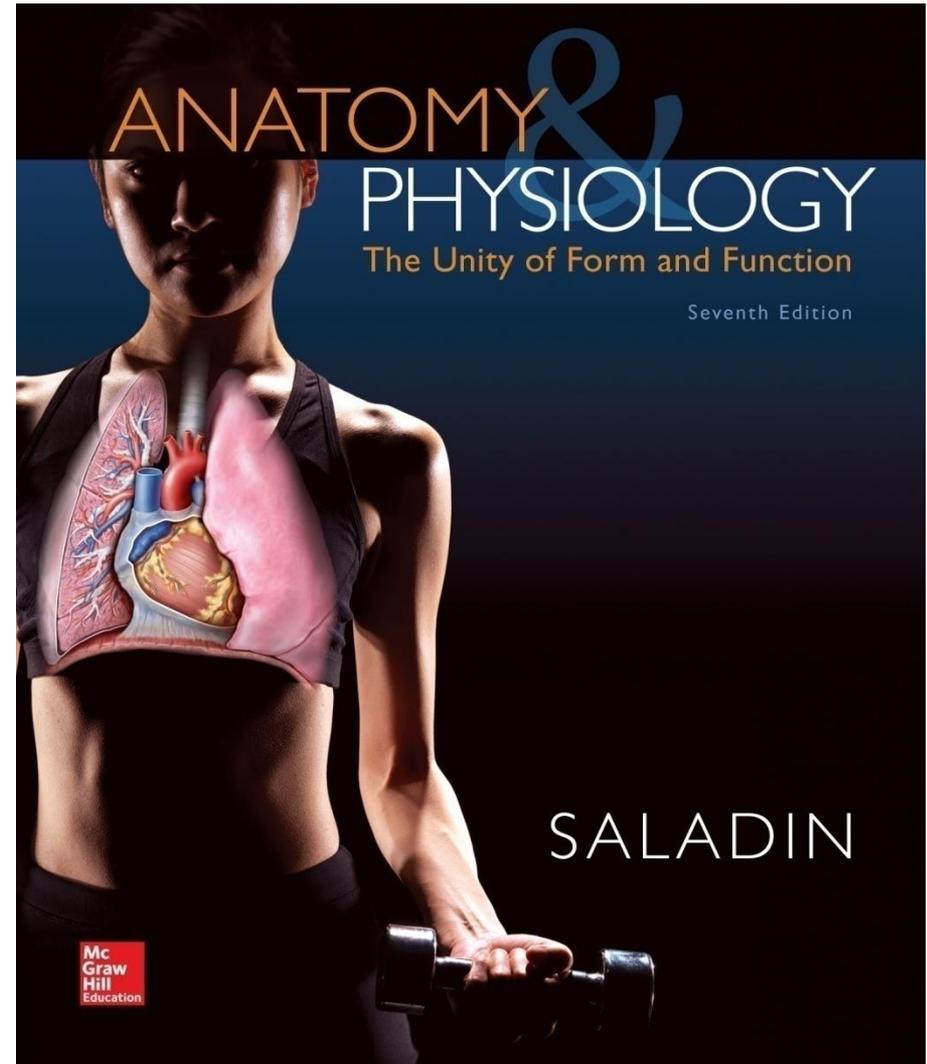


Chapter 22

Lecture Outline

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.



Introduction

- Breathing represents **life!**
 - First breath of a newborn baby
 - Last gasp of a dying person
- All body processes directly or indirectly require **ATP**
 - Most ATP synthesis **requires oxygen** and **produces carbon dioxide**
 - Drives the need to **breathe** to take in oxygen, and eliminate carbon dioxide

Introduction

- The **respiratory system** consists of a system of tubes that delivers air to the lungs
 - 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 affect the heart and vice versa
- **Respiratory system** and the **urinary system** collaborate to regulate the body's acid–base balance

Anatomy of the Respiratory System

- **Expected Learning Outcomes**

- State the functions of the respiratory system.
- Name and describe the organs of this system
- Trace the flow of air from the nose to the pulmonary alveoli.
- Relate the function of any portion of the respiratory tract to its gross and microscopic anatomy.

Anatomy of the Respiratory System

- **Respiration** is a term used to refer to ventilation of the lungs (breathing)
 - In other contexts it can be used to refer to part of cellular metabolism
- **Functions** of respiration include:
 - **Gas exchange:** O₂ and CO₂ exchanged between blood and air
 - **Communication:** speech and other vocalizations
 - **Olfaction:** sense of **smell**
 - **Acid-Base balance:** influences **pH** of body fluids by eliminating CO₂

Anatomy of the Respiratory System

Functions of respiration (Continued)

- **Blood pressure regulation:** by helping in synthesis of angiotensin II
- **Blood and lymph flow:** breathing creates pressure gradients between thorax and abdomen that promote flow of lymph and blood
- **Blood filtration:** lungs filter small clots
- **Expulsion of abdominal contents:** breath-holding assists in urination, defecation, and childbirth (Valsalva maneuver)

Anatomy of the Respiratory System

- **Principal organs: 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 respiratory system
 - Includes those passages that serve only for airflow
 - No gas exchange
 - Nostrils through major bronchioles

Anatomy of the Respiratory System

- **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

The Respiratory System

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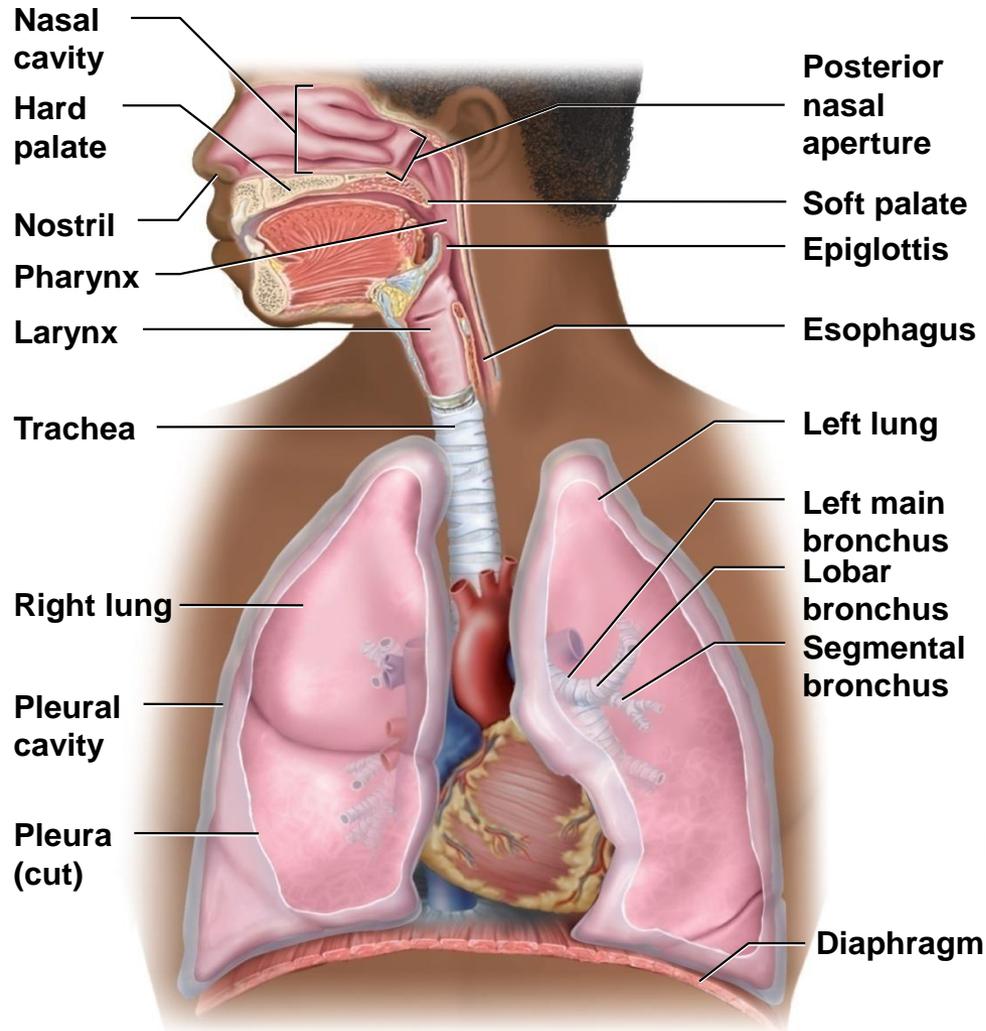


Figure 22.1

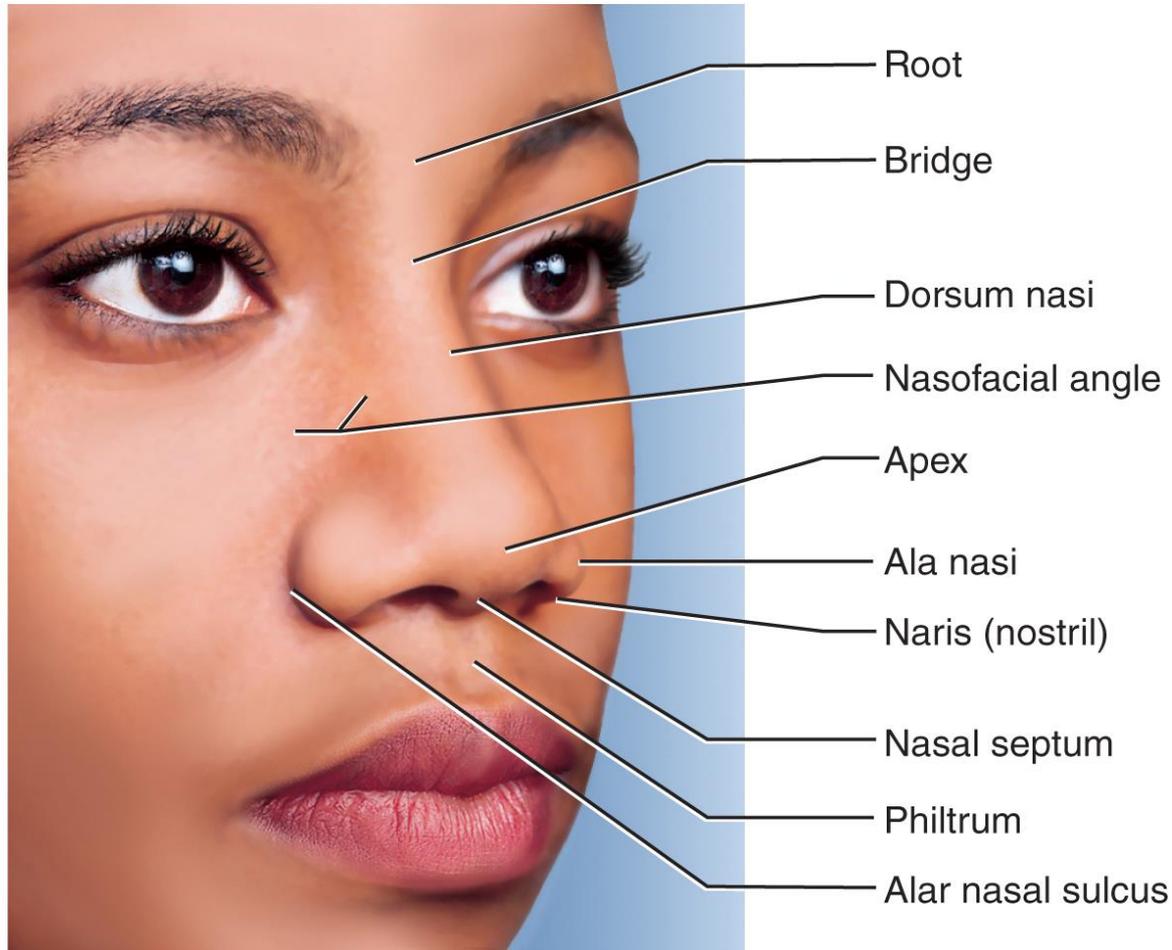
- **Nose, pharynx, larynx, trachea, bronchi, lungs**

The Nose

- **Functions of the nose**
 - Warms, cleanses, and humidifies inhaled air
 - Detects odors
 - Serves as a resonating chamber that amplifies voice
- Nose extends from **nostrils (nares)** to **posterior nasal apertures (choanae)**—posterior openings
- **Facial part is shaped by bone and hyaline cartilage**
 - Superior half: **nasal bones** and **maxillae**
 - Inferior half: lateral and **alar cartilages**
 - **Ala nasi**: flared portion at lower end of nose shaped by alar cartilages and dense connective tissue

Anatomy of the Nasal Region

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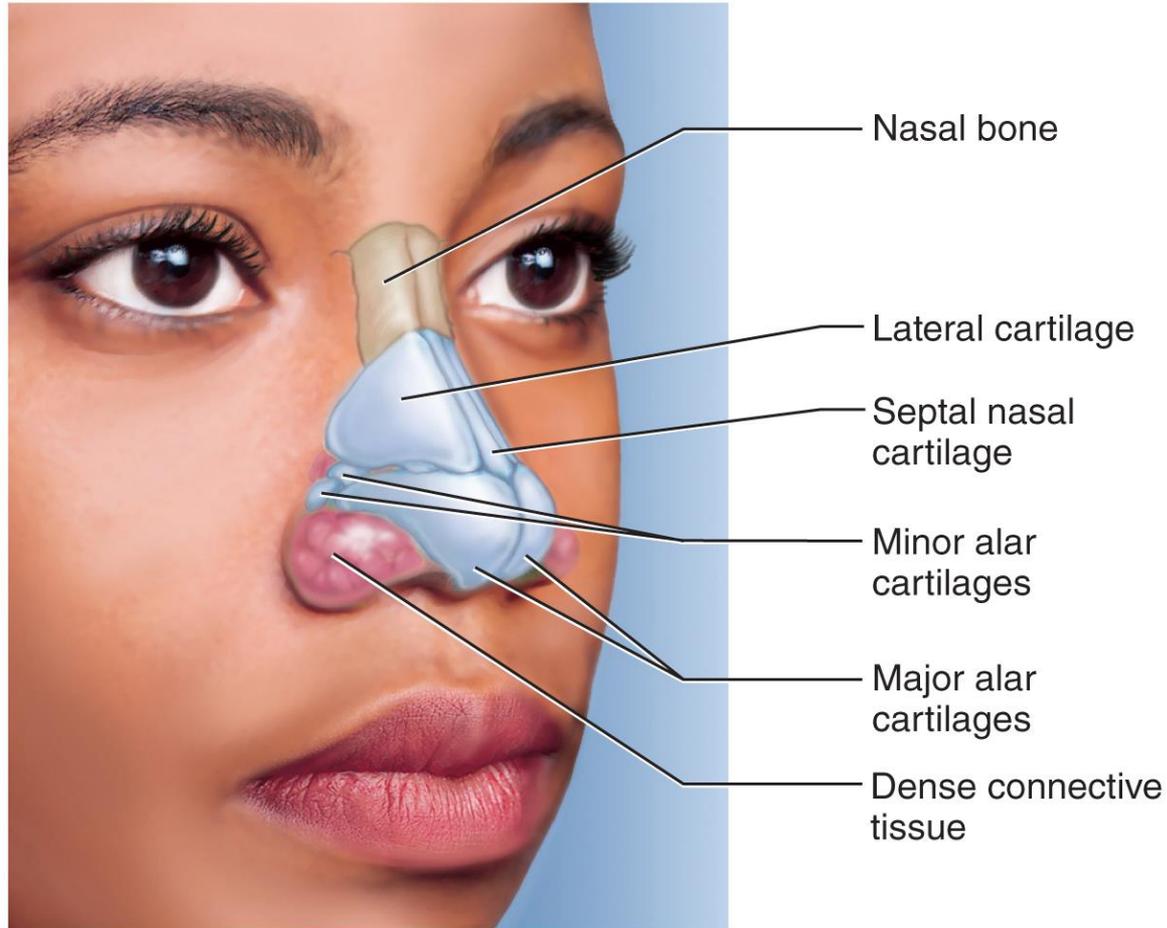
(a)

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Figure 22.2a

Anatomy of Nasal Region

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Figure 22.2b

The Nose

- **Nasal fossae**—right and left halves of nasal cavity
 - **Nasal septum** divides nasal cavity
 - Composed of bone and hyaline cartilage
 - **Vomer** forms inferior part
 - **Perpendicular plate of ethmoid** forms superior part
 - **Septal cartilage** forms anterior part
 - **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
 - **Paranasal sinuses** and **nasolacrimal duct** drain into nasal cavity

The Nose

- **Vestibule**—beginning of nasal cavity; small, dilated chamber just inside nostrils
 - Lined with **stratified squamous epithelium**
 - **Vibrissae**: stiff guard hairs that block insects and debris from entering nose
- **Posteriorly the nasal cavity expands into a larger chamber with not much open space**

The Nose

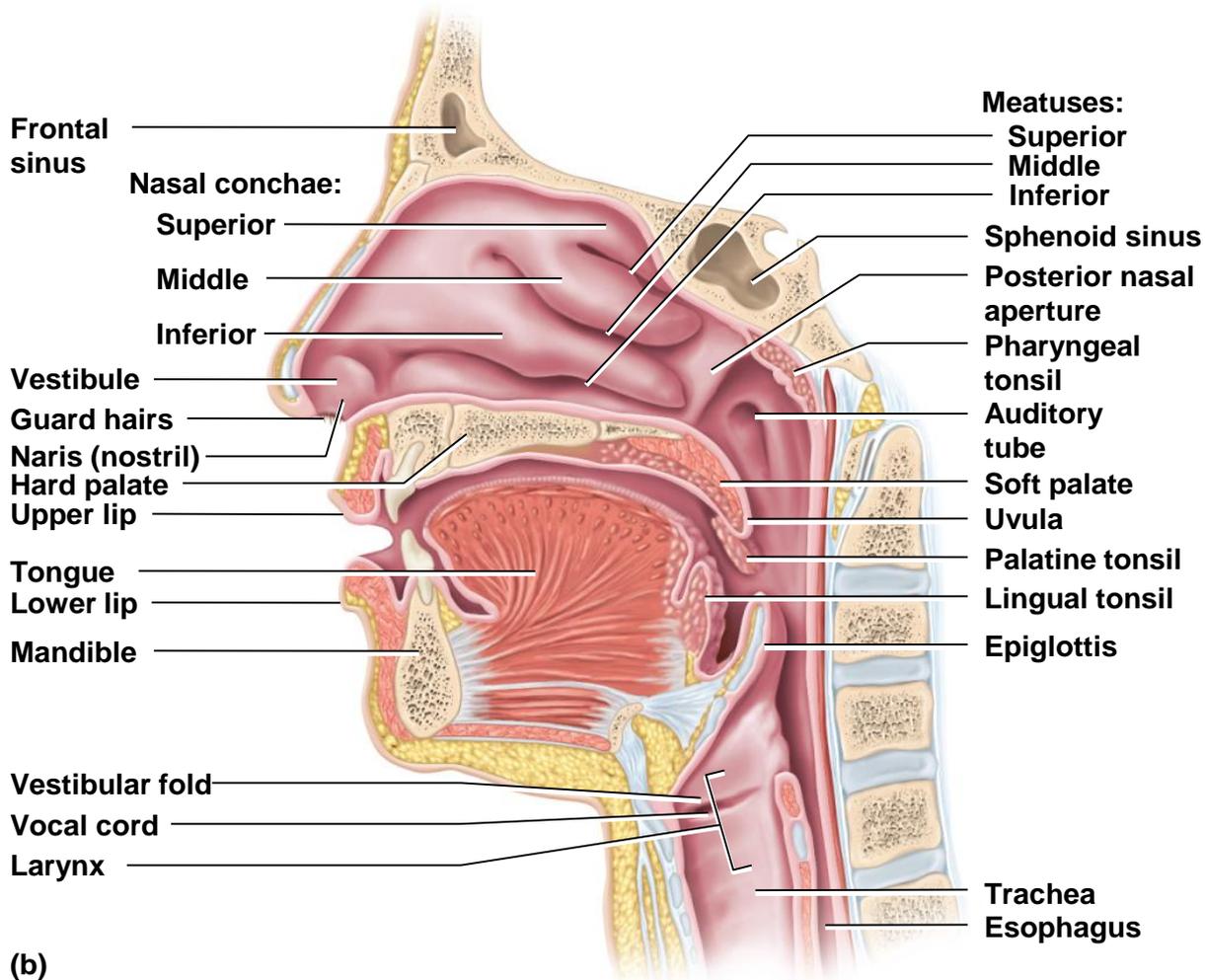
- Chamber behind vestibule is occupied by three folds of tissue—**nasal conchae**
 - **Superior, middle, and inferior nasal conchae (turbinates)**
 - Project from lateral walls toward septum
 - **Meatus**—narrow air passage beneath each concha
 - Narrowness and turbulence ensure that most air contacts mucous membranes
 - Cleans, warms, and moistens the air
- **Olfactory epithelium**—detects 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
 - Immobile cilia on sensory cells bind odorant molecules

The Nose

- **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 mucus posteriorly toward pharynx
 - Swallowed into digestive tract
- **Erectile tissue (swell body)**—extensive venous plexus in epithelium of inferior concha
 - Every 30 to 60 minutes, tissue on one side swells with blood
 - Restricts airflow through that fossa, so most air directed through other nostril
 - Allows engorged side time to recover from drying
 - Preponderant flow of air shifts between the right and left nostrils once or twice an hour

Anatomy of the Upper Respiratory Tract

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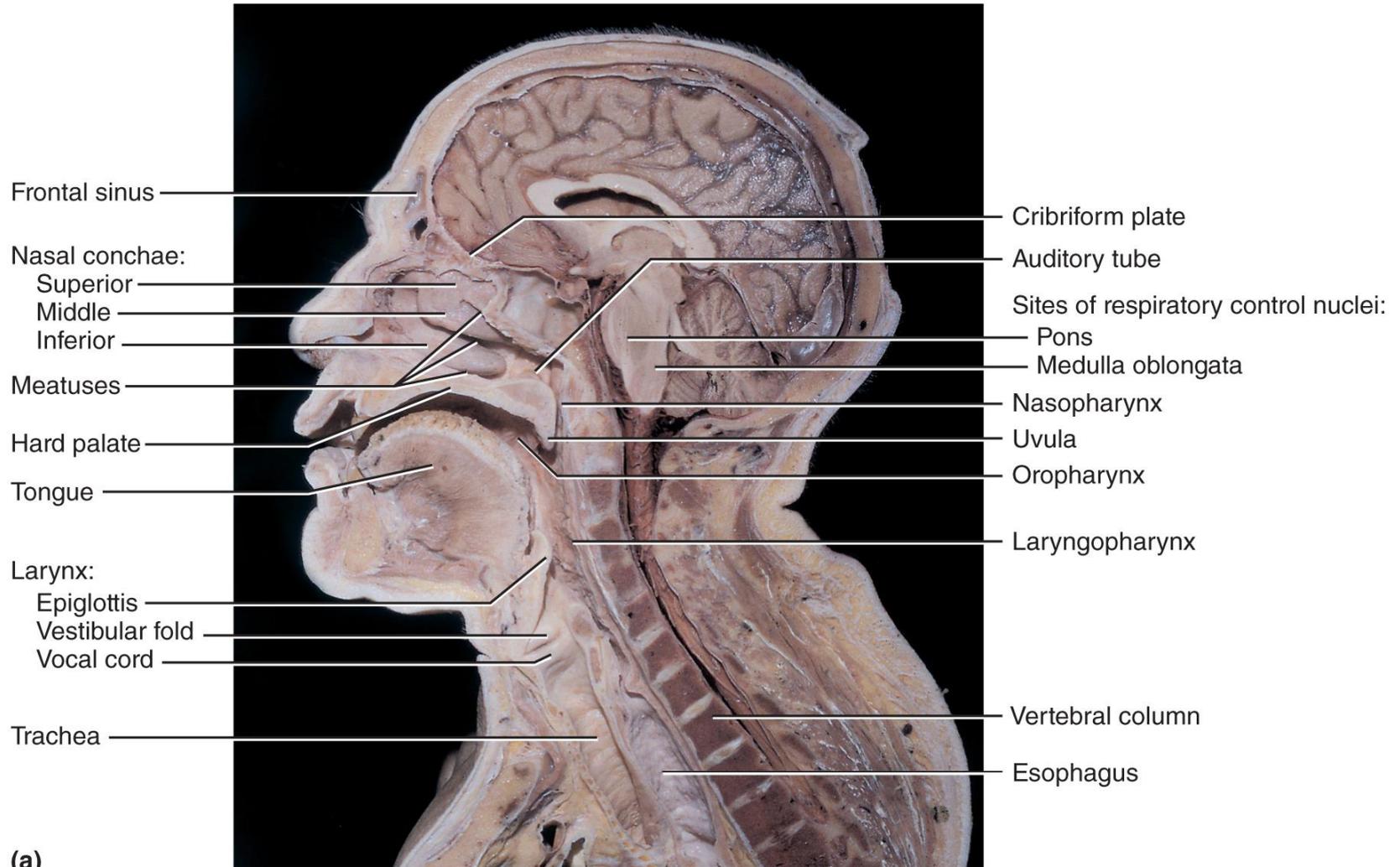


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Figure 22.3b

Anatomy of the Upper Respiratory Tract

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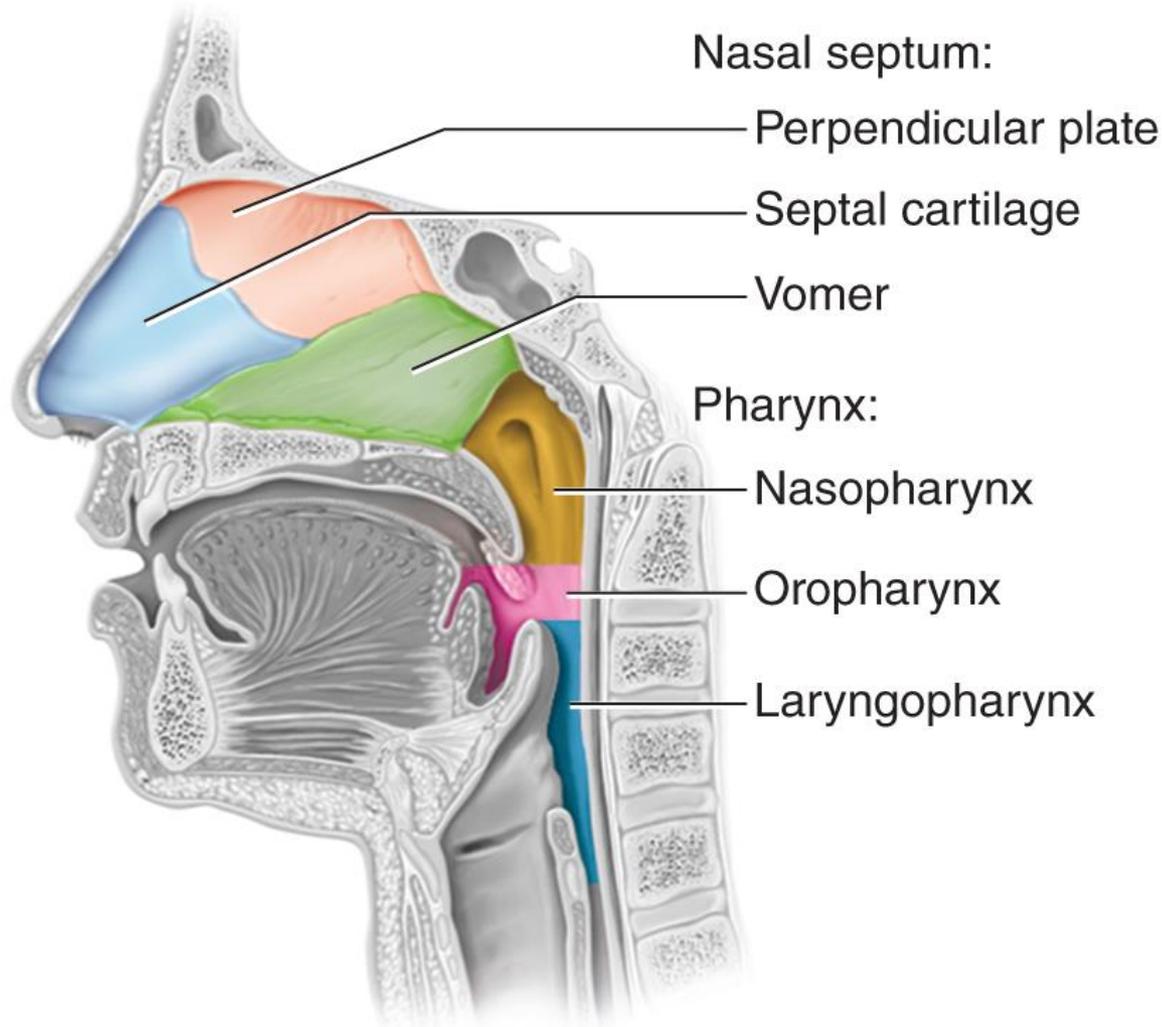


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Figure 22.3a

Anatomy of the Upper Respiratory Tract

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(c)

Figure 22.3c

The Pharynx

- **Pharynx (throat)**—muscular funnel extending about 5 in. from the **choanae** to the **larynx**
- **Three regions of pharynx**
 - **Nasopharynx**
 - Posterior to nasal apertures and above soft palate
 - Receives auditory tubes and contains pharyngeal tonsil
 - 90° downward turn traps large particles (>10 μm)
 - **Oropharynx**
 - Space between soft palate and epiglottis
 - Contains palatine tonsils
 - **Laryngopharynx**
 - Epiglottis to cricoid cartilage
 - Esophagus begins at that point

The Pharynx

- **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**
- Muscles of the pharynx assist in **swallowing** and **speech**

The Larynx

- **Larynx (voice box)**—cartilaginous chamber about 4 cm (1.5 in.) long
- **Primary function** is to keep food and drink out of the airway
 - In several animals it has evolved the additional role of **phonation**—the production of sound

The Larynx

- **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 esophagus behind it
 - **Vestibular folds** of the larynx play greater role in keeping food and drink out of the airway

The Larynx

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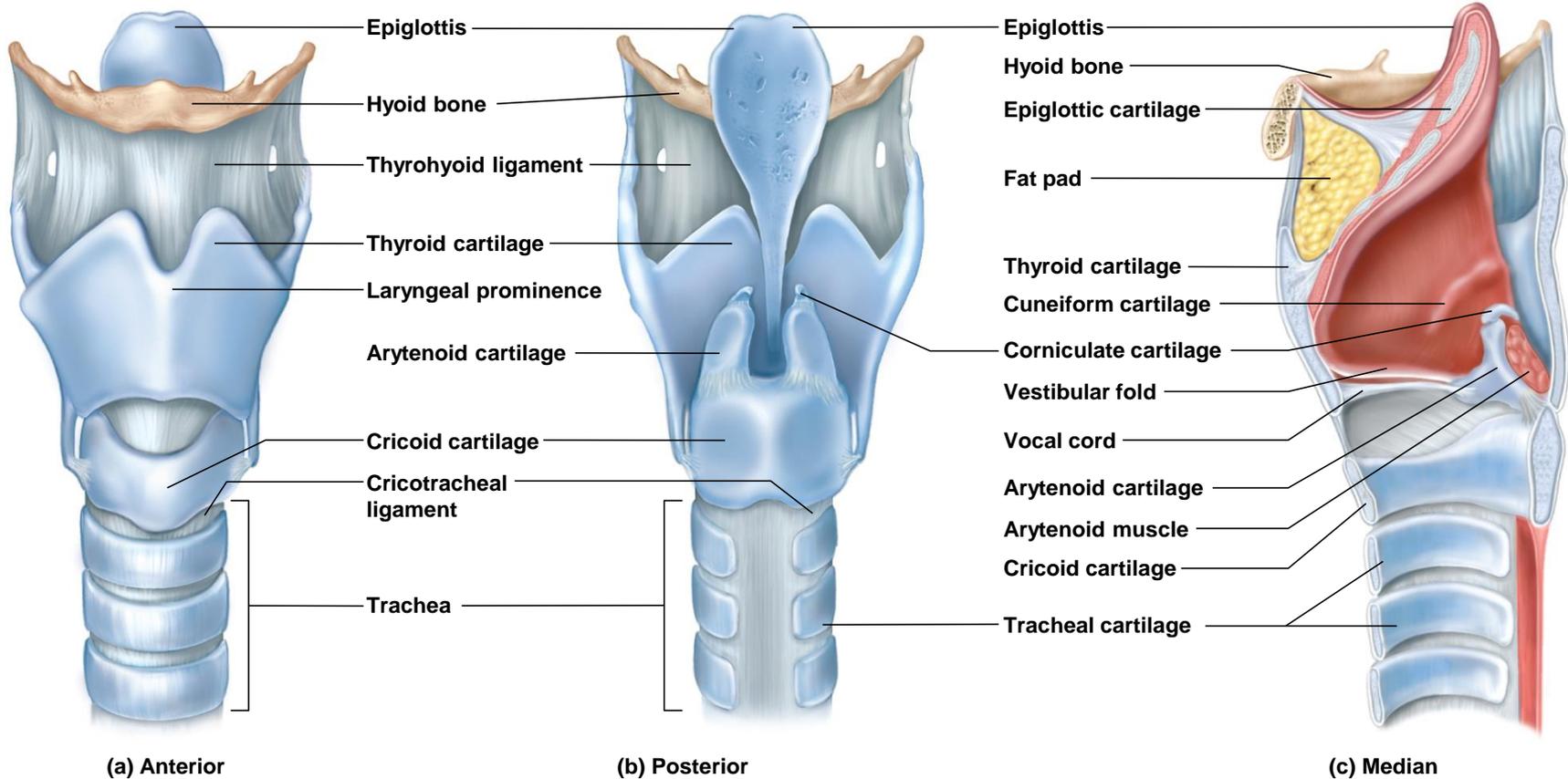


Figure 22.4a–c

The Larynx

- **Nine cartilages** make up framework of larynx
- **First three are solitary and relatively large**
 - **Epiglottic cartilage:** spoon-shaped supportive plate in epiglottis; most superior one
 - **Thyroid cartilage:** largest, laryngeal prominence (**Adam's apple**); shield-shaped
 - Testosterone stimulates growth, larger in males
 - **Cricoid cartilage:** connects larynx to trachea, ring-like

The Larynx

- **Three smaller, paired cartilages**
 - **Arytenoid cartilages (2)**: posterior to thyroid cartilage
 - **Corniculate cartilages (2)**: attached to arytenoid cartilages like a pair of little horns
 - **Cuneiform cartilages (2)**: support soft tissue between arytenoids and epiglottis
- **Ligaments suspends larynx from hyoid and hold it together**
 - Thyrohyoid ligament suspends it from hyoid
 - Cricotracheal ligament suspends trachea from larynx
 - Intrinsic ligaments hold laryngeal cartilages together

The Larynx

- Interior wall has **two folds** on each side that extend from thyroid cartilage in front to arytenoid cartilages in back
 - 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 stratified squamous epithelium
 - Suited to endure vibration and contact
 - **Glottis**—the vocal cords and the opening between them

The Larynx

- **Walls of larynx are quite muscular**
 - Deep **intrinsic muscles** operate the vocal cords
 - Superior **extrinsic muscles** connect larynx to hyoid bone
 - Elevate the larynx during swallowing
 - Infrahyoid group

The Larynx

- **Intrinsic muscles** control vocal cords
 - Pull on corniculate and arytenoid cartilages causing cartilages to pivot
 - Abduct or adduct vocal cords, depending on direction of rotation
 - Air forced between adducted vocal cords vibrates them producing high-pitched sound when cords are taut
 - Produces lower-pitched sound when cords are more slack

The Larynx

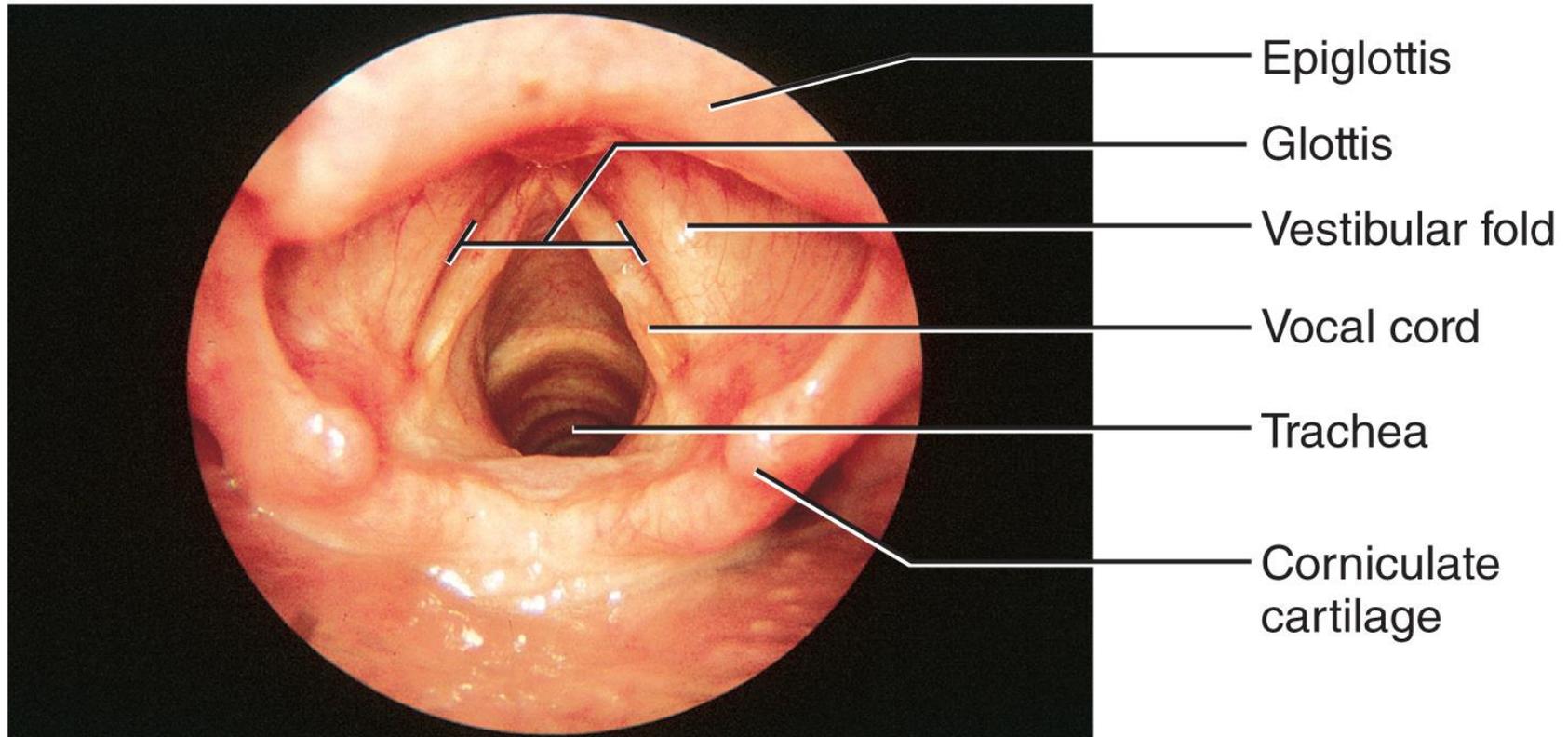
(Continued)

- Adult male vocal cords, when compared to female cords
 - Usually longer and thicker
 - Vibrate more slowly
 - Produce lower-pitched sound
- **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

Endoscopic View of the Respiratory Tract

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Anterior



Posterior

(a)

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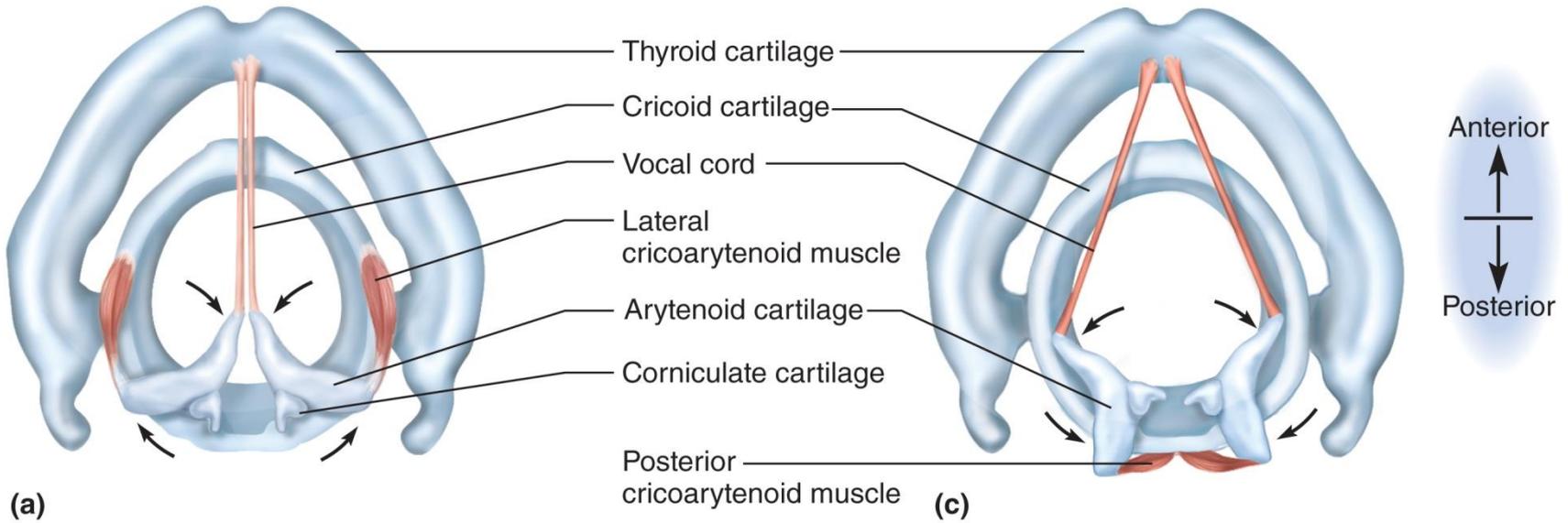
Figure 22.5a

Action of Muscles on the Vocal Cords

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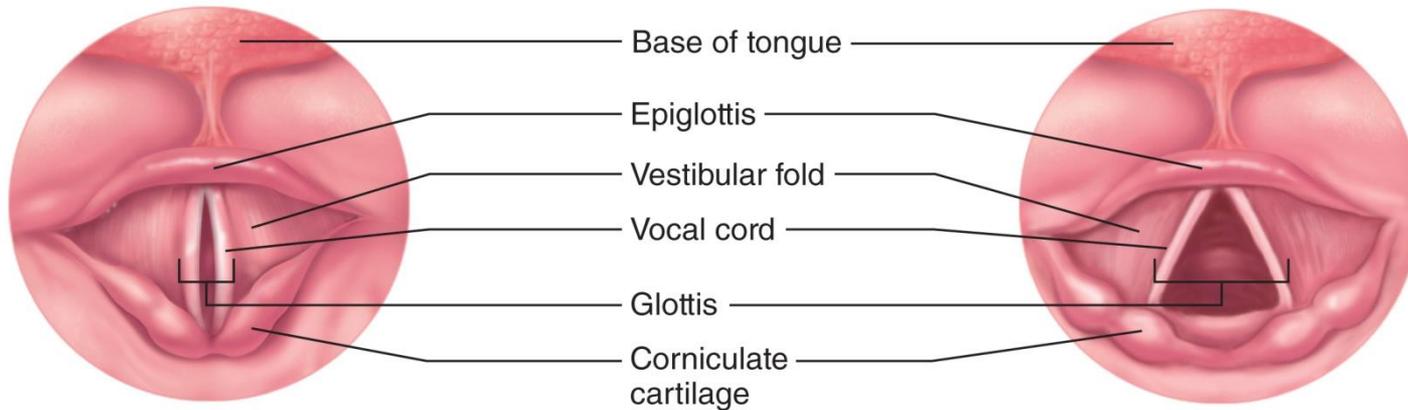
Adduction of vocal cords

Abduction of vocal cords



(a)

(c)



(b)

(d)

Figure 22.6

The Trachea

- **Trachea (windpipe)**—a rigid tube about 12 cm (4.5 in.) long and 2.5 cm (1 in.) in diameter
 - Anterior to esophagus
 - Supported by 16 to 20 **C-shaped** rings of **hyaline cartilage** that reinforce trachea and prevent collapse during inhalation
 - Opening in rings faces posteriorly toward 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 airflow

The Trachea

- Inner lining of trachea is **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
- **Middle tracheal layer—connective tissue beneath the tracheal epithelium**
 - Contains lymphatic nodules, mucous and serous glands, and the tracheal cartilages

The Trachea

- **Adventitia—outermost layer of trachea**
 - Fibrous connective tissue that blends into adventitia of other organs of mediastinum
- **Right and left main bronchi**
 - Trachea forks at level of sternal angle
 - **Carina:** internal medial ridge in the lowermost tracheal cartilage
 - Directs the airflow to the right and left

The Tracheal Epithelium

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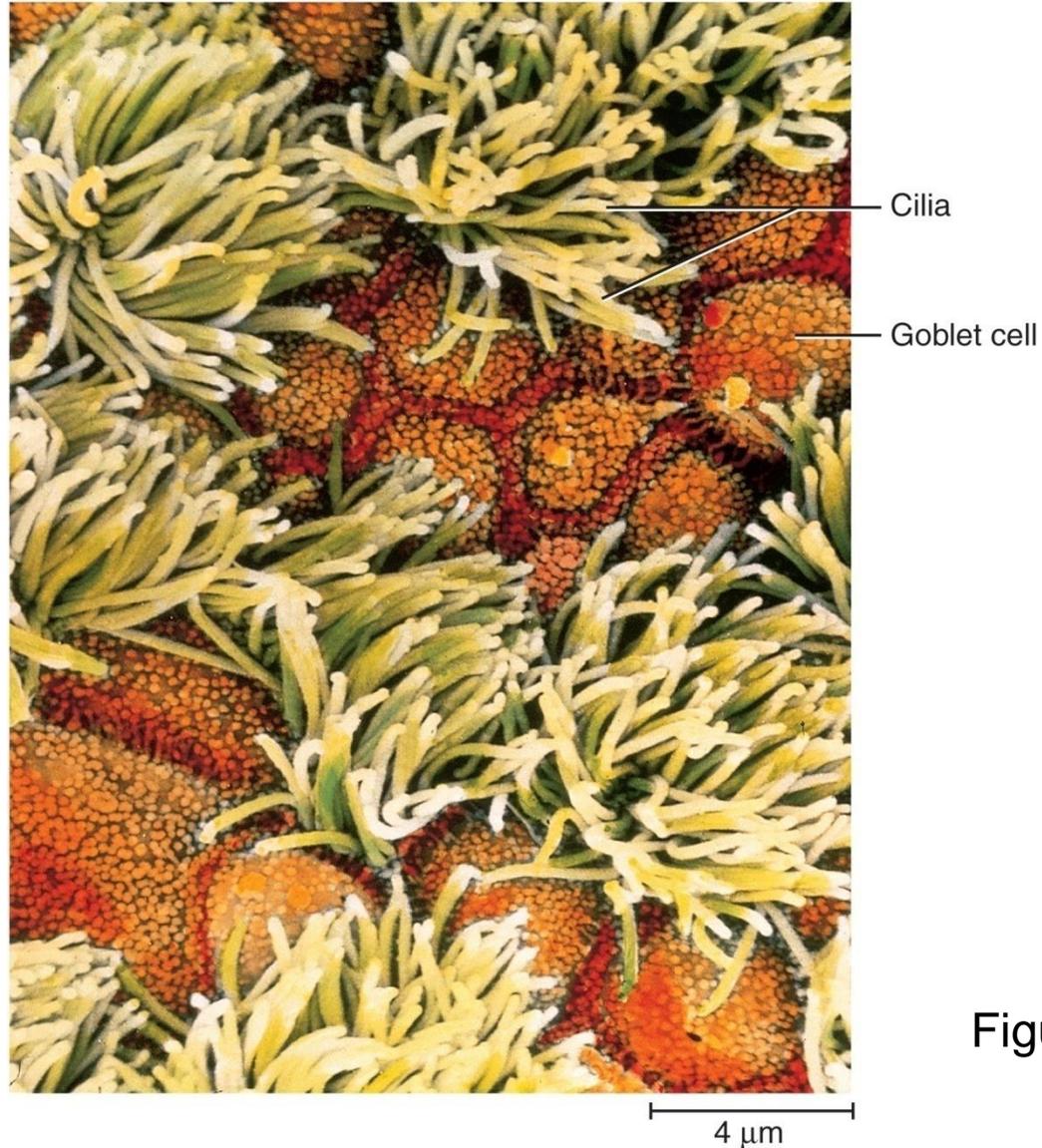


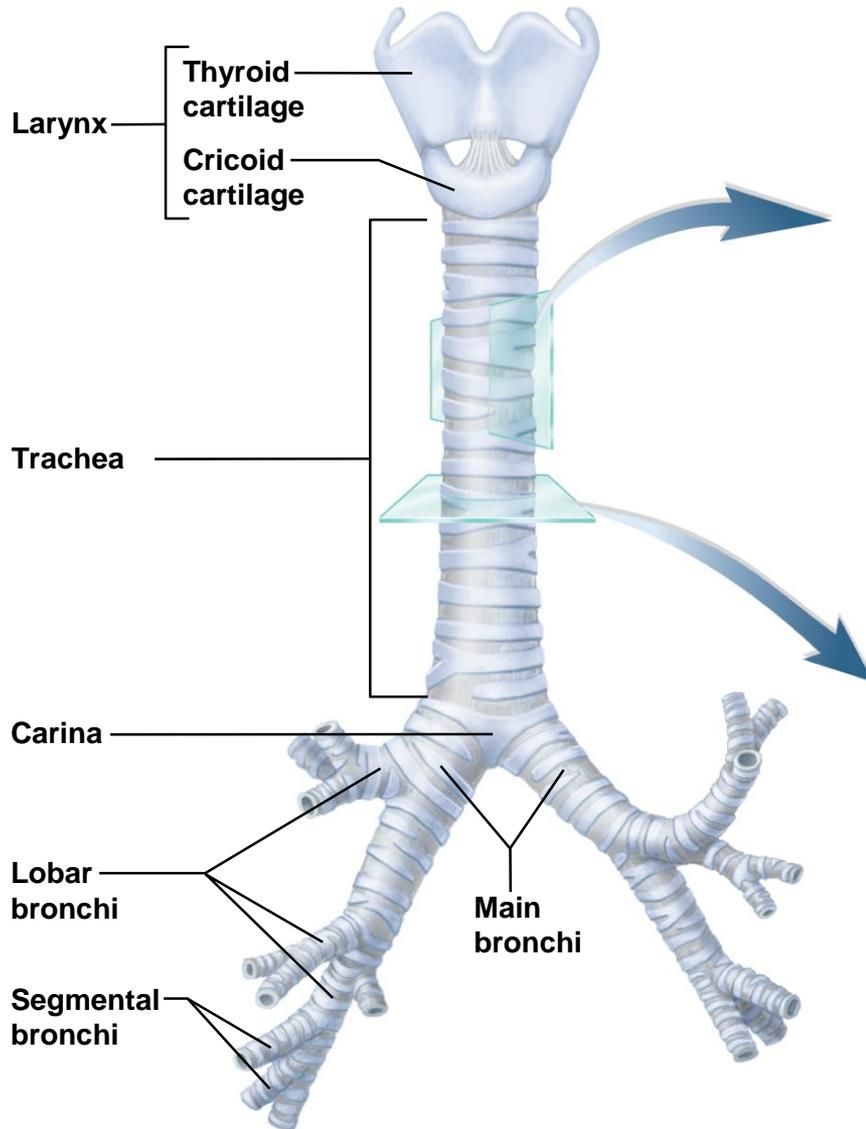
Figure 22.8

Tracheostomy

- **Tracheostomy**—to make a temporary opening in the trachea and insert a tube to allow airflow
 - Prevents asphyxiation due to upper airway obstruction
 - Inhaled air bypasses the nasal cavity and is hot humidified
 - If left for long, will dry out mucous membranes of respiratory tract
 - Become encrusted and interfere with clearance of mucus from tract, thereby promoting infection

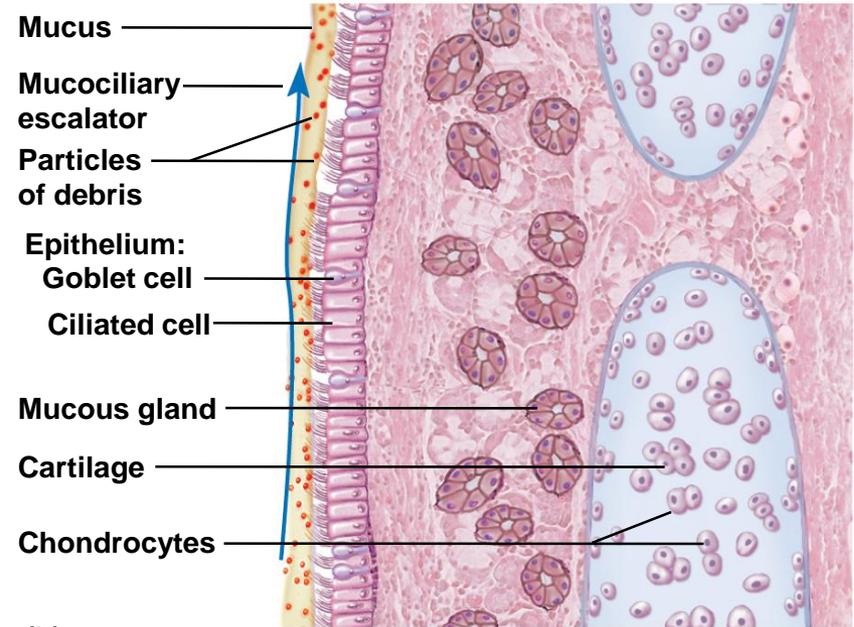
Anatomy of the Lower Respiratory Tract

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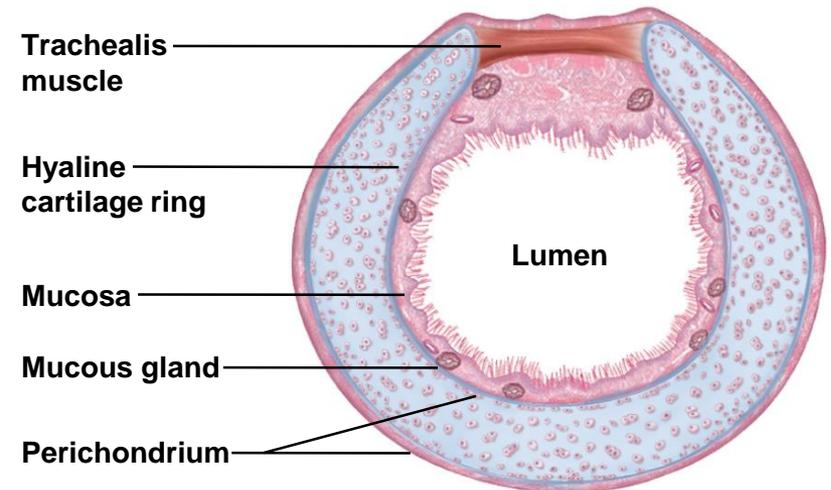


(a)

Figure 22.7a–c



(b)



(c)

Gross Anatomy of the Lungs

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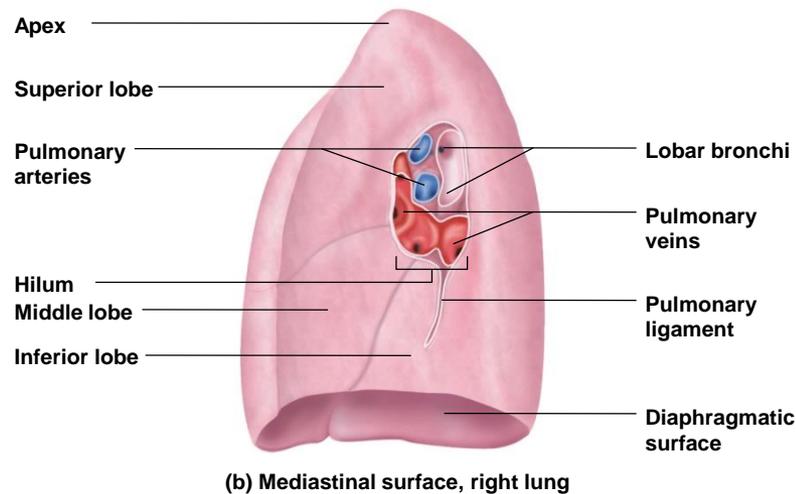
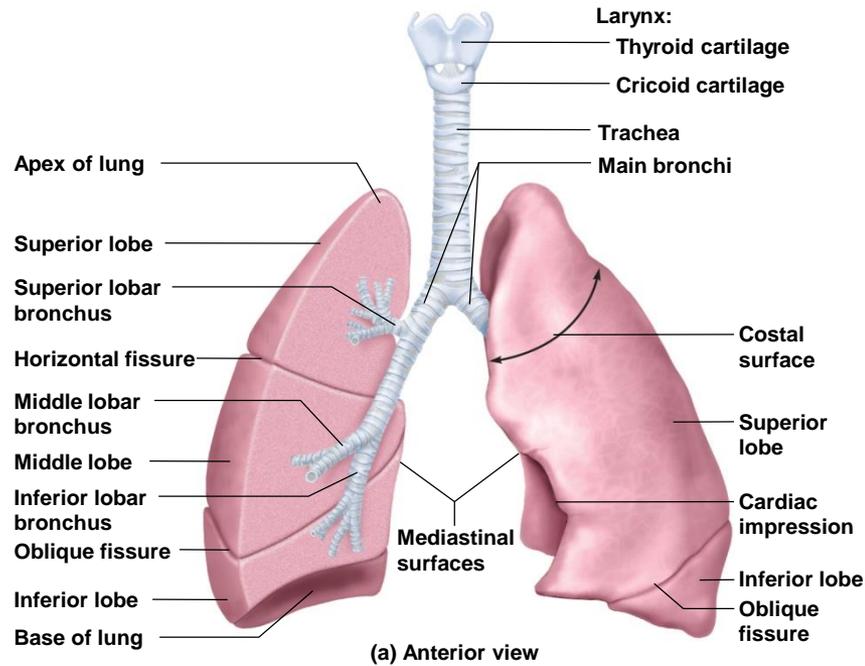
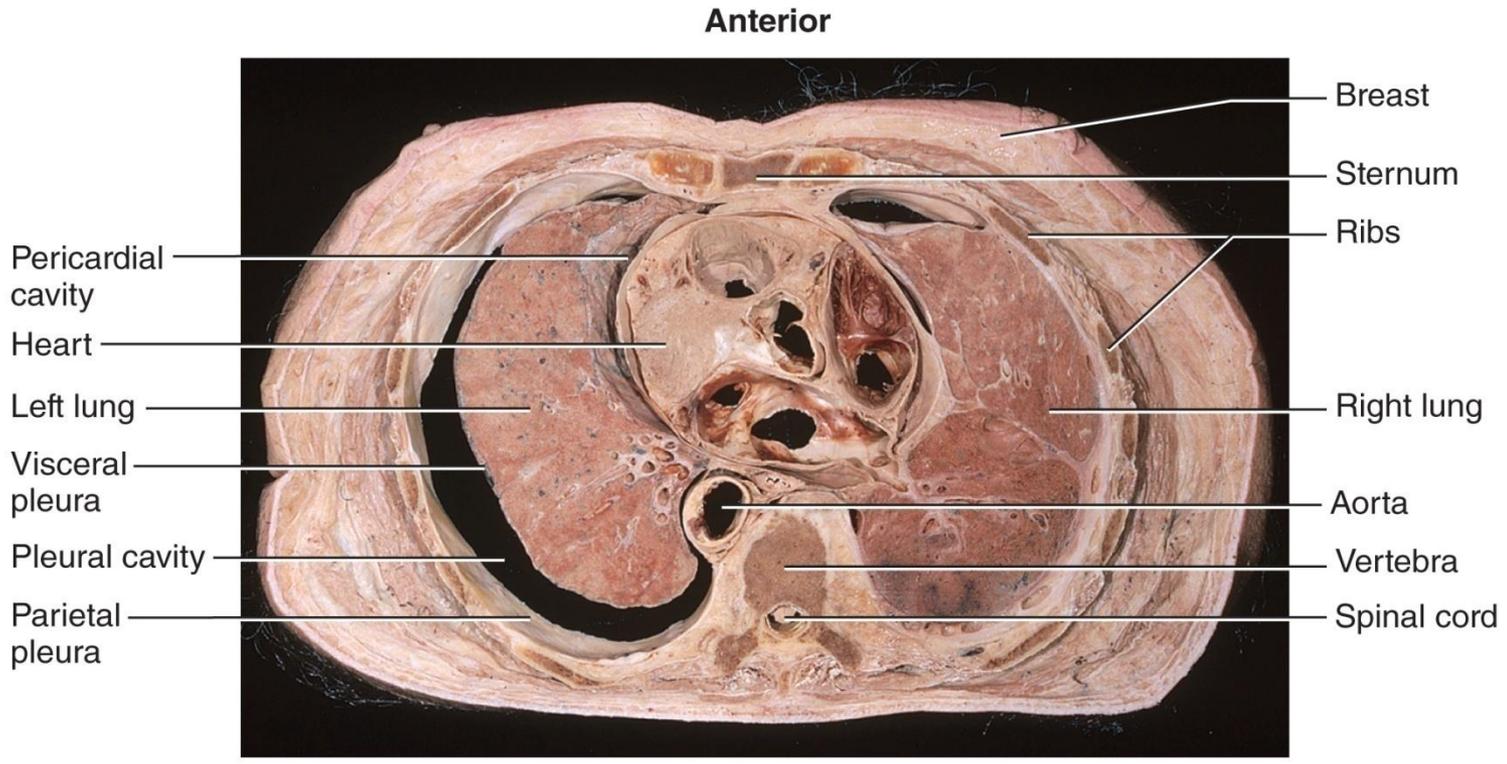
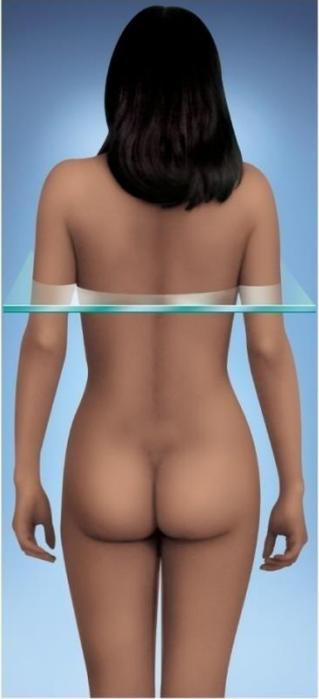


Figure 22.9a,b

Cross Section Through the Thoracic Cavity

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Figure 22.10

The Lungs and Bronchial Tree

- **Lung**
 - **Base:** broad concave portion resting on diaphragm
 - **Apex:** tip that projects just above the clavicle
 - **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
 - These structures near the hilum constitute the **root** of the lung

The Lungs and Bronchial Tree

- **Lungs are crowded by adjacent organs; they neither fill the entire ribcage, nor are they symmetrical**
 - **Right lung**
 - Shorter than left because liver rises higher on the right
 - Has **three lobes—superior, middle, and inferior—**separated by **horizontal and oblique fissure**
 - **Left lung**
 - Tall and narrow 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**

The 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
 - **Rt. main bronchus** is a branch 2 to 3 cm long, arising from fork of trachea
 - Right bronchus slightly wider and more vertical than left
 - **Aspirated (inhaled)** foreign objects lodge in the right main bronchus more often than in the left
 - **Lt. main bronchus** is about 5 cm long
 - Slightly narrower and more horizontal than the right

The Bronchial Tree

- **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, 8 on left
 - **Bronchopulmonary segment:** functionally independent unit of the lung tissue

The Bronchial Tree

- All bronchi are lined with **ciliated pseudostratified columnar epithelium**
 - Cells grow shorter and the epithelium thinner as we progress distally
 - **Lamina propria** has an abundance of mucous glands and lymphocyte nodules (**mucosa-associated lymphoid tissue, MALT**)
 - Positioned to 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

The Bronchial Tree

(Conintued)

- **Mucosa** has a well-developed layer of **smooth muscle**
 - **Muscularis mucosae** contracts or relaxes to constrict or dilate the airway, regulating airflow
- **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

The Bronchial Tree

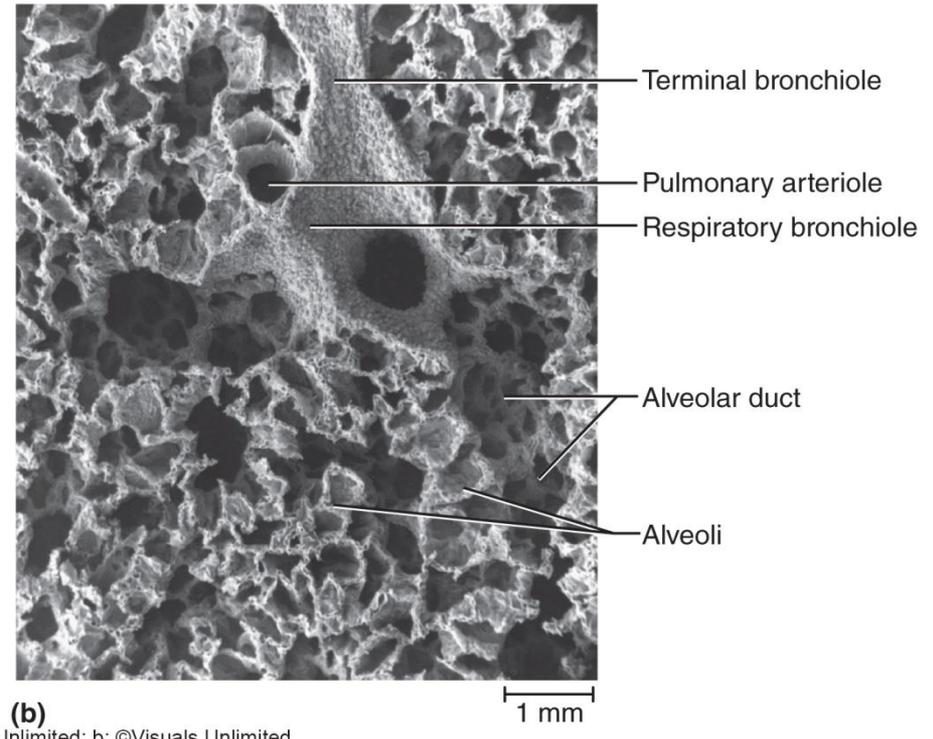
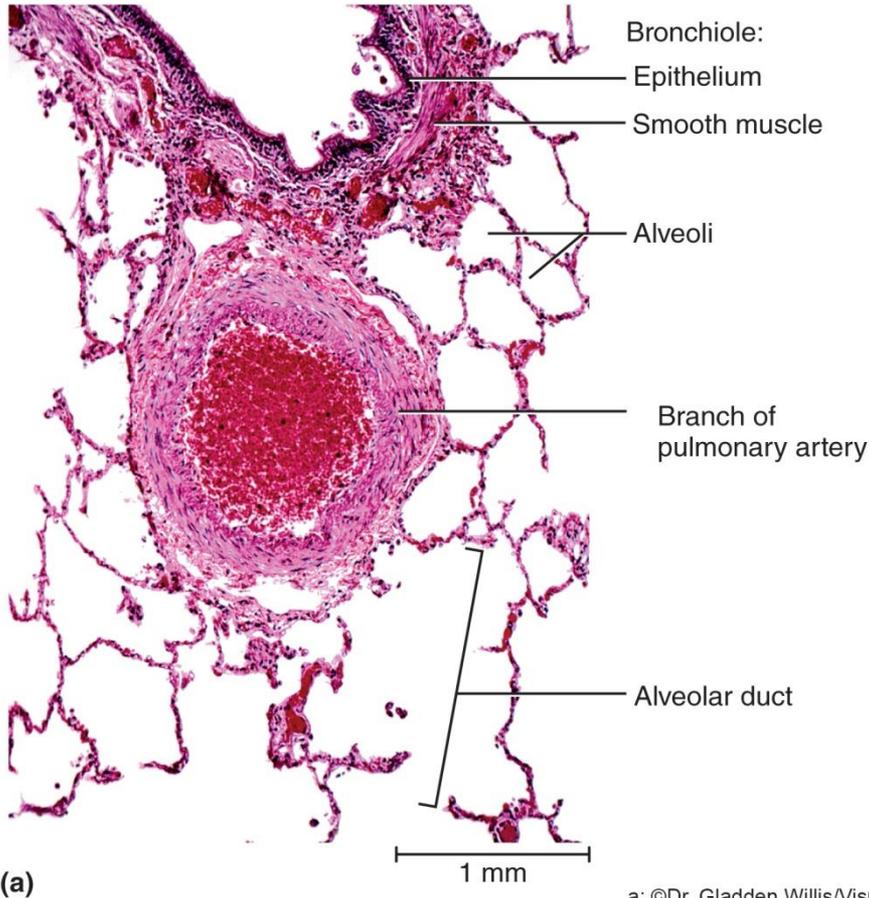
- **Bronchioles**
 - 1 mm or less in diameter
 - **Pulmonary lobule:** portion of lung ventilated by one bronchiole
 - Have ciliated cuboidal epithelium
 - Well-developed layer of smooth muscle
 - Divides into 50 to 80 **terminal bronchioles**
 - **Final branches of conducting division**
 - Measure 0.5 mm or less in diameter
 - Have no mucous glands or goblet cells
 - Have cilia that move mucus draining into them back by mucociliary escalator
 - Each terminal bronchiole gives off two or more smaller respiratory bronchioles

The Bronchial Tree

- **Respiratory bronchioles**
 - Have alveoli budding from their walls
 - Considered the **beginning of the respiratory division** since alveoli participate in gas exchange
 - Divide into 2 to 10 **alveolar ducts**
 - End in **alveolar sacs**: clusters of alveoli arrayed around a central space called the **atrium**

Histology of the Lung

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Figure 22.11a,b

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

Alveoli

Cells of the alveolus (Continued)

– **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 during exhalation

Alveoli

Cells of the alveolus (Continued)

– Alveolar macrophages (dust cells)

- Most numerous of all cells in the lung
- Wander the lumens of alveoli and the connective tissue between them
- Keep alveoli free from debris by phagocytizing dust particles
- 100 million dust cells die each day as they ride up the mucociliary escalator to be swallowed and digested with their load of debris

Pulmonary Alveoli

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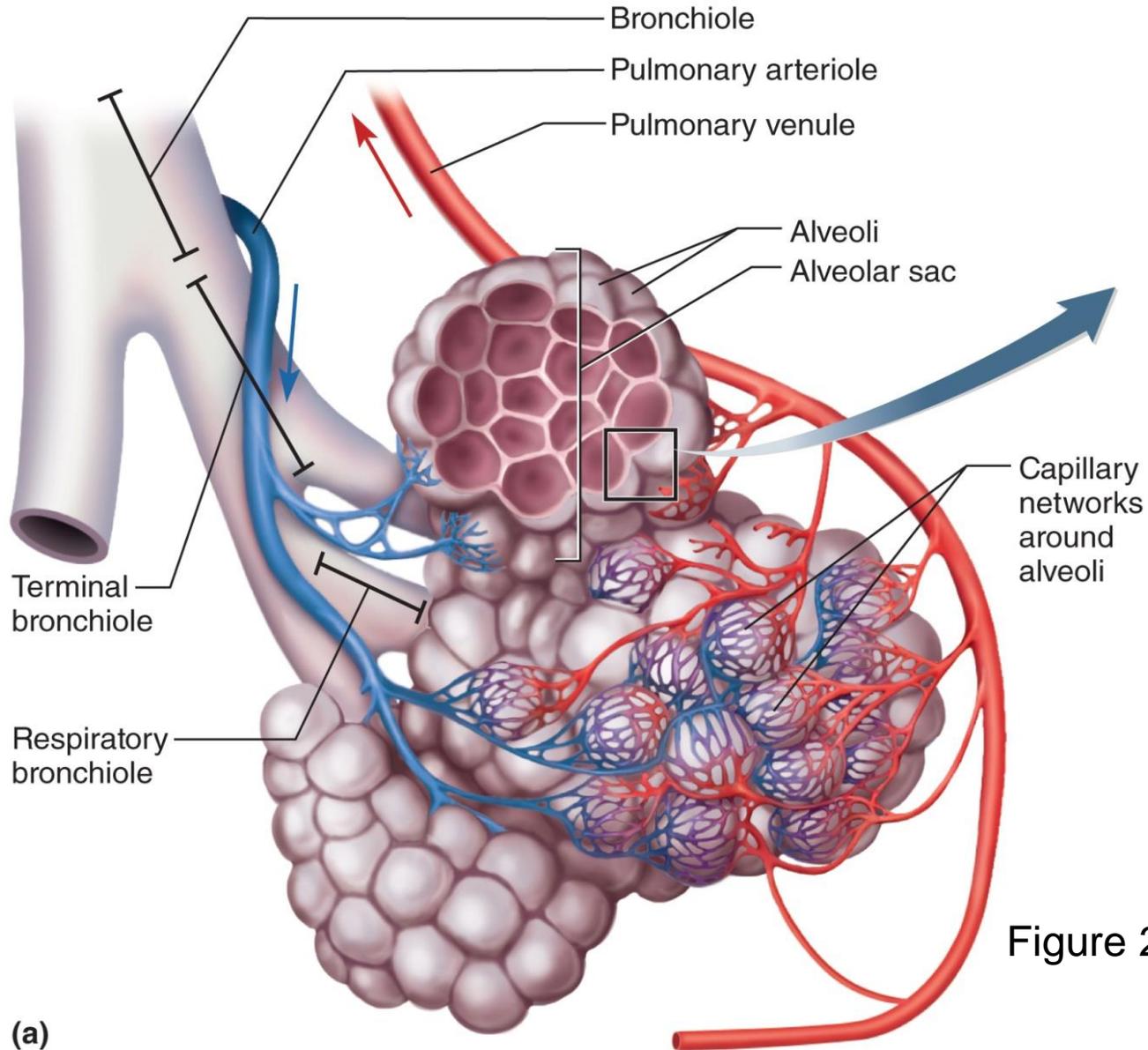


Figure 22.12a

(a)

Alveoli

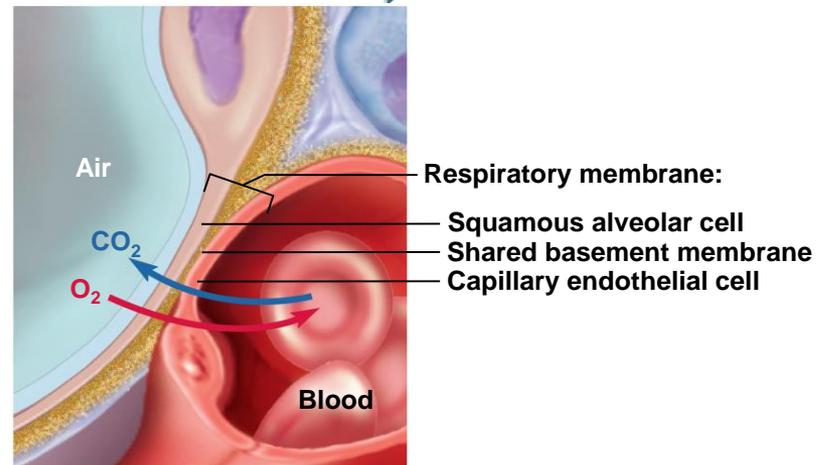
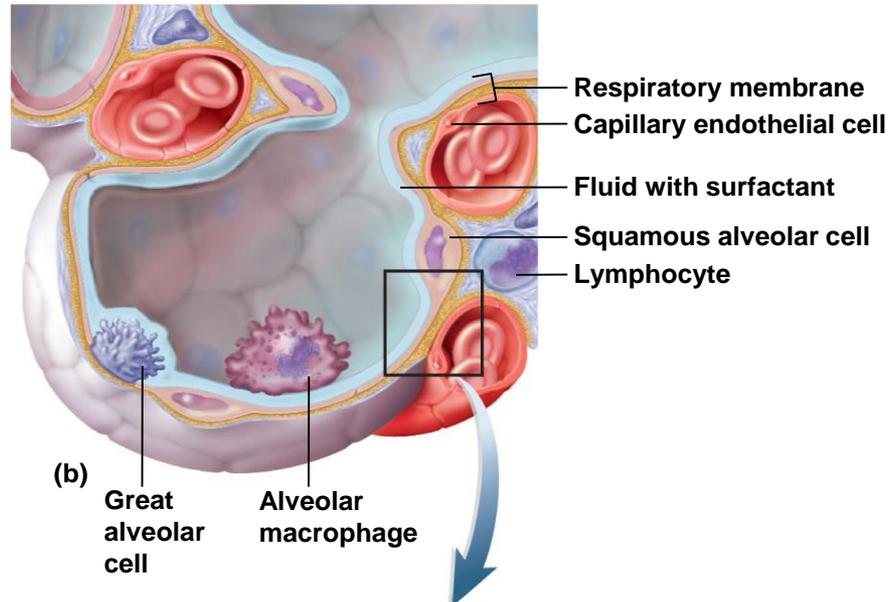
- Each alveolus surrounded by a basket of capillaries supplied by the **pulmonary artery**
- **Respiratory membrane**—thin barrier between the alveolar air and blood
- **Respiratory membrane consists of:**
 - Squamous alveolar cells
 - Endothelial cells of blood capillary
 - Their shared basement membrane

Alveoli

- **Important to prevent fluid from accumulating in alveoli**
 - Gases diffuse too slowly through liquid to sufficiently aerate the blood
 - Alveoli are kept dry by absorption of excess liquid by blood capillaries
 - Lungs have a more extensive lymphatic drainage than any other organ in the body
 - Low capillary blood pressure also prevents rupture of the delicate respiratory membrane

Pulmonary Alveoli

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(c)

Figure 22.12b,c

The Pleurae

- **Visceral pleura**—serous membrane that covers lungs
- **Parietal pleura**—adheres to mediastinum, inner surface of the rib cage, and superior surface of the diaphragm
- **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; assists lung inflation
 - **Compartmentalization**
 - Prevents spread of infection from one organ in mediastinum to others

Pulmonary Ventilation

- **Expected Learning Outcomes**

- Name the muscles of respiration and describe their roles.
- Describe brainstem centers that control breathing and the inputs they receive from other parts of the nervous system.
- Explain how pressure gradients account for flow of air into and out of lungs, and how those gradients are produced.
- Identify the sources of resistance to airflow and discuss their relevance to respiration.
- Explain the significance of anatomical dead space to alveolar ventilation.
- Define clinical measurements of pulmonary volume and capacity.
- Define terms for deviations from the normal pattern of breathing.

Pulmonary Ventilation

- **Breathing (pulmonary ventilation)**—consists of a repetitive cycle of **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 within lungs and outside body
- **Respiratory muscles** change lung volumes and create differences in pressure relative to the atmosphere

The Respiratory Muscles

- **Diaphragm**
 - Prime mover of respiration
 - Contraction flattens diaphragm, 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

The Respiratory Muscles

- **Internal and external intercostal muscles**
 - Synergists to diaphragm
 - Located between ribs
 - Stiffen the thoracic cage during respiration
 - Prevent it from caving inward when diaphragm descends
 - Contribute to enlargement and contraction of thoracic cage
 - Add about one-third of the air that ventilates the lungs
- **Scalenes**
 - Synergist to diaphragm
 - Fix or elevate ribs 1 and 2

The Respiratory Muscles

- **Accessory muscles** of respiration act mainly in **forced respiration**
- **Forced inspiration**
 - Erector spinae, sternocleidomastoid, pectoralis major, pectoralis minor, and serratus anterior muscles and scalenes
 - Greatly increase thoracic volume

The Respiratory Muscles

- **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 airflow out of the lungs

- **Forced expiration**

- Rectus abdominis, internal intercostals, and other lumbar, abdominal, and pelvic muscles
- Greatly increased abdominal pressure pushes viscera up against diaphragm increasing thoracic pressure, forcing air out
- Important for “abdominal breathing”

The 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 push organ contents out
 - Childbirth, urination, defecation, vomiting

The Respiratory Muscles

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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 stimulation of skeletal muscles from brain and will cease if spinal cord is severed high in neck**
 - Skeletal muscles require nervous stimulation
 - Interaction of multiple respiratory muscles requires coordination

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
 - In quiet breathing (eupnea), inspiratory neurons fire for about 2 seconds
 - Expiratory neurons in eupnea fire for about 3 seconds allowing inspiratory muscles to relax
 - Produces a respiratory rhythm of 12 breaths per minute
 - **Dorsal respiratory group (DRG)**
 - Modifies the rate and depth of breathing
 - Receives influences from external sources

Brainstem Respiratory Centers

- **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

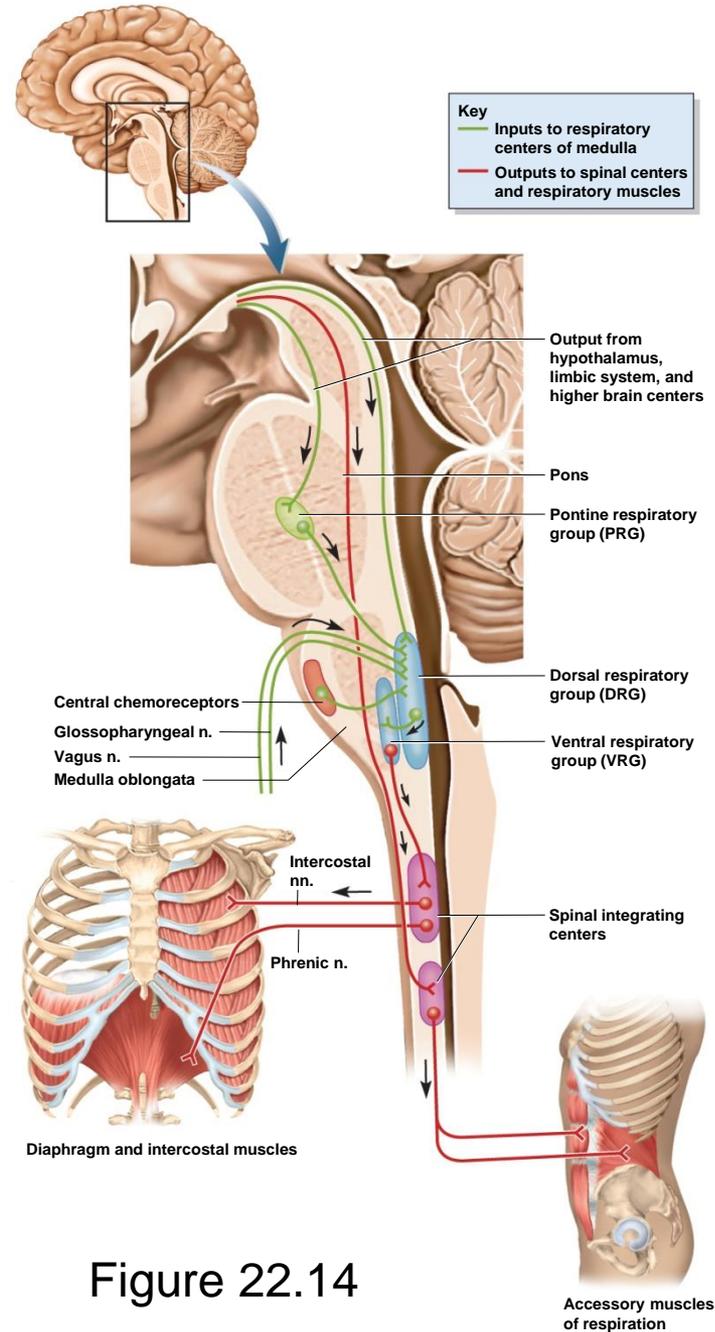


Figure 22.14

Central and Peripheral Input to the Respiratory Centers

- **Hyperventilation**—anxiety-triggered state in which breathing is so rapid that it expels CO_2 from the body faster than it is produced
 - As blood CO_2 levels drop, the pH rises causing the cerebral arteries to constrict
 - This reduces cerebral perfusion which may cause dizziness or fainting
 - Can be brought under control by having the person rebreathe the expired CO_2 from a paper bag

Central and Peripheral Input to the Respiratory Centers

- **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 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 the 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 and stops inspiration

Central and Peripheral Input to the Respiratory Centers

- **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

The Peripheral Chemoreceptors

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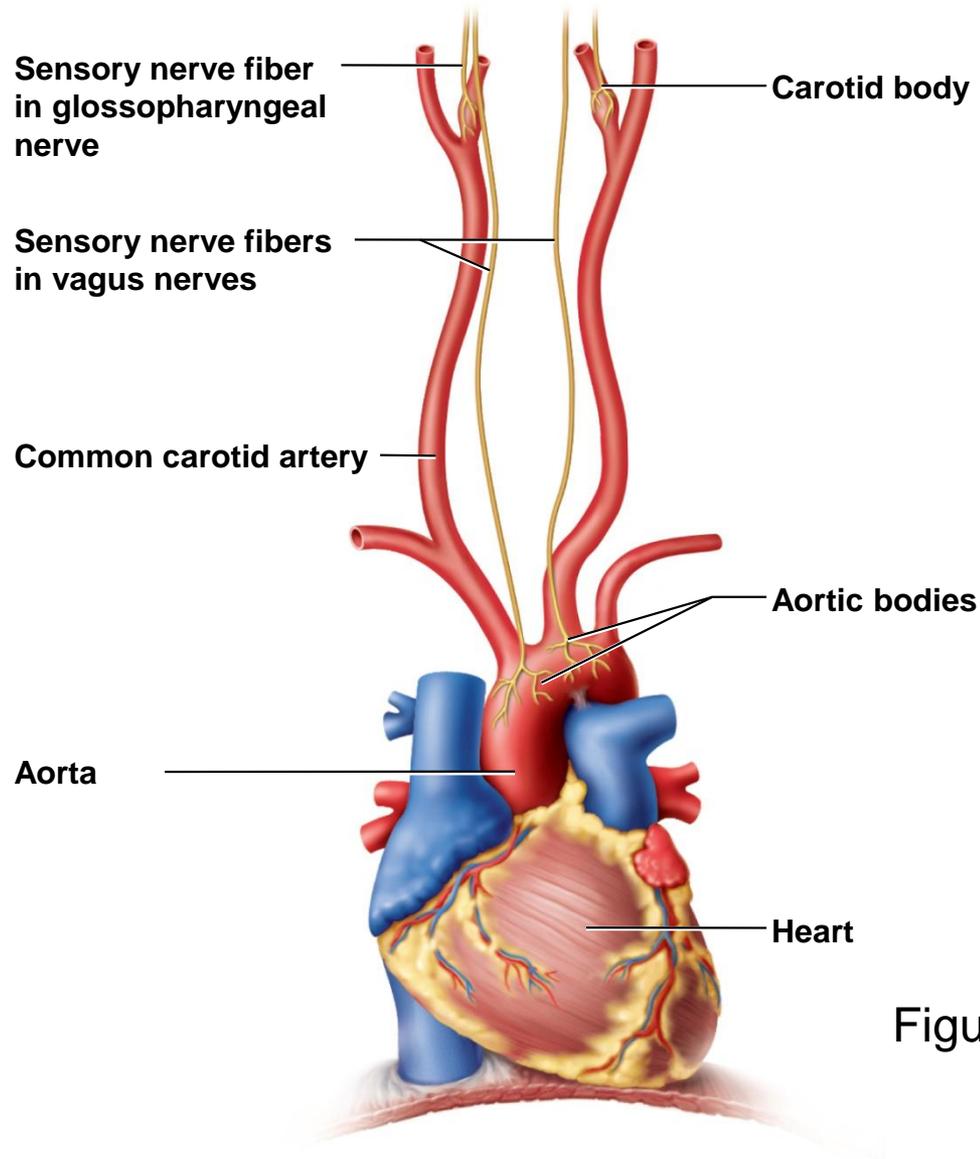


Figure 22.15

Voluntary Control of Breathing

- Voluntary control over breathing originates in the **motor cortex of frontal lobe of the cerebrum**
 - Sends impulses down corticospinal tracts to respiratory neurons in spinal cord, bypassing brainstem
- **Limits to voluntary control**
 - **Breaking point:** when CO₂ levels rise to a point where automatic controls override one's will

Pressure, Resistance, 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, or **1 atmosphere (1 atm)**
 - Lower at higher elevations

Pressure, Resistance, and Airflow

- **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, air moves into the lungs
 - If the lung volume decreases, intrapulmonary pressure rises
 - If the pressure rises above atmospheric pressure, air moves out of the lungs

Pressure, Resistance, and Airflow

- **The unit for pressure used by respiratory physiologists is cm H₂O**
 - This measures how far a column of water would be moved by a given pressure
 - This is more sensitive than mm Hg, since Hg (mercury) is a heavy liquid
 - 1 mm Hg is equal to about 1.4 cm H₂O

Inspiration

- **Intrapleural pressure**—the slightly negative pressure that exists between the two pleural layers
 - Recoil of lung tissue and tissues of thoracic cage causes lungs and chest wall to be pulling in opposite directions
 - The small space between the parietal and visceral pleura is filled with watery fluid, and so these layers stay together
 - About -5 cm H₂O of intrapleural pressure results

Inspiration

- The **two pleural layers** cling together due to the cohesion of water
 - 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

Inspiration

- **Another force that expands the lungs is explained by Charles's law**
- **Charles's law**—volume 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

Inspiration

- 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

The Respiratory Cycle

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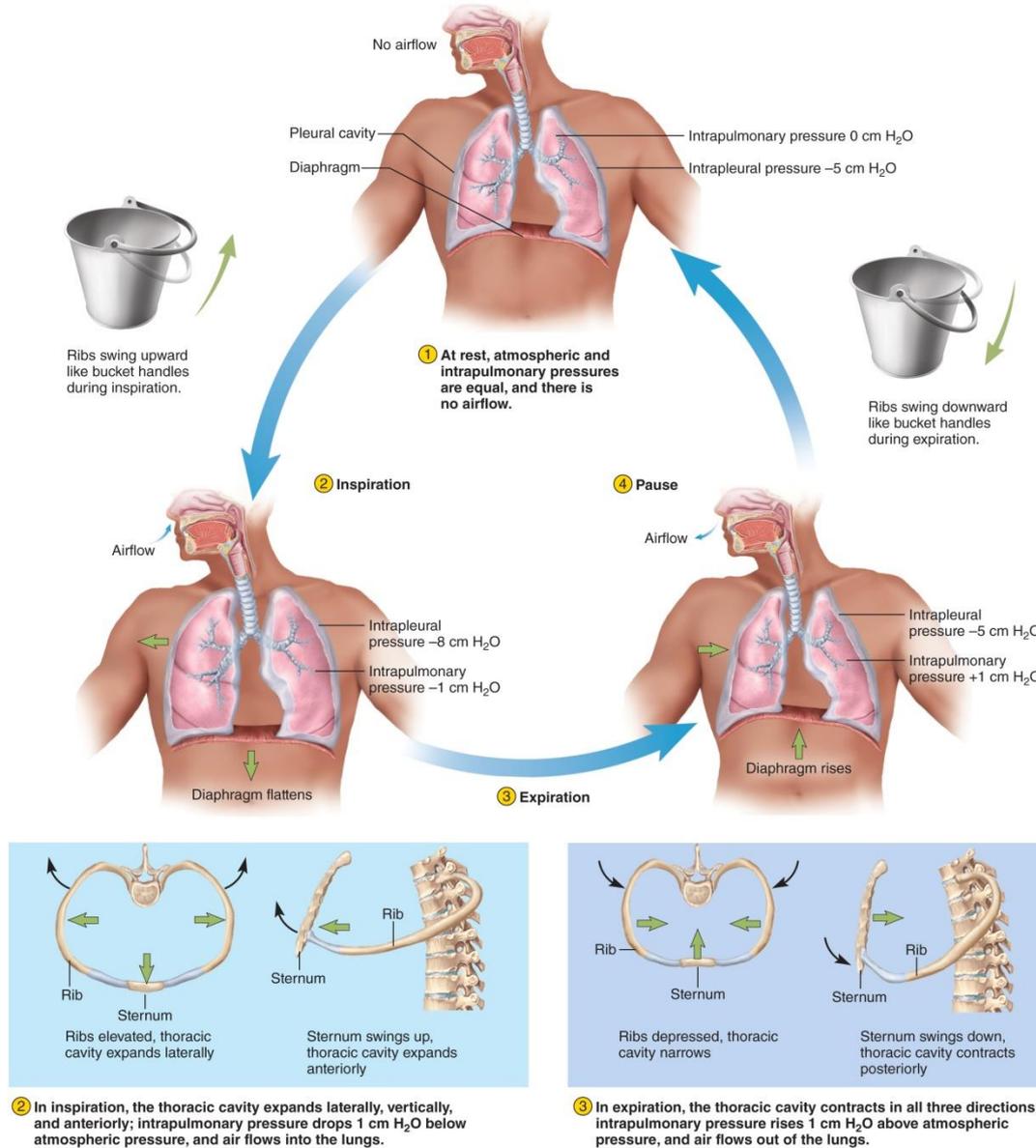


Figure 22.16

Expiration

- **Relaxed breathing**

- Passive process achieved mainly by elastic recoil of thoracic cage
- Recoil compresses the lungs
- Volume of thoracic cavity decreases
- Raises intrapulmonary pressure to about 1 cm H₂O
- Air flows down the pressure gradient and out of the lungs

- **Forced breathing**

- Accessory muscles raise intrapulmonary pressure as high as +40 cm H₂O

Expiration

- **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 as blood absorbs gases from blood

Resistance to Airflow

- Increasing **resistance** decreases airflow
- **Two factors influence airway resistance: bronchiole diameter and pulmonary compliance**
 - **Diameter of the bronchioles**
 - **Bronchodilation**—increase in diameter of a bronchus or bronchiole
 - Epinephrine and sympathetic stimulation stimulate dilation
 - Increased airflow
 - **Bronchoconstriction**—decrease in diameter of a bronchus or bronchiole
 - Histamine, parasympathetic nerves, cold air, and chemical irritants stimulate bronchoconstriction
 - Decreases airflow
 - Suffocation can occur from extreme bronchoconstriction brought about by anaphylactic shock and asthma

Resistance to Airflow

- **Two factors influencing airway resistance (Continued)**
 - **Pulmonary compliance:** ease with which the lungs can expand
 - The change in lung volume relative to a given pressure change
 - Compliance is reduced by degenerative lung diseases in which the lungs are stiffened by scar tissue
 - Compliance is limited by the surface tension of the water film inside alveoli
 - **Surfactant** secreted by great cells of alveoli disrupts hydrogen bonds between water molecules and thus reduces the surface tension
 - Infant respiratory distress syndrome (IRDS)—premature babies lacking surfactant are treated with artificial surfactant until they can make their own

Alveolar Ventilation

- **Only air that enters alveoli is available for gas exchange**
- **Not all inhaled air gets there—about 150 mL fills the conducting division of the airway**
- **Anatomic dead space**
 - Conducting division of airway where there is no gas exchange
 - Can be altered somewhat by sympathetic and parasympathetic stimulation
 - Sympathetic dilation increases dead space but allows greater flow
- **In pulmonary diseases, some alveoli may be unable to exchange gases**
 - **Physiologic (total) dead space**—sum of anatomic dead space and any pathological alveolar dead space

Alveolar Ventilation

- **If a person inhales 500 mL of air, and 150 mL stays in anatomical dead space, then 350 mL reaches alveoli**
- **Alveolar ventilation rate (AVR)**
 - Air that ventilates alveoli (350 mL) X respiratory rate (12 bpm) = 4,200 mL/min.
 - This measurement is crucially relevant to the body's ability to get oxygen to the tissues and dispose of carbon dioxide
- **Residual volume**—1,300 mL that cannot be exhaled with maximum effort

Spirometry—The Measurement of Pulmonary Ventilation

- **Spirometer**—a device that recaptures expired breath and records such variables 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 of breathing (500 mL)
 - **Inspiratory reserve volume:** air in excess of tidal volume that can be inhaled with maximum effort (3,000 mL)
 - **Expiratory reserve volume:** air in excess of tidal volume that can be exhaled with maximum effort (1,200 mL)

Respiratory Volumes and Capacities

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(a)

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Figure 22.17a

Respiratory Volumes and Capacities

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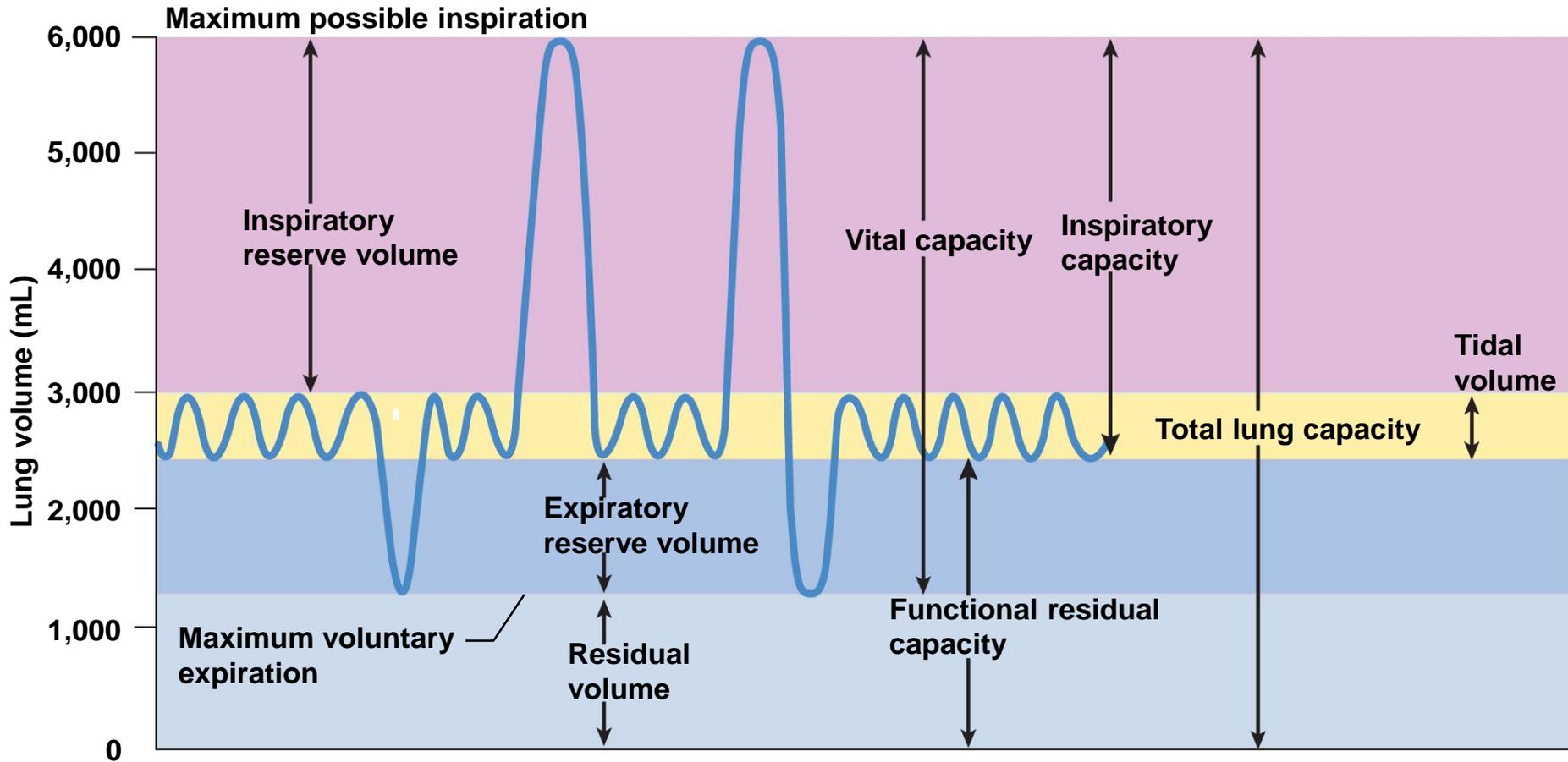


Figure 22.17b

Spirometry—The Measurement of Pulmonary Ventilation

(Continued)

- **Residual volume:** air remaining in lungs after maximum expiration (1,300 mL)
 - Allows some gas exchange with blood before next breath of fresh air arrives
- **Vital capacity:** total amount of air that can be inhaled and then exhaled with maximum effort
 - $VC = ERV + TV + IRV$ (4,700 mL)
 - Important measure of pulmonary health
- **Inspiratory capacity:** maximum amount of air that can be inhaled after a normal tidal expiration
 - $IC = TV + IRV$ (3,500 mL)

Spirometry—The Measurement of Pulmonary Ventilation

(Continued)

- **Functional residual capacity:** amount of air remaining in lungs after a normal tidal expiration
 - $FRC = RV + ERV$ (2,500 mL)
- **Total lung capacity:** maximum amount of air the lungs can contain
 - $TLC = RV + VC$ (6,000 mL)

Spirometry—The Measurement of Pulmonary Ventilation

- **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 disease, tuberculosis

Spirometry—The Measurement of Pulmonary Ventilation

- **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

Spirometry—The Measurement of Pulmonary Ventilation

- **Forced expiratory volume (FEV)**
 - Percentage of the vital capacity that can be exhaled in a given time interval
 - Healthy adult reading is 75% to 85% in 1 second
- **Peak flow**
 - Maximum speed of expiration
 - Blowing into a handheld meter
- **Minute respiratory volume (MRV)**
 - Amount of air inhaled per minute
 - $TV \times \text{respiratory rate}$ (at rest $500 \times 12 = 6,000 \text{ mL/min.}$)
- **Maximum voluntary ventilation (MVV)**
 - MRV during heavy exercise
 - May be as high as 125 to 170 L/min

Variations in the Respiratory Rhythm

- **Eupnea**—relaxed, quiet breathing
 - Characterized by tidal volume 500 mL and the respiratory rate of 12 to 15 bpm
- **Apnea**—temporary cessation of breathing
- **Dyspnea**—labored, gasping breathing; shortness of breath
- **Hyperpnea**—increased rate and depth of breathing in response to exercise, pain, or other conditions
- **Hyperventilation**—increased pulmonary ventilation in excess of metabolic demand

Variations in the Respiratory Rhythm

- **Hypoventilation**—reduced pulmonary ventilation leading to an increase in blood CO₂
- **Kussmaul respiration**—deep, rapid breathing often induced by acidosis
- **Orthopnea**—dyspnea that occurs when person is lying down
- **Respiratory arrest**—permanent cessation of breathing
- **Tachypnea**—accelerated respiration

Gas Exchange and Transport

- **Expected Learning Outcomes**

- Define *partial pressure* and discuss its relationship to a gas mixture such as air.
- Contrast the composition of inspired and alveolar air.
- Discuss how partial pressure affects gas transport by the blood.
- Describe the mechanism of transporting O₂ and CO₂.
- Describe the factors that govern gas exchange in the lungs and systemic capillaries.
- Explain how gas exchange is adjusted to the metabolic needs of different tissues.
- Discuss the effect of blood gases and pH on the respiratory rhythm.

Composition of Air

- **Composition of air**

- 78.6% nitrogen, 20.9% oxygen, 0.04% carbon dioxide, 0% to 4% water vapor, depending on temperature and humidity, and minor gases argon, neon, helium, methane, and ozone

Composition of Air

- **Dalton's law**—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 mm Hg
 - 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 Air

- **Composition of inspired and alveolar air differs because of three influences**
 - Air is **humidified** by contact with mucous membranes
 - Alveolar P_{H_2O} is more than 10 times higher than inhaled air
 - Air in alveoli **mixes with residual air** left from previous respiratory cycle
 - Oxygen gets diluted and air is enriched with CO_2
 - Alveolar air **exchanges O_2 and CO_2 with blood**
 - PO_2 of alveolar air is about 65% that of inspired air
 - PCO_2 is more than 130 times higher

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TABLE 22.4		Composition of Inspired (Atmospheric) and Alveolar Air		
Gas	Inspired Air*		Alveolar Air	
N_2	78.6%	597 mm Hg	74.9%	569 mm Hg
O_2	20.9%	159 mm Hg	13.7%	104 mm Hg
H_2O	0.5%	3.7 mm Hg	6.2%	47 mm Hg
CO_2	0.04%	0.3 mm Hg	5.3%	40 mm Hg
Total	100%	760 mm Hg	100%	760 mm Hg

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

Alveolar Gas Exchange

- **Alveolar gas exchange**—the swapping of O_2 and CO_2 across the respiratory membrane
 - 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, and pass through the respiratory membrane separating the air from the bloodstream
 - **For carbon dioxide to leave the blood** it must pass the other way, and then diffuse out of the water film into the alveolar air

Alveolar Gas Exchange

- **Gases diffuse down their own gradients until the partial pressure of each gas in the air is equal to its partial pressure in water**
- **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 PO_2 in the alveolar air, the more O_2 the blood picks up
 - Since blood arriving at an alveolus has a higher PCO_2 than air, it releases CO_2 into the air

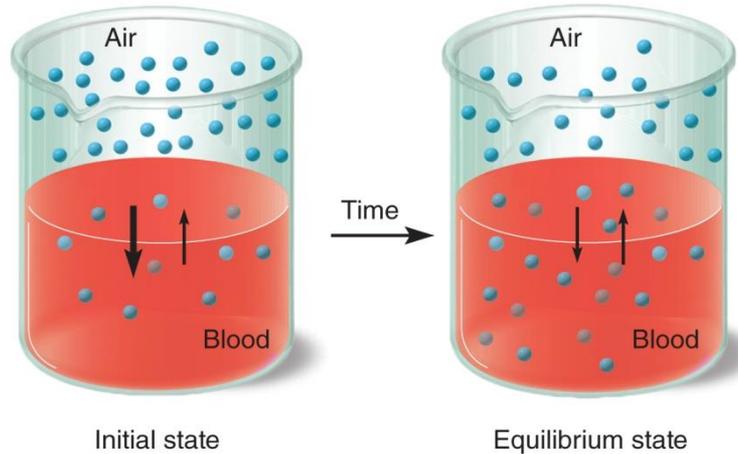
Alveolar Gas Exchange

Henry's Law (Continued)

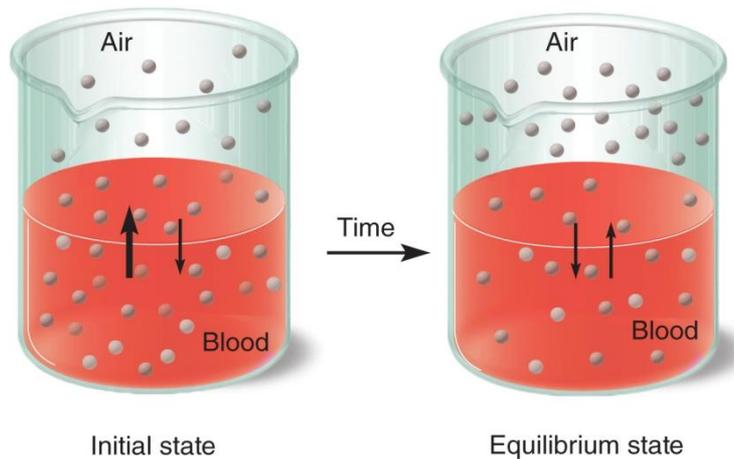
- At the alveolus, the blood is said to **unload** CO₂ and **load** O₂
 - Unloading CO₂ and loading O₂ involves erythrocytes
 - Efficiency depends on how long an RBC stays in alveolar capillaries
 - 0.25 second necessary to reach equilibrium
 - At rest, RBC spends 0.75 second in alveolar capillaries
 - In strenuous exercise, 0.3 second, 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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(a) Oxygen



(b) Carbon dioxide

Figure 22.18

Alveolar Gas Exchange

- **Pressure gradient of the gases**
 - Normally:
 - $PO_2 = 104$ mm Hg in alveolar air versus 40 mm Hg in blood
 - $PCO_2 = 46$ mm Hg in blood arriving versus 40 mm Hg in alveolar air
 - **Hyperbaric oxygen therapy:** treatment with oxygen at greater than 1 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

Changes in Gases

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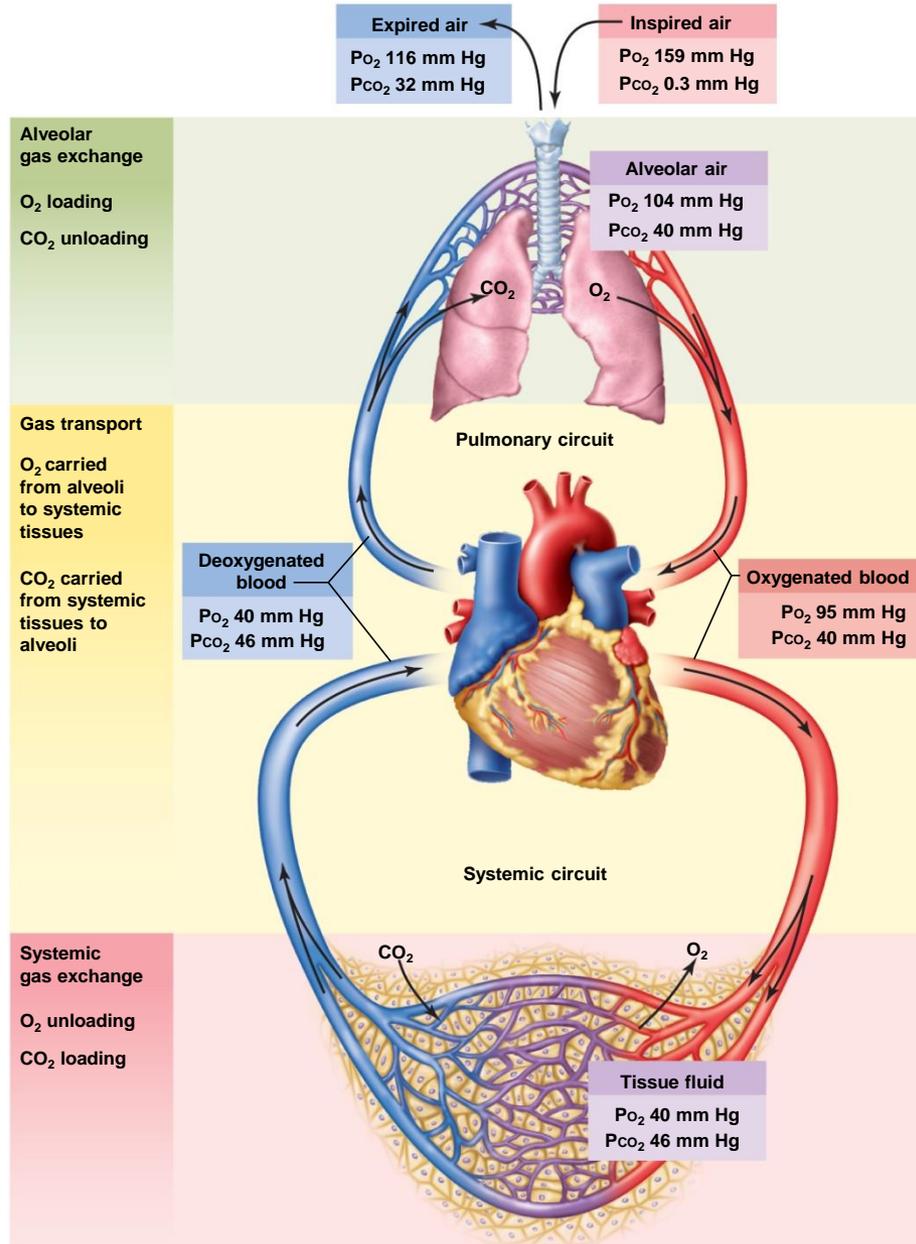


Figure 22.19

Oxygen Loading in Relation to Partial Pressure Gradient

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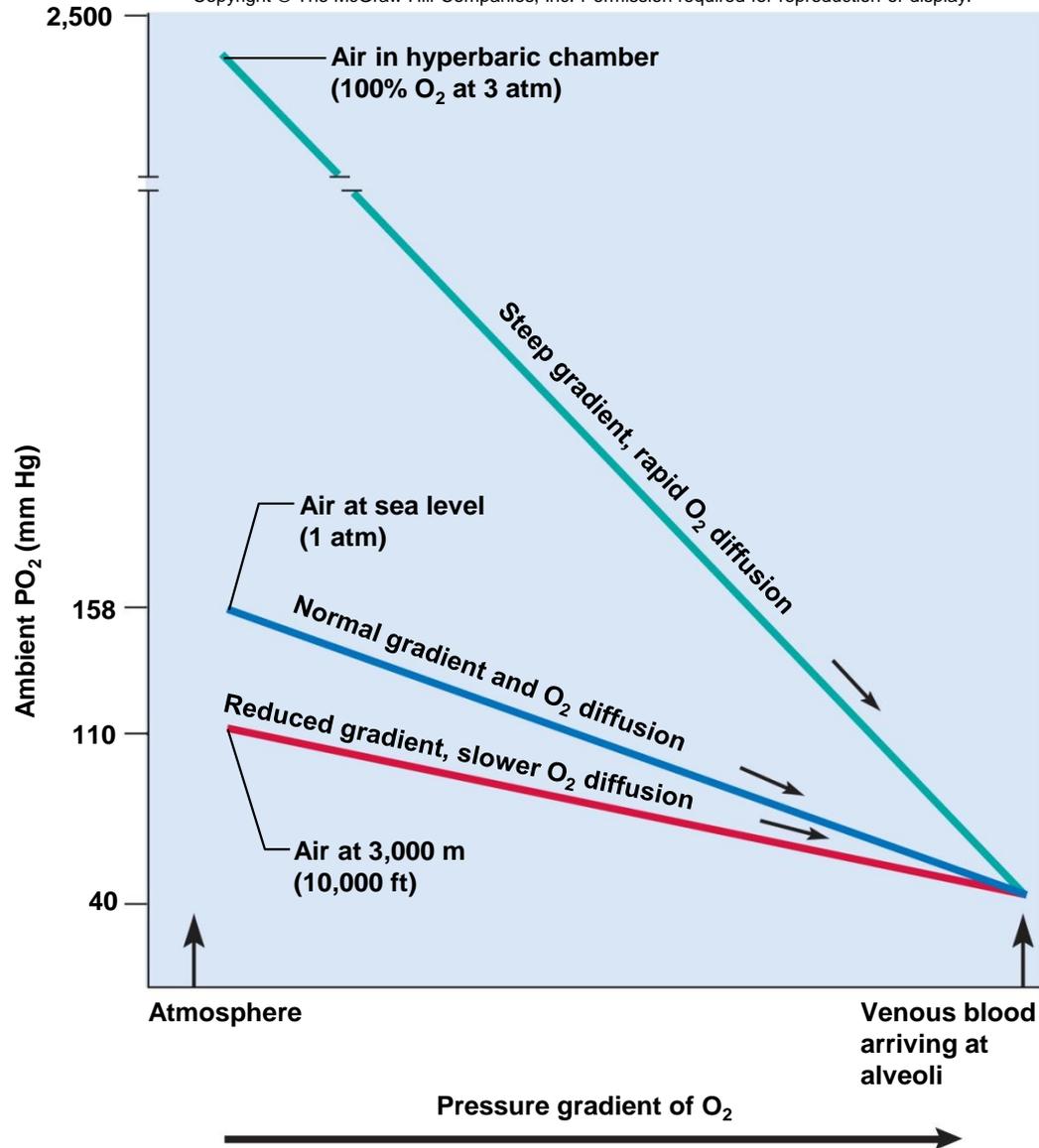


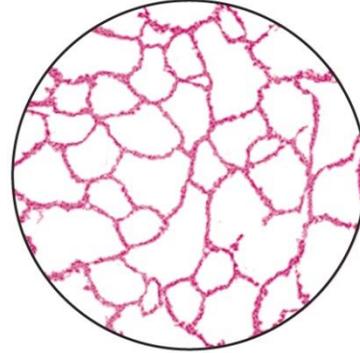
Figure 22.20

Alveolar Gas Exchange

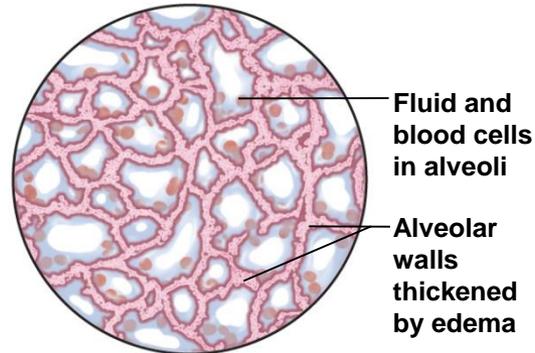
- **Solubility of the gases**
 - CO₂ is 20 times as soluble as O₂
 - Equal amounts of O₂ and CO₂ are exchanged across the respiratory membrane because CO₂ is much more soluble and diffuses more rapidly
- **Membrane surface area**—100 mL blood in alveolar capillaries, spread thinly over 70 m²
 - Emphysema, lung cancer, and tuberculosis decrease surface area for gas exchange

Pulmonary Alveoli in Health and Disease

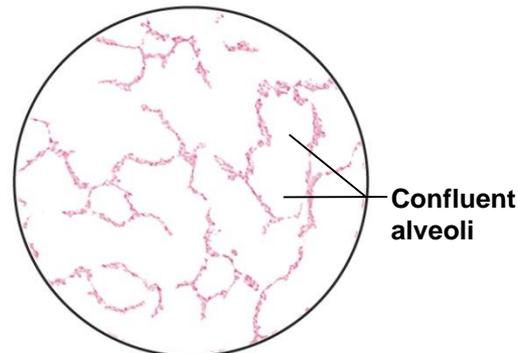
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(a) Normal



(b) Pneumonia



(c) Emphysema

Figure 22.21

Alveolar Gas Exchange

- **Membrane thickness**—only 0.5 μm thick
 - Presents little obstacle to diffusion
 - Pulmonary edema in left ventricular failure causes edema and thickening of the respiratory membrane
 - Pneumonia causes thickening of respiratory membrane
 - When membrane is thicker, gases have farther to travel between blood and air and cannot equilibrate fast enough to keep up with blood flow

Alveolar Gas Exchange

- **Ventilation–perfusion coupling**—the ability to match air flow and blood flow to each other
 - Gas exchange requires both good ventilation of alveolus and good perfusion of the capillaries
 - Pulmonary blood vessels change diameter depending on air flow to an area of the lungs
 - Example: If an area is poorly ventilated, pulmonary vessels constrict
 - Bronchi change diameter depending on blood flow to an area of the lungs
 - Example: If an area is well perfused, bronchodilation occurs

Ventilation–Perfusion Coupling

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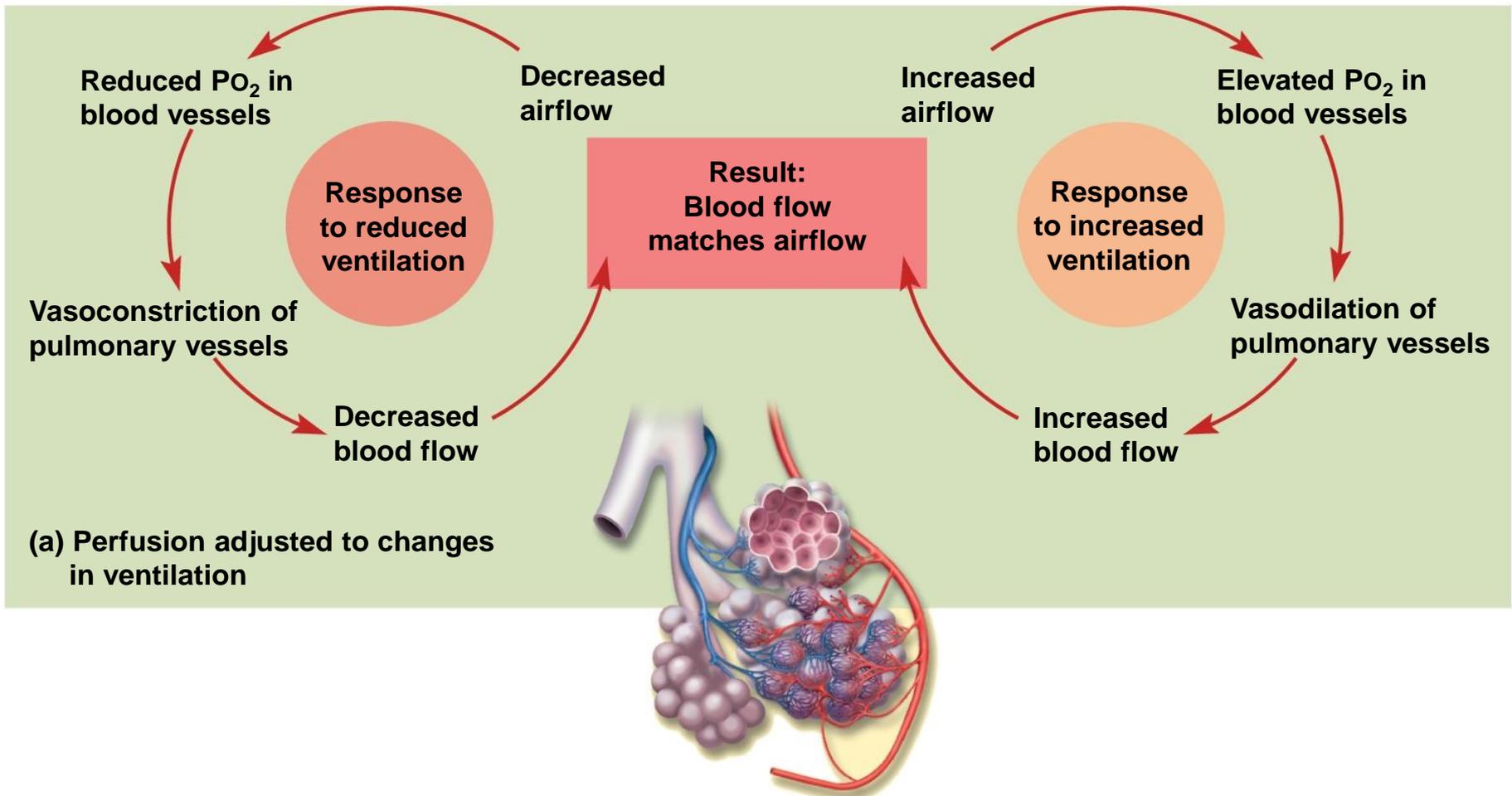
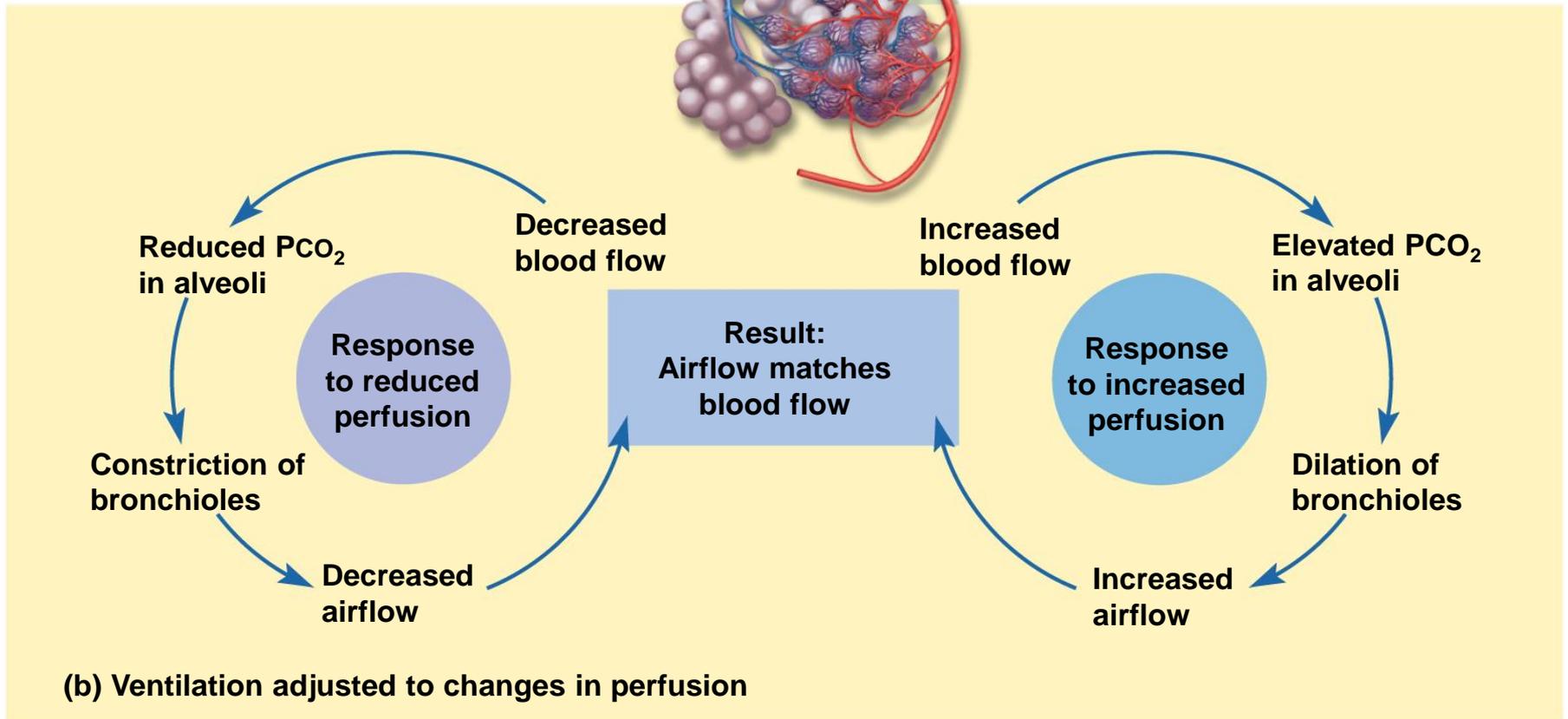
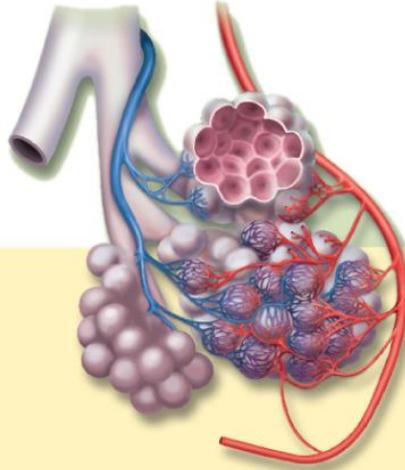


Figure 22.22a

Ventilation–Perfusion Coupling

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(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 vice versa
- **Oxygen transport**
 - 98.5% bound to hemoglobin
 - 1.5% dissolved in plasma
- **Carbon dioxide transport**
 - In transport: 90% is hydrated to form carbonic acid (dissociates into bicarbonate ions); 5% is bound to proteins; and 5% is dissolved as a gas in plasma
 - In exchange: 70% of CO₂ comes from carbonic acid; 23% comes from proteins; and 7% comes straight from plasma

Oxygen

- **Arterial blood carries about 20 mL of O₂ per deciliter**
- **Hemoglobin**—molecule specialized for oxygen transport
 - Four protein (**globin**) portions
 - Each with a heme group that binds one O₂ to an iron atom
 - One hemoglobin molecule can carry up to 4 O₂
 - 100% saturation Hb with 4 O₂ molecules per Hb
 - 50% saturation Hb with 2 O₂ molecules per Hb
 - Oxyhemoglobin (HbO₂)—O₂ bound to hemoglobin
 - Deoxyhemoglobin (HHb)—hemoglobin with no O₂

Oxyhemoglobin Dissociation Curve

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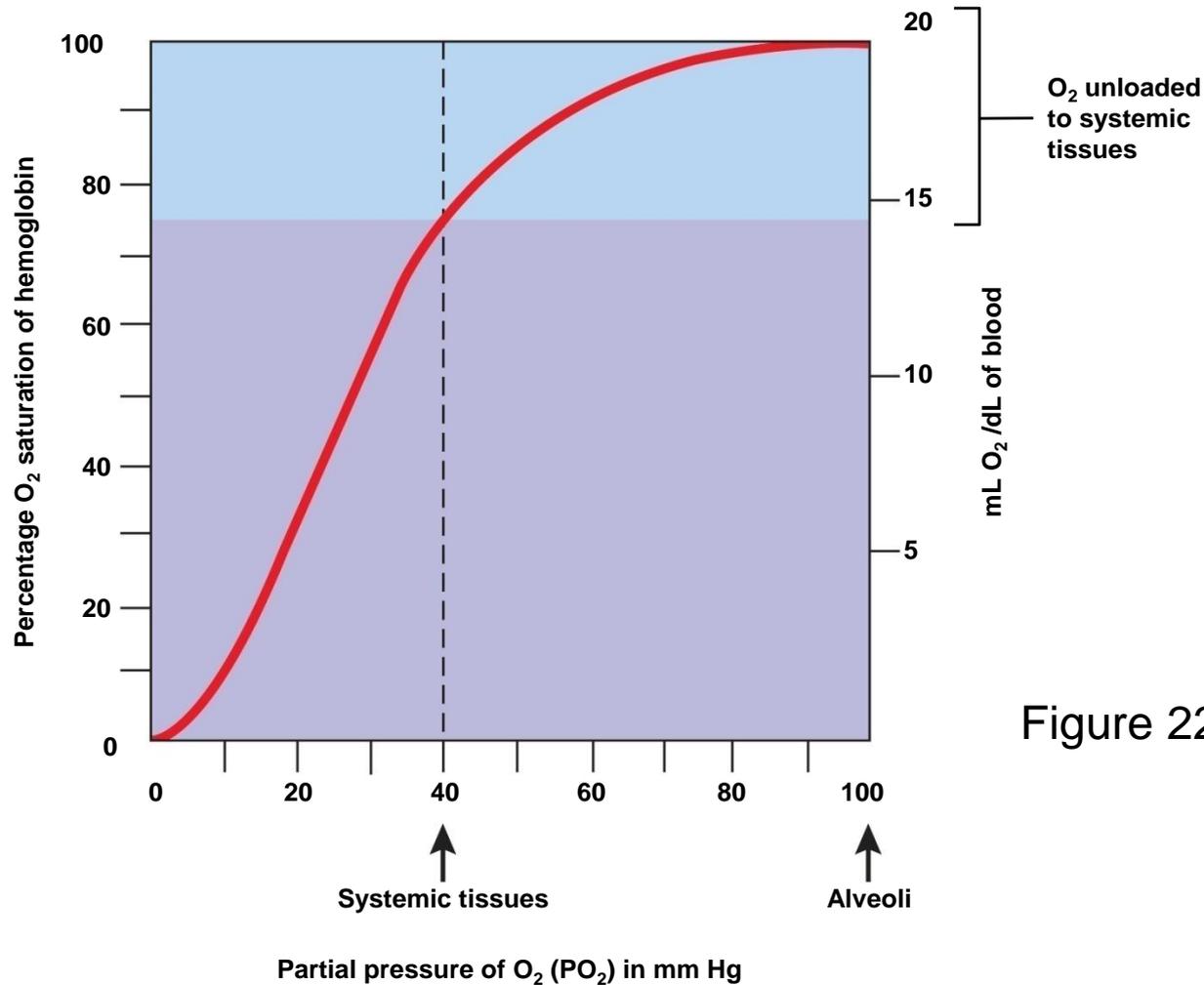


Figure 22.23

Relationship between hemoglobin saturation and PO_2 is nonlinear (binding facilitates loading; ultimate saturation)

Carbon Dioxide

- **Carbon dioxide transported in three forms**
 - Carbonic acid, carbamino compounds, and dissolved in plasma
- **90% of CO₂ is hydrated to form carbonic acid**
 - $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+$
 - Then dissociates into bicarbonate and hydrogen ions
- **5% binds to the amino groups of plasma proteins and hemoglobin to form carbamino compounds—chiefly carbaminohemoglobin (HbCO₂)**
 - Carbon dioxide does not compete with oxygen
 - They bind to different moieties on the hemoglobin molecule
 - Hemoglobin can transport O₂ and CO₂ simultaneously

Carbon Dioxide

(Continued)

- **5% is carried in the blood as dissolved gas**
- **Relative amounts of CO₂ exchange between the blood and alveolar air differs**
 - 70% of exchanged CO₂ comes from carbonic acid
 - 23% from carbamino compounds
 - 7% dissolved in the plasma
 - Blood gives up the dissolved CO₂ gas and CO₂ from the carbamino compounds more easily than CO₂ in bicarbonate

Carbon Monoxide Poisoning

- **Carbon monoxide (CO)**—competes for the O₂ binding sites on the hemoglobin molecule
- **Colorless, odorless gas in cigarette smoke, engine exhaust, fumes from furnaces and space heaters**
- **Carboxyhemoglobin**—CO binds to iron of hemoglobin (Hb)
 - Binds 210 times as tightly as oxygen and ties up Hb for a long time
 - Nonsmokers: less than 1.5% of Hb occupied by CO
 - Smokers: 10% of Hb occupied by CO in heavy smokers
 - Atmospheric concentration of 0.2% CO is quickly lethal

Systemic Gas Exchange

- **Systemic gas exchange—the unloading of O₂ and loading of CO₂ at the systemic capillaries**
- **CO₂ loading**
 - CO₂ diffuses into the blood
 - **Carbonic anhydrase** in RBC catalyzes
 - **CO₂ + H₂O → H₂CO₃ → HCO₃⁻ + H⁺**
 - Chloride shift
 - Keeps reaction proceeding, exchanges HCO₃⁻ for Cl⁻
 - H⁺ binds to hemoglobin

Systemic Gas Exchange

- **Oxygen 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
 - **Utilization coefficient:** given up 22% of its oxygen load
 - **Venous reserve:** oxygen remaining in the blood after it passes through the capillary beds

Systemic Gas Exchange

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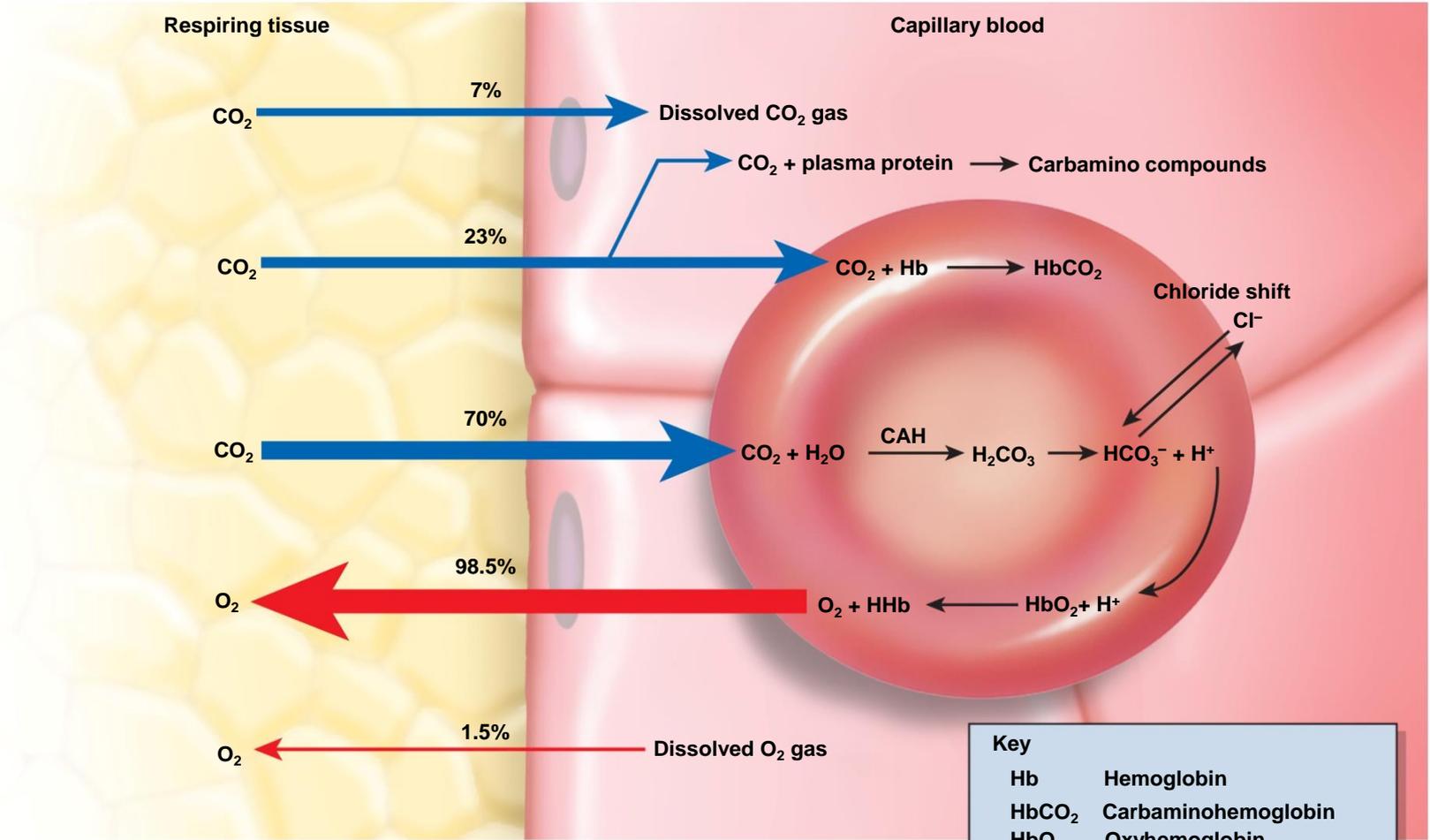


Figure 22.24

Alveolar Gas Exchange Revisited

- **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 binds with HCO₃⁻
 - **CO₂ + H₂O ← H₂CO₃ ← HCO₃⁻ + H⁺**
 - Reverse **chloride shift**
 - HCO₃⁻ diffuses back into RBC in exchange for Cl⁻, free CO₂ that is generated diffuses into alveolus to be exhaled

Alveolar Gas Exchange

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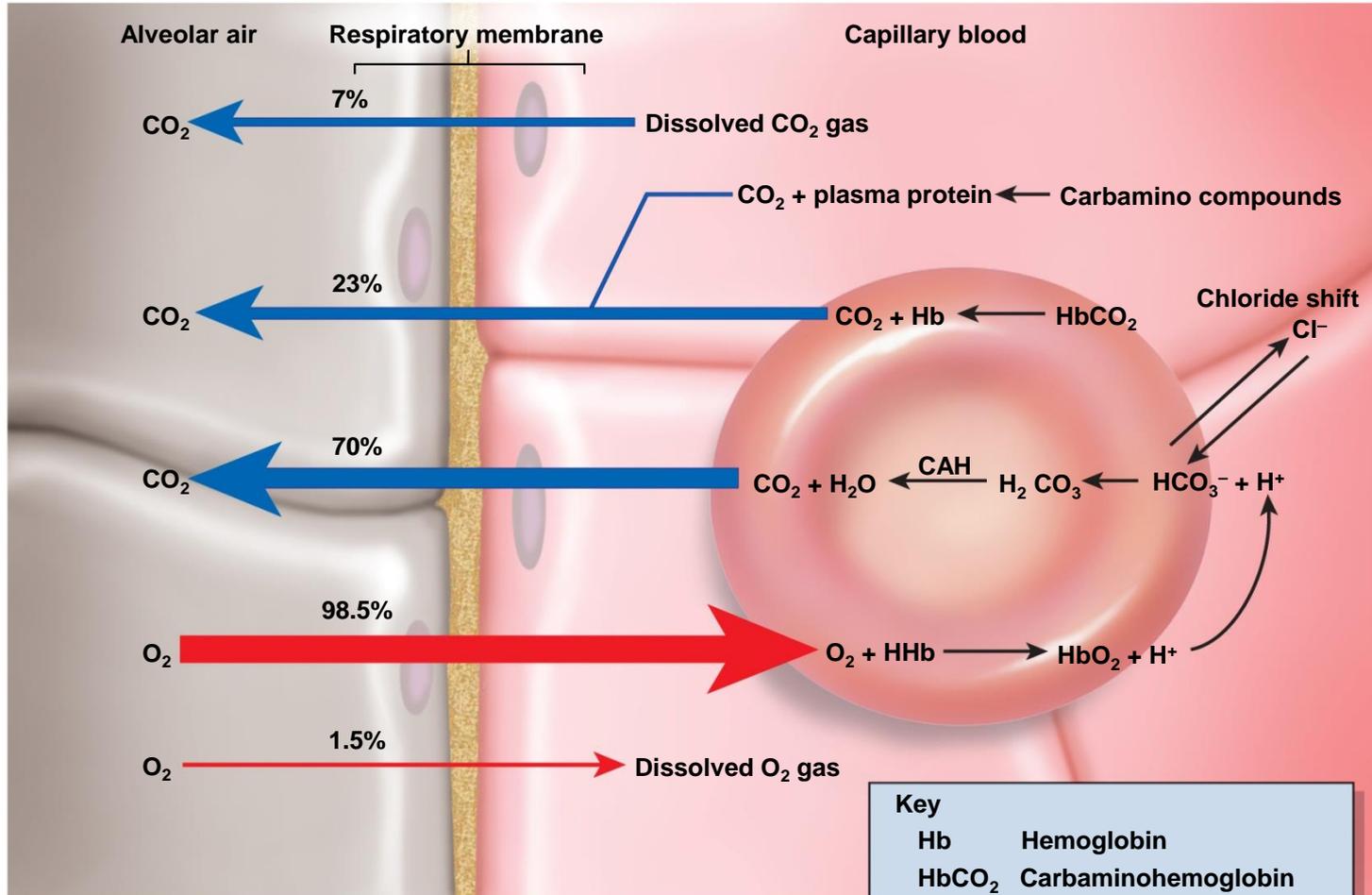


Figure 22.25

Adjustment to the Metabolic Needs of Individual Tissues

- Hemoglobin unloads O_2 to match metabolic needs of different states of activity of the tissues
- Four factors adjust the rate of oxygen unloading to match need: ambient PO_2 , temperature, the Bohr effect, concentration of biphosphoglycerate (BPG)
 - Ambient PO_2
 - Active tissue has $\downarrow PO_2$; O_2 is released from Hb
 - Temperature
 - Active tissue has \uparrow temp; promotes O_2 unloading

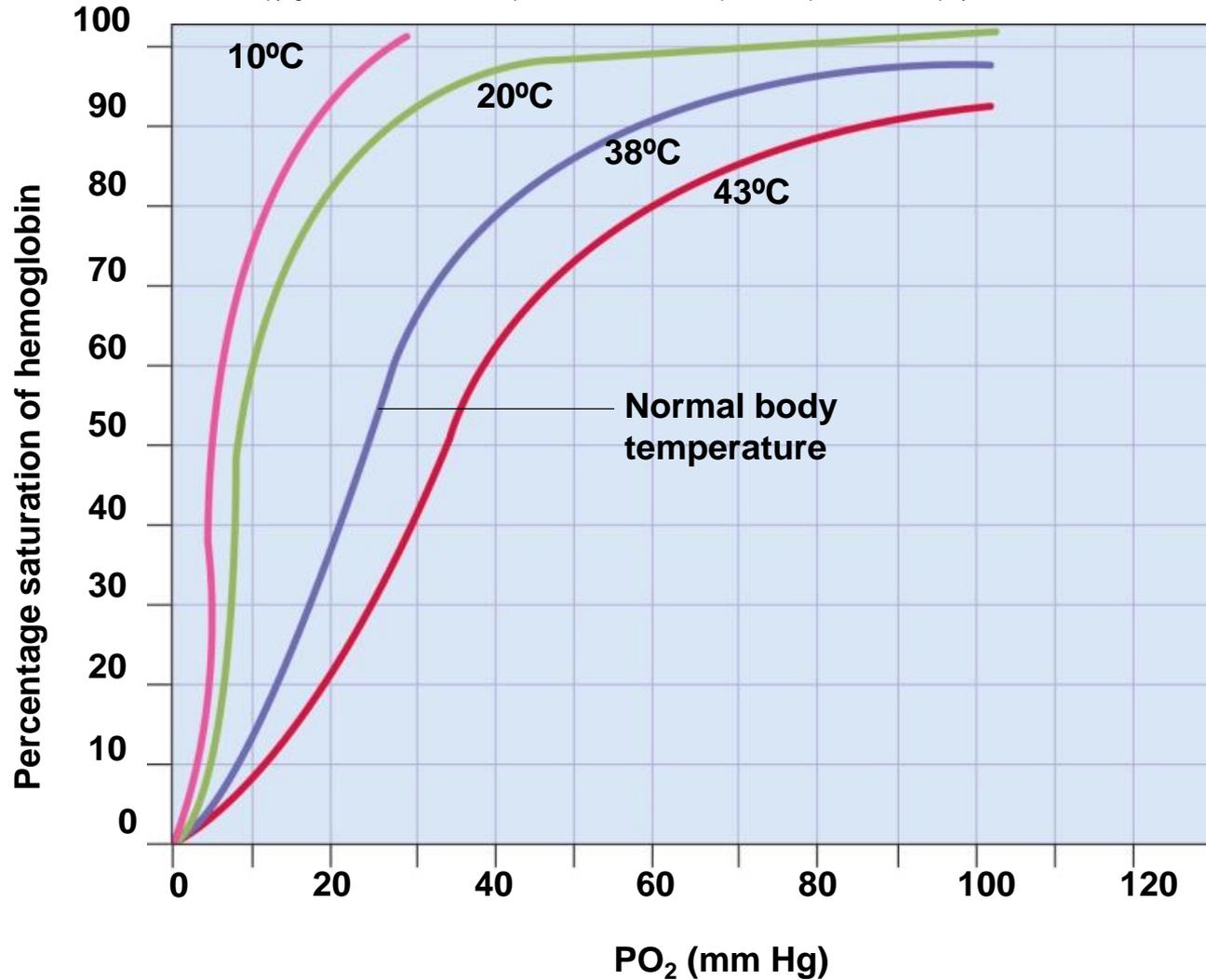
Adjustment to the Metabolic Needs of Individual Tissues

Adjustment of oxygen unloading (Continued)

- **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
 - \uparrow body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and promote O_2 unloading
- **Rate of CO_2 loading also adjusted to meet needs**
 - **Haldane effect**—low level of oxyhemoglobin enables the blood to transport more CO_2

Effects of Temperature on Oxyhemoglobin Dissociation

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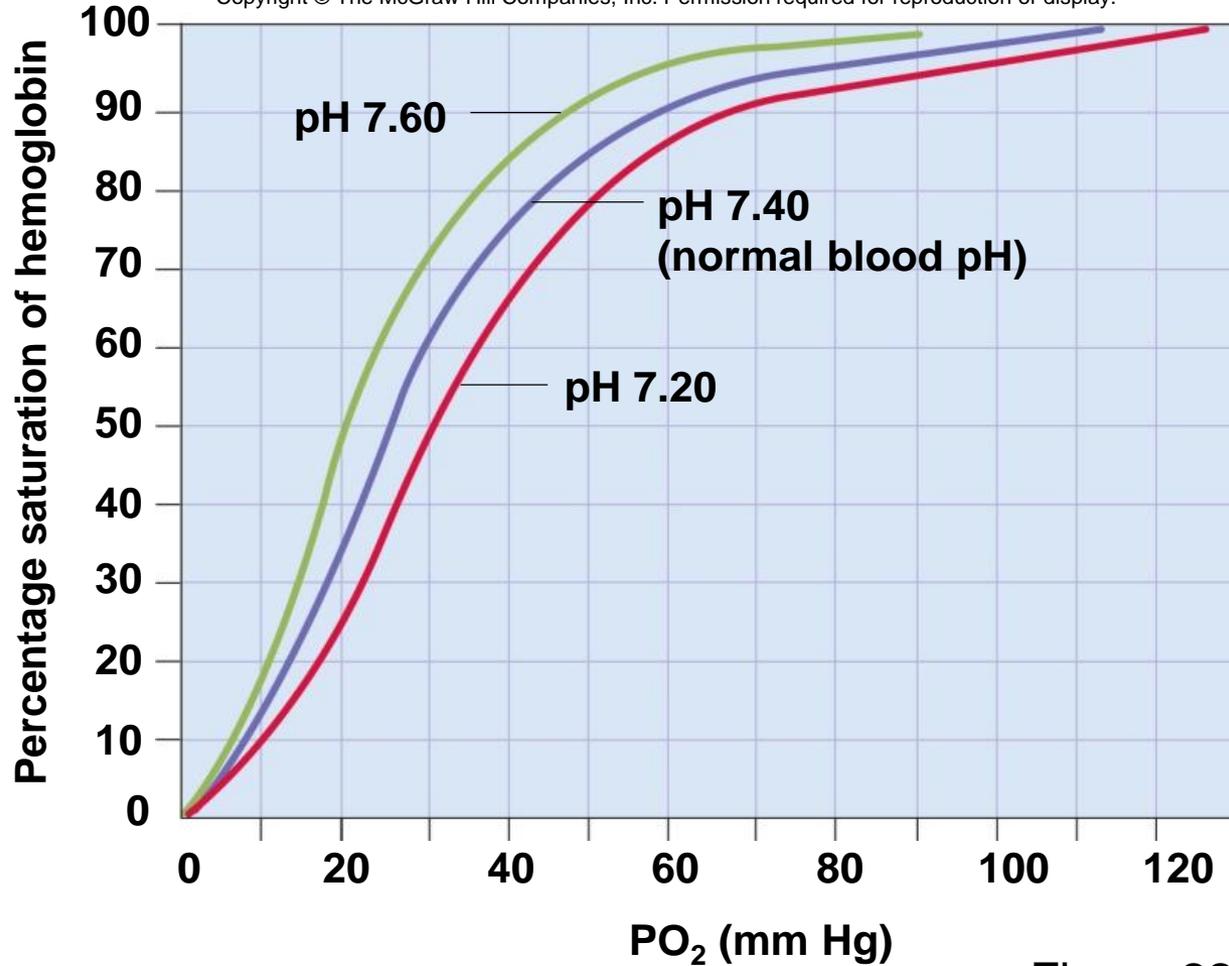


(a) Effect of temperature

Figure 22.26a

Effects of pH on Oxyhemoglobin Dissociation

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(b) Effect of pH

Figure 22.26b

Bohr effect: release of O₂ in response to low pH

Blood Gases and the Respiratory Rhythm

- **Rate and depth** of breathing adjust to maintain levels of:
 - **pH** **7.35 to 7.45**
 - **P_{CO₂}** **40 mm Hg**
 - **P_{O₂}** **95 mm Hg**
- **Brainstem respiratory centers** receive input from central and peripheral chemoreceptors that monitor composition of CSF and blood
- **Most potent stimulus for breathing** is **pH**, followed by **CO₂**, and least significant is **O₂**

Hydrogen Ions

- **Pulmonary ventilation is adjusted to maintain pH of the brain**
 - **Central chemoreceptors** in medulla produce about 75% of the change in respiration induced by pH shift
 - CO₂ crosses blood-brain-barrier and reacts with water in CSF to produce carbonic acid
 - The H⁺ from carbonic acid strongly stimulates central chemoreceptors, since CSF does not contain much protein buffer
- Hydrogen ions also stimulate **peripheral chemoreceptors** which produce 25% of the respiratory response to pH changes

Hydrogen Ions

- **Acidosis**—blood pH lower than 7.35
- **Alkalosis**—blood pH higher than 7.45
- **Hypocapnia**—PCO₂ less than 37 mm Hg (normal 37 to 43 mm Hg)
 - Most common cause of alkalosis
- **Hypercapnia**—PCO₂ greater than 43 mm Hg
 - Most common cause of acidosis

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** can be a corrective homeostatic **response to acidosis**
 - “Blowing off” CO₂ faster than the body produces it
 - Pushes reaction to the left:
$$\text{CO}_2 \text{ (expired)} + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \downarrow \text{H}^+$$
 - Reduces H⁺ (reduces acid), raises blood pH toward normal

Hydrogen Ions

- **Hypoventilation** can be a corrective homeostatic response to alkalosis
 - Allows CO₂ to accumulate in 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

Hydrogen Ions

- **Ketoacidosis**—acidosis brought about by rapid fat oxidation releasing acidic ketone bodies (seen in diabetes mellitus)
 - Induces **Kussmaul respiration**: hyperventilation that reduces CO₂ concentration and compensates (to some degree) for the acidity of ketone bodies

Carbon Dioxide

- CO₂ has strong **indirect** effects on respiration
 - Through pH, as described previously
- **Direct effects**
 - ↑ CO₂ at beginning of exercise may directly stimulate peripheral chemoreceptors and trigger ↑ ventilation more quickly than central chemoreceptors

Oxygen

- **PO₂ usually has little effect on respiration**
- Chronic hypoxemia, PO₂ less than 60 mm Hg, can significantly stimulate ventilation
 - **Hypoxic drive:** respiration driven more by low PO₂ than by CO₂ or pH
 - Emphysema, pneumonia
 - High elevations after several days

Respiration and Exercise

- **Causes of increased respiration during exercise**
 - When the brain sends motor commands to the muscles
 - It also sends this information to the respiratory centers
 - They increase pulmonary ventilation in anticipation of the needs of the exercising muscles
 - Exercise stimulates proprioceptors of muscles and joints
 - They transmit excitatory signals to brainstem respiratory centers
 - Increase breathing because they are informed that muscles are moving
 - Increase in pulmonary ventilation keeps blood gas values at their normal levels in spite of the elevated O₂ consumption and CO₂ generation by the muscles

Respiratory Disorders

- **Expected Learning Outcomes**
 - Describe the forms and effects of oxygen deficiency and oxygen excess.
 - Describe the chronic obstructive pulmonary diseases and their consequences.
 - Explain how lung cancer begins, progresses, and exerts its lethal effects.

Oxygen Imbalances

- **Hypoxia**—a deficiency of oxygen in a tissue or the inability to use oxygen
 - A consequence of respiratory diseases
- **Hypoxemic hypoxia**—state of low arterial PO_2
 - Usually due to inadequate pulmonary gas exchange
 - Oxygen deficiency at high elevations, impaired ventilation: drowning, aspiration of a foreign body, respiratory arrest, degenerative lung diseases
- **Ischemic hypoxia**—inadequate circulation of blood
 - Congestive heart failure

Oxygen Imbalances

- **Anemic hypoxia**—due to anemia resulting from the inability of the blood to carry adequate oxygen
- **Histotoxic hypoxia**—metabolic poisons such as cyanide prevent tissues from using oxygen
- **Cyanosis**—blueness of the skin
 - Sign of hypoxia

Oxygen Imbalances

- Although safe to breathe 100% oxygen at 1 atm for a few hours, **oxygen toxicity** develops when pure O₂ breathed at 2.5 atm or greater
 - Generates free radicals and H₂O₂
 - Destroys enzymes
 - Damages nervous tissue
 - Leads to seizures, coma, death
- **Hyperbaric oxygen**
 - Formerly used to treat premature infants, caused retinal damage, was discontinued

Chronic Obstructive Pulmonary Diseases

- **Chronic obstructive pulmonary disease (COPD)**— long-term obstruction of airflow and substantial reduction in pulmonary ventilation
- Major COPDs are **chronic bronchitis** and **emphysema**
 - Almost always associated with smoking
 - Other risk factors include: air pollution, occupational exposure to airborne irritants, hereditary defects

Chronic Obstructive Pulmonary Diseases

- **Chronic bronchitis**

- Severe, persistent inflammation of lower respiratory tract
- Goblet cells enlarge and produce excess mucus
- Immobilized cilia fail to remove mucus
- Thick, stagnant mucus – ideal for bacterial growth
- Smoke compromises alveolar macrophage function
- Develop chronic cough to bring up **sputum** (thick mucus and cellular debris)
- Symptoms include hypoxemia and cyanosis

Chronic Obstructive Pulmonary Diseases

- **Emphysema**

- Alveolar walls break down

- Lung has fewer and larger spaces
- Much less respiratory membrane for gas exchange

- Lungs fibrotic and less elastic

- Lungs become flabby and cavitated with large spaces

- Air passages collapse

- Obstructs outflow of air
- Air trapped in lungs; person becomes barrel-chested

- Weaken thoracic muscles

- Spend three to four times the amount of energy just to breathe

Chronic Obstructive Pulmonary Diseases

- **COPD reduces vital capacity**
- **COPD causes: hypoxemia, hypercapnia, and respiratory acidosis**
 - Hypoxemia stimulates erythropoietin release from kidneys, and leads to polycythemia
- **Cor pulmonale**
 - Hypertrophy and potential failure of right heart due to obstruction of pulmonary circulation

Smoking and Lung Cancer

- **Lung cancer** accounts for more deaths than any other form of cancer
 - Most important cause is smoking (at least 60 carcinogens)
- **Squamous-cell carcinoma** (most common form)
 - Begins with transformation of bronchial epithelium into stratified squamous from ciliated pseudostratified epithelium
 - Dividing cells invade bronchial wall, cause bleeding lesions
 - Dense swirls of keratin replace functional respiratory tissue

Smoking and Lung Cancer

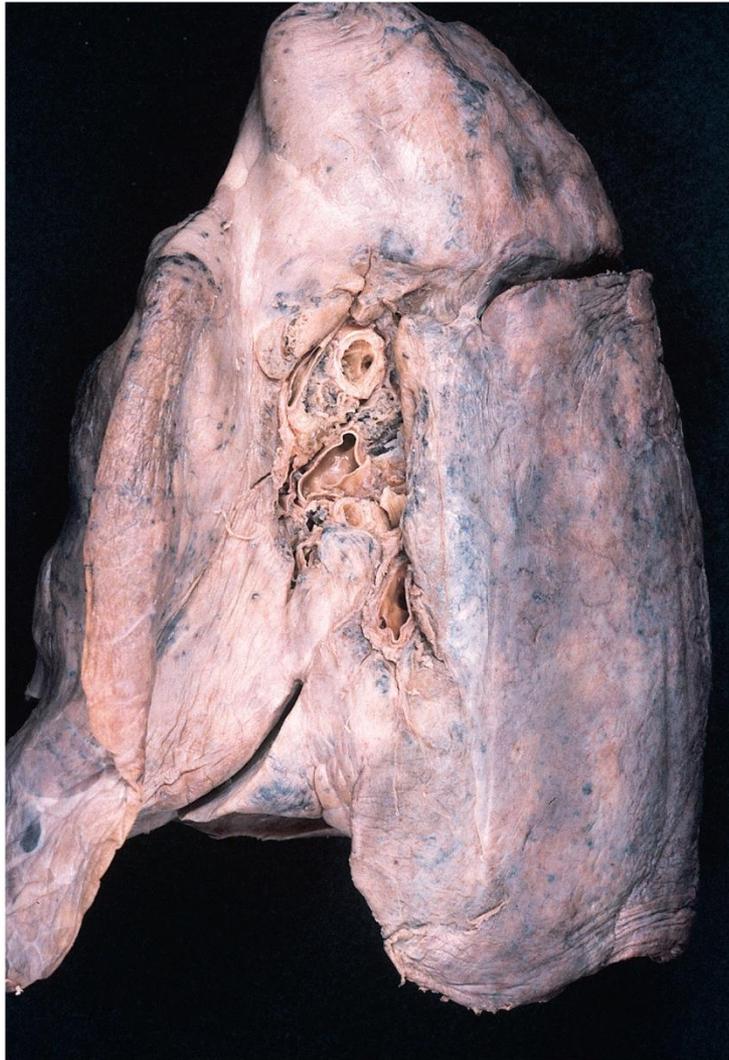
- **Adenocarcinoma**
 - Originates in mucous glands of lamina propria
- **Small-cell (oat cell) carcinoma**
 - Least common, most dangerous
 - Named for clusters of cells that resemble oat grains
 - Originates in primary bronchi, invades mediastinum, metastasizes quickly to other organs

Smoking and Lung Cancer

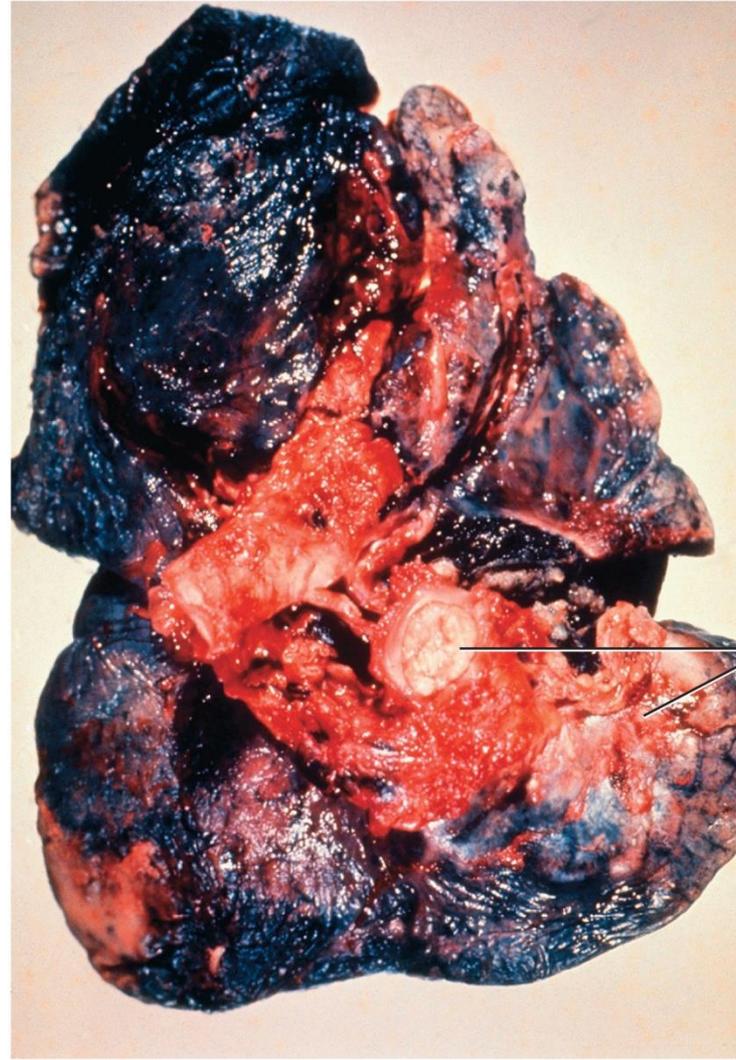
- **90% originate in mucus membranes of large bronchi**
- **Tumor invades bronchial wall, compresses airway; may cause atelectasis**
- **Often first sign is coughing up blood**
- **Metastasis is rapid; usually occurs by time of diagnosis**
 - Common sites: pericardium, heart, bones, liver, lymph nodes, and brain
- **Prognosis poor after diagnosis**
 - Only 7% of patients survive 5 years

Smoking and Lung Cancer

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(a) Healthy lung, mediastinal surface



(b) Smoker's lung with carcinoma

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