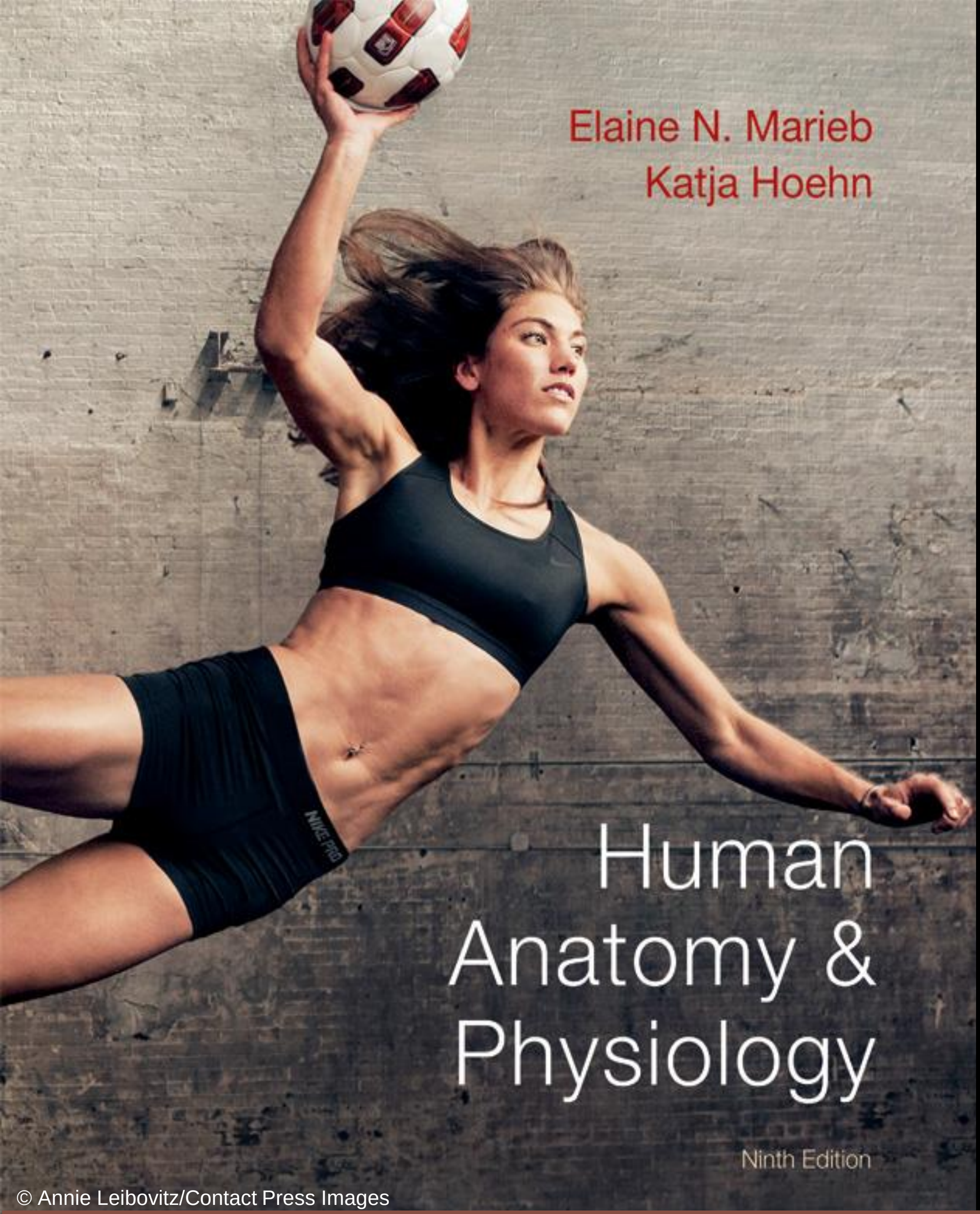

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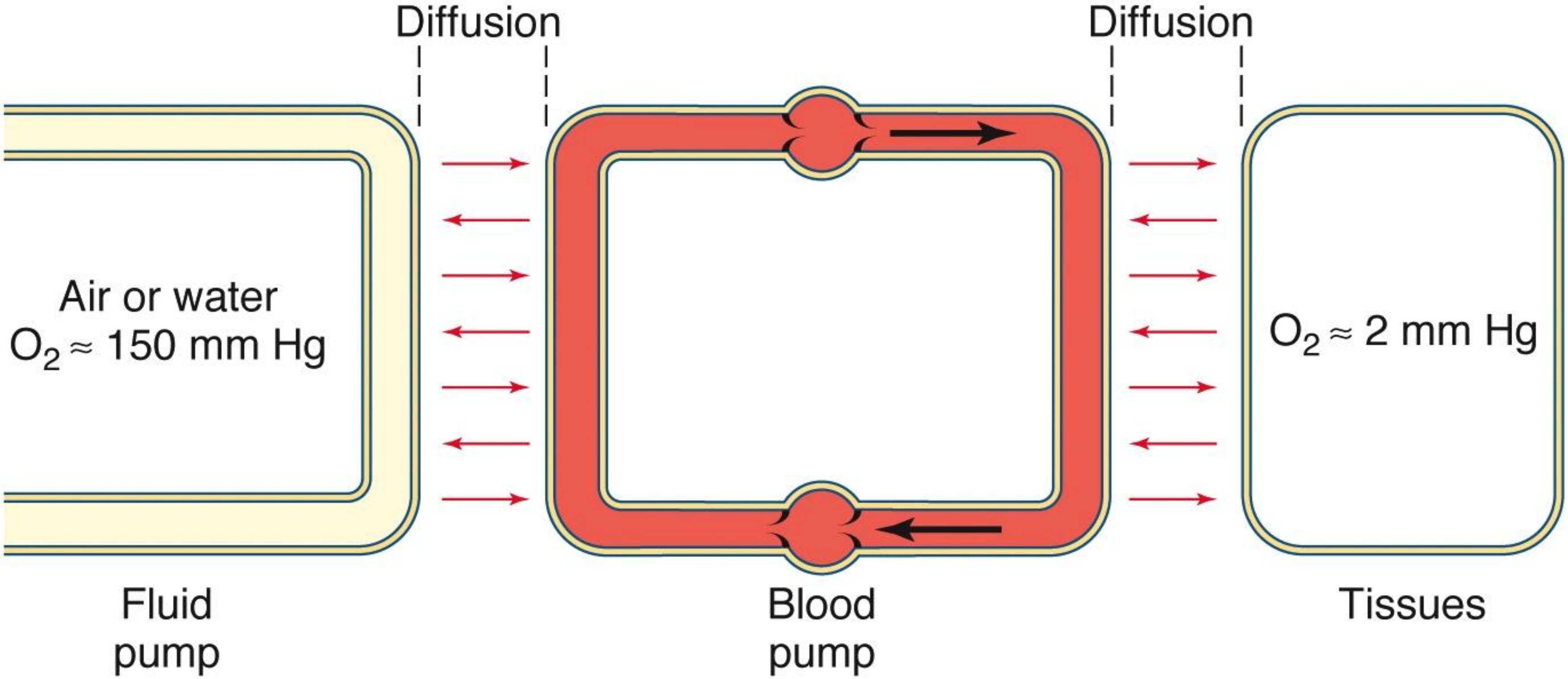
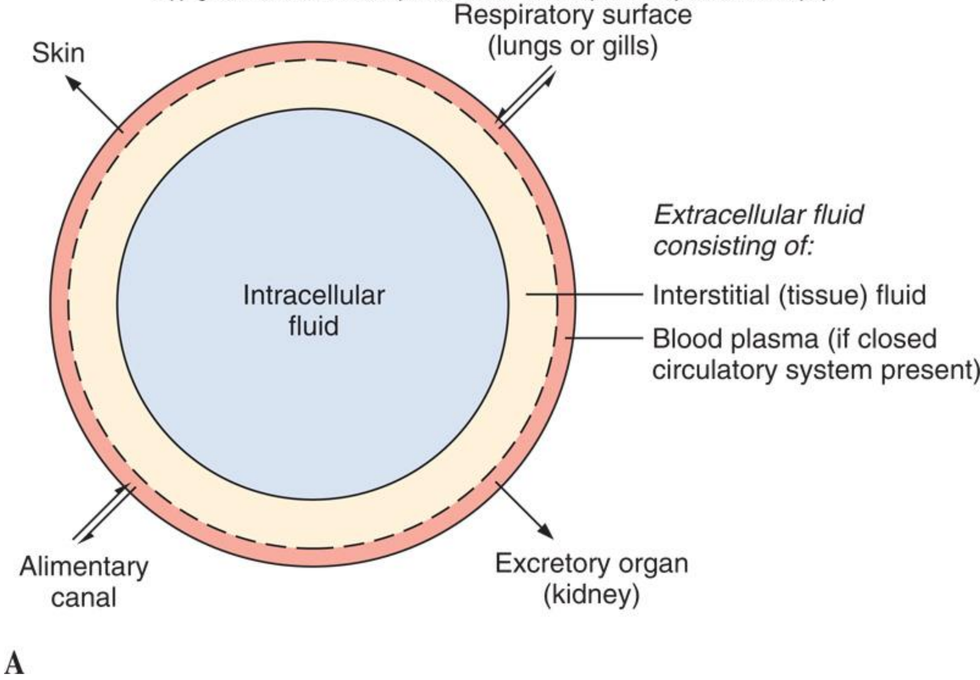
CHAPTER 22

The Respiratory System: Part A


Diffusion
Diffusion
Air or water
$O_2 \approx 150$ mm Hg
$O_2 \approx 2$ mm Hg
Fluid
pump
Blood
pump
Tissues

Exchanging Materials

- Every organism must exchange materials with its environment.
  - This exchange ultimately occurs at the cellular level.



Circulatory Systems Reflect Phylogeny

- Transport systems functionally connect the organs of exchange with the body cells.

Solubility of Gases in Distilled Water

°C	*Oxygen*	*Carbon Dioxide*	*Nitrogen*	*Helium*
0	21.7	767.5	—	—
10	16.9	531.2	—	—
20	13.7	386.8	6.82	—
30	11.6	294.9	—	—
37	10.6	250.5	5.61	3.75
40	10.2	234.8	—	—

Effect of Salinity on Oxygen Solubility

°C	Salinity	0‰	10‰	20‰	30‰	40‰
0		21.7	20.2	18.9	17.7	16.6
10		16.9	15.8	14.8	13.9	13.1
20		13.7	12.9	12.2	11.5	10.8
30		11.6	11.0	10.4	9.86	9.33
40		10.2	9.71	9.26	8.73	8.35

Effects of high altitude on atmospheric pressure (P_b; kPa), ambient pO_2 (kPa), and alveolar pO_2 and pCO_2 ($p_A O_2$, and $p_A CO_2$; kPa) for a human.

Altitude	P_b	Ambient pO_2	$p_A O_2$	$p_A CO_2$
0	101	21.1	13.8	5.3
3100	70.6	14.6	8.9	4.8
4340	61.9	12.8	6.0	—
6200	46	9.7	5.3	3.2
7100	———	normal "ceiling"		———
8848	33	6.9	4.0	1.5
9200	30	6.3	2.8	—
12300	19	3.9	1.1	—
14460	———	"ceiling" with pure O_2		———
15400	12	2.4	0.1	—
20000	6	1.3	0	0

Sea level

P_{O2} =760*0.2094 = 159 mmHg

P_{O2} =(760-18)*0.2094 = 155 mmHg

Partial pressures (kPa) for oxygen and nitrogen (dry, CO_2-free values for ambient air), alveolar carbon dioxide, and plasma-dissolved O_2 (ml O_2 per liter plasma; assuming plasma solubility of O_2 is 0.209 ml liter^{-1} kPa^{-1}) and fat N_2 content (ml N_2 per liter body fat; assuming fat solubility of N_2 is 0.67 ml liter^{-1} kPa^{-1} dissolved N_2) for a human scuba diver in equilibrium with the ambient hydrostatic pressure as a function of depth of diving.

Depth (m)	**0**	**50**	**100**	**500**
Ambient Pressure	101	202	1111	5151
pO_2	21.1	42.4	233.5	1082.6
pN_2	79.8	159.7	878.3	4072.5
Alveolar pCO_2	5.32	5.32	5.32	5.32
Plasma O_2	4.4	8.8	48.3	223.9
Fat N_2	53	106	582	2700

The Respiratory System

- Major function-**respiration**
  - Supply body with O_2 for *cellular respiration;* dispose of CO_2, a waste product of *cellular respiration*
  - Its four processes involve both respiratory and circulatory systems
- Also functions in olfaction and speech

Processes of Respiration

- **Pulmonary ventilation** (breathing)- movement of air into and out of lungs
- **External respiration**-O_2 and CO_2 exchange between lungs and blood
- **Transport**-O_2 and CO_2 in blood
- **Internal respiration**-O_2 and CO_2 exchange between systemic blood vessels and tissues

Respiratory system

Circulatory system

Bronchi and Subdivisions

- Air passages undergo 23 orders of branching → **bronchial** (respiratory) **tree**
- From tips of bronchial tree → conducting zone structures → respiratory zone structures

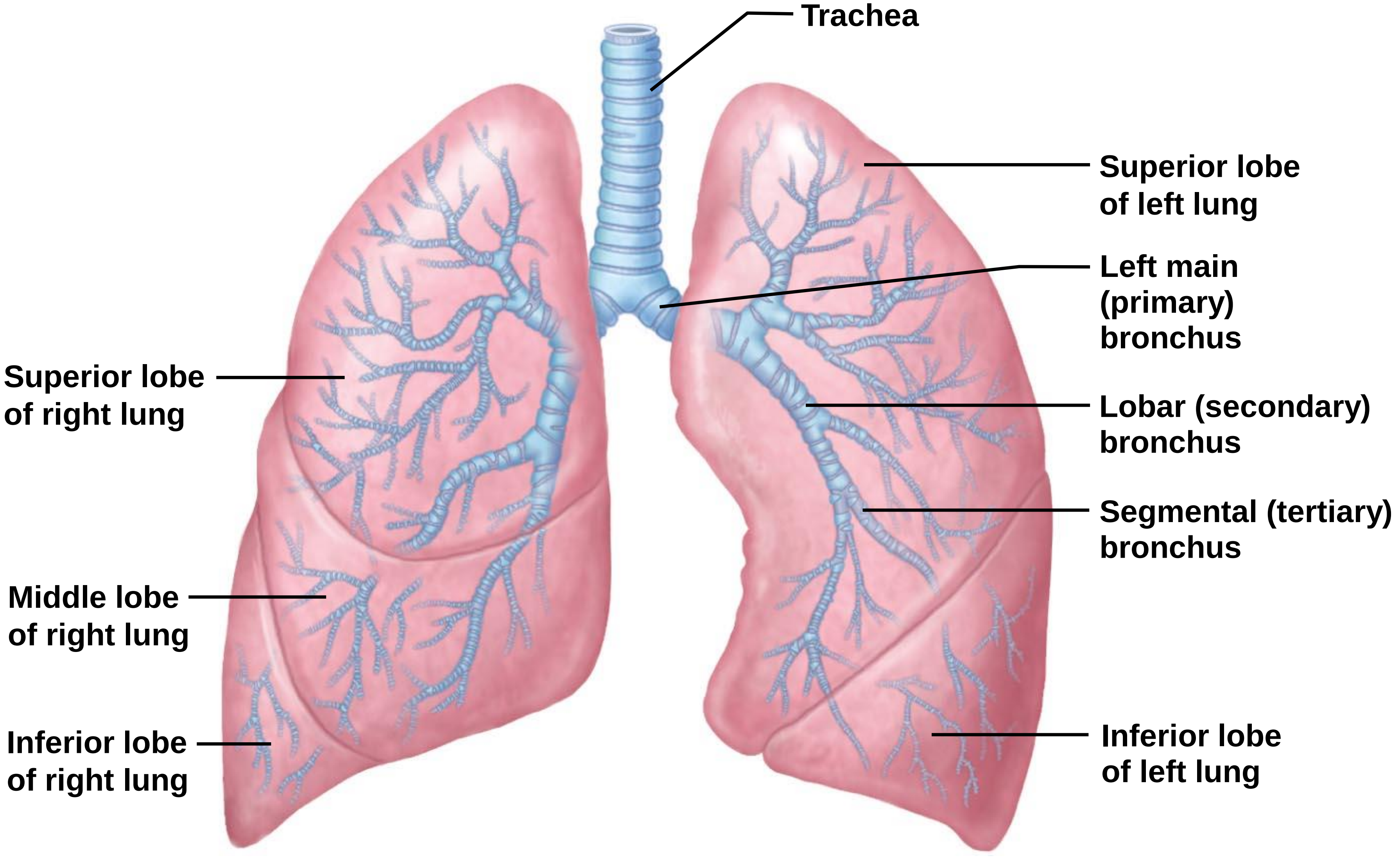
Conducting Zone Structures

- Trachea → **right and left main** (primary) **bronchi**
- Each main bronchus enters hilum of one lung
  - Right main bronchus wider, shorter, more vertical than left
- Each main bronchus branches into **lobar** (secondary) **bronchi** (three on right, two on left)
  - Each lobar bronchus supplies one lobe

Conducting Zone Structures

- Each lobar bronchus branches into **segmental** (tertiary) **bronchi**
  - Segmental bronchi divide repeatedly
- Branches become smaller and smaller →
  - **Bronchioles**-less than 1 mm in diameter
  - **Terminal bronchioles**-smallest-less than 0.5 mm diameter

Figure 22.7 Conducting zone passages.



Conducting Zone Structures

- From bronchi through bronchioles, structural changes occur
  - Cartilage rings become irregular plates; in bronchioles elastic fibers replace cartilage
  - Epithelium changes from pseudostratified columnar to cuboidal; cilia and goblet cells become sparse
  - Relative amount of smooth muscle increases
    - Allows constriction

Respiratory Zone

- Begins as terminal bronchioles → **respiratory bronchioles → alveolar ducts → alveolar sacs**
  - Alveolar sacs contain clusters of **alveoli**
    - ~300 million alveoli make up most of lung volume
    - Sites of gas exchange

Figure 22.8a Respiratory zone structures.

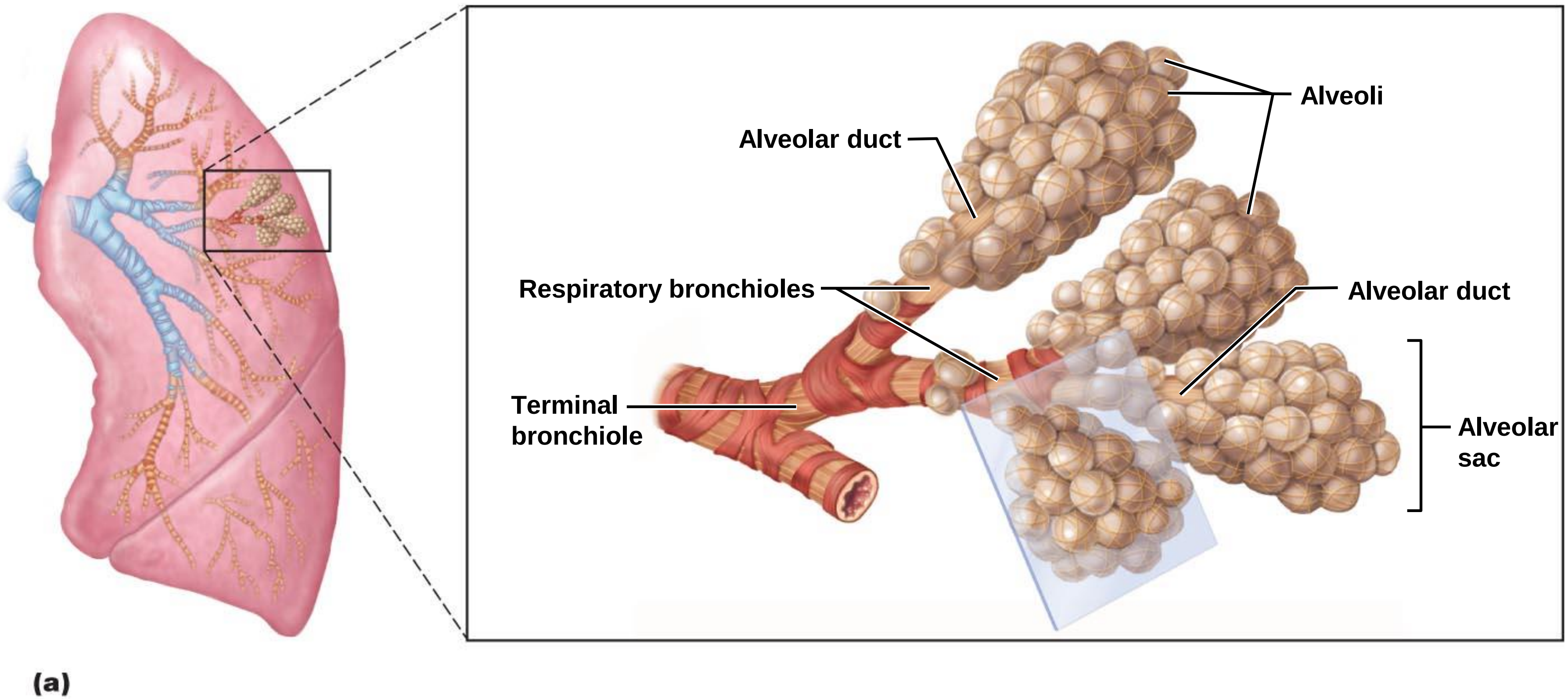
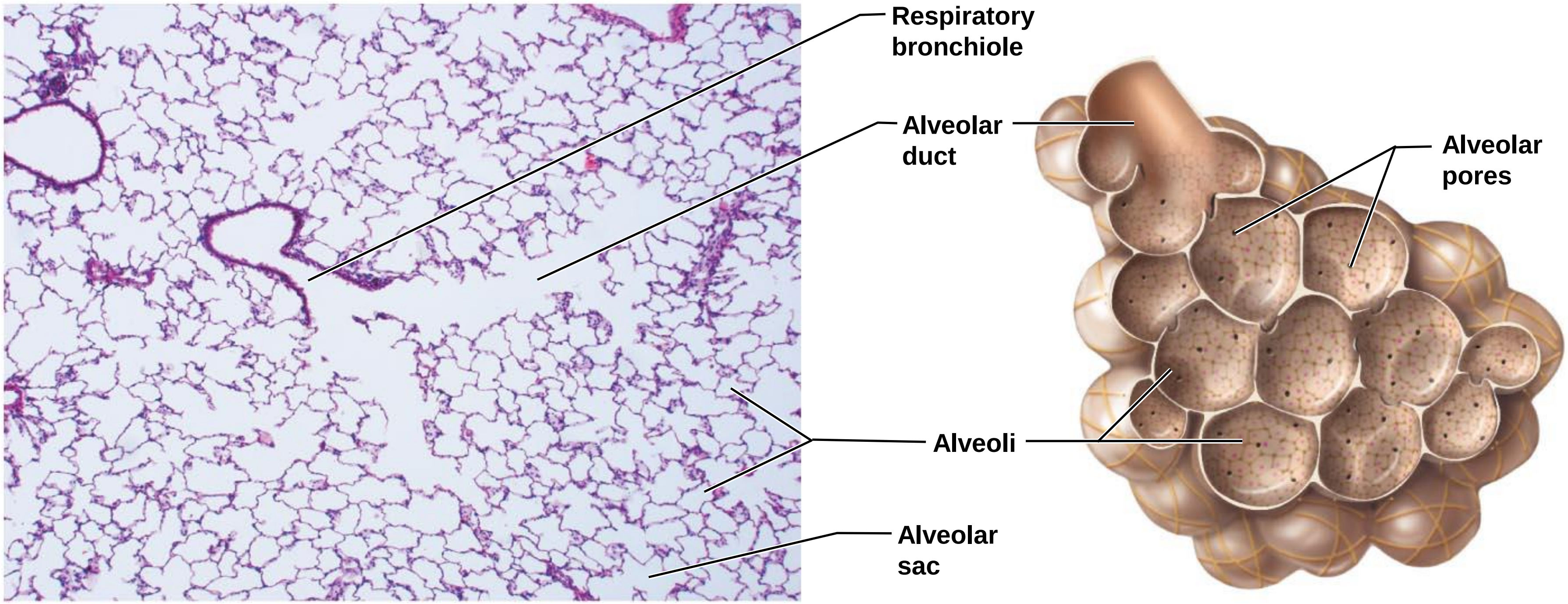


Figure 22.8b Respiratory zone structures.

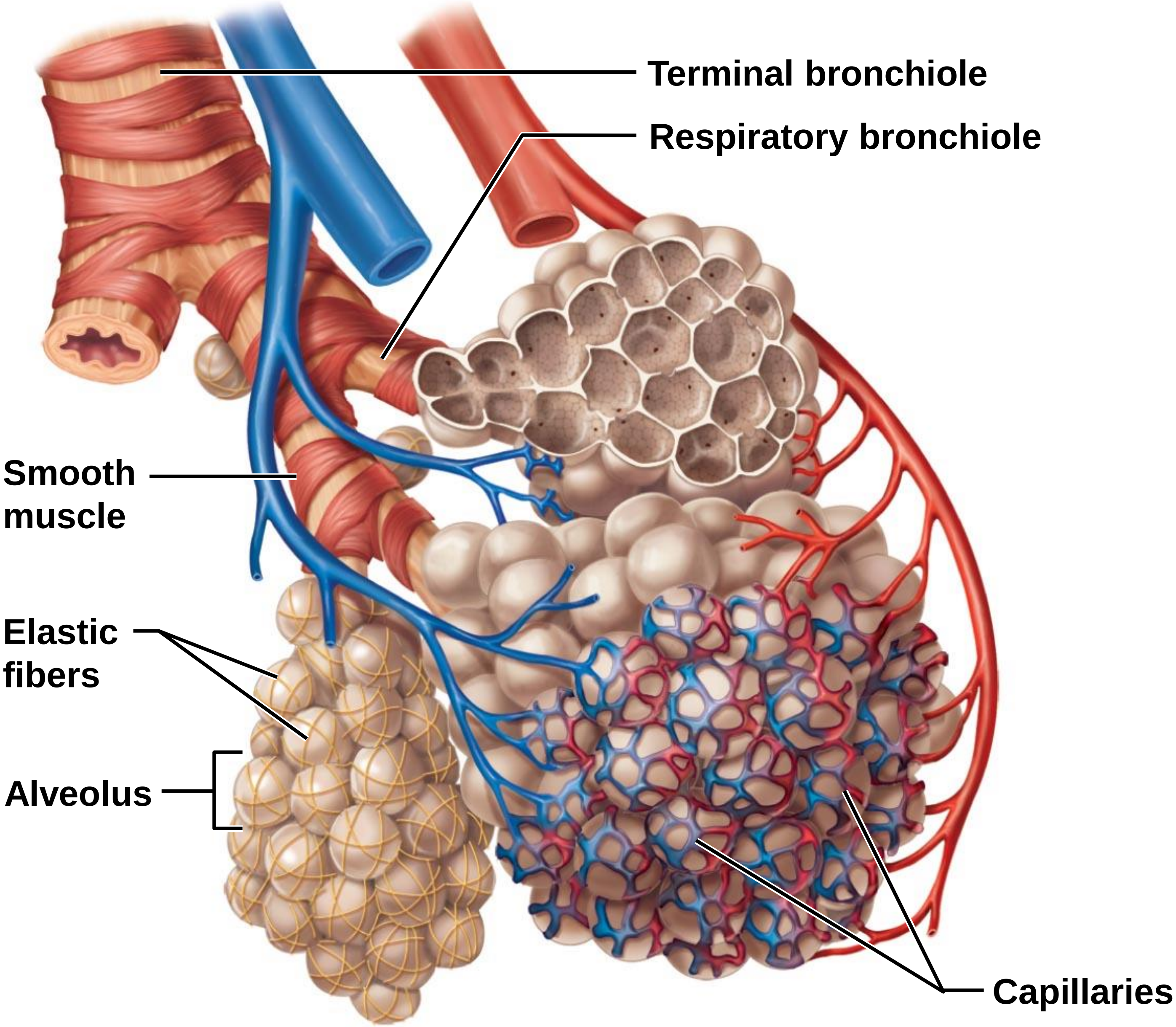


(b)

Respiratory Membrane

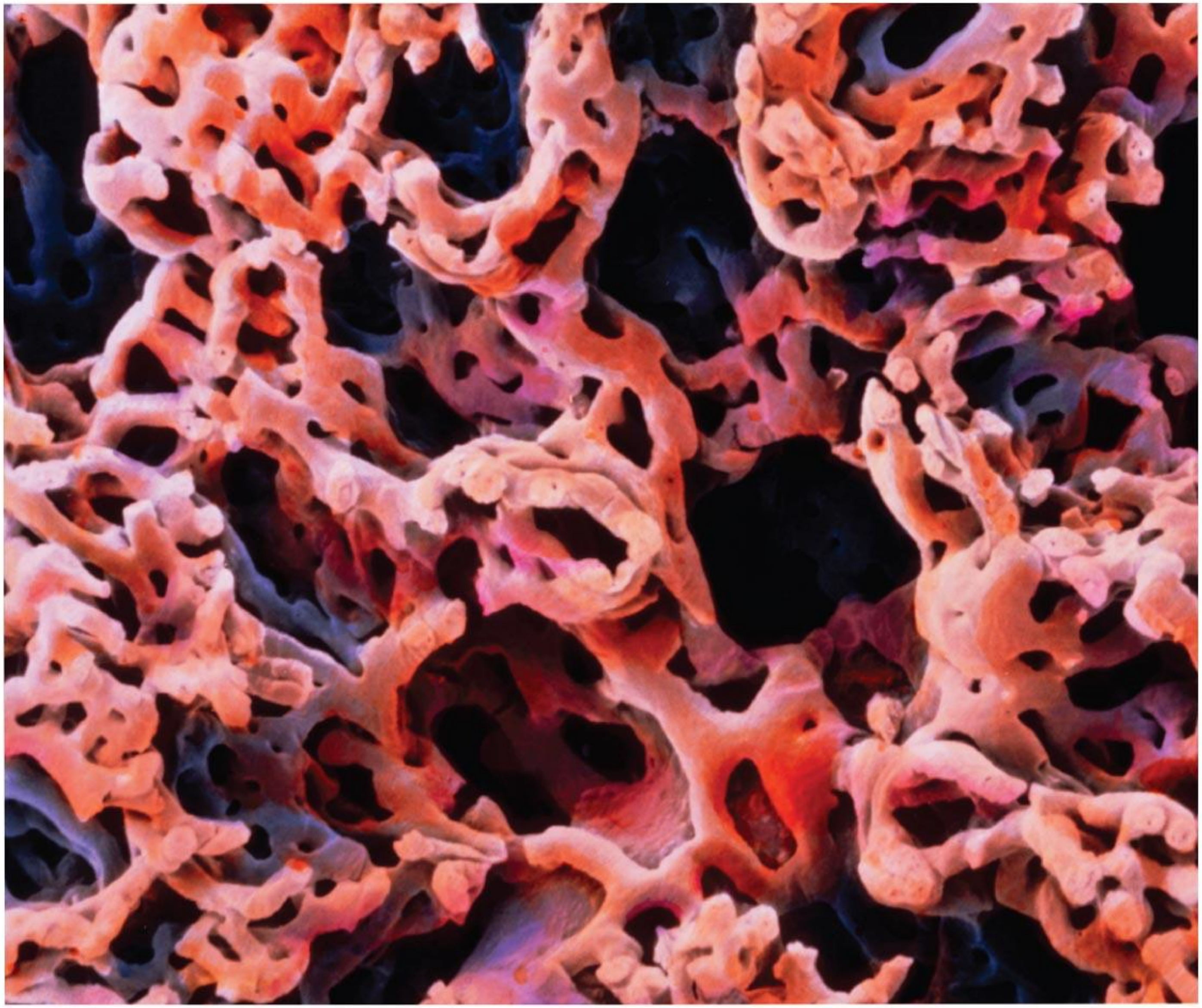
- Alveolar and capillary walls and their fused basement membranes
  – ~0.5-µm-thick; gas exchange across membrane by simple diffusion
- Alveolar walls
  – Single layer of squamous epithelium (**type I alveolar cells**)
- Scattered cuboidal **type II alveolar cells** secrete **surfactant** and antimicrobial proteins

Figure 22.9a Alveoli and the respiratory membrane.



(a) Diagrammatic view of capillary-alveoli relationships

Figure 22.9b Alveoli and the respiratory membrane.

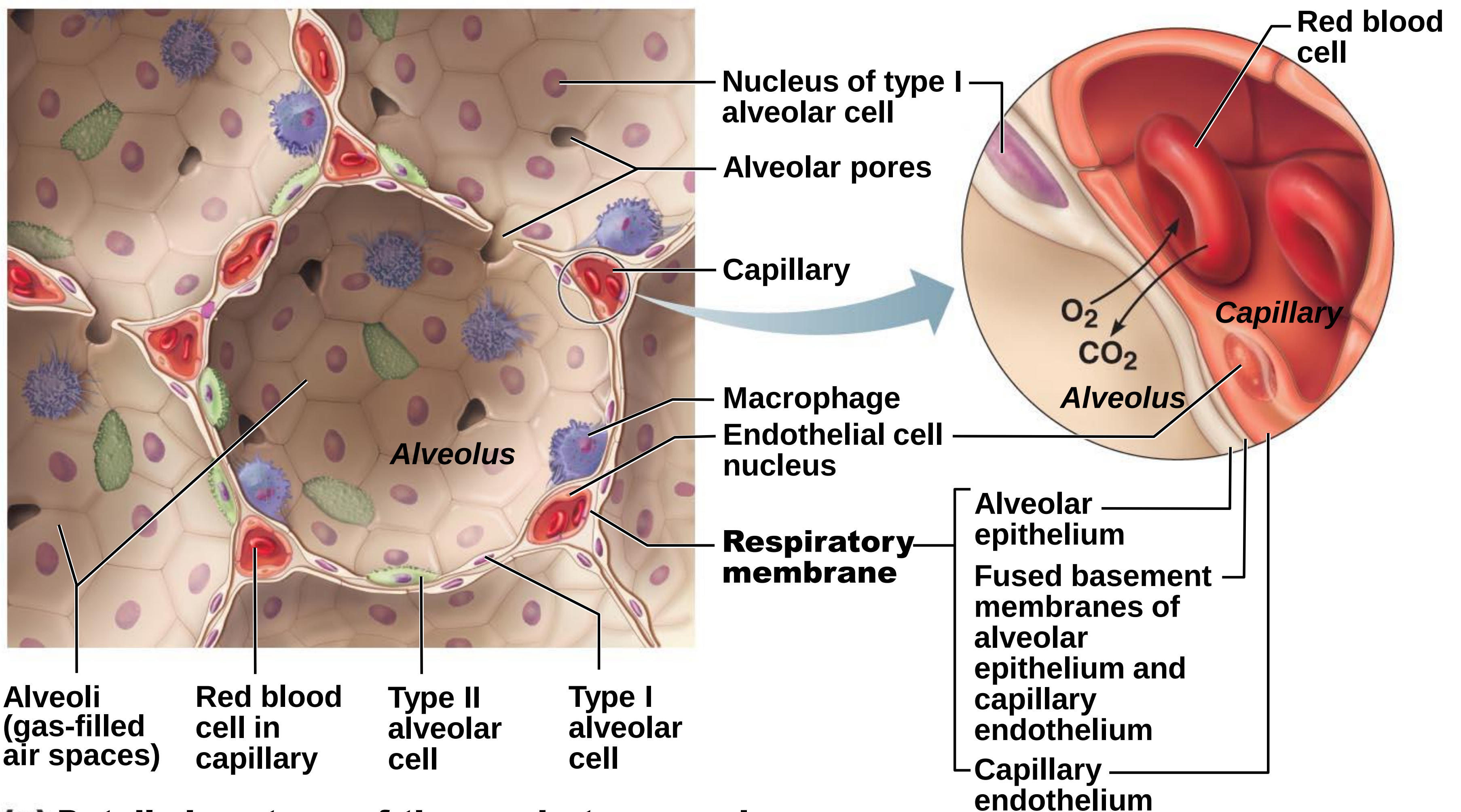


(b) Scanning electron micrograph of pulmonary capillary casts (70x)

Alveoli

- Surrounded by fine elastic fibers and pulmonary capillaries
- **Alveolar pores** connect adjacent alveoli
    - Equalize air pressure throughout lung
- **Alveolar macrophages** keep alveolar surfaces sterile
    - – 2 million dead macrophages/hour carried by cilia → throat → swallowed

Figure 22.9c Alveoli and the respiratory membrane.

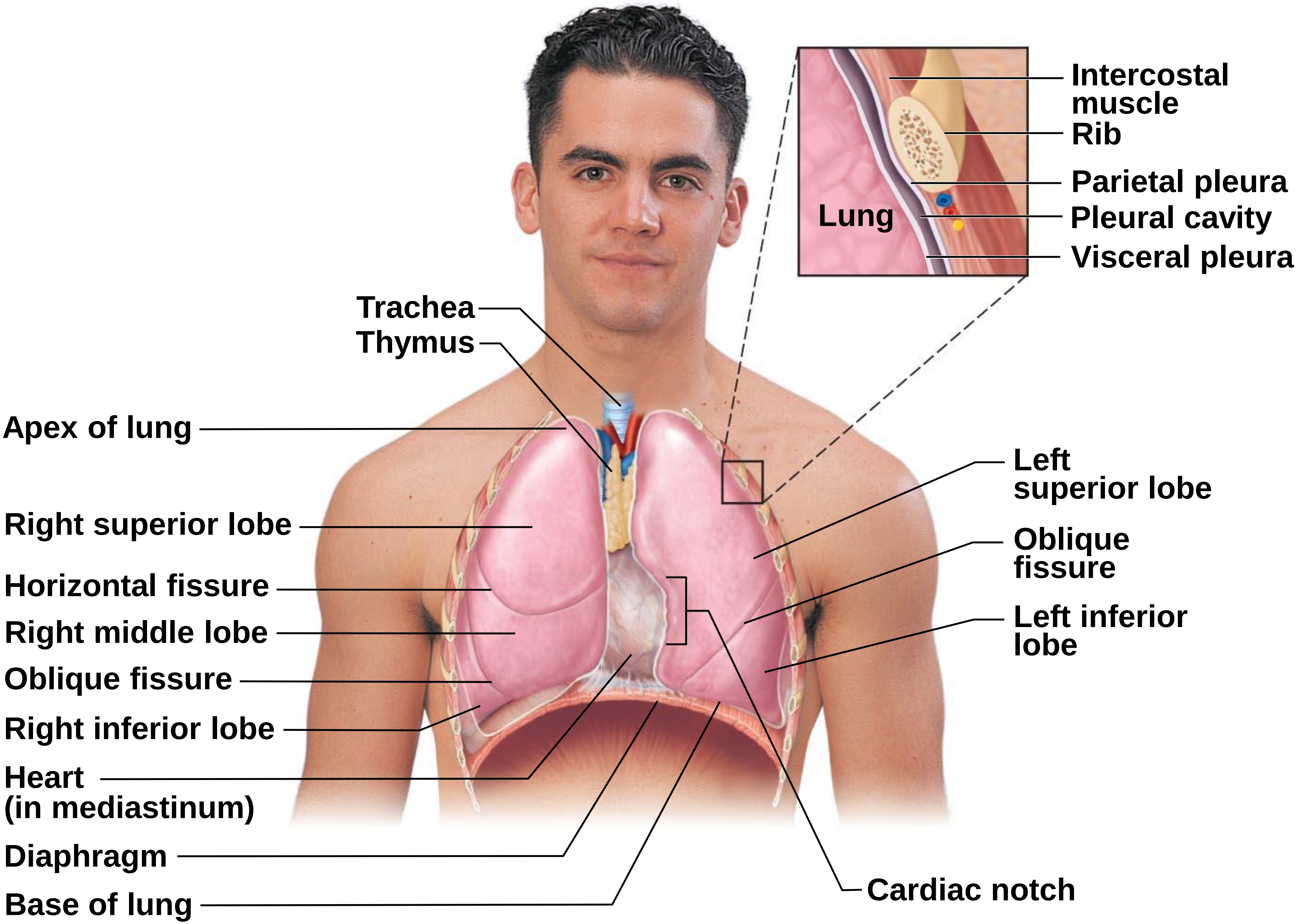


(c) Detailed anatomy of the respiratory membrane

Lungs

- **Apex**-superior tip; deep to clavicle
- **Base**-inferior surface; rests on diaphragm
- **Hilum**-on mediastinal surface; site for entry/exit of blood vessels, bronchi, lymphatic vessels, and nerves
- Left lung smaller than right
  - **Cardiac notch**-concavity for heart
  - Separated into *superior* and *inferior* **lobes** by *oblique fissure*

Figure 22.10a Anatomical relationships of organs in the thoracic cavity.



(a) Anterior view. The lungs flank mediastinal structures laterally.

Mechanics of Breathing

- Pulmonary ventilation consists of two phases
  - **Inspiration**-gases flow into lungs
  - **Expiration**-gases exit lungs

Pressure Relationships in the Thoracic Cavity

- **Atmospheric pressure (P_{atm})**
  - Pressure exerted by air surrounding body
  - 760 mm Hg at sea level = 1 atmosphere
- Respiratory pressures described relative to P_{atm}
  - Negative respiratory pressure-less than P_{atm}
  - Positive respiratory pressure-greater than P_{atm}
  - Zero respiratory pressure = P_{atm}

Intrapulmonary Pressure

- **Intrapulmonary** (intra-alveolar) **pressure** (**P_{pul}**)
  - Pressure in alveoli
  - Fluctuates with breathing
  - Always eventually equalizes with P_{atm}

Intrapleural Pressure

- **Intrapleural pressure (P_{ip})**
  - Pressure in pleural cavity
  - Fluctuates with breathing
  - Always a negative pressure ($<P_{atm}$ and $<P_{pul}$)
  - Fluid level must be minimal
    - Pumped out by lymphatics
    - If accumulates → positive P_{ip} pressure → lung collapse

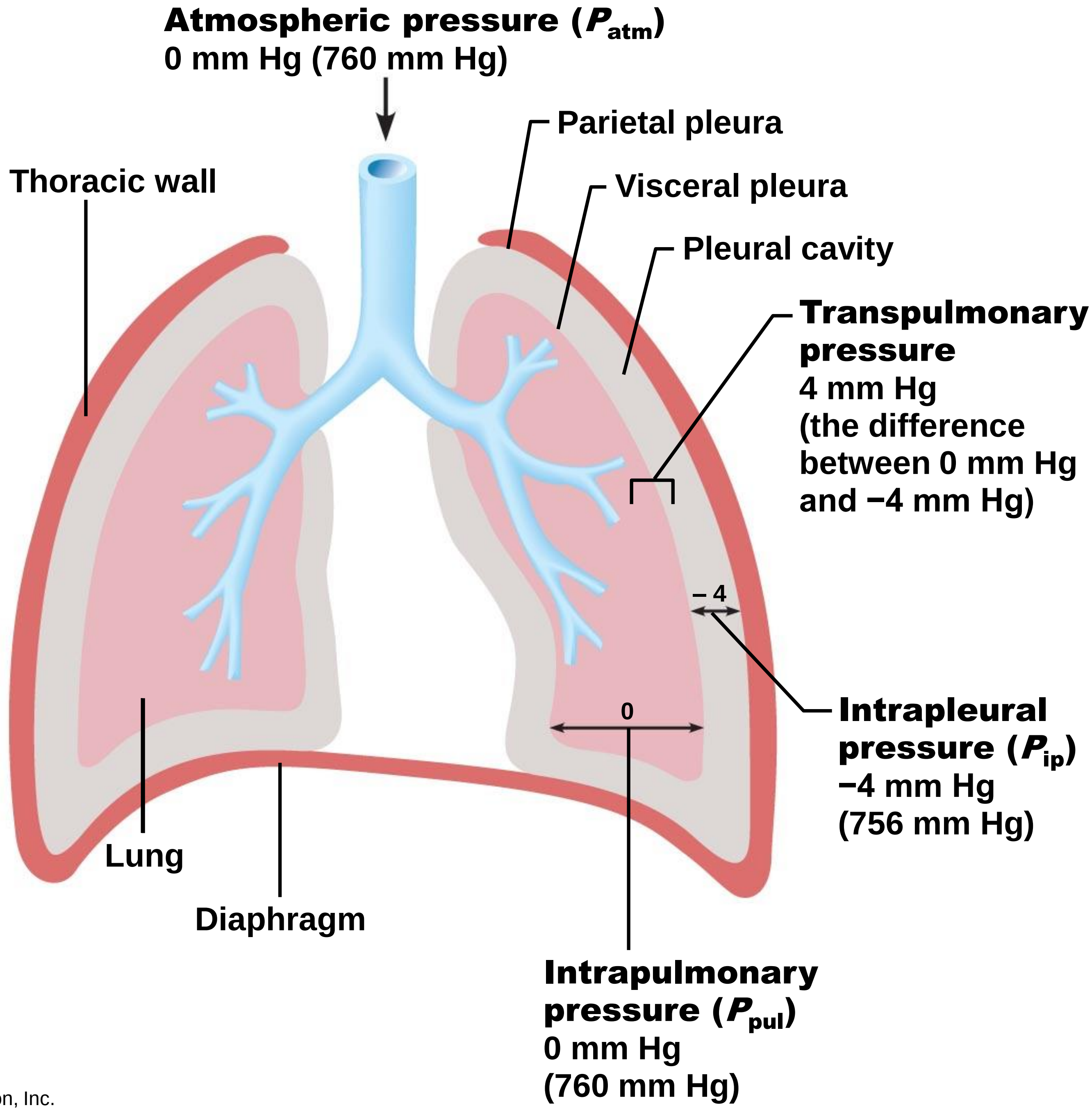
Intrapleural Pressure

- Negative P_{ip} caused by opposing forces
  - Two inward forces promote *lung collapse*
    - Elastic recoil of lungs decreases lung size
    - Surface tension of alveolar fluid reduces alveolar size
  - One outward force tends to enlarge lungs
    - Elasticity of chest wall pulls thorax outward

Pressure Relationships

- If $P_{ip} = P_{pul}$ or P_{atm} → lungs collapse
- $(P_{pul} – P_{ip})$ = **transpulmonary pressure**
  - Keeps airways open
  - Greater transpulmonary pressure → larger lungs

Figure 22.12 Intrapulmonary and intrapleural pressure relationships.



Homeostatic Imbalance

- **Atelectasis** (lung collapse) due to
  - Plugged bronchioles → collapse of alveoli
  - **Pneumothorax**-air in pleural cavity
    - From either wound in parietal or rupture of visceral pleura
    - Treated by removing air with chest tubes; pleurae heal → lung reinflates

Pulmonary Ventilation

- Inspiration and expiration
- Mechanical processes that depend on volume changes in thoracic cavity
  - Volume changes $\rightarrow$ pressure changes
  - Pressure changes $\rightarrow$ gases flow to equalize pressure

Boyle's Law

- Relationship between pressure and volume of a gas
  - Gases fill container; if container size reduced → increased pressure
- Pressure (P) varies inversely with volume (V):
  - $P_1V_1 = P_2V_2$

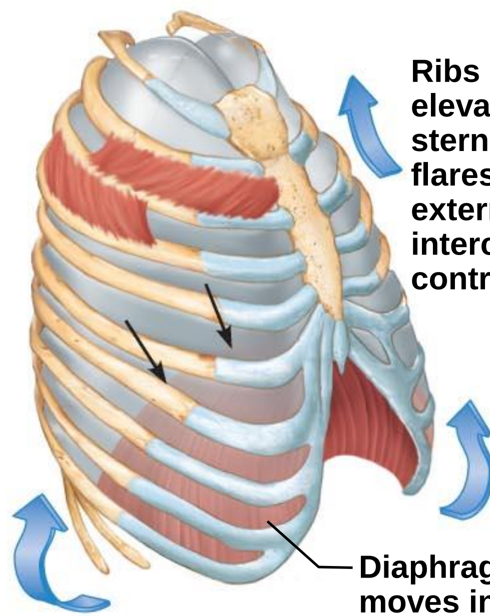
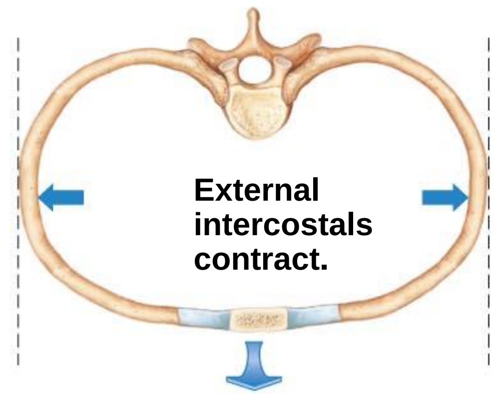
Inspiration

- Active process
  - Inspiratory muscles (diaphragm and external intercostals) contract
  - Thoracic volume increases → intrapulmonary pressure drops (to –1 mm Hg)
  - Lungs stretched and intrapulmonary volume increases
  - Air flows into lungs, down its pressure gradient, until $P_{pul} = P_{atm}$

Forced Inspiration

- Vigorous exercise, COPD → accessory muscles (scalenes, sternocleidomastoid, pectoralis minor) → further increase in thoracic cage size

Figure 22.13 Changes in thoracic volume and sequence of events during inspiration and expiration. (1 of 2)

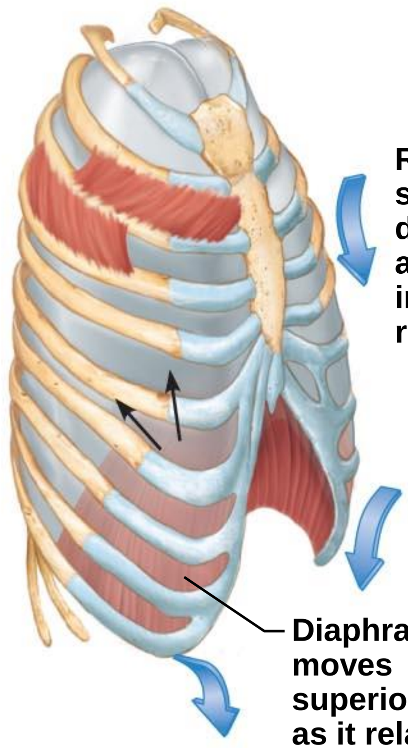
	Sequence of events	Changes in anterior-posterior and superior-inferior dimensions	Changes in lateral dimensions (superior view)
Inspiration	① Inspiratory muscles contract (diaphragm descends; rib cage rises). ↓ ② Thoracic cavity volume increases. ↓ ③ Lungs are stretched; intrapulmonary volume increases. ↓ ④ Intrapulmonary pressure drops (to –1 mm Hg). ↓ ⑤ Air (gases) flows into lungs down its pressure gradient until intrapulmonary pressure is 0 (equal to atmospheric pressure).		

Expiration

- Quiet expiration normally passive process
  - Inspiratory muscles relax
  - Thoracic cavity volume decreases
  - Elastic lungs recoil and intrapulmonary volume decreases → pressure increases (P_{pul} rises to +1 mm Hg) →
  - Air flows out of lungs down its pressure gradient until $P_{pul} = 0$
- Note: *forced expiration*-active process; uses abdominal (oblique and transverse) and internal intercostal muscles

Figure 22.13 Changes in thoracic volume and sequence of events during inspiration and expiration. (2 of 2)

	Sequence of events	Changes in anterior-posterior and superior-inferior dimensions	Changes in lateral dimensions (superior view)
Expiration	① Inspiratory muscles relax (diaphragm rises; rib cage descends due to recoil of costal cartilages). ↓ ② Thoracic cavity volume decreases. ↓ ③ Elastic lungs recoil passively; intrapulmonary Volume decreases. ↓ ④ Intrapulmonary pressure rises (to +1 mm Hg). ↓ ⑤ Air (gases) flows out of lungs down its pressure gradient until intrapulmonary pressure is 0.	see image 1	see image 2



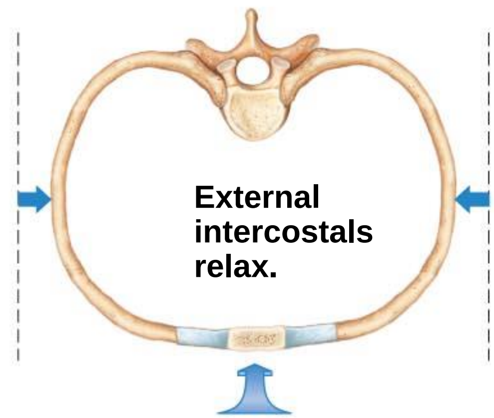
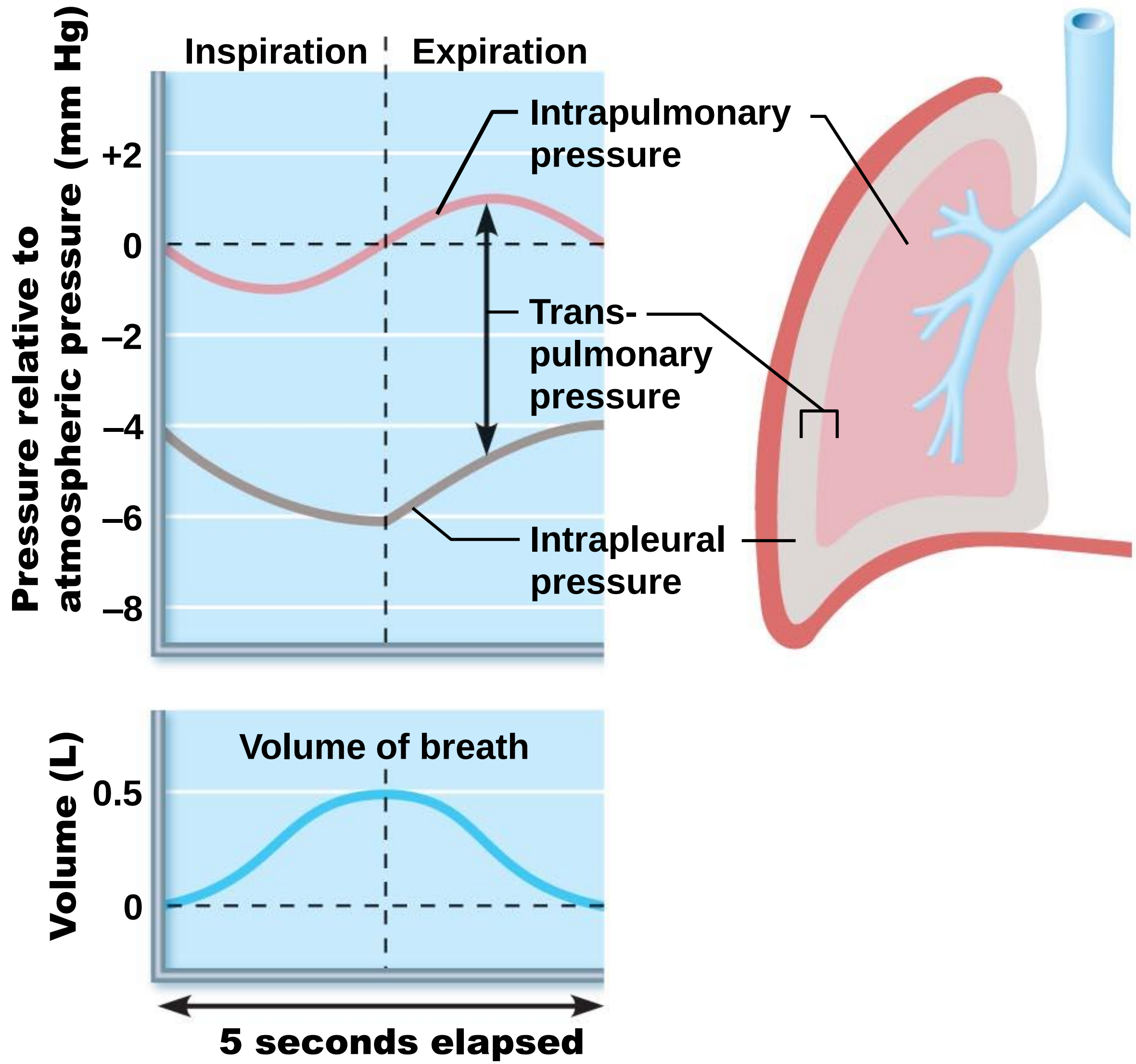


Figure 22.14 Changes in intrapulmonary and intrapleural pressures during inspiration and expiration.

Intrapulmonary pressure. Pressure inside lung decreases as lung volume increases during inspiration; pressure increases during expiration.

Intrapleural pressure. Pleural cavity pressure becomes more negative as chest wall expands during inspiration. Returns to initial value as chest wall recoils.

Volume of breath. During each breath, the pressure gradients move 0.5 liter of air into and out of the lungs.



Physical Factors Influencing Pulmonary Ventilation

- Three physical factors influence the ease of air passage and the amount of energy required for ventilation.
  - **Airway resistance**
  - **Alveolar surface tension**
  - **Lung compliance**

Airway Resistance

- Friction-major *nonelastic* source of resistance to gas flow; occurs in airways
- Relationship between flow (F), pressure (P), and resistance (R) is:

$$F = \frac{\Delta P}{R}$$

  - ΔP - pressure gradient between atmosphere and alveoli (2 mm Hg or less during normal quiet breathing)
  - Gas flow changes inversely with resistance

Airway Resistance

- Resistance usually insignificant
  - Large airway diameters in first part of conducting zone
  - Progressive branching of airways as get smaller, increasing total cross-sectional area
  - Resistance greatest in medium-sized bronchi
- Resistance disappears at terminal bronchioles where diffusion drives gas movement

Homeostatic Imbalance

- As airway resistance rises, breathing movements become more strenuous
- Severe constriction or obstruction of bronchioles
  - Can prevent life-sustaining ventilation
  - Can occur during acute asthma attacks; stops ventilation
- Epinephrine dilates bronchioles, reduces air resistance

Alveolar Surface Tension

- **Surface tension**
  - Attracts liquid molecules to one another at gas-liquid interface
  - Resists any force that tends to increase surface area of liquid
  - Water–high surface tension; coats alveolar walls → reduces them to smallest size

Alveolar Surface Tension

- **Surfactant**
  - Detergent-like lipid and protein complex produced by type II alveolar cells
  - Reduces surface tension of alveolar fluid and discourages alveolar collapse
  - Insufficient quantity in premature infants causes **infant respiratory distress syndrome**
    - → alveoli collapse after each breath

Lung Compliance

- Measure of change in lung volume that occurs with given change in transpulmonary pressure
- Higher lung compliance → easier to expand lungs
- Normally high due to
  - Distensibility of lung tissue
  - Surfactant, which decreases alveolar surface tension

Lung Compliance

- Diminished by
  - Nonelastic scar tissue replacing lung tissue (fibrosis)
  - Reduced production of surfactant
  - Decreased flexibility of thoracic cage

Total Respiratory Compliance

- The total compliance of the respiratory system is also influenced by compliance (distensibility) of the thoracic wall, which is decreased by:
  - Deformities of thorax
  - Ossification of costal cartilage
  - Paralysis of intercostal muscles

Respiratory Volumes

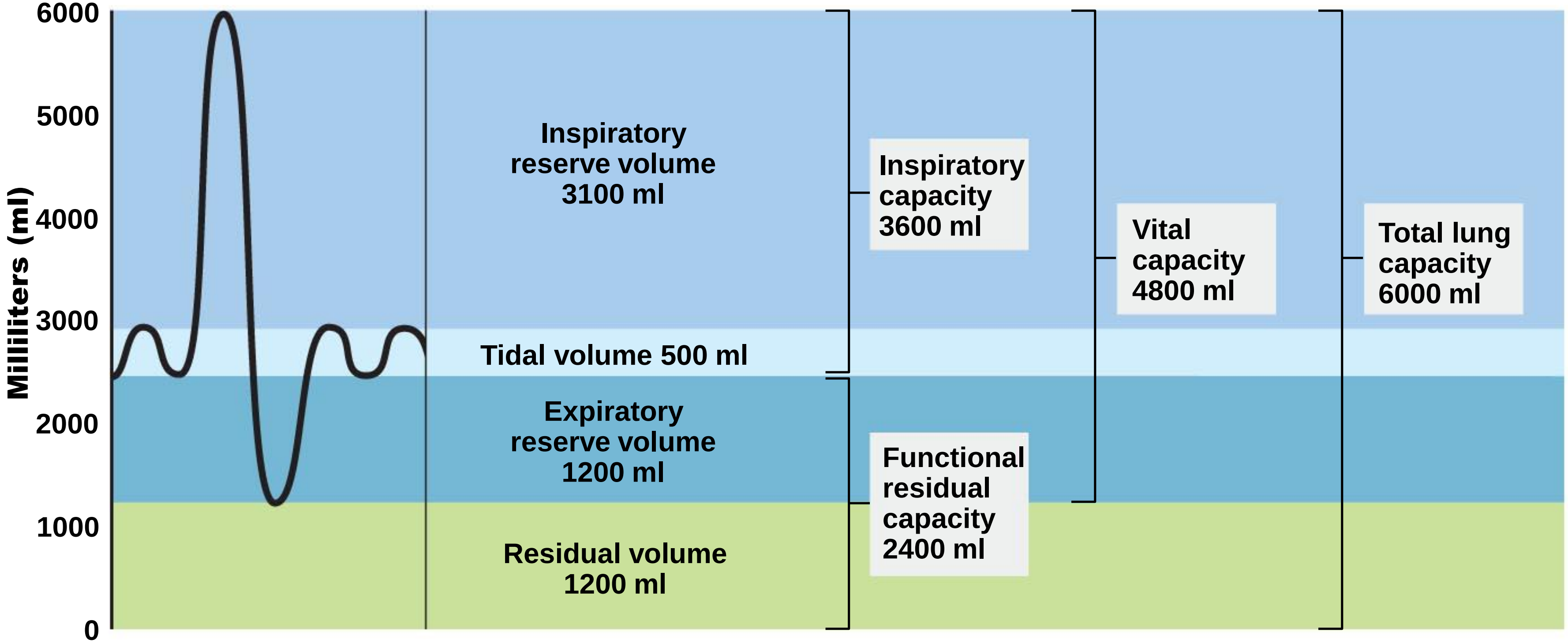
- Used to assess respiratory status
  - **Tidal volume (TV)**
  - **Inspiratory reserve volume (IRV)**
  - **Expiratory reserve volume (ERV)**
  - **Residual volume (RV)**

Figure 22.16b Respiratory volumes and capacities.

	Measurement	Adult male average value	Adult female average value	Description
Respiratory volumes	Tidal volume (TV)	500 ml	500 ml	Amount of air inhaled or exhaled with each breath under resting conditions
	Inspiratory reserve volume (IRV)	3100 ml	1900 ml	Amount of air that can be forcefully inhaled after a normal tidal volume inspiration
	Expiratory reserve volume (ERV)	1200 ml	700 ml	Amount of air that can be forcefully exhaled after a normal tidal volume expiration
	Residual volume (RV)	1200 ml	1100 ml	Amount of air remaining in the lungs after a forced expiration
Respiratory capacities	Total lung capacity (TLC)	6000 ml	4200 ml	Maximum amount of air contained in lungs after a maximum inspiratory effort: TLC = TV + IRV + ERV + RV
	Vital capacity (VC)	4800 ml	3100 ml	Maximum amount of air that can be expired after a maximum inspiratory effort: VC = TV + IRV + ERV
	Inspiratory capacity (IC)	3600 ml	2400 ml	Maximum amount of air that can be inspired after a normal tidal volume expiration: IC = TV + IRV
	Functional residual capacity (FRC)	2400 ml	1800 ml	Volume of air remaining in the lungs after a normal tidal volume expiration: FRC = ERV + RV

(b) Summary of respiratory volumes and capacities for males and females

Figure 22.16a Respiratory volumes and capacities.



(a) Spirographic record for a male

Dead Space

- **Anatomical dead space**
  - No contribution to gas exchange
  - Air remaining in passageways; ~150 ml
- **Alveolar dead space**–non-functional alveoli due to collapse or obstruction
- **Total dead space**-sum of anatomical and alveolar dead space

Pulmonary Function Tests

- **Spirometer**-instrument for measuring respiratory volumes and capacities
- Spirometry can distinguish between
  - **Obstructive pulmonary disease**—increased airway resistance (e.g., bronchitis)
    - TLC, FRC, RV may increase
  - **Restrictive disorders**—reduced TLC due to disease or fibrosis
    - VC, TLC, FRC, RV decline

Pulmonary Function Tests

- To measure *rate* of gas movement
  - **Forced vital capacity** (FVC)—gas forcibly expelled after taking deep breath
  - **Forced expiratory volume** (FEV)—amount of gas expelled during specific time intervals of FVC

Alveolar Ventilation

- **Minute ventilation**—total amount of gas flow into or out of respiratory tract in one minute
  - Normal at rest = ~ 6 L/min
  - Normal with exercise = up to 200 L/min
  - Only rough estimate of respiratory efficiency

Table 22.2 Effects of Breathing Rate and Depth on Alveolar ventilation of Three Hypothetical Patients

Table 22.2 Effects of Breathing Rate and Depth on Alveolar Ventilation of Three Hypothetical Patients

BREATHING PATTERN OF HYPOTHETICAL PATIENT	DEAD SPACE VOLUME (DSV)	TIDAL VOLUME (TV)	RESPIRATORY RATE*	MINUTE VENTILATION (MVR)	ALVEOLAR VENTILATION (AVR)	% EFFECTIVE VENTILATION (AVR/MVR)
I—Normal rate and depth	150 ml	500 ml	20/min	10,000 ml/min	7000 ml/min	70%
II—Slow, deep breathing	150 ml	1000 ml	10/min	10,000 ml/min	8500 ml/min	85%
III—Rapid, shallow breathing	150 ml	250 ml	40/min	10,000 ml/min	4000 ml/min	40%

*Respiratory rate values are artificially adjusted to provide equivalent minute ventilation as a baseline for comparing alveolar ventilation.

Gas Exchanges Between Blood, Lungs, and Tissues

- *External respiration*–diffusion of gases in lungs
- *Internal respiration*–diffusion of gases at body tissues
- Both involve
  - Physical properties of gases
  - Composition of alveolar gas

Basic Properties of Gases: Dalton's Law of Partial Pressures

- Total pressure exerted by mixture of gases = sum of pressures exerted by each gas
- **Partial pressure**
  - Pressure exerted by each gas in mixture
  - Directly proportional to its percentage in mixture

Basic Properties of Gases: Henry's Law

- Gas mixtures in contact with liquid
  – Each gas dissolves in proportion to its partial pressure
  – At equilibrium, partial pressures in two phases will be equal
  – Amount of each gas that will dissolve depends on
    - Solubility–CO_2 20 times more soluble in water than O_2; little N_2 dissolves in water
    - Temperature–as temperature rises, solubility decreases

Composition of Alveolar Gas

- Alveoli contain more CO_2 and water vapor than atmospheric air
  - Gas exchanges in lungs
  - Humidification of air
  - Mixing of alveolar gas with each breath

Table 22.4 Comparison of Gas Partial Pressures and Approximate Percentages in the Atmosphere and in the Alveoli

Table 22.4 Comparison of Gas Partial Pressures and Approximate Percentages in the Atmosphere and in the Alveoli

	ATMOSPHERE (SEA LEVEL)		*ALVEOLI*	
GAS	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)
N_2	78.6	597	74.9	569
O_2	20.9	159	13.7	104
CO_2	0.04	0.3	5.2	40
H_2O	0.46	3.7	6.2	47
	100.0%	760	100.0%	760

External Respiration

- Exchange of O_2 and CO_2 across respiratory membrane
- Influenced by
  - Thickness and surface area of respiratory membrane
  - Partial pressure gradients and gas solubilities
  - Ventilation-perfusion coupling

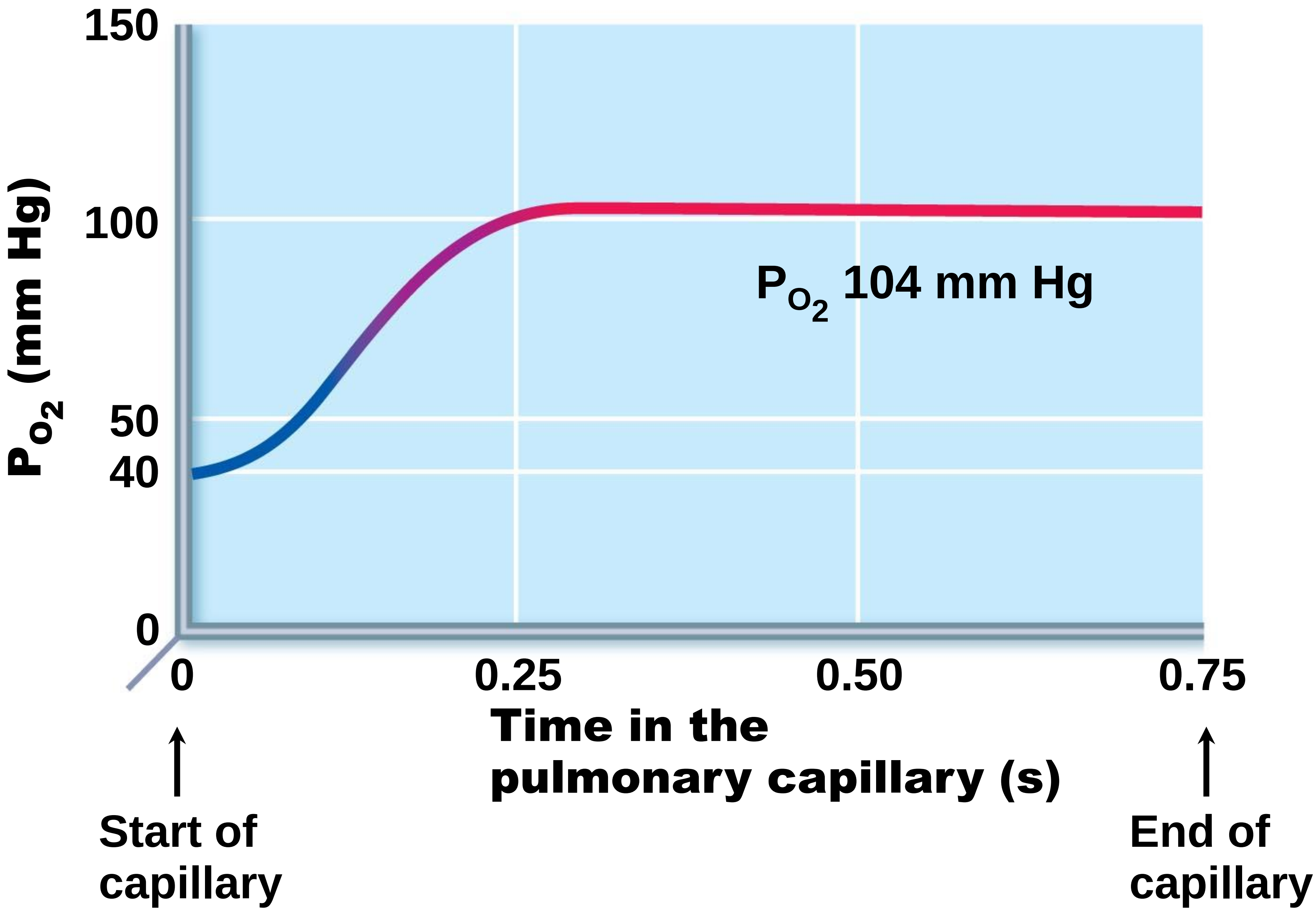
Thickness and Surface Area of the Respiratory Membrane

- Respiratory membranes
  - 0.5 to 1 μ m thick
  - Large total surface area (40 times that of skin) for gas exchange
- Thicken if lungs become waterlogged and edematous → gas exchange inadequate
- Reduced surface area in emphysema (walls of adjacent alveoli break down), tumors, inflammation, mucus

Partial Pressure Gradients and Gas Solubilities

- Steep partial pressure gradient for O_2 in lungs
  - Venous blood Po_2 = 40 mm Hg
  - Alveolar Po_2 = 104 mm Hg
    - Drives oxygen flow to blood
    - Equilibrium reached across respiratory membrane in ~0.25 seconds, about 1/3 time a red blood cell in pulmonary capillary →
      - Adequate oxygenation even if blood flow increases 3X

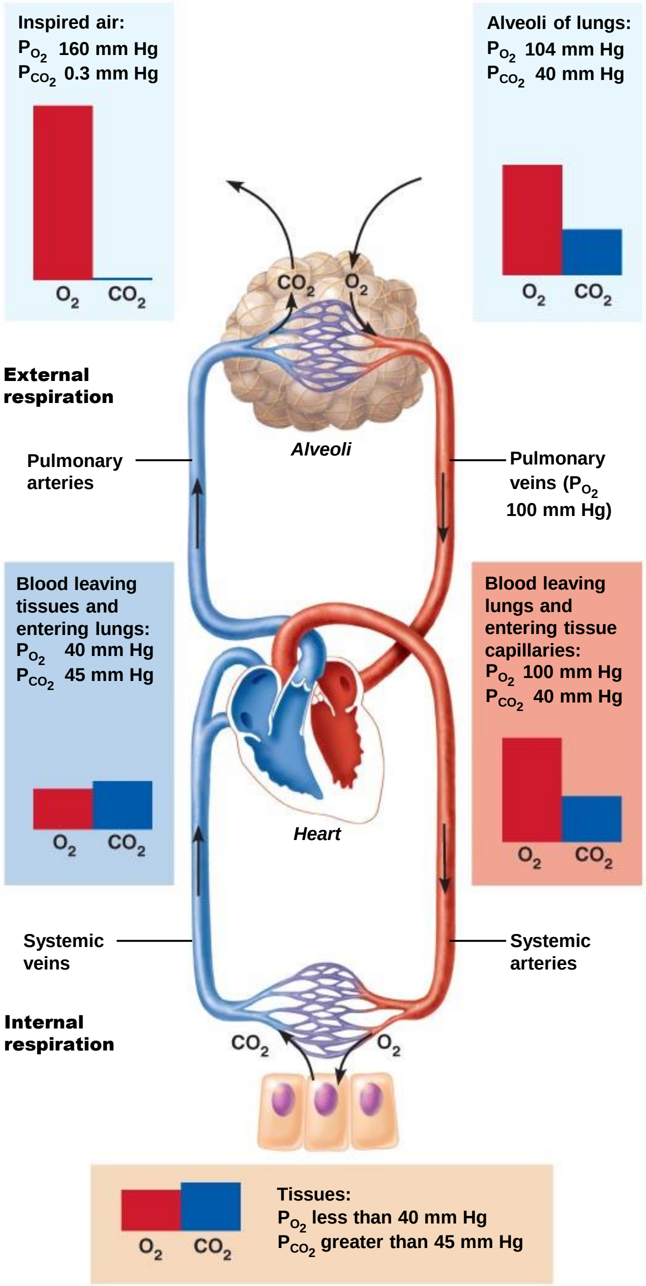
Figure 22.18 Oxygenation of blood in the pulmonary capillaries at rest.



Partial Pressure Gradients and Gas Solubilities

- Partial pressure gradient for CO_2 in lungs less steep
  - Venous blood P_{CO_2} = 45 mm Hg
  - Alveolar P_{CO_2} = 40 mm Hg
- Though gradient not as steep, CO_2 diffuses in equal amounts with oxygen
  - CO_2 20 times more soluble in plasma than oxygen

Figure 22.17 Partial pressure gradients promoting gas movements in the body.



Ventilation-Perfusion Coupling

- **Perfusion**-blood flow reaching alveoli
- **Ventilation**-amount of gas reaching alveoli
- Ventilation and perfusion matched (coupled) for efficient gas exchange
  - Never balanced for all alveoli due to
    - Regional variations due to effect of gravity on blood and air flow
    - Some alveolar ducts plugged with mucus

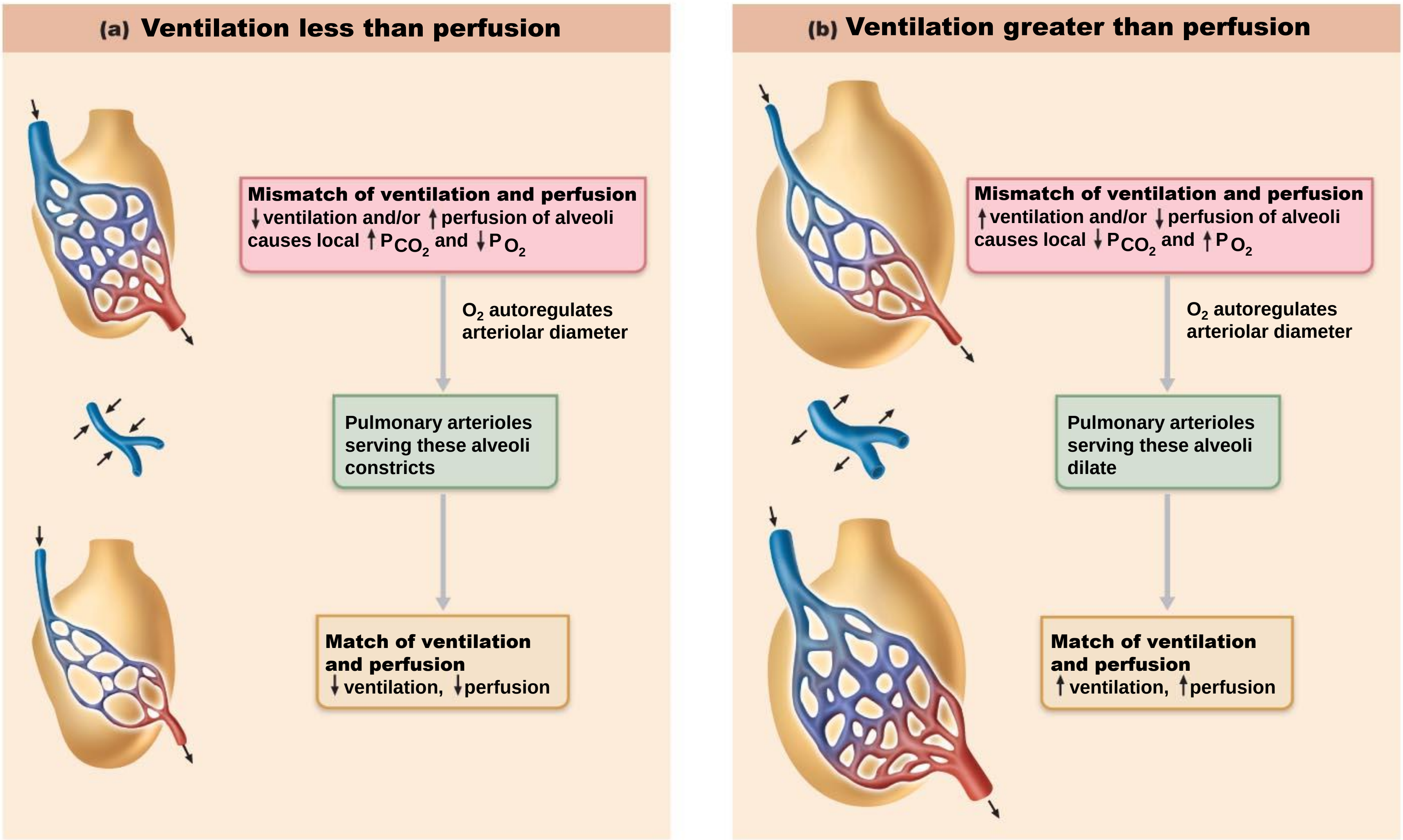
Ventilation-Perfusion Coupling

- Perfusion
  - Changes in Po_2 in alveoli cause changes in diameters of arterioles
    - Where alveolar O_2 is high, arterioles dilate
    - Where alveolar O_2 is low, arterioles constrict
    - Directs most blood where alveolar oxygen high

Ventilation-Perfusion Coupling

- Changes in Pco_2 in alveoli cause changes in diameters of bronchioles
  - Where alveolar CO_2 is high, bronchioles dilate
  - Where alveolar CO_2 is low, bronchioles constrict
  - Allows elimination of CO_2 more rapidly

Figure 22.19 Ventilation-perfusion coupling.



Transport of Respiratory Gases by Blood

- Oxygen (O_2) transport
- Carbon dioxide (CO_2) transport

O_2 Transport

- Molecular O_2 carried in blood
  - 1.5% dissolved in plasma
  - 98.5% loosely bound to each Fe of hemoglobin (Hb) in RBCs
    - 4 O_2 per Hb

O_2 and Hemoglobin

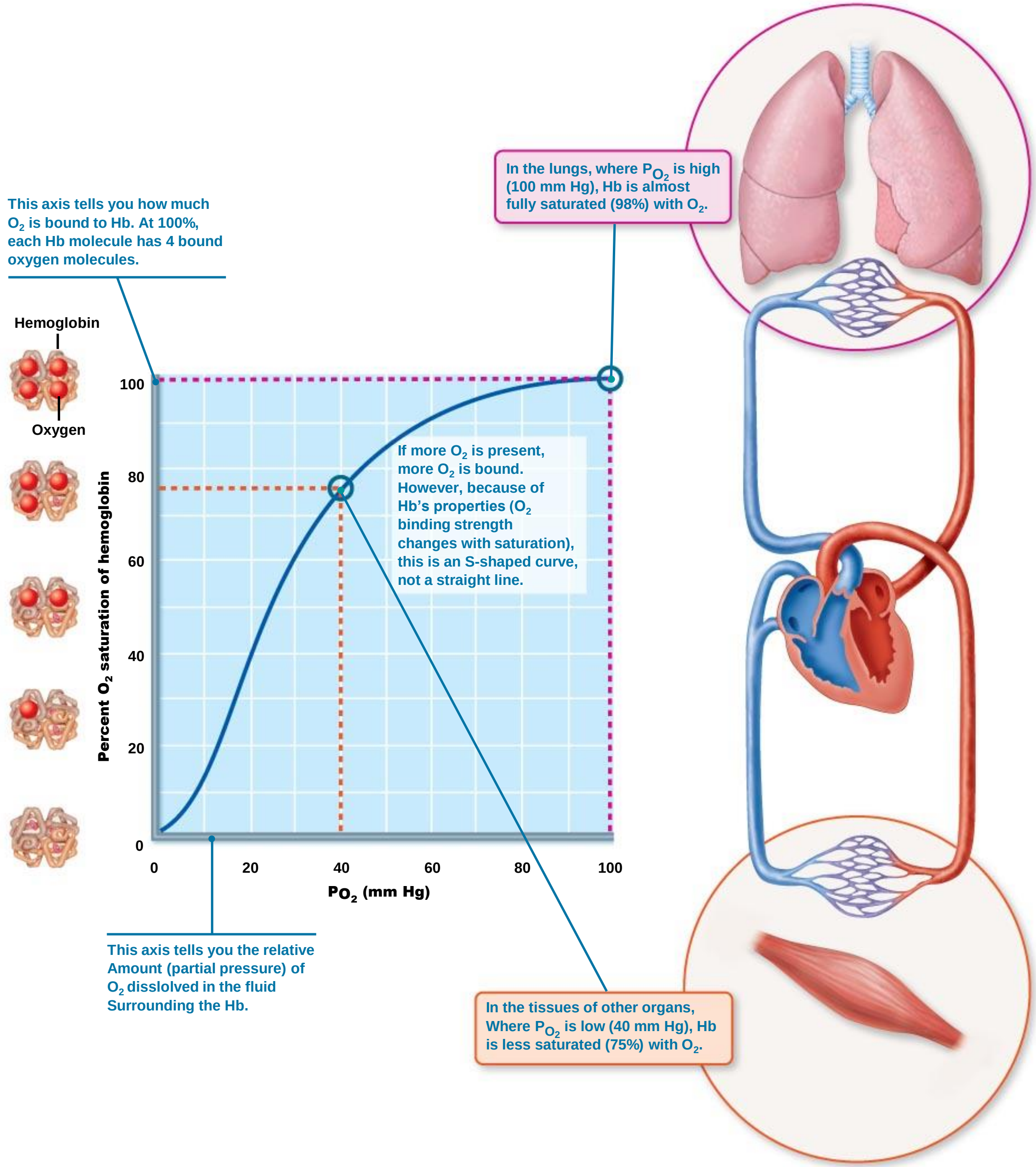
- **Oxyhemoglobin** (HbO_2)-hemoglobin-O_2 combination
- **Reduced hemoglobin** (**deoxyhemoglobin**) (HHb)-hemoglobin that has released O_2

$$HHb + O_2 \underset{\text{Tissues}}{\overset{\text{Lungs}}{\longleftrightarrow}} HbO_2 + H^+$$

O_2 and Hemoglobin

- Loading and unloading of O_2 facilitated by change in shape of Hb
  - As O_2 binds, Hb affinity for O_2 increases
  - As O_2 is released, Hb affinity for O_2 decreases
- *Fully saturated* (100%) if all four heme groups carry O_2
- *Partially saturated* when one to three hemes carry O_2

Figure 22.20 The amount of oxygen carried by hemoglobin depends on the P_{O_2} (the amount of oxygen) available locally. (1 of 3)



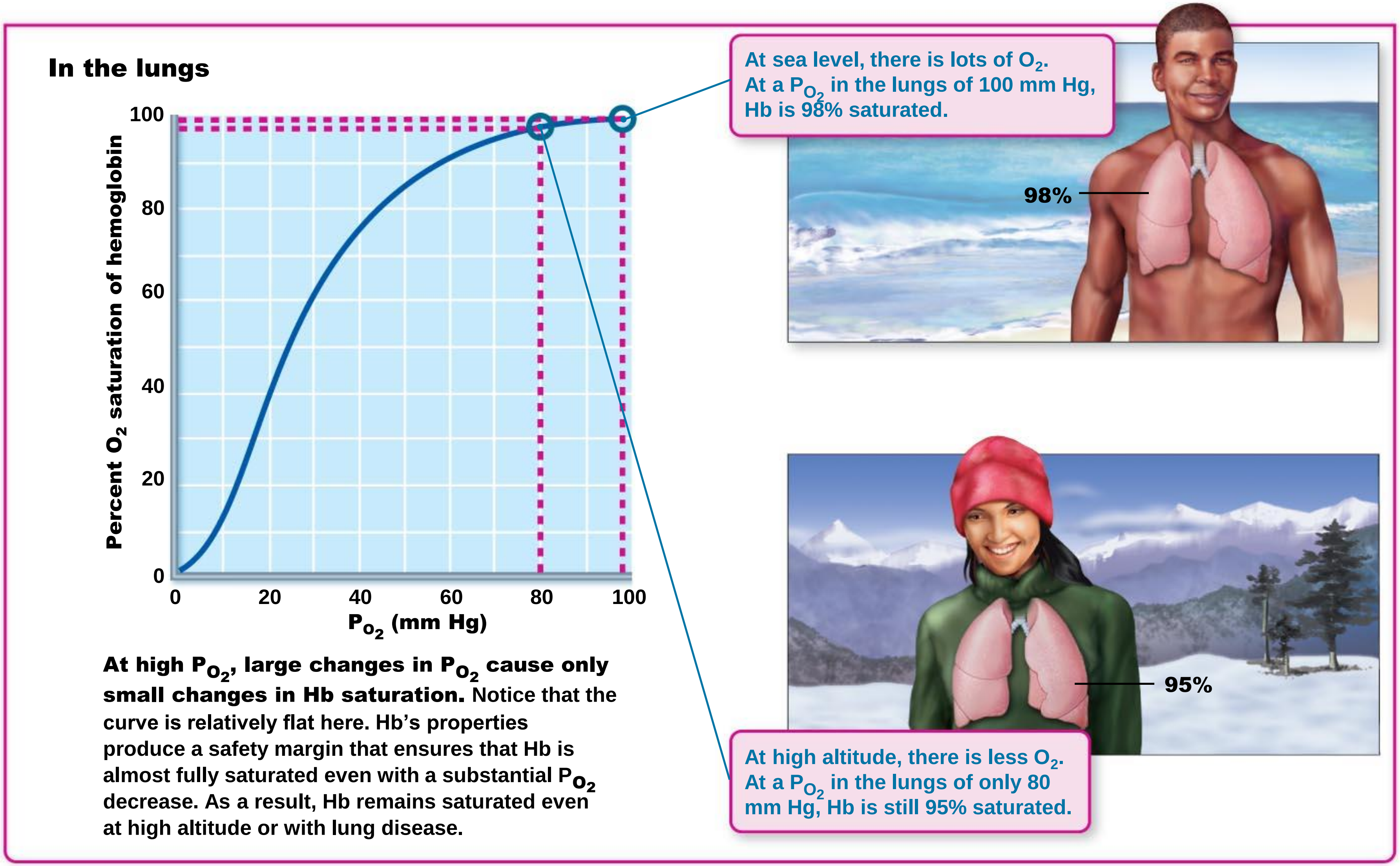
Influence of Po_2 on Hemoglobin Saturation

- In arterial blood
  - Po_2 = 100 mm Hg
  - Contains 20 ml oxygen per 100 ml blood (20 vol %)
  - Hb is 98% saturated
- Further increases in Po_2 (e.g., breathing deeply) produce minimal increases in O_2 binding

Influence of Po_2 on Hemoglobin Saturation

- In venous blood
  - Po_2 = 40 mm Hg
  - Contains 15 vol % oxygen
  - Hb is 75% saturated
  - **Venous reserve**
    - Oxygen remaining in venous blood

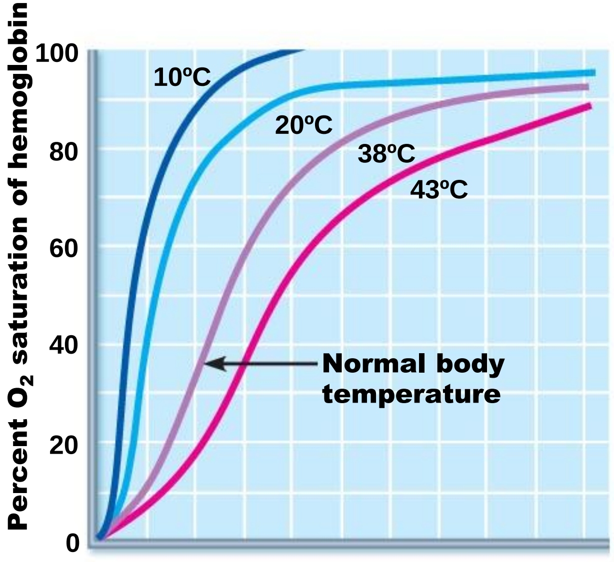
Figure 22.20 The amount of oxygen carried by hemoglobin depends on the P_{O_2} (the amount of oxygen) available locally. (2 of 3)



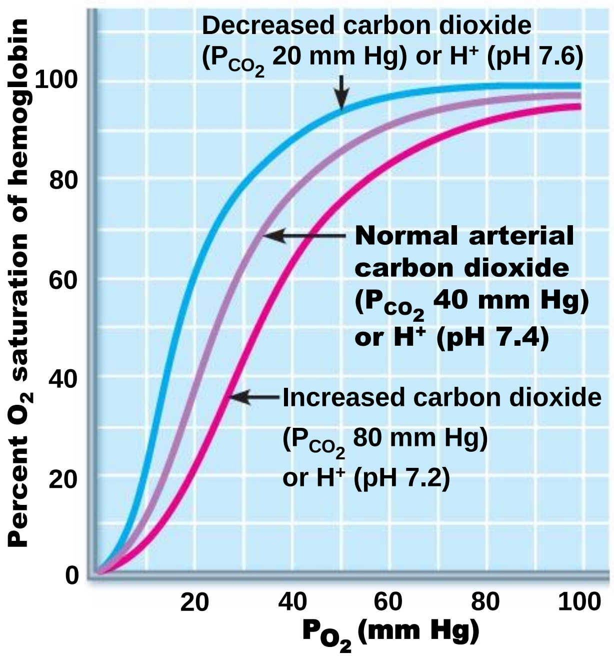
Other Factors Influencing Hemoglobin Saturation

- Increases in temperature, H^+, Pco_2, and BPG
  - Modify structure of hemoglobin; decrease its affinity for O_2
  - Occur in systemic capillaries
  - Enhance O_2 unloading from blood
  - Shift O_2-hemoglobin dissociation curve to right
- Decreases in these factors shift curve to left
  - Decreases oxygen unloading from blood

Figure 22.21 Effect of temperature, P_{CO_2}, and blood pH on the oxygen-hemoglobin dissociation curve.



(a)



(b)

Factors that Increase Release of O_2 by Hemoglobin

- As cells metabolize glucose and use O_2
  - Pco$_2$ and H^+ increase in capillary blood →
  - Declining blood pH and increasing Pco$_2$ →
    - **Bohr effect** - Hb-O_2 bond weakens → oxygen unloading where needed most
  - Heat production increases → directly and indirectly decreases Hb affinity for O_2 → increased oxygen unloading to active tissues

Homeostatic Imbalance

- **Hypoxia**
  - Inadequate O_2 delivery to tissues → **cyanosis**
  - **Anemic hypoxia**–too few RBCs; abnormal or too little Hb
  - **Ischemic hypoxia**–impaired/blocked circulation
  - **Histotoxic hypoxia**–cells unable to use O_2, as in metabolic poisons
  - **Hypoxemic hypoxia**–abnormal ventilation; pulmonary disease
  - **Carbon monoxide poisoning**–especially from fire; 200X greater affinity for Hb than oxygen

CO_2 Transport

- CO_2 transported in blood in three forms
  - 7 to 10% dissolved in plasma
  - 20% bound to *globin* of hemoglobin (**carbaminohemoglobin**)
  - 70% transported as **bicarbonate ions** (HCO_3^-) in plasma

Transport and Exchange of CO_2

- CO_2 combines with water to form carbonic acid (H_2CO_3), which quickly dissociates

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

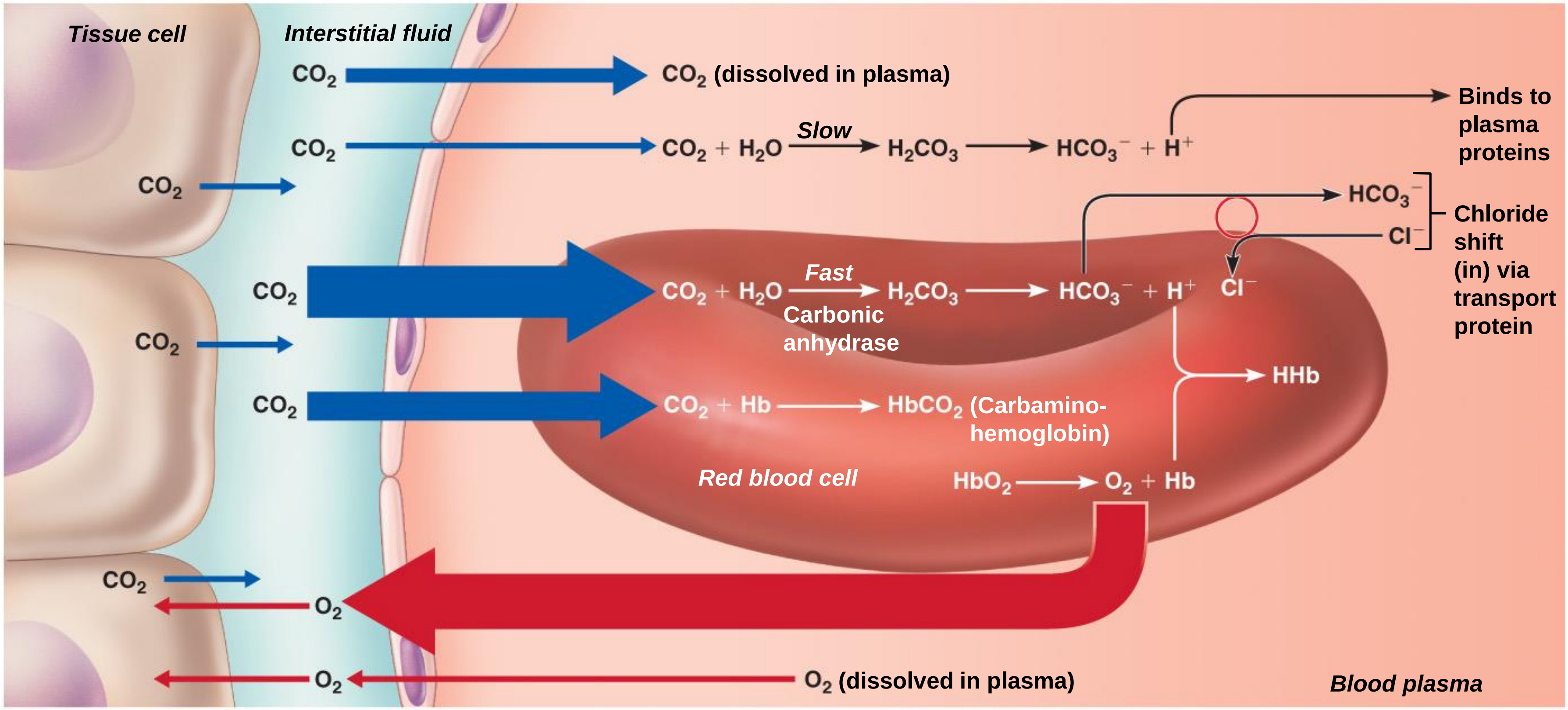
CO_2	H_2O	H_2CO_3	H^+	HCO_3^-
carbon dioxide	water	carbonic acid	hydrogen ion	bicarbonate ion

- Occurs primarily in RBCs, where **carbonic anhydrase** reversibly and rapidly catalyzes reaction

Transport and Exchange of CO_2

- In systemic capillaries
  - HCO_3^- quickly diffuses from RBCs into plasma
    - **Chloride shift** occurs
      - Outrush of HCO_3^- from RBCs balanced as Cl^- moves into RBCs from plasma

Figure 22.22a Transport and exchange of CO_2 and O_2.

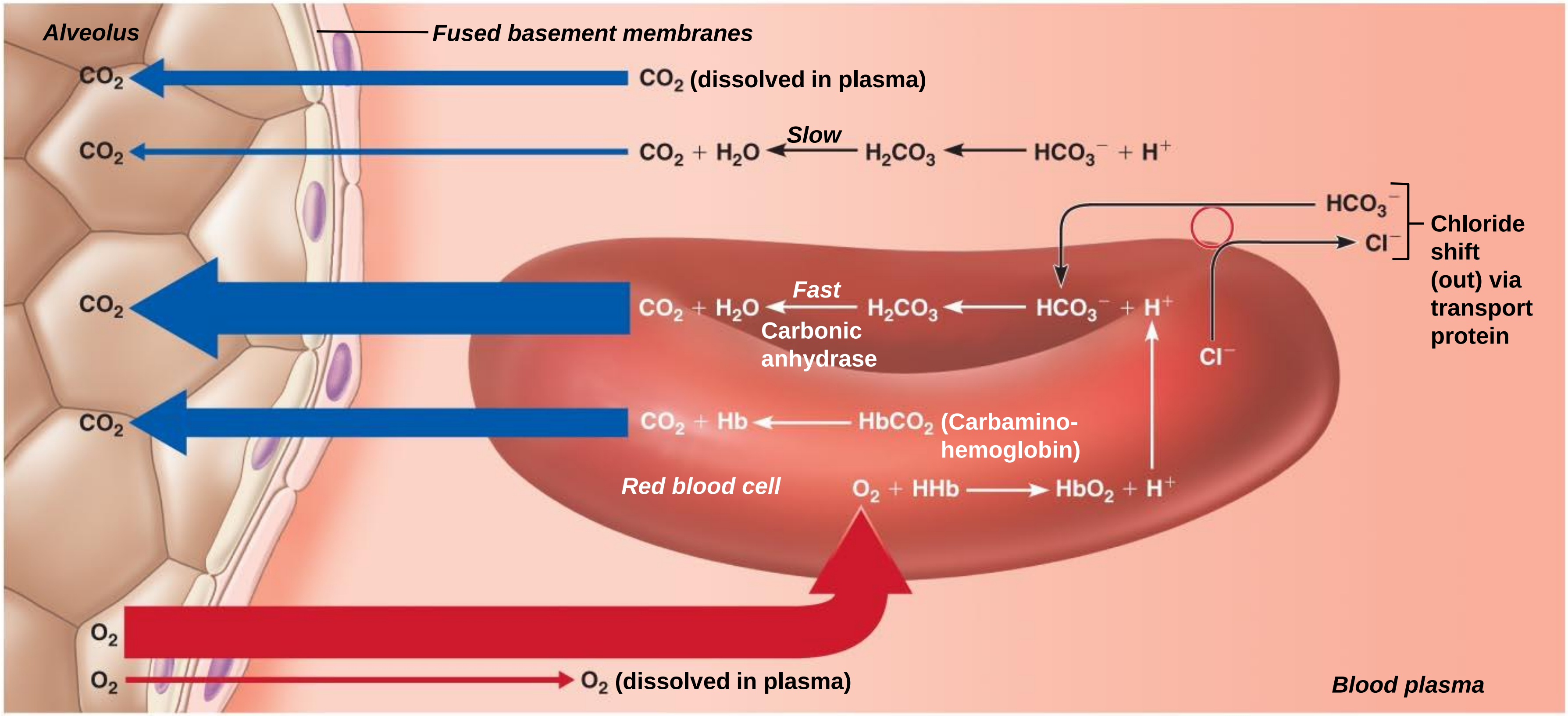


(a) Oxygen release and carbon dioxide pickup at the tissues

Transport and Exchange of CO_2

- In pulmonary capillaries
  - HCO_3^- moves into RBCs (while Cl^- move out); binds with H^+ to form H_2CO_3
  - H_2CO_3 split by carbonic anhydrase into CO_2 and water
  - CO_2 diffuses into alveoli

Figure 22.22b Transport and exchange of CO_2 and O_2.



(b) **Oxygen pickup and carbon dioxide release in the lungs**

Haldane Effect

- Amount of CO_2 transported affected by Po_2
  - Reduced hemoglobin (less oxygen saturation) forms carbaminohemoglobin and buffers H^+ more easily →
  - Lower Po_2 and hemoglobin saturation with O_2; more CO_2 carried in blood
- Encourages CO_2 exchange in tissues and lungs

Haldane Effect

- At tissues, as more CO_2 enters blood
  - More oxygen dissociates from hemoglobin (**Bohr effect**)
  - As HbO_2 releases O_2, it more readily forms bonds with CO_2 to form carbaminohemoglobin

Influence of CO_2 on Blood pH

- **Carbonic acid–bicarbonate buffer system**–resists changes in blood pH
  - If H^+ concentration in blood rises, excess H^+ is removed by combining with $HCO_3^- \rightarrow H_2CO_3$
  - If H^+ concentration begins to drop, H_2CO_3 dissociates, releasing H^+
  - HCO_3^- is **alkaline reserve** of carbonic acid-bicarbonate buffer system

Control of Respiration

- Involves higher brain centers, chemoreceptors, and other reflexes
- Neural controls
  - Neurons in reticular formation of medulla and pons
  - Clustered neurons in medulla important
    - **Ventral respiratory group**
    - **Dorsal respiratory group**

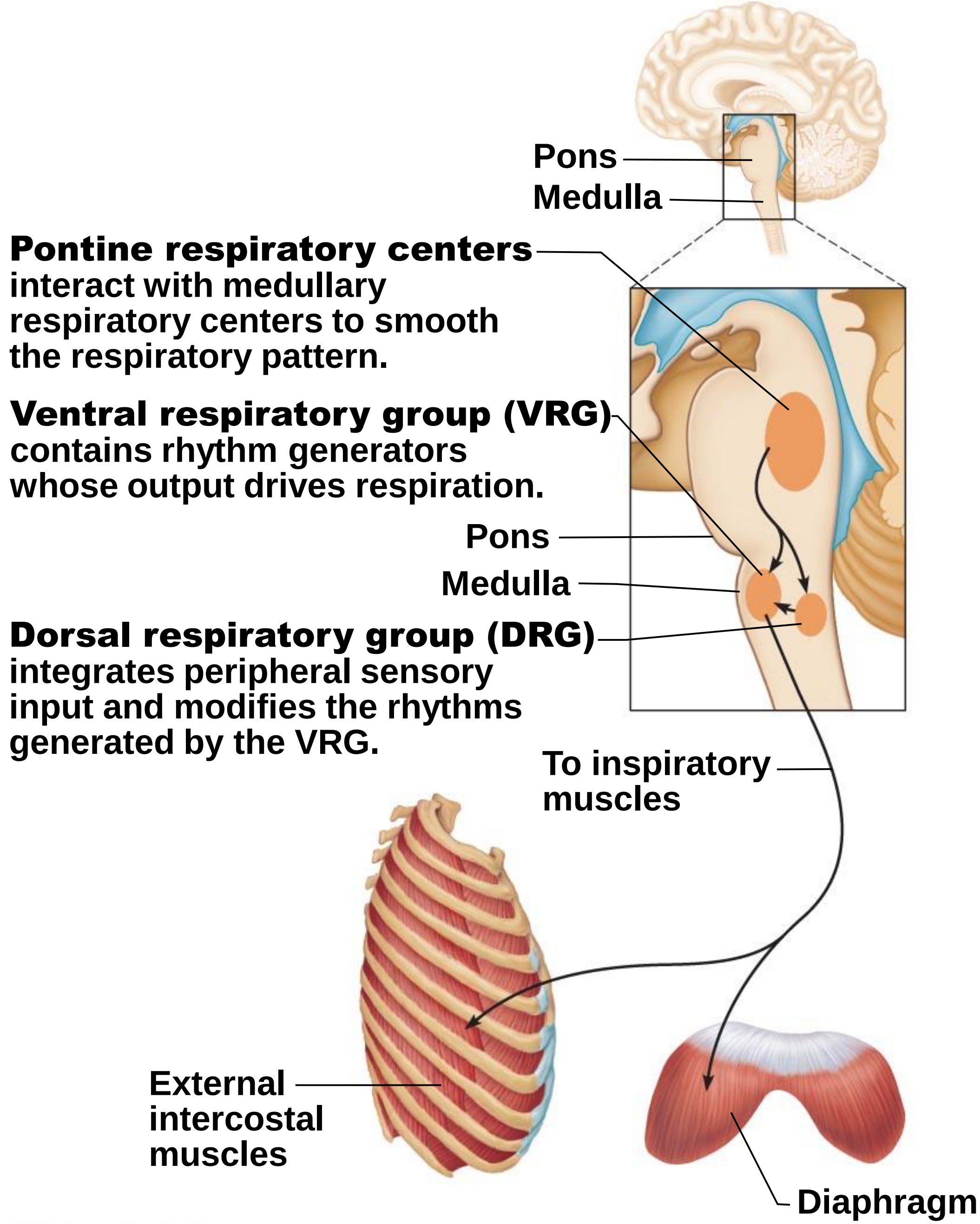
Medullary Respiratory Centers

- Ventral respiratory group (VRG)
  - – Rhythm-generating and integrative center
  - – Sets **eupnea** (12–15 breaths/minute)
    - Normal respiratory rate and rhythm
  - – Its inspiratory neurons excite inspiratory muscles via **phrenic** (diaphragm) and **intercostal nerves** (external intercostals)
  - – Expiratory neurons inhibit inspiratory neurons

Medullary Respiratory Centers

- Dorsal respiratory group (DRG)
  - Near root of cranial nerve IX
  - Integrates input from peripheral stretch and chemoreceptors; sends information → VRG

Figure 22.23 Locations of respiratory centers and their postulated connections.



Generation of the Respiratory Rhythm

- Not well understood
- One hypothesis
  - Pacemaker neurons with intrinsic rhythmicity
- Most widely accepted hypothesis
  - Reciprocal inhibition of two sets of interconnected pacemaker neurons in medulla that generate rhythm

Figure 22.25 Changes in P_{CO_2} and blood pH regulate ventilation by a negative feedback mechanism.

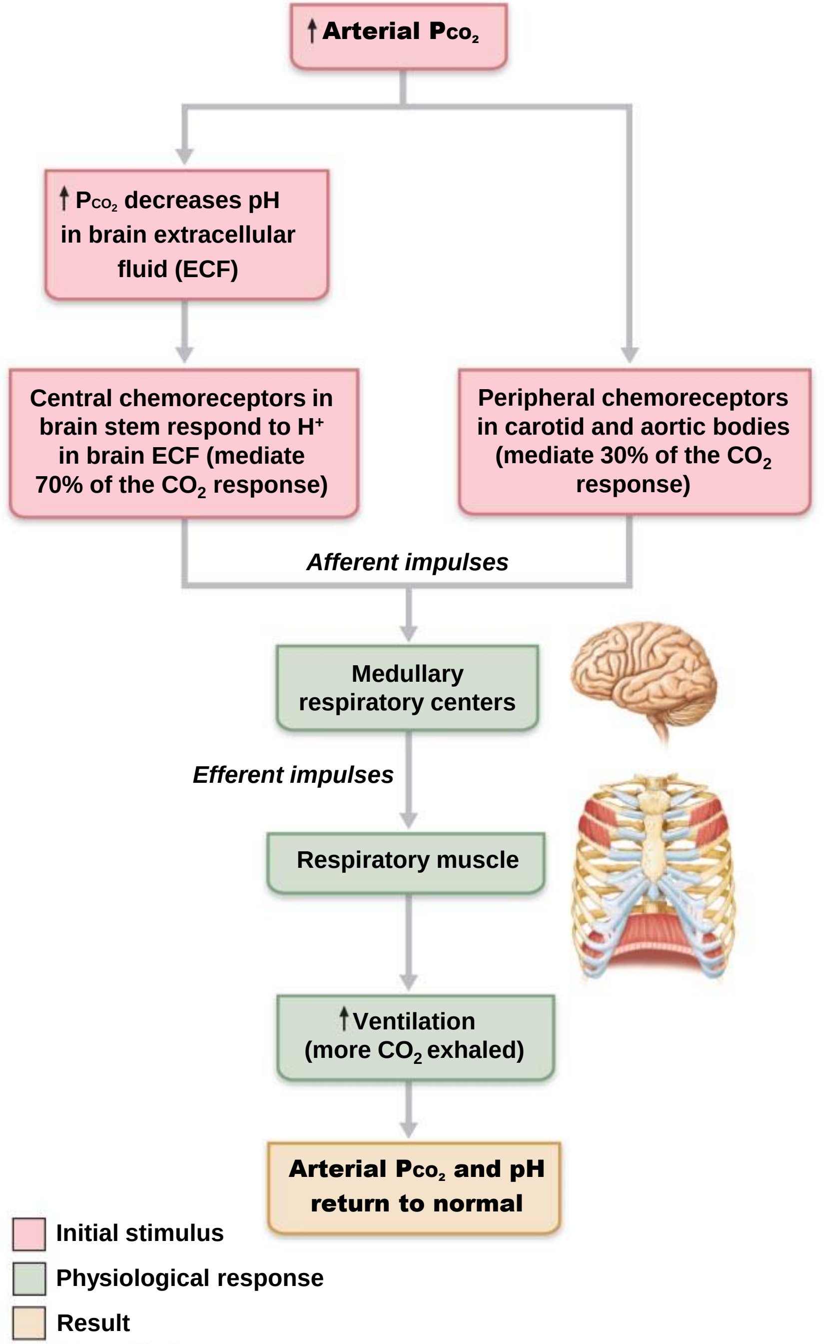
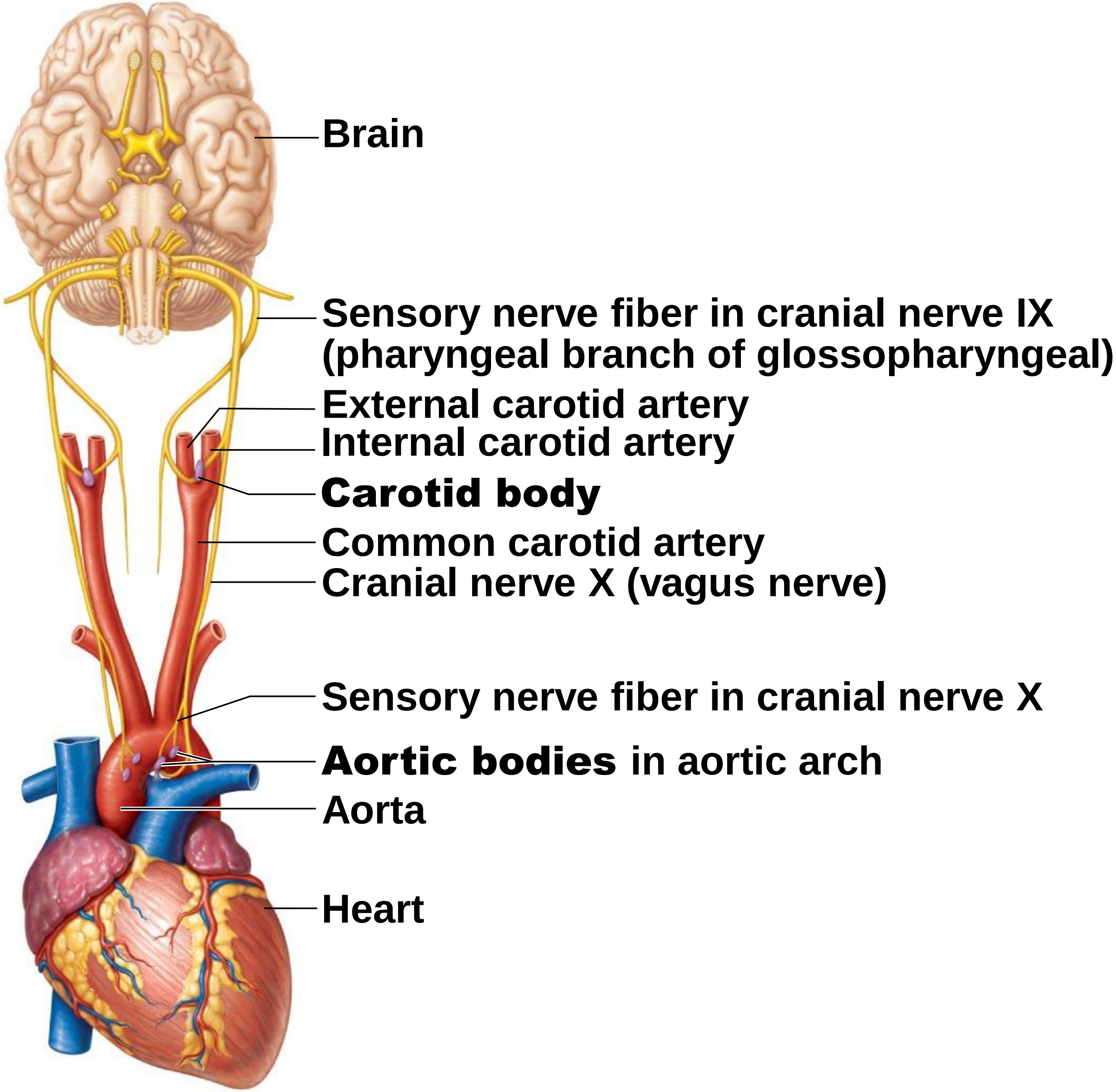


Figure 22.26 Location and innervation of the peripheral chemoreceptors in the carotid and aortic bodies.



Chemical Factors

- Influence of arterial pH
  - Can modify respiratory rate and rhythm even if CO_2 and O_2 levels normal
  - Mediated by peripheral chemoreceptors
  - Decreased pH may reflect
    - CO_2 retention; accumulation of lactic acid; excess ketone bodies
  - Respiratory system controls attempt to raise pH by increasing respiratory rate and depth

Summary of Chemical Factors

- Rising CO_2 levels most powerful respiratory stimulant
- Normally blood Po_2 affects breathing only indirectly by influencing peripheral chemoreceptor sensitivity to changes in Pco_2

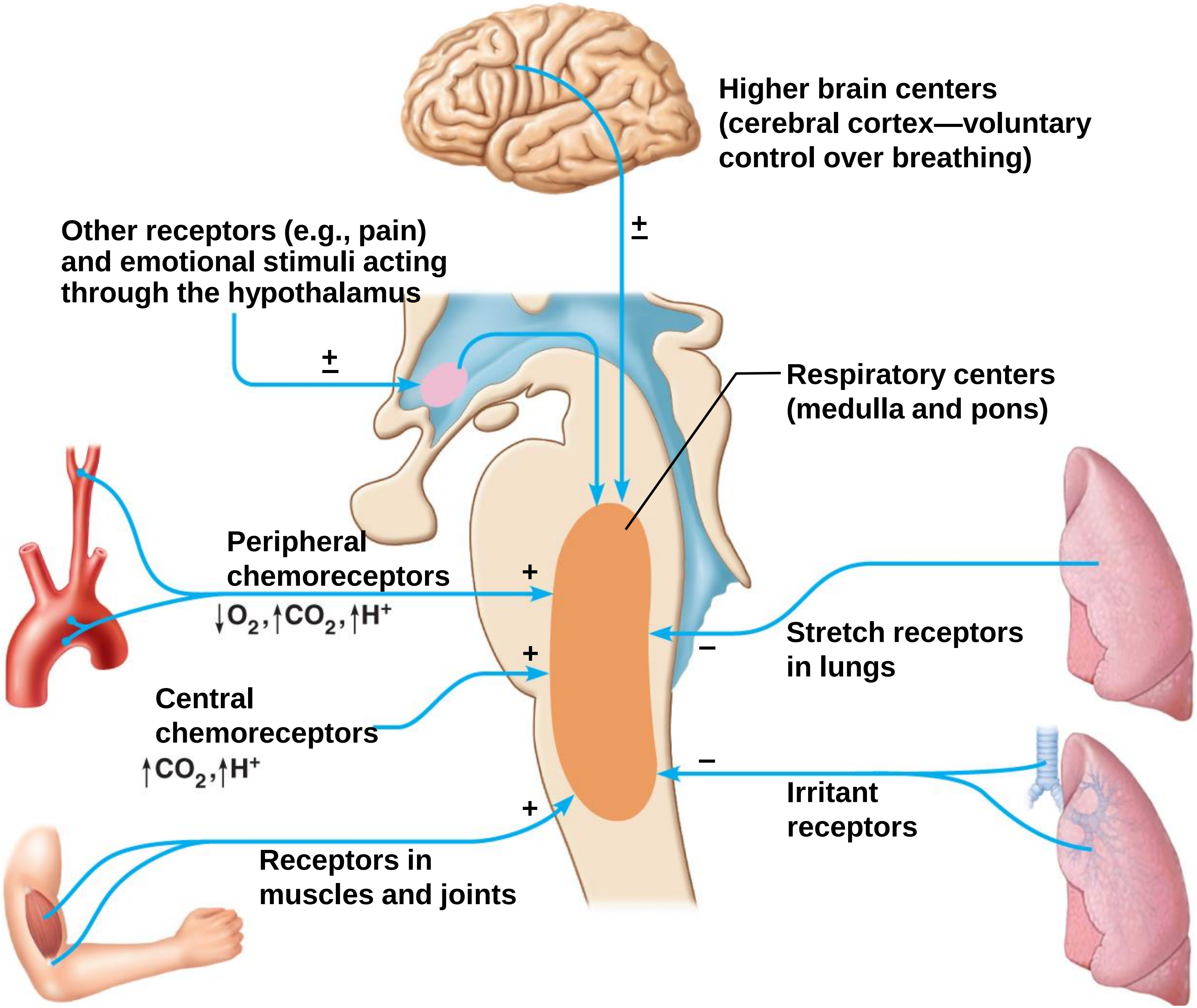
Summary of Chemical Factors

- When arterial Po_2 falls below 60 mm Hg, it becomes major stimulus for respiration (via peripheral chemoreceptors)
- Changes in arterial pH resulting from CO_2 retention or metabolic factors act indirectly through peripheral chemoreceptors

Inflation Reflex

- **Hering-Breuer Reflex (inflation reflex)**
  - Stretch receptors in pleurae and airways stimulated by lung inflation
    - Inhibitory signals to medullary respiratory centers end inhalation and allow expiration
    - Acts as protective response more than normal regulatory mechanism

Figure 22.24 Neural and chemical influences on brain stem respiratory centers.



Respiratory Adjustments: Exercise

- Adjustments geared to both intensity and duration of exercise
- **Hyperpnea**
  - Increased ventilation (10 to 20 fold) in response to metabolic needs
- Pco_2, Po_2, and pH remain surprisingly constant during exercise

Respiratory Adjustments: Exercise

- Three neural factors cause increase in ventilation as exercise begins
  - Psychological stimuli—anticipation of exercise
  - Simultaneous cortical motor activation of skeletal muscles and respiratory centers
  - Excitatory impulses to respiratory centers from proprioceptors in moving muscles, tendons, joints

Respiratory Adjustments: High Altitude

- Quick travel to altitudes above 2400 meters (8000 feet) may → symptoms of acute mountain sickness (AMS)
  - Atmospheric pressure and Po_2 levels lower
  - Headaches, shortness of breath, nausea, and dizziness
  - In severe cases, lethal cerebral and pulmonary edema

Acclimatization to High Altitude

- **Acclimatization**—respiratory and hematopoietic adjustments to long-term move to high altitude
  - Chemoreceptors become more responsive to P_{CO_2} when P_{O_2} declines
  - Substantial decline in P_{O_2} directly stimulates peripheral chemoreceptors
  - Result—minute ventilation increases and stabilizes in few days to 2–3 L/min higher than at sea level

Acclimatization to High Altitude

- Always lower-than-normal Hb saturation levels
  - Less O_2 available
- Decline in blood O_2 stimulates kidneys to accelerate production of EPO
- RBC numbers increase slowly to provide long-term compensation

Homeostatic Imbalances

- **Chronic obstructive pulmonary disease (COPD)**
  - Exemplified by chronic bronchitis and emphysema
  - Irreversible decrease in ability to force air out of lungs
  - Other common features
    - History of smoking in 80% of patients
    - **Dyspnea** - labored breathing ("air hunger")
    - Coughing and frequent pulmonary infections
    - Most develop respiratory failure (**hypoventilation**) accompanied by respiratory acidosis, hypoxemia

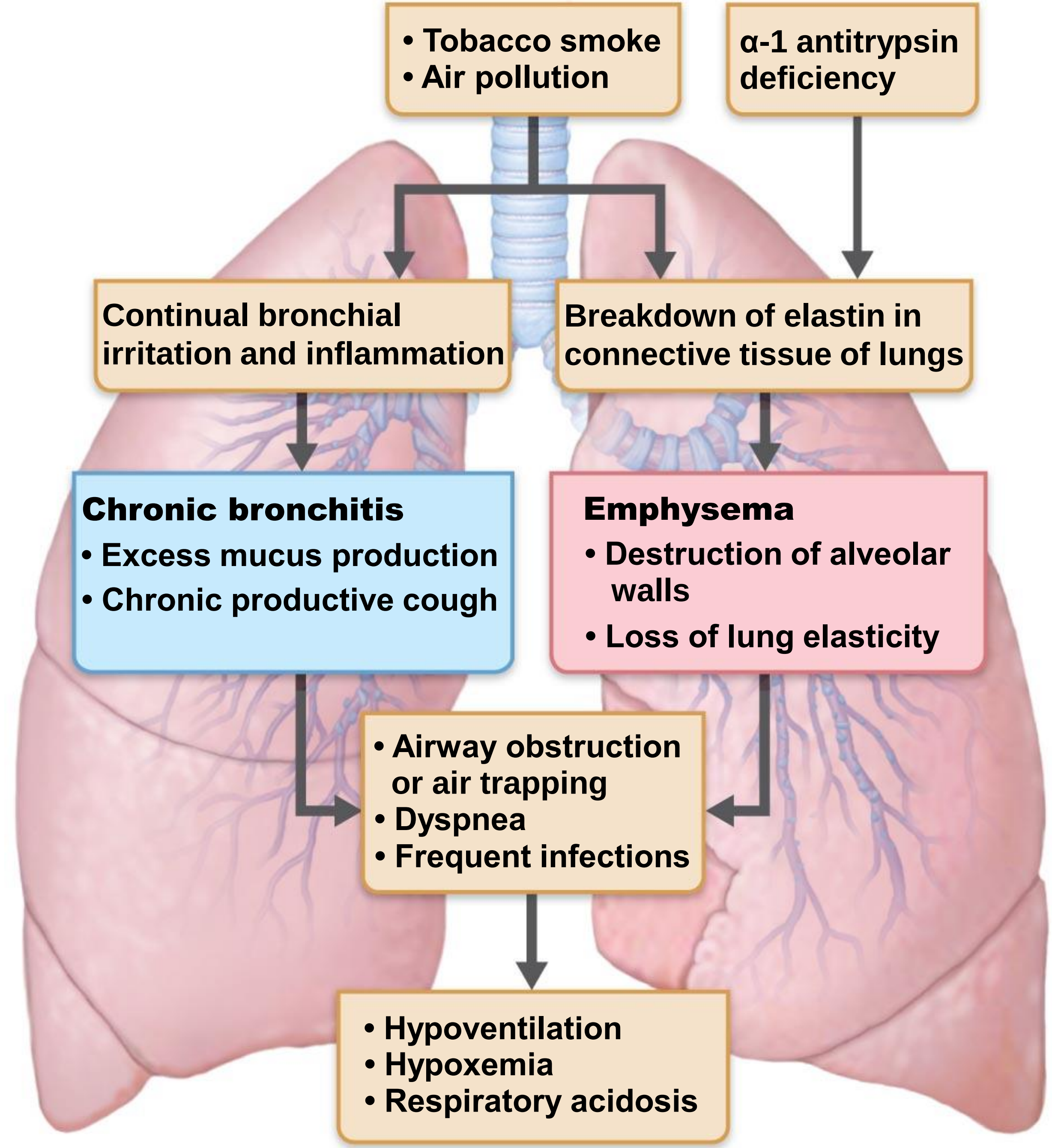
Homeostatic Imbalance

- Emphysema
  - Permanent enlargement of alveoli; destruction of alveolar walls; decreased lung elasticity →
    - Accessory muscles necessary for breathing
      - → exhaustion from energy usage
    - Hyperinflation → flattened diaphragm → reduced ventilation efficiency
    - Damaged pulmonary capillaries → enlarged right ventricle

Homeostatic Imbalance

- Chronic bronchitis
  - Inhaled irritants → chronic excessive mucus →
  - Inflamed and fibrosed lower respiratory passageways →
  - Obstructed airways →
  - Impaired lung ventilation and gas exchange →
  - Frequent pulmonary infections

Figure 22.27 The pathogenesis of COPD.



Homeostatic Imbalances

- Asthma–reversible COPD
  - Characterized by coughing, dyspnea, wheezing, and chest tightness
  - Active inflammation of airways precedes bronchospasms
  - Airway inflammation is immune response caused by release of interleukins, production of IgE, and recruitment of inflammatory cells
  - Airways thickened with inflammatory exudate magnify effect of bronchospasms

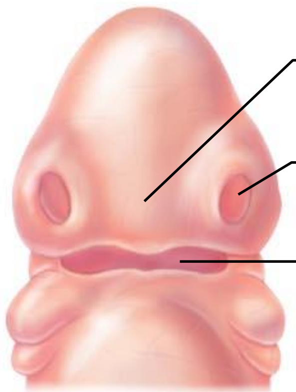
Homeostatic Imbalances

- **Tuberculosis (TB)**
  – Infectious disease caused by bacterium *Mycobacterium tuberculosis*
  – Symptoms-fever, night sweats, weight loss, racking cough, coughing up blood
  – Treatment- 12-month course of antibiotics
    - Are antibiotic resistant strains

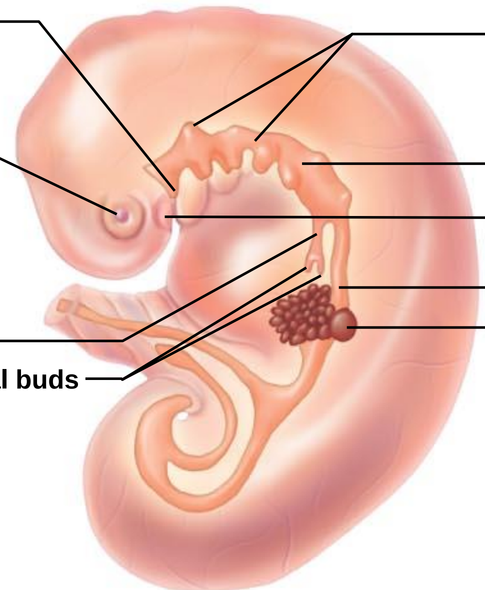
Homeostatic Imbalances

- **Lung cancer**
  - Leading cause of cancer deaths in North America
  - 90% of all cases result of smoking
  - Three most common types
    - **Adenocarcinoma** (~40% of cases) originates in peripheral lung areas - bronchial glands, alveolar cells
    - **Squamous cell carcinoma** (20–40% of cases) in bronchial epithelium
    - **Small cell carcinoma** (~20% of cases) contains lymphocyte-like cells that originate in primary bronchi and subsequently metastasize

Figure 22.28 Embryonic development of the respiratory system.



(a) 4 weeks: anterior superficial view of the embryo's head



(b) 5 weeks: left lateral view of the developing lower respiratory passageway mucosae

Developmental Aspects

- By 28th week, premature baby can breathe on its own
- During fetal life, lungs filled with fluid and blood bypasses lungs
- Gas exchange takes place via placenta

Homeostatic Imbalance

- Cystic fibrosis
  - Most common lethal genetic disease in North America
  - Abnormal, viscous mucus clogs passageways → bacterial infections
    - Affects lungs, pancreatic ducts, reproductive ducts
  - Cause–abnormal gene for Cl^- membrane channel

Homeostatic Imbalance

- Treatments for cystic fibrosis
  - Mucus-dissolving drugs; manipulation to loosen mucus; antibiotics
  - Research into
    - Introducing normal genes
    - Prodding different protein → Cl^- channel
    - Freeing patient's abnormal protein from ER to → Cl^- channels
    - Inhaling hypertonic saline to thin mucus