Chapter 22
The Respiratory System
Respiration

- Pulmonary ventilation (breathing): movement of air into and out of the lungs
- External respiration: $O_2$ and $CO_2$ exchange between the lungs and the blood
- Transport: $O_2$ and $CO_2$ in the blood
- Internal respiration: $O_2$ and $CO_2$ exchange between systemic blood vessels and tissues
Mechanics of Breathing

• Pulmonary ventilation consists of two phases
  1. Inspiration: gases flow into the lungs
  2. Expiration: gases exit the lungs
Pressure Relationships in the Thoracic Cavity

• Atmospheric pressure ($P_{atm}$)
  • Pressure exerted by air surrounding body
  • 760 mm Hg at sea level = 1 atmosphere

• Respiratory pressures described relative to $P_{atm}$
  • Negative respiratory pressure-less than $P_{atm}$
  • Positive respiratory pressure-greater than $P_{atm}$
  • Zero respiratory pressure = $P_{atm}$
Intrapulmonary Pressure

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

- Intrapleural pressure ($P_{ip}$):
  - Pressure in the pleural cavity
  - Fluctuates with breathing
  - Always a negative pressure ($<P_{atm}$ and $<P_{pul}$)
Intrapleural Pressure

- Negative $P_{ip}$ 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
Figure 22.12 Intrapulmonary and intrapleural pressure relationships.

Atmospheric pressure ($P_{\text{atm}}$)
0 mm Hg (760 mm Hg)

Thoracic wall

Parietal pleura

Visceral pleura

Transpulmonary pressure
4 mm Hg
(the difference between 0 mm Hg and −4 mm Hg)

Intrapleural pressure ($P_{\text{ip}}$)
−4 mm Hg
(756 mm Hg)

Intrapulmonary pressure ($P_{\text{pul}}$)
0 mm Hg
(760 mm Hg)
Pulmonary Ventilation

• Inspiration and expiration

• Mechanical processes that depend on volume changes in the thoracic cavity
  • Volume changes → pressure changes
  • Pressure changes → gases flow to equalize pressure
Boyle’s Law

• The relationship between the pressure and volume of a gas

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

\[
P_1 V_1 = P_2 V_2
\]

• \(P\) = pressure of a gas in mm Hg

• \(V\) = volume of a gas in cubic millimeters

• Subscripts 1 and 2 represent the initial and resulting conditions, respectively
<table>
<thead>
<tr>
<th>Inspiration</th>
<th>Sequence of events</th>
<th>Changes in anterior-posterior and superior-inferior dimensions</th>
<th>Changes in lateral dimensions (superior view)</th>
</tr>
</thead>
<tbody>
<tr>
<td>① Inspiratory muscles contract (diaphragm descends; rib cage rises).</td>
<td></td>
<td></td>
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<tr>
<td>② Thoracic cavity volume increases.</td>
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<tr>
<td>③ Lungs are stretched; intrapulmonary volume increases.</td>
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<tr>
<td>④ Intrapulmonary pressure drops (to −1 mm Hg).</td>
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<tr>
<td>⑤ Air (gases) flows into lungs down its pressure gradient until intrapulmonary pressure is 0 (equal to atmospheric pressure).</td>
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</tbody>
</table>

- Ribs are elevated and sternum flares as external intercostals contract.
- Diaphragm moves inferiorly during contraction.
- External intercostals contract.
Factors That Diminish Lung Compliance

- Scar tissue or fibrosis that reduces the natural resilience of the lungs
- Blockage of the smaller respiratory passages with mucus or fluid
- Reduced production of surfactant
- Decreased flexibility of the thoracic cage or its decreased ability to expand
Figure 22.13 Changes in thoracic volume and sequence of events during inspiration and expiration. (2 of 2)

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</tr>
</thead>
<tbody>
<tr>
<td>① Inspiratory muscles relax (diaphragm rises; rib cage descends due to recoil of costal cartilages).</td>
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<tr>
<td>② Thoracic cavity volume decreases.</td>
<td></td>
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<tr>
<td>③ Elastic lungs recoil passively; intrapulmonary Volume decreases.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>④ Intrapulmonary pressure rises (to +1 mm Hg).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>⑤ Air (gases) flows out of lungs down its pressure gradient until intrapulmonary pressure is 0.</td>
<td></td>
<td></td>
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</tbody>
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- Diaphragm moves superiorly as it relaxes.
- Ribs and sternum are depressed as external intercostals relax.
- External intercostals relax.
**Intrapulmonary pressure.**
Pressure inside lung decreases as lung volume increases during inspiration; pressure increases during expiration.

**Intrapleural pressure.**
Pleural cavity pressure becomes more negative as chest wall expands during inspiration. Returns to initial value as chest wall recoils.

**Volume of breath.** During each breath, the pressure gradients move 0.5 liter of air into and out of the lungs.
Clinical Applications

• Atelectasis – lung collapse – air entering plural cavity
• Pneumothorax
• Tension pneumothorax
• Hemothorax
• IRDS – Idiopathic Respiratory Distress Syndrome
Gas Exchanges Between Blood, Lungs, and Tissues

- External respiration
- Internal respiration

To understand the above processes, first consider

- Physical properties of gases
- Composition of alveolar gas
Basic Properties of Gases: Dalton's Law of Partial Pressures

• Total pressure exerted by mixture of gases = sum of pressures exerted by each gas

• Partial pressure
  • Pressure exerted by each gas in mixture
  • Directly proportional to its percentage in mixture
| GAS | ATMOSPHERE (SEA LEVEL) | | | ALVEOLI | | |
|-----|-----------------------|------------------|------------------|------------------|------------------|
|     | APPROXIMATE PERCENTAGE | PARTIAL PRESSURE (mm Hg) | APPROXIMATE PERCENTAGE | PARTIAL PRESSURE (mm Hg) |
| N₂  | 78.6                  | 597              | 74.9              | 569              |
| O₂  | 20.9                  | 159              | 13.7              | 104              |
| CO₂ | 0.04                  | 0.3              | 5.2               | 40               |
| H₂O | 0.46                  | 3.7              | 6.2               | 47               |
|     | 100.0%                | 760              | 100.0%            | 760              |
Basic Properties of Gases: Henry's Law

• Gas mixtures in contact with liquid
  • Each gas dissolves in proportion to its partial pressure
  • At equilibrium, partial pressures in two phases will be equal
  • Amount of each gas that will dissolve depends on
    • Solubility—CO₂ 20 times more soluble in water than O₂; little N₂ dissolves in water
    • Temperature—as temperature rises, solubility decreases
External Respiration

- Exchange of $O_2$ and $CO_2$ across the respiratory membrane

- Influenced by
  - Partial pressure gradients and gas solubilities
  - Ventilation-perfusion coupling
  - Structural characteristics of the respiratory membrane
Figure 22.18 Oxygenation of blood in the pulmonary capillaries at rest.

The graph shows the increase in oxygen partial pressure ($P_{O_2}$) over time in the pulmonary capillaries. At the start of the capillary, $P_{O_2}$ is 0 mm Hg. As the blood flows through the capillary, $P_{O_2}$ increases and reaches a plateau at approximately 104 mm Hg near the end of the capillary. The $P_{O_2}$ value of 104 mm Hg is indicated on the graph.
Ventilation-Perfusion Coupling

- **Perfusion**- blood flow reaching alveoli
- **Ventilation**- amount of gas reaching alveoli
- Ventilation and perfusion matched (coupled) for efficient gas exchange
  - Never balanced for all alveoli due to
    - Regional variations due to effect of gravity on blood and air flow
    - Some alveolar ducts plugged with mucus
Figure 22.19  Ventilation-perfusion coupling.

(a) Ventilation less than perfusion

Mismatch of ventilation and perfusion
↓ ventilation and/or ↑ perfusion of alveoli
causes local ↑ P CO₂ and ↓ P O₂

O₂ autoregulates arteriolar diameter

Pulmonary arterioles serving these alveoli constricts

Match of ventilation and perfusion
↓ ventilation, ↑ perfusion

(b) Ventilation greater than perfusion

Mismatch of ventilation and perfusion
↑ ventilation and/or ↓ perfusion of alveoli
causes local ↓ P CO₂ and ↑ P O₂

O₂ autoregulates arteriolar diameter

Pulmonary arterioles serving these alveoli dilate

Match of ventilation and perfusion
↑ ventilation, ↓ perfusion
Internal Respiration

• Capillary gas exchange in body tissues
• Partial pressures and diffusion gradients reversed compared to external respiration
  • Tissue $\text{Po}_2$ always lower than in systemic arterial blood $\rightarrow$ oxygen from blood to tissues
  • $\text{CO}_2$ $\rightarrow$ from tissues to blood
  • Venous blood $\text{Po}_2$ 40 mm Hg and $\text{Pco}_2$ 45 mm Hg
Figure 22.17 Partial pressure gradients promoting gas movements in the body.

Inspired air:
- $P_{O_2} = 160$ mm Hg
- $P_{CO_2} = 0.3$ mm Hg

Alveoli of lungs:
- $P_{O_2} = 104$ mm Hg
- $P_{CO_2} = 40$ mm Hg

Blood leaving tissues and entering lungs:
- $P_{O_2} = 40$ mm Hg
- $P_{CO_2} = 45$ mm Hg

Blood leaving lungs and entering tissue capillaries:
- $P_{O_2} = 100$ mm Hg
- $P_{CO_2} = 40$ mm Hg

Tissues:
- $P_{O_2}$ less than 40 mm Hg
- $P_{CO_2}$ greater than 45 mm Hg
O$_2$ Transport

• Molecular O$_2$ is carried in the blood
  • 1.5% dissolved in plasma
  • 98.5% loosely bound to each Fe of hemoglobin (Hb) in RBCs
• 4 O$_2$ per Hb
O₂ and Hemoglobin

• Oxyhemoglobin (HbO₂): hemoglobin-O₂ combination

• Reduced hemoglobin (HHb): hemoglobin that has released O₂

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

Lungs

Tissues
O₂ and Hemoglobin

- Loading and unloading of O₂ is facilitated by change in shape of Hb
  - As O₂ binds, Hb affinity for O₂ increases
  - As O₂ is released, Hb affinity for O₂ decreases
- Fully (100%) saturated if all four heme groups carry O₂
- Partially saturated when one to three hemes carry O₂
Carbon Monoxide Poisoning

- CO competes with O2
- Hemoglobin has higher affinity for CO
- Treatment – 100% O2

Cyanosis

- Skin has bluish color due to increased concentration of deoxyhemoglobin (HHb)
CO₂ Transport

• CO₂ is transported in the blood in three forms
  • 7 to 10% dissolved in plasma
  • 20% bound to globin of hemoglobin (carbaminohemoglobin)
  • 70% transported as bicarbonate ions (HCO₃⁻) in plasma
Transport and Exchange of CO$_2$

- CO$_2$ combines with water to form carbonic acid (H$_2$CO$_3$), which quickly dissociates

\[
\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \\
\text{carbon dioxide} \quad \text{water} \quad \text{carbonic acid} \quad \text{hydrogen ion} \quad \text{bicarbonate ion}
\]

- Occurs primarily in RBCs, where carbonic anhydrase reversibly and rapidly catalyzes reaction
Transport and Exchange of CO$_2$

• In systemic capillaries
  • HCO$_3^-$ quickly diffuses from RBCs into the plasma
  • The chloride shift occurs: outrush of HCO$_3^-$ from the RBCs is balanced as Cl$^-$ moves in from the plasma
Figure 22.22a Transport and exchange of $\text{CO}_2$ and $\text{O}_2$.

(a) Oxygen release and carbon dioxide pickup at the tissues
Transport and Exchange of CO$_2$

• In pulmonary capillaries
  • HCO$_3^-$ moves into the RBCs and binds with H$^+$ to form H$_2$CO$_3$
  • H$_2$CO$_3$ is split by carbonic anhydrase into CO$_2$ and water
  • CO$_2$ diffuses into the alveoli
(b) Oxygen pickup and carbon dioxide release in the lungs
Haldane Effect

• The lower the Po$_2$ and hemoglobin saturation with O$_2$, the more CO$_2$ can be carried in the blood

• At the tissues, as more carbon dioxide enters the blood
  • More oxygen dissociates from hemoglobin (Bohr effect)
  • As HbO$_2$ releases O$_2$, it more readily forms bonds with CO$_2$ to form carbaminohemoglobin
Influence of CO₂ on Blood pH

- HCO₃⁻ in plasma is the alkaline reserve of the carbonic acid–bicarbonate buffer system
- If H⁺ concentration in blood rises, excess H⁺ is removed by combining with HCO₃⁻
- If H⁺ concentration begins to drop, H₂CO₃ dissociates, releasing H⁺
Influence of CO$_2$ on Blood pH

- Changes in respiratory rate can also alter blood pH
  - For example, slow shallow breathing allows CO$_2$ to accumulate in the blood, causing pH to drop
- Changes in ventilation can be used to adjust pH when it is disturbed by metabolic factors
Control of Respiration - Medullary Respiratory Centers

1. Dorsal respiratory group (DRG)
   - Integrates input from peripheral stretch and chemoreceptors

2. Ventral respiratory group (VRG)
   - Rhythm-generating and integrative center
   - Sets eupnea (12–15 breaths/minute)
   - Inspiratory neurons excite the inspiratory muscles via the phrenic and intercostal nerves
   - Expiratory neurons inhibit the inspiratory neurons
Figure 22.23 Locations of respiratory centers and their postulated connections.

**Pontine respiratory centers** interact with medullary respiratory centers to smooth the respiratory pattern.

**Ventral respiratory group (VRG)** contains rhythm generators whose output drives respiration.

**Dorsal respiratory group (DRG)** integrates peripheral sensory input and modifies the rhythms generated by the VRG.
Depth and Rate of Breathing

• Depth is determined by how actively the respiratory center stimulates the respiratory muscles

• Rate is determined by how long the inspiratory center is active

• Both are modified in response to changing body demands
Hyperventilation - Compensatory

- Hyperventilation – increased depth and rate of breathing that:
  - Quickly flushes carbon dioxide from the blood
  - Occurs in response to hypercapnia (high CO$_2$)
- Though a rise CO$_2$ acts as the original stimulus, control of breathing at rest is regulated by the hydrogen ion concentration in the brain
- Exercise
- Drugs affecting CNS
Hyperventilation – Non-compensatory

- Rapid or extra deep breathing leads to hypocapnia -(low CO$_2$)
- Can lead to alkalosis with cramps and spasms
- Causes – acute anxiety or emotional tension
- CO$_2$ is vasodilator – low P$_{CO2}$ results in LOCAL vasoconstrictions = ischemia/hypoxia
- How do you fix it?
Hypoventilation – Non-compensatory

• Hypoventilation – slow and shallow breathing due to abnormally low $P_{CO_2}$ levels (initially)
  - Apnea (breathing cessation) may occur until $P_{CO_2}$ levels rise
• Leads to too much $CO_2$ which leads to drop in pH = acidosis
Summary of Chemical Factors

- Rising CO$_2$ levels are the most powerful respiratory stimulant.

- Normally blood Po$_2$ affects breathing only indirectly by influencing peripheral chemoreceptor sensitivity to changes in Pco$_2$.

- When arterial Po$_2$ falls below 60 mm Hg, it becomes the major stimulus for respiration (via the peripheral chemoreceptors).

- Changes in arterial pH resulting from CO$_2$ retention or metabolic factors act indirectly through the peripheral chemoreceptors.
Influence of Higher Brain Centers

- Hypothalamic controls act through the limbic system to modify rate and depth of respiration
  - Example: breath holding that occurs in anger or gasping with pain
- A rise in body temperature acts to increase respiratory rate
- Cortical controls are direct signals from the cerebral motor cortex that bypass medullary controls
  - Example: voluntary breath holding
Figure 22.24 Neural and chemical influences on brain stem respiratory centers.

Central chemoreceptors

Peripheral chemoreceptors

Higher brain centers (cerebral cortex—voluntary control over breathing)

Other receptors (e.g., pain) and emotional stimuli acting through the hypothalamus

Respiratory centers (medulla and pons)

Stretch receptors in lungs

Irritant receptors

Receptors in muscles and joints

\[ \downarrow O_2, \uparrow CO_2, \uparrow H^+ \]

\[ \uparrow CO_2, \uparrow H^+ \]
Respiratory Diseases

OYO

• Asthma
• Lung Cancer
• Effects of Cigarette Smoke on Cilia
• COPD
• Tuberculosis
What if ????

• Alveolar $P_{O_2}$ is 100, alveolar $P_{CO_2}$ is 38 and alveolar $P_{CO}$ is 1

• A child eats 20 aspirin tablets (aspirin is acetylsalicylic acid…. How will respiratory rate be affected?

• A few hours after surgery I am experiencing lots of pain, so I take a dose of my narcotic pain killer… 5 minutes later it still hurts so I take another ….How will RR be affected?