Pathophysiology of respiratory failure

Dr. Nagamani Nambiar.V.V.

Consultant
Anaesthesiologist & Critical Care Physician
Kormbayil Hospital and Diagnostic Centre(P)Ltd.Kerala

Respiratory Failure

Definition: It is a syndrome in which Respiratory system fails in one or both of its gas exchange function namely

Oxygenation and Ventilation.

The term respiratory failure implies the inability to maintain either the normal delivery of oxygen to tissues or the normal removal of carbon dioxide from the tissues. There are actually three processes involved: the transfer of oxygen across the alveolus, the transport of tissues (by cardiac output), and the removal of carbon dioxide from the blood into the alveolus with subsequent exhalation into the environment. Failure of any step in this process can lead to respiratory failure

Types of Respiratory failure

1. Type 1 Respiratory failure

In this type of respiratory failure arterial oxygen tension is below 60 mm of Hg (Hypoxemic, Pao2 < 60mm of Hg),PaCO2 may normal or low. This is the most common form of respiratory failure, and it can be associated with virtually all acute diseases of the lung, which generally involve fluid filling or collapse of alveolar units. Some examples of type I respiratory failure are cardiogenic or noncardiogenic pulmonary edema, pneumonia, and pulmonary hemorrhage and pulmonary fibrosis.Hypoxemia may be refractory to Oxygen therapy.

2. Type 2 Respiratory failure.

Hypercapnic respiratory failure (type II) is characterized by a $PaCO_2$ higher than 50 mm Hg. Hypoxemia is common in patients with hypercapnic respiratory failure who are breathing room air. The pH depends on the level of bicarbonate, which, in turn, is dependent on the duration of hypercapnia. Common etiologies include drug overdose, neuromuscular disease, chest wall abnormalities, and severe airway disorders (eg, asthma and chronic obstructive pulmonary disease).

3. *Type 3 Respiratory failure*

Type 3 respiratory failure can be considered as a subtype of type 1 failure. However, acute respiratory failure is common in the post-operative period with atelectasis being the most frequent cause. Thus measures to reverse atelectasis are paramount.In general residual anesthesia effects, post-operative pain, and abnormal abdominal mechanics contribute to decreasing FRC and progressive collapse of dependant lung units.

It can present as combined Oxygenation and Ventilation failure(PaO2 low and PCO2 high).

Alveolar – Arterial Oxygen partial pressure is increased.(PAO2-PaO2)

Causes of post-operative atelectasis include:

- decreased FRC
- Supine/ obese/ ascites
- anesthesia
- upper abdominal incision
- airway secretions

Therapy is directed at reversing the atelectasis are

- Turn patient q1-2h
- Chest physiotherapy
- Incentive spirometry
- Treat incisional pain (may include epidural anesthesia or patient controlled analgesia)
- Ventilate at 45 degrees upright
- Drain ascites
- Re-expansion of lobar collapse
- Avoid overhydration

Type 4 Respiratory failure

It due to cardiovascular abnormalities. Hypotension seen in septic shock patients leads to hypoperfusion at the level of alveolus and respiratory muscles.

DEPENDING ON THE TIME OF ONSET OF RESPIRATORY FAILURE IT IS ALSO CLASSIFIED AS FOLLOWS:

ACUTE RESPIRATORY FAILURE

It is a sudden onset of respiratory failure.Usually associated with acute respiratory illness like pneumonia,ARDS or sudden alveolar fluid filling as in acute left ventricular failure.Arterial blood gas analysis shows PH usually less than 7.3,Hypoxemia,PaCO2 and bicarbonate which is normal or low in initial stage.

CHRONIC RESPIRATORY FAILURE.

It is normally seen in patients who have pre existing respiratory disorders like COPD.Chronic respiratory acidosis stimulates kidneys to reabsorb bicarbonate for compensation and keeps the PH near normal. Renal compensation.ABG will show Hypoxemia,Hypercapnia,Increased bicarbonate and PH usually above 7.35.

Other features like Polycythemia,Corpulmonale may be seen in patients with chronic respiratory failure.

ACUTE ON CHRONIC RESPIRATORY FAILURE

Seen in advanced COPD patients.In an established chronic respiratory failure an acute exacerbation of COPD results in this type of respiratory failure.ABG may show hypoxemia,Hypercapnea,increased bicarbonate and PH usually < 7.3.

Pathophysiology of Respiratory failure.

Any of the following factors may be involved in the pathogenesis of the respiratory failure

- Airway diseases

- Alveolocapillary units

- CNS,Brain stem

- Peripheral Nervous System

- Respiratory muscles

- Chest wall and Pleura

- Shock

Cardiogenic , Hypovolemic , Septic.

Type 1 Respiratory Failure-Pathophysiology

- Low inspired partial pressure of O2-This can occur in industrial settings in closed spaces.If the inspired air has low Oxygen concentration than normal it can result in hypoxemia.

- Low barometric pressure- Seen in high altitude. Eg:At the summit of mount everest Barometric pressure is only 256 mm of Hg hence berathing atmospheric air,one will have PiO2 of 43 mm Hg and PaO2 28mm Hg. So it is not possible to stay alive here without supplemental Oxygen.

- Alveolar hypoventilation

- Diffusion impairment

- V/Q mismatch

- Right to Left shunt

Causes of Type 1 Respiratory failure

- Acute Asthma

- ARDS

- Pneumonia

- Pulmonary embolism

- Pulmonary Fibrosis

- Pulmonary oedema

- COPD

Impairment of diffusion: This means that equilibration does not occur between the P_{O2} in the pulmonary capillary blood and alveolar gas. Recall that the diffusion capacity of the lung for a gas is equal to:

DL(gas) = net rate of transfer/ΔP_{gas} betw. alveolus & capillary

Under typical resting conditions, the capillary P_{O_2} reaches that of alveolar gas when the red cell is about one-third of the way along the capillary. Even when the capillary transit time is shortened by exercise, the capillary blood equilibriates completely with alveolar air. However, in some abnormal circumstances when the diffusion properties of the lung are impaired, the blood does not reach the alveolar value by the end of the capillary. Diffusion limitation seldom causes systemic hypoxemia at rest, but may cause hypoxemia during exercise when there is less time for equilibration with alveolar gas.

Diseases in which diffusion impairment may contribute to hypoxemia include asbestosis, sarcoidosis and diffuse interstitial fibrosis. Impaired diffusion is also likely to develop when P_{AO_2} is abnormally low, such as at high altitudes. Here, the impairment occurs because the gradient for O_2-diffusion is low.

Carbon dioxide elimination is generally thought to be unaffected by diffusion abnormalities. This is because the diffusion of CO_2 is ≥20X faster than O_2. Clinically, significant hypercapnia (elevations in arterial PCO2) is never caused by a diffusion defect.

Hypoxemia can be easily corrected by breathing an enriched oxygen mixture.

V/Q ratio

V/Q ratio is amount of ventilation in relation to perfusion in any given part of the lung.V/Q relates to the efficiency of lung units with which it resaturates venous blood with O2 and eliminate CO2.

Since alveolar ventilation (VA) is normally 4 L/minute and Pulmonary capillary perfusion(Q)is 5 L/minute,the over all V/Q ratio is 0.8.
V/Q for each alveolar-capillary unit can range from zero(no ventilation) to infinity (no perfusion).Areas with no ventilation (V/Q=0) is referred as Intra pulmonary shunt and areas with no perfusion is referred as alveolar dead space.
V/Q normally ranges between 0.3 and 3.3 with majority of lung areas close to 1.0.
Perfusion increases at a greater rate from nondependent to dependent part of the lung when compared to ventilation.

V/Q at the top(Apex) of the lung 3.3 (Dead space)

- Ventilation is more in relation to perfusion – High V/Q areas (PAO2 132,PCO2 28 mm of Hg)

V/Q at the bottom(Base) of lung 0.3 (shunt)

- Perfusion is more in relation to Ventilation – Low V/Q areas (PAO2 89,PCO2 42 mm of Hg)

When lung is inadequately ventilated and optimally perfused V/Q<1

Low V/Q – Acts as a shunt

Results in Hypoxemia and Hypercapnia

When the lung is inadequately perfused and optimally ventilated V/Q >1

High V/Q – Acts as alveolar dead space (Wasted Ventilation)

Normally don't affect gas exchange unless severe.

Ventilation – Perfusion (V/Q) mismatch
V/Q mismatch is the presence of a degree of shunt and a degree of dead space in the same lung. It is a component of most causes of respiratory failure and is the commonest cause of hypoxaemia.
Because of the complicated structure of the lungs, it is impossible to describe this condition in anatomical terms. A patient with this condition is likely to have areas in the lungs that are better perfused than ventilated and areas that are better ventilated than perfused. This occurs in normal lungs to some extent. The difference in V/Q mismatch is that the extent to which this occurs is significantly increased.

OXYGEN DISSOCIATION CURVE
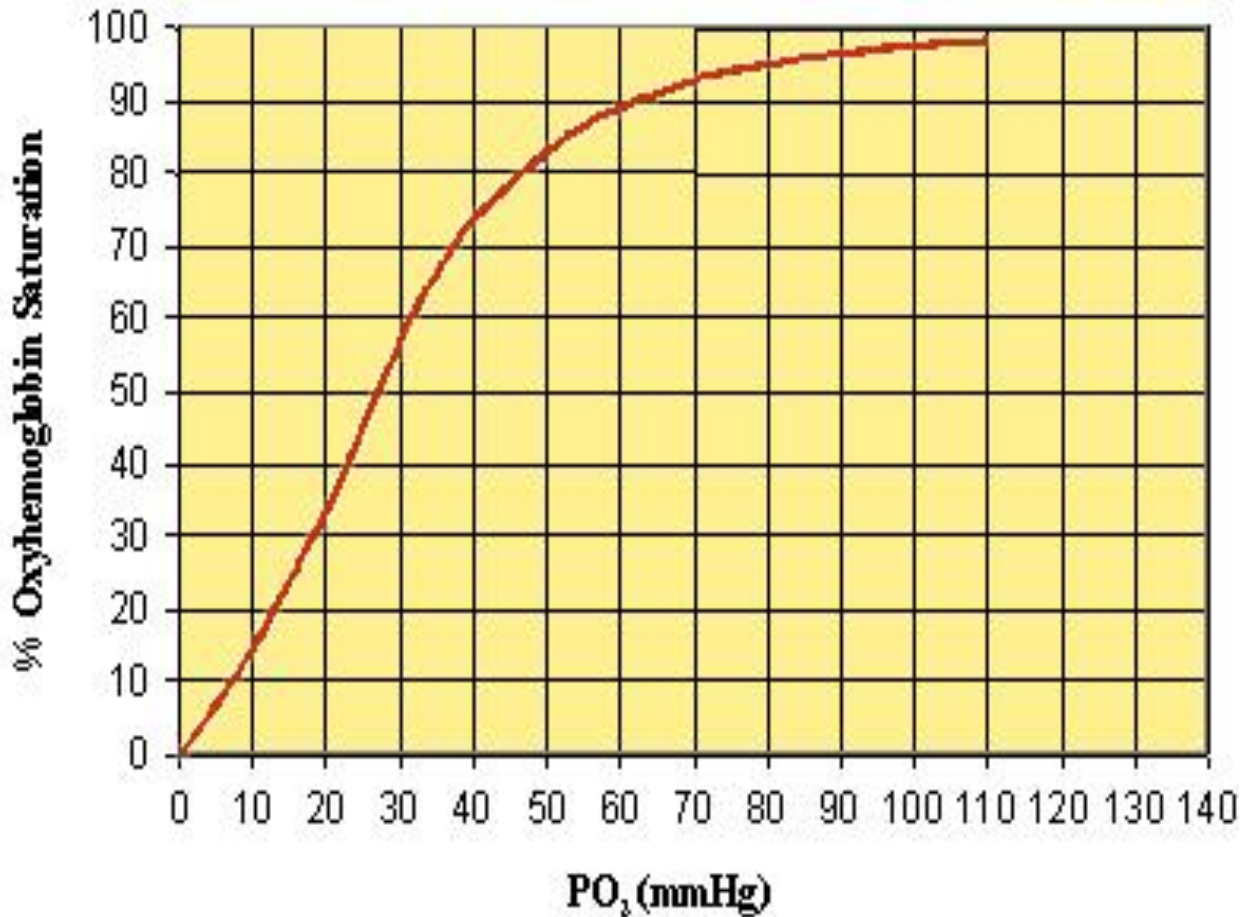
Because of the flat upper portion of the Oxyhaemoglobin dissociation curve , blood leaving the relatively healthy alveoli will have an oxygen saturation of about 97%. Blood leaving alveoli that do not have optimum V/Q ratios will have a much lower oxygen saturations . The admixture of all the blood leaving the alveoli results low oxygen saturations and hypoxaemia.

In general, this cause of respiratory failure responds to oxygen therapy, although the response varies depending on the precise nature and size of the V/Q mismatch

Intra pulmonary Shunt

Deoxygenated blood (Pulmonary artery-Mixed venous) bypasses the alveoli and mixes with oxygenated blood that has flowed through the ventilated alveoli resulting in decrease in arterial oxygen content in the Pulmonary vein.

Types of Intrapulmonary shunt

- **True Shunt- V/Q = 0**

Total absence of gas exchange between Capillary blood and Alveolar gas.This can occur in intra pulmonary arteriovenous fistulas.This does not respond to 100% oxygen.This shunt is equivalent to the anatomic shunt between right and left side of the heart.

- **<u>Venous admixture</u>**

Capillary flow does not equilibrate completely with Alveolar gas. Excessive perfusion in relation to ventilation. Blood passes through low V/Q areas (V/Q <1) and mixes with blood coming from normally ventilated and perfused alveoli.This mixing decreases the net Oxygen tension in pulmonary vein entering the left atrium.

100% Oxygen administration increases the Oxygen concentration in all the alveolus and hypoxemia improves to some extent.

SHUNT EQUATION:

Fraction of cardiac output that represents intra pulmonary shunt is known as shunt fraction.Intra pulmonary shunt fraction is derived by relationship between the Oxygen content in arterial blood,mixed venous blood and pulmonary capillary blood.

QS/QT=(CcO2-CaO2) / (CcO2-CvO2)

CcO2= Capillary O2 content (Calculated from ideal PAO2)

CaO2= Arterial O2 content (Derived from PaO2 by using ODC)

CvO2= Mixed venous O2 content (from pulmonary artery catheter)

QS/QT= Shunt fraction (Normal <10% of Cardiac output)

Problem with this formula is the inability to measure the pulmonary capillary Oxygen (CcO2)content directly.As a result pure Oxygen breathing to produce 100% Oxyhemoglobin saturation in the pulmonary capillary blood is recommended for shunt calculation.How ever in this situation,Qs/Qt measures only the true shunt.

Intrapulmonary shunt fraction is increased in

- Small air way occlusion- Asthma

- Fluid filled Alveoli- ARDS,Pneumonia,Pulmonary oedema.

- Alveolar collapse- Atelectasis.

- Excessive Capillary flow- Non embolised region of the lung in pulmonary embolism.

Influence of shunt on Oxygen and Carbon dioxide tension

PaO2 falls progressively as the shunt fraction increases but PaCO2 remains constant until the shunt fraction exceeds 50%.PaCO2 is often low in intrapulmonary shunting due to hyperventilation triggered by disease process like sepsis or by accompanying hypoxemia.

In10 to 50% of shunt, increasing FiO2 has very minimal effect on PaO2.More than50% shunt PaO2 is independent of changes in FiO2. Hypercapnia is seen when the shunt is >50% of Cardiac output. A-a Oxygen partial pressure gradient increases in shunt.

Implication:

In ARDS with a very high shunt fraction, FiO2 can be kept to a minimum safe level without further compromising arterial oxygenation thereby preventing pulmonary oxygen toxicity.

PaO2/FiO2 Ratio

It is used as an indirect estimate of shunt fraction.

- PaO2/FiO2 < 200 = shunt fraction indication Qs/Qt >20% ,usually seen in ARDS.

- PaO2/FiO2 >200 = shunt fraction indication Qs/Qt < 20%, Usually seen in Acute Lung Injury.

Shunt and V/Q mismatch can be differentiated by administering 100% Oxygen or by calculating the shunt fraction.

- Shunt poorly responds to 100% Oxygen.

- A-a gradient is high in shunt.

Alveolar to Arterial oxygen gradient= PAO2-PaO2

A-a PO2= (FiO2 X (PB-PH2O) - (PaCO2/R)) - PaO2

A-a PO2=0.21X(760-47)- (40/0.8) – 90 = 10 mm of Hg. In ventilated patients, mean airway pressure should be added to ambient barometric pressure while calculating A-a PO2 gradient

It normally ranges between 5-20 mm of Hg(Usually < 15). Alveolar to Arterial gradient of O2 above 15mm of Hg indicates pulmonary disease as the cause of Hypoxemia. A-a gradient increases with age.   For a given age, it can be calculated by (Patient's age/4) + 4 = Normal A-a gradient for that age.

A-aPO2 gradient increases by 5-7 mm Hg for every 10% increase in FiO2. Loss of regional pulmonary vasoconstriction during supplemental O2 breathing maintains blood

flow in poorly ventilated lung regions, and this increases intrapulmonary shunt fraction and there by A-a PO2 gradient.

V/Q mismatch and Shunt can increase the alveolar to arterial O2 gradient

A-a gradient is normal in hypoxemia due to low FiO2 and Alveolar hypoventilation

Normal A-a gradient with mixed venous Oxygen tension of 40mm of Hg or more indicates V/Q mismatch as the sole cause of Hypoxemia.

Normal A-a gradient with mixed venous Oxygen tension less than 40mm of Hg indicates that there is aDO2/VO2 imbalance adding to hypoxemia due to V/Q mismatch .This imbalance may be due to a decrease in DO2 (Anemia or decreased cardiac output) or an increased VO2(from hypermetabolism).

a/A PO2 ratio

A-a PaO2 gradient is influenced by FiO2. This influence of FiO2 can be avoided by calculating a/A ratio.

a/A PO2 ratio = 1 – (A-aPO2)/PaO2

- Normal a/A PO2 ratio = 0.74-0.77 room air.

- 0.80-0.82 with 100% O2.

Type II Respiratory Failure-Pathophysiology

- Abnormalities of central respiratory drive

- Neuromuscular dysfunction

- Abnormalities of the chest wall

- Abnormalities of the airways

- Abnormalities of the lungs

Hypercapnic Respiratory Failure.

- CO2 removal depends on Alveolar Ventilation

In steady state – Rate of CO2 production by tissue = Rate of CO2 removal.

VA = K X VCO2/PaCO2

PaCO2=K X VCO2/VA

- VA – Alveolar Ventilation

- K – Constant 0.863

- VCO2 – CO2 ventilation.

- PaCO2-Arterial CO2 partial pressure

Ventilatory Capacity – Maximum spontaneous ventilation that can be maintained without development of respiratory fatigue.

Ventilatory Demand – Spontanious minute ventilation that results in a stable PaCO2.

Normal state – Ventilatory Capacity > Ventilatory Demand. Most hypercapnic states result from inadequate clearance due to alveolar hypoventilation and increased dead space (dead space/tidal volume); this may happen in parenchymal diseases such as emphysema and in circulatory problems such as pulmonary embolism. Normally, the ventilatory drive adjusts the output of the muscular pump in proportion to metabolic activity, in order to maintain arterial blood pH within narrow limits (7.38–7.42). Causes of pump failure can be grouped into three major categories: central depression, mechanical defect of the ventilatory pump, and muscle fatigue. Exacerbation of chronic obstructive pulmonary disease is the most important cause of hypercapnic respiratory failure; the increased load of the respiratory system and reduced muscular force induce the patient to adopt a rapid shallow breathing pattern in order to preserve the ventilatory pump from fatigue and exhaustion.

Alveolar Dead space (Wasted ventilation)

Alveolar dead space is sum of the volumes of those alveoli which have little or no blood flowing through their adjacent pulmonary capillaries, i.e., alveoli that are ventilated but not perfused, and where, as a result, no gas exchange can occur. Alveolar dead space is negligible in healthy individuals, but can increase dramatically in some lung diseases due to ventilation-perfusion mismatch. Alveolar VD is increased in conditions COPD, Pul embolism, CCF, Pulmonary vasoconstriction.

Anatomical Dead space

Anatomical dead space is that portion of the airways (such as the mouth and trachea to the bronchioles) which conducts gas to the alveoli. No gas exchange is possible in these spaces. In healthy lungs where the alveolar dead space is small, Fowler's method accurately measures the anatomic dead space by a nitrogen washout technique.

The normal value for dead space volume (in ml) is approximately the lean mass of the body (in pounds), and averages about a third of the resting tidal volume (450-500 mL). (or 2 ml/kg)In Fowler's original study, the anatomic dead space was 156 ± 28 ml (n=45 males) or 26% of their tidal volume. Despite the flexibility of the trachea and smaller conducting airways, their overall volume (i.e. the anatomic dead space) changes little with bronchoconstriction or when breathing hard during exercise.

Alveolar + Anatomical dead space =Physiological dead space.

Dead space ventilation increases in:

- Alveolar-Capillary interface damage (Emphysema)

- Reduced blood flow (Decreased CO)

- Alveolar over distension (Positive pressure ventilation)

Bohr Equation = VD Phy / VT= PaCO2- PET CO2/PaCO2

O.25-0.40   Normal

Bohr Equation describes the amount of physiological dead space in a person's lungs. This is given as a ratio of dead space to tidal volume. It differs from anatomical dead space as measured by Fowler's method as it includes alveolar dead space.

PaCO2 begins to rise when dead space ventilation is > 50% of total ventilation.(VD/VT 0.5)

PCO2 and Alveolar Ventilation relationship is hyperbolic.As the Alveolar Ventilation decreases   PaCO2 rises precipitously. Hypoventilation is characterized by Hypercapnia and Hypoxemia. Hypoventilation can be differentiated from other causes of Hypoxemia by the presence of normal Alveolar to Arterial PO2 gradient. Increased CO2 production is an important factor in promoting hypercapnia only in patients with reduced ability to eliminate CO2. Overfeeding with Carbohydrates in ventilator dependent patients can promote hypercapnia and delay weaning.

Severe Hypercapnia

High level of PaCO2 can result in Hypoxemia by decreasing PAO2 if not supplemented by O2.

Example: At PaCO2 of 80mm Hg breathing room air will reduce the PAO2 to 50mm Hg.

PAO2= 0.21 X(760-47)- 80/0.8 = 150-100 = 50 mm of Hg

Causes of Type II Respiratory failure.

1.CNS Causes

- Coma

- Head injury,Increased ICP

- Head Injury

- Opioid,Sedatives

- Hypothyroidism

2.Neuromuscular causes

- Spinal Cord- Poliomylitis

- Cervical Cord leisons

- Peripheral Nerves – Guillion Barre Syndrome,Diphtheria,Critical illness Neuropathy.

- Neuromuscular Junction- Myasthenia Gravis,OP poisoning,Muscle relaxants,Botulism.

- Muscular Dystrophy.

3.Thoracic wall causes

- Chest wall trauma

- Rupture of Diaphragm

- Kyphoscoliosis

- Abdominal distension – Ascites,Blood,Surgical packs.

- Morbid obesity.

4.Pulmonary Causes.

- Acute severe Asthma

- Upper airway obstruction

- COPD

- Bronchiectasis

- OSA

Assessment of Respiratory failure

- History

- Clinical examination

- Pulse oximetry

- ABG

- X-ray chest

- ECG

- Echo

- PFT : Limited use in acute settings.FEV1/FVC

- CT-Thorax

- V/Q scan: In pulmonary embolism

- Pulmonary artery catheterization and mixed venous oxygen tension estimation

Conclusion: Pathophysiology of respiratory failure in a patient can be multifactorial , hence a good understanding of this syndrome helps the clinician to adapt the proper strategies in Oxygen therapy and Mechanical ventilation.