Respiratory System

- Consists of the respiratory and conducting zones

- Respiratory zone:
  - Site of gas exchange
  - Consists of bronchioles, alveolar ducts, and alveoli
Respiratory System

- Conducting zone:
  - Conduits for air to reach the sites of gas exchange
  - Includes all other respiratory structures (e.g., nose, nasal cavity, pharynx, trachea)
- Respiratory muscles – diaphragm and other muscles that promote ventilation
Major Functions of the Respiratory System

- Major function is to supply the body with oxygen and dispose of carbon dioxide

- Respiration – four distinct processes must happen
  - Pulmonary ventilation – moving air into and out of the lungs
  - External respiration – gas exchange between the lungs and the blood
  - Transport – transport of oxygen and carbon dioxide between the lungs and tissues
  - Internal respiration – gas exchange between systemic blood vessels and tissues
Framework of the Larynx

Figure 22.4a, b

- Body of hyoid bone
- Thyroid cartilage
- Laryngeal prominence (Adam’s apple)
- Cricothyroid ligament
- Cricotracheal ligament
- Epiglottis
- Thyrohyoid membrane
- Cuneiform cartilage
- Corniculate cartilage
- Arytenoid cartilage
- Arytenoid muscles
- Cricoid cartilage
- Tracheal cartilages
- Body of hyoid bone
- Thyrohyoid membrane
- Fatty pad
- Vestibular fold (false vocal cord)
- Thyroid cartilage
- Vocal fold (true vocal cord)
- Cricothyroid ligament
- Cricotracheal ligament
Vocal Ligaments

- Attach the arytenoid cartilages to the thyroid cartilage
- Composed of elastic fibers that form mucosal folds called true vocal cords
  - The medial opening between them is the glottis
  - They vibrate to produce sound as air rushes up from the lungs
- False vocal cords (vestibular folds)
  - Mucosal folds superior to the true vocal cords
  - Have no part in sound production
  - Help close the glottis when swallowing
Vocal Production

- Speech – intermittent release of expired air while opening and closing the glottis
- Pitch – determined by the length and tension of the vocal cords
  - Wide glottis: deep tones
  - Narrow glottis: high pitched tones
- Loudness – depends upon the force at which the air rushes across the vocal cords
  - Vocal cords do not move when we whisper
- The pharynx resonates, amplifies, and enhances sound quality
- Sound is “shaped” into language by action of the pharynx, tongue, soft palate, and lips
Movements of Vocal Cords

Figure 22.5

(a) Base of tongue

(b) Epiglottis

False vocal cord

True vocal cord

Glottis

Inner lining of trachea

Corniculate cartilage
Sphincter Functions of the Larynx

- The larynx is closed during Valsalva’s maneuver

- Valsalva’s maneuver
  - Air is temporarily held in the lower respiratory tract by closing the glottis
  - Causes intra-abdominal pressure to rise when abdominal muscles contract
  - Helps to empty the rectum
  - Stabilizes the trunk when lifting heavy loads
Respiratory Membrane

Figure 22.9b
Respiratory Membrane

Figure 22.9c, d
Breathing

- Breathing, or pulmonary ventilation, consists of two phases
  - Inspiration – air flows into the lungs
  - Expiration – gases exit the lungs
Pressure Relationships in the Thoracic Cavity

- Respiratory pressure is always described relative to atmospheric pressure

- Atmospheric pressure \( (P_{\text{atm}}) \)
  - Pressure exerted by the air surrounding the body
    - Negative respiratory pressure is less than \( P_{\text{atm}} \)
    - Positive respiratory pressure is greater than \( P_{\text{atm}} \)
Pressure Relationships in the Thoracic Cavity

- Intrapulmonary pressure ($P_{\text{pul}}$) – pressure within the alveoli
- Intrapleural pressure ($P_{\text{ip}}$) – pressure within the pleural cavity
Pressure Relationships

- Intrapulmonary pressure and intrapleural pressure fluctuate with the phases of breathing.
- Intrapulmonary pressure always eventually equalizes itself with atmospheric pressure.
- Intrapleural pressure is always less than intrapulmonary pressure and atmospheric pressure.
Pressure Relationships

- Two forces act to pull the lungs away from the thoracic wall, promoting lung collapse
  - Elasticity of lungs causes them to assume smallest possible size
  - Surface tension of alveolar fluid draws alveoli to their smallest possible size
- Opposing forces
  - Elasticity of the chest wall pulls the thorax outward to enlarge the lungs
  - Strong adhesion force between parietal and visceral pleura
Pressure Relationships

Figure 22.12

Atmospheric pressure

Parietal pleura

Visceral pleura

Pleural cavity

Transpulmonary pressure
760 mm Hg
−756 mm Hg
= 4 mm Hg

Intrapleural pressure
756 mm Hg
(−4 mm Hg)

Intrapulmonary pressure
760 mm Hg
(0 mm Hg)
Pulmonary Ventilation

- A mechanical process that depends on volume changes in the thoracic cavity

- Volume changes lead to pressure changes, which lead to the flow of gases to equalize pressure
Inspiration

- The diaphragm and external intercostal muscles (inspiratory muscles) contract and the rib cage rises

- The lungs are stretched and intrapulmonary volume increases

- Intrapulmonary pressure drops below atmospheric pressure (−1 mm Hg)

- Air flows into the lungs, down its pressure gradient, until intrapleural pressure = atmospheric pressure
Inspiration

Box of air model: if we increase the size of the box, more air rushes in.

<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</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>① Inspiratory muscles contract (diaphragm descends; rib cage rises)</td>
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<td></td>
<td>② Thoracic cavity volume increases</td>
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<td></td>
<td>③ Lungs stretched; intrapulmonary volume increases</td>
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<tr>
<td></td>
<td>④ Intrapulmonary pressure drops (to −1 mm Hg)</td>
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<td></td>
<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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<td>Inspiration</td>
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</tbody>
</table>
Deep (forced) Inspiration

- As in exercise

- Accessory muscles like the scalenes, sternocleidomastoid, and pectoralis minor contract and raise the ribs more
Expiration

- Inspiratory muscles relax and the rib cage descends due to gravity
- Thoracic cavity volume decreases
- Elastic lungs recoil passively and intrapulmonary volume decreases
- Intrapulmonary pressure is greater than atmospheric pressure (+1 mm Hg)
- Gases flow out of the lungs down the pressure gradient until intrapulmonary pressure is 0
## Expiration

<table>
<thead>
<tr>
<th>Sequence of events</th>
<th>Changes in anterior-posterior and superior-inferior dimensions</th>
<th>Changes in lateral dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>① Inspiratory muscles relax (diaphragm rises; rib cage descends due to recoil of costal cartilages)</td>
<td>Ribs and sternum depressed as external intercostals relax</td>
<td>External intercostals relax</td>
</tr>
<tr>
<td>② Thoracic cavity volume decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>③ Elastic lungs recoil passively; intrapulmonary volume decreases</td>
<td>Diaphragm moves superiorly as it relaxes</td>
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</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>
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</tbody>
</table>
Deep (forced) Expiration

- Involves the contraction of the abdominal wall muscles (e.g. oblique and transverse muscles)
- These muscles increase intra-abdominal pressure and the abdominal organs move superiorly against the diaphragm
- Transverse abdominus lowers the ribcage
Basic Properties of Gases: Dalton’s Law of Partial Pressures

- Total pressure exerted by a mixture of gases is the sum of the pressures exerted independently by each gas in the mixture

- The partial pressure of each gas is directly proportional to its percentage in the mixture
Basic Properties of Gases: Henry’s Law

- When a mixture of gases is in contact with a liquid, each gas will dissolve in the liquid in proportion to its partial pressure.

- The amount of gas that will dissolve in a liquid also depends upon its solubility:
  - Carbon dioxide is the most soluble
  - Oxygen is 1/20th as soluble as carbon dioxide
  - Nitrogen is practically insoluble in plasma

- Thus, more CO2 than O2 dissolves in a liquid and virtually no N2 goes into solution.
Composition of Alveolar Gas

- The atmosphere is mostly oxygen and nitrogen, while alveoli contain more carbon dioxide and water vapor.

- These differences result from:
  - Gas exchanges in the lungs – oxygen diffuses from the alveoli and carbon dioxide diffuses into the alveoli.
  - Humidification of air by conducting passages.
  - The mixing of alveolar gas that occurs with each breath.
  - Thus, high AVR (alveolar ventilation rate) brings in more O2 increasing P\text{O}_2 and rapidly eliminates CO2 from the lungs.
External Respiration: Pulmonary Gas Exchange

- Factors influencing the movement of oxygen and carbon dioxide across the respiratory membrane:
  - Partial pressure gradients and gas solubilities
  - Matching of alveolar ventilation and pulmonary blood perfusion
  - Structural characteristics of the respiratory membrane
Partial Pressure Gradients and Gas Solubilities

- The partial pressure oxygen (PO$_2$) of venous blood is 40 mm Hg; the partial pressure in the alveoli is 104 mm Hg
  - This steep gradient allows oxygen partial pressures to rapidly reach equilibrium (in 0.25 seconds)
  - Blood can move three times as quickly (0.75 seconds) through the pulmonary capillary and still be adequately oxygenated (e.g. resting heart @ 60 beats/min)
Partial Pressure Gradients and Gas Solubilities

- The partial pressure carbon dioxide (PCO$_2$) of venous blood is 45 mm Hg; the partial pressure in the alveoli is 40 mm Hg

- CO$_2$ travels down the gradient into the alveoli

- Although carbon dioxide has a lower partial pressure gradient:
  - It is 20 times more soluble in plasma than oxygen
  - It diffuses in equal amounts with oxygen
Figure 22.17

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

Expired air:
- $P_{O_2}$ 120 mm Hg
- $P_{CO_2}$ 27 mm Hg

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

External respiration

Blood entering alveolar capillaries:
- $P_{O_2}$ 40 mm Hg
- $P_{CO_2}$ 45 mm Hg

Blood leaving alveolar capillaries:
- $P_{O_2}$ 104 mm Hg
- $P_{CO_2}$ 40 mm Hg

Pulmonary veins ($P_{O_2}$ 100 mm Hg)

Pulmonary arteries

Systemic veins

Blood leaving tissue capillaries:
- $P_{O_2}$ 40 mm Hg
- $P_{CO_2}$ 45 mm Hg

Blood 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
Ventilation-Perfusion Coupling

- **Ventilation**: the amount of gas reaching the alveoli
- **Perfusion**: the blood flow reaching the alveoli

Local autoregulatory mechanisms respond to alveoli conditions.
Ventilation-Perfusion Coupling

- Changes in $P_{CO_2}$ in the alveoli cause changes in the diameters of the bronchioles
  - Passageways servicing areas where alveolar carbon dioxide is high dilate allowing CO2 to be eliminated rapidly
  - Those serving areas where alveolar carbon dioxide is low constrict
Internal Respiration: Capillary Gas Exchange in Body Tissues

- The factors promoting gas exchange between systemic capillaries and tissue cells are the same as those acting in the lungs.

- The partial pressures and diffusion gradients are reversed:
  - $P_{O_2}$ in tissue is always lower than in systemic arterial blood (40 vs. 100 mm Hg).

- Thus, $O_2$ moves rapidly from blood to tissues until equilibrium is met ($CO_2$ is the reverse).
Oxygen Transport

- Molecular oxygen is carried in the blood:
  - Bound to hemoglobin (Hb) w/i RBCs (98.5%)
  - Dissolved in plasma (1.5%)
Oxygen Transport: Role of Hemoglobin

- Each Hb molecule binds four oxygen atoms in a rapid and reversible process.
- The hemoglobin-oxygen combination is called oxyhemoglobin (HbO$_2$).
- Hemoglobin that has released oxygen is called reduced hemoglobin or deoxyhemoglobin (HHb).

\[
\text{Lungs: } \text{HHb} + \text{O}_2 \rightleftharpoons \text{HbO}_2 + \text{H}^+ \\
\text{Tissues: }
\]
Hemoglobin (Hb)

- Saturated hemoglobin – when all four hemes of the molecule are bound to oxygen

- Partially saturated hemoglobin – when one to three hemes are bound to oxygen
  - 1st O2 binds resulting in a conformational change in Hb allowing 2 more O2 to bind which results in yet another conformational change in Hb allowing 4th O2 to bind (fully saturated)
  - Unloading of O2 works the same way via affinity binding with the last bound O2 being the first released and so on
Hemoglobin (Hb)

- The rate that hemoglobin binds and releases oxygen is regulated by:
  - $P_{O_2}$, temperature, blood pH, $P_{CO_2}$, and the concentration of BPG (an organic chemical)
  - These factors ensure adequate delivery of oxygen to tissue cells
- BPG: In bonding to partially deoxygenated hemoglobin BPG allosterically upregulates the release of the remaining oxygen molecules bound to the hemoglobin, thus enhancing the ability of RBCs to release oxygen near tissues that need it most.
Influence of $P_{O_2}$ on Hemoglobin Saturation

- Hemoglobin saturation plotted against $P_{O_2}$ produces an oxygen-hemoglobin dissociation curve.

- 98% saturated arterial blood contains 20 ml oxygen per 100 ml blood (20 vol%).

- As arterial blood flows through capillaries, 5 ml oxygen are released.
  - 75-80% remains bound as the venous reserve that can be unloaded during vigorous exercise.
Hemoglobin Saturation Curve

- Only 20–25% of bound oxygen is unloaded during one systemic circulation

- If oxygen levels in tissues drop:
  - More oxygen dissociates from hemoglobin and is used by cells
  - Respiratory rate or cardiac output need not increase
Other Factors Influencing Hemoglobin Saturation

- Temperature, H⁺, PCO₂, and BPG (2,3-bisphosphoglycerate)
  - Modify the structure of hemoglobin and alter its affinity for oxygen
  - Increases of these factors:
    - Decrease hemoglobin’s affinity for oxygen
    - Enhance oxygen unloading from the blood
  - Decreases act in the opposite manner
- These parameters are all high in systemic capillaries where oxygen unloading is the goal
Carbon monoxide

- CO competes with O2 for heme sites
- CO has 200x greater affinity than O2 for heme sites
- The result is hypoxia: inadequate O2 delivery to tissues
Carbon Dioxide Transport

- Carbon dioxide is transported in the blood in three forms
  - Dissolved in plasma – 7 to 10%
  - Chemically bound to hemoglobin – 20% is carried in RBCs as carbaminohemoglobin
  - Bicarbonate ion in plasma – 70% is transported as bicarbonate (HCO$_3^-$)
Transport and Exchange of Carbon Dioxide

- Carbon dioxide diffuses into RBCs and combines with water to form carbonic acid ($H_2CO_3$), which quickly dissociates into hydrogen ions and bicarbonate ions.

<table>
<thead>
<tr>
<th>CO$_2$</th>
<th>+</th>
<th>H$_2$O</th>
<th>$\leftrightarrow$</th>
<th>H$_2$CO$_3$</th>
<th>$\leftrightarrow$</th>
<th>H$^+$</th>
<th>+</th>
<th>HCO$_3^-$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon dioxide</td>
<td>Water</td>
<td>Carbonic acid</td>
<td>Hydrogen ion</td>
<td>Bicarbonate ion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- In RBCs, **carbonic anhydrase** reversibly catalyzes the conversion of carbon dioxide and water to carbonic acid.
Transport and Exchange of Carbon Dioxide

(a) Oxygen release and carbon dioxide pickup at the tissues

- CO₂ (dissolved in plasma) → CO₂ + H₂O → H₂CO₃ → HCO₃⁻ + H⁺ (dissolved in plasma)
- CO₂ + Hb = HbCO₂ (Carbamino-hemoglobin)
- HbO₂ → O₂ + Hb
- CO₂ + H₂O → H₂CO₃ → HCO₃⁻ + H⁺ (dissolved in plasma)
- Binds to plasma proteins
- Chloride shift

Figure 22.22a
Transport and Exchange of Carbon Dioxide

- At the tissues:
  - Bicarbonate quickly diffuses from RBCs into the plasma
  - The chloride shift – to counterbalance the outrush of negative bicarbonate ions from the RBCs, chloride ions (Cl\(^-\)) move from the plasma into the RBCs
Transport and Exchange of Carbon Dioxide

- At the lungs, these processes are reversed
  - Bicarbonate ions move into the RBCs and bind with hydrogen ions to form carbonic acid
  - Carbonic acid is then split by carbonic anhydrase to release carbon dioxide and water
  - Carbon dioxide then diffuses from the blood into the alveoli
Transport and Exchange of Carbon Dioxide

(b) Oxygen pickup and carbon dioxide release in the lungs
Haldane Effect

- The amount of carbon dioxide transported is markedly affected by the $P_{O_2}$

- Haldane effect – the lower the $P_{O_2}$ and hemoglobin saturation with oxygen, the more carbon dioxide can be carried in the blood
Haldane Effect

- At the tissues, as more carbon dioxide enters the blood:
  - More oxygen dissociates from hemoglobin (Bohr effect)
  - More carbon dioxide combines with hemoglobin, and more bicarbonate ions are formed
- This situation is reversed in pulmonary circulation
Influence of Carbon Dioxide on Blood pH

- The carbonic acid–bicarbonate buffer system resists blood pH changes.

- If hydrogen ion concentrations in blood begin to rise, excess $\text{H}^+$ is removed by combining with $\text{HCO}_3^-$.

- If hydrogen ion concentrations begin to drop, carbonic acid dissociates, releasing $\text{H}^+$.
Influence of Carbon Dioxide on Blood pH

- Changes in respiratory rate can also:
  - Alter blood pH
  - Provide a fast-acting system to adjust pH when it is disturbed by metabolic factors
    - E.g. slow shallow breathing leads to increased CO2 levels which leads to increased H2CO3 which leads to a decrease in pH
    - E.g. rapid deep breathing leads to decreased CO2 levels which leads to decreased H2CO3 which leads to an increase in pH
Control of Respiration: Medullary Respiratory Centers

- Two areas of medulla oblongata are important in respiration:
  - dorsal respiratory group (DRG)
  - ventral respiratory group (VRG)

VRG is the rhythm-generating integrative center:
- Contains neurons that fire during inspiration and a different neural group that fire during expiration.
Control of Respiration: Medullary Respiratory Centers

- Inspiration: VRG neural impulse travels down the phrenic & intercostal nerves exciting the diaphragm & intercostal muscles, respectively
  - The thorax expands and air rushes in

- Expiration: when the VRG expiratory neurons fire, the inspiratory neurons stop firing and passive expiration occurs

- Mutual inhibition of the two neural areas

- Function of DRG: integrates input from peripheral stretch and chemoreceptors and communicates this information to the VRG
Depth and Rate of Breathing

- Chemical factors: CO2, O2, H+ sensed by chemoreceptors found in the ventrolateral medulla (central receptors) and aortic arch and carotid arteries (peripheral receptors)
Medullary Respiratory Centers

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)

Peripheral chemoreceptors
$O_2 \downarrow$, $CO_2 \uparrow$, $H^+ \uparrow$

Central chemoreceptors
$CO_2 \uparrow$, $H^+ \uparrow$

Receptors in muscles and joints

Stretch receptors in lungs

Irritant receptors
**Depth and Rate of Breathing: \( P_{CO_2} \)**

- CO2 is the most potent chemical influence and most controlled

- Changing PCO2 levels are monitored by chemoreceptors of the brain stem

- As PCO2 levels rise (hypercapnia), cerebrospinal fluid pH drops (CSF lacks pH buffering system) exciting the central chemoreceptors: depth & rate of breathing increase

- As PCO2 levels fall, respiration is inhibited and apnea (breathing cessation) may occur until PCO2 rises and stimulates respiration
Figure 22.26

Increased arterial PCO₂

Increased PCO₂ decreases pH in cerebrospinal fluid (CSF)

Central chemoreceptors in medulla respond to H⁺ in CSF (mediate 70% of the CO₂ response)

Peripheral chemoreceptors (carotid and aortic bodies) (mediate 30% of the CO₂ response)

Afferent impulses

Medullary respiratory centers

Efferent impulses

Respiratory muscles

Increased ventilation (more CO₂ exhaled)

Arterial PCO₂ and pH return to normal

Key:
- Initial stimulus
- Physiological response
- Result
Depth and Rate of Breathing: $P_{CO_2}$

- Hyperventilation – increased depth and rate of breathing that:
  - Quickly flushes carbon dioxide from the blood
  - Occurs in response to hypercapnia
- Though a rise in CO$_2$ acts as the original stimulus, control of breathing at rest is regulated by the hydrogen ion concentration in the brain
Depth and Rate of Breathing: $P_{CO_2}$

- Hypoventilation – slow and shallow breathing due to abnormally low $P_{CO_2}$ levels
  - Apnea (breathing cessation) may occur until $P_{CO_2}$ levels rise
Depth and Rate of Breathing: $P_{CO_2}$

- Arterial oxygen levels are monitored by the aortic and carotid bodies

- Substantial drops in arterial $P_{O_2}$ (to 60 mm Hg) are needed before oxygen levels become a major stimulus for increased ventilation

- If carbon dioxide is not removed (e.g., as in emphysema and chronic bronchitis), chemoreceptors become unresponsive to $P_{CO_2}$ chemical stimuli

- In such cases, $P_{O_2}$ levels become the principal respiratory stimulus (hypoxic drive)
Depth and Rate of Breathing: Arterial pH

- Changes in arterial pH can modify respiratory rate even if carbon dioxide and oxygen levels are normal.

- As pH falls, respiratory system controls attempt to compensate and increase pH by eliminating CO2 and carbonic acid from the blood by increasing respiration rate and depth.