Chapter 22
Respiration
Breathing

- all our body processes directly or indirectly require **ATP**
  - ATP synthesis **requires oxygen** and **produces carbon dioxide**
  - drives the need to **breathe** to take in oxygen, and eliminate carbon dioxide

- the **respiratory system** consists of a system of tubes that delivers air to the lung
  - oxygen diffuses into the **blood**, and carbon dioxide diffuses out

- **respiratory** and **cardiovascular systems** work together to deliver oxygen to the tissues and remove carbon dioxide
Fig. 24-1. Overview of respiratory physiology. This chapter is organized around the principle that respiratory function includes external respiration (ventilation and pulmonary gas exchange), transport of gases by blood, and internal respiration (systemic tissue gas exchange and cellular respiration). Cellular respiration is discussed separately (see Chapters 4 and 27). Regulatory mechanisms centered in the brainstem use feedback from blood gas sensors to regulate ventilation.
RESPIRATORY PHYSIOLOGY

• **External respiration**
  – Pulmonary ventilation (breathing)
  – Pulmonary gas exchange

• **Transport of gases by the blood**

• **Internal respiration**
  – Systemic tissue gas exchange
  – Cellular respiration
Functions of Respiratory System

- O₂ and CO₂ exchange between blood and air
- speech and other vocalizations
- affects pH of body fluids by eliminating CO₂
- affects blood pressure by synthesis of vasoconstrictor, angiotensin II
- Respiratory pump for lymph and venous blood
The respiratory system is divided into two structural divisions:

- **Upper respiratory tract**: organs are located outside the thorax and consist of the nose, nasopharynx, oropharynx, laryngopharynx, and larynx.

- **Lower respiratory tract**: organs are located within the thorax and consist of the trachea, the bronchial tree, and the lungs.

- **Accessory structures** include the oral cavity, ribcage, and diaphragm.
Fig. 23-1. **Structural plan of the respiratory system.** The inset shows the alveolar sacs where the interchange of oxygen and carbon dioxide takes place through the walls of the grapelike alveoli.
The Nose

- **functions** of the nose
  - warms, cleanses, and humidifies inhaled air
  - detects odors in the airstream
  - serves as a resonating chamber that amplifies the voice

- Openings form **nostrils** (nares).

- Nasal conchae increase surface area to promote the warming, cleansing and humidifying of air.
Pharynx

• **pharynx** (throat)
• **three regions of pharynx**
  – **nasopharynx**
    • above soft palate
    • receives auditory tubes and contains pharyngeal tonsil
  – **oropharynx**
    • space between soft palate and epiglottis
    • contains palatine tonsils
  – **laryngopharynx**
    • epiglottis to cricoid cartilage
    • esophagus begins at that point

• **nasopharynx** passes only air and is lined by **pseud stratified columnar epithelium**
• **oropharynx** and **laryngopharynx** pass air, food, and drink and are lined by **stratified squamous epithelium**
(b) Parasagittal section of left side of head and neck showing location of respiratory structures

Pharyngeal tonsil

NASOPHARYNX
Opening of auditory tube
Uvula
Palatine tonsil

OROPHARYNX
Epiglottis

LARYNGOPHARYNX
Esophagus

Trachea

Superior
Middle
Inferior

Nasal conchae

External naris
Oral cavity
Soft palate
Lingual tonsil
Hyoid bone

Ventricular fold (false vocal cord)
Vocal fold (true vocal cord)
Larynx
Thyroid cartilage
Cricoid cartilage

Regions of the pharynx

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Larynx

- **larynx** (voice box) – cartilaginous chamber
- **primary function** is to keep food and drink out of the airway
- **epiglottis** – flap of tissue that guards the superior opening of the larynx
Fig. 23-6. **Laryngeal cartilages.** Some softer tissues of the larynx and surrounding structures have been removed to make it possible to see the cartilages of the larynx. Note the position of the nearby thyroid gland. **A,** Anterior view. **B,** Posterior view.

Larynx

- **cartilages** that make up framework of larynx
  - *epiglottic cartilage* – spoon-shaped supportive plate in epiglottis
  - *thyroid cartilage* – largest, *(Adam’s apple)* shield-shaped
  - *cricoid cartilage* - connects larynx to trachea,
Walls of Larynx

- interior wall has **two folds** on each side that extend from thyroid cartilage in front to arytenoid cartilages in the back

  - superior **vestibular folds (false vocal cords)**
    - play no role in speech
    - close the larynx during swallowing

  - inferior **vocal cords**
    - produce sound when air passes between them
    - contain vocal ligaments

- **glottis** – the vocal cords and the opening between them

- **Rima glottidis** – opening between vocal cords
Action of Vocal Cords

• **intrinsic muscles** control the vocal cords
  
  – abduct or adduct vocal cords
  
  – air forced between adducted (closed) vocal cords vibrates them
  – producing **high pitched sound** when cords are taut
  
  – produce **lower-pitched sound** when cords are more abducted (open)
  
  – **loudness** – determined by the force of air passing between the vocal cords
  
  – vocal cords produce **crude sounds** that are formed into words by actions of pharynx, oral cavity, tongue, and lips
Thyroid cartilage
Cricoid cartilage
Vocal fold
Arytenoid cartilage
Posterior cricoarytenoid muscle

Superior view of cartilages and muscles

Tongue
Epiglottis
Glottis:
Vocal folds (true vocal cords)
Rima glottidis
Ventricular folds (false vocal cords)

View through a laryngoscope

(a) Movement of vocal folds apart (abduction)

Lateral cricoarytenoid muscle

(b) Movement of vocal folds together (adduction)
Trachea

• **trachea** (windpipe)
  – found anterior to esophagus

  – supported by 16 to 20 **C-shaped** rings of **hyaline cartilage**
  – reinforces the trachea and keeps it from collapsing when you inhale

  – opening in rings faces posteriorly towards esophagus

  – **muscle** spans opening in rings
    • gap in C allows room for the esophagus to expand as swallowed food passes by
Fig. 23-10. **Cross section of the trachea.** The inset at the top shows from where the section was cut. The scanning electron micrograph shows details of the mucous coat, the tip of a cartilage ring, and the adventitia that form the wall of the trachea (×300).
Lower Respiratory Tract

- right and left primary bronchi
  - carina – internal medial ridge in the lowermost tracheal cartilage
    - directs the airflow to the right and left
Lungs

- **lung** – conical organ with a broad, concave **base**, resting on the diaphragm, and a blunt peak called the **apex**
  - **hilum** – slit through which the lung receives the main bronchus, blood vessels, lymphatics and nerves
    - **right lung**
      - has **three lobes** – **superior, middle, and inferior** separated by **horizontal and oblique fissure**
    - **left lung**
      - has **two lobes** – **superior and inferior** separated by a single **oblique fissure**
Bronchial Tree

• bronchioles
  – lack cartilage
  – well developed layer of smooth muscle

  – terminal bronchioles
    • final branches of conducting division

  – respiratory bronchioles
    • have alveoli budding from their walls
    • divide into 2-10 alveolar ducts
    • end in alveolar sacs – grape-like clusters of alveoli arrayed around a central space called the atrium
Alveoli

• 150 million alveoli in each lung, providing about 70 m² of surface for gas exchange

• cells of the alveolus
  – squamous (type I) alveolar cells
    • thin, broad cells that allow for rapid gas diffusion between alveolus and bloodstream
  – great (type II) alveolar cells
    • secrete pulmonary surfactant

– alveolar macrophages (dust cells)
  • keep alveoli free from debris by phagocytizing dust particles
  • 100 million dust cells perish each day as they ride up the mucociliary escalator to be swallowed and digested with their load of debris
Respiratory Membrane

- each alveolus surrounded by a basket of blood capillaries supplied by the pulmonary artery

- respiratory membrane – the barrier between the alveolar air and blood

- respiratory membrane consists of:
  - squamous alveolar cells
  - endothelial (squamous)cells of blood capillary
  - their shared basement membrane
Alveolus

- Respiratory membrane
- Capillary endothelial cell
- Fluid with surfactant
- Squamous alveolar cell
- Lymphocyte
- Great alveolar cell
- Alveolar macrophage
- Oxygen ($O_2$)
- Carbon dioxide ($CO_2$)
- Air
- Blood
- Respiratory membrane:
  - Squamous alveolar cell
  - Shared basement membrane
  - Capillary endothelial cell

(c)
The Pleurae and Pleural Fluid

• **visceral pleura** – serous membrane that covers lungs

• **parietal pleura** – adheres to mediastinum, inner surface of the rib cage

• **pleural cavity** – potential space between pleurae
  – normally no room between the membranes, but contains a film of slippery **pleural fluid**

• **functions** of pleurae and pleural fluid
  – reduce friction
  – create pressure gradient
    • lower pressure than atmospheric pressure and assists lung inflation
Pulmonary Ventilation

- **breathing (pulmonary ventilation)** – consists of a repetitive cycle one cycle of **inspiration** (inhaling) and **expiration** (exhaling)

- **respiratory cycle** – one complete inspiration and expiration

- flow of air in and out of lung depends on a **pressure difference** between air pressure within lungs and outside body

- **breathing muscles** change lung volumes and create differences in pressure relative to the atmosphere
Respiratory Muscles

• **diaphragm**
  – prime mover of respiration
  – contraction flattens diaphragm and enlarging thoracic cavity and pulling air into lungs
  – relaxation allows diaphragm to bulge upward again, compressing the lungs and expelling air

• **internal and external intercostal muscles**
  – contribute to enlargement and contraction of thoracic cage
(a) Muscles of inhalation and their actions (left); muscles of exhalation and their actions (right)
REGULATION OF PULMONARY FUNCTION

• Respiratory control centers: the main integrators controlling the nerves that affect the inspiratory and expiratory muscles are located in the brainstem

  – Medullary rhythmicity center: generates the basic rhythm of the respiratory cycle

• Consists of two interconnected control centers
  – Inspiratory Area
  – Expiratory Area

These centers set the tidal breathing rate
REGULATION OF PULMONARY FUNCTION (cont.)

– The basic breathing rhythm can be altered by different inputs to the medullary rhythmicity center

– Pons
  • *apneustic center* in the pons stimulates the inspiratory center to increase the length and depth of inspiration
  • *Pneumotaxic center* in the pons inhibits the apneustic center and inspiratory center to prevent overinflation of the lungs
RESPIRATORY CENTER:

- Pneumotaxic area
- Apneustic area
- Medullary rhythmicity area:
  - Inspiratory area
  - Expiratory area

Sagittal section of brain stem

- Midbrain
- Pons
- Medulla oblongata
- Spinal cord

Sagittal plane
Central and Peripheral Input to Respiratory Centers

- **central chemoreceptors** – brainstem neurons that respond to changes in pH of cerebrospinal fluid
  - pH of cerebrospinal fluid reflects the CO₂ level in the blood

- **peripheral chemoreceptors** – located in the carotid and aortic bodies of the large arteries above the heart
  - respond to the O₂ and CO₂ content and the pH of blood
Central and Peripheral Input to Respiratory Centers

- **stretch receptors** – found in the smooth muscles of bronchi and bronchioles, and in the visceral pleura
  - respond to inflation of the lungs
  - **inflation (Hering-Breuer) reflex** – triggered by excessive inflation
    - protective reflex that inhibits inspiratory neurons stopping inspiration
    - Sets tidal breathing pattern in lungs
Fig. 24-30. Regulation of breathing. The dorsal respiratory group (DRG) and ventral respiratory group (VRG) of the medulla represent the medullary rhythmicity area. The pontine respiratory group (PRG, or pneumotaxic center) and apneustic center of the pons influence the basic respiratory rhythm by means of neural input to the medullary rhythmicity area. The brainstem also receives input from other parts of the body; information from chemoreceptors, baroreceptors, and stretch receptors can alter the basic breathing pattern, as can emotional (limbic) and sensory input. Despite these subconscious reflexes, the cerebral cortex can override the “automatic” control of breathing to some extent to do such activities as sing or blow up a balloon. Green arrows show flow of information to the respiratory control centers. The purple arrow shows the flow of information from the control centers to the respiratory muscles that drive breathing.
Voluntary Control of Breathing

• voluntary control over breathing originates in the motor cortex of frontal lobe of cerebrum
  –
• limits to voluntary control
  – breaking point – when CO₂ levels rise to a point when automatic controls override one’s will
Pressure and Airflow

• **atmospheric pressure** drives respiration
  – 760 mm Hg at sea level - 1 atmosphere (atm)
    • lower at higher elevations

• **Boyle’s Law** – at a constant temperature, the pressure of a given quantity of gas is inversely proportional to its volume
  – if the lung volume increases, their internal pressure (alveolar pressure) falls
    • if the pressure falls below atmospheric pressure the air moves into the lungs
  – if the lung volume decreases, alveolar pressure rises
    • if the pressure rises above atmospheric pressure the air moves out of the lungs
Fig. 24-7. Mechanism of inspiration. Note the role of the diaphragm and the chest-elevating muscles (pectoralis minor and external intercostals) in increasing thoracic volume, which decreases pressure in the lungs and thus draws air inward.
Figure 24-5 The respiratory cycle. During inspiration, the diaphragm contracts, increasing the volume of the thoracic cavity. This increase in volume results in a decrease in pressure, which causes air to rush into the lungs. During expiration, the diaphragm returns to an upward position, reducing the volume in the thoracic cavity. Air pressure thus increases, forcing air out of the lungs. See Table 24-1 for additional details.

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Fig. 24-8. Mechanism of expiration. Note that relaxation of the diaphragm plus contraction of chest-depressing muscles (internal intercostals) reduces thoracic volume, which increases pressure in the lungs and thus pushes air outward.

Animation: Alveolar Pressure Changes During Inspiration and Expiration

At the end of expiration, barometric air pressure ($P_a$) and alveolar air pressure ($P_{alveolar}$) are equal. Therefore, no movement of air into or out of the lungs takes place.
Figure 24-9 Rhythm of ventilation. Respiratory cycles repeat continuously in normal, quiet breathing. Notice the rhythmic rise and fall of the intrapleural pressure (PIP) and alveolar pressure (PA). You can easily see that PIP is always lower than PA (negative transpulmonary pressure), which helps keep the alveoli inflated. The lowest line shows the change in air volumes during the respiratory cycle.
Pneumothorax

- **pneumothorax** - presence of air in pleural cavity
  - thoracic wall is punctured
  - inspiration sucks air through the wound into the pleural cavity
  - potential space becomes an air filled cavity
  - loss of negative intrapleural pressure allows lungs to recoil and collapse
Resistance to Airflow

• three factors influencing airway resistance
  – diameter of the bronchioles
    • bronchodilation – increase in the diameter of a bronchus or bronchiole
      – epinephrine and sympathetic stimulation stimulate bronchodilation
    • bronchoconstriction – decrease in the diameter of a bronchus or bronchiole
      – parasympathetic nerves
      – anaphylactic shock and asthma
  – pulmonary compliance – the ease with which the lungs can expand
    • compliance reduced by degenerative lung diseases in which the lungs are stiffened by scar tissue
Alveolar Surface Tension

• thin film of water needed for gas exchange

• pulmonary **surfactant** produced by the great alveolar cells
  – decreases surface tension by disrupting the hydrogen bonding in water

• premature infants that lack surfactant suffer from **infant respiratory distress syndrome (IRDS)**
Alveolar Ventilation

• only air that enters the alveoli is available for gas exchange

• anatomic dead space
  – conducting division of airway where there is no gas exchange

• physiologic (total) dead space
  – sum of anatomic dead space and any pathological alveolar dead space

• alveolar ventilation rate (AVR)
  – Tidal Volume – approx 500 mL, 150 mL occupies airway
  – air that ventilates alveoli (350 mL) X respiratory rate (12 bpm) = 4200 mL/min
Measurements of Ventilation

• **spirometer** – a device that recaptures expired breath and records such variables such as rate and depth of breathing, speed of expiration, and rate of oxygen consumption

• **respiratory volumes**
  - **tidal volume** - volume of air inhaled and exhaled in one cycle during quiet breathing (500 mL)
  - **inspiratory reserve volume** - air in excess of tidal volume that can be inhaled with maximum effort (3000 mL)
  - **expiratory reserve volume** - air in excess of tidal volume that can be exhaled with maximum effort (1200 mL)
  - **residual volume** - air remaining in lungs after maximum expiration (1300 mL)
LUNG CAPACITIES
LUNG VOLUMES

6000 mL
5000 mL
4000 mL
3000 mL
2000 mL
1000 mL

INSPIRATORY RESERVE VOLUME
3100 mL
(1900 mL)

TIDAL VOLUME 500 mL

EXPIRATORY RESERVE VOLUME
1200 mL
(700 mL)

RESIDUAL VOLUME
1200 mL
(1100 mL)

INSPIRATORY RESERVE VOLUME
3100 mL
(1900 mL)

TIDAL VOLUME 500 mL

EXPIRATORY RESERVE VOLUME
1200 mL
(700 mL)

RESIDUAL VOLUME
1200 mL
(1100 mL)

INSPIRATORY CAPACITY
3600 mL
(2400 mL)

VITAL CAPACITY
4800 mL
(3100 mL)

TOTAL LUNG CAPACITY
6000 mL
(4200 mL)

FUNCTIONAL RESIDUAL CAPACITY
2400 mL
(1800 mL)
Respiratory Capacities

• **vital capacity** - total amount of air that can be inhaled and then exhaled with maximum effort

• **functional residual capacity** - amount of air remaining in lungs after a normal tidal expiration

• **total lung capacity** – maximum amount of air the lungs can contain
Respiratory Capacities

• **forced expiratory volume (FEV)**
  – percentage of the vital capacity that can be exhaled in a given time interval
  – Usually about 3 seconds

• **peak flow**
  – maximum speed of expiration
  – blowing into a handheld meter
Fig. 24-12, Forced expiratory volume (FEV). A normal individual forcefully exhales about 83% of the vital capacity (VC) during the first second, 94% at the end of 2 seconds, and 97% by the end of 3 seconds. The red line shows the results from a person with COPD (chronic obstructive pulmonary disease) who cannot forcefully exhale a large percentage of the vital capacity as quickly as a person without pulmonary obstruction.
Fig. 24-13. Flow-volume loops. The top of the loop represents expiratory flow (vertically) and volume (horizontally). The bottom of the loop represents inspiratory flow and volume. Notice that a person with COPD (chronic obstructive pulmonary disease) will produce a smaller loop with a “scooped-out” shape at the end of the expiratory curve. FVC, Forced vital capacity.
PULMONARY GAS EXCHANGE

• Partial pressure of gases: pressure exerted by a gas in a mixture of gases or a liquid
  – Law of partial pressures (Dalton’s law): the partial pressure of a gas in a mixture of gases is directly related to the concentration of that gas in the mixture and to the total pressure of the mixture
Fig. 24-14. Partial pressure of gases in atmospheric air. A, Composition of dry atmospheric air under standard conditions showing the concentrations of nitrogen, oxygen, carbon dioxide, and other gases. B, A mercury barometer. The weight of air pressing down on the surface of the mercury in the open dish pushes the mercury down into the dish and up the tube. The greater the air pressure pushing down on the mercury surface, the farther up the tube the mercury will be forced. Under standard conditions, air pressure causes the mercury column to rise 760 mm. A proportion of this pressure is exerted by each of the gases that comprise air, according to their relative concentrations (see A). That is, the total atmospheric air pressure is the sum of the partial pressures of nitrogen, oxygen, carbon dioxide, water vapor, and other gases.

Composition of Inspired and Alveolar Air

1. $O_2$ has atmospheric partial pressure of 159 mm, but is reduced to 104 mm by the time it gets to alveoli. Due to oxygen dissolving on mucous membrane of respiratory tract.

2. $CO_2$ has atmospheric partial pressure of 0.2 mm, but increases to 40 mm by the time it gets to alveoli. Due to mixing with residual volume

<table>
<thead>
<tr>
<th>Gas</th>
<th>Inspired Air*</th>
<th>Alveolar Air</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N_2$</td>
<td>78.6%</td>
<td>74.9%</td>
</tr>
<tr>
<td>$O_2$</td>
<td>20.9%</td>
<td>13.7%</td>
</tr>
<tr>
<td>$H_2O$</td>
<td>0.5%</td>
<td>6.2%</td>
</tr>
<tr>
<td>$CO_2$</td>
<td>0.04%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Typical values for a cool clear day; values vary with temperature and humidity. Other gases present in small amounts are disregarded.
CO2 exhaled
O2 inhaled

Atmospheric air:
P_{O2} = 159 \text{ mmHg}
P_{CO2} = 0.3 \text{ mmHg}

Alveolar air:
P_{O2} = 105 \text{ mmHg}
P_{CO2} = 40 \text{ mmHg}

Oxygenated blood:
P_{O2} = 100 \text{ mmHg}
P_{CO2} = 40 \text{ mmHg}

Deoxygenated blood:
P_{O2} = 40 \text{ mmHg}
P_{CO2} = 45 \text{ mmHg}

Systemic tissue cells:
P_{O2} = 40 \text{ mmHg}
P_{CO2} = 45 \text{ mmHg}

Pulmonary capillaries

(a) External respiration: pulmonary gas exchange
(b) Internal respiration: systemic gas exchange

Systemic capillaries

To lungs
To right atrium
To left atrium
To tissue cells

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Animation: Changes in the Partial Pressures of Oxygen and Carbon Dioxide

Fresh air entering the lung carries oxygen with a $P_{O_2}$ (partial pressure of oxygen) of 160. The presence of moisture in the lung results in reduction of the $P_{O_2}$ to 104.
Factors Affecting Gas Exchange

- **membrane thickness** - only 0.5 μm thick
  - presents little obstacle to diffusion

- **membrane surface area** - 100 ml blood in alveolar capillaries, spread thinly over 70 m²

- **ventilation-perfusion coupling** – the ability to match ventilation and perfusion to each other
  - gas exchange requires both good ventilation of alveolus and good perfusion of the capillaries
Lung Disease Affects Gas Exchange

(a) Normal

(b) Pneumonia
- Fluid and blood cells in alveoli
- Alveolar walls thickened by edema

(c) Emphysema
- Confluent alveoli
Figure 24-32A Ventilation and perfusion of the alveoli. Here, two alveoli represent typical alveoli in the lungs. A, Each alveolus is well ventilated with air and well perfused with blood, an efficient combination. B, Ventilation to the left alveolus is obstructed, but blood perfusion is unchanged—an inefficient arrangement because blood going to the poorly ventilated alveolus is not being fully oxygenated. C, Vasoconstriction of the pulmonary arteriole in the left (poorly ventilated) alveolus reduces blood perfusion—thus efficiently matching the perfusion to the ventilation.

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Figure 24-32B Ventilation and perfusion of the alveoli.
Here, two alveoli represent typical alveoli in the lungs.
A, Each alveolus is well ventilated with air and well perfused with blood, an efficient combination. B, Ventilation to the left alveolus is obstructed, but blood perfusion is unchanged—an inefficient arrangement because blood going to the poorly ventilated alveolus is not being fully oxygenated. C, Vasoconstriction of the pulmonary arteriole in the left (poorly ventilated) alveolus reduces blood perfusion—thus efficiently matching the perfusion to the ventilation.

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Gas Transport

• **gas transport** - the process of carrying gases from the alveoli to the systemic tissues and vise versa

• **oxygen transport**
  – 98.5% bound to hemoglobin
  – 1.5% dissolved in plasma

• **carbon dioxide transport**
  – 70% as bicarbonate ion
  – 23% bound to hemoglobin
  – 7% dissolved in plasma
Oxygen Transport

– 95% bound to hemoglobin in RBC
– 1.5% dissolved in plasma

• **hemoglobin** – molecule specialized in oxygen transport
  – four protein (globin) portions
    • each with a heme group which binds one $O_2$ to the **ferrous ion** ($Fe^{2+}$)
    • **oxyhemoglobin** ($HbO_2$) – $O_2$ bound to hemoglobin
Fig. 24-19. **Hemoglobin.** Sketch showing that hemoglobin is a quaternary protein consisting of four different tertiary (folded) polypeptide chains—two alpha (α) chains and two beta (β) chains. Each chain has an associated iron-containing heme group, as seen in detail in the inset. Oxygen (O₂) can bind to the iron (Fe) of the heme group, or carbon dioxide (CO₂) can bind to amine groups of the amino acids in the polypeptide chains.
Fig. 24-20. *Oxygen-carrying capacity of blood.* If blood consisted only of plasma, the maximum oxygen that could be transported would be only about 0.3 ml of O$_2$ per 100 ml of blood. Because the red blood cells contain hemoglobin molecules, which act as "oxygen sponges," the blood can actually carry up to 20 ml of dissolved O$_2$ per 100 ml of blood.
Carbon Monoxide Poisoning

- *carbon monoxide (CO)* - competes for the $O_2$ binding sites on the hemoglobin molecule

- colorless, odorless gas in cigarette smoke, engine exhaust, fumes from furnaces and space heaters
  - binds 210 times as tightly as oxygen
  - non-smokers - less than 1.5% of hemoglobin occupied by CO
  - smokers - 10% in heavy smokers
Carbon Dioxide Transport

• Transport of carbon dioxide
  – A small amount of CO$_2$ dissolves in plasma and is transported as a solute (10%)
  – 20% of CO$_2$ combines with NH$_2$ (amine) groups of Hb and other proteins to form carbaminohemoglobin
  – CO$_2$’s association with Hb is accelerated by an increase in blood PCO$_2$
  – More than two thirds of the CO$_2$ is carried in plasma as bicarbonate ions (70%)
Systemic Gas Exchange

• systemic gas exchange - the unloading of O$_2$ and loading of CO$_2$ at the systemic capillaries

• CO$_2$ loading
  – CO$_2$ diffuses into the blood
  – **carbonic anhydrase** in RBC catalyzes
    • CO$_2$ + H$_2$O $\rightarrow$ H$_2$CO$_3$ $\rightarrow$ HCO$_3^-$ + H$^+$
  – chloride shift
    • keeps reaction proceeding, exchanges HCO$_3^-$ for Cl$^-$
    • H$^+$ binds to hemoglobin

• O$_2$ unloading
  – H$^+$ binding to HbO$_2$ reduces its affinity for O$_2$
    • tends to make hemoglobin release oxygen
Systemic Gas Exchange

Respiring tissue

CO₂ → Dissolved CO₂ gas

CO₂ → CO₂ + plasma protein → Carbamino compounds

CO₂ → CO₂ + Hb → HbCO₂

CO₂ + H₂O → CO₂ + H₂O → H₂CO₃ → HCO₃⁻ + H⁺

O₂ → 98.5%

O₂ → Dissolved O₂ gas

Capillary blood

Key

Hb Hemoglobin
HbCO₂ Carbaminohemoglobin
HbO₂ Oxyhemoglobin
HHb Deoxyhemoglobin
CAH Carbonic anhydrase
Alveolar Gas Exchange

- reactions that occur in the lungs are reverse of systemic gas exchange

- **CO₂ unloading**
  - as Hb loads O₂ its affinity for H⁺ decreases, H⁺ dissociates from Hb and bind with HCO₃⁻
    - **CO₂ + H₂O ↔ H₂CO₃ ↔ HCO₃⁻ + H⁺**
    - reverse chloride shift
      - HCO₃⁻ diffuses back into RBC in exchange for Cl⁻, free CO₂ generated diffuses into alveolus to be exhaled
Alveolar Gas Exchange

Key:
- Hb: Hemoglobin
- HbCO₂: Carboxyhemoglobin
- HbO₂: Oxyhemoglobin
- HHb: Deoxyhemoglobin
- CAH: Carbonic anhydrase

**Alveolar air**
- CO₂: 7%

**Respiratory membrane**
- CO₂: 23%

**Capillary blood**
- CO₂: 70%
- CO₂ + H₂O → CO₂ + H⁺ + HCO₃⁻
- CO₂ + Hb → HbCO₂
- CO₂ + plasma protein → Carbaminohemoglobin

**Dissolved CO₂ gas**
- CO₂: 1.5%

**Dissolved O₂ gas**
- O₂: 98.5%
- O₂ + Hb → HbO₂ + H⁺
Blood Gases and the Respiratory Rhythm

• **rate** and **depth** of breathing adjust to maintain levels of:
  – pH \( 7.35 – 7.45 \)
  – \( \text{Pco}_2 \) 40 mm Hg
  – \( \text{Po}_2 \) 95 mm Hg

• **brainstem respiratory centers** receive input from central and peripheral chemoreceptors that monitor the composition of blood and CSF

• **most potent stimulus for breathing** is pH, followed by \( \text{CO}_2 \), and least significant is \( \text{O}_2 \)
Fig. 24-30. Regulation of breathing. The dorsal respiratory group (DRG) and ventral respiratory group (VRG) of the medulla represent the medullary rhythmicity area. The pontine respiratory group (PRG, or pneumotaxic center) and apneustic center of the pons influence the basic respiratory rhythm by means of neural input to the medullary rhythmicity area. The brainstem also receives input from other parts of the body; information from chemoreceptors, baroreceptors, and stretch receptors can alter the basic breathing pattern, as can emotional (limbic) and sensory input. Despite these subconscious reflexes, the cerebral cortex can override the “automatic” control of breathing to some extent to do such activities as sing or blow up a balloon. Green arrows show flow of information to the respiratory control centers. The purple arrow shows the flow of information from the control centers to the respiratory muscles that drive breathing.
Hydrogen Ions

- **acidosis** – blood pH lower than 7.35
- **alkalosis** – blood pH higher than 7.45
- **hypocapnia** – $P_{CO_2}$ less than 37 mm Hg
  - most common cause of alkalosis
- **hypercapnia** – $P_{CO_2}$ greater than 43 mm Hg
  - most common cause of acidosis
Effects of Hydrogen Ions

- **hyperventilation** is a corrective homeostatic response to acidosis
  - “blowing off” CO₂ faster than the body produces it
  - pushes reaction to the left
    \[
    \text{CO}_2 \text{(expired)} + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \downarrow \text{H}^+
    \]
Effects of Hydrogen Ions

- **hypoventilation** is a corrective homeostatic response to alkalosis
  - allows CO$_2$ to accumulate in the body fluids faster than we exhale it
  - shifts reaction to the right
  - CO$_2$ + H$_2$O $\rightarrow$ H$_2$CO$_3$ $\rightarrow$ HCO$_3^-$ + H$^+$
  - raising the H$^+$ concentration, lowering pH to normal
Chronic Obstructive Pulmonary Disease

• **COPD** – refers to any disorder in which there is a long-term obstruction of airflow and a substantial reduction in pulmonary ventilation

• major COPDs are chronic bronchitis, asthma, and emphysema
Effects of COPD

• reduces pulmonary compliance and vital capacity

• hypoxemia, hypercapnia, respiratory acidosis