Chapter 22

Respiratory System
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
  – considered jointly as **cardiopulmonary system**
  – disorders of lungs directly effect the heart and vise versa

• **respiratory system** and the **urinary system** collaborate to regulate the body’s acid base balance
Respiration

Respiration has three meanings:

1. ventilation of the lungs (breathing)

1. the exchange of gases between the air and blood, and between blood and the tissue fluid

1. the use of oxygen in cellular metabolism
Functions of Respiratory System

- **O₂ and CO₂ exchange** between blood and air
- **speech** and other vocalizations
- sense of **smell**
- affects **pH** of body fluids by eliminating CO₂
- affects **blood pressure** by synthesis of vasoconstrictor, angiotensin II
- breathing creates pressure gradients between thorax and abdomen that promote the **flow of lymph and venous blood**
- breath-holding helps **expel abdominal contents** during urination, defecation, and childbirth (Valsalva maneuver)
Principal Organs of Respiratory System

- **nose, pharynx, larynx, trachea, bronchi, lungs**
  - incoming air stops in the **alveoli**
    - millions of thin-walled, microscopic air sacs
    - exchanges gases with the bloodstream through the alveolar wall, and then flows back out

- **conducting division** of the respiratory system
  - those passages that serve only for airflow
  - no gas exchange
  - nostrils through major bronchioles

- **respiratory division** of the respiratory system
  - consists of alveoli and other gas exchange regions

- **upper respiratory tract** – in head and neck
  - nose through larynx

- **lower respiratory tract** – organs of the thorax
  - trachea through lungs
Organs of Respiratory System

- nose, pharynx, larynx, trachea, bronchi, lungs

Figure 22.1
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
Nasal Cavity

• **nasal fossae** – right and left halves of the nasal cavity
  – **nasal septum** divides nasal cavity

  – roof and floor of nasal cavity
    • **ethmoid and sphenoid bones** form the roof
    • **hard palate** forms floor
      – separates the nasal cavity from the oral cavity and allows you to breathe while you chew food
Nasal Cavity

• **vestibule** – beginning of nasal cavity – small dilated chamber just inside nostrils

• **Nasal conchae** - occupied by three folds of tissue
  - narrowness and turbulence insure that most air contacts mucous membranes
  - cleans, warms, and moistens the air

• **olfactory epithelium** – detect odors
  - covers a small area of the roof of the nasal fossa and adjacent parts of the septum and superior concha
  - ciliated pseudostratified columnar epithelium with goblet cells
  - immobile cilia to bind odorant molecules
Nasal Cavity

• **respiratory epithelium** lines rest of nasal cavity except vestibule
  – ciliated pseudostratified columnar epithelium with goblet cells
  – cilia are motile
  – goblet cells secrete mucus and cilia propel the mucous posteriorly toward pharynx
  – swallowed into digestive tract

• **erectile tissue**
  – every 30 to 60 minutes, erectile tissue on one side swells with blood
  – restricts air flow through that fossa
  – most air directed through other nostril and fossa
  – allowing engorged side time to recover from drying
  – preponderant flow of air shifts between the right and left nostrils once or twice an hour
Regions of Pharynx

Pharynx:
- Nasopharynx
- Oropharynx
- Laryngopharynx

Nasal septum:
- Perpendicular plate
- Septal cartilage
- Vomer

Figure 22.3c
Pharynx

- **pharynx** (throat) – a muscular funnel extending about 13 cm (5 in.)

- **three regions of pharynx**
  - **nasopharynx**
    - receives auditory tubes and contains pharyngeal tonsil
    - 90° downward turn traps large particles (>10µm)
  - **oropharynx**
    - space between soft palate and epiglottis
    - contains palatine tonsils
  - **laryngopharynx**

- **nasopharynx** passes only air and is lined by *pseudostratified columnar epithelium*

- **oropharynx** and **laryngopharynx** pass air, food, and drink and are lined by *stratified squamous epithelium*
Larynx

- **larynx** (voice box) – cartilaginous chamber about 4 cm (1.5 in.)

- **primary function** is to keep food and drink out of the airway
  - has evolved to produce sound

- **epiglottis** – flap of tissue that guards the superior opening of the larynx
  - at rest, stands almost vertically
  - during swallowing, extrinsic muscles of larynx pull larynx upward
  - tongue pushes epiglottis down to meet it
  - closes airway and directs food to the esophagus behind it
Views of Larynx

(a) Anterior  (b) Posterior  (c) Median

Figure 22.4 a-c
Walls of Larynx

• walls of larynx are quite muscular
  – deep **intrinsic muscles** operate the vocal cords
  – superior **extrinsic muscles** connect the larynx to hyoid bone
    • elevate the larynx during swallowing

• interior wall has **two folds**
  – superior **vestibular folds**
    • play no role in speech
    • close the larynx during swallowing
  – inferior **vocal cords**
    • produce sound when air passes between them
    • contain vocal ligaments
    • covered with stratifies squamous epithelium
      • best suited to endure vibration and contact between the cords
  • **glottis** – the vocal cords and the opening between them
Endoscopic View of the Larynx

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Anterior

Epiglottis
Glottis
Vestibular fold
Vocal cord
Trachea

Posterior

Figure 22.5a
Adduction of vocal cords

- Thyroid cartilage
- Cricoid cartilage
- Vocal cord
- Lateral cricoarytenoid muscle
- Arytenoid cartilage
- Corniculate cartilage
- Posterior cricoarytenoid muscle

Abduction of vocal cords

- Base of tongue
- Epiglottis
- Vestibular fold
- Vocal cord
- Glottis
- Corniculate cartilage

Figure 22.6 a-d
Trachea

- **trachea** (windpipe) – a rigid tube about 12 cm (4.5 in.) long and 2.5 cm (1 in.) in diameter
  - 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
- **trachealis muscle** spans opening in rings
  - gap in C allows room for the esophagus to expand as swallowed food passes by
  - contracts or relaxes to adjust air flow
Trachea

- inner lining of trachea is a **ciliated pseudostratified columnar epithelium**
  - composed mainly of mucus-secreting cells, ciliated cells, and stem cells
  - **mucociliary escalator** – mechanism for debris removal
    - mucus traps inhaled particles
    - upward beating cilia drives mucus toward pharynx where it is swallowed
Tracheal Epithelium

Figure 22.8
Lower Respiratory Tract

Larynx
Trachea
Main bronchi
Lobar bronchi

Thyroid cartilage
Cricoid cartilage
Trachealis muscle
Hyaline cartilage ring
Lumen

Mucus
Mucociliary escalator
Particles of debris
Epithelium: Goblet cell
Ciliated cell
Mucous gland
Cartilage
Chondrocytes

Trachealis muscle
Hyaline cartilage ring
Mucosa
Mucous gland

Figure 22.7 a-c
Lungs - Surface Anatomy

(a) Anterior view

- Apex of lung
- Superior lobe
- Superior lobar bronchus
- Horizontal fissure
- Middle lobar bronchus
- Middle lobe
- Inferior lobar bronchus
- Oblique fissure
- Inferior lobe
- Base of lung

(b) Mediastinal surface, right lung

- Apex
- Superior lobe
- Pulmonary arteries
- Hilum
- Middle lobe
- Inferior lobe

Larynx:
- Thyroid cartilage
- Cricoid cartilage
- Trachea
- Main bronchi

Costal surface
- Superior lobe
- Cardiac impression
- Inferior lobe
- Oblique fissure

Mediastinal surfaces

Diaphragmatic surface

Figure 22.9
Thorax - Cross Section

Ralph Hutchings/Visuals Unlimited

Figure 22.10
Lungs

- **lung**
  - **costal surface** – pressed against the ribcage
  - **mediastinal surface** – faces medially toward the heart
    - **hilum** – slit through which the lung receives the main bronchus, blood vessels, lymphatics and nerves

- **right lung**
  - shorter than left because the liver rises higher on the right
  - has **three lobes** – **superior, middle, and inferior** separated by **horizontal and oblique fissure**

- **left lung**
  - taller and narrower because the heart tilts toward the left and occupies more space on this side of mediastinum
  - has indentation – **cardiac impression**
  - has **two lobes** – **superior and inferior** separated by a single **oblique fissure**
Bronchial Tree

- **bronchial tree** – a branching system of air tubes in each lung
  - from main bronchus to 65,000 terminal bronchioles

- **main (primary) bronchi** – supported by c-shaped hyaline cartilage rings

- **lobar (secondary) bronchi** – supported by crescent shaped cartilage plates
  - three **rt. lobar (secondary) bronchi** – **superior, middle, and inferior**
    - one to each lobe of the right lung
  - two **lt. lobar bronchi** - **superior** and **inferior**
    - one to each lobe of the left lung

- **segmental (tertiary) bronchi** - supported by crescent shaped cartilage plates
  - 10 on right, and 8 on left
  - **bronchopulmonary segment** – functionally independent unit of the lung tissue
Bronchial Tree

- all bronchi are lined with **ciliated pseudostratified columnar epithelium**

  - **lamina propria** has an abundance of mucous glands and lymphocyte nodules (bronchus-associated lymphoid tissue, BALT)
    - intercept inhaled pathogens

  - all divisions of bronchial tree have a large amount of **elastic connective tissue**
    - contributes to the recoil that expels air from lungs

- **mucosa** also has a well-developed layer of **smooth muscle**
  - **muscularis mucosae** which contracts or relaxes to constrict or dilate the airway, regulating air flow

- **pulmonary artery** branches closely follow the bronchial tree on their way to the alveoli

- **bronchial artery** – services bronchial tree with systemic blood
  - arises from the aorta
Bronchial Tree

- bronchioles
  - lack cartilage
  - 1 mm or less in diameter
  - **pulmonary lobule** - portion of lung ventilated by one bronchiole
  - **terminal bronchioles**
    - Final branches of conducting division
    - each terminal bronchiole gives off two or more smaller respiratory bronchioles
  - **respiratory bronchioles**
    - have alveoli budding from their walls
    - considered the **beginning of the respiratory division** since alveoli participate in gas exchange
    - divide into 2-10 **alveolar ducts**
    - end in **alveolar sacs** – grape-like clusters of alveoli arrayed around a central space called the **atrium**
Path of Air Flow

Conducting division

nasal cavity > pharynx > larynx > trachea > main bronchus > lobar bronchus > segmental bronchus > bronchiole > terminal bronchiole >

respiratory division

respiratory bronchiole > alveolar duct > atrium > alveolars
Lung Tissue

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Figure 22.11

(a) Bronchiole: Epithelium Smooth muscle Alveoli Branch of pulmonary artery Alveolar duct

(b) Terminal bronchiole Pulmonary arteriole Respiratory bronchiole Alveolar duct Alveoli

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Alveolar Blood Supply

- Terminal bronchiole
- Respiratory bronchiole
- Pulmonary arteriole
- Pulmonary venule
- Alveoli
- Alveolar sac
- Capillary networks around alveoli

Figure 22.12a
**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
    - cover 95% of alveolus surface area
  - **great (type II) alveolar cells**
    - round to cuboidal cells that cover the remaining 5% of alveolar surface
    - repair the alveolar epithelium when the squamous (type I) cells are damaged
    - secrete **pulmonary surfactant**
      - a mixture of phospholipids and proteins that coats the alveoli and prevents them from collapsing when we exhale
  - **alveolar macrophages (dust cells)**
    - most numerous of all cells in the lung
    - wander the lumen and the connective tissue between alveoli
    - 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

- capillaries supplied by the **pulmonary artery**
- **respiratory membrane** – the barrier between the alveolar air and blood
- **respiratory membrane consists of:**
  - squamous alveolar cells
  - endothelial cells of blood capillary
  - their shared basement membrane
- important to prevent fluid from accumulating in alveoli
  - gases diffuse too slowly through liquid to sufficiently aerate the blood
  - Capillaries absorb excess liquid
  - extensive lymphatic drainage
Alveolus

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Figure 22.12 b-c
The Pleurae and Pleural Fluid

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

- **parietal pleura** – adheres to inner surface of the rib cage, and superior surface of the diaphragm

- **pleural cavity** – 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
  - compartmentalization
    - prevents spread of infection from one organ to others
Pulmonary Ventilation

• breathing (pulmonary ventilation) – inspiration (inhaling) and expiration (exhaling)

• respiratory cycle – one complete inspiration and expiration
  – quiet respiration – while at rest, effortless, and automatic
  – forced respiration – deep rapid breathing, such as during exercise

• 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
  - accounts for two-thirds of airflow

• **internal and external intercostal muscles**
  - synergist to diaphragm
  - between ribs
  - stiffen the thoracic cage during respiration
  - prevents it from caving inward when diaphragm descends
  - contribute to enlargement and contraction of thoracic cage
  - adds about one-third of the air that ventilates the lungs

• **scalenes**
  - synergist to diaphragm
  - quiet respiration holds ribs 1 and 2 stationary
Accessory Respiratory Muscles

- **accessory muscles** of respiration act mainly in **forced respiration**

- **forced inspiration**
  - Accessory muscles greatly increase thoracic volume

- **normal quiet expiration**
  - an energy-saving **passive process** achieved by the elasticity of the lungs and thoracic cage
  - as muscles relax, structures recoil to original shape and original (smaller) size of thoracic cavity, results in air flow out of the lungs

- **forced expiration**
  - greatly increased abdominal pressure pushes viscera up against diaphragm increasing thoracic pressure, forcing air out
Accessory Respiratory Muscles

• **Valsalva maneuver** – consists of taking a deep breath, holding it by closing the glottis, and then contracting the abdominal muscles to raise abdominal pressure and pushing organ contents out
  – childbirth, urination, defecation, vomiting
Respiratory Muscles

Inspiration

Sternocleidomastoid (elevates sternum)

Scalenes (fix or elevate ribs 1–2)

External intercostals (elevate ribs 2–12, widen thoracic cavity)

Pectoralis minor (cut) (elevates ribs 3–5)

Internal intercostals, intercartilaginous part (aid in elevating ribs)

Diaphragm (descends and increases depth of thoracic cavity)

Forced expiration

Internal intercostals, interosseous part (depress ribs 1–11, narrow thoracic cavity)

Diaphragm (ascends and reduces depth of thoracic cavity)

Rectus abdominis (depresses lower ribs, pushes diaphragm upward by compressing abdominal organs)

External abdominal oblique (same effects as rectus abdominis)

Figure 22.13
Neural Control of Breathing

- no autorhythmic pacemaker cells for respiration, as in the heart
- exact mechanism for setting the rhythm of respiration remains unknown
- breathing depends on repetitive stimuli of skeletal muscles from brain
- neurons in medulla oblongata and pons control unconscious breathing
- voluntary control provided by motor cortex
- inspiratory neurons: fire during inspiration
- expiratory neurons: fire during *forced* expiration
Brainstem Respiratory Centers

- automatic, unconscious cycle of breathing is controlled by three pairs of respiratory centers in the reticular formation of the medulla oblongata and the pons

- respiratory nuclei in medulla
  - ventral respiratory group (VRG)
    - primary generator of the respiratory rhythm
    - inspiratory neurons in quiet breathing fire for about two seconds
    - expiratory neurons fire for about three seconds allowing inspiratory muscles to relax
    - produces a respiratory rhythm of ~12 breath per minute
  - dorsal respiratory group (DRG)
    - modifies the rate and depth of breathing
    - receives influences from external sources

- pons
  - pontine respiratory group (PRG)
    - modifies rhythm of the VRG by outputs to both the VRG and DRG
    - adapts breathing to special circumstances such as sleep, exercise, vocalization, and emotional responses
Respiratory Control Centers

Figure 22.14
Central and Peripheral Input to Respiratory Centers

• **hyperventilation** – anxiety triggered state
  • breathing is so rapid that it expels CO\(_2\) from the body faster than it is produced.
  • blood CO\(_2\) levels drop, the pH rises > cerebral arteries constrict

• **central chemoreceptors** – brainstem neurons that respond to changes in pH of cerebrospinal fluid
  – pH of cerebrospinal fluid reflects the CO\(_2\) level in the blood
  – by regulating respiration to maintain stable pH, respiratory center also ensures stable CO\(_2\) level in the blood

• **peripheral chemoreceptors** – located in the carotid and aortic bodies of the large arteries above the heart
  – respond to the O\(_2\) and CO\(_2\) 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

- **irritant receptors** – nerve endings amid the epithelial cells of the airway
  - respond to smoke, dust, pollen, chemical fumes, cold air, and excess mucus
  - trigger protective reflexes such as bronchoconstriction, shallower breathing, breath-holding (apnea), or coughing
Peripheral Chemoreceptors

Figure 22.15

Sensory nerve fiber in glossopharyngeal nerve

Sensory nerve fibers in vagus nerves

Common carotid artery

Aortic bodies

Aorta

Heart
Voluntary Control of Breathing

• voluntary control over breathing originates in the **motor cortex of frontal lobe of cerebrum**
  – sends impulses down corticospinal tracts to respiratory neurons in spinal cord, bypassing brainstem

• limits to voluntary control
  – **breaking point** – when CO$_2$ levels rise to a point when automatic controls override one’s will
Pressure and Airflow

• respiratory airflow is governed by the same principles of flow, pressure, and resistance as blood flow
  – the flow of a fluid is directly proportional to the pressure difference between two points
  – the flow of a fluid is inversely proportional to the resistance

• atmospheric pressure drives respiration
  – the weight of the air above us
  – 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 lungs contain a quantity of a gas and the lung volume increases, their internal pressure (intrapulmonary pressure) falls
    • if the pressure falls below atmospheric pressure the air moves into the lungs
  – if the lung volume decreases, intrapulmonary pressure rises
    • if the pressure rises above atmospheric pressure the air moves out of the lungs
Inspiration

• the two pleural layers, their cohesive attraction to each other, and their connections to the lungs and their lining of the rib cage bring about inspiration
  – when the ribs swing upward and outward during inspiration, the parietal pleura follows them
  – the visceral pleura clings to it by the cohesion of water and it follows the parietal pleura
  – it stretches the alveoli within the lungs
  – the entire lung expands along the thoracic cage
  – as it increases in volume, its internal pressure drops, and air flows in

• intrapleural pressure – the slight vacuum that exists between the two pleural layers
  – about -4 mm Hg
  – drops to -6 mm Hg during inspiration as parietal pleura pulls away
  – some of this pressure change transfers to the interior of the lungs
  • intrapulmonary pressure – the pressure in the alveoli drops -3 mm Hg
  • pressure gradient from 760 mm Hg atmosphere to 757 mm Hg in alveoli allows air to flow into the lungs
Inspiration

• another force that expands the lungs is Charles’s Law

• **Charles’s Law** – the given quantity of a gas is directly proportional to its absolute temperature
  - on a cool day, 16°C (60°F) air will increase its temperature by 21°C (39°F) during inspiration
  - inhaled air is warmed to 37°C (99°F) by the time it reaches the alveoli
  - inhaled volume of 500 mL will expand to 536 mL and this thermal expansion will contribute to the inflation of the lungs

• in **quiet breathing**, the dimensions of the thoracic cage increase only a few millimeters in each direction
  - enough to increase its total volume by 500 mL.
  - thus, 500 mL of air flows into the respiratory tract
Respiratory Cycle

At rest, atmospheric and intrapulmonary pressures are equal, and there is no airflow.

In inspiration, the thoracic cavity expands laterally, vertically, and anteriorly; intrapulmonary pressure drops 3 mm Hg below atmospheric pressure, and air flows into the lungs.

In expiration, the thoracic cavity contracts in all three directions; intrapulmonary pressure rises 3 mm Hg above atmospheric pressure, and air flows out of the lungs.

Figure 22.16
Expiration

**relaxed breathing**
- passive process achieved mainly by the elastic recoil of the thoracic cage
- recoil compresses the lungs
- volume of thoracic cavity decreases
- raises intrapulmonary pressure to about +3 mm Hg
- air flows down the pressure gradient and out of the lungs

**forced breathing**
- accessory muscles raise intrapulmonary pressure as high as +30 mmHg
- massive amounts of air moves out of the lungs
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

• **atelectasis** - collapse of part or all of a lung
  – can also result from an airway obstruction
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
      - increase air flow
    - **bronchoconstriction** – decrease in the diameter of a bronchus or bronchiole
      - histamine, parasympathetic nerves, cold air, and chemical irritants stimulate bronchoconstriction
      - suffocation from extreme bronchoconstriction brought about by anaphylactic shock and asthma
  - **pulmonary compliance** – the ease with which the lungs can expand
    - the change in lung volume relative to a given pressure change
    - compliance reduced by degenerative lung diseases in which the lungs are stiffened by scar tissue
  - **surface tension of the alveoli and distal bronchioles**
    - **surfactant** – reduces surface tension of water
Alveolar Surface Tension

• thin film of water needed for gas exchange
  – creates surface tension that acts to collapse alveoli and distal bronchioles

• 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)
  – great difficulty in breathing
  – treated with artificial surfactant until lungs can produce own
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 Volumes and Capacities

Maximum possible inspiration

Inspiratory reserve volume

Vital capacity

Inspiratory capacity

Total lung capacity

Tidal volume

Maximum voluntary expiration

Expiratory reserve volume

Residual volume

Functional residual capacity

Tidal volume
Respiratory Capacities

• **vital capacity** - total amount of air that can be inhaled and then exhaled with maximum effort
  – \(VC = ERV + TV + IRV\) (4700 mL)
  • important measure of pulmonary health

• **inspiratory capacity** - maximum amount of air that can be inhaled after a normal tidal expiration
  – \(IC = TV + IRV\) (3500 mL)

• **functional residual capacity** - amount of air remaining in lungs after a normal tidal expiration
  – \(FRC = RV + ERV\) (2500 mL)

• **total lung capacity** – maximum amount of air the lungs can contain
  – \(TLC = RV + VC\) (6000 mL)
Respiratory Capacities

• **spirometry** – the measurement of pulmonary function
  – aid in diagnosis and assessment of *restrictive* and *obstructive* lung disorders

• **restrictive disorders** – those that reduce pulmonary compliance
  – limit the amount to which the lungs can be inflated
  – any disease that produces pulmonary fibrosis
  – black-lung, tuberculosis

• **obstructive disorders** – those that interfere with airflow by narrowing or blocking the airway
  – make it harder to inhale or exhale a given amount of air
  – asthma, chronic bronchitis
  – emphysema combines elements of restrictive and obstructive disorders
Gas Exchange and Transport

• composition of air
  - 78.6 % nitrogen, 20.9% oxygen, 0.04% carbon dioxide, 0 – 4% water vapor depending on temperature and humidity, and minor gases argon, neon, helium, methane and ozone
Daltons Law

The total atmospheric pressure is the sum of the contributions of the individual gases

**partial pressure** – the separate contribution of each gas in a mixture

at sea level 1 atm. of pressure = 760 mmHg

nitrogen constitutes 78.6\% of the atmosphere, thus

\[ P_{N_2} = 78.6\% \times 760 \text{ mm Hg} = 597 \text{ mm Hg} \]

\[ P_{O_2} = 20.9\% \times 760 \text{ mm Hg} = 159 \text{ mm Hg} \]

\[ P_{H_2O} = 0.5\% \times 760 \text{ mm Hg} = 3.7 \text{ mm Hg} \]

\[ P_{CO_2} = 0.04\% \times 760 \text{ mm Hg} = 0.3 \text{ mm Hg} \]

\[ P_{N_2} + P_{O_2} + P_{H_2O} + P_{CO_2} = 760 \text{ mmHg} \]
Composition of Inspired and Alveolar Air

- composition of inspired air and alveolar is different because of three influences:
  1. air is humidifies by contact with mucous membranes
     - alveolar $P_{H_2O}$ is more than 10 times higher than inhaled air
  1. freshly inspired air mixes with residual air left from the previous respiratory cycle
     - oxygen is diluted and it is enriched with $CO_2$
  1. alveolar air exchanges $O_2$ and $CO_2$ with the blood
     - $PO_2$ of alveolar air is about 65% that of inspired air
     - $PCO_2$ is more than 130 times higher
<table>
<thead>
<tr>
<th>Gas</th>
<th>Inspired Air*</th>
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<th>Alveolar Air</th>
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<td></td>
<td>%</td>
<td>mm Hg</td>
<td>%</td>
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<td>78.6%</td>
<td>597 mm Hg</td>
<td>74.9%</td>
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<tr>
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<td>20.9%</td>
<td>159 mm Hg</td>
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<tr>
<td>H₂O</td>
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<td>0.04%</td>
<td>0.3 mm Hg</td>
<td>5.3%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
<td>760 mm Hg</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.
Alveolar Gas Exchange

• air in the alveolus is in contact with a film of water covering the alveolar epithelium
  – for oxygen to get into the blood it must dissolve in this water
  – pass through the respiratory membrane separating the air from the bloodstream
  – for carbon dioxide to leave the blood it must pass the other way
  – diffuse out of the water film into the alveolar air

• gases diffuse down their own concentration gradient until the partial pressure of each gas in the air is equal to its partial pressure in water
Alveolar Gas Exchange

• **Henry’s law** – at the air-water interface, for a given temperature, the amount of gas that dissolves in the water is determined by its solubility in water and its partial pressure in air
  – the greater the P\textsubscript{O\textsubscript{2}} in the alveolar air, the more O\textsubscript{2} the blood picks up
  – since blood arriving at an alveolus has a higher P\textsubscript{CO\textsubscript{2}} than air, it releases CO\textsubscript{2} into the air
  – at the alveolus, the blood is said to **unload** CO\textsubscript{2} and **load** O\textsubscript{2}

  • **unload** CO\textsubscript{2} and **load** O\textsubscript{2} involves erythrocytes
  • efficiency depends on how long RBC stays in alveolar capillaries
    – 0.25 sec necessary to reach equilibrium
    – at rest, RBC spends 0.75 sec in alveolar capillaries
    – strenuous exercise, 0.3, which is still adequate
  – each gas in a mixture behaves independently
  – one gas does not influence the diffusion of another
Alveolar Gas Exchange

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Figure 22.18

(a) Oxygen

(b) Carbon dioxide
Factors Affecting Gas Exchange

• pressure gradient of the gases
  – \( P_{O_2} = 104 \text{ mm Hg in alveolar air versus 40 mm Hg in blood} \)
  – \( P_{CO_2} = 46 \text{ mm Hg in blood arriving versus 40 mm Hg in alveolar air} \)
  – hyperbaric oxygen therapy – treatment with oxygen at greater than one atm of pressure
    • gradient difference is more, and more oxygen diffuses into the blood
    • treat gangrene, carbon monoxide poisoning
  – at high altitudes the partial pressures of all gases are lower
    • gradient difference is less, and less oxygen diffuses into the blood

• solubility of the gases
  – \( CO_2 \) 20 times as soluble as \( O_2 \)
    • equal amounts of \( O_2 \) and \( CO_2 \) are exchanged across the respiratory membrane because \( CO_2 \) is much more soluble and diffuses more rapidly
  – \( O_2 \) is twice as soluble as \( N_2 \)
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
  - emphysema, lung cancer, and tuberculosis decrease surface area for gas exchange
Concentration Gradients of Gases

Figure 22.19

Alveolar gas exchange
- O2 loading
- CO2 unloading

Gas transport
- O2 carried from alveoli to systemic tissues
- CO2 carried from systemic tissues to alveoli

Systemic gas exchange
- O2 unloading
- CO2 loading

Expired air
- PO2 116 mm Hg
- PCO2 32 mm Hg

Inspired air
- PO2 159 mm Hg
- PCO2 0.3 mm Hg

Alveolar air
- PO2 104 mm Hg
- PCO2 40 mm Hg

Deoxygenated blood
- PO2 40 mm Hg
- PCO2 46 mm Hg

Oxygenated blood
- PO2 95 mm Hg
- PCO2 40 mm Hg

Tissue fluid
- PO2 40 mm Hg
- PCO2 46 mm Hg

Pulmonary circuit

Systemic circuit

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Ambient Pressure & Concentration Gradients

Air in hyperbaric chamber
(100% O₂ at 3 atm)

Air at sea level
(1 atm)

Normal gradient and O₂ diffusion

Reduced gradient, slower O₂ diffusion

Air at 3,000 m
(10,000 ft)

Atmosphere

Venous blood arriving at alveoli

Figure 22.20
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 22.21
Perfusion Adjustments

(a) Perfusion adjusted to changes in ventilation

- Reduced $\text{PO}_2$ in blood vessels
- Vasoconstriction of pulmonary vessels
- Decreased blood flow
- Response to reduced ventilation

- Increased $\text{PO}_2$ in blood vessels
- Vasodilation of pulmonary vessels
- Increased blood flow
- Response to increased ventilation

- Decreased airflow

Result: Blood flow matches airflow

- Increased airflow

Response to increased ventilation

- Decreased airflow

Response to reduced ventilation

Figure 22.22a
Ventilation Adjustments

- Reduced \( \text{PCO}_2 \) in alveoli
  - Decreased blood flow
  - Response to reduced perfusion
  - Constriction of bronchioles
  - Decreased airflow

- Increased blood flow
  - Increased perfusion
  - Dilation of bronchioles
  - Increased airflow

Result: Airflow matches blood flow

- Elevated \( \text{PCO}_2 \) in alveoli
  - Response to increased perfusion
  - Increased airflow

(b) Ventilation adjusted to changes in perfusion

Figure 22.22b
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

- **hemoglobin** – molecule specialized in oxygen transport
  - four protein (globin) portions
    - each with a heme group which binds one $O_2$ to the **ferrous ion** ($Fe^{2+}$)
    - one hemoglobin molecule can carry up to 4 $O_2$
    - oxyhemoglobin (HbO$_2$) – $O_2$ bound to hemoglobin
    - deoxyhemoglobin (HHb) – hemoglobin with no $O_2$
    - 100% saturation Hb with 4 oxygen molecules
    - 50% saturation Hb with 2 oxygen molecules
Carbon Monoxide Poisoning

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

- colorless, odorless gas

- **carboxyhemoglobin** – CO binds to ferrous ion of hemoglobin
  - binds 210 times as tightly as oxygen
  - non-smokers - less than 1.5% of hemoglobin occupied by CO
  - smokers - 10% in heavy smokers
  - atmospheric concentrations of 0.2% CO is quickly lethal
Oxyhemoglobin Dissociation Curve

Figure 22.23

relationship between hemoglobin saturation and $P_O^2$
Carbon Dioxide Transport

• 90% of CO$_2$ is hydrated to form carbonic acid
  – CO$_2$ + H$_2$O $\rightarrow$ H$_2$CO$_3$ $\rightarrow$ HCO$_3^-$ + H$^+$
  – then dissociates into bicarbonate and hydrogen ions

• 5% binds to the amino groups of plasma proteins and hemoglobin to form carbamino compounds – chiefly carbaminohemoglobin (HbCO$_2$)
  – carbon dioxide does not compete with oxygen
  – they bind to different moieties on the hemoglobin molecule
  – hemoglobin can transport O$_2$ and CO$_2$ simultaneously

• 5% is carried in the blood as dissolved gas
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
    - $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
  - 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
    - HbO$_2$ arrives at systemic capillaries 97% saturated, leaves 75% saturated
      - venous reserve – oxygen remaining in the blood after it passes through the capillary beds
Systemic Gas Exchange

Respiring tissue

- CO₂: 7%
- CO₂: 23%
- CO₂: 70%
- O₂: 98.5%
- O₂: 1.5%

Capillary blood

- CO₂ + Hb → HbCO₂
- CO₂ + H₂O → H₂CO₃ → HCO₃⁻ + H⁺
- CO₂ + plasma protein → Carbamino compounds
- Chloride shift

Key

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

Figure 22.24
Alveolar Gas Exchange Revisited

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

- **CO$_2$ unloading**
  - as Hb loads O$_2$ its affinity for H$^+$ decreases, H$^+$ dissociates from Hb and bind with HCO$_3^-$

  - $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$

  - reverse chloride shift

    - HCO$_3^-$ diffuses back into RBC in exchange for Cl$^-$, free CO$_2$ generated diffuses into alveolus to be exhaled
Alveolar Gas Exchange

Figure 22.25

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

Dissolved CO2 gas

CO2 + plasma protein → Carbamino compounds

O2 + HHb → HbO2 + H+

CO2 + H2O → H2CO3 → HCO3− + H+

Cl− → Chloride shift

HbCO2 → CO2 + Hb
Adjustment to the Metabolic Needs of Individual Tissues

- hemoglobin unloads $O_2$ to match metabolic needs of different states of activity of the tissues
  - ambient $P_{O_2}$
    - active tissue has $\downarrow P_{O_2}$; $O_2$ is released from Hb
  - temperature
    - active tissue has $\uparrow$ temp; promotes $O_2$ unloading
  - Bohr effect
    - active tissue has $\uparrow CO_2$, which lowers pH of blood; promoting $O_2$ unloading
  - bisphosphoglycerate (BPG)
    - RBCs produce BPG which binds to Hb; $O_2$ is unloaded
    - Haldane effect – rate of $CO_2$ loading is also adjusted to varying needs of the tissues, low level of oxyhemoglobin enables the blood to transport more $CO_2$
      - $\uparrow$ body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and cause $O_2$ unloading
        - $\uparrow$ metabolic rate requires $\uparrow$ oxygen
Oxygen Dissociation and Temperature

Figure 22.26a

(a) Effect of temperature

Temperature: 10°C, 20°C, 38°C, 43°C

Percentage saturation of hemoglobin vs. PO₂ (mm Hg)

Normal body temperature
Oxygen Dissociation and pH

(b) Effect of pH

Bohr effect: release of $O_2$ in response to low pH
Blood Gases and the Respiratory Rhythm

- **rate** and **depth** of breathing adjust to maintain levels of:
  - pH \( 7.35 \) – \( 7.45 \)
  - \( P_{\text{CO}_2} \) 40 mm Hg
  - \( P_{\text{O}_2} \) 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 \( CO_{2} \), and least significant is \( O_{2} \)
Hydrogen Ions

- pulmonary ventilation is adjusted to maintain the pH of the brain
  - central chemoreceptors in the medulla oblongata produce about 75% of the change in respiration induced by pH shift
  - yet H\(^+\) does not cross the blood-brain barrier very easily
  - CO\(_2\) does and in CSF reacts with water and produces carbonic acid
    - dissociates into bicarbonate and hydrogen ions
    - most H\(^+\) remains free and greatly stimulates the central chemoreceptors
  - hydrogen ions are also a potent stimulus to the peripheral chemoreceptors which produce about 25% of the respiratory response to pH change
Effects of Hydrogen Ions

• respiratory acidosis and respiratory alkalosis – pH imbalances resulting from a mismatch between the rate of pulmonary ventilation and the rate of CO₂ production

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

• hypoventilation is a corrective homeostatic response to alkalosis
  – allows CO₂ to accumulate in the body fluids faster than we exhale it
  – shifts reaction to the right
  – \( \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+ \)
  – raising the H⁺ concentration, lowering pH to normal

• ketoacidosis – acidosis brought about by rapid fat oxidation releasing acidic ketone bodies (diabetes mellitus)
  – induces Kussmaul respiration – hyperventilation cannot remove ketone bodies, but blowing off CO₂, it reduces the CO₂ concentration and compensates for the ketone bodies to some degree
Carbon Dioxide

• indirect effects on respiration
  – through pH as seen previously

• direct effects
  ↑CO₂ at beginning of exercise may directly stimulate peripheral chemoreceptors and trigger ↑ventilation more quickly than central chemoreceptors
Effects of Oxygen

- $P_O_2$ usually has little effect on respiration
- chronic hypoxemia, $P_O_2$ less than 60 mm Hg, can significantly stimulate ventilation
  - hypoxic drive – respiration driven more by low $P_O_2$ than by $CO_2$ or pH
  - emphysema, pneumonia
  - high elevations after several days
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** and **emphysema**
  - usually associated with smoking
  - other risk factors include air pollution or occupational exposure to airborne irritants
**Chronic Obstructive Pulmonary Disease**

- **chronic bronchitis**
  - inflammation and hyperplasia of the bronchial mucosa
  - cilia immobilized and reduced in number
  - goblet cells enlarge and produce excess mucus
  - develop chronic cough to bring up extra mucus with less cilia to move it
  - **sputum** formed (mucus and cellular debris)
    - ideal growth media for bacteria
    - incapacitates alveolar macrophages
  - leads to chronic infection and bronchial inflammation
Chronic Obstructive Pulmonary Disease

- **emphysema**
  - alveolar walls break down
    - lung has larger but fewer alveoli
    - much less respiratory membrane for gas exchange
  - lungs fibrotic and less elastic
    - healthy lungs are like a sponge; in emphysema, lungs are more like a rigid balloon
  - air passages collapse
    - obstructs outflow of air
    - air trapped in lungs
  - weaken thoracic muscles
    - spend three to four times the amount of energy just to breathe
Smoking and Lung Cancer

- lung cancer accounts for more deaths than any other form of cancer
  - most important cause is smoking (15 carcinogens)

- squamous-cell carcinoma (most common)
  - transformation of bronchial epithelium
  - dividing cells invade bronchial wall, cause bleeding lesions
  - dense swirls of keratin replace functional respiratory tissue
Lung Cancer

• adenocarcinoma
  – originates in mucous glands

• small-cell (oat cell) carcinoma
  – least common, most dangerous
  – named for clusters of cells that resemble oat grains
  – originates in primary bronchi, metastasizes quickly to other organs
Progression of Lung Cancer

• 90% originate in primary bronchi

• tumor invades bronchial wall, compresses airway; may cause atelectasis

• often first sign is coughing up blood

• metastasis is rapid; usually occurs by time of diagnosis
  – common sites: pericardium, heart, bones, liver, lymph nodes and brain

• prognosis poor after diagnosis
  – only 7% of patients survive 5 years
Effect of Smoking

(a) Healthy lung, mediastinal surface
(b) Smoker’s lung with carcinoma

Tumors

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Figure 22.27 a-b