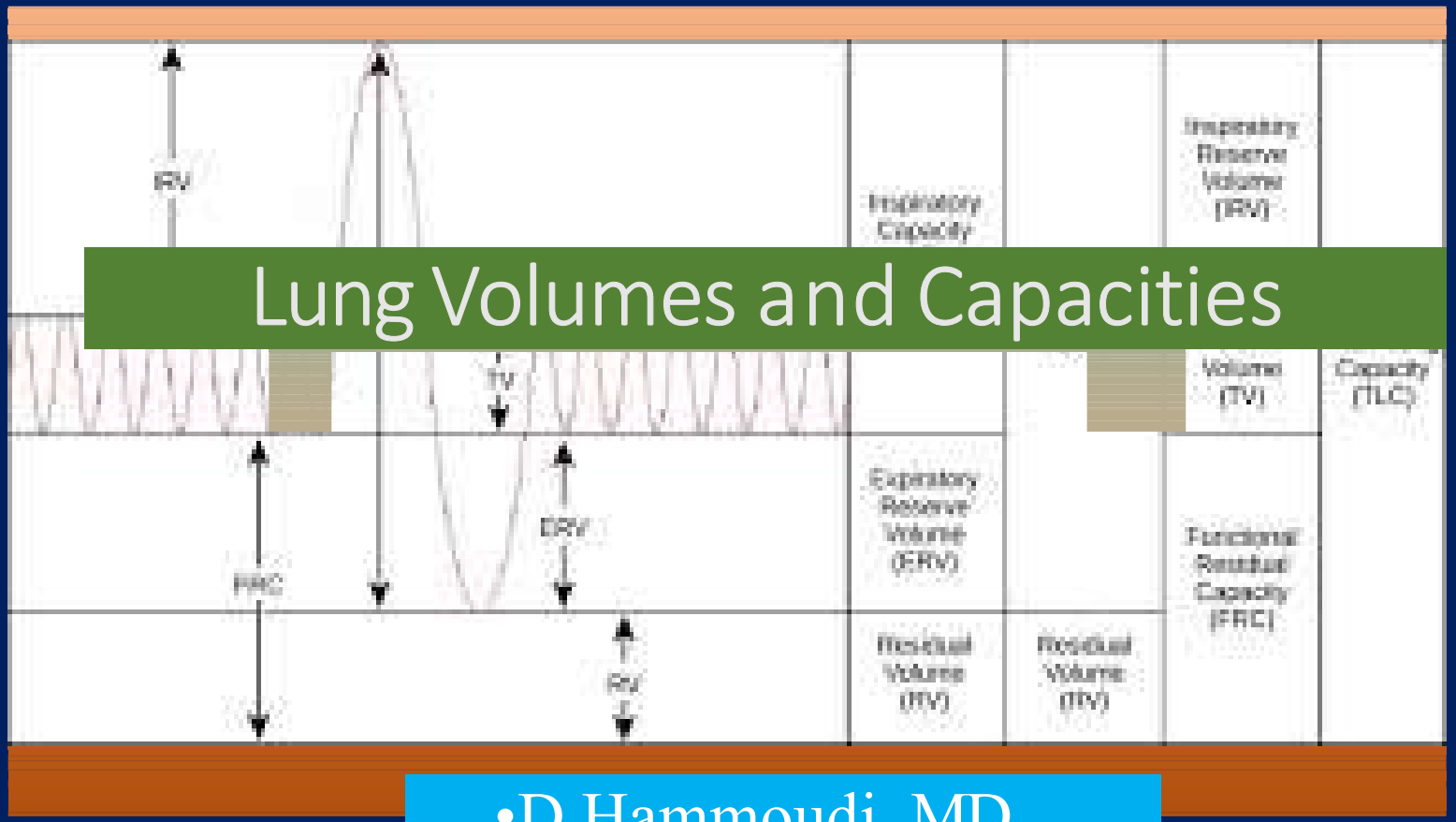
Lung Volumes and Capacities



•D.Hammoudi. MD

Respiratory System Functions

- **Gas exchange:** Oxygen enters blood and carbon dioxide leaves
- **Regulation of blood pH**: Altered by changing blood carbon dioxide levels
- **Voice production:** Movement of air past vocal folds makes sound and speech
- **Olfaction**: Smell occurs when airborne molecules drawn into nasal cavity
- **Protection** Against microorganisms by preventing entry and removing them

Major Functions of the Respiratory System

- To supply the body with oxygen and dispose of carbon dioxide
- Respiration – four distinct processes must happen
  - **Pulmonary ventilation** – moving air into and out of the lungs
  - **External respiration** – gas exchange between the lungs and the blood
  - **Transport** – transport of oxygen and carbon dioxide between the lungs and tissues
  - **Internal respiration** – gas exchange between systemic blood vessels and tissues

Function of the Nose

- **The only externally visible part of the respiratory system that functions by:**
  - Providing an airway for respiration
  - Moistening and warming the entering air
  - Filtering inspired air and cleaning it of foreign matter
  - Serving as a resonating chamber for speech
  - Housing the olfactory receptors

Age-old story: Age-related respiratory changes

Structural changes

- Nose enlargement (from continued cartilage growth)
- General atrophy of the tonsils
- Tracheal deviations (from changes in the aging spine)
- Increased anteroposterior chest diameter (resulting from altered calcium metabolism)
- Calcification of costal cartilages (resulting in reduced mobility of the chest wall)
- Kyphosis (due to osteoporosis and vertebral collapse)
- Increased lung rigidity
- Decreased number and dilation of alveoli
- Reduction in respiratory fluids by 30% (heightening the risk of pulmonary infection and mucus plugs)
- Reduction in respiratory muscle strength

Pulmonary function changes

- Diminished ventilatory capacity
- Decline in diffusing capacity
- Diminished vital capacity (due to decreased inspiratory and expiratory muscle strength)
- Decreased elastic recoil capability (resulting in an elevated residual volume)
- Decreased ventilation of basal areas (due to closing of some airways)

Patterns of Breathing

- **Eupnea**
  - **normal breathing (12-17 B/min, 500-600 ml/B)**
- **Hyperpnea**
  - **⇑ pulmonary ventilation matching ⇑ metabolic demand**
- **Hyperventilation (⇓ CO2)**
  - **⇑ pulmonary ventilation > metabolic demand**
- **Hypoventilation (⇑ CO2)**
  - **⇓ pulmonary ventilation < metabolic demand**

Patterns of breathing (cont.)

- **Tachypnea**
  - ⇑ frequency of respiratory rate
- Apnea
  - Absense of breathing. e.g. Sleep apnea
- **Dyspnea**
  - Difficult or labored breathing
- Orthopnea
  - Dyspnea when recumbent, relieved when upright. e.g. congestive heart failure, asthma, lung failure

1. Eupnea (normal)

2. Tachypnea

3. Bradypnea

4. Apnea

5. Cheyne-Stokes

6. Biot's

7. Apneustic

8. Agonal

9. Shallow

10. Hyperpnea

11. Air trapping

12. Kussmaul's

13. Sighing

SURFACTANT

- Lines the inner layer of alveolar epithelium.
- Synthesized by SER of type II pneumocytes.
- **Function –**

  1. To reduce the surface tension of alveoli mainly during expiration, thus reduces the work of lung inflation.
  2. Waterproofing.

- Surfactant synthesis starts after 26 weeks of fetal life. Therefore premature infants,with insufficient surfactant suffer from HMD.

Important lung products

1. Surfactant—produced by type II pneumocytes, ↓ alveolar surface tension, ↑ compliance, ↓ work of inspiration
2. Prostaglandins
3. Histamine ↑ bronchoconstriction
4. Angiotensin-converting enzyme (ACE)—angiotensin I → angiotensin II; inactivates bradykinin (ACE inhibitors ↑ bradykinin and cause cough, angioedema)
5. Kallikrein—activates bradykinin

Surfactant––dipalmitoyl phosphatidylcholine (lecithin) deficient in neonatal RDS.

Collapsing pressure = $\frac{2\ (\text{tension})}{\text{radius}}$

Lecithin/Sphingomyelin (L/S) Ratio: This ratio in the amniotic fluid is measured. A ratio of 2:1 or higher typically indicates mature fetal lungs.

Surfactant measurement in a fetus is crucial for assessing lung maturity, particularly when there is a risk of preterm birth.

Surfactant is a substance that reduces surface tension in the lungs, preventing the alveoli from collapsing and allowing for proper gas exchange.
Insufficient surfactant production in premature infants can lead to respiratory distress syndrome (RDS).

Methods for Assessing Fetal Lung Maturity

1.Amniocentesis: This is the most common method for assessing fetal lung maturity. A sample of amniotic fluid is taken and analyzed for surfactant levels.

2.Lecithin/Sphingomyelin (L/S) Ratio: This ratio in the amniotic fluid is measured. A ratio of 2:1 or higher typically indicates mature fetal lungs.

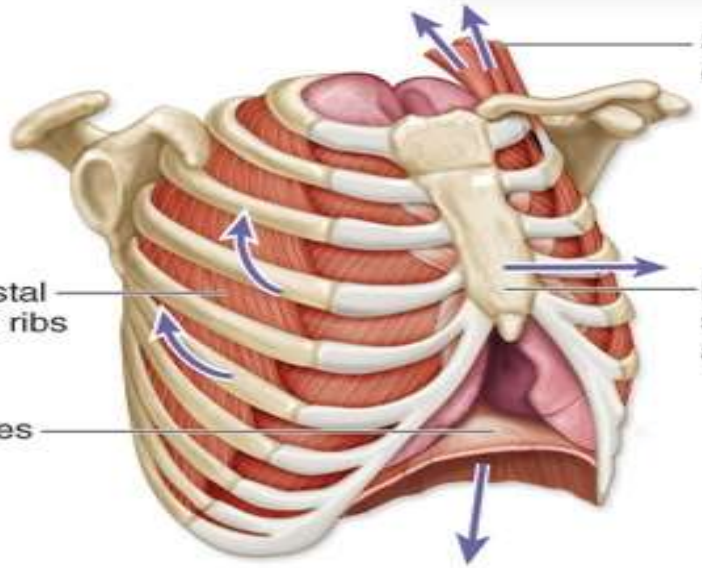
3.Phosphatidylglycerol (PG): The presence of phosphatidylglycerol in the amniotic fluid is a good indicator of lung maturity and is often measured alongside the L/S ratio.

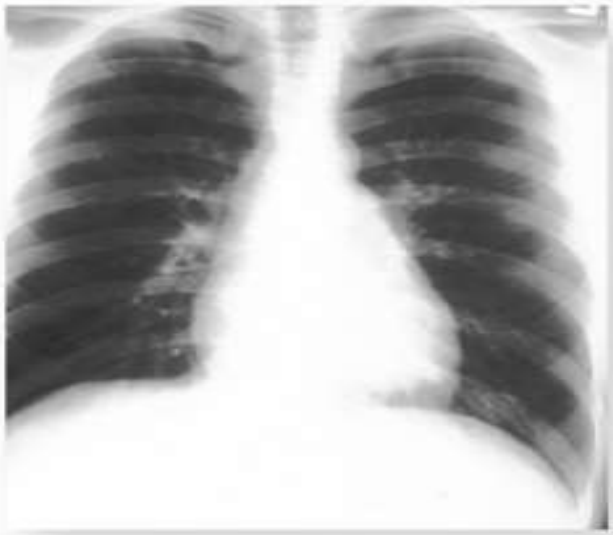
4.Surfactant/Albumin (S/A) Ratio: This method uses fluorescence polarization to measure the ratio of surfactant to albumin in the amniotic fluid. Higher ratios indicate greater lung maturity.

5.Foam Stability Index (FSI): This test measures the ability of surfactant in the amniotic fluid to create a stable foam. The presence of foam indicates adequate surfactant levels.

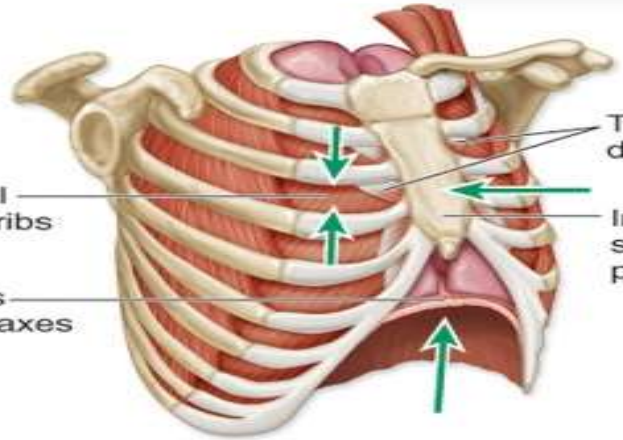
6.Lamellar Body Count (LBC): Lamellar bodies are surfactant storage granules found in amniotic fluid. Their count can be determined using a hematology analyzer, with higher counts indicating lung maturity.

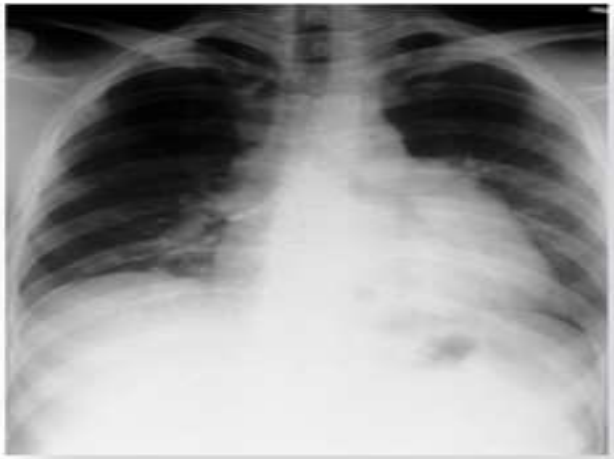
Inhalation

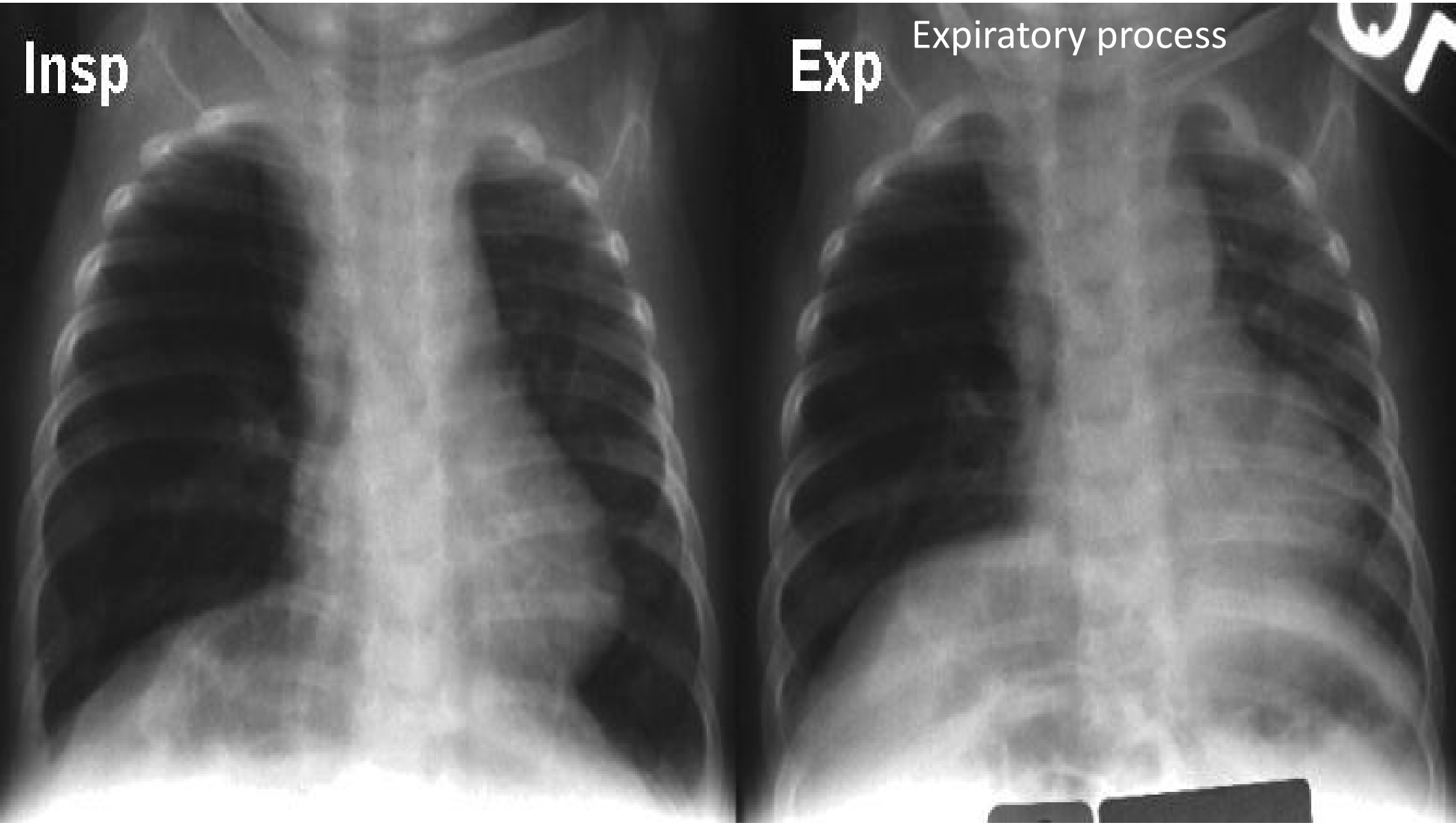




Exhalation






Insp
Exp
Expiratory process

Muscles of inspiration

Accessory

Sternocleidomastoid (elevates sternum)

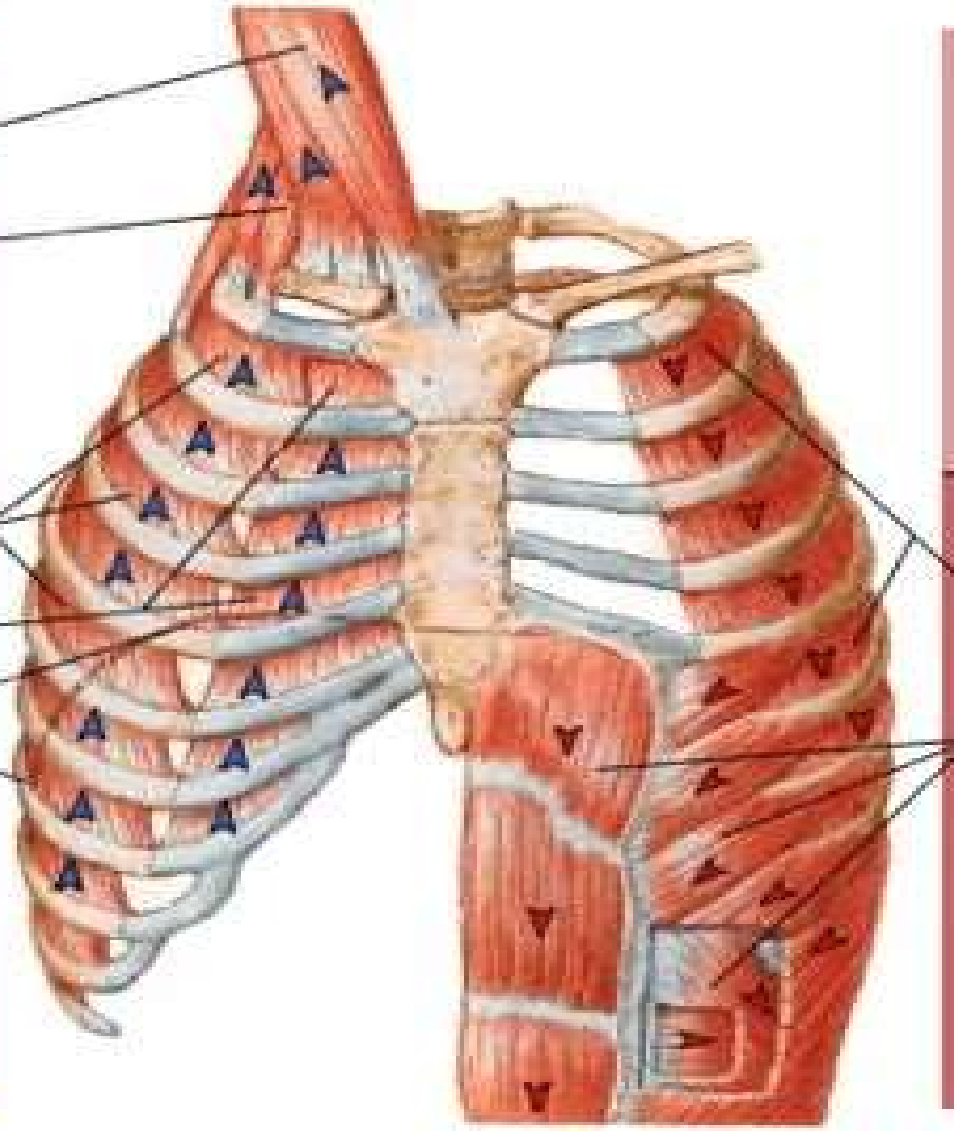
Scalenes Group (elevate upper ribs)

Not shown:
Pectoralis minor

Principal

External intercostals Interchondral part of internal intercostals (also elevates ribs)

Diaphragm (dome descends, thus increasing vertical dimension of thorac cavity; also elevates lower ribs)



Muscles of expiration

Quiet breathing

Expiration results from passive, elastic recoil of the lungs, dib cage and diaphragm

Active breathing

Internal intercostals, except interchondral part (pull ribs down)

Abdominals (pull ribs down, compress abdominal contents thus pushing diaphragm up)

Note shown:
Quadratus lumborum (pulls ribs down)

Skeletal Muscles of Breathing

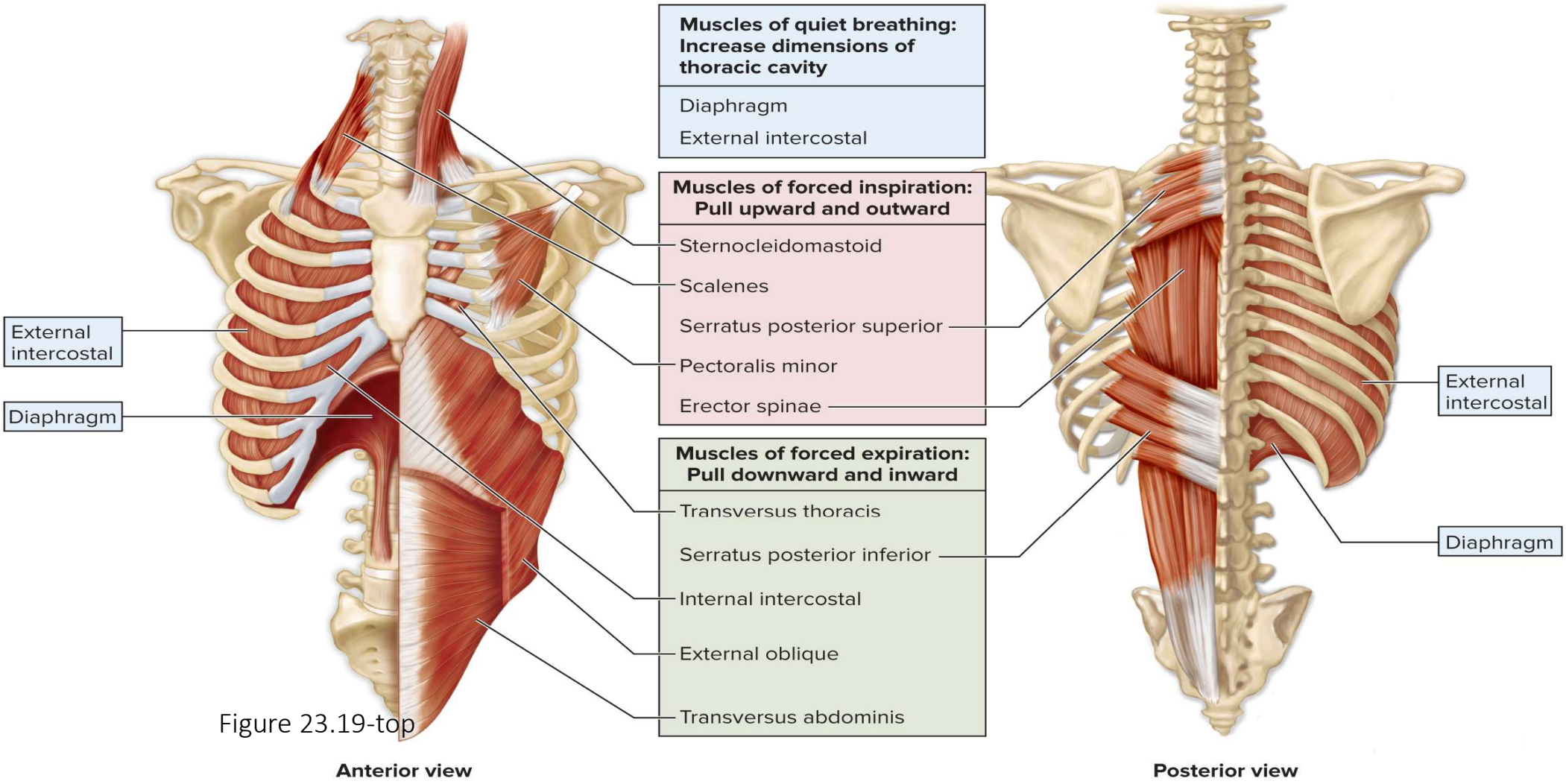


Figure 23.19-top

Intrapulmonary Pressures

- **Air entering the lungs during inspiration because the atmospheric pressure is greater than the intrapulmonary pressure**..
- **Usually during quiet inspiration, intrapulmonary pressure is at 3 mmHg below the pressure of the atmosphere. But it shows as -3mmHg.**
- **Expiration occurs when the intrapulmonary pressure is greater than the atmospheric pressure.**
- During quiet expiration it's shown as +3mmHg above atmospheric pressure.

Intrapleural Pressure

The opposing elastic recoil of the lungs and the chest wall produces a subatmospheric pressure in the intrapleural space between the two structures.

- **This intrapleural pressure is lower during inspiration because of the expansion of the thoracic cavity than it is during expiration.**
- **The intrapleural pressure is normally lower than the intraplumonary pressure during both inspiration and expiraiton.**

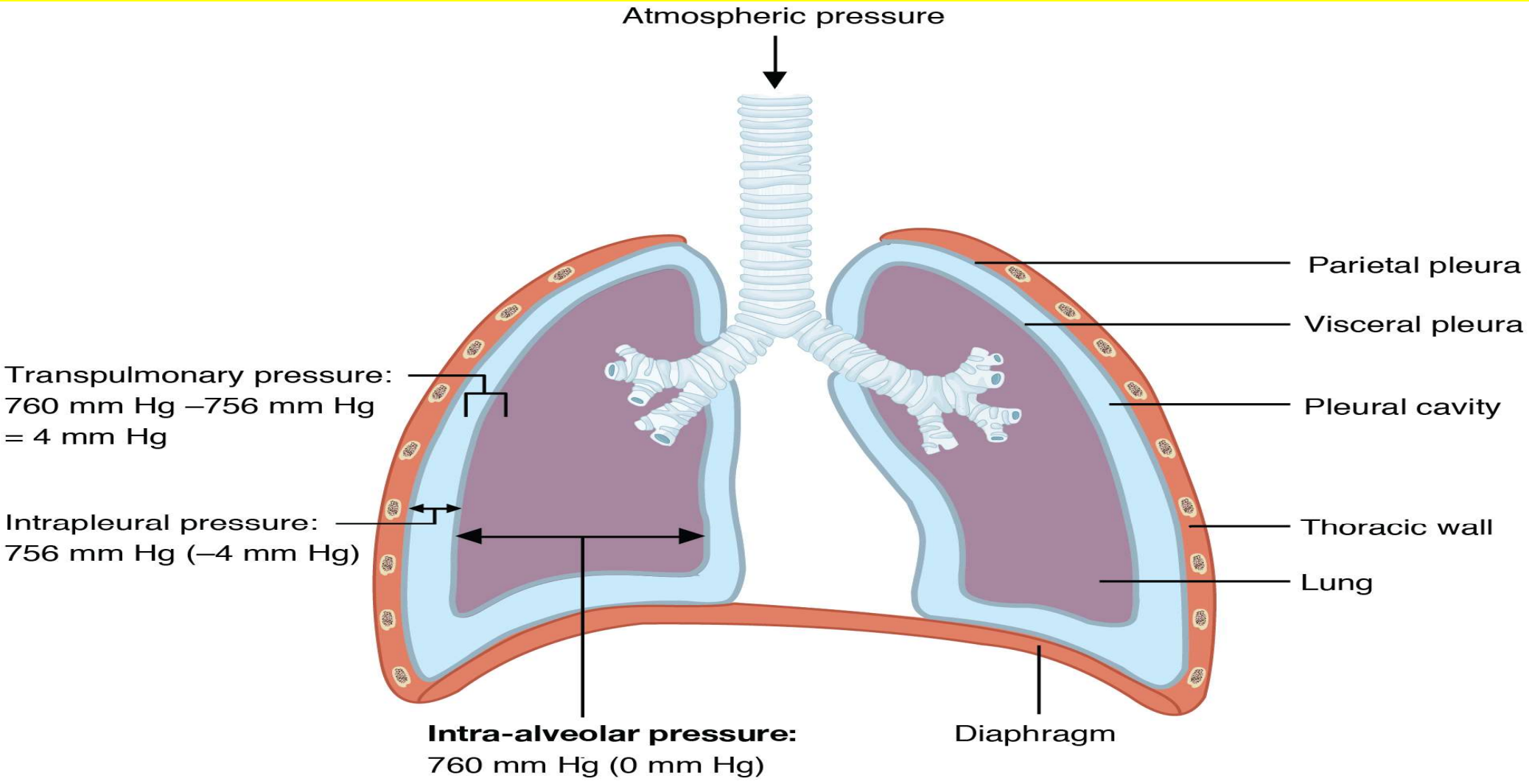
Transpulmonary Pressure

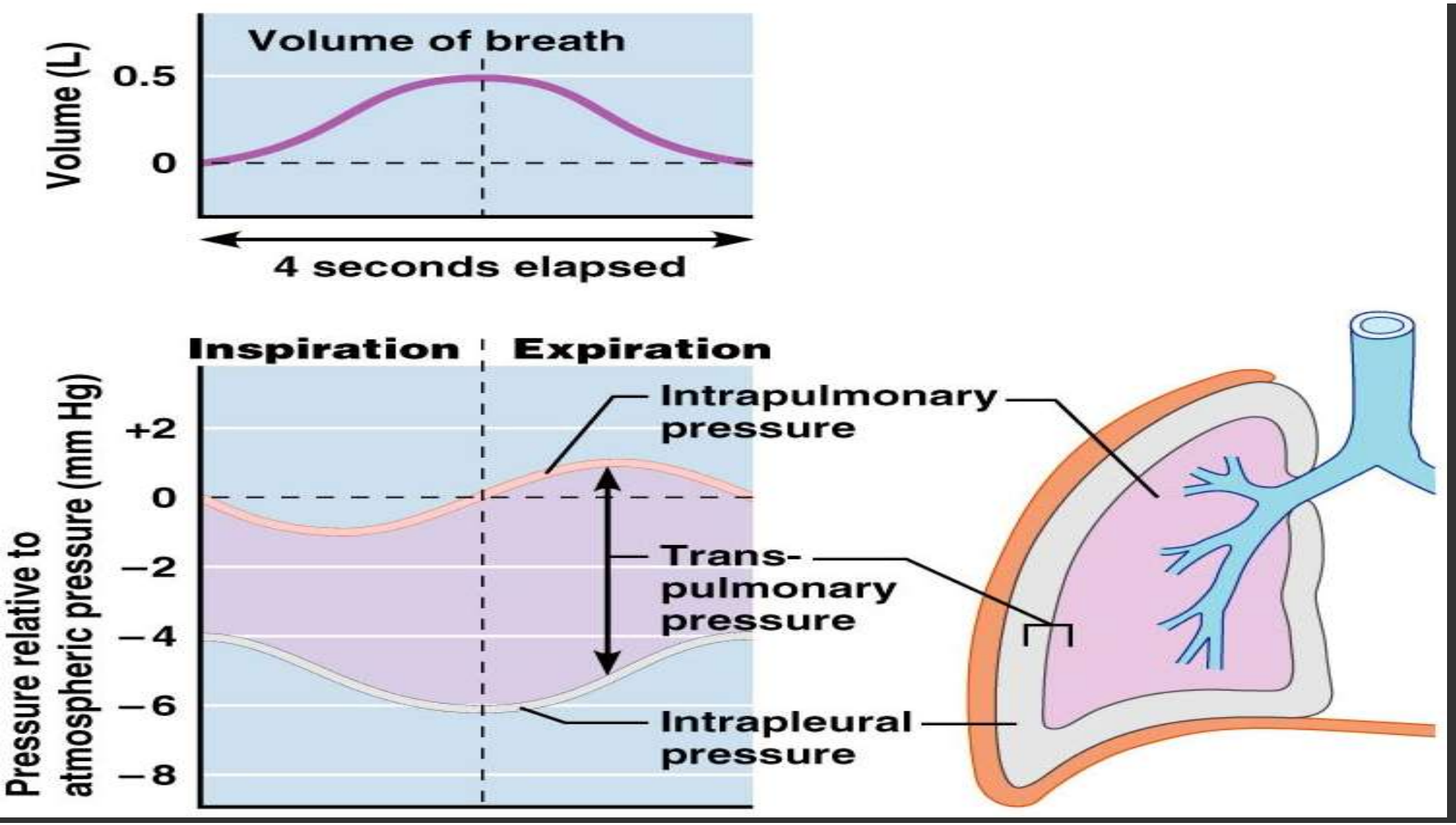
The pressure difference across the wall of the lung is transpulmonary pressure, which can also be the difference between the intrapulmonary pressure and the intrapleural pressure and keeps the lungs against the chest wall.

Pressures

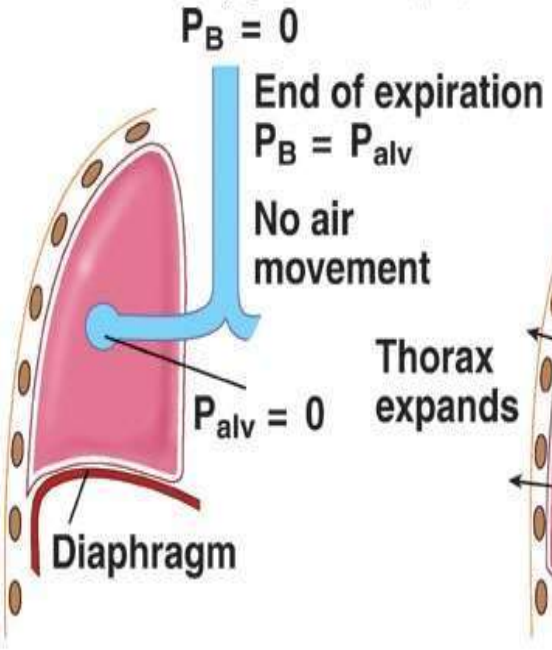
- **Atmospheric pressure – 760 mm Hg, 630 mm Hg here**
- **Intrapleural pressure – 756 mm Hg – pressure between pleural layers**
- **Intrapulmonary pressure – varies, pressure inside lungs**

Pressure Relationships

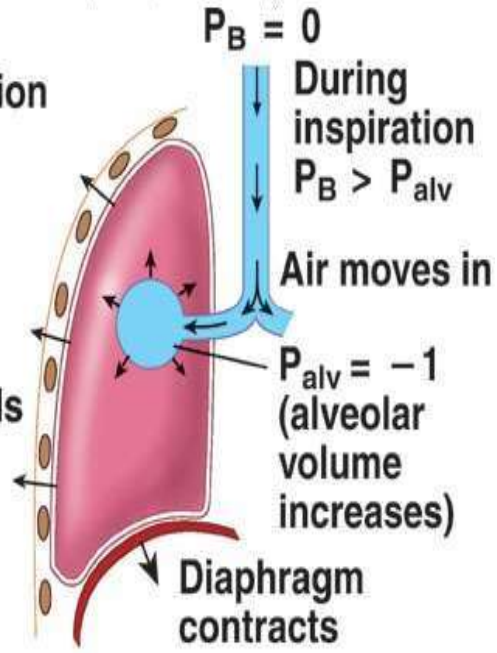



Volume of breath
Volume (L)
0.5
0
4 seconds elapsed
Inspiration
Expiration
Pressure relative to atmospheric pressure (mm Hg)
+2
0
−2
−4
−6
−8
Intrapulmonary pressure
Trans-pulmonary pressure
Intrapleural pressure

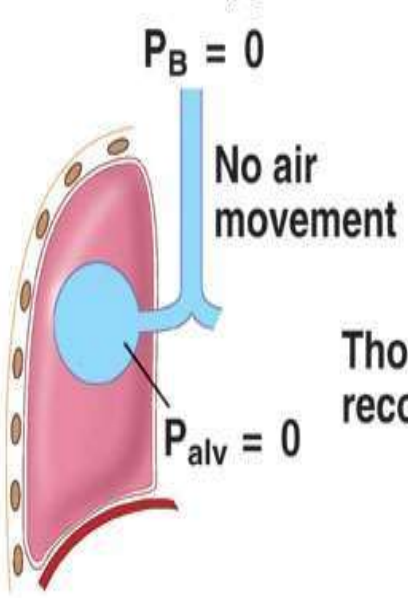
Alveolar Pressure Changes



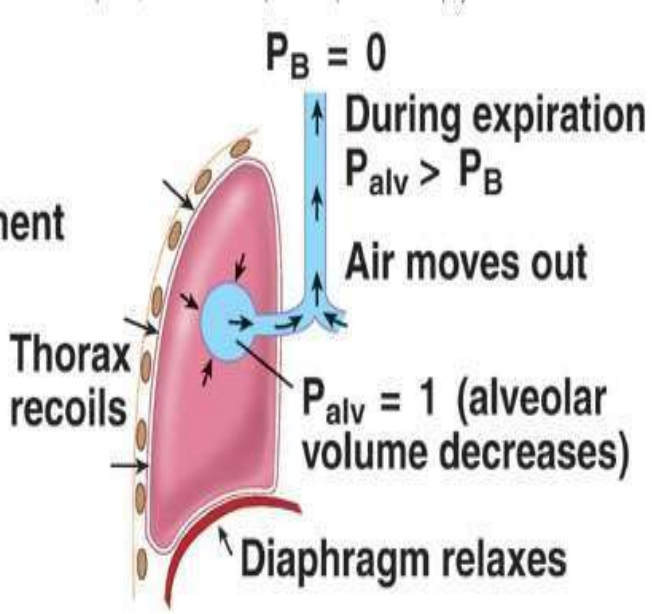
1. Barometric air pressure (P_B) is equal to alveolar pressure (P_{alv}) and there is no air movement.



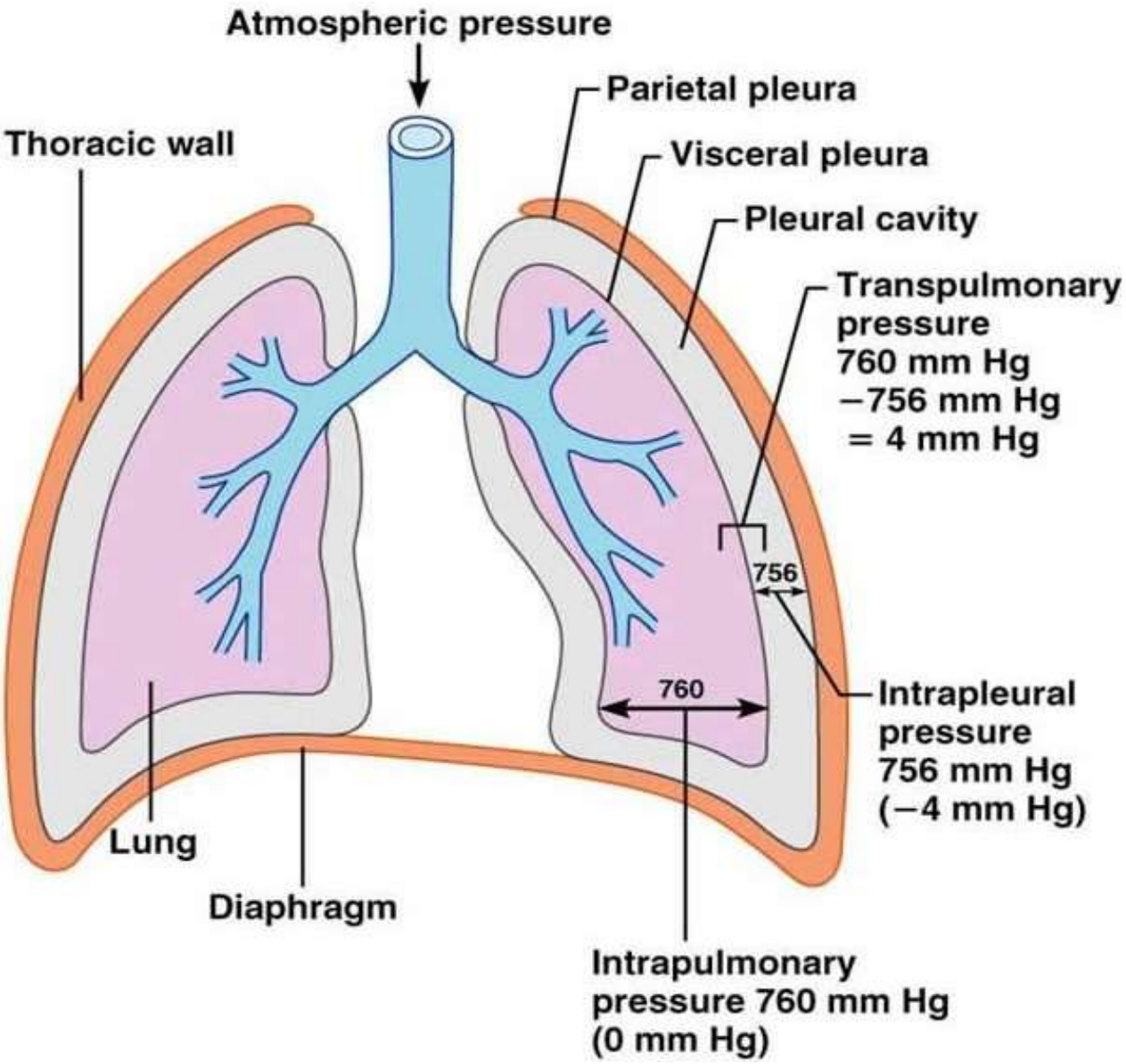
2. Increased thoracic volume results in increased alveolar volume and decreased alveolar pressure. Barometric air pressure is greater than alveolar pressure, and air moves into the lungs.



3. End of inspiration.



4. Decreased thoracic volume results in decreased alveolar volume and increased alveolar pressure. Alveolar pressure is greater than barometric air pressure, and air moves out of the lungs.

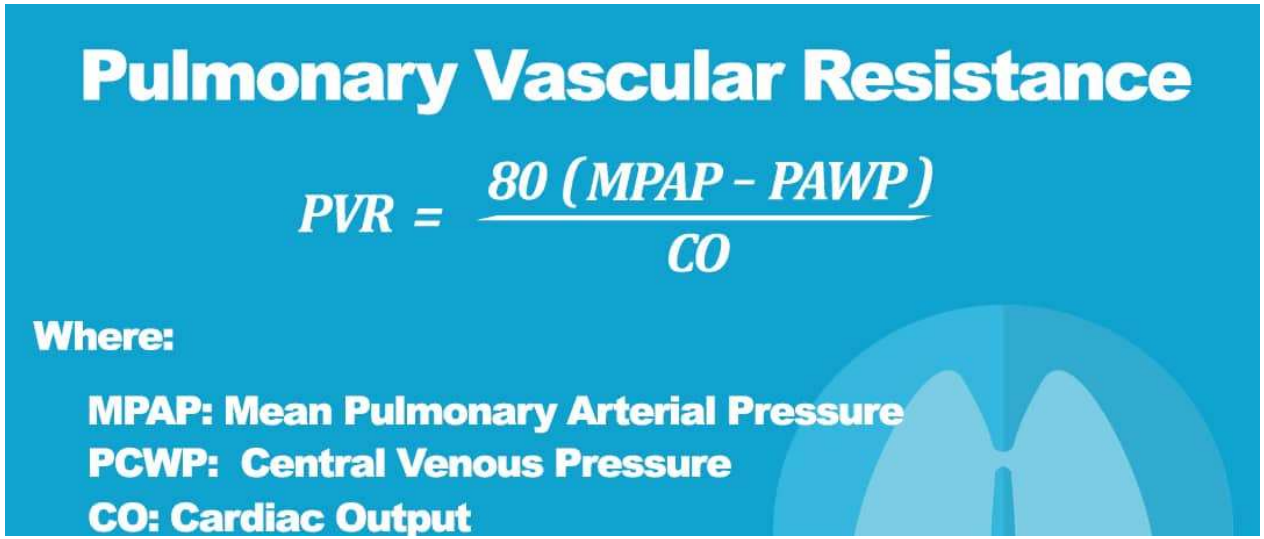


Laplace's law:
Pressure =(4 x surface tension) / radius

The surface tension contributes a large part of the static recoil force of the lung (expiration)

FRC (Functional residual capcity) is the volume in the **lungs** at the end of a natural exhalation.

- At FRC (functional residual capacity) , inward pull of lung is balanced by outward pull of chest wall, and system pressure is atmospheric.
- At FRC, airway and alveolar pressures equal atmospheric pressure (called zero), and intrapleural pressure is negative (prevents atelectasis).
- The inward pull of the lung is balanced by the outward pull of the chest wall.
- System pressure is atmospheric.
- PVR (Pulmonary vascular resistance) is at a minimum.



Compliance

- **Describes distensibility of respiratory system=** change in lung volume for a change in pressure (Lung compliance refers to the ability of the lungs to stretch and expand in response to pressure.)
- Describes change in lung volume for a given change in pressure (**C = V/P)** expressed as ΔV/ΔP and is
- inversely proportional to wall stiffness
- ↑ compliance in emphysema
- ↓ compliance in pulmonary fibrosis, pulmonary edema, ARDS, chest wall disease

- Measure of the ease with which lungs and thorax expand
  - The greater the compliance, the easier it is for a change in pressure to cause expansion
  - A lower-than-normal compliance means the lungs and thorax are harder to expand
    - Conditions that decrease compliance
      - **Pulmonary fibrosis**
      - **Pulmonary edema**
      - **Respiratory distress syndrome**

High compliance = lung easier to fill (emphysema, normal aging),

lower compliance = lung harder to fill (pulmonary fibrosis, pneumonia, NRDS, pulmonary edema).

Surfactant increases compliance

. Compliant lungs comply (cooperate) and fill easily with air

Elastance

- **Describes elastic properties (inverse of compliance, elastance = P/V)**
- Lungs tend to collapse inward
- Chest wall tends to expand outward

High lung compliance indicates that the lungs can expand easily, while low lung compliance means that the lungs are stiff and require more effort to expand.

Factors Affecting Lung Compliance

- **Elastic Fibers**: The presence of elastic fibers in the lung tissue contributes to its elasticity.

- **Surface Tension**: Surfactant reduces the surface tension within the alveoli, thereby increasing lung compliance.

- **Lung Volume**: Compliance is higher at lower lung volumes and decreases as the lungs approach their total lung capacity.

- **Increased Lung Compliance**: Seen in conditions like **emphysema,** where the elastic tissue of the lungs is damaged, making the lungs overly compliant and less effective at expelling air.

- **Decreased Lung Compliance**: Seen in conditions such as **pulmonary fibrosis, acute respiratory distress syndrome (ARDS), and pulmonary edema,** where the lungs become stiff and difficult to inflate.

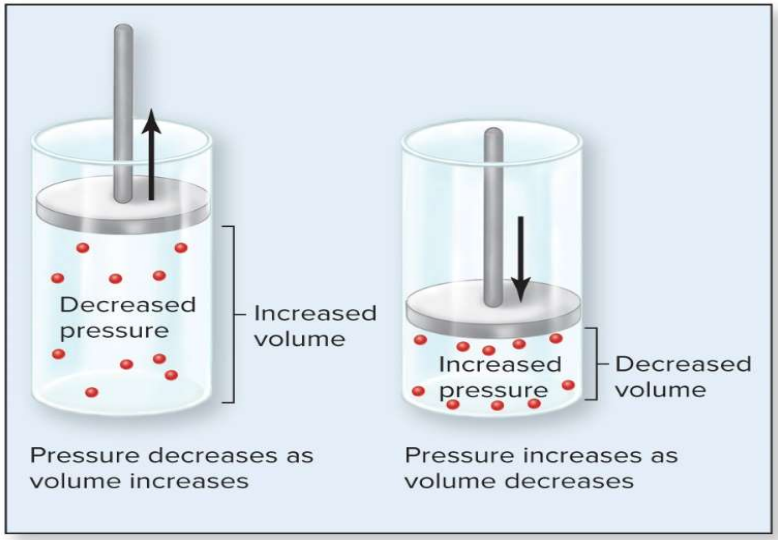
Importance in Neonates and Fetuses

•**Fetal Lung Development**: Lung compliance is low in fetuses and preterm neonates due to the underdevelopment of alveoli and insufficient surfactant production.

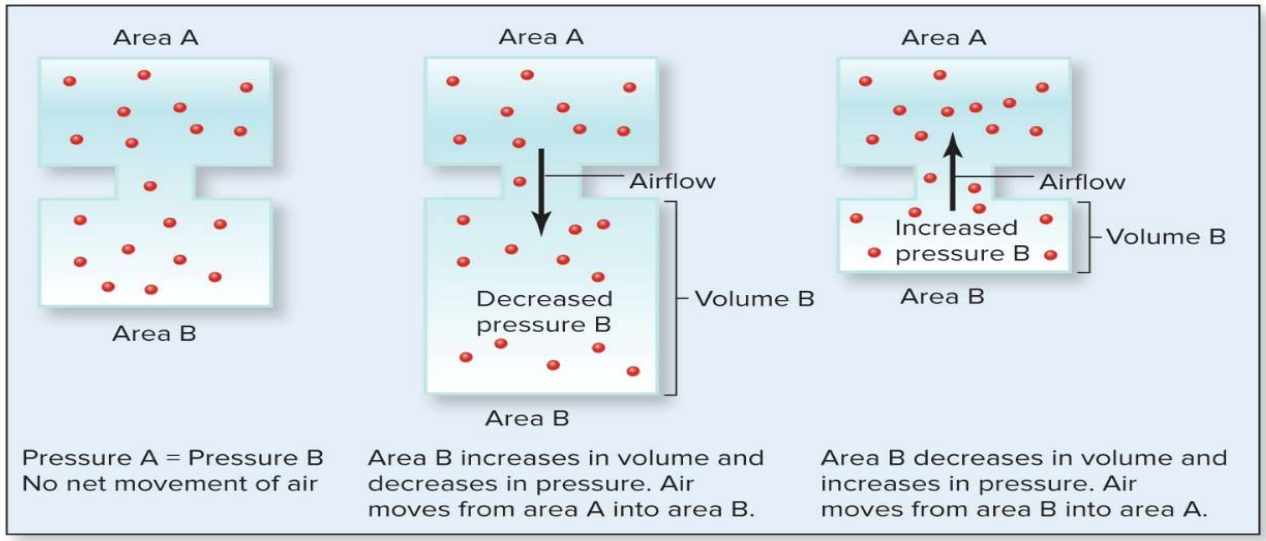
•**Surfactant Therapy**: Administering exogenous surfactant to preterm infants can improve lung compliance, reduce the risk of respiratory distress syndrome, and improve overall outcomes.

- During inspiration intrapleural pressure becomes more negative
- Respiration stops in late expiration because of dynamic compression of airways
- Total lung capacity depends on compliance
- Nitrogen wash out method detects functional residual capacity
- FRC (FUNCTIONAL RESIDUAL CAPACITY) is not estimated by spirometry
- Slow and deep breathing are the most economical way of breathing.

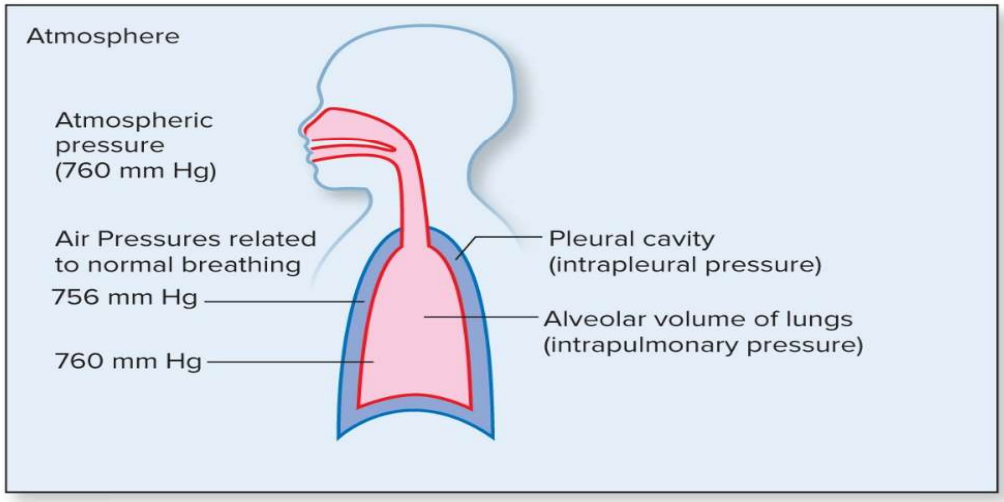
Elastic recoil—tendency for lungs to collapsinward and chest wall to spring outward.



(a) Boyle's law



(b) Pressure gradients



(c) Volumes and pressures with breathing (at the end of an expiration)

Boyle's gas law: Relationship of volume and pressure

At constant temperature, pressure (P) of a gas decreases if volume (V) of the container increases, and vice versa

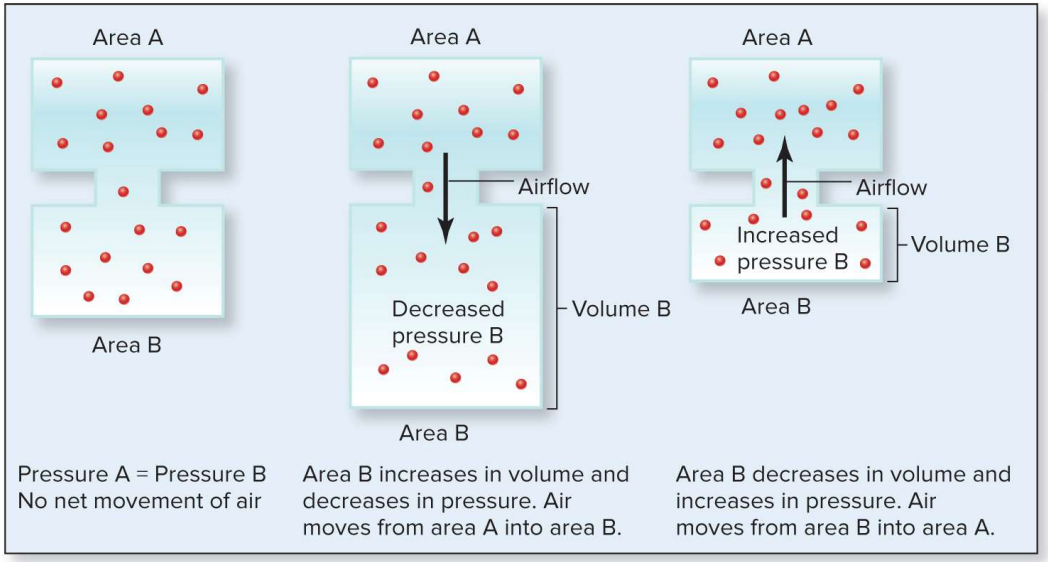
P_1 and V_1 represent initial conditions and P_2 and V_2 the changed conditions

$P_1V_1 = P_2V_2$

Inverse relationship between gas pressure and volume

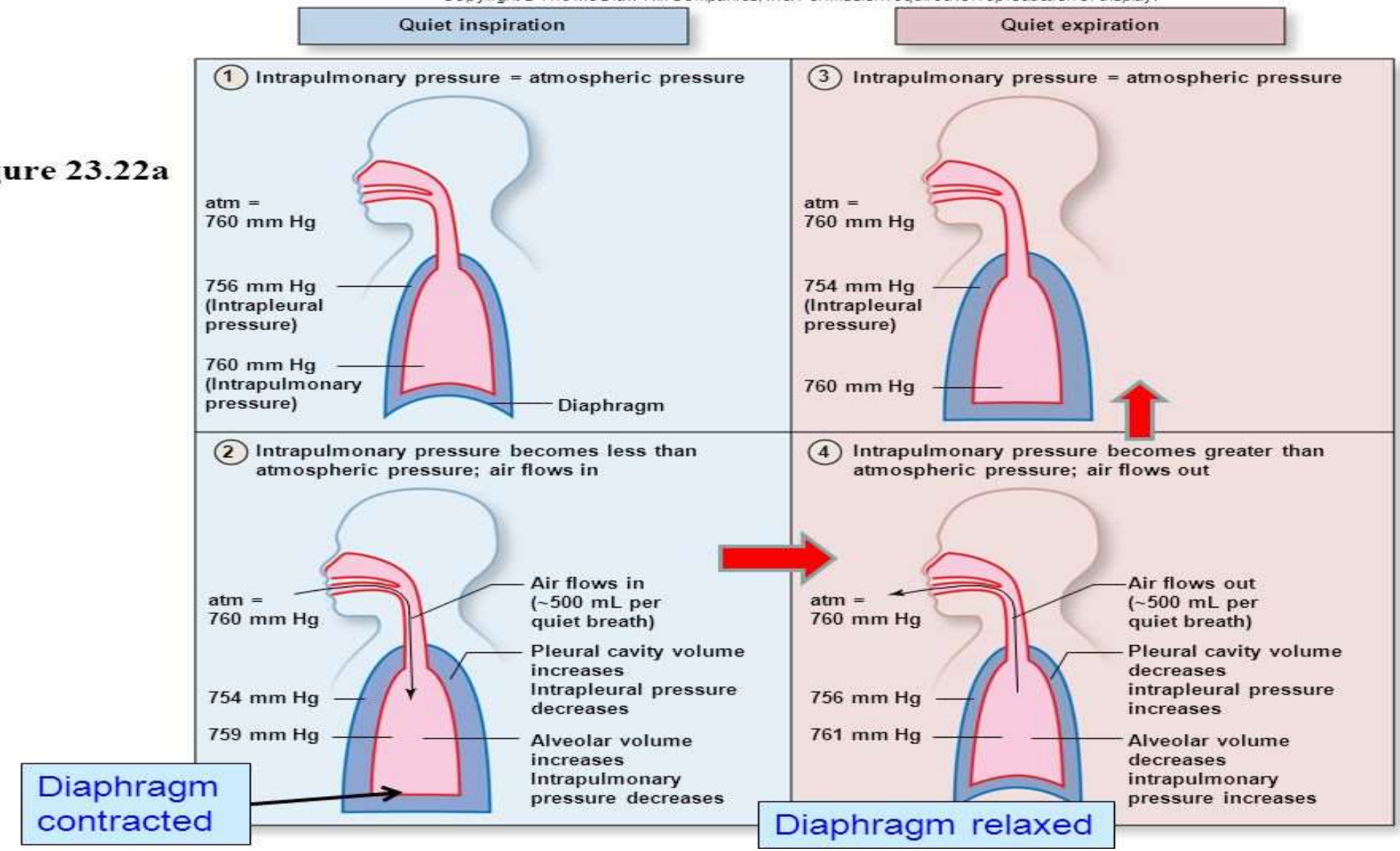
Pressure Gradients

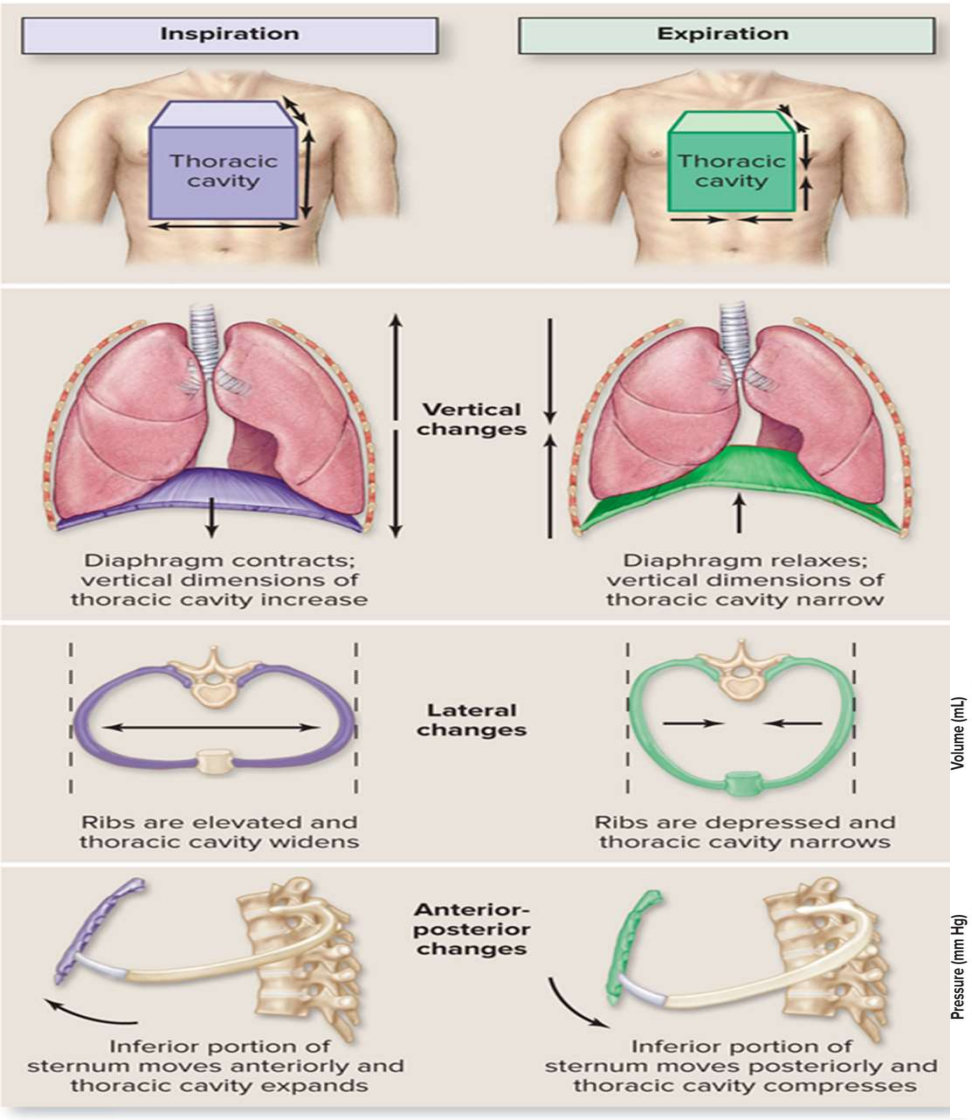
- An air pressure gradient exists when force per unit area is greater in one place than another
  - If the two places are interconnected, air flows from high to low pressure until pressure is equal

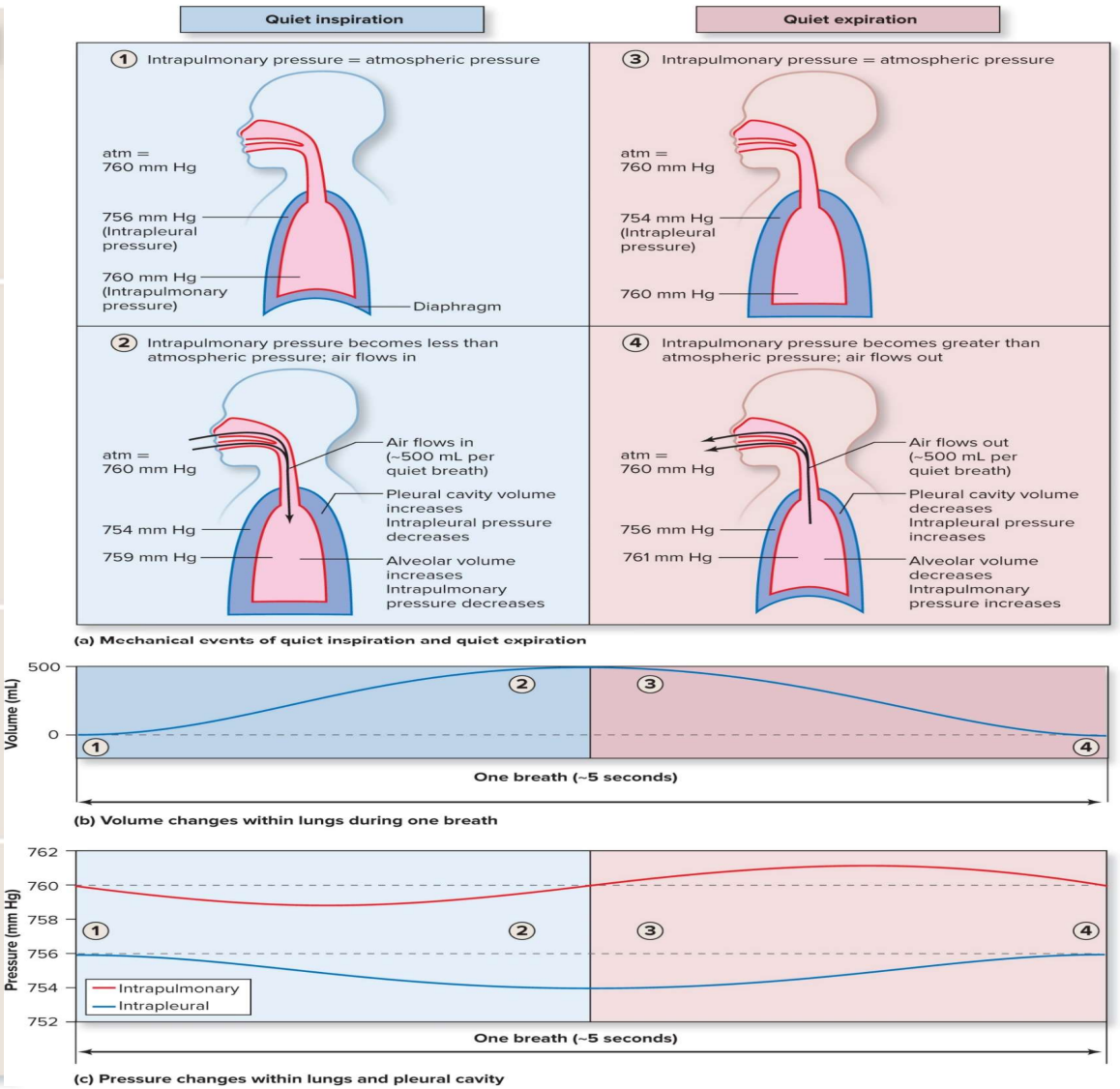


(b) Pressure gradients

Figure 23.22a







Respiration—Pulmonary Ventilation: Mechanics of Breathing

What is the sequence of events in quiet inspiration?

- Diaphragm and external intercostals contract;
- Pleural cavity volume increases;
- Lungs expand;
- Intrapulmonary pressure decreases below atmospheric pressure;
- Air moves into the lungs, moving down pressure gradient until intrapulmonary pressure equals atmospheric pressure.

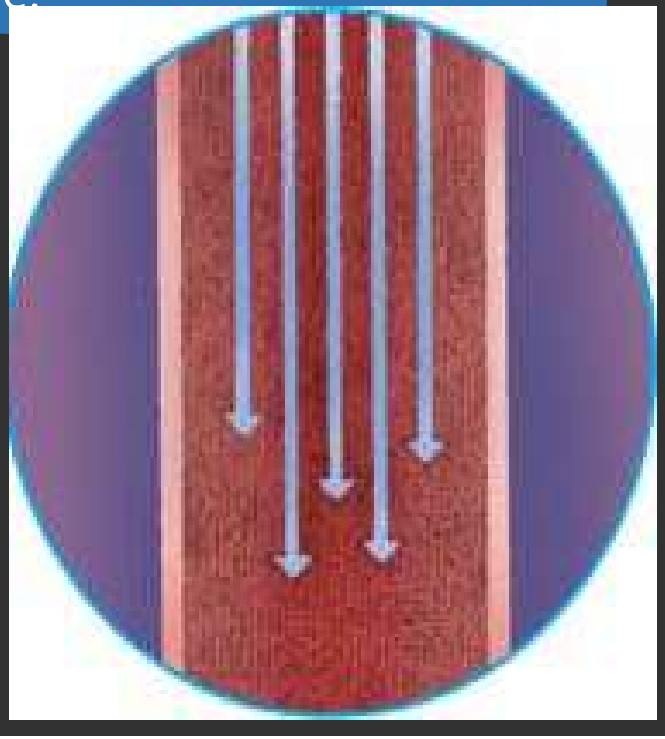
Table 23.3 Changes Associated with Quiet Breathing

Variable	Inspiration	Expiration
Diaphragm and external intercostals	Contracting (active)	Relaxing (passive)
Pleural cavity	Volume increases; pressure decreases	Volume decreases; pressure increases
Lungs	Volume increases; pressure decreases	Volume decreases; pressure increases
Air movement	Into lungs	Out of lungs

Laminar flow

Laminar flow, a linear pattern that occurs at low flow rates, offers minimal resistance.

This flow type occurs mainly in the small peripheral airways of the bronchial tree.

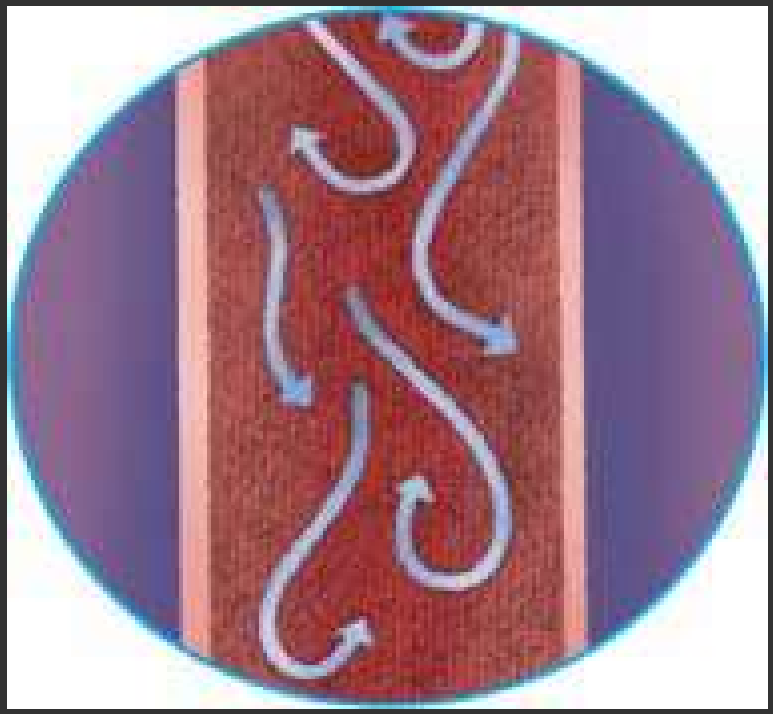


Turbulent flow

The eddying pattern of turbulent flow creates friction and increases resistance.

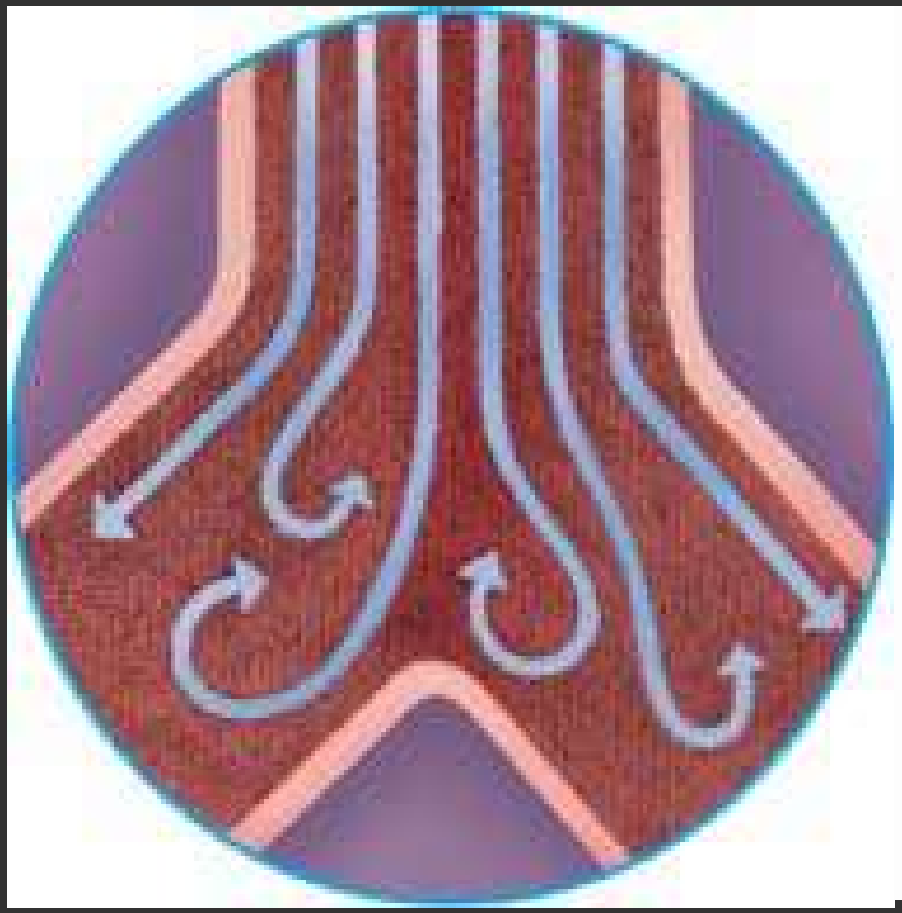
Turbulent flow is normal in the trachea and large central bronchi.

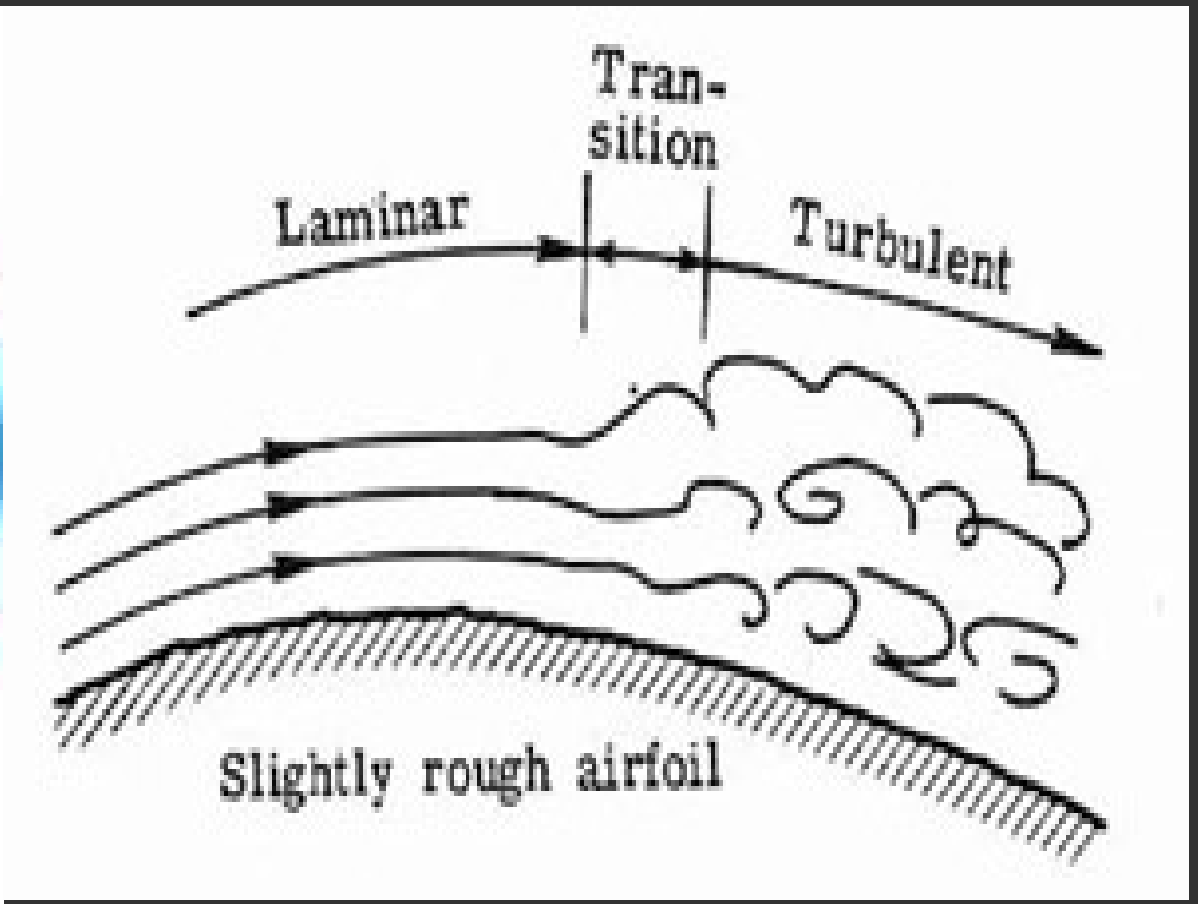
If the smaller airways become constricted or clogged with secretions, however, turbulent flow may also occur there.



Transitional flow

A mixed pattern known as transitional flow is common at lower flow rates in the larger airways, especially where the airways narrow from obstruction, meet, or branch.





Respiration—Pulmonary Ventilation: Airflow, Pressure Gradients, and Resistance

What changes to breathing must occur to maintain adequate airflow if resistance is increased?

More forceful respirations with use of the accessory muscles and greater energy expenditure

Respiration—Pulmonary Ventilation: Airflow, Pressure Gradients, and Resistance

What are the three major factors that increase resistance to airflow?

1) Change in bronchiole diameter or size of passageway through which air moves
2) Decrease in elasticity of chest wall and lungs
3) Collapse of alveoli

PART 2

Respiration division

Respiration is divided into 4 processes:

1. **Pulmonary ventilation is the movement of air into/out of the lungs**

2. **External respiration is the movement of O2 from the lungs to the blood and CO2 from the blood to the lungs.**

3. **Internal respiration is the movement of O2 from the blood to the cell interior and CO2 from the cell interior to the blood.**

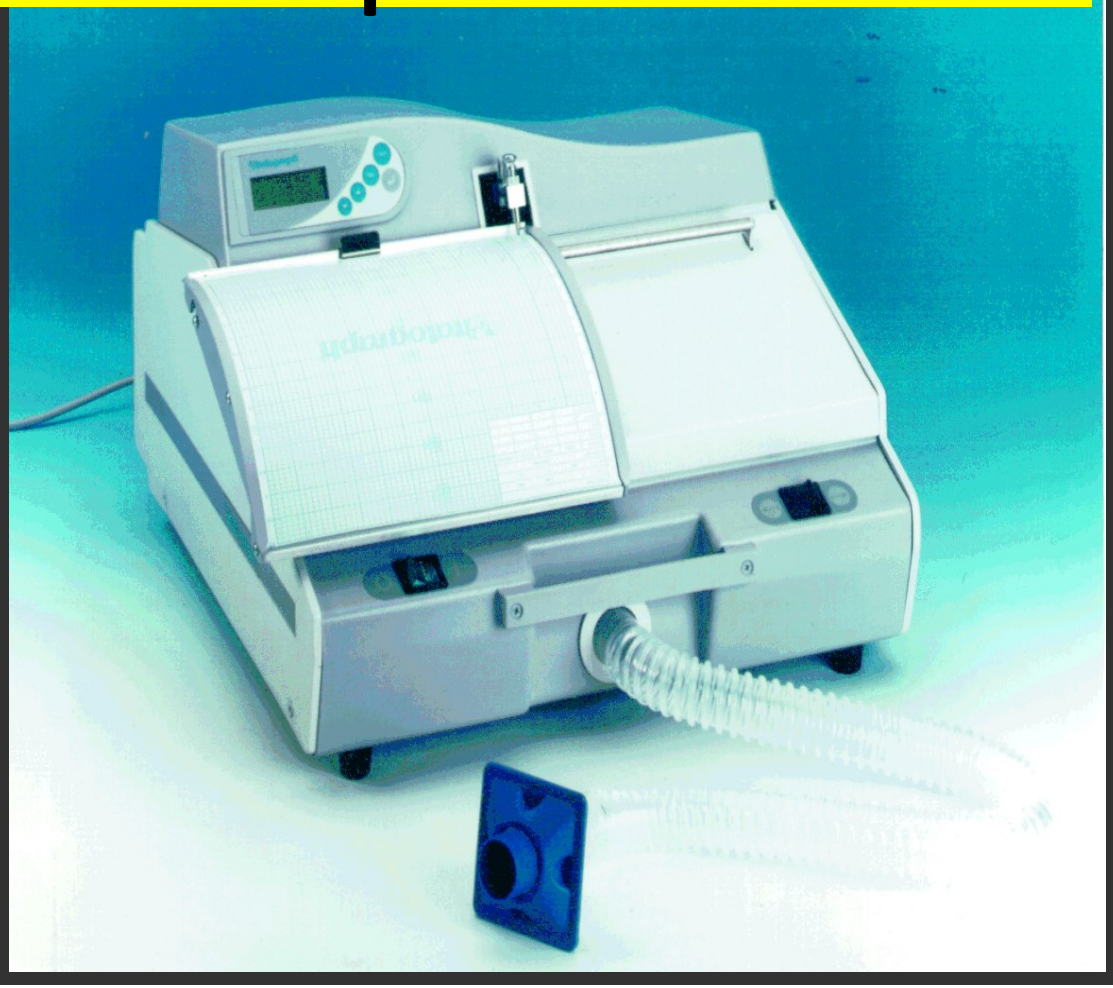
4. **Cellular respiration is the breakdown of glucose, fatty acids and amino acids that occurs in mitochondria and results in production of ATP.**
   It requires O2 and produces CO2. (Note that this type of cellular respiration, which requires O2, is known as "aerobic metabolism," whereas breakdown of glucose that produces ATP but does not require O2 is "anaerobic metabolism.")

Breathing Rate and Homeostasis: Effects of Hyperventilation and Hypoventilation

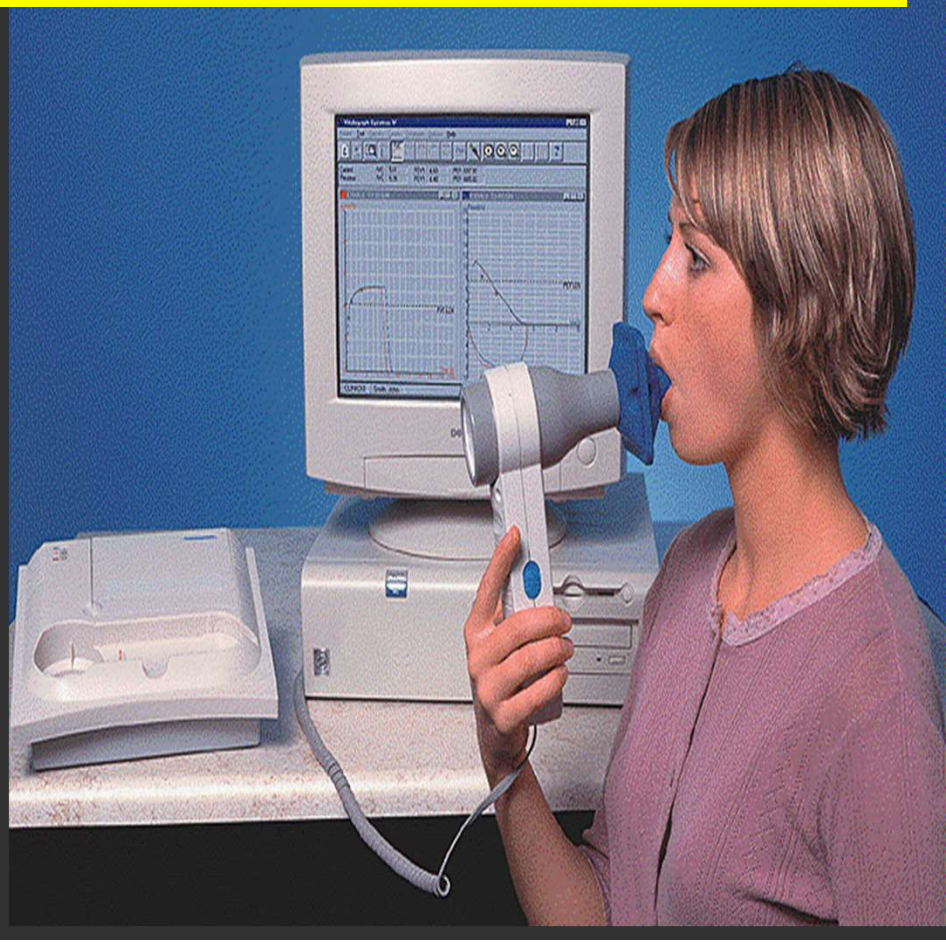
How do blood PO_2 and PCO_2 change if an individual is hyperventilating?

PO_2 remains the same. PCO_2 decreases.

Volume Measuring Spirometer



Flow Measuring Spirometer



Desktop Electronic Spirometers

Small Hand-held Spirometers

Respiration: Pulmonary and Alveolar Ventilation

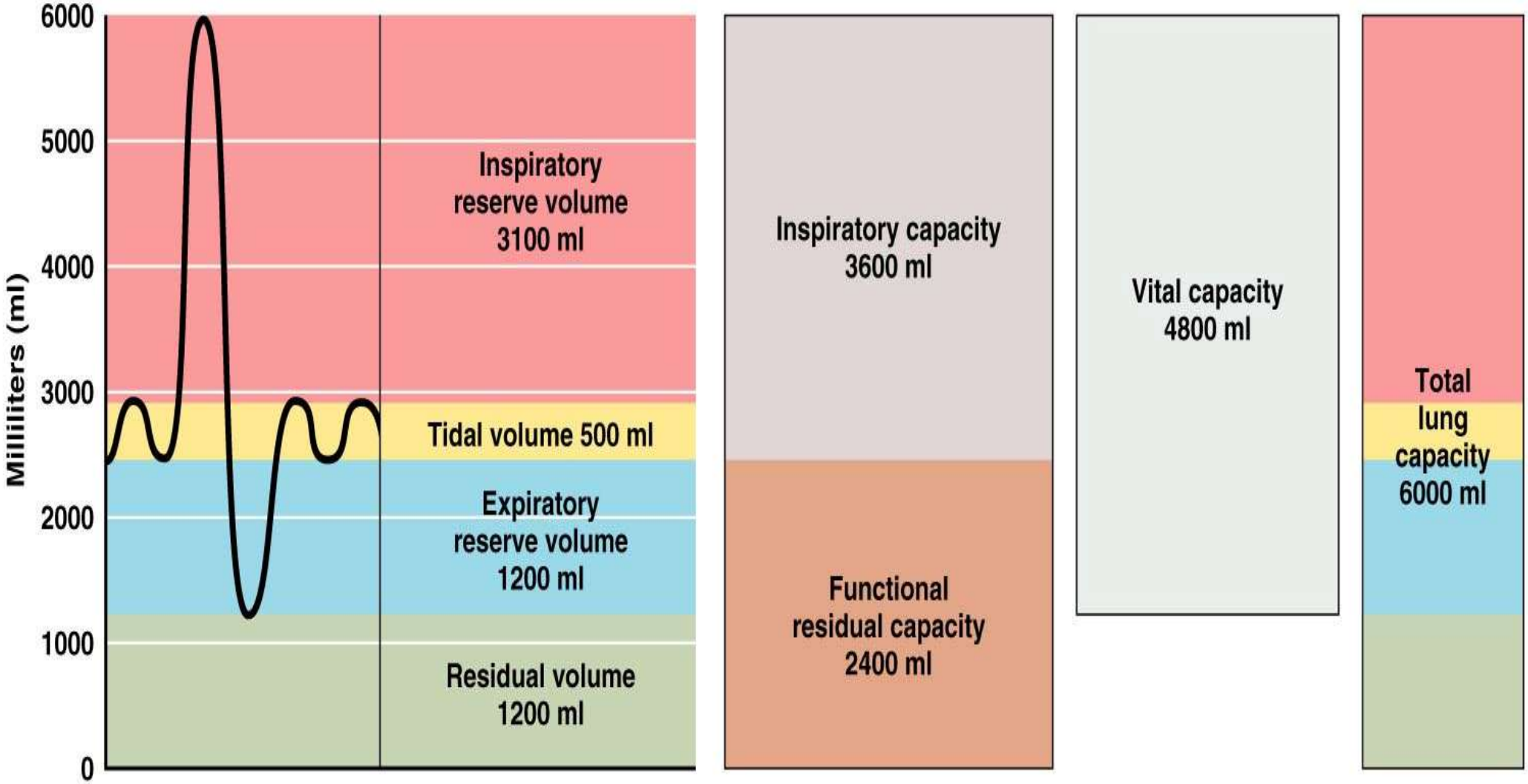
Does a person taking long deep breaths have greater or less alveolar ventilation than someone taking more shallow breaths?

Greater alveolar ventilation. Extra inhaled breath is available for gas exchange. Smaller percentage of air ends up in the anatomic dead space.

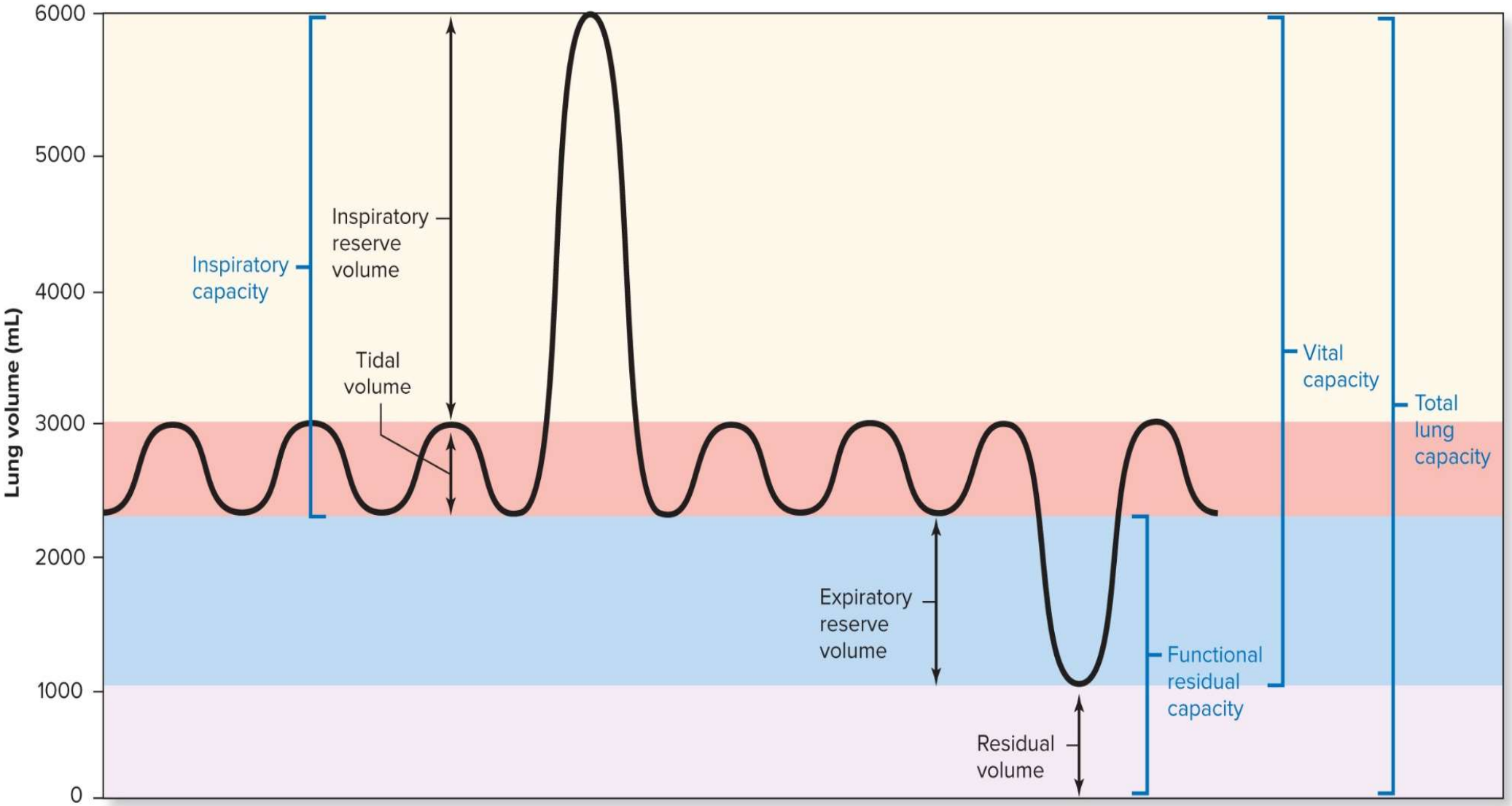
Respiratory volumes

	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 inhalation
	Expiratory reserve volume (ERV)	1200 ml	700 ml	Amount of air that can be forcefully exhaled after a normal tidal volume exhalation
	Residual volume (RV)	1200 ml	1100 ml	Amount of air remaining in the lungs after a forced exhalation
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 (should be 80% TLC)
	Inspiratory capacity (IC)	3600 ml	2400 ml	Maximum amount of air that can be inspired after a normal 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



(a) Spirographic record for a male



- **The following terms describe the various lung (respiratory) volumes:**
- **The tidal volume (TV),** about 500 ml, is the ***amount of air inspired during normal, relaxed breathing***.
- **The inspiratory reserve volume (IRV),** about 3,100 ml, is the ***additional air that can be forcibly inhaled after the inspiration of a normal tidal volume***.
- **The expiratory reserve volume (ERV),** about 1,200 ml, is ***the additional air that can be forcibly exhaled after the expiration of a normal tidal volume.***
- **Residual volume (RV),** about 1,200 ml, ***is the volume of air still remaining in the lungs after the expiratory reserve volume is exhaled.***

Summing specific lung volumes produces the following lung capacities:

- **The total lung capacity (TLC),** about **6,000 ml**, **is the maximum amount of air that can fill the lungs**
  - (***TLC = TV + IRV + ERV + RV***).
- **The vital capacity (VC),** about **4,800 ml**, is **the total amount or air that can be expired after fully inhaling**
  - ***(VC = TV + IRV + ERV = approximately 80% TLC).***
- **The inspiratory capacity (IC),** about **3,600 ml**, is **the maximum amount of air that can be inspired**
  - ***(IC = TV + IRV).***
- **The functional residual capacity (FRC),** about **2,400 ml**, **is the amount of air remaining in the lungs after a normal expiration**
  - (FRC = RV + ERV).
- Some of the air in the lungs does not participate in gas exchange. Such air is located in the anatomical dead space within bronchi and bronchioles—that is, outside the alveoli.

Alveolar Ventilation

- **Alveolar ventilation rate (AVR)**

  Alveolar ventilation = Volume of gas that reaches alveoli each minute

- Slow, deep breathing increases AVR and rapid, shallow breathing decreases AVR

AVR	=	frequency	X	(TV – dead space)
(ml/min)		(breaths/min)		(ml/breath)

- Total volume of gas entering lungs per minute= VE = VT× RR = **Minute ventilation**

Normal values:
Respiratory rate (RR) = 12–20 breaths/min
VT= 500 mL/breath = TIDAL VOLUME
VD= 150 mL/breath

Dead Space

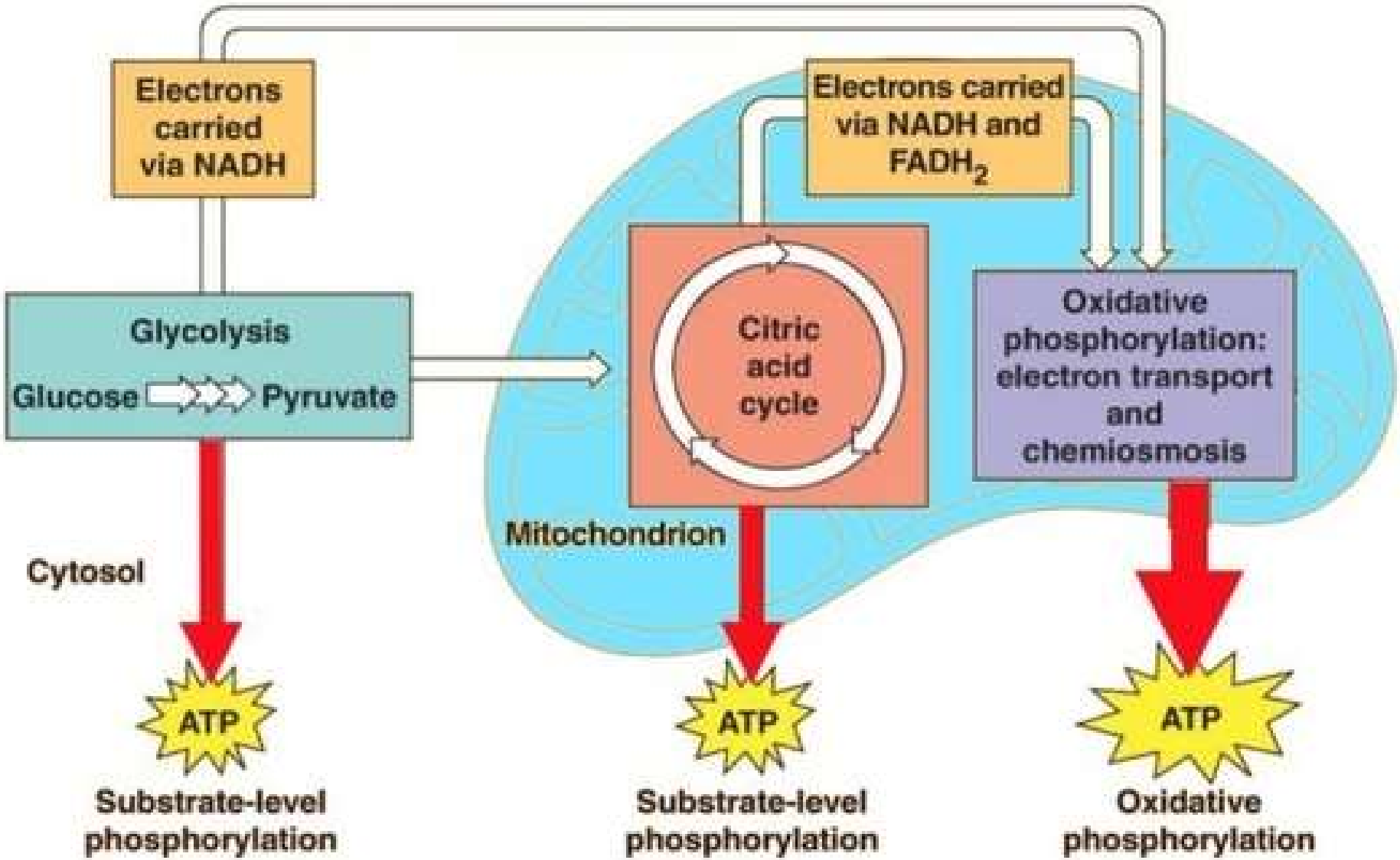
- **Anatomical dead space** – volume of the conducting respiratory passages (150 ml)
- **Alveolar dead space** – alveoli that cease to act in gas exchange due to collapse or obstruction
- **Total dead space** – sum of alveolar and anatomical dead spaces

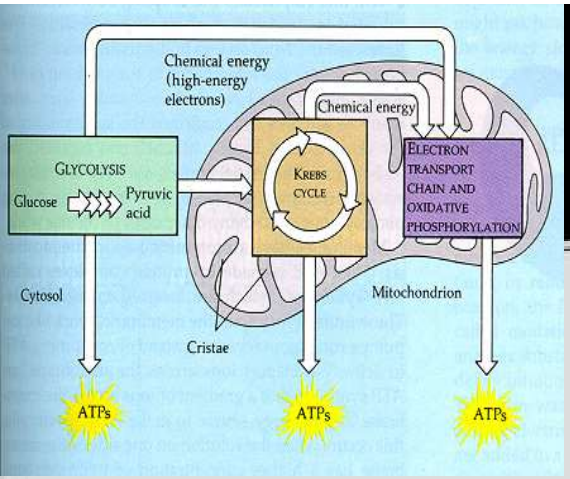
Determination of physiologic dead space

$$VD = VT \times \frac{Paco2 - Peco2}{Paco2}$$

VD= physiologic dead space = anatomic dead space of conducting airways plus alveolar dead space; apex of healthy lung is largest contributor of alveolar dead space.
Volume of inspired air that does not take part in gas exchange.
VT= tidal volume.
Paco 2 = arterial Pco2
.**Peco2**= expired air Pco2
.

Physiologic dead space—approximately equivalent to anatomic dead space in normal lungs.
May be greater than anatomic dead space in lung diseases with V/Q DEFECT(VENTILATION PERFUSION)


Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
Mitochondrion
Cytosol
ATP
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation
Oxidative phosphorylation



Glucose

Cytosol

ATP

Glycolysis

NAD^+

replenishment

NADH

Oxygen present

NADH

Pyruvate

NADH

NAD^+

Electron transport

NADH $FADH_2$

TCA Cycle

Acetyl Co-A

Fermentation

In absence of oxygen

ATP

ATP

ATP

Mitochondrion

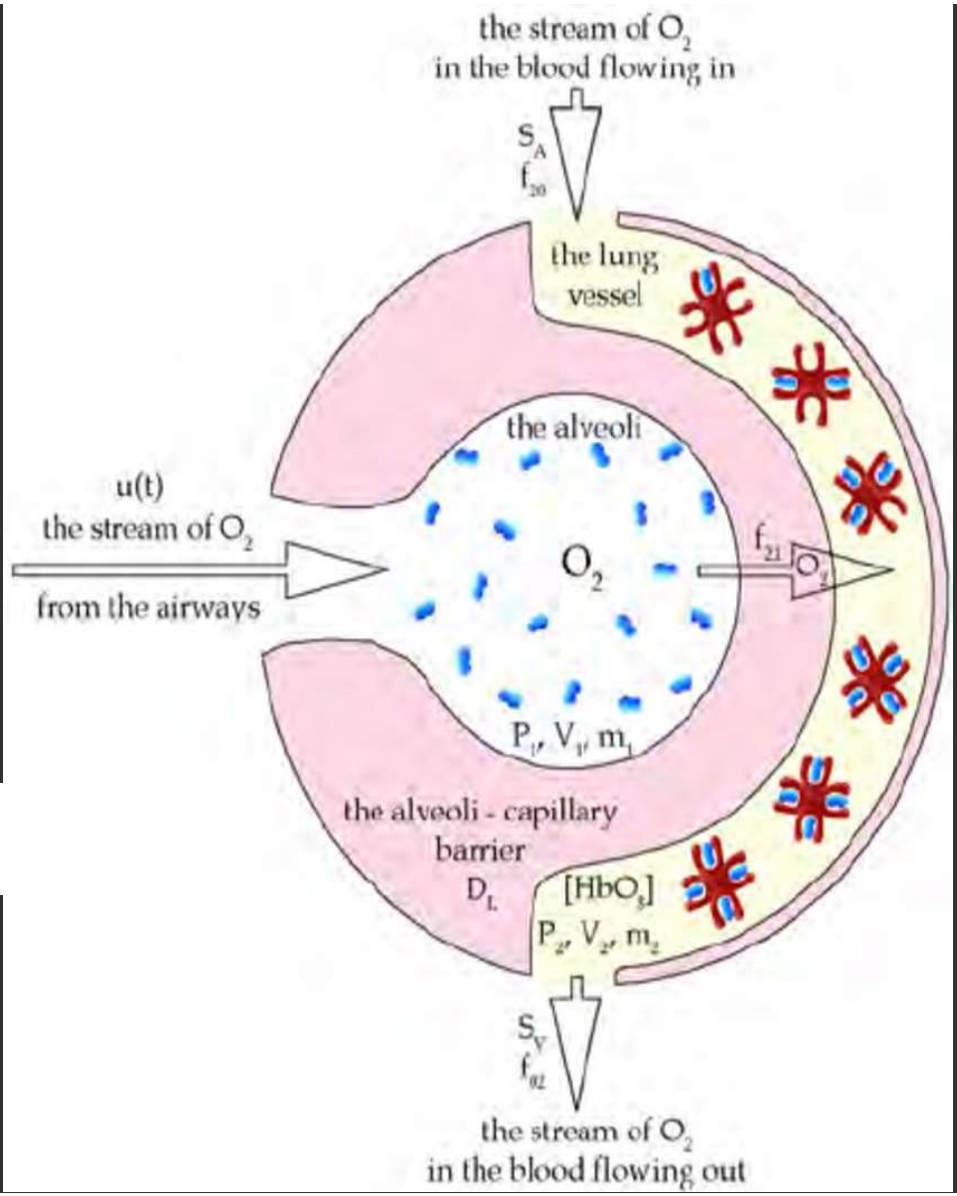
CO_2 H_2O

Lactate

4 rules for diffusion of gas

- Surface area
- Thickness
- Concentration
- Distance

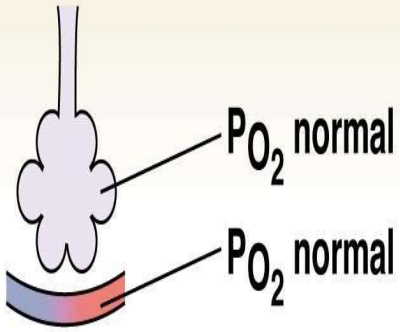
Laplace's law:
Pressure =(4 x surface tension) / radius



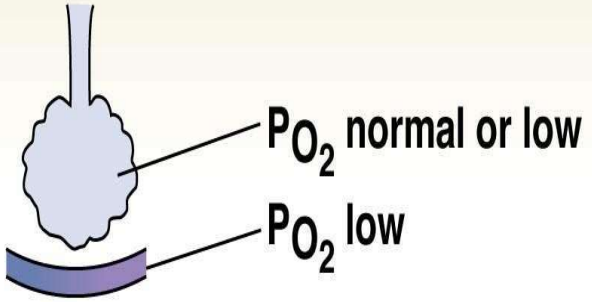
$$\text{collapsing pressure (P)} = \frac{2\ (\text{surface tension})}{\text{radius}}$$

- **Alveoli have increased tendency to collapse on expiration as radius decreased (law of Laplace).**
- **Pulmonary surfactant is a complex mix of lecithins, the most important of which is dipalmitoylphosphatidylcholine (DPPC).**
- **Surfactant synthesis begins around week 26 of gestation, but mature levels are not achieved until around week 35.**

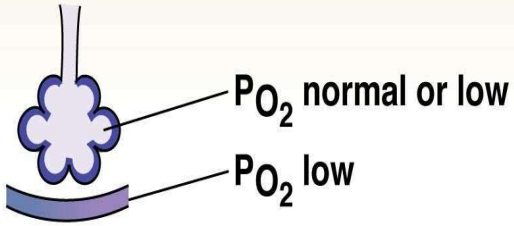
(a) Normal lung



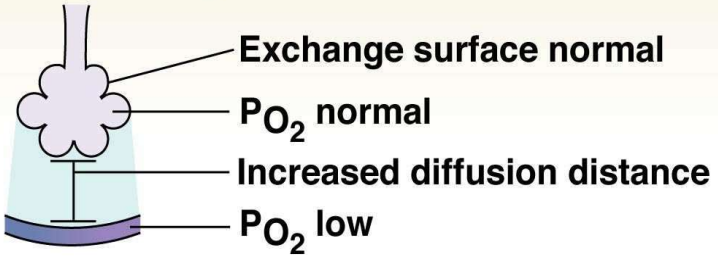
(b) **Emphysema:** destruction of alveoli reduces surface area for gas exchange.



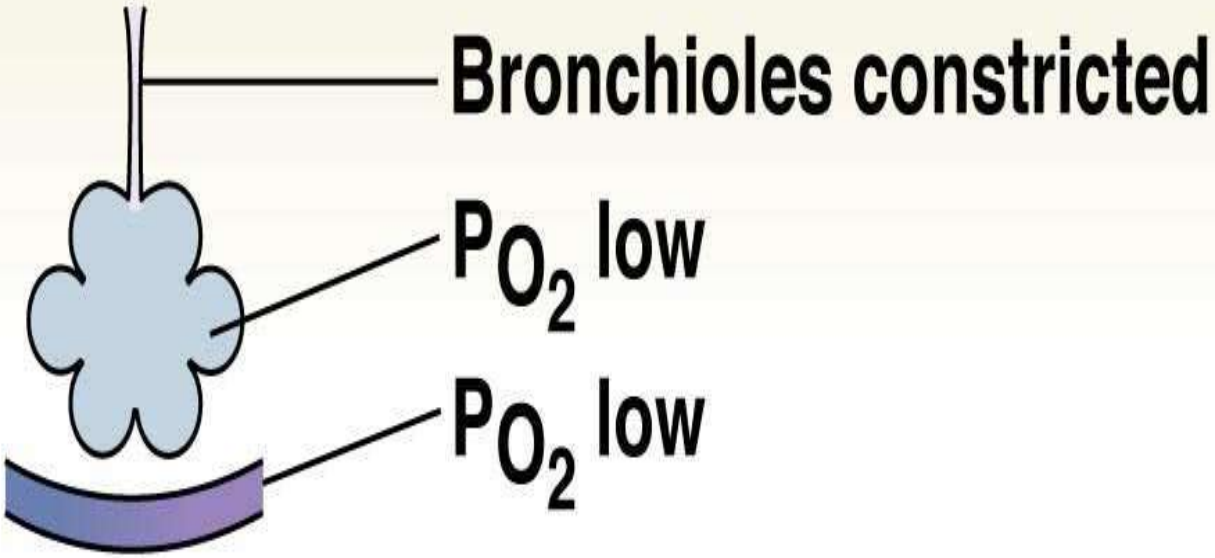
(c) **Fibrotic lung disease:** thickened alveolar membrane slows gas exchange. Loss of lung compliance may decrease alveolar ventilation.



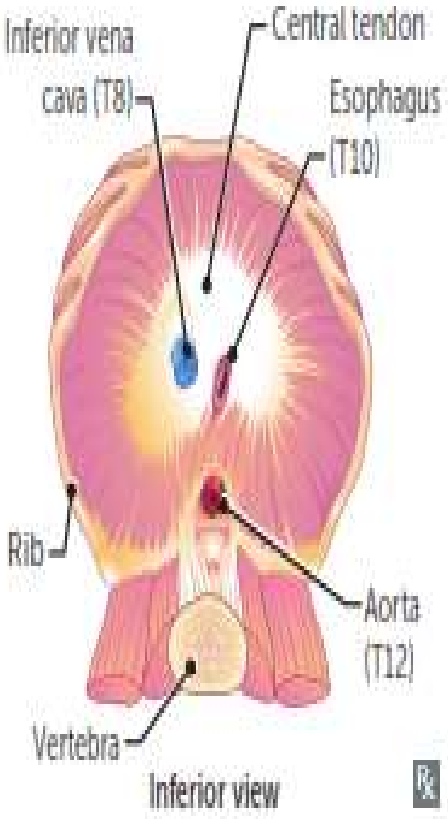
(d) **Pulmonary edema:** fluid in interstitial space increases diffusion distance. Arterial P_{CO_2} may be normal due to higher CO_2 solubility in water.



(e) Asthma: increased airway resistance decreases airway ventilation.



Diaphragm structures



Structures perforating diaphragm:

- At T8: IVC, right phrenic nerve
- At T10: esophagus, vagus (CN 10; 2 trunks)
- At T12: aorta (red), thoracic duct (white), azygos vein (blue) ("At T-1-2 it's the red, white, and blue")

Diaphragm is innervated by C3, 4, and 5 (phrenic nerve). Pain from diaphragm irritation (eg, air, blood, or pus in peritoneal cavity) can be referred to shoulder (C5) and trapezius ridge (C3, 4).

Number of letters = T level:

T8: vena cava

T10: "oesophagus"

T12: aortic hiatus

I (IVC) ate (8) ten (10) eggs (esophagus) at (aorta) twelve (12).

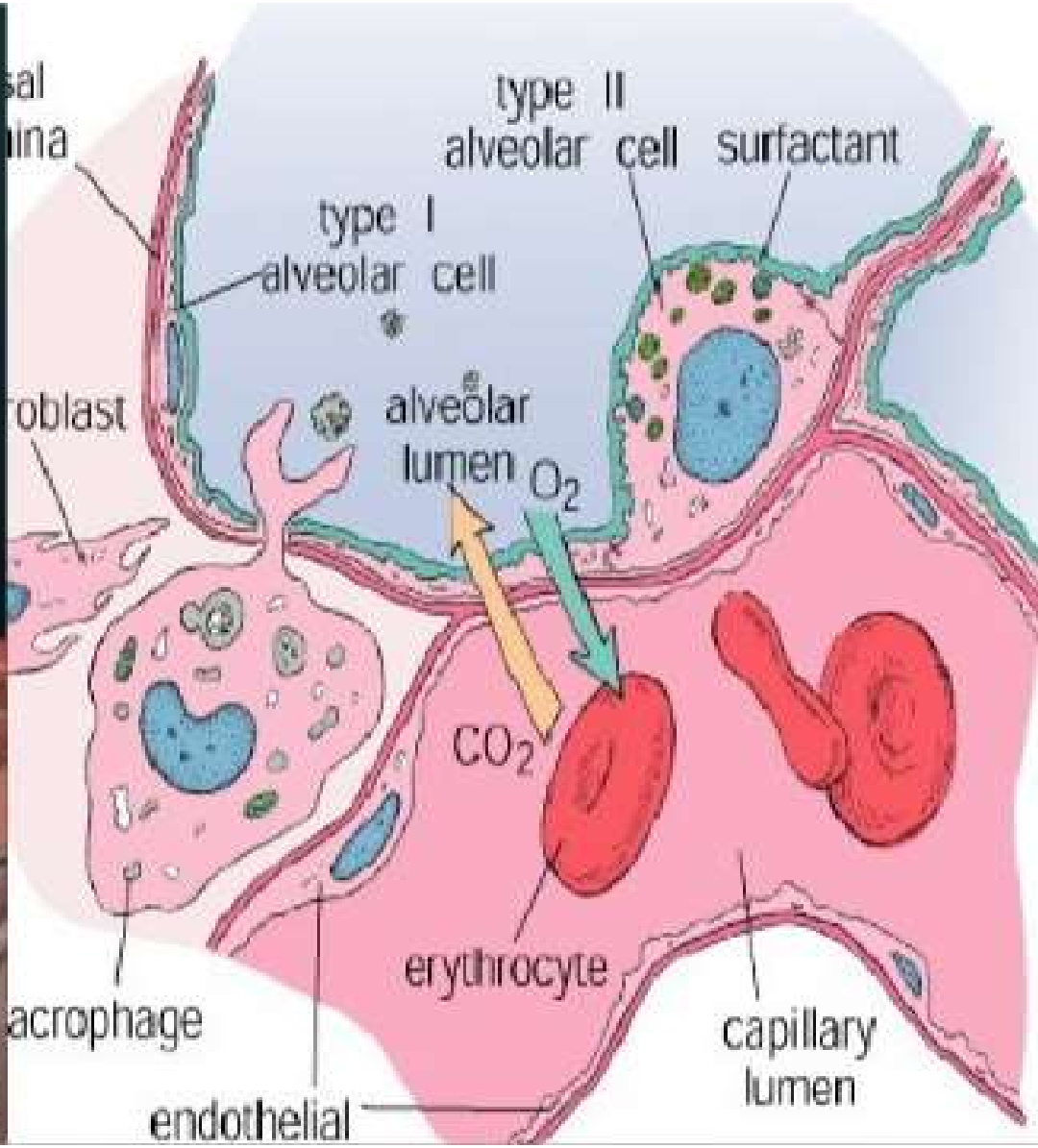
C3, 4, 5 keeps the diaphragm alive.

Other bifurcations:

- The common carotid bifourcates at C4.
- The trachea bifourcates at T4.
- The abdominal aorta bifourcates at L4.

Blood air barrier:

Wall through which gas exchange occur. It is present in() blood in the capillaries & air within lung alveoli.



Respiration—Alveolar and Systemic Gas Exchange: Alveolar Gas Exchange

How do the partial pressure of oxygen and carbon dioxide in blood change during alveolar gas exchange?

Oxygen levels rise from 40 mm Hg to 104 mm Hg. Carbon dioxide levels drop from 45 mm Hg to 40 mm Hg.

Figure 23.26

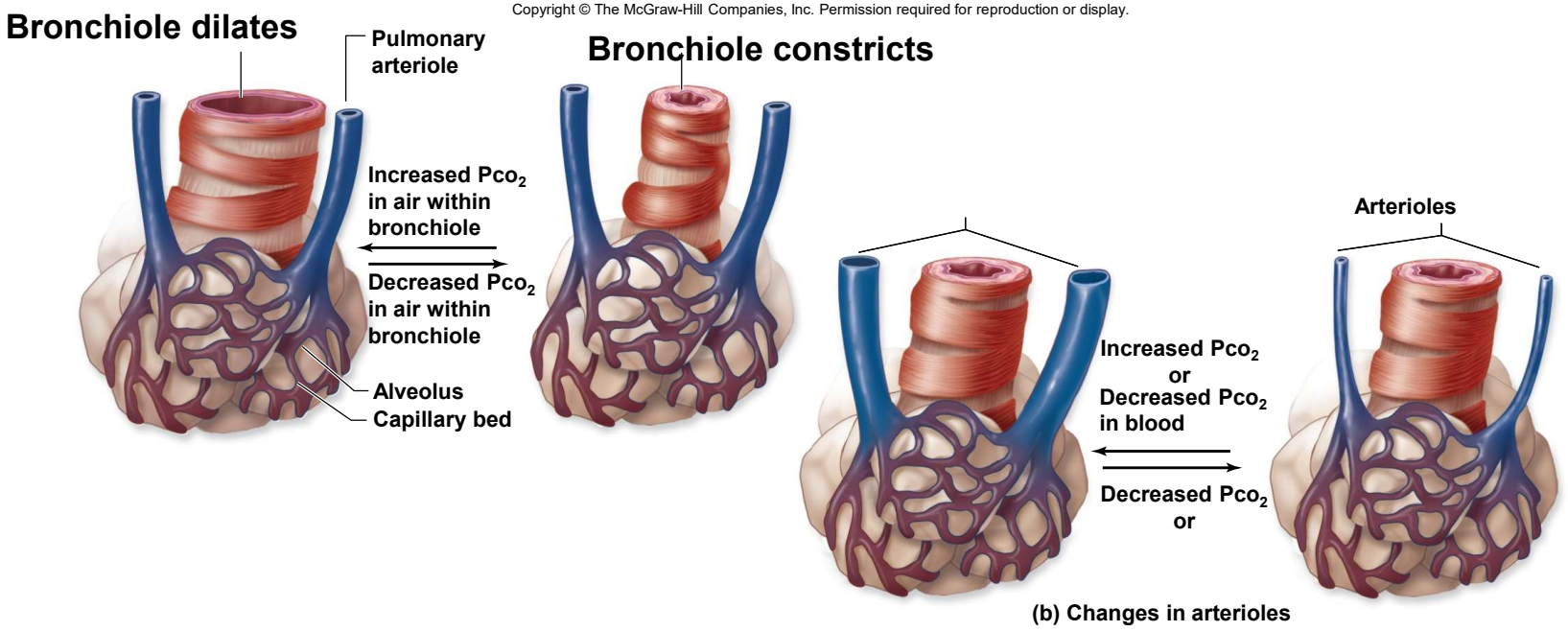


Table 23.2 Respiration Processes

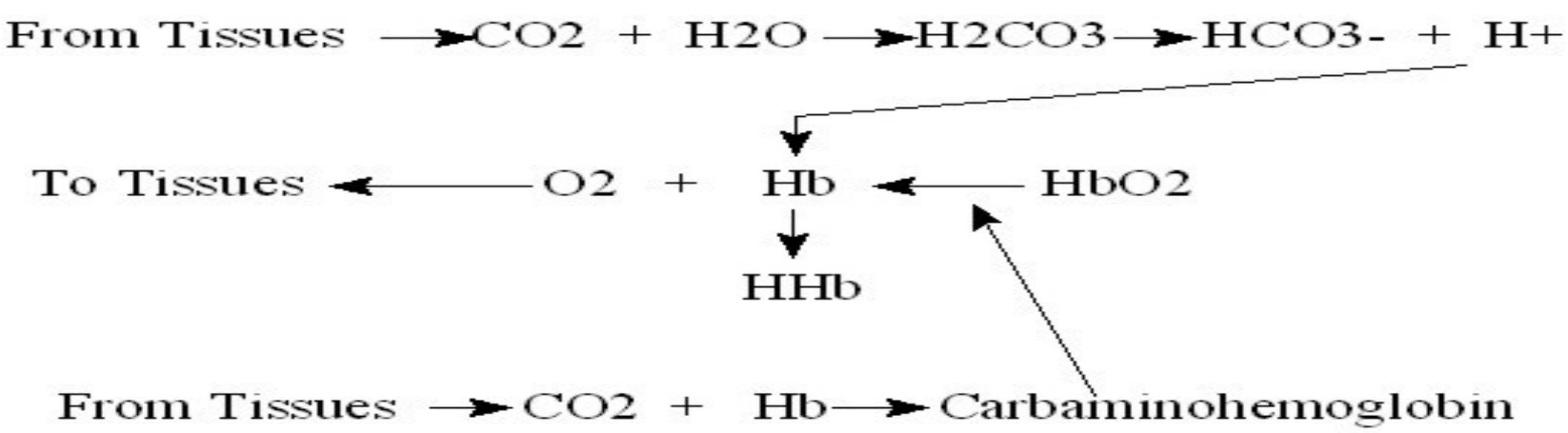
Process	Description	Body Systems
Pulmonary ventilation	Movement of air between atmosphere and the alveoli • Net movement of oxygen from atmosphere to alveoli during inspiration (step 1) • Net movement of carbon dioxide from alveoli to atmosphere during expiration (step 8)	Respiratory, skeletal, muscular, and nervous
Alveolar gas exchange	Exchange of respiratory gases between alveoli of the lungs and the blood • Oxygen diffuses from alveoli into blood (step 2) • Carbon dioxide diffuses from blood into alveoli (step 7)	Respiratory and cardiovascular
Gas transport	Blood transport of respiratory gases between lungs and tissue cells of the body • Oxygen is transported from lungs to tissue cells (step 3) • Carbon dioxide is transported from systemic cells to lungs (step 6)	Cardiovascular
Systemic gas exchange	Exchange of respiratory gases between blood and systemic cells • Oxygen diffuses from blood into tissue cells (step 4) • Carbon dioxide diffuses from systemic cells into blood (step 5)	Cardiovascular

Breathing Rate and Homeostasis:
Breathing and Exercise

How do blood PO_2 and PCO_2 change during exercise?

They both remain relatively the same.

The Bohr Effect Occurs in the Systemic Capillaries



The **Bohr Effect** describes the result of increasing CO2 in causing more oxygen unloading from hemoglobin.

It results from two circumstances:

the effect of lowering pH as described above,

2) the effect of carbaminohemoglobin in stimulating oxygen unloading

Main Gases of the Atmosphere

Gas	Symbol	Approximate %
Nitrogen	N_2	78.6
Oxygen	O_2	20.9
Carbon Dioxide	CO_2	0.04
Water Vapor	H_2O	0.46

Respiration—Alveolar and Systemic Gas Exchange: Chemical Principles

Given the same partial pressure for oxygen and carbon dioxide, which gas enters a water solution more readily?

Carbon dioxide. It has a higher solubility coefficient and dissolves in water more readily. According to Henry's law, solubility is dependent on partial pressure and the solubility coefficient.

Gas Exchange

- Partial Pressure
  - Each gas in atmosphere contributes to the entire atmospheric pressure, denoted as P
- Gases in liquid
  - Gas enters liquid and dissolves in proportion to its partial pressure
- O_2 and CO_2 Exchange by DIFFUSION
  - PO_2 is 105 mmHg in alveoli and 40 in alveolar capillaries
  - PCO_2 is 45 in alveolar capillaries and 40 in alveoli

Partial Pressures

- Oxygen is 21% of atmosphere
- 760 mmHg x .21 = 160 mmHg PO2
- This mixes with “old” air already in alveolus to arrive at PO2 of 105 mmHg

Partial Pressures

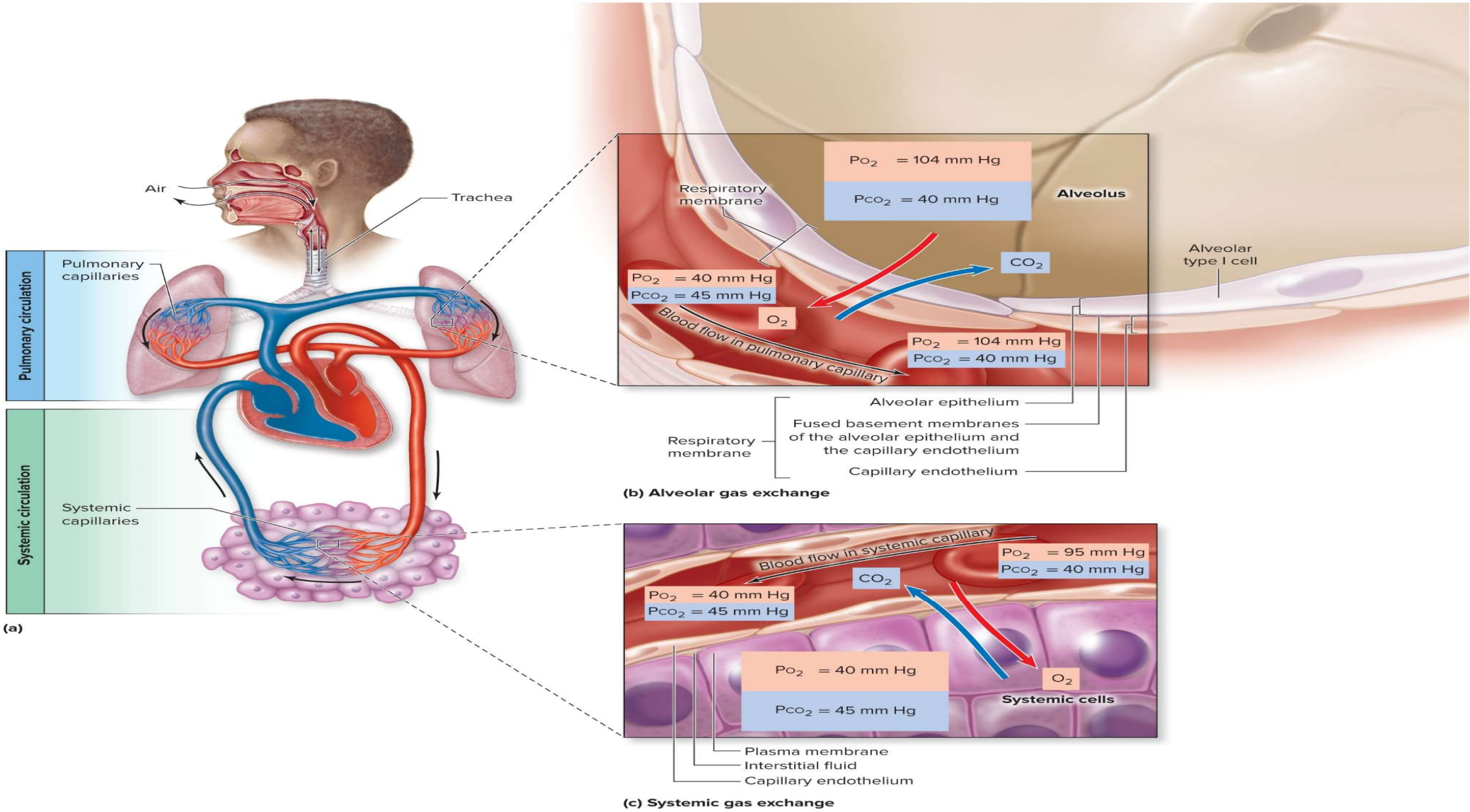
- Carbon dioxide is .04% of atmosphere
- 760 mmHg x .0004 = .3 mm Hg PCO_2
- This mixes with high CO_2 levels from residual volume in the alveoli to arrive at PCO_2 of 40 mmHg

Carbon Dioxide Transport

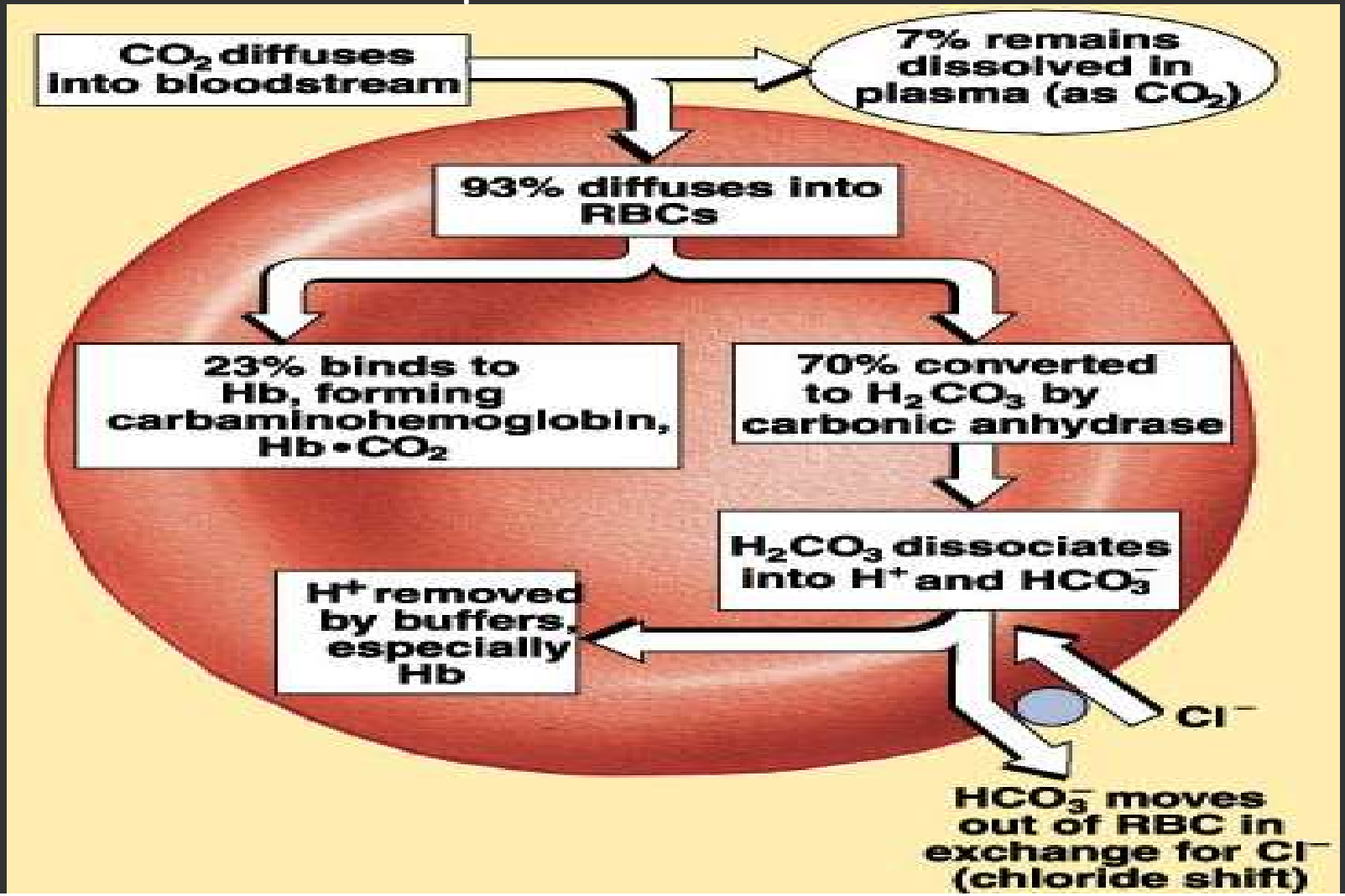
• **Method**	**Percentage**
•Dissolved in Plasma	7 - 10 %
•Chemically Bound to •Hemoglobin in RBC's	20 - 30 %
•As Bicarbonate Ion in •Plasma	60 -70 %

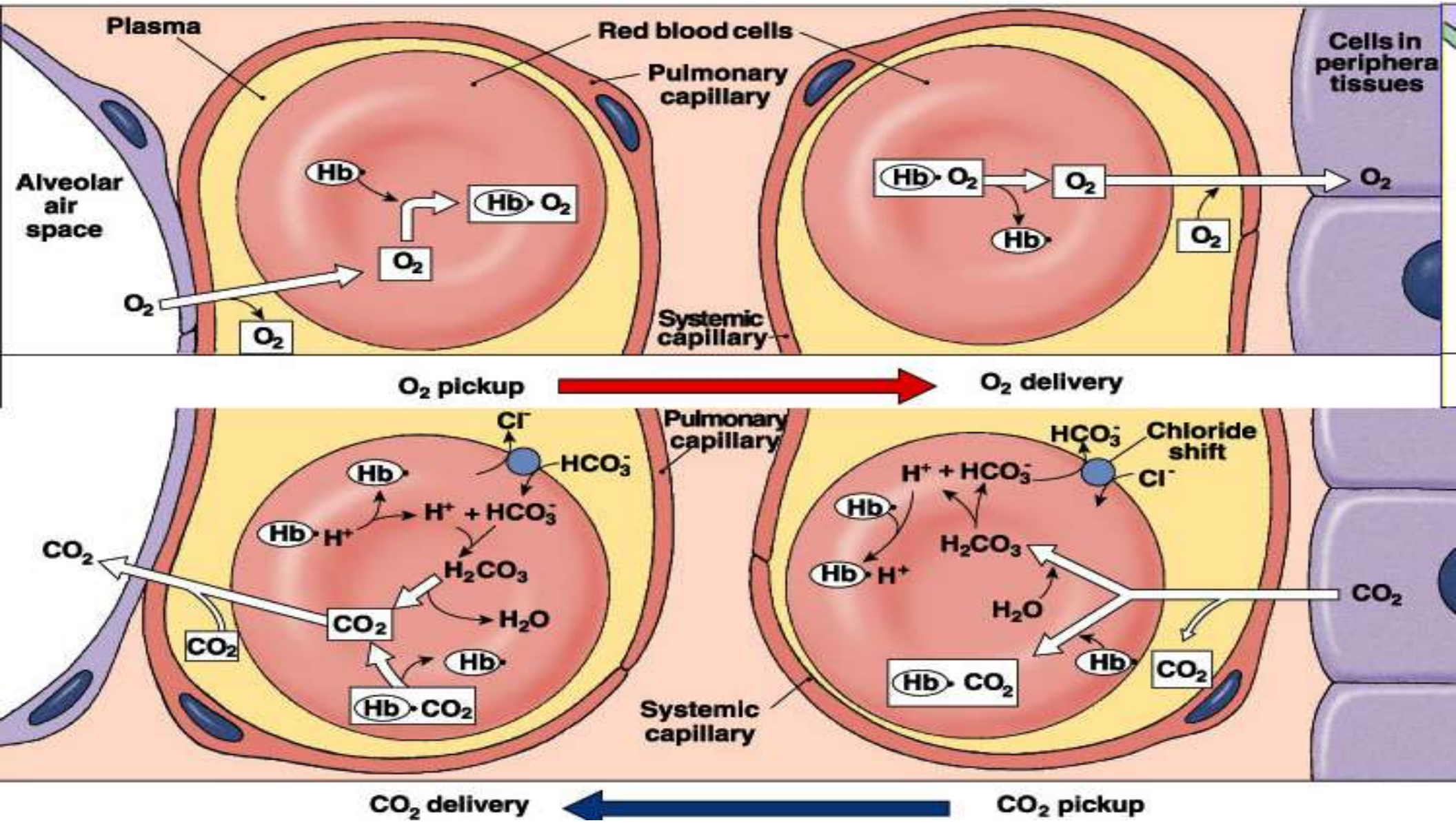
Oxygen Transport

Method	**Percentage**
Dissolved in Plasma	1.5 %
Combined with Hemoglobin	98.5 %

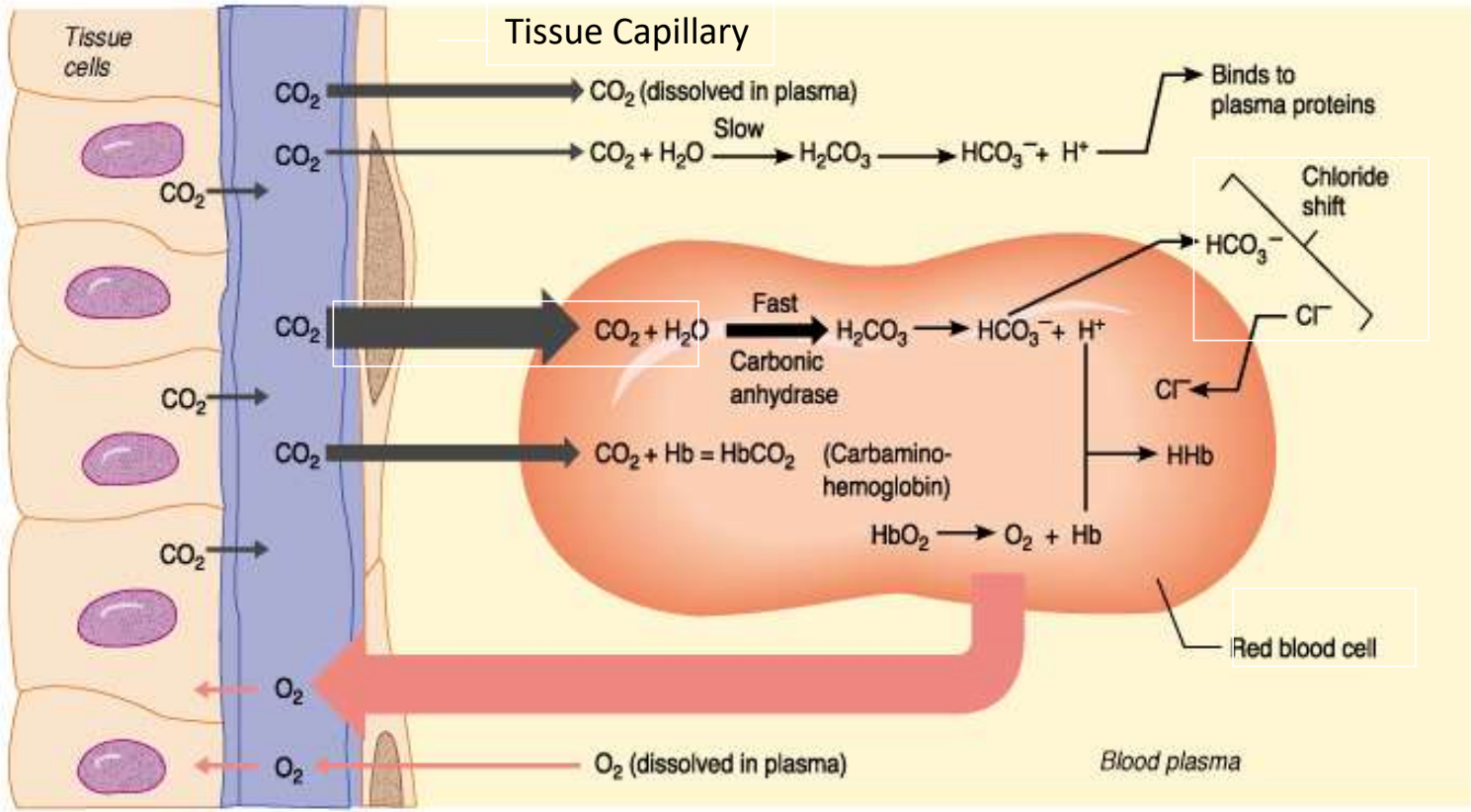


CO2 Transport and Cl- Movement



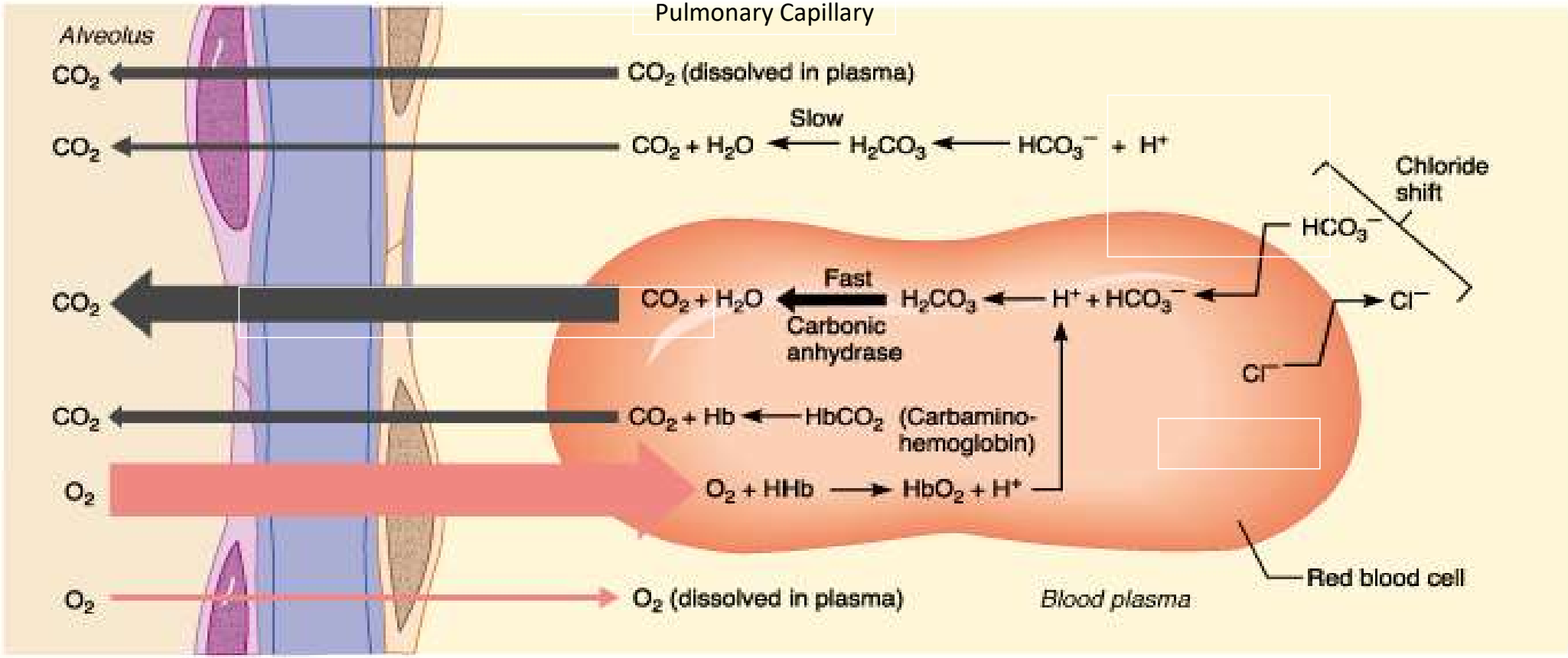

Plasma
Red blood cells
Pulmonary capillary
Cells in peripheral tissues
Alveolar air space
Hb
Hb·O2
O2
O2
O2
Hb·O2
O2
Hb
O2
O2
Systemic capillary
O2 pickup
O2 delivery
Cl-
HCO3-
Pulmonary capillary
HCO3-
Chloride shift
Hb
H+ + HCO3-
Cl-
Hb·H+
H+ + HCO3-
H2CO3
CO2
H2CO3
Hb·H+
H2O
CO2
CO2
CO2
Hb
Hb
Hb·CO2
Hb·CO2
CO2
Systemic capillary
CO2 delivery
CO2 pickup

Chloride Shift in Tissue Capillaries

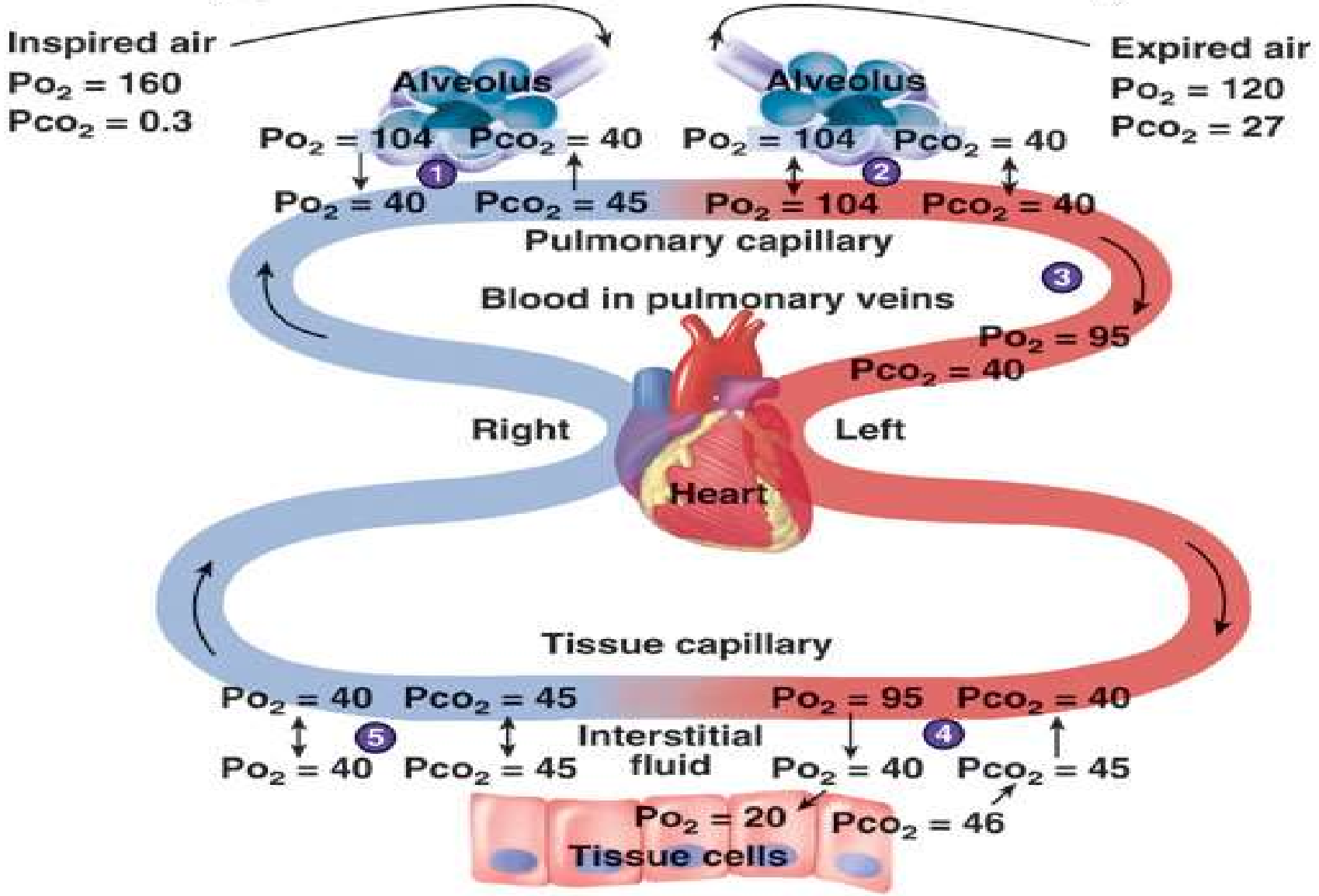


(a) Oxygen release and carbon dioxide pickup at the tissues

Chloride Shift in Pulmonary Capillaries

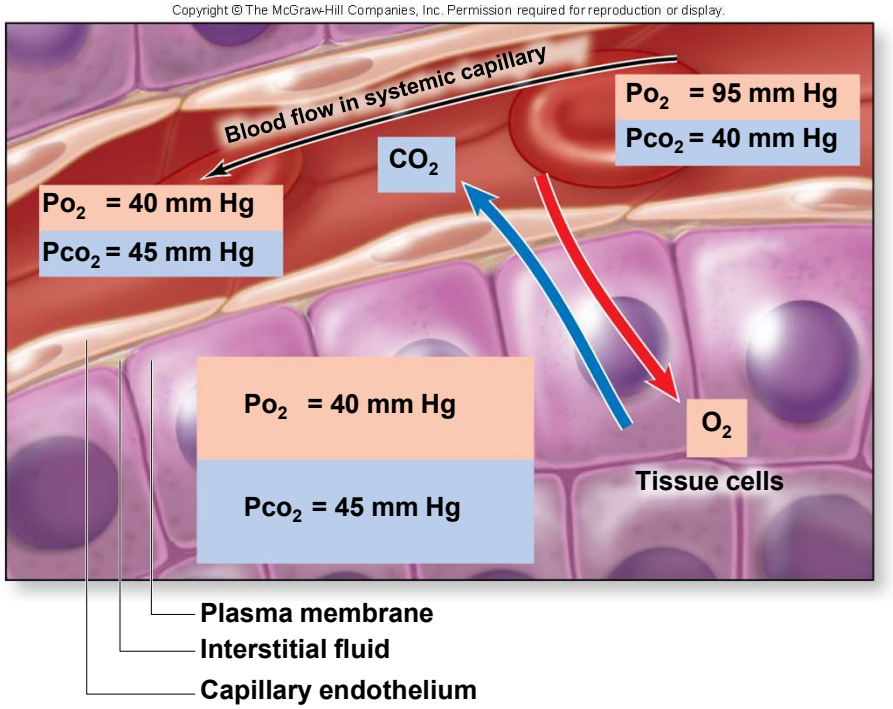


(b) Oxygen pickup and carbon dioxide release in the lungs



Respiration—Alveolar and Systemic Gas Exchange: Systemic Gas Exchange

- Carbon dioxide
  - Diffuses from systemic cells to blood
  - Partial pressure gradient driving process
    - PCO_2 in systemic cells 45mm Hg
    - PCO_2 in systemic capillaries 40 mm Hg
  - Diffusion continuing until blood PCO_2 is 45 mm Hg

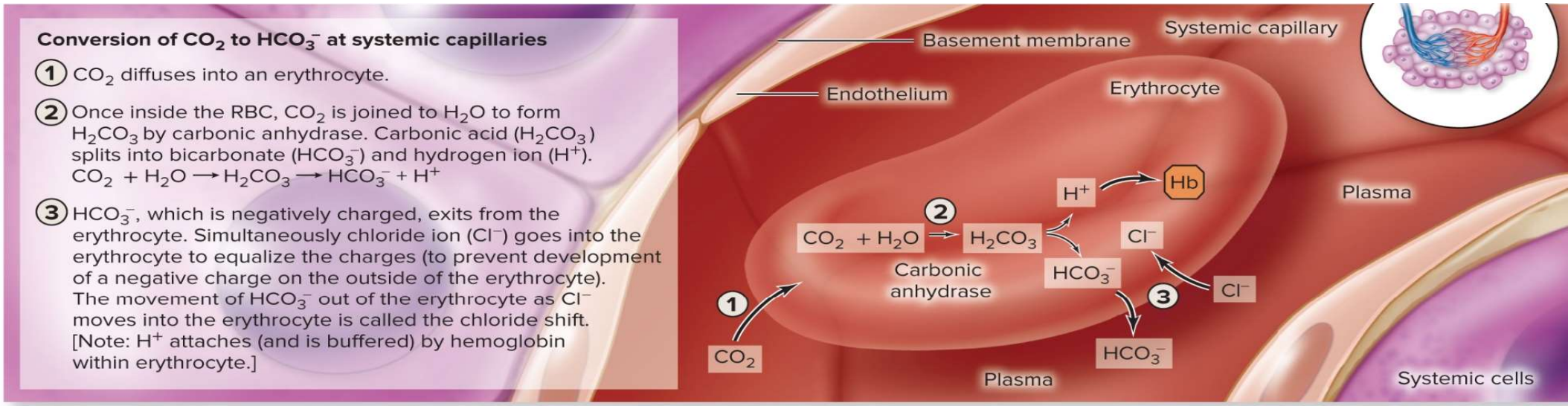


(c) Systemic gas exchange

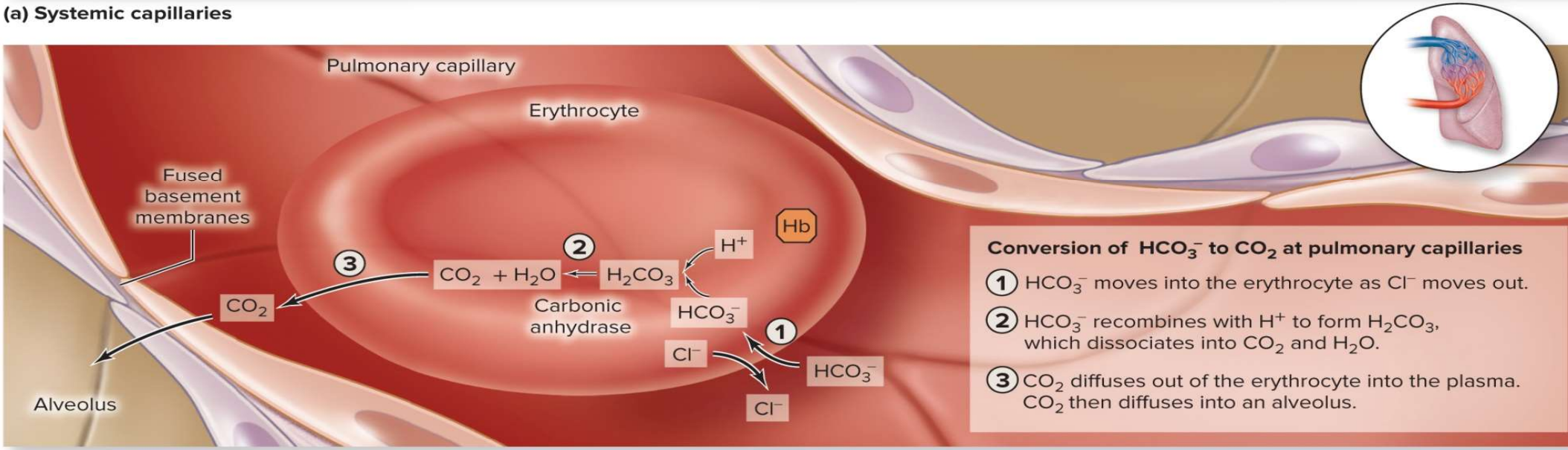
Table 23.5 Gas Exchange[1]

Characteristic	Alveolar Gas Exchange	Systemic Gas Exchange
Definition	Exchange of respiratory gases between alveoli in lungs and blood in pulmonary capillaries	Exchange of respiratory gases between systemic cells and blood in systemic capillaries
Changes in Blood Po_2	Blood Po_2 increases from 40 to 104 mm Hg	Blood Po_2 decreases from 95 to 40 mm Hg
Changes in Blood Pco_2	Blood Pco_2 decreases from 45 to 40 mm Hg	Blood Pco_2 increases from 40 to 45 mm Hg

1. General Conditions: Location is at sea level and individual is at rest



(a) Systemic capillaries



(b) Pulmonary capillaries

Respiration—Gas Transport:
Oxygen Transport

How is the majority of carbon dioxide transported within the blood?

As bicarbonate dissolved in the blood plasma

Respiration—Gas Transport:
Oxygen Transport

Why is such a small percentage of oxygen dissolved in plasma and most transported on hemoglobin?

Because oxygen's solubility coefficient is very low, and not much dissolves in the plasma.

Respiration—Alveolar and Systemic Gas Exchange: Alveolar Gas Exchange

How do the partial pressure of oxygen and carbon dioxide in blood change during systemic gas exchange?

Oxygen levels decrease from 95 to 40 mm Hg.
Carbon dioxide levels increase from 40 to 45 mm Hg.

Pulmonary vascular resistance

$$PVR = \frac{P_{\text{pulm artery}} - P_{\text{L atrium}}}{\text{cardiac output}}$$

Remember: $\Delta P = Q \times R$, so $R = \Delta P / Q$

$R = 8\eta l / \pi r^4$

$P_{\text{pulm artery}}$ = pressure in pulmonary artery
$P_{\text{L atrium}} \approx$ pulmonary capillary wedge pressure
Q = cardiac output (flow)
R = resistance
η = viscosity of blood
l = vessel length
r = vessel radius

Alveolar gas equation

$$P_{A}O_2 = PIO_2 - \frac{PaCO_2}{R}$$

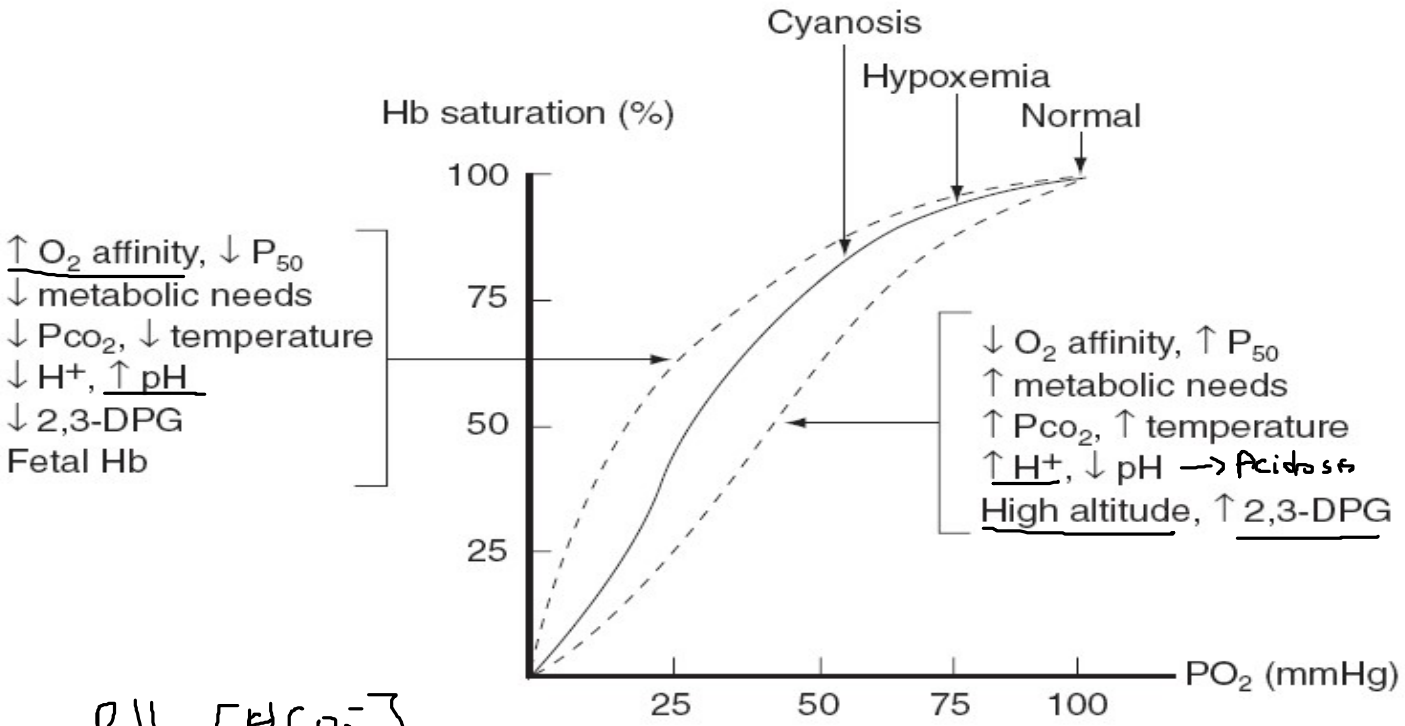
$$\approx 150 \text{ mm Hg}^{a} - \frac{PaCO_2}{0.8}$$

[a]At sea level breathing room air

$P_{A}O_2$ = alveolar P_{O_2} (mm Hg)
PIO_2 = P_{O_2} in inspired air (mm Hg)
$PaCO_2$ = arterial P_{CO_2} (mm Hg)
R = respiratory quotient = CO_2 produced/O_2 consumed
A-a gradient = $P_{A}O_2 - PaO_2$. Normal range = 10–15 mm Hg
↑ A-a gradient may occur in hypoxemia; causes include shunting, $\dot{V}/\dot{Q}$ mismatch, fibrosis (impairs diffusion)

Oxygen-hemoglobin dissociation curve

2,3-Diphosphoglycerate (2,3-DPG) is a special intermediate of **glycolysis** in erythrocytes which is rapidly consumed under conditions of normal oxygen tension.
However, when hypoxia is encountered in peripheral tissues, the concentration of 2,3-DPG can accumulate to significant levels within hours.



$$pH = \frac{[HCO_3^-]}{[CO_2]}$$
$$[H^+]$$

Sigmoidal shape due to positive cooperativity, i.e., hemoglobin can bind 4 oxygen molecules and has higher affinity for each subsequent oxygen molecule bound.

When curve shifts to the right, ↓ affinity of hemoglobin for O_2 (facilitates unloading of O_2 to tissue).

An ↑ in all factors (except pH) causes a shift of the curve to the right.

A ↓ in all factors (except pH) causes a shift of the curve to the left.

Fetal Hb has a higher affinity for oxygen than adult Hb, so its dissociation curve is shifted left.

Right shift—**CADET** face **right**:

CO_2
Acid/Altitude
DPG (2,3-DPG)
Exercise
Temperature

Respiration—Gas Transport:
Hemoglobin as a Transport Molecule

How is oxygen released from hemoglobin during systemic gas exchange altered by temperature? By 2,3-BPG? By hydrogen ions? By CO2?

Increased temperature, increased 2,3-BPG, increased hydrogen ions, and increased CO_2 all cause greater oxygen release from hemoglobin.

- P_{50} is PO_2 at which hemoglobin is 50% saturated
- ↑ P_{50} → ↓ hemoglobin affinity for O_2
- 50% saturation achieved at higher-than-normal P_{50}
- ↓ P_{50} → ↑ hemoglobin affinity for O_2
- 50% saturation achieved at lower-than-normal P_{50}

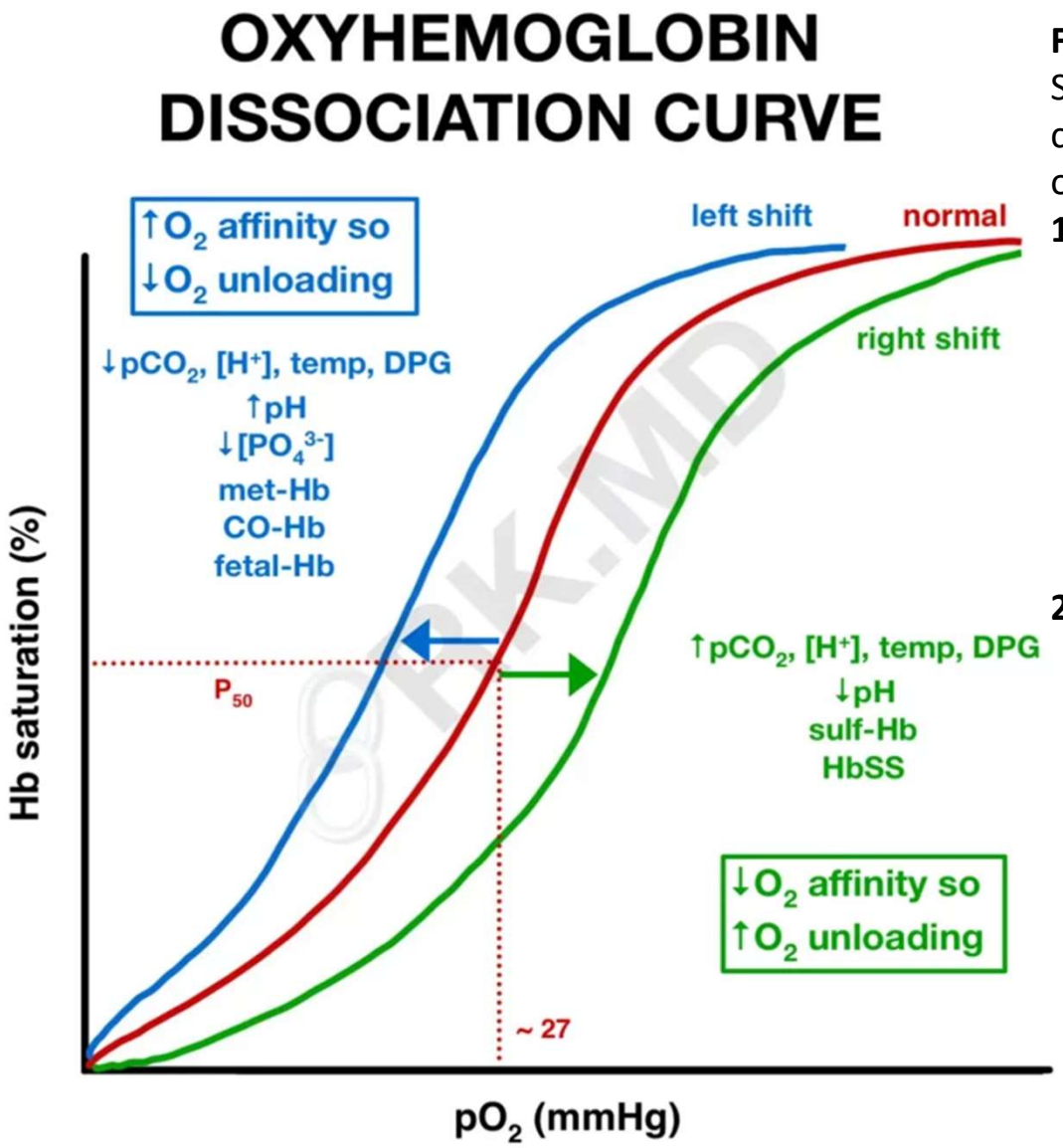
Loading and unloading of oxygen

-in lungs

- PaO_2 ≈ 100 mm Hg
- hemoglobin % saturation ≈ 100%
- facilitates maximal O_2 loading into arterial blood in lungs

-in peripheral tissues

- PvO_2 ≈ 40 mm Hg
- hemoglobin % saturation ≈ 75%
- facilitates O_2 unloading into peripheral tissues



Factors Influencing the Curve

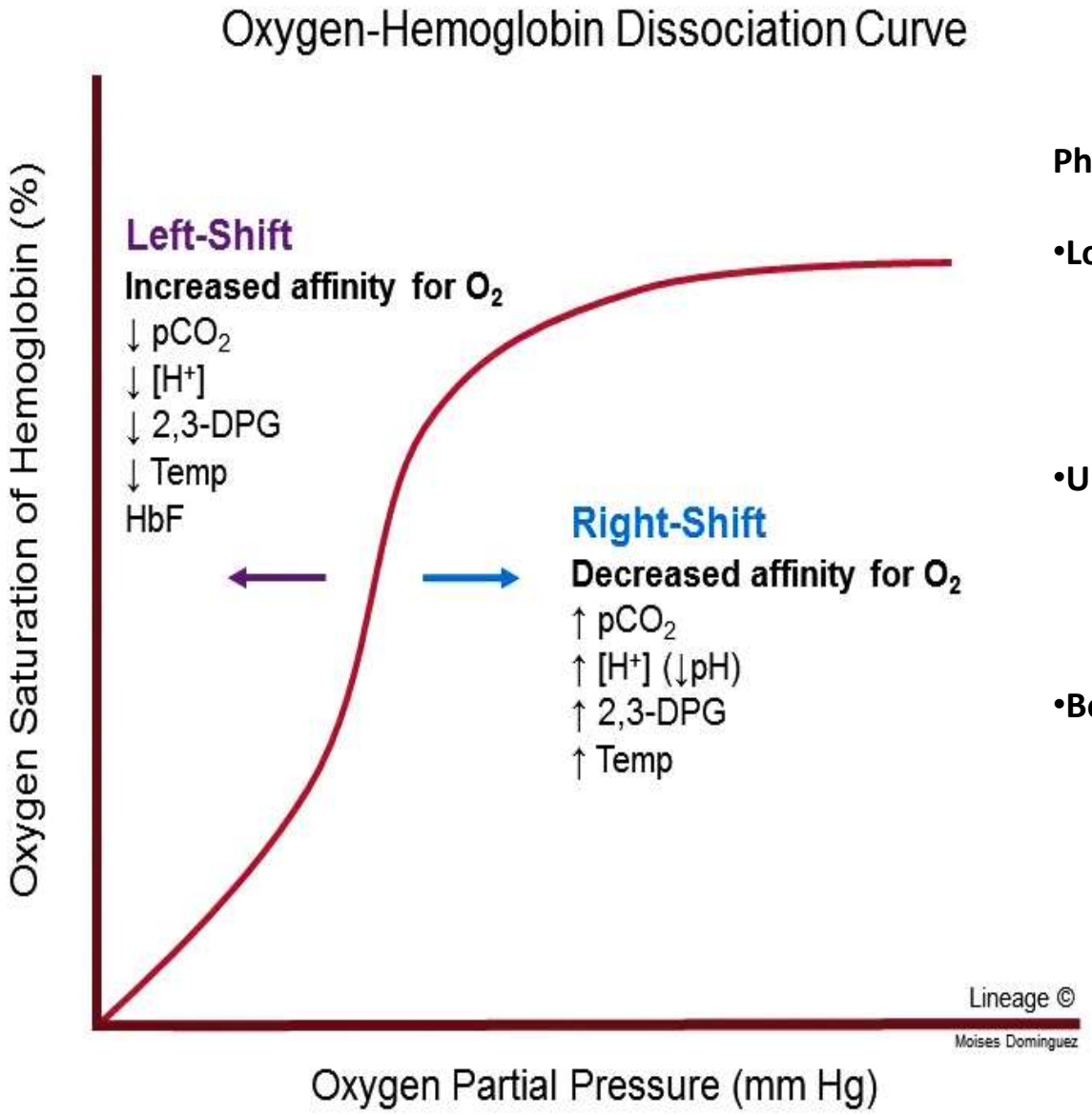
Several factors can shift the oxygen-hemoglobin dissociation curve to the right or left, affecting hemoglobin's affinity for oxygen:

1.Right Shift:

1. **Decreased Affinity:** Hemoglobin releases oxygen more readily.
2. **Factors:**
    1. Increased CO_2 (Bohr effect)
    2. Increased H^+ concentration (lower pH, acidosis)
    3. Increased temperature
    4. Increased 2,3-bisphosphoglycerate (2,3-BPG) levels

2.Left Shift:

1. **Increased Affinity:** Hemoglobin holds on to oxygen more tightly.
2. **Factors:**
    1. Decreased CO_2
    2. Decreased H^+ concentration (higher pH, alkalosis)
    3. Decreased temperature
    4. Decreased 2,3-BPG levels
    5. Presence of fetal hemoglobin (HbF), which has a higher affinity for oxygen than adult hemoglobin (HbA)



Physiological Importance

•Loading in Lungs:

- At the high pO_2 in the alveoli (around 100 mmHg), hemoglobin becomes almost fully saturated with oxygen.

•Unloading in Tissues:

- At the lower pO_2 in tissues (around 40 mmHg or lower during exercise), hemoglobin releases oxygen where it is needed most.

•Bohr Effect:

- In tissues with high metabolic activity, increased CO_2 and H^+ (resulting from metabolism) cause a right shift, promoting oxygen release.

Bohr Effect Explained

1.Mechanism:

1. The Bohr Effect refers to the shift in the oxygen-hemoglobin dissociation curve in response to changes in pH and CO_2 levels.
2. In conditions where CO_2 is high and pH is low (acidic environment), the oxygen-hemoglobin dissociation curve shifts to the right.
3. This shift decreases hemoglobin's affinity for oxygen, promoting oxygen release to tissues that need it most.

Physiological Relevance:

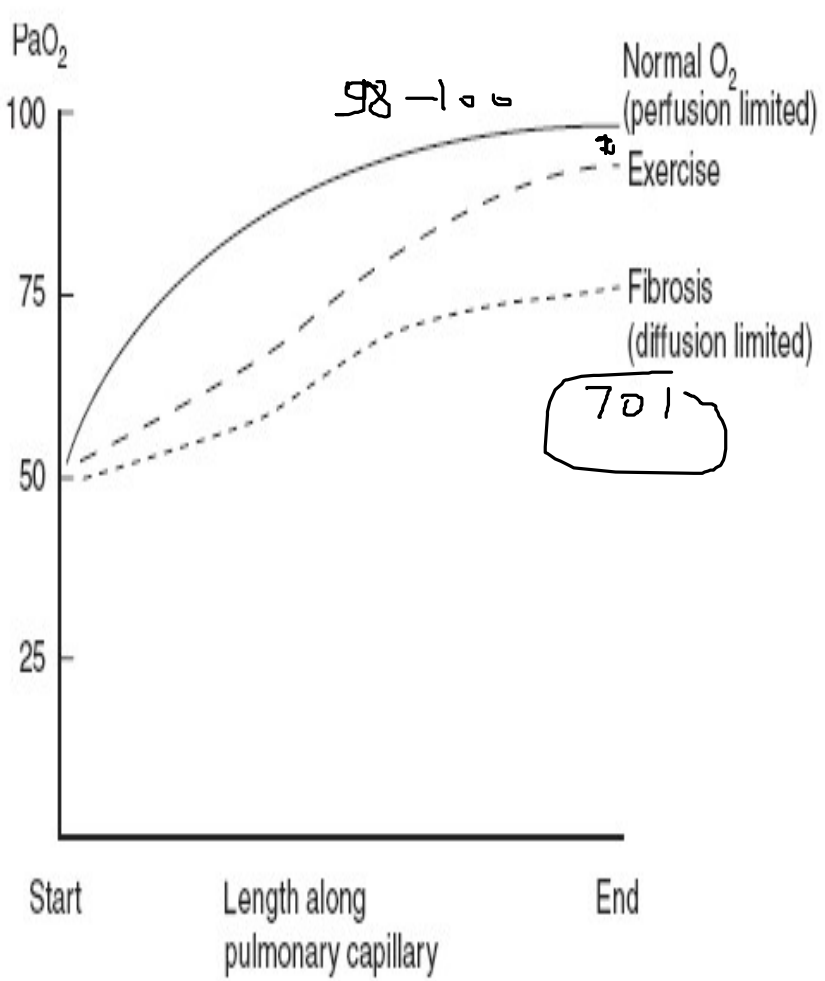
•**Tissue Level:**

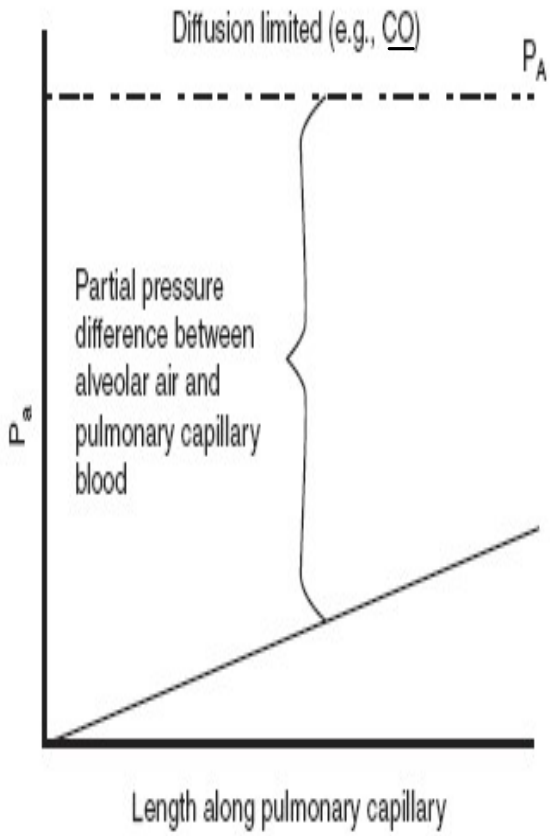
- **Active tissues produce more CO_2 and H^+ ions** (lowering pH) due to increased metabolic activity.
- The rightward shift facilitates more oxygen being released from hemoglobin, thus supplying active tissues with the oxygen they need.

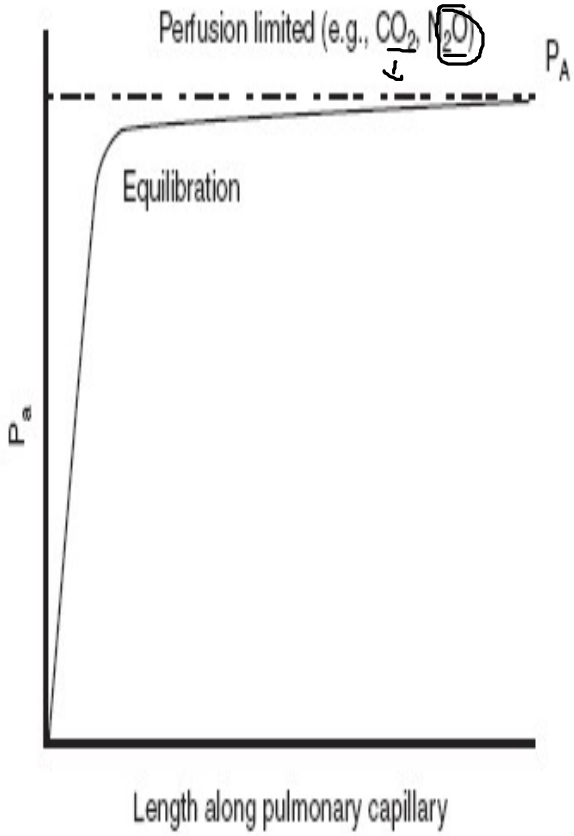
•**Lung Level:**

- In the lungs, **where CO_2 is expelled and pH is higher** (more basic environment**), the curve shifts to the left**.
- This leftward shift increases hemoglobin's affinity for oxygen, enhancing oxygen uptake in the lungs.

Pulmonary circulation	Normally a low-resistance, high-compliance system. P_{O_2} and P_{CO_2} exert opposite effects on pulmonary and systemic circulation. A ↓ in Pa_{O_2} causes a hypoxic vasoconstriction that shifts blood away from poorly ventilated regions of lung to well-ventilated regions of lung. 1. Perfusion limited—O_2 (normal health), CO_2, N_2O. Gas equilibrates early along the length of the capillary. Diffusion can be ↑ only if blood flow ↑. 2. Diffusion limited—O_2 (emphysema, fibrosis), CO. Gas does not equilibrate by the time blood reaches the end of the capillary.	A consequence of pulmonary hypertension is cor pulmonale and subsequent right ventricular failure (jugular venous distention, edema, hepatomegaly).







P_a = partial pressure of gas in pulmonary capillary blood
P_A = partial pressure of gas in alveolar air

Pulmonary vascular resistance (PVR)

$$PVR = \frac{P_{pulm\ artery} - P_{L\ atrium}}{Cardiac\ output}$$

Remember: $\Delta P = Q \times R$, so $R = \Delta P / Q$.

$R = 8\eta l / \pi r^4$

$P_{pulm\ artery}$ = pressure in pulmonary artery.

$P_{L\ atrium}$ = pulmonary wedge pressure.

η = the viscosity of inspired air;

l = airway length;

r = airway radius.

Oxygen content of blood

O_2 content = (O_2 binding capacity × % saturation) + dissolved O_2.

Normally 1 g Hb can bind 1.34 mL O_2; normal Hb amount in blood is 15 g/dL.

Cyanosis results when Hb is < 5 g/dL.

O_2 binding capacity ≈ 20.1 mL O_2 / dL.

O_2 content of arterial blood ↓ as Hb falls, but O_2 saturation and arterial P_{O_2} do not.

Arterial P_{O_2} ↓ with chronic lung disease because physiologic shunt ↓ O_2 extraction ratio.

Oxygen delivery to tissues = cardiac output × oxygen content of blood.

Alveolar gas equation

$$PAO_2 = PIO_2 - \frac{PACO_2}{R}$$

- Can normally be approximated:

$$PAO_2 = 150 - PaCO_2 / 0.8$$

PAO_2 = alveolar PO_2 (mmHg).

PIO_2 = PO_2 in inspired air (mmHg).

$PACO_2$ = alveolar PCO_2 (mmHg).

R = respiratory quotient.

A-a gradient = $PAO_2 - PaO_2$ = 10–15 mmHg.

↑ A-a gradient may occur in hypoxemia; causes include shunting, V/Q mismatch, fibrosis (diffusion block).

	Hb CONCENTRATION	% O_2 SAT OF Hb	DISSOLVED O_2 (Pao_2)	TOTAL O_2 CONTENT
CO poisoning	Normal	↓ (CO competes with O_2)	Normal	↓
Anemia	↓	Normal	Normal	↓
Polycythemia	↑	Normal	Normal	↑

V/Q mismatch

Ideally, ventilation is matched to perfusion (i.e., $V/Q = 1$) in order for adequate gas exchange to occur.

Lung zones:

1. Apex of the lung—$V/Q = 3$ (wasted ventilation)
2. Base of the lung—$V/Q = 0.6$ (wasted perfusion)

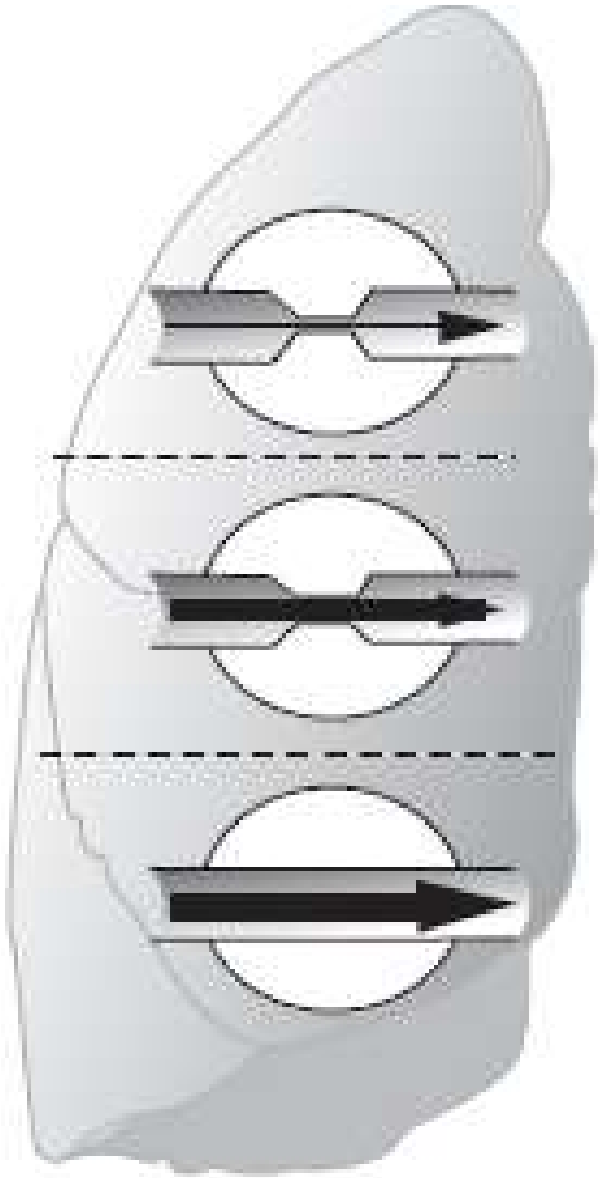
Both ventilation and perfusion are greater at the base of the lung than at the apex of the lung.

With exercise (↑ cardiac output), there is vasodilation of apical capillaries, resulting in a V/Q ratio that approaches 1.

Certain organisms that thrive in high O_2 (e.g., TB) flourish in the apex.

$V/Q \rightarrow 0$ = airway obstruction (shunt). In shunt, 100% O_2 does not improve P_{O_2}.

$V/Q \rightarrow \infty$ = blood flow obstruction (physiologic dead space). Assuming < 100% dead space, 100% O_2 improves P_{O_2}.

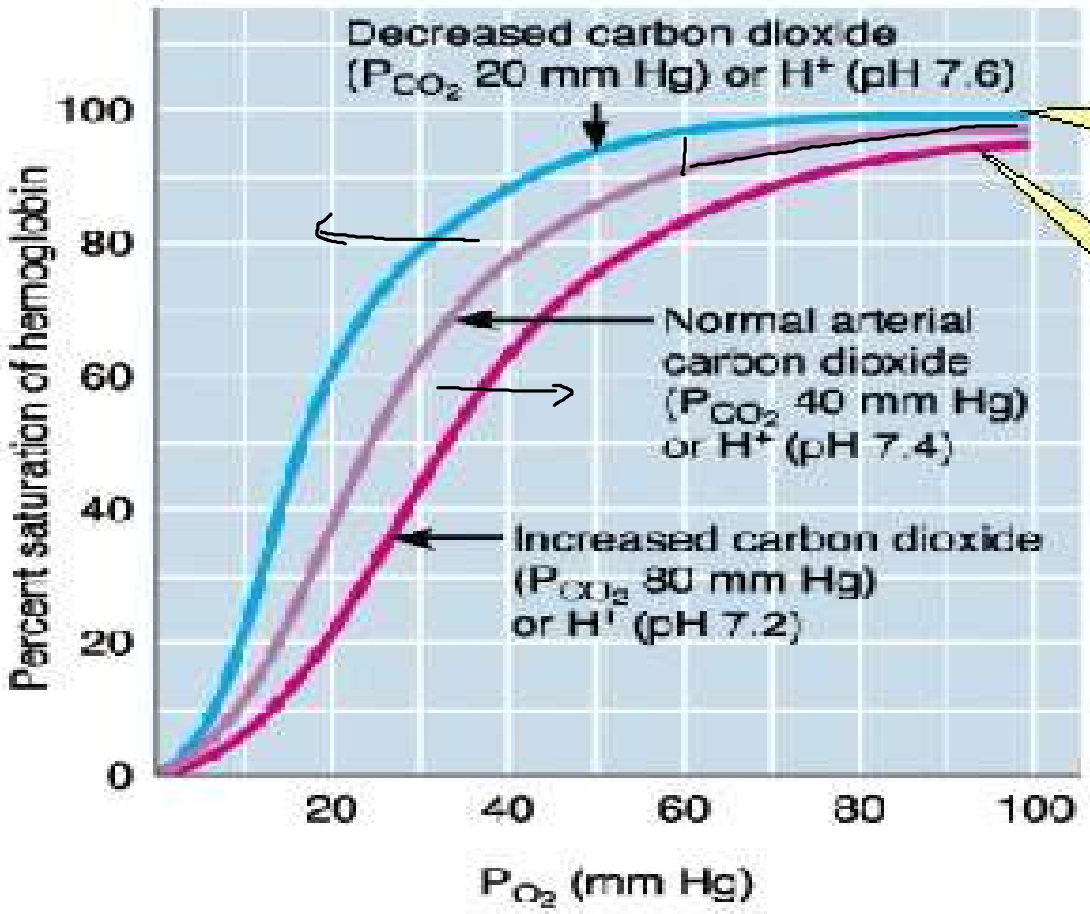


Apex: $P_A > P_a > P_v \rightarrow V/Q = 3$
(wasted ventilation)

$P_a > P_A > P_v$

Base: $P_a > P_v > P_A \rightarrow V/Q = 0.6$
(wasted perfusion); NOTE: both ventilation and perfusion are greater at the base of the lung than at the apex

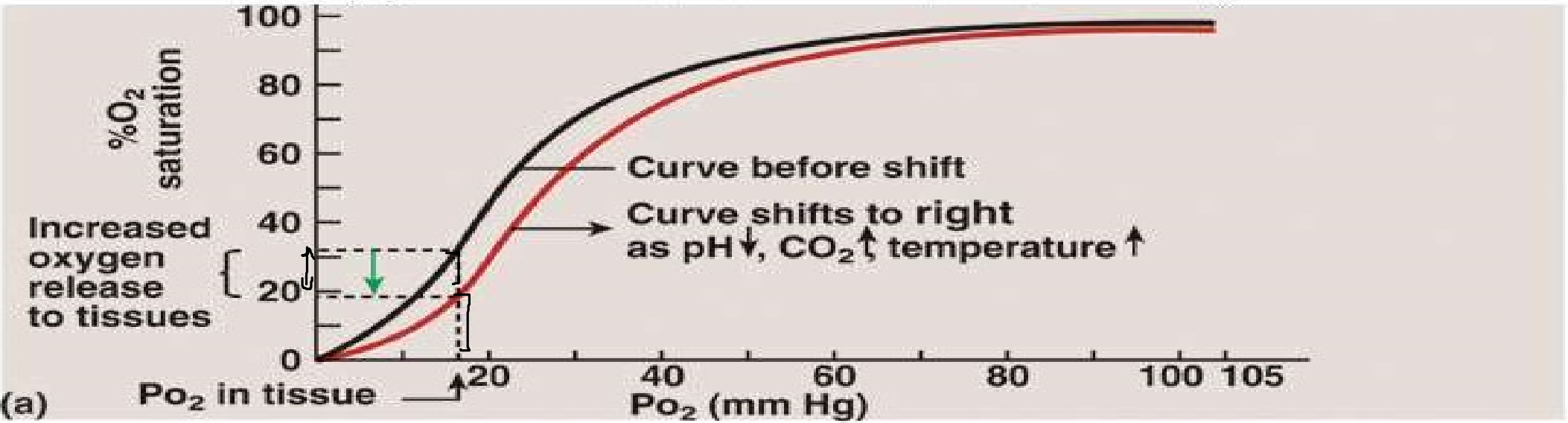
Effect of pH on Respiration

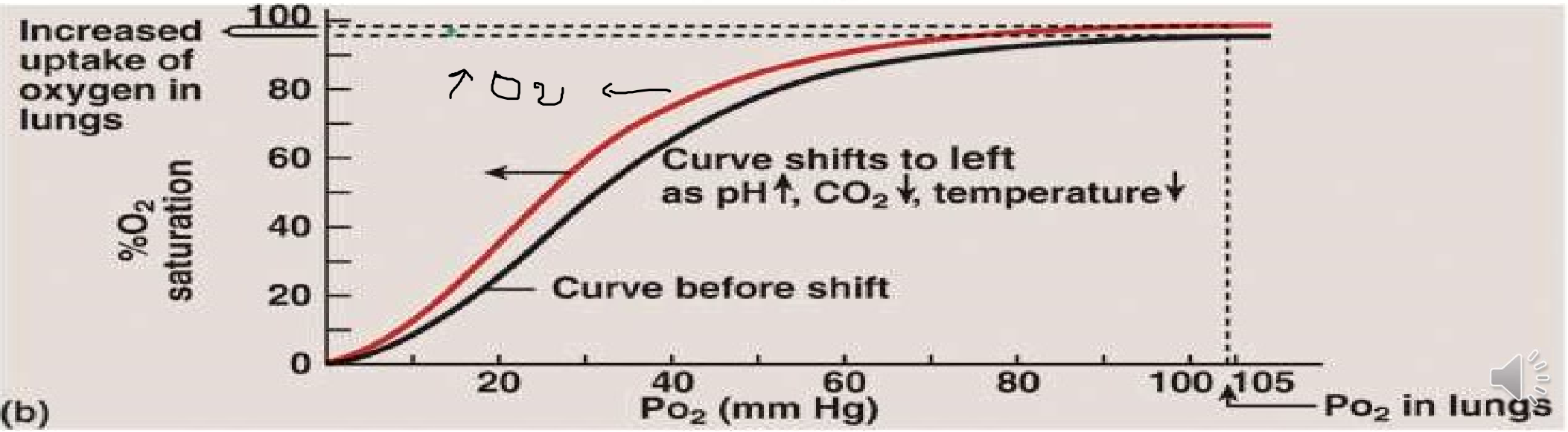


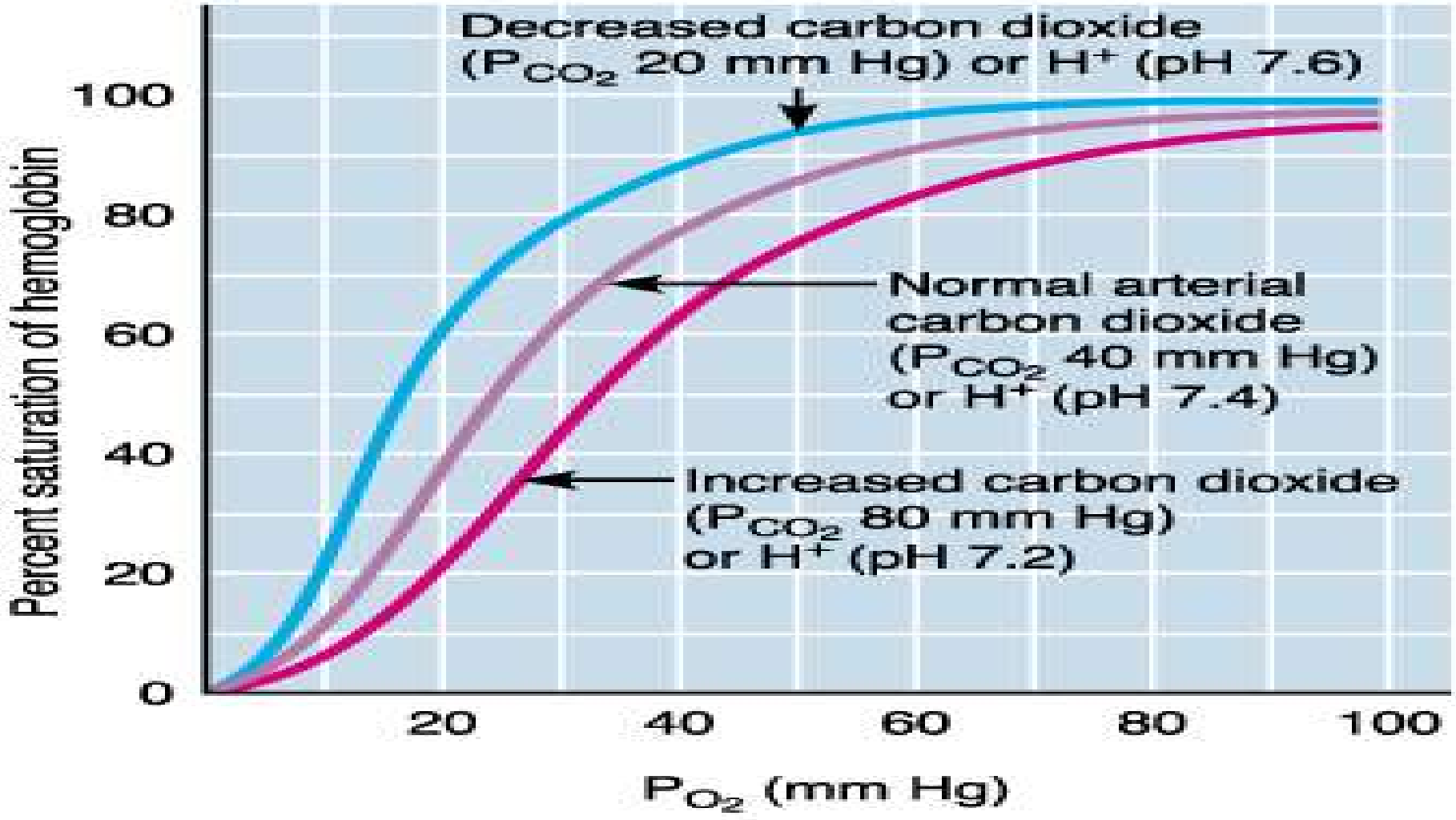
(b)

↑ pH resulting from ↓CO2 or H+ increases the association of oxygen with hemoglobin.

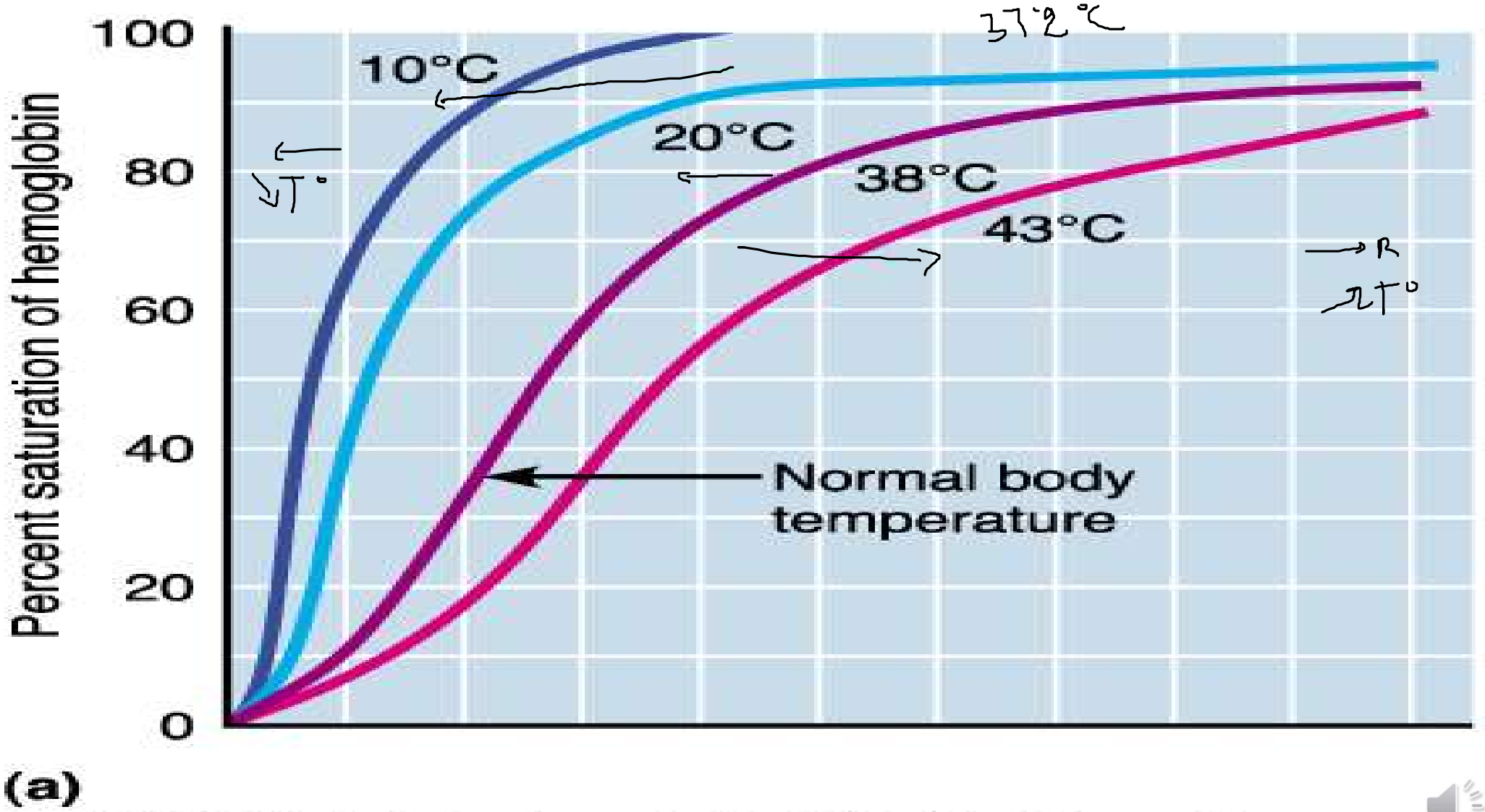
↓ pH resulting from ↑CO2 or H+ decreases the association of oxygen with hemoglobin.



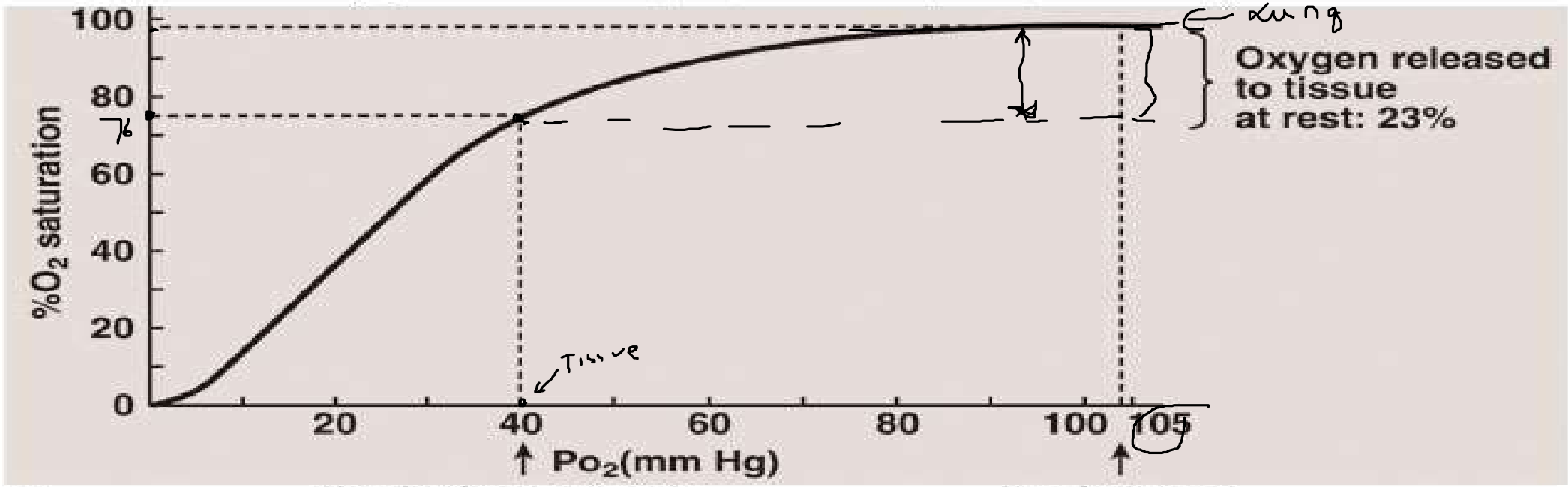




(b)



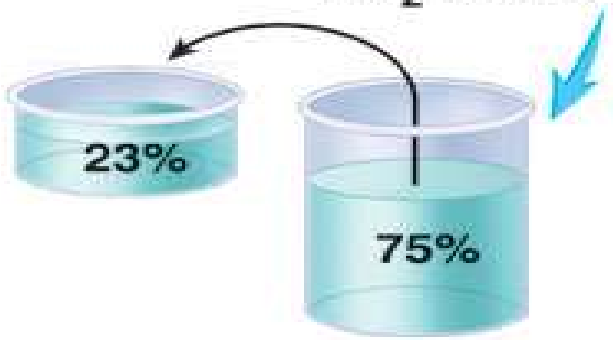
(a)



(a)

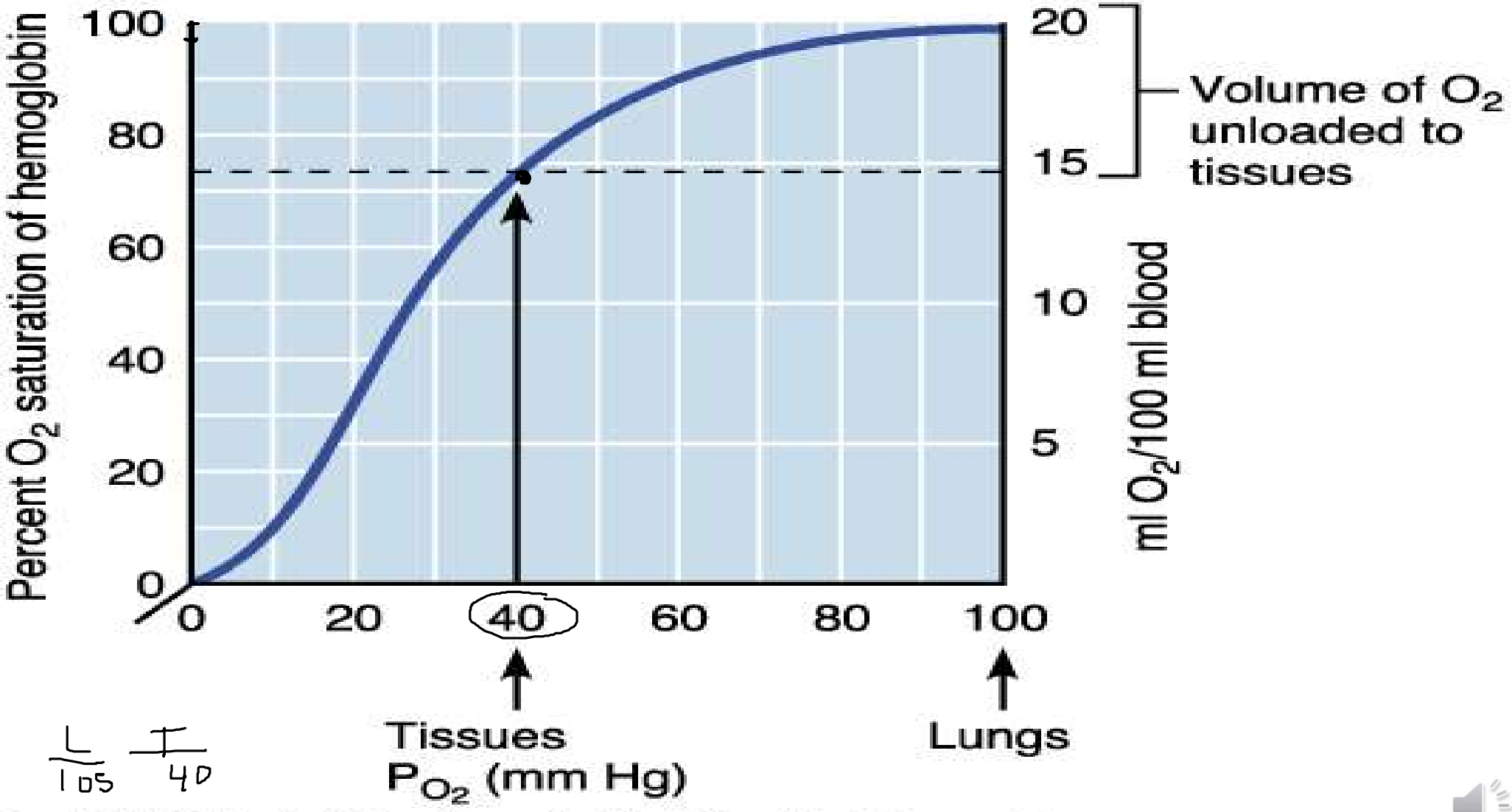
Po_2 in tissue at rest

Po_2 in lungs



(b) In resting tissues, hemoglobin releases some oxygen, which is like partially emptying the glass.

Hemoglobin saturated with oxygen in the lungs is like a nearly full glass.



Response to High Altitude

- increased Ventilation (EARLIEST CHANGE)
- increased Sensitivity of central receptors
- increased Response of carotid bodies
- increased Erythropoietin
- increased 2 3 DPG
- increased Mitochondria
- increased Renal excretion of Bicarbonate
- Respiratory alkalosis
- Pulmonary edema when occurs is due to increased pulmonary capillary pressure

•High altitude → ↓ atmospheric pressure (Patm) and ↓ alveolar PO_2

•Ventilation

- •↓ alveolar PO_2 → ↑ respiratory rate (hyperventilation)
- ↓ alveolar PO_2 stimulates peripheral chemoreceptors in aortic bodies and carotid bodies to instruct medullary inspiration center to increase respiratory rate

•Arterial blood

•↑ ventilation rate → ↑ PaO_2 and ↓ $PaCO_2$ → respiratory alkalosis

•A number of physiologic changes occur in a person living at high altitude.

- The diminished barometric pressure at high altitude
- causes alveolar hypoxia and arterial hypoxia.
- Pulmonary vasoconstriction occurs in response to alveolar hypoxia; therefore, the diameter of the pulmonary vessels would be greater in the brother living at sea level.
- Increased erythropoietin production , caused by arterial hypoxia, leads to increases in hematocrit in people living at high altitude

•Mitochondrial density increases in people chronically exposed to the hypoxemia caused by living at high altitude

•At high altitudes, the ventilation rate increases, causing a respiratory alkalosis.

The kidney then compensates by increasing the excretion of HCO3

•Increasing the rate of respiration is a very useful adaptation to the hypoxic conditions of high altitude. The primary stimulus is the hypoxic stimulation of peripheral chemoreceptors.

Oxygen deprivation

Hypoxia (↓ O_2 delivery to tissue)	Hypoxemia (↓ Pao_2)	Ischemia (loss of blood flow)
↓ cardiac output	Normal A-a gradient	Impeded arterial flow
Hypoxemia	▪ High altitude	↓ venous drainage
Anemia	▪ Hypoventilation (eg, opioid use)	
CO poisoning	↑ A-a gradient	
	▪ $\dot{V}/\dot{Q}$ mismatch	
	▪ Diffusion limitation (eg, fibrosis)	
	▪ Right-to-left shunt	

Response to high altitude

↓ atmospheric oxygen (PO_2) → ↓ Pa_{O_2} → ↑ ventilation → ↓ Pa_{CO_2} → respiratory alkalosis → altitude sickness.

Chronic ↑ in ventilation.

↑ erythropoietin → ↑ Hct and Hb (due to chronic hypoxia).

↑ 2,3-BPG (binds to Hb causing left shift so that Hb releases more O_2).

Cellular changes (↑ mitochondria).

↑ renal excretion of HCO_3^- to compensate for respiratory alkalosis (can augment with acetazolamide).

Chronic hypoxic pulmonary vasoconstriction results in pulmonary hypertension and RVH.

Response to exercise

↑ CO_2 production.

↑ O_2 consumption.

↑ ventilation rate to meet O_2 demand.

$\dot{V}/\dot{Q}$ ratio from apex to base becomes more uniform.

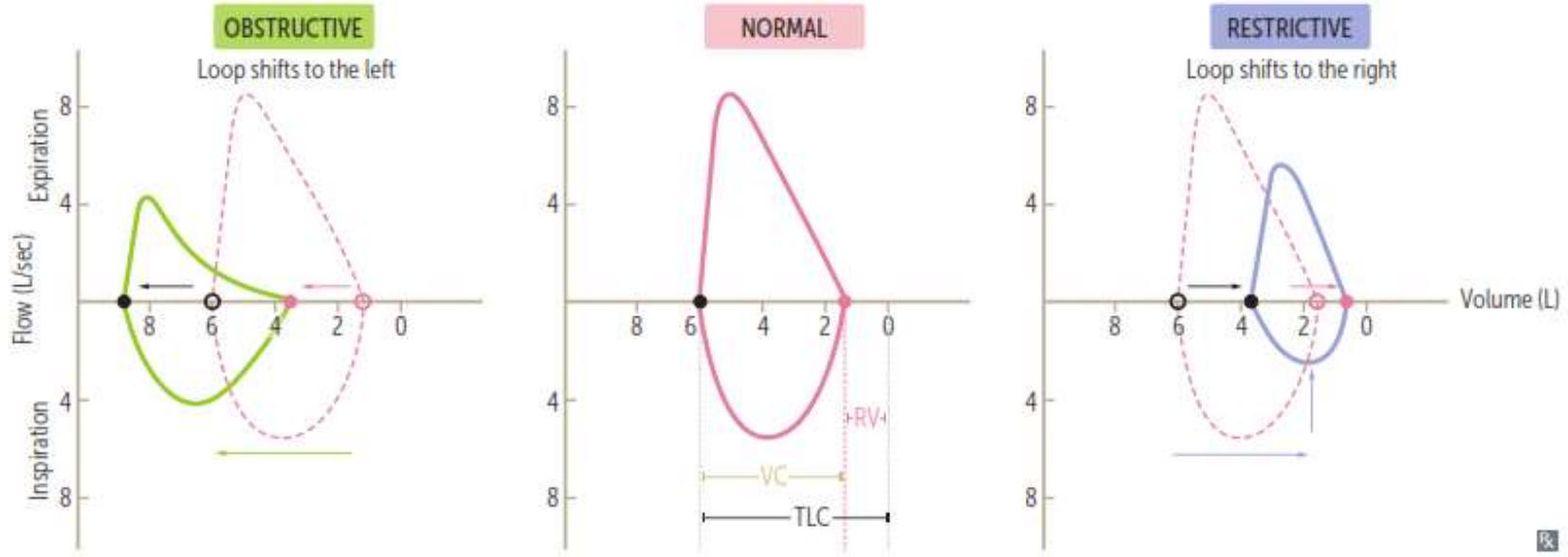
↑ pulmonary blood flow due to ↑ cardiac output.

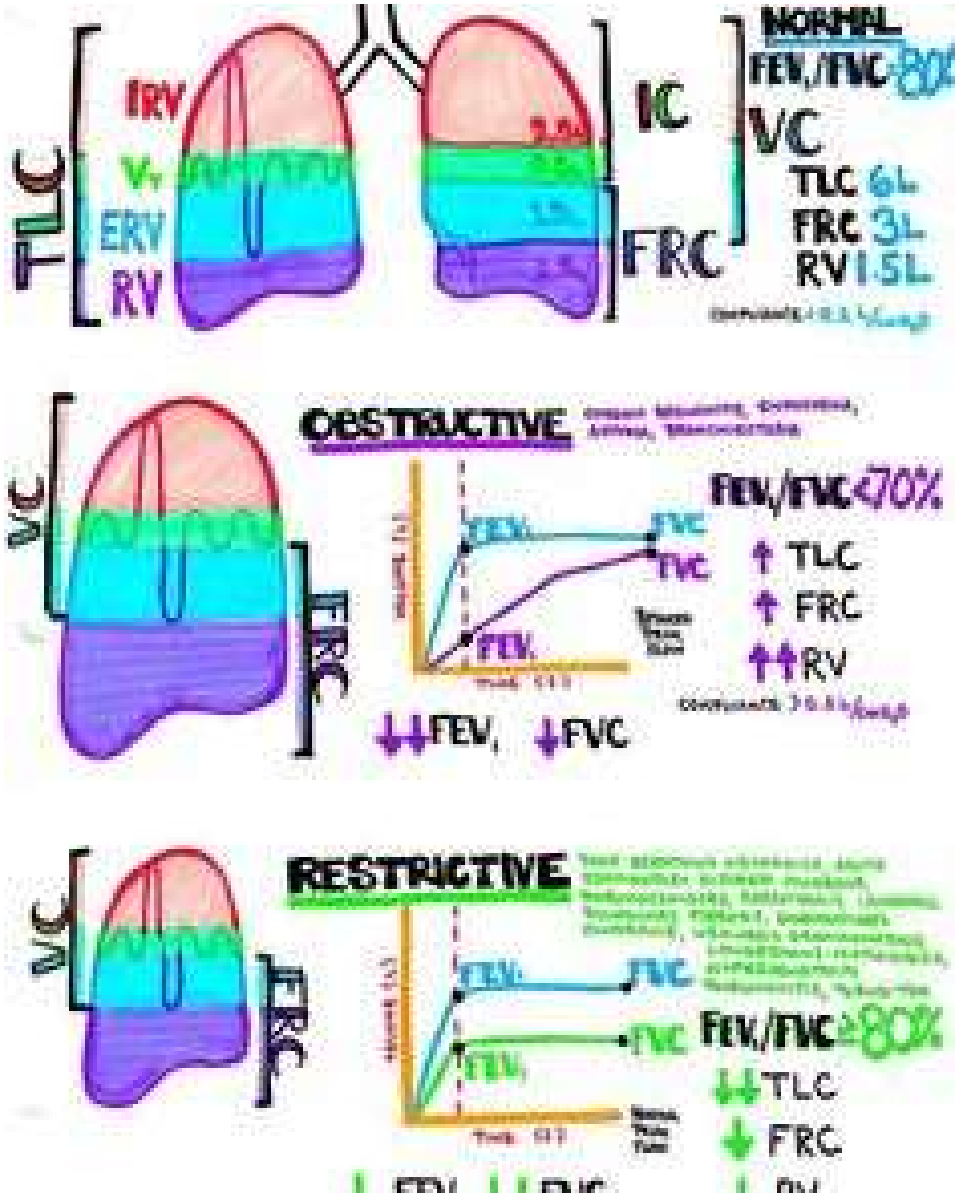
↓ pH during strenuous exercise (2° to lactic acidosis).

No change in Pa_{O_2} and Pa_{CO_2}, but ↑ in venous CO_2 content and ↓ in venous O_2 content.

Flow-volume loops

FLOW-VOLUME PARAMETER	Obstructive lung disease	Restrictive lung disease
RV	↑	↓
FRC	↑	↓
TLC	↑	↓
FEV_1	↓↓	↓
FVC	↓	↓
FEV_1/FVC	↓ FEV_1 decreased more than FVC	Normal or ↑ FEV_1 decreased proportionately to FVC




NORMAL
FEV1/FVC 80%
IRV
VT
ERV
RV
TLC
IC
FRC
VC
TLC 6L
FRC 3L
RV 1.5L
OBSTRUCTIVE
FEV1/FVC <70%
FEV1
FVC
↑ TLC
↑ FRC
↑↑ RV
↓↓FEV1 ↓FVC
RESTRICTIVE
FEV1/FVC ≥80%
↓↓TLC
↓ FRC

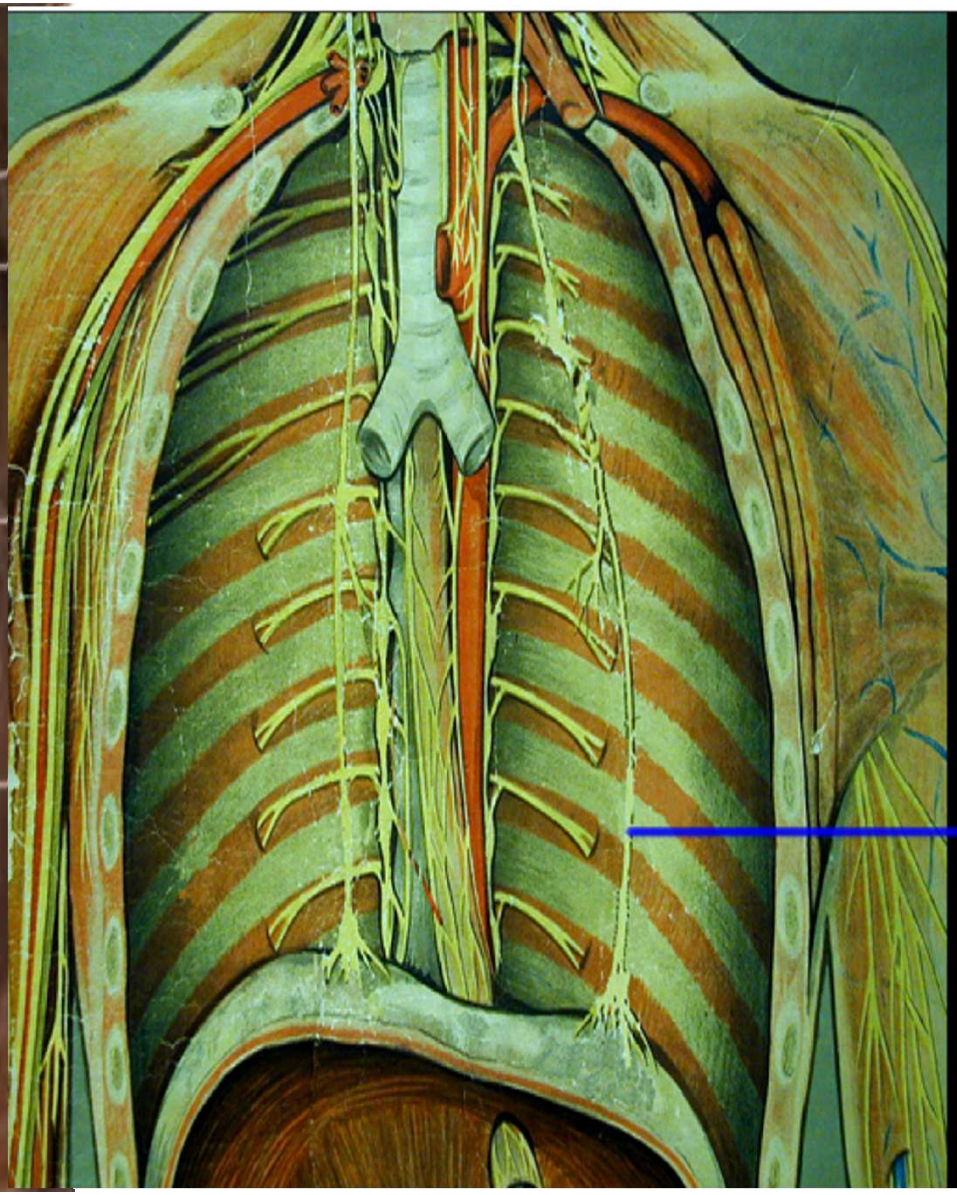
Categories of Disease

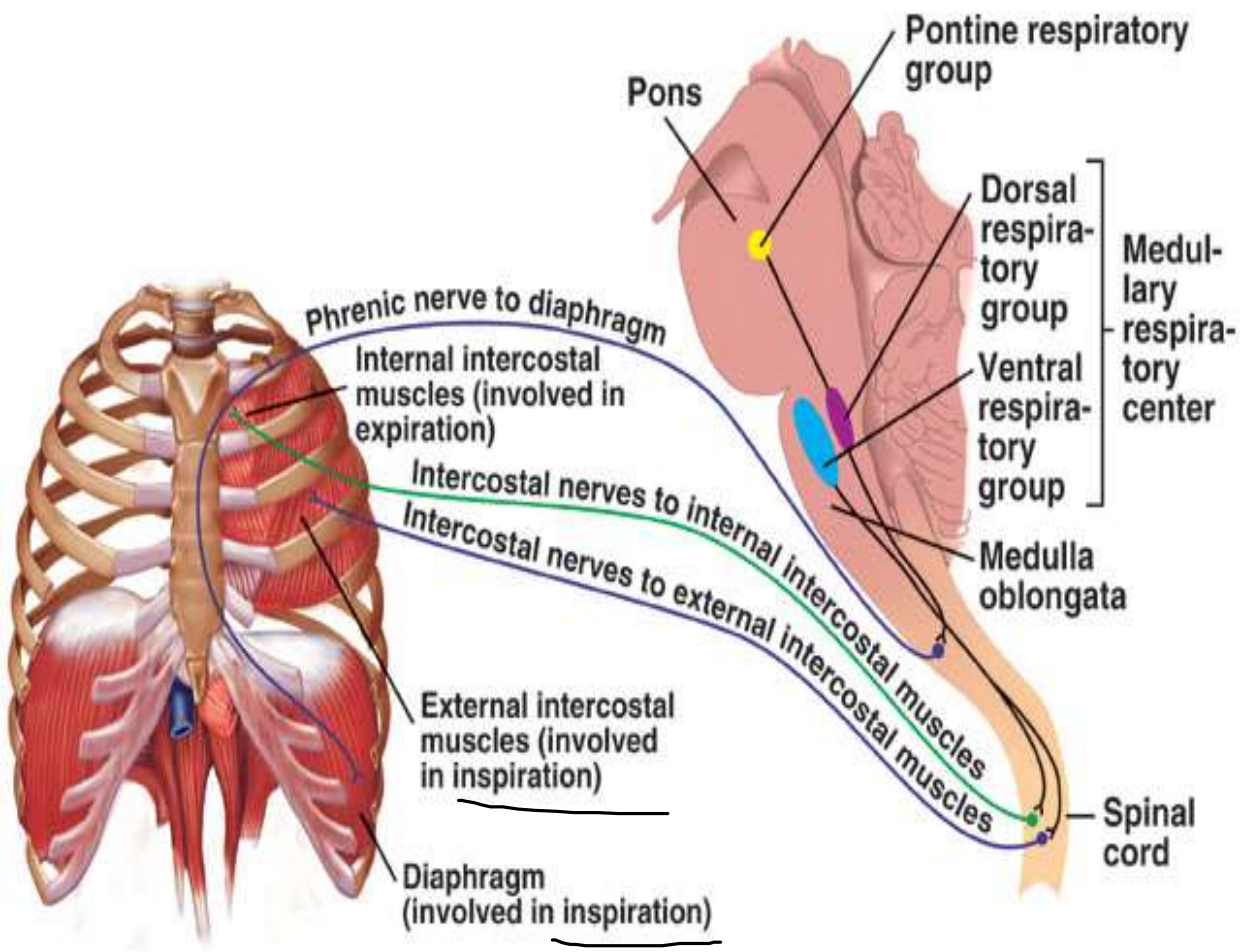
	OBSTRUCTIVE	MIXED	RESTRICTIVE
FEV1/FVC	↓70%	↓ 70-79%	Normal or ↑
FEV1	↓(marked)	↓	Normal or ↓(slight)
FVC	Normal or ↓	↓	↓
PEFR	↓	↓	N or ↑ with linear decrease in flow versus lung volume
MVV	↓	↓	Normal or ↓
TLC	Normal or ↑	↓	↓

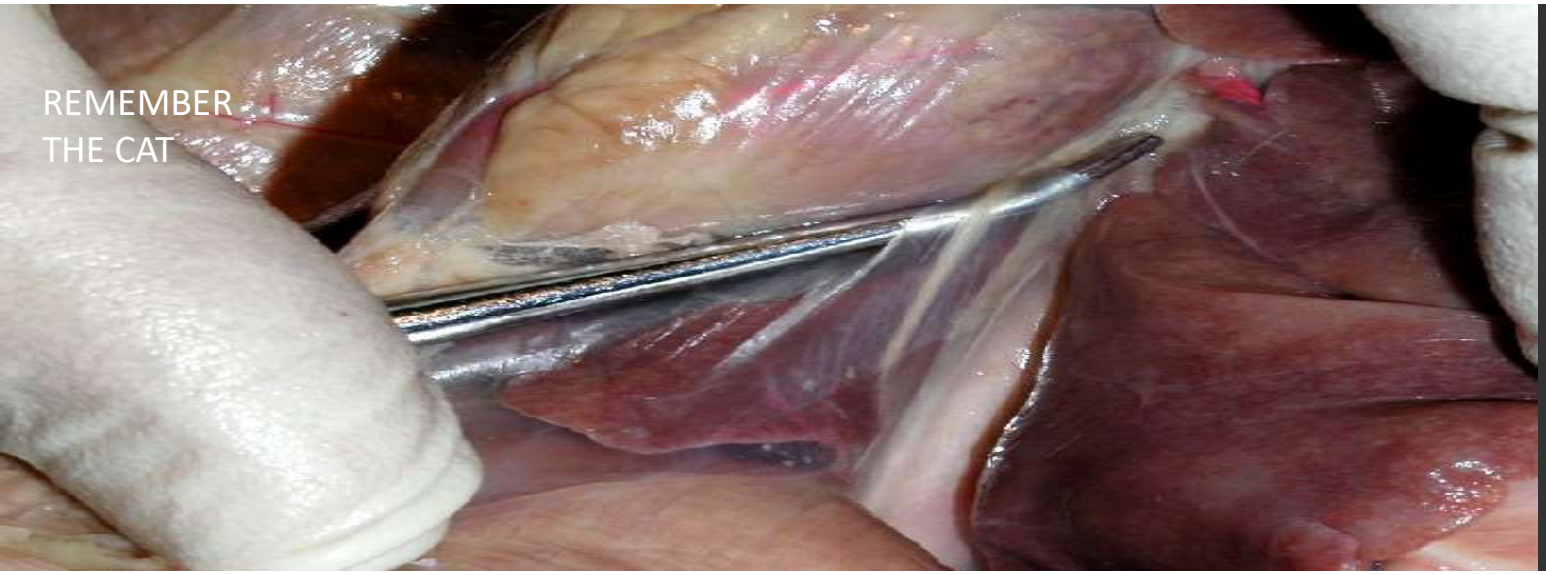
OBSTRUCTIVE VS. RESTRICTIVE

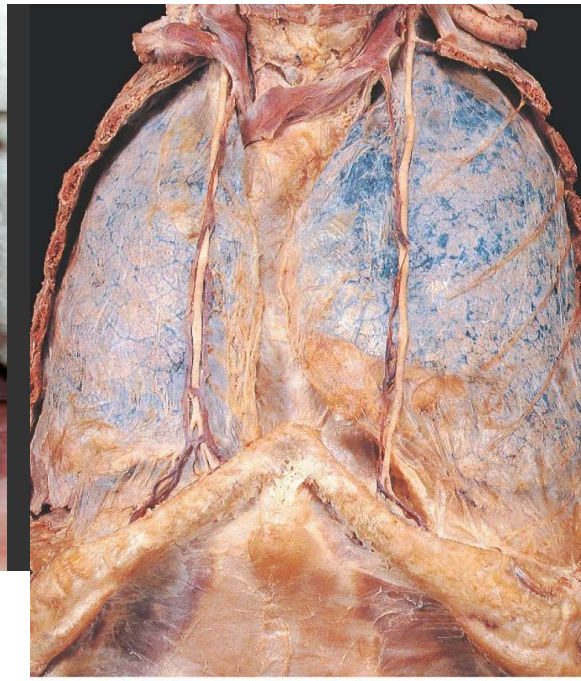
Obstructive disorders	Restrictive disorders
• **Characterized by:** reduction in airflow. • So, shortness of breath → in exhaling air. (the air will remain inside the lung after full expiration) 1. COPD 2. Asthma 3. Bronchiectasis	• **Characterized by** a reduction in lung volume. • So, Difficulty in taking air inside the lung. (DUE TO stiffness inside the lung tissue or chest wall cavity) 1. Interstitial lung disease. 2. Scoliosis 3. Neuromuscular cause 4. Marked obesity

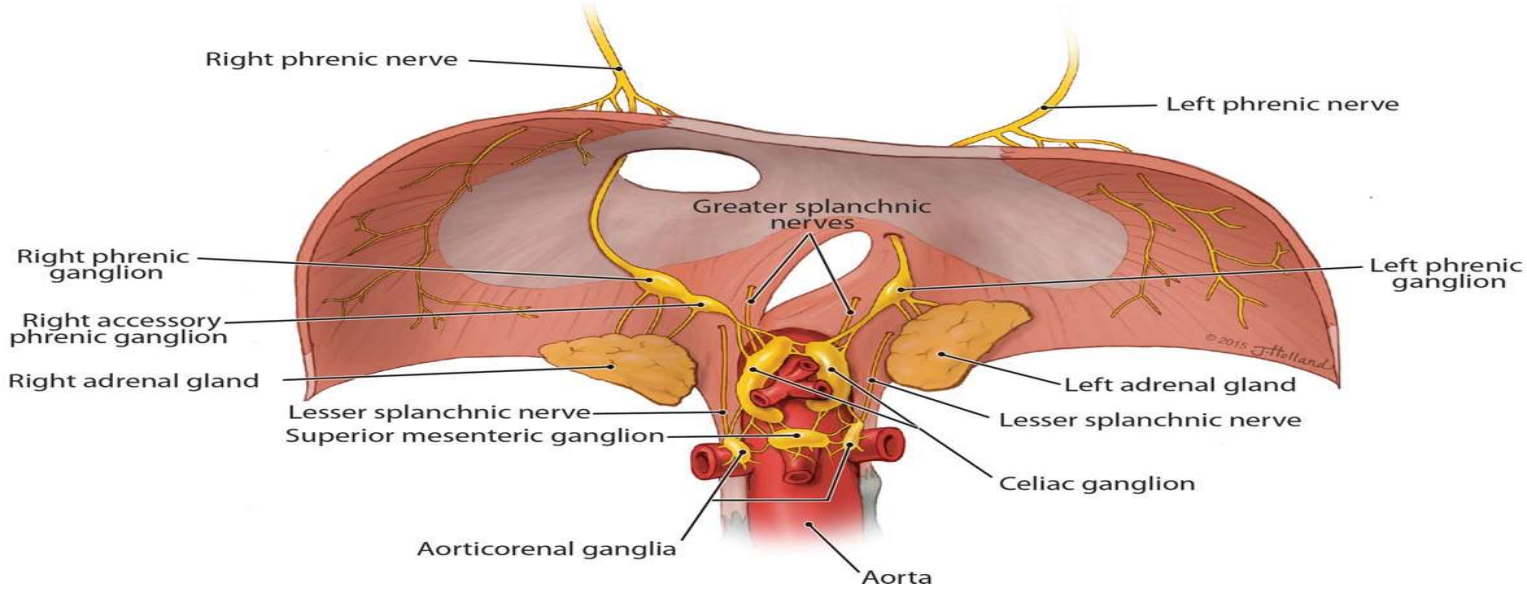
Part 3

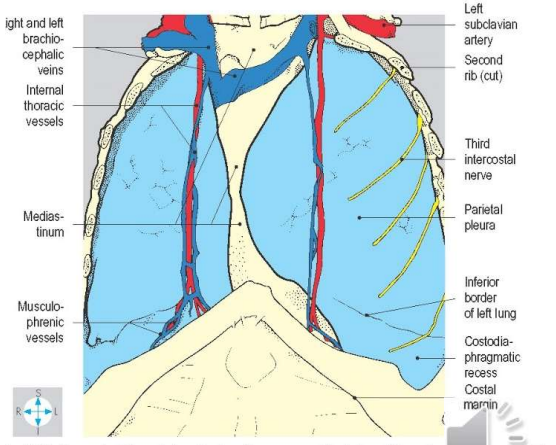

Phrenic Nerve









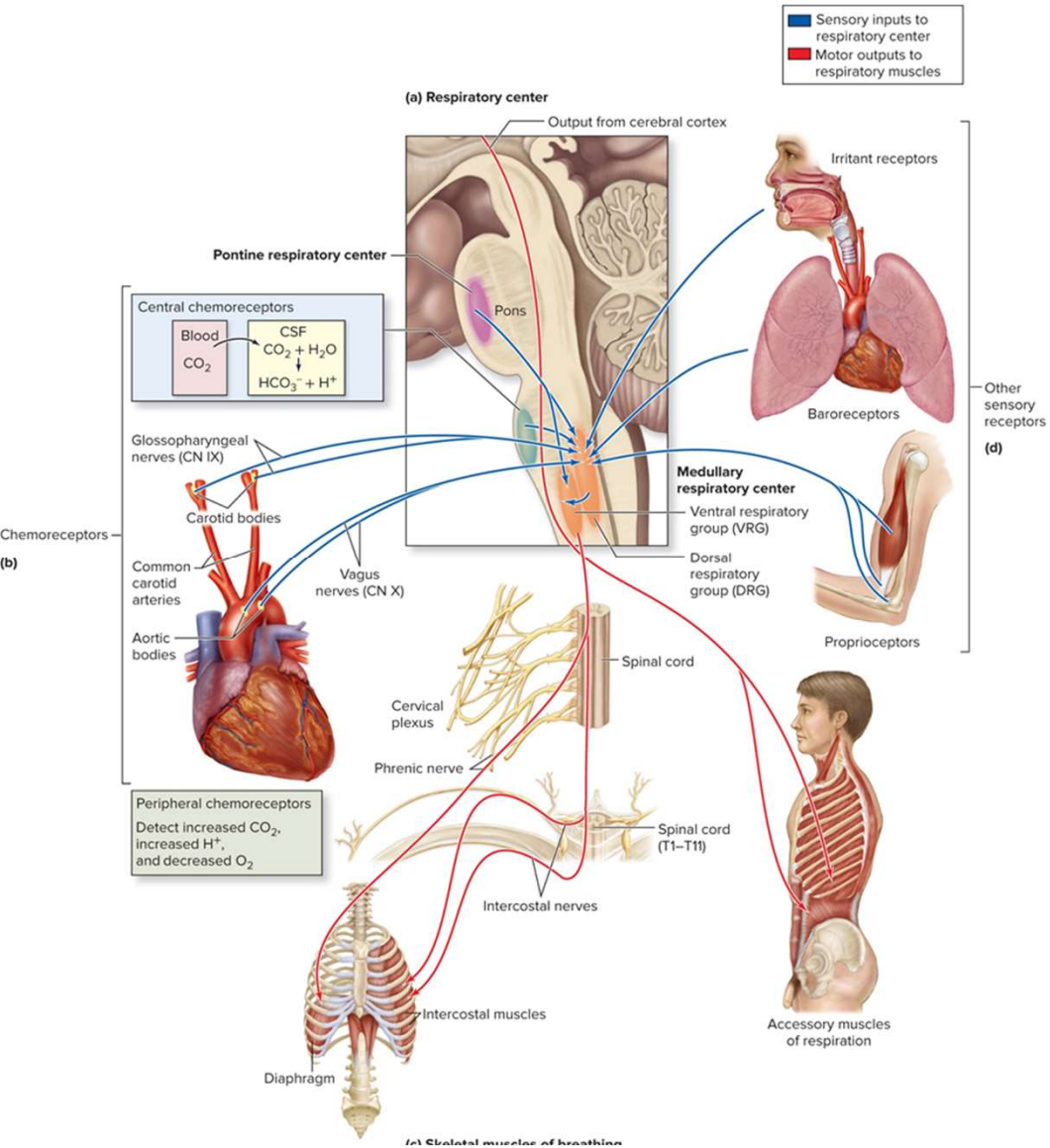


ig. 2.17 Removal of the anterior chest wall has exposed the internal thoracic vessels and costal pa f the parietal pleura, through which the lungs are visible.

Respiration—Pulmonary Ventilation: Nervous Control of Breathing

What is the consequence of a spinal cord injury below C5? (Phrenic nerve is innervated by C1-C5; intercostal nerves by T1-T12)

This person would have full use of the diaphragm but no use of the intercostal muscles. This person could breathe without a ventilator, but would breathe abnormally.



•Medullary Respiratory Centers:

•**Dorsal Respiratory Group (DRG):** Located in the medulla oblongata, the **DRG is primarily responsible for the initiation of inspiration (inhalation).**

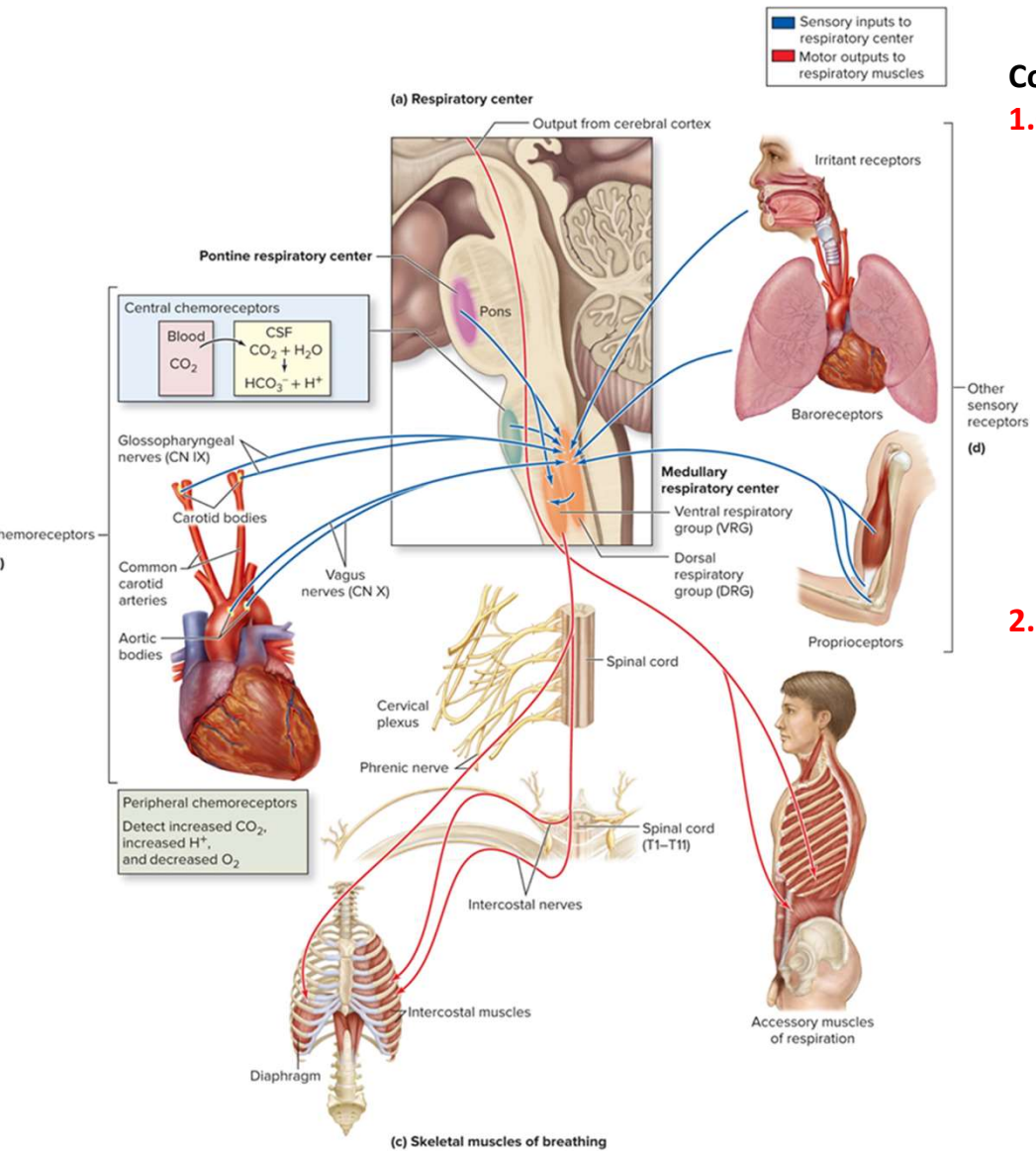
• It **generates basic rhythmic breathing patterns and sends signals to the diaphragm and intercostal muscles**.

•**Ventral Respiratory Group (VRG):** Also in the medulla, the VRG contains neurons that are active during both inspiration and expiration (exhalation**). It plays a crucial role in controlling forced breathing and is involved in both the rhythmic generation and modulation of respiratory patterns**.

•Pontine Respiratory Centers:

•**Pneumotaxic Center:** Located in the upper part of the pons, this center **regulates the rate and pattern of breathing by inhibiting the activity of the DRG,** thus controlling the transition between inspiration and expiration.

•**Apneustic Center:** Located in the lower part of the pons, this center **promotes deep, prolonged inspiratory gasps by stimulating the DRG and inhibiting the pneumotaxic center**. It helps to fine-tune the breathing rhythm.



Control Mechanisms

1.Chemical Control:

1. **Central Chemoreceptors:** Located in the medulla, these receptors respond to changes in the pH of the cerebrospinal fluid, which reflects the levels of carbon dioxide (CO_2) in the blood. Increased CO_2 levels lead to a drop in pH, stimulating the respiratory center to increase the rate and depth of breathing to expel CO_2.
2. **Peripheral Chemoreceptors:** Located in the carotid bodies and aortic bodies, these receptors respond to changes in blood oxygen (O_2), CO_2, and pH levels. A decrease in O_2 or pH, or an increase in CO_2, stimulates these receptors to signal the respiratory center to adjust breathing accordingly.

2.Neural Control:

1. **Stretch Receptors:** Found in the lungs, these receptors prevent over-inflation by sending inhibitory signals to the respiratory center when the lungs expand too much.
2. **Irritant Receptors:** Located in the airways, these receptors respond to harmful substances by initiating reflexes such as coughing, sneezing, or rapid shallow breathing to protect the respiratory system.
3. **Higher Brain Centers:** The cerebral cortex can voluntarily override the respiratory centers, allowing conscious control of breathing, such as holding your breath or speaking.

Respiration—Pulmonary Ventilation: Nervous Control of Breathing

What is the function of the VRG?

The DRG?

The VRG initiates neural impulses for inspiration and expiration.

The DRG receives sensory impulses from sensory receptors and relays them to the VRG.

- **Respiratory muscles** – diaphragm and other muscles that promote ventilation

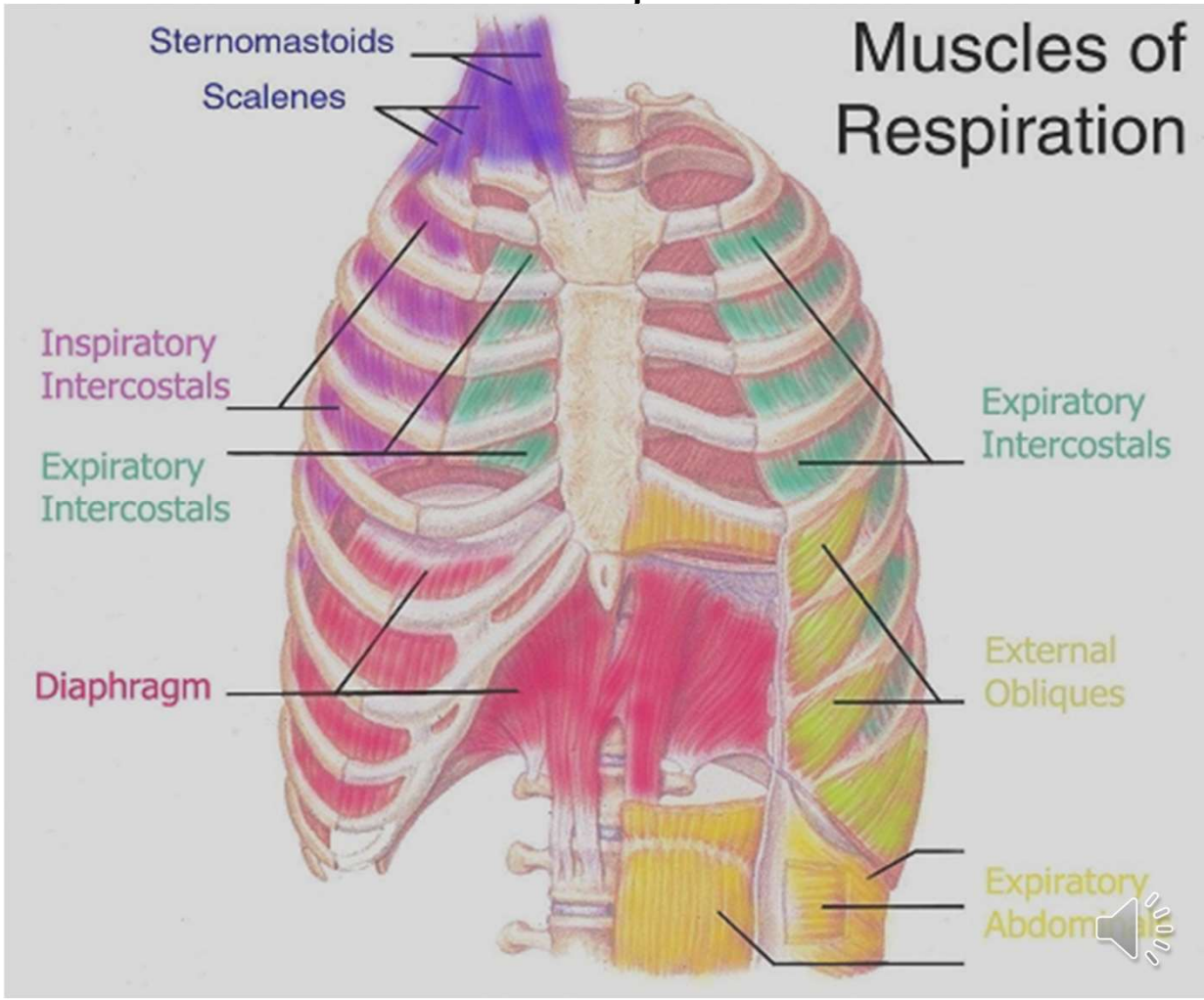
Contraction of external intercostal muscles

- > elevation of ribs & sternum
- > increased front- to-back dimension of thoracic cavity
- > lowers air pressure in lungs
- > air moves into lungs

Contraction of diaphragm

> diaphragm moves downward

- ➢ increases vertical dimension of thoracic cavity
- ➢ > lowers air pressure in lungs
- ➢ > air moves into lungs:



•Diaphragm:

•The primary muscle of respiration.

•Located at the base of the thoracic cavity.

•Contracts during inspiration, creating negative pressure to draw air into the lungs.

•Relaxes during expiration, allowing air to be expelled from the lungs.

•Intercostal Muscles:

•External Intercostal Muscles:

- Located between the ribs.
- Contract during inspiration to elevate the ribs and expand the chest cavity.

•Internal Intercostal Muscles:

- Located deeper between the ribs.
- Contract during forced expiration to depress the ribs and decrease the chest cavity volume.

•Accessory Muscles of Inspiration:

•Sternocleidomastoid:

- Elevates the sternum.

•Scalenes:

- Elevate the first two ribs.

•Pectoralis Minor:

- Elevates the third, fourth, and fifth ribs.

•Accessory Muscles of Expiration:

•Abdominal Muscles:

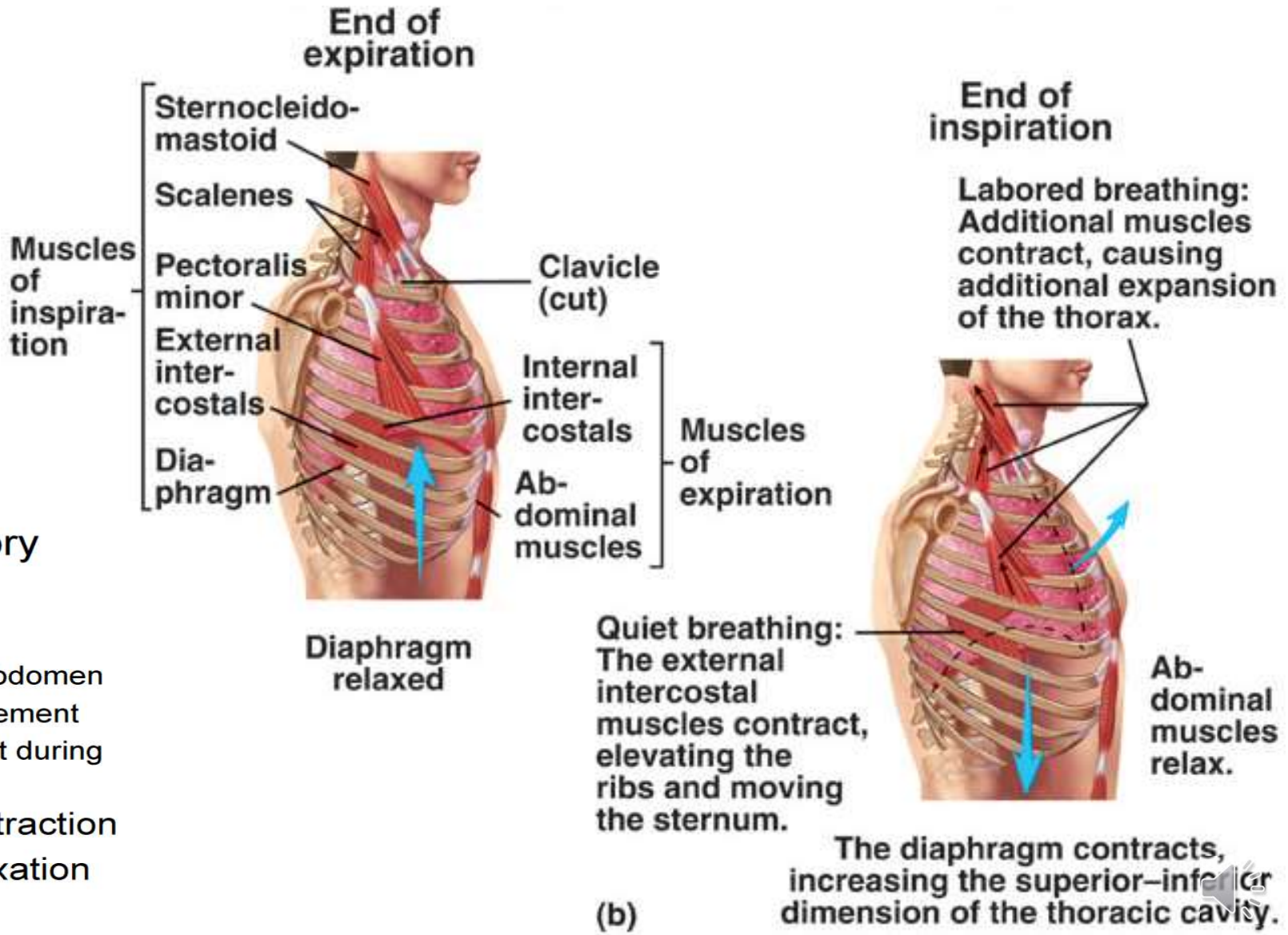
- Include the rectus abdominis, external oblique, internal oblique, and transversus abdominis.
- Contract to increase intra-abdominal pressure, pushing the diaphragm upward and aiding in forced expiration.

•Quadratus Lumborum:

- Stabilizes the lower ribs and assists in forced expiration.

Thoracic Walls Muscles of Respiration

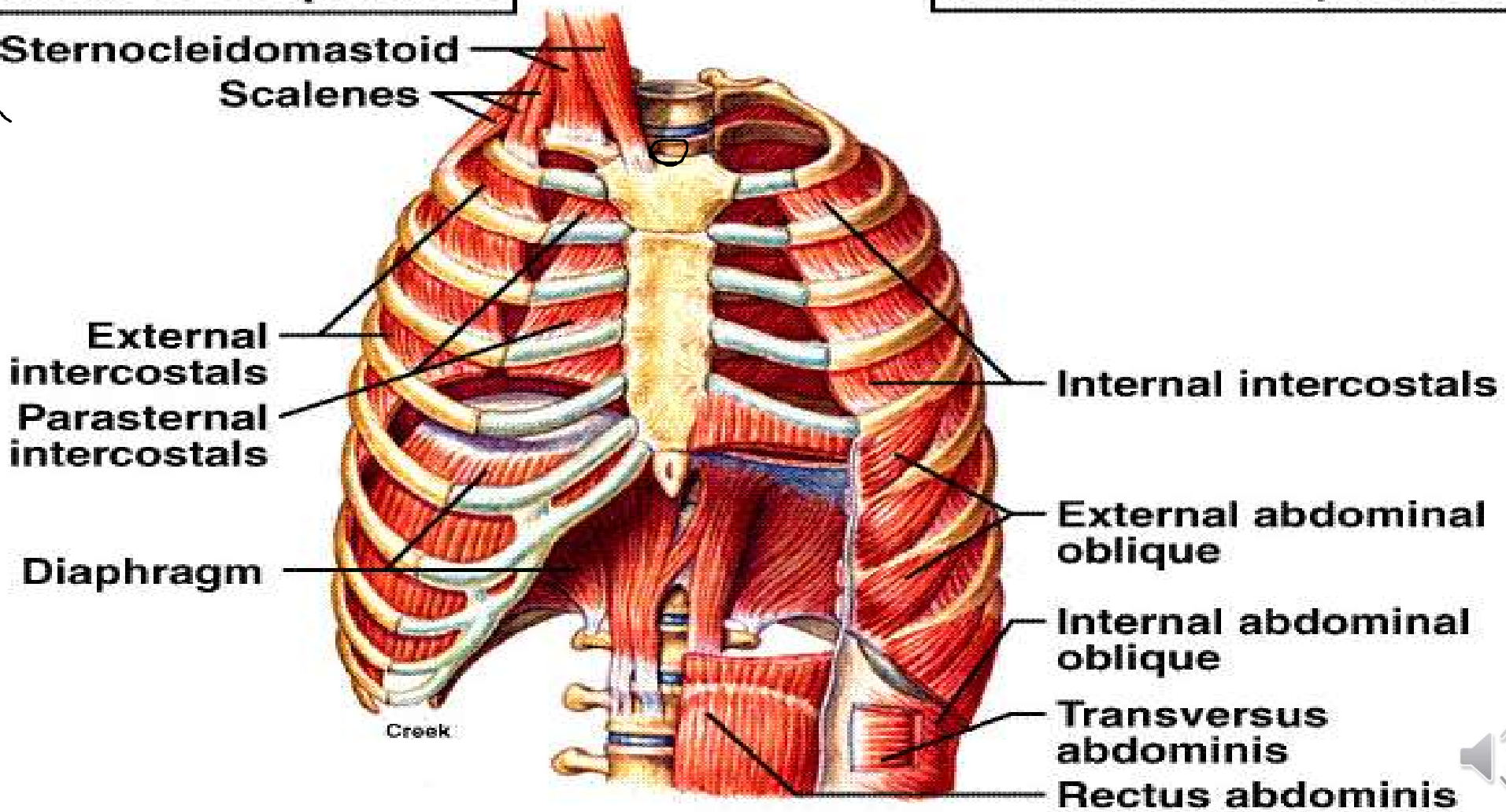
- Primary Ventilatory Muscles
  - Diaphragm
    - Divides Chest/Abdomen
    - 75% of gas movement
    - 1.5cm movement during quiet breathing
  - Inspiration – contraction
  - Expiration – relaxation
    - Elastic Recoil



Muscles Involved in Breathing

Muscles of inspiration

Muscles of expiration



Muscles of respiration

Quiet breathing:

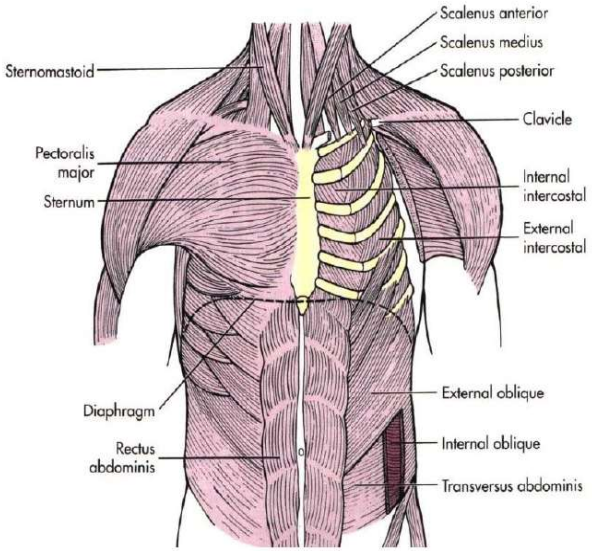
Inspiration––diaphragm.

Expiration––passive.

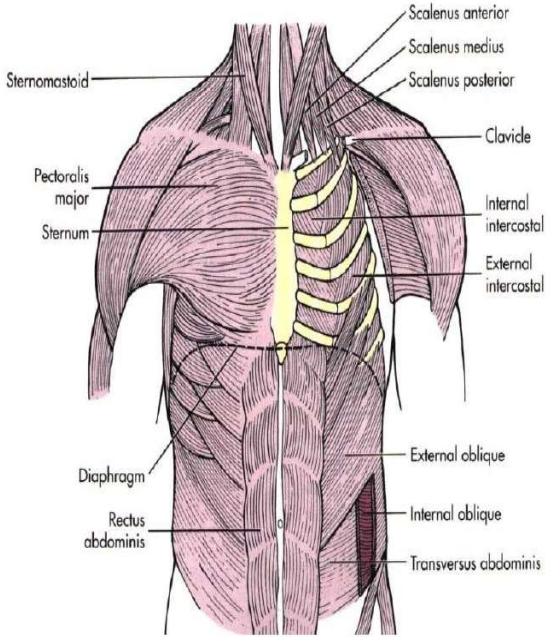
Exercise:

Inspiration––external intercostals, scalene muscles, sternomastoids.

Expiration––rectus abdominis, internal and external obliques, transversus abdominis, internal intercostals.



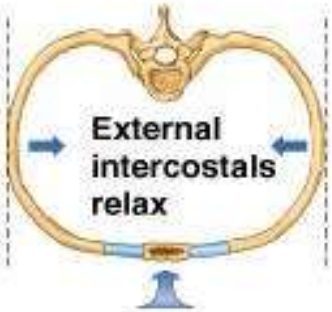
- Scalene Muscles
  - Neck muscles
  - Attach to 1st /2nd rib
  - Assist ventilatory demands
- Sternomastoid
  - Manubrium / clavicle
- Pectoralis Major
  - Clavicle / sternum



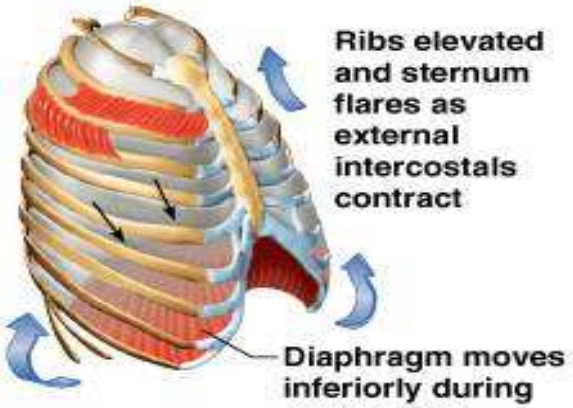
- Abdominal Muscles
  - External oblique
  - Internal oblique
  - Transverse abdominus
  - Rectus abdominus
- Inactive during quiet breathing
- Active > 40L/min

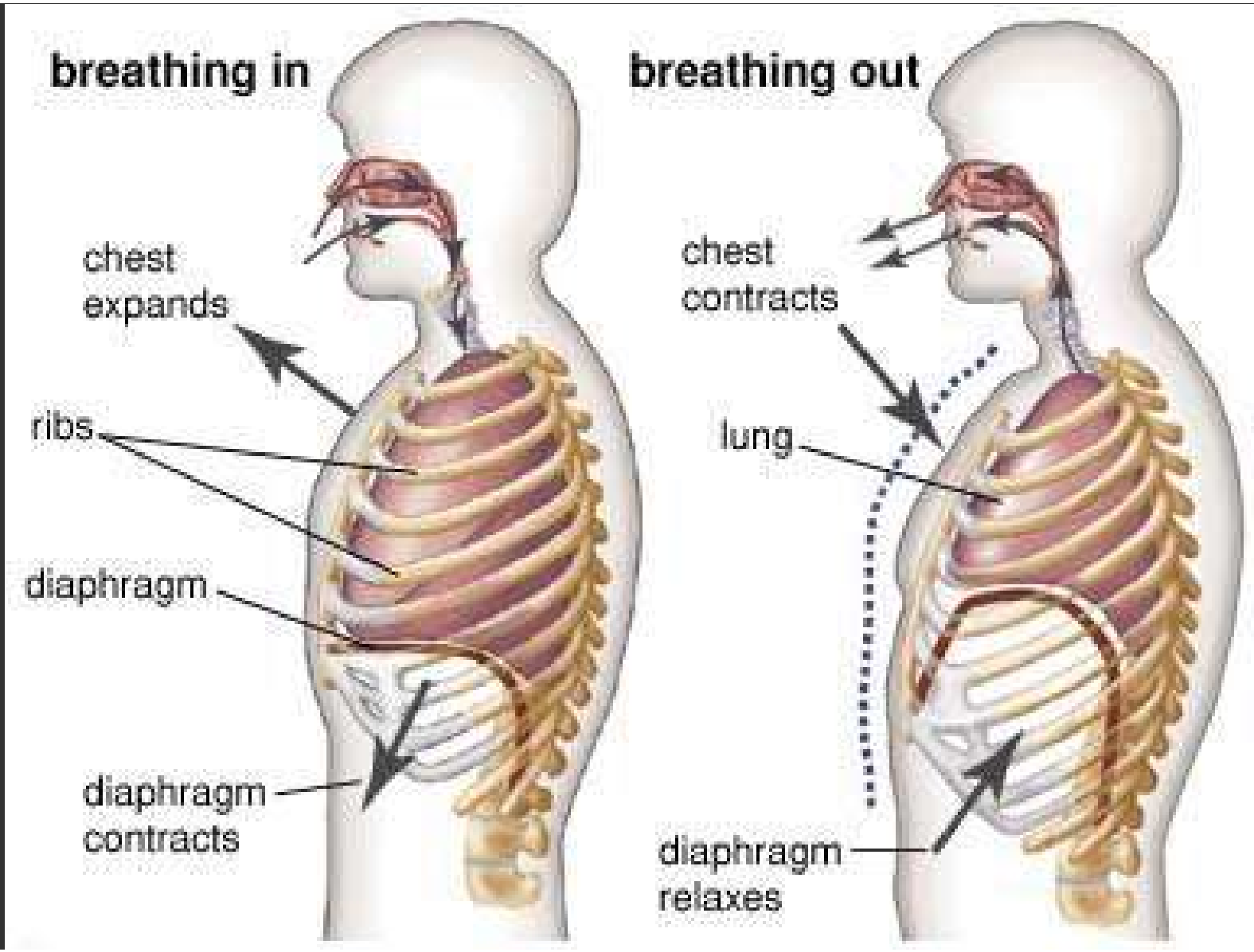
Expiration

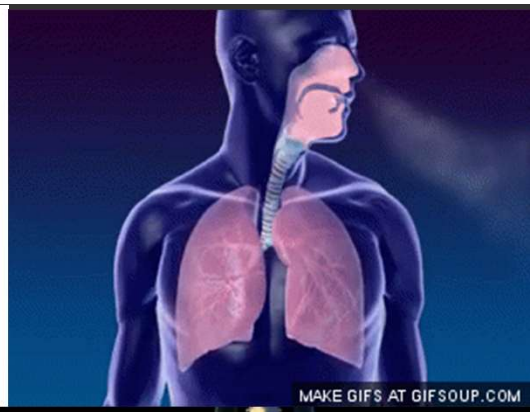
① Inspiratory muscles relax (diaphragm rises; rib cage descends due to recoil of costal cartilages)
↓
② Thoracic cavity volume decreases
↓
③ Elastic lungs recoil passively; intrapulmonary volume decreases
↓
④ Intrapulmonary pressure rises (to +1 mm Hg)
↓
⑤ Air (gases) flows out of lungs down its pressure gradient until intrapulmonary pressure is 0



Inspiration

Sequence of events	Changes in anterior-posterior and superior-inferior dimensions	Changes in lateral dimensions
① Inspiratory muscles contract (diaphragm descends; rib cage rises) ↓ ② Thoracic cavity volume increases ↓ ③ Lungs 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)		


breathing in
chest expands
ribs
diaphragm
diaphragm contracts
breathing out
chest contracts
lung
diaphragm relaxes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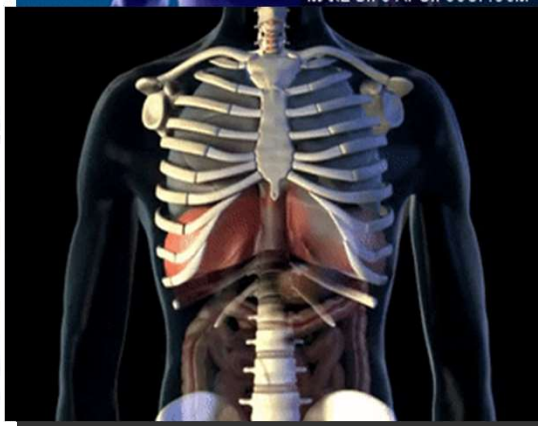
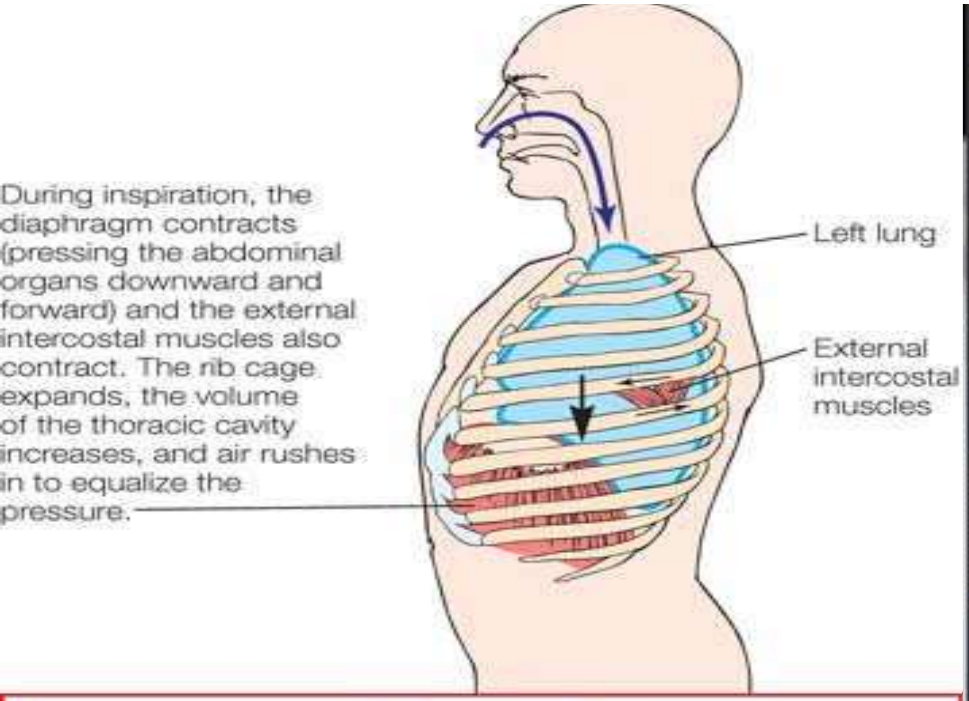
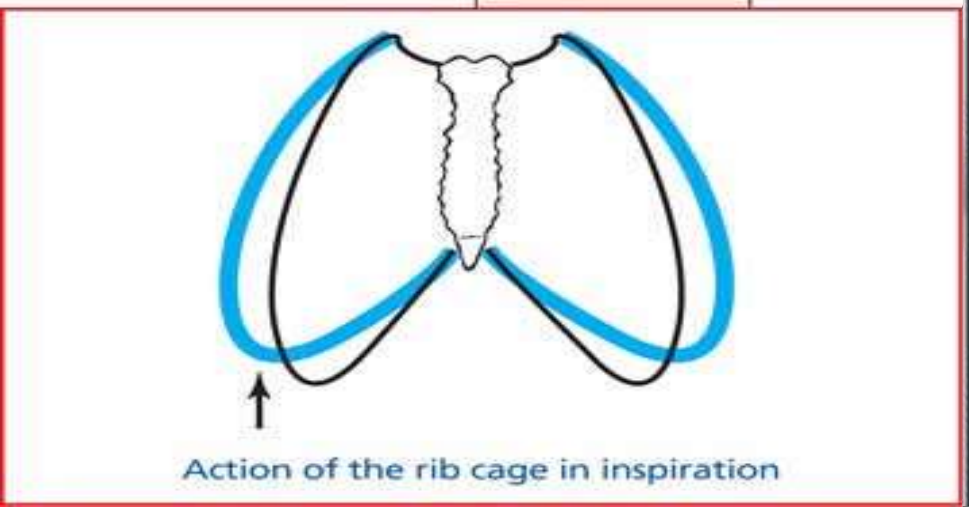
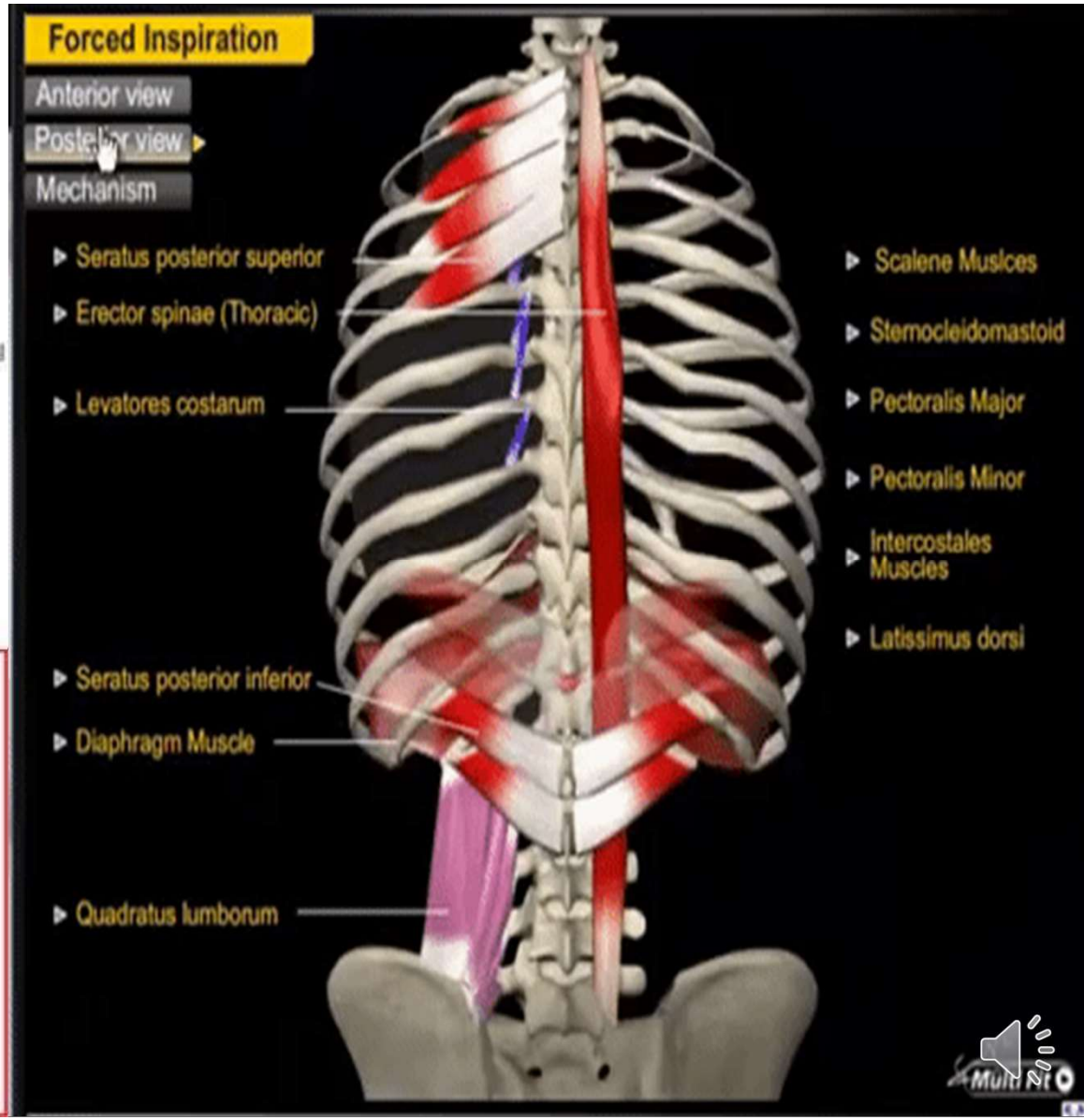


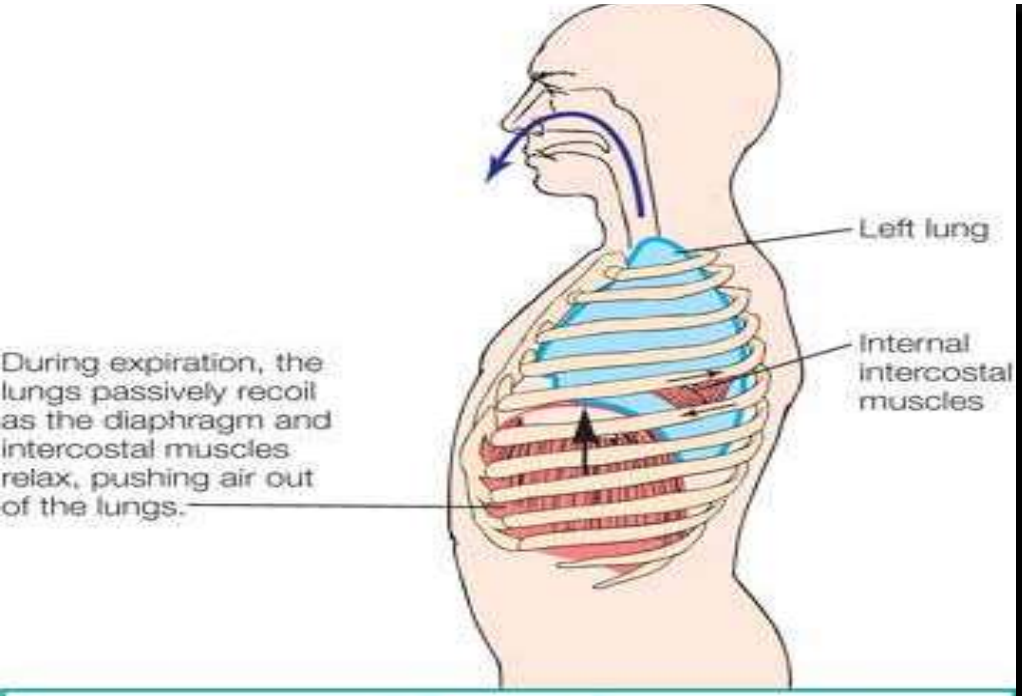
During inspiration, the diaphragm contracts (pressing the abdominal organs downward and forward) and the external intercostal muscles also contract. The rib cage expands, the volume of the thoracic cavity increases, and air rushes in to equalize the pressure.

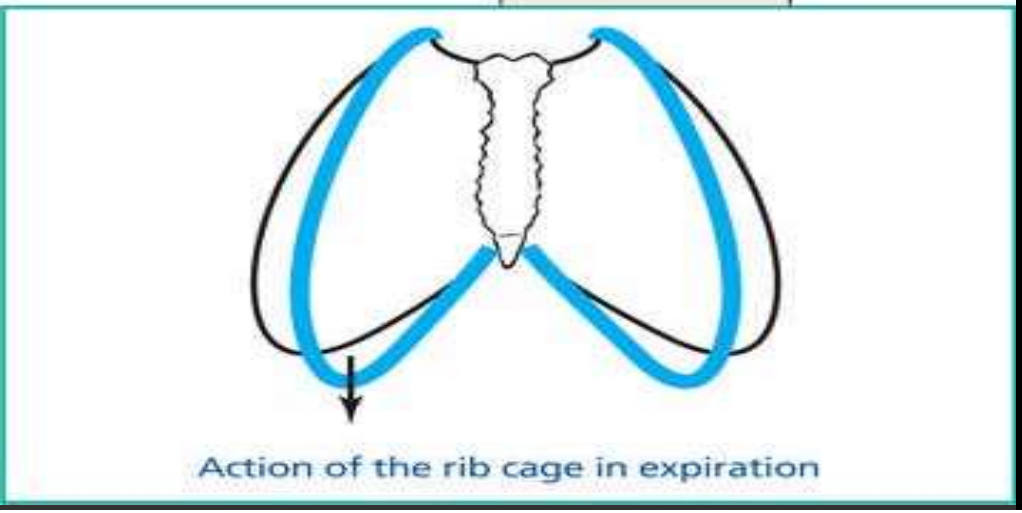


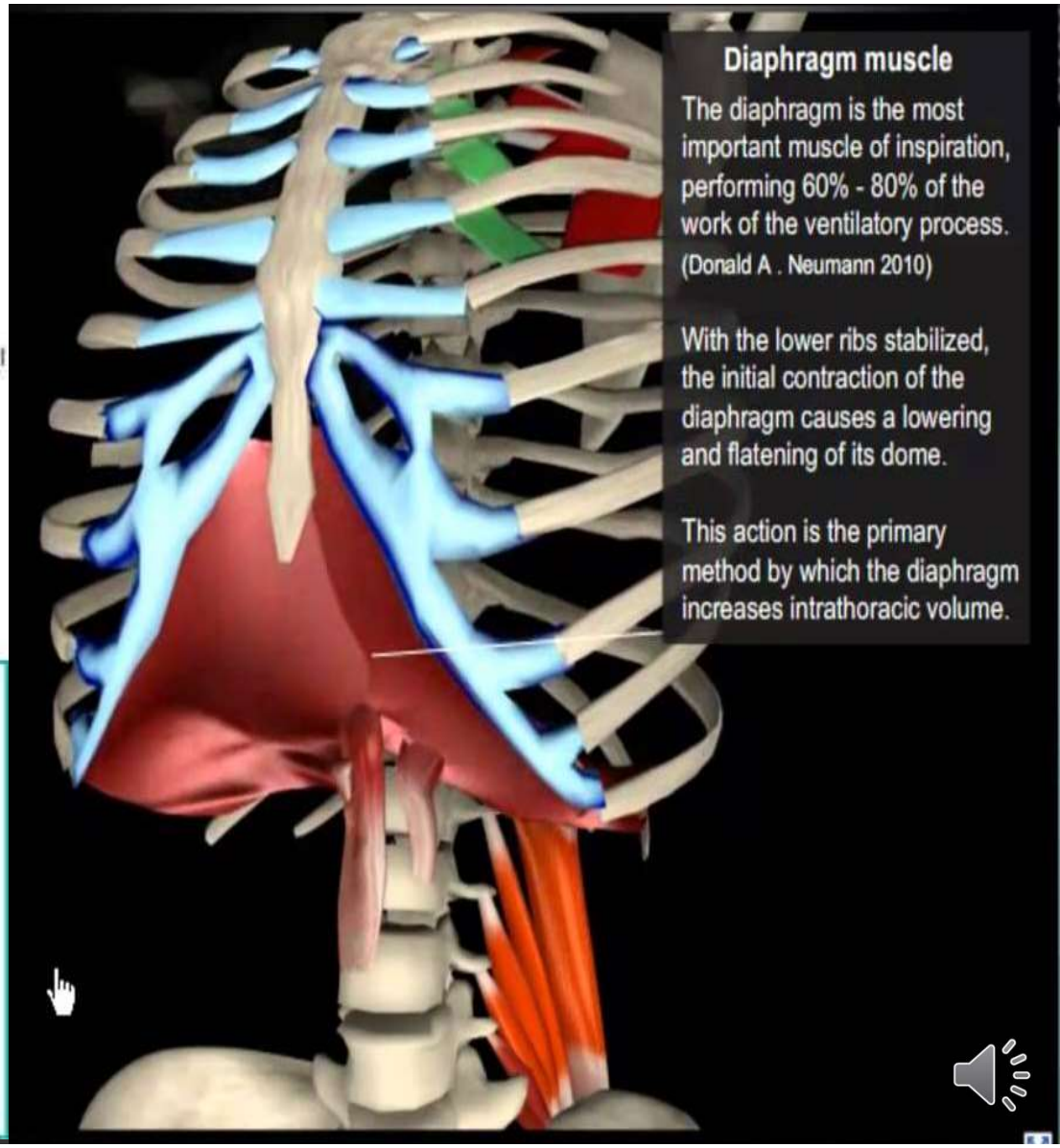


Action of the rib cage in inspiration



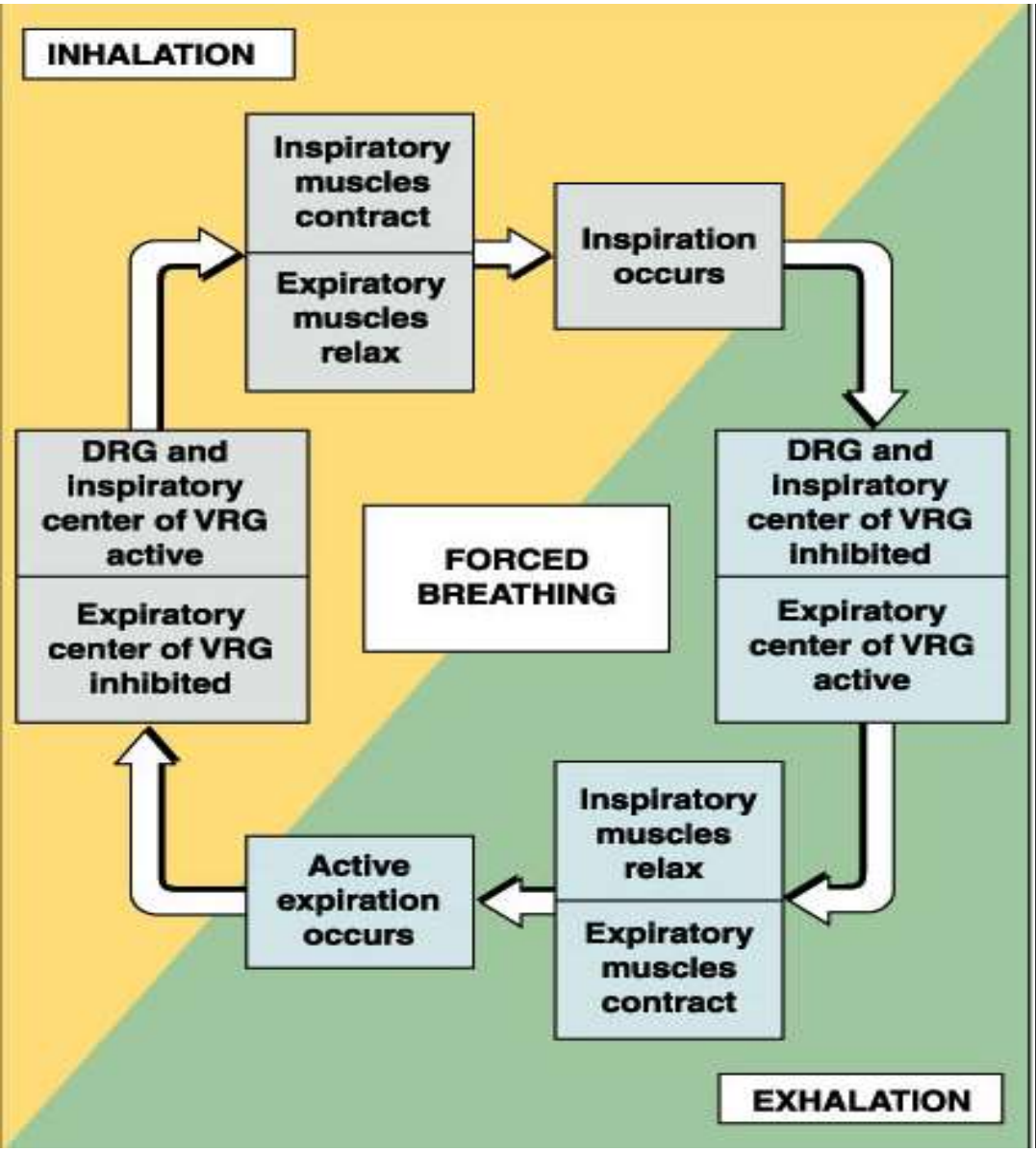

Left lung
Internal intercostal muscles
During expiration, the lungs passively recoil as the diaphragm and intercostal muscles relax, pushing air out of the lungs.

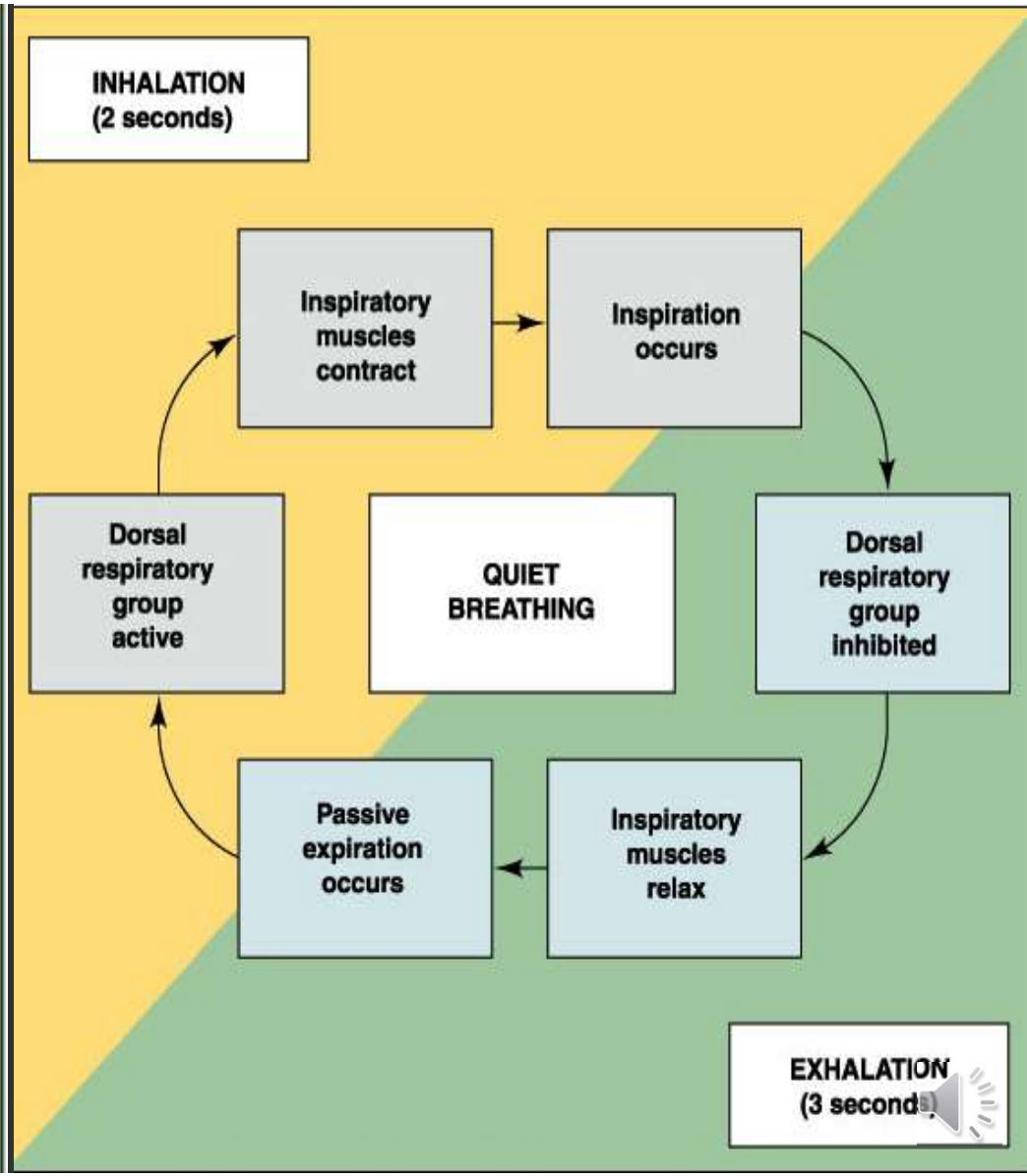

Action of the rib cage in expiration


Diaphragm muscle
The diaphragm is the most important muscle of inspiration, performing 60% - 80% of the work of the ventilatory process.
(Donald A . Neumann 2010)
With the lower ribs stabilized, the initial contraction of the diaphragm causes a lowering and flatening of its dome.
This action is the primary method by which the diaphragm increases intrathoracic volume.

Deep Forceful Breathing

- ***Deep Inhalation***
  - During deep forceful inhalation accessory muscles of inhalation participate to increase size of thoracic cavity
    - **Sternocleidomastoid – elevate sternum**
    - **Scalenes – elevate first two ribs**
    - **Pectoralis minor – elevate 3rd–5th ribs**
- ***Deep Exhalation***
  - Exhalation during forceful breathing is active process
    - **Muscles of exhalation increase pressure in abdomen and thorax**
      - Abdominals
      - Internal intercostals


INHALATION
Inspiratory muscles contract
Expiratory muscles relax
Inspiration occurs
DRG and inspiratory center of VRG active
Expiratory center of VRG inhibited
FORCED BREATHING
DRG and inspiratory center of VRG inhibited
Expiratory center of VRG active
Inspiratory muscles relax
Expiratory muscles contract
Active expiration occurs
EXHALATION


INHALATION (2 seconds)
Inspiratory muscles contract
Inspiration occurs
Dorsal respiratory group active
QUIET BREATHING
Dorsal respiratory group inhibited
Passive expiration occurs
Inspiratory muscles relax
EXHALATION (3 seconds)

Respiratory center

Regulation of respiration takes place centrally in the respiratory center located in the reticular formation of the medulla oblongata and pons.

Medullary center

Function: creates rhythmic innervation of the respiratory muscles and is influenced by various respiratory stimuli

Dorsal respiratory group

- Responsible for inspiration
- Input: peripheral chemoreceptors and mechanoreceptors (via the vagus and glossopharyngeal nerve)
- Output: phrenic nerve

Ventral respiratory group

- Responsible for expiration
- Expiration is usually passive, only becoming active during physical exercise.

Expiration at rest is mainly driven by elastic properties of the lung tissue.

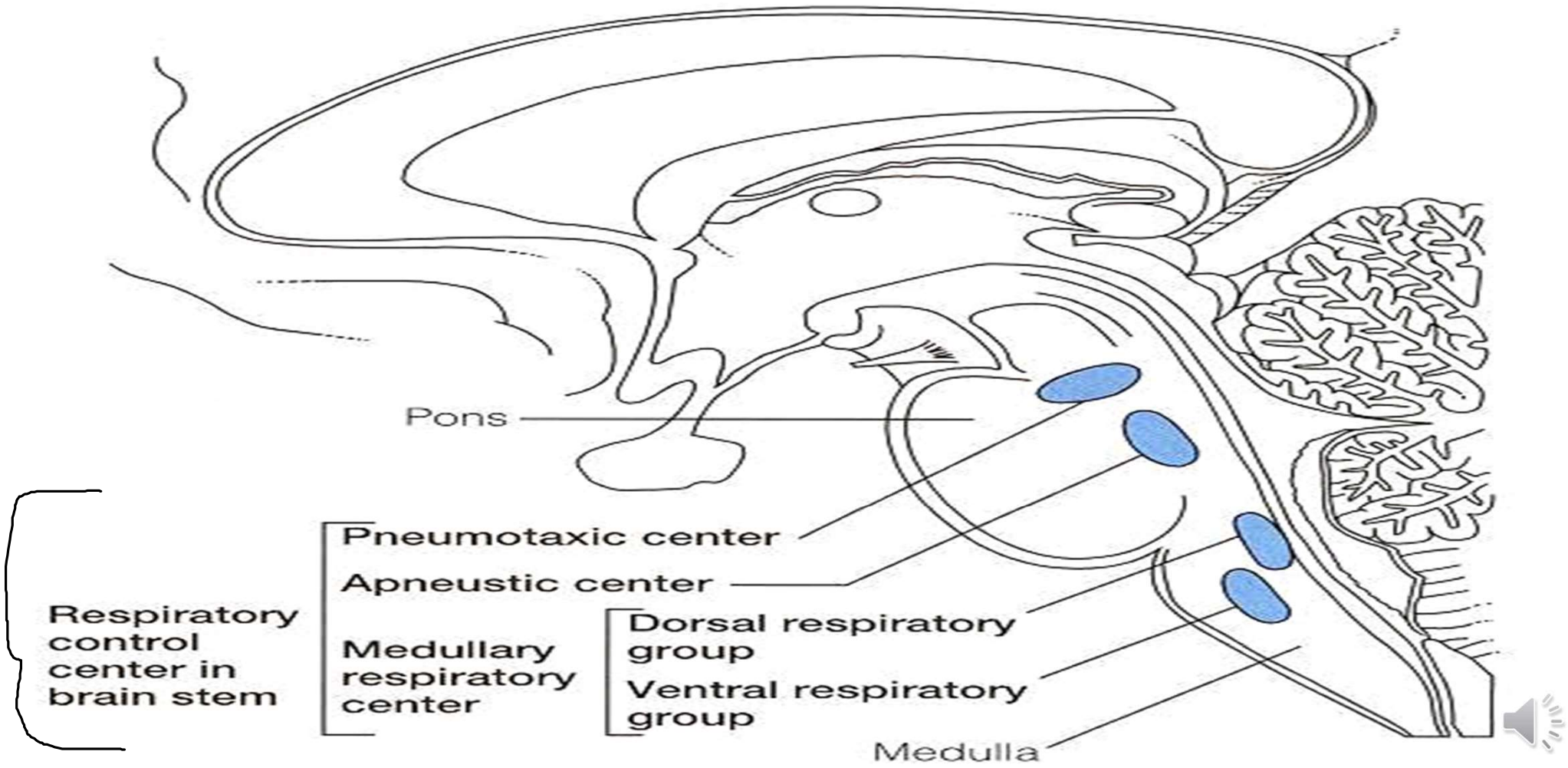
Pontine center

- **Function**: modifies the activity of the medullary center

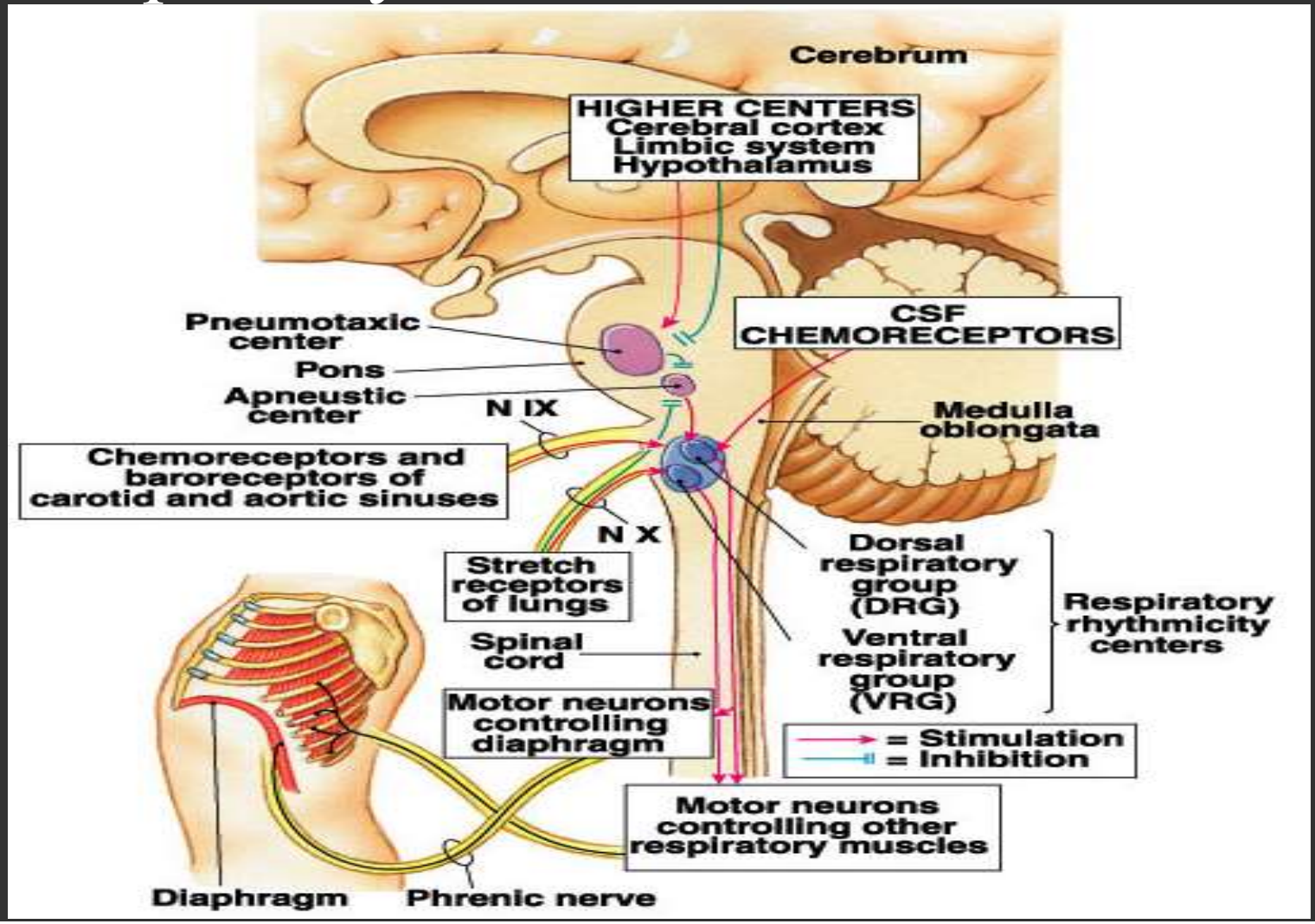
- **Apneustic center**
  - **Controls the intensity of breathing**
  - Promotes deep gasping inspiration (apneusis) by stimulation of the dorsal respiratory group and inhibition of the pneumotaxic center

- **Pneumotaxic center**
  - **Controls the respiratory rate** and pattern of breathing
  - Limits or delays inspiration

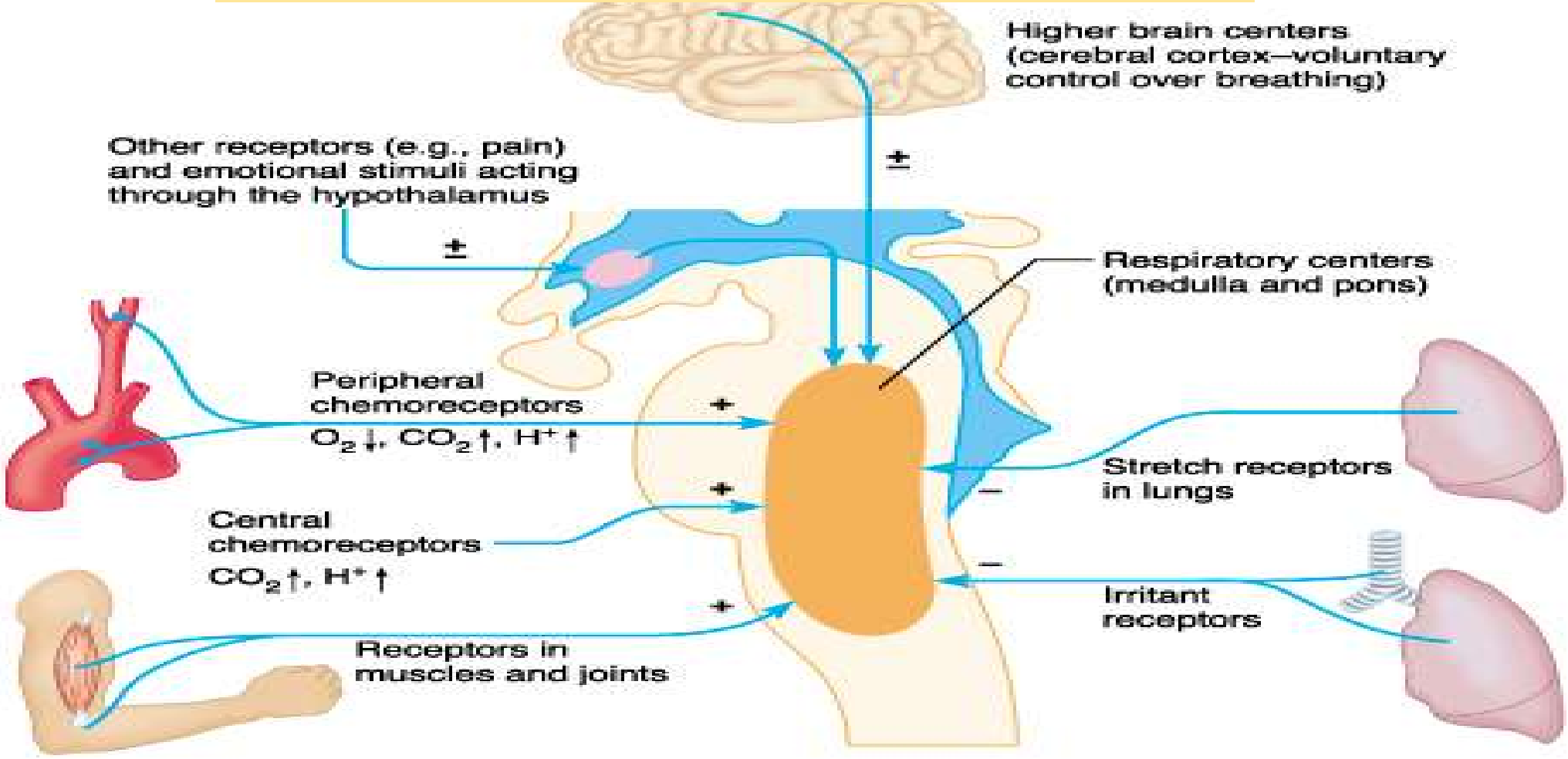
Respiratory Centers



Respiratory Structures in Brainstem



Factors Influencing Respiration



Two Sets of Chemoreceptors Exist

Central Chemoreceptors

Responsive to increased arterial PCO2

Act by way of CSF [H+] .

Peripheral Chemoreceptors

Responsive to decreased arterial PO2

Responsive to increased arterial PCO2

Responsive to increased H+ ion concentration.

Peripheral Chemoreceptors

Carotid bodies

Sensitive to: PaO_2, $PaCO_2$, and pH

Afferents in glossopharyngeal nerve.

Aortic bodies

Sensitive to: PaO_2, $PaCO_2$, but not pH

Afferents in vagus

Receptors

Central chemoreceptors in the medulla oblongata: detect ↑ pCO_2 and ↓ pH

Peripheral chemoreceptors in aorta and carotids (carotid body) via CN IX and CN X : detect ↓ pO_2 (< 60 mmHg), ↑ pCO_2, and ↓ pH

Mechanoreceptors in the airways and respiratory muscles

Respiratory stimuli

- ↑ pCO_2 : strongest respiratory drive under normal conditions
- ↓ pO_2
    - **Strongest respiratory drive in chronic hypercapnia (e.g., in COPD)**
    - **The respiratory center** develops a tolerance for increased pCO_2..
- ↓ pH
- **Nonspecific stimuli:** fever, pain, norepinephrine

- **A chronically elevated pCO_2 ≥ 70 mmHg (e.g., in COPD) inhibits the respiratory center instead of stimulating it.**
- **Hyperventilation can reduce the $PaCO_2$ and thus the respiratory drive; this technique is used, for example, by divers before a dive.**

Significance of Hering-Breuer

Limits the degree of inspiration and prevents overinflation of the lungs

Normal adults. Receptors are not activated at end normal tidal volumes.

Become Important during exercise when tidal volume is increased.

Become Important in Chronic obstructive lung diseases when lungs are more distended.

Infants. Probably help terminate normal inspiration.

Hering-Breuer Reflex or Pulmonary Stretch Reflex

Including pulmonary inflation reflex and pulmonary deflation reflex

Receptor: Slowly adapting stretch receptors (SARs) in bronchial airways.

Afferent: vagus nerve

Pulmonary inflation reflex:

- Terminate inspiration.
- By speeding inspiratory termination they increase respiratory frequency.
- **Sustained stimulation of SARs:** causes activation of expiratory neurons

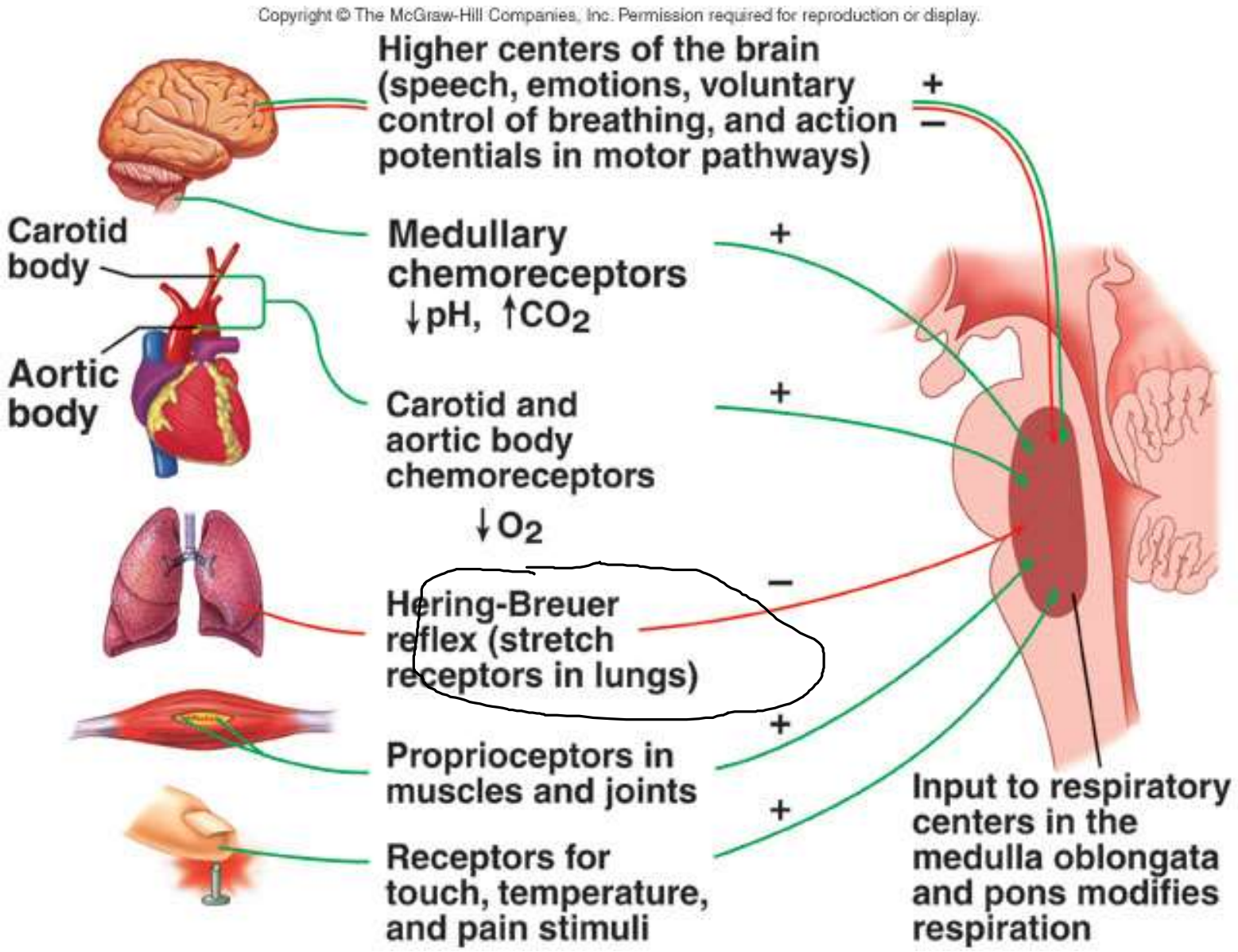
•**Hering-Breuer inflation reflex**

- Inhibits inspiration to prevent over-inflation of the lungs and alveolar damage
- Mediated by pulmonary stretch receptors and vagal afferents

•**Diving reflex:** immersion of the head triggers peripheral vasoconstriction redirection of blood to the heart and brain, and slowed pulse rate, which optimizes respiration

•**Spinal cord responses:** recruitment of additional respiratory muscles (e.g., to compensate hypoventilation) via stimulation of motor neurons by the respiratory center

•**Upper airway** responses (e.g., coughing, sneezing)



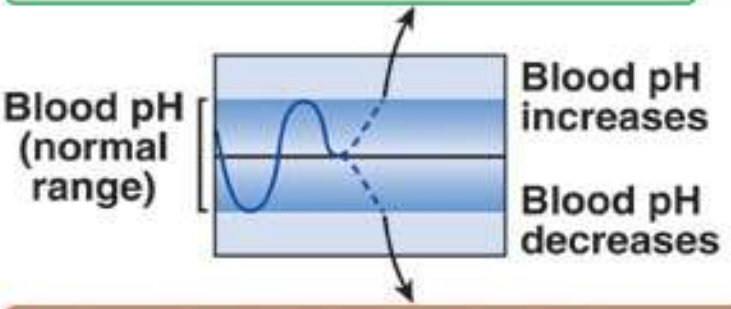
Modifying Respiration

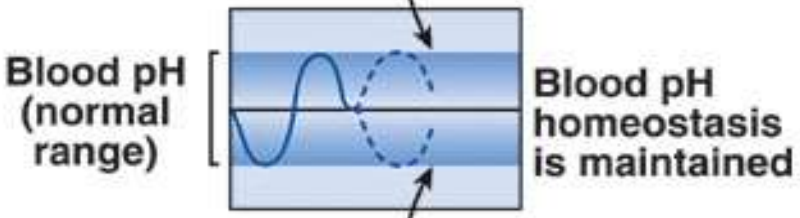
Decreased stimulation of the respiratory centers results.

Decreased stimulation of the respiratory muscles by the respiratory centers results in decreased ventilation, which decreases gas exchange.

An increase in blood pH (often caused by a decrease in blood CO_2) is detected by the medullary chemoreceptors.

A decrease in blood pH is caused by the increase in blood CO_2.





- A decrease in blood pH (often caused by an increase in blood CO_2) is detected by the medullary chemoreceptors.
- A decrease in blood O_2 is detected by the carotid and aortic body chemoreceptors.

- An increase in blood pH is caused by the decrease in blood CO_2.
- Blood O_2 increases.

Increased stimulation of the respiratory centers results.

Increased stimulation of the respiratory muscles by the respiratory centers results in increased ventilation, which increases gas exchange.

Regulation of Blood pH and Gases

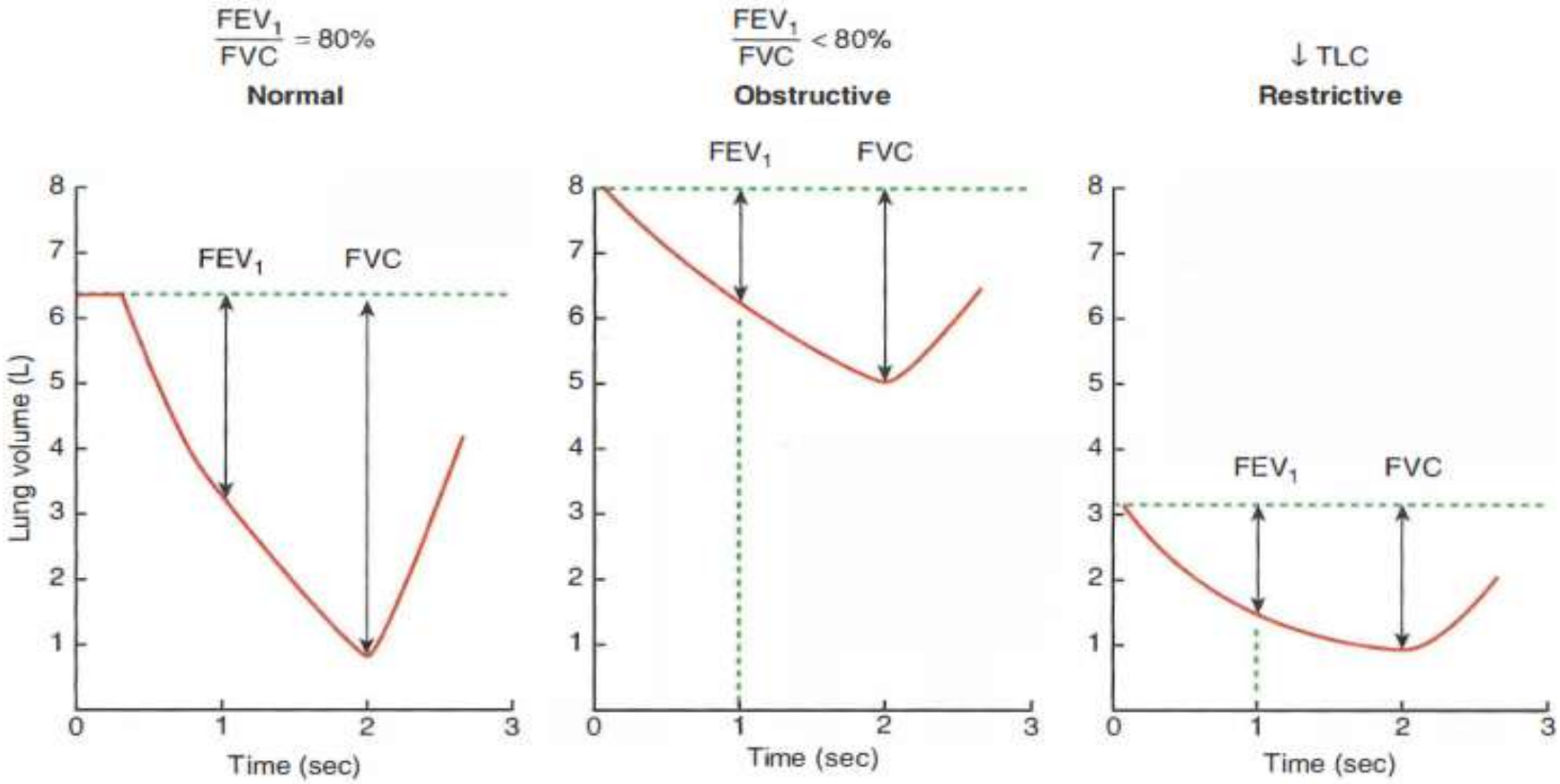
- **Pulmonary circulation**
- In healthy individuals the resistance is low and the compliance is high.
- Blood flow is equivalent to cardiac output (~ 5 L/min).
- **Distribution of blood flow**: depends on the position of the body and is precisely regulated in relation to the ventilation to optimize gas exchange
- **Standing and sitting position:** due to gravity, circulation is highest in the lung base
- **Supine position:** nearly equal distribution of the blood throughout the lung

Characteristics of pulmonary blood flow THE REMINDER		
Location	**Blood flow**	**Pressures**
Apical segments	Lowest	Alveolar pressure > arterial pressure > venous pressure
Middle segments	Medium	Arterial pressure > alveolar pressure > venous pressure
Basal segments	Highest	Arterial pressure > venous pressure > alveolar pressure

In order to keep the ventilation-perfusion ratio constant, the vessels of the lungs react to hypoxia with vasoconstriction.
In contrast, hypoxia in other organs causes vasodilation to increase perfusion

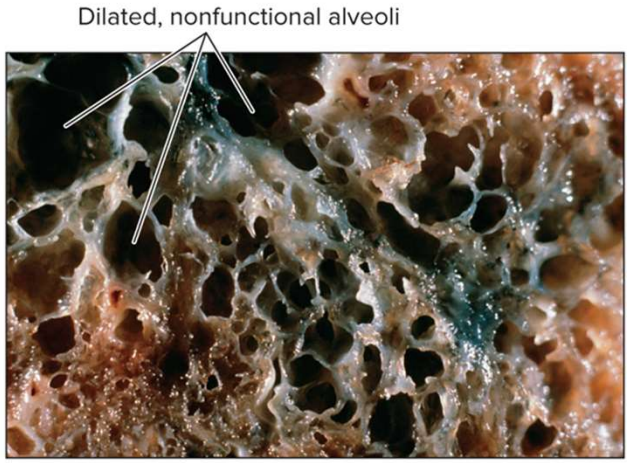
.

Obstructive vs. restrictive lung disease

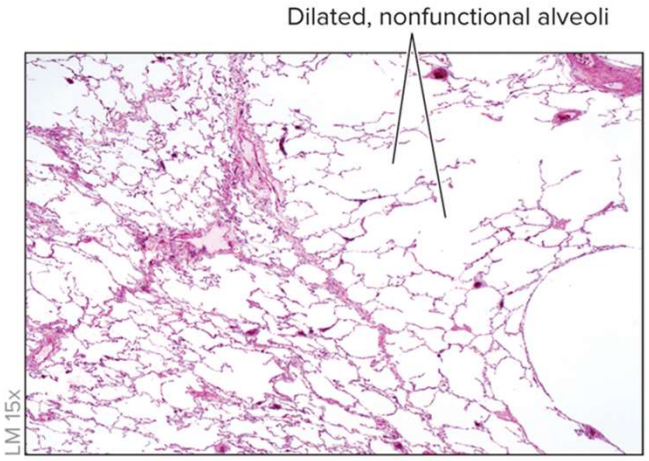


Note: Obstructive lung volumes > normal (↑ TLC, ↑ FRC, ↑ RV); restrictive lung volumes < normal. In both obstructive and restrictive, FEV_1 and FVC are reduced, but in obstructive, FEV_1 is more dramatically reduced, resulting in a ↓ FEV_1/FVC ratio.

Characteristics of pathological breathing patterns just for your information for your future		
Pathological breathing patterns	**Characteristics**	**Common causes**
Kussmaul breathing	•Hyperventilation • with a deep, labored, breathing pattern (to eliminate excess CO_2)	•Metabolic acidosis(e.g., diabetic ketoacidosis •, uremia)
Cheyne-Stokes respiration	•Cyclic, crescendo-decrescendo pattern of breathing with intermittent periods of apnea •	•Damage to respiratory center • (e.g., stroke) •Central sleep apnea •Heart failure
Biot respirations (cluster breathing)	•Irregular breathing followed by regular or irregular periods of apnea	•↑ Intracranial pressure •Brain damage (e.g., trauma, stroke) •Opioid • use
Agonal respirations	•Labored breaths, gasping, myoclonus • and grunting, often prior to terminal apnea • and death; can last seconds to hours.	•Cardiocirculatory arrest
Rapid, shallow breathing	•Rapid, shallow breaths with low tidal volume •.	•Pain (e.g., rib fracture) •Post-extubation, weaning from mechanical ventilation •Pneumonia •, pulmonary edema •Asthma •, COPD •Anxiety



(a) Gross section of an emphysemic lung



(b) Microscopic view of an emphysemic lung

(a) ©CNRI/Science Source; (b) ©McGraw-Hill Education/Al Telser

What is the approximate cross-sectional area of the trachea?
2.5 cm_2
How many alveoli are there present in a normal adult?
About 300 million
How many branches are there in the respiratory tree?
23
How many generations until alveoli are present; that is, how many branch generations
in the conducting zone?
16 (trachea to the terminal bronchioles)
What type of epithelium lines the conducting zone?
Ciliated, pseudostratified columnar (also known as respiratory epithelium)
At what point in the respiratory tree does gas exchange begin?
Respiratory bronchioles

What are the barriers to gas exchange at the alveolar-capillary interface?
- Surfactant
- Alveolar epithelium
- Interstitial space
- Capillary endothelium

What types of cells compose the alveolar surface?
- Type I pneumocytes: thin cells that constitute 90% of the surface area, even though less abundant than type II cells in numbers
- Type II pneumocytes: most abundant, but only constitute 10% of surface, and produce surfactant
- Phagocytic alveolar macrophages: ingests and clears foreign, inhaled particles

What are the two types of dead space?
1. Anatomic dead space (respiratory tree with no alveoli present)
2. Alveolar dead space (alveoli with no perfusion)

How is anatomic dead space approximated?
Ideal body weight in pounds is roughly equivalent to anatomic dead space in milliliters.

What is the function of anatomic dead space?
Warm and humidity inspired air Removal of foreign particles

In which locations and by what mechanisms is air filtered?
1. In vibrissae (aka nasal hairs)
2. By mucus in bronchi and bronchioles
3. Alveolar macrophages remove particles that make it to alveoli

What is the mucociliary escalator?
As foreign particles are trapped in the mucus that lines the epithelium of the respiratory tract, the cilia on the epithelium beat upwards, away from alveoli and lower respiratory structures.

What common inhalant inhibits the mucociliary escalator?
Cigarette smoke
Why do particles in venous blood not reach the arterial circulation?
They are filtered out by the pulmonary circulation (these particles can vary, but can be clots, agglutinated red blood cells, gas bubbles, etc).
What does this "filter" prevent?
Thrombotic or occlusive events on the left side of circulation (such as stroke, MI, etc)

Define the following lung volumes:

Tidal volume (V_T)

Volume of a normal breath at rest (average 500 mL)

Inspiratory reserve volume (IRV)

Additional volume of gas that can be inspired above the V_T (average 3 L)

Expiratory reserve volume (ERV)

Volume of gas that can be forcefully expired after a normal passive expiration (average 1.3 L)

Residual volume (RV)

Volume of gas that remains after maximal expiration (average 1.5 L)

How are lung volumes and capacities related?

A capacity is the sum of two or more volumes

Define the following lung capacities:

Total lung capacity (TLC)

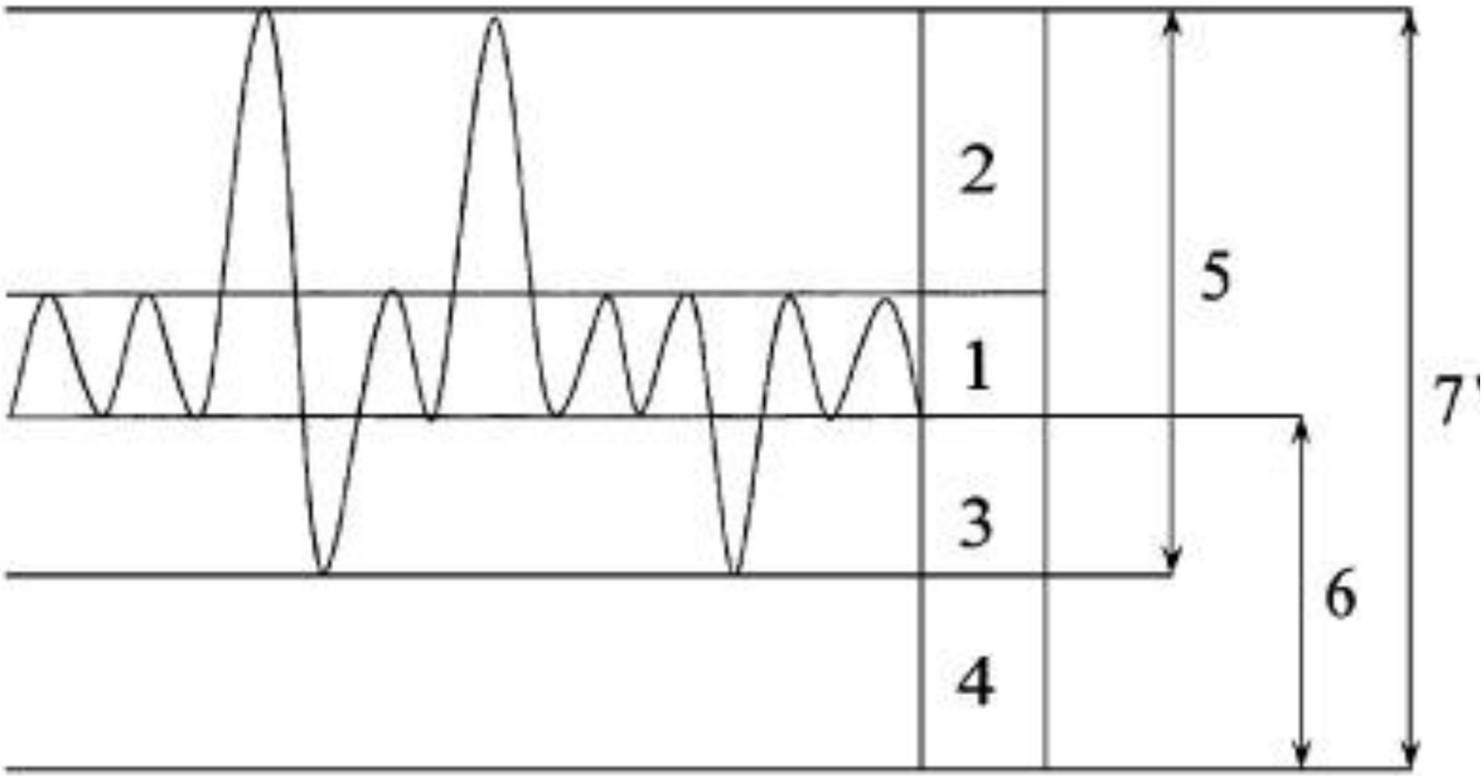
Volume of gas present after a maximal inspiration (average 6 L)

Vital capacity (VC)

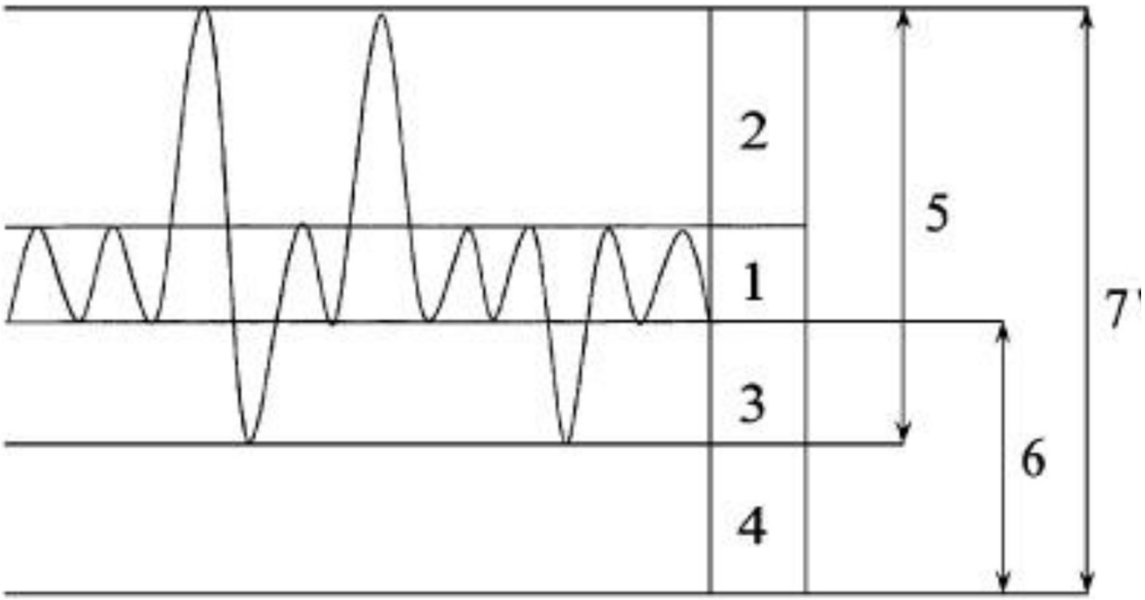
- Maximal volume that can be expelled after a maximal inspiration (average 4.5 L).
- This is the maximal volume that can be exchanged in a single breath

Functional residual capacity (FRC)

Volume remaining at the end of a normal breath at rest (average 3 L)



Identify the labeled lung volumes on the spirogram above.



1. Tidal volume (V_T)
2. Inspiratory reserve volume (IRV)
3. Expiratory reserve volume (ERV)
4. Residual volume (RV)
5. Vital capacity (VC)
6. Functional reserve capacity (FRC)
7. Total lung capacity (TLC)

What are the volumes that make up the following capacities?

Inspiratory capacity (IC)

IC = V_T + IRV

FRC

FRC = RV + ERV

VC

VC = ERV + V_T + IRV

TLC

TLC = RV + ERV + V_T + IRV

Which lung volumes and capacities cannot be measured using spirometry?

RV, FRC, and TLC

How does FRC change with position?

FRC increases when standing/sitting and decreases when supine

How does age affect the following parameters of pulmonary function tests (PFTs)?

TLC

Decreased

RV

Increased

VC

Decreased

FRC

Does not change

Define minute ventilation (V_E):

Volume of air inspired or expired per minute: $V_E = V_T \times$ frequency

What are:
Forced vital capacity (FVC)
Volume exhaled with maximal expiratory effort
Forced expiratory volume in 1 second (FEV_1)
Volume that can be forcefully expired in 1 second
What is the normal ratio of FEV_1 per FVC?
80% ($FEV_1/FVC = 0.8$)
What is alveolar ventilation?
The volume of air reaching the alveoli per minute
Why is alveolar ventilation less than minute ventilation?
Last part of inspired air only reaches the conducting zone and never reaches the respiratory zone
How does shallow versus deep breathing affect alveolar ventilation?
Rapid shallow breathing produces much less alveolar ventilation; most of each breath ventilates the conducting zone

What are the muscles of inspiration?
1. Diaphragm (majority of work at rest)
2. External intercostals (increase thoracic size and prevent retraction)
3. Accessory muscles of inspiration (not used during quiet breathing)

What are the accessory muscles of inspiration?
Sternocleidomastoid, scalenes, strap muscles of neck
What is the innervation of the diaphragm?
Phrenic nerve (C3,4,5 keep the diaphragm alive)
Where does referred diaphragmatic pain occur?
Ipsilateral shoulder (remember the dermatomes of the nerve roots!)

Does the diaphragm contribute more to inspiration while supine or standing?
Supine; when standing, external intercostals contribute significantly
What action does the diaphragm perform?
As it contracts it flattens into the abdominal cavity, increasing the volume of the thoracic cavity
Which muscles are involved in normal, quiet expiration?
None. It is a passive process due to the elastic recoil by the lungs.

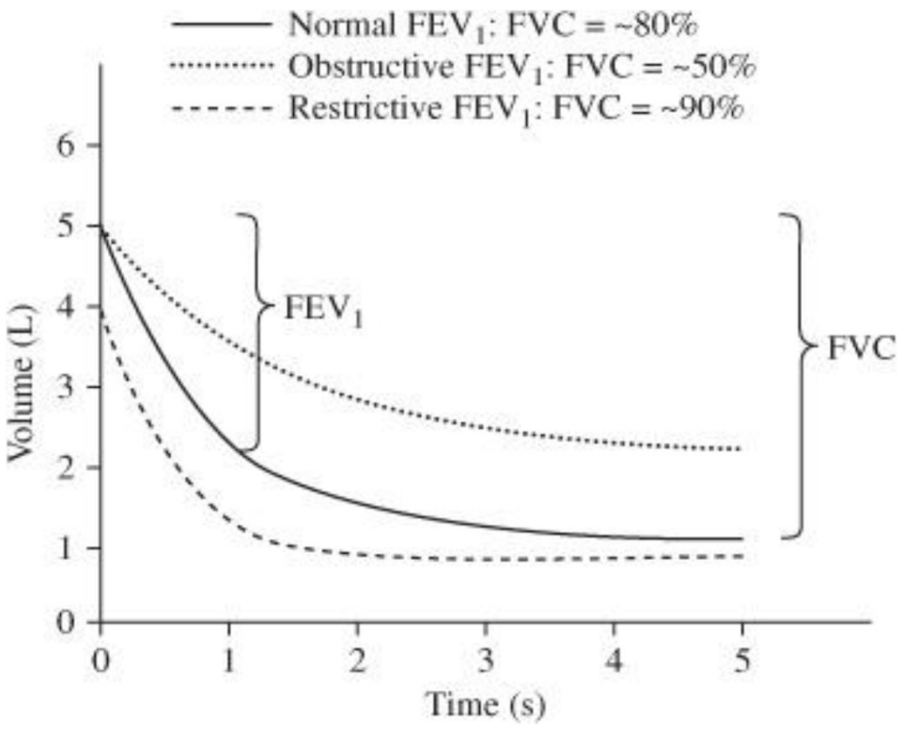
Which muscles are active in active expiration (e.g., exercise)?
Abdominal muscles and internal intercostals
During quiet breathing, which is longer, inspiration or expiration?
Expiration, in about a 2:1 ratio
Where is the intrapleural space?
It is between the lung and the chest wall. It is actually only a "potential space" under normal conditions because the visceral and parietal pleural layers are usually closely apposed.
What is the normal intrapleural pressure at rest?
Slightly subatmospheric (−3 to −5 cm H_2O)
How can the intrapleural pressure be measured?
A swallowed balloon can measure the intrathoracic pressure, which approximates the intrapleural pressure

Define compliance (C):
An indication of how easily the lungs and chest wall can be stretched or inflated.
In general terms, it refers to the lungs ability to accommodate incoming volume.
What is the equation for compliance?
$C = \Delta V/\Delta P$
ΔV = change in volume
ΔP = change in pressure
What physiologic elements influence compliance?
Most widely discussed are things like intrinsic recoil of pulmonary tissues, but remember that lung volume and alveolar surface tension also contribute

What is the normal series of events during inspiration?

Respiration initiated by central
nervous system
↓
Diaphragm contracts, along with
other external intercostals ↓ Thoracic volume increases
Decrease in intrapleural pressure
↓
Alveoli expand
↓
Alveolar pressure becomes
subatmospheric
↓
Air flows into alveoli to equilibrate
with atmospheric pressure

What processes can cause a decrease in compliance?
Pulmonary congestion and various restrictive lung diseases
What causes an increase in compliance?
Destruction of lung tissue with concomitant loss of elastic tissues (e.g., emphysema)



Comparison of spirograms between normal and diseased lungs.
Compare the FEV1: FVC ratio of a normal lung to a lung with emphysema or chronic bronchitis (COPD)
Normal lung has an FEV1: FVC ratio of 80%, emphysematous lung has an FEV1:
FVC ratio of <80% (usually 60%-70% or less).
What other obstructive lung disease cause this pattern?
Asthma, bronchiectasis
What physical examination findings correlate with obstructive lung disease?
Increased anteroposterior diameter of the chest (barrel chested), and prolonged expiratory phase
How does the FVC compare between a normal lung and one with restrictive disease?
Total FVC is lower due to decreased lung compliance

How does compliance change with lung volumes?
Increases at low volumes, decreases at high volumes
Define elasticity:
The recoil force generated by distension of a structure
How is compliance related to elasticity?
Inversely (*C*= 1/*E*)
What contributes to the lungs' recoil properties?
Lung parenchyma (elastin, collagen, etc)
Surface tension at air-liquid interface in alveoli

How does Laplace law relate to surface tension, and how does that affect the collapsibility of alveoli?
P = collapsing pressure (dyne/cm$_2$)
T = surface tension (dyne/cm)
r= alveolar radius (cm)

$$P = \frac{2T}{r}$$

Which is easier to keep open, a large alveoli or a small one?
Large alveoli (alveolar radius is inversely proportional to collapsing pressure, see above equation)
Which cells produce surfactant?
Type II alveolar epithelial cells

What are the functions of pulmonary surfactant?

1. Reduce surface tension at low lung volumes (prevent atelectasis)
2. Increase surface tension at high lung volumes (contribute to lung recoil)
3. Increase alveolar radius
4. Reduce pulmonary capillary infiltration

What is the effect of surfactant on compliance and elasticity?

Surfactant increases compliance, and decreases elasticity

What is surfactant composed of?

1. Dipalmitoyl phosphatidylcholine (aka lecithin)-major
2. Phosphatidylglycerol
3. Other lipids
4. Neutral lipids
5. Proteins

How may surfactant synthesis be reduced?

- Developmental deficiency (e.g., prematurity)
- Hypovolemia
- Hypothermia
- Acidosis
- Hypoxemia
- Rare genetic disorders of surfactant synthesis

What is the significance of surfactant in infant respiratory distress syndrome (IRDS)?

In this condition a surfactant deficiency results in high surface tension in the alveoli of the lungs, leading to alveolar collapse and atelectasis.
Because of this, there is decreased FRC with subsequent arterial hypoxemia.

By what week do the fetal lungs make surfactant?
Week 34 to 36

What may indicate fetal pulmonary maturity?
The ratio of lecithin to sphingomyelin or L/S ratio in the amniotic fluid. Over the course of gestation, lecithin gradually increases with pulmonary maturity while the sphingomyelin remains constant, so it serves as a useful meter.
The presence of minor phospholipids (e.g., phosphatidylglycerol) is also indicative in cases where the L/S ratio is borderline.

What L/S ratio usually indicates pulmonary maturity?
2:1

What can be used to help accelerate the maturation of surfactant in the lungs of a fetus?
Glucocorticoid hormones

Under normal conditions, what structural feature of individual alveoli helps to prevent them from collapsing?
Alveolar walls and airway walls are structurally connected so that tension on alveolar walls created by one collapsing alveolus helps to hold adjacent alveoli open.

What is the above theory called?
Alveolar interdependence

What two types of resistance make up pulmonary resistance?
1. Airway resistance (~80%)
2. Pulmonary tissue resistance (~20%)

In what pathologic states is pulmonary tissue resistance increased?
Fibrosis from any cause, examples include amyloidosis and sarcoidosis

What factors determine airway resistance?

Gas viscosity
Diameter of the airway
Length of the airway

$$R = \frac{8\eta l}{\pi r^4}$$

What law describes airway resistance?

Poiseuille law:
R = resistance
η = viscosity of inspired gas
l = length of airway
r= radius of airway

How are airway resistance and airflow related?

Much like flow through the cardiovascular system, they are inversely related:
Q = airflow (L/min)
Δ *P*= pressure gradient (cm H_2O)
R = airway resistance (cm/H_2O/L/min)

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

Which part of the respiratory system is the major site of airway resistance?

Medium-sized bronchi

Which part of the respiratory system has the highest individual resistance?

Small terminal airways; they are not the major site of airway resistance because they are far more numerous and are arranged in parallel

What causes bronchoconstriction?
Parasympathetic discharge
Substance P
Adenosine
Hypersensitivity response (e.g., histamines)
Arachidonic acid metabolites (e.g., prostaglandins and leukotrienes)

How does bronchoconstriction affect airways?
1. Reduces airway radius
2. Increases resistance
3. Via the above two changes, limits airflow during inspiration or expiration

What causes bronchodilation?
Sympathetic discharge and sympathetic agonists via ***β2*** receptors

How do obstructive diseases affect respiratory mechanics?
Increase airway resistance; it creates air trapping which increases lung volumes

How do restrictive diseases affect respiratory mechanics?
Decrease compliance, affecting inspiration mechanics; more on this later

What is the fraction of oxygen in ambient air?
21%

What is the fraction of carbon dioxide in ambient air?
0.04% (can assume atmospheric CO_2 is equal to zero)

What are the partial pressures of O_2 and CO_2 in the following locations?

Atmospheric air
O_2: 160 mm Hg, CO_2: 0 mm Hg

Air in the trachea
O_2: 150 mm Hg, CO_2: 0 mm Hg

Alveolar air
O_2: 100 mm Hg, CO_2: 40 mm Hg

Arterial blood
O_2: slightly < 100 mm Hg, CO_2: 40 mm Hg

Mixed venous blood
O_2: 40 mm Hg, CO_2: 46 mm Hg

Why is the PO_2 in the trachea less than that of the atmosphere?
The air in the trachea is humidified (addition of H_2O, which decreases PO_2)

Why is the PO_2 in arterial blood slightly less than 100 mm Hg?
Regional *V/Q* mismatching and normal physiologic shunt

What is a *physiologic shunt?*
The ~2% of systemic cardiac output that bypasses the pulmonary circulation (bronchial circulation)

True or false? The composition of alveolar gas remains relatively constant at rest.
True

Why does alveolar gas composition remain constant at rest?
Because the FRC (2.8 L on average) is much larger than the tidal volume (0.5 L on average), creating a steady state environment for P_AO_2 and P_ACO_2

Define gas exchange:
Transport of gas from alveoli to hemoglobin (Hb) in the blood across the respiratory membrane

Where in the respiratory system does gas exchange occur?
In the terminal portions of the airways (respiratory bronchioles, alveolar ducts, and alveoli)

At rest, how long does it take for the blood to traverse the pulmonary capillaries?
It takes only 0.75 second for blood to move through the portion of the capillary where gas exchange occurs

What happens to this time during exercise?
Decreases (down to 0.25 seconds under strenuous exercise)

What factors determine pulmonary gas diffusion?
1. Surface area for diffusion
2. Partial pressure difference across membrane
3. Thickness of barrier
4. Diffusivity of gas

How is O_2 transported in blood?
In arterial blood at PO_2 100 mm Hg, PCO_2 40 mm Hg, and Hb 97% saturated
Major: chemical combination with Hb (19.5 mL O_2/100 mL blood)
Minor: dissolved in the plasma (0.29 mL O_2/100 mL blood)

What is the partial pressure (oxygen tension) of normal O_2 arterial blood?
85 to 100 mm Hg

In normal adults, what are hemoglobin molecules (HbA) composed of?
Two α and two β chains. There are exceptions: fetal hemoglobin and disease states

What are the functions of hemoglobin?
1. Facilitates O_2 transport
2. Facilitates CO_2 transport
3. Buffers p_H of the blood
4. Facilitates NO transport

What is heme?
Complex made up of a porphyrin ring and one atom of ferrous iron (there is one heme group per chain)

What is the role of the ferrous iron (Fe^{2+})?
Each ferrous iron reversibly binds one O_2 molecule making four binding sites per hemoglobin molecule

What is the significance of the iron in heme?
It has six available orbitals for binding, four to the pyrole groups of the porphyrin ring, one to the polypeptide chain, and one that can associate with oxygen

How does the hemoglobin structure affect its oxygen-carrying capacity?
Hemoglobin has a quaternary structure that varies in its affinity for oxygen depending on the number of oxygen bound to it.

How are the hemoglobin subunits affected in a deoxygenated state?
Hemoglobin subunits are in a *tense (tight)* configuration with a relatively lower affinity for O_2

How are the hemoglobin subunits affected when they have oxygen attached to them?
With each progressive O_2 molecule, hemoglobin takes on a *relaxed* configuration where subsequent binding of O_2 is facilitated as each O_2-binding site is exposed (called allosterism)

How does Hb affect the O_2 content in blood?
Increases the amount of O_2 that can be carried in the blood almost 70-fold

What percent of O_2 in arterial blood is carried by hemoglobin?
~98.5%

Define hemoglobin saturation:
Percent of hemoglobin that is combined with O_2

What influences the amount of O_2 that combines with hemoglobin?
O_2 tension (PO_2) or O_2 saturation

Define O_2 capacity:
The maximal amount of O_2 that can be carried in the blood by hemoglobin

What is the hemoglobin-oxygen dissociation curve?
The curve relating percent saturation of the O_2-carrying capacity of hemoglobin to the PO_2

What does decreased oxygen affinity mean?
A higher PO_2 is required for hemoglobin to bind a given amount of O_2.

What factors decrease the affinity of hemoglobin for oxygen?
In general, think of exercise and altitude
1. Low pH (acidosis—increased H)
2. Increased PCO_2
3. Increased temperature
4. Increased 2,3-diphosphoglycerate (2,3-DPG) concentration

What factors cause an increase in 2, 3-DPG concentrations?
1. High pH
2. Thyroid hormone
3. Growth hormone
4. Androgens
5. High altitudes

What is meant by a "left shift"?
As the Hb dissociation curve shifts to the left, it saturates *at a lower* PO_2, but is more reluctant to unload O_2.
As an example, think of fetal Hb. It has a higher affinity for O_2 (a "left shift"), so it will "steal" O_2 from maternal Hb, but it is less eager to unload O_2 in the fetal tissues.

What is the *P*50?
It is the PO_2 where the Hb is 50% saturated with oxygen. It is a useful measure of Hb kinetics

What does decreased oxygen affinity favor?
Oxygen delivery to tissue
In the above diagram, does the line labeled "b" have a higher or lower P_{50}?
Higher
How does that new *P*50 value relate to O_2 affinity/unloading?
That line represents decreased affinity/increased oxygen unloading. The opposite is true for the line labeled "a."
What is the Bohr effect?
Decreased Hb affinity for oxygen due to lowered pH. This is related to the fact that protonated Hb (HbH) binds oxygen less avidly.
Where is the Bohr effect used physiologically?
In the peripheral tissue (helps unload oxygen in metabolically active tissues)

How does fetal hemoglobin (HbF) differ from adult hemoglobin (HbA)?
HbF contains γ-polypeptide chains instead of ***β*** chains

What is the significance of the βchains versus the β-chains HbF?
There is poor binding of 2, 3-DPG by the βchains causing HbF to have greater affinity for O_2 than HbA.

How does anemia affect 2,3-DPG concentration in red blood cells (RBCs)?
Increases it

How is myoglobin in muscle different from hemoglobin in blood?
Myoglobin binds one, rather than four, molecules of O_2 per protein

Where is much of the myoglobin found?
In skeletal muscles
What does decreased arterial O_2 content cause?
Decreased hemoglobin saturation and reduced arterial O_2 tension
For which does Hb have more affinity, CO or O_2?
CO (~200 × greater affinity)
What is formed as a result of CO reacting with hemoglobin?
Carboxyhemoglobin
How does carboxyhemoglobin formation affect O_2 content?
- Decreases the functional Hb concentration
- Reduces oxygen-carrying capacity of blood
- Lowers the tissue O_2 tension

How is CO_2 transported in blood?
1. As HCO_3^- in plasma (major)
2. Dissolved in plasma or in RBCs (minor)
3. Formation of carbamino-Hb in RBCs (minor)
4. Formation of carbamino compounds with plasma protein (minor)

How does HCO_3^- enter the plasma?
Cl^- antiporter in RBC membrane (chloride shift)
Which two factors determine arterial or alveolar CO_2 tensions.
1. Rate of CO_2 production
2. Alveolar ventilation

What is the Haldane effect?
Binding of O_2 to hemoglobin reduces its affinity for CO_2
Where does the Haldane effect occur physiologically?
Lungs
What is methemoglobin?
Hb that contains ferric (Fe^{3+}) has a very high affinity for oxygen, resulting in decreased ability of Hb to unload oxygen.

What is the physiologic response of the lungs to hypoxia?
Vasoconstriction (opposite from the systemic response to hypoxia!)
Why does this occur?
To shunt blood away from non-ventilated regions of the lungs toward ventilated regions

Define ventilation (*V*):
Transport of gas from the environment to the alveoli for gas exchange (normal about 4-6 L/min)
Define perfusion (*Q*):
Pulmonary blood flow to the alveolar capillaries
What is the normal *V/Q* ratio?
0.8 to 1.2
What is the most common cause of hypoxemia?
V/Q mismatch
What occurs to alveolar gas partial pressures with an increase in *V/Q?*
Decrease in PCO_2, increase in PO_2
What occurs to alveolar gas partial pressures with a decrease in *V/Q?*
Increase in PCO_2, decrease in PO_2
In other words, which area of the lung has greater dead space?
The apices; they are ventilated, but are poorly perfused.

What is the normal distribution of ventilation and perfusion in a standing person?
- Ventilation: highest at base, lowest at apex
- Perfusion: highest at base, lowest at apex

Which has a higher *V/Q:* bases or apices?
Apices (ventilation > perfusion)
Which has a lower *V/Q:* bases or apices?
Bases (perfusion > ventilation)
Why is the *V/Q* ratio low at the base and high at the apex?
The change in blood flow from the apex to the base is *relatively greater* than the change in ventilation
What is a shunt?
Perfusion with no/low ventilation

Where is respiration centrally controlled?
Reticular formation in the medulla (medullary respiration center)
Where do the nerve fibers that mediate inspiration converge?
On the phrenic motor neurons located in the ventral horns from C3 to C5 and the external intercostal motor neurons in the ventral horns throughout the thoracic cord
Where do fibers concerned with expiration converge?
Primarily on the internal intercostal motor neurons in the thoracic cord
What is the dorsal respiratory group (DRG)?
Inspiratory cells that may act as the primary rhythm generator for respiration
What stimulates DRG activity?
1. Low O_2 tensions
2. High CO_2 tensions
3. Low pH levels
4. Increased electrical traffic resulting from renal artery stenosis (RAS)

What nerves mediate input to the DRG?
- Vagus: peripheral chemoreceptors and lung mechanoreceptors
- Glossopharyngeal: peripheral chemoreceptors

Where does the outflow from DRG project?
Contralateral phrenic and intercostals motor neurons, and the ventral respiratory group (VRG)

What makes up the VRG?
Upper motor neurons of the vagus and the nerves to the accessory muscles of respiration

What is the role of the VRG?
Activated to control expiration when it is an active process (e.g., exercise)
Where is the apneustic center?
Caudal area of the lower pons
What is the significance of the apneustic center?
Efferent outflow increases the duration of inspiration
Where is the pneumotaxic center?
Upper part of the pons
What is the function of the pneumotaxic center?
Unknown, it is thought to inhibit the apneustic center and shortens inspiration. It
may play a role in switching between inspiration and expiration.
How does damage to the pneumotaxic center affect respiration?
Respiration becomes slower and V_T greater
Where are central chemoreceptors located?
Beneath the ventral surface of the medulla
What do central chemoreceptors respond to?
H^+ concentration in the cerebrospinal fluid (CSF) and the surrounding interstitial fluid
What is the major chemical drive of respiration?
CO_2 (H^+) effects on the central chemoreceptors

Where are the peripheral chemoreceptors located?
Carotid and aortic bodies

What do peripheral chemoreceptors respond to?
1. Lowered O_2 tensions
2. Increased CO_2 tensions
3. Increased H^+ concentrations in arterial blood

What stimuli affect the respiratory center?

Chemical control:
1. CO_2 (via CSF and brain interstitial fluid H^+ concentration)
2. O_2 (via carotid and aortic bodies)
3. H^+ (via carotid and aortic bodies)

Nonchemical control:
1. Vagal afferents from receptors in the airways and lungs
2. Afferents from the pons, hypothalamus, and limbic system
3. Afferents from proprioceptors
4. Afferents from baroreceptors

How does the respiratory system respond to exercise?

- Increase minute ventilation (through initially increased tidal volume and then increased frequency)
- A-a gradient widens (excessive exercise)
- Respiratory (CO_2/O_2) exchange ratio exceeds 1, but < 1.25

How does the pulmonary blood flow change during exercise?

Increases, due to increased pulmonary artery pressures and a decrease in pulmonary vascular resistance (as well as more venous return to the heart due to deeper inspirations)

What occurs to the *V/Q* matching during exercise?

V/Q increases (ventilation increases more than perfusion increases)

How does the amount of O_2 in the body change with exercise?

Total O_2 content increases, but PaO_2 remains steady

How does the PO_2 of blood flowing into the pulmonary capillaries change with exercise?

Falls to 25 mm Hg or less because of increased extraction

How does CO_2 excretion change with exercise?

Increases to as much as 40-fold because of increased amount of CO_2 produced

What happens to the mean values for arterial PO_2 and PCO_2 during exercise?

No change in oxygen, CO_2 constant during aerobic respiration (decreases slightly with anaerobic respiration and lactic acid production).

What happens to arterial pH during exercise?

No change with moderate exercise, but it decreases with strenuous exercise due to lactic acidosis

What is hypoxia?

O2 deficiency at the tissue level

What are the signs of hypoxia?

Cyanosis, tachycardia, and tachypnea

A 46-year-old plumber presents to the doctor with slowly progressing difficulty breathing. He is diagnosed with restrictive lung disease secondary to exposure at work. How would his lung compliance be affected? Which part of breathing would he have difficulty with, inspiration or expiration? How would his FEV1/FVC be affected?

His compliance would be decreased due to stiffness of his lungs. He would have trouble with inspiration, as the stiffness of his lungs would prevent him from expanding his lungs fully. His FEV1/FVC would be unchanged, as his FEV1 and FVC would be decreased in the same proportion.

A healthy, 25-year-old friend of yours asks you why exercise makes you feel short of breath. What is your answer?

You explain to him that during exercise, the limiting factor in oxygenation to tissues is not the amount of oxygen you are getting into your lungs, rather it is because of the amount of blood traversing the pulmonary vasculature per unit time (flow limitation).

The body demands O2 in excess of what is being delivered and central receptors perceive this as shortness of breath

A 40-minute-old male neonate of an 18-year-old Caucasian female at 27 weeks gestation is noted to have central cyanosis. His respirations are shallow and rapid at 65/min. Other vital signs are stable. On examination, there is nasal flaring, audible grunting, and duskiness with intercostal and subcostal retractions. Fine rales are
heard over both lung bases. Nasal O2 does not improve his cyanosis. A chest x-ray (CXR) reveals fine reticular granularity, predominantly in lower lobes. Arterial blood gas (ABG) reveals hypoxemia with metabolic acidosis. What is the underlying cause of his condition?

Decreased production and secretion of surfactant resulting in atelectasis and shunting (perfused but non-ventilated alveoli). This ventilatory defect leads to the bodies inability to excrete its acid load