For the body to survive, there must be a constant supply of O₂ and a constant disposal of CO₂.
Chapter 21: Respiratory System

Respiratory System:

Respiratory System Functions:

1) **Provides surface area for gas exchange** (between air / blood)
2) **Moves air to / from gas exchange surface**
3) **Protect system** (dehydration / temp. change / pathogens)
4) **Sound production**
5) **Assist in detection of olfactory cues**

Functional Anatomy:

Overview of Respiratory System:

1) External nares
2) Nasal cavity
   • Resonance chamber
3) Uvula
4) Pharynx
   • Nasopharynx
   • Oropharynx
   • Laryngopharynx
5) Larynx
   • Provide open airway
   • channel air / food
   • voice production
6) Trachea
7) Bronchial tree
8) Alveoli

---

Marieb & Hoehn – Figure 21.1
Trachea
Primary Bronchus
Bronchi bifurcation (23 orders)

Naming of pathways:
- > 1 mm diameter = bronchus
- < 1 mm diameter = bronchiole
- < 0.5 mm diameter = terminal bronchiole

Bronchi = Conducting Zone
Terminal Bronchiole = Respiratory Zone

Mucosa:
Mucous membrane
( epithelium / areolar tissue )

Epithelium:
Pseudostratified columnar
Cilia
Lamina Propria (areolar tissue layer):
Smooth muscle
Mucous glands
Cartilage:
Rings

Respiratory Mucosa / Submucosa (Variable):
Location in Bronchial Tree:
Near Trachea → Near Alveoli

Epithelium:
Pseudostratified columnar → Simple cuboidal
Cilia → No cilia

Lamina Propria (areolar tissue layer):
↓ Smooth muscle → Smooth muscle
Mucous glands → No mucous glands

Cartilage:
Rings → Plates / none
Functional Anatomy:

How are inhaled debris / pathogens cleared from respiratory tract?

Nasal Cavity:
- Particles > 10 µm

Conducting Zone:
- Particles 5 – 10 µm

Respiratory Zone:
- Particles 1 – 5 µm

Mucus Escalator

Trachea
- Tough, flexible tube (~ 1” diameter)
- 15 – 20 tracheal cartilages (hyaline)
  - Protect airway (prevent collapse)
  - Allow for food passage (‘C’-shaped)

Bronchi (> 1 mm diameter)
- $1^\circ$ = Extrapulmonary bronchi
- $2^\circ$ → = Intrapulmonary bronchi
  - Smooth muscle layer
  - Cartilaginous plates

Bronchitis:
Inflammation of airways
Functional Anatomy:

**Bronchioles** (< 1 mm diameter)
- Loss of cartilage
- Mucous glands rare – Why?
- Thick smooth muscle layer
  
  **Sympathetic stimulation:**
  Bronchodilation
  
  **Parasympathetic stimulation:**
  Bronchoconstriction

**Terminal Bronchioles**
- Ciliated epithelium (columnar / cuboidal)
- No mucous glands

**Respiratory Bronchioles**
- Ciliated → non-ciliated epithelium
- Actively participates in respiration

**Alveoli** (~ 1.5 million / lung)
- Cup-shaped, thin-walled sacs
  
  **Type I cells:** Simple squamous; forms wall of alveoli
  - Alveolar pores (1 – 6 / alveoli)
  
  **Type II cells:** Cuboidal / round
  - **Surfactant:** Secretion; reduces surface tension (prevents alveoli collapse)
    - Respiratory Distress Syndrome (e.g., pre-mature babies)
  - **Dust cells:** Macrophages; clear debris on alveolar surface

**Respiratory Membrane:**
1) Type I cells of the alveoli
2) Endothelial cells of capillaries
3) Fused basement membranes

0.1 – 0.5 \( \mu \text{m} \) thick

**Pneumonia:** Thickening of respiratory membrane

Pseudostratified ciliated columnar epithelium

Allergic Attack = Histamine Release = Bronchoconstriction

Chapter 21: Respiratory System

Marieb & Hoehn – Figure 21.8
Respiration includes:

1) **Pulmonary ventilation** (pumping air in / out of lungs)
2) **External respiration** (gas exchange @ blood-gas barrier)
3) **Transport of respiratory gases** (blood)
4) **Internal respiration** (gas exchange @ tissues)
Pressure relationships in the thoracic cavity:

1) **Intrapulmonary Pressure** (within the alveoli):
   - Static conditions = 0 mm Hg
   - Inhalation (inspiration) = \( P_{pul} \) slightly negative
   - Exhalation (expiration) = \( P_{pul} \) slightly positive

2) **Intrappeural pressure** (within the pleural cavity):
   - Always relatively negative (~ -4 mm Hg)
   - Prevents lungs from collapsing

**Atmospheric pressure** = ~ 760 mm Hg
(Consider \( P_{atmospheric} = 0 \) mm Hg)
1) Pulmonary Ventilation:

Why is the intrapleural pressure negative?

Answer: Interaction of opposing forces

Forces acting to collapse lung:
1) Elasticity of lungs
2) Alveolar surface tension

Force resisting lung collapse:
1) Rigid chest wall

Surface tension of serous fluids keep lungs “stuck” to chest wall

Forces equilibrate at $P_{ip} = -4$ mm Hg

Pneumothorax:
("sucking chest wound")
Puncture of chest wall — results in inability to generate negative pressure and expand the lungs

Boyle’s Law

$P_1 V_1 = P_2 V_2$

- $P$ = pressure of gas (mm Hg)
- $V$ = volume of gas (mm$^3$)
- $P_1$ = initial pressure; $V_1$ = initial volume
- $P_2$ = resulting pressure; $V_2$ = resulting volume

Example: $4$ mm Hg ($2$ mm$^3$) = $P_2$ ($4$ mm$^3$)  \[ P_2 = 2 \text{ mm Hg} \]

CHANGING THE VOLUME RESULTS IN INVERSE CHANGE OF PRESSURE!
1) Pulmonary Ventilation:
Mechanisms of Ventilation:

1) **Inspiration:** Muscular expansion of thoracic cavity

A) Contraction of diaphragm
   • Lengthens thorax (pushes liver down)

B) Contraction of external intercostal muscles
   • Widens thorax

Results in:
• Reduced intrapleural pressure ($P_{ip}$)
• Reduced intrapulmonary pressure ($P_{pul}$)
1) Pulmonary Ventilation:

Mechanisms of Ventilation:

2) Expiration: Retraction of thoracic cavity

A) Passive Expiration
   - Diaphragm relaxes
   - External intercostals relax
   - Elastic rebound (lungs rebound)

B) Active ("Forced") Expiration
   - Abdominal muscles contract
   - Internal intercostals contract

Eupnea:
Quiet breathing
(active inspiration; passive expiration)

Hyperpnea:
Forced breathing
(active inspiration; active expiration)
Chapter 21: Respiratory System

1) Pulmonary Ventilation:

Physical Factors Influencing Pulmonary Ventilation:

A) Airway resistance
   - Flow of air = change in pressure / resistance (F = ΔP / R)
     ➢ Asthma - allergic response to irritants
       • Constriction of bronchioles = ↓ radius = ↑ resistance

B) Surface tension in alveoli
   - Moist alveolar surfaces attract to one another (H₂O polarity – collapses alveoli)
   - Alveolar cells secrete surfactant (e.g., detergents)

C) Lung compliance
   - “Stretchiness” of lung (↑ compliance = easier to expand lung)
   - Determined by:
     a) Elasticity of lung
     b) Surface tension
     ➢ Emphysema: Lungs lose elasticity (too compliant)

---

Respiratory Volumes:

Tidal Volume:
Amount of air moved into / out of lung during single respiratory cycle

- Resting Tidal Volume (~ 500 ml)
- Inspiratory reserve volume (~ 3100 ml)
- Expiratory reserve volume (~ 1200 ml)
- Residual volume (~ 1200 ml)
- Vital capacity (~ 4800 ml)
- Total lung capacity (~ 6000 ml)

(Male)
(Female ~ 4200 ml)
1) Pulmonary Ventilation:

Respiratory Rates:

**Respiratory Minute Volume:**

\[ V_M = f \text{ (breaths / minute)} \times V_T \text{ (tidal volume)} \]

\[ = 12 \text{ breaths / minute} \times 500 \text{ ml} \]

\[ = 6000 \text{ ml / minute} \]

\[ = 6.0 \text{ liters / minute} \]

**Alveolar Ventilation:**

\[ V_A = f \text{ (breaths / minute)} \times (V_T \text{ (tidal volume)} - V_D \text{ (anatomic dead space)}) \]

\[ = 12 \text{ breaths / minute} \times (500 \text{ ml} - 150 \text{ ml}) \]

\[ = 4200 \text{ ml / minute} \]

\[ = 4.2 \text{ liters / minute} \]

Respiration includes:

1) Pulmonary ventilation (pumping air in / out of lungs)

2) External respiration (gas exchange @ blood-gas barrier)

3) Transport of respiratory gases (blood)

4) Internal respiration (gas exchange @ tissues)
2) External / Internal Respiration:

Physical Properties of Gases:

A) **Dalton’s Law of Partial Pressures:**
   - The total pressure of a gas is equal to the sum of the pressure of its constituents

\[
P_{\text{atmosphere}} = 760 \text{ mm Hg}
\]

\[
P_{O_2} = 0.21 \times 760 \text{ mm Hg} = 159 \text{ mm Hg}
\]

\[
P_{N_2} = 0.79 \times 760 \text{ mm Hg} = 601 \text{ mm Hg}
\]

\[
P_{CO_2} = 0.0004 \times 760 \text{ mm Hg} = 0.30 \text{ mm Hg}
\]

B) **Henry’s Law:**
   - Gases diffuse down pressure gradients

Additional factors affecting gas / liquid interchange:

A) **Solubility of gas in water**
   - \( CO_2 >> O_2 >> N_2 \) (the “bends”)

B) **Temperature**
   - Solubility inversely related to temperature
2) External / Internal Respiration:

Why is alveolar gas high in CO₂ and water vapor?

Lung air modified by gas exchange:
1) O₂ into blood; CO₂ out of blood
2) Humidification of air (conducting pathways)
3) Mixture of fresh and residual air / breath

% Composition of Air
\[ \text{H₂O} = 6.2\% \]
\[ \text{O₂} = 21\% \]
\[ \text{N₂} = 79\% \]
\[ \text{CO₂} = 0.04\% \]

% Composition of Lung Air
\[ \text{H₂O} = 6.2\% \]
\[ \text{O₂} = 13\% \]
\[ \text{N₂} = 74.5\% \]
\[ \text{CO₂} = 6\% \]

Approximately the same amount of CO₂ and O₂ cross membrane

Lung – Blood Interface
- \( P_{ \text{O₂} } \) in alveoli = ~ 100 mm Hg
- \( P_{ \text{CO₂} } \) in blood = ~ 40 mm Hg
  Net movement into blood
- \( P_{ \text{CO₂} } \) in alveoli = ~ 40 mm Hg
- \( P_{ \text{CO₂} } \) in blood = ~ 45 mm Hg
  Net movement into alveoli

Blood – Tissue Interface
- \( P_{ \text{O₂} } \) in blood = ~ 100 mm Hg
- \( P_{ \text{CO₂} } \) in tissues = ~ 40 mm Hg
  Net movement into tissues
- \( P_{ \text{CO₂} } \) in blood = ~ 40 mm Hg
- \( P_{ \text{CO₂} } \) in tissue = ~ 45 mm Hg
  Net movement into blood
2) External / Internal Respiration:
Gas exchange at the respiratory membrane is efficient:

A) Differences in partial pressure across respiratory membrane substantial

B) Exchange area thin (thickness < 1.0 µm) and expansive (~ 50 - 70 m²)

C) Ventilation – Perfusion Coupling:

↓ O₂ / ↑ CO₂ in alveoli triggers:
1) constriction of arterioles feeding area
2) dilation of bronchioles feeding area

↑ O₂ / ↓ CO₂ in alveoli triggers:
1) dilation of arterioles feeding area
2) constriction of bronchioles feeding area
Respiration includes:

1) Pulmonary ventilation (pumping air in / out of lungs)
2) External respiration (gas exchange @ blood-gas barrier)
3) **Transport of respiratory gases** (blood)
4) Internal respiration (gas exchange @ tissues)

3) Gas Transport:

A) **Oxygen Transport:**
   - Most $O_2$ in blood bound to **hemoglobin** (Hb) (> 98.5%)
     - **Hemoglobin saturation** = % of heme units bound to $O_2$ in blood
     - $O_2$ solubility low in plasma (~ 1.5%)

\[
\begin{align*}
\text{Hb} + O_2 & \rightarrow \text{HbO}_2 \\
\text{lungs} & \rightarrow \text{tissues}
\end{align*}
\]
3) Gas Transport:
A) Oxygen Transport:
   • Rate of $O_2$ binding to hemoglobin dependent on partial pressure of $O_2$

   **Oxygen Dissociation Curve**
   Describes relationship between percent saturation of Hb and partial pressure of oxygen

   **Sub-unit Cooperativity** (hemoglobin)
   Oxygenation of first heme group facilitates oxygenation of other heme groups

Factors influencing $O_2$ binding to Hb:
1) $P_{O_2}$ ($\downarrow P_{O_2} = \uparrow$ release of $O_2$)
2) Temperature ($\uparrow$ temp. = $\uparrow$ release of $O_2$)
3) pH ($\downarrow$ pH = $\uparrow$ release of $O_2$)
4) $P_{CO_2}$ ($\uparrow P_{CO_2} = \uparrow$ release of $O_2$)
3) Gas Transport:
B) Carbon Dioxide Transport:
   • Dissolved directly in plasma (7 – 10%)
   • Bound to amino acids of Hb (20 – 30%)
     • Carbaminohemoglobin
   • Converted to bicarbonate ion (60 – 70%)

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

1) Carbon dioxide (CO₂) combines with water (H₂O) to form carbonic acid (H₂CO₃)
   • Reaction catalyzed by carbonic anhydrase (CA - enzyme)
2) H₂CO₃ dissociates into hydrogen ion (H⁺) and bicarbonate ion (HCO₃⁻)
   • HCO₃⁻ released into plasma

3) Gas Transport:
B) Carbon Dioxide Transport:
   Chloride Shift:
   Mass influx of Cl⁻ into RBC to offset efflux of HCO₃⁻

   Bohr Effect:
   \(\downarrow\) pH due to HCO₃⁻ production leads to \(\uparrow\) in O₂ release from Hb
3) Gas Transport:

B) Carbon Dioxide Transport:

- $CO_2$ transport allows for blood buffering:
  - $HCO_3^-$ acts as a proton acceptor ($H^+$) in plasma
    - If blood $[H^+]$ rises, $H^+$ combines with $HCO_3^-$
    - If blood $[H^+]$ drops, $H^+$ dissociates from $H_2CO_3$
  - Mechanism maintains stable blood pH ~ 7.4

Control of Respiration:

1) Medullary Respiratory Centers

A) Ventral Respiratory Group (VRG):
  - Inspiratory center ("pacesetter"); 12 – 15 breaths / min
  - Excites diaphragm / external intercostals

B) Dorsal Respiratory Group (DRG):
  - Integration of peripheral signals (e.g., chemical)
Control of Respiration:
2) Chemoreceptor Reflexes

A) $P_{CO_2}$
- Most potent respiratory stimulant
- **Hypercapnia**: Increased $P_{CO_2}$ in arterial blood
- **Hypocapnia**: Decreased $P_{CO_2}$ in arterial blood

Hyperventilation:
Rate / depth of respiration exceeds demands for $O_2$ delivery / $CO_2$ removal

$\downarrow P_{CO_2}$

(strenuous exercise)

$\downarrow$ Ventilation Rate

$\downarrow$ Oxygen Starvation

B) $P_{O_2}$
- Minor respiratory stimulant ($\downarrow O_2 = \uparrow$ respiratory rate)
- Mediated via peripheral chemoreceptors (e.g., carotid artery)
- Stimulated by $P_{O_2} < 60$ mm Hg in arterial blood

C) Arterial pH
- Mediated via peripheral chemoreceptors ($\downarrow$ pH = $\uparrow$ respiratory rate)

3) Hering-Breuer Reflexes

A) Inflation Reflex
- Lung stretch inhibits inspiratory center (prevents lung over-inflation)

B) Deflation Reflex
- Lung deflation inhibits expiratory center (during active expiration)
Control of Respiration:

4) Protective Reflexes:
   A) Pulmonary Irritant Reflexes:
      • Irritant stimulates sneezing (nasal cavity) or coughing (lower conduction system)

   B) Laryngeal Spasm
      • Irritant around glottis leads to closure of epiglottis (protect lung)

5) Voluntary Control:
   A) Emotion:
      • ↑ respiratory rate via hypothalamic input (limbic system)
   B) Anticipation of Strenuous Exercise:
      • ↑ respiratory rate via sympathetic input
   C) Conscious Control (bypass / block respiratory centers)

Increase in lung cancer rates correlated with rise in smoking among adult men and women:

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>Rare…</td>
</tr>
<tr>
<td>1956</td>
<td>29,000 deaths</td>
</tr>
<tr>
<td>1978</td>
<td>105,000 deaths</td>
</tr>
<tr>
<td>2004</td>
<td>160,440 deaths</td>
</tr>
</tbody>
</table>

Formaldehyde, benzene, vinyl chloride, arsenic, ammonia, hydrogen cyanide, ~ 3,400 deaths/year contributed to second-hand smoke…