# The Respiratory System

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# LEARNING OUTCOMES

## As a result of the lesson you will be able to:

- *List state the functions of the respiratory system;*
- *Name and Identify the organs forming the respiratory passageway from the nasal cavity to the alveoli of the lungs (on a diagram or model), and describe the function of each.*
- *Describe the structure and function of the lungs, the pleural coverings and the respiratory membrane.*
- *Name the muscles of respiration and describe their roles in inspiration and expiration;*
- *Describe the brainstem centers that control breathing and the inputs they receive from other parts of the nervous system.*
- *Define partial pressure and explain how it affects diffusion of gases across the respiratory membrane;*
- *Describe gas exchange in the lungs and systemic capillaries;*
- *Describe how $O_2$ and $CO_2$ are transported in the blood;*
- *Explain the effect of blood gases and pH on the respiratory rhythm*

# Breathing

- breathing represents **life**!
  - first breath of a newborn baby
  - last gasp of a dying person
- 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)
2. **the exchange of gases between the air and blood, and between blood and the tissue fluid**
3. **the use of oxygen in cellular metabolism**

# Functions of Respiratory System

- **$O_2$ and $CO_2$ exchange** between blood and air
- **speech** and other vocalizations
- sense of **smell**
- affects **pH** of body fluids by eliminating $CO_2$
- 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



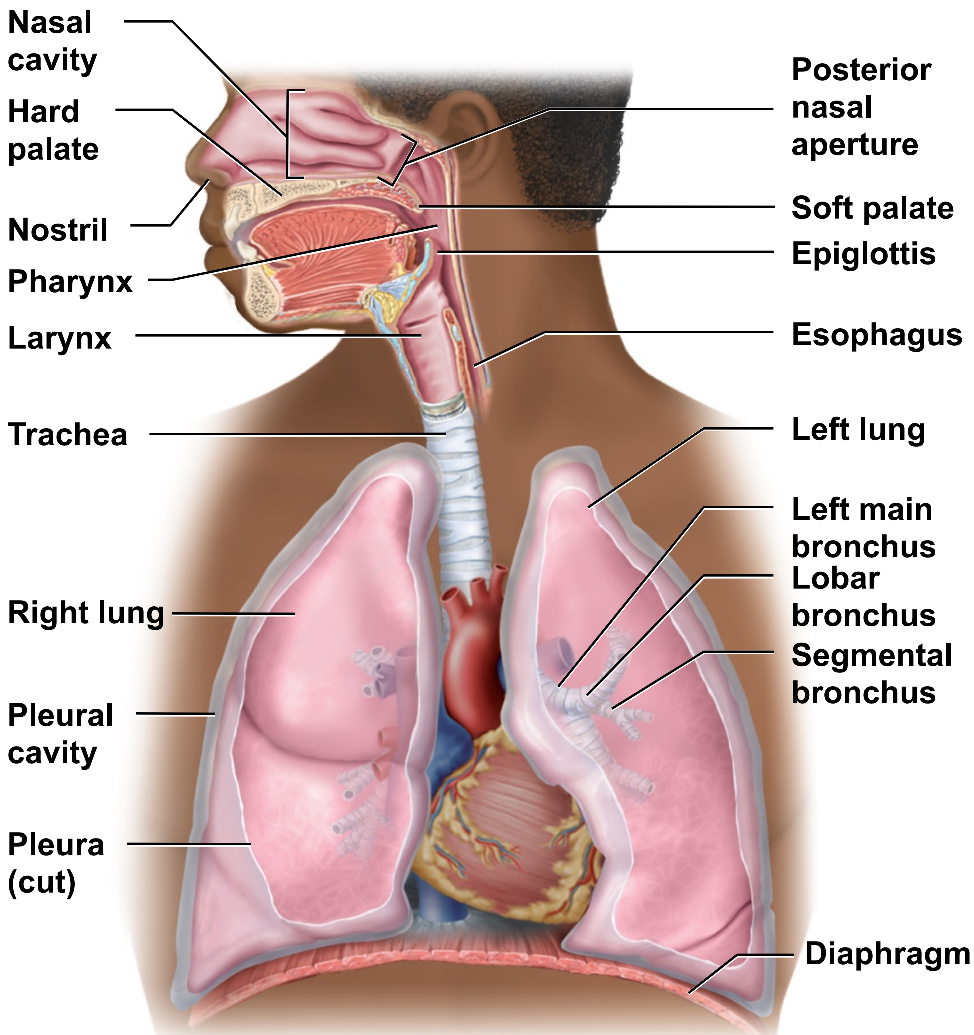



Figure 22.1

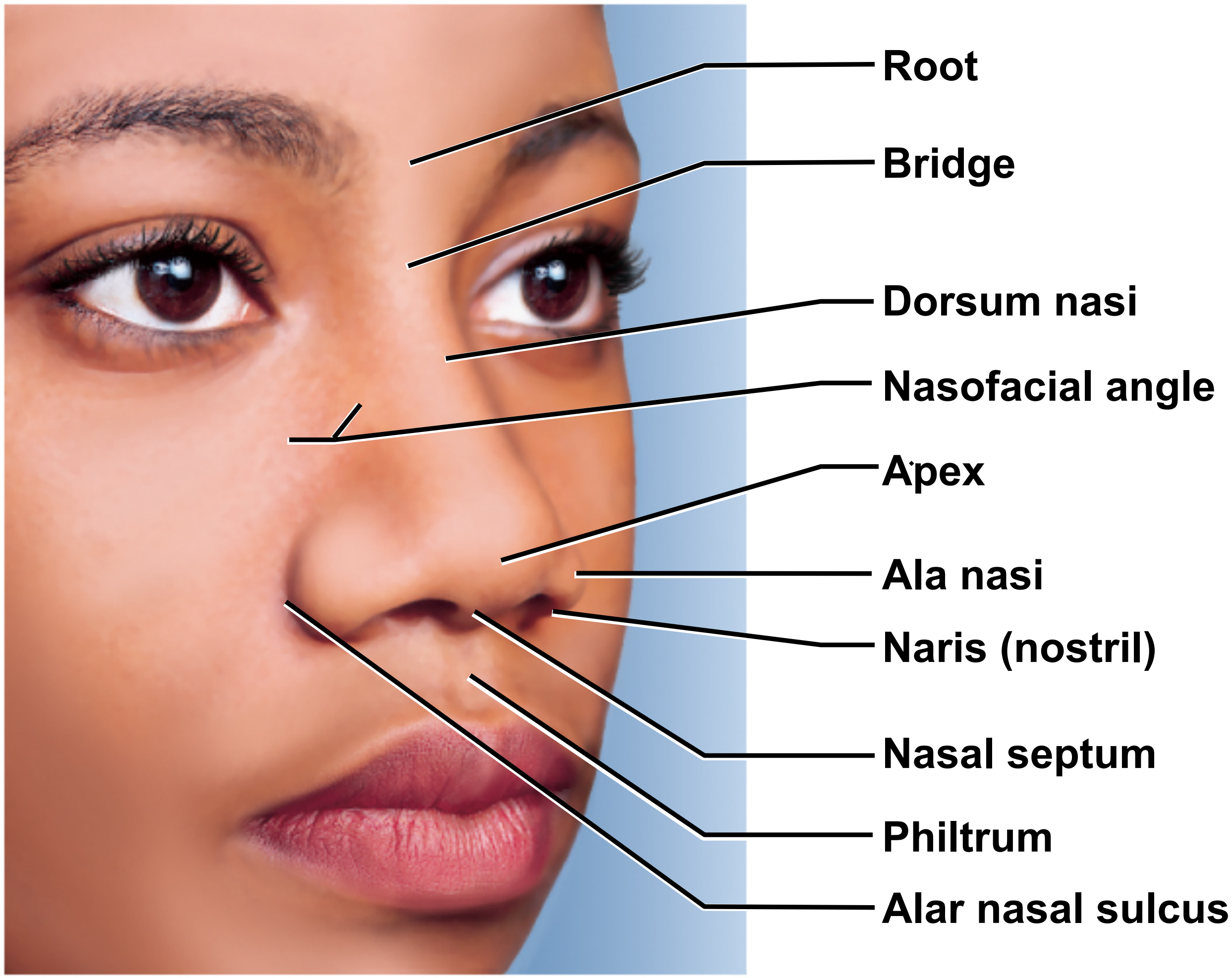
- nose, pharynx, larynx, trachea, bronchi, lungs

# 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
- nose extends from **nostrils** (nares), to a pair of posterior openings called the **posterior nasal apertures** (choanae)
- 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 the lower end of nose shaped by alar cartilages and dense connective tissue

# Anatomy of Nasal Region






(a)

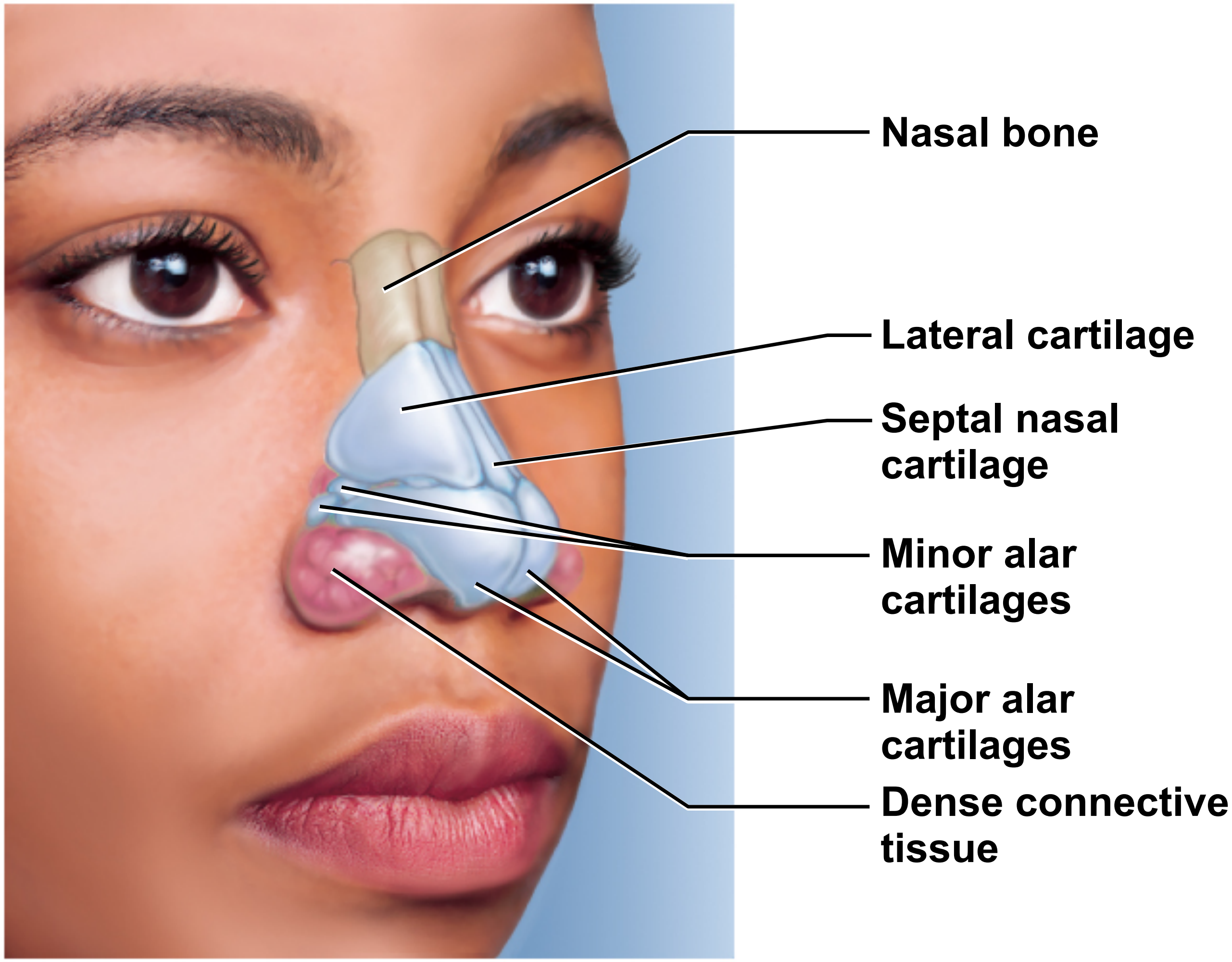




Figure 22.2a

# Anatomy of Nasal Region






(b)





Figure 22.2b

# Nasal Cavity

- **nasal fossae** – right and left halves of the 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

# Nasal Cavity

- **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.
- 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 insure that most air contacts mucous membranes
    - cleans, warms, and moistens the air
- **olfactory epithelium** – detect odors
  - covers a small area of the roof of the nasal fossa and adjacent parts of the septum and superior concha
  - ciliated pseudostratified columnar epithelium with goblet cells
  - immobile cilia to bind odorant molecules

# Nasal Cavity

- **respiratory epithelium** lines rest of nasal cavity except vestibule
  - ciliated pseudostratified columnar epithelium with goblet cells
  - cilia are motile
  - goblet cells secrete mucus and cilia propel the mucous posteriorly toward pharynx
  - swallowed into digestive tract
- **erectile tissue** - extensive venous plexus in inferior concha
  - every 30 to 60 minutes, erectile tissue on one side swells with blood
  - restricts air flow through that fossa
  - most air directed through other nostril and fossa
  - allowing engorged side time to recover from drying
  - preponderant flow of air shifts between the right and left nostrils once or twice an hour

# Upper Respiratory Tract



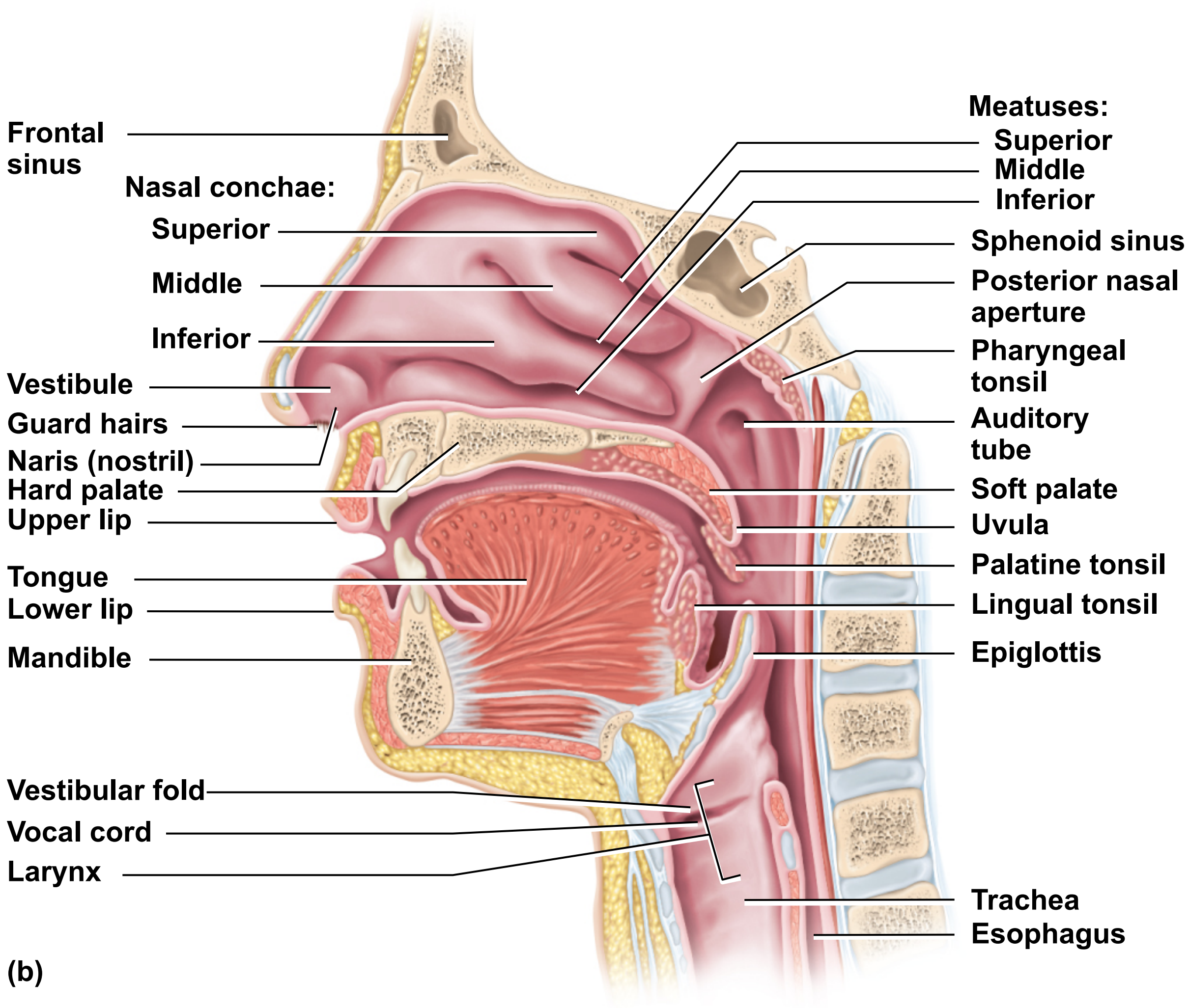



Figure 22.3b

# Upper Respiratory Tract



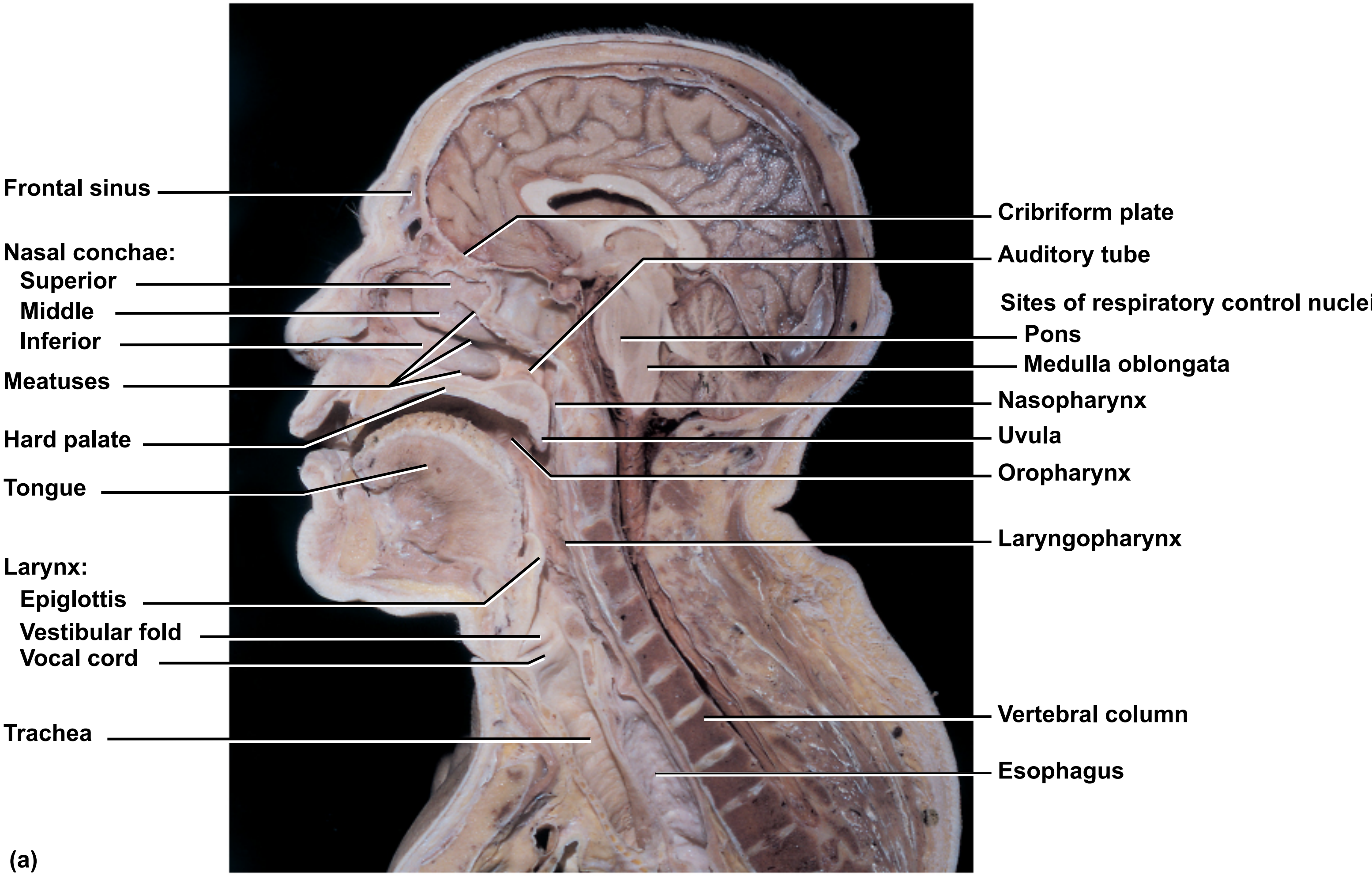





Figure 22.3a

# Regions of Pharynx



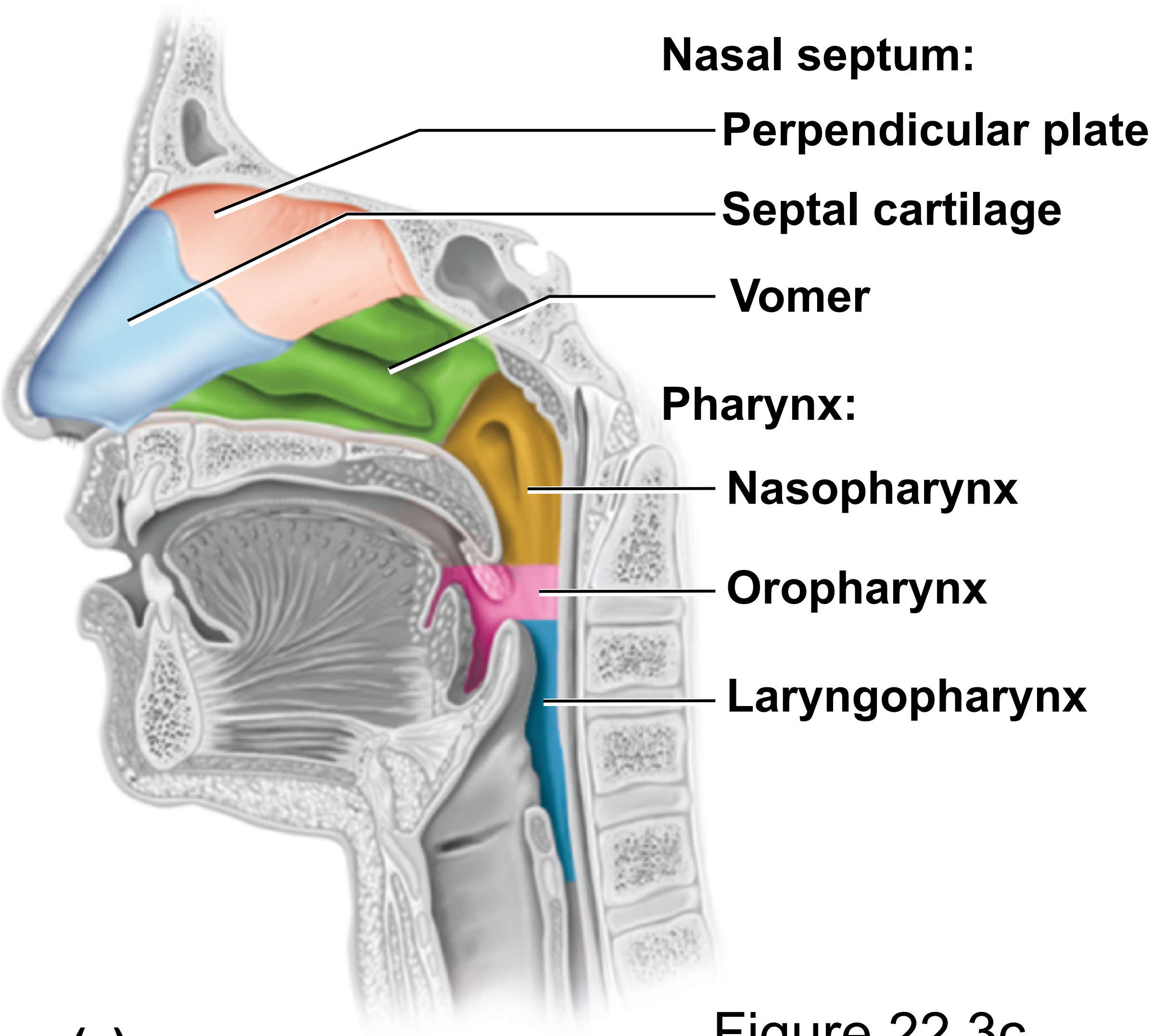



Figure 22.3c

# Pharynx

- **pharynx** (throat) – a muscular funnel extending about 13 cm (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$\mu$m)
  - **oropharynx**
    - space between soft palate and epiglottis
    - contains palatine tonsils
  - **laryngopharynx**
    - epiglottis to cricoid cartilage
    - esophagus begins at that point

- **nasopharynx** passes only air and is lined by **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 additional role – **phonation** – production of 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
  – **vestibular folds** of the larynx play greater role in keeping food and drink out of the airway

# Views of Larynx



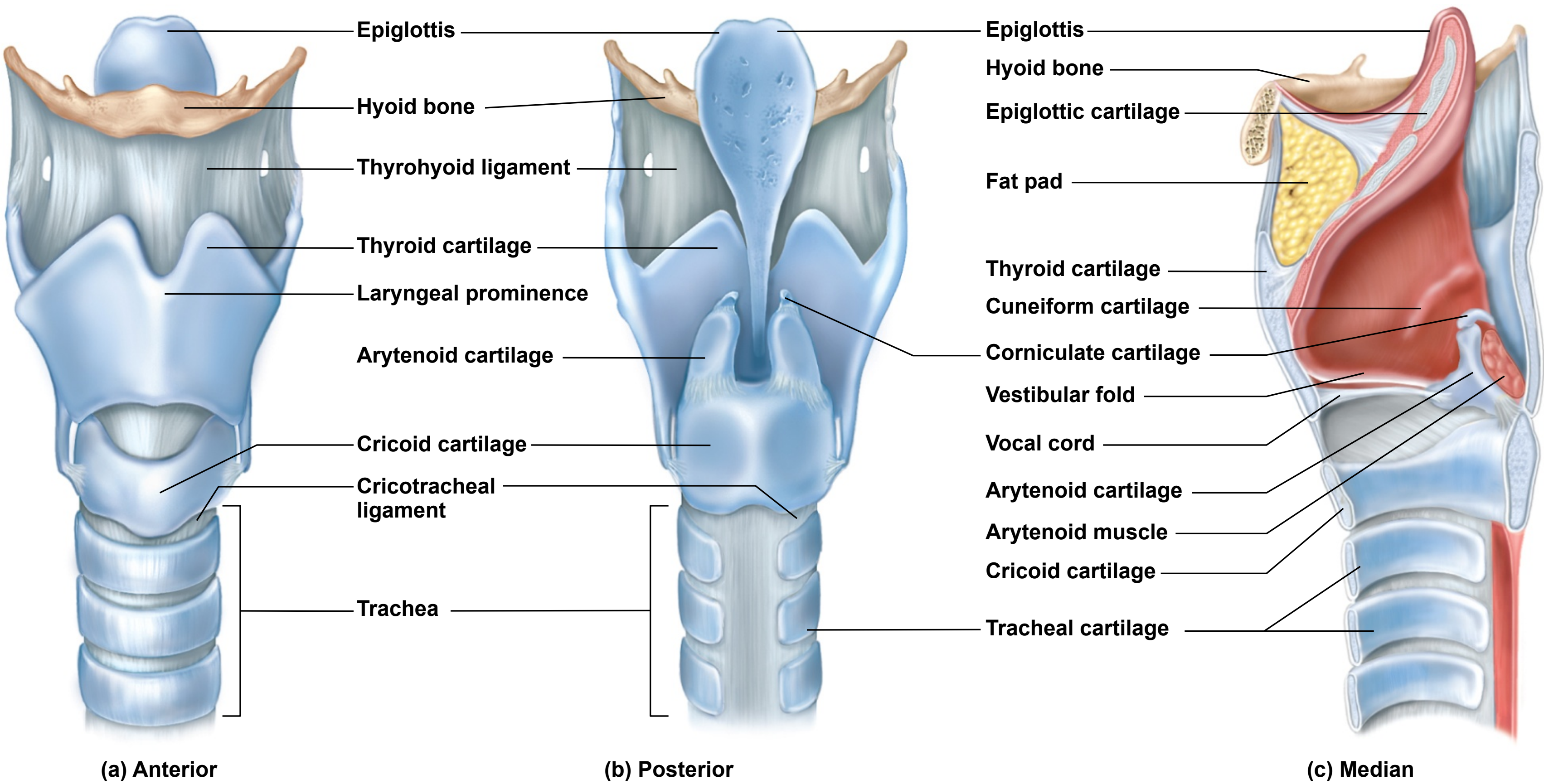



Figure 22.4 a-c

# Larynx

- **nine cartilages** that 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 stimulated growth, larger in males
  - **cricoid cartilage** - connects larynx to trachea, ringlike

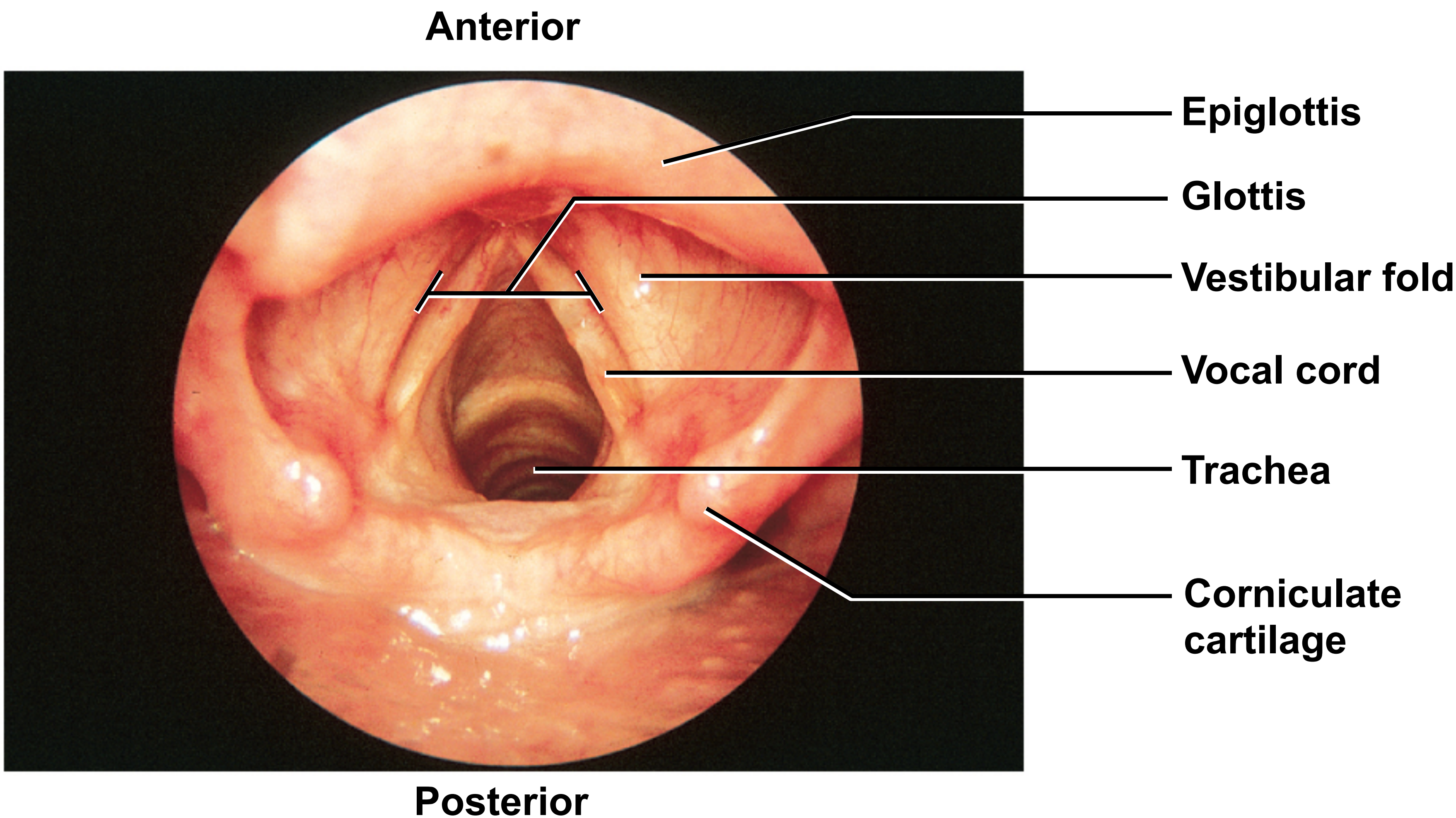
- three smaller, paired cartilages
  - **arytenoid cartilages** (2) - posterior to thyroid cartilage
  - **corniculate cartilages** (2) - attached to arytenoid cartilages like a pair of little horns
  - **cuneiform cartilages** (2) - support soft tissue between arytenoids and epiglottis

# 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
    - infrahyoid group
- interior wall has **two folds** on each side that extend from thyroid cartilage in front to arytenoid cartilages in the 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 stratifies squamous epithelium
      - best suited to endure vibration and contact between the cords
    - **glottis** – the vocal cords and the opening between them

# Endoscopic View of the Larynx






(a)

Figure 22.5a

# Action of Vocal Cords



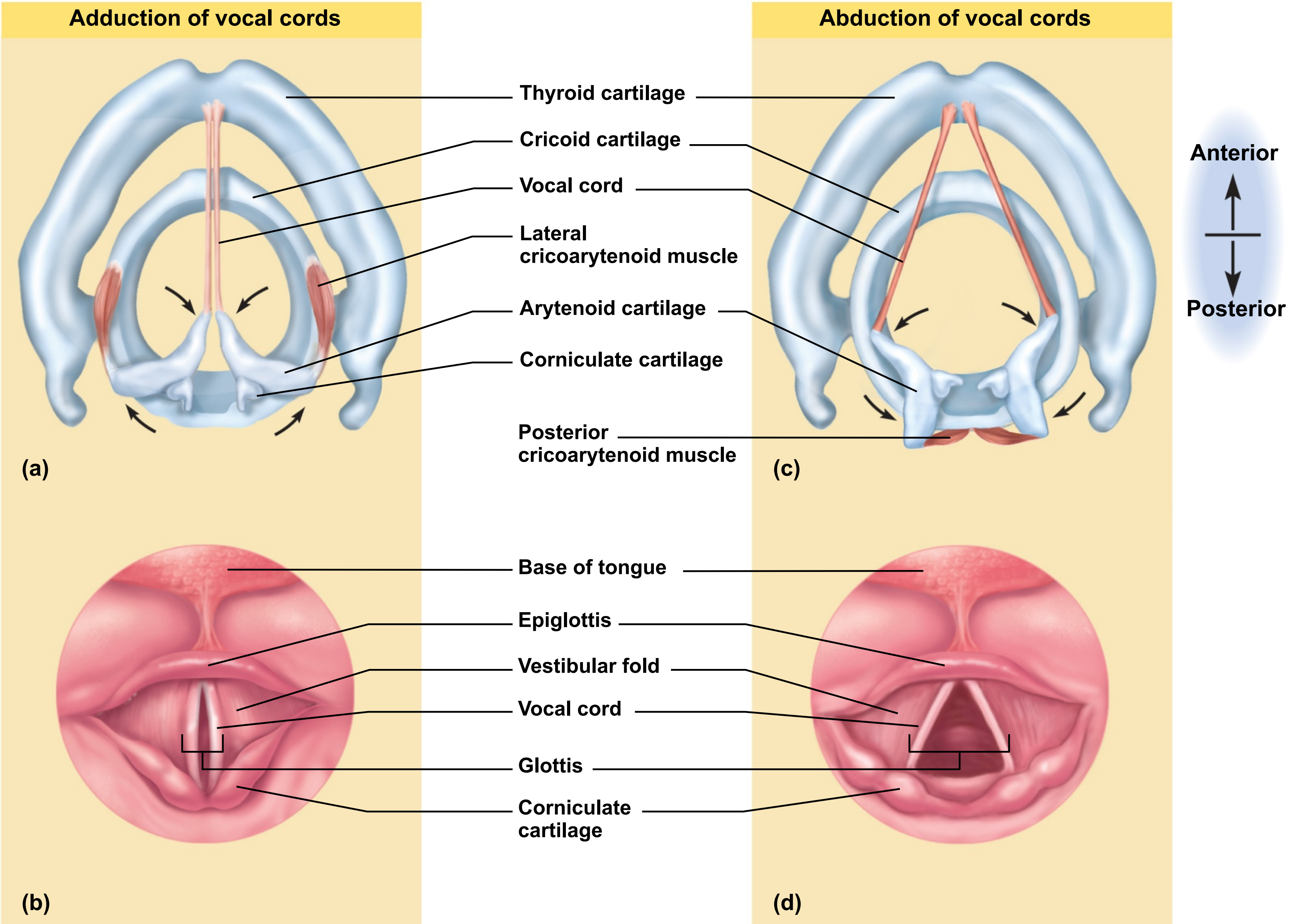



Figure 22.6 a-d

# Action of Vocal Cords

- **intrinsic muscles** control the vocal cords
  - pull on the corniculate and arytenoid cartilages
  - causing the 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
  - produce lower-pitched sound when cords are more slack
  - adult male vocal cords are:
    - 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

# Trachea

- **trachea** (windpipe) – a rigid tube about 12 cm (4.5 in.) long and 2.5 cm (1 in.) in diameter
  – found anterior to esophagus
  – supported by 16 to 20 **C-shaped** rings of **hyaline cartilage**
  – reinforces the trachea and keeps it from collapsing when you inhale
  – opening in rings faces posteriorly towards esophagus
  **– 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
- middle tracheal layer - connective tissue beneath the tracheal epithelium
  - contains lymphatic nodules, mucous and serous glands, and the tracheal cartilages
- 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

# Tracheal Epithelium



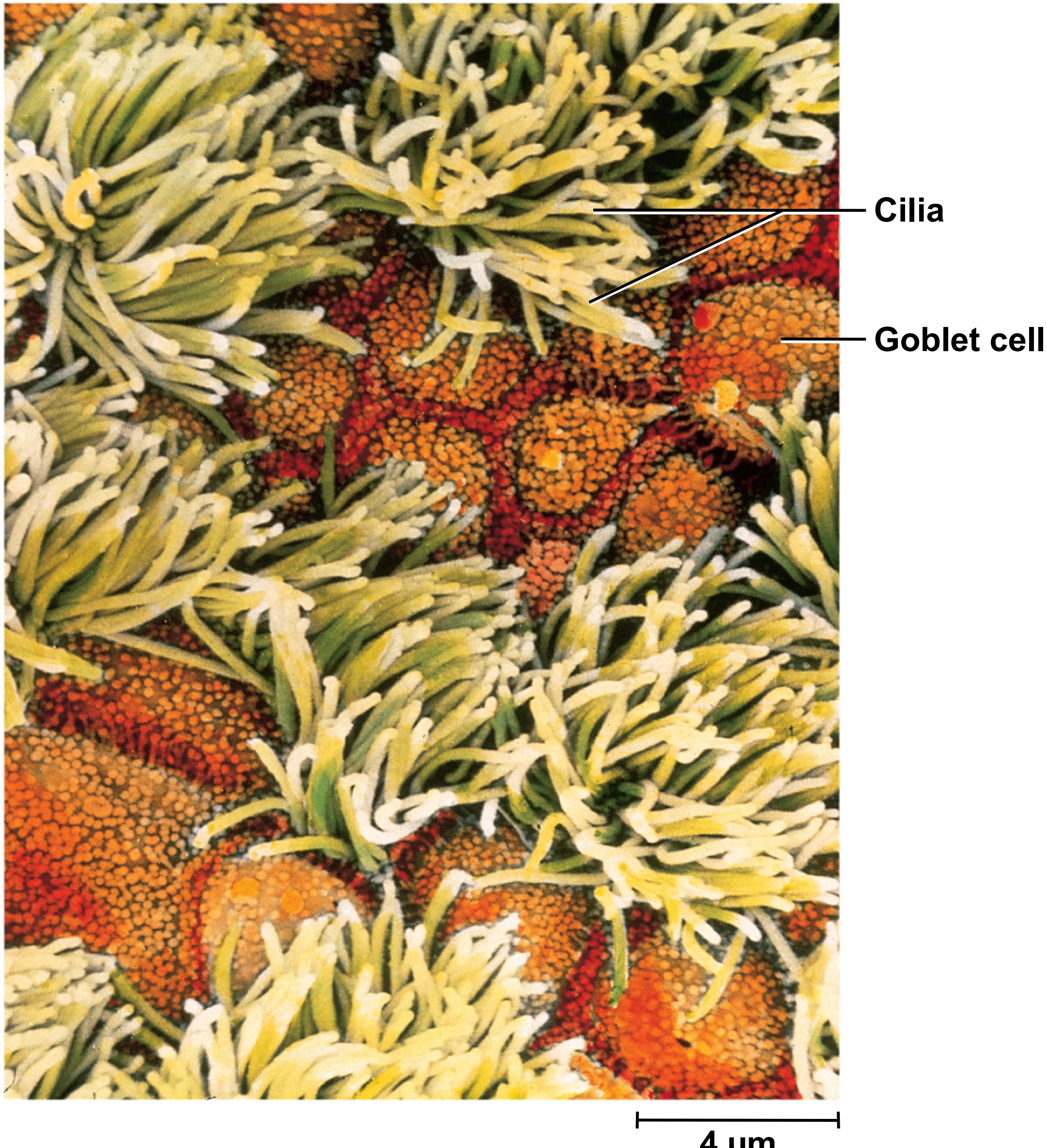



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Figure 22.8

# Tracheostomy

- **tracheostomy** – to make a temporary opening in the trachea inferior to the larynx 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 the mucous membranes of the respiratory tract
  - become encrusted and interfere with clearance of mucus from tract
  - promoting infection

# Lower Respiratory Tract



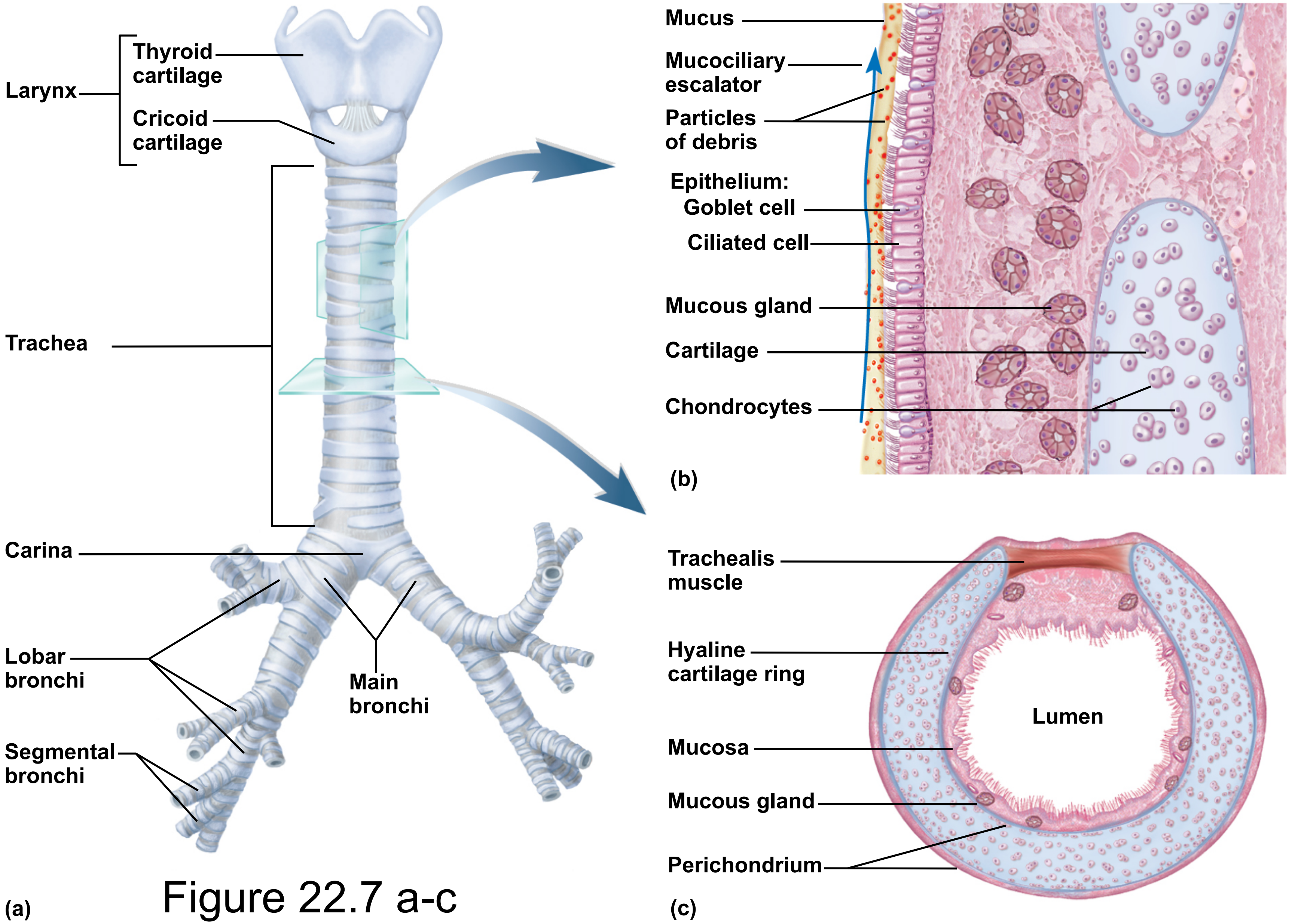
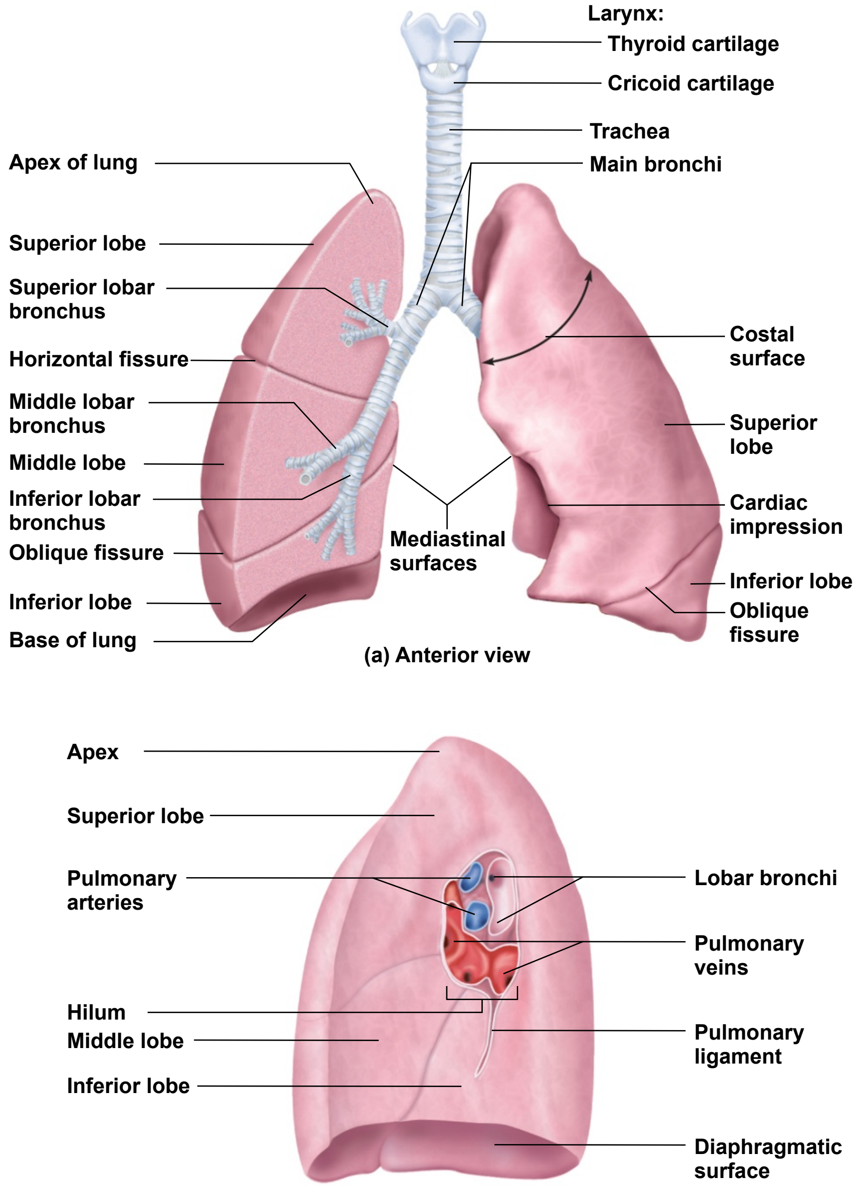



Figure 22.7 a-c

# Lungs - Surface Anatomy





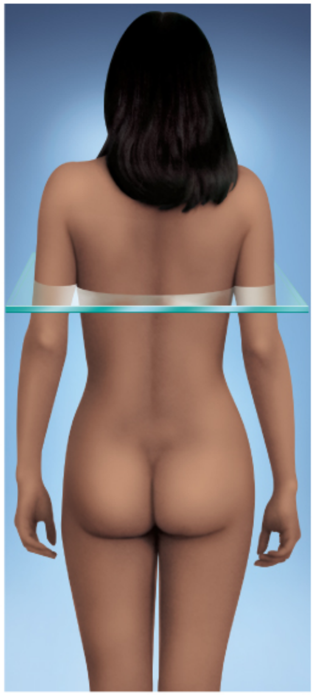

(a) Anterior view

(b) Mediastinal surface, right lung

Figure 22.9

# Thorax - Cross Section





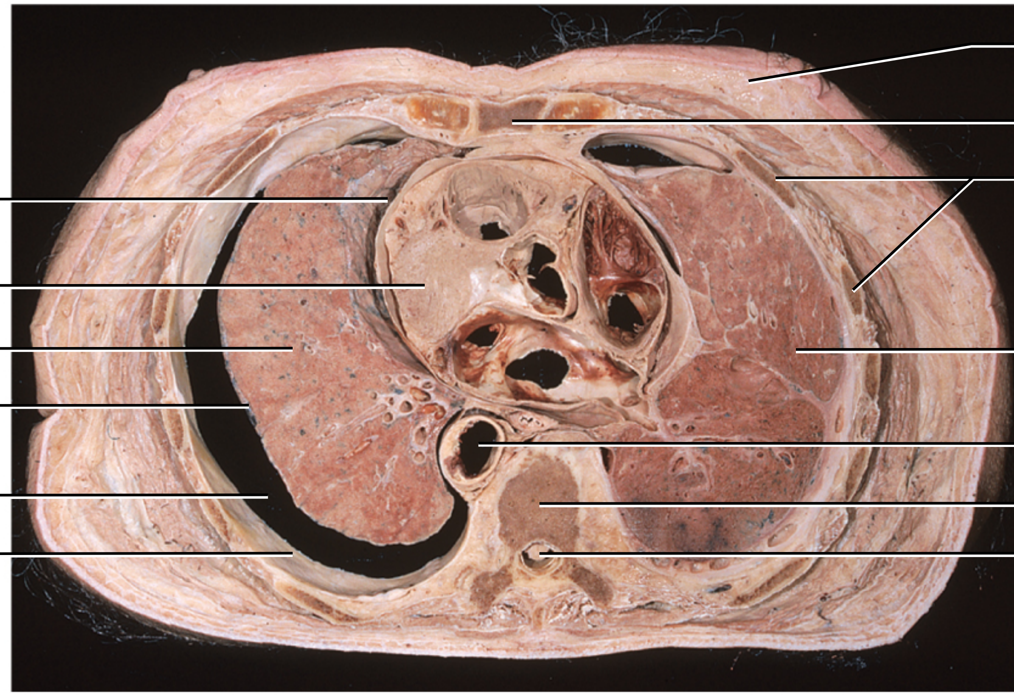



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Figure 22.10

# Lungs

- **lung** – conical organ with a broad, concave **base**, resting on the diaphragm, and a blunt peak called the **apex** projecting slightly 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 constitute the **root** of the lung

- lungs are crowded by adjacent organs, neither fill the entire ribcage, nor are they symmetrical.
  - **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
  - **rt. main bronchus** is a 2-3 cm branch arising from fork of trachea
    - right bronchus slightly wider and more vertical than left
    - **aspirated** (inhaled) foreign objects lodge right bronchus more often the left
  - **lt. main bronchus** is about 5 cm long
    - slightly narrower and more horizontal than the right
- **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**
  - cells grow shorter and the epithelium thinner as we progress distally
  - **lamina propria** has an abundance of mucous glands and lymphocyte nodules **(bronchus-associated lymphoid tissue, BALT)**
    - 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
  - **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

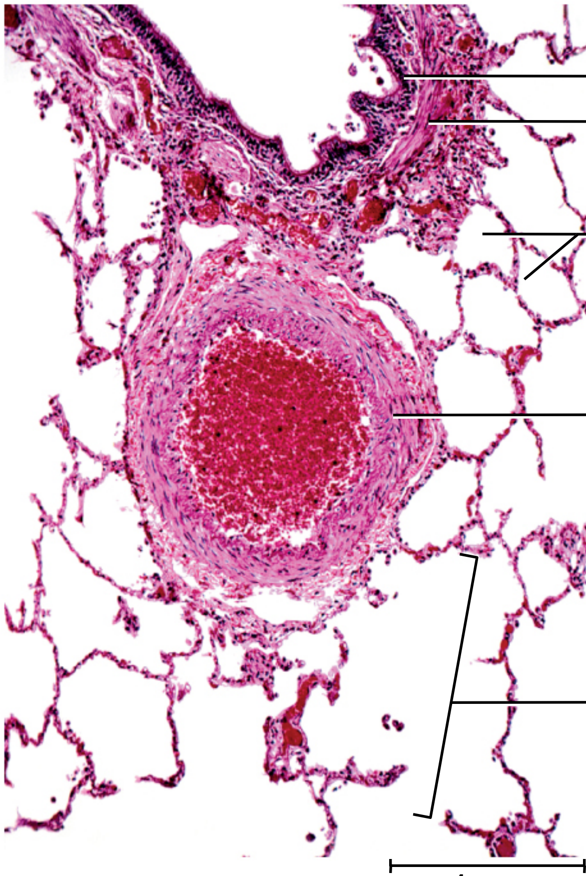
- **bronchioles**
  - lack cartilage
  - 1 mm or less in diameter
  - **pulmonary lobule** - portion of lung ventilated by one bronchiole
  - have ciliated cuboidal epithelium
  - well developed layer of smooth muscle
  - divides into 50 - 80 **terminal bronchioles**
    - **final branches of conducting 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
  - **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

**nasal cavity → pharynx → larynx → trachea → main bronchus → lobar bronchus → segmental bronchus → bronchiole → terminal bronchiole → respiratory division → respiratory bronchiole → alveolar duct → atrium → alveolus**

# Lung Tissue





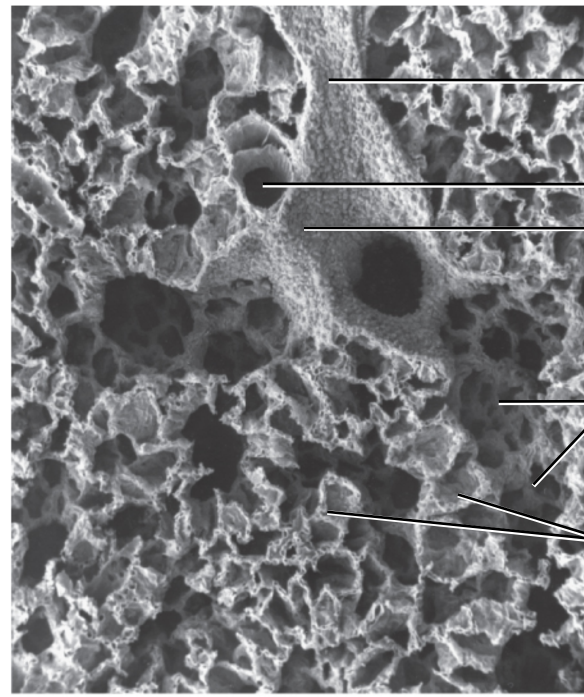




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Figure 22.11

# Alveolar Blood Supply



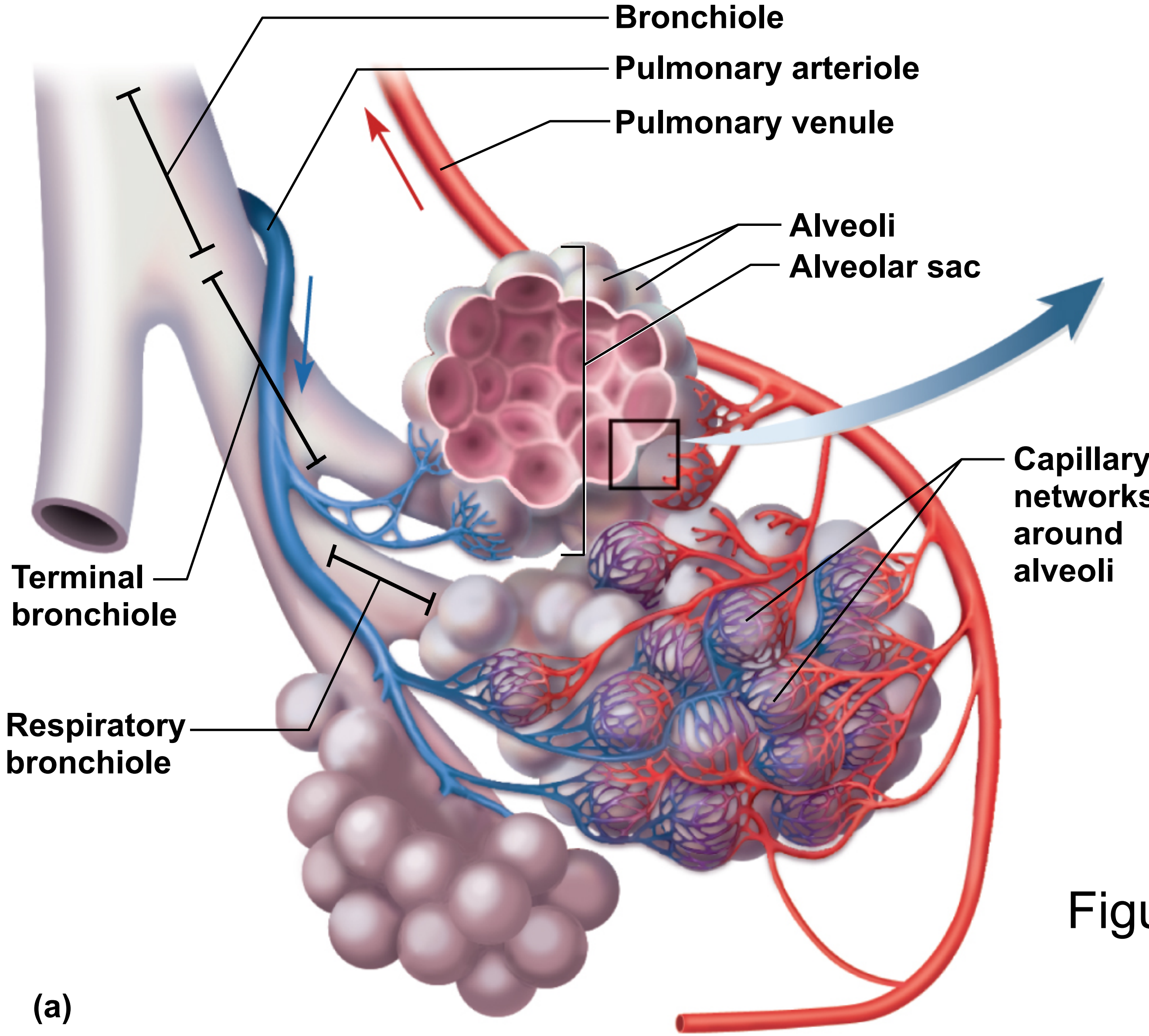



Figure 22.12a

# Alveoli

- 150 million alveoli in each lung, providing about 70 $m^2$ of surface for gas exchange
- cells of the alveolus
  - **squamous (type I) alveolar cells**
    - thin, broad cells that allow for rapid gas diffusion between alveolus and bloodstream
    - cover 95% of alveolus surface area
  - **great (type II) alveolar cells**
    - round to cuboidal cells that cover the remaining 5% of alveolar surface
    - **repair** the alveolar epithelium when the squamous (type I) cells are damaged
    - secrete **pulmonary surfactant**
      - a mixture of phospholipids and proteins that coats the alveoli and prevents them from collapsing when we exhale
  - **alveolar macrophages (dust cells)**
    - most numerous of all cells in the lung
    - wander the lumen and the connective tissue between alveoli
    - keep alveoli free from debris by phagocytizing dust particles
    - 100 million dust cells perish each day as they ride up the mucociliary escalator to be swallowed and digested with their load of debris

# Respiratory Membrane

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

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

- **respiratory membrane consists of:**
  - squamous alveolar cells
  - endothelial 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
  - 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 the rupture of the delicate respiratory membrane

# Alveolus



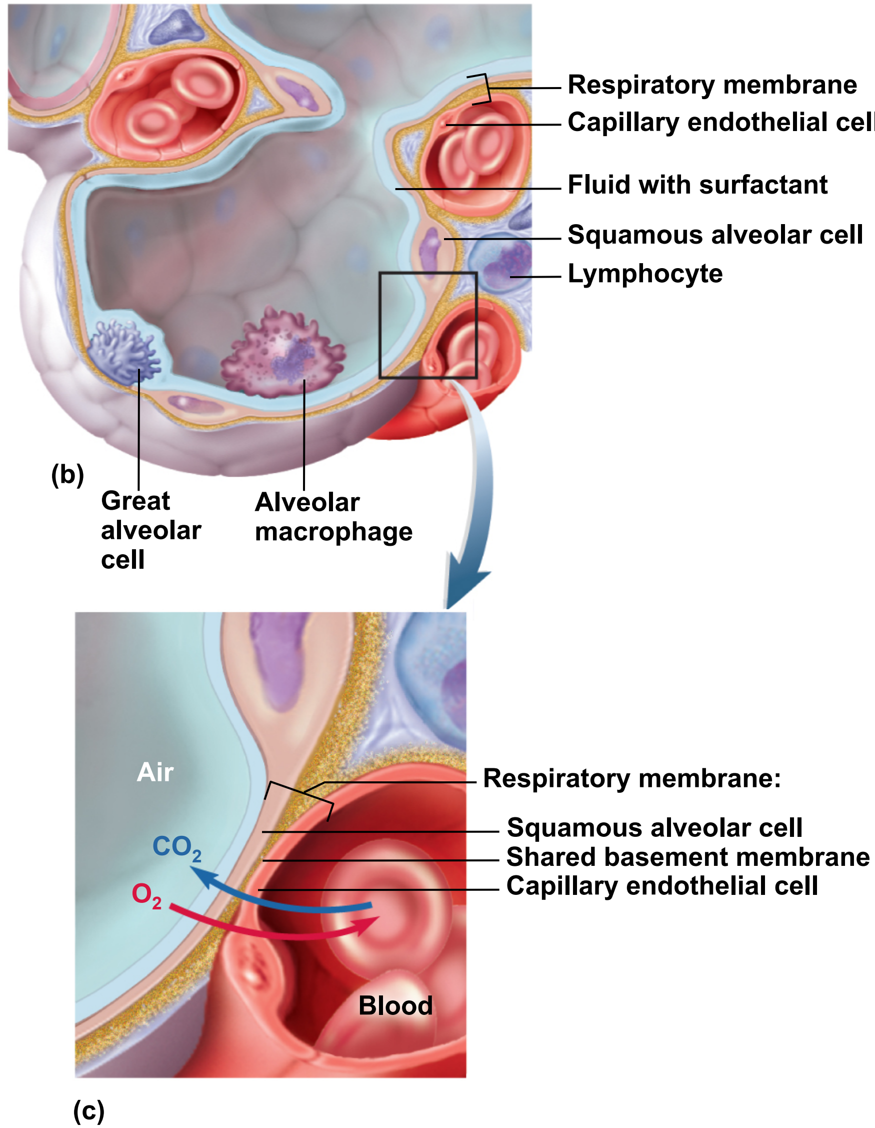



Figure 22.12 b-c

# The Pleurae and Pleural Fluid

- **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 and assists lung inflation
  - **compartmentalization**
    - prevents spread of infection from one organ in the mediastinum to others

# Pulmonary Ventilation

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

- **respiratory cycle** – one complete inspiration and expiration
  - **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**
  - erector spinae, sternocleidomastoid, pectoralis major, pectoralis minor, and serratus anterior muscles and scalenes
  - 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**
  - rectus abdominis, internal intercostals, other lumbar, abdominal, and pelvic muscles
  - greatly increased abdominal pressure pushes viscera up against diaphragm increasing thoracic pressure, forcing air out

# Accessory Respiratory Muscles

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

# Respiratory Muscles



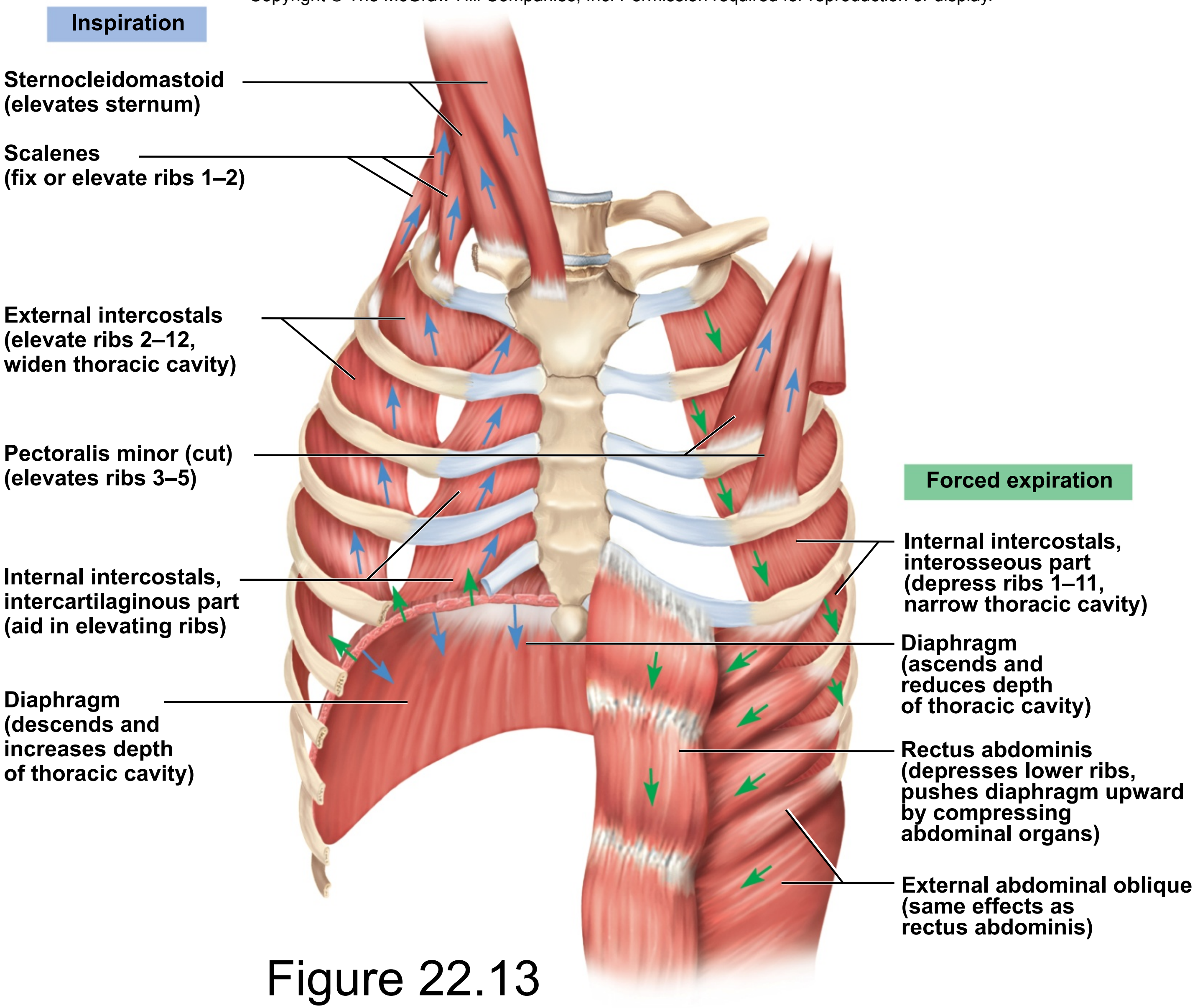



Figure 22.13

# Neural Control of Breathing

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

# 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 (eupnea) fire for about two seconds
    - expiratory neurons in eupnea fire for about three seconds allowing inspiratory muscles to relax
    - produces a respiratory rhythm of 12 breath per minute
  - **dorsal respiratory group (DRG)**
    - modifies the rate and depth of breathing
    - receives influences from external sources

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

# Respiratory Control Centers



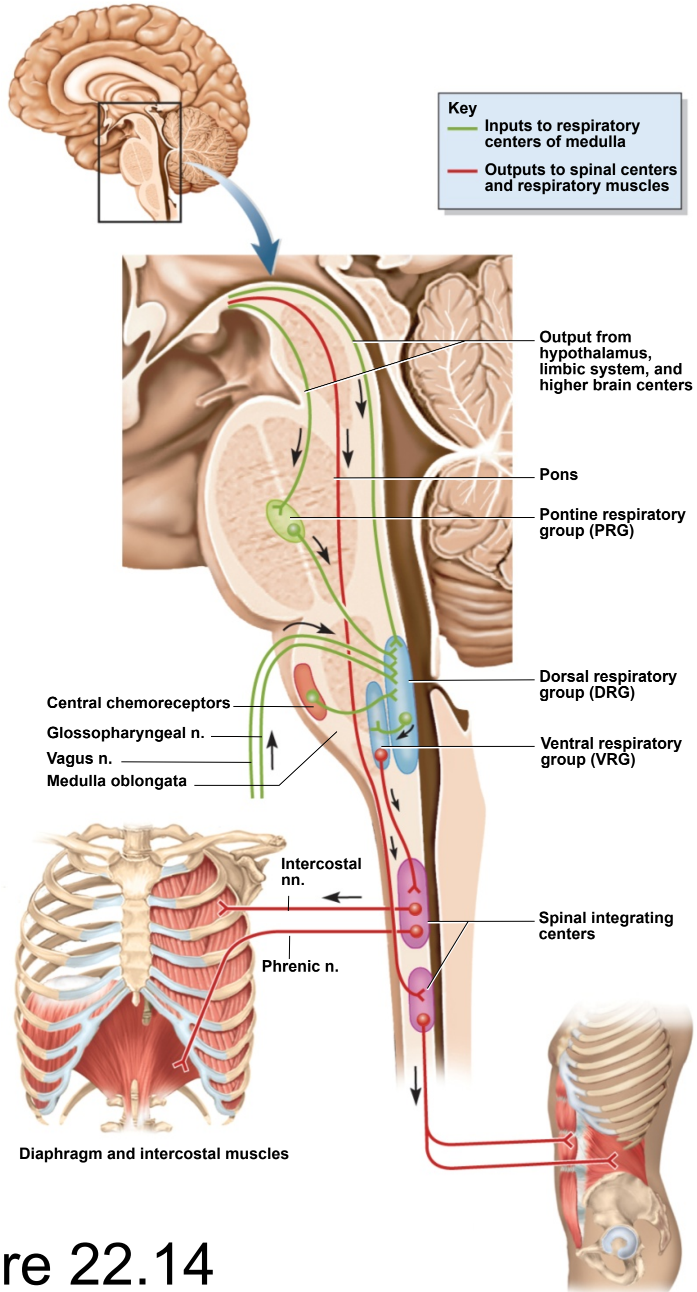



Figure 22.14

# Central and Peripheral Input to Respiratory Centers

- **hyperventilation** – anxiety triggered state 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 reducing 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 chemoreceptors** – brainstem neurons that respond to changes in pH of cerebrospinal fluid
  - pH of cerebrospinal fluid reflects the $CO_2$ level in the blood
  - by regulating respiration to maintain stable pH, respiratory center also ensures stable $CO_2$ level in the blood
- **peripheral chemoreceptors** – located in the carotid and aortic bodies of the large arteries above the heart
  - respond to the $O_2$ and $CO_2$ content and the pH of blood

# Central and Peripheral Input to Respiratory Centers

- **stretch receptors** – found in the smooth muscles of bronchi and bronchioles, and in the visceral pleura
  - respond to inflation of the lungs
  - **inflation (Hering-Breuer) reflex** – triggered by excessive inflation
    - protective reflex that inhibits inspiratory neurons stopping inspiration

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

# Peripheral Chemoreceptors



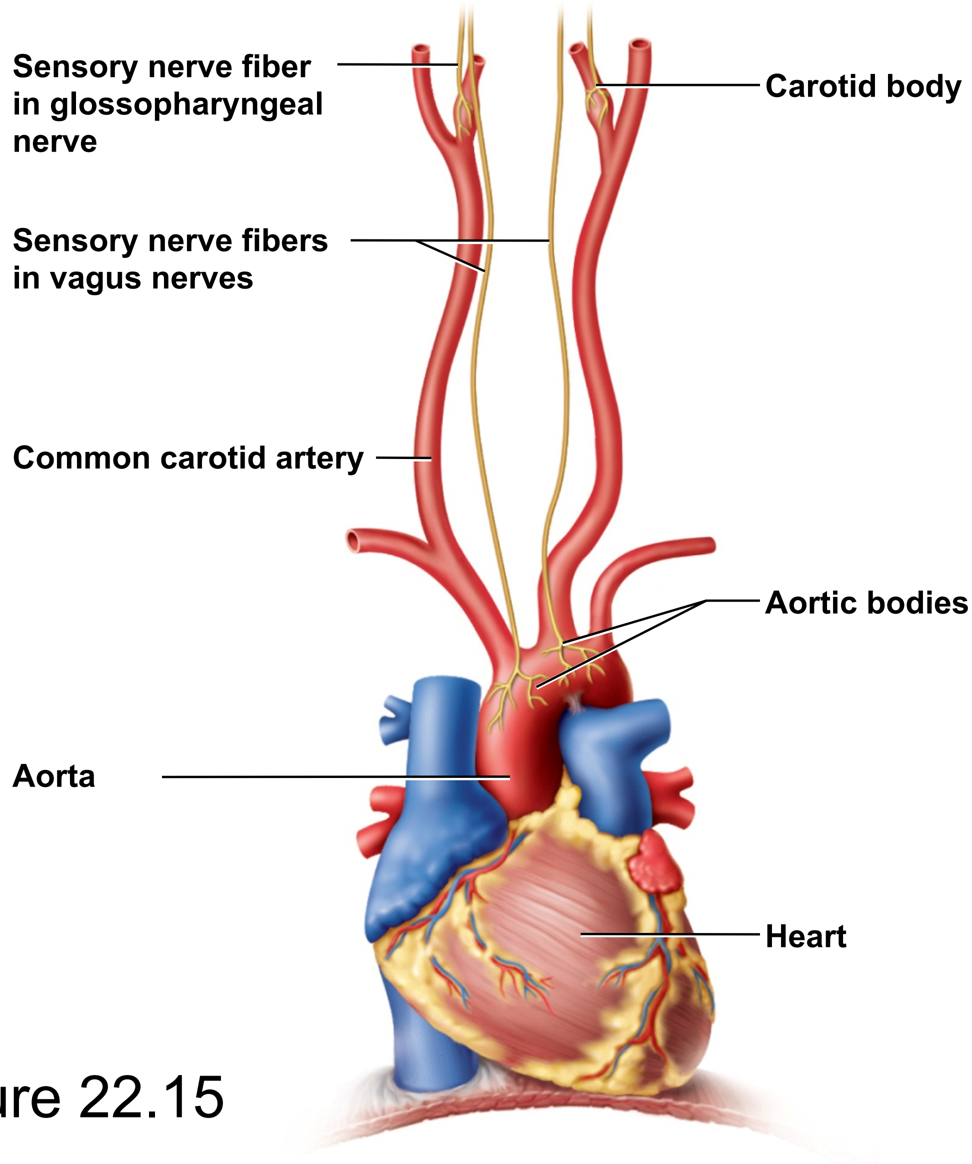



Figure 22.15

# Voluntary Control of Breathing

- voluntary control over breathing originates in the **motor cortex of frontal lobe of cerebrum**
  - sends impulses down corticospinal tracts to respiratory neurons in spinal cord, bypassing brainstem
- limits to voluntary control
  - **breaking point** – when $CO_2$ levels rise to a point when automatic controls override one's will

# Pressure and Airflow

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

- **atmospheric pressure** drives respiration
  - the weight of the air above us
  - **760 mm Hg** at sea level - **1 atmosphere (atm)**
    - lower at higher elevations

- **Boyle's Law** – at a constant temperature, the pressure of a given quantity of gas is inversely proportional to its volume
  - if the lungs contain a quantity of a gas and the lung volume increases, their internal pressure (**intrapulmonary pressure**) falls
    - if the pressure falls below atmospheric pressure the air moves into the lungs
  - if the lung volume decreases, intrapulmonary pressure rises
    - if the pressure rises above atmospheric pressure the air moves out of the lungs

# Inspiration

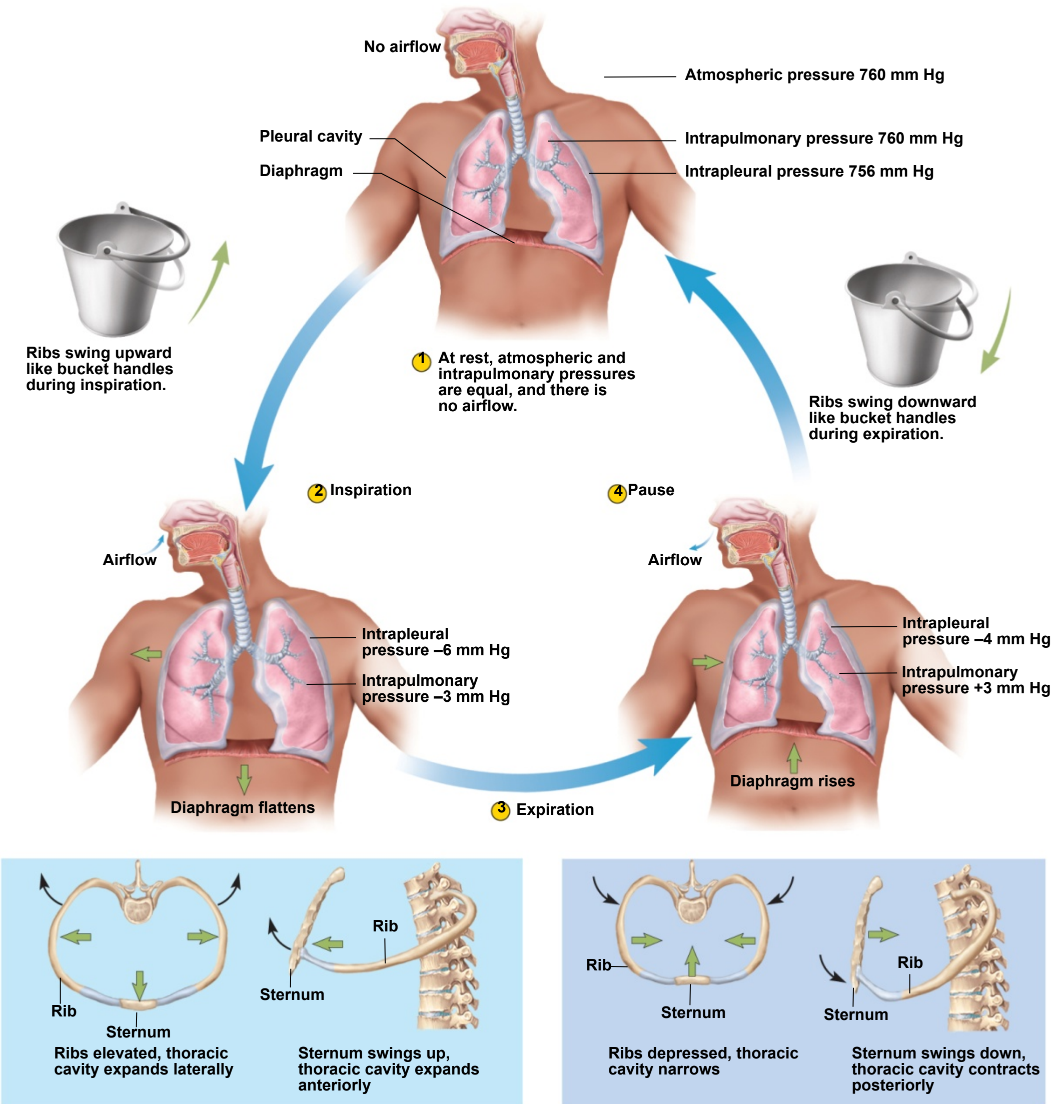
- the two pleural layers, their cohesive attraction to each other, and their connections to the lungs and their lining of the rib cage bring about inspiration
  - when the ribs swing upward and outward during inspiration, the parietal pleura follows them
  - the visceral pleura clings to it by the cohesion of water and it follows the parietal pleura
  - it stretches the alveoli within the lungs
  - the entire lung expands along the thoracic cage
  - as it increases in volume, its internal pressure drops, and air flows in
- **intrapleural pressure** – the slight vacuum that exists between the two pleural layers
  - about -4 mm Hg
  - drops to -6 mm Hg during inspiration as parietal pleura pulls away
  - some of this pressure change transfers to the interior of the lungs
    - **intrapulmonary pressure** – the pressure in the alveoli drops -3 mm Hg
    - pressure gradient from 760 mm Hg atmosphere to 757 mm Hg in alveoli allows air to flow into the lungs

# Inspiration

- another force that expands the lungs is Charles's Law
- **Charles's Law** – the given quantity of a gas is directly proportional to its absolute temperature
  - on a cool day, 16°C (60°F) air will increase its temperature by 21°C (39°F) during inspiration
  - inhaled air is warmed to 37°C (99° F) by the time it reaches the alveoli
  - inhaled volume of 500 mL will expand to 536 mL and this thermal expansion will contribute to the inflation of the lungs
- in **quiet breathing**, the dimensions of the thoracic cage increase only a few millimeters in each direction
  - enough to increase its total volume by 500 mL.
  - thus, 500 mL of air flows into the respiratory tract

# Respiratory Cycle






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

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

Figure 22.16

# Expiration

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

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

# Pneumothorax

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

- **atelectasis** - collapse of part or all of a lung
  - can also result from an airway obstruction

# Resistance to Airflow

- **pressure** is one determinant of airflow - **resistance** is the other
  - the greater the resistance the slower the flow
- 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
    - infant respiratory distress syndrome (IRDS) – premature babies

# 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

# Alveolar Ventilation

- only air that enters the 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
- in pulmonary diseases, some alveoli may be unable to exchange gases because they lack blood flow or there respiratory membrane has been thickened by edema or fibrosis
- **physiologic (total) dead space**
  - sum of anatomic dead space and any pathological alveolar dead space
- 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) = 4200 mL/min
  - of all the measurements, this one is most directly relevant to the body's ability to get oxygen to the tissues and dispose of carbon dioxide
- **residual volume** – 1300 mL that cannot be exhaled with max. effort

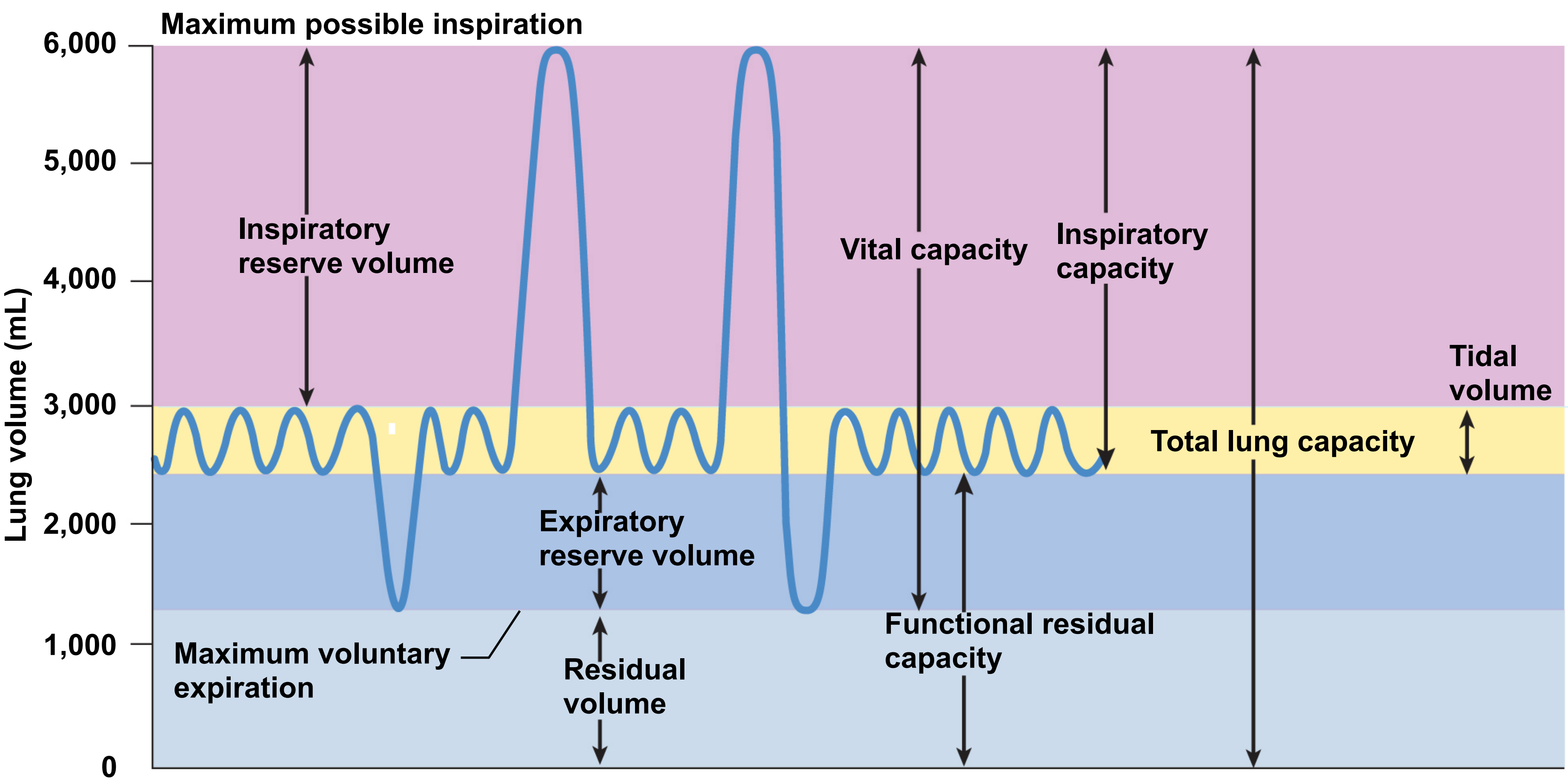
# Measurements of Ventilation

- **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





# 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

# Respiratory Capacities

- **forced expiratory volume** (FEV)
  - percentage of the vital capacity that can be exhaled in a given time interval
  - healthy adult reading is 75 - 85% in 1 sec
- **peak flow**
  - maximum speed of expiration
  - blowing into a handheld meter
- **minute respiratory volume** (MRV)
  - amount of air inhaled per minute
  - TV x respiratory rate (at rest 500 x 12 = 6000 mL/min)
- **maximum voluntary ventilation** (MVV)
  - MRV during heavy exercise
  - may be as high as 125 to 170 L/min

# Variations in Respiratory Rhythm

- **eupnea** – relaxed quiet breathing
  - characterized by tidal volume 500 mL and the respiratory rate of 12 – 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
- **hypoventilation** – reduced pulmonary ventilation
- **Kussmaul respiration** – deep, rapid breathing often induced by acidosis
- **orthopnea** – dyspnea that occurs when a person is lying down
- **respiratory arrest** – permanent cessation of breathing
- **tachypnea** – accelerated respiration

# 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
- **Dalton's 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% x 760 mm Hg = 597 mm Hg
    - $P_{O_2}$ = 20.9% x 760 mm Hg = 159 mm Hg
    - $P_{H_2O}$ = 0.5% x 760 mm Hg = 3.7 mm Hg
    - $P_{CO_2}$ = 0.04% x 760 mm Hg = 0.3 mm Hg
    - $P_{N_2} + P_{O_2} + P_{H_2O} + P_{CO_2}$ = 760 mmHg

# Composition of Inspired and Alveolar Air

- composition of inspired air and alveolar is different because of three influences:
  1. **air is humidifies by contact with mucous membranes**
     - alveolar $P_{H_2O}$ is more than 10 times higher than inhaled air
  2. **freshly inspired air mixes with residual air left from the previous respiratory cycle**
     - oxygen is diluted and it is enriched with $CO_2$
  3. **alveolar air exchanges $O_2$ and $CO_2$ with the blood**
     - $P_{O_2}$ 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 |
| $H_2O$ | 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

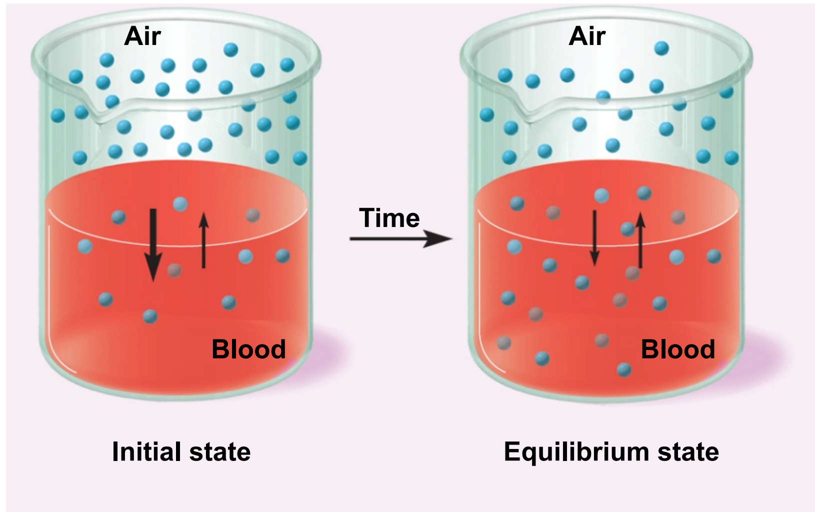
- **alveolar gas exchange** – the back-and-forth traffic of $O_2$ and $CO_2$ across the respiratory membrane
  - air in the alveolus is in contact with a film of water covering the alveolar epithelium
  - **for oxygen to get into the blood** it must dissolve in this water
  - pass through the respiratory 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

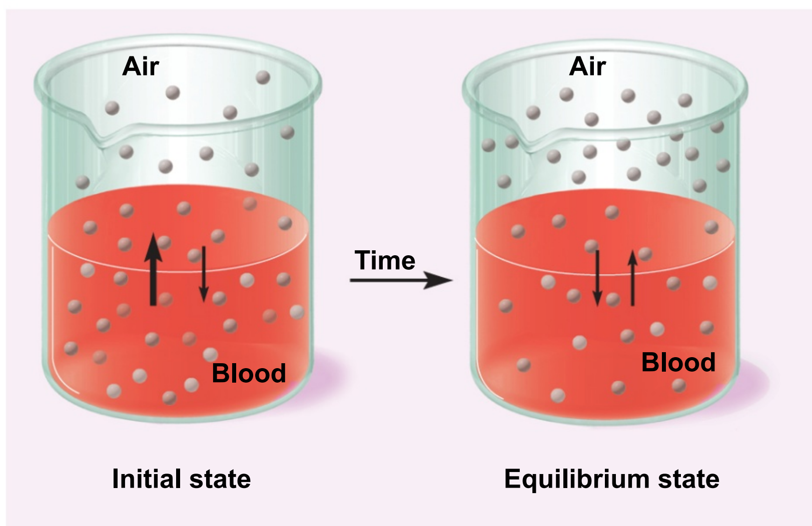
- **Henry's law** – at the air-water interface, for a given temperature, the amount of gas that dissolves in the water is determined by its solubility in water and its partial pressure in air
  - the greater the $PO_2$ in the alveolar air, the more $O_2$ the blood picks up
  - since blood arriving at 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






(a) Oxygen




(b) Carbon dioxide

Figure 22.18

# Factors Affecting Gas Exchange

- **pressure gradient of the gases**
  - $P_{O_2}$ = 104 mm Hg in alveolar air versus 40 mm Hg in blood
  - $P_{CO_2}$ = 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
  - pulmonary edema in left side ventricular failure causes edema and thickening of the respiratory membrane
  - pneumonia causes thickening of respiratory membrane
  - farther to travel between blood and air
  - cannot equilibrate fast enough to keep up with blood flow
- **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
- **ventilation-perfusion coupling** –the ability to match ventilation and perfusion to each other
  - gas exchange requires both good ventilation of alveolus and good perfusion of the capillaries
  - ventilation-perfusion ratio of 0.8 – a flow of 4.2 L of air and 5.5 L of blood per minute at rest

# Concentration Gradients of Gases



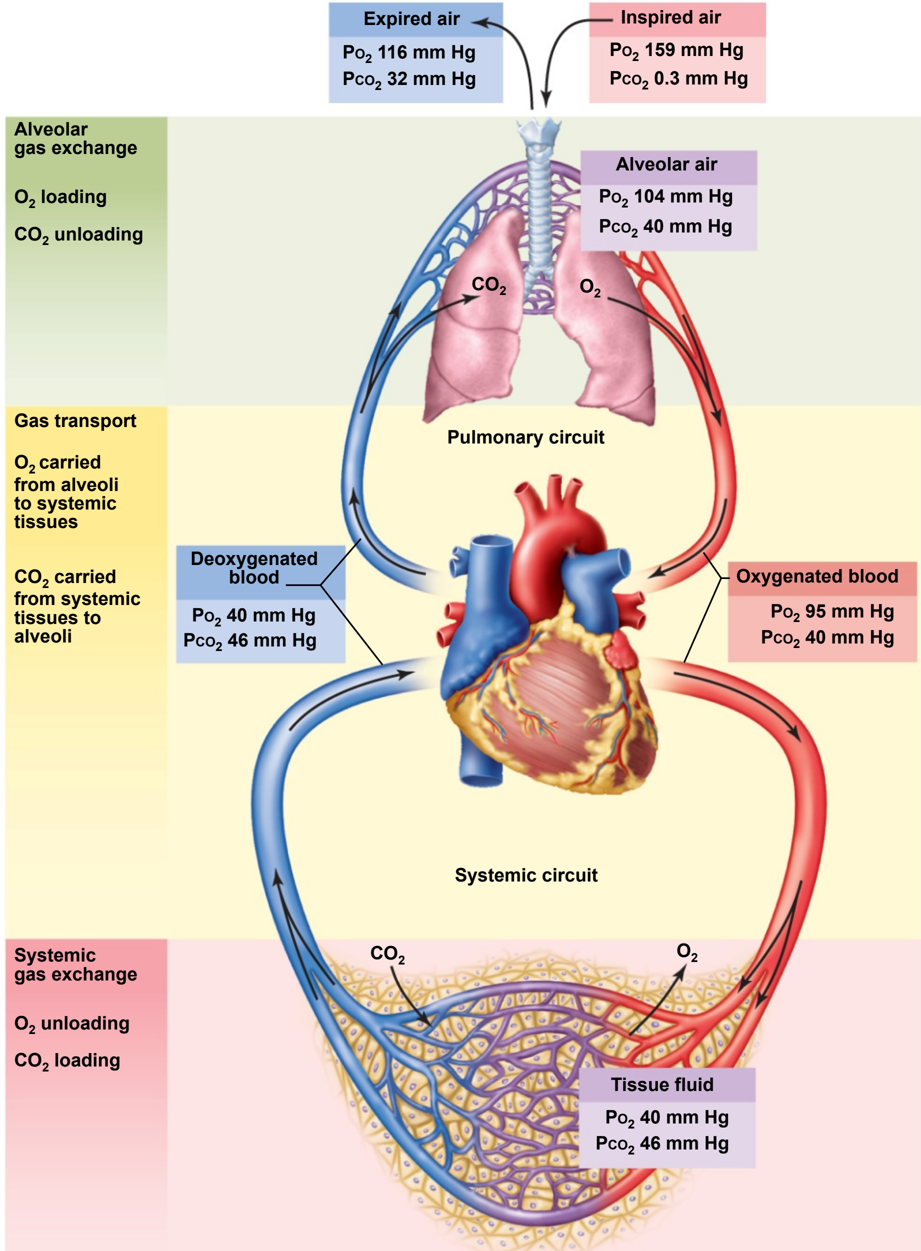



Figure 22.19

# Ambient Pressure & Concentration Gradients



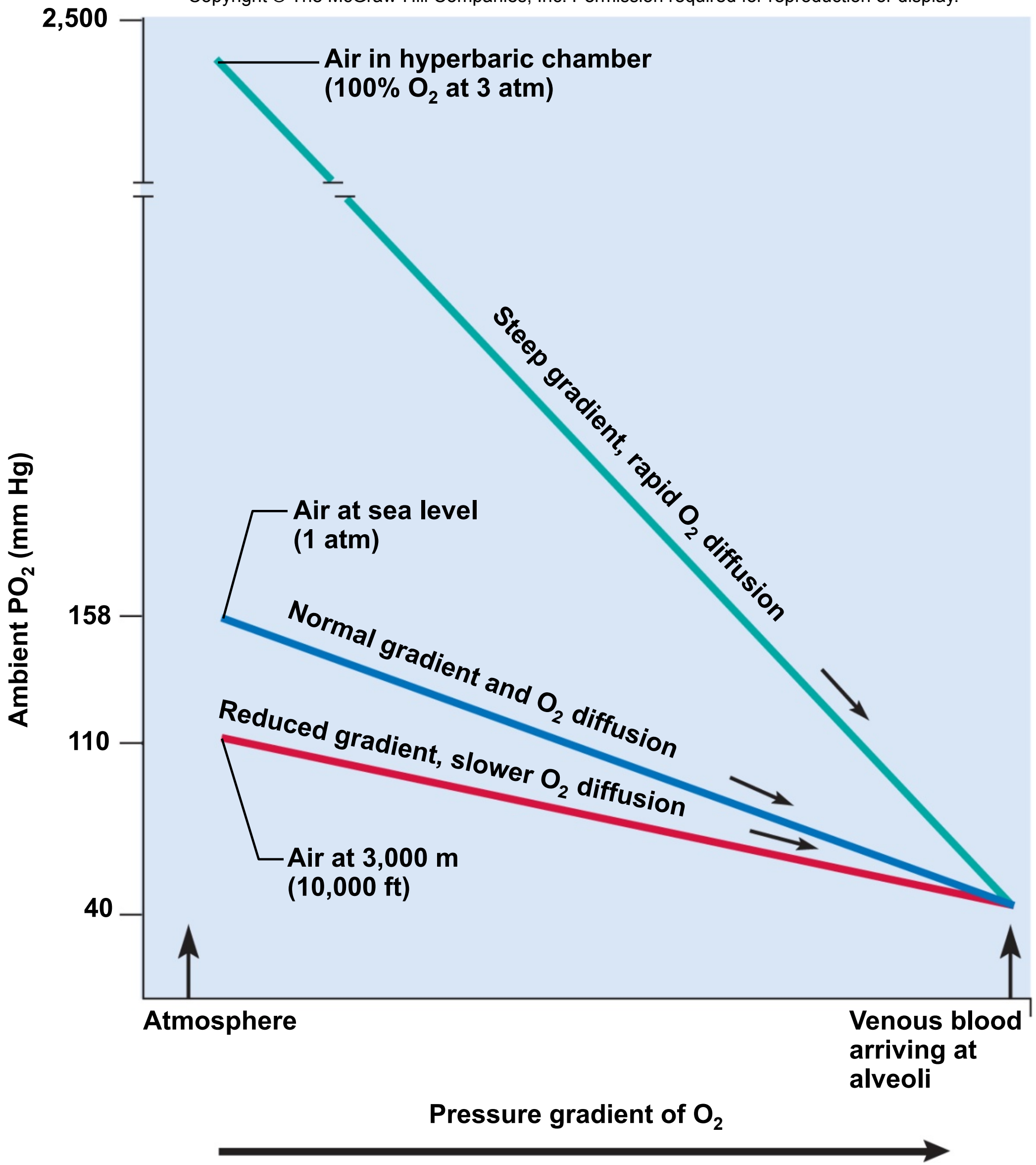



Figure 22.20

# Lung Disease Affects Gas Exchange



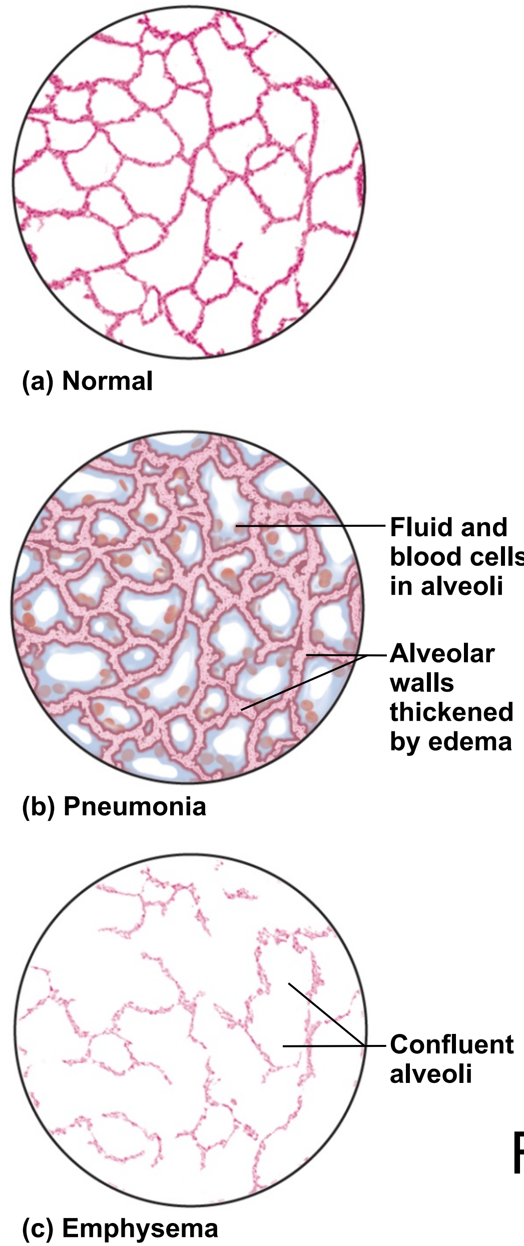
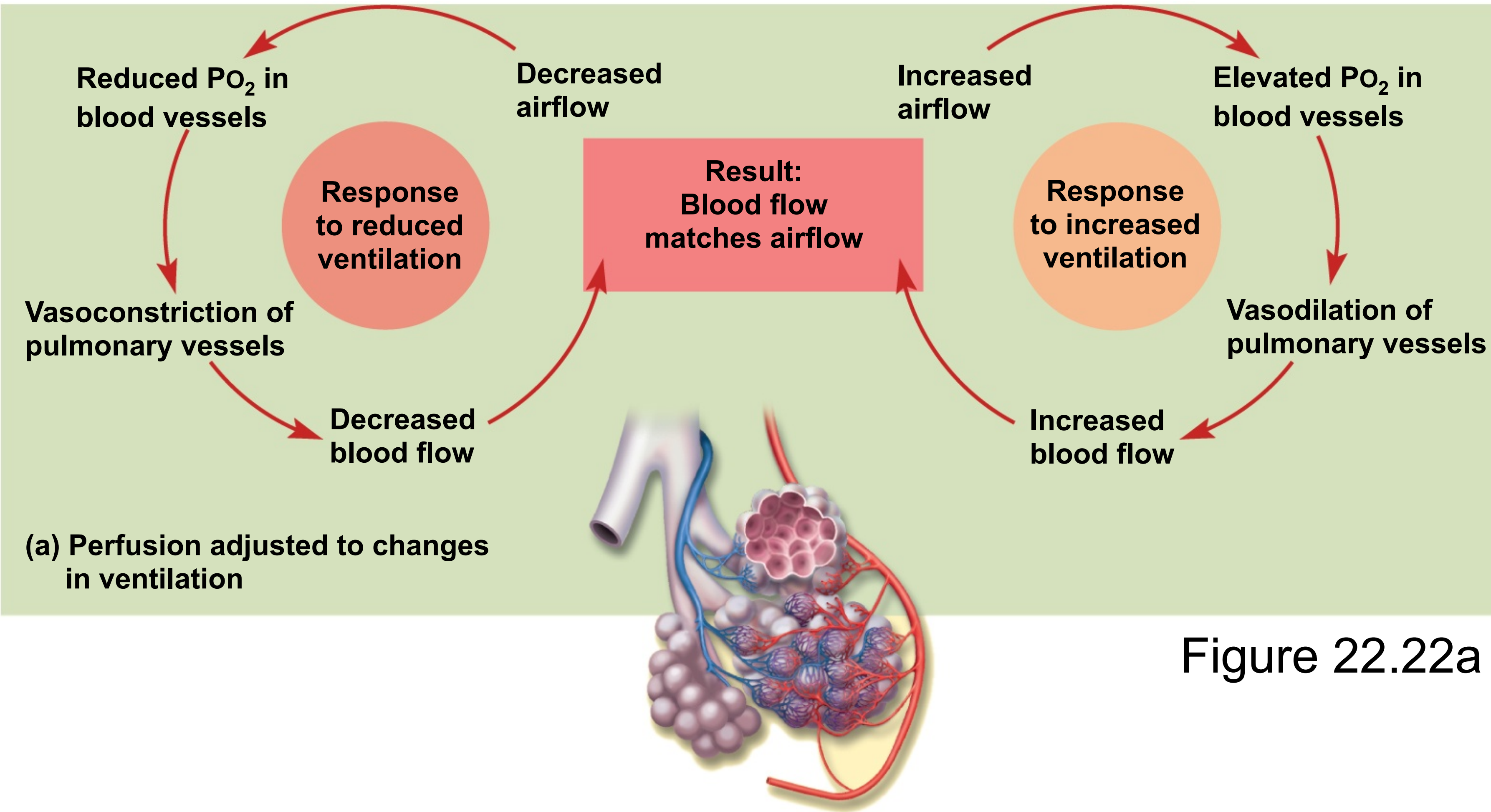



Figure 22.21

# Perfusion Adjustments



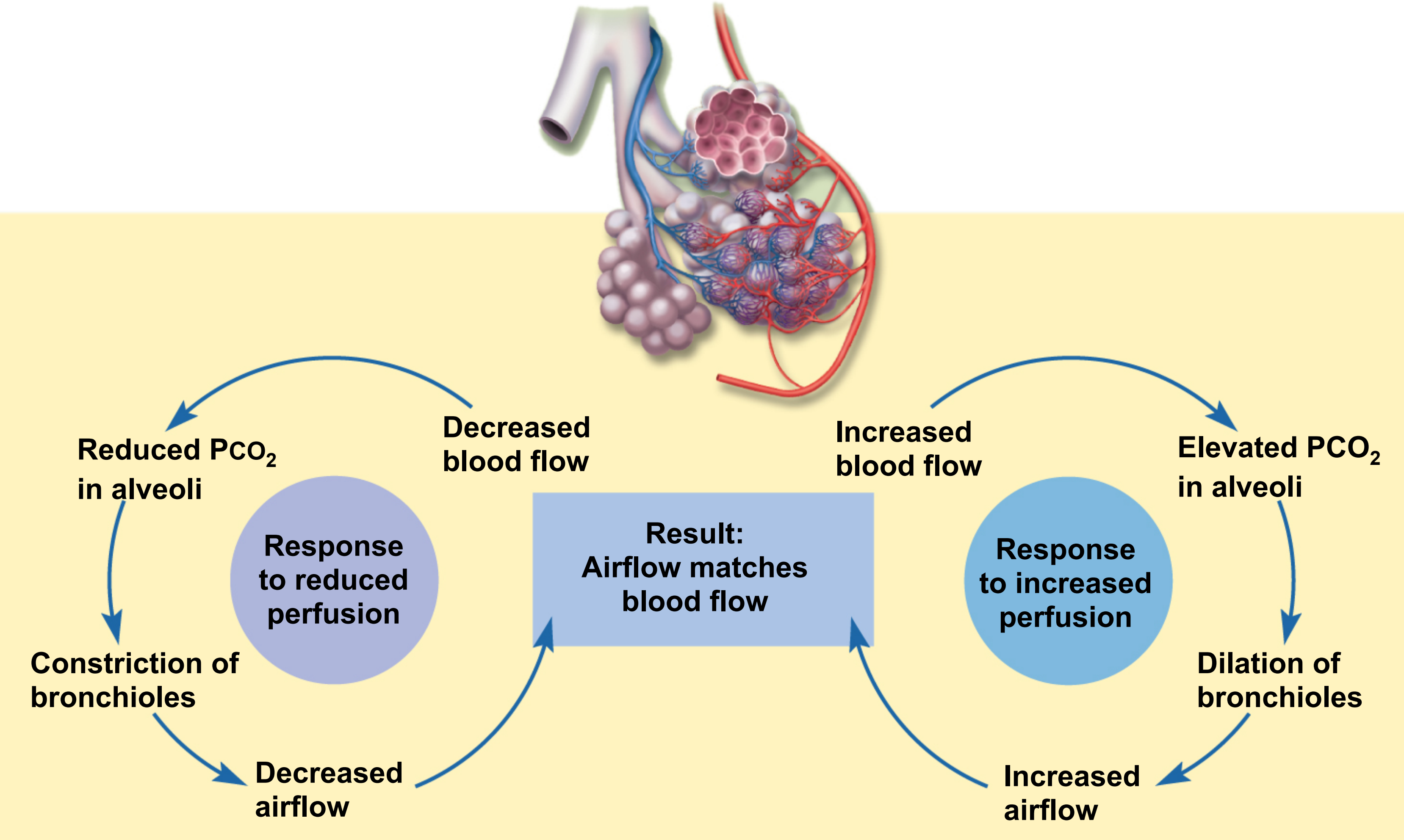



(a) Perfusion adjusted to changes in ventilation

Figure 22.22a

# Ventilation Adjustments






(b) Ventilation adjusted to changes in perfusion

Figure 22.22b

# Gas Transport

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

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

- **carbon dioxide transport**
  - 70% as bicarbonate ion
  - 23% bound to hemoglobin
  - 7% dissolved in plasma

# Oxygen Transport

- arterial blood carries about 20 mL of $O_2$ per deciliter
  - 95% bound to hemoglobin in RBC
  - 1.5% dissolved in plasma
- **hemoglobin** – molecule specialized in oxygen transport
  - four protein (**globin**) portions
    - each with a heme group which binds one $O_2$ to the **ferrous ion** ($Fe^{2+}$)
    - one hemoglobin molecule can carry up to 4 $O_2$
    - oxyhemoglobin ($HbO_2$) – $O_2$ bound to hemoglobin
    - deoxyhemoglobin (HHb) – hemoglobin with no $O_2$
    - 100 % saturation Hb with 4 oxygen molecules
    - 50% saturation Hb with 2 oxygen molecules

# Carbon Monoxide Poisoning

- **carbon monoxide (CO) -** competes for the $O_2$ binding sites on the hemoglobin molecule
- colorless, odorless gas in cigarette smoke, engine exhaust, fumes from furnaces and space heaters
- **carboxyhemoglobin** – CO binds to ferrous ion of hemoglobin
  - binds 210 times as tightly as oxygen
  - ties up hemoglobin for a long time
  - non-smokers - less than 1.5% of hemoglobin occupied by CO
  - smokers- 10% in heavy smokers
  - atmospheric concentrations of 0.2% CO is quickly lethal

# Oxyhemoglobin Dissociation Curve



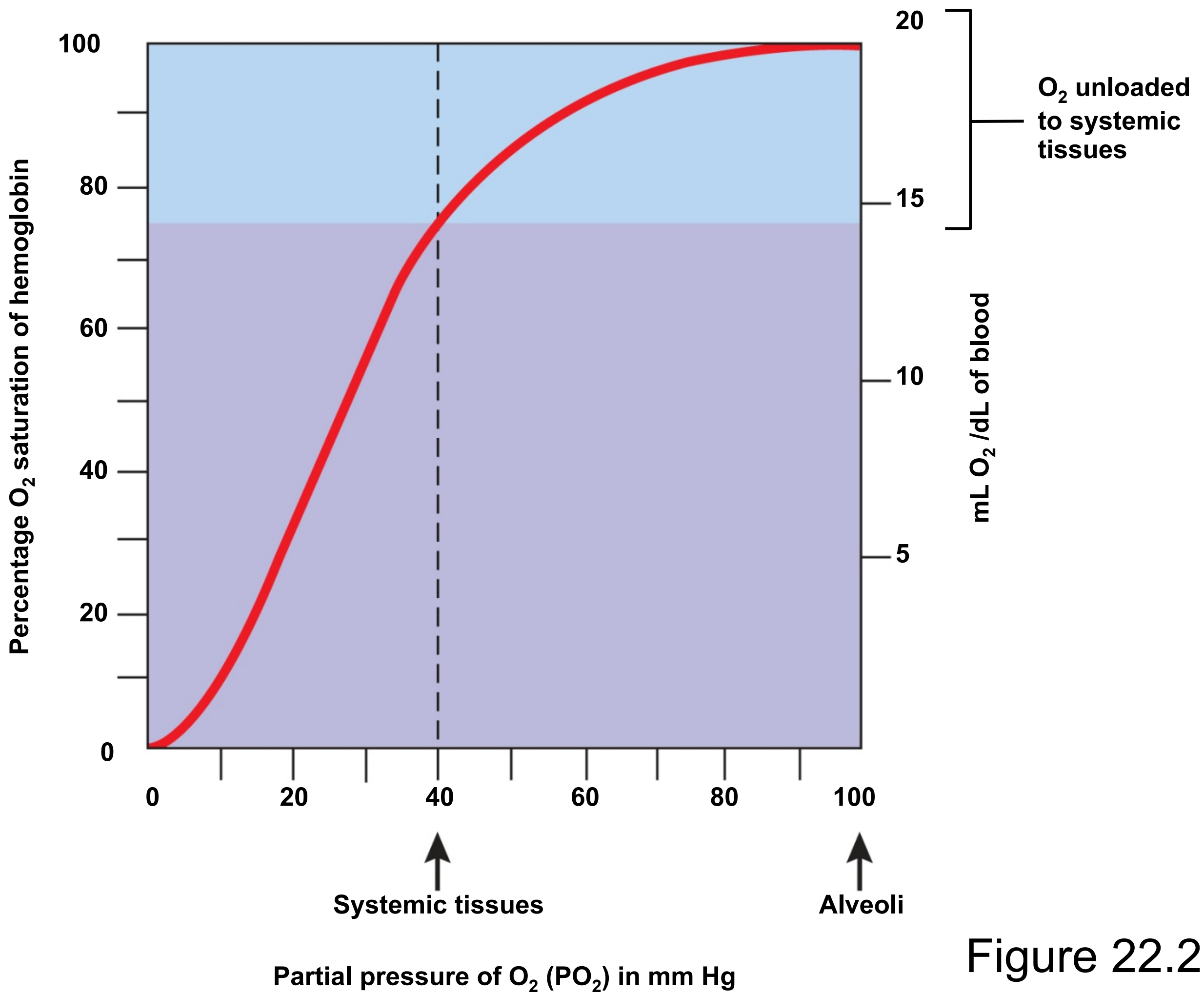



Figure 22.23

relationship between hemoglobin saturation and $PO_2$

# Carbon Dioxide Transport

- carbon dioxide transported in three forms
  - carbonic acid, carbamino compounds, and dissolved in plasma
- 90% of $CO_2$ is hydrated to form carbonic acid
  - $CO^2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO3^- + H^+$
  - then dissociates into bicarbonate and hydrogen ions
- 5% binds to the amino groups of plasma proteins and hemoglobin to form carbamino compounds – chiefly carbaminohemoglobin ($HbCO_2$)
  - carbon dioxide does not compete with oxygen
  - they bind to different moieties on the hemoglobin molecule
  - hemoglobin can transport $O_2$ and $CO_2$ simultaneously
- 5% is carried in the blood as dissolved gas
- relative amounts of $CO_2$ exchange between the blood and alveolar air differs:
  - 70% of exchanged $CO_2$ comes from carbonic acid
  - 23% from carbamino compounds
  - 7% dissolved in the plasma
    - blood gives up the dissolved $CO_2$ gas and $CO_2$ from the carbamino compounds more easily than $CO_2$ in bicarbonate

# Systemic Gas Exchange

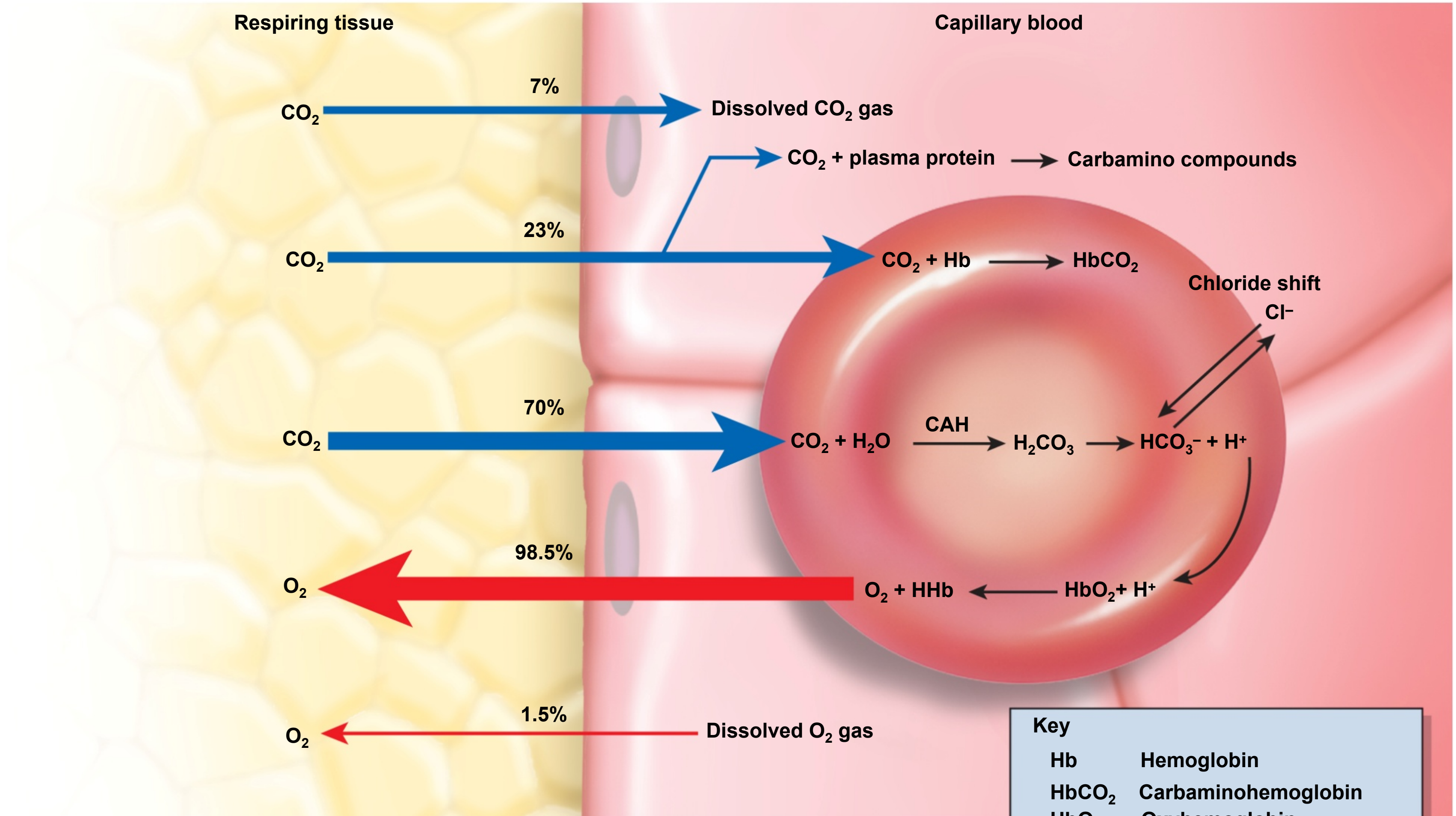
- systemic gas exchange - the unloading of $O_2$ and loading of $CO_2$ at the systemic capillaries

- **$CO_2$ loading**
  - $CO_2$ diffuses into the blood
  - **carbonic anhydrase** in RBC catalyzes
    - **$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$**
  - chloride shift
    - keeps reaction proceeding, exchanges $HCO_3^-$ for $Cl^-$
    - $H^+$ binds to hemoglobin

- **$O_2$ unloading**
  - $H^+$ binding to $HbO_2$ reduces its affinity for $O_2$
    - tends to make hemoglobin release oxygen
    - $HbO_2$ arrives at systemic capillaries 97% saturated, leaves 75% saturated –
      - **venous reserve** – oxygen remaining in the blood after it passes through the capillary beds
  - **utilization coefficient** – given up 22% of its oxygen load

# Systemic Gas Exchange






**Key**

| | |
|---|---|
| Hb | Hemoglobin |
| $HbCO_2$ | Carbaminohemoglobin |
| $HbO_2$ | Oxyhemoglobin |
| HHb | Deoxyhemoglobin |
| CAH | Carbonic anhydrase |

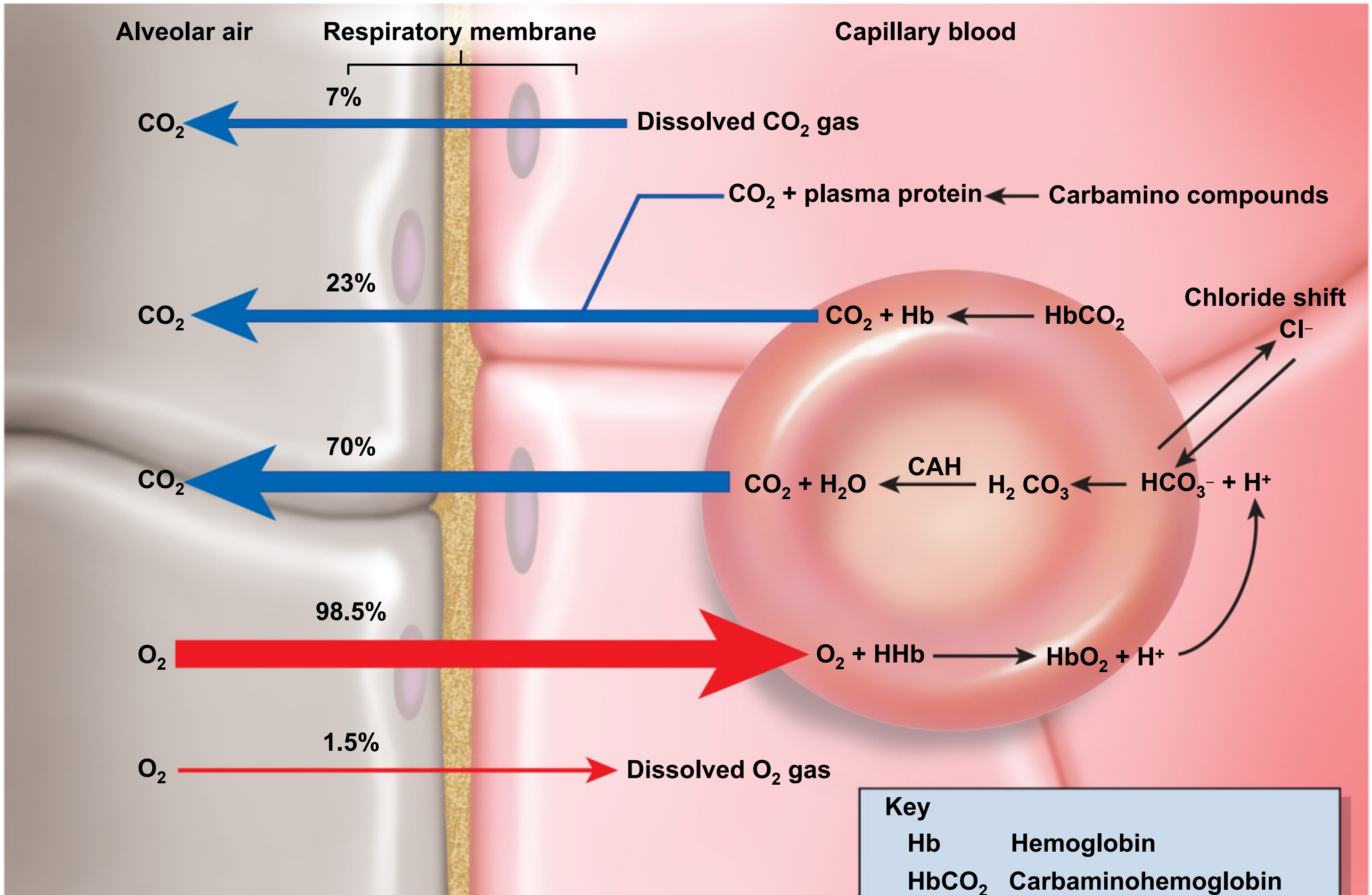
Figure 22.24

# Alveolar Gas Exchange Revisited

- reactions that occur in the lungs are reverse of systemic gas exchange
- **$CO_2$ unloading**
  - as Hb loads $O_2$ its affinity for $H^+$ decreases, $H^+$ dissociates from Hb and bind with $HCO_3^-$
    - $\mathbf{CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+}$
  - reverse **chloride shift**
    - $HCO_3^-$ diffuses back into RBC in exchange for $Cl^-$, free $CO_2$ generated diffuses into alveolus to be exhaled

# Alveolar Gas Exchange






**Key**

| | |
|---|---|
| Hb | Hemoglobin |
| $HbCO_2$ | Carbaminohemoglobin |
| $HbO_2$ | Oxyhemoglobin |
| HHb | Deoxyhemoglobin |
| CAH | Carbonic anhydrase |

Figure 22.25

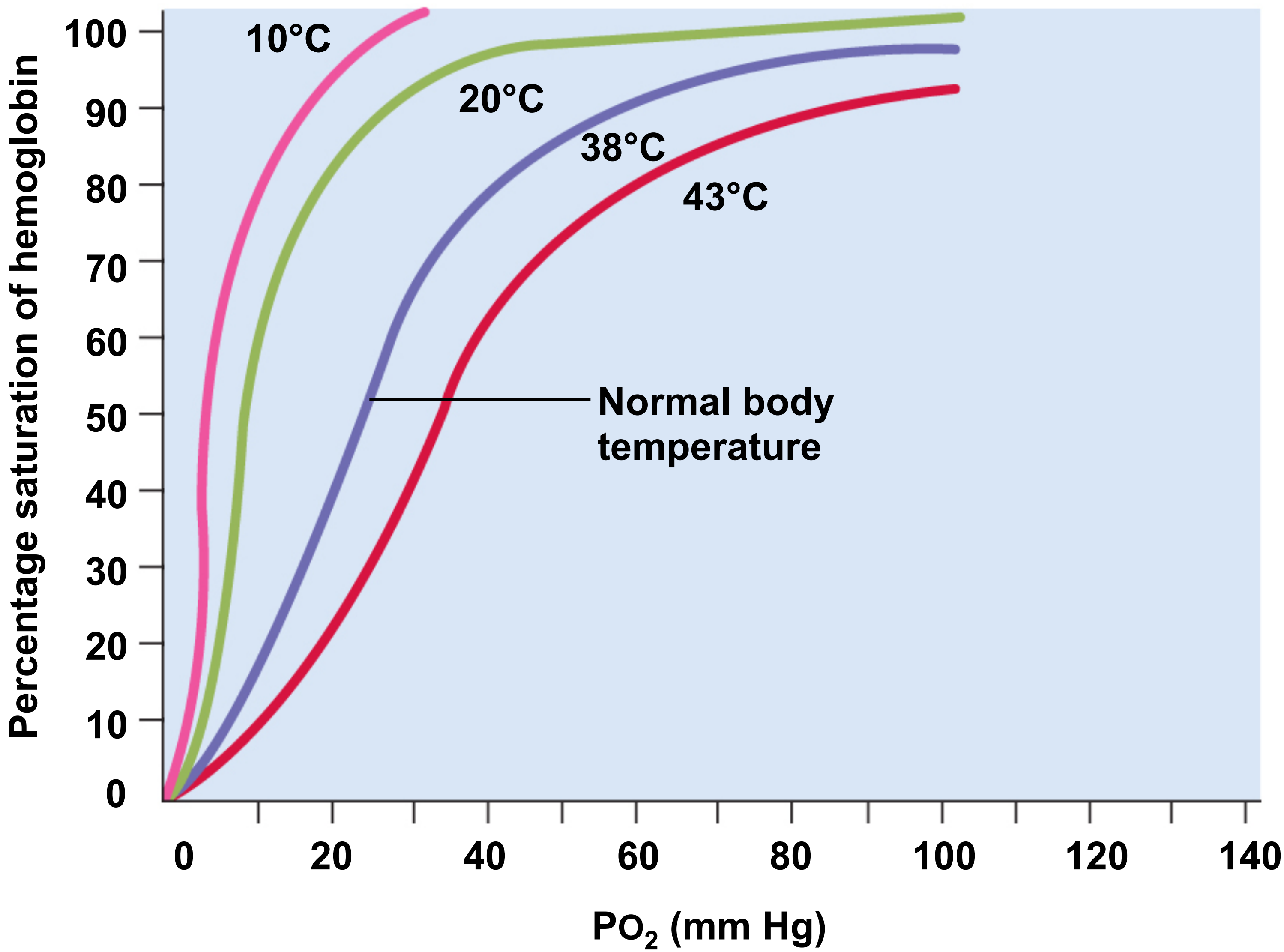
# Adjustment to the Metabolic Needs of Individual Tissues

- hemoglobin unloads $O_2$ to match metabolic needs of different states of activity of the tissues

- four factors that adjust the rate of oxygen unloading
  - **ambient $Po_2$**
    - active tissue has ↓ $Po_2$ ; $O_2$ is released from Hb
  - **temperature**
    - active tissue has ↑ temp; promotes $O_2$ unloading
  - **Bohr effect**
    - active tissue has ↑ $CO_2$, 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 $CO_2$
    - ↑ body temp (fever), thyroxine, growth hormone, testosterone, and epinephrine all raise BPG and cause $O_2$ unloading
    - ↑ metabolic rate requires ↑ oxygen

# Oxygen Dissociation and Temperature



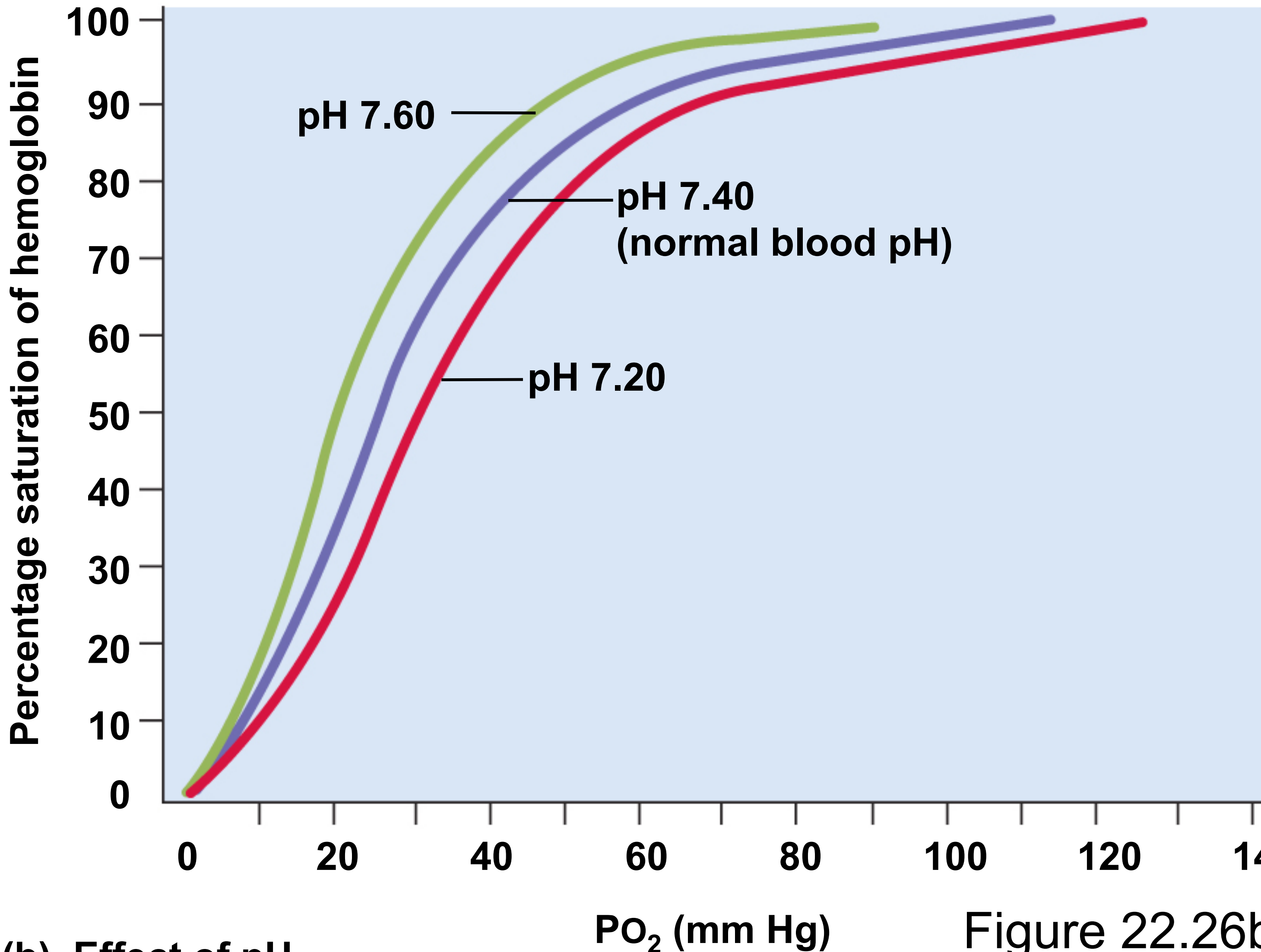



(a) Effect of temperature

Figure 22.26a

# Oxygen Dissociation and pH






(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**
  - **$P_{CO_2}$ 40 mm Hg**
  - **$P_{O_2}$ 95 mm Hg**

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

- **most potent stimulus for breathing** is **pH**, followed by $CO_2$, and least significant is $O_2$

# Hydrogen Ions

- pulmonary ventilation is adjusted to maintain the pH of the brain
  - **central chemoreceptors** in the medulla oblongata produce about 75% of the change in respiration induced by pH shift
  - yet $H^+$ does not cross the blood-brain barrier very easily
  - $CO_2$ does and in CSF reacts with water and produces carbonic acid
    - dissociates into bicarbonate and hydrogen ions
    - most $H^+$ remains free and greatly stimulates the central chemoreceptors
  - hydrogen ions are also a potent stimulus to the **peripheral chemoreceptors** which produce about 25% of the respiratory response to pH change

# Hydrogen Ions

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

# Effects of Hydrogen Ions

- **respiratory acidosis** and **respiratory alkalosis** – pH imbalances resulting from a mismatch between the rate of pulmonary ventilation and the rate of $CO_2$ production

- **hyperventilation** is a corrective homeostatic **response to acidosis**
  - "blowing off" $CO_2$ faster than the body produces it
  - pushes reaction to the left

    $CO_2$ (expired) + $H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + \downarrow H^+$
  - 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
  - $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
  - 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
  - ↑ $CO_2$ 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

# Respiration and Exercise

- causes of increased respiration during exercise

1. 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
2. exercise stimulates proprioceptors of the muscles and joints
   - they transmit excitatory signals to the brainstem respiratory centers
   - increase breathing because they are informed that the muscles have been told to move or are actually moving
   - increase in pulmonary ventilation keeps blood gas values at their normal levels in spite of the elevated $O_2$ consumption and $CO_2$ generation by the muscles

# Respiratory Disorders 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 $P_{O_2}$
  - usually due 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
- **anemic hypoxia** – due to anemia resulting from the inability of the blood to carry adequate oxygen
- **histotoxic hypoxia** – metabolic poisons such as cyanide prevent the tissues from using oxygen delivered to them
- **cyanosis** – blueness of the skin
  - sign of hypoxia

# Oxygen Excess

- **oxygen toxicity** - pure $O_2$ breathed at 2.5 atm or greater
  – safe to breathe 100% oxygen at 1 atm for a few hours
  – generates free radicals and $H_2O_2$
  – destroys enzymes
  – damages nervous tissue
  – leads to seizures, coma, death

- **hyperbaric oxygen**
  – formerly used to treat premature infants, caused retinal damage, was discontinued