

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

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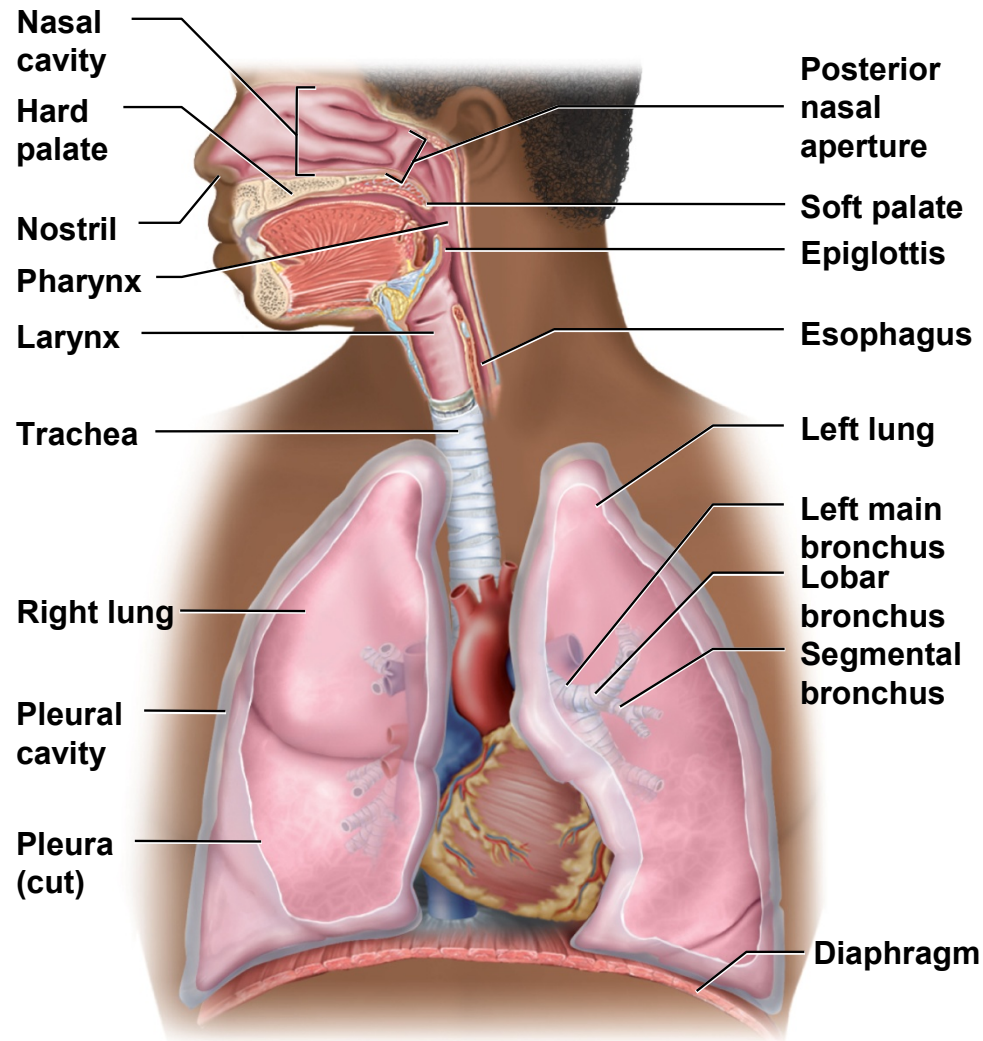


Figure 22.1

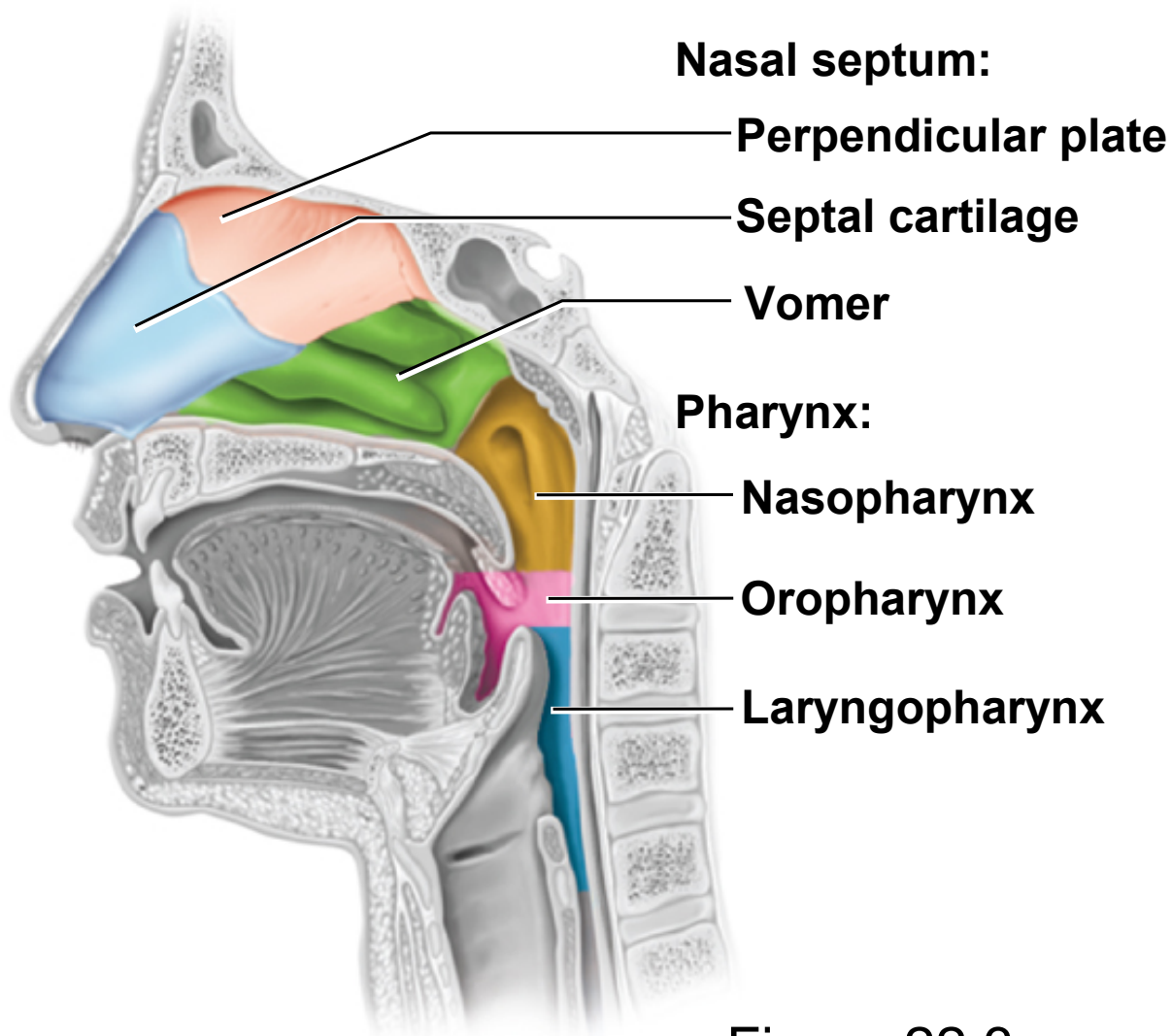
- nose, pharynx, larynx, trachea, bronchi, lungs

The Nose

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

Regions of Pharynx

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(c)

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 ($>10\ \mu\text{m}$)
 - **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

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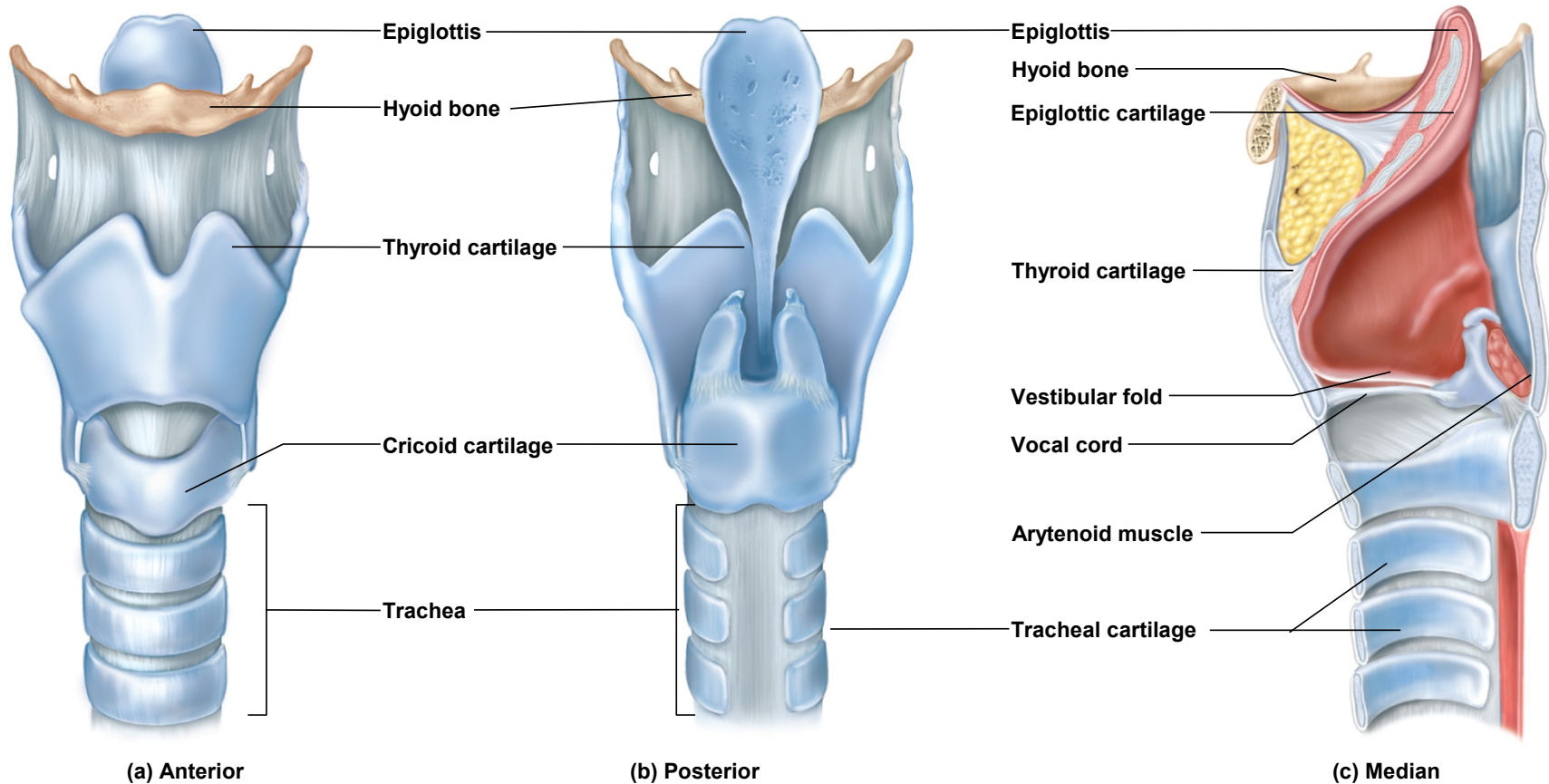


Figure 22.4 a-c

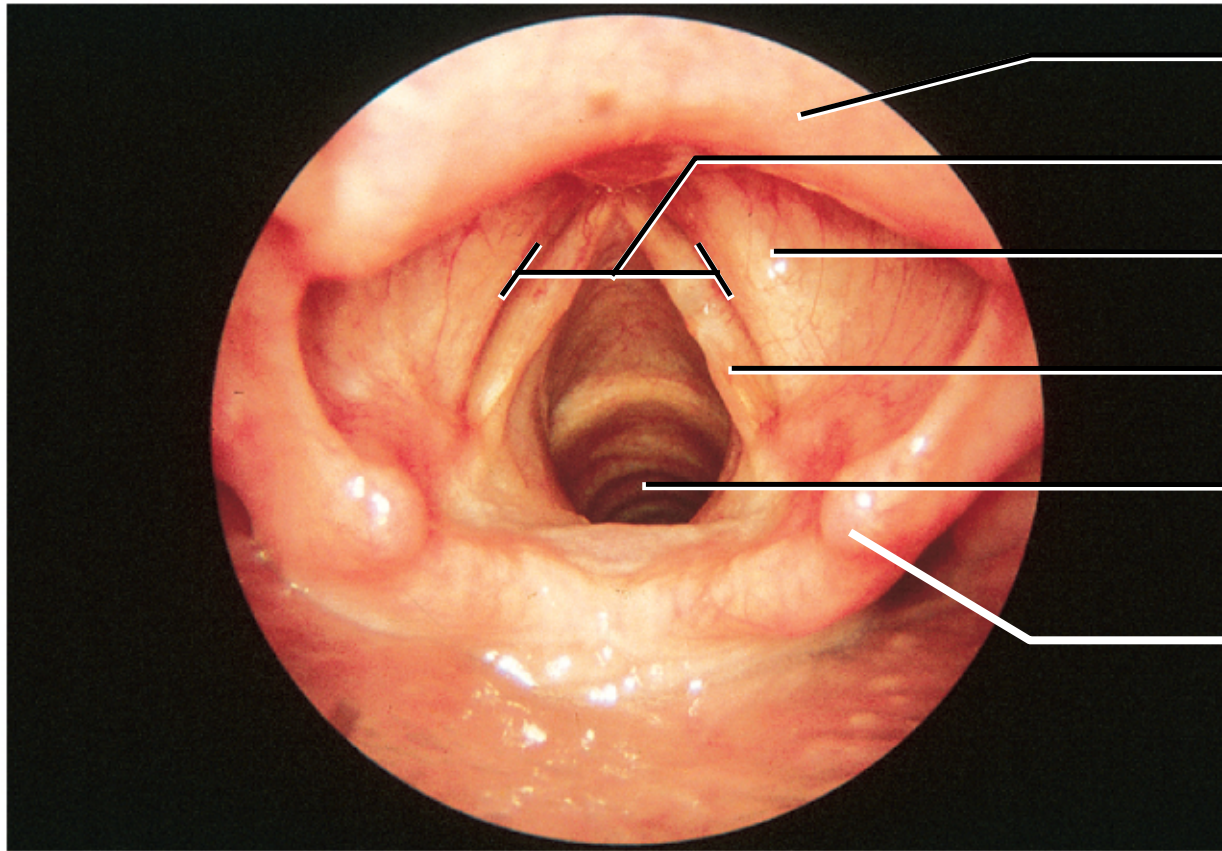
Walls of Larynx

- 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 stratified 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

(a)

Figure 22.5a

Action of Vocal Cords

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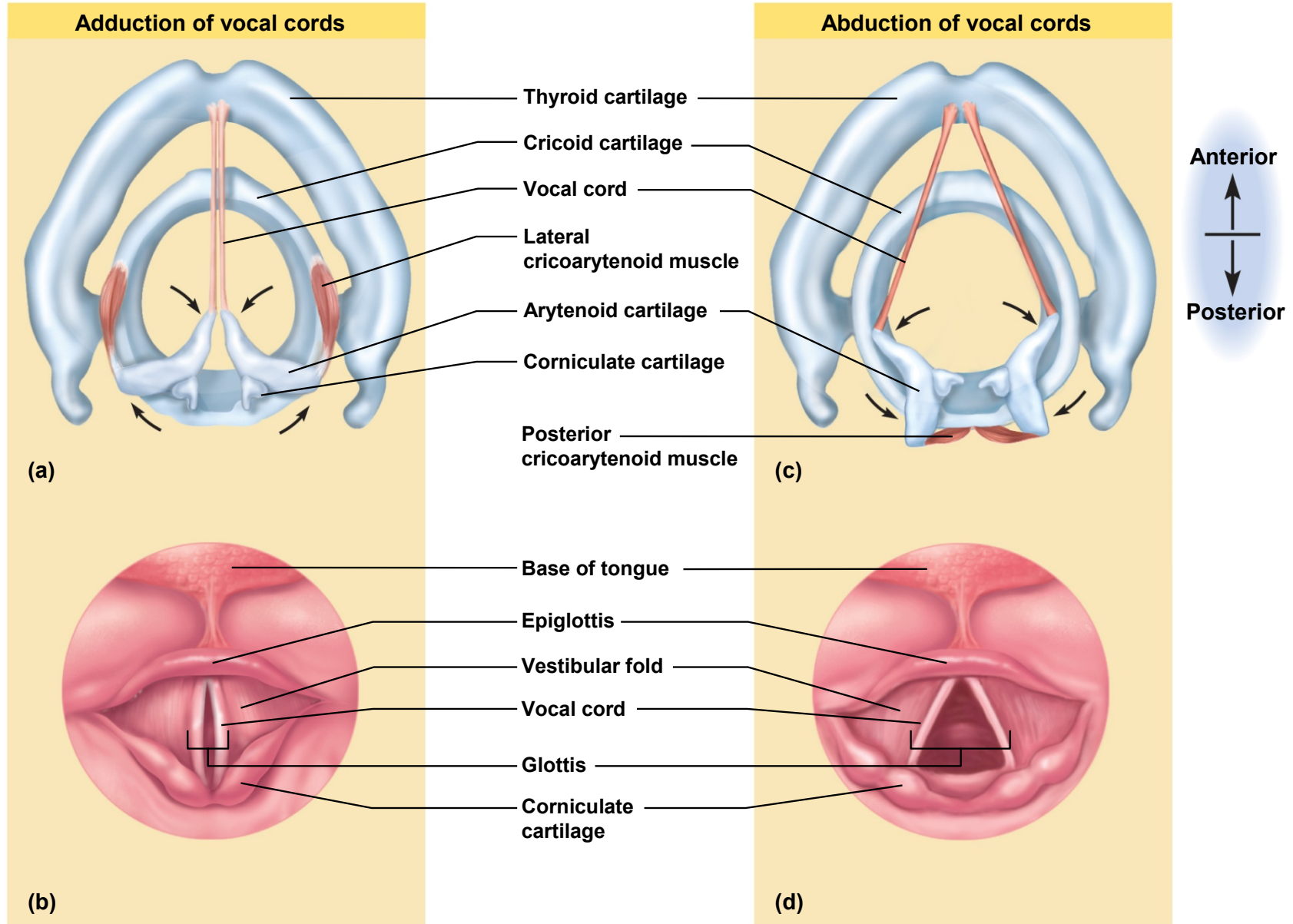


Figure 22.6 a-d

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

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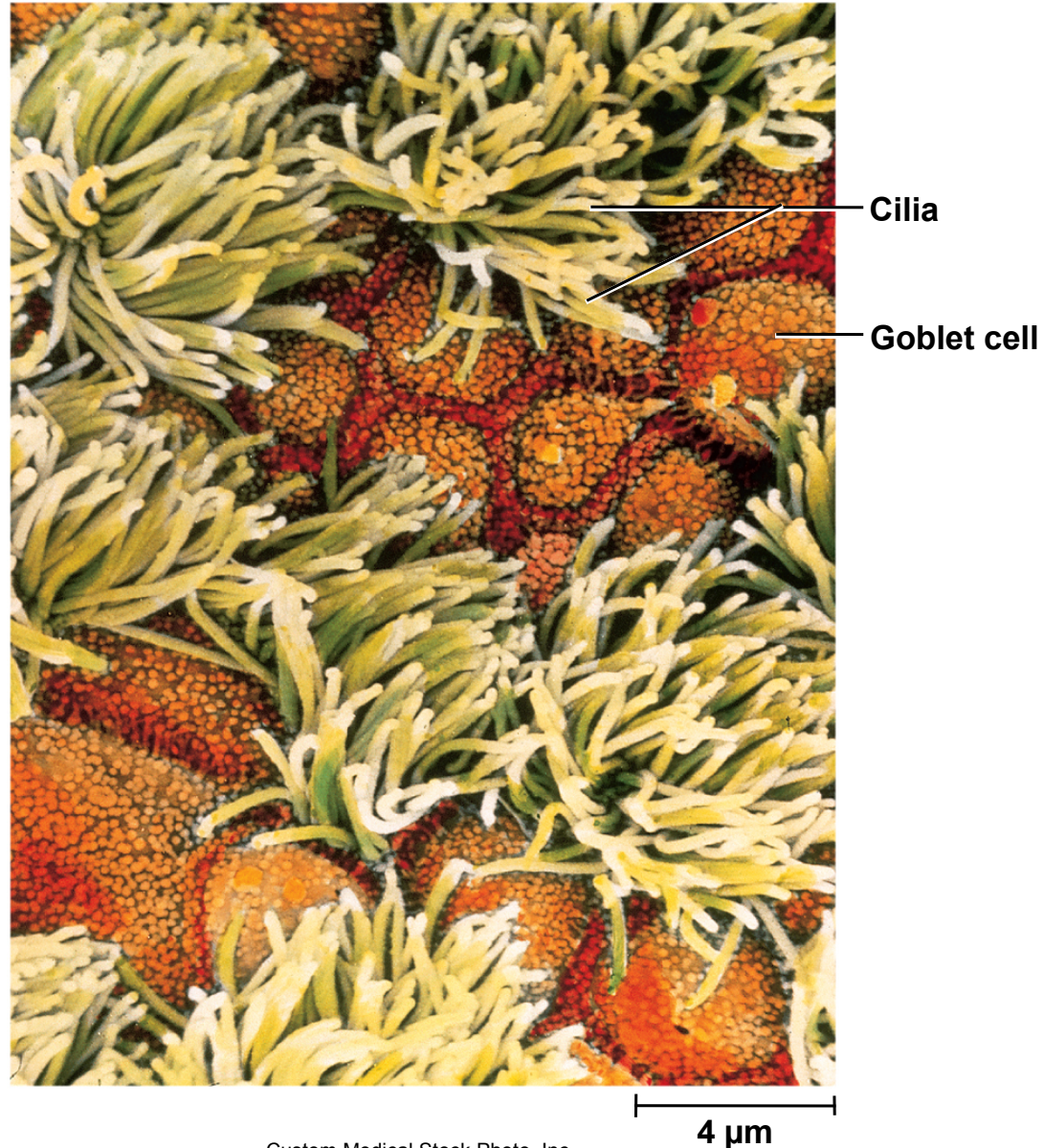
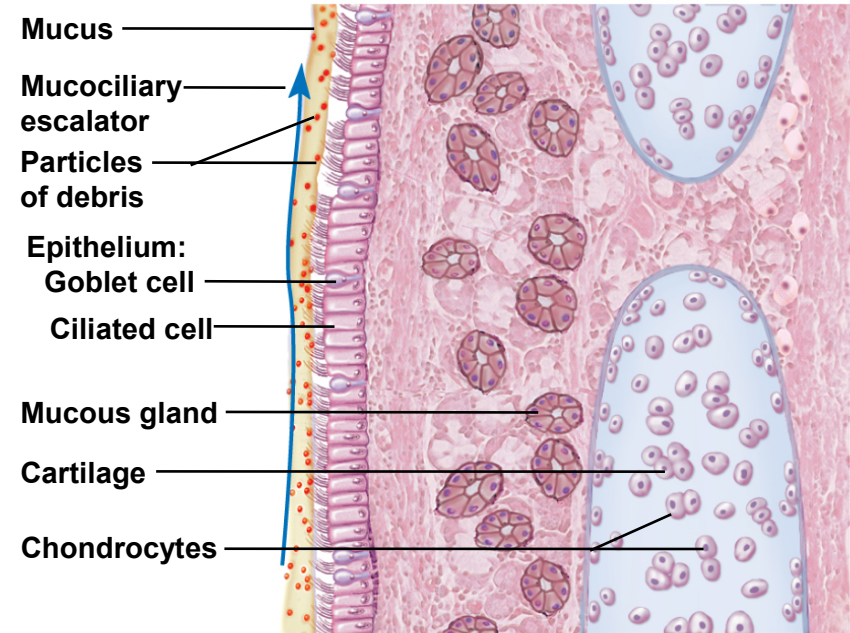
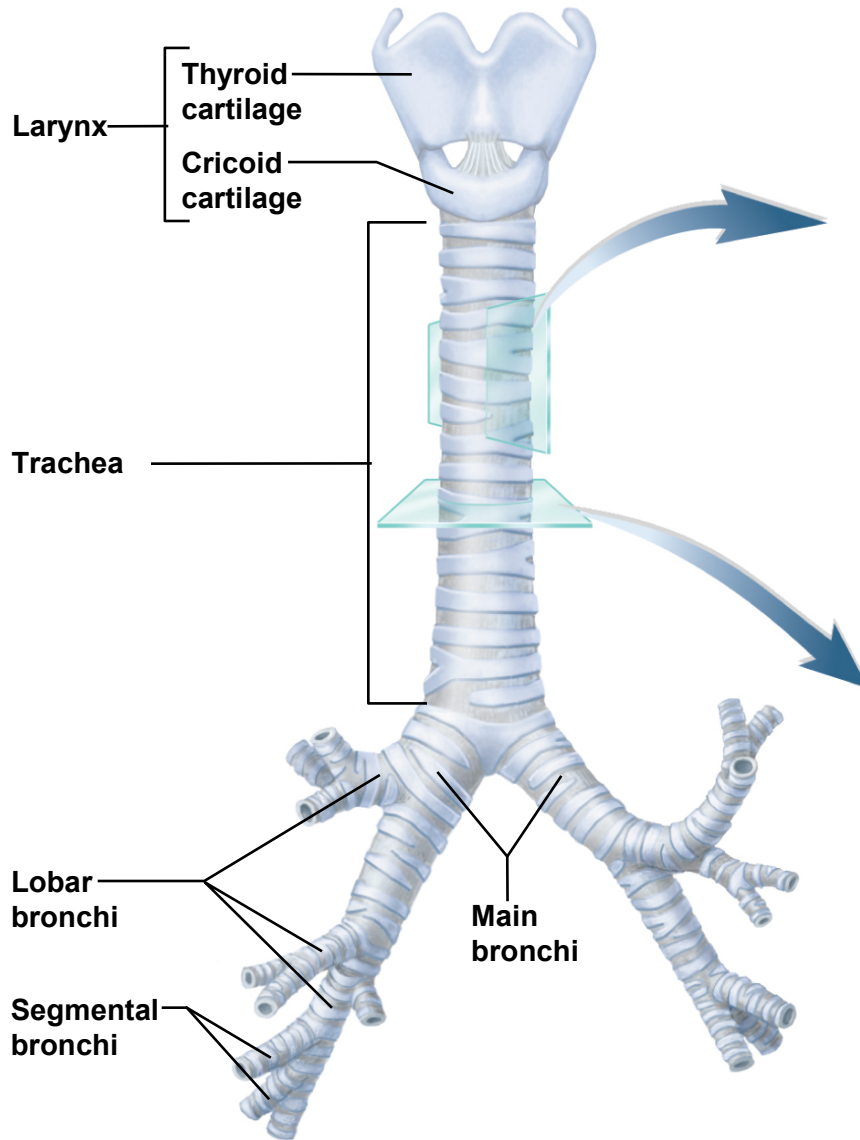


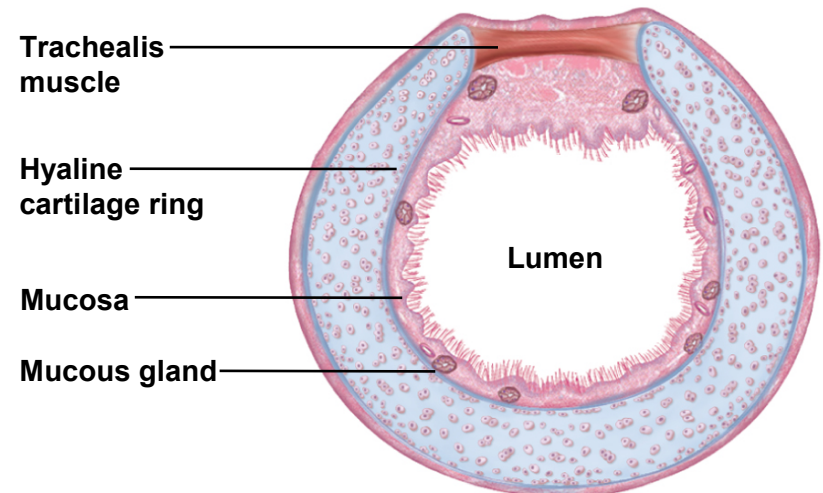
Figure 22.8

Lower Respiratory Tract

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Figure 22.7 a-c

Lungs - Surface Anatomy

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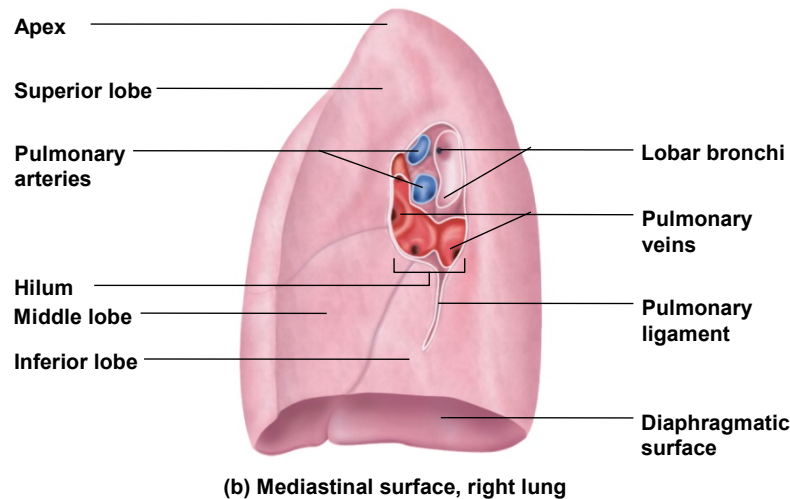
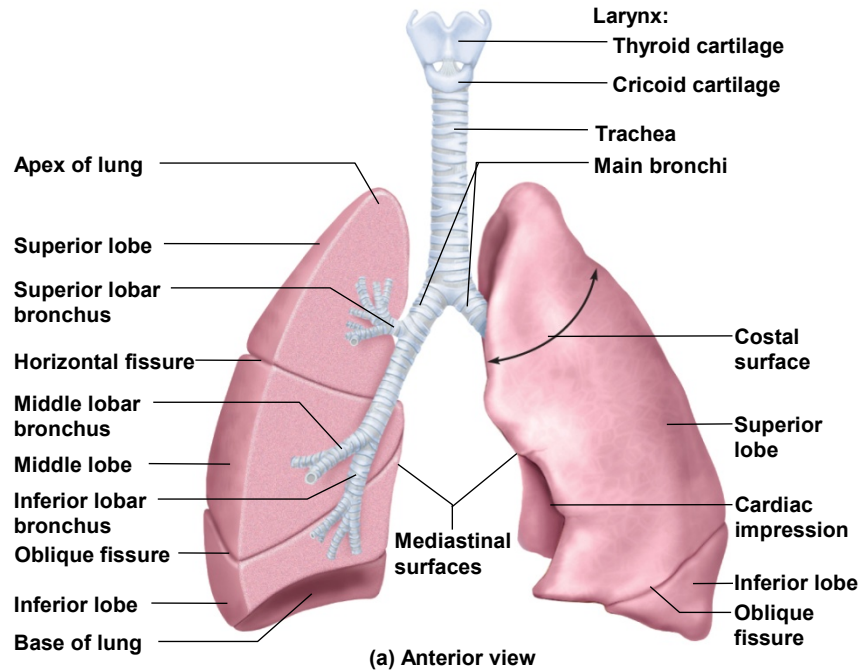
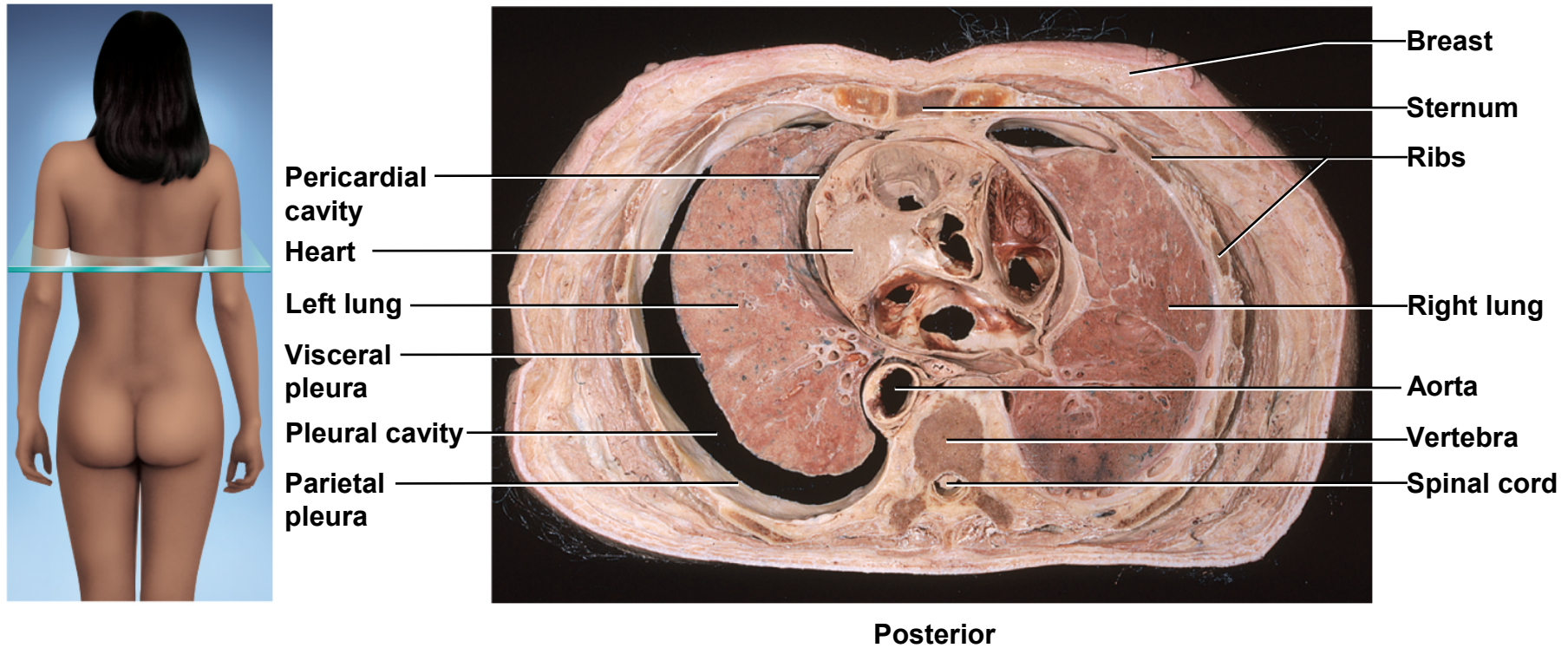


Figure 22.9

Thorax - Cross Section

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Ralph Hutchings/Visuals Unlimited

Figure 22.10

Lungs

- **lung**
 - **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

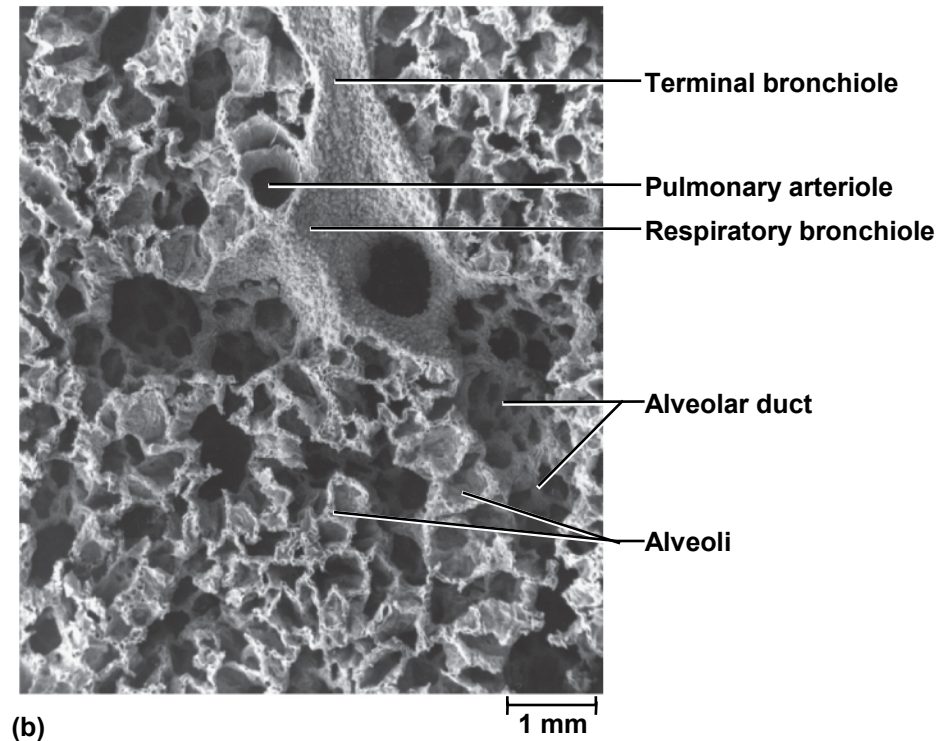
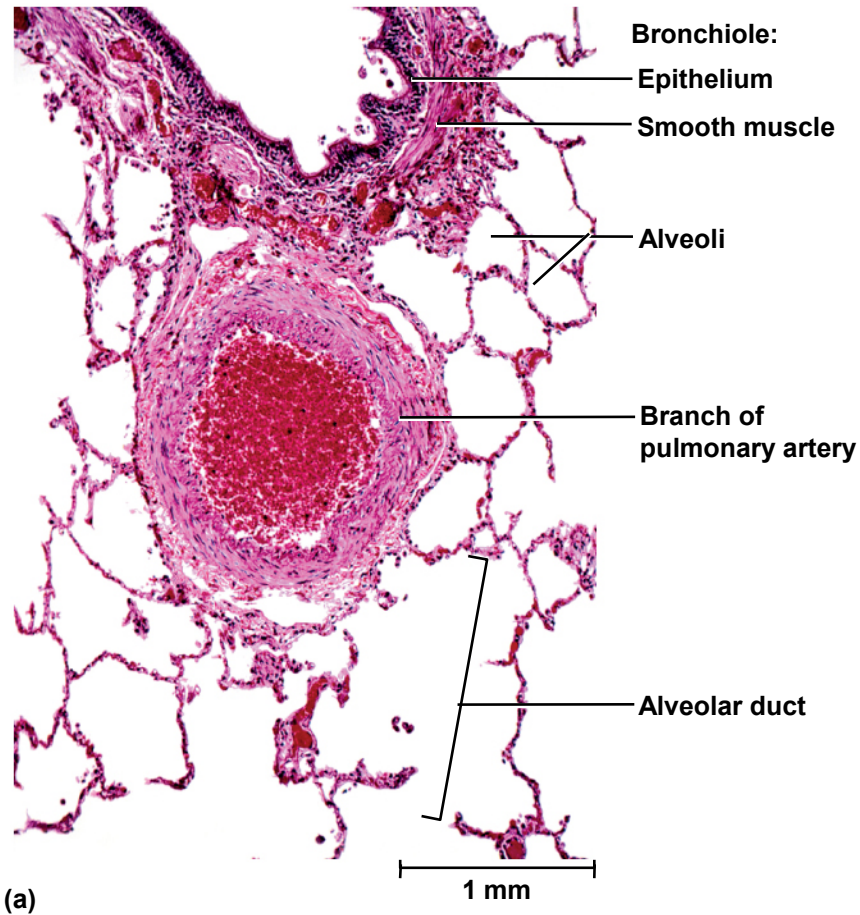
nasal cavity > pharynx > larynx > trachea > main bronchus > lobar bronchus > segmental bronchus > bronchiole > terminal bronchiole >

respiratory division

respiratory bronchiole > alveolar duct > atrium > alveolars

Lung Tissue

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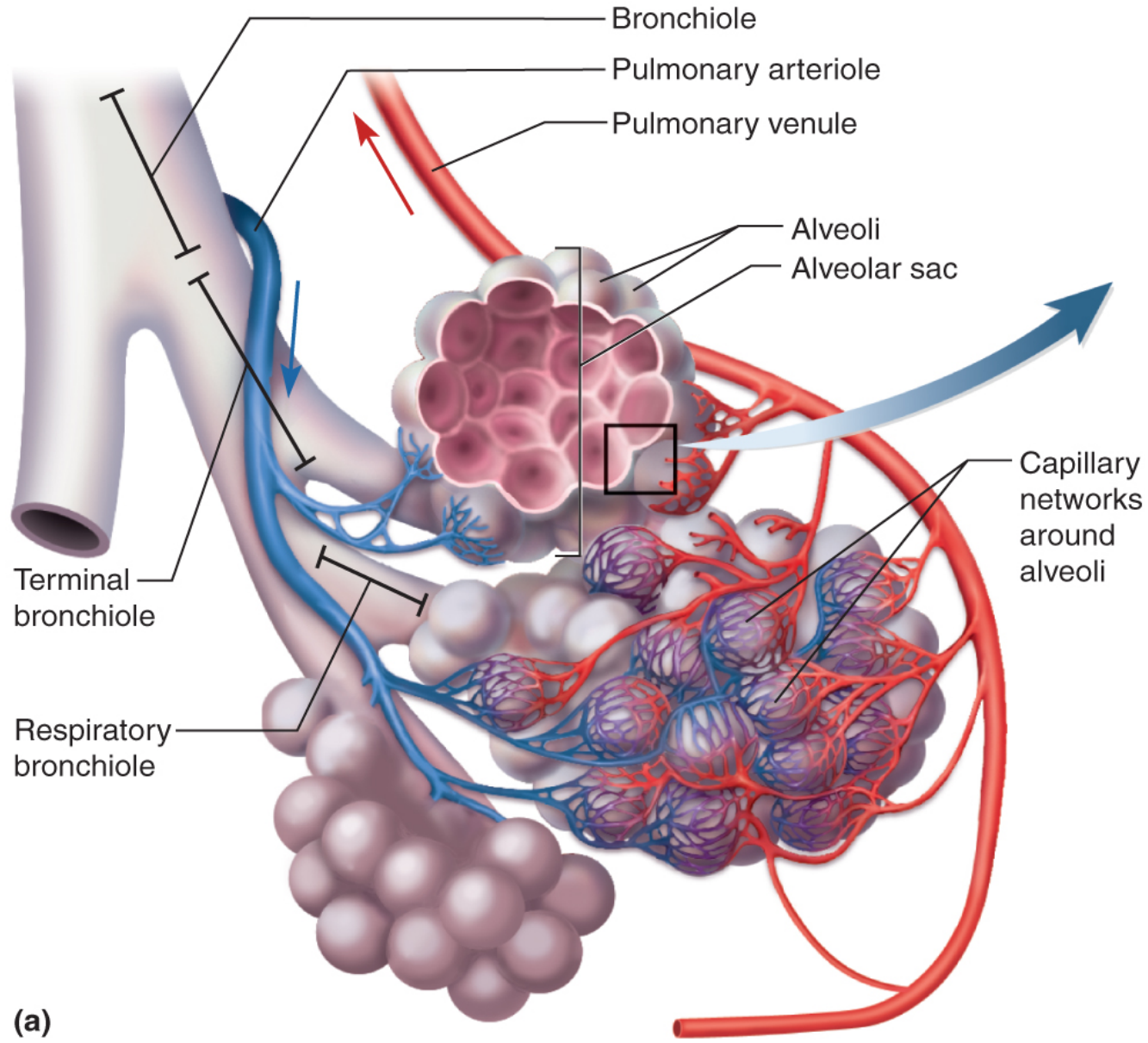
Figure 22.11

Alveoli

- 150 million alveoli in each lung, providing about 70 m² of surface for gas exchange
- cells of the alveolus
 - **squamous alveolar cells**
 - thin, broad cells that allow for rapid gas diffusion between alveolus and bloodstream
 - cover 95% of alveolus surface area
 - **great 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

Alveolar Blood Supply

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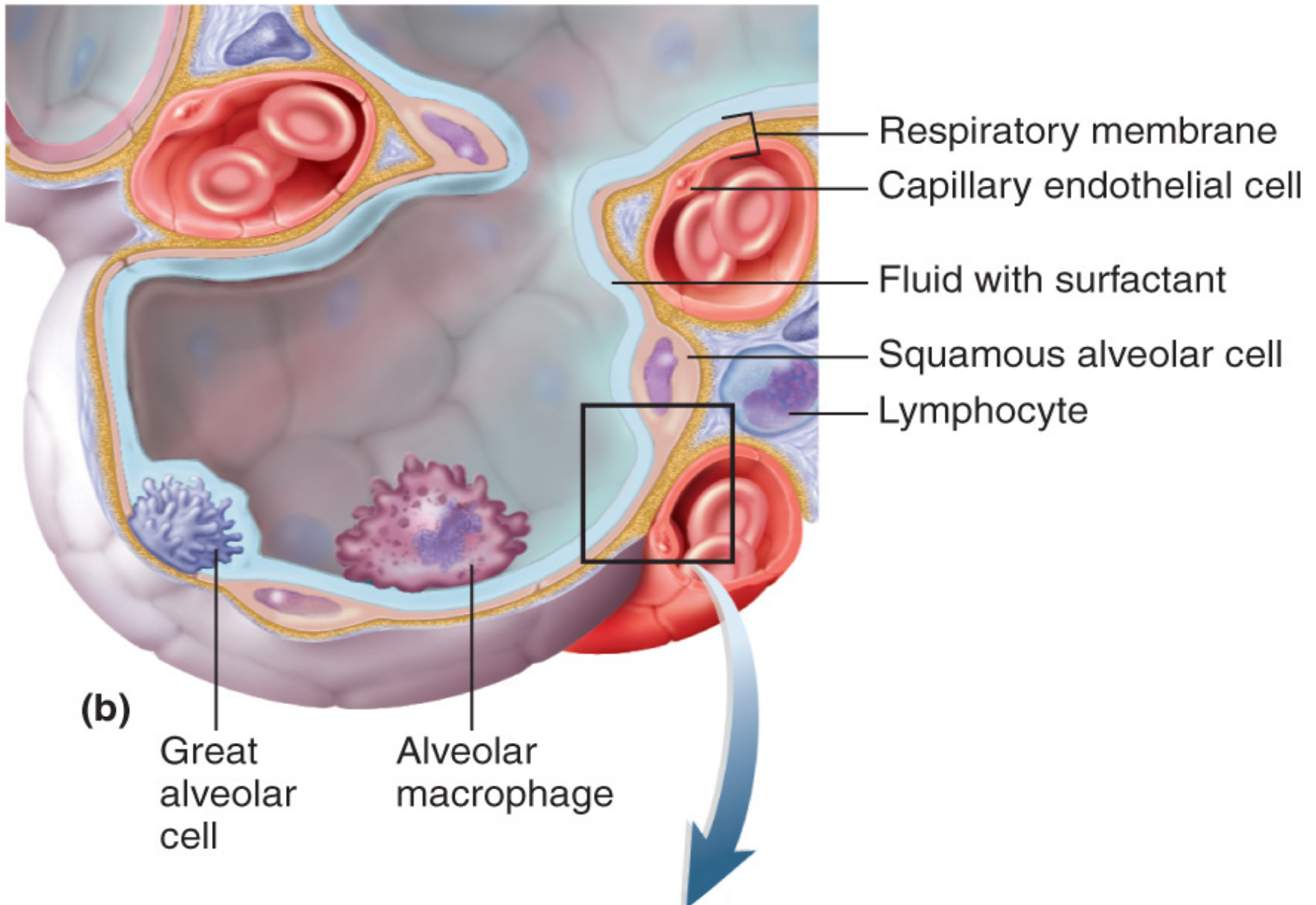


Respiratory Membrane

- 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

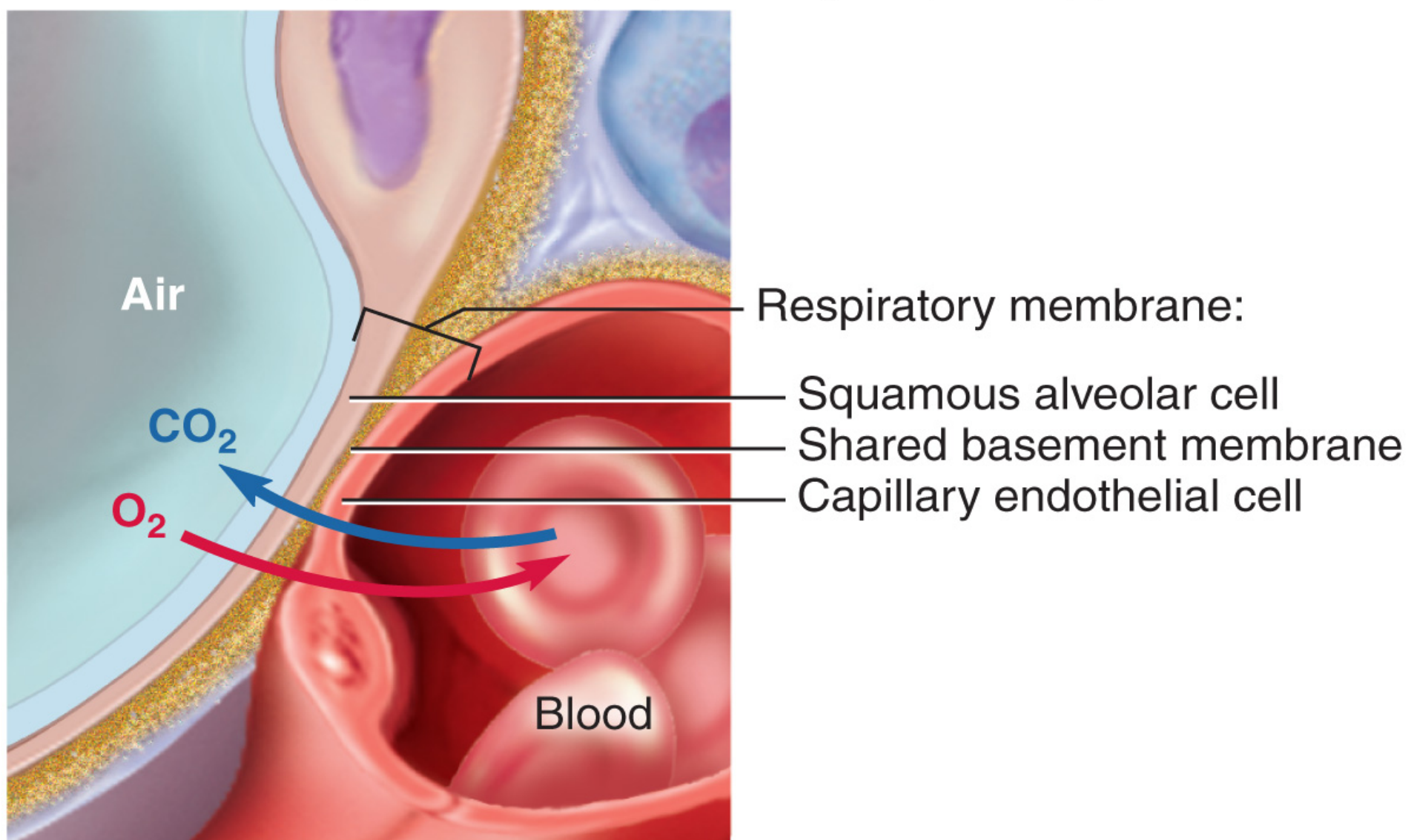
Alveolus

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Alveolus

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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

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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

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Inspiration

Sternocleidomastoid—
(elevates sternum)

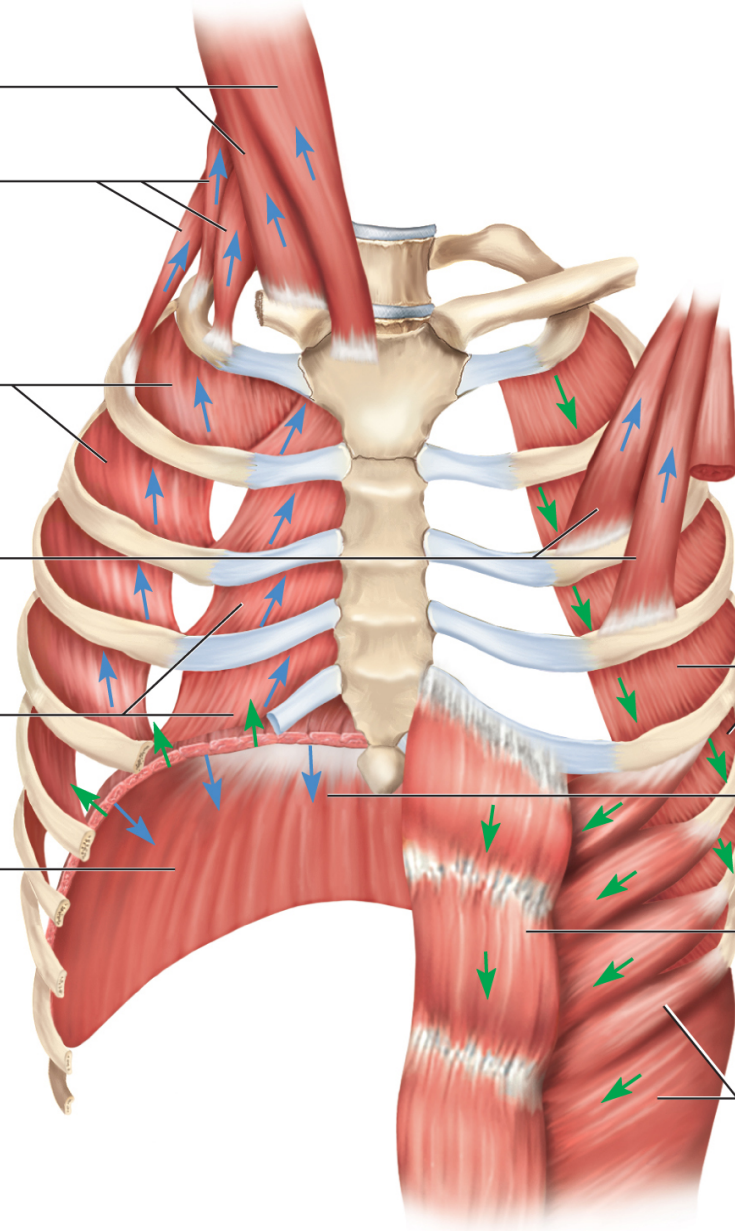
Scalenes—
(fix or elevate ribs 1–2)

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)

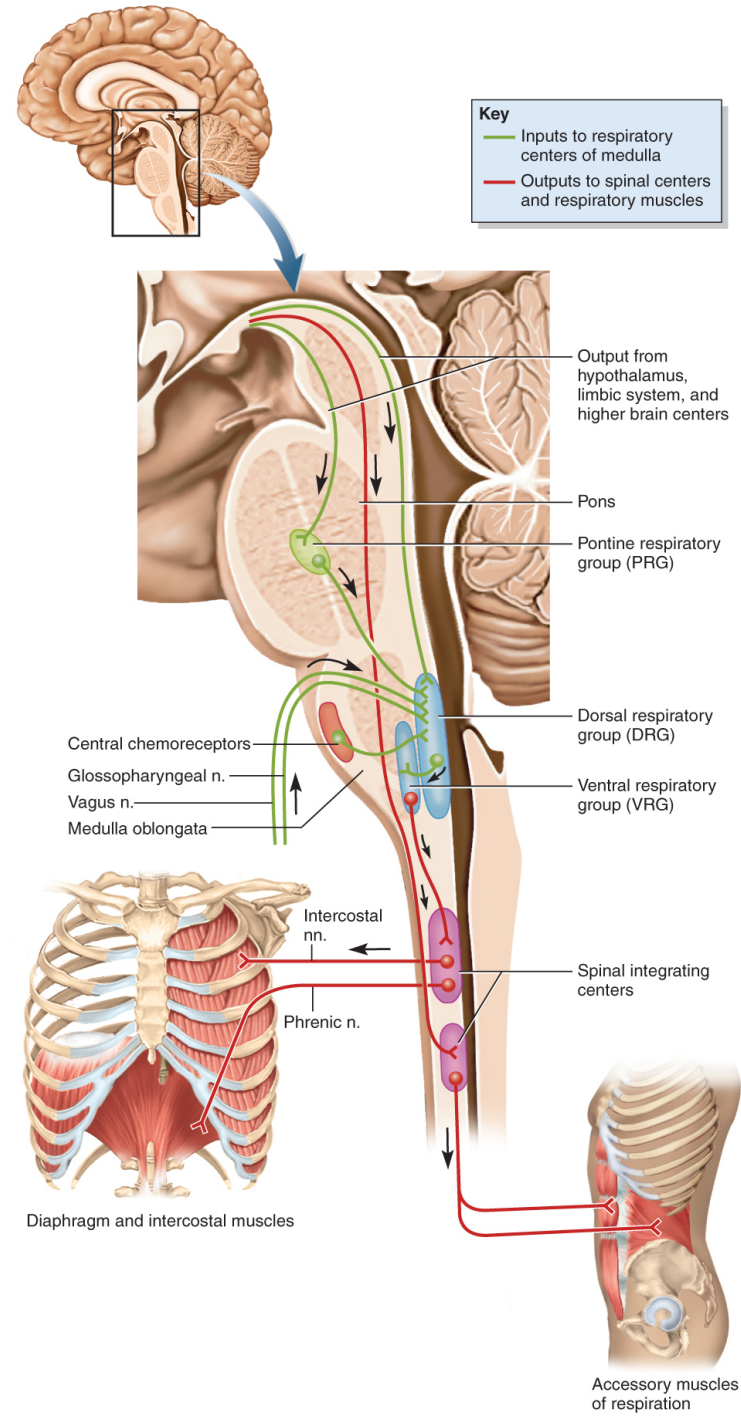
Neural Control of Breathing

- 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



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

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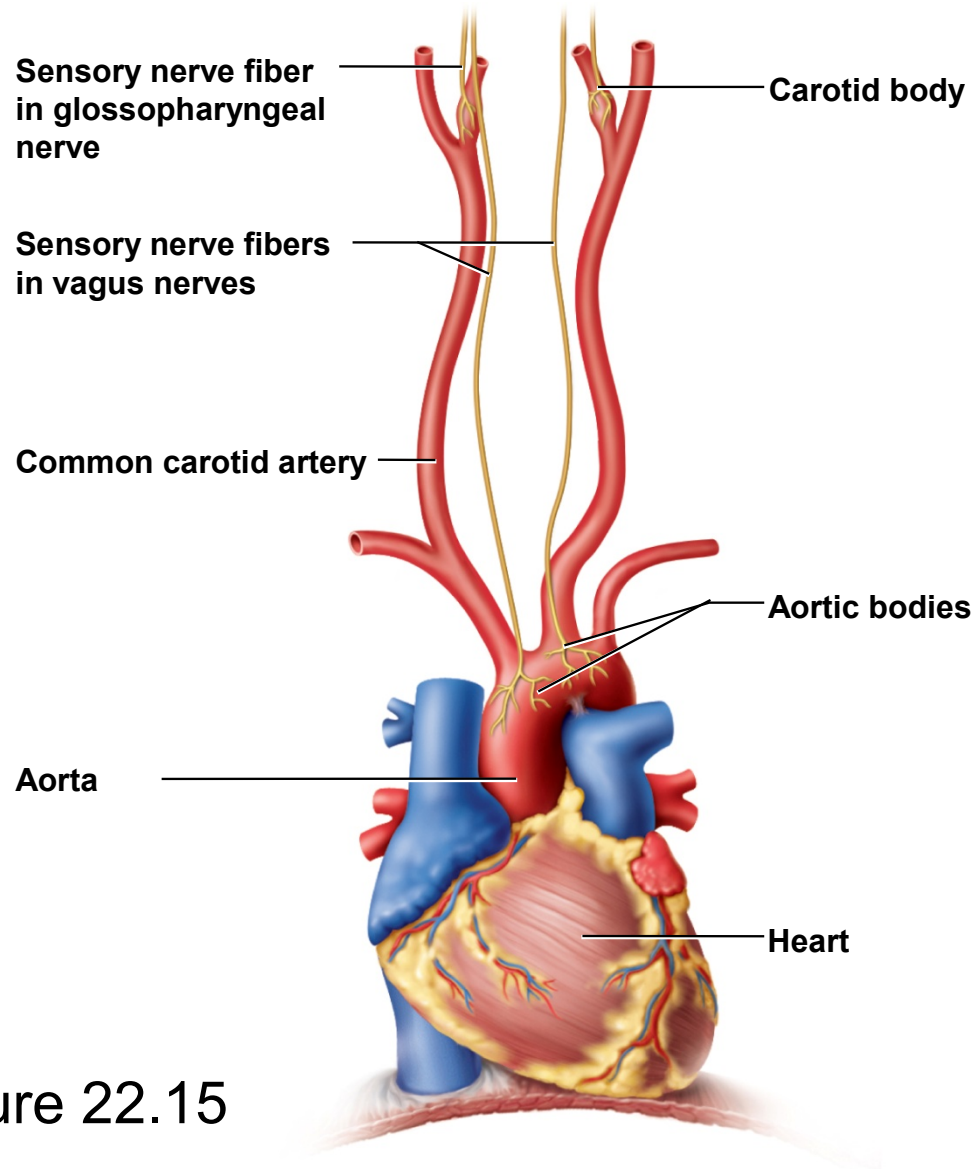


Figure 22.15

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 CO₂ 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

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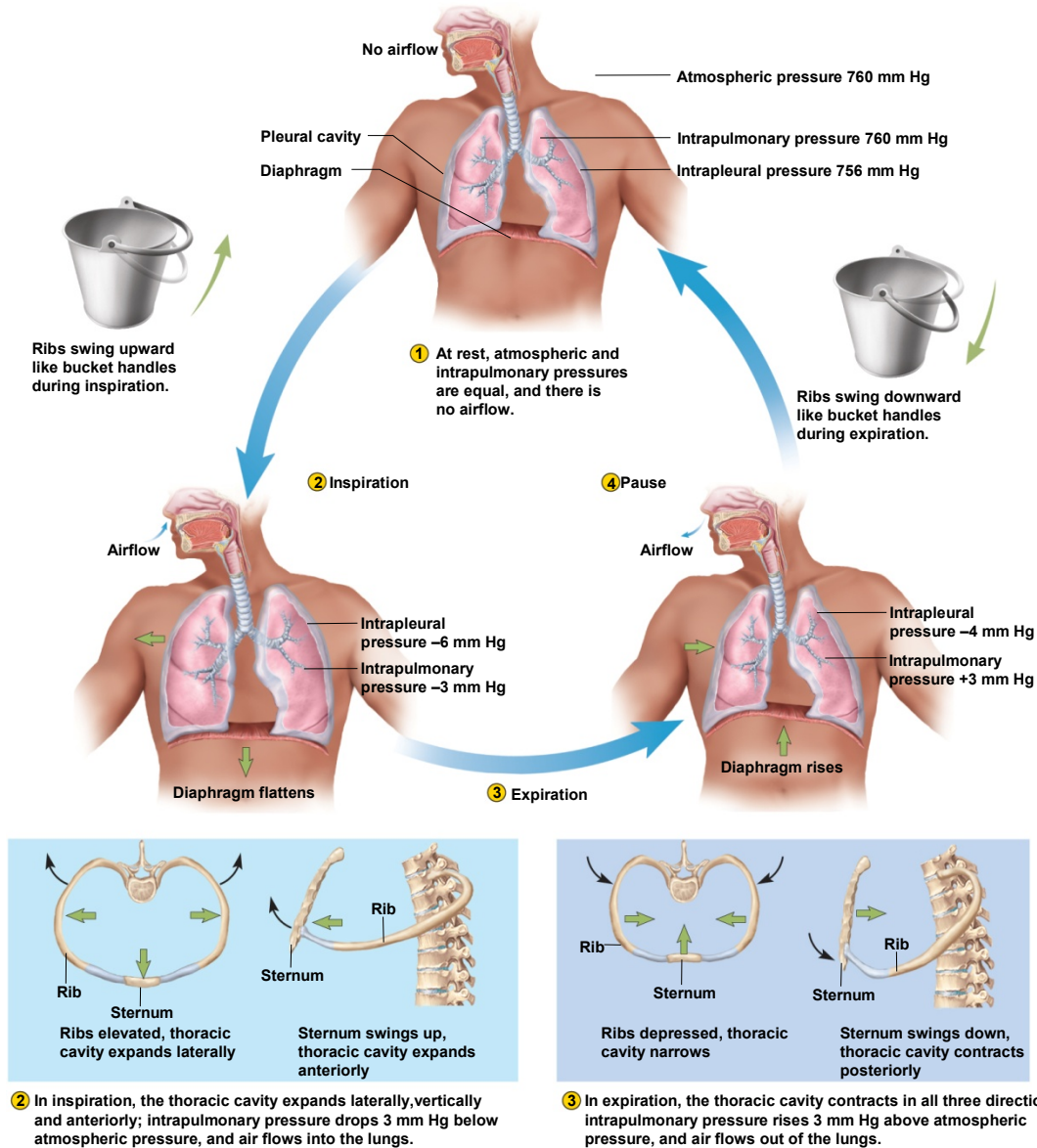


Figure 22.16

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

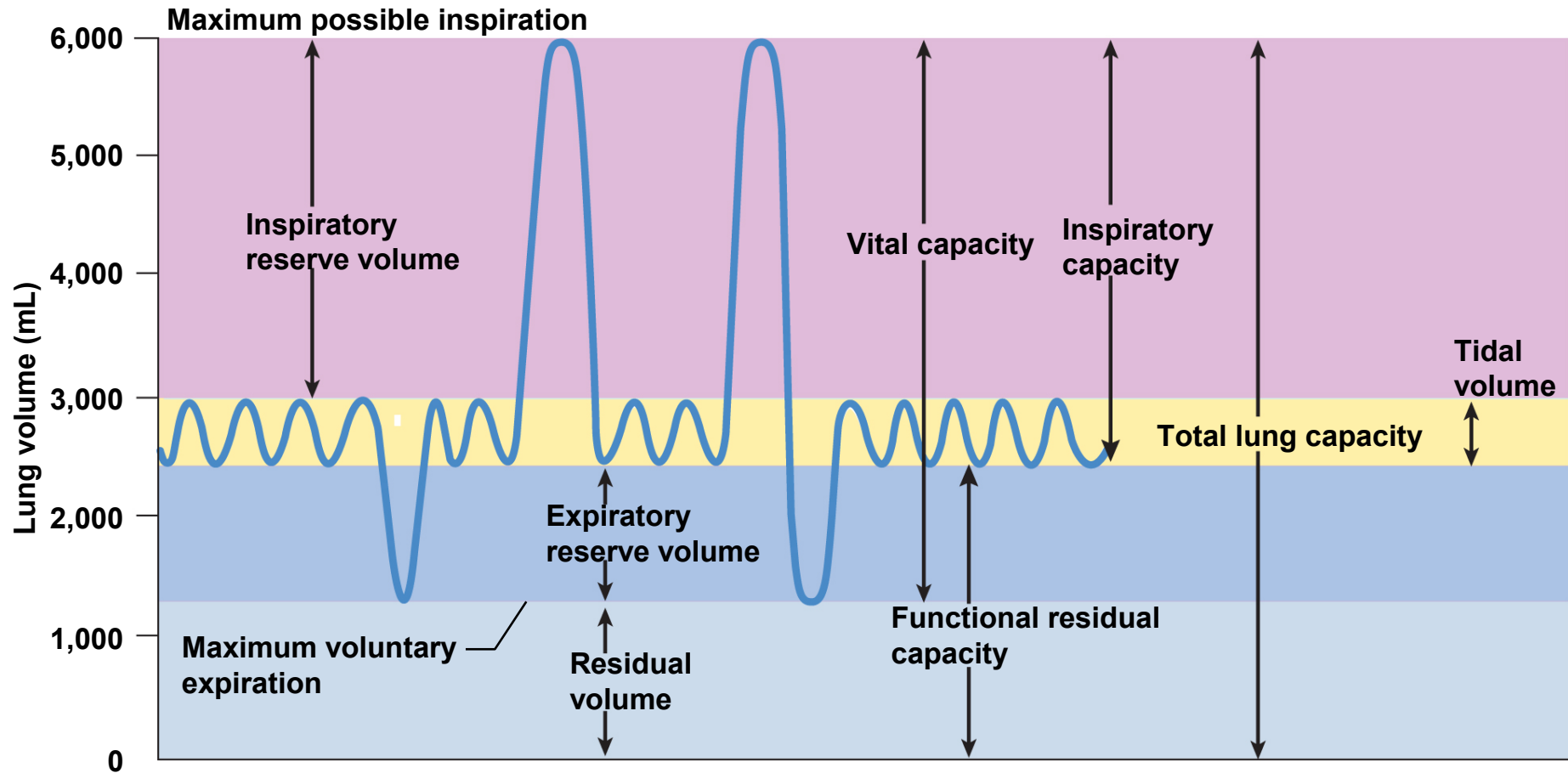
- thin film of water needed for gas exchange
 - creates surface tension that acts to collapse alveoli and distal bronchioles
- pulmonary **surfactant** produced by the great alveolar cells
 - decreases surface tension by disrupting the hydrogen bonding in water
- premature infants that lack surfactant 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

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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

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

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

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

$$\underline{P_{CO_2} = 0.04\% \times 760 \text{ mm Hg} = 0.3 \text{ mm Hg}}$$

$$P_{N_2} + P_{O_2} + P_{H_2O} + P_{CO_2} = 760 \text{ mmHg}$$

Composition of Inspired and Alveolar Air

- composition of inspired air and alveolar is different because of three influences:
 1. **air is humidified 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
 - P_{CO_2} is more than 130 times higher

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 ₂ O	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

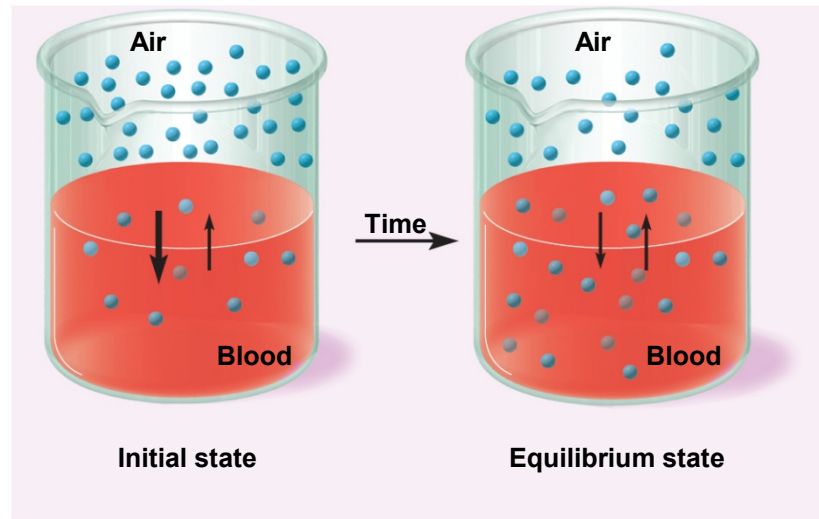
- air in the alveolus is in contact with a film of water covering the alveolar epithelium
 - **for oxygen to get into the blood** it must dissolve in this water
 - pass through the respiratory membrane separating the air from the bloodstream
 - **for carbon dioxide to leave the blood** it must pass the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

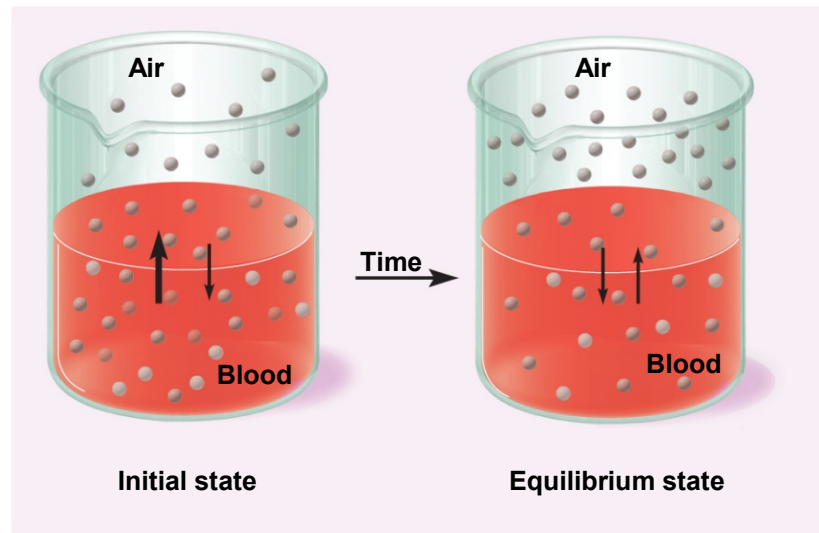
- **Henry's law** – at the air-water interface, for a given temperature, the amount of gas that dissolves in the water is determined by its solubility in water and its partial pressure in air
 - the greater the PO_2 in the alveolar air, the more O_2 the blood picks up
 - since blood arriving at an alveolus has a higher PCO_2 than air, it releases CO_2 into the air
 - at the alveolus, the blood is said to **unload** CO_2 and **load** O_2
 - **unload** CO_2 and **load** O_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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(a) Oxygen



(b) Carbon dioxide

Figure 22.18

Factors Affecting Gas Exchange

- **pressure gradient of the gases**

- $PO_2 = 104$ 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 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 m^2
 - emphysema, lung cancer, and tuberculosis decrease surface area for gas exchange

Concentration Gradients of Gases

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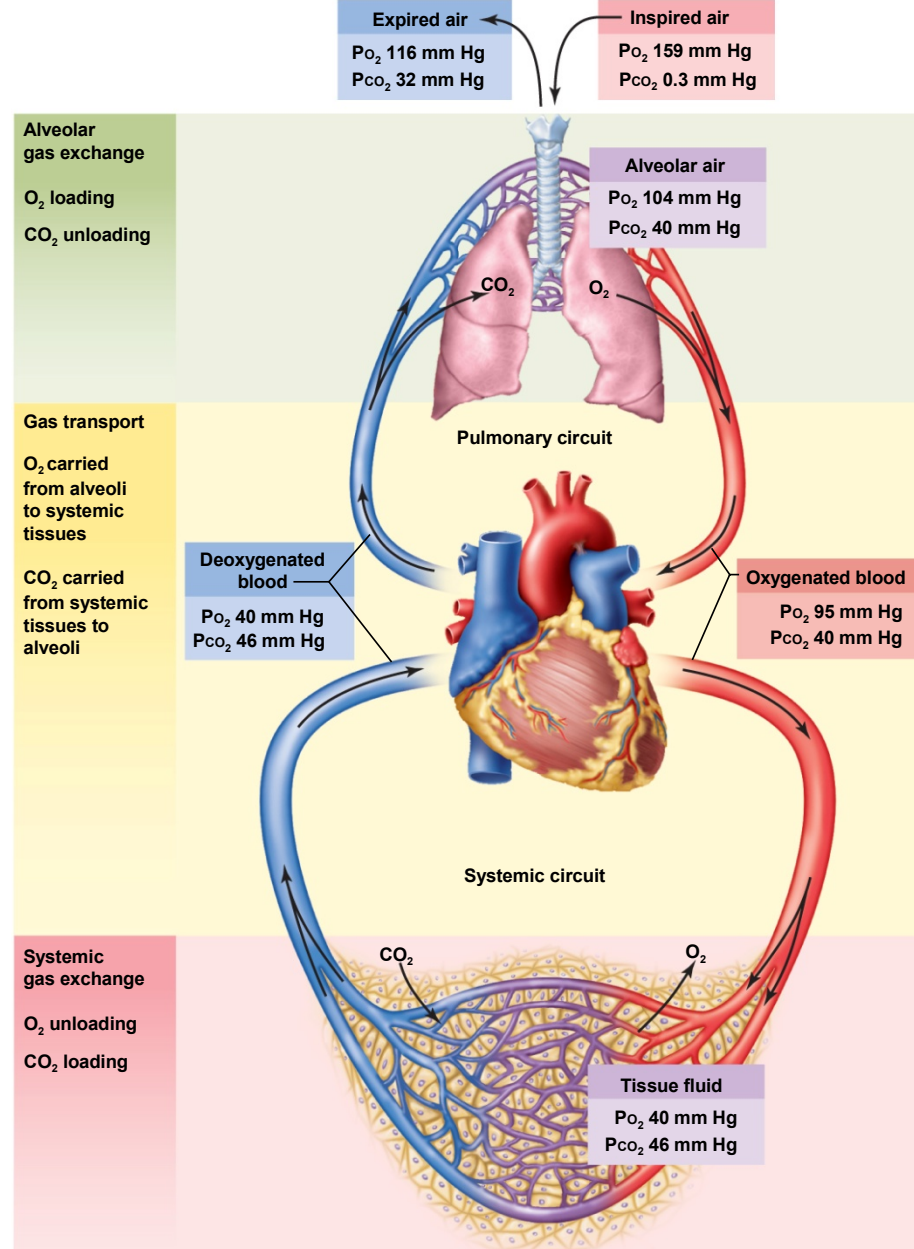


Figure 22.19

Ambient Pressure & Concentration Gradients

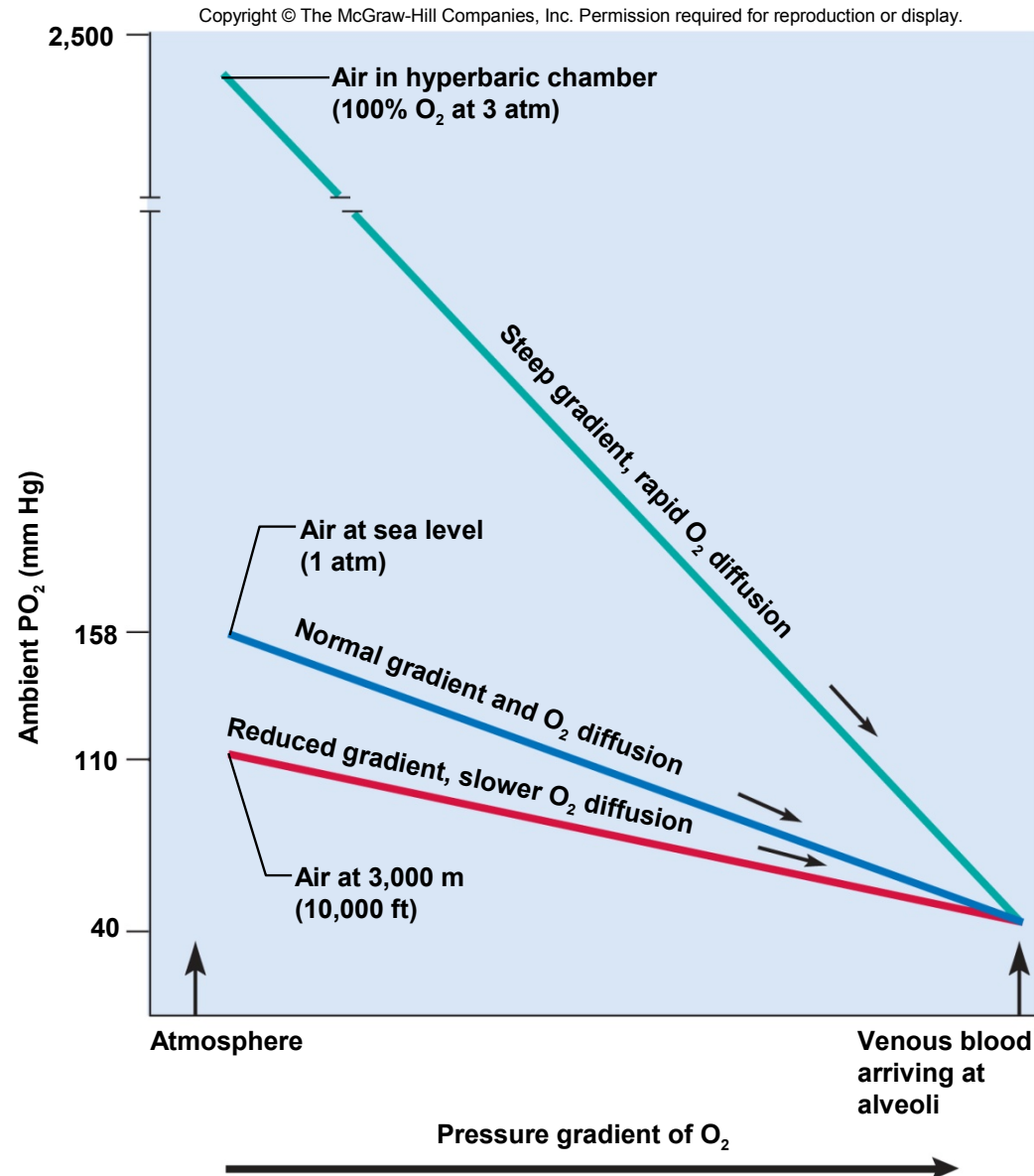
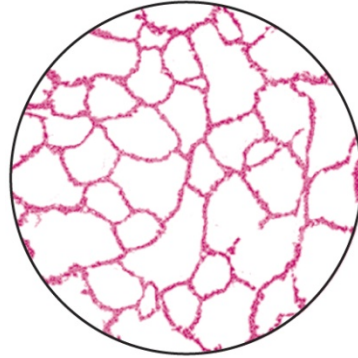


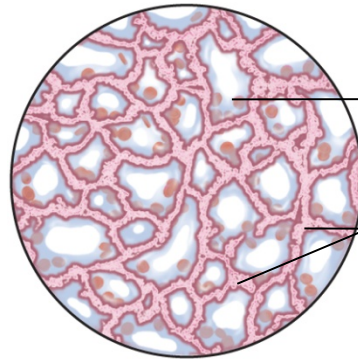
Figure 22.20

Lung Disease Affects Gas Exchange

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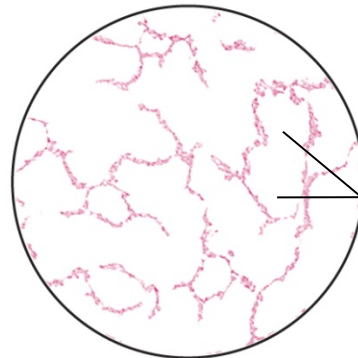
(a) Normal



Fluid and
blood cells
in alveoli

Alveolar
walls
thickened
by edema

(b) Pneumonia



Confluent
alveoli

(c) Emphysema

Figure 22.21

Perfusion Adjustments

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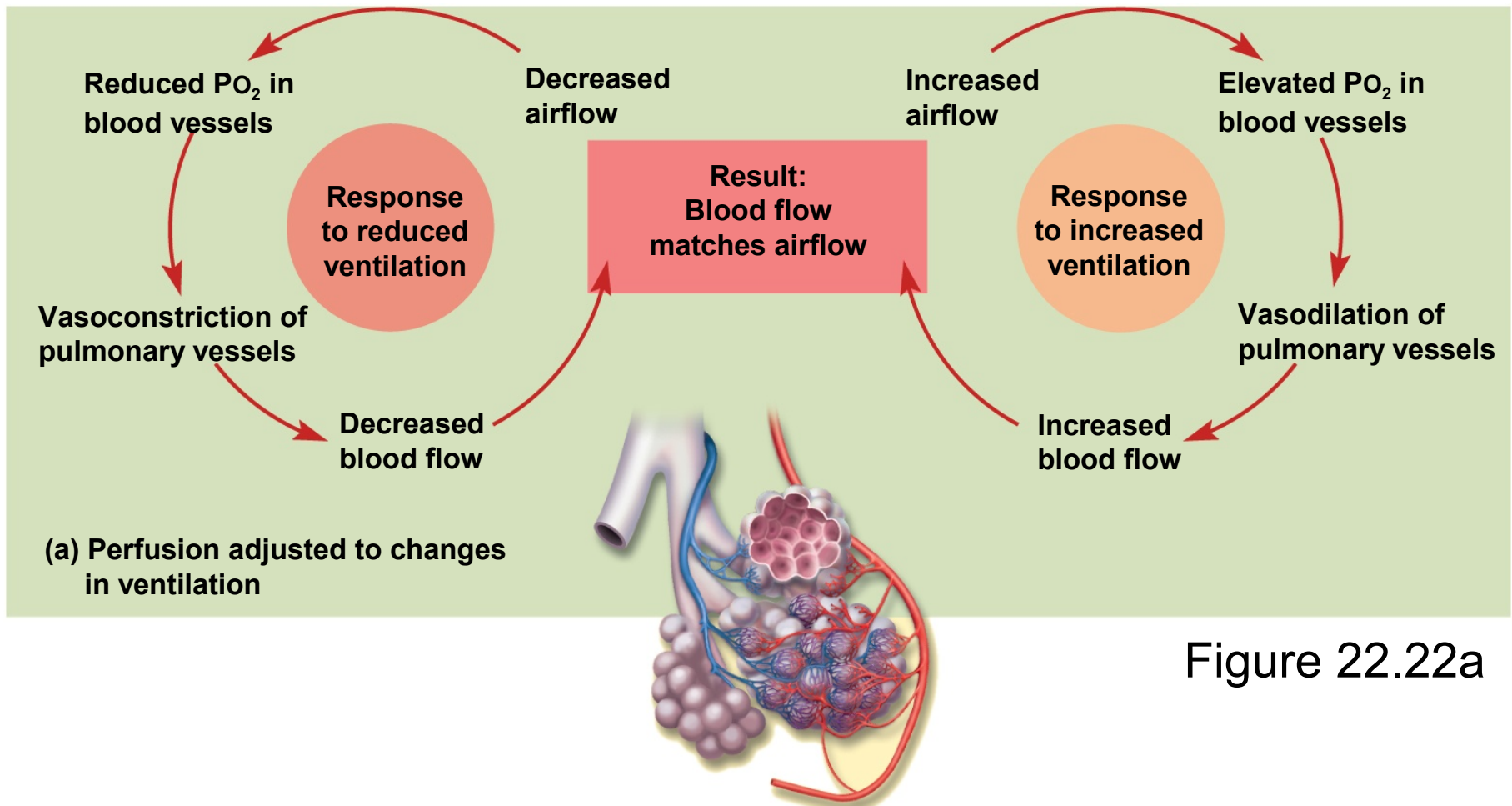
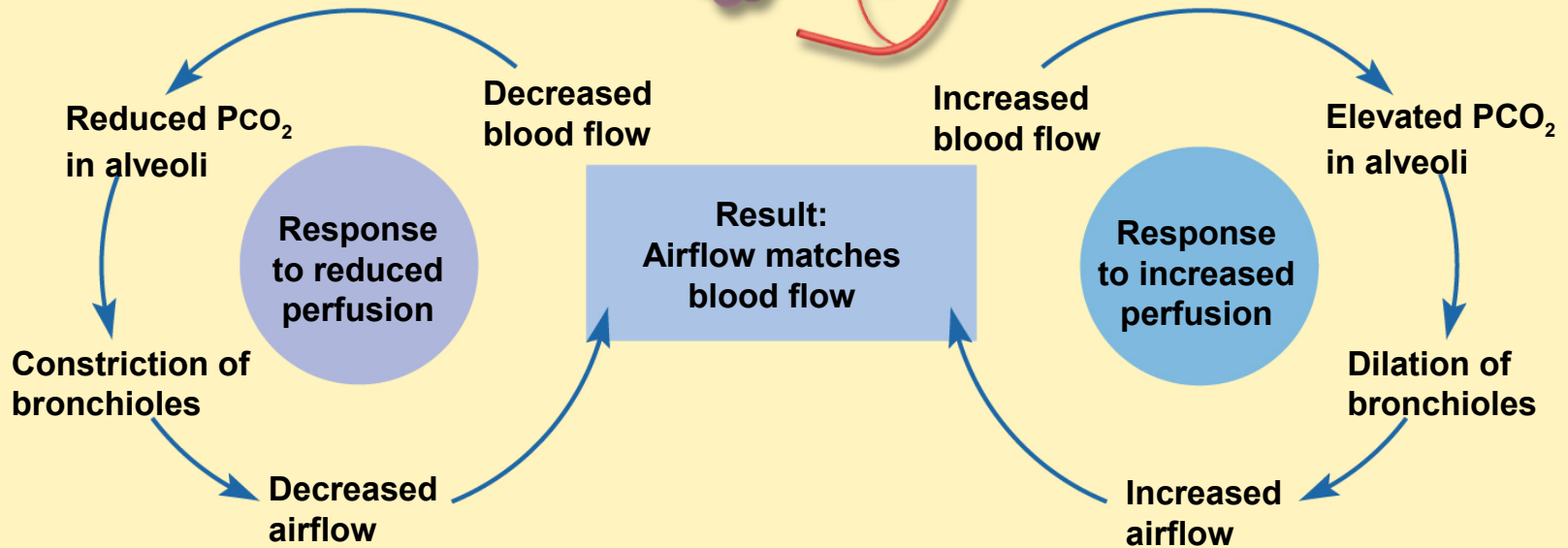
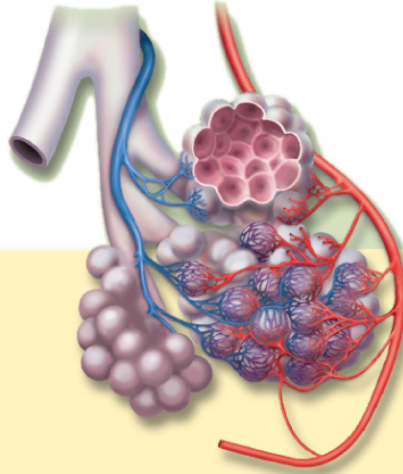


Figure 22.22a

Ventilation Adjustments

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(b) Ventilation adjusted to changes in perfusion

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**
 - 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 O₂ 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

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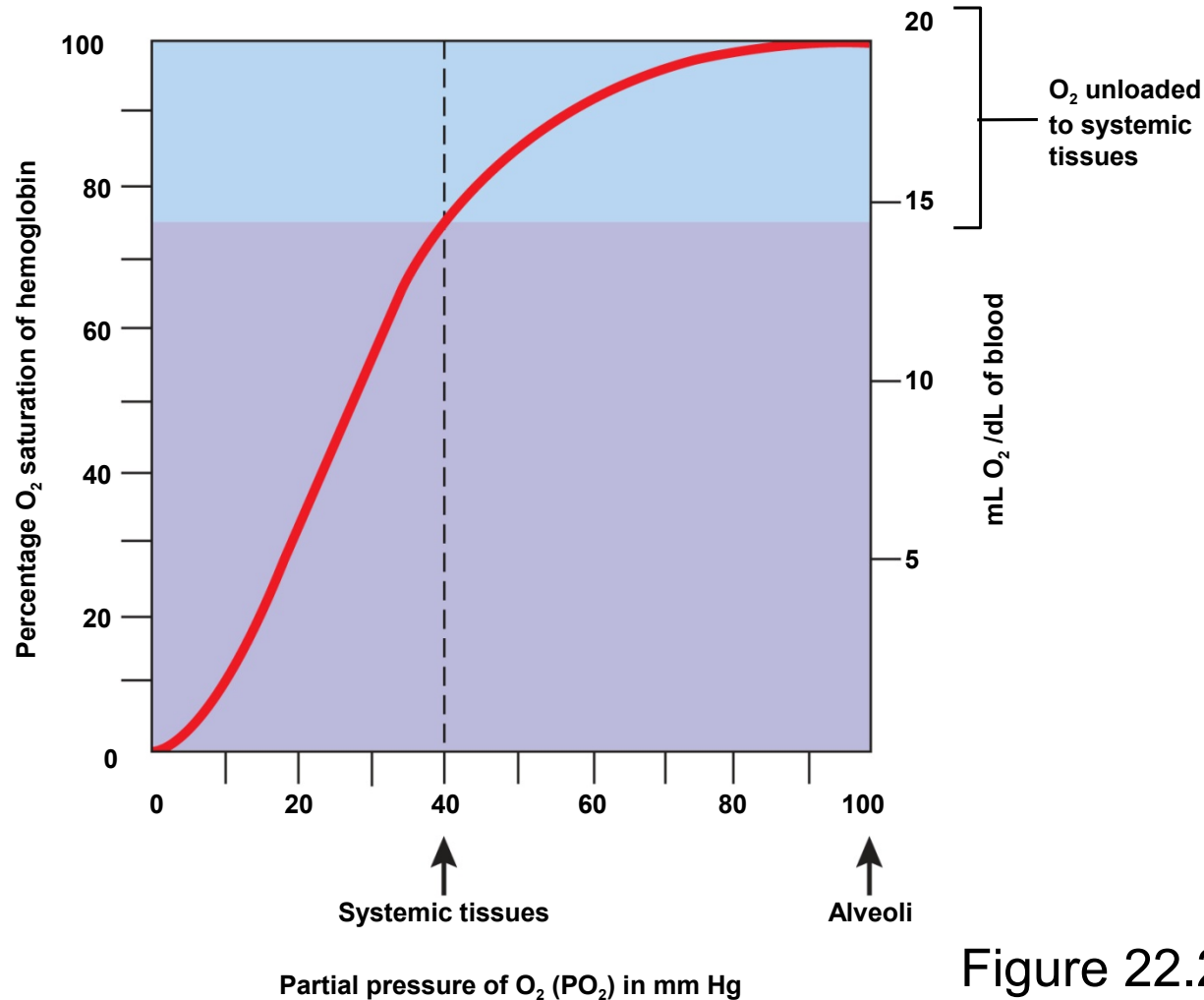


Figure 22.23

relationship between hemoglobin saturation and PO_2

Carbon Dioxide Transport

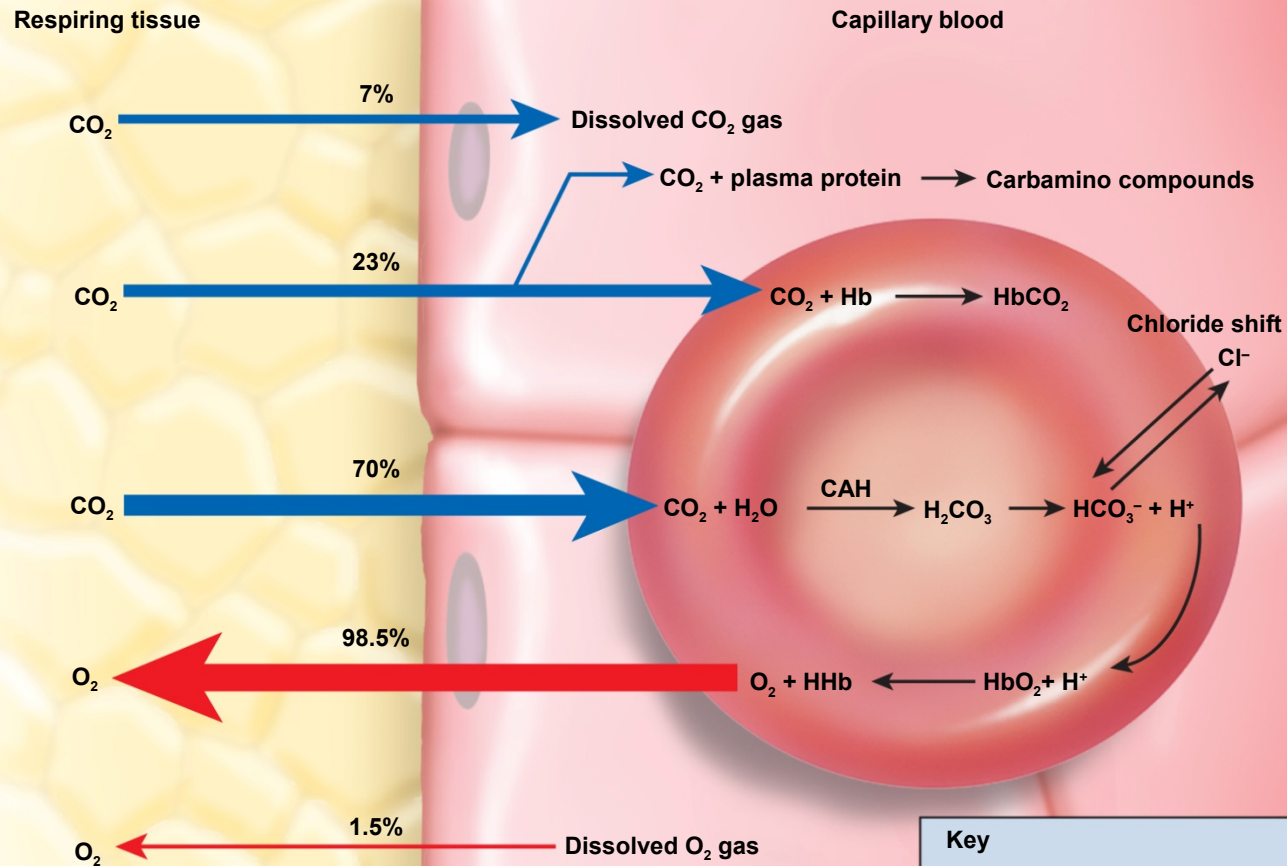
- 90% of CO₂ is hydrated to form carbonic acid
 - $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+$
 - then dissociates into bicarbonate and hydrogen ions
- 5% binds to the amino groups of plasma proteins and hemoglobin to form carbamino compounds – 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
- 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
 - $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons HCO_3^- + H^+$
 - 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

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Key	
Hb	Hemoglobin
HbCO ₂	Carbaminohemoglobin
HbO ₂	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
- **CO₂ unloading**
 - as Hb loads O₂ its affinity for H⁺ decreases, H⁺ dissociates from Hb and bind with HCO₃⁻
 - **CO₂ + H₂O ★ H₂CO₃ ★ HCO₃⁻ + H⁺**
 - reverse **chloride shift**
 - HCO₃⁻ diffuses back into RBC in exchange for Cl⁻, free CO₂ generated diffuses into alveolus to be exhaled

Alveolar Gas Exchange

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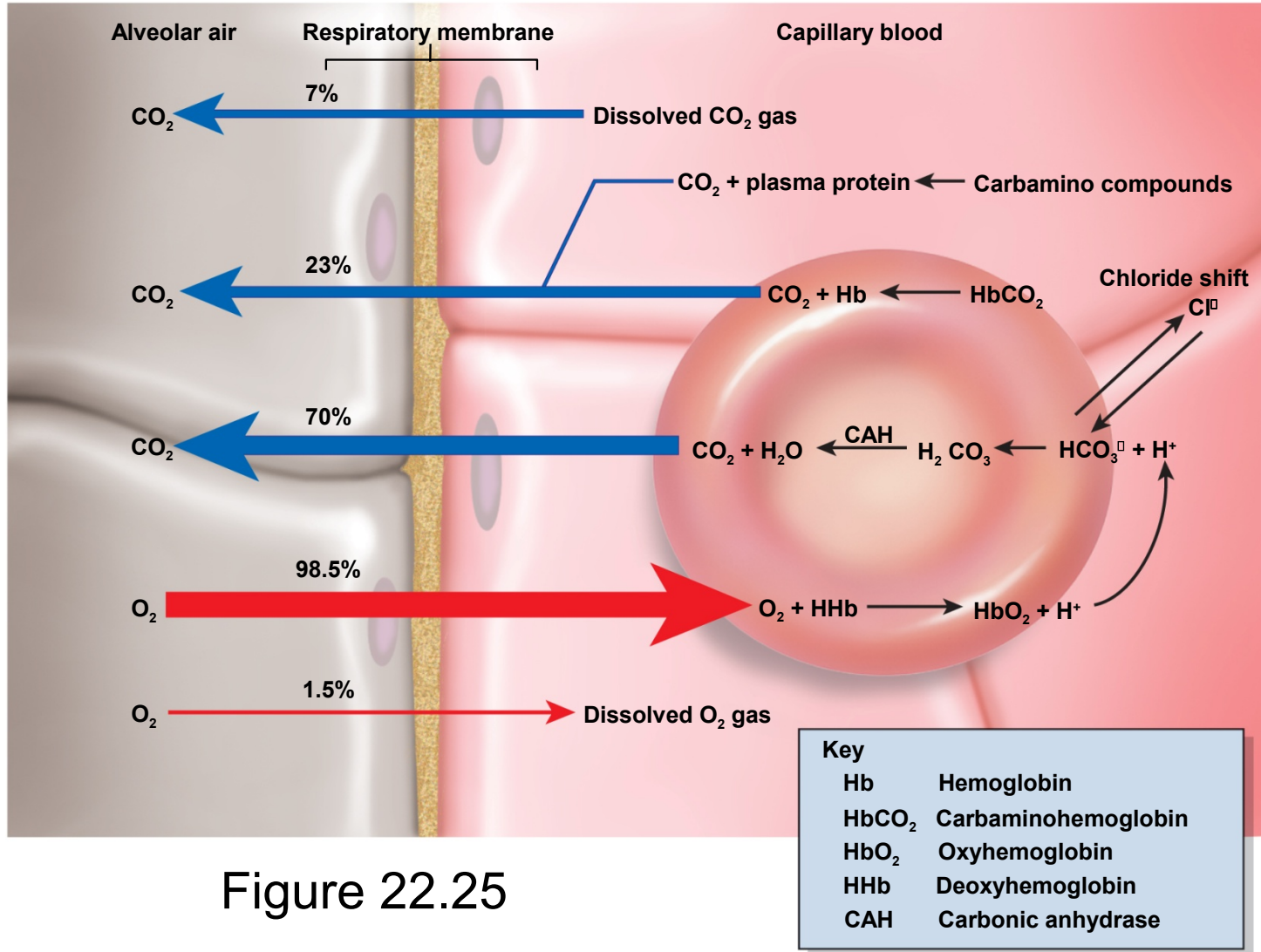


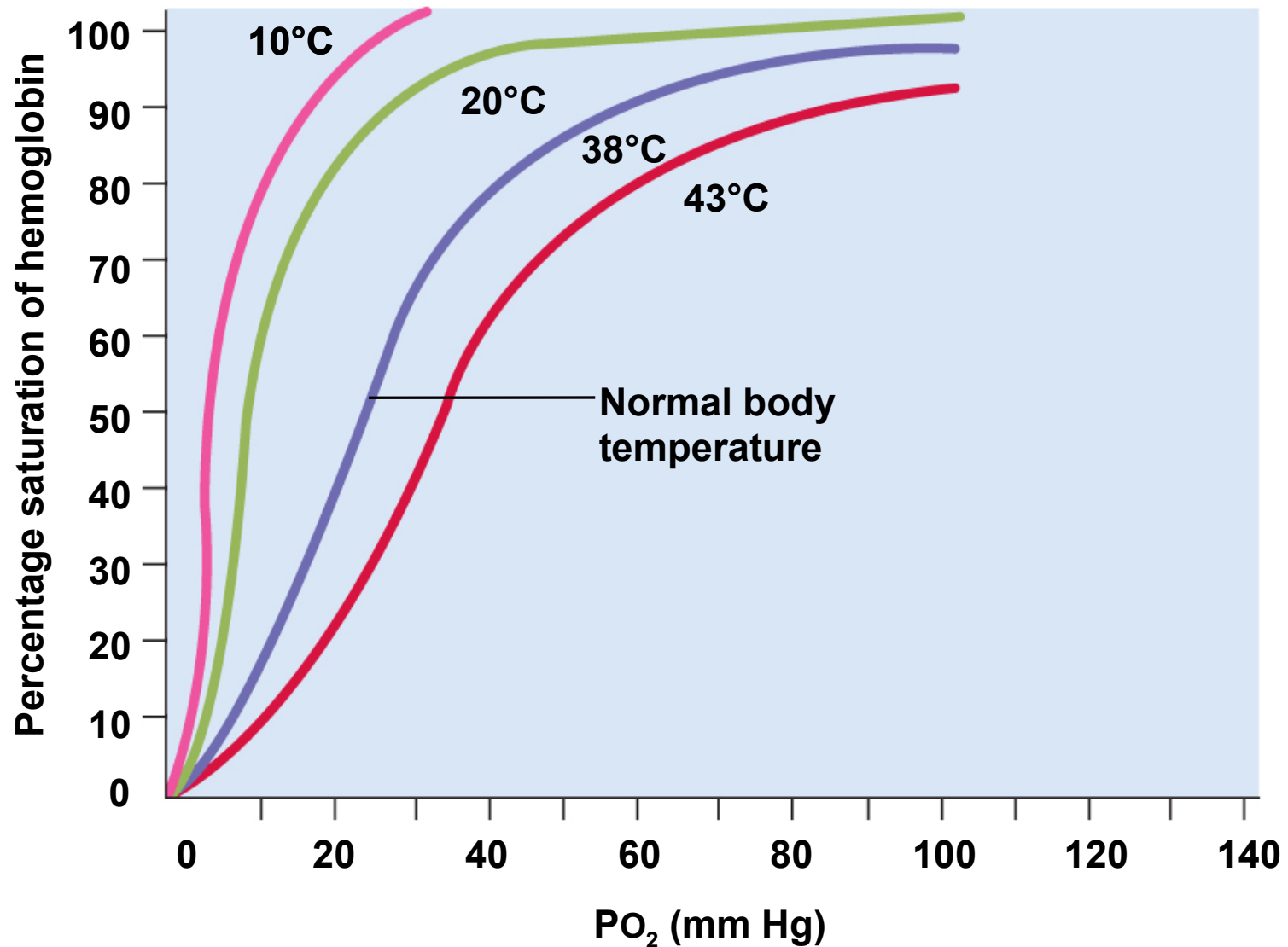
Figure 22.25

Adjustment to the Metabolic Needs of Individual Tissues

- hemoglobin unloads O_2 to match metabolic needs of different states of activity of the tissues
 - **ambient P_{O_2}**
 - active tissue has $\star P_{O_2}$; O_2 is released from Hb
 - **temperature**
 - active tissue has $\star \text{temp}$; promotes O_2 unloading
 - **Bohr effect**
 - active tissue has $\star CO_2$, 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
 - \star body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and cause O_2 unloading
 - » \star metabolic rate requires \star oxygen

Oxygen Dissociation and Temperature

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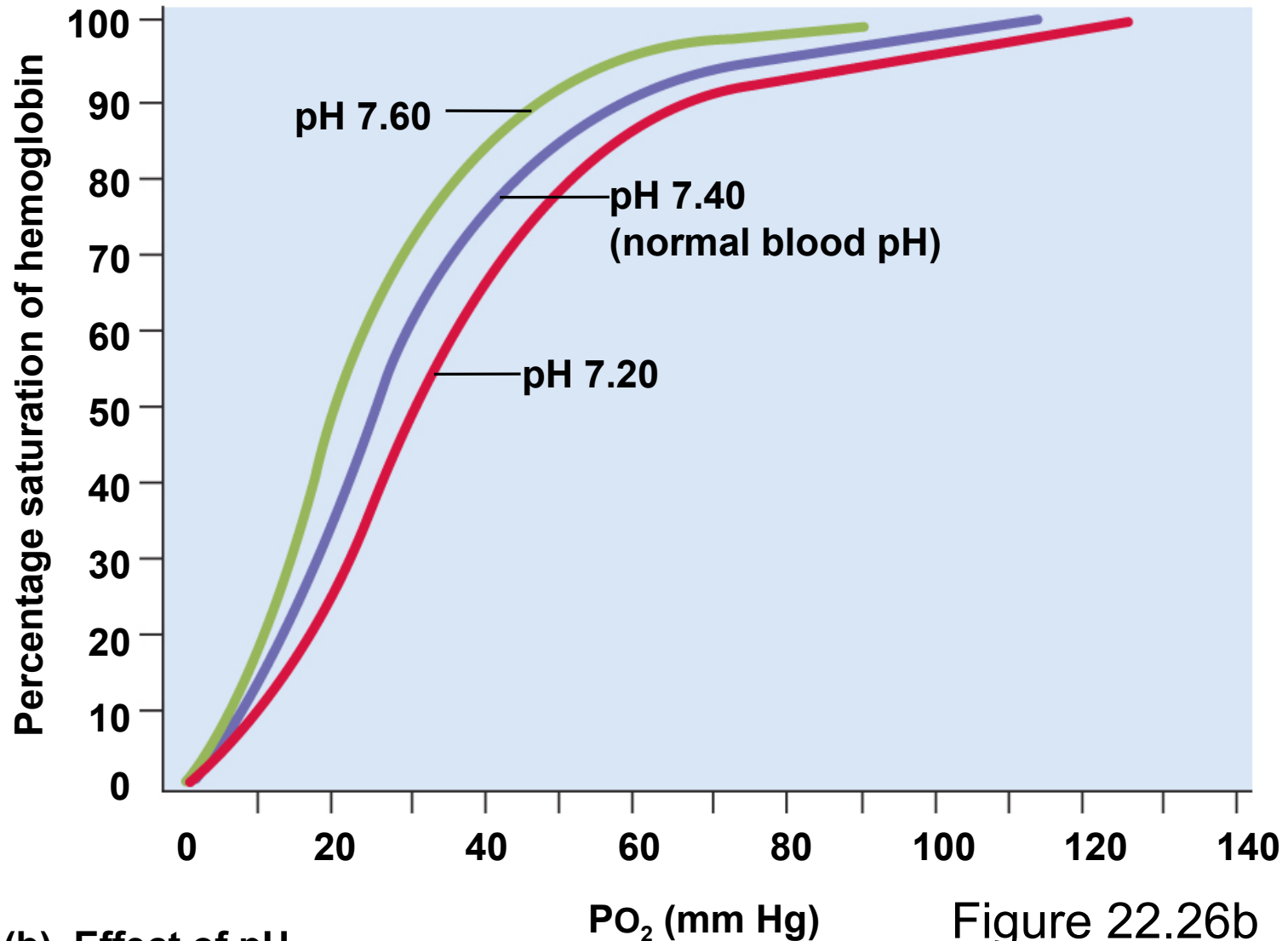


(a) Effect of temperature

Figure 22.26a

Oxygen Dissociation and pH

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(b) Effect of pH

Figure 22.26b

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**
 - **Pco₂** **40 mm Hg**
 - **Po₂** **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 CO₂, and least significant is O₂

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
$$\text{CO}_2 (\text{expired}) + \text{H}_2\text{O} \star \text{H}_2\text{CO}_3 \star \text{HCO}_3^- + \star \text{H}^+$$
 - reduces H⁺ (reduces acid) raises blood pH towards normal

Effects of Hydrogen Ions

- **hypoventilation** is a corrective homeostatic **response to alkalosis**
 - allows CO_2 to accumulate in the body fluids faster than we exhale it
 - shifts reaction to the right
 - $\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{HCO}_3^- + \text{H}^+$
 - 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 CO_2 , it reduces the CO_2 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

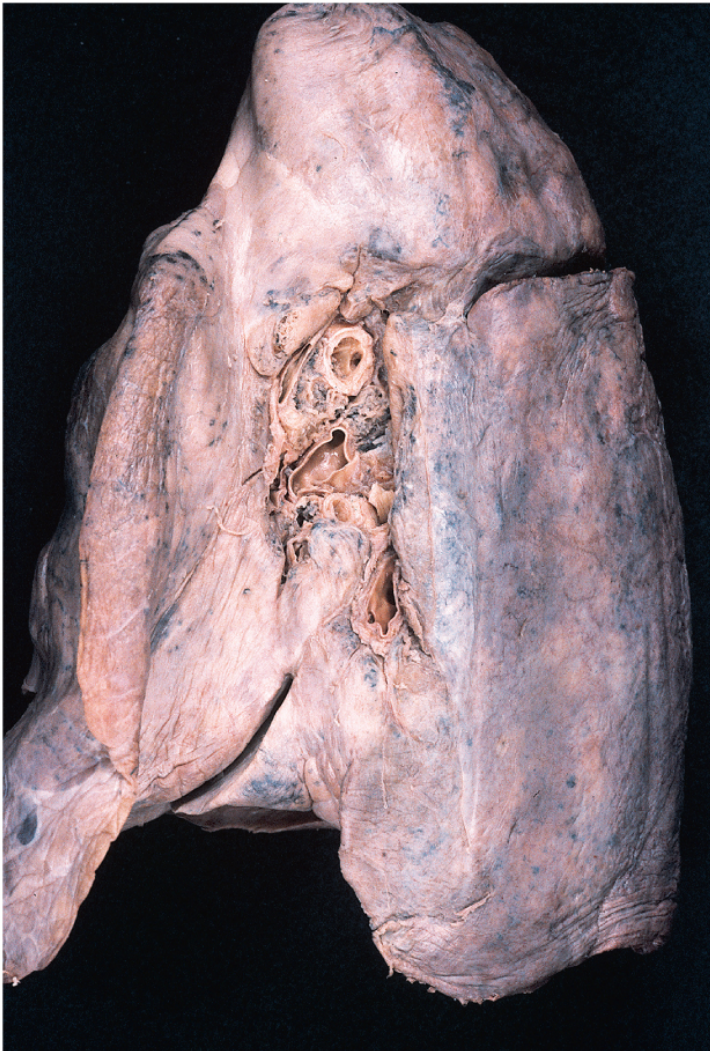
- **adenocarcinoma**
 - originates in mucous glands
- **small-cell (oat cell) carcinoma**
 - least common, most dangerous
 - named for clusters of cells that resemble oat grains
 - originates in primary bronchi, metastasizes quickly to other organs

Progression of Lung Cancer

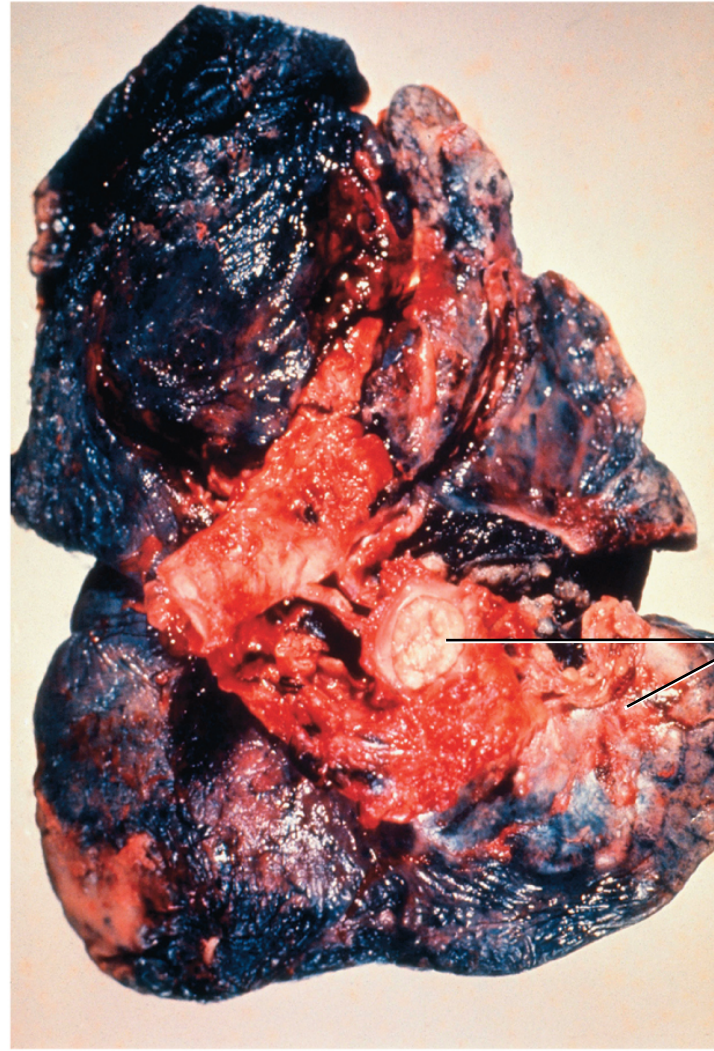
- 90% originate in primary bronchi
- tumor invades bronchial wall, compresses airway; may cause atelectasis
- often first sign is coughing up blood
- metastasis is rapid; usually occurs by time of diagnosis
 - common sites: pericardium, heart, bones, liver, lymph nodes and brain
- prognosis poor after diagnosis
 - only 7% of patients survive 5 years

Effect of Smoking

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(a) Healthy lung, mediastinal surface



(b) Smoker's lung with carcinoma

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Figure 22.27 a-b