Respiratory physiology

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Learning objectives

Pulmonary ventilation

Mechanism of breathing – breathing muscles, intrathoracic and intrapulmonary pressure. Surface tension in alveoli, surfactant. Application of the law of Laplace in lungs. Respiratory work. Pneumothorax.

Transport of gases through alveolar-capillary membrane

Composition of atmospheric and alveolar air. Diffusion through the alveolar-capillary membrane. Oxygen –haemoglobin dissociation curve, the Bohr effect. CO_2 dissociation curve.

Regulation of breathing

Neuronal regulation – respiratory centre. Chemoreceptors – effect of hypoxia and hypercapnia. Mechanoreceptors in lungs – Hering–Breuer reflexes. Protective reflexes of respiratory system. Response of the ventilation to physical activity.

Diagnostic and therapeutic methods in clinical practice

Spirometry – flow-volume loop. Pneumotachography. Pneumography. Measurement of the death space. Measurement of residual volume of the lungs. Artificial ventilation.

Overview of respiratory system

OVERVIEW OF AIRWAY PHYSIOLOGY

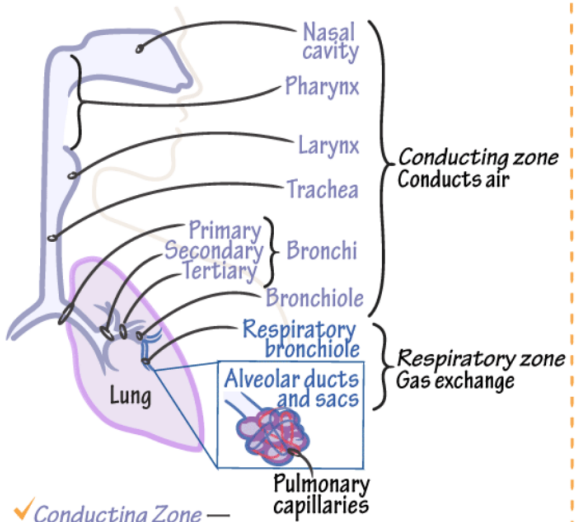
Respiratory Zones

- ✓ *Conducting* —
  - ✓ Conducts air into and out of the lungs. Lined with ciliated mucous membranes that remove foreign materials.
- ✓ *Respiratory* —
  - ✓ Provides surfaces for gas exchange with pulmonary capillaries.

Asthma

- ✓ Narrow airways prevent sufficient airflow and oxygen intake to meet tissue demands.
- ✓ Certain treatments induce bronchial dilation to increase airflow.

2 Functional Divisions



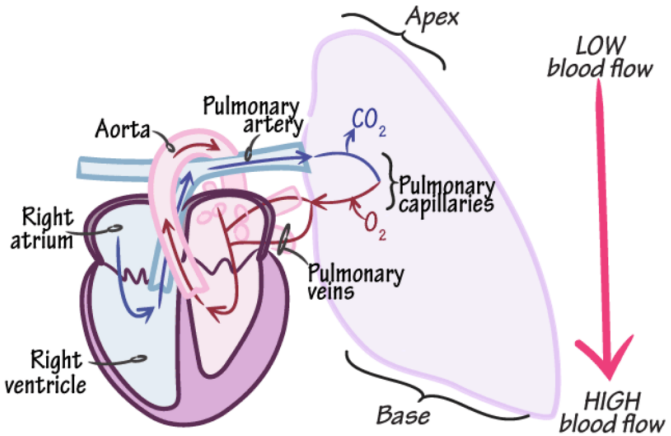
✓ *Conducting Zone* —
Regulate airflow;
Most easily achieved by changing bronchial diameter:

↓ Diameter = ↑ Resistance = ↓ Airflow

↑ Diameter = ↓ Resistance = ↑ Airflow

✓ *Respiratory Zone* —
Alveoli are sac-like pouches;
- Type I — Flat epithelial cells w/ large surface area; predominant type.
- Type II — Cuboidal cells Synthesize surfactant, reduce surface tension.

Pulmonary Circulation

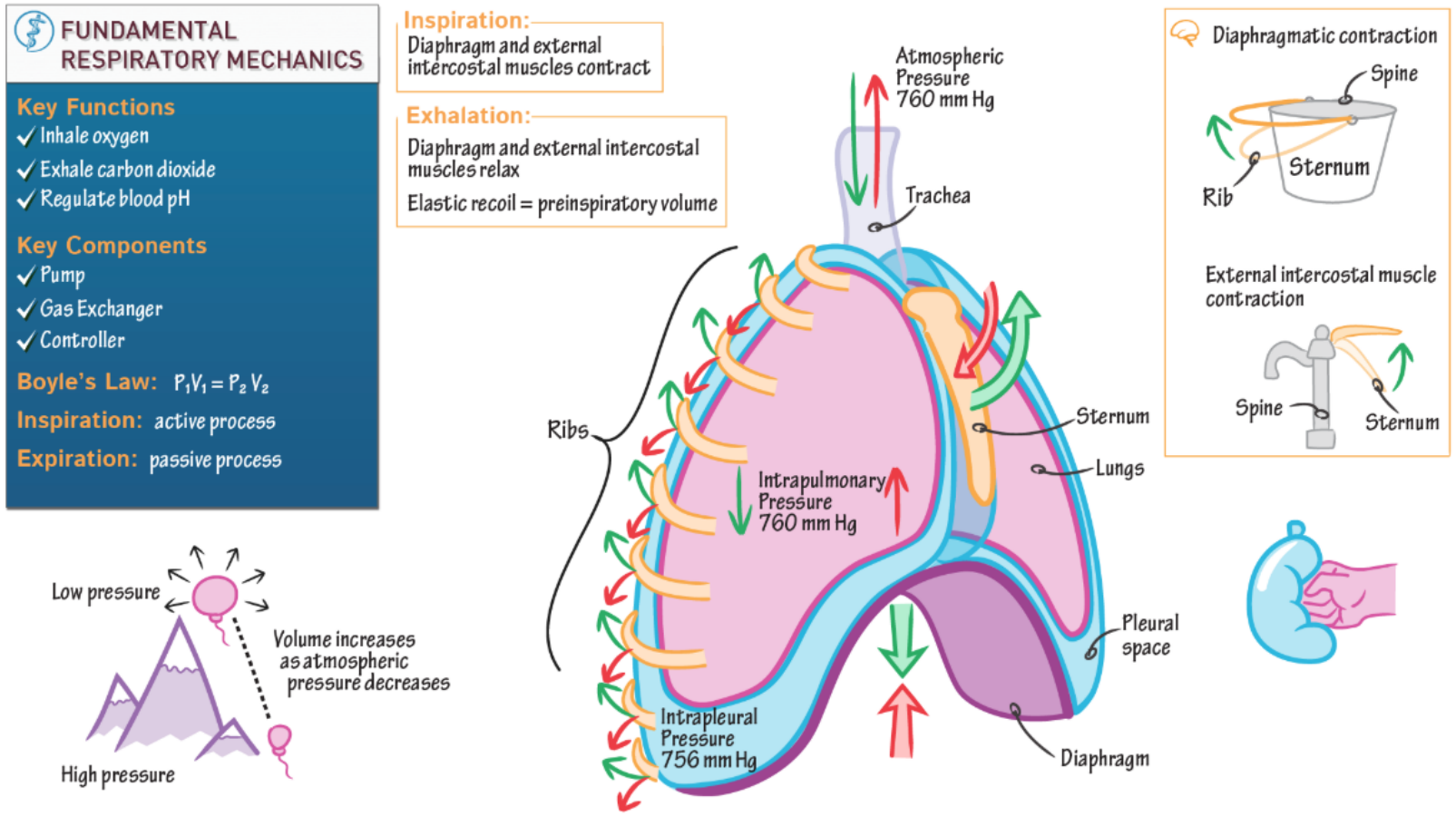


✓ *Pulmonary blood flow* —
Equal to the cardiac output of the right ventricle.

✓ *Bronchial circulation* —
Blood supply to conducting zone; small portion of total blood flow that does not take part in gas exchange.

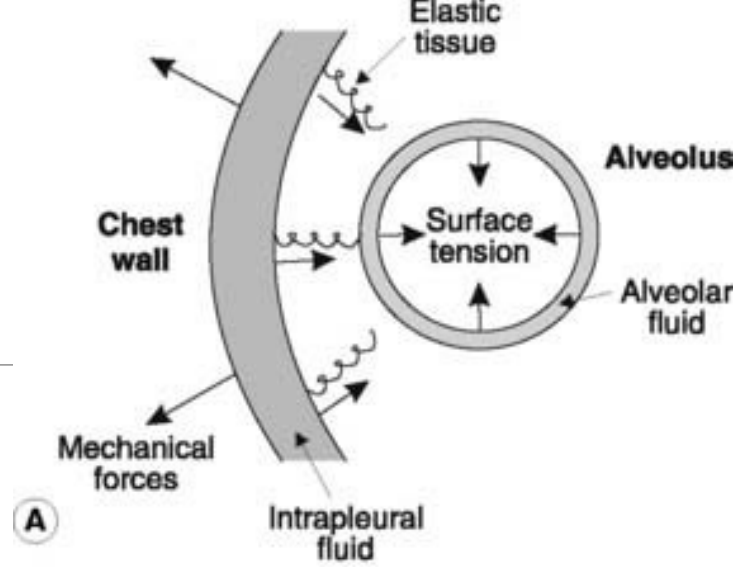
✓ *Gravitational effects* —
In upright position, pulmonary blood flow is not equally distributed.

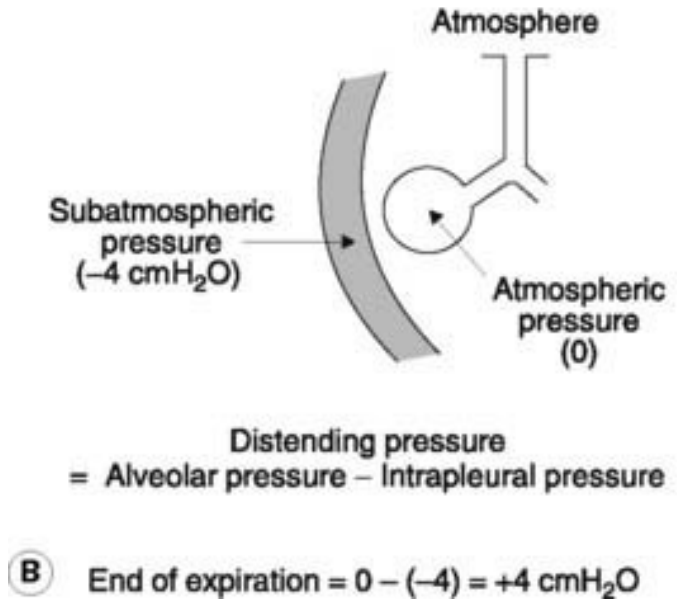
Respiratory mechanics



Forces acting on the lung

1. elasticity of lung (elastic recoil) (collapsing force)
2. Lung surface tension (collapsing force)
3. Chest wall recoil (opening force)
4. Intrapleural pressure-IPP (opening force)





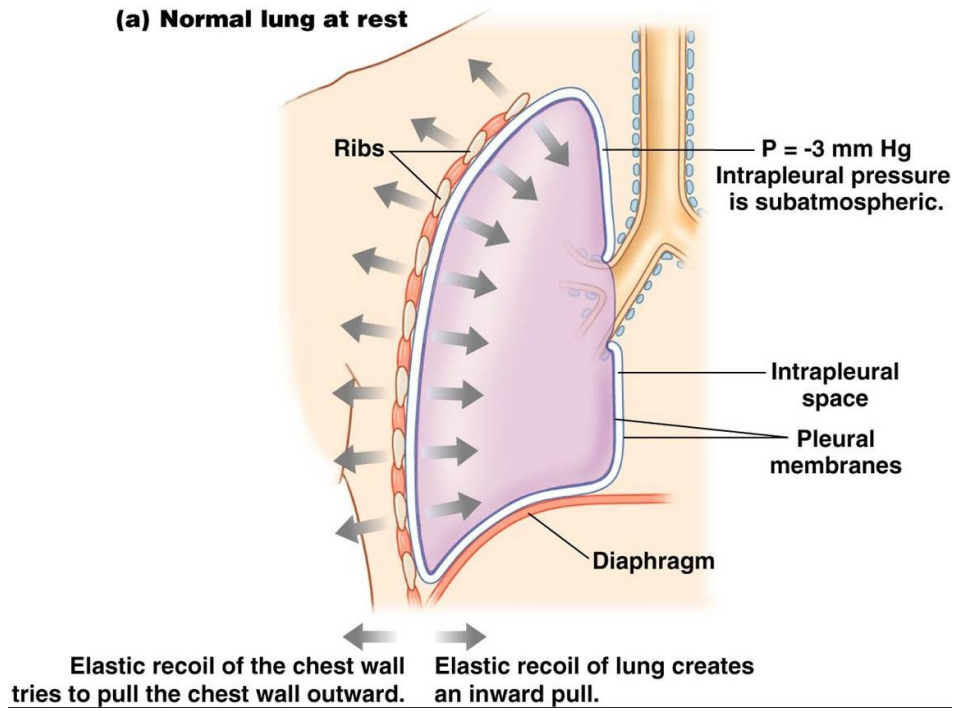
Lung recoil and chest wall recoil

Lung Recoil

- Represents the inward force created by the elastic recoil properties of alveoli.
- As the lung expands, recoil increases; as the lung gets smaller, recoil decreases.
- Recoil, as a force, always acts to collapse the lung.

Chest Wall Recoil

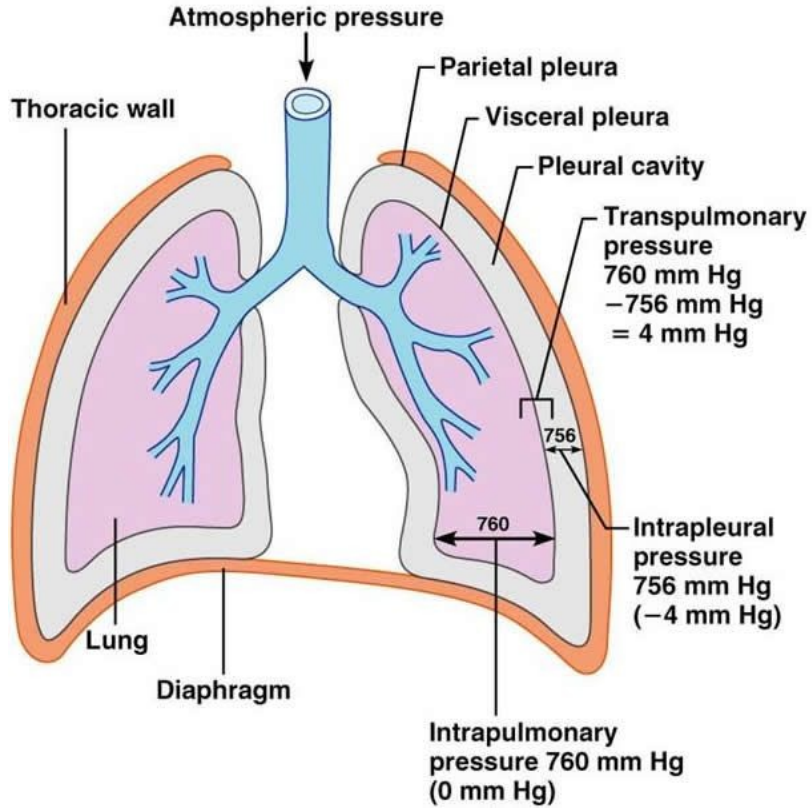
- Outward force of the chest wall
- FRC represents the point where this outward recoil of the chest wall is counterbalanced by the inward recoil of the lung.



Intrapleural pressure

Intrapleural Pressure (IPP)

- Represents the pressure inside the thin film of fluid between the visceral pleura, which is attached to the lung, and the parietal pleura, which is attached to the chest wall.
- The outward recoil of the chest and inward recoil of the lung create a negative (subatmospheric) IPP.
- IPP is the outside pressure for all structures inside the chest wall.



Major forces acting on the lung

Important points

- Intrapleural pressure > Lung recoil → **Lung Expands**
- Intapleural pressure < lung recoil → **lung collapse**
- Intrapleural pressure = Lung recoil → **lung size constant**

Transmural pressure

BIOPHYSICS OF BREATHING

1. Transthoracic (P_{tt}) - difference between alveolar pressure and body surface pressure

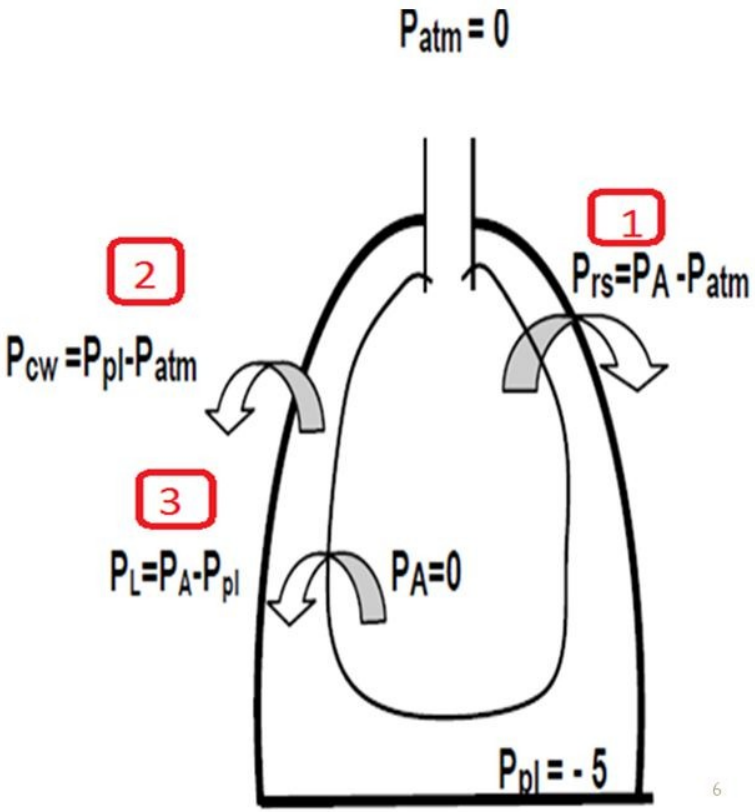
$(P_{tt}) = (P_{alv}) - (P_{atml})$

2 . Transchest pressure (P_{ta})- tdifference between the alveoli pressure (P_{alv}) and atmospheric pressure

$(P_{cw}).= P_{pl}- P_{atm}$

3. Transpulmonary pressure (P_{tp}) - difference between the alveolar pressure and the pleural pressure

$(P_{tp}) = (P_{alv}) - (P_{pl})$



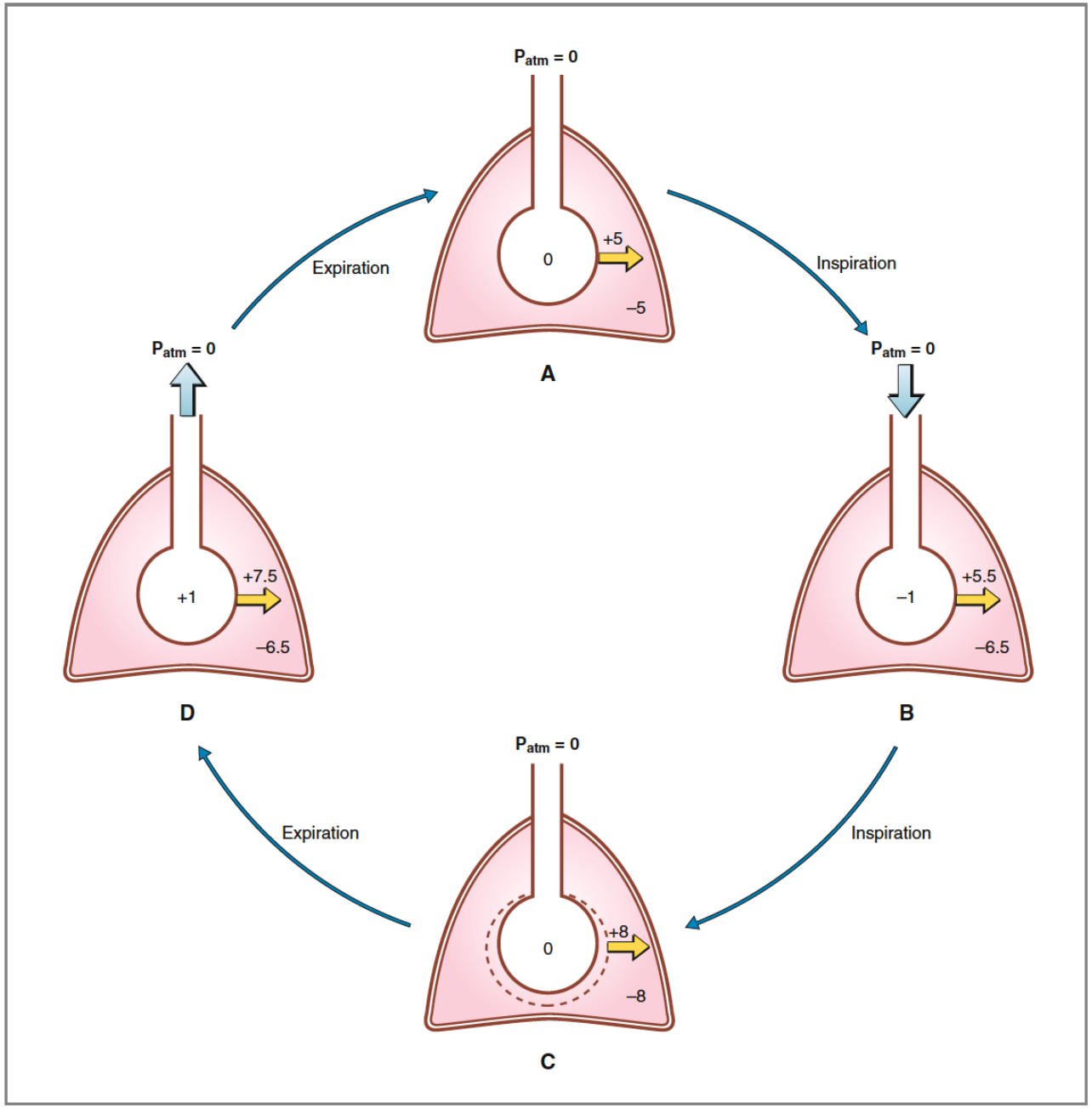
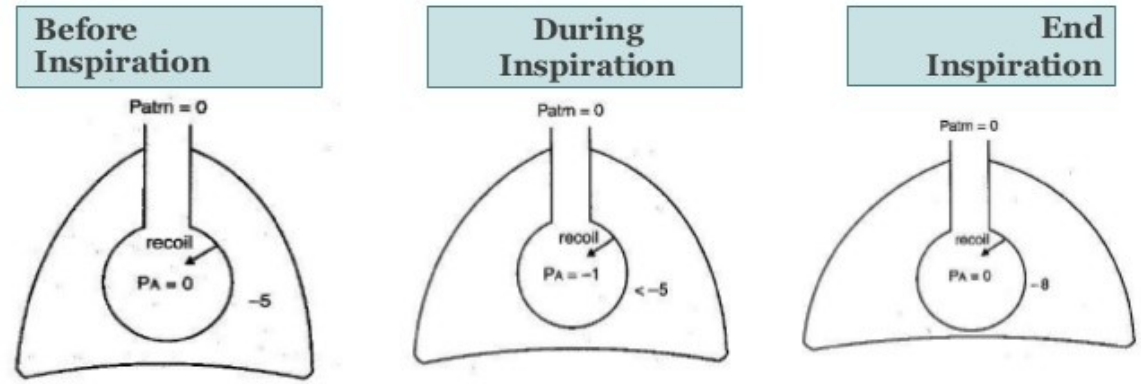


Figure 5-14 **Pressures during normal breathing cycle.** The numbers give pressures in cm H_2O relative to atmospheric pressure (P_{atm}). The numbers over the yellow arrows give the magnitude of transmural pressures. The *wide blue arrows* show airflow into and out of the lungs. **A**, Rest; **B**, halfway through inspiration; **C**, end of inspiration; **D**, halfway through expiration.

Mechanics Under Resting Condition



	Before	During	End Of
Intra pleural Pressure (cm H_2O)	-5	More negative less than -5	-8
Lung Recoil Force (cm H_2O)	5	More positive More than 5	8
Alveolar Pressure	0	slightly negative (-1)	0

Respiratory compliance

- is described by the following equation:

$$C = V/P$$

where:
C = compliance (mL/mm Hg)
V = volume (mL)
P = pressure (mm Hg)

- describes the **distensibility** of the lungs and chest wall.
- is **inversely related to elastance**, which depends on the amount of elastic tissue.
- is inversely related to stiffness.
- is the **slope of the pressure–volume curve.**
- is the change in volume for a given change in pressure. Pressure refers to transmural, or transpulmonary, pressure (i.e., the pressure difference across pulmonary structures).

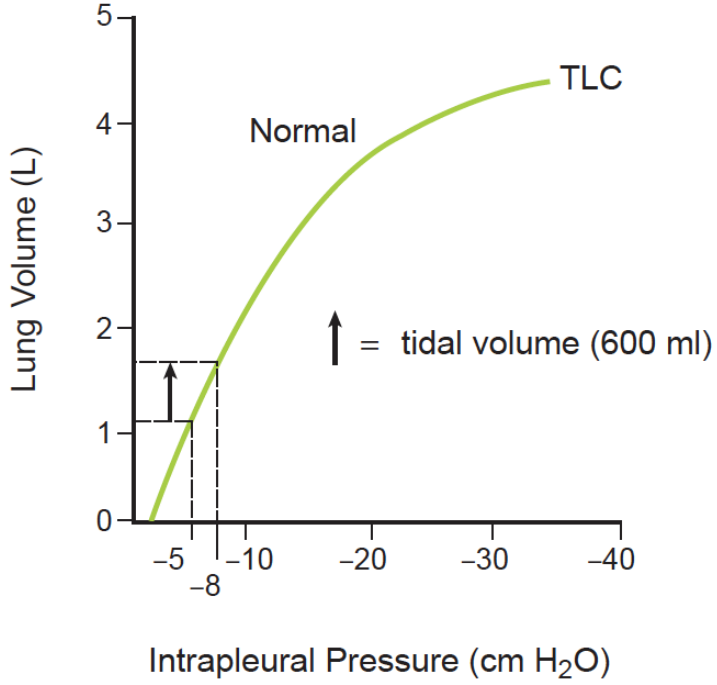


Figure VII-1-9. Lung Inflation Curve

Compliance vs elastance

Compliance Vs Elastance

- Compliance is a measure of distensibility
- Elastance is a measure of elastic recoil
- These both oppose each other!
  - Compliance decreases as Elastance increases:
    - » Pulmonary fibrosis (restrictive lung disease)
    - » Pulmonary hypertension/congestion
    - » Decreased surfactant – increased surface tension (prematurity, artificial ventilation)
  - Compliance increases as Elastance decreases
    - » Normal ageing (alteration in elastic tissue)
    - » Asthma (unknown reason)
    - » Emphysema* (obstructive lung disease)

Lung compliance changes

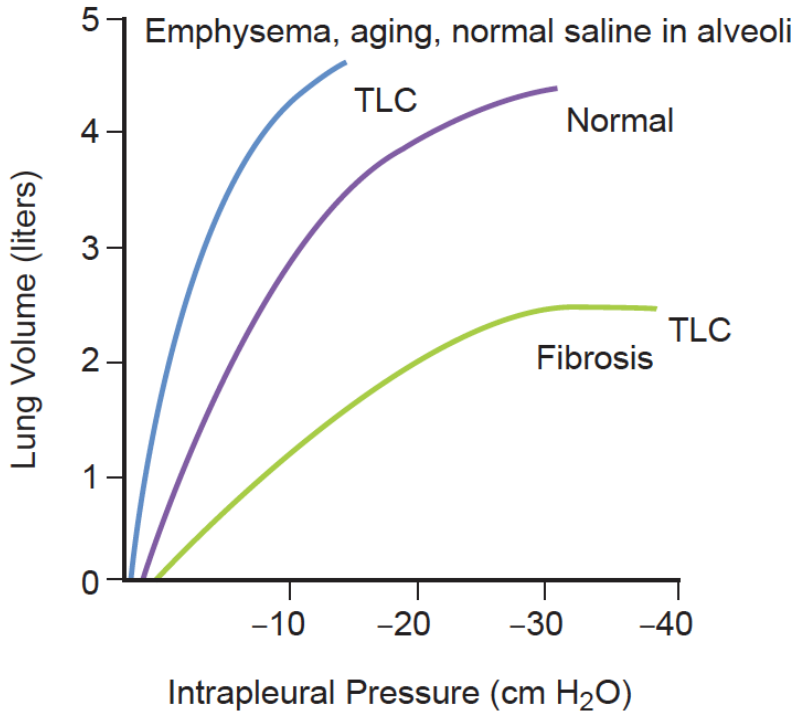


Figure VII-1-10. Lung Compliance

Surface tension

1. **Surface tension of the alveoli** (Figure 4-5)
   - results from the attractive forces between liquid molecules lining the alveoli.
   - creates a collapsing pressure that is directly proportional to surface tension and inversely proportional to alveolar radius **(Laplace's law)**, as shown in the following equation:

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

where:
P = collapsing pressure on alveolus (or pressure required to keep alveolus open) [dynes/cm^2]
T = surface tension (dynes/cm)
r = radius of alveolus (cm)

   a. **Large alveoli** (large radii) have low collapsing pressures and are easy to keep open.
   b. **Small alveoli** (small radii) have high collapsing pressures and are more difficult to keep open.
      - In the **absence of surfactant**, the small alveoli have a tendency to collapse **(atelectasis)**.

Surface tension

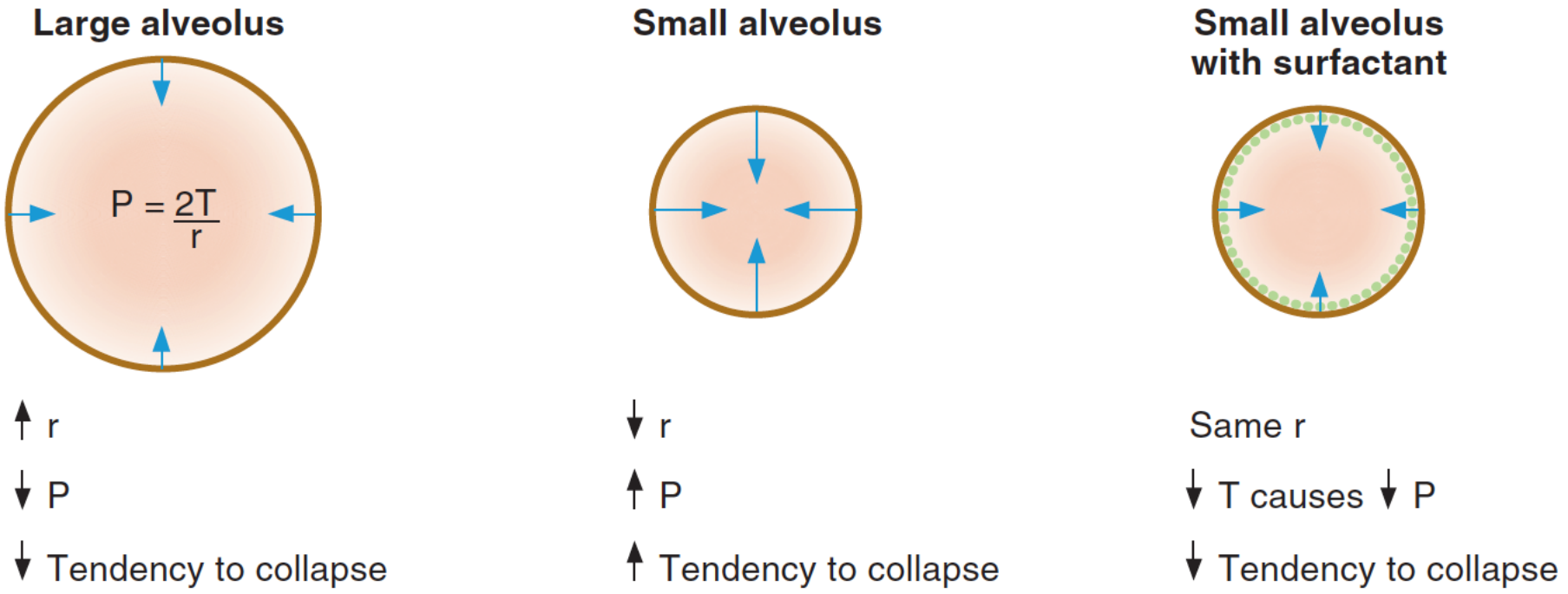


FIGURE 4-5 Effect of alveolar size and surfactant on the pressure that tends to collapse the alveoli. P = pressure; r = radius; T = surface tension.

Pneumothorax

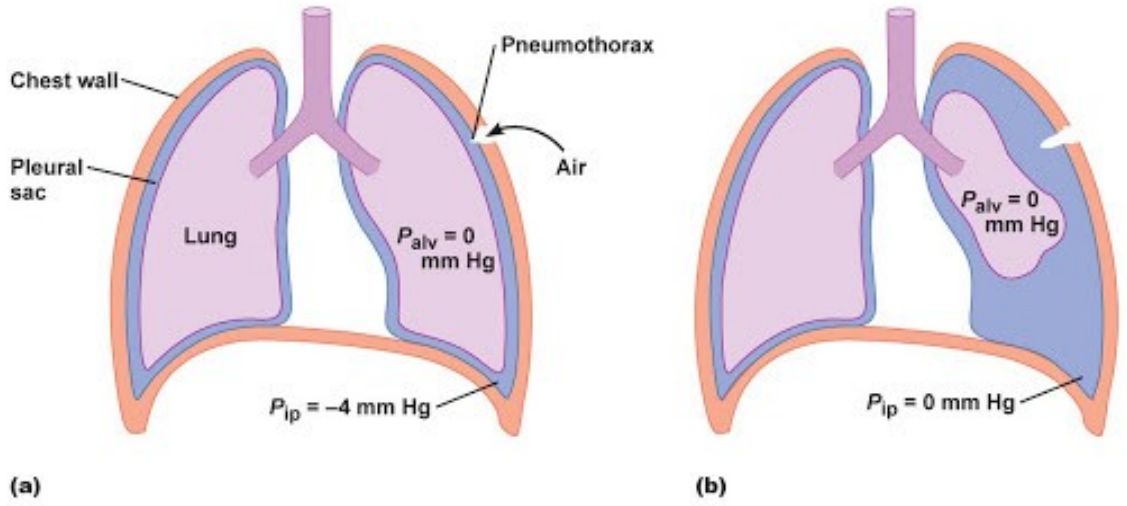
The following changes occur with the development of a simple pneumothorax. The pneumothorax may be (1) traumatic: perforation of the chest wall, or (2) spontaneous: rupture of an alveolus:

- Intrapleural pressure increases from a mean at –5 cm H_2O to equal atmospheric pressure.
- Lung recoil decreases to zero as the lung collapses.
- Chest wall expands. At FRC, the chest wall is under a slight tension directed outward. It is this tendency for the chest wall to spring out and the opposed force of recoil that creates the intrapleural pressure of –5 cm H_2O.
- Transpulmonary pressure is negative.

In some cases, the opening of the lung to the pleural space may function as a valve allowing the air to enter the pleural space but not to leave. This creates a tension pneumothorax.

Pneumothorax

- Strong inspiratory efforts promote the entry of air into the pleural space, but during expiration, the valve closes and positive pressures are created in the chest cavity. Ventilation decreases but the positive pressures also decrease venous return and cardiac output.
- Tension pneumothorax most commonly develops in patients on a positive-pressure ventilator.



Clinical Correlate

The common clinical signs of a tension pneumothorax include:

- Respiratory distress
- Asymmetry of breath sounds
- Deviation of the trachea to the side opposite the tension pneumothorax
- Markedly depressed cardiac output

Total work of respiratory muscles at quiet breathing

Elastic (static) work (65%)

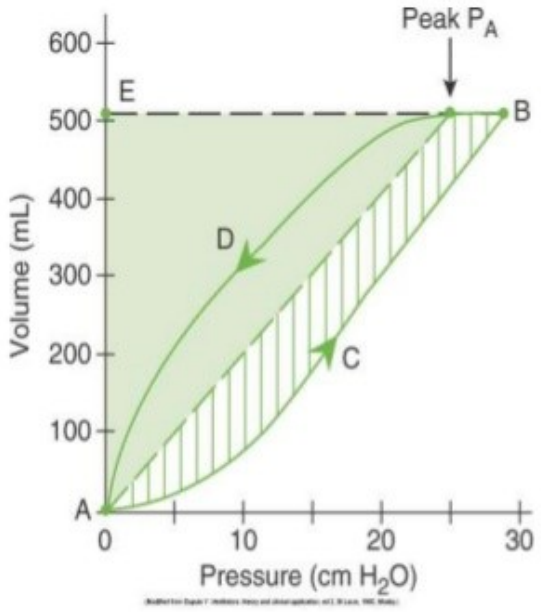
- To overcome the elastic forces of the chest and lungs

Dynamic work (35%)

- To overcome the resistence of air passage during the air movement - **aerodynamic resistence (28%)**
- To overcome the friction during mutual movement of inelastic tissue – **Viscous resistence (7%)**

Respiratory work

WORK OF BREATHING



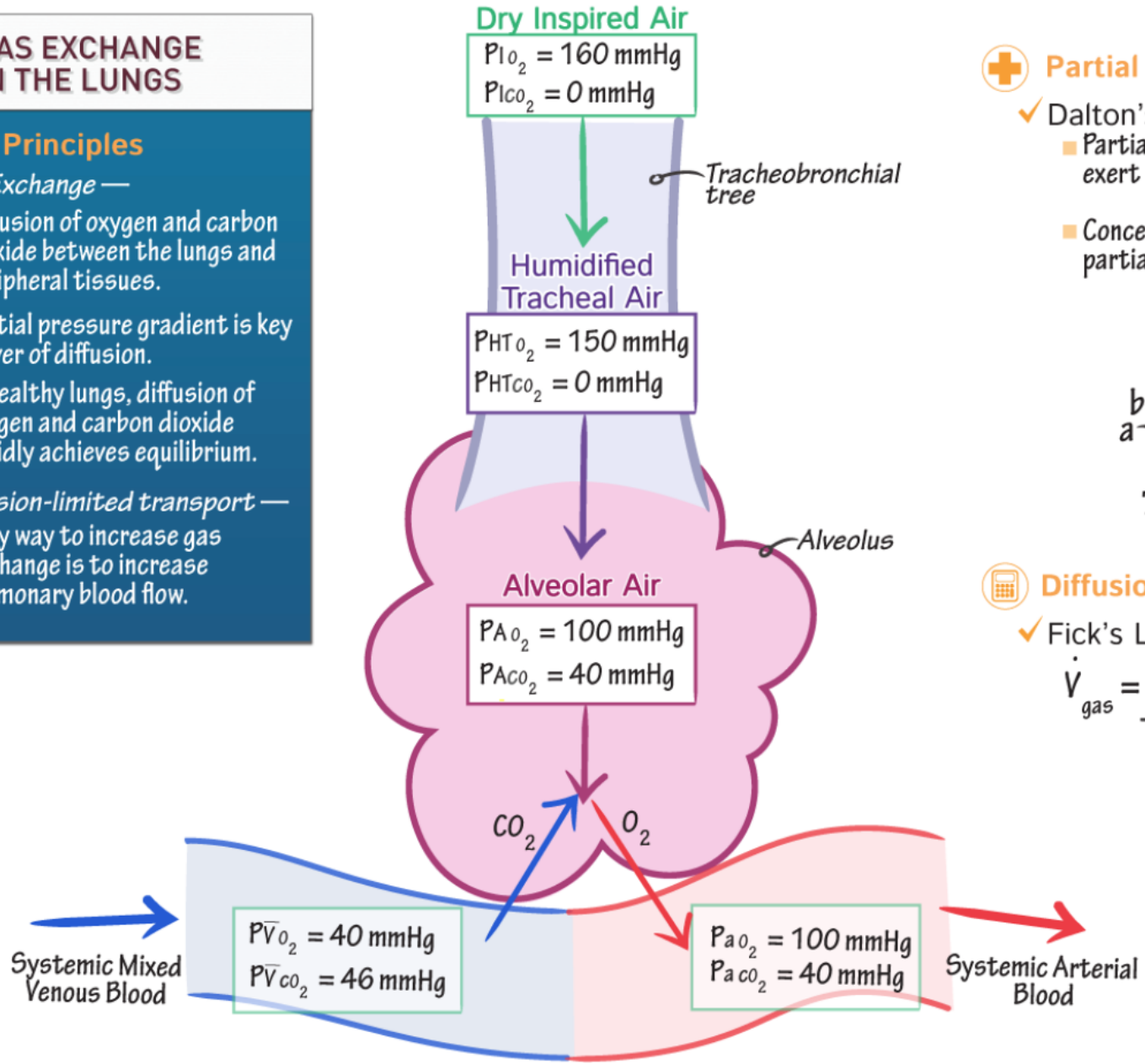
- Triangle AP_AE represents the **Compliance work**.
- Area $ACBP_A$ represents **Inspiratory Resistance work**.
- Triangle AP_AD represents **Expiratory Resistance work**.
- The area within the hysteresis represents total **Resistance work**.

GAS EXCHANGE IN THE LUNGS

Key Principles

✓ *Gas Exchange —*
- ✓ Diffusion of oxygen and carbon dioxide between the lungs and peripheral tissues.
- ✓ Partial pressure gradient is key driver of diffusion.
- ✓ In healthy lungs, diffusion of oxygen and carbon dioxide rapidly achieves equilibrium.

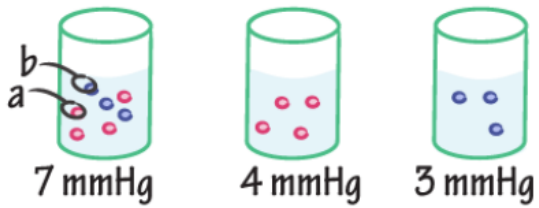
✓ *Perfusion-limited transport —*
- ✓ Only way to increase gas exchange is to increase pulmonary blood flow.



Partial Pressure

✓ Dalton's Law —
- Partial pressure is the pressure a gas would exert if it occupied the total volume of a mixture.
- Concentration of a gas depends, in part, on its partial pressure (Henry's Law).

$$P_{total} = P_a + P_b$$



Diffusion Rate Equation

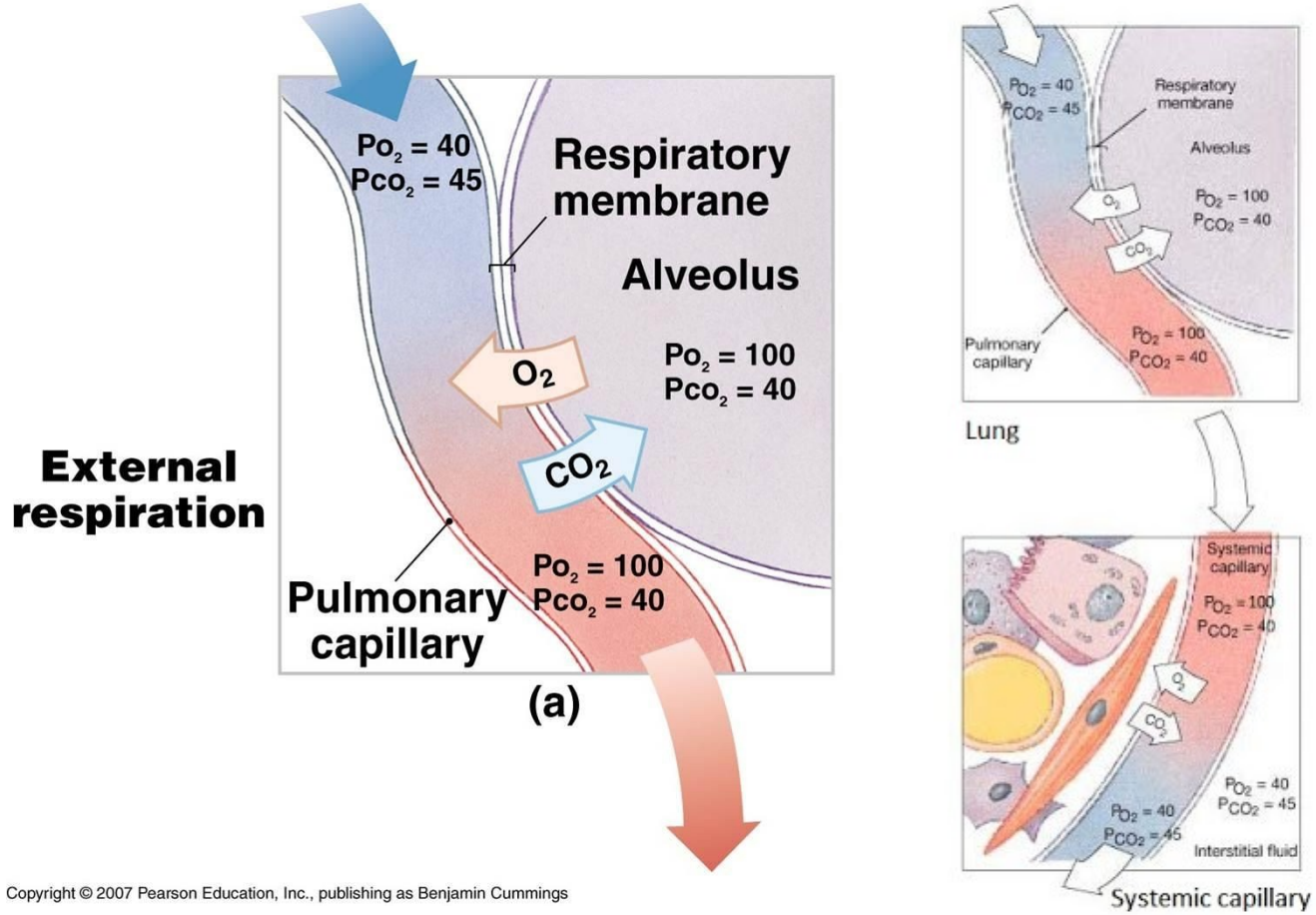
✓ Fick's Law

$$\dot{V}_{gas} = \frac{D * (P_1 - P_2) * A}{T}$$

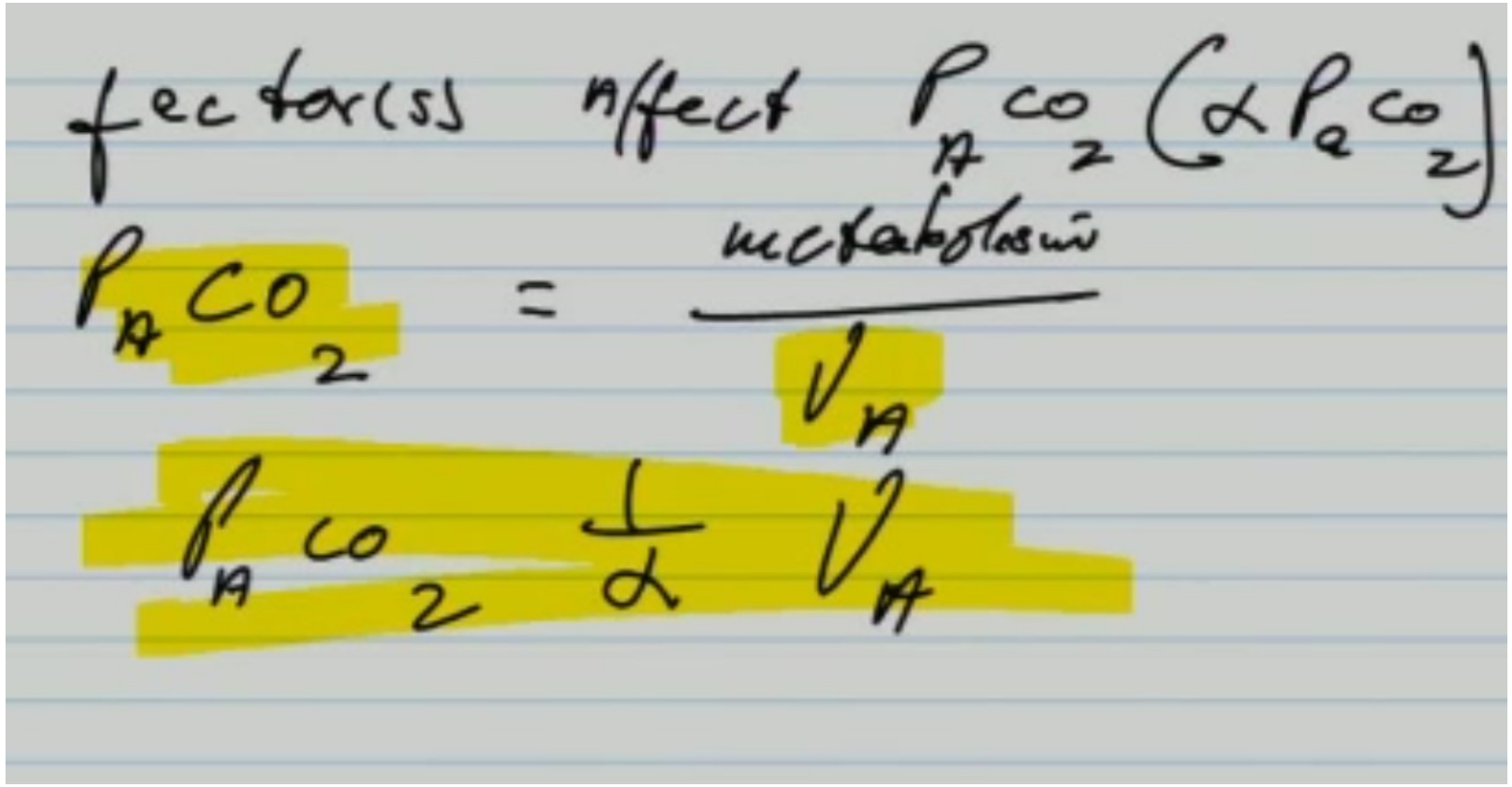
- Diffusion Coefficient (D)
- Partial pressure gradient ($P_1 - P_2$)
- Surface area (A)
- Thickness of barrier (T)

Respiratory diseases negatively affect diffusion rate
- Emphysema: Surface area decreases
- Fibrosis: Membrane thickness increases

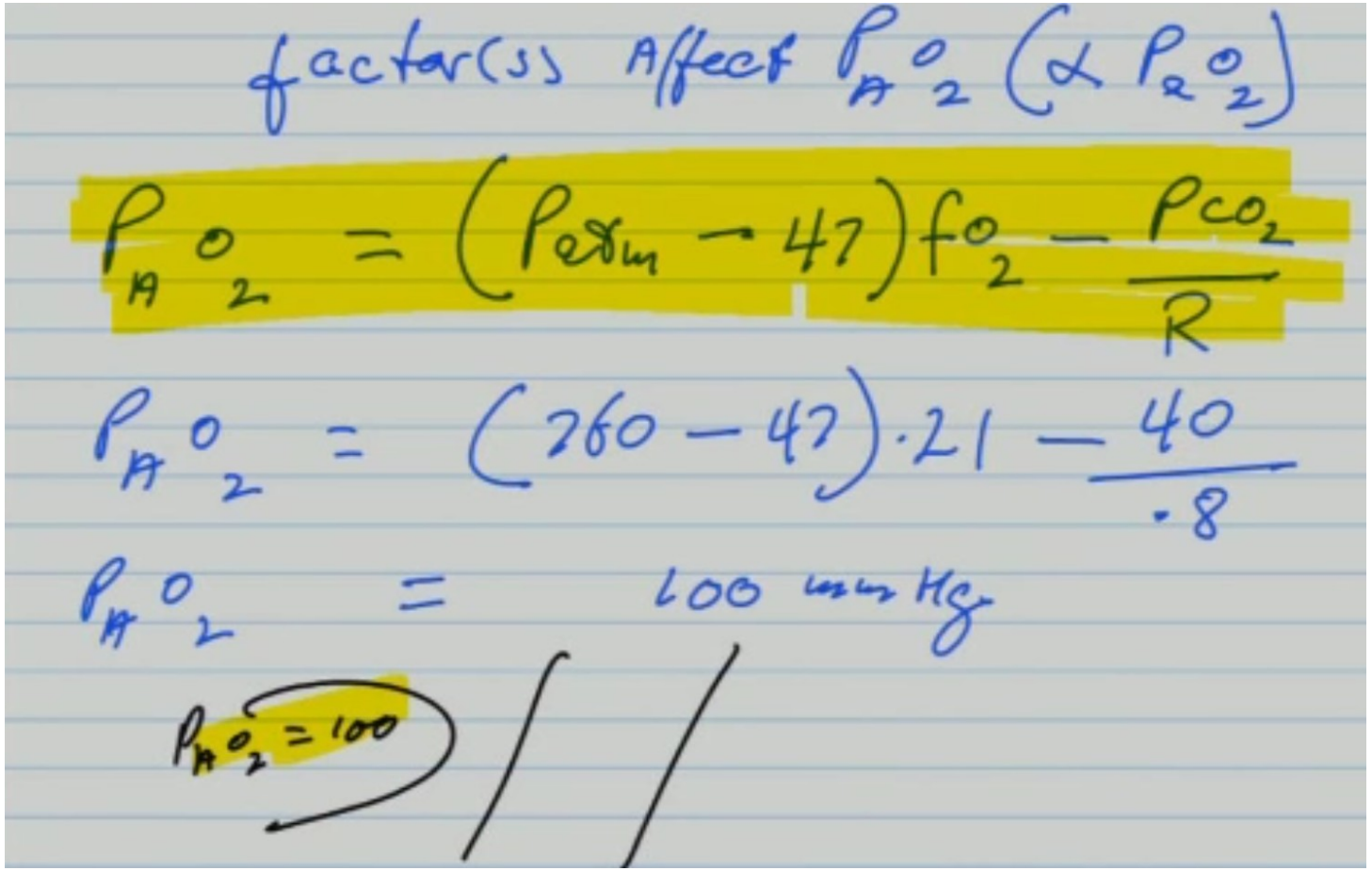
The lung and the transport of O2



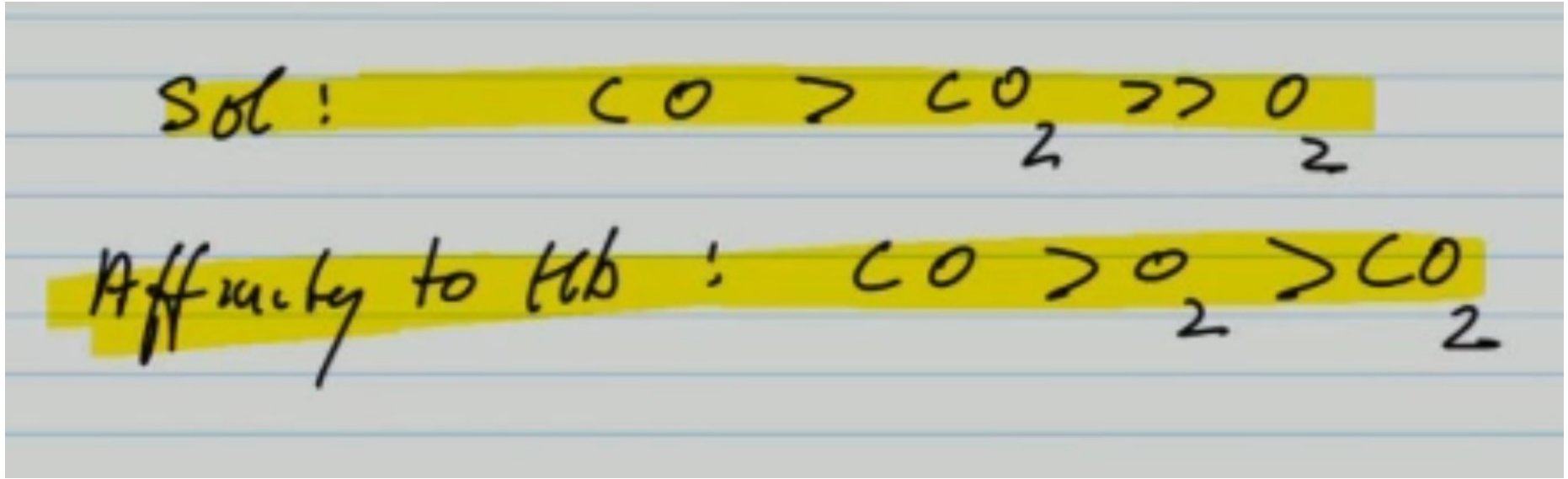
Factors affecting PACO2



Factors affecting PAO2



Solubility vs Hem affinity of Gasses



Oxygen-hemoglobin dissociation curve

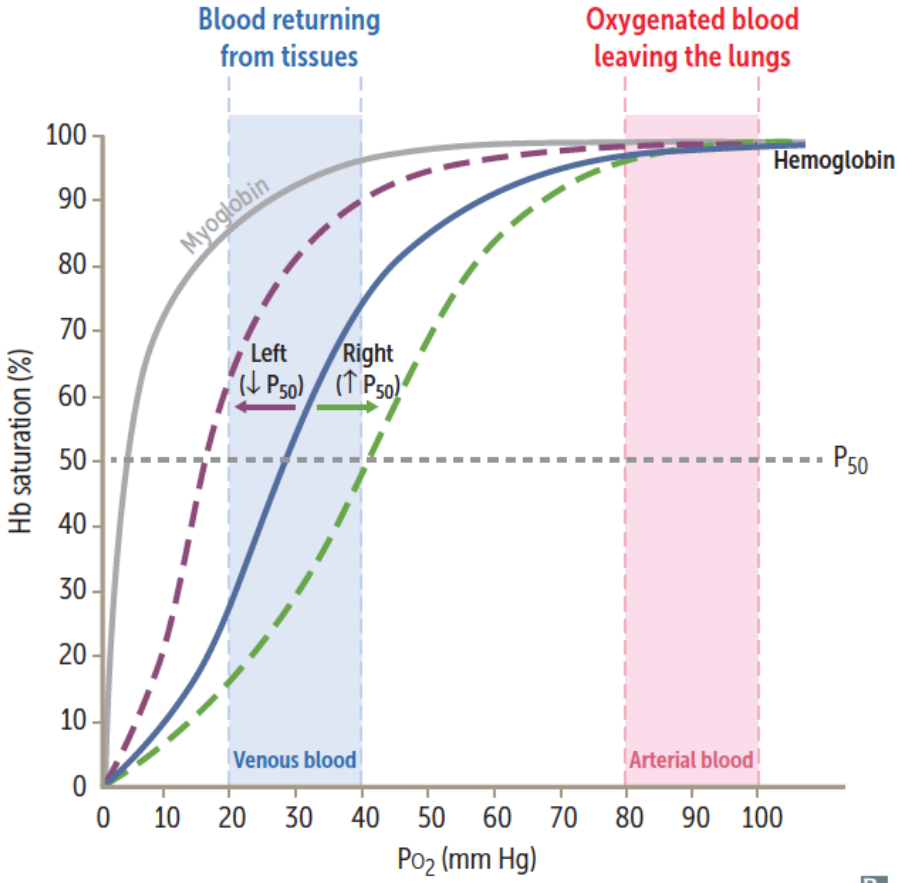
ODC has a sigmoidal shape due to positive cooperativity (ie, tetrameric Hb molecule can bind 4 O_2 molecules and has higher affinity for each subsequent O_2 molecule bound). Myoglobin is monomeric and thus does not show positive cooperativity; curve lacks sigmoidal appearance.

Shifting the curve to the right → ↓ Hb affinity for O_2 (facilitates unloading of O_2 to tissue) → ↑ P_{50} (higher Po_2 required to maintain 50% saturation).

Shifting the curve to the left → ↓ O_2 unloading → renal hypoxia → ↑ EPO synthesis → compensatory erythrocytosis.

Fetal Hb has higher affinity for O_2 than adult Hb (due to low affinity for 2,3-BPG), so its dissociation curve is shifted left.

Shift to the Right	Shift to the Left
Easier for tissues to extract oxygen	More difficult for tissues to extract oxygen
Steep part of curve, O_2 content decreased	Steep part of curve, O_2 content increased
P_{50} increased	P_{50} decreased



Left shift (↓ O_2 unloading to tissue) Left = Lower	Right shift (↑ O_2 unloading to tissues) ACE Bats right handed
↓ H^+ (↑ pH, base)	↑ H^+ (↓ pH, Acid)
↓ Pco_2	↑ Pco_2
↓ 2,3–BPG	Exercise
↓ Temperature	↑ 2,3–BPG
↑ CO	High Altitude
↑ MetHb	↑ Temperature
↑ HbF	

Carbon dioxide transport

Carbon dioxide transport

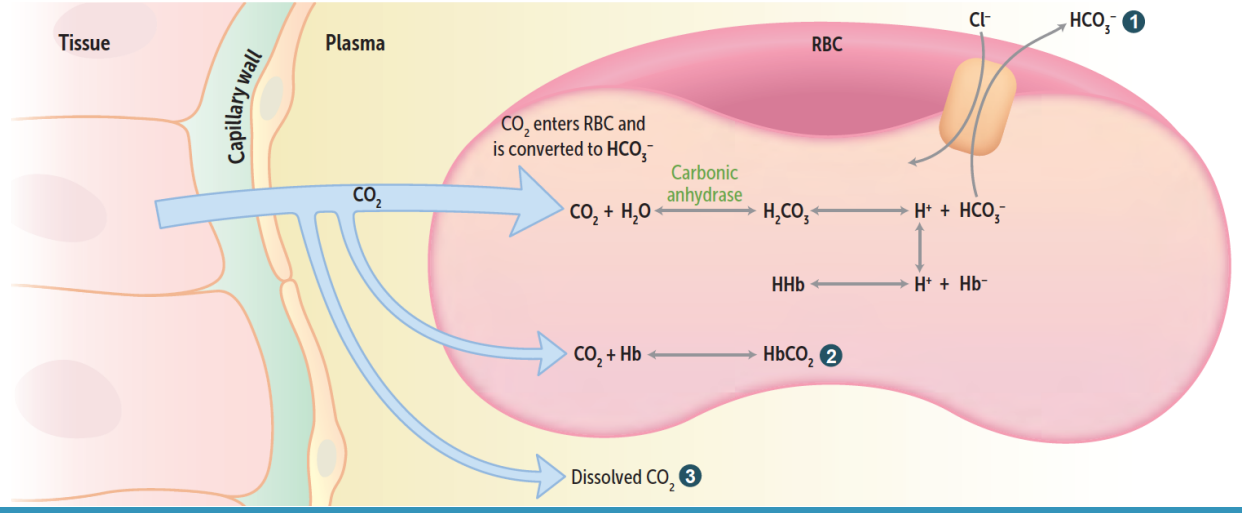
CO_2 is transported from tissues to lungs in 3 forms:

1. HCO_3^- (70%).
2. Carbaminohemoglobin or $HbCO_2$ (21–25%). CO_2 bound to Hb at N-terminus of globin (not heme). CO_2 favors deoxygenated form (O_2 unloaded).
3. Dissolved CO_2 (5–9%).

In lungs, oxygenation of Hb promotes dissociation of H^+ from Hb. This shifts equilibrium toward CO_2 formation; therefore, CO_2 is released from RBCs (Haldane effect).

In peripheral tissue, ↑ H^+ from tissue metabolism shifts curve to right, unloading O_2 (Bohr effect).

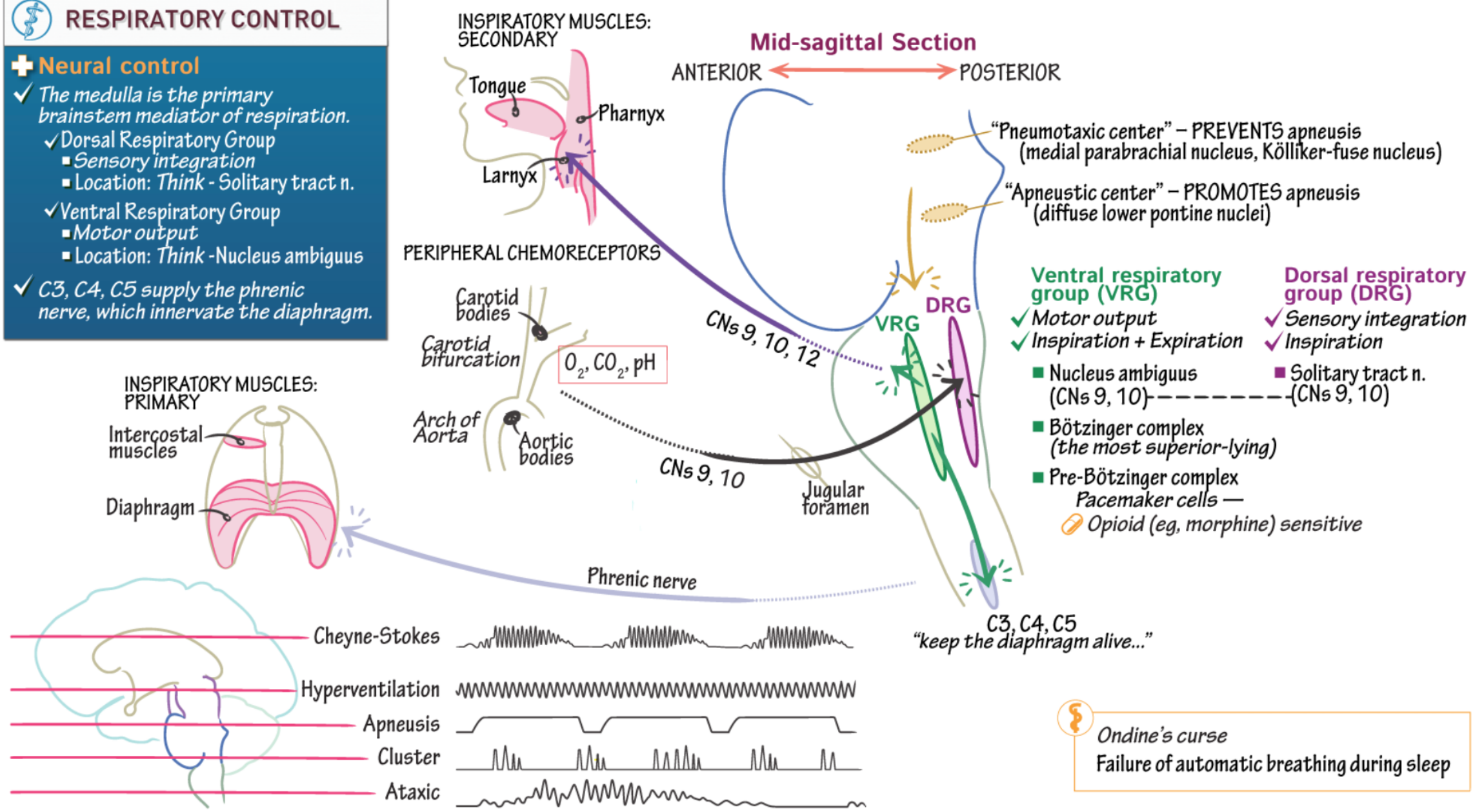
Majority of blood CO_2 is carried as HCO_3^- in the plasma.



RESPIRATORY CONTROL

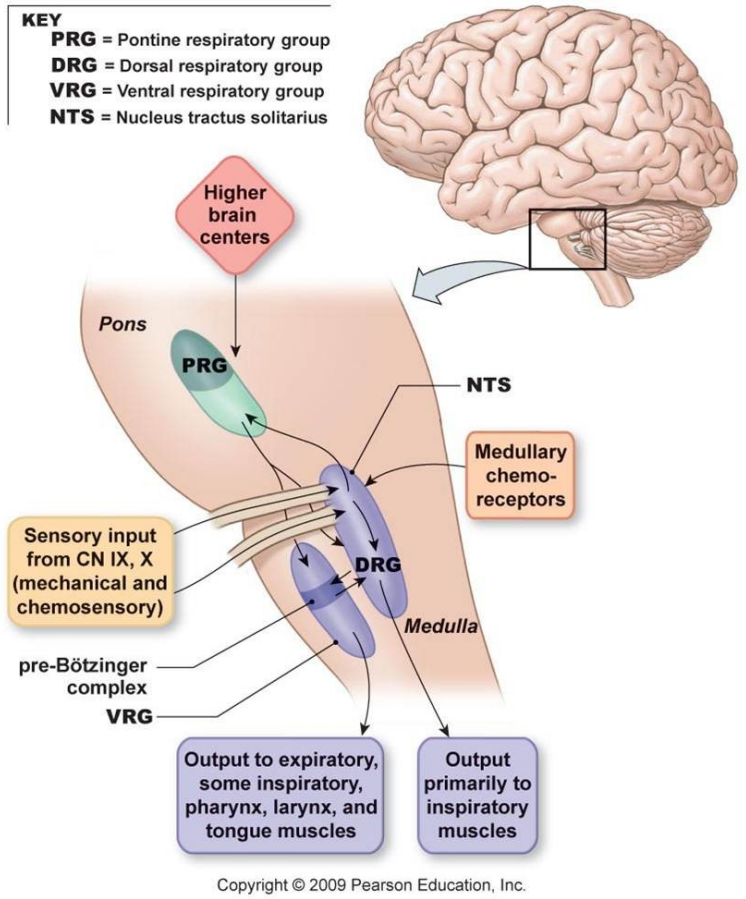
Neural control

- ✓ *The medulla is the primary brainstem mediator of respiration.*
  - ✓ Dorsal Respiratory Group
    - *Sensory integration*
    - Location: *Think* - Solitary tract n.
  - ✓ Ventral Respiratory Group
    - *Motor output*
    - Location: *Think* - Nucleus ambiguus
- ✓ *C3, C4, C5 supply the phrenic nerve, which innervate the diaphragm.*

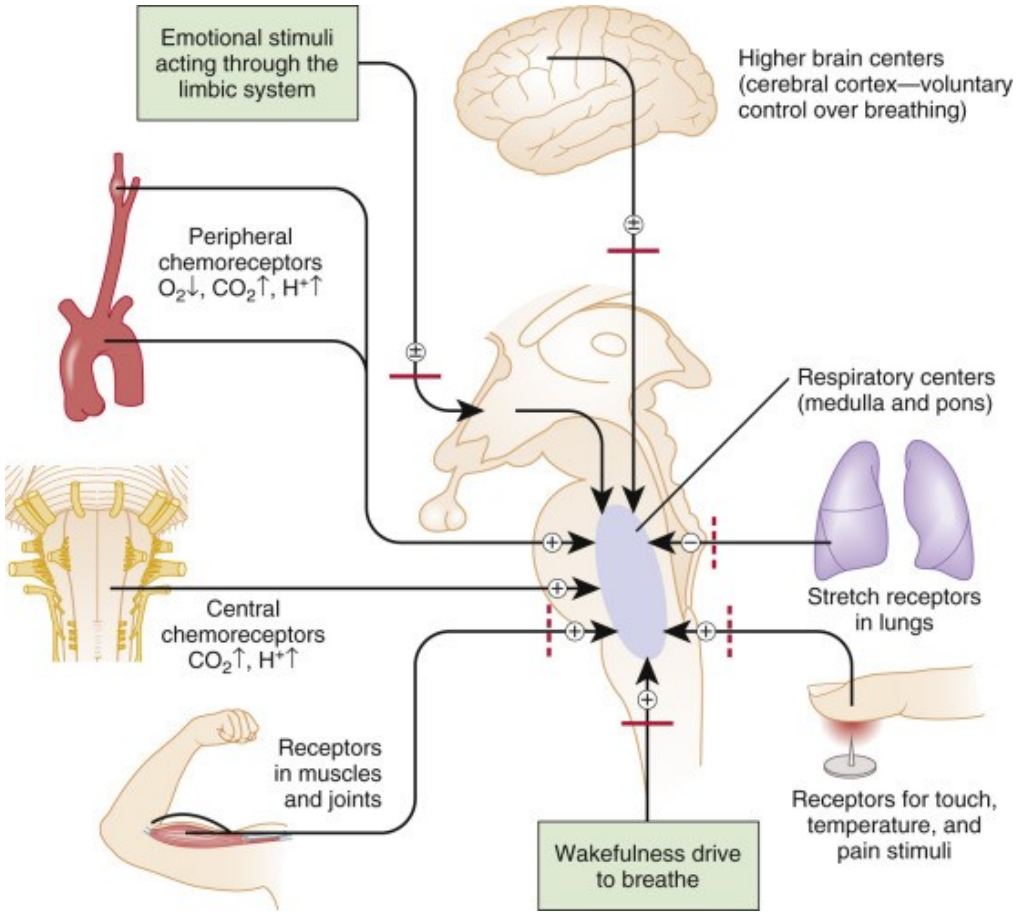


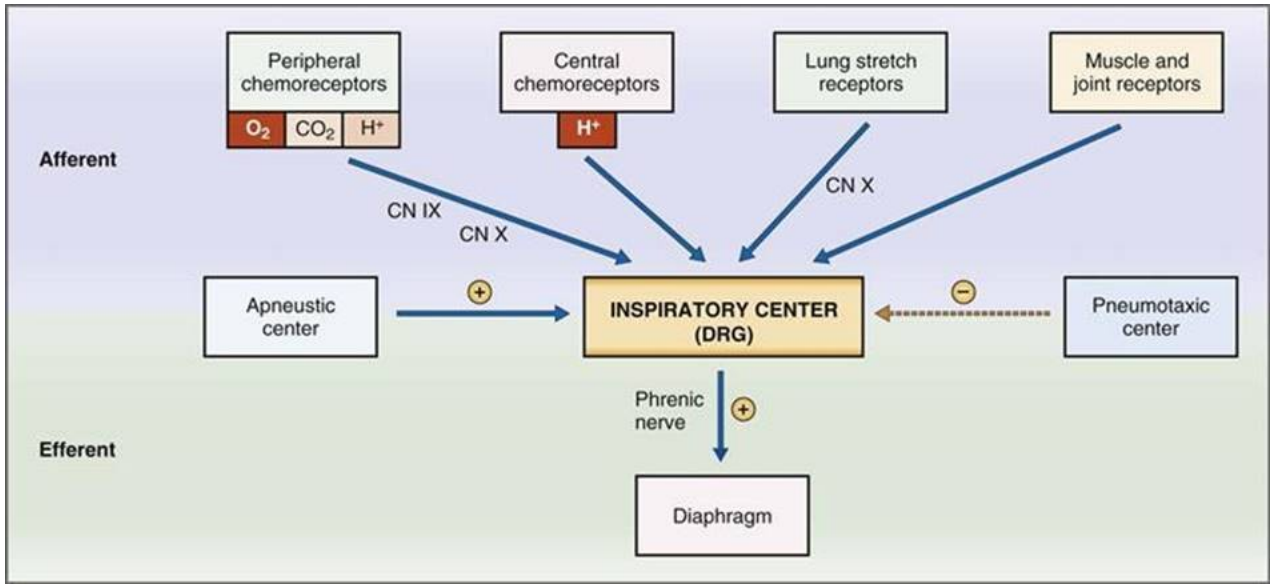
Ondine's curse
Failure of automatic breathing during sleep

Respiratory center



Regulation of Respiration





Other receptors

Irritants receptors on mucose of respiratory system – quickly adaptated,

Stimulus: chemical substances (histamin, serotonin, cigarette smoke).

Respons: increase mucus secretion, constriction of larynx and brochus

C-receptors (=J receptors)– free nerve ending of n.vagus (type C) in intersticium of bronchus and alveolus;

Mechanical irritans (pulmonary hypertension, pulmonary oedema)

Response: hypopnoe, bronchoconstriction, cough

Stretch receptors slowly adaptation, in smooth muscle trachea and bronchus; its irritants triggered decrese activity of respiratory centre – **Hering-Breuer´s reflexes**.

Respiratory response to high altitude

Response to high altitude

↓ atmospheric oxygen (PiO_2) → ↓ Pao_2 → ↑ ventilation → ↓ $Paco_2$ → respiratory alkalosis → altitude sickness.

Chronic ↑ in ventilation.

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

↑ 2,3-BPG (binds to Hb causing rightward shift of the ODC so that Hb releases more O_2).

Cellular changes (↑ mitochondria).

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

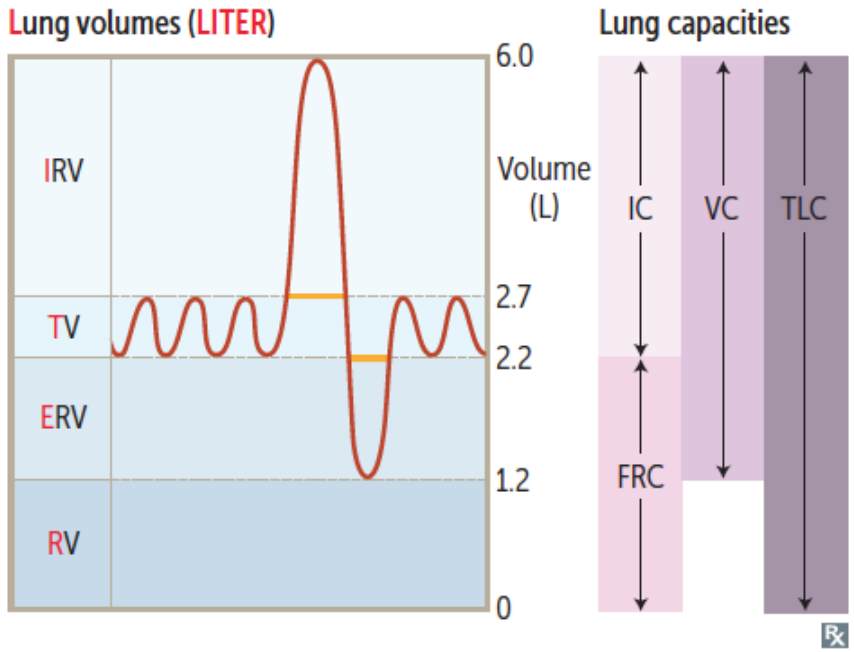
Chronic hypoxic pulmonary vasoconstriction results in pulmonary hypertension and RVH.

Respiratory response to Exercise

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 Pao_2 and $Paco_2$, but ↑ in venous CO_2 content and ↓ in venous O_2 content.

Lung volumes	Note: a capacity is a sum of ≥ 2 physiologic volumes.
Inspiratory reserve volume	Air that can still be breathed in after normal inspiration
Tidal volume	Air that moves into lung with each quiet inspiration, typically 500 mL
Expiratory reserve volume	Air that can still be breathed out after normal expiration
Residual volume	Air in lung after maximal expiration; RV and any lung capacity that includes RV cannot be measured by spirometry
Inspiratory capacity	IRV + TV Air that can be breathed in after normal exhalation
Functional residual capacity	RV + ERV Volume of gas in lungs after normal expiration
Vital capacity	TV + IRV + ERV Maximum volume of gas that can be expired after a maximal inspiration
Total lung capacity	IRV + TV + ERV + RV Volume of gas present in lungs after a maximal inspiration



(FEV1/FCV < 80%) = Obstructive pattern

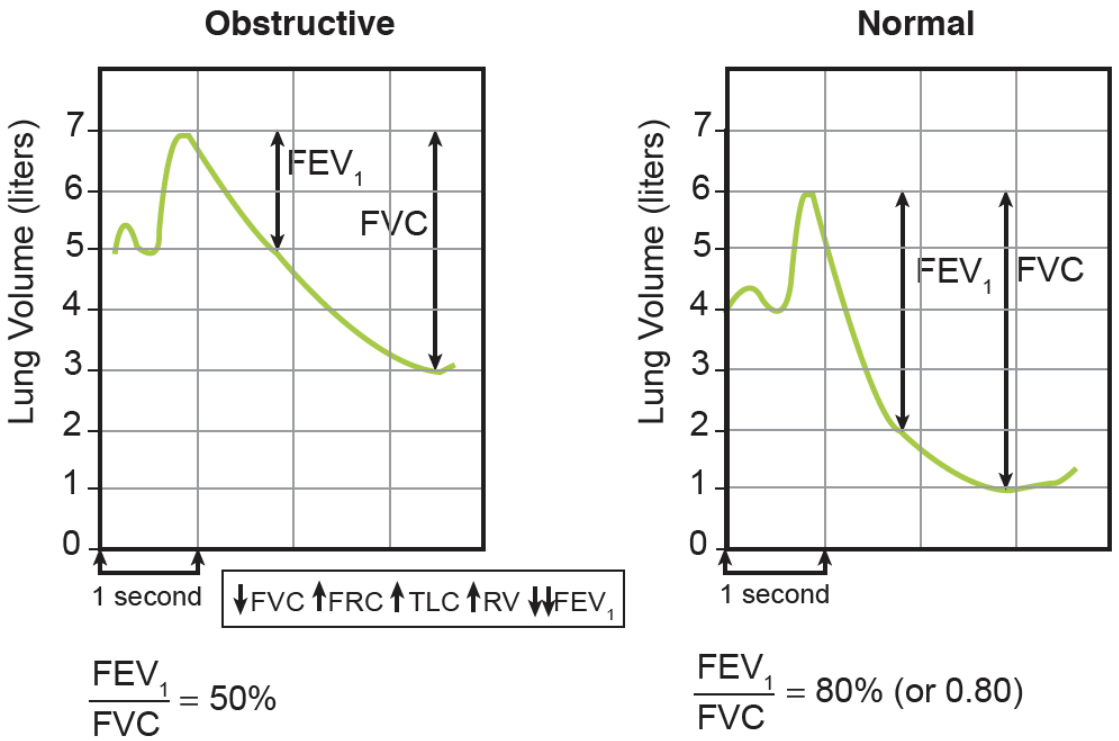


Figure VII-1-17. Obstructive Pattern

FEV1/FVC = or > 80% (restrictive pattern)

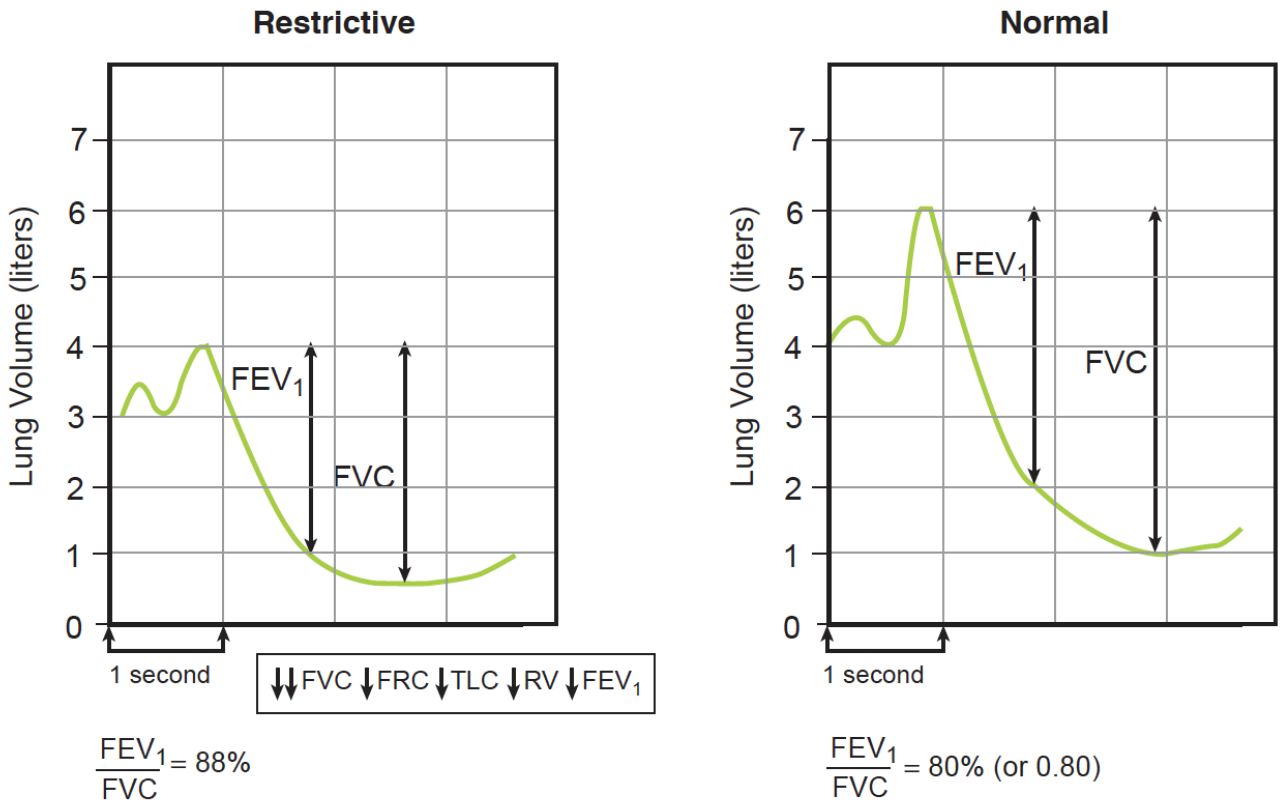


Figure VII-1-18. Restrictive Pattern

Obstructive vs restrictive diseases studies

Table VII-1-1. Summary of Obstructive Versus Restrictive Pattern

Variable	Obstructive Pattern (e.g., Emphysema)	Restrictive Pattern (e.g., Fibrosis)
TLC	↑	↓↓
FEV_1	↓↓	↓
FVC	↓	↓↓
FEV_1/FVC	↓	↑ or normal
Peak fl w	↓	↓
FRC	↑	↓
RV	↑	↓

Flow-volume loop

Flow–Volume Loops

The instantaneous relationship between fl w (liters/sec) and lung volume is useful in determining whether obstructive or restrictive lung disease is present. In the loop shown in Figure VII-1-19, expiration starts at total lung capacity and continues to residual volume. The width of the loop is the FVC.

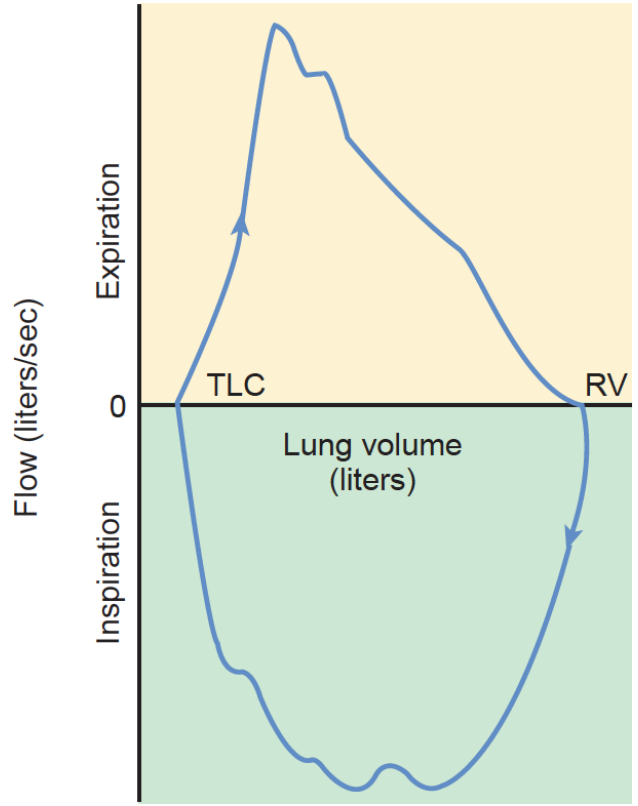


Figure VII-1-19. Flow–Volume Loop

Obstructive vs restrictive lung diseases

Obstructive disease

In obstructive disease, the fl w–volume loop begins and ends at abnormally high lung volumes, and the expiratory fl w is lower than normal. In addition, the downslope of expiration "scallops" or "bows" inward. Th s scalloping indicates that at any given lung volume, fl w is less. Thus, airway resistance is elevated (obstructive).

Restrictive disease

In restrictive disease, the fl w–volume loop begins and ends at unusually low lung volumes. Peak fl w is less, because overall volume is less. However, when expiratory fl w is compared at specific lung volumes, the fl w in restrictive disease is somewhat greater than normal.

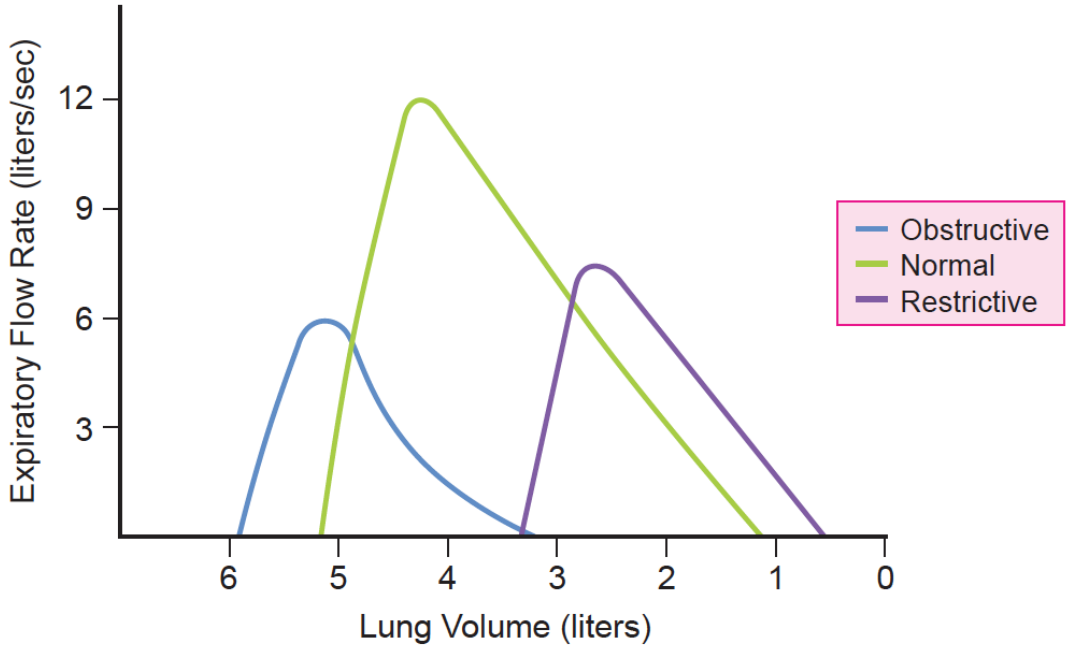


Figure VII-1-20. Forced Expiratory Flow–Volume Loop

DEAD SPACES & VENTILATION RATES

Key Principles

- ✓ *Gas exchange requires the close association of ventilated alveoli and perfused pulmonary capillaries.*
- ✓ *Dead Space —*
  - ✓ *Gas exchange does not occur.*
  - ✓ *Anatomic dead space comprises conducting zones of airways.*
  - ✓ *Physiologic dead space comprises anatomical dead space + functional dead space.*

$PAO_2 - PaO_2$ Gradient

- ✓ *In healthy lungs, Alveolar - Arterial partial pressure of 02 ~ 5-15 mmHg.*
- ✓ *Gradient > ~ 30 can indicate pulmonary malfunction.*

Use Ventilation Rates to Calculate PAO_2 —

1. Calculate Minute Ventilation Rate

   $\dot{V}E$ = Tidal Volume * Breaths/min

2. Calculate Alveolar Ventilation Rate

   $\dot{V}A = \dot{V}E - \dot{V}D$

3. Solve for $PAco_2$
   - Alveolar ventilation equation
   - K = 863 mmHg

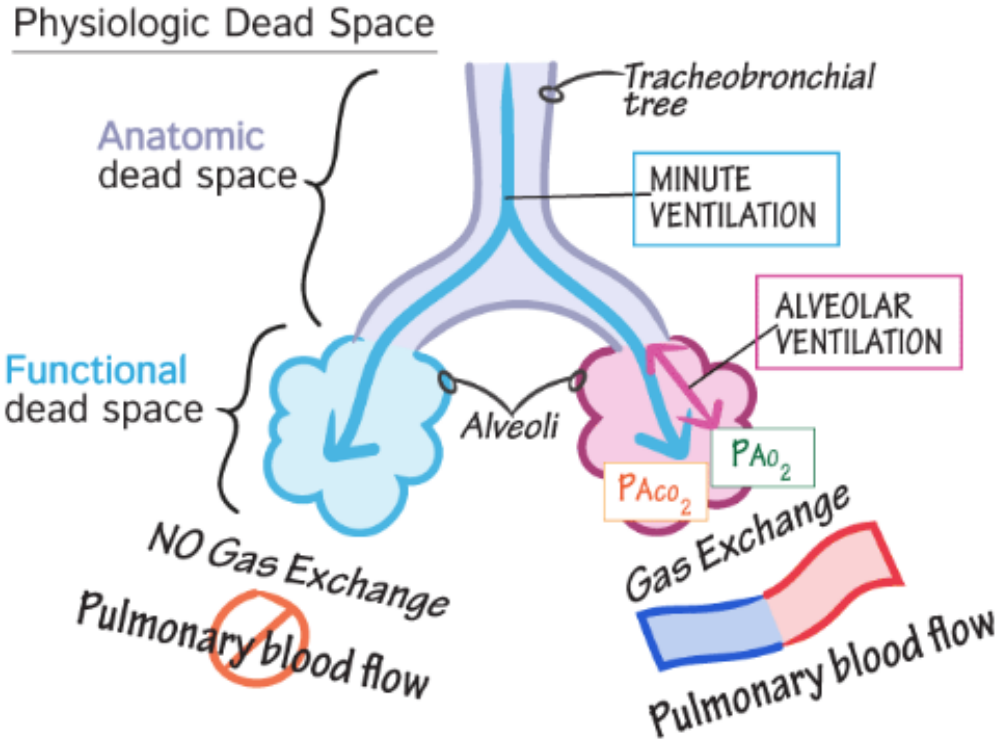
   $$PAco_2 = \frac{\dot{V}co_2 * K}{\dot{V}A}$$

4. Use Alveolar Gas Equation to solve for PAo_2
   - RQ = 0.8

   $$PAo_2 = Pio_2 - \frac{PAco_2}{RQ}$$

Conclusions —

- ✓ When $\dot{V}A \downarrow$, $PAco_2 \uparrow$ & $PAo_2 \downarrow$
- ✓ CO_2 is held w/in lungs; O_2 intake slows
  - If $\dot{V}A$ is halved, $PAco_2 \uparrow$ * 2; $PAo_2 \downarrow$ >1/2.



MINUTE VENTILATION RATE =
Total rate of air flow into and out of lungs.

ALVEOLAR VENTILATION RATE =
Rate of air flow into and out of functioning alveoli, only.

Anatomic dead space

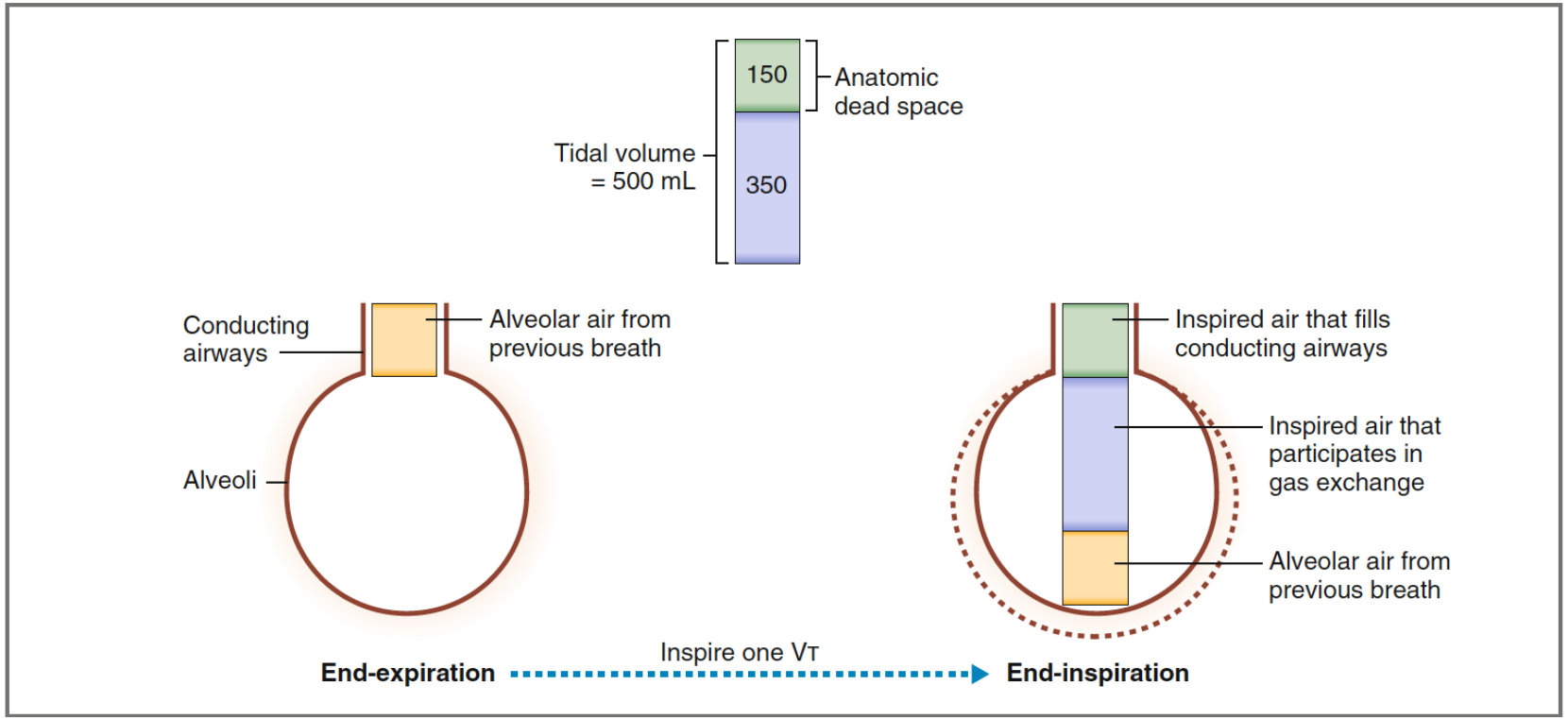
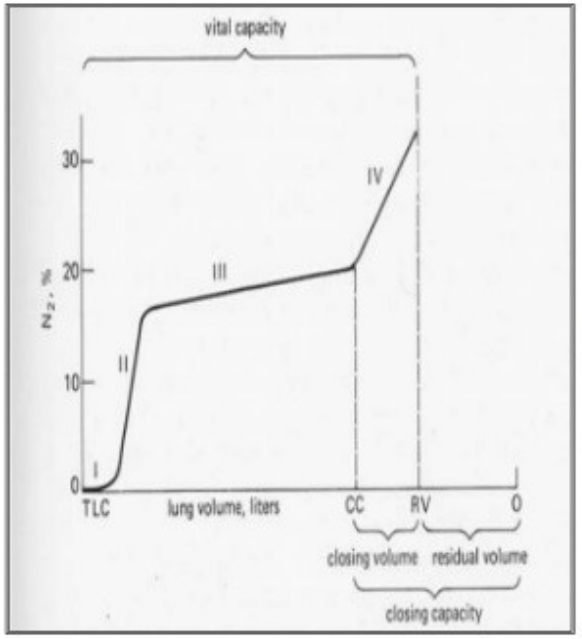


Figure 5-3 **Anatomic dead space.** One third of each tidal volume fills the anatomic dead space. V_T, Tidal volume.

Measurement of Dead space (nitrogen wash out) -video

A- Single breath nitrogen washout(closing volume)



- In phase I, the nitrogen concentration is close to 0% as this represents anatomical dead space.
- During phase II, there is a sharp rise in the expired nitrogen concentration as dead space gas mixes with resident alveolar gas.
- Phase III represents alveolar gas and the expired nitrogen concentration begins to plateau.
- Finally, in phase IV, there is a steep rise in expired N2 concentration as the most poorly ventilated areas (with little O2 mixing) empty. This is also the point at which the small airways start to and is known as the closing volume (CV).

Pneumograph

Table 2-2 BREATHING PATTERNS

	Condition	Description	Causes
	Eupnea	Normal breathing rate and pattern	
	Tachypnea	Increased respiratory rate	Fever, anxiety, exercise, shock
	Bradypnea	Decreased respiratory rate	Sleep, drugs, metabolic disorder, head injury, stroke
	Apnea	Absence of breathing	Deceased patient, head injury, stroke
	Hyperpnea	Normal rate, but deep respirations	Emotional stress, diabetic ketoacidosis
	Cheyne-Stokes	Gradual increases and decreases in respirations with periods of apnea	Increasing intracranial pressure, brain stem injury
	Biot's	Rapid, deep respirations (gasps) with short pauses between sets	Spinal meningitis, many CNS causes, head injury
	Kussmaul's	Tachypnea and hyperpnea	Renal failure, metabolic acidosis, diabetic ketoacidosis
	Apneustic	Prolonged inspiratory phase with shortened expiratory phase	Lesion in brain stem

Hyperventilation

Definition: Both, accelerated and deep breathing

- In humans, hyperventilation coming as combination of anxiety and pain
- During hyperventilation is expired CO_2 (hypocapnia) and the increase of pO_2 (hyperoxia) → vasoconstriction of cerebral vessels

- **Symptoms**: tingling in the ears, feeling light in the head, headache etc.

- **Tx :** by increasing pCO_2 in the body – e.g.: by breathing into and out of the bag (re-breathing)

Hypoxia

- Hypoxia is a general name for a lack of oxygen in the body or individual tissues.
- Hypoxemia is lack of oxygen in arterial blood.
- Complete lack of oxygen is known as anoxia.

Classification of hypoxia

Classification of Hypoxia

TYPE	DEFINITION	TYPICAL CAUSES
Hypoxic hypoxia	Low arterial P_{O_2}	High altitude; alveolar hypoventilation; decreased lung diffusion capacity; abnormal ventilation-perfusion ratio
Anemic hypoxia	Decreased total amount of O_2 bound to hemoglobin	Blood loss; anemia (low [Hb] or altered HbO_2 binding); carbon monoxide poisoning
Ischemic hypoxia	Reduced blood flow	Heart failure (whole-body hypoxia); shock (peripheral hypoxia); thrombosis (hypoxia in a single organ)
Histotoxic hypoxia	Failure of cells to use O_2 because cells have been poisoned	Cyanide and other metabolic poisons

THANK YOU

Resources

1. First Aid for USMLE Step 1 2020
2. Costanzo Physiology
3. Kaplan Physiology
4. Illustrations → Drawittoknowit