4
CHAPTER

Respiratory System

Introduction

The respiratory system is concerned with delivery of oxygen from the atmosphere to tissues and excretion of carbon dioxide from the tissues to atmosphere. Oxygen diffuses into blood from the alveoli and at the same time carbon dioxide is evolved out of blood into lungs. Exchange of gases at the level of lungs is known as external respiration.

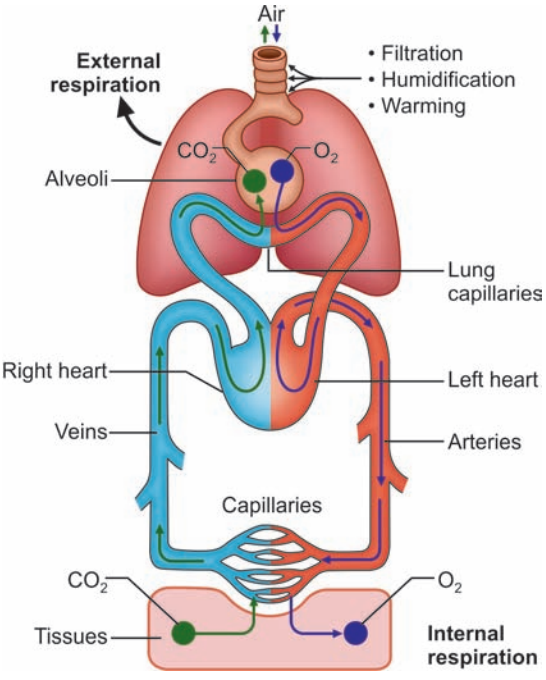

Fig. 4.1: The areas of external and internal respiration

At the level of tissues, the reversal occurs. Oxygen diffuses into tissues from blood and at the same time carbon dioxide diffuses into blood from the tissues. This is known as internal respiration (Fig. 4.1).

Respiratory Tract

Parts of respiratory system starting from the nasal apertures, extends through pharynx, larynx, trachea, bronchi, bronchioles and into alveoli. Alveolus is the structural and functional unit of respiratory system. The part extending from the nasal apertures up to terminal bronchioles forms the respiratory tract and is known as conducting zone. This region is also known as anatomical dead space (Fig. 4.2).

The concept of dead space is part of respiratory system in which in spite of air being present, it does not take part in exchange of respiratory gases. The normal anatomical dead space volume (DSV) is about 150 ml.

Functions of Upper Respiratory Tract (Fig. 4.2)

1. Warming up of air, as the temperature of air reaching the alveoli should be brought to body temperature, for better diffusion of gas.
2. The epithelial cells lining the respiratory tract add on water molecules to the air getting into the alveoli. This is known as humidifying of air.
3. Filtration of air is essential before the air reaches alveoli. Partial filtration of dust particles will be taking place due to the presence of hairs in the nose

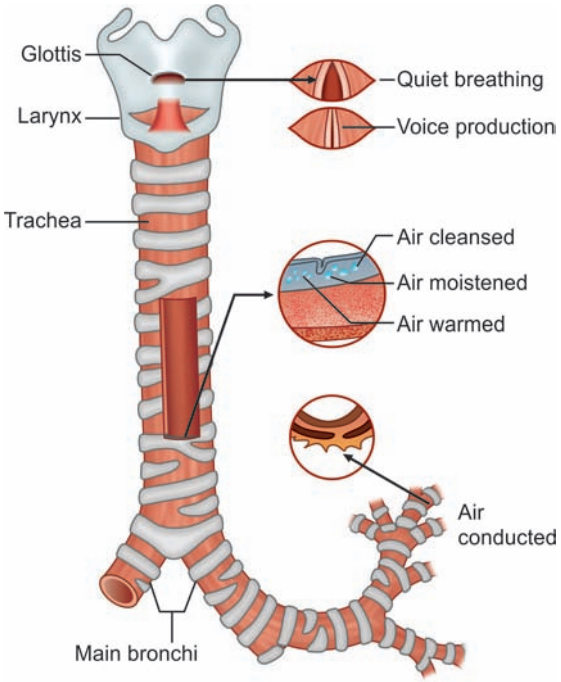

Fig. 4.2: Parts of respiratory tract (that is a dead space region) showing various functions of the tract while air is passing through

and also because of the ciliated cells on which a layer of mucus is present.

All the aforesaid aspects in general are known as air conditioning. In addition to this, the passage of air through the larynx is responsible for production of sound.

Functions of respiratory system can be broadly classified into:

a. Respiratory
b. Non-respiratory.

Respiratory Function

It is to provide adequate volume of oxygen to the tissues. Normal person at rest needs about 250 ml of oxygen per minute. Atmospheric air enters the lungs during inspiration. Oxygen from the air diffuses through the alveoli into pulmonary capillary blood. The oxygenated blood reaches the left ventricle and from there it gets pumped to reach all parts of the body.

About 200 ml of carbon dioxide is produced in the body every minute because of tissue metabolism. From the tissues, carbon dioxide enters the blood to reach the lungs for the process of excretion. When deoxygenated blood reaches the lungs, carbon dioxide gets diffused from the pulmonary capillaries into the alveoli. The air from the alveoli is expelled out from the lungs by the process of expiration.

Non-respiratory Functions

1. Regulation of acid-base (pH) balance.
2. Mast cells present in the lungs produce heparin, which acts as an anticoagulant.
3. Macrophages in the alveoli have phagocytic function.
4. Converting enzyme present in the lungs play a role in converting angiotensin I to angiotensin II, which is a powerful vasoconstrictor.
5. The passage of the air through the larynx is essential for vocalization and has role in communication by speech.
6. Plays a minor role in body temperature regulation.

Parts of Respiratory System

Nose

a. Hairs are present in the nasal cavity. These hairs serve to filter the air that is entering the respiratory system. Any particle whose size is more than 6 μ gets filtered in the nose.
b. The mucous membrane of the nose is highly vascular. As the air passes through the nose, it gets:
   i. Warmed up to the body temperature,
   ii. Its water vapor content is also increased. This is essential because if dry air passes through the trachea, it may lead to drying up of the trachea and it can produce a cough reflex.

Trachea

a. It is made up of a number of incomplete cartilaginous rings, which prevent the trachea from kinking when the neck is rotated. The posterior 1/6th of the trachea is free from cartilage and is made up of fibrous tissue, which permits certain amount of expansion of trachea during inspiration.
b. The trachea is lined by ciliated columnar epithelium. Underneath this lining, lot of goblet cells are present. These goblet cells secrete certain amount of mucus. The particles which escape filtration at nose, get trapped in the mucus present here and swept towards the nose by the movements of the cilia. These particles are get rid off from the body by the process of coughing. Some of the finest

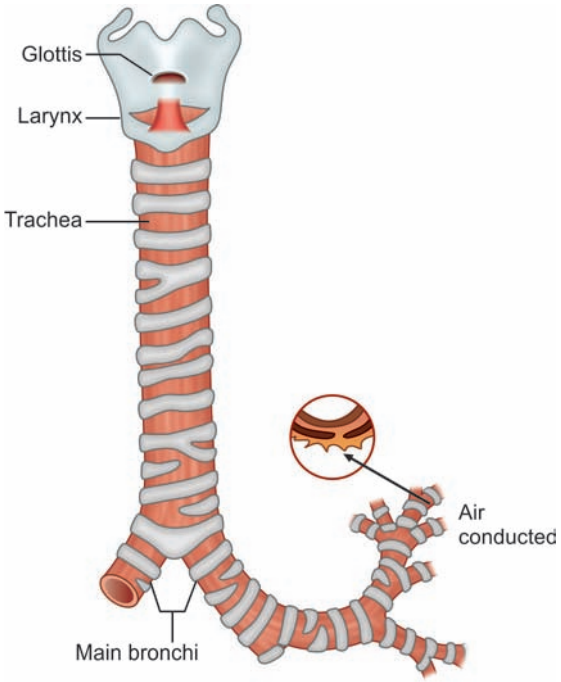

Fig. 4.3: The branching of bronchi from the trachea

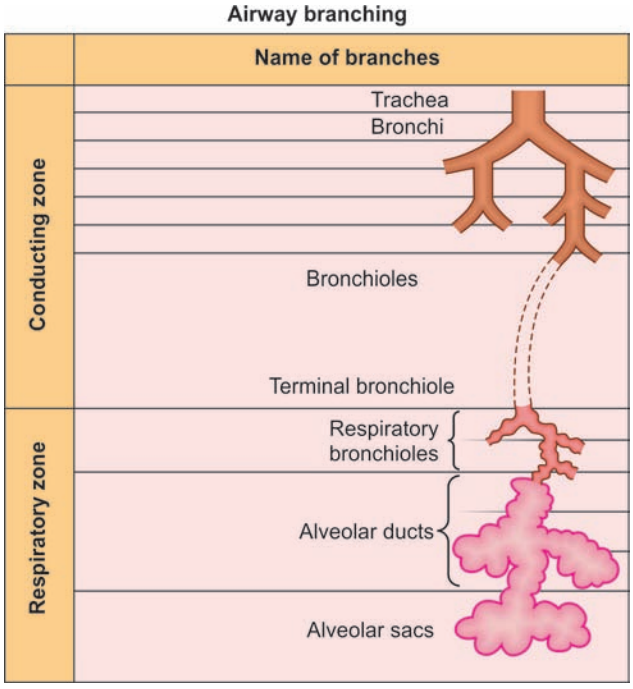

Fig. 4.4: Branching of airways until the alveoli

particles may escape from getting filtered here and reach alveoli. They are removed by the macrophages lining of the alveoli or the parenchyma of the lungs.

The trachea divides into right and left bronchi (Fig. 4.3). The branching of the trachea is the most sensitive part of the tracheobronchial tree. The right bronchus is larger than the left and the angle at which it originates from the trachea is also less acute. Because of this reason, any foreign body entering the trachea is found more commonly in the right lung than in the left.

Bronchi

The bronchi, which are the branches of the trachea, divide further. These branches are called as lobar bronchi that again divide into segmental bronchi. As the branching proceeds, the amount of cartilage present in the walls goes on decreasing. They also acquire a coat of smooth muscle fibers. These smooth muscle fibers are supplied by both sympathetic and parasympathetic nerve fibers. Sympathetic nerve stimulation or administration of sympathomimetic drugs (adrenaline) brings about relaxation of smooth muscle and hence bronchodilation. This leads to decrease of the airway resistance. This knowledge is useful in the treatment of bronchial asthma. Parasympathetic nerve stimulation brings about bronchoconstriction.

The bronchi divide to form bronchioles. These bronchioles further divide to form terminal and respiratory bronchioles. The respiratory bronchioles lead to alveolar duct and finally into the alveoli (Fig. 4.4).

Changes that occur as the branching proceeds from trachea to bronchioles:

1. The cross-sectional area goes on increasing. The branching decreases the resistance offered to the flow of airflow (particularly during inspiration).
2. The amount of cartilaginous tissue also goes on decreasing to be replaced by smooth muscle fibers.
3. The mucous membrane which is lined by columnar ciliated epithelium is changed to flattened non-ciliated at the level of alveoli.

Flattened epithelial cells line the alveoli. Alveolus is approximately 70–300 μ in diameter. The total surface area of all the alveoli together will be approximately 70 m^2. At any given time approximately 60–80 ml of blood will be present in the capillaries surrounding the alveoli. Therefore, any given time about 1 ml of blood is spread over 1 m^2. This facilitates rapid

exchange of gases between air in alveoli and blood in pulmonary capillaries.

Normal respiratory rate is about 12–16/min and is known as rate of respiration (RR). The volume of air that is taken in or expired out of respiratory system during a normal quiet breathing is known as tidal volume and is about 500 ml.

Pulmonary ventilation: It is defined as the volume of air entering or leaving the respiratory system per minute. It is the product of rate of respiration (RR) multiplied by tidal volume (TV), which is about 6 L/min (12 × 500 = 6000 ml/min).

Alveolar ventilation: It is defined as the volume of air taking part in the exchange of gases at the level of alveoli per minute. As stated already, the alveolar area region is where the exchange of gas occurs but the air present in the conducting zone does not take part in exchange of gases (dead space air). It can be calculated by the following formula:

$$\text{Alveolar ventilation} = RR \times (TV - DSV)$$
$$= 12 \times (500 - 150)$$
$$= 4200 \text{ ml/min}$$

RR—rate of respiration
TV—tidal volume
DSV—dead space volume

Covering of the Lungs

The lungs are covered by pleura that are closely adherent to the surface of the lung tissue. This layer of pleura is known as visceral pleura. Another layer of pleura adheres to the inner surface of the wall of the thorax. This layer is known as parietal pleura. A thin film of fluid is present between the two layers of pleura in the potential space known as pleural space. This fluid keeps the pleural layers adherent to each other. The two layers cannot be separated but can slide over one on the other. In animals, introduction of needle into the pleural space allows us to record the pressure in the intrapleural space. In the case of human beings, it can be measured from the lower one-third of esophagus by balloon technique. Normally intrapleural pressure is always negative (less than the atmospheric pressure). Sometime the pleural space may get filled with fluid/air giving rise to pleural effusion and pneumothorax, respectively.

Mechanics of Respiration

Respiration has two phases namely inspiration and expiration. During normal quiet inspiration due to contraction of muscles of inspiration, the chest and lungs expand. The pressure inside the alveoli (intra-alveolar pressure) falls below the atmospheric pressure. Due to the pressure gradient developed in the direction of the alveolus, air moves from the atmosphere into the lungs. Because inspiration is brought about by the contraction of the muscles, the process of inspiration is an active one.

However, the process of expiration is normally a passive process. The relaxation of the muscles of inspiration and the recoiling of the elastic fibers present in the lungs is more than enough to bring about the expiration. During expiration, since the alveoli are trying to recoil, the intra-alveolar pressure becomes more than the atmospheric pressure and hence air can be driven out of the lungs into the atmosphere. In forced expiratory states, expiration needs the active contraction of certain muscles. Hence in such states even expiration becomes an active process.

Muscles of inspiration: Diaphragm and external intercostals are the muscles of inspiration during a normal quiet breathing. However, during forced inspiration, contraction of sternocleidomastoid, scalene, serratus anterior and platysma muscles is very much required. These muscles are known as accessory muscles of inspiration.

Muscles of expiration: The normal quiet expiration is a passive process. However, in forced expiration, even this phase becomes an active process and requires active contraction of certain muscles. The muscles that are involved in forced expiration are known as accessory muscles of expiration and they are internal intercostals and muscles of the anterior abdominal wall.

Thorax is separated from the abdominal cavity by the diaphragm, a dome-shaped muscle. The thorax has three different diameters namely vertical, transverse and anteroposterior. During inspiration, the thoracic volume gets increased because of increase in the diameters of chest. The increase in the thoracic volume decreases the intra-alveolar pressure.

The most important muscle of inspiration is diaphragm supplied by the phrenic nerve. This is

responsible for about 70% increase in the thoracic volume and the rest volume increase in thorax is contributed by the contraction of external intercostals supplied by the intercostal nerves. This type of respiration is called as abdominothoracic type. In case the external intercostals play a major role in expansion of thorax, the type of respiration is known as thoraco-abdominal type.

Contraction of the diaphragm alters the vertical diameter whereas the contraction of the external intercostals increases the anteroposterior and transverse diameters of the thoracic cavity.

Intrapleural and Intra-alveolar Pressure (Fig. 4.5)

Intrapleural Pressure

- It is the pressure that is prevalent in the pleural space.
- It is always sub-atmospheric (less than 760 mm Hg).
- At the beginning of inspiration, it is minus 3 mm Hg (3 mm Hg less than the atmospheric pressure).
- As the inspiration proceeds, it becomes more negative and in normal quiet inspiration, it reaches a value of about minus 6 mm Hg at the end of inspiration.

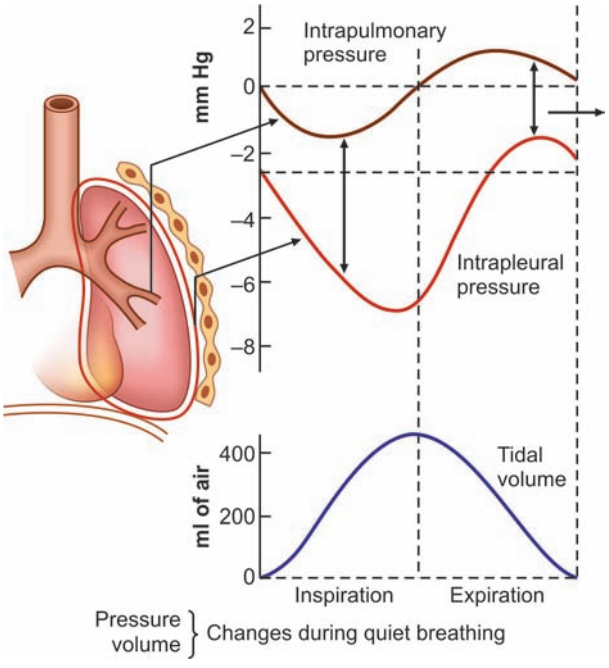

Fig. 4.5: Graph of intrapleural and intra-alveolar (intrapulmonary) pressures tidal volume during a normal quiet respiration

- During expiration, it becomes less negative as the expiration proceeds. And reaches minus 3 mm Hg at the end of expiration.
- During forced inspiration, it becomes much more negative and can be as low as minus 60 mm Hg.
- When there is forced expiration against closed glottis (as occurs in coughing, sneezing, etc.), the pressure can become positive and can be as high as plus 40 mm Hg.
- During inspiration, as the chest wall expands, the two layers of pleura have a tendency to recoil in the opposing directions. The visceral pleura along with the lungs tend to recoil in the direction of the hilum of the lungs and the parietal pleura towards the chest wall. This makes the intrapleural pressure to become more negative. When the inspiration becomes deeper, the recoiling tendency becomes greater because of further increase in the expansion of the alveoli. The intrapleural pressure becomes more negative in forced inspiration.
- The intrapleural pressure can be measured in animals by introduction of needle into the pleural space and connecting it to a manometer. In the case of human beings, it can be recorded by introduction of balloon into the lower one-third of esophagus.

Significance or Functions of Negative Intrapleural Pressure

1. Facilitates the venous return from dependent parts of the body into the heart.
2. Maintains the patency of bronchioles both during inspiration and expiration and decreases airway resistance during inspiration.
3. This decreases the intra-alveolar pressure, which facilitates air entry into the alveoli.
4. Prevents the collapsing tendency of the alveoli.
5. Facilitates lymph flow.

Pressure Changes in the Alveoli during Respiration

- Alveoli are connected to the atmosphere outside the body through the respiratory tract. The entry or exit of air through this tract is always in the direction of the pressure gradient (along a pressure gradient).
- The pressure recorded from the alveoli is known as intra-alveolar pressure.

- At the beginning of inspiration, the pressure is 0 mm Hg. As the inspiration proceeds, it becomes negative. It can be as little as minus 1 or 2 mm Hg by mid-inspiration. During the later part of inspiration, it starts becoming less negative and at the end of inspiration, it will be 0 mm Hg once again.
- The pressure gradient during inspiration facilitates the entry of air from atmosphere into the alveoli.
- The accumulation of air in the alveoli, gradually makes the pressure to become less negative and at the end of inspiration it becomes 0 mm Hg. This puts an end to the pressure gradient and hence air entry into the alveoli ceases.
- The recoiling tendency of the alveoli during expiration brings about the compression of air present in the alveoli. This increases the intra-alveolar pressure and becomes positive (more than the atmospheric pressure), and it can be as much as plus 1 or 2 mm Hg by mid-expiration. This forces air from the alveoli into the atmosphere. As the air moves out of the alveoli, the pressure inside decreases and at the end of expiration the pressure returns to 0 mm Hg. Pressure gradient ceases and hence expiration comes to an end.

Lung Compliance (Fig. 4.6)

- It is the change in the volume of lungs per unit change in transpulmonary pressure (pressure difference between intrapleural and intra-alveolar compartments).
- The unit being cm H_2O for pressure and ml for the volume.
- It is about 130 ml per cm H_2O pressure (for lungs and chest wall put together).
- It is about 200 ml per cm H_2O for lungs alone.
- When it is plotted in the form of graph for inspiratory and expiratory phases, the curves will not overlap but bring about the formation of hysteresis loop. It is due to a change in the elastic property of the lungs and chest walls.

Factors influencing the compliance of the lungs are:

a. Presence or absence of surfactant
b. Initial lung volume
c. Posture

Compliance of lung decreases in conditions, namely:

1. Pulmonary edema.

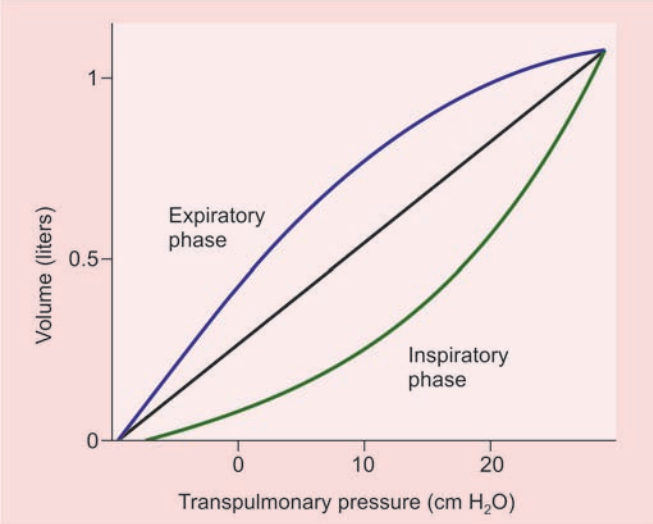

Fig. 4.6: Compliance of lungs during inspiration and expiration phases

2. Fibrosis.
3. Atelectasis.
4. In the lying down posture, due to accumulation of blood in the lungs (increase in pulmonary blood volume).

Compliance can be measured by making the person to inspire 50 ml of air at a time and a short time is allowed for pressure equilibration to occur. Then the pressure measurements are made. This is continued till the person breathes 500 ml of air (tidal inspiration). Procedure is repeated by expiring 50 ml of air at a time and recording of the pressure. The result is plotted on the graph paper. With the help of this, the airway resistance and non-elastic tissue resistance can also be measured. This measures the static lung compliance. If pressure measurements are made as the air is entering into or coming out of lungs, this is known as dynamic lung compliance.

Collapsing Tendency of the Lungs

- It is because of the presence of layer of water molecules in the alveoli, which exert surface tension (get attracted towards each other). This is responsible for about two-thirds of the collapsing tendency.
- The lungs contain large amount of elastic fibers that have a tendency to recoil. This is responsible for the remaining one-third of the collapsing tendency.

Factors preventing collapsing tendency of lungs/alveoli:

- A layer of surfactant opposes the collapsing tendency of the lungs, which is present in the alveoli. The surfactant covers the layer of water molecule present in the alveoli. Hence, prevents the air–water molecular interface.
- Recoiling tendency of the chest walls in the opposite direction.
- The negative intrapleural pressure also contributes for preventing the collapsing tendency of the alveoli by maintaining a distension force on the lungs.
- Another factor that also has a role in preventing the collapsing tendency of the alveoli is interdependence of the alveoli. The walls of the adjacent alveoli are adhering to each other. When one alveolus tries to recoil, the elastic fibers in the surrounding alveoli gets stretched. As a result of which they try to recoil in the opposite direction.

Blood flowing through the collapsed alveoli is unable to take part in diffusion of gases and hence this blood remains as deoxygenated blood. When this blood mixes with oxygenated blood coming from other alveoli, it can lead to some amount of shunting (Fig. 4.7). This type of shunting is detrimental to body functioning.

Surfactant

- It is a chemical substance namely dipalmitoyl-phosphatidylcholine (DPPC).

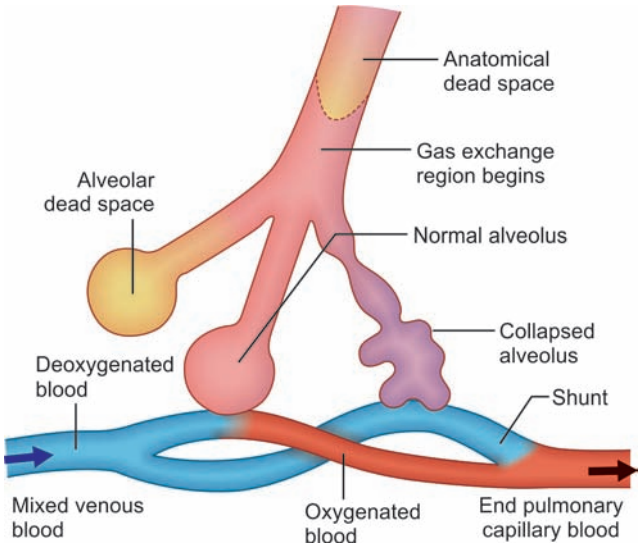

Fig. 4.7: Collapsed alveoli thereby contributing for shunting of blood

- It is secreted by type II pneumocytes (alveolar epithelial cells)
- Covers the thin layer of water molecules present in the alveoli and instead of air–water interface, there will be air-surfactant interface. This decreases the surface tension exerted by the water molecules by about 10–14 times.
- Two-thirds of collapsing tendency of the lungs is prevented by this.
- The secretion of surfactant starts from the 7th month of intrauterine life. The secretion is affected by the hormones thyroxine and cortisol.
- In the premature newborn infant when surfactant is deficient, the lungs remain collapsed. This leads to respiratory distress syndrome or hyaline membrane disease. In this condition, fluid is retained in lungs.
- Steroids or injection of surfactant may help these patients.
- In adult when surfactant is deficient, it leads to adult respiratory distress syndrome (ARDS). In smokers, the production of surfactant is decreased and may lead to ARDS.

Spirogram

Spirometry is a technique by which recording of the different lung volumes and capacities can be done.

Spirogram is the graphical recording of the lung volumes (Fig. 4.8) and capacities.

- *Tidal volume* (TV) is the volume of air inspired or expired during a normal quiet respiration and it is about 500 ml.
- *Inspiratory reserve volume* (IRV) is the volume of air inspired forcibly over and above a tidal inspiration—3000 ml.
- *Expiratory reserve volume* (ERV) is the volume of air expired forcibly after tidal expiration—1100 ml.
- *Residual volume* (RV) is the volume of air still remaining in the lungs even after a forced expiration—1200 ml.

  A capacity is sum of two or more different lung volumes.
- *Functional residual capacity* (FRC) is the volume of air remaining in the lungs after a normal expiration (RV + ERV) and is about 2300 ml. This air is responsible for making the exchange of respiratory gases a continuous process. Because of this, the partial pressure of the gases in artery gets maintained constant.

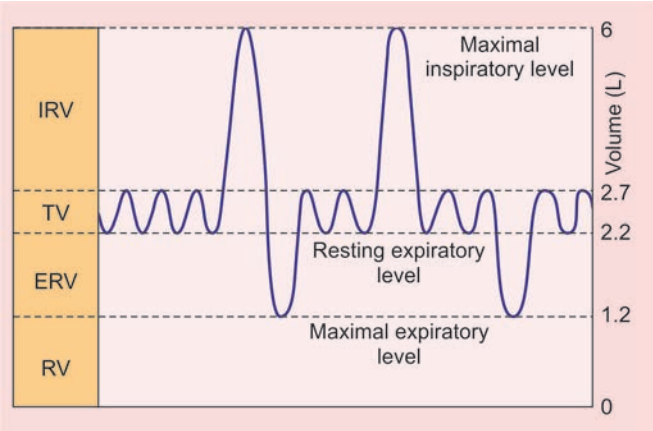

Fig. 4.8: Spirogram showing different lung volumes

- *Total lung capacity* is the maximum volume of air present in the lungs at the end of forced inspiration. It is sum of IRV, TV, ERV and RV, which is around 5800 ml.
- *Vital capacity* (VC) is the volume of air expired forcibly after a maximal inspiration. It includes TV, ERV and IRV. Normally in a male, it is about 4600 ml.
  a. In relation to body surface area, vital capacity is about 2.8 l/mts^2 in males and 2.3 l/mts^2 in females.
  b. Vital capacity determination forms one of the important lung function tests. It is normal in obstructive type of lung diseases and decreased in restrictive type of lung diseases.
  c. Vital capacity is also dependent on the age, sex, posture and build of the individual.
  d. Vital capacity decreases in fibrosis of lungs, paralysis of respiratory muscles, pleural effusion, poorly developed respiratory muscles, restricted movement of diaphragm (due to increased intra-abdominal pressure).

Timed vital capacity is the percentage volume of vital capacity expired at the end of successive seconds. Usually it is denoted as FEV_1, FEV_2 and FEV_3 wherein FEV refers to the forced expiratory volume and the number suffixed refers to the end of a particular second. To calculate timed vital capacity at the end of first second, the following formula is applied

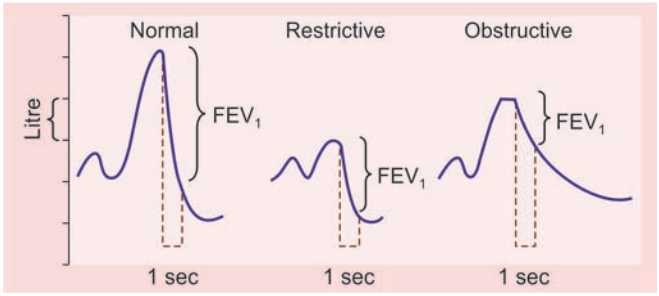

Fig. 4.9: Timed vital capacity and vital capacity in different types of lung diseases when compared to normal

$$FEV_1 = \frac{\text{Volume of air expired at the end of first second}}{\text{Vital capacity}} \times 100$$

Normal value:

- FEV_1 is 75–80%
- FEV_2 is 85–90%
- FEV_3 is about 97%

Timed vital capacity decreases in obstructive type of lung diseases (bronchial asthma) even though vital capacity remains normal. Vital capacity is decreased in restrictive type of lung diseases but the timed vital capacity remains normal (Fig. 4.9; Table 4.1).

Ventilation Perfusion Ratio

- It is the ratio between the volumes of air taking part in the exchange of gases at the alveoli to the volume of blood flow through the lungs per minute.

$$\text{V-P ratio} = \frac{\text{Ventilation (alveolar ventilation l/min)}}{\text{Perfusion (pulmonary blood flow l/min)}}$$

- Normal value is 0.8 because, alveolar ventilation is about 4 liters and pulmonary blood flow is 5 liters per minute, respectively.
- This value is mean for the lungs assuming that all the parts of the lungs have proportionate ventilation and perfusion.

Table 4.1: Differences between obstructive and restrictive type of lung diseases

Type of lung disease	*Vital capacity*	*Timed vital capacity*	*Occurs in conditions*
Obstructive type	Almost normal	Decreases	Bronchial asthma, emphysema
Restrictive type	Decreases	Normal	Paralysis of respiratory muscles, pleural effusion, lobectomy, hydrothorax

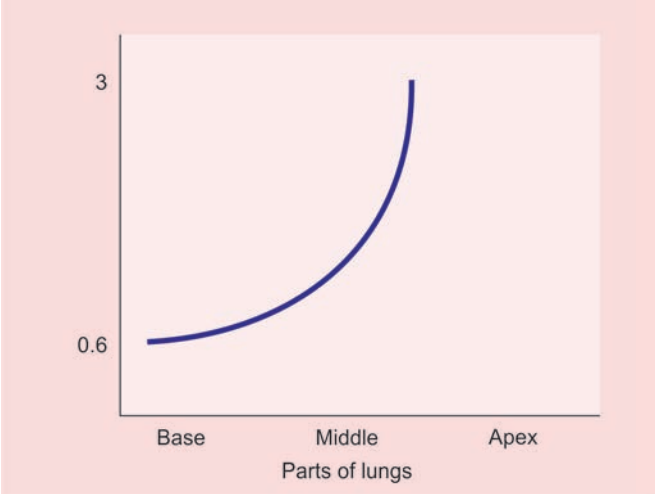

Fig. 4.10: Graph showing the difference in V-P ratio in different parts of lungs

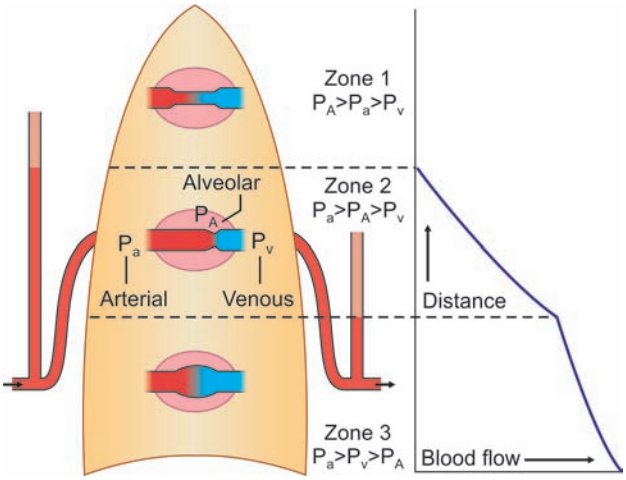

Fig. 4.11: Model tries to explain variation in the blood flow in different parts of lungs based on the pressure in artery, vein and alveoli (P_a–pressure in artery, P_v–pressure in vein, P_A–pressure in alveoli)

- In the sitting posture, it is slightly different between the apical, middle and basal parts of the lungs. In erect posture, the perfusion of blood to the apical parts will be low as against a high perfusion to the basal parts. Hence at the apical parts, the V:P ratio will be more than 0.8 and at base it will be less than 0.8 (Figs 4.10 and 4.11). It is the middle part, which has V:P ratio of almost 0.8.
- A higher value (>0.8) indicates wastage of ventilation (physiologic dead space) and low value (<0.8) indicates wastage of blood flow (blood is not getting oxygenated adequately).

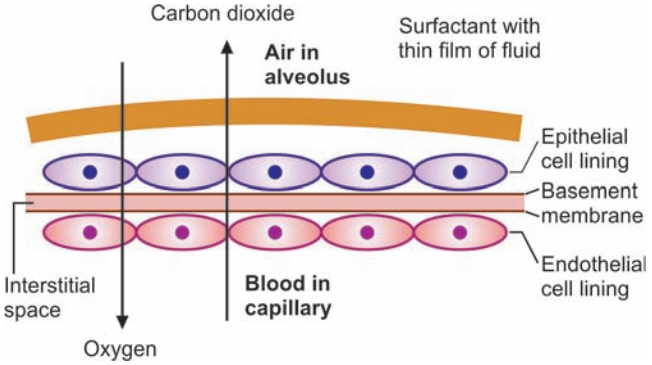

Fig. 4.12: Diagram of respiratory membrane

Respiratory Membrane (Fig. 4.12) and Exchange of Gases

- It is also known as alveolocapillary membrane or blood–gas barrier.
- The average thickness of the membrane is about 0.5 µ.
- The average surface area available for gas exchange will be about 60–80 sq mts.
- The membrane is made up of different layers.
- On one of the sides of the membrane will be air and on the other side will be blood. Hence the name blood–gas barrier.

Factors affecting diffusion of gas across the membrane: The volume of gases diffusion across the membrane can be explained based on the Fick's law of diffusion. According to this law,

$$D = \frac{\text{Pressure gradient available for the gas, } S, A}{\text{Square root of mol. wt of gas, } T}$$

D–volume of gas diffused.
A–surface area available for diffusion
T–thickness of respiratory membrane.
S–solubility of the gas

Square root of molecular weight of the gas and solubility of the gas are constant. So, the alterations in any of the other factors affect gas diffusion across the respiratory membrane, the three factors namely pressure gradient for the gas, surface area available for diffusion and thickness of respiratory membrane affect the volume of gas diffused.

Pressure Gradients (Fig. 4.13)

In the alveolar air, the pO_2 is around 104 mm Hg and pCO_2 is 40 mm Hg, whereas, in the pulmonary capillary blood pO_2 is 40 mm Hg and pCO_2 is 46 mm

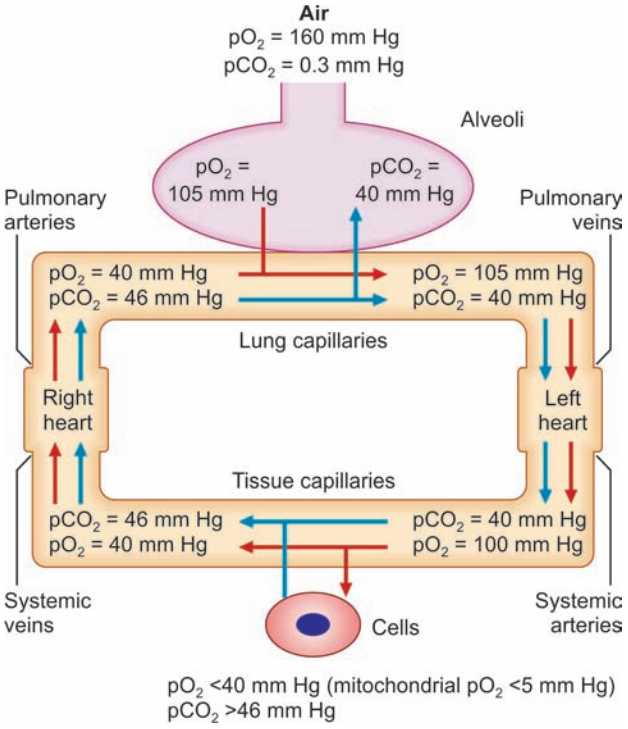

Fig. 4.13: Partial pressure of gases at different regions in the body

Hg. For O_2 to diffuse into blood from the alveolar air, the pressure gradient available will be about 64 mm Hg. And for CO_2 to diffuse out from pulmonary blood into the alveolar air, it is about 6 mm Hg. Though the pressure gradient available for CO_2 diffusion is only 6 mm Hg (10 times less than for oxygen) when compared to 64 mm Hg available for O_2, still CO_2 can diffuse easily because the rate of diffusion ratio between CO_2 and O_2 is 20:1. CO_2 has a high diffusion coefficient. Because of this, in respiratory disorders where the respiratory membrane is affected (pulmonary edema), the patient will have more of signs and symptoms of hypoxia (decreased oxygen supply to tissues) and not of hypercapnia (increased pCO_2 in circulation).

Diffusion coefficient of a gas: Can be defined as the volume of gas that is diffused per unit area (cm^2) area of respiratory membrane for a pressure gradient of 1 mm Hg per unit time.

Diffusing capacity is the volume of gas diffusing across the respiratory membrane per minute per mm Hg pressure gradient. For oxygen, it is about 21 ml/mm Hg/minute.

When the gases start diffusing across the membrane the equilibration point (the partial pressure of the gas on either side of the respiratory membrane when gets equaled) is achieved when blood has traversed only about one-third of the distance and time available in the capillary. So the pulmonary capillary blood pO_2 will have got increased to 104 from 40 mm Hg and pCO_2 will have got decreased to 40 from 46 mm Hg. Rest of the distance along the capillary, the blood flows without there being any net diffusion of gas. This distance and time will act as a safety factor in certain demanding situations like in muscular exercise during which the velocity of blood flow increases considerably and the volume of gas has to diffuse will also be more than normal in unit time.

Pressure gradient gets decreased in conditions, like:

- Hypoventilation of alveoli (bronchial asthma, paralysis of respiratory muscles)
- Hyperventilation of alveoli (at high altitudes)

Surface area availability is normally around 60–80 sq mts.

Decrease in surface area occurs in:

- Emphysema
- Collapse of the lungs
- Pneumonia
- Collapse of lung lobes (atelectasis) due to pleural effusion, pneumothorax, etc.

Thickness of the respiratory membrane is only 0.5–1 micron. It is increased in conditions, like pulmonary edema.

Muscular exercise: During muscular exercise, the oxygen demand by the body is increased and the volume of carbon dioxide produced will also be more. So, certain respiratory adjustments have to be brought about by which the rate of diffusion of gas can be

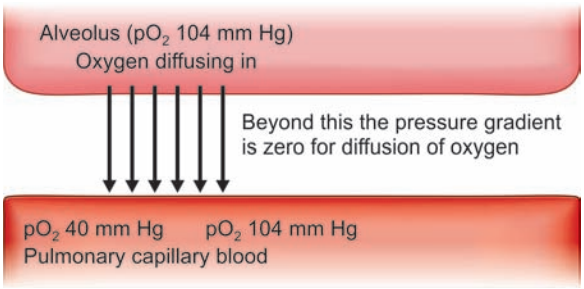

Fig. 4.14: Diffusion of gas across the respiratory membrane (that is between alveolar air and pulmonary, capillary blood)

enhanced. The respiratory adjustments that are brought about to meet the increased demands are:

- Increase in rate and depth of respiration.
- Further distension of the alveoli.
- The almost dormant alveoli are opened up for diffusion of gases.
- Opening of new capillaries

Oxygen Transport

Oxygen transport from the atmospheric air to the tissues is "down the hill" transport along a pressure gradient.

Along a pressure gradient (Fig. 4.15), oxygen diffuses from the alveolar air into the pulmonary capillary blood. The diffusion takes hardly 0.3 sec though blood remains in the pulmonary capillary for about 0.8 sec. Within this short duration (Fig. 4.16), the pO_2 of the pulmonary capillary blood gets increased from 40 to 104 mm Hg and thereby equilibration is achieved. To start with, during diffusion of oxygen there will be a pressure gradient of 64 mm Hg.

Safety factor of time for diffusion of gas along the respiratory membrane.

By the time oxygenated blood is pumped out from the left ventricle, the pO_2 is reduced to about 95 mm Hg. This is due to admixture of venous blood (physiologic shunt). The reasons for the physiologic shunt are:

- A small volume of venous blood from bronchial veins gets directly mixed with the oxygenated blood present in the pulmonary veins (Fig. 4.17).
- A small volume of venous blood from the coronary circulation supplying the myocardium gets drained directly into the chamber of the left ventricle that contains oxygenated blood.

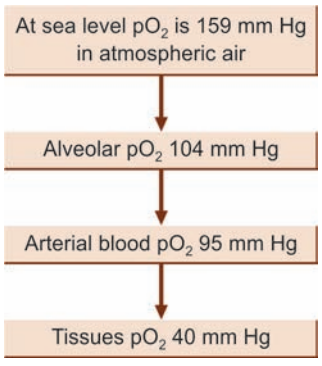

Fig. 4.15: The pressure profile from atmosphere until the tissues

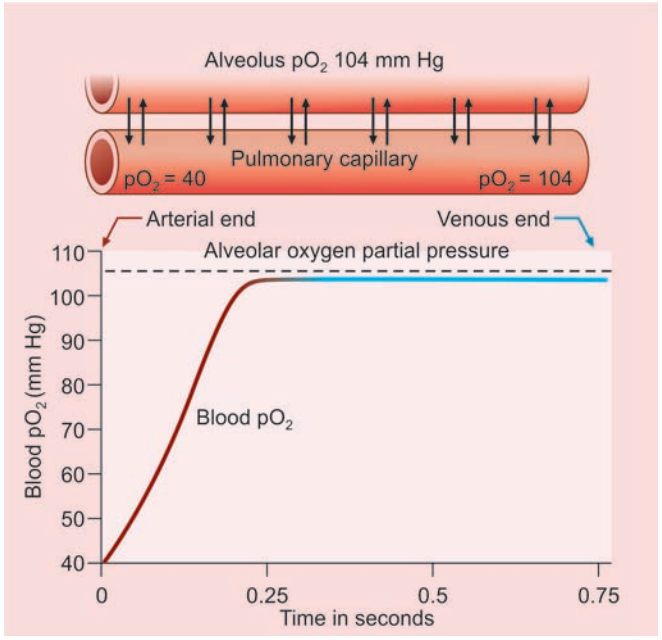

Fig. 4.16: Length and time in which the oxygen equilibration of pressure is achieved with that of alveolar air in capillary blood

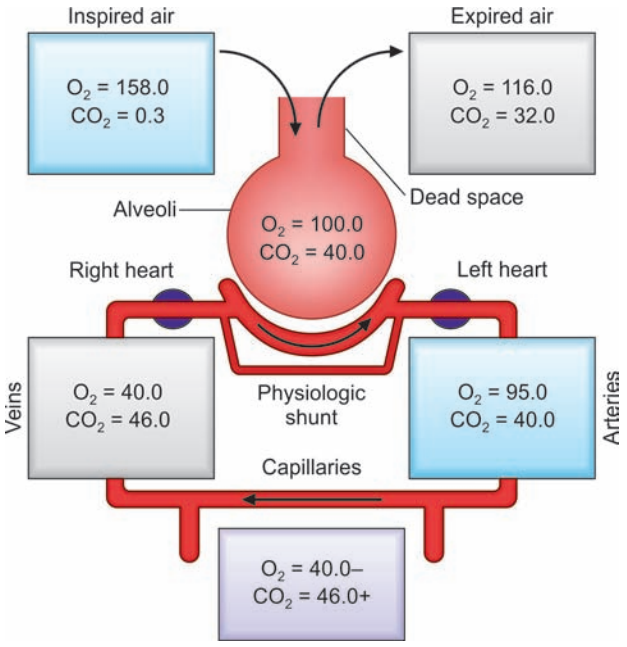

Fig. 4.17: pO_2 and pCO_2 in different regions and the vessels contributing for physiologic shunt

Details of Oxygen Transport

- Volume present in 100 ml of blood
- Partial pressure at different regions
- Forms of transport
- Importance of dissolved form
- In combination with hemoglobin
- Oxygen hemoglobin dissociation curve and factors influencing

In 100 ml of blood, the volume of oxygen present will be:

- Arterial blood about 20 ml
- Venous blood about 15 ml (mixed venous blood in pulmonary artery).

Partial pressure at different regions will be:

- Alveoli—104 mm Hg at sea level.
- Arterial blood—95 mm Hg.
- Tissues—<40 mm Hg.
- Venous blood—40 mm Hg (mixed venous blood in pulmonary artery)

	Arterial blood	*Venous blood (mixed venous blood)*
pO_2 (mm Hg)	95	40
% saturation of Hb	95–97	70–75
Content (ml/100 ml)	20	15

So when pulmonary arterial blood, which contains mixed venous blood, flows through the lungs, to start with there will be a pressure gradient of about 64 mm Hg for the diffusion of oxygen into blood from the alveoli. Because of this, oxygen starts getting diffused from the alveolar air into pulmonary capillary blood. By the time blood has traversed about one-third the distance along the pulmonary capillary, the pressure equilibration is brought about between alveolar air and blood. This acts as safety factor for better oxygenation during muscular exercise wherein the velocity of flow of blood through the pulmonary circulation will be very fast (Fig. 4.16).

Forms of Transport

- Dissolved form
- In combination with hemoglobin.

In the dissolved form, it is about 0.3 ml/100 ml in the arterial blood and 0.1 ml/100 ml in the venous blood. But still this particular form of transport is very essential as this form of gas alone can exert partial pressure that is necessary for diffusion of any gas. Oxygen gets dissolved in water available both in plasma and red blood cells. The volume of oxygen that is getting into the dissolved form in blood is directly proportional to the partial pressure.

As the pO_2 is increased, the volume of oxygen getting dissolved will also increase (Fig. 4.18). At pO_2 of 104 mm Hg, it is about 0.3 ml of oxygen goes into the solution form. At pO_2 of 1000 mm Hg, it is about 3 ml. In cases of severe anemia, oxygen in the dissolved form alone can cope up with the demands of oxygen supply to the tissues. This can be achieved by allowing the patient to breathe oxygen under high pressure (pO_2 1000–2000 mm Hg) intermittent hyperbaric oxygen administration.

Oxygen is transported mainly by hemoglobin. Volume of oxygen transported by hemoglobin in the arterial blood is about 19.5 ml/100 ml and in venous blood it is about 14.5 ml/100 ml. Presence of Hb increases the oxygen carrying capacity of blood by about 65 times.

$$Hb + O_2 \rightleftharpoons HbO_2$$

The percentage saturation of hemoglobin is about:

- 97% in arterial blood (oxygenated blood)
- 70% in the venous blood (deoxygenated blood)

One gram of hemoglobin can maximally carry about 1.34 ml of oxygen on full saturation.

Even though about 20 ml of oxygen is available in arterial blood for utilization by the tissues, the tissues normally use only about 5 ml of oxygen when 100 ml of blood flows through them in one minute. In other

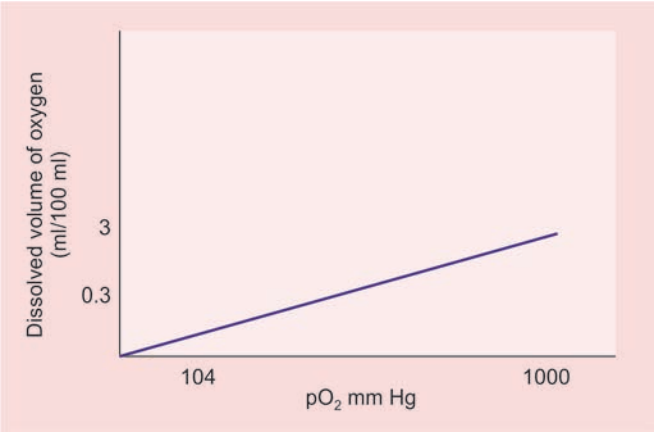

Fig. 4.18: Graph showing relationship between dissolved form of oxygen and partial pressure (note the direct relatioship between the volume of O_2 present in dissolved form when there is increase in pO_2)

words, only a part of oxygen available to them will be utilized. This is known as utilization coefficient. The ratio between the volume of oxygen used to the volume of oxygen available for utilization by the tissues is known as utilization coefficient. The utilization coefficient of oxygen is normally about 25%. In severe muscular exercise, it can go up to about 75%.

Oxygen binds to the heme part of hemoglobin. The reaction is a physical one. The reaction will be oxygenation and not oxidation, as the ferrous form of iron in hemoglobin does not get oxidsed to ferric form. Each molecule of hemoglobin with 4 atoms of iron can carry 4 molecules of oxygen. The reactions occur in stepwise fashion and it is known as heme-heme interaction. This type of binding of oxygen facilitates the rate of binding of oxygen to hemoglobin.

Details of heme—heme interaction steps:

$$Hb_4 + O_2 \longleftrightarrow Hb_4O_2$$
$$Hb_4O_2 + O_2 \longleftrightarrow Hb_4O_4$$
$$Hb_4O_4 + O_2 \longleftrightarrow Hb_4O_6$$
$$Hb_4O_6 + O_2 \longleftrightarrow Hb_4O_8$$

Reaction between oxygen and hemoglobin can be studied by plotting an oxygen dissociation curve.

- A series of (at least 10) tonometers are used. These are conical-shaped glass tubes of 5 ml capacity.
- In each one of these tonometers, 1 ml of blood is taken.
- These blood samples are exposed to different partial pressure of oxygen starting from 10 to 110 mm Hg, sealed and centrifuged.
- Oxygen combines with Hb and Hb gets saturated to different extents depending on the pO_2 to which it is exposed.
- The oxygen content of each of the tonometer is determined.
- Then one sample of blood is also exposed to 760 mm Hg pO_2 to fully saturate the Hb. This will give us the oxygen combining capacity of Hb.
- The amount of oxygen after full saturation is found out.
- From these figures available, the % saturation of Hb is calculated.

Percentage saturation of hemoglobin is ratio between volume of oxygen carried by hemoglobin to the maximum oxygen carrying capacity of hemoglobin times hundred.

$$\% \text{ Saturation of Hb} = \frac{O_2 \text{ carried (content)}}{O_2 \text{ carrying ability (capacity)}} \times 100$$

Oxygen dissociation curve: It is the graphical representation of % saturation of hemoglobin in relation to partial pressure of oxygen (Fig. 4.19). For adult Hb, it is sigmoid in shape whereas for fetal Hb, it has different configuration. Fetal Hb has greater affinity for oxygen as has been depicted in the graph. It is for this reason, fetal Hb dissociation curve when plotted is to the left of the adult Hb dissociation curve.

pO_2 mm Hg	% Saturation of HbA	% Saturation of HbF
20	35	70
40	70	95
104	97	

Factors affecting dissociation are:

1. Partial pressure of carbon dioxide.
2. H^+ in blood (decrease pH).
3. Temperature.
4. Conc. of 2–3 DPG.

Increase in all above factors shift the oxygen dissociation curve to the right. Converse happens (shift to left) when there is decrease in any of the above mentioned factors. Increase in pCO_2 or decrease in pH, which shifts the curve to right, is known as Bohr's effect. The extra oxygen requirement by the tissues during exercise is, therefore, met with by the above factors and hence the utilization coefficient is increased from 25 to about 75%. Therefore, oxygen

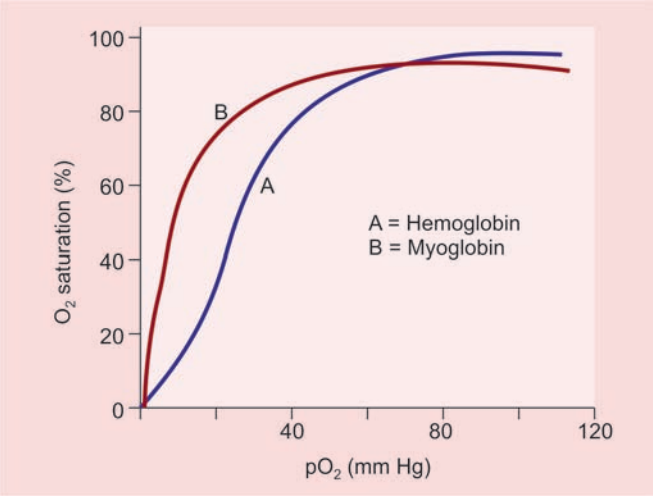

Fig. 4.19: Graph comparing oxygen-Hb dissociation curve with that of myoglobin

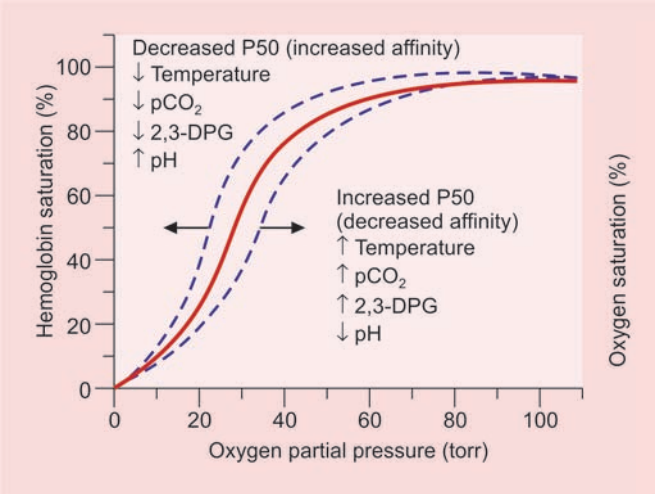

Fig. 4.20: Variation in P50 depending on various factors influencing the O_2 dissociation curve

supply to the tissues during exercise can be increased from 250 to 750 ml/min by the above mechanism only. Another 5–7-fold increase in the supply of oxygen can be achieved by increasing the cardiac output to about 25–35 l/min.

P50 is the partial pressure of oxygen at which hemoglobin is saturated to 50%. At sea level, P50 is about 28 mm Hg (Fig. 4.20).

Carbon Dioxide Transport

Carbon dioxide is the end product of oxidative tissue metabolism. When arterial blood flows through the tissues, because of pressure gradient, carbon dioxide diffuses from tissues into blood.

Carbon dioxide transport will be discussed under the following headings:

- Content
- Partial pressure at different levels
- Forms of transport
- Importance of dissolved form
- In combination with hemoglobin/plasma protein
- In HCO_3 form
- Carbon dioxide dissociation curve and factors influencing the same.

Content

In the arterial blood, it is about 48 ml/100 ml and in the venous blood (mixed) is about 52 ml/100 ml. Partial pressure at different regions:

a. In arterial blood is 40 mm Hg.
b. In tissues is about 46 mm Hg.
c. In venous blood, it is 46 mm Hg (mixed venous blood)
d. In alveoli, around 40 mm Hg.

	Arterial blood	*Venous blood*
pCO_2 (mm Hg)	40	46
Content (ml/100 ml)	48	52

Forms of Transport (Fig. 4.21)

1. As dissolved form 10%
2. As bicarbonate 68%
3. As carbamino compound 22%

Dissolved form: In arterial blood, it is about 2.5 ml and in venous blood it is about 2.8 ml per 100 ml of blood. It is this form of gas which exerts partial pressure. It gets dissolved in water available in plasma and in red blood cells. The volume of carbon dioxide getting transported in the dissolved form is directly proportional to partial pressure of the gas (Fig. 4.22).

As carbamino compound form: When hemoglobin reacts with hydrogen ion, the hemoglobin now is called reduced hemoglobin. The reduced hemoglobin reacts with carbon dioxide to form carbamino hemoglobin, which is also one of the forms of carbon dioxide transport. Unlike oxygen that binds to the heme part, carbon dioxide is attached to the globin part of hemoglobin.

Carbon dioxide is transported as bicarbonate both in red blood cells and plasma. But the formation of bicarbonate occurs mostly in erythrocytes because of the presence of the enzyme carbonic anhydrase. Bicarbonate thus formed inside the red blood cells, diffuse into the plasma along the concentration gradient.

At the tissue level, carbon dioxide diffuses from tissues into blood. This carbon dioxide apart from getting dissolved in water presents in the plasma, some amount also gets diffused into the red blood cells. In the erythrocytes also, some amount is transported in the dissolved form. However, the presence of carbonic anhydrase enzyme in red blood cell facilitates the reaction between carbon dioxide and water and there will be formation of carbonic acid. This acid is an unstable weak acid. Immediately, it dissociates to form bicarbonate and hydrogen ion.

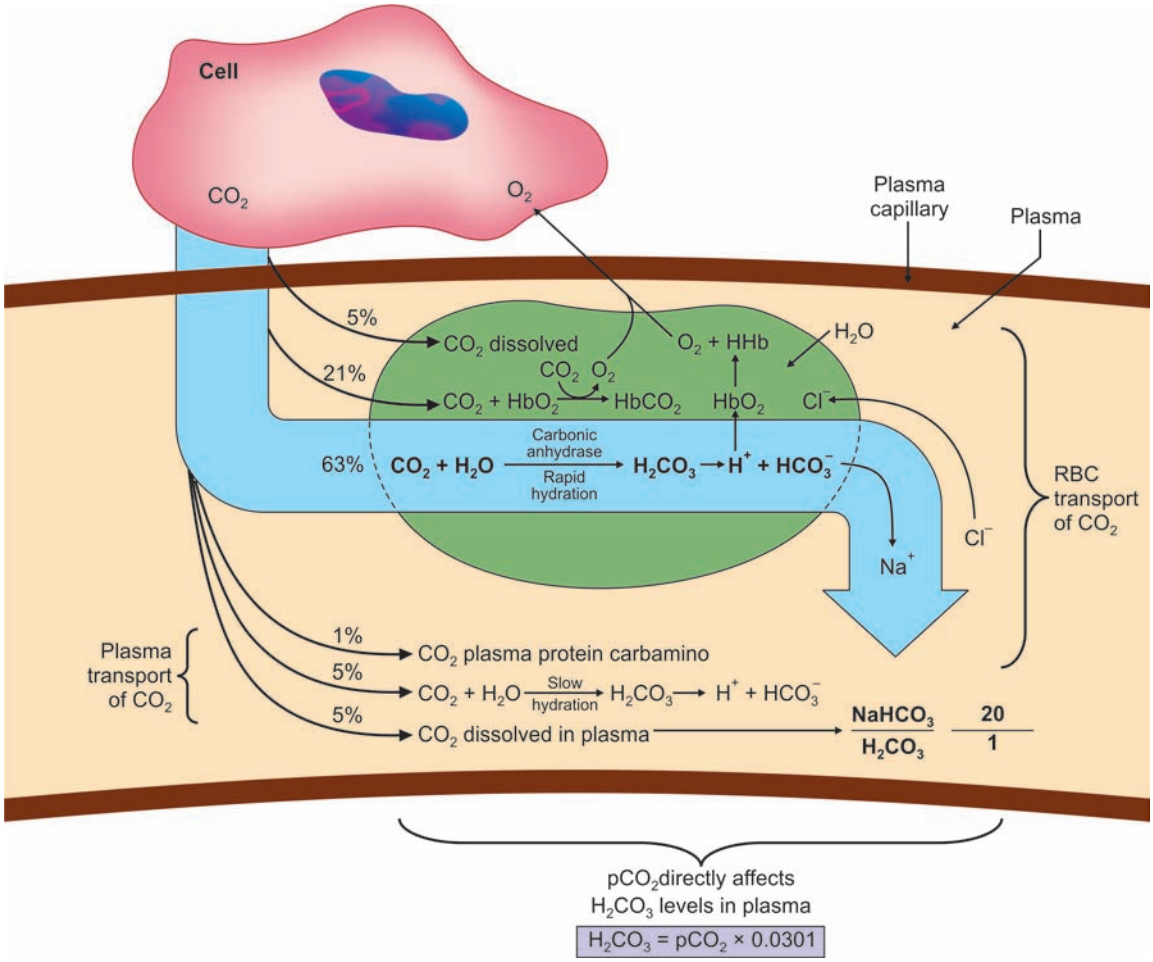

Fig. 4.21: Details of CO_2 transport in RBCs and plasma

Hemoglobin present in RBCs buffers the hydrogen ion that is formed during the reaction between carbon dioxide and water (Fig. 4.23).

Bicarbonate thus formed inside the red blood cell diffuses into plasma along the concentration gradient. Electrical activity of both red blood cells and plasma gets affected since bicarbonate is a charged ion. In order to maintain electrical neutrality, when bicarbonate diffuses out of cells, chloride ion diffuses into red blood cells from the plasma. This is known as *chloride shift* or *Hamburger's phenomenon*. This will be followed by diffusion of water into the red blood cells to maintain the tonicity. This increases the volume of RBCs. Hence PCV of venous blood will be slightly more than the arterial blood.

The whole set of reactions get reversed at the level of lungs during the process of diffusion of gas and thereby leads to the removal of carbon dioxide from the blood.

Carbon Dioxide Dissociation Curve (Fig. 4.24)

Graphical relation between partial pressure of carbon dioxide and the volume of carbon dioxide present in 100 ml of blood.

Haldane's effect: When venous blood flows through the pulmonary capillaries carbon dioxide diffuses out from blood into alveoli. Because of this, the pCO_2 of blood falls to 40 mm Hg from 46 mm Hg. If diffusion of carbon dioxide alone were to happen in the alveoli, what will happen to the volume of carbon dioxide at 40 mm Hg? When carbon dioxide dissociation curve is plotted for venous blood (pO_2–40 mm Hg), it is seen that when pCO_2 has fallen from 46 to 40 mm Hg, the

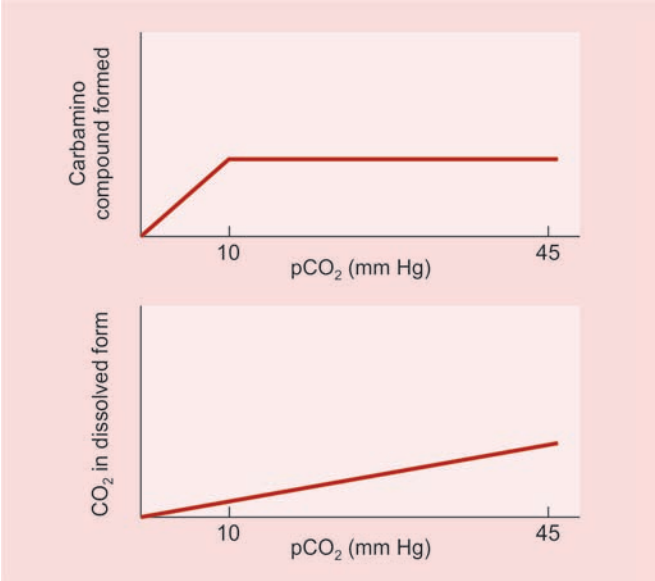

Fig. 4.22: Relationship between volume of CO_2 in dissolved form, carbamino compound form and partial pressure of CO_2

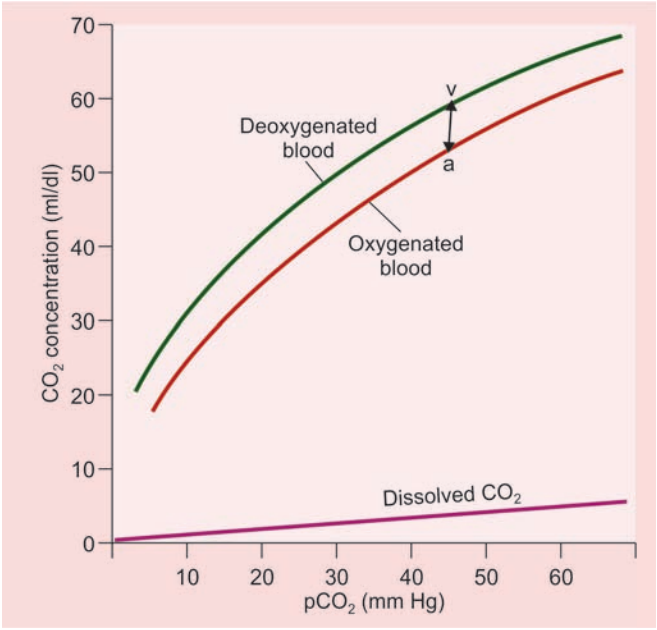

Fig. 4.24: Carbon dioxide dissociation curve

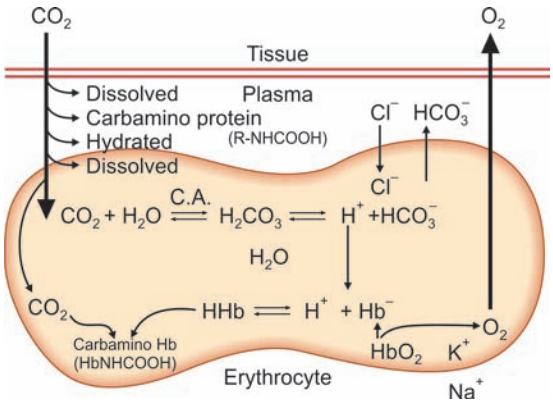

Fig. 4.23: Reactions within RBCs during carbon dioxide transport

carbon dioxide content gets reduced from 52 to 50 ml (point B in graph) only and not to 48 ml. For every 100 ml of blood flowing through the pulmonary capillaries only about 2 ml of carbon dioxide is removed.

But the important aspect to be remembered here is that at the lungs when carbon dioxide is diffusing out, there will be simultaneous oxygenation of capillary blood. This will increase the pO_2 of blood from 40 to 104 mm Hg. The increase in pO_2 shifts carbon dioxide dissociation curve to the right, so that point B on the dissociation curve gets shifted to point C. This facilitates an additional 2 ml of carbon dioxide being removed from blood. Because of this, when pCO_2 falls from 46 to 40 mm Hg due to simultaneous increase of pO_2, the content of carbon dioxide in blood falls from 52 to 48 ml/100 ml. This enables the removal of 4 ml of carbon dioxide from every 100 ml of blood flowing through the pulmonary capillaries. This is made possible because when oxygen enters blood, it combines with Hb to form oxyhemoglobin. This compound has a much lower affinity for carbon dioxide. Exactly the opposite happens when blood flows through the tissue capillaries.

In the lungs, when carbon dioxide is diffusing out, there is simultaneous diffusion of oxygen into blood. The increase in pO_2 (formation of oxy Hb) facilitates the release of more amount of carbon dioxide. Increase of pO_2, which shifts CO_2 dissociation curve to right, is known as Haldane's effect. Haldane's effect will help both the uptake (at tissue level) as well as giving out of carbon dioxide (at lungs).

Regulation of Respiration

Oxygen requirement by the body differs depending on the activity. It is lowest at rest and increases during routine activity and further increases in muscular exercise. Similarly production of carbon dioxide also is dependent on the rate of metabolic activity in the

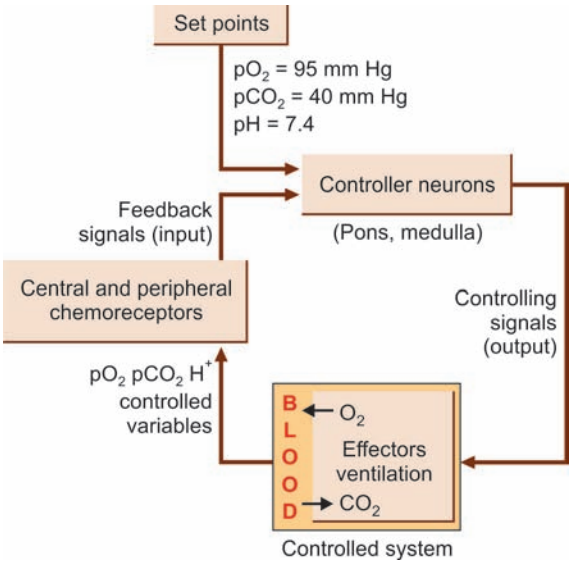

Fig. 4.25: Feedback circuit involved in the regulation of respiration

body. Respiratory system has the responsibility of meeting needs of the body by altering the rate and depth of respiration in order to keep the pO_2 and pCO_2 at normal levels.

The regulation of respiration can be brought about by:

1. Neural mechanism.
2. Chemical influence.
3. Non-chemical influence.

The chemical and non-chemical influence has to act through the neural mechanism only (Fig. 4.25).

Neural Mechanism

Centers are present in brainstem. The brainstem centers are required for rhythmic respiration whether during asleep or awake. The cerebral cortical center is required for voluntary alterations in respiration.

Brainstem centers are present in the reticular formation of pons and medulla oblongata. In the pons, the centers present are:

- Pneumotaxic
- Apneustic

In medulla oblongata, the centers present are:

- Inspiratory (dorsomedial group of neurons)
- Expiratory (ventrolateral group of neurons)

There is a lot of interconnection between the various centers. The interplay of the different centers is essential for a proper regulation of respiration. The medullary centers are termed as basic centers, whereas the pontine centers are called regulatory centers. The pontine centers act through the medullary centers and bring about smooth rhythmic respiration.

From the medullary centers, which are also spontaneously active, the impulses are sent to spinal cord through the reticulospinal pathway, which ends on the anterior horn cells in spinal cord. Both the phrenic (C3–C5) and intercostal nerve (T1–T11) take origin from spinal cord and influence the activity of diaphragm and intercostals muscles, respectively.

So if there is a complete transverse section of spinal cord at the level of

- *C*2 segment person dies of respiratory paralysis.
- *C*6 person survives because the diaphragmatic respiration continues.

In a normal person, the inspiratory center (IC) appears to generate impulse on its own. During the course of the generation of impulse, it is presumed that the rate of impulse generation goes on increasing till it reaches a certain point and then there will be sudden cessation of impulse generation. Because of this, IC is known to act as a ramp generator. The impulses from the apneustic center have a regulatory influence on the inspiratory center. The apneustic center activity in turn is controlled by the impulses coming from the pneumotaxic center and through the vagus nerve from the stretch receptors of lungs. When the influence by the vagus and pneumotaxic center over the apneustic center is lost, there will be prolonged inspiration and a sudden expiration. This type of breathing is known as apneustic breathing (Fig. 4.26).

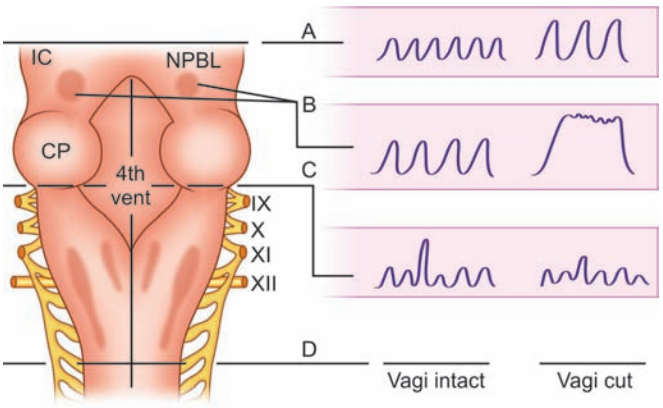

Fig. 4.26: Role of pontine respiratory centers over the medullary centers and also the role of vagus in control of breathing

Sequence of events during normal regulation of respiration by neural mechanism:

- Onset and gradual increase in the number of impulses production in the inspiratory center because of the ramp generator.
- This leads to:
  a. Impulses being sent from IC to spinal cord for stimulation of phrenic and intercostals nerves.
  b. Reciprocal inhibition of expiratory center by IC.
  c. Excitatory impulses from IC sent to pneumotaxic center through multisynaptic pathway.
- When inspiration is going on, there will be gradual inhibition of the apneustic center by the impulses coming from the pneumotaxic center and also from the afferent vagal fibers coming from the distended alveoli.
- Apneustic center influence over the IC ceases completely. Hence the activity of inspiratory center stops and leads to no inhibition influence over the expiratory center (EC). No more impulses from the inspiratory center to motor neurons in the spinal cord.
- The muscles of inspiration start relaxing. This starts the process of expiration which normally lasts for about 3 sec.
- After this, once again the activity in the IC starts, leading to the next respiratory cycle.

Location of the respiratory centers in CNS for rhythmic respiration can be experimentally studied from the following observations:

1. If transection is done above pons, the rhythmic respiration continues as usual.
2. If a mid-pontine section is done along with bilateral vagotomy, there will be a prolonged inspiration followed by a sudden short expiration (apneustic type of breathing).
3. If transection is done between pons and medulla oblongata, though respiration continues on its own, it will be irregular. Sometimes it becomes shallow and sometimes it is deeper. This type of breathing is known as gasping.
4. If transection is done below medulla (at the beginning of the spinal cord), it leads to complete cessation of breathing.

So by the above studies, it can be concluded that the centers are present in brainstem. The pontine centers play role in smooth and rhythmic respiration.

Hering-Brueur reflex: Inflation of alveoli brings about cessation of inspiration and expiration commences. The details are as under:

- Inflation of alveoli
- Leads of stimulation of stretch receptors present in the alveoli.
- Afferent impulses are carried by vagal fibers.
- Inhibit the activity of the respiratory center, cessation of inspiration.
- Leads to relaxation of muscles of inspiration.
- Expiration commences.

This reflex is not very well seen in adults. The reflex probably helps to prevent over distension of the alveoli.

Chemical Influence on Respiration

This is brought about by the chemoreceptors. They are called:

- Peripheral
- Central chemoreceptors.

Peripheral Chemoreceptors (Fig. 4.27)

a. Carotid bodies which are present at the branching of internal carotid artery.
b. Aortic bodies are present in the arch of aorta.

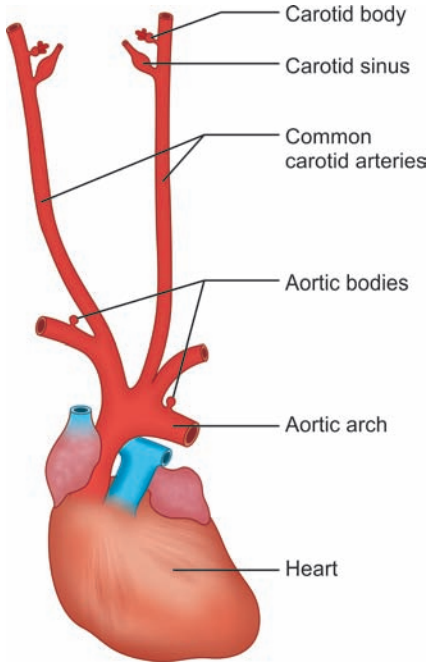

Fig. 4.27: Location of peripheral chemoreceptors

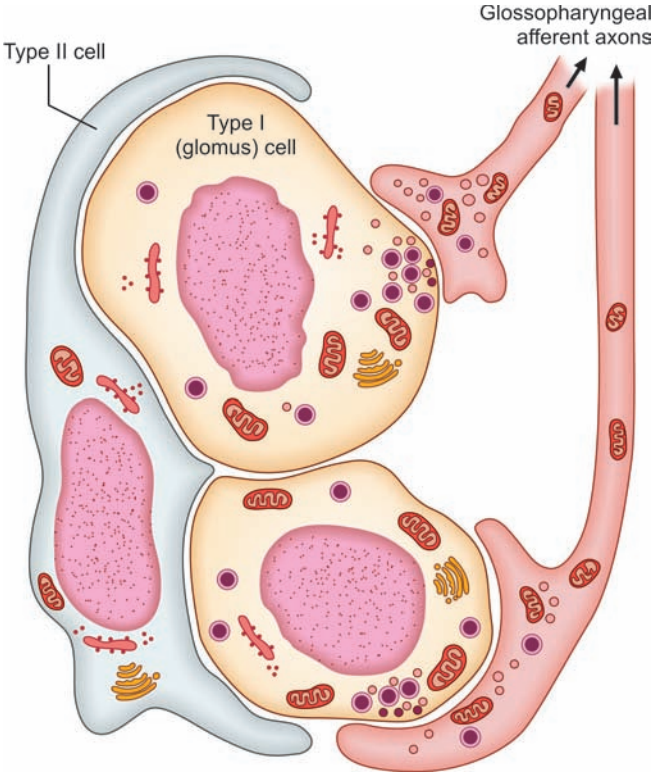

Fig. 4.28: Afferent nerve carrying impulse from carotid body

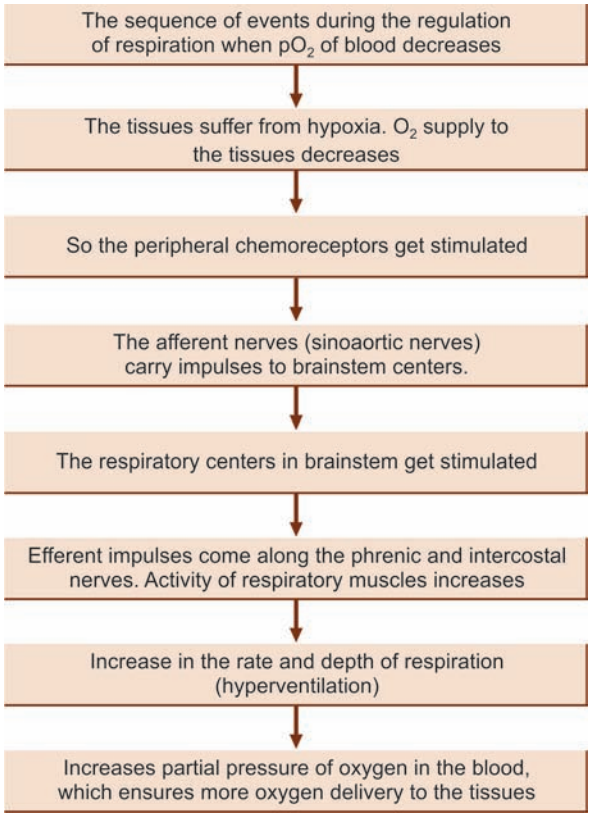

Fig. 4.29: Sequence of events during the regulation of respiration by peripheral chemoreceptors

From the carotid bodies, the afferent impulses will be carried by the sinus nerve (Fig. 4.28) a branch of glossopharyngeal nerve and from the aortic bodies by the aortic nerve branch of vagus nerve.

The peripheral chemoreceptors respond to:

- Decrease in pO_2
- Increase in H^+
- Increase of pCO_2 of blood.

Details of the role of peripheral chemoreceptors in regulation of respiration are shown in Figs 4.29 to 4.33.

Central Chemoreceptors

They are present in the brainstem near the respiratory centers. They are more sensitive to hydrogen ions, but the hydrogen ion of blood cannot stimulate them because the blood brain–barrier is impermeable for the hydrogen ion to diffuse through. Hence, the increase in partial pressure of carbon dioxide forms the stimulus (Fig. 4.34).

Decreased pO_2, increased pCO_2 together (asphyxia) will have an additive effect on chemoreceptors. Hence there will be maximum respiratory response in such a situation (Fig. 4.35). Asphyxia occurs in conditions, like drowning or strangulation.

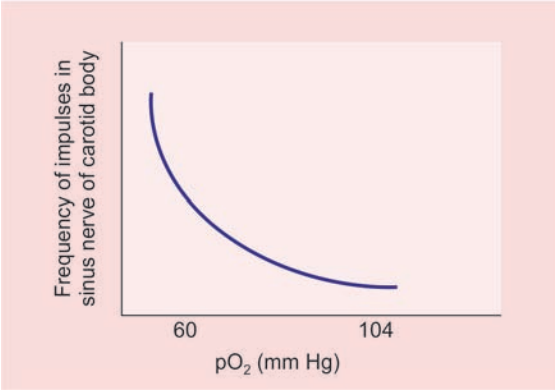

Fig. 4.30: Relationship between pO_2 and frequency of impulses in the sinus nerve from the carotid body

Non-chemical influence on respiratory centers pertains to impulses coming from:

- Baroreceptors
- Muscle spindles of respiratory muscles to control depth of respiration.

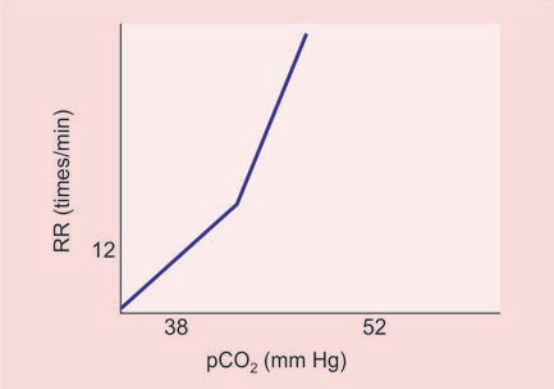

Fig. 4.31: Relationship between pCO_2 and rate of respiration

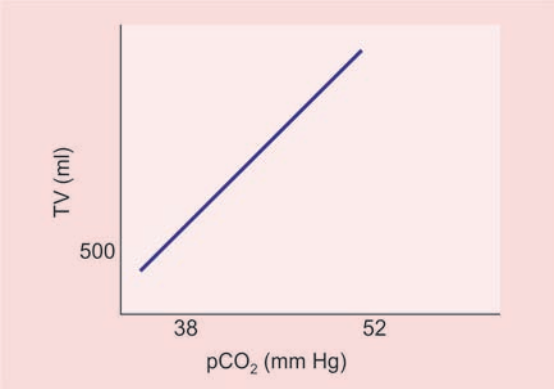

Fig. 4.32: Relationship between pCO_2 and tidal volume

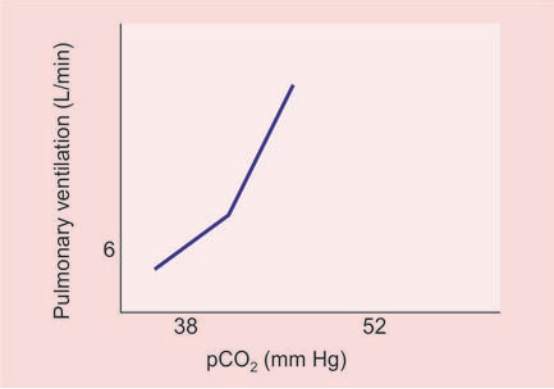

Fig. 4.33: Relationship between pCO_2 and pulmonary ventilation

- Pain receptors
- Intracranial tension
- Irritant receptors stimulation in lungs while coughing.

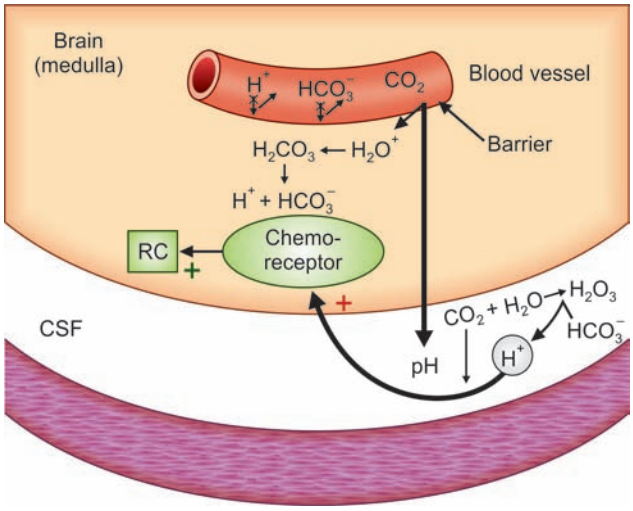

Fig. 4.34: Reactions occurring in the brain and the consequent stimulation of central chemoreceptos

- Higher parts of CNS
- Irritation of nasal mucosa (sneezing)
- Mechanoreceptors in pharynx (deglutition).
- Receptors of muscles and joints.

Depending on the location of the receptors influencing the respiratory centers, there will be appropriate alterations in the respiration.

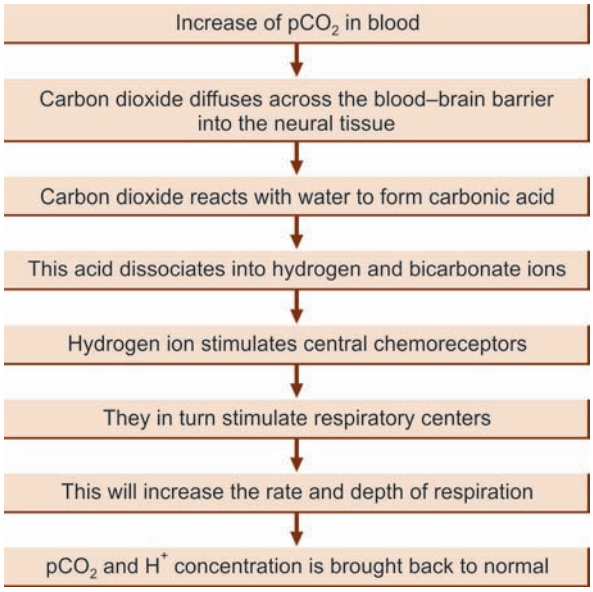

Fig. 4.35: Sequence of events during the regulation of respiration by central chemoreceptors

Hypoxia

When there is deficient oxygen supply to the tissues it is called hypoxia. There are 4 types of hypoxias. They are:

1. Hypoxic hypoxia (hypoxemia)
2. Anemic hypoxia
3. Stagnant hypoxia
4. Histotoxic hypoxia

Some of the characteristic features and causes for different types of hypoxia are given in Table 4.2.

Hypoxic Hypoxia

- Arterial pO_2 and oxygen content will be less than normal because most of the times the problem will be for the diffusion of oxygen at the level of alveolus.
- Hb cannot get oxygenated completely due to faulty diffusion or decreased pO_2 at high altitude, % saturation of Hb is decreased. More amount of reduced Hb (Hb that is not oxygenated) remains in circulation.
- At the level of tissues, reduction of Hb occurs further due to release of oxygen and hence the reduced Hb concentration increases. This leads to cyanosis.

Anemic Hypoxia

- Arterial pO_2 remains normal because diffusion of gas at the alveolus is normal. So the dissolved form of oxygen transported remains normal.
- Arterial oxygen content decreases because of either qualitative (carbon monoxide poisoning) or quantitative (anemia) defect in Hb.

Stagnant Hypoxia

- In this case, both the oxygen diffusion at alveoli and Hb function will be normal. Hence partial pressure, content, % saturation of Hb remain normal in arterial blood.
- Since circulation has slowed down or almost no circulation (cardiac failure) or hypokinetic (obstruction in venous drainage), it results in more oxygen being extracted by the tissues from the capillary blood. It leads more than normal amount of reduced Hb formation, and therefore, cyanosis will be present.

Table 4.2: Types of hypoxia—characteristic features and causes

Type of hypoxia	*Arterial blood*			*Venous blood*				
	pO_2 (95 mm Hg)	*% saturation of Hb (97%)*	*O_2 content (20 ml%)*	*pO_2 (40 mm Hg)*	*% saturation of Hb (70%)*	*O_2 content (15 ml%)*	*Cyanosis*	*Occurs in conditions*
Hypoxic	↓	↓	↓	↓	↓		Seen	Alveolar hypoventilation (bronchial asthma), pulmonary edema, at high altitude
Anemic	N	N	↓	N	N	↓	No	Anemia, carbon monoxide poisoning
Stagnant	N	N	N	↓	↓	↓	Seen	Cardiac failure, myocardial infarction, venous obstruction for any reason
Histotoxic	N	N	N	↑	↑	↑	No	Cyanide poisoning

Histotoxic Hypoxia

- Alveolar diffusion of oxygen, Hb function and the circulation is normal and hence all the parameters in arterial blood remain normal.
- Since there is poisoning of the enzyme system (cytochrome oxidase), the tissues are unable to take up oxygen from blood. The amount of oxygen used by the tissue gets decreased. So, less amount of reduced Hb is formed. The venous blood oxygen content will be more than normal. Hence A-V oxygen difference will be less than normal (parameters in the venous blood will be increased when compared to any normal situation).

Dyspnea

It means difficulty to breathe. The point at which a conscious necessity to increase the breathing occurs is known as dyspnea point. Dyspnea is seen in bronchial asthma, pneumothorax, respiratory and cardiac disorders. It can also be seen in physiological condition like in severe muscular exercise.

Cyanosis

a. Cyanosis is the bluish discoloration of skin and mucous membrane.
b. It occurs due to an increase in the concentration of reduced hemoglobin in capillary blood.
c. The concentration of reduced hemoglobin when exceeds 5 g%, there will be cyanosis.
d. Cyanosis can be central or peripheral.
e. Usually it is obvious in lips, nail beds, tongue, and finger tips.
f. Cyanosis occurs in hypoxic hypoxia and stagnant hypoxia.
g. It can occur due to diseases of lungs or heart.

Mountain Sickness

When people living at higher barometric pressure areas/low altitude get exposed suddenly to higher altitude, they are exposed to lower barometric pressure environment. Because of this, they will suffer from certain problems. All the symptoms are basically due to acute hypoxia especially on the neurons of central nervous system. The neurons of cerebral cortex are most susceptible for hypoxic effects when compared to either the brainstem or spinal cord. Some of the milder symptoms of mountain sickness are:

- Drowsiness
- Confusion
- Headache
- Nausea
- Impairment of judgment.
- Alteration of behavior.
- Motor incoordination.

Severe symptoms include cerebral and pulmonary edema, loss of consciousness, which may lead to death. To avoid such symptoms, people are advised to climb slowly so that body can get acclimatized to the atmosphere.

Acclimatization

Acclimatization can be defined as the physiological changes that are brought about to adjust for an altered atmosphere when exposed for prolonged duration.

Some of the physiological changes occur when the body is exposed to high altitudes are:

- Increase in rate and depth of respiration due to hypoxic stimulus acting through the peripheral chemoreceptors. However, the increase in rate and depth of respiration brings about washout of carbon dioxide. This reduces pCO_2 (respiratory alkalosis) and the fall in pCO_2 depresses the respiratory center activity. Hence there will be final increase of ventilation.
- There will be increased production of 2–3 DPG which helps for shifting of oxygen dissociation curve to right even though pCO_2 is less than normal.
- There will be increase in the diffusion capacity. Normal diffusion capacity is about 21 ml/min/mm Hg. Increase in diffusion capacity is because of increased surface area available for diffusion due to opening of the normally dormant capillaries and further distension of the already functional alveoli.
- Increase in myoglobin content to store as much of oxygen as possible.
- Increase in cytochrome oxidase enzyme activity to extract as much of oxygen from blood as possible.
- Increase in mitochondria to increase the supply of energy.
- Increase of red blood cell count because of hypoxic stimulus increasing the secretion of erythropoietin.
- Increase of cardiac output.

All the above changes help the person to sustain life easily even at a higher altitude.

Decompression Sickness/Caisson's Disease/Dysbarism

It occurs when people exposed to high barometric pressure suddenly get exposed to low atmospheric pressure. Usually, it is seen in divers who are exposed to high pO_2 below sea level. At high pressures, more gas will have gone into the dissolved state in all the tissues of body including blood. Among the gases, nitrogen which is neither utilized nor excreted also will be dissolved more in the tissues. It escapes from blood and enters organs and tissues. As it is fat-soluble, comparatively more of nitrogen is dissolved in fatty tissue and one of the vital organs in which a lot of nitrogen goes into dissolved state is brain.

When such people ascend up (come back to sea level) all of a sudden, nitrogen is decompressed. The gas starts escaping from the tissues at a faster rate leading to bubbling. When these bubbles enter blood vessels, it may obstruct the blood flow producing embolism. Because of the bubbling of gases either in tissues or in blood, it can lead to certain problems. Some of the features of the condition are:

- Compression in chest (chokes)
- Pain in the joints (bends)
- Pain at the back
- At times there can be damage to brain tissue as well, which may lead to paresis/paralysis.

Treatment

1. Avoid ascending up suddenly.
2. Promote recompression in a chamber and perform slow decompression.

Apnea

Apnea is temporary cessation of breathing. The different types are:

- Deglutition apnea (during deglutition) occurs during 2nd phase of swallowing.
- Voluntary apnea when breath is held voluntarily. Holding of breath cannot continue beyond a particular time. This is because, when breath is held, carbon dioxide accumulates in blood. This increases pCO_2 in circulation. The increased pCO_2 will override the voluntary breath holding effort and the person respires. The point at which the override effect is observed is known as breaking point.
- Hyperventilation apnea is because of washout of carbon dioxide leads to fall in pCO_2. The pCO_2 in arterial blood can be as little as 15 mm Hg from a normal value of 40 mm Hg.
- Vagal apnea
- Adrenaline apnea

Asphyxia

Asphyxia is a condition in which simultaneously there will be hypoxia (decrease in pO_2) and hypercapnia (increase in pCO_2) occurring in the body. Asphyxia occurs in strangulation, drowning, obstruction to the airway, etc. Asphyxia also occurs when newborn infant fails to breath. Since this condition could be fatal, immediate intervention to restore normal respiration must be initiated.

Periodic Breathing

Periodic breathing is when the breaths are interposed with some amount of apnea. The different types of periodic breathing are (Fig. 4.36):

- Cheyne-Stokes
- Biot's

Effects of hyperventilation: The increase in the rate and depth of respiration will bring about certain alterations in the body. They are:

- Decreased arterial pCO_2 which can fall to as low as 15 mm Hg.
- Increased arterial pO_2, which can be as high as 140 mm Hg.
- The increased voluntary hyperventilation cannot go for any length of time, because the washout of CO_2 from the body decreases the stimulatory influence on the respiratory center.

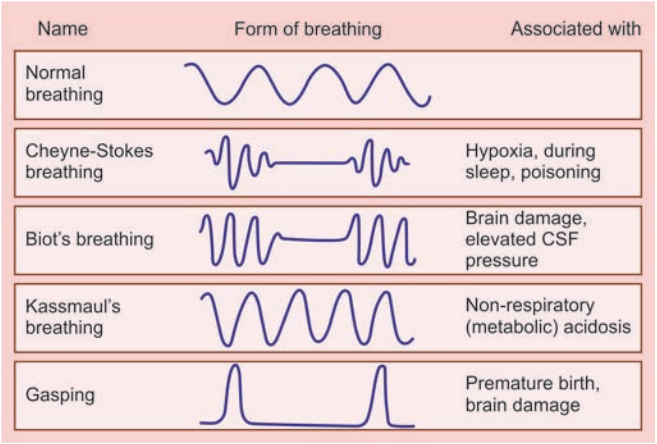

Fig. 4.36: Periodic breathing in different conditions

- When pCO_2 has fallen down to around 15 mm Hg, the respiration arrests for some time. This is known as hyperventilation apnea.
- Because of more of CO_2 elimination from the body, the pH of blood increases. In order to maintain the pH of blood, H^+ from the plasma proteins get liberated. Now the sites occupied by the H^+ are free. To these sites, the ionic calcium binds. This leads to decreased concentration of ionic calcium circulation. Hence can lead to tetany.
- The washout of CO_2 decreases the pCO_2 in blood. The vasodilator effect of carbon dioxide on the cerebral vessels decreases. There will be vasoconstriction in cerebral vessels and leads to decreased blood flow. This can lead to dizziness and loss of consciousness.

Artificial Respiration

When normal breathing has stopped for any reason, it is very essential to induce artificial respiration as early as possible. It is because if oxygen is not supplied to the brain for more than 3 minutes, it causes irreversible damage to brain. Artificial respiration has to be continued till the automatic respiration resumes.

There are different methods of artificial respiration. They can be broadly classified into:

1. Manual methods
2. Instrumental methods.

Some of the important manual methods are:

a. Mouth to mouth breathing.
b. Arm lift back pressure method (Holger Nielsen method)
c. Sylvester's method.
d. Eve's rocking method.

The most important advantage of manual methods is they can be employed anywhere and everywhere without any time delay. But the disadvantage will be they cannot be continued for longer duration. Each one of the manual methods has certain advantages and disadvantages.

Instrumental method: They are mechanical ventilators and basically are of two types, namely:

1. Positive pressure ventilator (air is forced into lungs from the respirator by positive pressure)
2. Negative pressure ventilator (air is made to enter lungs as the negative pressure applied by the respirator will act on the chest wall and bring about the expansion of same)

In both the type of methods, expiration will be brought about by a passive process.

The biggest advantage of the instrumental methods is they can be employed to continue artificial respiration for any length of time. On the other hand, these methods are available only at bigger hospitals and expensive and hence may not be within the reach of common man.