104 mm Hg

  Oxygen readily diffuses from alveoli to lung capillaries
External Respiration

- Partial pressure gradient for CO₂ in the lungs
  - Venous blood pCO₂ = 45 mm Hg
  - Alveolar pCO₂ = 40 mm Hg
- But...
  - CO₂ is 20 times more soluble in plasma than oxygen
  - CO₂ diffuses in equal amounts with oxygen!

Factors Affecting External Respiration

Anatomical adaptations
- Moist surfaces
- Thickness and surface area
- Narrow capillaries = RBC’s single file

Physiological and physical factors
- Pulmonary disease
- Affect of drugs on minute volume
- Partial pressure changes with altitude

Internal Respiration

- Capillary gas exchange in body tissues
- Partial pressures and diffusion gradients are reversed compared to external respiration
  - pO₂ in tissue is always lower than in systemic arterial blood
  - pCO₂ in tissue is higher than in systemic arterial blood
Gas Transport (page 12)

- Oxygen (O\textsubscript{2}) transport
- Carbon dioxide (CO\textsubscript{2}) transport

O\textsubscript{2} Transport

- Molecular O\textsubscript{2} is carried in the blood
  - Solubility in plasma low
  - Few O\textsubscript{2} = partial pressure
  - Only 1.5% dissolved in plasma
  - paO\textsubscript{2} does not include O\textsubscript{2} bound to hemoglobin
    - Poor measure of total O\textsubscript{2}

O\textsubscript{2} Transport

- Hemoglobin
  - Bound O\textsubscript{2} does not contribute to partial pressure
    - Maintaining partial pressure gradient → diffusion
    - 98.5% loosely bound to each Fe of hemoglobin (Hb) in RBCs
      - (4) O\textsubscript{2} per hemoglobin
- Oxyhemoglobin (HbO\textsubscript{2})
  - Hemoglobin-O\textsubscript{2} combination
- Reduced hemoglobin (HHb)
  - Hemoglobin that has released O\textsubscript{2}

\[
\text{HHb} + \text{O}_2 \rightarrow \text{HbO}_2 + \text{H}^+ 
\]

\[
\begin{align*}
\text{Lungs} & \\
\text{Tissues} & \\
\end{align*}
\]
O₂ Transport

- Loading and unloading of O₂ is facilitated by change in shape of Hb
  - As O₂ binds, Hb affinity for O₂ increases
- 4 heme groups bound to O₂
  - Saturated
- 1, 2 or 3 heme groups bound to O₂
  - Partially saturated
- Measure of oxygen saturation

O₂ Transport

- Rate of loading and unloading of O₂ is regulated by
  - pO₂
  - Temperature
  - Blood pH
  - pCO₂
  - Products of metabolism

O₂ Transport

- Factors that promote oxyhemoglobin formation
  - ↑ pO₂
  - ↓ pCO₂

*Conditions found in the lungs promote O₂ binding to Hb*

O₂ Transport

- Factors that promote oxyhemoglobin dissociation
  - ↓ pO₂
  - ↑ temperature
  - ↑ pCO₂
  - ↑ products of metabolism

*Conditions found in the tissues promote O₂ unloading*

Oxyhemoglobin Dissociation

- Influence of pO₂ on hemoglobin saturation
  - Arterial blood
    - paO₂ = 100 mm Hg
    - Hb is 97-100% saturated
  - Venous blood (resting tissues)
    - pO₂ = 40 mm Hg
    - Hb is 75% saturated
    - Venous blood still contains oxyhemoglobin!
Oxyhemoglobin Dissociation

- **Utilization coefficient**
  - Difference between arterial and venous $SO_2$
    - Example: arterial $SO_2 = 100%$, venous $SO_2 = 75%$
    - Utilization coefficient 25%
  - $↑$ metabolism = $↓$ paO$_2$ = larger partial pressure difference

- **Only 20–25% of bound O$_2$ is unloaded during one systemic circulation (at rest)**
- If O$_2$ levels in tissues drop:
  - More oxygen dissociates from hemoglobin and is used by cells
    - Blood flow and heart rate need not increase!

- **Other factors influencing hemoglobin saturation**
  - $↑$ temperature and $↑$ H$^+$
    - Conditions found at cells enhance O$_2$ unloading
    - Shift the O$_2$-hemoglobin dissociation curve to the right

---

**CO$_2$ Transport**

- CO$_2$ is transported in the blood in three forms
  - 7-10% dissolved in plasma
  - 20% bound to globin of hemoglobin
    - carboxyhemoglobin or HbCO$_2$
  - 70% transported as bicarbonate ions (HCO$_3^-$) in plasma

---

**Factors promoting Oxyhemoglobin dissociation shift curve to the right**

- Increased carbon dioxide ($P_{CO_2}$ 80 mm Hg or $↓$ pH 7.2)
- Decreased carbon dioxide ($P_{CO_2}$ 20 mm Hg or $↑$ pH 7.6)
- Normal arterial concentrations

---

**CO$_2$ Transport**

\[
\begin{align*}
H_2O + CO_2 & \leftrightarrow H_2CO_3 \\
H_2CO_3 & \leftrightarrow HCO_3^- + H^+
\end{align*}
\]

Key:
- H$_2$O = water
- CO$_2$ = carbon dioxide
- H$_2$CO$_3$ = carbonic acid
- HCO$_3^-$ = bicarbonate ion
- H$^+$ = hydrogen ion
- CA = carbonic anhydrase
CO₂ Transport

- Reaction happens in plasma but is 1,000X faster in the RBC because of CA
- H⁺ ions = acid = decrease pH = improved O₂ unloading from hemoglobin
- HCO₃⁻ diffuses out, replaced by Cl⁻ to maintain equilibrium = Chloride Shift

CO₂ Transport

- In pulmonary capillaries reaction is reversed
  - HCO₃⁻ moves into the RBCs and binds with H⁺ to form H₂CO₃
  - H₂CO₃ is split by carbonic anhydrase into CO₂ and water
  - CO₂ diffuses into the alveoli

\[
\text{CA} \quad \text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+
\]