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Respiratory Failure

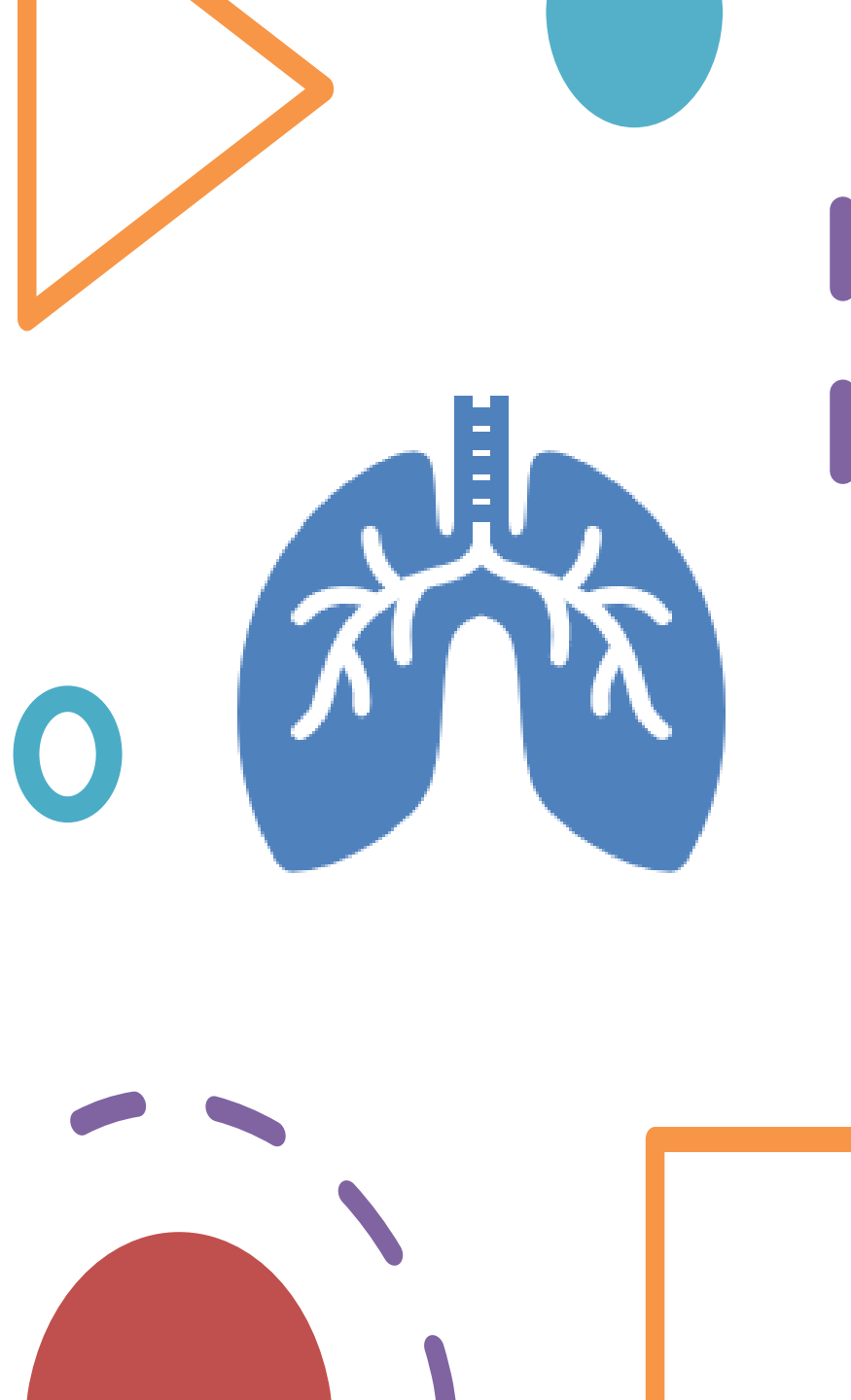
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- University of Jordan

Lecture outline

- ***Definition and Classification***
- ***Pathophysiology***
- ***Etiology***
- ***Clinical Presentation***
- ***Diagnosis***
- ***Management***

Definition

- **Respiratory failure is a life-threatening condition in which the respiratory system fails in one or both of its main functions:**
 - ❖ *Gas exchange (oxygenation)*
 - ❖ *Ventilation (CO_2 elimination)*
- **It is defined physiologically as:**
 - ❖ $\text{PaO}_2 < 60 \text{ mmHg}$ (hypoxemia) on room air
 - ❖ $\text{PaCO}_2 > 50 \text{ mmHg}$ (hypercapnia) with $\text{pH} < 7.35$





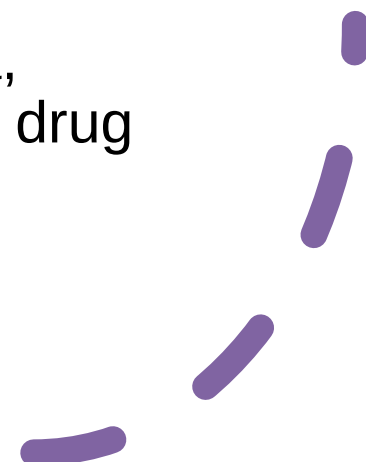
Classification

Based on Gas Abnormalities

Type I (Hypoxemic):

- $\text{PaO}_2 < 60$, PaCO_2 normal/low.
- Mechanism: V/Q mismatch, shunt, diffusion impairment.
- Examples: ARDS, pneumonia, pulmonary edema, pulmonary embolism.

Type II (Hypercapnic):

- $\text{PaCO}_2 > 50$, often with hypoxemia.
 - Mechanism: hypoventilation (alveolar).
 - Examples: COPD, asthma, neuromuscular weakness, drug overdose.
- 

Based on Gas Abnormalities

Type III (Perioperative/Atelectatic):

- Postoperative atelectasis → reduced FRC.
- Examples: abdominal/thoracic surgery, obesity.

Type IV (Shock-related):

- Respiratory muscle hypoperfusion and fatigue in shock.

Based on Onset

- **Acute respiratory failure** – develops within minutes to hours (e.g., trauma, acute asthma, ARDS).
- **Chronic respiratory failure** – develops gradually with compensatory mechanisms (e.g., advanced COPD, obesity hypoventilation).
- **Acute on chronic** – acute decompensation in a chronically compromised patient (e.g., COPD with pneumonia).

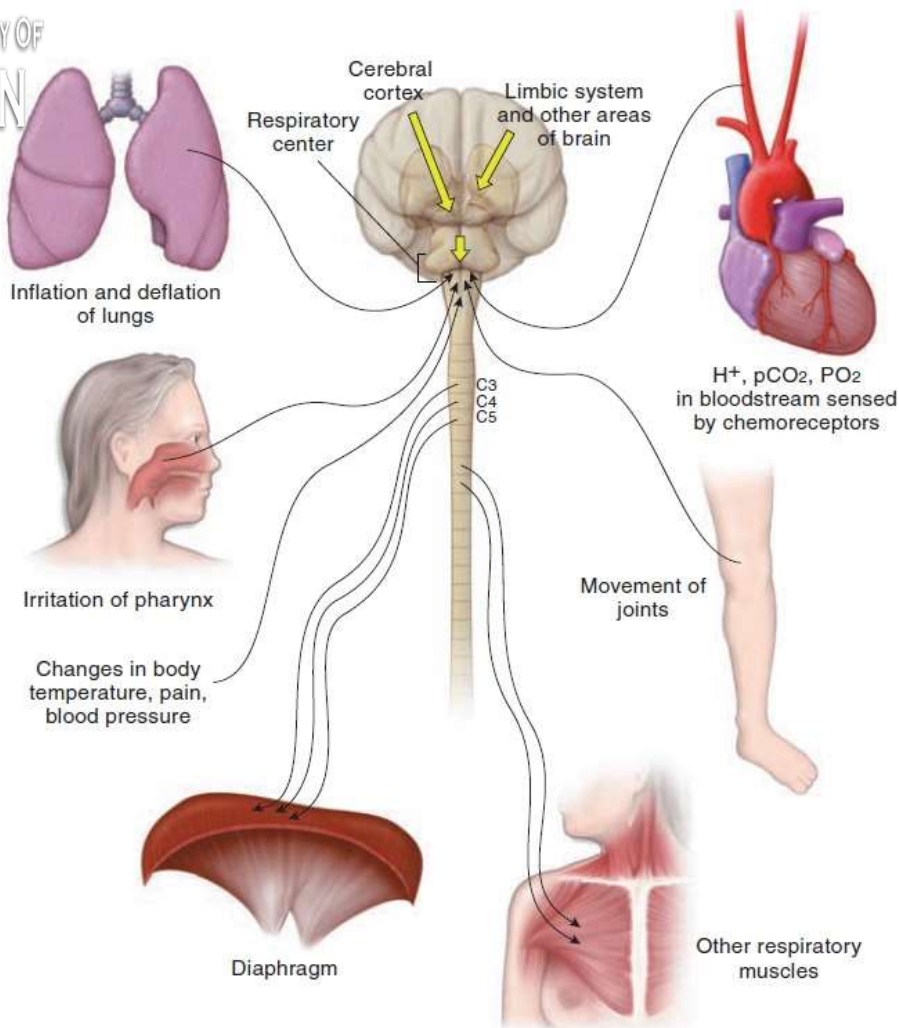


FIGURE 10.16. A Schematic Representation of the Regulation of Respiration

Respiratory system function depends on :

- CNS control.
- Neuromuscular function.
- Upper airway muscles and reflexes.
- Thorax and pleura.
- Alveolar function.

Gas Exchange & Physiology

- Three key processes:
 1. Oxygen transfer across alveoli
 2. Oxygen transport to tissues
 3. CO₂ removal from blood → alveolus → environment

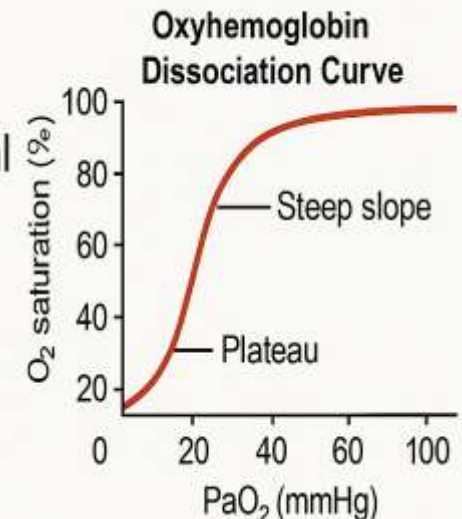


Gas Exchange & Physiology

- O_2 transport: binds to Hb (1 g Hb = 1.36 mL O_2)
- Oxyhemoglobin dissociation curve = sigmoid (steep at 10–50 mmHg)
- CO_2 transport: dissolved, bicarbonate, carbamino compounds

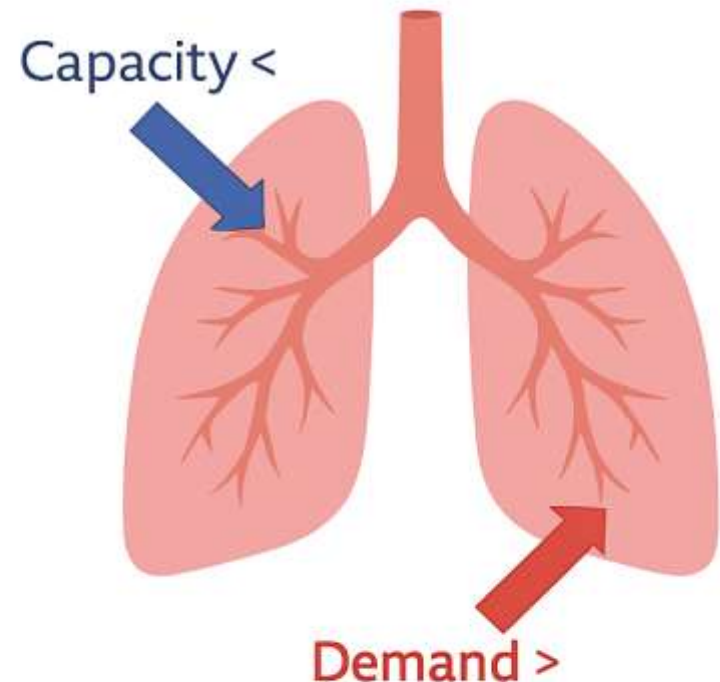
O_2 Transport

- Hemoglobin carries most O_2 (1 g Hb = 1.36 mL O_2)
- Oxyhemoglobin dissociation curve: sigmoid shape
Steep slope (PaO_2 10–50 mmHg)
small $\downarrow PaO_2 \rightarrow$ large saturation
- Plateau (>70 mmHg): safety margin against hypoxemia



Respiratory Failure Basics

- Inability to maintain adequate O_2 and/or CO_2 exchange
- Causes:
 - Airways, alveoli, CNS, PNS, respiratory muscles, and chest wall
 - Shock states: cardiogenic, hypovolemic, septic
- Ventilatory capacity vs demand
 - Capacity = max ventilation sustainable without fatigue
 - Demand = ventilation needed for stable $PaCO_2$
 - Failure occurs when capacity < demand





Alveolar Ventilation & A—a Gradient

Alveolar Ventilation

- At steady state:
 CO_2 produced by tissues = CO_2 eliminated by lungs.
- Expressed mathematically:
- $$V_A = K \times \frac{V_{\text{CO}_2}}{P_a\text{CO}_2}$$



Alveolar–Arterial (A–a) Gradient

- The efficiency of lungs at carrying out of respiration
- *A–a Gradient* = $PAO_2 - PaO_2$
- Normal values:
 - 5–15 mmHg (young adults)
 - Increases with age $\rightarrow$ normal $\approx$ (Age/4 + 4) mmHg

Alveolar Gas Equation

- $PAO_2 = FiO_2 (P_B - P_{water}) - PaCO_2/0.8,$
 - ✓ PAO_2 = Alveolar partial pressure of oxygen
 - ✓ FiO_2 = Fraction of inspired oxygen
 - ✓ P_B = Barometric (Atmospheric) pressure
 - ✓ P_{water} = Vapor pressure of water at body temperature (37°C)=47 mmHg
 - ✓ $PaCO_2$ = Partial pressure of arterial carbon dioxide

Clinical Application

PaCO₂ reflects ventilation.

A-a gradient reflects oxygenation efficiency.

Even in normal lungs:

Markedly increased A-a gradient is a hallmark of **pulmonary disease causing hypoxemia** (e.g., ARDS, pneumonia, PE).

Mild V/Q mismatch

Small **right-to-left shunt**
→ causes PAO₂ to be slightly higher than PaO₂.

- The pathophysiologic mechanisms

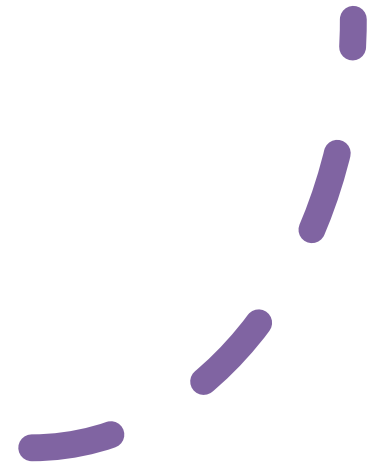




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Hypoxemic respiratory failure

- V/Q mismatch
- Shunt





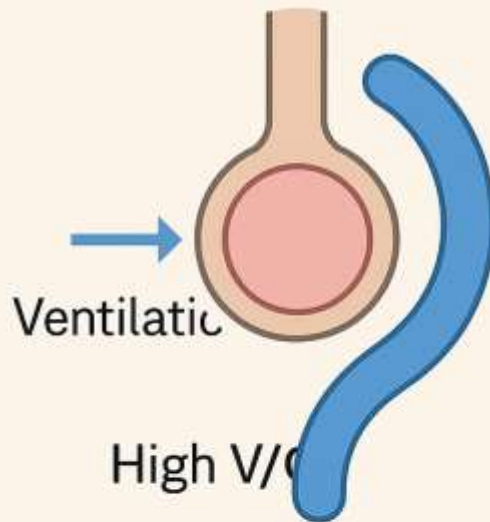
V/Q mismatch

- Most common cause of hypoxemia
- Caused by
 - ventilation of non-perfused alveoli. (high V/Q ratio)
 - Perfusion to non-ventilated alveoli (Low V/Q ratio)
- Admin. of 100% O₂ eliminate hypoxemia

V/Q Mismatch

Dead Space

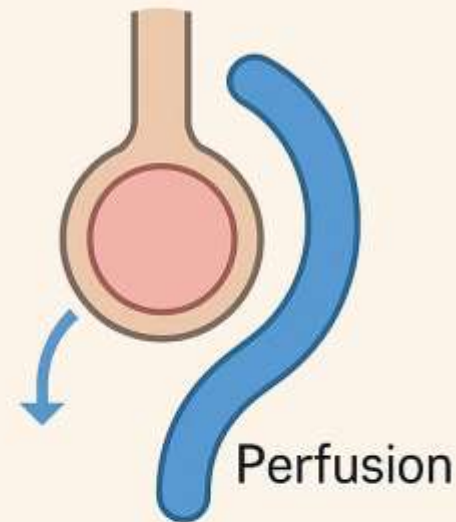
Ventilation



- High V/Q
- Acts like dead space

Shunt

No Ventilation



- Low V/Q
- Acts like a shunt

Shunt

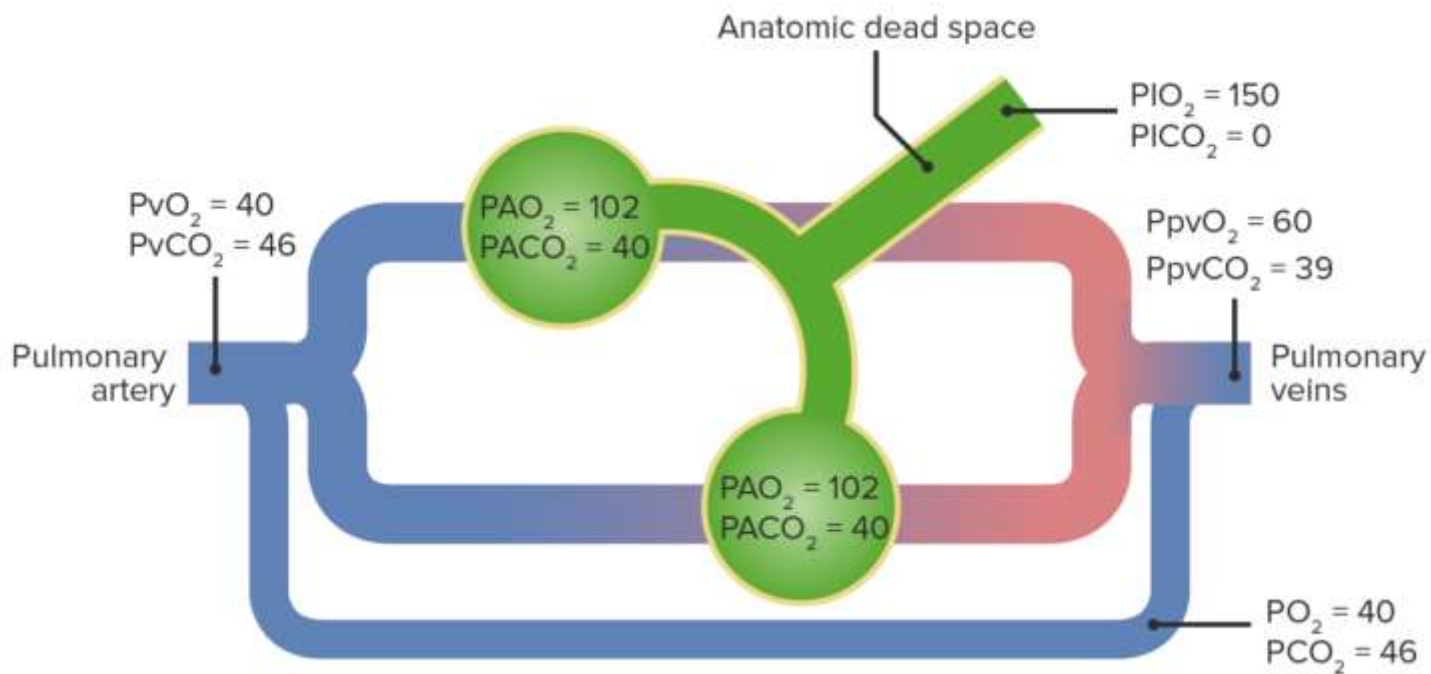
- Right-to-left shunt
- Blood is shunted from the right side of the heart to the left side without undergoing oxygenation.
- Deoxygenated blood mixes with oxygenated blood →
↓ arterial pressure of O₂

Shunt

- The deoxygenated blood bypasses the ventilated alveoli and mixes with oxygenated blood → hypoxemia
- Persistent of hypoxemia despite 100% O₂ inhalation
- Hypercapnia occur when shunt is excessive > 60%

Shunt

- Anatomic shunt exists in normal lungs because of the bronchial and thebesian circulations, which account for 2-3% of shunt.
- A normal right-to-left shunt may occur from atrial septal defect, ventricular septal defect, patent ductus arteriosus, or arteriovenous malformation in the lung.





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Hypercapnic
respiratory
failure

- Hypoventilation



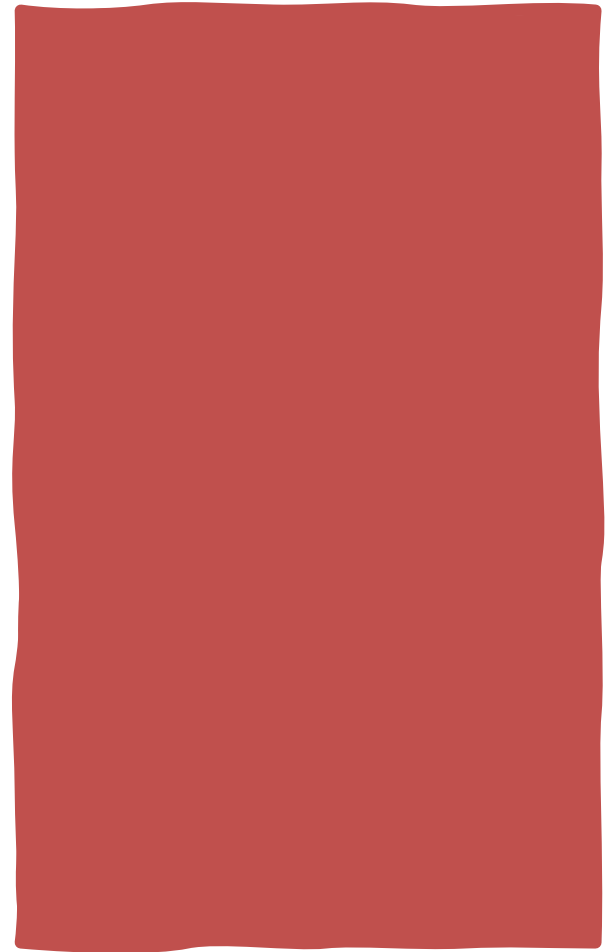
Hypoventilation

- Occurs when ventilation $\downarrow$ 4-6 l/min
- Causes
 - Depression of CNS from drugs
 - Neuromuscular disease of respiratory muscles
- $\uparrow$ PaCO₂ and $\downarrow$ PaO₂
- Alveolar –arterial PO₂ gradient is normal
- COPD

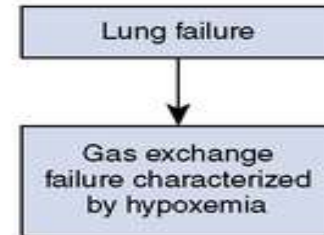
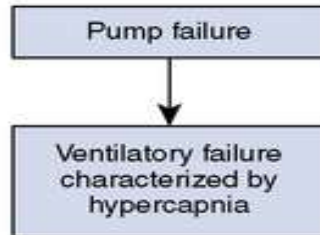
Respiratory pathway affecting carbon dioxide elimination

Central nervous system ↓	"Won't breathe" "Can't breathe"
Peripheral nervous system ↓	
Respiratory muscles ↓	
Chest wall and pleura ↓	
Upper airway ↓	
Lungs	Abnormal gas exchange: "Can't breathe enough"

Etiology



Respiratory Failure



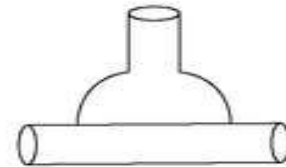
Central
nervous system
component



Peripheral
nervous system/
chest wall
component



Airway
component



Alveolar
component

Etiology of hypoxemic respiratory failure

- ✓ Right-to-left shunt:
 - ✓ [Pulmonary edema](#) (cardiogenic and noncardiogenic)
 - ✓ [Pneumonia](#)
 - ✓ Pulmonary hemorrhage
 - ✓ Aspiration
 - ✓ [Atelectasis](#)
 - ✓ ARDS
- ✓ V/Q mismatch:
 - ✓ [Pulmonary embolism](#)
 - ✓ [Asthma](#)
 - ✓ Chronic obstructive [pulmonary disease](#) ([COPD](#))
 - ✓ [Cystic fibrosis](#)
 - ✓ Interstitial lung disease
 - ✓ [Pulmonary hypertension](#)
- ✓ Low inspired oxygen: high altitude
- ✓ Hypoventilation:
 - ✓ Sedative medications
 - ✓ Neuromuscular conditions

Mechanisms, etiology, and management of acute hypoxemic respiratory failure

Cause of hypoxemia*	Definition	Etiologies	A-a gradient	PaCO ₂	Response to oxygen	Treatment
V/Q mismatch	■ Imbalance of lung perfusion relative to ventilation: ■ Low V/Q – Regions underventilated relative to perfusion (shunt is extreme form of low V/Q mismatch; refer to below) ■ High V/Q – Regions that are overventilated relative to perfusion (dead space is extreme form of high V/Q mismatch)	■ Embolic disease (venous pulmonary embolism, fat embolism, amniotic fluid embolism, malignant cells) ■ Pulmonary vascular disease (destroys capillary beds and limits perfusion to alveoli) ■ Chronic obstructive lung disease/emphysema (destroys the pulmonary capillary-alveolar interface) ■ Interstitial diseases (eg, pulmonary edema, pulmonary inflammation) ■ Low flow cardiac output states	High	Typically normal (unless associated with hypoventilation or significant increase in dead space)	Yes (unless due to shunt)	■ Supplemental oxygen ■ Treat underlying cause
Right-to-left shunt	■ Extreme form of low V/Q mismatch: ■ Anatomic (ie, mechanical shunt) ■ Physiologic (ie, typically capillary shunt)	■ Anatomic: ■ Cardiac shunt (eg, ASD, PFO, VSD) ■ Intravascular shunt (pulmonary or other AVM, hepatopulmonary syndrome) ■ Physiologic: ■ Capillary shunt (eg, atelectasis, edema, pneumonia) ■ Alveolar filling disorders (eg, fluid, hemorrhage, pus, cells, protein, lipid) ■ Complete airway obstruction (including angioedema)	High	Normal	No	■ Oxygen; however, it is frequently minimally responsive or unresponsive to oxygen ■ Treat underlying cause
Hypoventilation	■ Reduced minute ventilation "can't breathe, won't breathe, can't breathe enough"†	■ Central neurologic disease (eg, stroke, sedation, hypothyroidism) ■ Respiratory neuromuscular and chest wall diseases (eg, cervical-spine or phrenic nerve injury, Guillain-Barré syndrome, bilateral diaphragmatic weakness) ■ Airway/alveolar disease (acute exacerbation of COPD, COPD, asthma, ILD)	Normal	Elevated	Yes	■ Supplemental oxygen (oxygen will improve oxygenation but will not resolve hypercapnia) ■ Increase minute ventilation (eg, noninvasive ventilation or invasive ventilation) ■ Treat underlying cause
Diffusion defect	■ Impairment of gas exchange between alveoli and pulmonary capillaries ■ Often overlaps with shunt or V/Q mismatch pathophysiology	■ ILD ■ Lung resection ■ Emphysema ■ Pulmonary vascular disease	High (occasionally normal)	Normal	Yes	■ Supplemental oxygen ■ Treat underlying cause
Reduced PiO ₂	■ Reduced PiO₂‡	■ Sudden change in elevation or new altitude ■ Reduction in pressure during air travel in aircraft	Normal	Normal or low (if hyperventilation present)	Yes	■ Descent if altitude is the cause ■ Supplemental oxygen ■ Consider acetazolamide
Increased oxygen extraction	■ Reduced mixed venous oxygen content of blood returning to the right side of the heart	■ Decreased cardiac output ■ Anemia ■ Hypermetabolism (eg, fever, sepsis, hyperthyroidism, burns, trauma)	High	Normal	Yes	■ Supplemental oxygen ■ Treat underlying cause

A-a gradient: alveolar-arterial gradient; PaCO₂: arterial carbon dioxide tension; V/Q: ventilation/perfusion; ASD: atrial septal defect; PFO: patent foramen ovale; VSD: ventricular septal defect; AVM: arteriovenous malformation; COPD: chronic obstructive pulmonary disease; ILD: interstitial lung disease; PiO₂: inspired oxygen tension.

* Rare causes of hypoxemia include hemoglobinopathies, cyanide toxicity, methemoglobinemia, and leukocyte larceny.

† Refer to UpToDate content on hypercapnia.

Etiology of hypercapnic respiratory failure

- Diminished respiratory drive:
 - Sedative medications ([opioids](#), [benzodiazepines](#))
 - [Brain](#) stem lesions (affecting the central respiratory center)
 - Multiple [sclerosis](#) (bulbar dysfunction leading to central respiratory drive depression)
 - [Hypothermia](#)

- Impaired respiratory muscle function:
 - Guillain–Barré syndrome
 - [Myasthenia gravis](#)
 - Amyotrophic lateral [sclerosis](#)
 - Multiple [sclerosis](#)
 - [Botulism](#)
 - [Tetanus](#)
 - [Spinal cord](#) lesions
 - Muscle [fatigue](#) (seen with hypoxemic respiratory failure)
 - [Malnutrition](#)
 - [Myopathy](#)

Etiology of hypercapnic respiratory failure

- Airway obstruction:
 - COPD
 - Asthma
 - Obstructive sleep apnea
 - Cystic fibrosis
 - Airway edema
- Diminished lung elasticity/compliance:
 - Alveolar edema
 - Pneumonia
 - Atelectasis
 - ARDS
- Diminished chest wall elasticity:
 - Pleural effusion
 - Obesity
 - Kyphoscoliosis
 - Abdominal distention
 - Pneumothorax





Clinical Presentation

General signs and symptoms

- Vitals:
 - Tachypnea
 - Tachycardia
 - Low transcutaneous oxygen saturation in hypoxemic respiratory failure (late sign)
- Dyspnea
- Increased work of breathing and use of accessory muscles of breathing
- Diaphoresis
- Altered mental status:
 - Restlessness and anxiety
 - Confusion
 - Somnolence
 - Coma

Hypoxemic Respiratory Failure (Type 1):

- **Dyspnea:** Shortness of breath, especially with exertion, or even at rest if severe.
- **Cyanosis:** Bluish discoloration of the skin, lips, or nail beds due to low oxygen levels.
- **Tachypnea:** Increased respiratory rate as the body attempts to compensate for low oxygen levels.
- **Use of Accessory Muscles:** This is a sign of increased work of breathing as the body attempts to recruit additional muscles to aid in ventilation.
- **Confusion/Agitation:** Decreased oxygen supply to the brain can cause cognitive impairment and agitation.
- **Fatigue:** Severe cases can lead to exhaustion as the body's energy is used to compensate.



Hypercapnia Respiratory Failure (Type 2)

- ❑ **Dyspnea:** More often with shallow breathing.
- ❑ **Headache:** Elevated CO₂ levels lead to vasodilation in the brain, causing increased intracranial pressure.
- ❑ **Drowsiness or Confusion:**
Hypercapnia can depress the CNS, leading to confusion or even coma in severe cases.
- ❑ **Tachypnea:** Initially, the body tries to compensate by increasing the breathing rate to expel CO₂.
- ❑ **Peripheral Edema:** If associated with chronic conditions like COPD or heart failure

Laboratory assessment

- ABG analysis
 -
- Lung function
- Vitalogram(pulmonary function tests)
- Chest Radiograph
- ECG
- Echocardiography
- CBC and blood cultures.

Arterial blood gas

- Diagnosis
- An arterial blood gas (ABG) analysis is required in the diagnosis of respiratory failure. It measures and calculates components in arterial blood:
- **Measured:**
 - pH
 - Partial pressure of oxygen (PaO_2)
 - Partial pressure of CO_2 (PaCO_2)
- **Calculated:**
 - Bicarbonate (HCO_3)
 - Base excess
 - Oxygen saturation (SaO_2)



PH **acidosis** **< 7.4** **>** **alkalosis**

PH	7.35 - 7.45
PaCo₂	35 - 45
HCo₃	22 - 28



Respiratory



Metabolic

R **Respiratory**

O **Opposite**

M **Metabolic**

E **Equal**

PH ↑ **PCo₂** ↓ **Alkalosis**

PH ↓ **PCo₂** ↑ **Acidosis**

PH ↑ **HCo₃** ↑ **Alkalosis**

PH ↓ **HCo₃** ↓ **Acidosis**

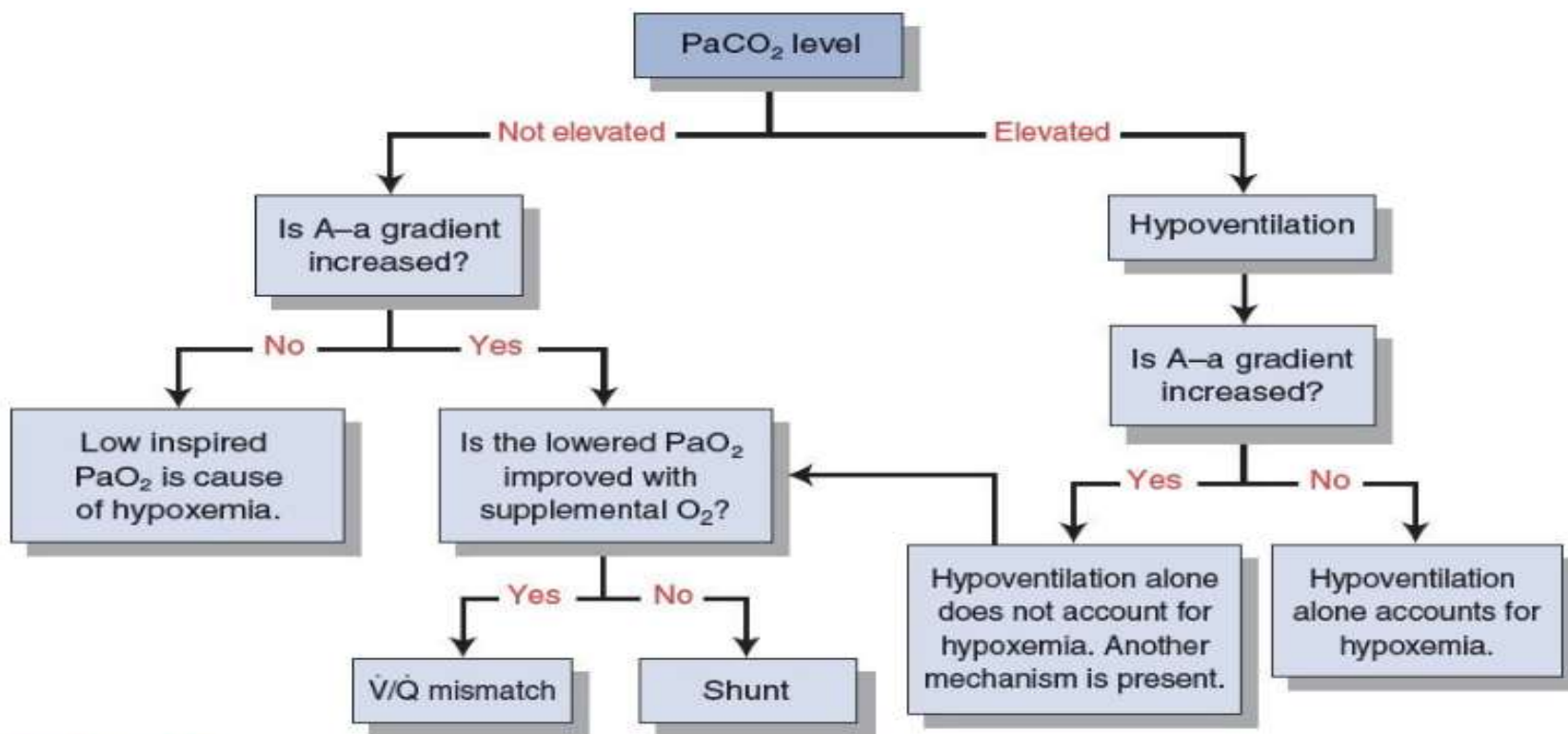
ARTERIAL BLOOD GAS INTERPRETATION

• 6-step approach:

- **Step 1:** Assess the internal consistency of the values using the Henderseon-Hasselbach equation: $[H^+] = 24(P_aCO_2) / [HCO_3^-]$
- **Step 2** Is there alkalemia or acidemia present? pH < 7.35 acidemia pH > 7.45 alkalemia
- **Step 3** Is the disturbance respiratory or metabolic?
- **Step 4** Is there appropriate compensation for the primary disturbance? Usually, compensation does not return the pH to normal (7.35 – 7.45).
- **Step 5:** Calculate the anion gap (if a metabolic acidosis exists):
 $AG = [Na^+] - ([Cl^-] + [HCO_3^-]) - 12 \pm 2$ (normaly 12)
- **Step 6:** If an increased anion gap is present, assess the relationship between the increase in the anion gap and the decrease in $[HCO_3^-]$.
 ✓ Assess the ratio of the change in the anion gap (ΔAG) to the change in $[HCO_3^-]$ ($\Delta[HCO_3^-]$): $\Delta AG / \Delta[HCO_3^-]$
 ✓ *This ratio should be between 1.0 and 2.0 if an uncomplicated anion gap metabolic acidosis is present*

ARTERIAL BLOOD GAS INTERPRETATION

1° DISORDER	pH	P_aCO_2	$[HCO_3^-]$	COMPENSATION
AG/non-AG Metabolic Acidosis	↓	↓ (2°)	↓ (1°)	$P_aCO_{2, \text{expect}} = 1.5 [HCO_3^-] + 8 \pm 2$ If $P_aCO_{2, \text{actual}} < P_aCO_{2, \text{expect}}$ also 1° respiratory alkalosis If $P_aCO_{2, \text{actual}} > P_aCO_{2, \text{expect}}$ also 1° respiratory acidosis
AG Acidosis "Delta/Delta"	For AG metabolic acidosis, calculate $\Delta AG / \Delta[HCO_3^-] = (AG - 12) / (24 - [HCO_3^-])$ if < 0.8, non-AG acidosis; if > 2, metabolic alkalosis			
Metabolic Alkalosis	↑	↑ (2°)	↑ (1°)	$P_aCO_2 = 0.7 \times [HCO_3^-] + 20 \pm 5$ If $P_aCO_{2, \text{actual}} < P_aCO_{2, \text{expect}}$ also 1° respiratory alkalosis If $P_aCO_{2, \text{actual}} > P_aCO_{2, \text{expect}}$ also 1° respiratory acidosis
Respiratory Acidosis	↓	↑ (1°)	↑ (2°)	For each ↑ 10 mmHg in P_aCO_2 Acute: ↑ $[HCO_3^-]$ 1 mmol/L and ↓ pH 0.08 Chronic: ↑ $[HCO_3^-]$ 4 mmol/L and ↓ pH 0.03
Respiratory Alkalosis	↑	↓ (1°)	↓ (2°)	For each ↓ 10 mmHg in P_aCO_2 Acute: ↓ $[HCO_3^-]$ 2 mmol/L and ↑ pH 0.08 Chronic: ↓ $[HCO_3^-]$ 5 mmol/L and ↑ pH 0.03
Primary disorder (1°), compensation (2°); arrows relative to "normal" baseline values: pH 7.35 - 7.45, P_aCO_2 35 - 45 mmHg and $[HCO_3^-]$ 22 - 26 mEq/L				



FIGURE

2.12

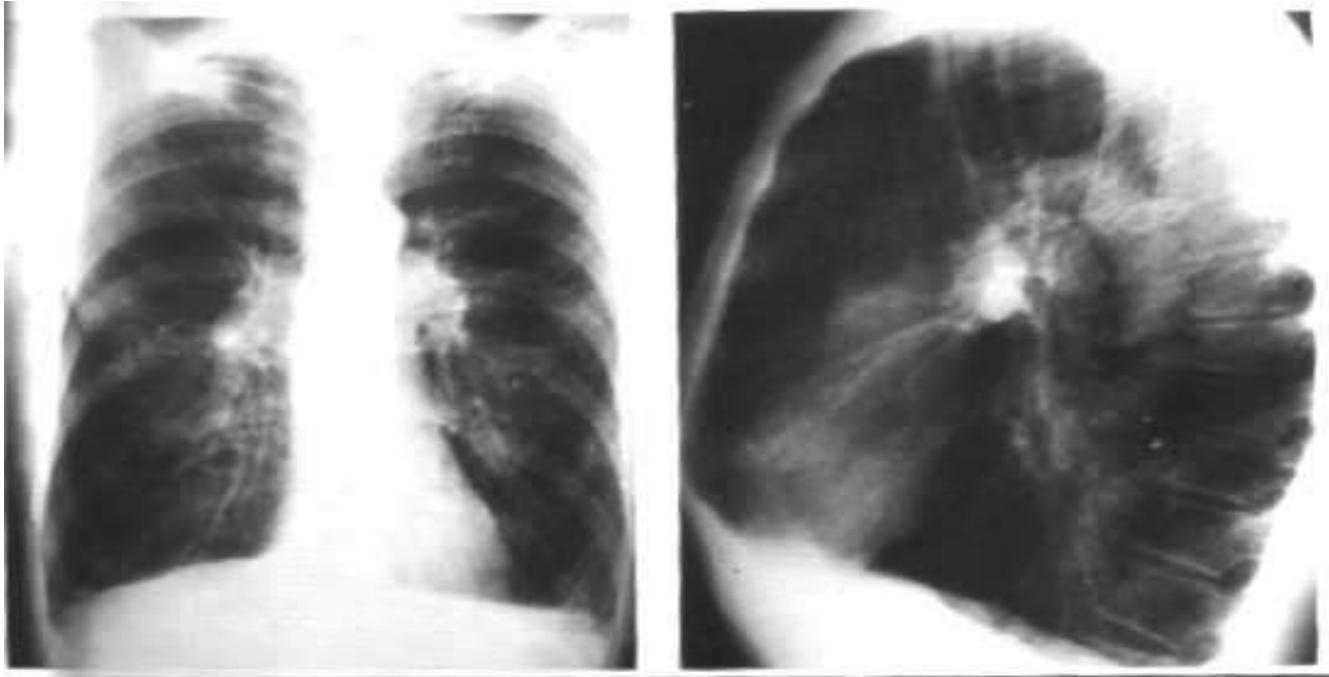
Evaluation of a patient with hypoxemia.

Chest X-ray/CT Scan

Provides imaging of the lungs to help identify conditions such as

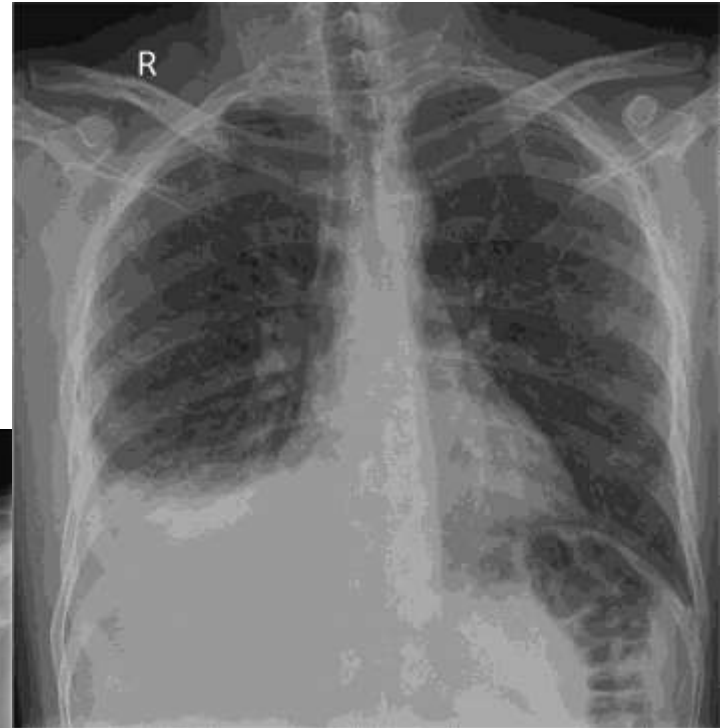
- pneumonia
- pulmonary edema
- Pneumothorax
- Pleural effusion
- COPD
- ARDS

Hyperinflated Lungs : COPD





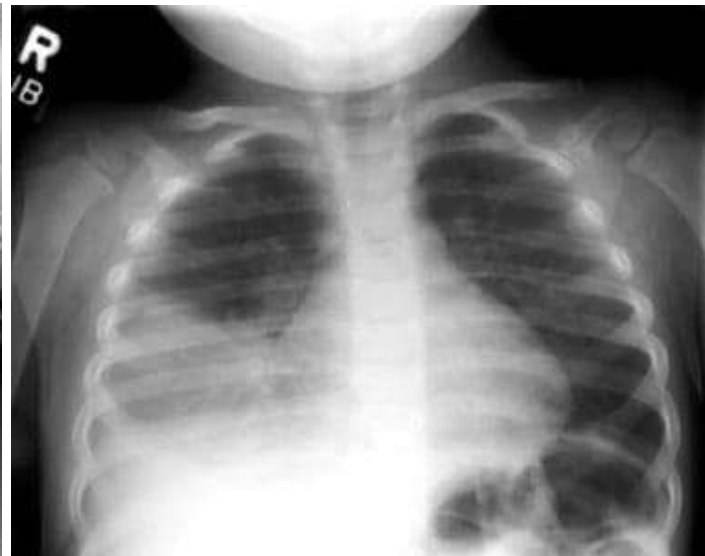
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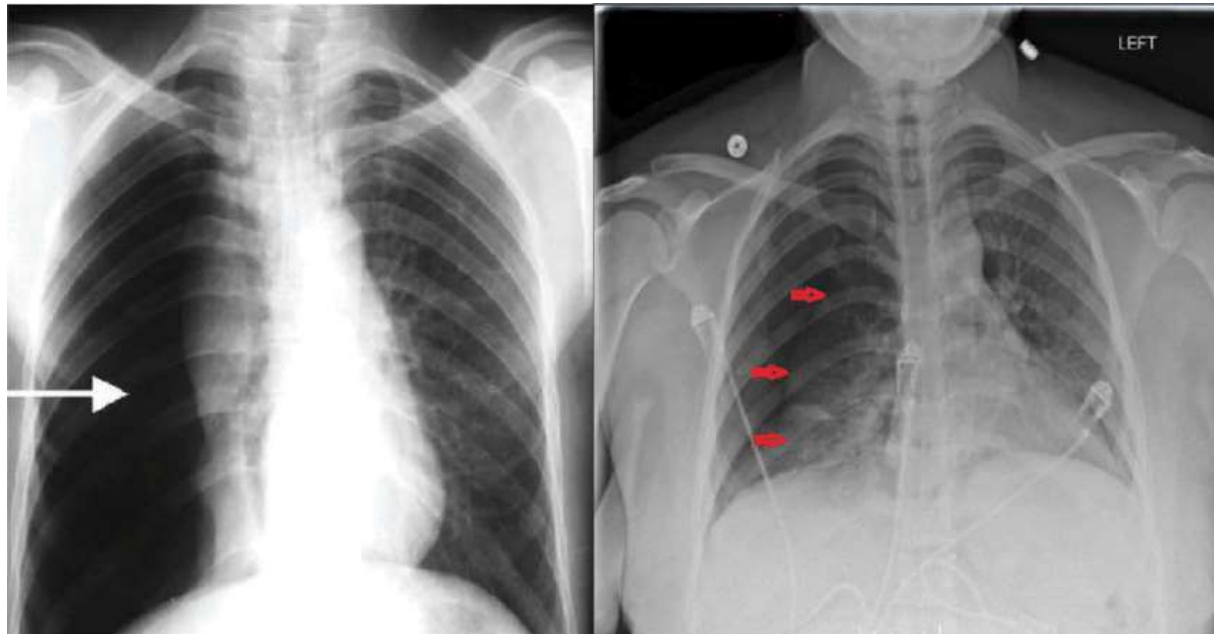
Pleural effusion



ARDS



Pneumonia



Pneumothorax

- **Pulmonary Function Tests:**

- Useful for assessing lung function, particularly in chronic conditions like COPD and asthma.

- **Electrocardiogram (ECG):**

- May help rule out cardiac causes, such as arrhythmias or ischemia, which may lead to respiratory failure.

- **Pulse Oximetry:**

- Non-invasive monitoring of oxygen saturation. While helpful for continuous monitoring, it

Management of Respiratory Failure

Management of Respiratory Failure

Principles

- Hypoxemia may cause death in RF
- Primary objective is to reverse and prevent hypoxemia
- Secondary objective is to control PaCO_2 and respiratory acidosis
- Treatment of underlying disease
- Patient's CNS and CVS must be monitored and treated

Oxygen Therapy

- Supplemental O₂ therapy essential
- titration based on SaO₂, PaO₂ levels and PaCO₂
- Goal is to prevent tissue hypoxia
- Increase arterial PaO₂ > 60 mmHg (SaO₂ > 90%) or venous SaO₂ > 60%
- O₂ dose either flow rate (L/min) or FiO₂ (%)

oxygen

OXYGEN DELIVERY SYSTEMS



Device: Nasal Cannula
Flow: 1 - 6 L/min
FiO₂: 25 - 40%
(~4%/L of flow)



Device: Face Mask
Flow: 5 - 10 L/min
FiO₂: 40 - 60%



Device: Face Tent
Flow: 10 - 15 L/min
FiO₂: ~40%



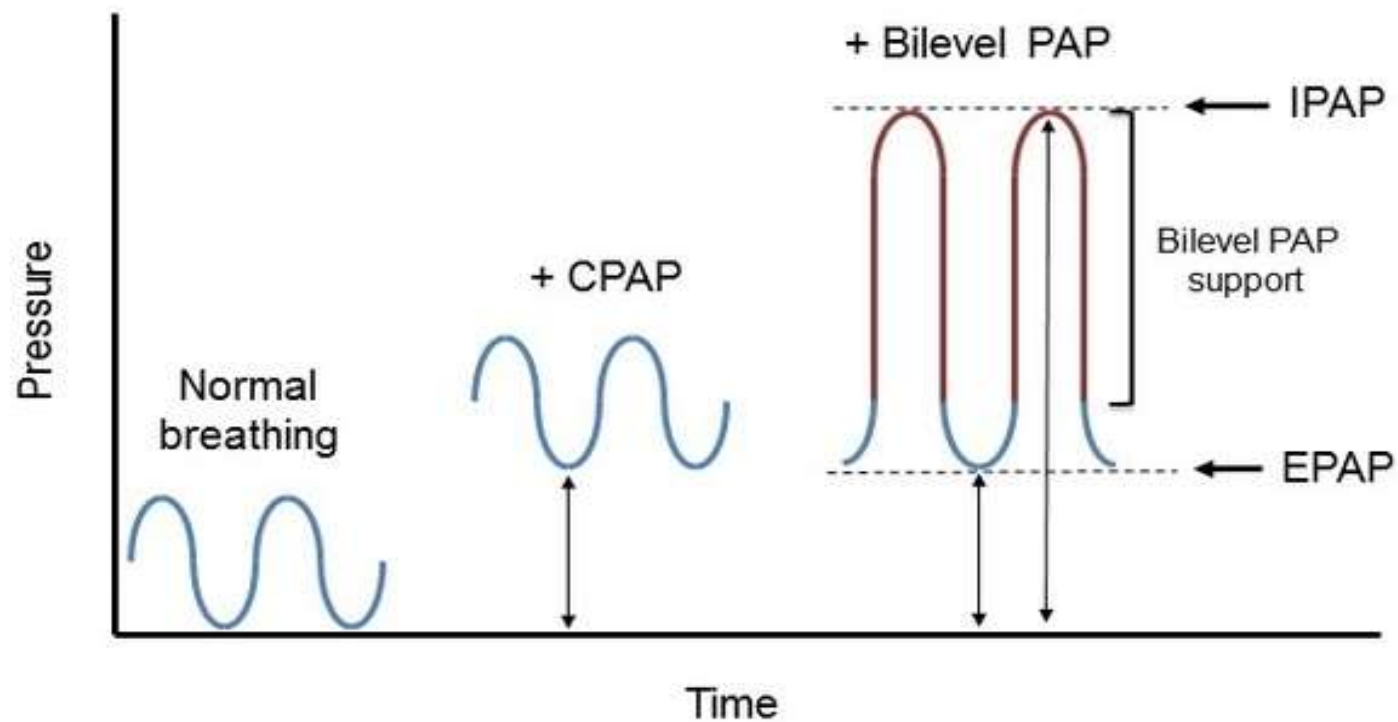
Device: Venturi Mask
Flow: 2 - 15 L/min
(based on valve)
FiO₂: 24 - 60%
(precisely controlled)



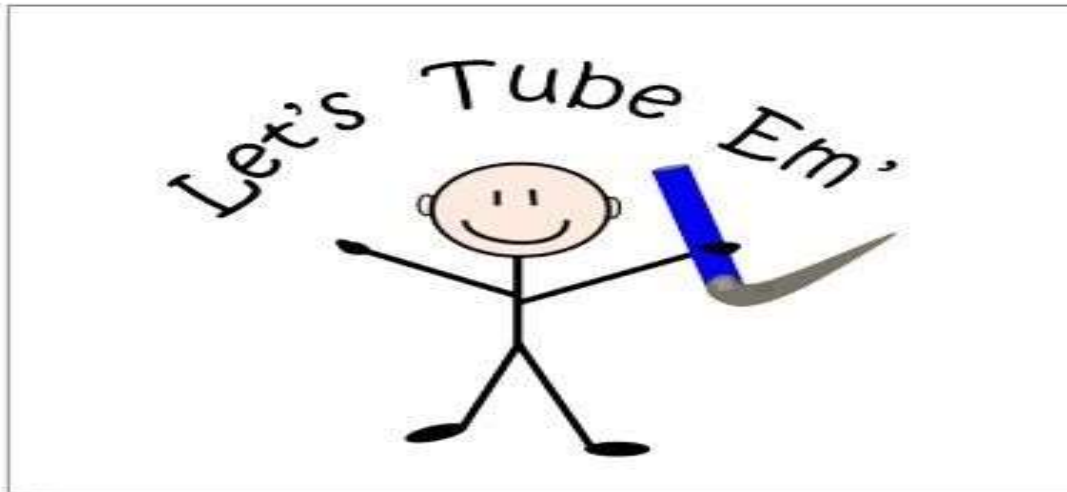
Device: Non-Rebreather
Flow: 10 - 15 L/min
FiO₂: 80 - 95%



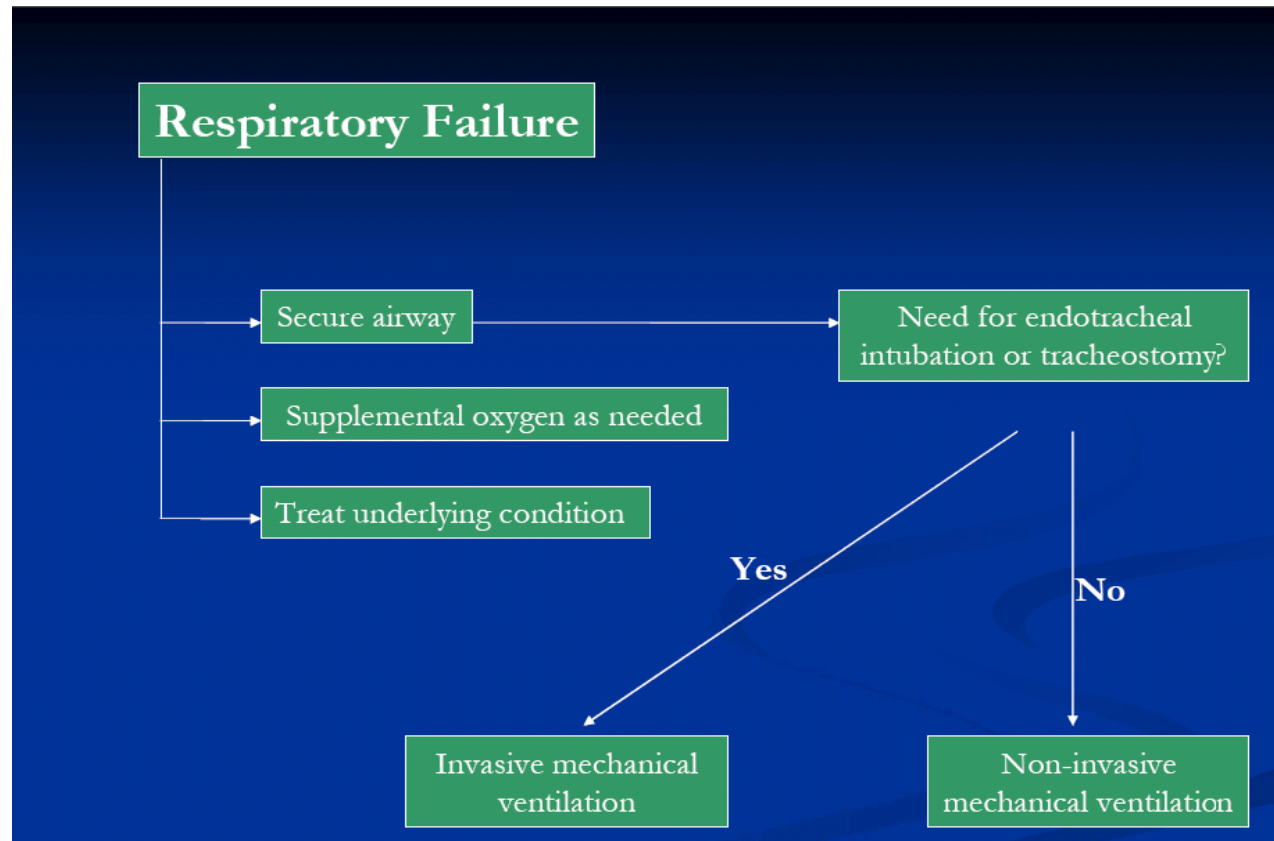
Device: High Flow
Nasal Cannula
Flow: up to 60 L/min
FiO₂: 21 - 100%



If noninvasive devices failed



ACUTE RESPIRATORY FAILURE



Complications of ARF

- Pulmonary
 - Pulmonary embolism
 - barotrauma
 - pulmonary fibrosis (ARDS)
 - Nosocomial pneumonia
- Cardiovascular
 - Hypotension, ↓COP
 - Arrhythmia
 - MI, pericarditis
- GIT
 - Stress ulcer, ileus, diarrhea, hemorrhage
- Infections
 - Nosocomial infection
 - Pneumonia, UTI, catheter related sepsis
- Renal
 - ARF (hypoperfusion, nephrotoxic drugs)
 - Poor prognosis
- Nutritional
 - Malnutrition, diarrhea, hypoglycemia, electrolyte disturbances

Prognosis of ARF

- Respiratory failure is a syndrome caused by a multitude of pathological states; therefore, the prognosis of this disease process is difficult to ascertain.
- In 2017, in the United States of America, however, the in-hospital respiratory failure mortality rate was 12%.
- In-hospital mortality rates for patients requiring intubation with mechanical ventilation for asthma exacerbation, acute exacerbation of chronic obstructive pulmonary disease, and pneumonia were found to be 9.8%, 38.3%, and 48.4%, respectively.
- Lastly, the in-hospital mortality rate for acute respiratory distress syndrome was found to be 44.3%

Thank You