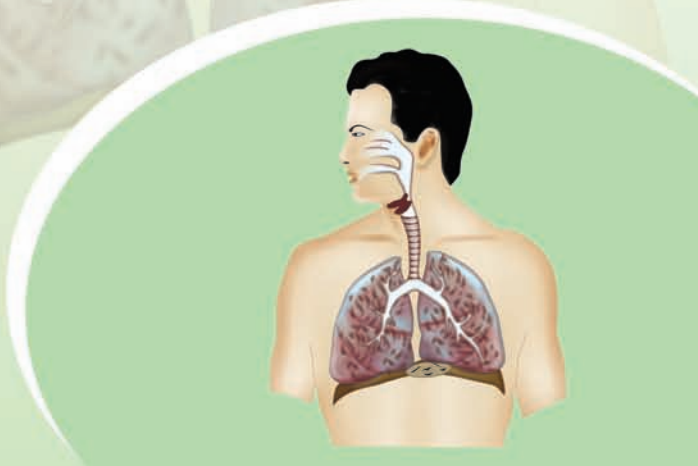
Section

9

Respiratory System and Environmental Physiology



Physiological Anatomy of Respiratory Tract

Chapter 118

INTRODUCTION

Respiration is the process by which oxygen is taken in and carbon dioxide is given out. The first breath takes place only after birth. **Fetal lungs** are **non-functional.** So, during intrauterine life the exchange of gases between fetal blood and mother's blood occurs through placenta.

After the first breath, the respiratory process continues throughout the life. Permanent stoppage of respiration occurs only at death.

Normal Respiratory Rate at Different Age

Newborn	:	30 to 60/minute
Early childhood	:	20 to 40/minute
Late childhood	:	15 to 25/minute
Adult	:	12 to 16/minute.

TYPES OF RESPIRATION

Respiration is classified into two types:

1. **External respiration** that involves exchange of respiratory gases, i.e. oxygen and carbon dioxide between lungs and blood
2. **Internal respiration,** which involves exchange of gases between blood and tissues.

PHASES OF RESPIRATION

Respiration occurs in two phases:

1. **Inspiration** during which air enters the lungs from atmosphere

2. **Expiration** during which air leaves the lungs.

During normal breathing, inspiration is an active process and expiration is a passive process.

■ FUNCTIONAL ANATOMY OF RESPIRATORY TRACT

Respiratory tract is the anatomical structure through which air moves in and out. It includes nose, pharynx, larynx, trachea, bronchi and lungs (Fig. 118.1).

Pleura

Each lung is enclosed by a bilayered serous membrane called pleura or **pleural sac.** Pleura has two layers namely inner **visceral** and outer **parietal** layers. Visceral layer is attached firmly to the surface of the lungs. At hilum, it is continuous with parietal layer, which is attached to the wall of thoracic cavity.

Intrapleural Space or Pleural Cavity

Intrapleural space or pleural cavity is the narrow space in between the two layers of pleura.

Intrapleural Fluid

Intrapleural space contains a thin film of serous fluid called intrapleural fluid, which is secreted by the visceral layer of the pleura.

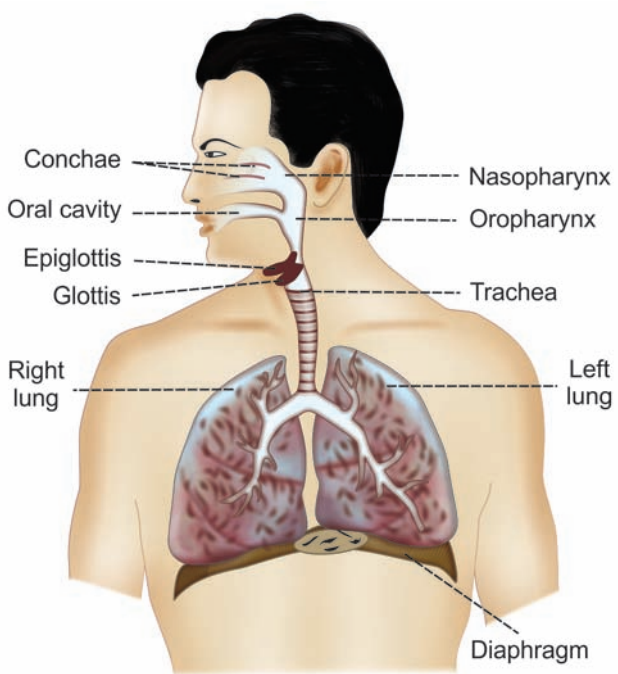


FIGURE 118.1: Respiratory tract

Functions of intrapleural fluid

1. It functions as the lubricant to prevent friction between two layers of pleura
2. It is involved in creating the negative pressure called **intrapleural pressure** within intrapleural space.

Pleural Cavity in Abnormal Conditions

In some pathological conditions, the pleural cavity expands with accumulation of air **(pneumothorax),** water **(hydrothorax),** blood **(hemothorax)** or pus **(pyothorax).**

Tracheobronchial Tree

Trachea and bronchi are together called tracheobronchial tree. It forms a part of air passage.

Components of tracheobronchial tree

1. **Trachea** bifurcates into two main or **primary bronchi** called right and left bronchi
2. Each primary bronchus enters the lungs and divides into **secondary bronchi**
3. Secondary bronchi divide into **tertiary bronchi.** In right lung, there are 10 tertiary bronchi and in left lung, there are eight tertiary bronchi
4. Tertiary bronchi divide several times with reduction in length and diameter into many generations of **bronchioles**
5. When the diameter of bronchiole becomes 1 mm or less, it is called **terminal bronchiole**
6. Terminal bronchiole continues or divides into **respiratory bronchioles,** which have a diameter of 0.5 mm.

Upper and Lower Respiratory Tracts

Generally, respiratory tract is divided into two parts:

1. Upper respiratory tract that includes all the structures from nose up to vocal cords; vocal cords are the folds of mucous membrane within larynx that vibrates to produce the voice
2. Lower respiratory tract, which includes trachea, bronchi and lungs.

■ RESPIRATORY UNIT

Parenchyma of lungs is formed by respiratory unit that forms the **terminal portion** of respiratory tract. Respiratory unit is defined as the structural and functional unit of lung. Exchange of gases occurs only in this part of the respiratory tract.

■ STRUCTURE OF RESPIRATORY UNIT

Respiratory unit starts from the respiratory bronchioles (Fig. 118.2). Each respiratory bronchiole divides into

alveolar ducts. Each alveolar duct enters an enlarged structure called the **alveolar sac.** Space inside the alveolar sac is called **antrum.** Alveolar sac consists of a cluster of **alveoli.** Few alveoli are present in the wall of alveolar duct also.

Thus, respiratory unit includes:

1. Respiratory bronchioles
2. Alveolar ducts
3. Alveolar sacs
4. Antrum
5. Alveoli.

Each **alveolus** is like a pouch with the diameter of about 0.2 to 0.5 mm. It is lined by epithelial cells.

Alveolar Cells or Pneumocytes

Alveolar epithelium consists of alveolar cells or pneumocytes, which are of two types namely type I alveolar cells and type II alveolar cells.

Type I alveolar cells

Type I alveolar cells are the squamous epithelial cells forming about 95% of the total number of cells. These cells form the site of gaseous exchange between the alveolus and blood.

Type II alveolar cells

Type II alveolar cells are cuboidal in nature and form about 5% of alveolar cells. These cells are also called **granular pneumocytes.** Type II alveolar cells secrete **alveolar fluid** and **surfactant.**

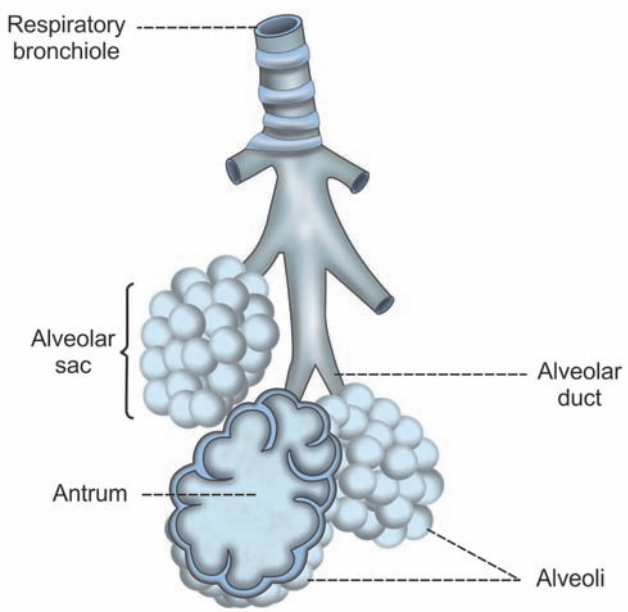


FIGURE 118.2: Respiratory unit

■ RESPIRATORY MEMBRANE

Respiratory membrane is the membranous structure through which the exchange of gases occurs.

Respiratory membrane separates air in the alveoli from the blood in capillary. It is formed by the **alveolar membrane** and **capillary membrane.** Respiratory membrane has a surface area of 70 square meter and thickness of 0.5 micron. Structure of respiratory membrane is explained in Chapter 124 (See Fig. 124.1).

■ NON-RESPIRATORY FUNCTIONS OF RESPIRATORY TRACT

Besides primary function of gaseous exchange, the respiratory tract is involved in several non-respiratory functions of the body. Particularly, the lungs function as a defense barrier and metabolic organs, which synthesize some important compounds. Non-respiratory functions of the respiratory tract are:

■ 1. OLFACTION

Olfactory receptors present in the mucous membrane of nostril are responsible for **olfactory sensation.**

■ 2. VOCALIZATION

Along with other structures, larynx forms the **speech apparatus.** However, larynx alone plays major role in the process of vocalization. Therefore, it is called **sound box.**

■ 3. PREVENTION OF DUST PARTICLES

Dust particles, which enter the nostrils from air, are prevented from reaching the lungs by **filtration action** of the hairs in nasal mucous membrane. Small particles, which escape the hairs, are held by the **mucus** secreted by nasal mucous membrane. Those dust particles, which escape nasal hairs and nasal mucous membrane, are removed by the **phagocytic action** of **macrophages** in the alveoli.

Particles, which escape the protective mechanisms in nose and alveoli are thrown out by **cough** reflex and **sneezing** reflex (Chapter 126).

■ 4. DEFENSE MECHANISM

Lungs play important role in the **immunological** defense system of the body. Defense functions of the lungs are performed by their own defenses and by the presence of various types of cells in mucous membrane lining the alveoli of lungs. These cells are leukocytes, macrophages, mast cells, natural killer cells and dendritic cells.

i. *Lung's Own Defenses*

Epithelial cells lining the air passage secrete some innate immune factors called **defensins** and **cathelicidins.** These substances are the antimicrobial peptides, which play an important role in lung's natural defenses. Refer Chapter 17 for detail.

ii. *Defense through Leukocytes*

Leukocytes, particularly the neutrophils and lymphocytes present in the alveoli of lungs provide defense mechanism against bacteria and virus. **Neutrophils** kill the bacteria by phagocytosis. **Lymphocytes** develop immunity against bacteria.

iii. *Defense through Macrophages*

Macrophages engulf the dust particles and the pathogens, which enter the alveoli and thereby act as **scavengers** in lungs. Macrophages are also involved in the development of immunity by functioning as **antigen presenting cells.** When foreign organisms invade the body, the macrophages and other antigen presenting cells kill them. Later, the antigen from the organisms is digested into polypeptides. Polypeptide products are presented to T lymphocytes and B lymphocytes by the macrophages.

Macrophages secrete interleukins, tumor necrosis factors (TNF) and chemokines (Chapter 24). Interleukins and TNF activate the general immune system of the body (Chapter 17). Chemokines attract the white blood cells towards the site of any inflammation.

iv. *Defense through Mast Cell*

Mast cell is a large cell resembling the basophil. Mast cell produces the **hypersensitivity reactions** like allergy and anaphylaxis (Chapter 17). It secretes heparin, histamine, serotonin and hydrolytic enzymes.

v. *Defense through Natural Killer Cell*

Natural killer (NK) cell is a large granular cell, considered as the third type of lymphocyte. Usually NK cell is present in lungs and other lymphoid organs. Its granules contain hydrolytic enzymes, which destroy the microorganisms.

NK cell is said to be the first line of defense in specific immunity particularly **against viruses.**

It destroys the viruses and viral infected or damaged cells, which may form the tumors. It also destroys the malignant cells and prevents development of cancerous tumors. NK cells secrete interferons and the tumor necrosis factors (Chapter 17).

vi. *Defense through Dendritic Cells*

Dendritic cells in the lungs play important role in immunity. Along with macrophages, these cells function as antigen presenting cells.

■ 5. MAINTENANCE OF WATER BALANCE

Respiratory tract plays a role in water loss mechanism. During expiration, water evaporates through the expired air and some amount of body water is lost by this process.

■ 6. REGULATION OF BODY TEMPERATURE

During expiration, along with water, heat is also lost from the body. Thus, respiratory tract plays a role in heat loss mechanism.

■ 7. REGULATION OF ACID-BASE BALANCE

Lungs play a role in maintenance of acid-base balance of the body by regulating the carbon dioxide content in blood. Carbon dioxide is produced during various metabolic reactions in the tissues of the body. When it enters the blood, carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it splits into hydrogen and bicarbonate ions.

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

Entire reaction is reversed in lungs when carbon dioxide is removed from blood into the alveoli of lungs (Chapter 125).

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

As carbon dioxide is a **volatile gas,** it is practically blown out by ventilation.

When metabolic activities are accelerated, more amount of carbon dioxide is produced in the tissues. Concentration of hydrogen ion is also increased. This leads to reduction in pH. Increased hydrogen ion concentration causes increased pulmonary ventilation (hyperventilation) by acting through various mechanisms like chemoreceptors in aortic and carotid bodies and in medulla of the brain (Chapter 126). Due to hyperventilation, excess of carbon dioxide is removed from body fluids and the pH is brought back to normal.

■ 8. ANTICOAGULANT FUNCTION

Mast cells in lungs secrete **heparin.** Heparin is an anticoagulant and it prevents the intravascular clotting.

■ 9. SECRETION OF ANGIOTENSIN-CONVERTING ENZYME

Endothelial cells of the pulmonary capillaries secrete the angiotensin-converting enzyme **(ACE).** It converts

the angiotensin I into active angiotensin II, which plays an important role in the regulation of ECF volume and blood pressure (Chapter 50).

■ 10. SYNTHESIS OF HORMONAL SUBSTANCES

Lung tissues are also known to synthesize the hormonal substances, prostaglandins, acetylcholine and serotonin, which have many physiological actions in the body including regulation of blood pressure (Chapter 73).

■ RESPIRATORY PROTECTIVE REFLEXES

Respiratory protective reflexes are the reflexes that protect lungs and air passage from foreign particles. Respiratory process is modified by these reflexes in order to eliminate the foreign particles or to prevent the entry of these particles into the respiratory tract. Following are the respiratory protective reflexes:

■ COUGH REFLEX

Cough is a modified respiratory process characterized by forced expiration. It is a protective reflex and it is caused by **irritation of respiratory tract** and some other areas such as **external auditory canal** (see below).

Causes

Cough is produced mainly by irritant agents. It is also produced by several disorders such as cardiac disorders (congestive heart failure), pulmonary disorders (chronic obstructive pulmonary disease – COPD) and tumor in thorax, which may exert pressure on larynx, trachea, bronchi or lungs.

Mechanism

Cough begins with deep inspiration followed by forced expiration with closed glottis. This increases the intrapleural pressure above 100 mm Hg. Then, glottis opens suddenly with explosive outflow of air at a high velocity. Velocity of the airflow may reach 960 km/hour. It causes expulsion of irritant substances out of the respiratory tract.

Reflex Pathway

Receptors that initiate the cough are situated in several locations such as nose, paranasal sinuses, larynx, pharynx, trachea, bronchi, pleura, diaphragm, pericardium, stomach, external auditory canal and tympanic membrane.

Afferent nerve fibers pass via vagus, trigeminal, glossopharyngeal and phrenic nerves. The center for cough reflex is in the medulla oblongata.

Efferent nerve fibers arising from the medullary center pass through the vagus, phrenic and spinal motor nerves. These nerve fibers activate the primary and accessory respiratory muscles.

■ SNEEZING REFLEX

Sneezing is also a modified respiratory process characterized by forced expiration. It is a protective reflex caused by **irritation of nasal mucous** membrane.

Causes

Irritation of the nasal mucous membrane occurs because of dust particles, debris, mechanical obstruction of the airway and excess fluid accumulation in the nasal passages.

Mechanism

Sneezing starts with deep inspiration, followed by forceful expiratory effort with opened glottis resulting in expulsion of irritant agents out of respiratory tract.

Reflex Pathway

Sneezing is initiated by the irritation of nasal mucous membrane, the olfactory receptors and trigeminal nerve endings present in the nasal mucosa.

Afferent nerve fibers pass through the trigeminal and olfactory nerves. Sneezing center is in medulla oblongata. It is located diffusely in spinal nucleus of trigeminal nerve, nucleus solitarius and the reticular formation of medulla.

Efferent nerve fibers from the medullary center pass via trigeminal, facial, glossopharyngeal, vagus and intercostal nerves. These nerve fibers activate the pharyngeal, tracheal and respiratory muscles.

■ SWALLOWING (DEGLUTITION) REFLEX

Swallowing reflex is a respiratory protective reflex that prevents entrance of food particles into the air passage during swallowing.

While swallowing of the food, the respiration is arrested for a while. Temporary arrest of respiration is called apnea. Arrest of breathing during swallowing is called **swallowing apnea** or **deglutition apnea.** It takes place during pharyngeal stage, i.e. second stage of deglutition and prevents entry of food particles into the respiratory tract. Refer Chapter 43 for details.

Pulmonary Circulation

Chapter 119

PULMONARY BLOOD VESSELS

Pulmonary blood vessels include **pulmonary artery,** which carries **deoxygenated blood** to alveoli of lungs and **bronchial artery,** which supply **oxygenated blood** to other structures of lungs (see below).

PULMONARY ARTERY

Pulmonary artery supplies deoxygenated blood pumped from right ventricle to alveoli of lungs (pulmonary circulation). After leaving the right ventricle, this artery divides into **right and left branches.** Each branch enters the corresponding lung along with primary bronchus. After entering the lung, branch of the pulmonary artery divides into small vessels and finally forms the **capillary plexus** that is in intimate relationship to alveoli. Capillary plexus is solely concerned with alveolar gas exchange. Oxygenated blood from the alveoli is carried to left atrium by one pulmonary vein from each side.

BRONCHIAL ARTERY

Bronchial artery arises from descending thoracic aorta. It supplies arterial blood to bronchi, connective tissue and other structures of lung stroma, visceral pleura and pulmonary lymph nodes. Venous blood from these structures is drained by two **bronchial veins** from each side. Bronchial veins from right side drain into **azygos vein** and the left bronchial veins drain into **superior hemiazygos** or **left superior intercostal veins.** However, the blood from distal portion of bronchial circulation is drained directly into the tributaries of **pulmonary veins.**

PHYSIOLOGICAL SHUNT

Definition

Physiological shunt is defined as a diversion through which the venous blood is mixed with arterial blood.

Components

Physiological shunt has two components:

1. Flow of deoxygenated blood from **bronchial circulation** into pulmonary veins without being oxygenated makes up part of normal physiological shunt
2. Flow of deoxygenated blood from **thebesian veins** into cardiac chambers directly (Chapter 108).

Venous Admixture and Wasted Blood

Physiological shunt results in venous admixture. Venous admixture refers to mixing of deoxygenated blood with oxygenated blood. Fraction of venous blood, which is not fully oxygenated is generally considered as wasted blood.

Normal Shunt Level and its Variations

Normal physiological shunt of venous blood to the left side of heart is 1% to 2% of cardiac output. In normal persons, it may increase up to 5% of cardiac output, which may be due to mismatching of ventilation-perfusion ratio within physiological limits.

Pathological increase in the shunt occurs in several conditions such as acute pulmonary infections and bronchiectasis (permanent dilatation of bronchi due to chronic pulmonary infections and inflammatory processes).

Physiological Shunt Vs Physiological Dead Space

Physiological shunt is analogous to physiological dead space (Chapter 122). Physiological shunt includes wasted blood and physiological dead space includes wasted air. Both wasted blood and wasted air exist on either side of alveolar membrane and both affect the ventilation-perfusion ratio (Chapter 122).

■ CHARACTERISTIC FEATURES OF PULMONARY BLOOD VESSELS

Following are the characteristic features of pulmonary blood vessels:

1. Pulmonary artery has a **thin wall.** Its thickness is only about one third of thickness of the systemic aortic wall. Wall of other pulmonary blood vessels is also thin.
2. Pulmonary blood vessels are **highly elastic** and more distensible
3. Smooth muscle coat is **not well developed** in the pulmonary blood vessels
4. True arterioles have less **smooth muscle** fibers
5. Pulmonary capillaries are **larger** than systemic capillaries. Pulmonary capillaries are also dense and have multiple anastomosis, so, each alveolus occupies a capillary basket.
6. Vascular resistance in pulmonary circulation is **very less;** it is only one tenth of systemic circulation
7. Pulmonary vascular system is a **low pressure system.** Pulmonary arterial pressure and pulmonary capillary pressure are very low (see below).
8. Pulmonary artery carries deoxygenated blood from heart to lungs and pulmonary veins carry oxygenated blood from lungs to heart
9. Physiological shunt is present.

■ PULMONARY BLOOD FLOW

Lungs receive the whole amount of blood that is pumped out from right ventricle. Output of blood per minute is same in both right and left ventricle. It is about 5 liter.

Thus, the lungs accommodate amount of blood, which is equal to amount of blood accommodated by all other parts of the body.

■ PULMONARY BLOOD PRESSURE

Pulmonary blood vessels are more distensible than systemic blood vessels. So the blood pressure is less in pulmonary blood vessels. Thus, the entire pulmonary vascular system is a **low pressure bed.**

Pulmonary Arterial Pressure

Systolic pressure	:	25 mm Hg
Diastolic pressure	:	10 mm Hg
Mean arterial pressure	:	15 mm Hg.

Pulmonary Capillary Pressure

Pulmonary capillary pressure is about 7 mm Hg. This pressure is sufficient for exchange of gases between alveoli and blood.

■ MEASUREMENT OF PULMONARY BLOOD FLOW

Pulmonary blood flow is measured by applying Fick principle. Details are given in Chapter 98.

■ REGULATION OF PULMONARY BLOOD FLOW

Pulmonary blood flow is regulated by the following factors:

1. Cardiac output
2. Vascular resistance
3. Nervous factors
4. Chemical factors
5. Gravity and hydrostatic pressure.

■ 1. CARDIAC OUTPUT

Pulmonary blood flow is **directly proportional** to cardiac output. So, any factor that alters the cardiac output, also affects pulmonary blood flow.

Cardiac output is in turn regulated by four factors:

i. Venous return
ii. Force of contraction
iii. Rate of contraction
iv. Peripheral resistance.

Refer Chapter 98 for details of factors affecting cardiac output.

■ 2. VASCULAR RESISTANCE

Pulmonary blood flow is **inversely proportional** to the pulmonary vascular resistance. Pulmonary vascular resistance is low compared to systemic vascular resistance. Pulmonary vascular resistance is altered in different phases of respiration. During inspiration, pulmonary blood vessels are distended because of decreased intrathoracic pressure. This causes decrease in vascular resistance resulting in increased pulmonary blood flow (Fig. 119.1). During expiration, the pulmonary vascular resistance increases resulting in decreased blood flow.

During the conditions like exercise, the vascular resistance decreases and blood flow increases. It is influenced by the exercise-induced hypoxia and hypercapnea.

■ 3. NERVOUS FACTORS

Stimulation of sympathetic nerves under experimental conditions increases the pulmonary vascular resistance by vasoconstriction and the stimulation of parasympathetic, i.e. vagus nerve decreases the vascular resistance by vasodilatation.

However, under physiological conditions, it is doubtful whether autonomic nerves play any role in regulating the blood flow to lungs.

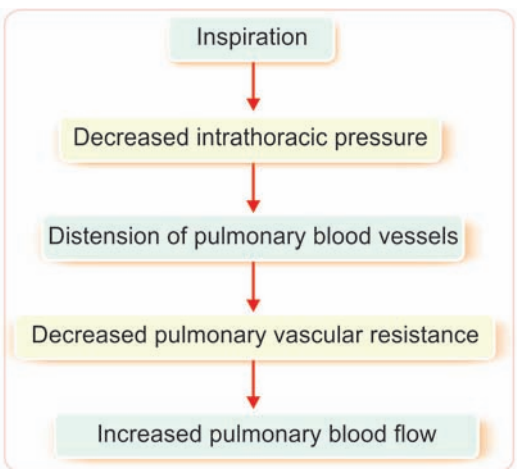


FIGURE 119.1: Schematic diagram showing increase in pulmonary blood flow during inspiration

■ 4. CHEMICAL FACTORS

Excess of carbon dioxide or lack of oxygen causes vasoconstriction. The cause for pulmonary vasoconstriction by hypoxia is not known. But it has some significance. If some part of lungs is affected by hypoxia, there is constriction of capillaries in that area. Thus, blood is directed to the alveoli of neighboring area where gaseous exchange occurs.

■ 5. GRAVITY AND HYDROSTATIC PRESSURE

Normally in standing position, blood pressure in lower extremity of the body is very high and in upper parts above the level of heart, the pressure is low. This is because of the effect of gravitational force.

A similar condition is observed to some extent in lungs also. Pulmonary vascular pressure varies in different parts of the lungs:

i. *Apical Portion – Zone 1*

Normally, in the apical portion of lungs, pulmonary capillary pressure is almost same as alveolar pressure. So, the pulmonary arterial pressure is just sufficient for flow of blood into alveolar capillaries. However, if pulmonary arterial pressure decreases or if alveolar pressure increases, the capillaries are collapsed. This prevents flow of blood to alveoli. So, this zone of lung is called **area of zero blood flow** (Fig. 119.2).

Under these conditions, there is no gaseous exchange in this zone of lungs. So, it is considered as the part of physiological dead space, which is ventilated but not perfused. And, the ventilation-perfusion ratio increases. It may lead to growth of bacteria, particularly tubercle bacilli making this part of lungs susceptible for tuberculosis.

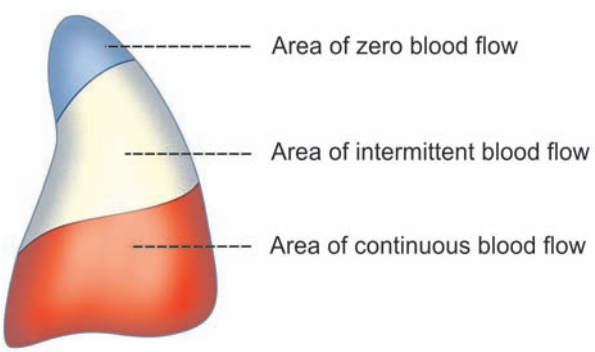


FIGURE 119.2: Pattern of blood flow in various areas of lungs

ii. *Midportion – Zone 2*

In the midportion of lungs, the pressure in alveoli is less than pulmonary systolic pressure and more than the pulmonary diastolic pressure. Because of this, the blood flow to the alveoli increases during systole and decreases during diastole. So, this zone of the lung is called **area of intermittent flow.** Ventilation-perfusion ratio is normal.

iii. *Lower Portion – Zone 3*

In the lower portion of lungs, the pulmonary arterial pressure is high and it is more than alveolar pressure both during systole and diastole. So the blood flows continuously. Hence, this part of lungs is called **area of continuous blood flow.** Ventilation-perfusion ratio decreases because of increased blood flow.

Chapter 120

Mechanics of Respiration

- RESPIRATORY MOVEMENTS
  - INTRODUCTION
  - MUSCLES OF RESPIRATION
  - MOVEMENTS OF THORACIC CAGE
  - MOVEMENTS OF LUNGS
- RESPIRATORY PRESSURES
  - INTRAPLEURAL PRESSURE
  - INTRA-ALVEOLAR PRESSURE
- COMPLIANCE
  - DEFINITION
  - NORMAL VALUES
  - TYPES
  - MEASUREMENT
  - APPLIED PHYSIOLOGY
- WORK OF BREATHING
  - WORK DONE BY RESPIRATORY MUSCLES
  - UTILIZATION OF ENERGY

RESPIRATORY MOVEMENTS

INTRODUCTION

Respiration occurs in two phases namely inspiration and expiration.

During inspiration, thoracic cage enlarges and lungs expand so that air enters the lungs easily. During expiration, the thoracic cage and lungs decrease in size and attain the preinspiratory position so that air leaves the lungs easily.

During normal quiet breathing, inspiration is the **active process** and expiration is the **passive process.**

MUSCLES OF RESPIRATION

Respiratory muscles are of two types:

1. Inspiratory muscles
2. Expiratory muscles.

However, respiratory muscles are generally classified into two types:

1. Primary or major respiratory muscles, which are responsible for change in size of thoracic cage during normal quiet breathing
2. Accessory respiratory muscles that help primary respiratory muscles during forced respiration.

Inspiratory Muscles

Muscles involved in inspiratory movements are known as inspiratory muscles.

Primary inspiratory muscles

Primary inspiratory muscles are the diaphragm, which is supplied by phrenic nerve (C3 to C5) and external intercostal muscles, supplied by intercostal nerves (T1 to T11).

Accessory inspiratory muscles

Sternocleidomastoid, scalene, anterior serrati, elevators of scapulae and pectorals are the accessory inspiratory muscles.

Expiratory Muscles

Primary expiratory muscles

Primary expiratory muscles are the internal intercostal muscles, which are innervated by intercostal nerves.

Accessory expiratory muscles

Accessory expiratory muscles are the abdominal muscles.

■ MOVEMENTS OF THORACIC CAGE

Inspiration causes enlargement of thoracic cage. Thoracic cage enlarges because of increase in **all diameters,** viz. anteroposterior, transverse and vertical diameters. Anteroposterior and transverse diameters of thoracic cage are increased by the elevation of ribs. Vertical diameter is increased by the descent of diaphragm.

In general, change in the size of thoracic cavity occurs because of the movements of four units of structures:

1. Thoracic lid
2. Upper costal series
3. Lower costal series
4. Diaphragm.

1. *Thoracic Lid*

Thoracic lid is formed by **manubrium sterni** and the first pair of ribs. It is also called **thoracic operculum.**

Movement of thoracic lid increases the **anteroposterior diameter** of thoracic cage. Due to the contraction of scalene muscles, the first ribs move upwards to a more horizontal position. This increases the anteroposterior diameter of upper thoracic cage.

2. *Upper Costal Series*

Upper costal series is constituted by second to sixth pair of ribs. Movement of upper costal series increases the **anteroposterior** and **transverse diameter** of the thoracic cage.

Movement of upper costal series is of two types:

i. Pump handle movement
ii. Bucket handle movement.

Pump handle movement

Contraction of external intercostal muscles causes elevation of these ribs and upward and forward movement of sternum. This movement is called pump handle movement. It increases **anteroposterior diameter** of the thoracic cage.

Bucket handle movement

Simultaneously, the central portions of these ribs (arches of ribs) move upwards and outwards to a more horizontal position. This movement is called bucket handle movement and it increases the **transverse diameter** of thoracic cage.

3. *Lower Costal Series*

Lower costal series includes seventh to tenth pair of ribs. Movement of lower costal series increases the **transverse diameter** of thoracic cage by bucket handle movement.

Bucket handle movement

Lower costal series of ribs also show bucket handle movement by swinging outward and upward. This movement increases the **transverse diameter** of the thoracic cage.

Eleventh and twelfth pairs of ribs are the floating ribs. These ribs are not involved in changing the size of thoracic cage.

4. *Diaphragm*

Movement of diaphragm increases the vertical diameter of thoracic cage. Normally, before inspiration the diaphragm is dome shaped with convexity facing upwards. During inspiration, due to the contraction, muscle fibers are shortened. But the central tendinous portion is drawn downwards so the diaphragm is flattened. Flattening of diaphragm increases the **vertical diameter** of the thoracic cage.

■ MOVEMENTS OF LUNGS

During inspiration, due to the enlargement of thoracic cage, the negative pressure is increased in the thoracic cavity. It causes expansion of the lungs. During expiration, the thoracic cavity decreases in size to the **preinspiratory position.** Pressure in the thoracic cage also comes back to the preinspiratory level. It compresses the lung tissues so that, the air is expelled out of lungs.

Collapsing Tendency of Lungs

Lungs are under constant threat to collapse even in resting conditions because of certain factors.

Factors Causing Collapsing Tendency of Lungs

Two factors are responsible for the collapsing tendency of lungs:

1. *Elastic property of lung tissues:* Elastic tissues of lungs show constant recoiling tendency and try to collapse the lungs
2. *Surface tension:* It is the tension exerted by the fluid secreted from alveolar epithelium on the surface of alveolar membrane.

Fortunately, there are some factors, which save the lungs from collapsing.

Factors Preventing Collapsing Tendency of Lungs

In spite of elastic property of lungs and surface tension in the alveoli of lungs, the collapsing tendency of lungs is prevented by two factors:

1. *Intrapleural pressure:* It is the pressure in the pleural cavity, which is always negative (see below). Because of negativity, it keeps the lungs expanded and prevents the collapsing tendency of lungs produced by the elastic tissues.
2. *Surfactant:* It is a substance secreted in alveolar epithelium. It reduces surface tension and prevents the collapsing tendency produced by surface tension.

Surfactant

Surfactant is a **surface acting material** or agent that is responsible for lowering the surface tension of a fluid. Surfactant that lines the epithelium of the alveoli in lungs is known as **pulmonary surfactant** and it decreases the **surface tension** on the alveolar membrane.

Source of secretion of pulmonary surfactant

Pulmonary surfactant is secreted by two types of cells:

1. **Type II alveolar epithelial cells** in the lungs, which are called surfactant secreting alveolar cells or pneumocytes. Characteristic feature of these cells is the presence of microvilli on their alveolar surface.
2. **Clara cells,** which are situated in the bronchioles. These cells are also called bronchiolar exocrine cells.

Chemistry of surfactant

Surfactant is a **lipoprotein complex** formed by lipids especially phospholipids, proteins and ions.

1. *Phospholipids:* Phospholipids form about 75% of the surfactant. Major phospholipid present in the surfactant is **dipalmitoylphosphatidylcholine** (DPPC).
2. *Other lipids:* Other lipid substances of surfactant are triglycerides and phosphatidylglycerol (PG).
3. *Proteins:* Proteins of the surfactant are called specific surfactant proteins. There are four main surfactant proteins, called SP-A, SP-B, SP-C and SP-D. SP-A and SP-D are hydrophilic, while SP-B and SP-C are hydrophobic. Surfactant proteins are vital components of surfactant and the surfactant becomes inactive in the absence of proteins.
4. *Ions:* Ions present in the surfactant are mostly calcium ions.

Formation of surfactant

Type II alveolar epithelial cells and Clara cells have a special type of membrane bound organelles called **lamellar bodies,** which form the intracellular source of surfactant. Laminar bodies contain surfactant phospholipids and surfactant proteins. These materials are synthesized in endoplasmic reticulum and stored in laminar bodies.

By means of exocytosis, lipids and proteins of lamellar bodies are released into surface fluid lining the alveoli. Here, in the presence of surfactant proteins and calcium, the phospholipids are arranged into a **lattice** (meshwork) structure called **tubular myelin.** Tubular myelin is in turn converted into surfactant in the form of a **film** that spreads over the entire surface of alveoli.

Most of the surfactant is absorbed into the type II alveolar cells, catabolized and the products are loaded into lamellar bodies for recycling.

Factors necessary for the formation and spreading of surfactant

Formation of surfactant requires many substances. Formation of tubular myelin requires DPPC, PG and the hydrophobic proteins, SP-B and SP-C. Formation of surfactant film requires SP-B, SP-C and PG.

Type II alveolar epithelial cells occupy only about 5% of alveolar surface. However, the surfactant must spread over the entire alveolar surface. It is facilitated by PG and calcium ions.

Glucocorticoids play important role in the formation of surfactant.

Functions of surfactant

1. Surfactant reduces the **surface tension** in the alveoli of lungs and prevents **collapsing tendency** of lungs.

Surfactant acts by the following mechanism:

Phospholipid molecule in the surfactant has two portions. One portion of the molecule is **hydrophilic.** This portion dissolves in water and lines the alveoli. Other portion is **hydrophobic** and it is directed towards the alveolar air. This surface of the phospholipid along with other portion spreads over the alveoli and reduces the surface tension. SP-B and SP-C play active role in this process.

2. Surfactant is responsible for stabilization of the alveoli, which is necessary to withstand the collapsing tendency.
3. It plays an important role in the inflation of lungs after birth. In fetus, the secretion of surfactant begins after the 3rd month. Until birth, the lungs are solid and not expanded. Soon after birth, the first breath starts because of the stimulation of respiratory centers by hypoxia and hypercapnea. Although the respiratory movements are attempted by the infant, the lungs tend to collapse repeatedly. And, the presence of surfactant in the alveoli prevents the lungs from collapsing.
4. Another important function of surfactant is its role in defense within the lungs against infection and inflammation. Hydrophilic proteins SP-A and SP-D destroy the bacteria and viruses by means of opsonization. These two proteins also control the formation of inflammatory mediators.

Effect of deficiency of surfactant – respiratory distress syndrome

Absence of surfactant in infants, causes collapse of lungs and the condition is called respiratory distress syndrome or hyaline membrane disease. Deficiency of surfactant occurs in adults also and it is called **adult respiratory distress syndrome (ARDS).**

In addition, the deficiency of surfactant increases the susceptibility for bacterial and viral infections.

■ RESPIRATORY PRESSURES

Two types of pressures are exerted in the thoracic cavity and lungs during process of respiration:

1. Intrapleural pressure or intrathoracic pressure
2. Intra-alveolar pressure or intrapulmonary pressure.

■ INTRAPLEURAL PRESSURE

Definition

Intrapleural pressure is the pressure existing in pleural cavity, that is, in between the visceral and parietal layers of pleura. It is exerted by the suction of the fluid that lines the pleural cavity (Fig. 120.1). It is also called **intrathoracic pressure** since it is exerted in the whole of thoracic cavity.

Normal Values

Respiratory pressures are always expressed in relation to atmospheric pressure, which is 760 mm Hg. Under physiological conditions, the intrapleural pressure is always negative.

Normal values are:

1. At the end of normal inspiration:
   –6 mm Hg (760 – 6 = 754 mm Hg)
2. At the end of normal expiration:
   –2 mm Hg (760 – 2 = 758 mm Hg)
3. At the end of forced inspiration:
   –30 mm Hg
4. At the end of forced inspiration with closed glottis (Müller maneuver):
   –70 mm Hg
5. At the end of forced expiration with closed glottis (Valsalva maneuver):
   +50 mm Hg.

Cause for Negativity of Intrapleural Pressure

Pleural cavity is always lined by a thin layer of fluid that is secreted by the visceral layer of pleura. This fluid is constantly pumped from the pleural cavity into the lymphatic vessels. Pumping of fluid creates the negative pressure in the pleural cavity.

Intrapleural pressure becomes positive in **Valsalva maneuver** (Chapter 104) and in some pathological conditions such as pneumothorax, hydrothorax, hemothorax and pyothorax.

Measurement

Intrapleural pressure is measured by direct method and indirect method. In the direct method, the intrapleural pressure is determined by introducing a needle into the pleural cavity and connecting the needle to a mercury manometer. In indirect method, intrapleural pressure is measured by introducing the esophageal balloon, which is connected to a manometer. Intrapleural pressure is considered as equivalent to the pressure existing in the esophagus.

Significance of Intrapleural Pressure

Throughout the respiratory cycle intrapleural pressure remains lower than intra-alveolar pressure. This keeps the lungs always inflated.

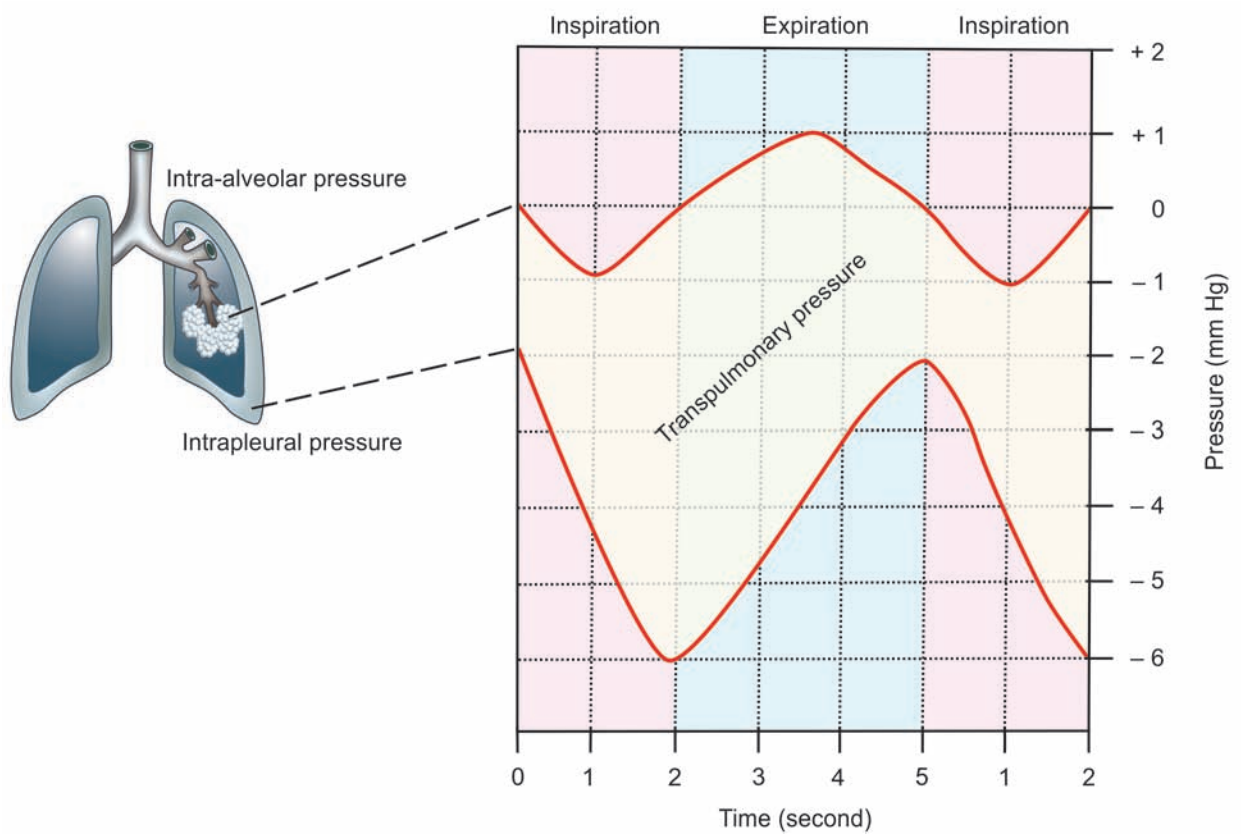


FIGURE 120.1: Changes in respiratory pressures during inspiration and expiration. '0' indicates the normal atmospheric pressure (760 mm Hg).

Intrapleural pressure has two important functions:

1. It prevents the collapsing tendency of lungs
2. Because of the negative pressure in thoracic region, larger veins and vena cava are enlarged, i.e. dilated. Also, the negative pressure acts like suction pump and pulls the venous blood from lower part of body towards the heart against gravity. Thus, the intrapleural pressure is responsible for venous return. So, it is called the **respiratory pump** for venous return (Chapter 98).

■ INTRA-ALVEOLAR PRESSURE

Definition

Intra-alveolar pressure is the pressure existing in the alveoli of the lungs. It is also known as **intrapulmonary pressure.**

Normal Values

Normally, intra-alveolar pressure is equal to the atmospheric pressure, which is 760 mm Hg. It becomes negative during inspiration and positive during expiration.

Normal values are:

1. During normal inspiration:
   –1 mm Hg (760 – 1 = 759 mm Hg)
2. During normal expiration:
   +1 mm Hg (760 + 1 = 761 mm Hg)
3. At the end of inspiration and expiration:
   Equal to atmospheric pressure (760 mm Hg)
4. During forced inspiration with closed glottis (Müller maneuver): –80 mm Hg
5. During forced expiration with closed glottis (Valsalva maneuver): +100 mm Hg.

Measurement

Intra-alveolar pressure is measured by using plethysmograph (Chapter 121).

Significance of Intra-alveolar Pressure

1. Intra-alveolar pressure causes flow of air in and out of alveoli. During inspiration, the intra-alveolar pressure becomes negative, so the atmospheric air enters the alveoli. During

expiration, intra-alveolar pressure becomes positive. So, air is expelled out of alveoli.
2. Intra-alveolar pressure also helps in exchange of gases between the alveolar air and the blood.

Transpulmonary Pressure

Transpulmonary pressure is the pressure difference between intra-alveolar pressure and intrapleural pressure. It is the measure of elastic forces in lungs, which is responsible for collapsing tendency of lungs.

■ COMPLIANCE

■ DEFINITION

Compliance is the ability of the lungs and thorax to expand or it is the **expansibility** of lungs and thorax. It is defined as the change in volume per unit change in the pressure.

Significance of Determining Compliance

Determination of compliance is useful as it is the measure of stiffness of lungs. Stiffer the lungs, less is the compliance.

■ NORMAL VALUES

Compliance is expressed by two ways:
1. In relation to intra-alveolar pressure
2. In relation to intrapleural pressure.

Compliance in Relation to Intra-alveolar Pressure

Compliance is the volume increase in lungs per unit increase in the intra-alveolar pressure.
1. Compliance of lungs and thorax together:
   130 mL/1 cm H_2O pressure
2. Compliance of lungs alone:
   220 mL/1 cm H_2O pressure.

Compliance in Relation to Intrapleural Pressure

Compliance is the volume increase in lungs per unit decrease in the intrapleural pressure.
1. Compliance of lungs and thorax together:
   100 mL/1 cm H_2O pressure
2. Compliance of lungs alone:
   200 mL/1 cm H_2O pressure.

Thus, if lungs could be removed from thorax, the expansibility (compliance) of lungs alone will be doubled. It is because of the absence of inertia and restriction exerted by the structures of thoracic cage, which interfere with expansion of lungs.

Specific Compliance

The term specific compliance is introduced to assess the stiffness of lung tissues more accurately. Specific compliance is the compliance per liter of lung volume. It is usually reported for expiration at functional residual capacity. It is the compliance divided by functional residual capacity.

$$\text{Specific compliance of lungs} = \frac{\text{Compliance of lungs}}{\text{Functional residual capacity}}$$

Functional residual capacity is the volume of air present in lungs at the end of normal expiration.

■ TYPES OF COMPLIANCE

Compliance is of two types:
1. Static compliance
2. Dynamic compliance.

1. *Static Compliance*

Static compliance is the compliance measured under **static conditions,** i.e. by measuring pressure and volume when breathing does not take place (see below). Static compliance is the pressure required to overcome the elastic resistance of respiratory system for a given tidal volume under zero flow (static) condition.

2. *Dynamic Compliance*

Dynamic compliance is the compliance measured during **dynamic conditions,** i.e. during breathing.

Static Compliance Vs Dynamic Compliance

In healthy subjects, there is little difference between static and dynamic compliance. In patients with stiff lungs, the dynamic compliance decreases while little change occurs in the static compliance.

■ MEASUREMENT OF COMPLIANCE

Measurement of Static Compliance

To measure the static compliance, the subject is asked to inspire air periodically at regular steps from a spirometer. In each step, a known volume of air is inspired. At the end of each step, intrapleural pressure is measured by means of an **esophageal balloon.** Then, the air is expired in steps until the volume returns to original preinspiratory level. Intrapleural pressure is measured at the end of each step.

Values of volume and pressure are plotted to obtain a curve, which is called **pressure-volume curve.** From this curve compliance can be calculated. This curve also shows the difference in inspiration and expiration (Fig. 120.2).

Measurement of Dynamic Compliance

Dynamic compliance is measured during normal breathing. It is measured by determining the lung volume and esophageal pressure (intrapleural pressure) at the end of inspiration and expiration when the lungs are apparently stationary.

■ APPLIED PHYSIOLOGY

Increase in Compliance

Compliance increases due to loss of elastic property of lung tissues, which occurs both in physiological and pathological conditions:

1. Physiological condition: Old age
2. Pathological condition: Emphysema (Fig. 120.3).

Decrease in Compliance

Compliance decreases in several pathological conditions such as:

1. Deformities of thorax like kyphosis and scoliosis (Chapter 68)
2. Fibrotic pleurisy (inflammation of pleura resulting in fibrosis)
3. Paralysis of respiratory muscles
4. Pleural effusion (Chapter 127)
5. Abnormal thorax such as pneumothorax, hydrothorax, hemothorax and pyothorax (Chapter 127).

■ WORK OF BREATHING

Work of breathing is the work done by respiratory muscles during breathing to overcome the resistance in thorax and respiratory tract.

■ WORK DONE BY RESPIRATORY MUSCLES

During respiratory processes, inspiration is active process and the expiration is a passive process. So, during quiet breathing, respiratory muscles perform the work only during inspiration and not during expiration.

■ UTILIZATION OF ENERGY

During the work of breathing, the energy is utilized to overcome three types of resistance:

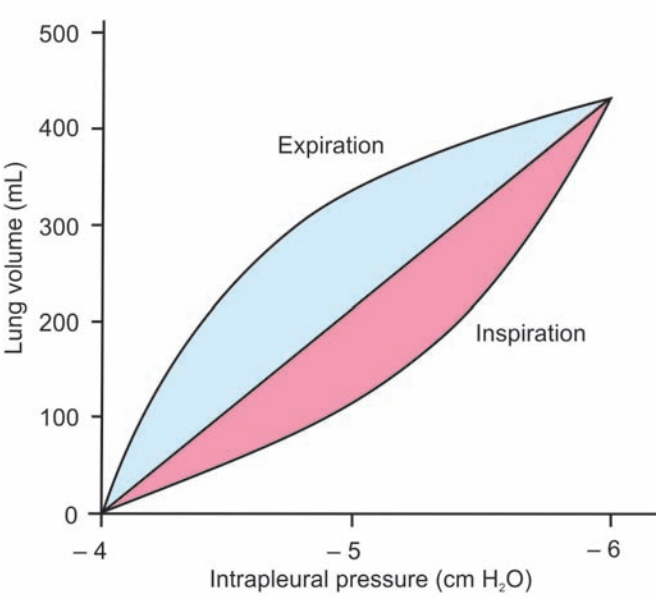


FIGURE 120.2: Pressure-volume curve

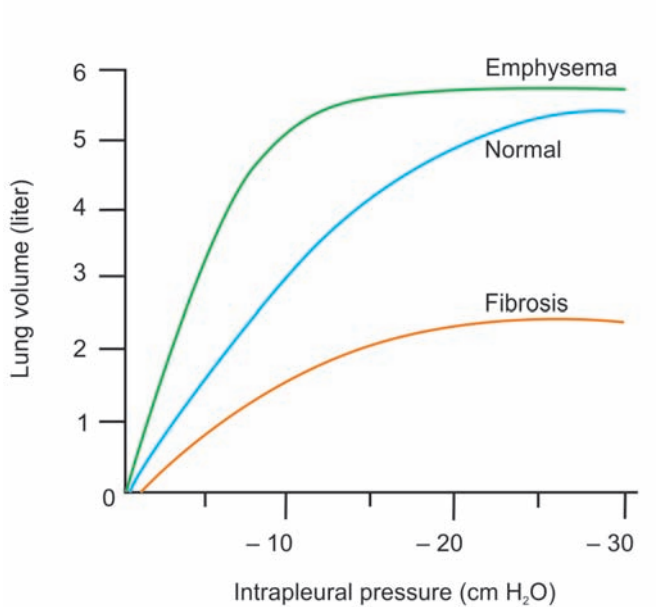


FIGURE 120.3: Variations in lung compliance

1. Airway resistance
2. Elastic resistance of lungs and thorax
3. Non-elastic viscous resistance.

1. *Airway Resistance*

Airway resistance is the resistance offered to the passage of air through respiratory tract. Resistance increases during bronchiolar constriction, which in-

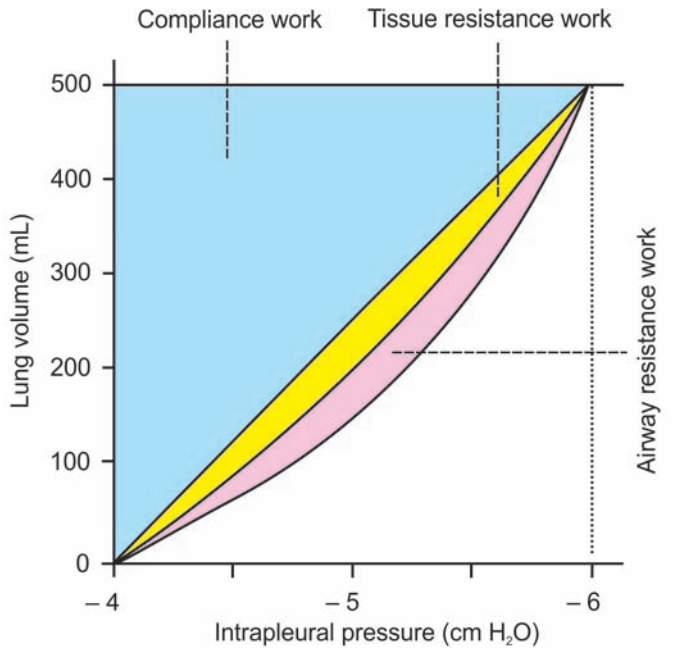


FIGURE 120.4: Work of breathing

creases the work done by the muscles during breathing. **Work done** to overcome the airway resistance is called **airway resistance work.**

2. *Elastic Resistance of Lungs and Thorax*

Energy is required to expand lungs and thorax against the elastic force. Work done to overcome this elastic resistance is called **compliance work.**

3. *Non-elastic Viscous Resistance*

Energy is also required to overcome the viscosity of lung tissues and tissues of thoracic cage. Work done to overcome this viscous resistance is called **tissue resistance work.**

Above factors are explained by the curve that shows the relation between lung volume and pleural pressure (Fig. 120.4).

Pulmonary Function Tests

Chapter 121

INTRODUCTION

Pulmonary function tests or lung function tests are useful in assessing the **functional status** of the respiratory system both in physiological and pathological conditions. Lung function tests are based on the measurement of volume of air breathed in and out in quiet breathing and forced breathing. These tests are carried out mostly by using spirometer.

TYPES OF LUNG FUNCTION TESTS

Lung function tests are of two types:

1. Static lung function tests
2. Dynamic lung function tests.

Static Lung Function Tests

Static lung function tests are based on **volume of air that flows** into or out of lungs. These tests do not depend upon the rate at which air flows.

Static lung function tests include static lung volumes and static lung capacities.

Dynamic Lung Function Tests

Dynamic lung function tests are based on time, i.e. the **rate at which air flows** into or out of lungs. These tests include forced vital capacity, forced expiratory volume, maximum ventilation volume and peak expiratory flow.

Dynamic lung function tests are useful in determining the severity of obstructive and restrictive lung diseases.

LUNG VOLUMES

Static lung volumes are the volumes of air breathed by an individual. Each of these volumes represents the volume of air present in the lung under a specified static condition (specific position of thorax).

Static lung volumes are of four types:

1. Tidal volume
2. Inspiratory reserve volume
3. Expiratory reserve volume
4. Residual volume.

■ TIDAL VOLUME

Tidal volume (TV) is the volume of air breathed in and out of lungs in a single normal quiet respiration. Tidal volume signifies the normal depth of breathing.

Normal Value

500 mL (0.5 L).

■ INSPIRATORY RESERVE VOLUME

Inspiratory reserve volume (IRV) is an additional volume of air that can be inspired forcefully after the end of normal inspiration.

Normal Value

3,300 mL (3.3 L).

■ EXPIRATORY RESERVE VOLUME

Expiratory reserve volume (EVR) is the additional volume of air that can be expired out forcefully, after normal expiration.

Normal Value

1,000 mL (1 L).

■ RESIDUAL VOLUME

Residual volume (RV) is the volume of air remaining in lungs even after forced expiration. Normally, lungs cannot be emptied completely even by forceful expiration. Some quantity of air always remains in the lungs even after the forced expiration.

Residual volume is significant because of two reasons:

1. It helps to aerate the blood in between breathing and during expiration
2. It maintains the contour of the lungs.

Normal Value

1,200 mL (1.2 L)

■ LUNG CAPACITIES

Static lung capacities are the combination of two or more lung volumes.

Static lung capacities are of four types:

1. Inspiratory capacity
2. Vital capacity
3. Functional residual capacity
4. Total lung capacity.

■ INSPIRATORY CAPACITY

Inspiratory capacity (IC) is the maximum volume of air that is inspired after normal expiration (end expiratory position). It includes tidal volume and inspiratory reserve volume (Fig. 121.1).

IC = TV + IRV
= 500 + 3,300 = 3,800 mL

■ VITAL CAPACITY (VC)

Vital capacity (VC) is the maximum volume of air that can be expelled out forcefully after a deep (maximal) inspiration. VC includes inspiratory reserve volume, tidal volume and expiratory reserve volume.

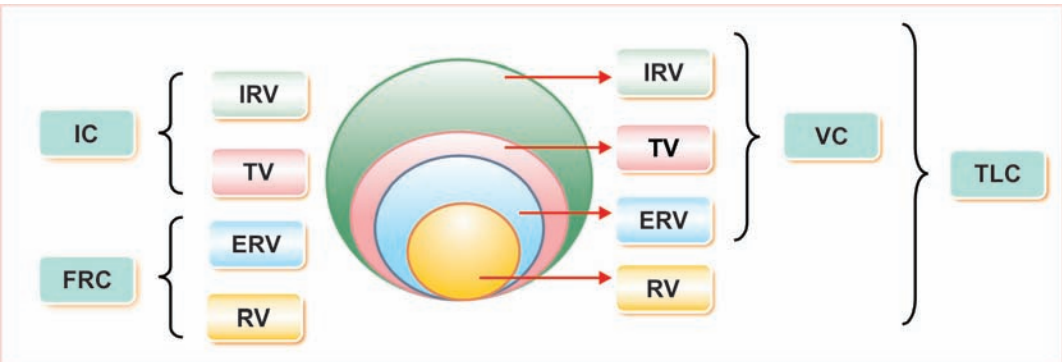


FIGURE 121.1: Lung volumes and capacities. TV = Tidal volume, IRV = Inspiratory reserve volume, ERV = Expiratory reserve volume, RV = Residual volume, IC = Inspiratory capacity, FRC = Functional residual capacity, VC = Vital capacity, TLC = Total lung capacity.

VC = IRV + TV + ERV
= 3,300 + 500 + 1,000 = 4,800 mL

Vital capacity is significant physiologically and its determination is useful in clinical diagnosis as explained later in this chapter.

■ FUNCTIONAL RESIDUAL CAPACITY

Functional residual capacity (FRC) is the volume of air remaining in lungs after normal expiration (after normal tidal expiration). Functional residual capacity includes expiratory reserve volume and residual volume.

FRC = ERV + RV
= 1,000 + 1,200 = 2,200 mL

■ TOTAL LUNG CAPACITY

Total lung capacity (TLC) is the volume of air present in lungs after a deep (maximal) inspiration. It includes all the volumes.

TLC = IRV + TV + ERV + RV
= 3,300 + 500 + 1,000 + 1,200 = 6,000 mL

■ MEASUREMENT OF LUNG VOLUMES AND CAPACITIES

Spirometry is the method to measure lung volumes and capacities. Simple instrument used for this purpose is called **spirometer.** Modified spirometer is known as **respirometer.** Nowadays **plethysmograph** is also used to measure lung volumes and capacities.

■ SPIROMETER

Spirometer is made up of metal and it contains two chambers namely outer chamber and inner chamber (Fig. 121.2). Outer chamber is called the **water chamber** because it is filled with water. A **floating drum** is immersed in the water in an inverted position. Drum is counter balanced by a **weight.** Weight is attached to the top of the inverted drum by means of string or chain. A **pen with ink** is attached to the counter weight. Pen is made to write on a **calibrated paper,** which is fixed to a recording device.

Inner chamber is inverted and has a small hole at the top. A long metal tube passes through the inner

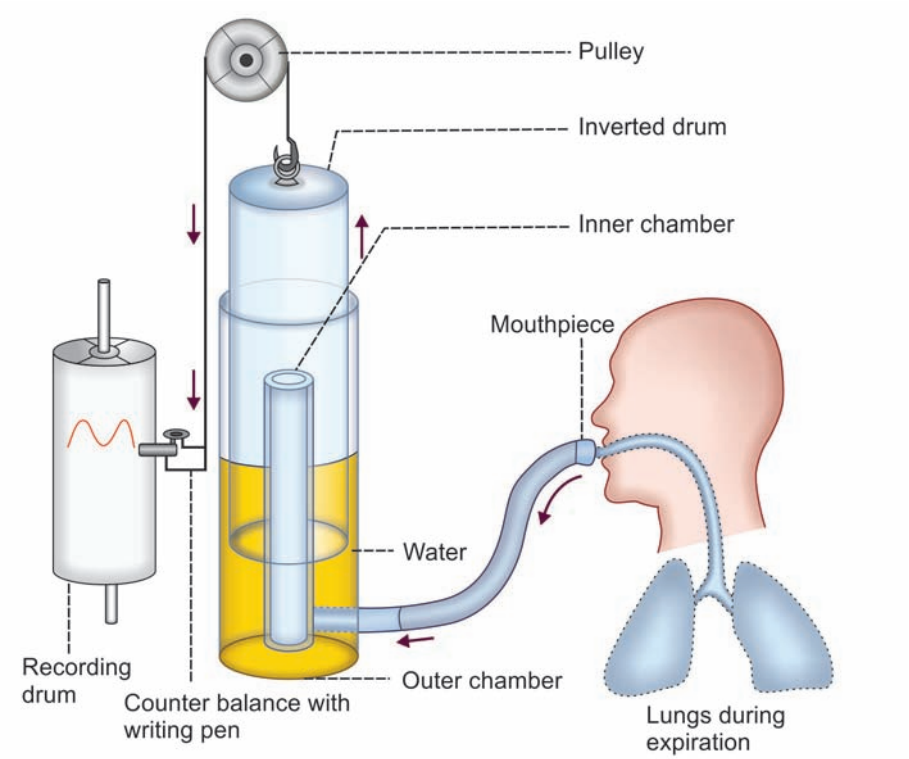


FIGURE 121.2: Spirometer. During expiration, the air enters the spirometer from lungs. Inverted drum moves up and the pen draws a downward curve on the recording drum.

chamber from the bottom towards the top. Upper end of this tube reaches the top portion of the inner chamber. Then the tube passes through a hole at the top of inner chamber and penetrates into outer water chamber above the level of water. A **rubber tube** is connected to the outer end of the metal tube. At the other end of this rubber tube, a mouthpiece is attached. Subject respires through this mouthpiece by closing the nose with a **nose clip.**

When the subject breathes with spirometer, during expiration, drum moves up and the counter weight comes down. Reverse of this occurs when the subject breathes the air from the spirometer, i.e. during inspiration. Upward and downward movements of the counter weight are recorded in the form of a graph. Upward deflection of the curve in the graph shows inspiration and the downward deflection denotes expiration.

Spirometer is used only for a **single breath.** Repeated cycles of respiration cannot be recorded by using this instrument because carbon dioxide accumulates in the spirometer and oxygen or fresh air cannot be provided to the subject.

Respirometer

Respirometer is the modified spirometer. It has provision for removal of carbon dioxide and supply of oxygen.

Carbon dioxide is removed by placing soda lime inside the instrument. Oxygen is supplied to the instrument from the oxygen cylinder, by a suitable valve system.

Oxygen is filled in the inverted drum above water level and the subject can breathe in and out with instrument for about 6 minutes and recording can be done continuously.

Spirogram

Spirogram is the graphical record of lung volumes and capacities using spirometer. Upward deflection of the spirogram denotes inspiration and the downward curve indicates expiration (Fig. 121.3). In order to determine the lung volumes and capacities, following four levels are to be noted in spirogram:

1. Normal end expiratory level
2. Normal end inspiratory level
3. Maximum expiratory level
4. Maximum inspiratory level.

■ COMPUTERIZED SPIROMETER

Computerized spirometer is the solid state electronic equipment. It does not contain a drum or water chamber. Subject has to respire into a sophisticated transducer, which is connected to the instrument by means of a cable.

Disadvantages of Spirometry

By using simple spirometer, respirometer or computerized spirometer, not all the lung volumes and lung capacities can be measured.

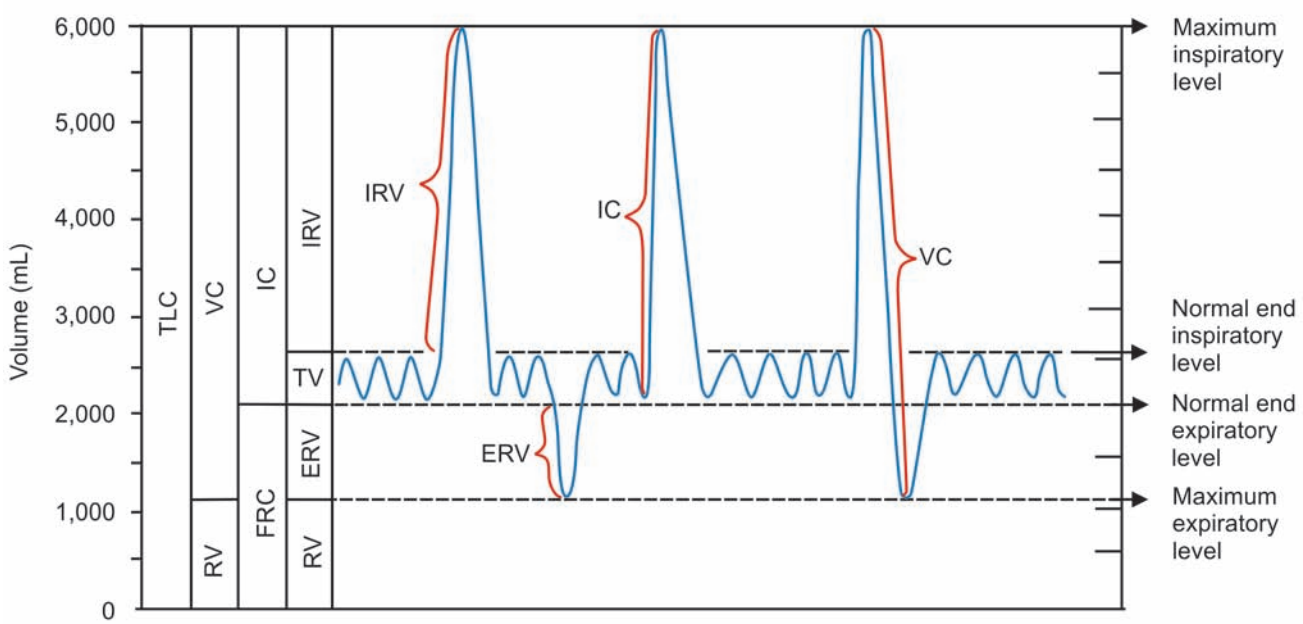


FIGURE 121.3: Spirogram. TV = Tidal volume, IRV = Inspiratory reserve volume, ERV = Expiratory reserve volume, RV = Residual volume, IC = Inspiratory capacity, FRC = Functional residual capacity, VC = Vital capacity, TLC = Total lung capacity.

Volume, which cannot be measured by spirometry, is the **residual volume.** Capacities, which include residual volume also cannot be measured. Capacities that include residual volume are **functional residual capacity** and **total lung capacity.**

Volume and capacities, which cannot be measured by spirometry, are measured by **nitrogen washout technique** or **helium dilution technique** or by **body plethysmograph.**

■ PLETHYSMOGRAPHY

Plethysmography is a technique used to measure all the lung volumes and capacities. It is explained later.

■ MEASUREMENT OF FUNCTIONAL RESIDUAL CAPACITY AND RESIDUAL VOLUME

Residual volume and the functional residual capacity cannot be measured by spirometer and can be determined by three methods:

1. Helium dilution technique
2. Nitrogen washout method
3. Plethysmography.

■ 1. HELIUM DILUTION TECHNIQUE

Procedure to Measure Functional Residual Capacity

Respirometer is filled with air containing a known quantity of **helium.** Initially, the subject breathes normally. Then, after the end of expiration, subject breathes from respirometer. Helium from respirometer enters the lungs and starts mixing with air in lungs. After few minutes of breathing, concentration of helium in the respirometer becomes equal to concentration of helium in the lungs of subject. It is called the equilibration of helium. After **equilibration of helium** between respirometer and lungs, concentration of helium in respirometer is determined (Fig. 121.4).

Functional residual capacity is calculated by the formula:

$$FRC = \frac{V\,(C_1 - C_2)}{C_2}$$

Where,

C_1 = Initial concentration of helium in the respirometer

C_2 = Final concentration of helium in the respirometer

V = Initial volume of air in the respirometer.

Measured Values

For example, the following data of a subject are obtained from the experiment:

1. Initial volume of air in respirometer = 5 L (5,000 mL)
2. Initial concentration of helium in respirometer = 15%
3. Final concentration of helium in respirometer = 10%.

Calculation

From the above data, the functional residual capacity of the subject is calculated in the following way:

$$FRC = \frac{V\,(C_1 - C_2)}{C_2}$$

$$FRC = \frac{5{,}000\ (15/100 - 10/100)}{10/100}\ mL$$

$$= \frac{5{,}000\ (5/100)}{10/100}\ mL$$

$$= \frac{5{,}000 \times 5}{10}\ mL$$

$$= 2{,}500\ mL$$

Thus, the functional residual capacity in this subject is 2,500 mL.

Procedure to Measure Residual Volume

To determine functional residual capacity, the subject starts breathing with respirometer after the end of normal expiration. To measure residual volume, the subject should start breathing from the respirometer after forced expiration.

■ 2. NITROGEN WASHOUT METHOD

Normally, concentration of nitrogen in air is 80%. So, if total quantity of nitrogen in the lungs is measured, the volume of air present in lungs can be calculated.

Procedure to Measure Functional Residual Capacity

Subject is asked to breathe normally. At the end of normal expiration, the subject inspires **pure oxygen** through a valve and expires into a Douglas bag. This procedure is repeated for 6 to 7 minutes, until the **nitrogen** in lungs is displaced by oxygen. Nitrogen comes to the **Douglas bag.** Afterwards, following factors are measured to calculate functional residual capacity.

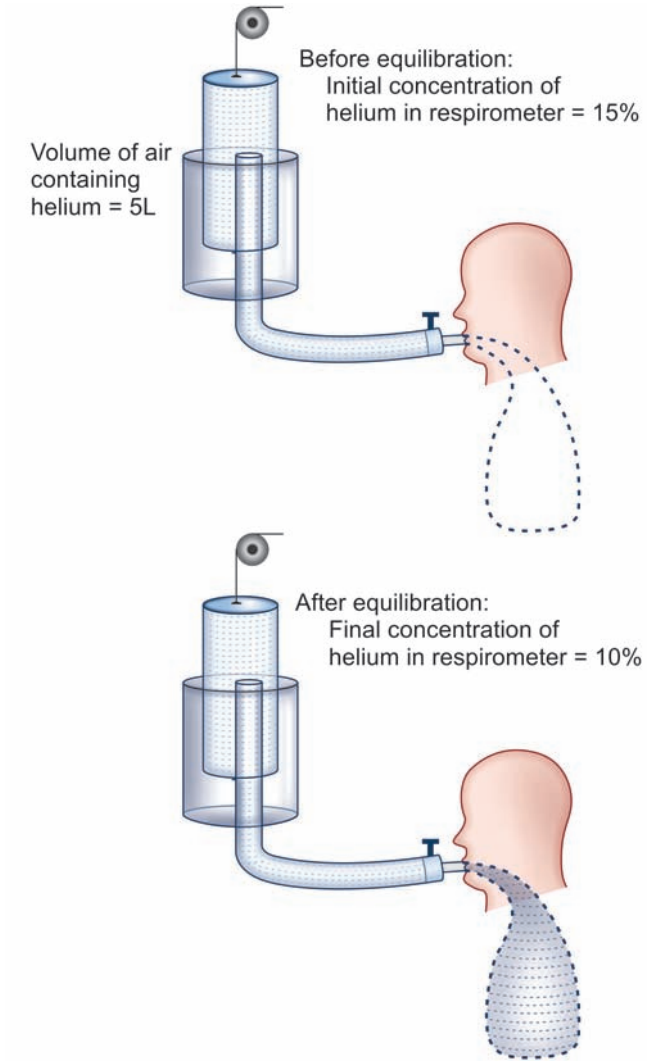


FIGURE 121.4: Measurement of functional residual capacity by using helium

Calculation

i. Volume of air collected in Douglas bag
ii. Concentration of nitrogen in Douglas bag.

By using the data, the functional residual capacity is calculated by using the formula:

$$FRC = \frac{C_1 \times V}{C_2}$$

Where,

V = Volume of air collected
C_1 = Concentration of nitrogen in the collected air
C_2 = Normal concentration of nitrogen in the air.

Measured Values

For example, the following data are obtained from the experiment with a subject:

i. Volume of air collected = 40 L (40,000 mL)
ii. Concentration of nitrogen in the collected air = 5%
iii. Normal concentration of nitrogen in the air. = 80%

Calculation

From the above data, the functional residual capacity of the subject is calculated in the following way:

$$FRC = \frac{C_1 \times V}{C_2}$$

$$FRC = \frac{5/100 \times 40{,}000}{80/100} \text{ mL}$$

$$= \frac{5 \times 40{,}000}{80} \text{ mL}$$

$$= 2{,}500 \text{ mL}.$$

Thus, functional residual capacity in this subject is 2,500 mL.

Procedure to Measure Residual Volume

To measure the functional residual capacity, the subject starts inhaling pure oxygen after the end of normal expiration and to determine the residual volume, the subject starts breathing pure oxygen after forceful expiration.

■ 3. PLETHYSMOGRAPHY

Plethysmography is a technique to study the variations in the size or volume of a part of the body such as limb. **Plethysmograph** is the instrument used for this purpose. Whole body plethysmograph is the instrument used to measure the lung volumes including residual volume.

Plethysmography is based on **Boyle's law of gas,** which states that the volume of a sample of gas is inversely proportional to the pressure of that gas at constant temperature.

Subject sits in an airtight chamber of the whole body plethysmograph and breathes normally through a mouthpiece connected to a flow transducer called **pneumotachograph.** It detects the volume changes

during different phases of respiration. After normal breathing for few minutes, the subject breathes rapidly with maximum force. During maximum expiration, the lung volume decreases very much. But volume of gas in the chamber increases with decrease in pressure. By measuring the volume and pressure changes inside the chamber, volume of lungs is calculated by using the formula:

$P_1 \times V = P_2 (V - \Delta V)$

Where,

P_1 and P_2 = Pressure changes

V = Functional residual capacity.

VITAL CAPACITY

DEFINITION

Vital capacity is the maximum volume of air that can be expelled out of lungs forcefully after a maximal or deep inspiration.

LUNG VOLUMES INCLUDED IN VITAL CAPACITY

Vital capacity includes inspiratory reserve volume, tidal volume and expiratory reserve volume.

NORMAL VALUE

VC = IRV + TV + ERV

= 3,300 + 500 + 1,000 = 4,800 mL.

VARIATIONS OF VITAL CAPACITY

Physiological Variations

1. *Sex:* In females, vital capacity is less than in males
2. *Body built:* Vital capacity is slightly more in heavily built persons
3. *Posture:* Vital capacity is more in standing position and less in lying position
4. *Athletes:* Vital capacity is more in athletes
5. *Occupation:* Vital capacity is decreased in people with sedentary jobs. It is increased in persons who play musical wind instruments such as bugle and flute.

Pathological Variations

Vital capacity is decreased in the following respiratory diseases:

1. Asthma
2. Emphysema
3. Weakness or paralysis of respiratory muscle
4. Pulmonary congestion
5. Pneumonia
6. Pneumothorax
7. Hemothorax
8. Pyothorax
9. Hydrothorax
10. Pulmonary edema
11. Pulmonary tuberculosis.

Measurement

Vital capacity is measured by spirometry. The subject is asked to take a deep inspiration and expire forcefully.

FORCED VITAL CAPACITY

Forced vital capacity (FVC) is the volume of air that can be exhaled forcefully and rapidly after a maximal or deep inspiration. It is a dynamic lung capacity.

Normally FVC is equal to VC. However in some pulmonary diseases, FVC is decreased.

FORCED EXPIRATORY VOLUME OR TIMED VITAL CAPACITY

DEFINITION

Forced expiratory volume (FEV) is the volume of air, which can be expired forcefully in a given unit of time (after a deep inspiration). It is also called timed vital capacity or forced expiratory vital capacity (FEVC). It is a dynamic lung volume.

FEV_1 = Volume of air expired forcefully in 1 second

FEV_2 = Volume of air expired forcefully in 2 seconds

FEV_3 = Volume of air expired forcefully in 3 seconds.

NORMAL VALUES

Forced expiratory volume in persons with normal respiratory functions is as follows:

FEV_1 = 83% of total vital capacity

FEV_2 = 94% of total vital capacity

FEV_3 = 97% of total vital capacity

After 3rd second = 100% of total vital capacity.

SIGNIFICANCE OF DETERMINING FEV

Vital capacity may be almost normal in some of the respiratory diseases. However, the FEV has great diagnostic value, as it is decreased significantly in some respiratory diseases.

It is very much decreased in obstructive diseases like asthma and emphysema. It is slightly reduced in some restrictive respiratory diseases like fibrosis of lungs (Fig. 121.5).

RESPIRATORY MINUTE VOLUME

DEFINITION

Respiratory minute volume (RMV) is the volume of air breathed in and out of lungs every minute. It is the product of tidal volume (TV) and respiratory rate (RR).

$$\text{RMV} = \text{TV} \times \text{RR}$$
$$= 500 \times 12 = 6{,}000 \text{ mL.}$$

NORMAL VALUE

Normal respiratory minute volume is 6 L.

VARIATIONS

Respiratory minute volume increases in physiological conditions such as voluntary hyperventilation, exercise and emotional conditions. It is reduced in respiratory diseases.

MAXIMUM BREATHING CAPACITY OR MAXIMUM VENTILATION VOLUME

DEFINITION

Maximum breathing capacity (MBC) is the maximum volume of air, which can be breathed in and out of lungs by forceful respiration (hyperventilation: increase in rate and force of respiration) per minute. It is also called maximum ventilation volume (MVV).

MBC is a dynamic lung capacity and it is reduced in respiratory diseases.

NORMAL VALUE

In healthy adult male, it is 150 to 170 L/minute and in females, it is 80 to 100 L/minute.

MEASUREMENT

Subject is asked to breathe forcefully and rapidly with a **respirometer** for 15 seconds. Volume of air inspired and expired is measured from the spirogram. From this value, the MBC is calculated for 1 minute.

For example, MBC in 12 seconds = 32 L

$$\text{MBC per minute} = \frac{32}{12} \times 60 \text{ L}$$
$$= 160 \text{ L}$$

PEAK EXPIRATORY FLOW RATE

DEFINITION

Peak expiratory flow rate (PEFR) is the maximum rate at which the air can be expired after a deep inspiration.

NORMAL VALUE

In normal persons, it is 400 L/minute.

MEASUREMENT

Peak expiratory flow rate is measured by using **Wright peak flow meter** or a mini peak flow meter.

SIGNIFICANCE OF DETERMINING PEFR

Determination of PEFR rate is useful for assessing the respiratory diseases especially to differentiate the obstructive and restrictive diseases. Generally, PEFR is reduced in all type of respiratory disease. However, reduction is more significant in the obstructive diseases than in the restrictive diseases.

Thus, in restrictive diseases, the PEFR is 200 L/minute and in obstructive diseases, it is only 100 L/minute.

RESTRICTIVE AND OBSTRUCTIVE RESPIRATORY DISEASES

Diseases of respiratory tract are classified into two types:

1. Restrictive respiratory disease
2. Obstructive respiratory disease.

These two types of respiratory diseases are determined by lung functions tests, particularly FEV.

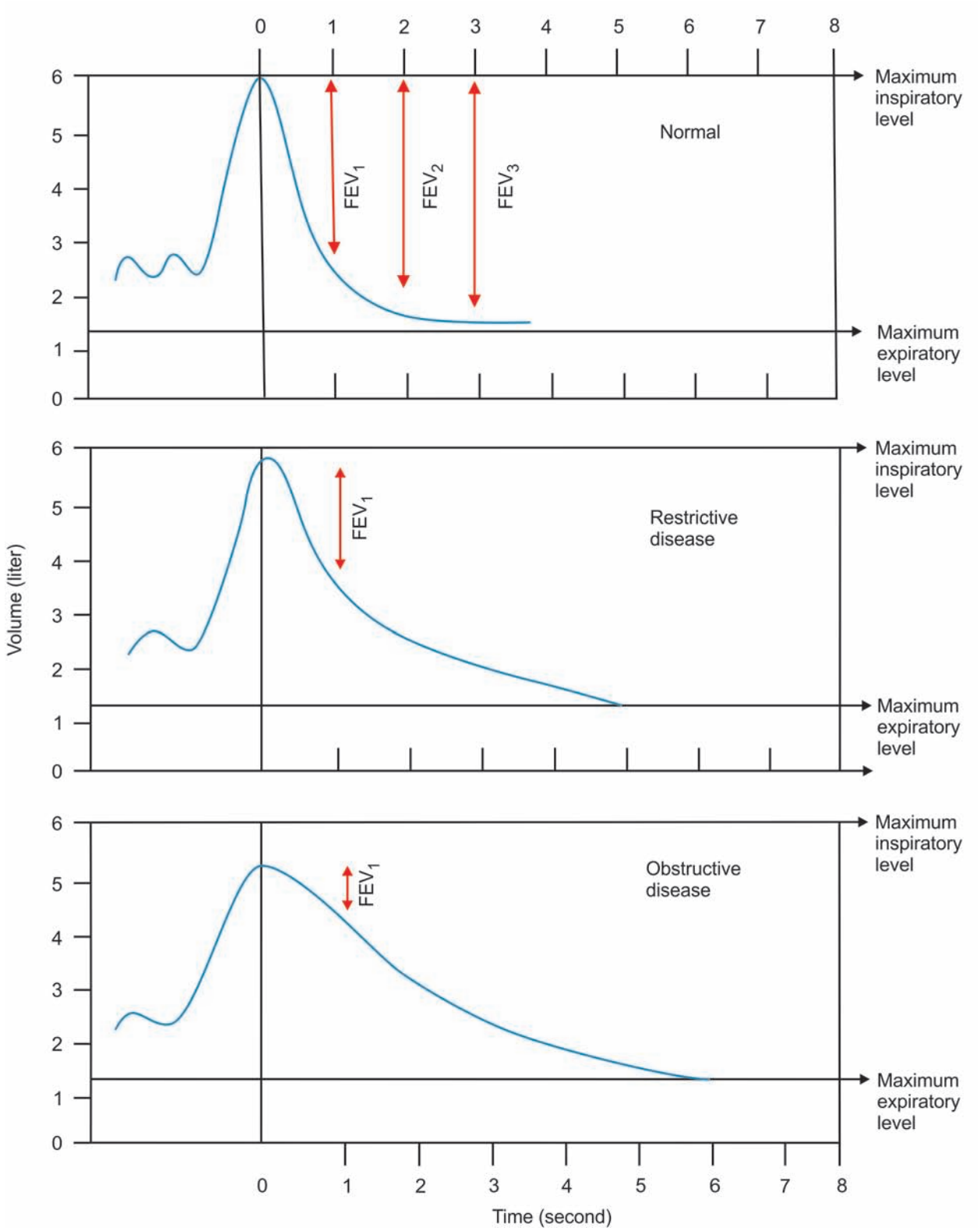


FIGURE 121.5: Forced expiratory volume. FEV = Forced expiratory volume.

TABLE 121.1: Restrictive and obstructive respiratory diseases

Type	Disease	Structures involved
Restrictive respiratory diseases	Polio myelitis	CNS
	Myasthenia gravis	CNS and thoracic cavity
	Flail chest (broken ribs)	Thoracic cavity
	Paralysis of diaphragm	CNS
	Spinal cord diseases	CNS
	Pleural effusion	Thoracic cavity
Obstructive respiratory diseases	Asthma Chronic bronchitis Emphysema Cystic fibrosis	Lower respiratory tract
	Laryngotracheobronchitis Epiglottis Tumors Severe cough and cold with phlegm	Upper respiratory tract

■ RESTRICTIVE RESPIRATORY DISEASE

Restrictive respiratory disease is the abnormal respiratory condition characterized by difficulty in inspiration. Expiration is not affected. Restrictive respiratory disease may be because of abnormality of lungs, thoracic cavity or/and nervous system.

■ OBSTRUCTIVE RESPIRATORY DISEASE

Obstructive respiratory disease is the abnormal respiratory condition characterized by difficulty in expiration.

Obstructive and respiratory diseases are listed in Table 121.1.

Ventilation

Chapter 122

- VENTILATION
- PULMONARY VENTILATION
  - DEFINITION
  - NORMAL VALUE AND CALCULATION
- ALVEOLAR VENTILATION
  - DEFINITION
  - NORMAL VALUE AND CALCULATION
- DEAD SPACE
  - DEFINITION
  - TYPES
  - NORMAL VALUE
  - MEASUREMENT
- VENTILATION-PERFUSION RATIO
  - DEFINITION
  - NORMAL VALUE AND CALCULATION
  - SIGNIFICANCE
  - WASTED AIR AND WASTED BLOOD
  - VARIATIONS

VENTILATION

In general, the word 'ventilation' refers to circulation of replacement of air or gas in a space. In respiratory physiology, ventilation is the rate at which air enters or leaves the lungs. Ventilation in **respiratory physiology** is of two types:

1. Pulmonary ventilation
2. Alveolar ventilation.

PULMONARY VENTILATION

DEFINITION

Pulmonary ventilation is defined as the volume of air moving in and out of respiratory tract in a given unit of time during quiet breathing. It is also called **minute ventilation** or **respiratory minute volume** (RMV).

Pulmonary ventilation is a cyclic process, by which fresh air enters the lungs and an equal volume of air leaves the lungs.

NORMAL VALUE AND CALCULATION

Normal value of pulmonary ventilation is 6,000 mL (6 L)/minute. It is the product of tidal volume (TV) and the rate of respiration (RR).

It is calculated by the formula:

Pulmonary ventilation
= Tidal volume × Respiratory rate
= 500 mL × 12/minute
= 6,000 mL/minute.

ALVEOLAR VENTILATION

DEFINITION

Alveolar ventilation is the amount of air utilized for gaseous exchange every minute.

Alveolar ventilation is different from pulmonary ventilation. In pulmonary ventilation, 6 L of air moves in and out of respiratory tract every minute. But the

whole volume of air is not utilized for exchange of gases. Volume of air subjected for exchange of gases is the alveolar ventilation. Air trapped in the respiratory passage (dead space) does not take part in gaseous exchange.

■ NORMAL VALUE AND CALCULATION

Normal value of alveolar ventilation is 4,200 mL (4.2 L)/minute.

It is calculated by the formula:

Alveolar ventilation
= (Tidal volume – Dead space) x Respiratory rate
= (500 – 150) mL × 12/minute
= 4,200 mL (4.2 L)/minute.

■ DEAD SPACE

■ DEFINITION

Dead space is defined as the part of the respiratory tract, where gaseous exchange does not take place. Air present in the dead space is called dead space air.

■ TYPES OF DEAD SPACE

Dead space is of two types:

1. Anatomical dead space
2. Physiological dead space.

Anatomical Dead Space

Anatomical dead space extends from nose up to terminal bronchiole. It includes nose, pharynx, trachea, bronchi and branches of bronchi up to terminal bronchioles. These structures serve only as the passage for air movement. Gaseous exchange does not take place in these structures.

Physiological Dead Space

Physiological dead space includes anatomical dead space plus two additional volumes.

Additional volumes included in physiological dead space are:

1. Air in the alveoli, which are **non-functioning**. In some respiratory diseases, alveoli do not function because of dysfunction or destruction of alveolar membrane.
2. Air in the alveoli, which do not receive adequate blood flow. Gaseous exchange does not take place during inadequate blood supply.

These two additional volumes are generally considered as wasted ventilation.

Wasted ventilation and wasted air

Wasted ventilation is the volume of air that ventilates physiological dead space. Wasted air refers to air that is not utilized for gaseous exchange. Dead space air is generally considered as wasted air.

■ NORMAL VALUE OF DEAD SPACE

Volume of normal dead space is 150 mL. Under normal conditions, physiological dead space is equal to anatomical dead space. It is because, all the alveoli are functioning and all the alveoli receive adequate blood flow in normal conditions.

Physiological dead space increases during respiratory diseases, which affect the pulmonary blood flow or the alveoli.

■ MEASUREMENT OF DEAD SPACE – NITROGEN WASHOUT METHOD

Dead space is measured by single breath nitrogen washout method. The subject respires normally for few minutes. Then, he takes a sudden inhalation of pure oxygen.

Oxygen replaces the air in dead space (air passage), i.e. the dead space air contains only oxygen and it pushes the other gases into alveoli.

Now, the subject exhales through a nitrogen meter. Nitrogen meter shows the concentration of nitrogen in expired air continuously.

First portion of expired air comes from upper part of respiratory tract or air passage, which contains only oxygen. Next portion of expired air comes from the alveoli, which contains nitrogen. Now, the nitrogen meter shows the nitrogen concentration, which rises sharply and reaches the plateau soon. By using data obtained from nitrogen meter, a graph is plotted. From this graph, the dead space is calculated (Fig. 122.1).

The graph has two areas, area without nitrogen and area with nitrogen. Area of the graph is measured by a planimeter or by computer. Area without nitrogen indicates dead space air.

It is calculated by the formula:

$$\text{Dead space} = \frac{\text{Area without } N_2}{\text{Area with } N_2 + \text{Area without } N_2} \times \text{Volume of expired air}$$

For example, in a subject:
Area with nitrogen = 70 sq cm
Area without nitrogen = 30 sq cm
Volume of air expired = 500 mL

$$\text{Dead space} = \frac{30}{70 + 30} \times 500$$

$$= \frac{30}{100} \times 500$$

$$= 150 \text{ mL.}$$

VENTILATION-PERFUSION RATIO

DEFINITION

Ventilation-perfusion ratio is the ratio of alveolar ventilation and the amount of blood that perfuse the alveoli.

It is expressed as V_A/Q. V_A is alveolar ventilation and Q is the blood flow (perfusion).

NORMAL VALUE AND CALCULATION

Normal Value

Normal value of ventilation-perfusion ratio is about 0.84.

Calculation

Alveolar ventilation is calculated by the formula:

$$\text{Ventilation-perfusion ratio} = \frac{\text{Alveolar ventilation}}{\text{Pulmonary blood flow}}$$

$$\text{Alveolar ventilation} = (\text{Tidal volume} - \text{Dead space}) \times \text{Respiratory rate}$$

$$= (500 - 150) \text{ mL} \times 12/\text{minute}$$

$$= 4{,}200 \text{ mL/minute}$$

$$\text{Blood flow through alveoli (Pulmonary blood flow)} = 5{,}000 \text{ mL/minute}$$

Therefore,

$$\text{Ventilation-perfusion ratio} = \frac{4{,}200}{5{,}000}$$

$$= 0.84$$

SIGNIFICANCE OF VENTILATION-PERFUSION RATIO

Ventilation-perfusion ratio signifies the gaseous exchange. It is affected if there is any change in alveolar ventilation or in blood flow.

Ventilation without perfusion = dead space

Perfusion without ventilation = shunt

WASTED AIR AND WASTED BLOOD

Ventilation-perfusion ratio is not perfect because of existence of two factors on either side of alveolar membrane.

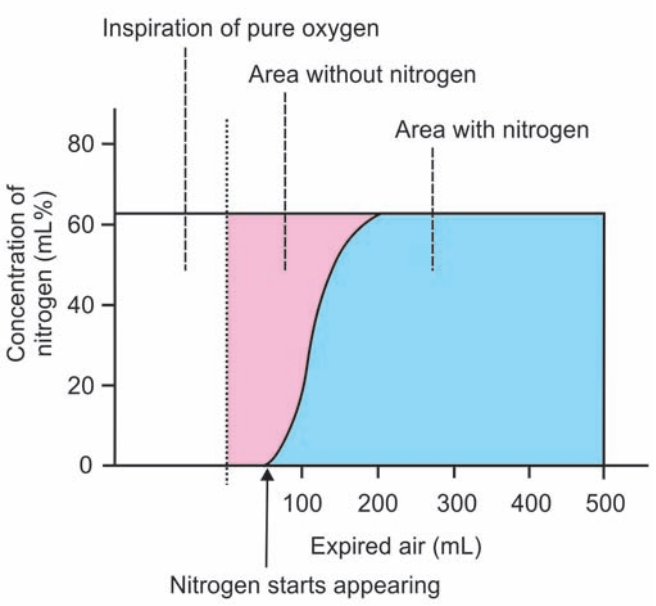


FIGURE 122.1: Measurement of dead space

These factors are:

1. Physiological dead space, which includes wasted air (see above)
2. Physiological shunt, which includes wasted blood (Chapter 119).

VARIATIONS IN VENTILATION-PERFUSION RATIO

Physiological Variation

1. Ratio increases, if ventilation increases without any change in blood flow
2. Ratio decreases, if blood flow increases without any change in ventilation
3. In sitting position, there is reduction in blood flow in the upper part of the lungs (zone 1) than in the lower part (zone 3). Therefore, in zone 1 of lungs ventilation-perfusion ratio increases three times. At the same time, in zone 3 of the lungs, because of increased blood flow ventilation-perfusion ratio decreases (Chapter 119).

Pathological Variation

In chronic obstructive pulmonary diseases (COPD), ventilation is affected because of obstruction and destruction of alveolar membrane. So, ventilation-perfusion ratio reduces greatly.

Inspired Air, Alveolar Air and Expired Air

Chapter 123

- INSPIRED AIR
  - DEFINITION
  - COMPOSITION
- ALVEOLAR AIR
  - DEFINITION
  - COMPOSITION
  - RENEWAL
  - METHOD OF COLLECTION
- EXPIRED AIR
  - DEFINITION
  - COMPOSITION
  - METHOD OF COLLECTION

INSPIRED AIR

DEFINITION

Inspired air is the atmospheric air, which is inhaled during inspiration.

COMPOSITION

Composition of inspired air is given in Table 123.1.

ALVEOLAR AIR

DEFINITION

Alveolar air is the air present in alveoli of lungs. Its composition is given in Table 123.1.

Alveolar Air Vs Inspired Air

Alveolar air is different from inspired air in four ways:

TABLE 123.1: Composition of inspired air, alveolar air and expired air

Air	Inspired (atmospheric) air		Alveolar air		Expired air	
Gas	Content (mL%)	Partial pressure (mm Hg)	Content (mL%)	Partial pressure (mm Hg)	Content (mL%)	Partial pressure (mm Hg)
Oxygen	20.84	159.00	13.60	104.00	15.70	120.00
Carbon dioxide	0.04	0.30	5.30	40.00	3.60	27.00
Nitrogen	78.62	596.90	74.90	569.00	74.50	566.00
Water vapor, etc.	0.50	3.80	6.20	47.00	6.20	47.00
Total	100.00	760.00	100.00	760.00	100.00	760.00

1. Alveolar air is partially replaced by the atmospheric air during each breath
2. Oxygen diffuses from the alveolar air into pulmonary capillaries constantly
3. Carbon dioxide diffuses from pulmonary blood into alveolar air constantly
4. Dry atmospheric air is humidified, while passing through respiratory passage before entering the alveoli (Table 123.1).

■ COMPOSITION

Composition of alveolar air is given in Table 123.1.

■ RENEWAL

Alveolar air is constantly renewed. Rate of renewal is slow during normal breathing. During each breath, out of 500 mL of tidal volume only 350 mL of air enters the alveoli and the remaining quantity of 150 mL (30%) becomes dead space air. Hence, the amount of alveolar air replaced by new atmospheric air with each breath is only about 70% of the total alveolar air.

Thus,

$$\text{Alveolar air} = \frac{350}{500} \times 100 = 70\%$$

Slow renewal of alveolar air is responsible for prevention of sudden changes in concentration of gases in the blood.

■ METHOD OF COLLECTION

Alveolar air is collected by using **Haldane-Priestely tube.** This tube consists of a canvas rubber tube, which is 1 m long and having a diameter of 2.5 cm. It is opened on both ends.

A mouthpiece is fitted at one end of the tube. Near the mouthpiece, there is a side tube, which is fixed with a sampling tube. Mouthpiece and the side tube are interconnected by means of a three-way cock. By keeping the mouthpiece in the mouth, the subject makes a forceful expiration through the mouthpiece. Alveolar air is expired at the end of forced expiration. So, by using the three-way cock, the last portion of expired air (alveolar air) is collected in the sampling tube.

■ EXPIRED AIR

■ DEFINITION

Expired air is the amount of air that is exhaled during expiration. It is a combination of dead space air and alveolar air.

■ COMPOSITION

Concentration of gases in expired air is somewhere between inspired air and alveolar air. Composition of expired air is given in Table 123.1 along with composition of inspired air and alveolar air.

■ METHOD OF COLLECTION

Expired air is collected by using **Douglas bag.**

Exchange of Respiratory Gases

Chapter 124

INTRODUCTION

Oxygen is essential for the cells. Carbon dioxide, which is produced as waste product in the cells must be expelled from the cells and body. Lungs serve to exchange these two gases with blood.

EXCHANGE OF RESPIRATORY GASES IN LUNGS

In the lungs, exchange of respiratory gases takes place between the alveoli of lungs and the blood. Oxygen enters the blood from alveoli and carbon dioxide is expelled out of blood into alveoli. Exchange occurs through **bulk flow diffusion** (Chapter 3).

Exchange of gases between blood and alveoli takes place through respiratory membrane. Refer Chapter 118 for details.

RESPIRATORY MEMBRANE

Respiratory membrance is a membranous structure through which exchange of respiratory gases takes place. It is formed by **epithelium** of respiratory unit and **endothelium** of pulmonary capillary. Epithelium of respiratory unit is a very thin layer (Chapter 118). Since, the capillaries are in close contact with this membrane, alveolar air is in close proximity to capillary blood. This facilitates gaseous exchange between air and blood (Fig. 124.1).

Respiratory membrane is formed by different layers of structures belonging to the alveoli and capillaries.

Layers of Respiratory Membrane

Different layers of respiratory membrane from within outside are given in Table 124.1.

In spite of having many layers, respiratory membrane is very thin with an average thickness of 0.5 µ. Total

surface area of the respiratory membrane in both the lungs is about 70 square meter.

Average diameter of pulmonary capillary is only 8 µ, which means that the RBCs with a diameter of 7.4 µ actually squeeze through the capillaries. Therefore, the membrane of RBCs is in close contact with capillary wall. This facilitates quick exchange of oxygen and carbon dioxide between the blood and alveoli.

■ DIFFUSING CAPACITY

Diffusing capacity is defined as the volume of gas that diffuses through the respiratory membrane each minute for a pressure gradient of 1 mm Hg.

TABLE 124.1: Layers of respiratory membrane

Portion	Layers
Alveolar portion	1. Monomolecular layer of surfactant, which spreads over the surface of alveoli 2. Thin fluid layer that lines the alveoli 3. Alveolar epithelial layer, which is composed of thin epithelial cells resting on a basement membrane
Between alveolar and capillary portions	4. An interstitial space
Capillary portion	5. Basement membrane of capillary 6. Capillary endothelial cells

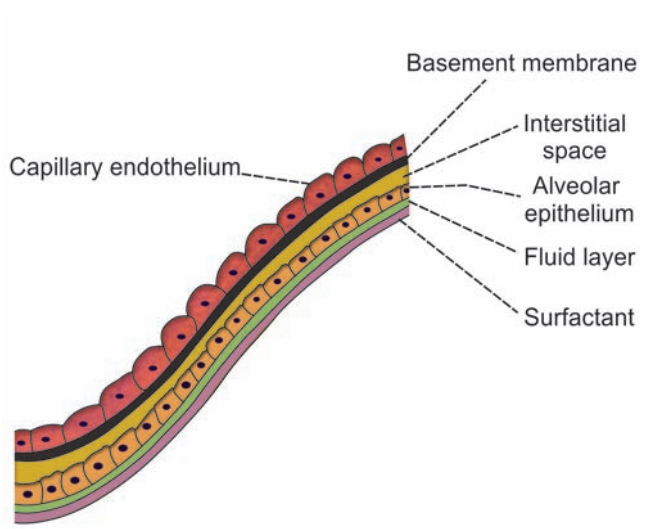


FIGURE 124.1: Structure of respiratory membrane

Diffusing Capacity for Oxygen and Carbon Dioxide

Diffusing capacity for oxygen is 21 mL/minute/1 mm Hg. Diffusing capacity for carbon dioxide is 400 mL/minute/1 mm Hg. Thus, the diffusing capacity for carbon dioxide is about 20 times more than that of oxygen.

Factors Affecting Diffusing Capacity

1. *Pressure gradient*

Diffusing capacity is **directly proportional** to pressure gradient. Pressure gradient is the difference between the partial pressure of a gas in alveoli and pulmonary capillary blood (see below). It is the major factor, which affects the diffusing capacity.

2. *Solubility of gas in fluid medium*

Diffusing capacity is **directly proportional** to solubility of the gas. If the solubility of a gas is more in the fluid medium, a large number of molecules dissolve in it and diffuse easily.

3. *Total surface area of respiratory membrane*

Diffusing capacity is **directly proportional** to surface area of respiratory membrane. Surface area of respiratory membrane in each lung is about 70 sq m. If the total surface area of respiratory membrane decreases, the diffusing capacity for the gases is decreased. Diffusing capacity is decreased in emphysema in which many of the alveoli are collapsed because of heavy smoking or oxidant gases.

4. *Molecular weight of the gas*

Diffusing capacity is **inversely proportional** to molecular weight of the gas. If the molecular weight is more, the density is more and the rate of diffusion is less.

5. *Thickness of respiratory membrane*

Diffusion is **inversely proportional** to the thickness of respiratory membrane. More the thickness of respiratory membrane less is the diffusion. It is because the distance through which the diffusion takes place is long. In conditions like fibrosis and edema, the diffusion rate is reduced, because the thickness of respiratory membrane is increased.

Relation between Diffusing Capacity and Factors Affecting it

Relation between diffusing capacity and the factors affecting it is expressed by the following formula:

$$DC \propto \frac{Pg \times S \times A}{Mw \times D}$$

DC = Diffusing capacity
Pg = Pressure gradient
S = Solubility of gas
A = Surface area of respiratory membrane
Mw = Molecular weight
D = Thickness of respiratory membrane.

■ DIFFUSION COEFFICIENT AND FICK LAW OF DIFFUSION

Diffusion Coefficient

Diffusion coefficient is defined as a constant (a factor of proportionality), which is the measure of a substance diffusing through the concentration gradient. It is also known as **diffusion constant.** It is related to size and shape of the molecules of the substance.

Fick Law of Diffusion

Diffusion is well described by Fick law of diffusion. According to this law, amount of a substance crossing a given area is directly proportional to the area available for diffusion, concentration gradient and a constant known as diffusion coefficient.

Thus,
Amount diffused = Area × Concentration gradient × Diffusion coefficient

Formula of Fick law:

$$J = -D \times A \times \frac{dc}{dx}$$

Where,
J = Amount of substance diffused
D = Diffusion coefficient
A = Area through which diffusion occurs
dc/dx = Concentration gradient.

Negative sign in the formula indicates that diffusion occurs from region of higher concentration to region of lower concentration. Diffusion coefficient reduces when the molecular size of diffusing substance is increased. It increases when the size is decreased, i.e. the smaller molecules diffuse rapidly than the larger ones.

■ DIFFUSION OF OXYGEN

Diffusion of Oxygen from Atmospheric Air into Alveoli

Partial pressure of oxygen in the atmospheric air is 159 mm Hg and in the alveoli, it is 104 mm Hg. Because of

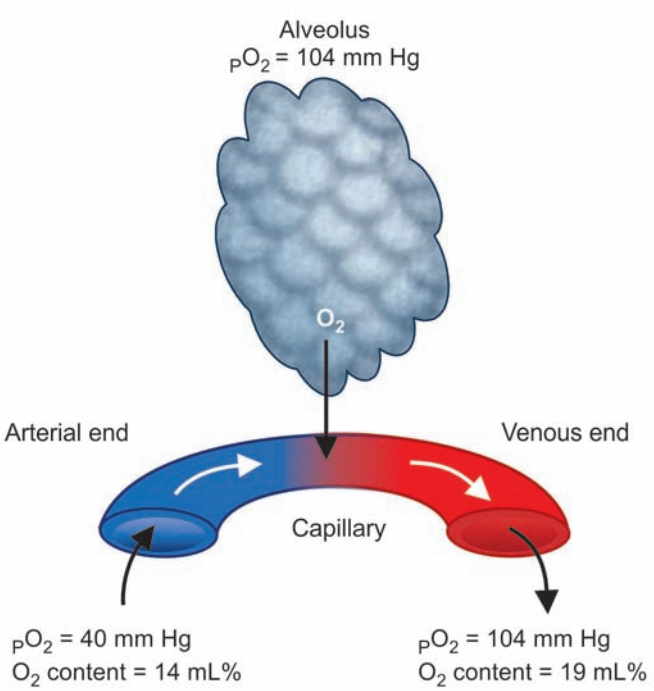


FIGURE 124.2: Diffusion of oxygen from alveolus to pulmonary capillary

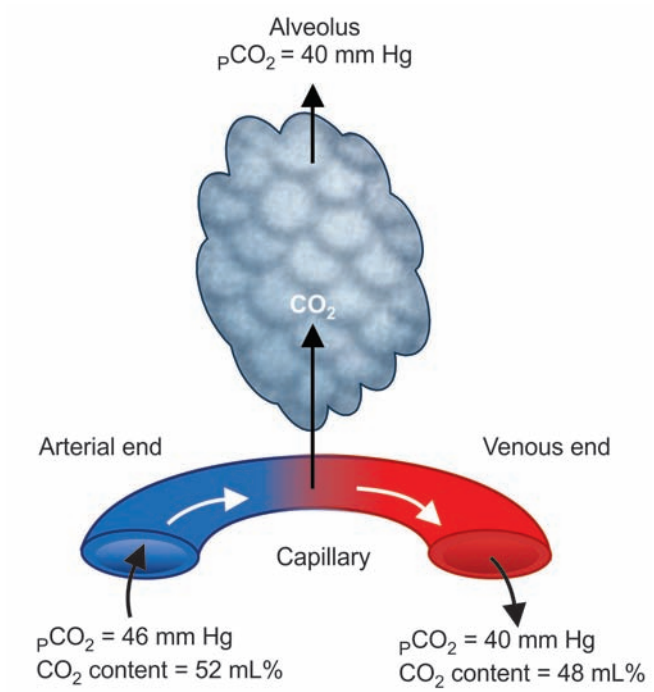


FIGURE 124.3: Diffusion of carbon dioxide from pulmonary capillary to alveolus

TABLE 124.2: Partial pressure and content of oxygen and carbon dioxide in alveoli, capillaries and tissue

Gas	Arterial end of pulmonary capillary	Alveoli	Venous end of pulmonary capillary	Arterial end of systemic capillary	Tissue	Venous end of systemic capillary
pO_2 (mm Hg)	40	104	104	95	40	40
Oxygen content (mL%)	14	–	19	19	–	14
pCO_2 (mm Hg)	46	40	40	40	46	46
Carbon dioxide content (mL%)	52	–	48	48	–	52

the pressure gradient of 55 mm Hg, oxygen easily enters from atmospheric air into the alveoli (Table 124.2).

Diffusion of Oxygen from Alveoli into Blood

When blood passes through pulmonary capillary, RBC is exposed to oxygen only for 0.75 second at rest and only for 0.25 second during severe exercise. So, diffusion of oxygen must be quicker and effective. Fortunately, this is possible because of pressure gradient.

Partial pressure of oxygen in the pulmonary capillary is 40 mm Hg and in the alveoli, it is 104 mm Hg. Pressure gradient is 64 mm Hg. It facilitates the diffusion of oxygen from alveoli into the blood (Fig. 124.2).

■ DIFFUSION OF CARBON DIOXIDE

Diffusion of Carbon Dioxide from Blood into Alveoli

Partial pressure of carbon dioxide in alveoli is 40 mm Hg whereas in the blood it is 46 mm Hg. Pressure gradient of 6 mm Hg is responsible for the diffusion of carbon dioxide from blood into the alveoli (Fig. 124.3).

Diffusion of Carbon Dioxide from Alveoli into Atmospheric Air

In atmospheric air, partial pressure of carbon dioxide is very insignificant and is only about 0.3 mm Hg whereas, in the alveoli, it is 40 mm Hg. So, carbon dioxide enters passes to atmosphere from alveoli easily.

■ EXCHANGE OF RESPIRATORY GASES AT TISSUE LEVEL

Oxygen enters the cells of tissues from blood and carbon dioxide is expelled from cells into the blood.

■ DIFFUSION OF OXYGEN FROM BLOOD INTO THE TISSUES

Partial pressure of oxygen in venous end of pulmonary capillary is 104 mm Hg. However, partial pressure of

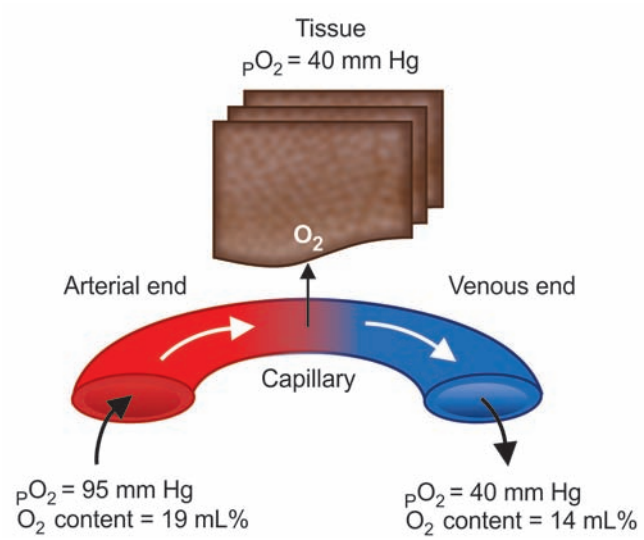


FIGURE 124.4: Diffusion of oxygen from capillary to tissue

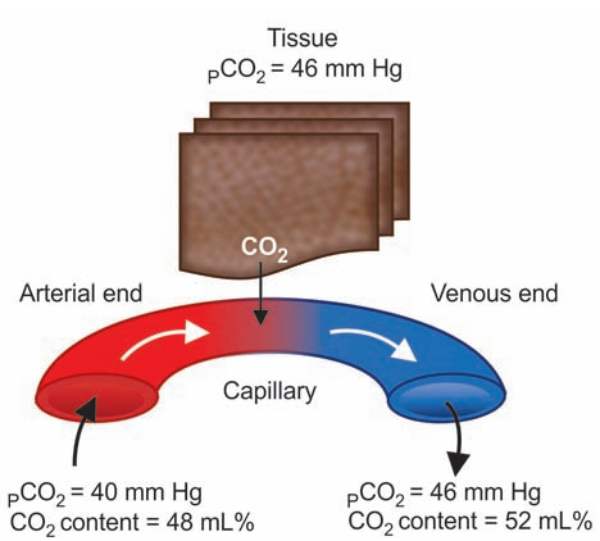


FIGURE 124.5: Diffusion of carbon dioxide from tissue to capillary

oxygen in the arterial end of systemic capillary is only 95 mm Hg. It may be because of physiological shunt in lungs. Due to **venous admixture** in the **shunt** (Chapter 119), 2% of blood reaches the heart without being oxygenated.

Average oxygen tension in the tissues is 40 mm Hg. It is because of continuous metabolic activity and constant utilization of oxygen. Thus, a pressure gradient of about 55 mm Hg exists between capillary blood and the tissues so that oxygen can easily diffuse into the tissues (Fig. 124.4).

Oxygen content in arterial blood is 19 mL% and in the venous blood, it is 14 mL%. Thus, the diffusion of oxygen from blood to tissues is 5 mL/100 mL of blood.

■ DIFFUSION OF CARBON DIOXIDE FROM TISSUES INTO THE BLOOD

Due to continuous metabolic activity, carbon dioxide is produced constantly in the cells of tissues. So, the partial pressure of carbon dioxide is high in the cells and is about 46 mm Hg. Partial pressure of carbon dioxide in arterial blood is 40 mm Hg. Pressure gradient of 6 mm Hg is responsible for the diffusion of carbon dioxide from tissues to the blood (Figs. 124.5 and 124.6).

Carbon dioxide content in arterial blood is 48 mL%. And in the venous blood, it is 52 mL%. So, the diffusion of carbon dioxide from tissues to blood is 4 mL/100 mL of blood (Fig. 124.5).

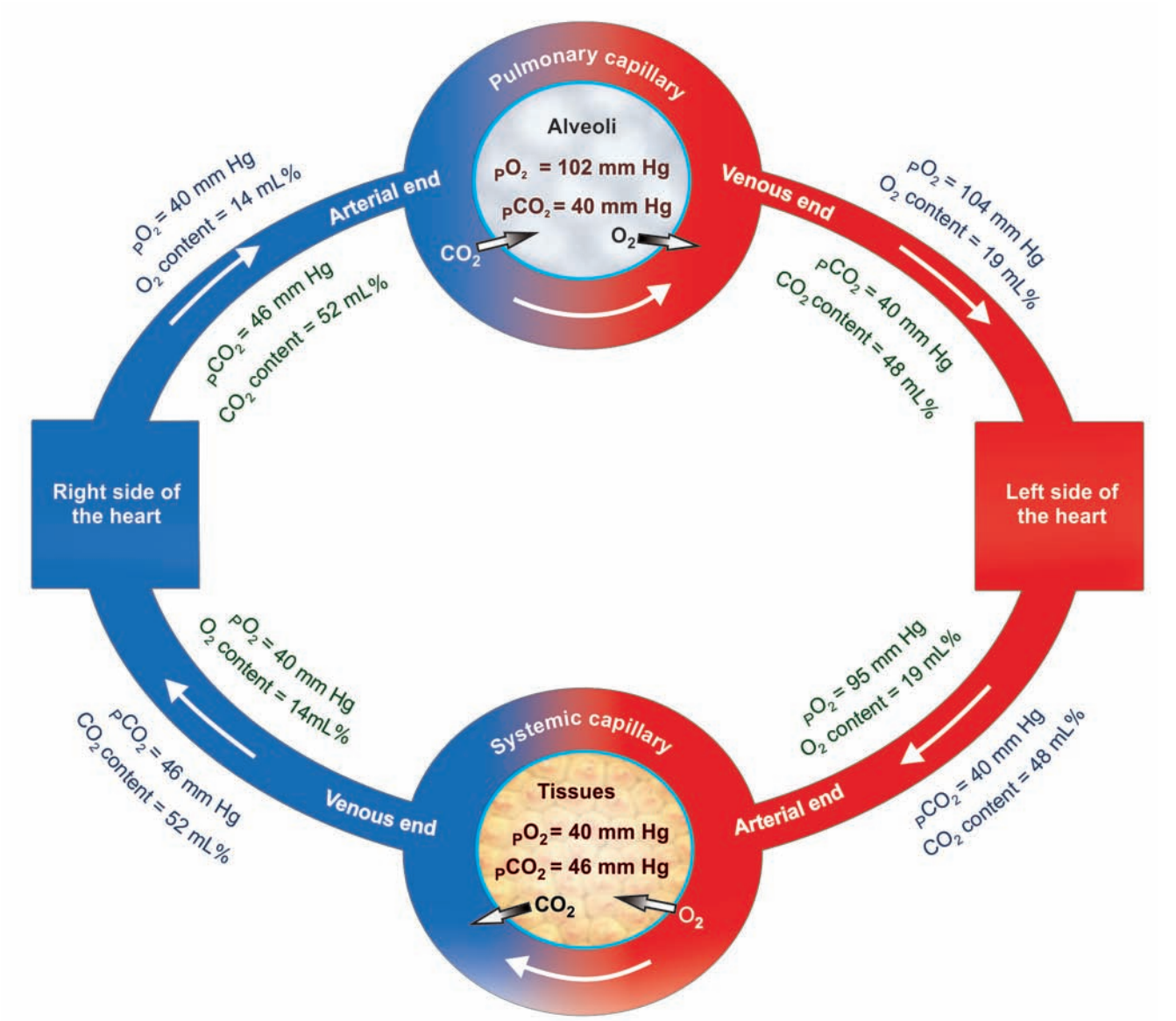


FIGURE 124.6: Partial pressure and content of oxygen and carbon dioxide in blood, alveoli and tissues

RESPIRATORY EXCHANGE RATIO

DEFINITION

Respiratory exchange ratio (R) is the ratio between the net output of carbon dioxide from tissues to simultaneous net uptake of oxygen by the tissues.

$$R = \frac{CO_2 \text{ output}}{O_2 \text{ uptake}}$$

NORMAL VALUES

Value of R depends upon the type of food substance that is metabolized.

When a person utilizes only carbohydrates for metabolism, R is 1.0. That means during carbohydrate metabolism, the amount of carbon dioxide produced in the tissue is equal to the amount of oxygen consumed.

If only fat is used for metabolism, the R is 0.7. When fat is utilized, oxygen reacts with fats and a large portion of oxygen combines with hydrogen ions to form water instead of carbon dioxide. So, the carbon dioxide output is less than the oxygen consumed. And the R is less.

If only protein is utilized, R is 0.803.

However, when a balanced diet containing average quantity of proteins, carbohydrates and lipids is utilized, the R is about 0.825. In steady conditions, respiratory exchange ratio is equal to respiratory quotient.

RESPIRATORY QUOTIENT

DEFINITION

Respiratory quotient is the molar ratio of carbon dioxide production to oxygen consumption. It is used to determine the utilization of different foodstuffs.

NORMAL VALUE

For about 1 hour after meals the respiratory quotient is 1.0. It is because usually, immediately after taking meals, only the carbohydrates are utilized by the tissues. During the metabolism of carbohydrates, one molecule of carbon dioxide is produced for every molecule of oxygen consumed by the tissues. Respiratory quotient is 1.0, which is equal to respiratory exchange ratio.

After utilization of all the carbohydrates available, body starts utilizing fats. Now the respiratory quotient becomes 0.7. When the proteins are metabolized, it becomes 0.8.

During exercise, the respiratory quotient increases (Chapter 132).

Transport of Respiratory Gases

Chapter 125

INTRODUCTION

Blood serves to transport the respiratory gases. Oxygen, which is essential for the cells is transported from alveoli of lungs to the cells. Carbon dioxide, which is the waste product in cells is transported from cells to lungs.

TRANSPORT OF OXYGEN

Oxygen is transported from alveoli to the tissue by blood in two forms:

1. As simple physical solution
2. In combination with hemoglobin.

Partial pressure and content of oxygen in arterial blood and venous blood are given in Table 125.1.

TABLE 125.1: Gases in arterial and venous blood

Gas		Arterial blood	Venous blood
Oxygen	Partial pressure (mm Hg)	95	40
	Content (mL%)	19	14
Carbon dioxide	Partial pressure (mm Hg)	40	46
	Content (mL%)	48	52

AS SIMPLE SOLUTION

Oxygen dissolves in water of plasma and is transported in this **physical form.** Amount of oxygen transported in this way is very negligible. It is only 0.3 mL/100 mL of plasma. It forms only about 3% of total oxygen in blood. It is because of poor solubility of oxygen in water content of plasma. Still, transport of oxygen in this form becomes important during the conditions like muscular exercise to meet the excess demand of oxygen by the tissues.

IN COMBINATION WITH HEMOGLOBIN

Oxygen combines with hemoglobin in blood and is transported as **oxyhemoglobin.** Transport of oxygen in this form is important because, maximum amount (97%) of oxygen is transported by this method.

Oxygenation of Hemoglobin

Oxygen combines with hemoglobin only as a physical combination. It is only **oxygenation** and not **oxidation.** This type of combination of oxygen with hemoglobin has got some advantages. Oxygen can be readily released from hemoglobin when it is needed.

Hemoglobin accepts oxygen readily whenever the partial pressure of oxygen in the blood is more. Hemoglobin gives out oxygen whenever the partial pressure of oxygen in the blood is less.

Oxygen combines with the iron in heme part of hemoglobin. Each molecule of hemoglobin contains 4 atoms of iron. Iron of the hemoglobin is present in ferrous form. Each iron atom combines with one molecule of oxygen. After combination, iron remains in ferrous form only. That is why the combination of oxygen with hemoglobin is called oxygenation and not oxidation.

Oxygen Carrying Capacity of Hemoglobin

Oxygen carrying capacity of hemoglobin is the amount of oxygen transported by 1 gram of hemoglobin. It is 1.34 mL/g.

Oxygen Carrying Capacity of Blood

Oxygen carrying capacity of blood refers to the amount of oxygen transported by blood. Normal hemoglobin content in blood is 15 g%.

Since oxygen carrying capacity of hemoglobin is 1.34 mL/g, blood with 15 g% of hemoglobin should carry 20.1 mL% of oxygen, i.e. 20.1 mL of oxygen in 100 mL of blood.

But, blood with 15 g% of hemoglobin carries only 19 mL% of oxygen, i.e. 19 mL of oxygen is carried by 100 mL of blood (Table 125.1). Oxygen carrying capacity of blood is only 19 mL% because the hemoglobin is not fully saturated with oxygen. It is saturated only for about 95%.

Saturation of Hemoglobin with Oxygen

Saturation is the state or condition when hemoglobin is unable to hold or carry any more oxygen. Saturation of hemoglobin with oxygen depends upon partial pressure of oxygen. And it is explained by oxygen-hemoglobin dissociation curve.

■ OXYGEN-HEMOGLOBIN DISSOCIATION CURVE

Oxygen-hemoglobin dissociation curve is the curve that demonstrates the relationship between partial pressure of oxygen and the percentage saturation of hemoglobin with oxygen. It explains hemoglobin's affinity for oxygen.

Normally in the blood, hemoglobin is saturated with oxygen only up to 95%. Saturation of hemoglobin with oxygen depends upon the partial pressure of oxygen. When the partial pressure of oxygen is more, hemoglobin accepts oxygen and when the partial pressure of oxygen is less, hemoglobin releases oxygen.

Method to Plot Oxygen-hemoglobin Dissociation Curve

Ten flasks or tonometers are taken. Each one is filled with a known quantity of blood with known concentration of hemoglobin. Blood in each tonometer is exposed to oxygen at different partial pressures. Tonometer is rotated at a constant temperature till the blood takes as much of oxygen as it can. Then, blood is analyzed to measure the percentage saturation of hemoglobin with oxygen. Partial pressure of oxygen and saturation of hemoglobin are plotted to obtain the oxygen-hemoglobin dissociation curve.

Normal Oxygen-hemoglobin Dissociation Curve

Under normal conditions, oxygen-hemoglobin dissociation curve is 'S' shaped or **sigmoid shaped** (Fig.125.1). Lower part of the curve indicates dissociation of oxygen from hemoglobin. Upper part of the curve indicates the uptake of oxygen by hemoglobin depending upon partial pressure of oxygen.

P_{50}

P_{50} is the partial pressure of oxygen at which hemoglobin saturation with oxygen is 50%. When the partial pressure of oxygen is 25 to 27 mm Hg, the hemoglobin is

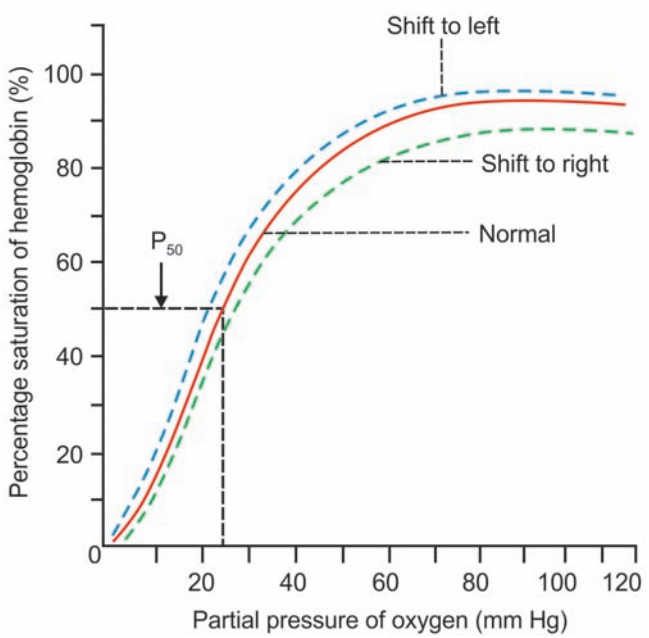


FIGURE 125.1: Oxygen-hemoglobin dissociation curve

saturated to about 50%. That is, the blood contains 50% of oxygen. At 40 mm Hg of partial pressure of oxygen, the saturation is 75%. It becomes 95% when the partial pressure of oxygen is 100 mm Hg.

Factors Affecting Oxygen-hemoglobin Dissociation Curve

Oxygen-hemoglobin dissociation curve is shifted to left or right by various factors:

1. Shift to left indicates acceptance **(association)** of oxygen by hemoglobin
2. Shift to right indicates **dissociation** of oxygen from hemoglobin.

1. *Shift to right*

Oxygen-hemoglobin dissociation curve is shifted to right in the following conditions:

i. Decrease in partial pressure of oxygen
ii. Increase in partial pressure of carbon dioxide (Bohr effect)
iii. Increase in hydrogen ion concentration and decrease in pH (acidity)
iv. Increased body temperature
v. Excess of 2,3-diphosphoglycerate (DPG) in RBC. It is also called 2,3-biphosphoglycerate (BPG). DPG is a byproduct in Embden-Meyerhof pathway of carbohydrate metabolism. It combines with β-chains of hemoglobin. In conditions like muscular exercise and in high attitude, the DPG increases in RBC. So, the oxygen-hemoglobin dissociation curve shifts to right to a great extent.

2. *Shift to left*

Oxygen-hemoglobin dissociation curve is shifted to left in the following conditions:

i. In fetal blood because, fetal hemoglobin has got more affinity for oxygen than the adult hemoglobin
ii. Decrease in hydrogen ion concentration and increase in pH (alkalinity).

Bohr Effect

Bohr effect is the effect by which presence of carbon dioxide decreases the affinity of hemoglobin for oxygen. Bohr effect was postulated by **Christian Bohr** in 1904. In the tissues, due to continuous metabolic activities, the partial pressure of carbon dioxide is very high and the partial pressure of oxygen is low.

Due to this pressure gradient, carbon dioxide enters the blood and oxygen is released from the blood to the tissues. Presence of carbon dioxide decreases the affinity of hemoglobin for oxygen. It enhances further release of oxygen to the tissues and oxygen-dissociation curve is shifted to right.

Factors influencing Bohr effect

All the factors, which shift the oxygen-dissociation curve to right (mentioned above) enhance the Bohr effect.

■ TRANSPORT OF CARBON DIOXIDE

Carbon dioxide is transported by the blood from cells to the alveoli.

Carbon dioxide is transported in the blood in four ways:

1. As dissolved form (7%)
2. As carbonic acid (negligible)
3. As bicarbonate (63%)
4. As carbamino compounds (30%).

■ AS DISSOLVED FORM

Carbon dioxide diffuses into blood and dissolves in the fluid of plasma forming a simple solution. Only about 3 mL/100 mL of plasma of carbon dioxide is transported as dissolved state. It is about 7% of total carbon dioxide in the blood.

■ AS CARBONIC ACID

Part of dissolved carbon dioxide in plasma combines with the water to form carbonic acid. Transport of carbon dioxide in this form is negligible.

■ AS BICARBONATE

About 63% of carbon dioxide is transported as bicarbonate. From plasma, carbon dioxide enters the RBCs. In the RBCs, carbon dioxide combines with water to form carbonic acid. The reaction inside RBCs is very rapid because of the presence of carbonic anhydrase. This enzyme accelerates the reaction. Carbonic anhydrase is present only inside the RBCs and not in plasma. That is why carbonic acid formation is at least 200 to 300 times more in RBCs than in plasma.

Carbonic acid is very unstable. Almost all carbonic acid (99.9%) formed in red blood corpuscles, dissociates into bicarbonate and hydrogen ions. Concentration of bicarbonate ions in the cell increases more and more. Due to high concentration, bicarbonate ions diffuse through the cell membrane into plasma.

Chloride Shift or Hamburger Phenomenon

Chloride shift or Hamburger phenomenon is the exchange of a chloride ion for a bicarbonate ion across RBC membrane. It was discovered by **Hartog Jakob Hamburger** in 1892.

Chloride shift occurs when carbon dioxide enters the blood from tissues. In plasma, plenty of sodium chloride is present. It dissociates into sodium and chloride ions (Fig. 125.2). When the negatively charged bicarbonate ions move out of RBC into the plasma, the negatively charged chloride ions move into the RBC in order to maintain the **electrolyte equilibrium (ionic balance).**

Anion exchanger 1 (band 3 protein), which acts like antiport pump in RBC membrane is responsible for the exchange of bicarbonate ions and chloride ions. Bicarbonate ions combine with sodium ions in the plasma and form sodium bicarbonate. In this form, it is transported in the blood.

Hydrogen ions dissociated from carbonic acid are buffered by hemoglobin inside the cell.

Reverse Chloride Shift

Reverse chloride shift is the process by which chloride ions are moved back into plasma from RBC shift. It occurs in lungs. It helps in elimination of carbon dioxide from the blood. Bicarbonate is converted back into carbon dioxide, which has to be expelled out. It takes place by the following mechanism:

When blood reaches the alveoli, sodium bicarbonate in plasma dissociates into sodium and bicarbonate ions. Bicarbonate ion moves into the RBC. It makes chloride ion to move out of the RBC into the plasma, where it combines with sodium and forms sodium chloride.

Bicarbonate ion inside the RBC combines with hydrogen ion forms carbonic acid, which dissociates into water and carbon dioxide. Carbon dioxide is then expelled out.

■ AS CARBAMINO COMPOUNDS

About 30% of carbon dioxide is transported as carbamino compounds. Carbon dioxide is transported in blood in combination with hemoglobin and plasma proteins. Carbon dioxide combines with hemoglobin to form carbamino hemoglobin or carbhemoglobin. And it combines with plasma proteins to form carbamino proteins. Carbamino hemoglobin and carbamino proteins are together called carbamino compounds.

Carbon dioxide combines with proteins or hemoglobin with a loose bond so that, carbon dioxide is easily released into alveoli, where the partial pressure of carbon dioxide is low. Thus, the combination of carbon dioxide with proteins and hemoglobin is a reversible one. Amount of carbon dioxide transported in combination with plasma proteins is very less compared to the amount transported in combination with hemoglobin. It is because the quantity of proteins in plasma is only half of the quantity of hemoglobin.

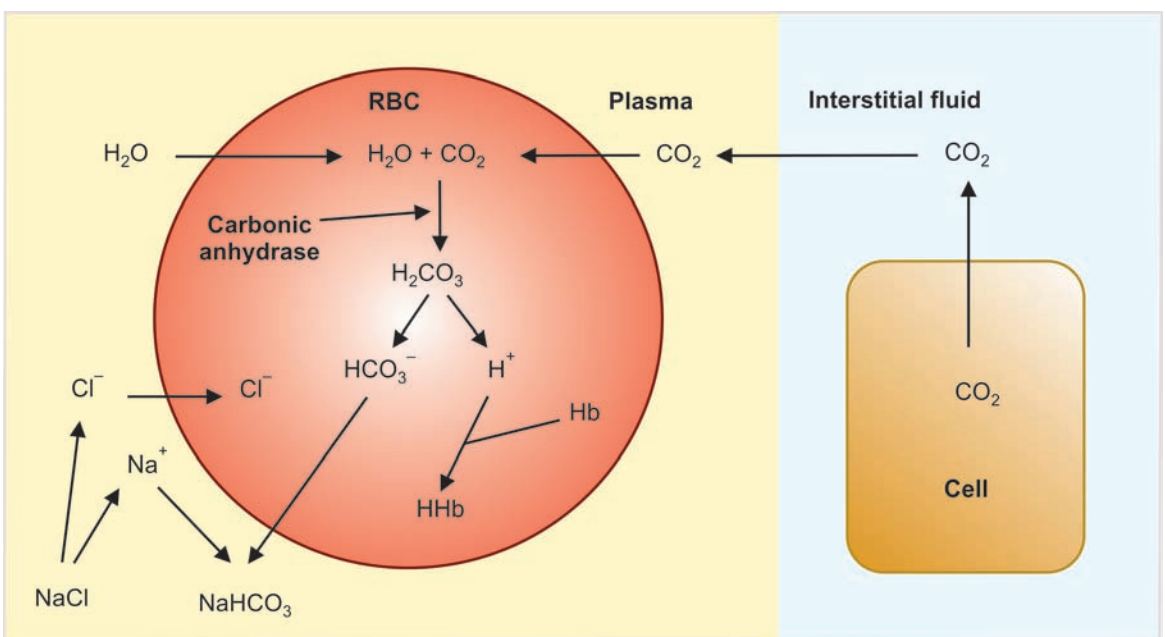


FIGURE 125.2: Transport of carbon dioxide in blood in the form of bicarbonate and chloride shift

■ CARBON DIOXIDE DISSOCIATION CURVE

Carbon dioxide is transported in blood as physical solution and in combination with water, plasma proteins and hemoglobin. The amount of carbon dioxide combining with blood depends upon the partial pressure of carbon dioxide.

Carbon dioxide dissociation curve is the curve that demonstrates the relationship between the partial pressure of carbon dioxide and the quantity of carbon dioxide that combines with blood.

Normal Carbon Dioxide Dissociation Curve

Normal carbon dioxide dissociation curve shows that the carbon dioxide content in the blood is 48 mL% when the partial pressure of carbon dioxide is 40 mm Hg and it is 52 mL% when the partial pressure of carbon dioxide is 48 mm Hg. Carbon dioxide content becomes 70 mL% when the partial pressure is about 100 mm Hg (Fig. 125.3).

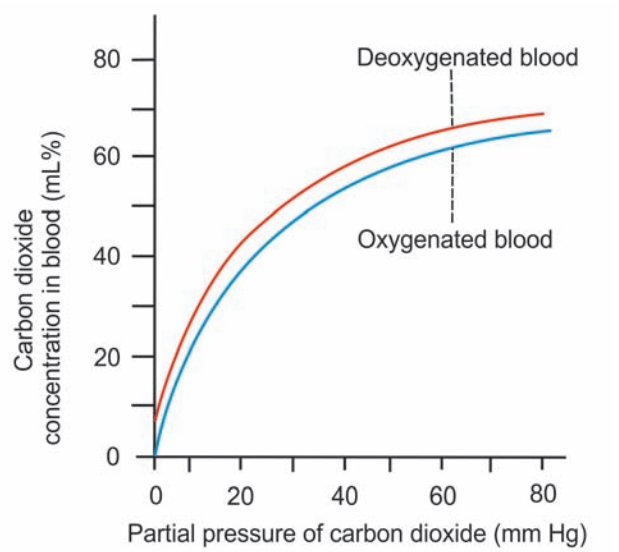


FIGURE 125.3: Carbon dioxide dissociation curve

Haldane Effect

Haldane effect is the effect by which combination of oxygen with hemoglobin displaces carbon dioxide from hemoglobin. It was first described by **John Scott Haldane** in 1860. Excess of oxygen content in blood causes shift of the carbon dioxide dissociation curve to right.

Causes for Haldane effect

Due to the combination with oxygen, hemoglobin becomes strongly acidic. It causes displacement of carbon dioxide from hemoglobin in two ways:

1. Highly acidic hemoglobin has low tendency to combine with carbon dioxide. So, carbon dioxide is displaced from blood.
2. Because of the acidity, hydrogen ions are released in excess. Hydrogen ions bind with bicarbonate ions to form carbonic acid. Carbonic acid in turn dissociates into water and carbon dioxide. Carbon dioxide is released from blood into alveoli.

Significance of Haldane effect

Haldane effect is essential for:

1. Release of carbon dioxide from blood into the alveoli of lungs
2. Uptake of oxygen by the blood.

Regulation of Respiration

Chapter 126

INTRODUCTION

Respiration is a reflex process. But it can be controlled voluntarily for a short period of about 40 seconds. However, by practice, breathing can be withheld for a long period. At the end of that period, the person is forced to breathe.

Respiration is subjected to variation, even under normal physiological conditions. For example, emotion and exercise increase the rate and force of respiration. But the altered pattern of respiration is brought back to normal, within a short time by some regulatory mechanisms in the body.

Normally, quiet regular breathing occurs because of two regulatory mechanisms:

1. Nervous or neural mechanism
2. Chemical mechanism.

NERVOUS MECHANISM

Nervous mechanism that regulates the respiration includes:

1. Respiratory centers
2. Afferent nerves
3. Efferent nerves.

RESPIRATORY CENTERS

Respiratory centers are group of neurons, which control the rate, rhythm and force of respiration. These centers are bilaterally situated in reticular formation of the brainstem (Fig. 126.1). Depending upon the situation in brainstem, the respiratory centers are classified into two groups:

A. Medullary centers consisting of
   1. Dorsal respiratory group of neurons
   2. Ventral respiratory group of neurons

B. Pontine centers
   3. Apneustic center
   4. Pneumotaxic center.

MEDULLARY CENTERS

1. *Dorsal Respiratory Group of Neurons*

Situation

Dorsal respiratory group of neurons are diffusely situated in the nucleus of **tractus solitarius** which is present in the upper part of the medulla oblongata (Fig. 126.1). Usually, these neurons are collectively called **inspiratory center.**

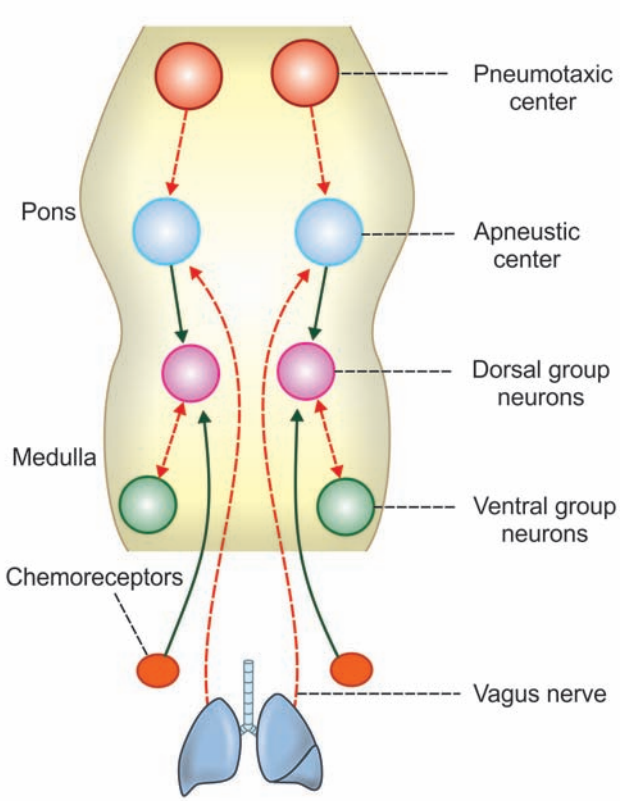


FIGURE 126.1: Nervous regulation of respiration.
Solid green line = Stimulation, Dotted red line = Inhibition.

All the neurons of dorsal respiratory group are **inspiratory neurons** and generate **inspiratory ramp** by the virtue of their **autorhythmic property** (Table 126.1).

Function

Dorsal group of neurons are responsible for basic rhythm of respiration (see below for details).

Experimental evidence

Electrical stimulation of these neurons in animals by using needle electrode causes contraction of inspiratory muscles and **prolonged inspiration.**

2. *Ventral Respiratory Group of Neurons*

Situation

Ventral respiratory group of neurons are present in **nucleus ambiguous** and **nucleus retroambiguous.** These two nuclei are situated in the medulla oblongata, anterior and lateral to the nucleus of tractus solitarius. Earlier, the ventral group neurons were collectively called **expiratory center.**

Ventral respiratory group has both **inspiratory** and **expiratory neurons.** Inspiratory neurons are found in the central area of the group. Expiratory neurons are in the caudal and rostral areas of the group.

Function

Normally, ventral group neurons are inactive during quiet breathing and become active during forced breathing. During forced breathing, these neurons stimulate both inspiratory muscles and expiratory muscles.

Experimental evidence

Electrical stimulation of the inspiratory neurons in ventral group causes contraction of inspiratory muscles and prolonged inspiration. Stimulation of expiratory neurons causes contraction of expiratory muscles and **prolonged expiration.**

■ PONTINE CENTERS

3. *Apneustic Center*

Situation

Apneustic center is situated in the reticular formation of lower pons.

Function

Apneustic center increases depth of inspiration by acting directly on dorsal group neurons.

Experimental evidence

Stimulation of apneustic center causes **apneusis.** Apneusis is an abnormal pattern of respiration, charac-

TABLE 126.1: Medullary centers

Features	Dorsal group	Ventral group
Situation	Diffusely situated in nucleus of tractus solitarius	In nucleus ambiguous and nucleus retroambiguous
Type of neurons	Inspiratory neurons	Inspiratory and expiratory neurons
Function	Always active Generate inspiratory ramp Has autorhythmic property	Inactive during quiet breathing Active during forced breathing

terized by prolonged inspiration followed by short, inefficient expiration.

4. Pneumotaxic Center

Situation

Pneumotaxic center is situated in the dorsolateral part of **reticular formation** in **upper pons.** It is formed by neurons of medial **parabrachial** and **subparabrachial nuclei.** Subparabrachial nucleus is also called **ventral parabrachial** or **Kölliker-Fuse nucleus.**

Function

Primary function of pneumotaxic center is to control the medullary respiratory centers, particularly the dorsal group neurons. It acts through apneustic center. Pneumotaxic center inhibits the apneustic center so that the dorsal group neurons are inhibited. Because of this, inspiration stops and expiration starts. Thus, pneumotaxic center influences the switching between inspiration and expiration.

Pneumotaxic center increases respiratory rate by reducing the duration of inspiration.

Experimental evidence

Stimulation of pneumotaxic center does not produce any typical effect, except slight **prolongation of expiration,** by inhibiting the dorsal respiratory group of neurons through apneustic center. Destruction or inactivation of pneumotaxic center results in apneusis.

■ CONNECTIONS OF RESPIRATORY CENTERS

Efferent Pathway

Nerve fibers from respiratory centers leave the brainstem and descend in anterior part of lateral columns of spinal cord.

These nerve fibers terminate on motor neurons in the anterior horn cells of cervical and thoracic segments of spinal cord. From motor neurons of spinal cord, two sets of nerve fibers arise:

1. Phrenic nerve fibers (C3 to C5), which supply the diaphragm
2. Intercostal nerve fibers (T1 to T11), which supply the external intercostal muscles.

Vagus nerve also contains some efferent fibers from the respiratory centers.

Afferent Pathway

Respiratory centers receive afferent impulses from:

1. Peripheral chemoreceptors and baroreceptors via branches of glossopharyngeal and vagus nerves
2. Stretch receptors of lungs via vagus nerve.

By receiving afferent impulses from these receptors, respiratory centers modulate the movements of thoracic cage and lungs through efferent nerve fibers.

■ INTEGRATION OF RESPIRATORY CENTERS

Role of Medullary Centers

Rhythmic discharge of inspiratory impulses

Dorsal respiratory group of neurons are responsible for the normal rhythm of respiration. These neurons maintain the normal rhythm of respiration by discharging impulses (action potentials) **rhythmically.** These impulses are transmitted to respiratory muscles by phrenic and intercostal nerves.

Inspiratory ramp

Inspiratory ramp is the pattern of impulse discharge from dorsal respiratory group of neurons. These impulses are characterized by steady increase in amplitude of the action potential. Impulse discharge from these neurons is not sudden and it is also not uniform.

Inspiratory ramp signals

To start with, the amplitude of action potential is low. It is due to the activation of only few neurons. Later, more and more neurons are activated, leading to gradual increase in the amplitude of action potential in a ramp fashion. Impulses of this type discharged from dorsal group of neurons are called inspiratory ramp signals.

Ramp signals are not produced continuously but only for a period of 2 seconds, during which inspiration occurs. After 2 seconds, ramp signals stop abruptly and do not appear for another 3 seconds. Switching off the ramp signals causes expiration. At the end of 3 seconds, inspriatory ramp signals reappear in the same pattern and the cycle is repeated.

Normally, during inspiration, dorsal respiratory group neurons inhibit expiratory neurons of ventral group. During expiration, the expiratory neurons inhibit the dorsal group neurons. Thus, the medullary respiratory centers control each other.

Significance of inspiratory ramp signals

Significance of inspiratory ramp signals is that there is a slow and steady inspiration, so that the filling of lungs with air is also steady.

Role of Pontine Centers

Pontine respiratory centers regulate the medullary centers. Apneustic center accelerates the activity of

dorsal group of neurons and the stimulation of this center causes prolonged inspiration.

Pneumotaxic center inhibits the apneustic center and restricts the duration of inspiration.

Pre-Bötzinger Complex

Pre-Bötzinger complex (**pre-BötC)** is an **additional respiratory center** found in animals. It is formed by a group of neurons called **pacemaker neurons,** located in the ventrolateral part of medulla. Pacemaker neurons generate the rhythmic respiratory impulses. Medullary centers send nerve fibers into this complex. Exact functioning mechanism of this complex is not known.

■ FACTORS AFFECTING RESPIRATORY CENTERS

Respiratory centers regulate the respiratory movements by receiving impulses from various sources in the body.

1. *Impulses from Higher Centers*

Higher centers alter the respiration by sending impulses directly to dorsal group of neurons. Impulses from anterior cingulate gyrus, genu of corpus callosum, olfactory tubercle and posterior orbital gyrus of cerebral cortex inhibit respiration. Impulses from motor area and Sylvian area of cerebral cortex cause **forced breathing.**

2. *Impulses from Stretch Receptors of Lungs: Hering-Breuer Reflex*

Hering-Breuer reflex is a **protective reflex** that restricts inspiration and prevents overstretching of lung tissues. It is initiated by the stimulation of stretch receptors of air passage.

Stretch receptors are the receptors which give response to stretch of the tissues. These receptors are situated on the wall of the bronchi and bronchioles.

Expansion of lungs during inspiration stimulates the stretch receptors. Impulses from stretch receptors reach the dorsal group neurons via vagal afferent fibers and inhibit them. So, inspiration stops and expiration starts (Fig. 126.2). Thus, the overstretching of lung tissues is prevented.

However, Hering-Breuer reflex does not operate during quiet breathing. It operates, only when the tidal volume increases beyond 1,000 mL.

Hering-Breuer inflation reflex and deflation reflex

The above mentioned reflex is called **Hering-Breuer inflation reflex** since it restricts the inspiration and limits the overstretching of lung tissues. Reverse of this reflex is called **Hering-Breuer deflation reflex** and it takes place during expiration. During expiration, as the stretching of lungs is absent, deflation occurs.

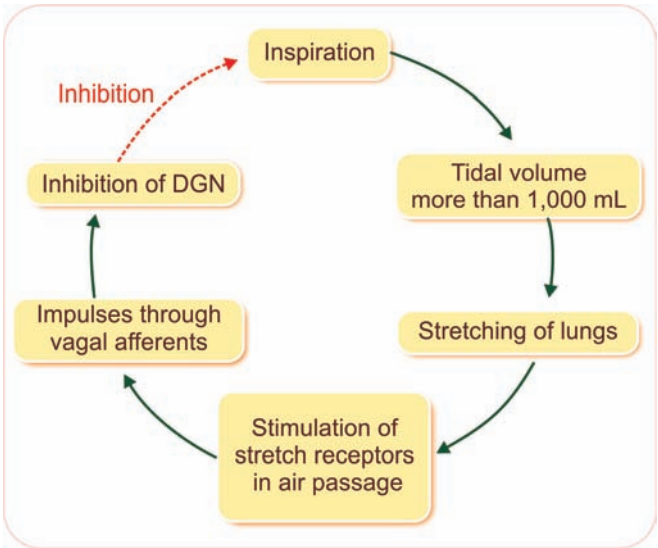


FIGURE 126.2: Hering-Breuer inflation reflex. DGN = Dorsal respiratory group of neurons. Dashed red arrow indicates inhibition.

3. *Impulses from 'J' Receptors of Lungs*

'J' receptors are **juxtacapillary receptors** which are present on the wall of the alveoli and have close contact with the pulmonary capillaries. **AS Paintal** discovered that these receptors are the sensory nerve endings of vagus. Nerve fibers from these receptors are non-myelinated and belong to C type. Few receptors are found on the wall of the bronchi.

Conditions when 'J' receptors are stimulated

i. Pulmonary congestion
ii. Pulmonary edema
iii. Pneumonia
iv. Over inflation of lungs
v. Microembolism in pulmonary capillaries
vi. Stimulation by exogenous and endogenous chemical substances such as histamine, halothane, bradykinin, serotonin and phenyldiguanide.

Effect of stimulation of 'J' receptors

Stimulation of the 'J' receptors produces a reflex response, which is characterized by **apnea.** Apnea is

followed by hyperventilation, bradycardia, hypotension and weakness of skeletal muscles.

Role of 'J' receptors in physiological conditions is not clear. However, these receptors are responsible for hyperventilation in patients affected by pulmonary congestion and left heart failure.

4. *Impulses from Irritant Receptors of Lungs*

Besides stretch receptors, there is another type of receptors in the bronchi and bronchioles of lungs, called irritant receptors. Irritant receptors are stimulated by irritant chemical agents such as ammonia and sulfur dioxide. These receptors send afferent impulses to respiratory centers via vagal nerve fibers.

Stimulation of irritant receptors produces **reflex hyperventilation** along with **bronchospasm.** Hyperventilation along with bronchospasm prevents further entry of harmful agents into the alveoli.

5. *Impulses from Baroreceptors*

Baroreceptors or **pressoreceptors** are the receptors which give response to change in blood pressure. Refer Chapter 101 for details of baroreceptors.

Function

Baroreceptors in carotid sinus and arch of aorta give response to increase in blood pressure. Whenever arterial blood pressure increases, baroreceptors are activated and send inhibitory impulses to vasomotor center in medulla oblongata. This causes decrease in blood pressure and inhibition of respiration. However, in physiological conditions, the role of baroreceptors in regulation of respiration is insignificant.

6. *Impulses from Chemoreceptors*

Chemoreceptors play an important role in the chemical regulation of respiration. Details of chemoreceptors and chemical regulation of respiration are explained later in this Chapter.

7. *Impulses from Proprioceptors*

Proprioceptors are the receptors which give response to change in the position of body. These receptors are situated in joints, tendons and muscles. Proprioceptors are stimulated during the muscular exercise and send impulses to brain, particularly cerebral cortex, through somatic afferent nerves. Cerebral cortex in turn causes hyperventilation by sending impulses to medullary respiratory centers.

8. *Impulses from Thermoreceptors*

Thermoreceptors are cutaneous receptors, which give response to change in the environmental temperature. Thermoreceptors are of two types, namely receptors for cold and receptors for warmth. When body is exposed to cold or when cold water is applied over the body, cold receptors are stimulated and send impulses to cerebral cortex via somatic afferent nerves. Cerebral cortex in turn, stimulates the respiratory centers and causes hyperventilation.

9. *Impulses from Pain Receptors*

Pain receptors are those which give response to pain stimulus. Whenever pain receptors are stimulated, the impulses are sent to cerebral cortex via somatic afferent nerves. Cerebral cortex in turn, stimulates the respiratory centers and causes hyperventilation (Fig. 126.3).

■ CHEMICAL MECHANISM

Chemical mechanism of regulation of respiration is operated through the chemoreceptors. Chemoreceptors are the sensory nerve endings, which give response to changes in chemical constituents of blood.

Changes in Chemical Constituents of Blood which Stimulate Chemoreceptors

1. Hypoxia (decreased pO_2)
2. Hypercapnea (increased pCO_2)
3. Increased hydrogen ion concentration.

Types of Chemoreceptors

Chemoreceptors are classified into two groups:

1. Central chemoreceptors
2. Peripheral chemoreceptors.

■ CENTRAL CHEMORECEPTORS

Central chemoreceptors are the chemoreceptors present in the brain.

Situation

Central chemoreceptors are situated in deeper part of medulla oblongata, close to the dorsal respiratory group of neurons. This area is known as **chemosensitive area** and the neurons are called chemoreceptors. Chemoreceptors are in close contact with blood and cerebrospinal fluid.

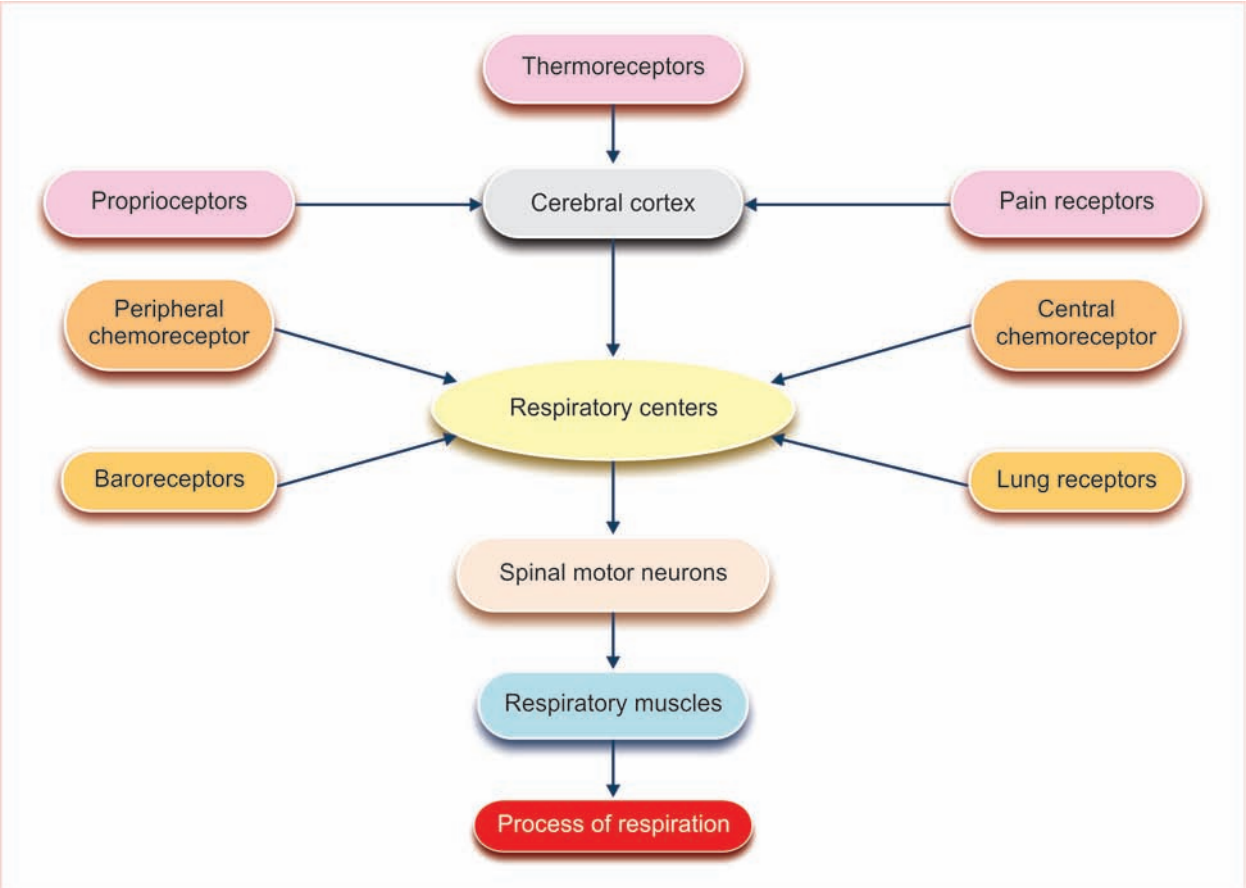


FIGURE 126.3: Factors affecting respiratory centers

Mechanism of Action

Central chemoreceptors are connected with respiratory centers, particularly the dorsal respiratory group of neurons through synapses. These chemoreceptors act slowly but effectively. Central chemoreceptors are responsible for 70% to 80% of increased ventilation through chemical regulatory mechanism.

Main stimulant for central chemoreceptors is the increased hydrogen ion concentration. However, if hydrogen ion concentration increases in the blood, it cannot stimulate the central chemoreceptors because, the hydrogen ions from blood cannot cross the **blood-brain barrier** and **blood-cerebrospinal fluid barrier.**

On the other hand, if carbon dioxide increases in the blood, it can easily cross the blood-brain barrier and blood-cerebrospinal fluid barrier and enter the interstitial fluid of brain or the cerebrospinal fluid. There, the carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it immediately dissociates into hydrogen ion and bicarbonate ion (Fig. 126.4).

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

Hydrogen ions stimulate the central chemoreceptors. From chemoreceptors, the excitatory impulses are sent to dorsal respiratory group of neurons, resulting in increased ventilation (increased rate and force of breathing). Because of this, excess carbon dioxide is washed out and respiration is brought back to normal. Lack of oxygen does not have significant effect on the central chemoreceptors, except that it generally depresses the overall function of brain.

■ PERIPHERAL CHEMORECEPTORS

Peripheral chemoreceptors are the chemoreceptors present in carotid and aortic region. Refer Chapter 101 for details.

Mechanism of Action

Hypoxia is the most potent stimulant for peripheral chemoreceptors. It is because of the presence of

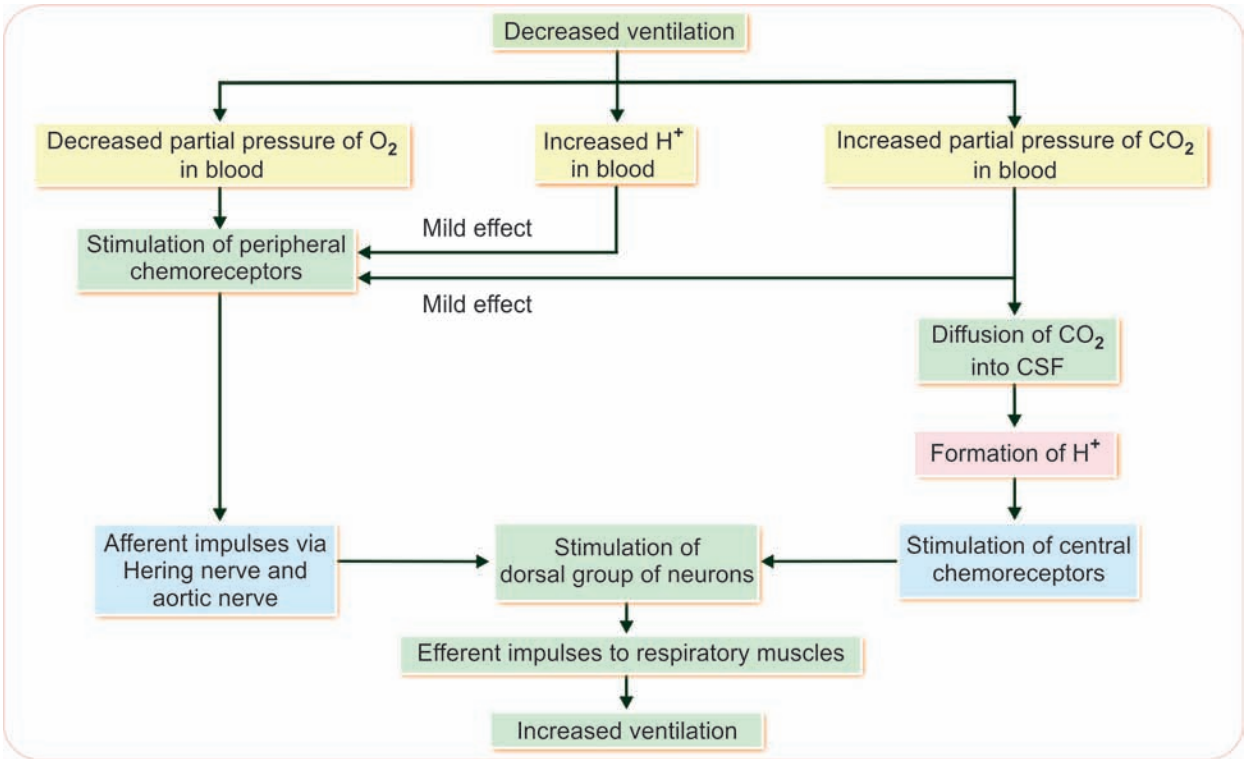


FIGURE 126.4: Chemical regulation of respiration. CSF = Cerebrospinal fluid.

oxygen sensitive potassium channels in the glomus cells of peripheral chemoreceptors.

Hypoxia causes closure of oxygen sensitive potassium channels and prevents potassium efflux. This leads to depolarization of **glomus cells** (receptor potential) and generation of action potentials in nerve ending.

These impulses pass through aortic and Hering nerves and excite the dorsal group of neurons. Dorsal group of neurons in turn, send excitatory impulses to respiratory muscles, resulting in increased ventilation. This provides enough oxygen and rectifies the lack of oxygen.

In addition to hypoxia, peripheral chemoreceptors are also stimulated by hypercapnea and increased hydrogen ion concentration. However, the sensitivity of peripheral chemoreceptors to hypercapnea and increased hydrogen ion concentration is mild.

Disturbances of Respiration

Chapter 127

- INTRODUCTION
- APNEA
- HYPERVENTILATION
- HYPOVENTILATION
- HYPOXIA
- OXYGEN TOXICITY (POISONING)
- HYPERCAPNEA
- HYPOCAPNEA
- ASPHYXIA
- DYSPNEA
- PERIODIC BREATHING
- CYANOSIS
- CARBON MONOXIDE POISONING
- ATELECTASIS
- PNEUMOTHORAX
- PNEUMONIA
- BRONCHIAL ASTHMA
- PULMONARY EDEMA
- PLEURAL EFFUSION
- PULMONARY TUBERCULOSIS
- EMPHYSEMA

INTRODUCTION

Normal respiratory pattern is called **eupnea.** Respiratory pattern is altered by many ways. Altered patterns of respiration are:

1. *Tachypnea:* Increase in the rate of respiration
2. *Bradypnea:* Decrease in the rate of respiration
3. *Polypnea:* Rapid, shallow breathing resembling panting in dogs. In this type of breathing, only the rate of respiration increases but the force does not increase significantly.
4. *Apnea:* Temporary arrest of breathing
5. *Hyperpnea:* Increase in pulmonary ventilation due to increase in rate or force of respiration. Increase in rate and force of respiration occurs after exercise. It also occurs in abnormal conditions like fever or other disorders.
6. *Hyperventilation:* Abnormal increase in rate and force of respiration, which often leads to dizziness and sometimes chest pain
7. *Hypoventilation:* Decrease in rate and force of respiration
8. *Dyspnea:* Difficulty in breathing
9. *Periodic breathing:* Abnormal respiratory rhythm.

APNEA

DEFINITION

Apnea is defined as the **temporary arrest** of breathing. Literally, apnea means absence of breathing. Apnea can also be produced voluntarily, which is called **breath holding** or **voluntary apnea.**

APNEA TIME

Breath holding time is known as apnea time. It is about 40 to 60 seconds in a normal person, after a deep inspiration.

CONDITIONS WHEN APNEA OCCURS

1. *Voluntary Effort*

Arrest of breathing by voluntary effort is known as **voluntary apnea** or **breath holding.** Breath holding time can be increased beyond 40 to 60 seconds by practice, exercise, willpower and yoga.

At the end of voluntary apnea, the subject is forced to breathe, which is called the **breaking point.** It is because of the accumulation of carbon dioxide in blood, which stimulates the respiratory centers. Besides increased carbon dioxide content in blood, hypoxia and increased hydrogen ion concentration are also responsible for stimulation of respiratory centers. Apnea is always followed by hyperventilation.

2. *Apnea after Hyperventilation*

Apnea occurs after hyperventilation. It is due to lack of carbon dioxide. During hyperventilation, more carbon dioxide is washed out. So, partial pressure of carbon dioxide in the blood decreases and the number of stimuli to the respiratory centers also decreases, leading to apnea. During apnea, carbon dioxide accumulates in the blood. When partial pressure of carbon dioxide increases, the respiratory centers are stimulated and respiration starts.

3. *Deglutition Apnea*

Arrest of breathing during deglutition is known as deglutition **(swallowing)** apnea. It occurs reflexly during pharyngeal stage of deglutition. When the bolus is pushed into esophagus from pharynx during pharyngeal stage of deglutition, there is possibility for bolus to enter the respiratory passage through larynx, causing serious consequences like choking. This is prevented by deglutition apnea, during which the larynx is closed by backward movement of epiglottis (Chapter 43).

4. *Vagal Apnea*

Vagal apnea is an **experimental apnea,** which is produced by the stimulation of vagus nerve in animals. Stimulation of vagus nerve causes apnea by inhibiting the inspiratory center.

5. *Adrenaline Apnea*

Adrenaline apnea is the apnea that occurs after injection of adrenaline. Administration of adrenaline produces marked increase in arterial blood pressure. It stimulates the baroreceptors, which in turn reflexly inhibit vasomotor center and the respiratory centers, causing fall in blood pressure and apnea.

CLINICAL CLASSIFICATION OF APNEA

Clinically, apnea is classified into three types:

1. Obstructive apnea
2. Central apnea
3. Mixed apnea.

1. *Obstructive Apnea*

Obstructive apnea occurs because of obstruction in the respiratory tract. Respiratory tract obstruction is mainly due to excess tissue growth like tonsils and adenoids. Common obstructive apnea is the sleep apnea.

Sleep apnea

Sleep apnea is the temporary stoppage of breathing that occurs repeatedly during sleep. It is also called **sleep disordered breathing** (SDB). It commonly affects overweight people.

Major cause for sleep apnea is obstruction of upper respiratory tract by excess tissue growth in airway, like enlarged tonsils and large tongue.

Characteristic feature of sleep apnea is loud **snoring.** Snoring without sleep apnea is called **simple** or **primary snoring.** But snoring with sleep apnea is serious and it may become life threatening. If left unnoticed, it may lead to hypertension, heart failure and stroke (refer Chapter 160 for sleep apnea syndrome).

2. *Central Apnea*

Central apnea occurs due to brain disorders, especially when the respiratory centers are affected. It is seen in premature babies. Typical feature of central apnea is a short pause in between breathing.

3. *Mixed Apnea*

Mixed apnea is a combination of central and obstructive apnea. It is usually seen in **premature babies** and in **full-term born infants.** Main reason for mixed apnea is the abnormal control of breathing due to immature or underdeveloped brain or respiratory system.

HYPERVENTILATION

DEFINITION

Hyperventilation means increased pulmonary ventilation due to forced breathing. It is also called **over ventilation.** In hyperventilation, both rate and force of breathing are increased and a large amount of air moves in and out of lungs. Thus, pulmonary ventilation is increased to a great extent. Very often, hyperventilation leads to dizziness, discomfort and chest pain.

CONDITIONS WHEN HYPERVENTILATION OCCURS

Hyperventilation mostly occurs in conditions like exercise when partial pressure of carbon dioxide (pCO_2) is increased. Excess of carbon dioxide stimulates the respiratory centers. Voluntarily also, hyperventilation can be produced. It is called voluntary hyperventilation.

EFFECTS OF HYPERVENTILATION

During hyperventilation, excessive carbon dioxide is washed out. In blood, the partial pressure of carbon dioxide is reduced. It causes suppression of respiratory centers, resulting in **apnea.** Apnea is followed by Cheyne-Stokes type of periodic breathing. After a period of **Cheyne-Stokes breathing,** normal respiration is restored (Fig. 127.1).

HYPOVENTILATION

DEFINITION

Hypoventilation is the decrease in pulmonary ventilation caused by decrease in rate or force of breathing. Thus, the amount of air moving in and out of lungs is reduced.

CONDITIONS WHEN HYPOVENTILATION OCCURS

Hypoventilation occurs when respiratory centers are suppressed or by administration of some drugs. It occurs during partial paralysis of respiratory muscles also.

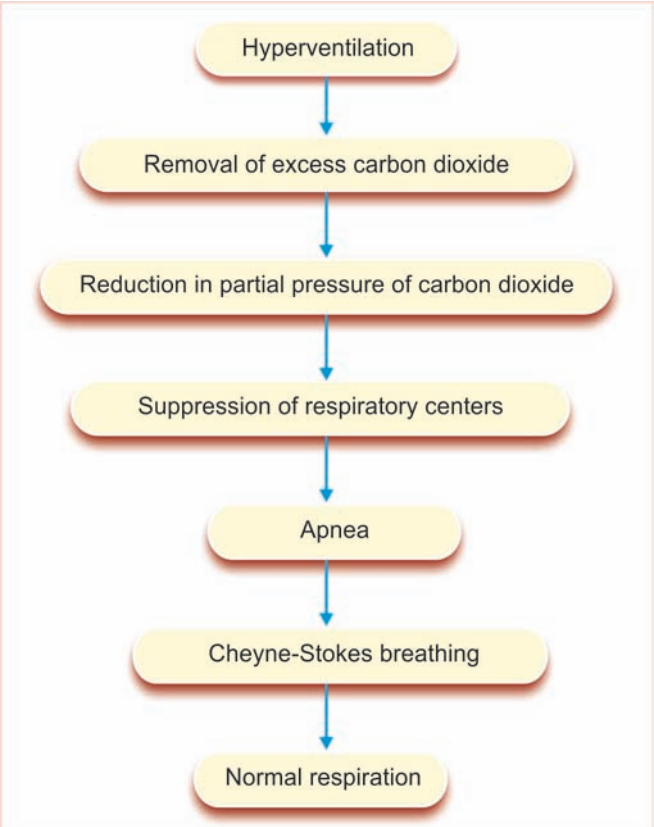


FIGURE 127.1: Effects of hyperventilation

EFFECTS OF HYPOVENTILATION

Hypoventilation results in development of hypoxia along with hypercapnea. It increases the rate and force of respiration, leading to dyspnea. Severe conditions result in lethargy, coma and death (Fig. 127.2).

HYPOXIA

DEFINITION

Hypoxia is defined as reduced availability of oxygen to the tissues. The term anoxia refers to absence of oxygen. In olden days, the term anoxia was in use. Since there is no possibility for total absence of oxygen in living conditions, use of this term is abandoned.

CLASSIFICATION AND CAUSES OF HYPOXIA

Four important factors which leads to hypoxia are:

1. Oxygen tension in arterial blood
2. Oxygen carrying capacity of blood
3. Velocity of blood flow
4. Utilization of oxygen by the cells.

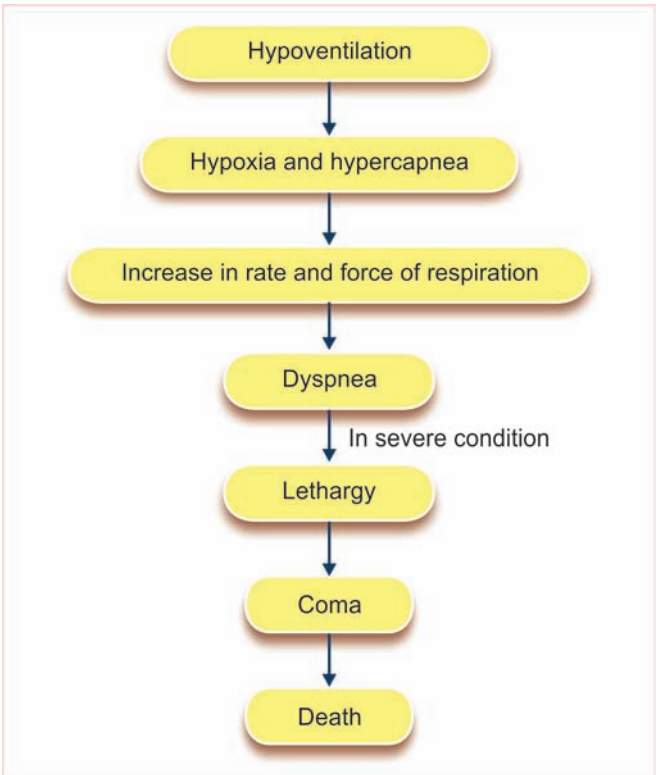


FIGURE 127.2: Effects of hypoventilation

On the basis of above factors, hypoxia is classified into four types:

1. Hypoxic hypoxia
2. Anemic hypoxia
3. Stagnant hypoxia
4. Histotoxic hypoxia.

Each type of hypoxia may be acute or chronic. Simultaneously, two or more types of hypoxia may be present.

1. *Hypoxic Hypoxia*

Hypoxic hypoxia means decreased oxygen content in blood. It is also called arterial hypoxia.

Causes for hypoxic hypoxia

Hypoxic hypoxia is caused by four factors.

i. Low oxygen tension in inspired (atmospheric) air, which does not provide enough oxygen
ii. Respiratory disorders associated with decreased pulmonary ventilation, which does not allow intake of enough oxygen
iii. Respiratory disorders associated with inadequate oxygenation in lungs, which does not allow diffusion of enough oxygen
iv. Cardiac disorders, in which enough blood is not pumped to transport oxygen.

i. *Low oxygen tension in inspired air*

Oxygen tension in inspired air is reduced in the following conditions:

a. High altitude
b. While breathing air in closed space
c. While breathing gas mixture containing low partial pressure of oxygen (PO_2).

Because of these conditions, required quantity of oxygen cannot enter the lungs.

ii. *Respiratory disorders associated with decreased pulmonary ventilation*

Pulmonary ventilation decreases in the following conditions:

a. Obstruction of respiratory passage as in asthma
b. Nervous and mechanical hindrance to respiratory movements as in poliomyelitis
c. Depression of respiratory centers as in brain tumors
d. Pneumothorax.

In these conditions, even though enough oxygen is available in the atmosphere, it cannot reach the lungs.

iii. *Respiratory disorders associated with inadequate oxygenation of blood in lungs*

Inadequate oxygenation of blood in lungs occurs in the following conditions:

a. Impaired alveolar diffusion as in emphysema
b. Presence of non-functioning alveoli as in fibrosis
c. Filling of alveoli with fluid as in pulmonary edema, pneumonia, pulmonary hemorrhage
d. Collapse of lungs as in bronchiolar obstruction
e. Lack of surfactant
f. Abnormal pleural cavity such as pneumothorax, hydrothorax, hemothorax and pyothorax
g. Increased venous admixture as in the case of bronchiectasis.

In these conditions, in spite of oxygen availability and entrance of oxygen into the alveoli, it cannot diffuse into the blood.

iv. *Cardiac disorders*

In congestive heart failure, oxygen availability and diffusion are normal, but the blood cannot be pumped from heart properly.

Characteristic features of hypoxic hypoxia

Hypoxic hypoxia is characterized by reduced oxygen tension in arterial blood. All other features remain normal (Table 127.1).

2. *Anemic Hypoxia*

Anemic hypoxia is the condition characterized by the inability of blood to carry enough amount of oxygen. Oxygen availability is normal. But the blood is not able to take up sufficient amount of oxygen due to anemic condition.

Causes for anemic hypoxia

Any condition that causes anemia can cause anemic hypoxia. It is caused by the following conditions:

i. Decreased number of RBCs
ii. Decreased hemoglobin content in the blood
iii. Formation of altered hemoglobin
iv. Combination of hemoglobin with gases other than oxygen and carbon dioxide.

i. *Decreased number of RBCs*

RBC decreases in conditions like bone marrow diseases, hemorrhage, etc.

ii. *Decreased hemoglobin content in the blood*

Conditions which decrease the RBC count or change the structure, shape and size of RBC (microcytes, macrocytes, spherocytes, sickle cells, poikilocytes, etc.) can decrease the hemoglobin content in blood.

iii. *Formation of altered hemoglobin*

Poisoning with chlorates, nitrates, ferricyanides, etc. causes oxidation of iron into ferric form and the hemoglobin is known as **methemoglobin.** Methemoglobin cannot combine with oxygen. Thus, the quantity of hemoglobin available for oxygen transport is decreased (Chapter 11).

iv. *Combination of hemoglobin with gases other than oxygen and carbon dioxide*

When hemoglobin combines with carbon monoxide, hydrogen sulfide or nitrous oxide, it looses the capacity to transport oxygen (Chapter 11).

Characteristic features of anemic hypoxia

Anemic hypoxia is characterized by decreased oxygen carrying capacity of blood. All other features remain normal (Table 127.1).

3. *Stagnant Hypoxia*

Stagnant hypoxia is the hypoxia caused by decreased velocity of blood flow. It is otherwise called hypokinetic hypoxia.

Causes for stagnant hypoxia

Stagnant hypoxia occurs mainly due to reduction in velocity of blood flow. Velocity of blood flow decreases in the following conditions:

i. Congestive cardiac failure
ii. Hemorrhage
iii. Surgical shock
iv. Vasospasm
v. Thrombosis
vi. Embolism.

Characteristic features of stagnant hypoxia

Stagnant hypoxia is characterized by decreased velocity of blood flow. All other features remain normal (Table 127.1).

4. *Histotoxic Hypoxia*

Histotoxic hypoxia is the type of hypoxia produced by the inability of tissues to utilize oxygen.

Causes for histotoxic hypoxia

Histotoxic hypoxia occurs due to cyanide or sulfide poisoning. These poisonous substances destroy the

TABLE 127.1: Characteristic features of different types of hypoxia

Features	Hypoxic hypoxia	Anemic hypoxia	Stagnant hypoxia	Histotoxic hypoxia
1. PO_2 in arterial blood	Reduced	Normal	Normal	Normal
2. Oxygen carrying capacity of blood	Normal	Reduced	Normal	Normal
3. Velocity of blood flow	Normal	Normal	Reduced	Normal
4. Utilization of oxygen by tissues	Normal	Normal	Normal	Reduced
5. Efficacy of oxygen therapy	100%	75%	< 50%	Not useful

cellular oxidative enzymes and there is a complete paralysis of **cytochrome oxidase system.** So, even if oxygen is supplied, the tissues are not in a position to utilize it.

Characteristic features of histotoxic hypoxia

Histotoxic hypoxia is characterized by inability of tissues to utilize oxygen even if it is delivered. All other features remain normal (Table 127.1).

■ EFFECTS OF HYPOXIA

Acute and severe hypoxia leads to unconsciousness. If not treated immediately, brain death occurs. Chronic hypoxia produces various symptoms in the body.

Effects of hypoxia are of two types:

1. Immediate effects
2. Delayed effects.

Immediate Effects

i. *Effects on blood*

Hypoxia induces secretion of **erythropoietin** from kidney. Erythropoietin increases production of RBC. This in turn, increases the oxygen carrying capacity of blood.

ii. *Effects on cardiovascular system*

Initially, due to the reflex stimulation of cardiac and vasomotor centers, there is an increase in rate and force of contraction of heart, cardiac output and blood pressure. Later, there is reduction in the rate and force of contraction of heart. Cardiac output and blood pressure are also decreased.

iii. *Effects on respiration*

Initially, respiratory rate increases due to chemoreceptor reflex. Because of this, large amount of carbon dioxide is washed out leading to **alkalemia.** Later, the respiration tends to be **shallow and periodic.** Finally, the rate and force of breathing are reduced to a great extent due to the failure of respiratory centers.

iv. *Effects on digestive system*

Hypoxia is associated with loss of appetite, nausea and vomiting. Mouth becomes dry and there is a feeling of thirst.

v. *Effects on kidneys*

Hypoxia causes increased secretion of erythropoietin from the juxtaglomerular apparatus. And **alkaline urine** is excreted.

vi. *Effects on central nervous system*

In mild hypoxia, the symptoms are similar to those of **alcoholic intoxication.**

Individual is depressed, apathetic with general loss of self control. The person becomes talkative, quarrelsome, ill-tempered and rude. The person starts shouting, singing or crying.

There is disorientation and loss of discriminative ability and loss of power of judgment. Memory is impaired. Weakness, lack of coordination and fatigue of muscles are common in hypoxia.

If hypoxia is acute and severe, there is a sudden loss of consciousness. If not treated immediately, **coma** occurs, which leads to **death.**

Delayed Effects of Hypoxia

Delayed effects appear depending upon the length and severity of the exposure to hypoxia.

The person becomes highly irritable and develops the symptoms of mountain sickness, such as nausea, vomiting, depression, weakness and fatigue.

■ TREATMENT FOR HYPOXIA – OXYGEN THERAPY

Best treatment for hypoxia is oxygen therapy, i.e. treating the affected person with oxygen. Pure oxygen or oxygen combined with another gas is administered.

Oxygen therapy is carried out by two methods:

1. By placing the patient's head in a 'tent' containing oxygen
2. By allowing the patient to breathe oxygen either from a mask or an intranasal tube.

Depending upon the situation, oxygen therapy can be given either under normal atmospheric pressure or under high pressure (hyperbaric oxygen).

In Normal Atmospheric Pressure

With normal atmospheric pressure, i.e. at one atmosphere (760 mm Hg), administration of pure oxygen is well tolerated by the patient for long hours. However, after 8 hours or more, lung tissues show fluid effusion and edema. Other tissues are not affected very much because of **hemoglobin-oxygen buffer system.**

In High Atmospheric Pressure – Hyperbaric Oxygen

Hyperbaric oxygen is the pure oxygen with high atmospheric pressure of 2 or more than 2 atmosphere. Hyperbaric oxygen therapy with 2 to 3 atmosphere

is tolerated by the patient for about 5 hours. During this period, the dissolved form of oxygen increases in arterial blood because the oxygen carrying capacity of hemoglobin is limited. At this level, tissue oxygen tension also increases to about 200 mm Hg. However, tissues tolerate the high partial pressure of oxygen, without much adverse effects. But, oxygen toxicity develops when pure oxygen is administered for long periods. Refer oxygen toxicity below.

Efficacy of Oxygen Therapy in Different Types of Hypoxia

Oxygen therapy is the best treatment for hypoxia. But it is not effective equally in all types of hypoxia. Value of oxygen therapy depends upon the type of hypoxia. So, before deciding the oxygen therapy, one should recall the physiological basis of different types of hypoxia.

In hypoxic hypoxia, the oxygen therapy is 100% useful. In anemic hypoxia, oxygen therapy is moderately effective to about 70%. In stagnant hypoxia, the effectiveness of oxygen therapy is less than 50%. In histotoxic hypoxia, the oxygen therapy is not useful at all. It is because, even if oxygen is delivered, the cells cannot utilize oxygen.

OXYGEN TOXICITY (POISONING)

DEFINITION AND CAUSE

Oxygen toxicity is the increased oxygen content in tissues, beyond certain critical level. It is also called oxygen poisoning. It occurs because of breathing pure oxygen with a high pressure of 2 to 3 atmosphere (hyperbaric oxygen). In this condition, an excess amount of oxygen is transported in plasma as dissolved form because oxygen carrying capacity of hemoglobin is limited to 1.34 mL/g.

EFFECTS OF OXYGEN TOXICITY

1. Lung tissues are affected first with tracheobronchial irritation and pulmonary edema
2. Metabolic rate increases in all the body tissues and the tissues are burnt out by excess heat. Heat also destroys **cytochrome system,** leading to damage of tissues.
3. When brain is affected, first hyperirritability occurs. Later, it is followed by increased muscular twitching, ringing in ears and dizziness.
4. Finally, the toxicity results in convulsions, coma and death.

HYPERCAPNEA

DEFINITION

Hypercapnea is the increased carbon dioxide content of blood.

CONDITIONS WHEN HYPERCAPNEA OCCURS

Hypercapnea occurs in conditions, which leads to blockage of respiratory pathway, as in case of asphyxia. It also occurs while breathing the air containing excess carbon dioxide content.

EFFECTS OF HYPERCAPNEA

1. *Effects on Respiration*

During hypercapnea, the respiratory centers are stimulated excessively. It leads to dyspnea.

2. *Effects on Blood*

The pH of blood reduces and blood becomes acidic.

3. *Effects on Cardiovascular System*

Hypercapnea is associated with tachycardia and increased blood pressure. There is flushing of skin due to peripheral vasodilatation.

4. *Effects on Central Nervous System*

During hypercapnea, the nervous system is also affected, resulting in headache, depression and laziness. These symptoms are followed by muscular rigidity, fine tremors and generalized convulsions. Finally, giddiness and loss of consciousness occur.

HYPOCAPNEA

DEFINITION

Hypocapnea is the decreased carbon dioxide content in blood.

CONDITIONS WHEN HYPOCAPNEA OCCURS

Hypocapnea occurs in conditions associated with hypoventilation. It also occurs after prolonged hyperventilation, because of washing out of excess carbon dioxide.

EFFECTS OF HYPOCAPNEA

1. *Effects on Respiration*

Respiratory centers are depressed, leading to decreased rate and force of respiration.

2. *Effects on Blood*

The pH of blood increases, leading to respiratory alkalosis. Calcium concentration decreases. It causes tetany, which is characterized by **neuromuscular hyperexcitability** and **carpopedal spasm.**

3. *Effects on Central Nervous System*

Dizziness, mental confusion, muscular twitching and loss of consciousness are the common features of hypocapnea.

ASPHYXIA

DEFINITION

Asphyxia is the condition characterized by combination of **hypoxia** and **hypercapnea,** due to obstruction of air passage.

CONDITIONS WHEN ASPHYXIA OCCURS

Axphyxia develops in conditions characterized by acute obstruction of air passage such as:

1. Strangulation
2. Hanging
3. Drowning, etc.

EFFECTS OF ASPHYXIA

Effects of asphyxia develop in three stages:

1. Stage of hyperpnea
2. Stage of convulsions
3. Stage of collapse.

1. *Stage of Hyperpnea*

Hyperpnea is the first stage of asphyxia. It extends for about 1 minute. In this stage, breathing becomes deep and rapid. It is due to the powerful stimulation of respiratory centers by excess of carbon dioxide. Hyperpnea is followed by **dyspnea** and **cyanosis.** Eyes become more prominent.

2. *Stage of Convulsions*

Stage of convulsions is characterized mainly by convulsions (uncontrolled involuntary muscular contractions). Duration of this stage is less than 1 minute. Hypercapnea acts on brain and produces the following effects:

i. Violent expiratory efforts
ii. Generalized convulsions
iii. Increase in heart rate
iv. Increase in arterial blood pressure
v. Loss of consciousness.

3. *Stage of Collapse*

Stage of collapse lasts for about 3 minutes. Severe hypoxia produces the following effects during this stage:

i. Depression of centers in brain and disappearance of convulsions
ii. Development of respiratory gasping occurs. During respiratory gasping, there is stretching of the body with opening of mouth, as if gasping for breath.
iii. Dilatation of pupils
iv. Decrease in heart rate
v. Loss of all reflexes.

Duration between the gasps is gradually increased and finally death occurs.

All together, asphyxia extends only for 5 minutes. The person can survive only by timely help such as relieving the respiratory obstruction, good aeration, etc.

DYSPNEA

DEFINITION

Dyspnea means difficulty in breathing. It is otherwise called the air hunger. Normally, the breathing goes on without consciousness. When breathing enters the consciousness and produces discomfort, it is called dyspnea. Dyspnea is also defined 'as a consciousness of necessity for increased respiratory effort'.

DYSPNEA POINT

Dyspnea point is the level at which there is increased ventilation with severe breathing discomfort. The normal person is not aware of any increase in breathing until the pulmonary ventilation is doubled. The real discomfort develops when ventilation increases by 4 or 5 times.

CONDITIONS WHEN DYSPNEA OCCURS

Physiologically, dyspnea occurs during severe muscular exercise. The pathological conditions when dyspnea occurs are:

1. *Respiratory Disorders*

Dyspnea occurs in the respiratory disorders, characterized by mechanical or nervous hindrance to respiratory movements and obstruction in any part of respiratory tract. Thus, dyspnea occurs in:

i. Pneumonia
ii. Pulmonary edema
iii. Pulmonary effusion
iv. Poliomyelitis
v. Pneumothorax
vi. Severe asthma, etc.

2. *Cardiac Disorders*

Dyspnea is common in left ventricular failure and decompensated mitral stenosis.

3. *Metabolic Disorders*

Metabolic disorders, which cause dyspnea are diabetic acidosis, uremia and increased hydrogen ion concentration.

■ DYSPNEIC INDEX

Dyspneic index is the index between breathing reserve and maximum breathing capacity (MBC). Breathing reserve is the balance (difference) between MBC and respiratory minute volume (RMV).

For example, in a normal subject, MBC is 116 L and RMV is 6 L.

$$\text{Dyspneic index} = \frac{\text{MBC} - \text{RMV}}{\text{MBC}} \times 100$$

$$= \frac{116 - 6}{116} \times 100$$

$$= 94.8\%.$$

Dyspnea develops when the dyspneic index decreases below 60%.

■ PERIODIC BREATHING

■ DEFINITION AND TYPES

Periodic breathing is the abnormal or uneven respiratory rhythm. It is of two types:

1. Cheyne-Stokes breathing
2. Biot breathing.

■ CHEYNE-STOKES BREATHING

Features of Cheyne-Stokes Breathing

Cheyne-Stokes breathing is the periodic breathing characterized by rhythmic hyperpnea and apnea. It is the most common type of periodic breathing. It is marked by two alternate patterns of respiration:

i. Hyperpneic period
ii. Apneic period.

Hyperpneic period – waxing and waning of breathing

To begin with, the breathing is shallow. Force of respiration increases gradually and reaches the maximum (hyperpnea). Then, it decreases gradually and reaches minimum and is followed by apnea. Gradual increase followed by gradual decrease in force of respiration is called **waxing** and **waning** of breathing (Fig. 127.3).

Apneic period

When, the force of breathing is reduced to minimum, cessation of breathing occurs for a short period. It is again followed by hyperpneic period and the cycle is repeated. Duration of one cycle is about 1 minute. Sometimes, waxing and waning of breathing occurs without apnea.

Causes for Waxing and Waning

Initially, during forced breathing, large quantity of carbon dioxide is washed out from blood. When partial pressure of carbon dioxide decreases, respiratory centers become inactive. It causes apnea. During

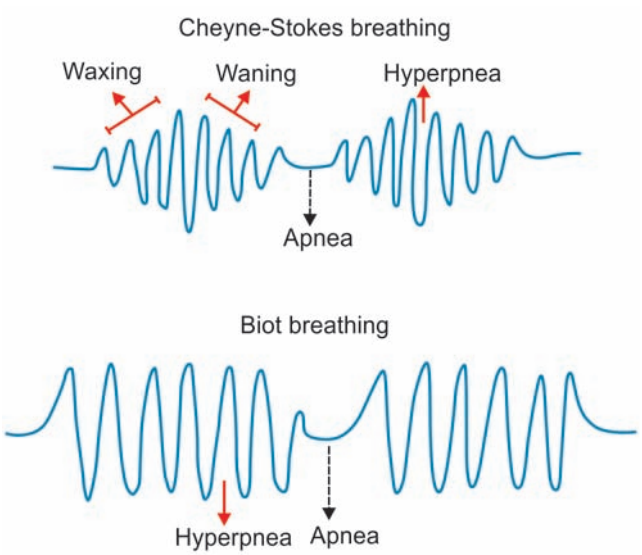


FIGURE 127.3: Periodic breathing

apnea, there is accumulation of carbon dioxide **(hypercapnea)** and reduction in oxygen tension **(hypoxia).** Now, the respiratory centers are activated, resulting in gradual increase in the force of breathing. When the force of breathing reaches maximum, the cycle is repeated (Fig. 127.4).

Conditions when Cheyne-Stokes Breathing Occurs

Cheyne-Stokes breathing occurs in both physiological and pathological conditions.

Physiological conditions when Cheyne-Stokes breathing occurs

i. During deep sleep
ii. In high altitude
iii. After prolonged voluntary hyperventilation
iv. During hibernation in animals
v. In newborn babies
vi. After severe muscular exercise.

Pathological conditions when Cheyne-Stokes breathing occurs

i. During increased intracranial pressure
ii. During advanced cardiac diseases, leading to cardiac failure
iii. During advanced renal diseases, leading to uremia
iv. Poisoning by narcotics
v. In premature infants.

■ BIOT BREATHING

Features of Biot Breathing

Biot breathing is another form of periodic breathing characterized by period of **apnea** and **hyperpnea.** Waxing and waning of breathing do not occur (Fig. 127.2). After apneic period, hyperpnea occurs abruptly.

Causes of Abrupt Apnea and Hyperpnea

Due to apnea, carbon dioxide accumulates and it stimulates the respiratory centers, leading to hyperventilation. During hyperventilation, lot of carbon dioxide is washed out. So, the respiratory centers are not stimulated and apnea occurs.

Conditions when Biot Breathing Occurs

Biot breathing does not occur in physiological conditions. It occurs only in pathological conditions. It occurs in conditions involving nervous disorders due to lesions or injuries to brain.

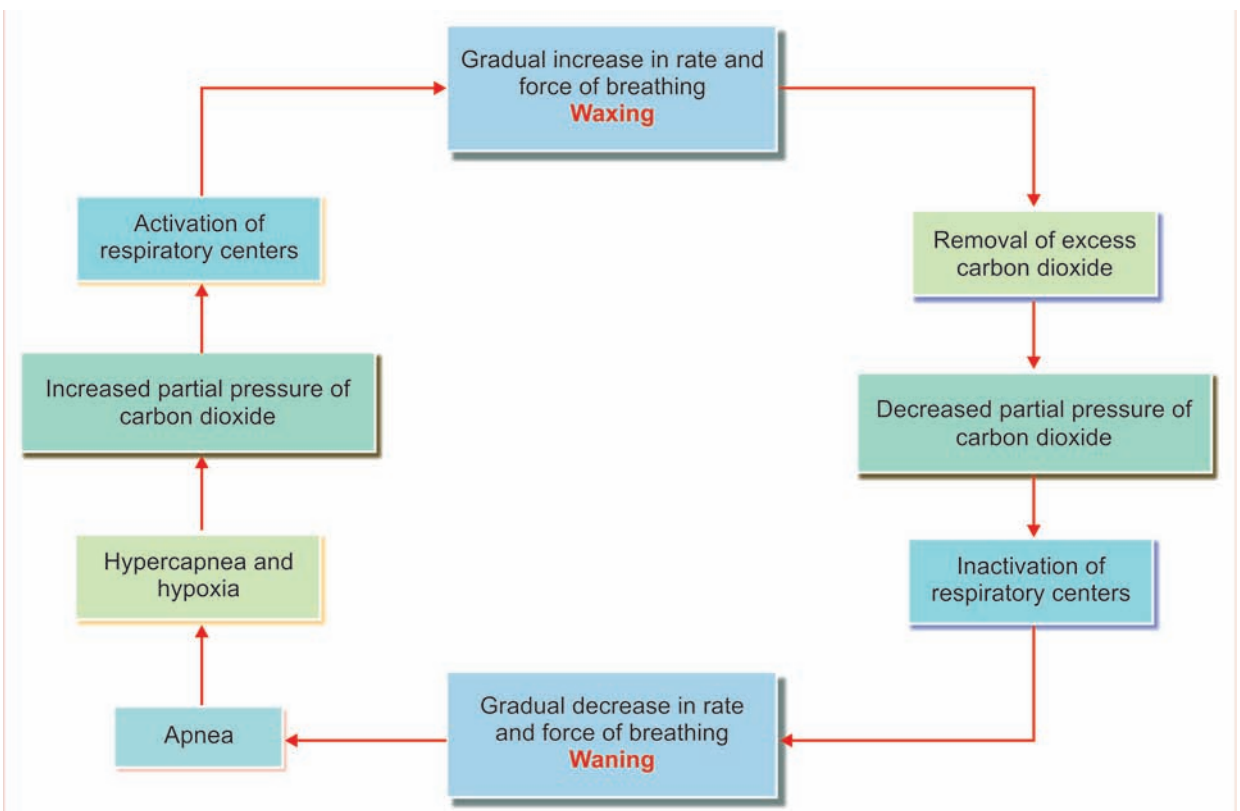


FIGURE 127.4: Cycle of waxing and waning

CYANOSIS

DEFINITION

Cyanosis is defined as the diffused **bluish coloration** of skin and mucus membrane. It is due to the presence of large amount of **reduced hemoglobin** in the blood. Quantity of reduced hemoglobin should be at least 5 to 7 g/dL in the blood to cause cyanosis.

DISTRIBUTION OF CYANOSIS

When it occurs, cyanosis is distributed all over the body. But, it is more marked in certain regions where the skin is thin. These areas are lips, cheeks, ear lobes, nose and fingertips above the base of the nail.

CONDITIONS WHEN CYANOSIS OCCURS

1. Any condition which leads to arterial hypoxia and stagnant hypoxia. Cyanosis does not occur in anemic hypoxia because the hemoglobin content itself is less. It does not occur in histotoxic hypoxia because of tissue damage.
2. Conditions when altered hemoglobin is formed. Due to poisoning, hemoglobin is altered into methemoglobin or sulfhemoglobin, which causes cyanosis. The **cyanotic discoloration** is due to the dark color of these compounds only and not due to reduced hemoglobin.
3. Conditions like polycythemia when blood flow is slow. During polycythemia, because of increased RBC count, the viscosity of blood is increased and it leads to **sluggishness of blood** flow. So the quantity of deoxygenated blood increases, which causes **bluish discoloration of skin.**

CYANOSIS AND ANEMIA

Cyanosis usually occurs only when the quantity of reduced hemoglobin is about 5 g/dL to 7 g/dL. But, in anemia, the hemoglobin content itself is less. So, cyanosis cannot occur in anemia.

CARBON MONOXIDE POISONING

INTRODUCTION

Carbon monoxide is a **dangerous gas** since it causes death. This gas was used by Greeks and Romans for the **execution of criminals.** Carbon monoxide causes more deaths than any other gases.

SOURCES OF CARBON MONOXIDE

Common sources for carbon monoxide are exhaust of gasoline engines, coal mines, gases from guns, deep wells and underground drainage system (Chapter 11).

TOXIC EFFECTS OF CARBON MONOXIDE

Carbon monoxide is a dangerous gas because it displaces oxygen from hemoglobin, by binding with same site in hemoglobin for oxygen. So, oxygen transport and oxygen carrying capacity of the blood are decreased.

Hemoglobin has got 200 times more affinity for carbon monoxide than for oxygen. So, even with low partial pressure of 0.4 mm Hg of carbon monoxide in alveoli, 50% of hemoglobin is saturated with it. It can be dangerous if the partial pressure increases to 0.6 mm Hg, (1/1,000 of volume concentration in air). Presence of carboxyhemoglobin decreases the release of oxygen from hemoglobin and the oxygen-hemoglobin dissociation curve shifts to left.

It is still more dangerous because, during carbon monoxide poisoning, the partial pressure of oxygen in blood may normal in spite of low oxygen content of blood. So, the regular feedback stimulation of respiratory centers by hypoxia does not take place because of normal partial pressure of oxygen.

However, low oxygen content in blood affects the brain, resulting in unconsciousness. The condition becomes fatal if immediate treatment is not given.

Carbon monoxide is toxic to the **cytochrome system** in cells also.

SYMPTOMS OF CARBON MONOXIDE POISONING

Symptoms of carbon monoxide poisoning depend upon its concentration:

1. While breathing air with 1% of carbon monoxide, saturation of hemoglobin with carbon monoxide becomes 15% to 20%. **Mild symptoms like headache** and **nausea** appear.
2. While breathing air containing carbon monoxide more than 1%, the saturation becomes 30% to 40%. It causes **convulsions, cardiorespiratory arrest, loss of consciousness** and **coma.**
3. When hemoglobin saturation is above 50%, death occurs.

TREATMENT FOR CARBON MONOXIDE POISONING

Treatment for carbon monoxide poisoning includes:

1. Immediate termination of exposure to carbon monoxide
2. Providing adequate ventilation and artificial respiration
3. Administration of 100% oxygen if possible. It is to replace carbon monoxide
4. Administration of air with few percent of carbon dioxide, if possible. It is done to stimulate the respiratory centers.

ATELECTASIS

DEFINITION

Atelectasis refers to partial or complete **collapse of lungs.** When a large portion of lung is collapsed, the partial pressure of oxygen is reduced in blood, leading to respiratory disturbances.

CAUSES

1. Deficiency or inactivation of surfactant. It causes collapse of lungs due to increased surface tension, which leads to respiratory distress syndrome.
2. Obstruction of a bronchus or a bronchiole. In this condition, the alveoli attached to the bronchus or bronchiole are collapsed.
3. Presence of air **(pneumothorax),** fluid **(hydrothorax),** blood **(hemothorax)** or pus **(pyothorax)** in the pleural space.

EFFECTS

Effects of atelectasis are decreased partial pressure of oxygen, leading to dyspnea.

PNEUMOTHORAX

DEFINITION

Pneumothorax is the presence of air in pleural space. Intrapleural pressure, which is always negative, becomes positive in pneumothorax and it causes collapse of lungs.

CAUSES

Air enters the pleural cavity because of damage of chest wall or lungs during accidents, bullet injury or stab injury.

TYPES AND EFFECTS

Pneumothorax is of three types:

1. Open pneumothorax
2. Closed pneumothorax
3. Tension pneumothorax.

1. *Open Pneumothorax*

After the injury, an open communication is developed between pleural cavity and exterior. It is known as open pneumothorax. Air enters the pleural cavity during inspiration and comes out during expiration. Collapse of lungs causes hypoxia, hypercapnea, dyspnea, cyanosis and asphyxia.

2. *Closed Pneumothorax*

During a mild injury, air enters into the pleural cavity and then the hole in the pleura is sealed and closed. It is called the closed pneumothorax. It does not produce hypoxia. Air from the pleural cavity is absorbed slowly.

3. *Tension Pneumothorax*

During injuries, sometimes the tissues over the hole in the chest wall or the lungs behave like a fluttering valve. It permits entrance of air into pleural cavity during inspiration but prevents the exit of air during expiration, due to its valvular nature. Because of this, the intrapleural pressure increases above atmospheric pressure. This condition is very fatal, since it results in collapse of the whole lung.

PNEUMONIA

DEFINITION

Pneumonia is the **inflammation** of lung tissues, followed by the accumulation of blood cells, fibrin and exudates in the alveoli. Affected part of the lungs becomes **consolidated.**

CAUSES

Inflammation of lung is caused by:

1. Bacterial or viral infection
2. Inhaling noxious chemical substance.

TYPES

Pneumonia is of two types, namely **lobar pneumonia** and **lobular pneumonia.** When it is lobular and associated with inflammation of bronchi, it is known as **bronchopneumonia.**

EFFECTS

Following are the effects of pneumonia:

1. Fever
2. Compression of chest and chest pain
3. Shallow breathing
4. Cyanosis
5. Sleeplessness (insomnia)
6. Delirium.

Delirium

Delirium is the extreme mental condition that is caused by cerebral hypoxia.

Features of delirium

i. Confused mental state (confused way of thought and speech)
ii. Illusion (misinterpretation of a sensory stimulus)
iii. Hallucination (feeling of sensations such as touch, pain, taste, smell, etc. without any stimulus)
iv. Disorientation (loss of ability to recognize place, time and other persons)
v. Hyperexcitability
vi. Loss of memory.

BRONCHIAL ASTHMA

DEFINITION

Bronchial asthma is the respiratory disease characterized by difficult breathing with **wheezing.** Wheezing refers to **whistling type** of respiration. It is due to bronchiolar constriction, caused by spastic contraction of smooth muscles in bronchioles, leading to obstruction of air passage. Obstruction is further exaggerated by the edema of mucus membrane and accumulation of mucus in the lumen of bronchioles.

CAUSES

1. *Inflammation of air passage:* Leukotrienes released from eosinophils and mast cells during inflammation cause bronchospasm.
2. *Hypersensitivity of afferent glossopharyngeal and vagal ending in larynx and afferent trigeminal endings in nose:* Hypersensitivity of these nerve endings is produced by some allergic substances like foreign proteins.
3. *Pulmonary edema and congestion of lungs caused by left ventricular failure:* Asthma developed due to this condition is called cardiac asthma.

FEATURES

Asthma is a **paroxysmal** (sudden) **disorder** because the attack commences and ends abruptly. During the attack, the difficulty is felt both during inspiration and expiration. Bronchioles have inherent tendency to dilate during inspiration and constrict during expiration. So, more difficulty is experienced during expiration. During expiration, great effort is exerted by all the expiratory muscles causing compression of chest. There is severe contraction of abdominal muscles also. So, air from lungs is pushed through the constricted bronchioles, producing a whistling sound.

Because of difficulty during expiration, the lungs are not deflated completely, so that the residual volume and functional residual capacity are increased.

There is reduction in:

i. Tidal volume
ii. Vital capacity
iii. Forced expiratory volume in 1 second (FEV1)
iv. Alveolar ventilation
v. Partial pressure of oxygen in blood.

Carbon dioxide accumulates, resulting in acidosis, dyspnea and cyanosis.

PULMONARY EDEMA

DEFINITION

Pulmonary edema is the accumulation of serous fluid in the alveoli and the interstitial tissue of lungs.

CAUSES

1. Increased pulmonary capillary pressure due to left ventricular failure or mitral valve disease
2. Pneumonia
3. Breathing harmful chemicals like chlorine or sulfur dioxide.

EFFECTS

Effects of pulmonary edema are severe dyspnea, cough with frothy bloodstained expectoration, cyanosis and cold extremities.

Chronic interstitial edema leads to asthma. Alveolar edema is fatal and causes sudden death due to suffocation.

PLEURAL EFFUSION

DEFINITION

Pleural effusion is the accumulation of large amount of fluid in the pleural cavity.

CAUSES

1. Blockage of lymphatic drainage
2. Excessive transudation of fluid from pulmonary capillaries due to increased pulmonary capillary pressure caused by left ventricular failure
3. Inflammation of pleural membrane which damages the capillary membrane, allowing leakage of fluid and plasma proteins into the pleural cavity.

FEATURES

Pleural effusion causes atelectasis, leading to dyspnea and other respiratory disturbances.

PULMONARY TUBERCULOSIS

DEFINITION

Tuberculosis is the disease caused by **tubercle bacilli.** This disease can affect any organ in the body. However, the lungs are affected more commonly. Infected tissue is invaded by macrophages and later it becomes fibrous. Affected tissue is called **tubercle.**

FEATURES

Initially, alveoli in the affected part become non-functioning, due to thickness of respiratory membrane. If a large part of lungs is involved, the diffusing capacity is very much reduced. In severe conditions, the destruction of the lung tissue is followed by formation of large **abscess cavities.**

EMPHYSEMA

DEFINITION AND CAUSES

Emphysema is one of the obstructive respiratory diseases in which lung tissues are extensively damaged. Damage of lung tissues results in loss of alveolar walls. Because of this, the elastic recoil of lungs is also lost.

Emphysema is caused by:

1. Cigarette smoking
2. Exposure to oxidant gases
3. Untreated bronchitis.

DEVELOPMENT OF EMPHYSEMA

1. Smoke or oxidant gases irritate the bronchi and bronchioles, leading to chronic infection
2. It increases the mucus secretion from the respiratory epithelial cells causing obstruction of air passage
3. Cilia of respiratory epithelial cells are partially paralyzed and the movement is very much reduced. Because of this, the mucus cannot be removed from the respiratory passage.
4. Destruction of alveolar mucus membrane
5. Destruction of elastic tissues occur. Normally, there is loss of some elastic tissues because of the proteolytic enzyme called **elastase.** But, that is very much negligible. Moreover, liver produces **elastase inhibitors** especially, **α_1-antitrypsin,** which prevents the destruction of elastic tissues. But, due to heavy smoking or because of constant exposure to oxidant gases, the pulmonary alveolar macrophages increase in number. Macrophages release a chemical substance, which attracts a large number of leukocytes. Leukocytes release proteases including elastase, which destroy the elastic tissues of the lungs.

EFFECTS OF EMPHYSEMA

1. Airway resistance increases several times due to the bronchiolar obstruction. So, the movement of air through the respiratory passage becomes very difficult. It is more pronounced during expiration.
2. Due to the destruction of alveolar membrane and elastic tissues, the lungs become loose and floppy. So, the diffusing capacity reduces to a great extent. However, lung compliance increases (Chapter 120) and the aeration of blood is impaired. Enough oxygen cannot diffuse into blood and carbon dioxide cannot diffuse out.
3. Obstruction also affects ventilation-perfusion ratio, resulting in poor aeration of blood
4. Due to the destruction of lung tissues, the number of pulmonary capillaries also decreases. It increases the pulmonary vascular resistance, leading to pulmonary hypertension.
5. Over the years, chronic emphysema could lead to hypoxia and hypercapnea. It will finally cause prolonged and severe air hunger (dyspnea), leading to death.

High Altitude and Space Physiology

Chapter 128

- HIGH ALTITUDE
- BAROMETRIC PRESSURE AND PARTIAL PRESSURE OF OXYGEN AT DIFFERENT ALTITUDES
- CHANGES IN THE BODY AT HIGH ALTITUDE
  - EFFECTS OF HYPOXIA
  - EFFECTS OF EXPANSION OF GASES ON THE BODY
  - EFFECTS OF REDUCED ATMOSPHERIC TEMPERATURE
  - EFFECTS OF LIGHT RAYS
- MOUNTAIN SICKNESS
  - DEFINITION
  - SYMPTOMS
  - TREATMENT
- ACCLIMATIZATION
  - DEFINITION
  - CHANGES DURING ACCLIMATIZATION
- AVIATION PHYSIOLOGY
  - ACCELERATIVE FORCE
  - GRAVITATIONAL FORCE
  - EFFECTS OF GRAVITATIONAL FORCES ON THE BODY
  - PREVENTION OF EFFECTS OF G FORCES ON THE BODY
- SPACE PHYSIOLOGY
  - EFFECTS OF TRAVEL BY SPACECRAFT

HIGH ALTITUDE

High altitude is the region of earth located at an altitude of above 8,000 feet from mean sea level. People can ascend up to this level, without any adverse effect. Different altitudes are given in Table 128.1.

Characteristic feature of high altitude is the **low barometric pressure.** However, amount of oxygen available in the atmosphere is same as that of sea level. Due to low barometric pressure, partial pressure of gases, particularly oxygen proportionally decreases. It leads to hypoxia.

Carbon dioxide in high altitude is very much negligible and it does not create any problem.

TABLE 128.1: Different altitudes

Altitude	Feet	Meter
High altitude	8,000 to 13,000	2,500 to 4,000
Very high altitude	13,000 to 18,000	4,000 to 5,500
Extreme altitude	> 18,000	> 5,500

BAROMETRIC PRESSURE AND PARTIAL PRESSURE OF OXYGEN AT DIFFERENT ALTITUDES

Barometric pressure decreases at different altitudes. Accordingly, partial pressure of oxygen also decreases

and produces various effects on the body. Barometric pressure and partial pressure of oxygen at different altitudes and their common effects on the body are given in Table 128.2.

■ CHANGES IN THE BODY AT HIGH ALTITUDE

When a person is exposed to high altitude, particularly by rapid ascent, the various systems in the body cannot cope with lowered oxygen tension and effects of hypoxia start. Besides hypoxia, some other factors are also responsible for the changes in functions of the body at high altitude.

Factors Affecting Physiological Functions at High Altitude

1. Hypoxia
2. Expansion of gases
3. Fall in atmospheric temperature
4. Light rays.

■ EFFECTS OF HYPOXIA

Refer Chapter 127 for effects of hypoxia.

■ EFFECTS OF EXPANSION OF GASES ON THE BODY

Volume of gases increases when the barometric pressure is reduced. So at high altitude, due to the decreased barometric pressure, volume of all gases increases in atmospheric air, as well as in the body.

At the sea level with atmospheric pressure of 760 mm Hg, if the volume of gas is 1 liter, at the height of 18,000 feet (where atmospheric pressure is 379 mm Hg), it becomes 2 liter. And it becomes 3 liter, at the height of 30,000 feet (where atmospheric pressure is 226 mm Hg).

Expansion of gases in GI tract causes painful distention of stomach and intestine. It is minimized by supporting the abdomen with a belt or by evacuation of the gases. Expansion of gases also destroys the alveoli.

During very rapid ascent from sea level to over 30,000 feet height, the gases evolve as bubbles, particularly nitrogen, resulting in decompression sickness. Refer Chapter 129 for details of decompression sickness.

TABLE 128.2: Barometric pressure, partial pressure of oxygen and common effects at different altitudes

Altitude (feet)	Barometric pressure (mm Hg)	Partial pressure of oxygen (mm Hg)	Common effects
Sea level	760	159	–
5,000	600	132	No hypoxia
10,000	523	110	Mild symptoms of hypoxia start appearing
15,000	400	90	Moderate hypoxia develops with following symptoms: – Reduction in visual acuity – Effects on mental functions: – Improper judgment and – Feeling of over confidence
20,000	349	73	Severe hypoxia appears with cardiorespiratory symptoms such as – Increase in heart rate and cardiac output – Increase in respiratory rate and respiratory minute volume This is the highest level for permanent inhabitants
25,000	250	62	This is the critical altitude for survival – Hypoxia becomes severe – Breathing oxygen becomes essential
29,628	235	49	This is the height of Mount Everest
30,000	226	47	Symptoms become severe even with oxygen
50,000	87	18	Hypoxia becomes more severe even with pure oxygen

EFFECTS OF REDUCED ATMOSPHERIC TEMPERATURE

Environmental temperature falls gradually at high altitudes. The temperature decreases to about 0°C at the height of 10,000 feet. It becomes –22°C at the height of 20,000 feet. At the altitude of 40,000 feet, the temperature falls to –44°C. Injury due to cold or frostbite occurs if the body is not adequately protected by warm clothing.

EFFECTS OF LIGHT RAYS

Skin becomes susceptible for injury due to many harmful rays like **ultraviolet rays** of sunlight. Moreover, the sunrays reflected by the snow might injure the retina of the eye, if it is not protected with suitable tinted glasses.

Severity of all these effects depends upon the speed at which one ascends in high altitude. The effects are comparatively milder or moderate in slow ascent and are severe in rapid ascent.

MOUNTAIN SICKNESS

DEFINITION

Mountain sickness is the condition characterized by adverse effects of hypoxia at high altitude. It is commonly developed in persons going to high altitude for the first time. It occurs within a day in these persons, before they get acclimatized to the altitude.

SYMPTOMS

In mountain sickness, the symptoms occur mostly in digestive system, cardiovascular system, respiratory system and nervous system. Symptoms of mountain sickness are:

1. *Digestive System*

Loss of appetite, nausea and vomiting occur because of expansion of gases in GI tract.

2. *Cardiovascular System*

Heart rate and force of contraction of heart increases.

3. *Respiratory System*

Pulmonary blood pressure increases due to increased blood flow. Blood flow increases because of vasodilatation induced by hypoxia. Increased pulmonary blood pressure results in pulmonary edema, which casus breathlessness.

4. *Nervous System*

Symptoms occuring in nervous system are headache, depression, disorientation, irritability, lack of sleep, weakness and fatigue. These symptoms are developed because of **cerebral edema.** Sudden exposure to hypoxia in high altitude causes vasodilatation in brain. **Autoregulation** mechanism of cerebral blood flow fails to cope with hypoxia. It leads to an increased capillary pressure and leakage of fluid from capillaries into the brain tissues.

TREATMENT

Symptoms of mountain sickness disappear by breathing oxygen.

ACCLIMATIZATION

DEFINITION

Acclimatization refers to the adaptations or the adjustments by the body in high altitude. While staying at high altitudes for several days to several weeks, a person slowly gets adapted or adjusted to the low oxygen tension, so that hypoxic effects are reduced. It enables the person to ascent further.

CHANGES DURING ACCLIMATIZATION

Various changes that take place during acclimatization help the body to cope with adverse effects of hypoxia at high altitude. Following changes occur in the body during acclimatization:

1. *Changes in Blood*

During acclimatization, RBC count increases and packed cell volume rises from normal value of 45% to about 59%. Hemoglobin content in the blood rises from 15 g% to 20 g%. So, the oxygen carrying capacity of the blood is increased. Thus, more oxygen can be carried to tissues, in spite of hypoxia. Increase in packed cell volume and hemoglobin content is due to erythropoietin actions.

Increase in RBC count, packed cell volume and hemoglobin content is due to erythropoietin, that is released from juxtaglomerular apparatus of kidney.

2. *Changes in Cardiovascular System*

Overall activity of cardiovascular system is increased in high altitude. There is an increase in rate and force of contraction of the heart and cardiac output. Vascularity in the body is increased due to vasodilatation induced

by hypoxia. So, blood flow to vital organs such as heart, brain, muscles, etc. increases.

3. *Changes in Respiratory System*

i. *Pulmonary ventilation*

Pulmonary ventilation increases up to 65%. This is the **immediate compensation** for hypoxia in high altitude and this alone helps the person to ascend several thousand feet. Increase in pulmonary ventilation is due to the stimulation of chemoreceptors (Chapter 126).

ii. *Pulmonary hypertension*

Increased cardiac output increases the pulmonary blood flow that leads to pulmonary hypertension. It is very common even in persons acclimatized to high altitude. In some of these persons, pulmonary hypertension is associated with right ventricular hypertrophy.

iii. *Diffusing capacity of gases*

Due to increased pulmonary blood flow and increased ventilation, diffusing capacity of gases increases in alveoli. It enables more diffusion of oxygen in blood.

4. *Changes in Tissues*

Both in human beings and animals residing at high altitudes permanently, the cellular oxidative enzymes involved in metabolic reactions are more than the inhabitants at sea level.

Even when a sea level inhabitant stays at high altitude for certain period, the amount of oxidative enzymes is not increased. So, the elevation in the amount of oxidative enzymes occurs only in fully acclimatized persons. An increase in the number of mitochondria is observed in these persons.

■ AVIATION PHYSIOLOGY

Aviation physiology is the study of physiological responses of the body in **aviation environment.**

Flying exerts great effects on the body through **accelerative forces** and **gravitational forces,** which are developed during the **flight maneuvering.** Pilots and other crew members of aircraft are trained to overcome the effects of these forces.

■ ACCELERATIVE FORCE

Acceleration means change in velocity. Flying straight in horizontal plane with constant velocity has minimum effects on the body. However, changes in velocity produce severe physiological effects. Accelerative forces are developed in the flight during linear, radial or centripetal and angular acceleration.

■ GRAVITATIONAL FORCE

Gravitational force (G force) is the major factor that develops accelerative force. **G force** and the direction in which body receives the force are responsible for physiological changes in the body during acceleration.

Force or pull of gravity upon the body is expressed in **G unit.** On the earth, this pull is responsible for body weight. Force of gravity while sitting, standing or lying position is considered to be equal to body weight and it is referred as 1 G. G unit increases in acceleration. If we say that G unit increases to 5 G during acceleration, it means that the force of gravity on body at that moment is equal to five times the body weight.

While traveling in an airplane, elevator or a car, if there is a sudden change in speed or direction, passengers are thrown or centrifuged in the opposite direction. It is because of change in the G unit. G unit may increase or decrease. Increase in G unit is called positive G and decrease in G unit is called **negative G. Positive G** occurs while increasing the speed (acceleration). Negative G occurs while decreasing the speed (slowing down; deceleration). G unit is altered during the change in direction also.

While flying, both positive G and negative G cause physiological changes in the body.

■ EFFECTS OF GRAVITATIONAL FORCES ON THE BODY

Effects of Positive G

Major effects of positive G during acceleration are on the blood circulation. When G unit increases to about 4 to 5 G, blood is pushed toward the lower parts of the body including abdomen. So the cardiac output decreases, resulting in reduced blood supply to the brain and eyes. Decreased blood flow in turn, decreases oxygen supply (hypoxia) to the head and leads to following disturbances:

1. *Grayout*

Grayout is the **graying of vision** that occurs when blood flow to eyes starts diminishing. It occurs because the retina is more sensitive to hypoxia than brain. Though physical impairment does not occur, grayout is considered as a warning for decreased blood flow to head.

2. *Blackout*

Blackout is the complete **loss of vision** that occurs when retinal function is affected by hypoxia. Consciousness and muscular activities are still retained. But it indicates the risk of loss of consciousness.

3. *Loss of consciousness*

When force increases beyond 5 G, hypoxia reaches the critical level and causes loss of consciousness. It may be associated with convulsions. Unconscious state may last for about 15 seconds. After recovery from unconsciousness, the person needs another 10 to 15 minutes for orientation. If the affected person happens to be a lone pilot, then he will loose control over his aircraft.

4. *Fracture of bones*

When force increases to about 20 G, bones, particularly the spine, becomes susceptible for fracture even during sitting posture.

Effects of Negative G

Negative G develops while flying downwards (inverted flying). It causes the following disturbances:

1. *Hyperemia*

When the force decreases to –4 to –6 G, **hyperemia** (abnormal increase in blood flow) occurs in head because the blood is pushed towards head. Sometimes the blood accumulates in head, resulting in **brain edema.** There is congestion, flushing of face and mild headache. Negative G at this level is tolerable and the effects are only momentary. Brain also can withstand hyperemia in such conditions.

2. *Redout and headache*

Redout is the **blurring of vision** and sudden reddening of visual field, caused by engorgement of blood vessels in head. When the negative G reaches to about –15 G to –20 G, there is dilatation and congestion of blood vessels in head and eyes, resulting in redout and headache. Blood vessels in brain may not be affected much because of CSF. When blood accumulates in brain, there is simultaneous pooling of CSF in cranium. The high pressure exerted by CSF acts as a cushion (buffer) and protects the blood vessels of brain.

3. *Loss of consciousness*

High negative G affects the body by other means. It increases the pressure in the blood vessels of chest and neck. It causes bradycardia or irregular heartbeat, which adds to stagnation of blood in head. All these factors ultimately lead to unconsciousness.

■ PREVENTION OF EFFECTS OF G FORCES ON THE BODY

Body can be protected from the effects of G forces, particularly positive G by the following methods:

1. *By Using Abdominal Belts*

Pooling of blood in the abdominal blood vessels is prevented by using abdominal belt and leaning forward while sitting in the aircraft. This procedure postpones grayout or blackout.

2. *By Using Anti-G Suit*

Anti-G suit exerts a positive pressure on lower limbs and abdomen and prevents the pooling of blood in lower part of the body.

■ SPACE PHYSIOLOGY

Space physiology is the study of physiological responses of the body in space and spacecrafts.

Major differences between the environments of earth and space are atmosphere, radiation and gravity. These three factors challenge the human survival in space. Atmospheric factors include atmospheric pressure, temperature, humidity and gas composition.

Spacecraft or **spacelab** is provided with stable and sophisticated environmental control system, which maintains all the atmospheric factors close to earth's environment. **Astronauts** also wear **launch and entry suit (LES).** LES is a pressurized suit that protects the body from space environment.

Another factor which affects the body in the space is **weightlessness.** Weightlessness is because of absence of gravity (microgravity).

■ EFFECTS OF TRAVEL BY SPACECRAFT

While traveling by spacecraft, the astronauts experience some intense symptoms only during blast off, due to acceleration and during landing because of deceleration. Otherwise, the accelerative forces are least while traveling in a spacecraft, since the spacecraft cannot make rapid changes in speed or direction like an aircraft.

Most of the physiological changes occur due to weightlessness in space travel. These changes are responsible for the adaptation of astronaut's body to space environment. Further, problems develop only when they return to earth. They require a longtime to readapt to earth environment.

Effects of weightlessness in spacecraft are:

1. *Effects on Cardiovascular Systems and Kidneys*

Cardiovascular changes are due to the fluid shift. Due to absence of gravity, blood moves from lower part to upper part of the body (upper trunk and head). It causes **enlargement of heart** to cope up with increased blood flow. In addition, there is an accumulation of other body fluids in upper part. Now, the compensatory mechanism in the body interprets the increase in blood and other fluids as a serious threat and starts correcting it by excreting large amount of fluid through kidneys. It causes decrease in blood volume and the heart need not pump the blood against gravity in space. So, initially enlarged heart starts shrinking slowly and becomes small. Thus during the initial fluid shift, astronauts experience dizziness or feeling of fainting.

Along with water, kidneys excrete electrolytes also. Because of this, osmolarity of body fluids is not altered. So the thirst center is not stimulated and the astronauts do not feel thirsty during space travel.

2. *Effects on Blood*

Plasma volume decreases due to excretion of fluid through urine. RBC count also decreases and it is called space anemia.

3. *Effects on Musculoskeletal System*

Because of microgravity in space, the muscles need not support the body against gravity. Astronauts move by floating instead of using their legs. This leads to decrease in muscle mass and muscle strength. **Endurance** of the muscles also decreases. Bones become weak. **Osteoclastic activity** increases during space travel. Calcium removed from bone is excreted through urine.

4. *Effects on Immune System*

Space travel causes suppression of immune system in the body.

5. *Space Motion Sickness*

After obtaining weightlessness, some astronauts develop space motion sickness. It is characterized by nausea, vomiting, headache and malaise (generalized feeling of discomfort or lack of well-being or illness that is associated with sensation of exhaustion). It persists for two or three days and then disappears. It is thought that the motion sickness occurs due to abnormal stimulation of vestibular apparatus and fluid shift.

Deep Sea Physiology

Chapter 129

INTRODUCTION

In high altitude, the problem is with **low atmospheric (barometric) pressure.** In deep sea or mines, the problem is with **high barometric pressure.** Increased pressure creates two major problems:

1. Compression effect on the body and internal organs
2. Decrease in volume of gases.

BAROMETRIC PRESSURE AT DIFFERENT DEPTHS

At sea level, the barometric pressure is 760 mm Hg, which is referred as 1 atmosphere. At the depth of every 33 feet (about 10 m), the pressure increases by 1 atmosphere. Thus, at the depth of 33 feet, the pressure is 2 atmospheres. It is due to the air above water and the weight of water itself. Pressure at different depths is given in Table 129.1.

EFFECT OF HIGH BAROMETRIC PRESSURE – NITROGEN NARCOSIS

Narcosis refers to unconsciousness or **stupor** produced by drugs. Stupor refers to lethargy with suppression of sensations and feelings. Nitrogen narcosis means narcotic effect produced by nitrogen at high pressure.

Nitrogen narcosis is common in deep sea divers, who breathe **compressed air** (air under high pressure). Breathing compressed air is essential for a deep sea diver or an underwater tunnel worker. It is to equalize the surrounding high pressure acting on thoracic wall and abdomen.

Eighty percent of the atmospheric air is nitrogen. Being an inert gas, it does not produce any known effect on the functions of the body at normal atmospheric pressure (sea level). When a person breathes **pressurized air** as in deep sea, the **narcotic effect** of nitrogen appears. It produces an altered mental state, similar to **alcoholic intoxication.**

TABLE 129.1: Barometric pressure and its effects at different depth

Depth (feet)	Atmospheric pressure (mm Hg)	Effects on the subject
Sea level	1	–
33	2	–
66	3	–
100	4	Symptoms of nitrogen narcosis appear
133	5	Lack of concentration Becomes jovial and careless
166	6	Starts feeling drowsy
200	7	Feels fatigued, weak and careless
233	8	Looses power of judgment Unable to do skilled work
266	9	Becomes unconscious
Barometric pressure: 1 atmosphere = 760 mm Hg		

■ MECHANISM

Nitrogen is soluble in fat. During compression by high barometric pressure in deep sea, nitrogen escapes from blood vessels and gets dissolved in the fat present in various parts of the body, especially the neuronal membranes. Dissolved nitrogen acts like an **anesthetic agent** suppressing the neuronal excitability. Nitrogen remains in dissolved form in the fat till the person remains in the deep sea.

■ SYMPTOMS

1. First symptom starts appearing at a depth of 120 feet. The person becomes very jovial, careless and does not understand the seriousness of the conditions.
2. At the depth of 150 to 200 feet, the person becomes drowsy
3. At 200 to 250 feet depth, the person becomes extremely fatigued and weak. There is loss of concentration and judgment. Ability to perform skilled work or movements is also lost.
4. Beyond the depth of 250 feet, the person becomes unconscious.

■ PREVENTION

Nitrogen narcosis can be prevented by mixing **helium** with oxygen. Helium is used as a substitute for nitrogen, to dilute oxygen during deep water diving. Helium also produces some effects like nausea and dizziness. But, the adverse effects of helium are less severe than nitrogen narcosis.

Nitrogen narcosis may be prevented by limiting the depth of dives. Effects of nitrogen narcosis may also be minimized by safe diving procedures such as proper maintenance of equipments and less work effort. In addition, alcohol consumption should be avoided 24 hours before diving.

■ TREATMENT

Symptoms of nitrogen narcosis completely disappear when the diver returns to a depth of 60 feet. There is no need for any further treatment since nitrogen narcosis does not have any hangover effect. However, the physician should be consulted if the diver loses consciousness.

■ DECOMPRESSION SICKNESS

■ DEFINITION

Decompression sickness is the disorder that occurs when a person returns rapidly to normal surroundings (atmospheric pressure) from the area of high atmospheric pressure like deep sea. It is also known as **dysbarism, compressed air sickness, caisson disease, bends** or **diver's palsy.**

■ CAUSE

High barometric pressure at deep sea leads to compression of gases in the body. Compression reduces the volume of gases.

Among the respiratory gases, oxygen is utilized by tissues. Carbon dioxide can be expired out. But,

nitrogen, which is present in high concentration, i.e. 80% is an inert gas. So, it is neither utilized nor expired. When nitrogen is compressed by high atmospheric pressure in deep sea, it escapes from blood vessels and enters the organs. As it is fat soluble, it gets dissolved in the fat of the tissues and tissue fluids. It is very common in the brain tissues.

As long as the person remains in deep sea, nitrogen remains in solution and does not cause any problem. But, if the person ascends rapidly and returns to atmospheric pressure, decompression sickness occurs.

Due to sudden return to atmospheric pressure, the nitrogen is decompressed and escapes from the tissues at a faster rate. Being a gas, it forms **bubbles** while escaping rapidly. The bubbles travel through blood vessels and ducts. In many places, the bubbles obstruct the blood flow and produce air **embolism,** leading to decompression sickness.

Underground tunnel workers who use the **caissons** (pressurized chambers) also develop decompression **(caisson disease)** sickness. Pressure in the chamber is increased to prevent the entry of water inside. Decompression sickness also occurs in a person who ascends up rapidly from sea level in an airplane without any precaution.

■ SYMPTOMS

Symptoms of decompression sickness are mainly due to the escape of nitrogen from tissues in the form of bubbles.

Symptoms are:

1. Severe pain in tissues, particularly the joints, produced by nitrogen bubbles in the myelin sheath of sensory nerve fibers
2. Sensation of numbness, tingling or pricking (paresthesia) and itching
3. Temporary paralysis due to nitrogen bubbles in the myelin sheath of motor nerve fibers
4. Muscle cramps associated with severe pain
5. Occlusion of coronary arteries followed by coronary ischemia, caused by bubbles in the blood
6. Occlusion of blood vessels in brain and spinal cord also
7. Damage of tissues of brain and spinal cord because of obstruction of blood vessels by the bubbles
8. Dizziness, paralysis of muscle, shortness of breath and choking occur
9. Finally, fatigue, unconsciousness and death.

■ PREVENTION

Decompression sickness is prevented by proper precautionary measures. While returning to mean sea level, the ascent should be very slow with short stay at regular intervals. **Stepwise ascent** allows nitrogen to come back to the blood, without forming bubbles. It prevents the decompression sickness.

■ TREATMENT

If a person is affected by decompression sickness, first recompression should be done. It is done by keeping the person in a **recompression chamber.** Then, he is brought back to atmospheric pressure by reducing the pressure slowly.

Hyperbaric oxygen therapy may be useful.

■ SCUBA

SCUBA (self-contained underwater breathing apparatus) is used by the deep sea divers and the underwater tunnel workers, to prevent the ill effects of increased barometric pressure in deep sea or tunnels.

This instrument can be easily carried and it contains air cylinders, valve system and a mask. By using this instrument, it is possible to breathe air or gas mixture without high pressure. Also, because of the valve system, only the amount of air necessary during inspiration enters the mask and the expired air is expelled out of the mask.

Disadvantage of this instrument is that the person using this can remain in the sea or tunnel only for a short period. Especially, beyond the depth of 150 feet, the person can stay only for few minutes.

Effects of Exposure to Cold and Heat

Chapter 130

- EFFECTS OF EXPOSURE TO COLD
  - HEAT PRODUCTION
  - PREVENTION OF HEAT LOSS
- EFFECTS OF EXPOSURE TO SEVERE COLD
  - LOSS OF TEMPERATURE REGULATING CAPACITY
  - FROSTBITE
- EFFECTS OF EXPOSURE TO HEAT
  - HEAT EXHAUSTION
  - DEHYDRATION EXHAUSTION
  - HEAT CRAMPS
  - HEATSTROKE – SUNSTROKE

EFFECTS OF EXPOSURE TO COLD

During exposure to cold, the body temperature is maintained by two mechanisms (Chapter 63).

1. Heat production
2. Prevention of heat loss.

HEAT PRODUCTION

When body is exposed to cold, heat is produced by the following activities:

1. *By Accelerating Metabolic Activities*

Heat gain center in hypothalamus is stimulated during exposure to cold. It activates the sympathetic centers, which cause secretion of adrenaline and noradrenaline. These hormones, especially adrenaline increase heat production by accelerating cellular metabolic activities.

2. *By Shivering*

Shivering is the increased **involuntary muscular activity** with slight vibration of the body in response to fear, onset of fever or exposure to cold. Shivering occurs when the body temperature falls to about 25°C (77°F). Primary motor center for shivering is situated in posterior hypothalamus near the wall of the III ventricle. During exposure to cold, heat gain center activates the motor center and shivering occurs. Enormous heat is produced during shivering due to severe muscular activities.

PREVENTION OF HEAT LOSS

When the body is exposed to cold, heat gain center in the posterior nucleus of hypothalamus is stimulated. It activates the sympathetic centers in posterior hypothalamus, resulting in cutaneous vasoconstriction and decrease in blood flow. Due to decrease in cutaneous blood flow, sweat secretion is decreased and heat loss is prevented.

EFFECTS OF EXPOSURE TO SEVERE COLD

Exposure of body to severe cold leads to death, if quick remedy is not provided. The survival time depends upon environmental temperature.

If a person is exposed to ice cold water, i.e. 0°C for 20 to 30 minutes, the body temperature falls below 25°C (77°F) and the person can survive if he is placed immediately in hot water tub with a temperature of 43°C

(110°F). Survival time at 9°C (28°F) is about 1 hour and at 15.5°C (60°F) it is about 5 hours.

Effects of exposure of body to extreme cold are:

1. Loss of temperature regulating capacity
2. Frostbite.

■ LOSS OF TEMPERATURE REGULATING CAPACITY

Temperature regulating capacity of hypothalamus is affected when the body temperature decreases to about 34.4°C (94°F). Hypothalamus totally looses the power of temperature regulation when body temperature falls below 25°C (77°F). Shivering does not occur.

In addition to loss of hypothalamic function, the metabolic activities are also suppressed. **Sleep or coma** develops due to depression of central nervous system.

■ FROSTBITE

Frostbite is the freezing of surface of the body when it is exposed to cold. It occurs due to sluggishness of blood flow. Most commonly, the exposed areas such as ear lobes and digits of hands and feet are affected. Frostbite is common in mountaineers. Prolonged exposure will lead to permanent damage of the cells, followed by **thawing** and **gangrene** (death and decay of tissues) formation.

■ EFFECTS OF EXPOSURE TO HEAT

Effects of exposure to heat are:

1. Heat exhaustion
2. Dehydration exhaustion
3. Heat cramps
4. Heatstroke (sunstroke).

■ HEAT EXHAUSTION

Heat exhaustion is the body's response to excess loss of water and salt through sweat, caused by exposure to hot environmental conditions. In fact, it is the warning that body is getting too hot. Heat exhaustion results in loss of consciousness and collapse. Before the loss of consciousness, following warning signs appear in the body:

i. Increased heart rate
ii. Increased cardiac output
iii. Dilatation of cutaneous blood vessels
iv. Increased moisture of the body
v. Fall in blood pressure
vi. Weakness and uneasiness
vii. Mild dyspnea.

■ DEHYDRATION EXHAUSTION

Prolonged exposure to heat results in dehydration. It is due to excessive sweating. Dehydration leads to fall in cardiac output and blood pressure. Collapse occurs if treatment is not given immediately.

■ HEAT CRAMPS

Severe painful cramps occur due to reduction in the quantity of salts and water as a result of increased sweating, during continuous exposure to heat.

■ HEATSTROKE – SUNSTROKE

Heatstroke

Heatstroke is an abnormal type of **hyperthermia** that occurs during exposure to extreme heat. It is characterized by increase in body temperature above 41°C (106°F), accompanied by some physical and neurological symptoms. Compared to other effects of exposure to heat such as heat exhaustion and heat cramps, heatstroke is very severe and often becomes fatal if not treated immediately. Hypothalamus loses the power of regulating body temperature.

Sunstroke

Sunstroke is the hyperthermia caused by prolonged exposure to sun during summer in desert or tropical areas.

Persons Susceptible to Heatstroke or Sunstroke

People more susceptible to heatstroke or sunstroke are:

i. Infants
ii. Old people with renal, cardiac or pulmonary disorders
iii. People doing physical labor under sun
iv. Sportsmen involved in continuous sports activities without break.

Features

Common features of heatstroke or sunstroke are:

i. Nausea and vomiting
ii. Dizziness
iii. Headache
iv. Abdominal pain
v. Difficulty in breathing
vi. Vertigo

vii. Confusion
viii. Muscle cramps and convulsions
ix. Paralysis
x. Unconsciousness.

If immediate and vigorous treatment is not given, damage of brain tissues occurs, resulting in coma and death.

Heatstroke and Humidity

Development of heatstroke depends upon humidity of the environment. If the environmental air is completely dry, exposure of body for several hours even to a temperature of 54.4°C (130°F) does not cause heatstroke. If air is 100% humid, even the temperature of 41°C (106.8°F) causes heatstroke.

Prevention

Heatstroke or sunstroke can be avoided by the following measures:

i. Avoiding dehydration by taking plenty of fluids such as water or sports drinks
ii. Taking frequent breaks during work or sports activity
iii. Wearing light clothes with hat.

Treatment

Person affected by heatstroke or sunstroke must be treated before the damage of organs. The subject should be immediately moved from hot environment and **hospitalized** as soon as possible. Immediate cooling of the body is the usual treatment. The person must be immersed in **cold water** or cold water may be sprayed on the skin. If water supply is not sufficient, cooling the head and neck of the subject should be done first. **Ice cubes** can be rubbed on head and neck. Ice packs must be kept under armpits and groin. Cooling efforts should be continued till the body temperature falls to about 35°C.

Artificial Respiration

Chapter 131

CONDITIONS WHEN ARTIFICIAL RESPIRATION IS REQUIRED

Artificial respiration is required whenever there is an arrest of breathing, without cardiac failure. Arrest of breathing occurs in the following conditions:

1. Accidents
2. Drowning
3. Gas poisoning
4. Electric shock
5. Anesthesia.

Stoppage of oxygen supply for 5 minutes causes irreversible changes in tissues of brain, particularly tissues of cerebral cortex. So, artificial respiration (resuscitation) must be started quickly without any delay, before the development of cardiac failure.

Purpose of artificial respiration is to ventilate the alveoli and to stimulate the respiratory centers.

METHODS OF ARTIFICIAL RESPIRATION

Methods of artificial respiration are of two types:

1. Manual methods
2. Mechanical methods.

MANUAL METHODS

Manual methods of **resuscitation** can be applied quickly without waiting for the availability of any mechanical aids.

Affected person must be provided with clear air. Clothes around neck and chest regions must be loosened. Mouth, face and throat should be cleared of mucus, saliva, foreign particles, etc. Tongue must be drawn forward and it must be prevented from falling posteriorly, which may cause airway obstruction.

Manual methods are of two types:

i. Mouth-to-mouth method
ii. Holger Nielsen method.

Mouth-to-mouth Method

The subject is kept in supine position and the **resuscitator** (person who give resuscitation) kneels at the side of the subject. By keeping the thumb on subject's mouth, the lower jaw is pulled downwards. Nostrils of the subject are closed with thumb and index finger of the other hand.

Resuscitator then takes a deep breath and exhales into the subject's mouth forcefully. Volume of exhaled air must be twice the normal tidal volume. This expands the subject's lungs. Then, the resuscitator removes his mouth from that of the subject. Now, a passive expiration occurs in the subject due to elastic recoil of the lungs. This procedure is repeated at a rate of 12 to 14 times a minute, till normal respiration is restored.

Mouth-to-mouth method is the most effective manual method because, carbon dioxide in expired air of the resuscitator can directly stimulate the respiratory centers and facilitate the onset of respiration. Only disadvantage is that the close contact between the mouths of resuscitator and subject may not be acceptable for various reasons.

Holger Nielsen Method or Back Pressure Arm Lift Method

Subject is placed in prone position with head turned to one side. Hands are placed under the cheeks with flexion at elbow joint and abduction of arms at the shoulders. Resuscitator kneels beside the head of the subject. By placing the palm of the hands over the back of the subject, the resuscitator bends forward with straight arms (without flexion at elbow) and applies pressure on the back of the subject.

Weight of the resuscitator and pressure on back of the subject compresses his chest and expels air from the lungs. Later, the resuscitator leans back. At the same time, he draws the subject's arm forward by holding it just above elbow.

This procedure causes expansion of thoracic cage and flow of air into the lungs. The movements are repeated at the rate of 12 per minute, till the normal respiration is restored.

■ MECHANICAL METHODS

Mechanical methods of artificial respiration become necessary when the subject needs artificial respiration for long periods. It is essential during the respiratory failure due to paralysis of respiratory muscles or any other cause.

Mechanical methods are of two types:

i. Drinker method
ii. Ventilation method.

Drinker Method

The machine used in this method is called **iron lung chamber** or **tank respirator.** The equipment has an airtight chamber, made of iron or steel. Subject is placed inside this chamber with the head outside the chamber.

By means of some pumps, the pressure inside the chamber is made positive and negative alternately. During the negative pressure in the chamber, the subject's thoracic cage expands and inspiration occurs and during positive pressure the expiration occurs.

By using tank respirator, the patient can survive for a longer time, even up to the period of one year till the natural respiratory functions are restored.

Ventilation Method

A rubber tube is introduced into the trachea of the patient through the mouth. By using a pump, air or oxygen is pumped into the lungs with pressure intermittently. When air is pumped, inflation of lungs and inspiration occur. When it is stopped, expiration occurs and the cycle is repeated. Apparatus used for ventilation is called **ventilator** and it is mostly used to treat acute respiratory failure.

Ventilator is of two types:

a. Volume ventilator
b. Pressure ventilator.

Volume ventilator

By volume ventilator, a constant volume of air is pumped into the lungs of patients intermittently with minimum pressure.

Pressure ventilator

By pressure ventilator, air is pumped into the lungs of subject with constant high pressure.

Effects of Exercise on Respiration

Chapter 132

- INTRODUCTION
- EFFECTS OF EXERCISE ON RESPIRATION
  - PULMONARY VENTILATION
  - DIFFUSING CAPACITY FOR OXYGEN
  - CONSUMPTION OF OXYGEN
  - OXYGEN DEBT
  - VO_2 MAX
  - RESPIRATORY QUOTIENT

INTRODUCTION

Muscular exercise brings about a lot of changes on various systems of the body. Degree of changes depends upon the severity of exercise. Refer Chapter 117 for types and severity of exercise.

EFFECTS OF EXERCISE ON RESPIRATION

EFFECT ON PULMONARY VENTILATION

Pulmonary ventilation is the amount of air that enters and leaves the lungs in 1 minute. It is the product of tidal volume and respiratory rate. It is about 6 liter/minute, with a normal tidal volume of 500 mL and respiratory rate of 12/minute.

During exercise, hyperventilation, which includes increase in rate and force of respiration occurs. In moderate exercise, respiratory rate increases to about 30/minute and tidal volume increases to about 2,000 mL. Thus, the pulmonary ventilation increases to about 60 L/minute during moderate exercise. In severe muscular exercise, it rises still further up to 100 L/minute.

Factors increasing pulmonary ventilation during exercise

1. Higher centers
2. Chemoreceptors
3. Proprioceptors
4. Body temperature
5. Acidosis.

1. *Higher Centers*

Rate and depth of respiration increase during the onset of exercise. Sometimes, before starting the exercise, thought or anticipation of exercise itself increases the rate and force of respiration. It is a **psychic phenomenon** due to the activation of higher centers like Sylvian cortex and motor cortex of brain. Higher centers, in turn accelerate the respiratory processes by stimulating respiratory centers.

2. *Chemoreceptors*

Chemoreceptors which are stimulated by exercise-induced hypoxia and hypercapnea, send impulses to the respiratory centers. Respiratory centers, in turn increase the rate and force of respiration. Chemoreceptors are described in detail in Chapter 126.

3. *Proprioceptors*

Proprioceptors, which are activated during exercise, send impulses to cerebral cortex through the somatic afferent nerves. Cerebral cortex, in turn causes hyperventilation by sending impulses to the medullary respiratory centers. Refer Chapter 156 for proprioceptors.

4. *Body Temperature*

Body temperature which increases by muscular activity, increases the ventilation by stimulating the respiratory centers.

5. *Acidosis*

Acidosis developed during exercise also stimulates the respiratory centers, resulting in hyperventilation.

■ EFFECT ON DIFFUSING CAPACITY FOR OXYGEN

Diffusing capacity for oxygen is about 21 mL/minute at resting condition. It rises to 45 to 50 mL/minute during moderate exercise because of increased blood flow through pulmonary capillaries.

■ EFFECT ON CONSUMPTION OF OXYGEN

Oxygen consumed by the tissues, particularly the skeletal muscles is greatly enhanced during exercise. Because of vasodilatation in muscles during exercise, more amount of blood flows through the muscles and more amount of oxygen diffuses into the muscles from blood. The amount of oxygen utilized by the muscles is directly proportional to the amount of oxygen available.

■ EFFECT ON OXYGEN DEBT

Oxygen debt is the extra amount of oxygen required by the muscles during recovery from severe muscular exercise. After a period of severe muscular exercise, amount of oxygen consumed is greatly increased. Oxygen required is more than the quantity available to the muscle. This much of oxygen is required not only for the activity of the muscle but also for reversal of some metabolic processes such as:

1. Reformation of glucose from lactic acid, accumulated during exercise
2. Resynthesis of ATP and creatine phosphate
3. Restoration of amount of oxygen dissociated from hemoglobin and myoglobin.

Thus, for the above reversal phenomena, an extra amount of oxygen must be made available in the body after severe muscular exercise. Oxygen debt is about six times more than the amount of oxygen consumed under resting conditions.

■ EFFECT ON VO_2 MAX

VO_2 max is the amount of oxygen consumed under maximal aerobic metabolism. It is the product of maximal cardiac output and maximal amount of oxygen consumed by the muscle.

In a normal active and healthy male, the VO_2 max is 35 to 40 mL/kg body weight/minute. In females, it is 30 to 35 mL/kg body weight/minute. During exercise, VO_2 max increases by 50%.

■ EFFECT ON RESPIRATORY QUOTIENT

Respiratory quotient is the molar ratio of carbon dioxide production to oxygen consumption. Refer Chapter 124 for details.

Respiratory quotient in resting condition is 1.0 and during exercise it increases to 1.5 to 2. However, at the end of exercise, the respiratory quotient reduces to 0.5.

QUESTIONS IN RESPIRATORY SYSTEM AND ENVIRONMENTAL PHYSIOLOGY

LONG QUESTIONS

1. Describe the various movements of thoracic cage and lungs during respiration.
2. Describe in detail the pulmonary circulation.
3. Give the definition and normal values of lung volumes and lung capacities and explain the measurement of the same.
4. Explain the transport of oxygen in blood.
5. Explain the transport of carbon dioxide in blood.
6. Describe the nervous regulation of respiration.
7. Describe the chemical regulation of respiration.
8. What is hypoxia? Describe the types, causes and effects of hypoxia. Add a note on oxygen therapy.
9. Describe the changes in the body at high altitude and explain the acclimatization.
10. Describe in detail the respiratory and cardio-vascular changes during exercise.

SHORT QUESTIONS

1. Respiratory unit.
2. Respiratory membrane.
3. Non-respiratory functions of respiratory tract.
4. Physiological shunt.
5. Characteristic features of pulmonary circulation.
6. Collapsing tendency of lungs.
7. Surfactant.
8. Respiratory pressures.
9. Compliance.
10. Work of breathing.
11. Spirometry.
12. Measurement of functional residual capacity.
13. Measurement of residual volume.
14. Vital capacity.
15. MBC or MVV.
16. Forced expiratory volume.
17. Plethysmography.
18. Peak expiratory flow rate.
19. Alveolar ventilation.
20. Dead space.
21. Ventilation perfusion ratio.
22. Respiratory quotient or respiratory exchange ratio.
23. Alveolar air.
24. Oxygen hemoglobin dissociation curve.
25. Carbon dioxide dissociation curve.
26. Bohr effect.
27. Haldane effect.
28. Chloride shift.
29. Diffusing capacity.
30. Exchange of gases between alveoli and blood.
31. Exchange of gases between blood and tissues.
32. Respiratory centers.
33. Inspiratory ramp.
34. Hering-Breuer reflex.
35. Receptors of lungs taking part in control of breathing.
36. Chemoreceptors.
37. Apnea.
38. Hypoxia.
39. Hyperventilation and hypoventilation.
40. Hypercapnea and hypocapnea.
41. Asphyxia.
42. Dyspnea.
43. Periodic breathing.
44. Cyanosis.
45. Oxygen toxicity (poisoning).
46. Carbon monoxide poisoning.
47. Pneumothorax.
48. Pneumonia.
49. Pulmonary edema.
50. Mountain sickness.
51. Acclimatization.
52. Effect of G force.
53. Decompression sickness.
54. Nitrogen narcosis.
55. Effects of sudden exposure to cold.
56. Effects of sudden exposure to heat.
57. Heatstroke or sunstroke.
58. Artificial respiration.
59. Respiratory changes during exercise.
60. Oxygen debt.
61. VO_2 max.
62. Fetal respiration and first breath.