7

Respiratory System

Functional Anatomy

Two lungs taken together can be viewed as a trumpet having two separate zones-

i. Conducting

ii. Respiratory zone.

Gaseous exchange occurs in the respiratory zone but not in the conducting zones (also called, dead space). Accordingly the respiratory zone presents a typical histological pattern conducive to the exchange. Mast cells of mucosa secrete histamine (H) when their membrane is perturbed and H_1 receptors are occupied by H → bronchospasm. Mast cells also produce SRS-A, which causes bronchospasm. Bronchial muscles supplied by sympathetic (relaxants = bronchodilator ; β_2 receptors) and parasympathetic (constrictor, muscarinic receptors). Besides, VIP secreting neurons also supply. β_2 stimulants (salbutamol) → bronchodilatation. Blood in pulmonary capillary is separated from air within alveolus by alveolo-capillary membrane (= capillary wall + alveolar wall; average thickness 0.5 mm).

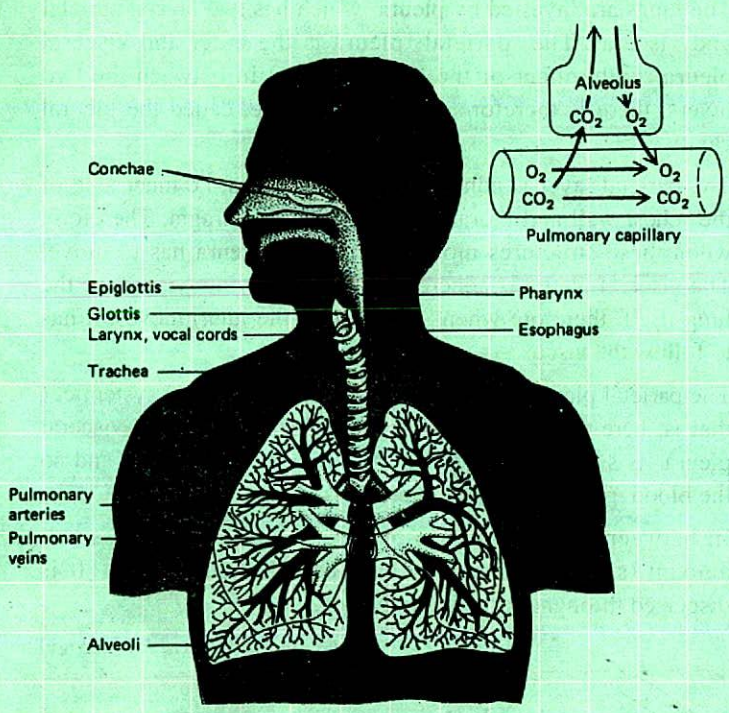


Fig. 7-1. *Respiratory tact or passage.*

Respiratory Tract

The organs which allow the entrance of air into the lungs and exchanges of gases with the blood in the air passages from the nose to the pulmonary alveoli.

Division of respiratory tract :

a. *Upper respiratory tract :* From nose (anterior nares) to the vocal fold. It consist of-
   i. Nose
   ii. Nasopharynx.
   iii. Oropharynx.
   iv. Larynx upto vocal folds.

b. *Lower respiratory tract :* From vocal folds to the alveoli of the lungs. It consist of-
   i. Larynx below the vocal folds
   ii. Trachea
   iii. Two bronchi
   iv. Bronchioles
   v. Terminal bronchioles
   vi. Respiratory bronchioles
   vii. Alveolar duct
   viii. Atria
   ix. Air sac
   x. Alveoli.

Linning epithelium of respiratory system

a. *Trachea & major bronchi :* Pseudostratified ciliated columnar epithelium.

b. *Bronchioles :* Ciliated columnar epithelium. Onwards from respiratory bronchioles : The cilia disappear and the epithelium becomes cubical.

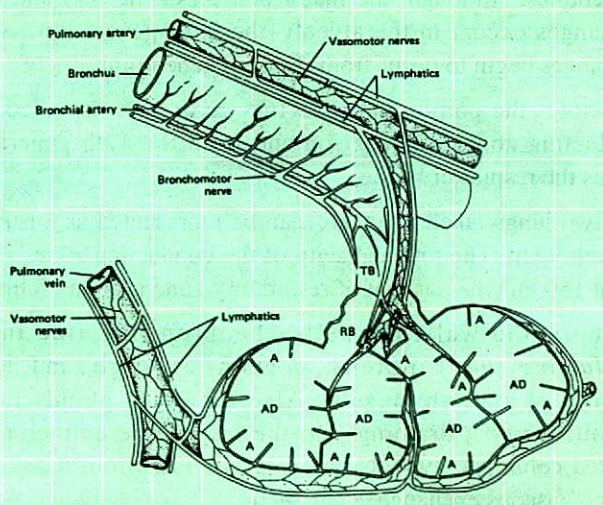


Fig. 7-2. *Respiratory passages or tract.*

c. *Alveolar wall :* Thin, simple squamous type. The linning epithelial cells are of two types.
   i. *Type I cells :* Squamous cells .
   ii. *Type II cells* (also called ***granular pneumocytes***) are interminged with the type I cells. They secrets surfactant a substance which reduce the surface tension in the alveoli. They constitute about 10 percent of the surface area of alveoli.

(Ref. Ganong 22th ed; Page-648, Guyton 11th ed; page-474)

Alveoli

a. *Total numbers*	: 300 million
b. *Total area of the alveolar walls in contact with capillaries in both lungs is about*	: 70 m^2
c. *Space between air and blood*	: 0.5 micro meter

Alveoli communicate with each other by small pores called *pores of khan*. Accessory communication sometimes occur between fine bronchioles and their adjacent alveoli and known as *Lamberts sinuses*.

(Ref. Ganong 22th edition, Page 649)

Conducting and respiratory zone

The whole lung can be divided into two major zones, conducting zone and respiratory zone.

Weibel numbered each generation of tracheobronchial tree.Thus the trachea is generation 0 (zero). The two major divisions of the trachea, viz, the right and left bronchi, constitute the first generation, and so on. In the 16th generation, the bronchi are called the terminal bronchiole.

The 17th generation bronchioles are the respiratory bronchioles. There are three generations of respiratory bronchiole. The alveolar sac is the 23rd and the last generation.

On and from the 17th generation, few alveoli can be found on bronchioles. Although, the major portion of the O_2 and CO_2 exchanges occurs in the alveoli (the 23rd generation), some exchanges begin to occur from the 17th generation.

Therefore the portion upto the 16th generation, is called the conducting zone, whereas on and from the 17th generation begins the respiratory zone.

The two lungs taken together, can be represented as a trumpet shaped organ. The total capacity of the conducting zone is only about 150 ml whereas that of respiratory zone is about 3 liters.

In short, the walls of the tracheobronchial tree in the ***conducting zone*** are thick, contain- cartilage and heavy amount of smooth muscles.Also there are glands in the submucous coat draining into the lumen.The epithelia are ciliated columnar type. No alveolus sprouts from these areas and no gaseous exchange occurs here.

On the other hand, ***respiratory zone*** is a big area containing large number of exceedingly thin walled alveoli, without any mucus secretion. Gaseous exchanges occur through the alveoli of this zone.

It will be seen afterwards that velocity of air flow is high in the conducting zone, whereas it is low in the respiratory zone.

These multiple divisions greatly increase the total cross-sectional area of the airways-

i. Trachea : 2.5 cm^2
ii. Alveoli : 11,800 cm^2.

(Ref. Ganong 21th edition, Page 650 & others)

Pleura

The lungs are invested by pleura which has two layers, parietal and visceral. The parietal pleura is the outer and visceral pleura is the inner of the double layer. In between the two layers, there is therefore a potential space, called the pleural cavity.

The parietal layer is adherent to the parieties, i,e inner side of the chest wall and thoracic side of the diaphragm. Therefore, when these structures move, the parietal pleura has to move. The visceral pleura is adherent to the underlying viscus, i,e the lung itself, therefore when the viscus (the lung) moves, it has to follow the viscus.

The parietal pleura is supplied by vessels which are systemic, (that is, here the blood pressure is higher) whereas the visceral pleura is supplied by vessels of pulmonary circulation and so the blood pressure in these vessels is low.

In between the two layers of pleura there is a very small amount (say about 2ml) of fluid, called ***pleural fluid.*** It is dispersed throughout the pleural cavity.

(Ref. Concise Medical Physiology)

Pulmonary Circulation

Pulmonary blood vessels

Anatomical peculiarities : The pulmonary vascular bed resembles the systemic, except that-

i. The walls of the pulmonary artery and its large branches are about 30% as thick as the wall of the aorta.
ii. The small arterial vessels, unlike the systemic arterioles, are endothelial tubes with relatively little muscle in their walls.
iii. There is also some smooth muscle in the walls of the postcapillary vessels.
iv. The pulmonary capillaries are large, and there are multiple anastomoses, so that each alveolus sits in a *capillary basket.*

(Ganong 22th Edition; page 661)

Pulmonary blood flow

With two quantitatively minor exceptions, the blood put out by the left ventricle returns to the right atrium and is ejected by the right ventricle, making the pulmonary vasculature unique in that

it accommodates a blood flow that is almost equal to that of all the other organs in the body. One of the exceptions is part of the bronchial blood flow. As noted above there are anastomoses between the bronchial capillaries and the pulmonary capillaries and veins, and although some of the bronchial blood enters the bronchial veins, some enters the pulmonary capillaries and veins, bypassing the right ventricle. The other exception is blood that flows from the coronary arteries into the chambers of the left side of the heart. Because of the small physiologic shunt created by those two exceptions, the blood in systemic arteries has a PO_2 about 2 mm Hg lower than that of blood that has equilibrated with alveolar air, and the saturation of hemoglobin is 0.5% less.

(Ganong 22th Edition; page 661)

(Q. 00. Define venous admixture of blood. Does it have any importance?)

Pulmonary blood volume

The blood volume of the lungs is about 450 milli liters, about 9 percent of the total blood volume of the circulatory system. The volume of blood in the pulmonary vessels at any one time is about 1 liter, of which less than 100 ml is in the capillaries. The mean velocity of the blood in the root of the pulmonary artery is the same as that in aorta (about 40 cm/second). It falls off rapidly, then rises slightly again in the larger pulmonary veins.

It takes red cell about 0.75 second to traverse the pulmonary capillaries at rest and 0.3 second or less during exercise.

(Ref. Guyton 11th edition, Page 484; Ganong 22th Edition; page 661)

Pulmonary blood pressure

The entire pulmonary vascular system is a distensible low-pressure system. The pulmonary arterial pressure is about 24/9 mm Hg, and the mean pressure is about 15 mm Hg. The pressure in the left atrium is about 8 mm Hg during diastole, so that the pressure gradient in the pulmonary system is about 7 mm Hg, compared with a gradient of about 90 mm Hg in the systemic circulation. It is interesting that the pressure fall from the pulmonary artery to the capillaries is relatively small and that there is an appreciable pressure drop in the veins.

(Ganong 22th Edition; page 662)

Pressures in the pulmonary artery and vein :

1. *Pressures in the pulmonary artery* :
   a. *Systolic* pulmonary arterial pressure averages approximately 25 mm of Hg in the normal human being,
   b. *Diastolic* pulmonary arterial pressure approximately 8 mm of Hg
   c. *Mean* pulmonary arterial pressure 15 mm of Hg.
2. *Pressures in the pulmonary capillary* : Mean capillary pressure about 7 mm of Hg.
3. *Left atrial and pulmonary venous pressure* : The mean pressure in the left atrium and major pulmonary veins varying from 1 to 5 mm of Hg, averages about 2 mm Hg.

(Ref. Guyton & Hall-11th edition, Page 483, 484)

Trans-pulmonary pressure

It is the pressure difference between the alveolar pressure and the pleural pressure. It is the pressure difference between the alveoli and the outer surface of the lungs, and it is a measure of the elastic forces in the lungs that tend to collapse the lungs at each point of expantion, called the recoil pressure.

(Ref. Guyton & Hall-11th Edition, Page-473)

Capillary pressure

Pulmonary capillary pressure is about 10 mm whereas the oncotic pressure is 25 mm Hg, so there is an inward-directed pressure gradient of about 15 mm Hg which keeps the alveoli free of fluid. When the pulmonary capillary pressure is more than 25 Hg- as it may be, for example, when there is 'back-ward failure' of the left ventricle- pulmonary congestion and edema result. Patients with mitral stenosis also have a chronic, progressive rise in pulmonary capillary pressure and extensive fibrotic changes in the pulmonary vessels.

(Ganong 22th Edition; page 662)

Pulmonary capillary dynamics

Exchange of gases between the alveolar air and the pulmonary capillary blood is discussed in the next chapter. However, it is important for us to note here that the alveolar walls are lined with so many capillaries that in most places, the capillaries almost touch one another side by side. Therefore, it has often been said that the capillary blood flows in the alveolar walls as a "sheet," rather than in individual capillaries.

(Ref. Guyton & Hall-11th edition, Page 487)

Pulmonary capillary pressure : No direct measurements of pulmonary capillary pressure have been made. However, "isogravimetric" measurement of pulmonary capillary pressure, using a technique has given a value of 7 mm Hg. This is probably nearly correct because the mean left atrial pressure is about 2 mm Hg and the mean pulmonary arterial pressure is only 15 mm Hg, so that the mean pulmonary capillary pressure must lie somewhere between these two values.

Length of time blood stays in the capillaries : From histological study of the total cross-sectional area of all the pulmonary capillaries, it can be calculated that when the cardiac output is normal, blood passes through the pulmonary capillaries in about 0.8 second. When the cardiac output increases, this can shorten to as little as 0.3 second. The shortening would be much greater were it not for the fact that additional capillaries, which normally are collapsed, open up to accommodate the increased blood flow. Thus, in only a fraction of a second, blood passing through the alveolar capillaries becomes oxygenated and loses its excess carbon dioxide.

(Ref. Guyton & Hall-11th edition, Page 487)

Capillary exchange of fluid in the lungs, and pulmonary interstitial fluid dynamics : The dynamics of fluid exchange across the lung capillary membranes are *qualitatively* the same

as for peripheral tissues. However, *quantitatively*, there are important differences, as follows :

a. *The pulmonary capillary pressure* is low, about 7 mm Hg, in comparison with a considerably higher functional capillary pressure in the peripheral tissues, about 17 mm Hg.

b. *The interstitial fluid pressure* in the lung is slightly more negative than that in the peripheral subcutaneous tissue. (This has been measured in two ways: by a micropipette inserted into the pulmonary interstitium, giving a value of about -5 mm Hg, and by measuring the absorption pressure of fluid from the alveoli, giving a value of about -8 mm Hg).

c. *The pulmonary capillaries* are relatively leaky to protein molecules, so that the colloid osmotic pressure of the pulmonary interstitial fluid is about 14 mm Hg in comparison with less than one half this in the peripheral tissues.

d. The alveolar walls are extremely thin, and the alveolar epithelium covering the alveolar surfaces is so weak that it can be ruptured by any positive pressure in the interstitial spaces greater than alveolar air pressure (greater than 0 mm Hg), which allows dumping of fluid from the interstitial spaces into the alveoli.

(Ref. Guyton & Hall 11th edition, Page 488)

Interrelations between interstitial fluid pressure and other pressures in the lungs : The balance of forces at the blood capillary membrane as follows :

Forces tending to cause movement of fluid outward from the capillaries and into the pulmonary interstitium :

1.	Capillary pressure	: 7
2.	Interstitial fluid colloid osmotic pressure	: 14
3.	Negative interstitial fluid pressure	: 8
	Total outward force	: *29*

Forces tending to cause absorption of fluid into the capillaries :

1.	Plasma colloid osmotic pressure	: 28
	Total inward force	: 28

Thus, the normal outward forces are slightly greater than the inward forces, providing a mean filtration pressure at the pulmonary capillary membrane; this can be calculated as follows :

	mm Hg
Total outward force	: + 29
Total inward force	: - 28
Mean filtration pressure	: + 1

This filtration pressure causes a slight continual flow of fluid from the pulmonary capillaries into the interstitial spaces, and except for a small amount that evaporates in the alveoli, this fluid is pumped back to the circulation through the pulmonary lymphatic system.

(Ref. Guyton Hall-11th edition, Page 488)

Negative pulmonary interstitial pressure and the mechanism for keeping the 'Alveoli Dry'

One of the most important problems in lung function is to understand why the alveoli do not fill with fluid. One's first impulse is to say that the alveolar epithelium keeps fluid from leaking out of the interstitial spaces into the alveoli. This is not true because there are always a small number of openings between the alveolar epithelial cells through which even large protein molecules as well as large quantities of water and electrolytes can pass.

However, if one remembers that the pulmonary capillaries and the pulmonary lymphatic system normally maintain a slight negative pressure in the interstitial spaces, then it is clear that whenever extra fluid appears in the alveoli, it will simply be sucked mechanically into the lung interstitium through the small openings between the alveolar epithelial cells. Then the excess fluid is either carried away through the pulmonary lymphatics or absorbed into the pulmonary capillaries. Thus, under normal conditions, the alveoli are kept in a "dry" state except for a small amount of fluid that seeps from the epithelium onto the lining surfaces of the alveoli to keep them moist.

(Ref. Guyton & Hall-11th edition, Page 488)

Regulation of pulmonary blood flow

It is unsettled whether pulmonary veins and pulmonary arteries are regulated separately, although constriction of the veins increases pulmonary capillary pressure and constriction of pulmonary arteries increases the load on the right side of the heart. Small arteries several hundred micrometers in diameter are the major site of vascular resistance.

Pulmonary blood flow is affected by both active and passive factors. There is an extensive autonomic innervation of the pulmonary vessels, and stimulation of the cervical sympathetic ganglia reduces pulmonary blood flow by as much as 30%. The vessels also respond to circulating humoral agents. Many of the dilator responses are endothelium-dependent and presumably operate via release of NO. In pulmonary hypertension, there is a deficiency of endothelial NOS.

Passive factors such as cardiac output and gravitational forces also have significant effects on pulmonary blood flow. Local adjustments of perfusion to ventialtion are determined by local effects of O_2 or its lack. With exercise, cardiac output increases and pulmonary arterial pressure rises proportionately with little or no vasodialation. More red cells move through the lungs without any reduction in the O_2 saturation of the hemoglobin in them,and consequently, the total amount of O_2 delivered to the systemic circulation is increased. Capillaries dilate, and previously underperfused capillaries are "recruited" to carry blood. The net effect is a marked incrase in pulmonary blood flow with few if any alterations in autonomic outflow to the the pulmonary vessels.

^{133}Xe can be used to survey local pulmonary blood flow by

injecting a saline solution of the gas intravenously while monitoring the chest. The gas rapidly enters the alveoli that are perfused normally but fails to enter those that are not perfused. Another technique for locating poorly perfused areas is injection of macroaggregates of albumin labeled with radioactive iodine. These aggregates are large enough to block capillaries and small arterioles, and they lodge only in vessels in which blood was flowing when they reached the lungs. Although it seems paradoxic to study patients with defective pulmonary blood flow by producing vascular obstruction, the technique is safe because relatively few particles are injected. The particles block only a small number of pulmonary vessels and are rapidly removed by the body.

When a bronchus or a bronchiole is obstructed, hypoxia develops in the underventilated alveoli beyond the obstruction. The O_2 deficiency apparently acts directly on vascular smooth muscle in the area to produce constriction, shunting blood away from the hypoxic area. Accumulation of CO_2 leads to a drop in pH in the area, and a decline in pH also produces vasoconstriction in the lungs, as opposed to the vasodilation it produces in other tissues. Conversely, reduction of the blood flow to a portion of the lung lowers the alveolar PCO_2 in that area, and this leads to constriction of the bronchi supplying it, shifting ventilation away from the poorly perfused area.

Systemic hypoxia also causes the pulmonary arterioles to constrict, with a resultant increase in pulmonary arterial pressure.

(Ref. Ganong 22th edition, Page 663)

Pulmonary edema

Pulmonary edema occurs in the same way that edema occurs elsewhere in the body. Any factor that causes the pulmonary interstitial fluid pressure to rise from the negative range into the positive range will cause sudden filling of the pulmonary interstitial spaces and alveoli with large amounts of free fluid.

The most common causes of pulmonary edema are as follows :

1. *Left-sided heart failure* or *mitral valvular disease* with consequent great increases in pulmonary venous pressure and pulmonary capillary pressure and flooding of the interstitial spaces and alveoli.
2. *Damage to the pulmonary capillary membrane* caused by infections such as pneumonia or by breathing noxious substances such as chlorine gas or sulfur dioxide gas.

Each of these causes rapid leakage of both plasma proteins and fluid out of the capillaries and into both the lung interstitial spaces and the alveoli.

(Ref. Guyton & Hall-11th edition, Page 488)

Pulmonary edema safety factor : In experiments in animals, it has been found that the pulmonary capillary pressure normally must rise to a value at least equal to the colloid osmotic pressure of the plasma inside the capillaries before significant pulmonary edema occurs. Remember that every time the left atrial pressure rises to high values, the pulmonary capillary pressure rises to a level 1 to 2 mm Hg greater than the left atrial pressure. As soon as the left atrial pressure rose above 23 mm Hg (With the pulmonary capillary pressure above about 25 mm Hg), fluid began to accumulate in the lungs; fluid accumulation increased even more rapidly with further increases in capillary pressure. Yet below 25 mm Hg pulmonary capillary pressure, there was no significant change in pulmonary fluid. The plasma colloid osmotic pressure in dogs is almost equal to this 25 mm Hg critical pressure level. Therefore, in the human being, who normally has a plasma colloid osmotic pressure of 28 mm Hg one can predict that the pulmonary capillary pressure must rise from the normal level of 7 mm Hg to more than 28 mm Hg to cause pulmonary edema, giving a safety factor against pulmonary edema of about 21 mm Hg.

Safety factor in chronic condition : When the pulmonary capillary pressure remains elevated chronically (for at least 2 weeks), the lungs become even more resistant to pulmonary edema because the lymph vessels expand greatly, increasing their capability of carrying fluid away from the interstitial spaces perhaps as much as 10-fold. Therefore, in patients with chronic mitral stenosis, pulmonary capillary pressures of 40 to 45 mm of Hg have been measured without the development of lethal pulmonary edema.

(Ref. Guyton & Hall-11th edition, Page 488, 489)

Broncho pulmonary segment

Each tertiary bronchus and its ramifications and the aleveoli connected with them, constitute a broncho-pulmonary segment, which is self-contained, functionally independent unit of lung tissue. It has its own blood, lymph & nerve supply and connective tissue investment. This is of surgical importance in dissection of a portion of the lung in diseased condition.

There are ten bronchopulmonary segments in the right lung & nine in the left lung. The medial basal or cardiac segment is absent in the left lung.

Broncho vascular units : Each segmental bronchus and its ramifications are not associates with independent vascular pattern, each having its own artery and being separate from its neighbours.

Lung unit/Primary lobule/Respiratory unit : The functional unit of lung, which is the clusters of structures around a single respiratory bronchiole.

It comprises :

i. A single respiratory bronchiole
ii. Five or six alveolar ducts.
iii. Atria
iv. Three to six alveolar sacs.

There are about 300 million alveoli in the two lungs, each alveolus having an average diameter of about 0.2 millimeter.

(Guyton & Hall-11th Edition)

Function of the lungs

A. ***Respiratory function*** :

1. *Gaseous exchanges :* Carriage of oxygen from the lungs to the site of tissue respiration for sub-sequent utilization and also carriage of CO_2 from that site to the lung alveoli for elimination.
2. *Metabolic function :* Oxygen is essen-tial for maintenance of metabolism in the tissue. Aerobic metabolism cannot take place in the abscence of oxygen.
3. *Excretion :* It excretes volatile substancess like ammonia, keton bodies, essential oils, alcohols, water vapours etc.
4. *Maintenance of acid-base balance :* This is done chiefly by adjusting the amount of CO_2 elimination, the normal P^H of the body fluid is 7.4. Any change in the P^H causes alteration in the rate and depth of breathing.
5. *Maintenance of temperature balance :* When water is transformed into gaseous form, heat is absorbed, so heat is lost through water vapours. About 10% of body heat is changed in this way.
6. *Maintenance of water balance* : 600-800 ml of water per day is lost as water vapour during expiration.
7. *Role of respiration on circulation :*
   a. During inspiration the intrathoracic pressure falls and intra-abdominal pressure rises, which helps in return of blood & lymph.
   b. Respiration affect heart rate & cardiac output through nervous mechanism. So changes in respirartion causes change in circulation.
   c. Blood pressure increases during the later part of inspiration & early part of expiration. During the remaining period blood pressure falls.
8. *Homeostatic function :* It helps in maintenance of homeostasis of the internal environment of the body.

B. ***Non-respiratory function of lungs*** :

i. Metabolic function.
ii. Excretory function.
iii. Maintenance of acid base balance.
iv. Maintenace of temperature balance.
v. Maintenance of water balance.
vi. Role on circulation.
vii. Maintenance of homeostasis of the internal environment of the body.
viii. *Lung defense mechanisms* :
   a. They humidify and cool or warm the inspired air. So that even very hot or very cold air is at or near body temperature by the time it reaches the alveoli.
   b. Bronchial secretions contain secretory immunoglobulins (IgA) and other substances that help to resist infection and maintain the integrity of the mucosa. In addition, the epithelium of the paranasal sinuses appears to produce NO, which is bacteriostatic and helps prevent infection.
   c. The Pulmonary alveolar macrophages (PAMS dust cell) are important components of the pulmonary defense mechanism.They are actively phagocytic and ingest inhaled bacteria and small particles.
   d. Various mechanism operate to prevent foreign matter from reaching the alveoli. The hairs in the nostrils strain out many particles larger than 10 mm in diameter.
   e. Particles 2-10 mm in diameter generally fall on the walls of the bronchi as the air flow slows in the smaller passages. There they initiate reflex brochial constriction and coughing.
   f. The epithelium of the respiratory passages from the anterior third of the nose to the begining of the respiratory bronchioles is ciliated, and the cilia beat at a frequency of 1000-1500 cycles per minute, is capable of moving particles at a rate of at least 16 mm/min. Particles less than 2 mm in diameter generally reach the alveoli, where they are ingested by the macrophages.

(Ref. Ganong 22th edition, Page 664 & others)

C. ***Biologically active substances metabolized by the lungs***
(Metabolic and Endocrine function of the lungs) :

a. Synthesized and used in the lung surfactant.
b. *Synthesized or stored and released into the blood* :
   Prostaglandins
   Histamine
   kallikrein.
c. *Partially removed from the blood* :
   Prostaglandins
   Adenine nucleotides
   Nor epinephrine
   Bradykinin
   Serotonin
   Acetylcholine
d. *Activated in the lungs* :
   Angiotensin-I → Angiotesnion-II.

(Ref. Ganong.22th edition, Page 665)

Function of the nose :

The nasal passage (nose) play for the conduction of air and also as efficient air conditioning and filtering units. Thus -

1. The dust particles and bacteria become cought up in the nasal mucous and are removed.
2. The air is cooled down and is made moist.
3. The sense organ of smell is situated in the nose & the odour of the inspired air can be easily taken.

Respiration

(Pulmonary ventilation)

Definition : Respiration is a physiological process which means the transport of O_2 from atmosphere to the body cell for oxidation of the ingested food materials and elemination of CO_2 and other volatile metabolic end products from the cell to the atmosphere.

Phages of respiration : Respiration has two phases -

A. *Inspiration (Active process) :* It means intake of air into lungs. Its duration is about 2 second.

B. *Expiration (passive process) :* It means output of air from lungs. Its duration is about 3 second.

Types of respiration : Respiration are of two types -

1. *External respiration :* Intake of O_2 and removal of CO_2 from body is called external respiration. It include four steps :
   a. Pulmonary ventilation : It means inflow and outflow of air between alveoli and atmosphere.
   b. Diffusion of O_2 and CO_2 between alveoli and blood.
   c. Transport of O_2 to the cells and CO_2 from the cells to the lungs.
   d. Regulation of respiration.
2. *Internal respiration :* The utilization of O_2 and production of CO_2 by cells and the gaseous exchanges between the cells and their fluid medium.

(Ref. Guyton 11th & Ganong 22th edition)

Rate of respiration : It is the total number of respiration per unit time. It is counted in minute. The normal rate of respiration varies in accordance with age, sex, size, work, rest & sleep.

Respiratory rate at different age groups :

Age in years	*Respiratory rate per minute*
At birth	14-60
First years	25-35
2-4 years	20-30
5-14 years	20-25
Adult (male)	10-18
Adult (Female)	10-18

Conditions increase rates of respiration : Rate of respiration is usually proportional to the level of metabolism. It increased in-

I. *Physiological factors* :
   1. Nervous excitement
   2. Muscular exercise.
   3. High altitude
   4. Increased temperature

II. *Chemical factors* :
   1. Increased CO_2
   2. Decreased O_2

III. *Pathological factors* :
   1. Fever
   2. Defective aeriation of blood.

Conditions decrease rates of respiration :

1. Opium
2. Barbiturate poisoning.

NB. Ratio between resipration & arterial pulse in health is 1 : 4. It altered in -

1. Pneumonia (1 : 1)
2. Narcotic poisoning (1 : 6).

Muscles of respiration

Movement of the diaphragm accounts for 75% of the change in intrathoracic volume during quiet inspiration. Attached around the bottom of the thoracic cage, this muscle arches over the liver and moves downward like a piston when it contracts. The distance it moves ranges from 1.5 cm to as much as 7 cm with deep inspiration.

(Ganong 22th Edition; page 652)

A. ***Muscles of inspiration :***
   1. *In quite inspiration :*
      i. *The diaphragm* (accounts 75% of the change in intrathoracic volume during qiute inspiration) : Contraction of the diaphragm pulls the lower surfaces of the lungs downward. The distance it moves ranges from 1.5 cm to as much as 7 cm with deep inspiration.
      ii. *External intercostal muscle* : When the external intercostals contract they elevate the lower ribs. This pushes the sternum outward and increases the antero-posterior diameter of the chest. The transverse diameter also increases, but to a lesser degree.
   2. *In forcefull inspiration :* (Additional muscles)
      i. Sternoclidomastoid muscles - which lift upward on the sternum.
      ii. Scaleni - which lift the first two ribs.
      iii. Anterior serrati - which lift many of the ribs.
      iv. Scalenus posterior
      v. Latissimus dorsi muscle.

B. ***Muscles of expiration :***
   1. *In quite expiration :* Does not involve any muscle. It occurs due to-
      a. Elastic recoil tendency of the lungs and chest wall and abdominal structures which compresses the lungs.
      b. Elastic forces exerted by the surface tension of the fluid lines the inside walls of the alveoli and lung air spaces.

2. *In forcefull expiration :* (Additional muscles)
   i. Abdominal recti
   ii. Internal intercostals
   iii. Serratus posterior inferior muscle.

(Ref. Ganong 22th edition, P-652; Guyton 11th ed, P-471 & others)

Pressure related to respiration

i. Intrapleural pressure.
ii. Intrapulmonary or intra-alveolar pressure.
iii. Intra abdominal pressure.

1. *Intrapulmonary pressure (alveolar pressure) :* It is the pressure within the alveoli of lungs. It is due to contraction and expansion of the lungs during pulmonary ventilation. During inspiration it becomes about (-)1 cm of H_2O. and in expiration it become (+)1 cm of H_2O.

   When glottis is open and no air is flowing into or out of the lungs, the pressure in all parts of the repiratory tree, all the way to the alveoli are all equal to atmospheric pressure , which is considered to be 0 centimeter of water pressure.

2. *Intrapleural pressure :* The potential space between the two layers of pleura contains a thin film of fluid keep the pleura apposed to each other by hydrolytic traction. This force of traction is called intrapleural pressure. It is normally a slightly negative pressure.The normal pleural pressure, at the beginning of inspiration is about (-)5 centimeters of water that is required to hold the lungs open to their resting level. During normal inspiration the expansion of the chest case pulls the surface of the lungs with still greater force and creats a still more negative pressure down to and average of about -7.5 centmeters of water.

(Ref. Guyton 11th edition; page-472)

N.B. Intrapleural pressure : (-) 2.5 to (-) 6 mm of Hg.

(Ref. Ganong 22th edition)

Difference between intrapleural pressure and intrapleural fluid pressure :

Intrapleural pressure	*Intrapleural fluid pressure*
1. It is the amount of negative pressure in the pleural space required to prevent the collapse of the lungs.	1. It is the force of traction between the two pleura.
2. It is the sum total of intrapleural fluid pressure & pleural surface pressure (-10 +6) -4 mm of Hg.	2. It is due to absorption of intrapleural fluid.
3. It is - 4 mm of Hg.	3. It is -10 mm of Hg.
4. It varies with the phage of respiration.	4. It varies with the rate of suction.

Explain- the intrapleural pressure is always negative :

Intrapleural pressure is alwas negative due to continual absorption of fluid or air that try to enter inside the intrapleural space. In addition, the intrapleural fluid contains a muco-polysaccharides which is continually absorbed by the pleural capillaries due to their low capillary pressure (7mm of Hg). This absorbtion creates a partial vacume and produces a negative pressure.

Recoil tendency of lung

The lungs have a continual elastic tendency to collapse and therefore to pull away from the chest wall. This is called the recoil tendency of lungs.

Causes :

i. Elastic fibres of the lungs that are stretched during inspiration and therefore attempt to shorten the lungs.
ii. The surface tension of the fluid lining the alveoli has a elastic tendency to collapse alveoli of the lungs.

This recoil tendency is prevented by :

i. The negetive intrapleural pressure.
ii. Presence of surfactant that reduces surface tension of the fluid lining the alveoli.
iii. Presence of residual volume.

(Ref. Guyton & Hall-11th edition)

Surfactant

Surfactant is a lipo-protein mixture secreted by the special surfactant secreting cells (type II granular pneumocytes) of alveolar epithelium. This mixture contains the phospholipid dipalmitoyl lecithin.

Composition :

Component	*Percent of surfactant*
Dipalmitoylphosphatidylchonile	62
Phosphatidylglycine	5
Other phospholipids	10
Neutral lipids	13
Proteins	8
Carbohoidrate	2

Formation & machenism of surfactant : Lamellar bodies (LB) are formed in type II alveolar epithelial cells and secreted by exocytosis. The released lamellar bodies is converted to tubular myelin (TM), and the TM is probably the source of the phospholipid surface film (SF).Some surfactant is taken up by alveolar macrophages, but more is taken up by endocytosis in type II epithelial cells.

Importance of surfactant :

i. Dipalmitoyl lecithin of surfactant decreases the surface tension of the fluid lining the alveoli thus prevents the collapsing of lungs.
ii. It helps in the expansion of lungs of a new born babies.

iii. It stabilizes the size of alveoli.

iv. It prevents the accumulation of edema fluid in the alveoli.

(Ref. Guyton 11th,edition, page-474; Ganong 22th edition, page-656)

Hyaline membrane disease

A few newborn babies, especially premature babies, do not secrete adequate quantities of surfactant, which makes lung expansion difficult. So, most of them die soon after birth because of inadequate ventilation. This condition is called hyaline membrane disease or respiratory distress syndrom.

(Ref. Guyton & Hall-11th edition)

Compliance

Definition : The extent to which the lungs expand for each unit increase in transpulmonary pressure is called their compliance.

It is determined by the elastic forces of the lungs-

1. The elastic forces of the lungs tissue itself.
2. The elastic force caused by the surface tension of the fluid that lines the inside walls of the alveoli and other lung air spaces. It accounts about two thirds of the total elastic forces in the normal lungs.

or

The expansibility of lungs and thorax is called compliance. This is expressed as, "the volume increase in the lungs for each unit increase in alveolar pressure or for each unit decrease in pleural pressure".

The normal total compliance of lungs together averages 200 ml/cm of water pressure. It means, "every time the alveolar pressure is increased by 1 cm of water the lungs expand 200 ml.

Factors that cause abnormal compliance :

i. Any condition that destroy the lung tissue, causes it to become fibrotic or edematous, blocks the bronchioles, impedes lung expansion and contraction causes decreased lung compliance.

ii. Deformities of chest such as kyphosis, severe sceliosis decreases chest compliance.

iii. Fibrotic pleurisy, paralized or fibrotic muscle reduces the chest compliance.

(Ref. Guyton & Hall-11th edition, page-474)

Work of breathing

During normal breathing contraction of respiratory muscle required only in inspiration, not in expiration which is a passive process caused by the elastic recoil of lungs and chest wall structures. So, the amount of work performed by the respiratory muscle to cause inspiration is called work of breathing.

It is divided into three fractions :

1. *Compliance work :* The work that is required to expand the lungs against the elastic forces is called compliance work.
2. *Airway resistance work :* The work that is required to over come the resistance to airflow through the respiratory passage .
3. *Tissue resistance work :* The work that is required to overcome the viscosity of the lungs and chest cage is called tissue resistance work.

(Ref. Guyton 10th edition, page-435)

Ventilation

Ventilation is of two types :

i. Pulmonary ventilation, and

ii. Alveolar ventilation.

i. *Pulmonary ventilation* : Pulmonary ventilation is the volume of air that is exchanged (i.e. inspired or expired) between the atmosphere and the lungs per minute. It is also called minute ventilation (V_E).

$V_E = V_T \times f$ (Here, VE = minute ventilation

$= 500 \times 12$ VT = tidal volume (averages 500 ml)

$= 6$ litres/minute. f = frequency of respiration/ minute = 12- 15/minute).

In a normal man at rest the V_E is of about : 6 - 7 L /minute.

ii. *Alveolar ventilation* : Alveolar ventilation is the volume of air that enters into the respiratory zone per minute and participates in the gas exchange.

During inspiration first 350 ml of the tidal volume (500 ml) with each breath enters into the alveoli (i.e. gas exchange area) and last 150 ml of the tidal volume remains in the conducting zone (dead space) of the respiratory tract. So, alveolar ventilation (V_A) per minute can be calculated as follows :

$V_A = (V_T - V_D) \times f$ Here, VA = alveolar ventilation

$= 350 \times 12$ VT = tidal volume : 500 ml

$= 4.2$ litres/minute. VD = air in the dead space (dead space volume) : 150 ml

f = frequency of respiration/minute = 12-15 / minute.

In a normal man at rest the V_A is of about 4.5-5 L/minute.

Distribution of ventilation : The alveolar ventilation is not evenly distributed throughout the lungs. In the upright position ventilation per unit lung -volume is greater at the base of the lung than at the apex, but in the supine position this difference tend to disappear. The unequal distributions of the ventilation are due to :

i. Intrapleural pressure is more subatmospheric (i.e. negative) at the apex than at the base

ii. The lung is more expanded (i.e. percentage of maximum lung volume is greater) at the apex than the base, and when the lungs is initially more expanded- the ventilation will be less.

Alveolar perfusion

The total pulmonary blood flow is approximately 5.5 litres/minute at rest. The distribution of pulmonary circulation at different zones of the vertical lungs depends on alveolar pressure (P_A), pulmonary artery pressure (Pa), and pulmonary venous pressure (Pv).

i. Zone 1 (apex) : PA > Pa. Pulmonary artery pressure is normally just sufficient to maintain perfusion. If P_A increased or Pa is reduced, no gas exchange occurs.

ii. Zone 2 (mid zone) : Pa> P_A > Pv : In this region blood flow occurs due to arterial alveolar pressure gradients. The Pa increase 1 cm H_2O for each cm descent from the apex of the lung, but the P_A remain constant. Therefore blood flow increases linearly from top to bottom of zone 2.

iii. Zone 3 (lower zone) : Pa > Pv > P_A : In this region blood flow is determined by the arterio-venous pressure difference.

Therefore in a vertical lung the base is more perfused than the apex of the lung.

Ventilation-Perfusion ratios

i. *Definition* : The ratio of alveolar ventilation to pulmonary blood flow for the whole lung is called ventilation-perfusion ratio.

Normally, alveolar ventilation (V_A)	= 4.2 L/minute
Pulmonary blood flow (Q)	= 5.5 L/minute
So, V_A/Q	= 4.2/5.5
	= 0.8

ii. *Relationships between alveolar ventilation and perfusion* : For efficient gas exchange it is important that there is a match between ventilation of the alveoli (V_A) and their perfusion (Q). In the normal lung the extreme relationships between alveolar ventilation and perfusion are-

i. Ventilation but no perfusion (physiological dead space)

ii. Perfusion but no ventilation (physiological shunting)

iii. *Defferences between alveolar ventilation and perfusion from apex to base of the lungs* : In normal lungs there is a tendency for ventilation not to be matched by perfusion towards the apices, with the reverse occurring at the bases.

a. At the apex : ventilation > perfusion

b. At the base : perfusion > ventilation

But, normally ventilation and perfusion vary in different regions of the normal lungs. The vertical lung base is *over perfused* compared to the ventilation (perfusion > ventilation) and the apex is *under perfused* compared to the ventilation (ventilation > perfusion).

Therefore V_A / Q varies from apex to base of the lungs :

i. VA / Q at apex = 3

ii. VA / Q at base = 0.6

So, in upright lungs V_A / Q is more in the apex than base.

iv. *Interpretation* :

i. The most efficient gas exchange occurs when the V_A/Q is approximately equal to 1.

ii. V_A / Q < 1 : no ventilation but perfusion (physiological shunt occur)

iii. V_A / Q = 0 : no ventilation but perfusion (anatomical shunt occur)

iv. V_A / Q > 1 : ventilation but no perfusion (physiological dead space)

v. V_A / Q ratio affects the PCO_2, and PO_2 in the alveoli. More V_A / Q ratio increases PO_2 in the alveoli and low V_A / Q ratio increases PCO_2 in the alveoli.

vi. V_A / Q is high at the apex (i.e. high PO_2), thus tuberculosis is common in the apical zone of the lungs (high PO_2 favors growth of mycobacteriurn).

Q. 00. **Give the example of ventilation perfusion imbalance with significance.**

Ans. *Ventilation-perfusion imbalance* : Patchy ventilation-perfusion imbalance is by far the most common cause of hypoxic hypoxia in clinical situations.

In disease processes that prevent ventilation of some of the alveoli, the ventilation-blood flow ratios in different parts of the lung determine the extent to which systemic arterial PO_2 declines. If nonventilated alveoli are perfused, the nonventilated but perfused portion of the lung is in effect a *right-to-left shunt*, dumping unoxygenated blood into the left side of the heart. Lesser degrees of ventilation-perfusion imbalance are more common. The underventilated alveoli have a low alveolar PO_2, whereas the overventilated alveoli have a high alveolar PO_2. Consequently, the arterial blood is unsaturated. On the other hand, the CO_2 content of the arterial blood is generally normal in such situations, since extra loss of CO_2 in overventilated regions can balance diminished loss in underventilated areas.

(Ganong 22th edition; page 687)

Respiratory exchange ratio (R)

Definition : Respiratory exchange ratio (R), is the ratio of CO_2 to O_2 at any given time whether or not equilibrium has been reached.

Factors : R is affected by factors other than metabolism.

R can be calculated for reactions outside the body, for individual organs and tissues, and for the whole body. The O_2 consumption and CO_2 production of an organ can be calculated at equilibrium by multiplying its blood flow per unit of time by the arteriovenous differences for O_2 and CO_2 across the organ.

Significance of respiratory exchange ratio (R) : R for the whole body differ in various conditions. For example-

i. *During hyperventilation* : R rises because CO_2 is being blown off.

ii. *During severe exercise* : R may reach 2.00 because CO_2 is

being blown off and lactic acid from anaerobic glycolysis is being converted to CO_2.

iii. *After exercise* : R may fall for a while to 0.50 or less.

iv. *In metabolic acidosis* : R rises because respiratory compensation for the acidosis causes the amount of CO_2 expired to rise.

v. *In severe acidosis* : R may be greater than 1.00.

vi. *In metabolic alkalosis* : R falls.

vii. *During secretion of gastric juice* : the stomach has a negative R because it takes up more CO_2 from the arterial blood than it puts into the venous blood.

(Ganong 22th Edition; page 280)

Normal quiet breathing is maintained by the diaphragm- Explain :

The diaphragm is the principal muscle for quiet breathing. It is dome shaped, and separates the thoracic cavity from the abodominal cavity.

Contraction of the diaphragm helps only in inspira-tion. The vertical descent during quiet normal inspiration, is about 1.5 cm, sufficient to accomodate 500-700 ml of air inside the lungs, which is the tidal volume. Therefore quiet breathing is mainly diaphragmatic.

The diaphragm may descent upto 7 cm, during force full inspiration. In paralysis of the intercostal muscle, the diaphragm maintains the respiration. This diaphragmatic respiration is known as abdominal type of respiration.

Mechanism of Respiration

(Pulmonary ventilation/ respiration or how air enters inside the lungs) :

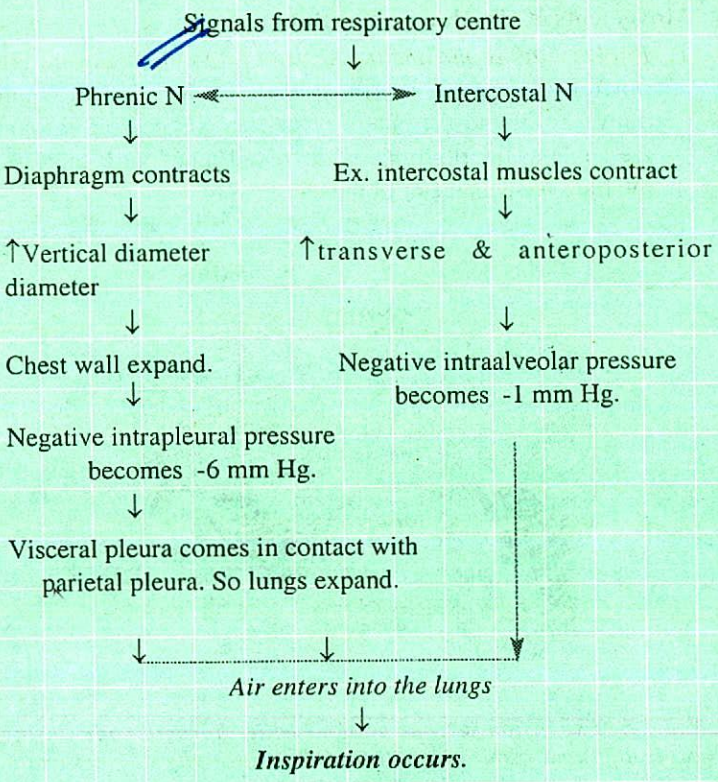
The basic mechanism of respiration (breathing) are expansion and contraction of lungs which can be achieved in two ways :

1. By downward and upward movement of the diaphragm to lengthen or shorten the vertical diameter of chest cavity.
2. By elevation and depression of ribs to increase or decrease the antero-posterior diameter of chest cavity.

During inspiration :

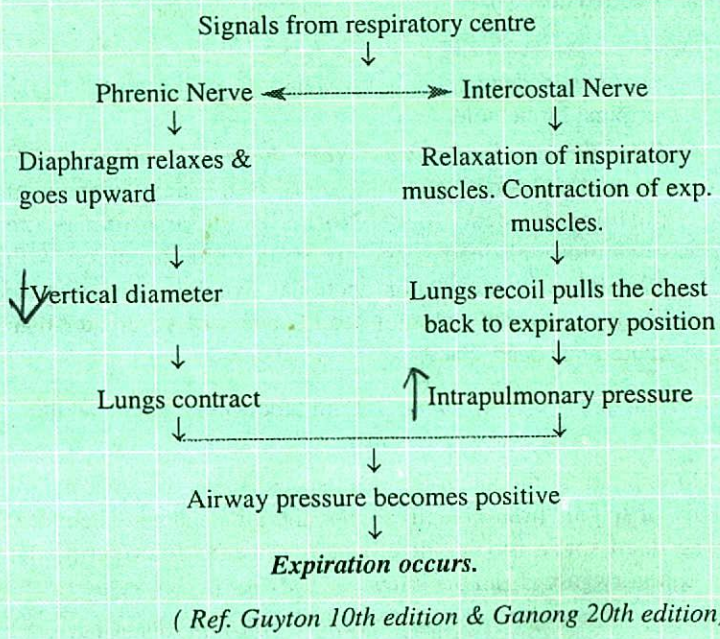
The inspiratory center stimulates and discharge impulses causes contraction of inspiratory muscles. Due to contraction of the diaphragm the vertical diameter of the chest cavity and by the contraction of external intercostal muscles antero-posterior and transverse diameter of the chest cavity increases. This increased chest cavity decrease the negative intrapleural pressure (from -2.5 to -6 mm of Hg or -7.5 cm of H_2O), which then pulls upon the visceral pleura causing enlargement of lungs and respiratory air passages, thereby creating a fall of intra alveolar pressure (-1cm of H_2O) in respect to atmosphere. Then the air will rushes inside the lungs from atmosphere.

(Ref. Guyton & Hall-11th edition & Ganong 22th edition)



During expiration :

Expiration is a passive process. It does not involve muscle except forcefull expiration. It occurs due to elastic recoil tendency of lungs and chest wall and elastic forces exerted by the surface tention of the fluid lies the inside walls of the alveoli and lung air spaces. The elasticity of lungs turn the diaphragm upwards and depress the ribs, the diameter of the chest cavity decreases, intra-alveolar (intra pulmonary) pressure rises which causes expulsion of air from lungs into atmosphere.



(Ref. Guyton 10th edition & Ganong 20th edition)

Movements of ribs during breathing

1. *Bucket handle movment :* In this movement the middle portion of ribs (from 7th to 10th) moves upwards and outwards around the antero-posterior axis passing through the angle of the rib to the costosternal junction. It increases the transverse diameter of the chest cavity.

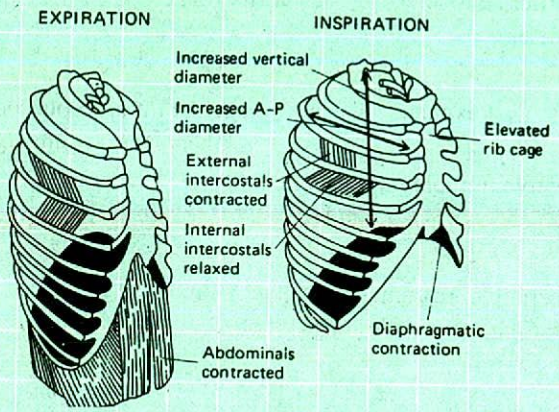


Fig.7-3. *Expansion & contraction of the thoracic cage during expiration and inspiration, illustrating especially diaphragmatic contraction, elevation of the rib cage, and function of the intercostals.*

2. *Pump handle movement :* In this movement anterior ends of the ribs (from 2nd to 6th) move upwards and forwards along the oblique axis passing through the neck of the ribs. It increases antero-posterior diameter of the chest cavity.

Dead Space

The space in the respiratory passage occupied by gas but does not allow in gaseous exchange but only acts as a reserviour of air is called dead space.

Types :

1. *Anatomical dead space :* It extends from the nostril to the terminal bronchiole.
2. *Physiological dead space :* When there is the alternation of ventilation perfusion ratio, there is the development of phsiological dead space. Normally the anatomical and physiological dead space are equal, but in person with partially functional or nonfunctional alveoli in some parts of the lung, the physiologiol dead space will be greater than anatomical dead space.

Normal dead space volume : 150 ml (about) in a young adult man.

On expiration, the air in the dead space is expired first, before any of the air from alveoli reaches the atmosphere. Therefore, the dead space is very disadvantageous for removal of the expiratory gases from the lungs.

(Ref. Guyton & Hall-11th edition, page500)

Dead space air

Definition : The amount of air that enters the respiratory passages but do not take part in the gaseous exchange is called dead space air.

Types :

a. *Anatomical dead space air* : The amount of air that remains in the conducting portion of the respiratory system that is from nose to terminal bronchiole with each phase of respiration is called anatomical dead space air. It is about 150 ml.

Improtance :

i. Saturates the inspired air by water vapour before reaching the alveoli.
ii. Helps in the removing of particles having a size more than 2 micron.

b. *Physiological dead space air* : It is the amount of air that is equal to anatomical dead space air plus the volume of air in the alveoli, having no blood supply. Usually this does not remain in normal condition.

Importance :

i. It gives an indication about the condition of the lungs.
ii. Indicates ventilatoin perfusion ratio.

(Ref. Guyton & Hall-11th edition, page478)

Pulmonary Volumes & Capacities

Pulmonary volumes

1. *Tidal volume :* It is the volume of air inspired or expired with each normal breath. It is about 500 ml.
2. *Inspiratory reserve volume :* It is the extra volume of air that can be inspired over and beyond the normal tidal volume. It is about 3000 ml.
3. *Expiratory reserve volume :* It is the amount of air that can be expired by forcefull expiration after the end of a normal tidal expiration. It is about 1100 ml.
4. *Residual volume :* It is the volume of air still remaining in the lungs after the most forcefull expiration. It is about 1200 ml.

(Ref. Guyton & Hall-11th edition, page 475)

Pulmonary Capacities

1. *Inspiratory capacity :* This is the amount of air that a person can inspired forcefully after a normal tidal expiration. It is about 3500 ml.

   Inspiratory capacity = Tidal volume + inspiratory reserve volume
   = 500 ml + 3000 ml
   = 3500 ml.

2. *Functional residual capacity :* This is the amount of air remaining in the lungs at the end of normal expiration. It is about 2300 ml.

Functional residual capacity = Expiratory reserve volume + residual volume
= 1100 ml + 1200 ml
= 2300 ml.

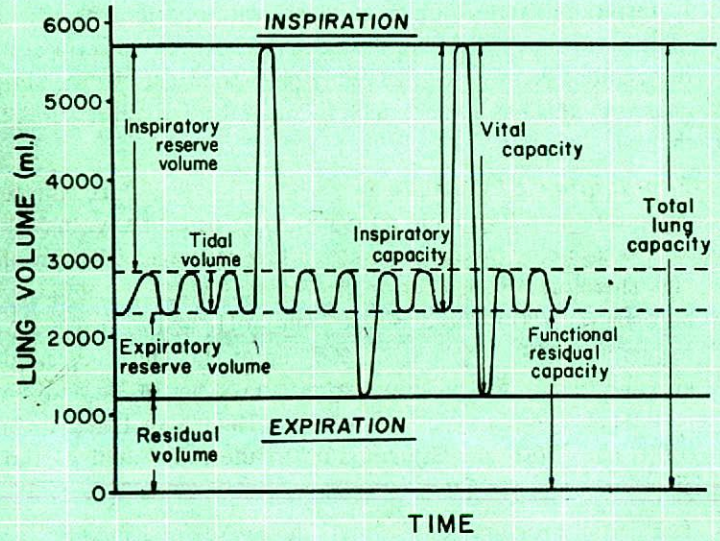


Fig. 7-4. *Diagram showing the lung volume & capacity.*

3. *Vital capacity :* The ***maximum*** amount of air that a person can *expired forcefully after the forcefull inspiration* is called vital capacity. It is about 4600 ml or 4.6 litre.

   Vital capacity = Tidal volume + Expiratory reserve volume + Inspiratory reserve volume.

   = 500 ml +1100 ml + 3000 ml
   = 4600 ml
   = 4.6 litres (male : 3.2-4.6 L; female : 2.9-4.2 L)

4. *Total lung capacity :* It is the maximum volume to which the lungs can be expanded with the greatest possible inspiratory effort.

   It is about 5800 ml.

   Total lung capacity = Vital capacity + Residual volume.
   = 4600 ml + 1200 ml
   = 5800 ml
   = 5.8 litres.

5. *Expiratory capacity :* It is the amount of air that a person can expired forcefully after a normal tidal inspiration.

   Expiratory capacity = Tidal volume + Expiratory reserve volume
   = 500 ml + 1100 ml
   = 1600 ml
   =1.6 litres.

N.B: All the pulmonary volume and capacities are about 20 to 25% less in women than in men and they are obviously greater in large and athlet persons than in small and asthenic persons.

(Ref. Guyton & Hall-11th edition, page476 & others)

Importance of residual volume :

i. It provides air in the alveoli to areate the blood (exchange of O_2 and CO_2) even between breath (expiration and inspiration) thereby prevents the sudden rise and fall of O_2 and CO_2 concentration in blood in each respiration.
ii. It prevents the collapse of alveoli of lungs.

(Ref. Guyton & hall-11th edition)

Vital Capacity

Definition : The ***maximum*** amount of air that a person can *expired forcefully after the forcefull inspiration* is called vital capacity.

Principle of measurement of vital capacity : Vital capacity is measured by spirometer. This consists of a drum inverted over a chamber of water, with the drum counter balanced by a weight. In the drum there is a breathing mixture of gases, usually air or oxygen. A tube connects the mouth with the gas chamber. When one breathes in and out of the chamber the drum rises and falls and an appropriate recording is made on a moving sheet of paper or on the meter.

Factors affecting vital capacity :

A. Air way resistance
B. Force of contraction of respiratory muscles
C. Elastic recoil tendency of the lungs.
D. Others :
   1. *Age :* It is more in young.
   2. *Sex :* 10% less in female due to
      i. Less surface area
      ii. Short thoracic cage
      iii. Less muscular strength.e.g.Adult man-4.6 liter. Adult female- 3.1 liter.
   3. *Posture :*
      Less in lying but more in erect posture due to
      i. Intra abdominal pressure
      ii. Pulmonary vascular blood volume.
   4. Surface area :
      Vital capacity is proportional to surface area.
   5. Anatomical built of the chest : Vital capacity decreases in some chest deformities such as
      i. Barrel shaped chest
      ii. Pigeons chest
      iii. Kyphosis.
   6. Diseases of lung and pleura :
      These decreases vital capacity by decreasing compliance.
   7. Paralysis of respiratory muscles :

Vital capacity decreases as low as 500-1000ml in this condition.

8. Congestive left heart failure :
   Causes pulmonary vascular congesion and edema which then decreases lung compliance and subsequently vital capacity.

Importance of vital capacity :

1. Measurement of the vital capacity give the idea of the condition of lungs i.e the maximum volume of air that can be tackled without any discomfort.
2. Indicates the efficiency in the acts of ventilation.
3. It is important in the lung functions tests as it decerases 500-1000ml after the paralysis of the respiratory muscles.
4. Clinically, it is important for the assesment of the different pulmonary fibrotic disease such as Tuberculosis(TB), Asthma, Emphysema.

Time vital capacity or Force expiratory volume (FEV_1)

Vital capacity is timed that means the percentage of vital capacity that is expired in 1st, 2nd and 3rd sec are determined. Normally FEV_1 is 83%-84% in 1st second; 93% in 2nd sec, 97% in 3rd sec.

The volume of air expired at one second is called *force expiratory volume at one second (FEV_1).*

Importance of FEV : If FEV_1 is found less than 80% in first second then there is obstruction some where in the air passage, such as in asthma.

Gaseous exchange between Lungs & Tissues

Composition of atmospheric, alveolar and expired air

	Atmospheric air (mm Hg.)		*Expired air (mm Hg.)*		*alveolar air (mm Hg.)*	
N_2	597.0	78.26%	563.4	74.9%	569.0	74.5%
O_2	159.0	20.84%	149.3	13.6%	104.0	15.5%
CO_2	0.3	0.04%	0.3	5.3%	40.0	3.6%
H_2O	3.7	0.50%	47.0	6.2%	47.0	6.2%
Total	760.0	100.0%	760.0	100.0%	760.0	100.0%

(Ref. Guyton 10th edition, page454)

Partial pressure :

The partial pressure of a gas in a mixture is the total amount of impaction force of the molecules of that particular gas alone against the surface.

Pressure is caused by the constant impact of kinetically moving molecules against a surface. Therefore, the pressure of a gas acting on the surfaces of the respiratory passages and alveoli is proportional to the summated force of impact of all the molecules striking the surface at any instant. This means that the total pressure is directly proportional to the concentration of the gas molecules.

In respiratory physiology, one deals with mixtures of gases, mainly of oxygen, carbondioxide, nitrogen etc. The rate of diffusion of these gases is directly proportional to the pressure caused by this gas alone, which is called the partial pressure of the gas.

Explanation : Consider air, which has an approximate composition of 79 percent nitrogen and 21 percent oxygen. The total pressure of this mixture at sea level averages 760 mm of Hg. Therefore, 79 percent of the 760 mm of Hg is caused by nitrogen (i.e 760 x .79) about 600 mm of Hg and 21 percent by oxygen (i.e 760 x 0.21) about 160 mm of Hg. Thus the partial pressure of nitrogen in the mixture is 600 mm of Hg and the partial pressure of oxygen is 160 mm of Hg; the total pressure is (600+160) 760 mm Hg, the sum of the individual partial pressure.

The partial pressures of the individual gases in a mixture are designated by the symbols Po_2, Pco_2, PN_2, PH_2o and so forth.

(Ref. Guyton & Hall-11th edition, page-492)

Partial pressure of O_2 (PO_2) :

Definition: Partial pressure of oxygen (Po_2) is the total amount of impaction force of oxygen (O_2) molecules on the surfaces.

Partial pressure of O_2 in various parts of the respiratory system and in the circulatory system is :

1. Lung alveoli : 104 mm of Hg
2. Pulmonary venous end : 104 mm of Hg
3. Arteries : 95 mm of Hg
4. Tissue arterial end : 95 mm of Hg
5. Tissue venous end : 40 mm of Hg
6. Interstitial fluid : 40 mm of Hg
7. Arterial blood entering the lungs or pulmonry arterial end. : 40 mm of Hg.

(Ref. Guyton & Hall-11th edition, page 502)

Partial pressure of CO_2 (PCO_2) :

Definition : Partial pressure of carbondioxide (Pco_2) is the total amount of impaction force of carbondioxide (Co_2) molecules on the surfaces.

PCO_2 in various parts :

1. Tissue : 46 mm of Hg
2. Interstitial fluid : 45 mm of Hg
3. Venous blood : 46 mm of Hg
4. Pulmonary artery : 46 mm of Hg

5. Alveoli : 40 mm of Hg
6. Arterial blood : 40 mm of Hg.

(Ref. Guyton & Hall-11th edition, page 502)

Partial pressure of respiratory gases in inspired and expired air :

Gas	*Inspired air mm Hg*	*Expired air mm Hg*
N_2	596.0	565.0
O_2	158.0	116.0
CO_2	0.3	32.0
H_2O	5.7	47.0

(Ref. Ganong 22th edition, Page 660)

Partial pressure of respiratory gases in circulatory system & alveoli :

Gas	*Alveolar air mm Hg*	*Arteries mm Hg*	*Tissues mm Hg*	*Veins mm Hg*
N_2	573.0	573.0	573.0	573.0
O_2	100.0	95.0	40.0 -	40.0
CO_2	40.0	40.0	46.0 +	46.0
H_2O	47.0	47.0	47.0	47.0

(Ref. Ganong 22th edition, Page 660)

Respiratory Membrane

Gaseous exchange between the alveolar air and the pulmonary blood occurs through the membranes of all the terminal portions of the lungs. These membrane are known as respiratory membrane.

(Ref. Guyton & Hall-11th edition, page 497)

Thickness : 0.3 to 1.0 micrometer, average 0.5 micromter.

Different layer of respiratory membrane :

1. A layer of fluid lining the alveolus and containing surfactant
2. The alveolar epithelium composed of thin epithelial cells.
3. An epithelial basement membrane.
4. A thin interstitial space between the alveolar epithelium and the capillary membrane.
5. A capillary basement membrane that in many places fuses with the alveolar epithelial basement membrane.
6. The capillary endothelial membrane.

(Ref. Guyton & Hall-11th edition, page 497)

Factors affecting gaseous exchange through the respiratory membrane :

1. *Thickness of the membrane :* The rate of diffusion through the membrane is inversely proportional to the thickness of the respiratory membrane. So any factor that increases the thickness of membrane such as edema of lungs, fibrosis of lungs also decrease the diffusion of gas through the membrane.
2. *The surface area of the membrane :* When the total surface area is decreased to approximately one-third to one-fourth normal, exchange of gases through the membrane impeded. So, any factor such as removal of part of lungs, cancer, tuberculus destruction and emphysema that decrease the area of membrane also decreases the rate of gases diffusion.
3. *The pressure difference of the gas between the two sides of the membrane :* When partial pressure of alveolar gas is greater than the pressure of gas in blood, net diffusion from the alveoli into the blood occurs. The opposite phenomenon occur when the pressure of the gas in the blood is greater than the alveolar gas.

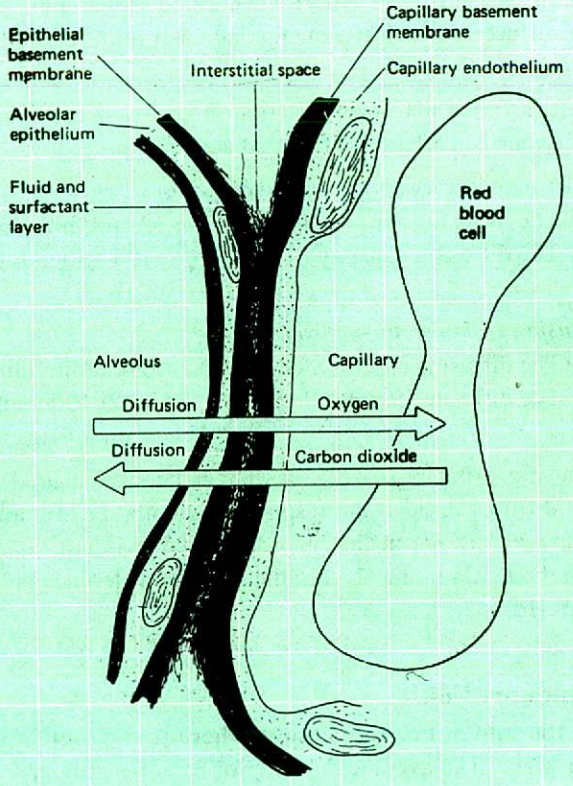


Fig. 7-5. *Ultrastructure of the respiratory membrane.*

4. *The diffusion co-efficient of the gas in the substance of the membrane :* The unit volume of a gas is measured in millimeters which diffuse through 1 sq.m of the membrane per minute when there is a pressure difference of 1 mm of Hg across the membrane is known as diffusion co-efficient.

   It depends on :

   a. Solubility of gases in the fluid of the membrane.

b. The molecular wt.

(Ref. Guyton & Hall-11th edition, page 498)

Factors increasing the thickness of respiratory membrane :

1. Edema fluid in the interstitial space of the membrane and in the alveoli.
2. Fibrosis of the lung.

(Ref. Guyton & Hall-11th edition, page 498)

Factors decreasing the surface area of respiratory membrane :

1. Removal of an entire lung or part of a lung.
2. Emphysema, in which many of the alveoli coalesce, with dissolution of many alveolar wall.
3. Cancer.
4. Tuberculous destruction.

(Ref. Guyton & Hall-11th edition, page 498)

Diffusing capacity of the respiratory membrane

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

Factors those affect the diffusion through the respiratory membrane can affect diffusing capacity.

Diffusing capacity under resting conditions :

1. The diffusing capacity for O_2 : 21 ml/min/mm of Hg
2. The diffusing capacity for CO_2 : 400-450 ml/min/mm of Hg.

Diffusing capacity during exercise :

1. The diffusing capacity for O_2 : 65 ml/min/mm of Hg
2. The diffusing capacity for CO_2 : 1200-1300 ml/min/mm of Hg.

Diffusing capacity of CO_2 has never been measured because CO_2 diffuses through the respiratory membrane so rapidly that the average PCO_2 in the pulmonary blood is not far different from the PCO_2 in the alveoli, the average difference is less than 1 mm Hg.

(Ref. Guyton & Hall-11th edition, page 498)

Respiratory Unit

It is the unit structure of lungs where the gaseous exchange takes place. The average diameter of each respiratory unit is 25 mm. There are 300 million of respiratory unit in the two lungs. Each respiratory unit composed of respiratory bronchiole, alveolar ducts, atria, and alveolus.

(Ref. Guyton & Hall-11th edition, page 496)

Transport of O_2

Transport of O_2 from alveolar air into tissue cell can be considered in 4 steps :

1. *Diffusion of O_2 from alveolar air into pulmonary capillary* : The partial pressure of oxygen (PO_2) in alveolus is 104 mm of Hg, where as the PO_2 in pulmonary capillary at arterial end is 40 mm of Hg. So, the pressure difference that causes O_2 to diffuse into the pulmonary capillary is (104 - 40) =64 mm of Hg. So, O_2 diffuse into pulmonary blood from alveolar air and the PO_2 of blood become equal to alveolar air by the time the blood has moved a third of the distance through the capillary.
2. *Transport of O_2 in the blood :* O_2 is transported in the blood in two ways :
   i. *In the form of oxy-haemoglobin : About 97% (19.5 ml/100 ml of blood)* of O_2 is carried in chemical combination with haemoglobin in the red cells by the process of oxygenation . The combination of O_2 with Hb is loose and reversible.
   ii. *As physical solution :* The *remaining 3% (0.29 ml/100 ml of blood)* of O_2 is transported in the dissolved state in the water of the plasma and cells.
   The arterial blood that enters the left atrium of heart is 97% saturated with O_2. Because of slight admixture of venous blood that passes through physiological shunts.

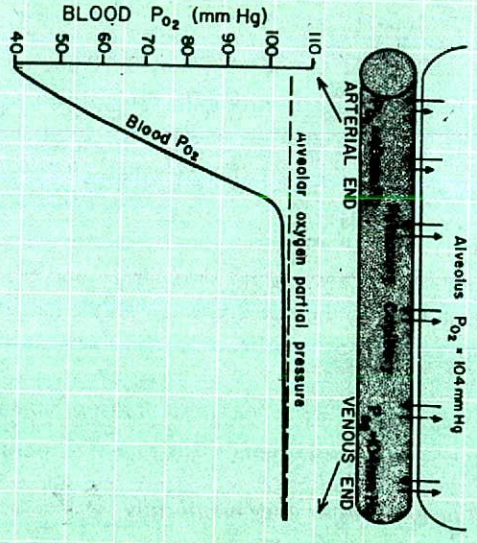


Fig. 7-6. *Uptake of O_2 by the pulmonary capillary blood.*

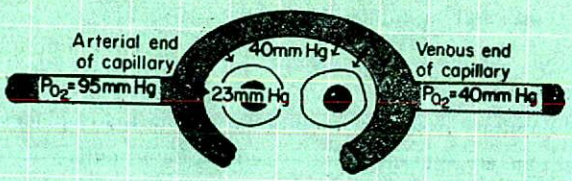


Fig. 7-7. *Diffusion of O_2 from a tissue capillary to the cell.*

3. *Diffusion of O_2 from blood to tissue interstitial fluid* : The blood PO_2 is 95 mm of Hg in tissue arterial end and PO_2 of interstitial fluid is 40 mm of Hg . So, the pressure difference is (95-40) 55 mm of Hg, and causes diffusion of O_2 into interstitial fluid.

4. *Diffusion of O_2 from interstitial fluid into cells* : The PO_2 of interstitial fluid is 40 mm of Hg and PO_2 inside the cell is ranging from 5 to 40 mm of Hg, averaging 23 mm of Hg. Because only 1 to 3 mm of Hg of oxygen pressure is normally required for full support of the chemical processes that use oxygen in the cell, one can see that even this low cellular PO_2 of 23 mm Hg is more than adequate and provides a large safety factor.

(Ref. Guyton 11th edition, P-502, 503; Ganong 22th edition, P-666)

PO_2 in aorta is 95 mm of Hg--explain ?

Ans.

About 98 % of the blood that enters the left atrium from the lung passes through the alveolar capillaries and becomes fully oxygenated that is PO_2 is approximately 104 mm of Hg. Another 2% of the blood leaving the lung passes through the bronchial circulation, which supplies mainly the pulmonary air. Therefore this blood flow represents 'shunt' and its PO_2 is approximately that of normal venous blood about 40 mm of Hg. This blood combines in the pulmonary veins with the oxygenated blood , this mixing of blood is called venous admixture of blood and it causes the PO_2 of the blood pumped by the left heart into aorta to fall to approximately 95 mm of Hg.

(Ref. Guyton 11th edition, page 503)

Oxygen-haemogblin dissociation curve

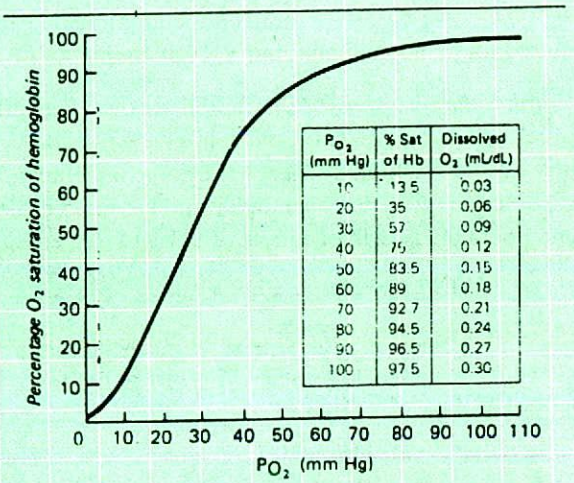
The dissociation of the oxygen from haemoglobin is studied by constructing a graph, where the relation of partial oxygen pressure and the percentage oxygen saturation of Hb in the blood are plotted as abscissa and ordinate, respectively.

Oxygen-hemoglobin dissociation curve is a graphical recording which shows a progressive increase in the *percentage saturation of the hemoglobin that is bound with oxygen as the PO_2 increases*. The curve is constructed by placing the percent saturation of Hb with O_2 at ordinate and tension of O_2 at abscissa.

(Ref. Guyton & Hall-11th edition, page 506)

The oxygen-hemoglobin dissociation curve, the curve relating percentage saturation of the O_2 carrying power of hemoglobin to the Po_2 has a characteristic sigmoid shape. When hemoglobin takes up a small amount of O_2, the R state is favoured and additional uptake of O_2 is facilitated. Combination of the first heme in the Hb molecule with O_2 increases the affinity of the second heme for O_2 and oxygenation of the second increases the affinity of the third, etc, so that the affinity of Hb for the fourth O_2 molecule is many times that for the first.

When blood is equi librated with 100% O_2 (Po_2 = 760 mm Hg), the normal hemoglobin becomes 100% saturated. When fully saturated , each gram of normal hemoglobin contains 1.39 mL of O_2. However, blood normally contains small amounts of inactive hemoglobin derivatives, and the measured value in vivo is lower. The traditional figure is 1.34 mL of O_2. The hemoglobin concentration in normal blood is about 15 g/dL (14 g/dL in women and 16 g/dL in men). Therefore, 1 dL of blood contain 20.1 mL (1.34 mL x 15) of O_2 bound to hemoglobin when the hemoglobin is 100% saturated. The amount of dissolved O_2 is a linear function of the Po_2 (0.003 mL/dL blood/mm Hg Po_2).



P_{O_2} (mm Hg)	% Sat of Hb	Dissolved O_2 (mL/dL)
10	13.5	0.03
20	35	0.06
30	57	0.09
40	75	0.12
50	83.5	0.15
60	89	0.18
70	92.7	0.21
80	94.5	0.24
90	96.5	0.27
100	97.5	0.30

Fig. 7-8. *Oxygen-haemoglobin dissociation curve.*

In vivo, the hemoglobin in the blood at the ends of the pulmonary capillaries is about 97.5% saturated with O_2 (Po_2 = 97 mm Hg). Because of a slight admixture with venous blood that by passes the pulmonary capillaries (physiologic shunt), the hemoglobin in systemic arterial blood is only 97% saturated. The arterial blood therefore contains a total of about 19.8 mL of O_2 per dL: 0.29 mL in solution and 19.5 mL bound to hemoglobin. In venous blood at rest, the hemoglobin is 70% saturated and the total O_2 content is about 15.2 mL/dL: 0.12 mL in solution and 15.1 mL bound to hemoglobin. Thus, at rest the tissues remove about (19.8-15.2) 4.6 mL of O_2 from each deciliter of blood passing through them; (0.29-0.12) 0.17 mL of this total represents O_2 that was in solution in the blood, and the remainder represents O_2 that was librated from hemoglobin. In this way, about 250 ml of O_2 per minute are transported from the blood to the tissues at rest.

$$\frac{4.6 \times 5500}{100} = 247.5 \text{ ml} \quad (\textit{Here, } CO = 5500 \text{ ml})$$

(Ref. Ganong 22th edition, Page-666)

Factors affecting the affinity of hemoglobin for oxygen :

A number of different factors can displace the dissociation curve in one direction or the other. These are-

1. *pH* : When blood becomes slightly acidic, with the pH decreasing from the normal value of 7.4 to 7.2, the oxygen-

hemoglobin dissociation curve shifts to the right. When the curve is shifted in this direction, a higher PO_2 is required for hemoglobin to bind a given amount of O_2.

On the other hand, an increase in the pH to 7.6 shifts the curve to the left and a lower PO_2 is required to bind a given amount of O_2.

2. *Blood temperature :* A rise in temperature decrease the hemoglobin saturation. It shifts the curve to the right. When the curve is shifted in this direction, a higher PO_2 is required for hemoglobin to bind a given amount of O_2.

3. *2,3 - diphosphoglyerate (DPG) :* 2,3 DPG is very plentiful in red cells. It is form from 3-phosphoglyceraldehde by EM pathway. It is a highly charged anion that bind to beta chains of deoxygenated haemoglobin. One mole of deoxy-hemoglobin binds with one mole of 2,3-DPG. In effect,

$HbO_2 + 2, 3\ DPG = Hb\text{-}\ 2, 3\ DPG + O_2$

In this equilibrium, an increase in the concentration of 2,3 DPG shift the reaction to the right, causing more O_2 to be liberated.

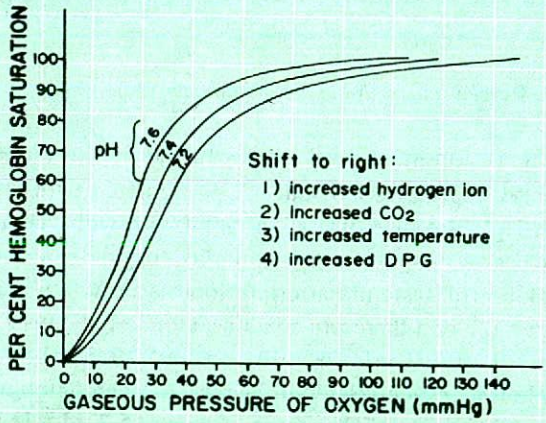


Fig. 7-9. *Shift of the oxygen-haemoglobin dissociation curve to the right by increasing -(i) H^+ (ii) CO_2 (iii) temparature (iv) 2,3-DPG.*

Factors affecting the concentration of 2,3-DPG in the red cells include p^H. Because acidosis inhibits red cell glycolysis. The 2,3-DPG concentration falls when the pH is low. Thyroid hormones, growth hormones, and androgens increase the concentration of 2,3-DPG and the P_{50}.

Exercise has been reported to produce an increase in 2,3-DPG within 60 minutes, although the rise may not occur in trained athlets. The P_{50} is also increased during exercise, because the temperature rises in active tissues and CO_2 & metabolites accumulate, lowering the pH. In addition much more O_2 is removed from each unit of blood flowing through active tissues because the tissues Po_2 declines. Finally, at low Po_2 values, the oxygen-hemoglobin dissociation curve is steep, and large amounts of O_2 are liberated per unit drop in Po_2.

Ascent to high altitude triggers a substantial rise in 2,3-DPG concentration in red cells, with a consequent increase in P_{50} and increase in the availability of O_2 to the tissues. The rise in 2,3-DPG which has a half-life of 6 hours, is secondary to the rise in blood pH. 2,3-DPG levels drop to normal upon return to sea level.

4. *CO_2 & Hydrogen ions :* Changes in the blood CO_2 & H^+ has very significant effect in enhancing oxygenation of the blood in the lung and then again in enhancing release of O_2 from the blood in the tissue. The P^H of blood falls as its CO_2 content increases, so that when the PCO_2 rises, the curve shifts to the right.

Most of the unsaturation of hemoglobin that occurs in the tissues is secondary to the decline in the PO_2, but an extra 1-2% unsaturation is due to the rise in PCO_2 and consequent shift of the dissociation curve to the right.

A convenient index of such shifts is the P_{50}, the PO_2 at which hemoglobin is half saturated with O_2. The higher the P_{50}, the lower the affinity of hemoglobin for O_2.

5. *Fetal hemoglobin* : The greater affinity of fetal hemoglobin than adult hemoglobin for O_2 fascilitates the movement of O_2 from the mother to the fetus. The cause of this greater affinity is the poor binding of 2,3-DPG by the gama polypeptide chains that replace beta chains in fetal hemoglobin.

(Ref. Ganong 22th edition, Page-667, 668)

N.B.

Red cell 2,3-DPG concentration is increased in anemia and in a variety of diseases in which there is chronic hypoxia. This fascilitates the delivary of O_2 to the tissues by raising the PO_2 at which O_2 is released in peripheral capillaries.

In blood bank, blood that is stored, the 2,3-DPG level falls and the ability of this blood to release O_2 to the tissues is reduced. This decrease, which obviously limits the benefit of the blood if it is transfused into a hypoxic patient, is less if the blood is stored in citrate-phosphate dextrose solution rather than the usual acid citrate dextrose solution.

(Ref. Ganong 22th edition, Page-669)

Shape of O_2-Hb dissociation curve :

The shape of the O_2-Hb dissociation curve is sigmoid shape. It is due to shifting affinity of the haem moiety of haemoglobin which is explained as follows- combination of the first haem with O_2 increases the affinity of the second haem for O_2, which increases the affinity of the 3rd and so forth. Oxygenation of Hb causes the two beta chains of the globin move closer together, when O_2 is given up, they move apart. This shift of beta chain is essential for the shifting affinity of haem for O_2.

(Ref. Ganong 22th edition, Page-669)

Importance of shape of O_2-Hb curve : Sigmoid shape of O_2-Hb

dissociation curve helps in quick saturation of Hb with oxygen in the lungs and binding with CO_2 in the tissue.

Function of hemoglobin : Hemoglobin has four functions-

i. It facilitates O_2 transport.
ii. It facilitates CO_2 transport.
i. It has an important role as a buffer.
i. It transports NO.

(Ref. Ganong 22th edition, Page-669)

Factors shifting the curve :

a. *Factor shifting the curve to the right :*
   i. Decreased pH (increase H^+ concentration)
   ii. Increased temperature.
   iii. Increased 2,3-diphosphoglycerate (DPG)
   iv. Increased $H^+$and increased CO_2

b. *Factors shifting to the left :*
   i. Foetal haemoglobin.
   ii. Increased p^H or decrease H^+
   iii. Decreased temperature.
   iv. Decreased PCO_2.

Reaction of Hemoglobin & Oxygen :

The dynamics of the reaction of hemoglobin with O_2 make it a particularly suitable O_2 carrier. Hemoglobin is a protein made up of sub-units each of which con-tains a haeme moiety. Haeme is a complex made up of a porphyrin and 1 atom of ferrous iron. Each of the 4 iron atoms can bind reversibly with one O_2 molecule. Since it contains 4Hb unit, the hemoglobin molecule can also be represented as Hb_4 and it actually reacts with 4 molecule of O_2 to form Hb_4O_8.

$$Hb_4 + O_2 = Hb_4O_2$$

$$Hb_4O_4 + O_2 = Hb_4O_6$$

$$Hb_4O_2 + O_2 = Hb_4O_4$$

$$Hb_4O_6 + O_2 = Hb_4O_8$$

(Ref. Ganong 22th edition, Page-666)

Difference between oxygenation and oxidation.

Oxygenation	*Oxidation*
1. No change of valency.	1. Change of valency.
2. Loose combination of O_2 occur.	2. Firm combination of O_2 occur.
3. Combination of O_2 is reversible.	3. Combination is irreversible.
4. It is temporary (transient).	4. It is permanent.

Utilization co-efficient : The percentage of blood that gives up its O_2 as it passes through the tissue capillaries is called utilization co-efficient. The normal value is about 25%.

(Ref. Guyton & Hall-11th edition, page 507).

Effect of hemoglobin to 'buffer' the tissue PO_2

(O_2 buffering action of Hb) :

Although hemoglobin is necessary for transport of O_2 to the tissue, it performs still another major function essential for life. This is its function as a "tissue oxygen buffer" system. That is the hemoglobin in the blood is mainly responsible for stabilizing the oxygen pressure in the tissues. This can be explained as follows :

1. ***Role of hemoglobin in maintaining constant PO_2 in the tissues*** : Under basal conditions the tissue require about 5 milliliters of oxygen from each deciliter (100ml) of blood passing through the tissue capillary. Again when 15 milliliters of oxygen is released, the PO_2 must fall to about 40 mm Hg. Therefore the tissue PO_2 normally can not rise above this 40 mm Hg level, for it such should occur; the oxygen needed by the tissue could not be released from the hemoglobin. In this way the hemoglobin nomally sets an upper limit on the gaseous pressure in the tissues at appro ximately 40 mm Hg.

   On the other hand, In heavy exercise extra large amounts of O_2 must be delivered from the hemoglobin to the tissue this can be achieved with very little furthur decrease in tissue PO_2 , that is a small fall in PO_2 causes large amount of O_2 to be released.

2. ***Value of hemoglobin for maintaining constant tissue PO_2 when atmospheric oxygen concentration changes markedly*** : The normal PO_2 in the alveoli is approximately 104 mm Hg. but as one ascends a mountain or ascends in a air plane, the PO_2 can easily fall to less than half this. *Or* when one enters areas of compressed air such as deep in the sea or in pressurized chambers, the PO_2 may rise to ten times this level. Even so, the tissue PO_2 changes very little.

   Let us explain - When the alveolar PO_2 is decreased to as low as 60 mm Hg, the arterial Hb is still 89% staturated, only 8% below the normal saturation of 97%. Further more, the tissues still remove approxi-mately 5 milliliters of O_2 from each deciliter of blood passing through the tissues, to remove this O_2, the PO_2 venous blood falls to 35 mm Hg, only 5 mm below the normal value. Thus the tissue PO_2 hardly changes, despite the marked fall in alveolar PO_2 from 104 to 60 mm Hg.

   On the other hand, when alveolar PO_2 rises as high as 500 mm Hg, the maximum oxygen saturation of Hb can never rise above 100%, which is only 3% above the normal level of 97%. Then when the blood passes through the tissue capillaries, it still loses several milliliters of O_2 to the tissues, which automatically reduces the Po_2 of the capillary blood to a value only a few millimeters greater than the normal 40 mm Hg.

Therefore, the level of alveolar O_2 may vary greatly from 60 to more than 500 mm of Hg Po_2 and still the Po_2 in the tissue does not vary more than a few millimeters from normal illustrating beautifully the tissue oxygen buffer function of the blood Hb.

(Ref. Guyton & Hall-11th edition, page 507)

N.B.

* 1 gm pure Hb contains 1.39 ml of O_2
* 1 gm impure Hb contains 1.34 ml of O_2
* 100 ml of arterial blood contains 19.8 ml of O_2
* 100 ml of venous blood contains 15.2 ml of O_2.

(Ref Ganong 22th edition, Page 667)

Formation and catabolism of 2, 3-BPG :

Glucose 6-PO_4
↓
3-Phosphoglyceraldehyde
↓
1,3-Biphosphoglycerate
2,3-BPG mutase →
Phospho glycerate kinase ↓
2,3-Biphosphoglycerat (2,3-BPG)
2,3-BPG phosphatase →
3-phosphoglycerate
↓
Pyruvate.

(Ref. Ganong 22th edition; page 668)

Transport of CO_2

CO_2 is continually produce in the tissue cells due to metabolic activity and this increases the intracellular Pco_2. So, CO_2 is released from the cell in the blood.

1. *Diffusion of CO_2 from cell into interstitial fluid :* Intracellular Pco_2 is about 46 mm of Hg. Interstitial fluid

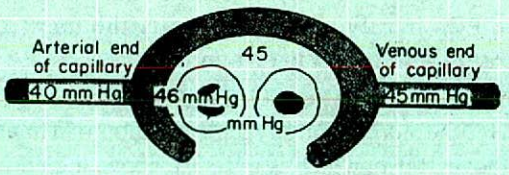


Fig. 7-10. *Uptake of CO_2 by the blood in the capillaries.*

Pco_2 is about 45 mm of Hg. Thus pressure difference is 1 mm of Hg that causes CO_2 to diffuse into interstitial fluid .

2. *Diffusion of CO_2 from interstitial fluid to blood :* Interstitial fluid Pco_2 about 45 mm of Hg . Arterial blood entering the tissue capillary Pco_2 is 40 mm of Hg. So, CO_2 diffuses into blood from interstitial fluid.

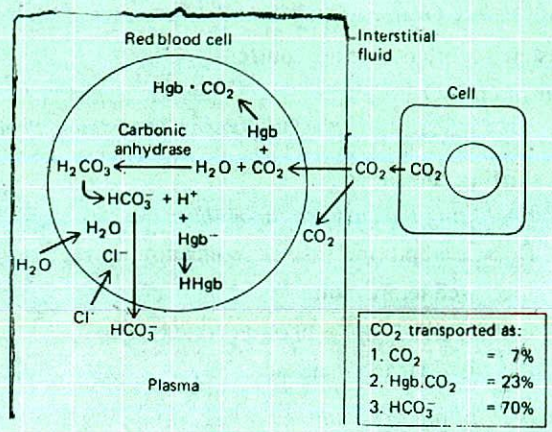


Fig. 7-11. *Transport of CO_2 in the blood.*

3. *Transport of CO_2 in the blood :* In blood CO_2 is transported in three form :
   i. In dissolved state : 7 %
   ii. In the form of HCO_3 and H^+ : 70 %
   iii. In combination with Hb : 23 %.

   i. *Transport of CO_2 in dissolved state :* The Pco_2 in venous blood is 45 mm of Hg and the amount of CO_2 dissolved in the fluid at 45 mm of Hg is about 2.7 ml per dL of blood.

   The CO_2 in arterial blood is 40 mm of Hg and the amount of CO_2 dissolved at 40 mm of Hg. is about 2.4 ml per dl. Therefore only, 0.3 ml (2.7-2.4) of CO_2 is transported in the form of dissolved state per dL of blood

   ii. *Transport of CO_2 in the form of HCO_3^- :* The dissolved CO_2 in the blood reacts with water catalyzes by carbonic anhydrase to form carbonic acid which inturn dissociate into HCO_3^- and H^+. Most of the H^+ then combine with Hb buffer system. Then almost all the HCO_3^- diffuses by the chloride shift mechan ism and this made possible by the presence of biocarbonate-chloride carrier protein in the membrane of the red cells.

   iii. *Transport of CO_2 as carbamino-haemoglobin or combination with Hb :* CO_2 also combine with haemoglobin to form carbaminohaemoglobin ($Hbco_2$) by very loose bond. So that CO_2 easily released into the alveoli where the Pco_2 is lower than tissue.

   A small amount of CO_2 also combine with plasma protein and transport in the same way.

4. *Diffusion of CO_2 from blood into alveoli of lung :* Pco_2 of

venous blood entering the lungs is 45 mm of Hg. Pco_2 of alveolar air is 40 mm of Hg. So the required amount of CO_2 diffuses out of pulmonary capillary into the alveoli and then into the atmosphere.

(Ref. Guyton & Hall-11th Edition, page 510, 511)

Chemical forms in which CO_2 is carried to the blood

In the form of chemical compound CO_2 is transported in two different ways :

1. As bicarbonate ions
2. As carbamino compound.
   a. Carbamino-hemoglobin.
   b. Carbamino-protein.

1. ***As bicarbonate ion*** :
   a. *In RBC :* The dissolve CO_2 in the blood reacts with water to form carbonic acid, catalized by an enzyme, carbonicanhydrase, accelerating the reaction about 5000 fold.

$$CO_2 + H_2O \xrightarrow{\text{Carbonic anhydrase}} H_2CO_3$$

As soon as carbonic acid is form in the red cells, dissociates into H^+ and HCO_3^-

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

Most of the H^+ then combine with Hb in the red blood cells, because Hb is a powerful acid base buffer.

$$H^+ + Hb \longrightarrow HbH^+$$

As the formation of HCO_3^- in RBC is much more rapid than plasma, the cell become alkaline and HCO_3 diffuses into the plasma, while choloride ions diffuse into the cells to take their place.

   b. *In plasma :*
      i. With the plasma proteins .

$$NaPr + H_2CO_3 = HPr + NaHCO_3$$

      ii. With phosphates -

$$Na_2HPO_4 + H_2CO_3 = NaHCO_3 + NaH_2PO_4$$

2. *As carbamino compound* :
   a. Carbamino-hemoglobin: CO_2 combines with- NH_2 group of globin part of hemoglobin to form carbamino hemoglobin.

$$CO_2 + HbNH_2 \longrightarrow HbNHCOOH.$$

   b. Carbamino-protein: In combination with plasma protein form carbamino - protein.

$$PrNH_2 + CO_2 = PrNHCOOH.$$

In these chemical form CO_2 is transported.

(Ref. Guyton & Hall-11th edition & others)

Fate of CO_2 in blood

A. *In plasma* :
   1. Dissolved
   2. Formation of carbamino compounds with plasma protein
   3. Hydration, H^+ buffered, HCO_3^- in plasma.

B. *In red blood cells* :
   1. Dissolved
   2. Formation of carbamino hemoglobin
   3. Hydration, H^+ buffered, 70% of HCO_3^- enters the plasma.
   4. Cl^- shifts into cells, mosm in cells increases.

(Ref. Ganong 22th edition, Page 670)

Summary of CO_2 transport :

1. *Each deciliter (100ml) of arterial blood contains 49 ml of CO_2.*
   a. Dissolved state : 2.6 mL
   b. Carbamino compounds : 2.6 mL
   c. As HCO_3^- : 43.8 mL
2. *In the tissues, 3.7 mL of CO_2 per deciliter (100mL) of blood is added.*:
   a. Stays in dissoved state : 0.4 ml
   b. Forms carbamino compound : 0.8 ml
   c. Forms HCO_3^- : 2.5 ml.
3. *The pH of the blood drops from 7.40 to 7.36.*
4. *Each deciliter (100ml) of venous blood contains (49 + 3.7) 52.7 ml of CO_2 :*
   a. Dissolved state : (2.6 + 0.4) 3.0 ml
   b. Carbamino compounds : (2.6 + 0.8) 3.4 ml
   c. As HCO_3^- : (43.8 + 2.5) 46.3 ml.
5. *In the lungs, the processes are reversed, and the 3.7 ml of CO_2 is discharged into the alveoli.*
6. About 200 ml ($\frac{3.7 \times 5500}{100}$ Here, cardiac output =5500 ml) of CO_2 per minute at rest and much larger amounts during exercise are transported from tissues to the lungs and exereted.

(Ref. Ganong 22th edition, Page-670)

Chloride shift mechanism

As a result of ionic imbalance due to more HCO_3^- formation in the red blood cells, they pass out of the red cells to the plasma and inturns Cl^- passes into the red cells from plasma. This phenomenon is called chloride shift or Hamburger shift.

CO_2 on entering into RBC binds with water and form carbonic acid which inturn with the help of carbonic anhydrase dissociates into hydrogen ion and bicarbonate ion (*Fig. 7-13*). The H^+ binds with the buffer system of haemoglobin. The

bicarbonate ion then increases the alkalinity of RBC. To correct this alkalinity of red blood cells bicarbonate ions diffuses into the plasma while chloride from plasma enters into red blood cells to take their place.

(Ref. Ganong 22th edition, Page-670 & Guyton 11th)

N.B. Note that for each CO_2 molecule added to a red cell, there is an increase of one osmotically active particle- either an HCO_3^- or a Cl^- in the red cell. Consequently, the red cells take up water and increase in size. For this reason, plus the fact that a small amount of fluid in the arterial blood returns via the lymphatics rather than the veins, the hematocrit of venous blood is normally 3% greater than that of the arterial blood. In the lungs the Cl^- moves out of the cells and they shrink.

(Ref. Ganong 22th edition, Page-670 & Guyton 11th)

Gas content of blood

ml/dl of blood containing 15 gm of haemoglobin

Gas	Arterial blood ($PO_2$95 mm Hg; PCO_2 40 mm Hg; Hb 97% saturated)		Venous blood (PO_2 40 mm Hg; PO_2 46 mm Hg; Hb 75% saturated)	
	Dissolved	Combined	Dissolved	Combined
O_2	0.29	19.5	0.12	15.1
CO_2	2.62	46.4	2.98	49.7
N_2	0.98	0	0.98	0

(Ref. Ganong 22th edition, Page-667)

Bohr Effect

Shift of oxygen-haemoglobin dissociation curve in response to changes in the blood carbon dioxide and hydrogen ions has a significant effect in enhancing oxygenation of blood in the lungs and then again in enhancing release of oxygen from the blood in the tissues. This is called Bohr effect.

It can be explained as follws : As the blood passes through the lungs, carbon dioxide diffuses from the blood into the alveoli. This reduces the blood PCO_2 and decreases the hydrogen ion concentration because of the resulting decrease in blood carbonic acid. Both these effects shift the oxygen-haemoglobin dissociation curve to the left and upwards. Therefore the quantity of oxygen that binds with the hemoglobin at any given alveolar PO_2 becomes considerably increased, thus allowing greater oxygen transport to the tissues.

Then when the blood reaches the tissue capillaries, exactly the opposite effects occur. Carbondioxide entering the blood from tissues shifts the curve to the right-ward, which displaces oxygen from the haemoglobin and therefore delivers oxygen to the tissues at a higher PO_2 than would otherwise occur.

(Ref. Guyton & Hall-11th edition, page 508)

Haldane Effect

Binding of oxygen with haemoglobin tends to displace carbon dioxide from blood, this effect is called the *Haldane effect*. It is important in promoting carbon dioxide transport.

The Haldane effect results from the simple fact that combination of oxygen with hemoglobin in the lungs causes the hemoglobin to become a stronger acid. This inturn displaces carbon dioxide from the blood and into the alveoli in two ways :

i. The more highly acidic hemoglobin has less tendency to combine with carbon dioxide to formcarbaminohemoglobin, thus displacing much much of the carbon dioxide that is present in the carbamino form from the blood.

ii. The increased acidity of the hemoglobin also causes it to release excess of hydrogen ions, and these in turn bind with bicarbonate ions to form carbonic acid; then this dissociates into carbon dioxide and water, and carbon dioxide is released from the blood into the alveoli.

In the tissue capillaries, the Haldane effect causes increased pickup of carbon dioxide because of oxygen removal from the hemoglobin, and in the lungs, it causes increased release of carbon dioxide because of oxygen pickup by the hemoglobin.

(Ref. Guyton & Hall-11th edition, page 511)

Control of Ventilation

Respiration is so adjusted that it keeps our bodily oxygen need satisfied, drives out carbon dioxide and hydrogen ions, yet it operates at low cost. Further, repiration can take care of the changes of our body needs by altering the frequency (normally about 14/min) and depth (normally 500 ml) of individual excursions and do that automatically. Further, respiratory movements are automatic and rhythmic.

These features, viz, automaticity, rhythmicity and adjustibility to the needs are dependent on the presence of a respiratory center (RC) which receives many feed backs from various parts of the body to adjust according to the needs.

The respiratory center consists of-

i. Medullary (DRG & VRG)
   a. Dorsal respiratory group (DRG)
   b. Ventral respiratory group (VRG)

ii. Pontine (apneustic and pneumotaxic) centers.

Inspiratory neurons, mostly in the DRG are always active, only the activity regularly increases and decreases. When it increases, the RC center discharges- inspiration begins. When decreases, the inspiration stops → expiration begins.

The inspiratory neurons are strongly influenced by reflexes (eg, load detecting reflex /Hering breuer reflex and so on), $PaCO_2$ and so on.

$PaCO_2$ acts mostly via central chemoreceptors (CC) of medulla. At exceptional times, depression of PaO_2 becomes an important (carotid and aortic bodies).

Finally, sometimes, higher centers (cortex/hypo thalamus) appear in the picture of control.

Cause of rhythmicity is rather speculative.

Breath Holding

Respiration can be voluntarily inhibited for some time, but eventually the voluntary control is overridden. *The point at which breathing can no longer be voluntarily inhibited is called the* ***breaking point***.

Breaking is due to the rise in arterial P_{CO_2}, and the fall in P_{O_2}. Individuals can hold their breath longer after removal of the carotid bodies.

Breathing 100% oxygen before breath holding raises alveolar P_{O_2} initially, so that the breaking point is delayed. The same is true of hyperventilating room air, because CO_2, is blown off and arterial P_{CO_2} is lower at the start.

Reflex or mechanical factors appear to influence the breaking point, since subjects who hold their breath as long as possible and then breathe a gas mixture low in O_2 and high in CO_2 can hold their breath for an additional 20 seconds or more.

Psychological factors also play a role, and subjects can hold their breath longer when they are told their performance is very good than they are not.

(Ref. Ganong 22th edition, Page 677)

Regulation of respiration

Spontaneous respiration is produced by rhythmic discharge of motor neurons that innervate the respiratory muscles. This discharge is totally dependent on nerve impulses from the brain; breathing stops if the spinal cord is transected above the origin of the phrenic nerves.

The rhythmic discharges from the brain that produce spontaneous respiration are regulated by alternations in arterial P_{O_2}, P_{CO_2} and H^+ concentration, and this chemical control of breathing is supplemented by a number of nonchemical influences.

(Ref. Ganong 22th edition, Page 671)

Respiratory centre

The respiratory center is composed of several groups of neurons located bilaterally in the medulla oblongata and pons. It is divided into three major collections of neurons :

i. *Dorsal respiratory group*, located in the dorsal portion of the medulla, which mainly causes inspiration.

ii. *Ventral respiratory group*, located in the ventrolateral part of the medulla, which can cause either expiration or inspiration, depending on which neurons in the group are stimulated.

iii. *Pneumotaxic center*, located dorsally in the superior portion of the pons, which helps control the rate and pattern of breathing.

The dorsal respiratory group of neurons plays the most fundamental role in the control of respiration.

(Ref. Guyton & HAll-11th Edition, page 514)

A. ***Dorsal respiratory group*** *(Inspiratory centre)* : The dorsal respiratory group of neurons extends most of the length of the medulla. All or most of its neurons are located within the *nucleus of the tractus solitarius*, although additional neurons in the adjacent reticular substance of the medulla also play important roles in respiratory control.

The *nucleus of the tractus solitarius* is the sensory termination of both the vagal and the glossopharyngeal nerves, which transmit sensory signals into the respiratory center :

1. from the peripheral chemoreceptors
2. from the baroreceptors
3. from several types of receptors in the lung.

All the signals from these peripheral areas help to control respiration.

Function : The basic rhythm of respiration is generated mainly in the dorsal respiratory group of neurons.

(Ref. Guyton & Hall-11th Edition, page 514)

B. ***Ventral respiratory group*** *(Functions in both inspiration and expiration)* : Located in each side of the medulla, about 5 millimeters anterior and lateral to the dorsal respiratory group of neurons, is the ventral respiratory group or neurons, found in the nucleus ambiguus rostrally and the nucleus retroambiguus caudally. The function of this neuronal group differs from that of the dorsal respiratory group in several important ways :

1. The neurons of the ventral respiratory group remain almost totally *inactive* during normal quiet respiration. Therefore, normal quiet breathing is caused only by repetitive inspiratory signals from the dorsal respiratory group transmitted mainly to the diaphragm, and expiration results from elastic recoil of the lungs and thoracic cage.
2. There is no evidence that the ventral respiratory neurons participate in the basic rhythmical oscillation that controls respiration.
3. When the respiratory drive for increased pulmonary ventilation becomes greater than normal, respiratory signals spill over into the ventral respiratory neurons from the basic oscillating mechanism of the dorsal respiratory area. As a consequence, the ventral respiratory area does then contribute its share to the respiratory drive as well.

4. Electrical stimulation of some of the neurons in the ventral group causes inspiration, whereas stimulation of others causes expiration. Therefore, these neurons contribute to both *inspiration* and *expiration*. They are especially important in providing the powerful expiratory signals to the abdominal muscles during very heavy expiration. Thus, this area operates more or less as an overdrive mechanism when high levels of pulmonary ventilation are required, especially during exercise.

(Ref. Guyton & HAll-11th Edition, page 515)

C. ***Pneumotaxic centre*** : The pneumotaxic center, located dorsally in the nucleus parabrachialis of the upper pons, transmits signals to the inspiratory area. The primary effect of this center is to control the "*switch-off*" point of the inspiratory ramp, thus controlling the duration of the filling phase of the lung cycle. When the pneumotaxic signal is strong, inspiration might last for as little as 0.5 second, thus filling the lungs only slightly; but when the pneumotaxic signals are weak, inspiration might continue for 5 or more seconds, thus filling the lungs with a great excess of air.

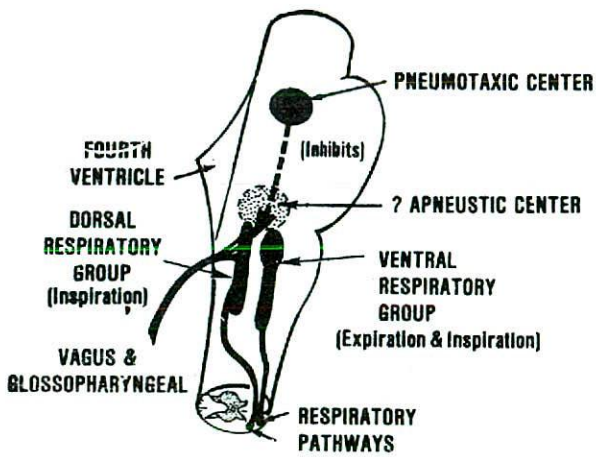


Fig. 7-12. *Location of Respiratory centre.*

Function : The function of the pneumotaxic center is primarily to limit inspiration. This has a secondary effect of increasing the rate of breathing, because limitation of inspiration also shortens expiration and the entire period of respiration. A strong pneumotaxic signal can increase the rate of breathing to 30 to 40 breaths per minute, whereas a weak pneumotaxic signal may reduce the rate to only 3 to 5 breaths per minute.

(Ref. Guyton & HAll-11th Edition, page 515)

D. ***Apneustic centre :*** To add confusion to our knowledge about respiratory center function, there is another strange center in the lower part of the pons called the apneustic center.

Function : Under a few conditions, this center sends signals to the dorsal respiratory group of neurons to prevent or retard the "switch-off" of the inspiratory ramp signal. Therefore, the lungs become almost completely filled with air, and only occasional short expiratory gasps occur.

The value of the apneustic center is not understood, but it presumably operates in association with the pneumotaxic center to control the intensity of inspiration.

(Ref. Guyton & HAll-10th Edition, page 475)

Airway and lung receptors

Vagal innervation :

i. *Myelinated fibers* :

Type	*Location in Interstitium*	*Stimulus*	*Response*
Slowly adapting	Among airway smooth muscle cells(?)	Lung inflation	Inspiratory time shortening Hering-Breuer inflation and deflation reflexes Bronchodilation Tachycardia
Rapidly adapting	Among airway epithelial cells	Lung hyperinflation Exogenous and endogenous substances (eg, histamine, prostaglandins)	Hyperpnea Cough Bronchoconstriction Mucus secretion

ii. *Unmyelinated C fibers* :

Type	*Location in Interstitium*	*Stimulus*	*Response*
Pulmonary C fibers	Close to blood vessels	Lung hyperinflation Exogenous and endogenous substances (eg, capsaicin, bradykinin, serotonin)	Apnea followed by rapid breathing Bronchoconstriction Bradycardia Hypotension Mucus secretion.

(Ref. Ganong 22th Edition; page 679)

Responses mediated by receptors in the airway and lungs :

Receptors in the airways and lungs are innervated by myelinated and unmyelinated vagal fibers. The unmyelinated fibers are C fibers. The receptors innervated by myelinated fibers are commonly divided into ***slowly adapting receptors*** and ***rapidly adapting receptors*** on the basis of whether sustained stimulation leads to prolonged or transient discharge in their afferent nerve fibers. The other group of receptors presumably consists of the endings of C fibers, and they are divided into pulmonary and bronchial subgroups on the basis of their location.

The shortening of inspiration produced by vagal afferent activity is mediated by slowly adapting receptors. So are the *Hering-Breuer reflexes.*

Hering-Breuer inflation reflex is an increase in the duration of expiration produced by steady lung inflation and *Hering-Breuer deflation reflex*1st is a decrease in the duration of expiration

produced by marked deflation of the lung. Because the rapidly adapting receptors are stimulated by chemicals such as histamine, they have been called ***irritant receptors***. Activation of rapidly adapting receptors in the trachea causes coughing, bronchoconstriction and mucus secretion, and activation of rapidly adapting receptors in the lung may produce hyperpnea.

Because the C fiber endings are close to pulmonary vessels, they have been called ***J*** *(juxtacapillary)* ***receptors***. They are stimulated by hyperinflation of the lung but they respond as well to intravenous or intracardiac administration of chemicals such as capsaicin. The reflex response that is produced is apnea followed by bradycardia, and hypotension (pulmonary reflex). A similar response is produced by receptors in the heart (Bezold-Jarisch reflex or the coronary chemoreflex). The physiologic role of this reflex is uncertain, but it probably occurs in pathologic states such as pulmonary congestion or embolization, in which it is produced by endogenously released substances. *(Q. Write short notes on J receptors)*

(Ref. Ganong 22th Edition; page 678)

Regulation of respiration

Respiration is regulated by the following ways :

1. *Nervous control of breathing*
   i. Voluntary control
   ii. Automatic control.
2. *Chemical control of respiration* :
   a. Direct chemical control of respiration affecting the respiratory centre by-
      i. Carbondioxide (PCO_2)
      ii. Hydrogen ions (H^+).
   b. Peripheral chemoreceptor system for control of respiratory activity-
      i. Role of oxygen
      ii. Role carbon dioxide
      ii. Role hydrogen ions.
3. *Non chemical influences on respiration* (other effects that affect respiration) :
   a. Responses mediated by receptors in the airways and lungs.
   b. Coughing and sneezing
   c. Responses in patients with heart-lung transplants
   d. Afferents from 'higher centers'
   e. Afferents from proprioceptors
   f. Respiratory components of visceral reflexes
   g. Respiratory effects of baroreceptor stimulation
   h. Effects of sleep.
4. *Hormonal effects on respiration.*

(Ref. Ganong 22th Edition & Guyton 11th Edition)

1. **Nervous control of breathing** : Two separate neural mechanisms regulate respiration. One is responsible for vlountary control and the other for automatic control. The voluntary system is located in the cerebral cortex and sends impulses to the respiratory motor neurons via corticospinal tracts. The automatic system is located in the pons and medulla, & the efferent output from this system to the respiratory motor neurons is located in the white matter of the spinal cord between the lateral and ventral corticospinal tracts. The nerve fibers mediating inspiration converge on the phrenic motor neurons located in the ventral horns from C_3 to C_5 and the external intercostal motor neurons in the ventral horns throughout the thoracic cord. The fibers concerned with the expiration converge primarily on the internal intercostal motor neurons in the thoracic cord.

   The motor neurons to the expiratory muscles are inhibited when those supplying the inspiratory muscles are active, and vice versa. *(Ref. Ganong 22th edition, Page-671)*

Rhythmic breathing *(Nervous regulation)* : Rhythmic breathing means normally inhaling and exhaling of air at a regular interval of time. The rhythmic breathing is controlled by the respiratory centres which are located in the grey mater of the pons and medulla of brain stem.

Mechanism of control : At first apneustic centre is stimulated either by excess Pco_2 in body fluid or by the stretch receptors of lungs and discharge stimulatory impulse to the inspiratory centre and slightly inhibitory impulse to the expiratory centre. The stimulated inspiratory centre then discharge stimulatory impulse to the diaphragm and the external intercostal muscle through 3rd, 4th and 5th cervical nerve and anterior horn cell of thoracic spinal nerve which causes contraction of the diaphragm and intercostal muscles.

By the action of the diaphragm and the intercostal muscles lungs expand and inspiration takes place. In normal respiration, it begins weakly and increases steadily in a ramp manner for about 2 seconds. Then it ceases abruptly for approximately the next 3 seconds, which turns off the excitation of the diaphragm and allows elastic recoil of the lungs and the chest wall to cause expiration.

When inspiration occurs, the stretch receptors which are present in the wall of the alveoli of lung stimulated, send inhibitory impulses through the vagus nerve to the apneustic centre. In the same time the pneumotaxic centre discharge inhibitory impulse to the apneustic centre and stimulatory impulse to the expiratory centre. As a result the apneustic centre ceases its activity and expiration takes place.

As a result of expiration the lungs contracts. So stretch receptor does not send impulse to apneustic centre and again inspiration takes place. By this process normal rhythmic breathing is regulated.

(Ref. Ganong 22th Edition & Guyton 11th Edition)

Hearing breuer inflation reflex : In addition to the neural

respiratory control mechanisms operating entirely within the brain stem, sensory nerve signals from the lungs also help to control respiration. Most important, located in the muscular portions of the walls of the bronchi and bronchioles throughout the lungs are stretch receptors that transmit signals through the vagi into the dorsal respiratory group of neurons when the lungs become overstretched. These signals affect inspiration in much the same way as signals from the pneumotaxic center; that is, when the lungs become overly inflated, the stretch receptors activate an appropriate feedback response that "switches off" the inspiratory ramp and thus stops further inspiration. This is called the *Hering-Breuer inflation reflex*. This reflex also increases the rate of respiration, the same as is true for signals from the pneumotaxic center.

In human beings, the Hering-Breuer reflex probably is not activated until the tidal volume increases to greater than about 1.5 liters. Therefore, this reflex appears to be mainly a protective mechanism for preventing excess lung inflation rather than an important ingredient in the normal control of ventilation.

(Ref. Guyton & Hall-11th Edition; Page 516)

2. **Chemical regulation** : The ultimate goal of respiration is to maintain proper concentrations of oxygen, carbon dioxide, and hydrogen ions in the tissues. It is fortunate, therefore, that respiratory activity is highly responsive to changes in each of these.

   a. *Excess carbon dioxide or excess hydrogen ions* in the blood mainly act directly on the *respiratory center* itself, causing greatly increased strength of both the inspiratory and the expiratory motor signals to the respiratory muscles.

   b. *Oxygen*, in contrast, does not have a significant direct effect on the respiratory center of the brain in controlling respiration. Instead, it acts almost entirely on *peripheral chemooreceptors* located in the carotid and aortic bodies, and these in turn transmit appropriate nervous signals to the respiratory center for control of respiration.

   a. ***Direct chemical control of respiratory center activity by carbon dioxide and hydrogen ions*** *(chemosensitive area of the respiratory center)* : There are three areas of the respiratory center- the dorsal respiratory group of neurons, the ventral respiratory group, and the pneumotaxic center. It is believed that none of these are affected directly by changes in blood carbon dioxide concentration or hydrogen ion concentration. Instead, an additional neuronal area, a sensitive chemosensative area, is located bilaterally lying only one-fifth millimeter beneath the ventral surface of the medulla. This area is highly sensitive to changes in either blood Pco_2, or hydrogen ion concentration, and it in turn excites the other portions of the respiratory center.

(Ref. Guyton & Hall-11th Edition; Page 516)

i. ***Response of the chemosensitive neurons to Hydrogen ions****- probably the primary stimulus* : The sensory neurons in the chemosensitive area are especially excited by hydrogen ions; in fact, it is believed that hydrogen ions are perhaps the only important direct stimulus for these neurons. However, hydrogen ions do not easily cross the blood brain barrier. For this reason, changes in hydrogen ion concentration in the blood have considerably less effect in stimulating the chemosensitive neurons than do changes in blood carbon dioxide, even though carbon dioxide is believed to stimulate these neurons secondarily by changing the hydrogen ion concentration.

(Ref. Guyton & Hall-11th Edition; Page 516)

ii. ***Effect of blood carbon dioxide*** *to stimulate the chemo sensitive area* : Although carbon dioxide has little direct effect in stimulating the neurons in the chemosensitive area, it does have a potent indirect effect. It does this by reacting with the water of the tissues to form carbonic acid. This in turn dissociates into hydrogen and bicarbonate ions; the hydrogen ions then have a potent direct stimulatory effect.

Why does blood carbon dioxide have a more potent effect in stimulating the chemosensitive neurons than do blood hydrogen ions? The answer is that the blood-brain barrier is almost completely impermeable to hydrogen ions, but carbon dioxide passes through this barrier almost as if the barrier did not exist. Consequently, whenever the blood Pco_2 increases, so does the Pco_2 of both the interstitial fluid of the medulla and the cerebrospinal fluid. In both these fluids, the carbon dioxide immediately reacts with the water to form hydrogen ions. Thus, paradoxically, more hydrogen ions are released into the respiratory chemosensitive sensory area when the blood carbon dioxide concentration increases than when the blood hydrogen ion concentration increases. For this reason, respiratory center activity is increased very strongly by changes in blood carbon dioxide, a fact that we subsequently discuss quantitatively.

Decreased stimulatory effect of carbon dioxide after the first 1 to 2 Days *:* Excitation of the respiratory center by carbon dioxide is great the first few hours after the carbon dioxide first increases but then gradually declines over the next 1 to 2 days, decreasing to about one fifth the initial effect. Part of this decline results from renal readjustment of the hydrogen ion

concentration back toward normal after the carbon dioxide first increases the hydrogen concentration. The kidneys achieve this by increasing the blood bicarbonate, which then binds with the hydrogen ions in the blood and cerebrospinal fluid to reduce their concentrations. But even more important, over a period of hours, the bicarbonate ions also slowly diffuse through the *blood-brain* and *blood-cerebrospinal fluid barriers* and combine directly with the hydrogen ions around the respiratory neurons as well, thus reducing the hydrogen ions back to near normal.

Therefore, a change in blood carbon dioxide concentration has a potent *acute effect* on controlling respiratory drive but only a weak *chronic effect* after a few days' adaptation.

(Ref. Guyton & Hall-11th Edition; Page 517)

Unimportant of oxygen for direct control of respiratory center : Changes in oxygen concentration have virtually no direct effect on the respiratory center itself to alter respiratory drive (although they do have an indirect effect, acting through the peripheral chemoreceptors).

We know that *hemoglobin-oxygen buffer system* delivers almost exactly normal amounts of oxygen to the tissues even when the pulmonary Po_2 changes from a value as low as 60 mm Hg up to a value as high as 1000 mm Hg. Therefore, except under special conditions, proper delivery of oxygen can occur despite changes in lung ventilation ranging from slightly below one-half normal to as high as 20 or more times normal. This is not true for *carbon dioxide*, because both the blood and tissue Pco_2, change almost exactly inversely with the rate of pulmonary ventilation; thus, evolution has made *carbon dioxide the major controller of respiration, not oxygen.*

Yet for those special condition in which the tissues get into trouble for lack of oxygen, the body has a special mechanism for respiratory control located in the peripheral chemoreceptors, outside the brain respiratory center; this mechanism responds when the blood oxygen falls too low, mainly below a Po_2 of 70 mm Hg.

(Ref. Guyton & Hall-11th Edition; Page 517)

b. ***Peripheral chemoreceptor system for control of respiratory activity*** *(Role of oxygen in respiratory control)* : In addition to control of respiratory activity by the respiratory center itself, still another mechanism is available for controlling respiration. This is the *peripheral chemoreceptor* system. Special nervous chemical receptors, called chemoreceptors, are located in several areas outside the brain. They are espicially important for detecting changes in the blood, although they also respond to a lesser extent to change in carbon dioxide and hydrogen ion concentrations. The chemoreceptors in turn transmit nervous signals to the respiratory center in the brain to help regulate respiratory activity.

Most of the chemoreceptors are located in the *carotid bodies*. However, a sizable number are also in the *aortic bodies*, and a few are located elsewhere in association with other arteries of the thoracic and abdominal regions of the body.

The *carotid bodies* are located bilaterally in the bifurcations of the common carotid arteries, and their afferent nerve fibers pass through Hering's nerves to the glossopharyngeal nerves and then to the dorsal respiratory area of the medulla. The *aortic bodies* are located along the arch of the aorta; their afferent nerve fibers pass through the vagi also to the dorsal respiratory area.

Each of the chemoreceptor bodies receives a special blood supply through a minute artery directly from the adjacent arterial trunk. Furthermore, blood flow through these bodies is extreme, 20 times the weight of the bodies themselves each minute. Therefore, the percentage removal of oxygen from the flowing blood is virtually zero. This means that the chemoreceptors are exposed at all times to arterial blood, not venous blood, and their Po_2s are arterial Po_2s.

(Ref. Guyton & Hall-11th Edition; Page 517)

Stimulation of the chemoreceptors by decreased arterial oxygen *:* When the oxygen concentration in the arterial blood falls below normal, the chemoreceptors become strongly stimulated. The impulse rate is particularly sensitive to changes in arterial Po_2, in the range from 60 down to 30 mm Hg, a range in which hemoglobin saturation with oxygen decreases rapidly.

Basic mechanism of stimulation of the chemoreceptors by oxygen deficiency : The exact means by which low Po_2 excites the nerve endings in the carotid and aortic bodies is still unknown. However, these bodies have multiple highly characteristic glandular-like cells, called *glomus cells*, that synapse directly or indirectly with the nerve endings. Some investigators have suggested that these glomus cells might function as the chemoreceptors and then in turn stimulate the nerve endings. But other studies suggest that the nerve endings themselves are directly sensitive to the low Po_2.

(Ref. Guyton & Hall-11th Edition; Page 518)

Effect of carbon dioxide and hydrogen ion concentration on chemoreceptor activity : An increase in either carbon dioxide concentration or hydrogen ion concentration also excites the chemoreceptors and in this way indirectly increases respiratory activity. However, the direct effects of both these factors in the respiratory center itself are so much more powerful than their effects mediated through the chemoreceptors (about seven times as powerful) that for most practical purposes, the indirect effects of carbon dioxide and hydrogen ions through the chemoreceptors do not need to be considered. Yet there is *one difference between the peripheral and central effects of carbon dioxide:* the stimulation by way of the peripheral chemoreceptors occurs as much as five times as rapidly as central stimulation, so that the peripheral chemoreceptors might be especially important to increase the rapidity of response to carbon dioxide at the onset of exercise.

(Ref. Guyton & Hall-11th Edition; Page 518)

3. **Non chemical influences on respiration** *(other effects that affect respiration)* :

   a. ***Responses mediated by receptors in the airways & lungs*** : Receptors in the airways and lungs are innervated by myelinated and unmyelinated vagal fibers. The unmyelinated fibers are C fibers. The receptors innervated by myelinated fibers are commonly divided into *slowly adapting receptors* and *rapidly adapting receptors* on the basis of whether sustained stimulation leads to prolonged or transient discharge in their afferent nerve fibers. The other group of receptors presumably consists of the endings of C fibers, and they are divided into pulmonary and bronchial subgroups on the basis of their location.

   The shortening of inspiration produced by vagal afferent activity is mediated by slowly adapting receptors. So are the *Hering-Breuer reflexes*. The *Hering-Breuer inflation reflex* is an increase in the duration of expiration produced by steady lung inflation, and the *Hering-Breuer deflation reflex* is a decrease in the duration of expiration produced by marked deflation of the lung.

   Because the rapidly adapting receptors are stimulated by chemicals such as histamine, they have been called *irritant receptors*. Activation of rapidly adapting receptors in the trachea *causes coughing, bronchoconstriction, and mucus secretion*, and activation of rapidly adapting receptors in the lung may produce *hyperpnea*.

   Because the C fiber endings are close to pulmonary vessels, they have been called *J (juxtacapillary) receptors*. They are stimulated by hyperinflation of the lung, but they respond as well to intravenous or intracardiac administration of chemicals such as capsaicin. The reflex response that is produced is apnea followed by rapid breathing, bradycardia, and hypotension (*pulmonary chemoreflex*). A similar response is produced by receptors in the heart (*Bezold-Jarisch reflex or the coronary chemoreflex*). The physiologic role of this reflex is uncertain, hut it probably occurs in pathologic states such as pulmonary congestion or embolization, in which it is produced by endogenously released substances.

   (Ref. Ganong 22th edition, Page 678)

   b. ***Coughing & sneezing*** : Coughing begins with a deep inspiration followed by forced expiration against a closed glottis. This increases the intrapleural pressure to 100 mm Hg or more. The glottis is then suddenly opened, producing an explosive outflow of air at velocities up to 965 km (600 miles) per hour. *Sneezing* is a similar expiratory effort with a continuously open glottis. These reflexes help expel irritants and keep airways clear.

   (Ref. Ganong 22th edition, Page 678)

   c. ***Responses in patients with heart-lung transplants*** : Trans plantation of the heart and lungs has progressed beyond experimental stage and is now established treatment for severe pulmonary disease and some other conditions. In individuals with transplants, the recipient's right atrium is sutured to the donor heart. and the donor heart does not reinnervate, so the resting heart rate is elevated. The donor trachea is sutured to the recipient's just above to carina, and afferent fibers from the lungs do not regrow. Consequently, healthy patients with heart-lung transplants provide an opportunity to evaluate the role of lung innervation in normal physiology. Their cough responses to stimulation of the trachea are normal, because the trachea remains innervated, but their cough responses to stimulation of the smaller airways are absent. Their bronchi tend to be dilated to a greater degree than normal. In addition, they have the normal number of yawns and sighs, indicating that these do not depend on innervation of the lungs. Finally, they lack Hering-Breuer reflexes, but their pattern of breathing at rest is normal, indicating that these reflexes do not play an important role in the regulation of resting respiration in humans.

   (Ref. Ganong 22th edition, Page 678)

   d. ***Afferents From "Higher Centers"*** : Pain and emotional stimuli affect respiration, so there must also be afferents from the limbic system and hypothalamus to the respiratory neurons in the brain stein. In addition, even though breathing is not usually a conscious event, both inspiration and expiration are under voluntary control.

The pathways for voluntary control pass from the neocortex to the motor neurons innervating the respiratory muscles, bypassing the medullary neurons.

Since voluntary and automatic control of respiration are separate, automatic control is sometimes disrupted without loss of voluntary control. The clinical condition that results has been called *Ondine's curse*. In German legend, Ondine was a water nymph who had an unfaithful mortal lover. The king of the water nymphs punished the lover by casting a curse upon him that took away all his automatic functions. In this state, he could stay alive only by staying awake and remembering to breathe. He eventually fell asleep from sheer exhaustion, and his respiration stopped. Patients with this intriguing condition generally have bulbar poliomyelitis or disease processes that compress the medulla.

(Ref. Ganong 22th edition, Page 679)

e. ***Afferents from proprioceptors*** : Carefully controlled experiments have shown that active and passive movements of joints stimulate respiration, presumably because impulses in afferent pathways from proprioceptors in muscles, tendons, and joints stimulate the inspiratory neurons. This effect probably helps increase ventilation during exercise.

(Ref. Ganong 22th edition, Page 679)

f. ***Respiratory components of visceral reflexes*** : The respiratory adjustments during *vomiting, swallowing, and sneezing* are inhibition of respiration and closure of the glottis. During these activities not only prevent the aspiration of food or vomitus into the trachea but, in the case of vomiting, fix the chest so that contraction of the abdoininal muscles increases the intra-abdominal pressure. Similar glottic closure and inhibition of respiration occur during voluntary and involuntary straining.

Hiccup is a spasmodic contraction of the diaphragm and other inspiratory muscles that produces an inspiration during which the glottis suddenly closes. The glottic closure is responsible for the characteristic sensation and sound. Hiccups occur in the *fetus in utero* as well as throughout extrauterine life. Their function is unknown. Most attacks of hiccups are of short duration, and they often respond to breath-holding or other measures that increase arterial Pco_2. Prolonged hiccuping can be debilitating. ***Yawning*** is a peculiar "infectious" respiratory act whose physiologic basis and significance are uncertain. Like hiccuping, it occurs in utero, and it occurs in fish and tortoises as well as mammals. Underventilated alveoli have a tendency to collapse, and it has been suggested that the deep inspiration and stretching open them and prevent the development of atelectasis. Yawning also increases venous return to the heart. Sighing may have a similar function. However, in actual experiments, no atelectatic effect of yawning could be demonstrated. It has also been suggested that yawning is a nonverbal signal used for communication between animals in a group, and one could argue that on a different level, the same thing is true in humans.

(Ref. Ganong 22th edition, Page 680)

g. ***Respiratory effects of baroreceptor stimulation*** : Afferent fibers from the baroreceptors in the carotid sinuses, aortic arch, atria, and ventricles relay to the respiratory neurons as well as the vasomotor and cardioinhibitory neurons in the medulla. Impulses in them inhibit respiration, but the inhibitory effect is slight and of little physiologic impor tance. The hyperventilation in shock is due to chemoreceptor stimulation caused by acidosis and hypoxia secondary to local stagnation of blood flow and is not baroreceptor-mediated. The activity of inspiratory neurons affects blood pressure and heart rate, and activity in the vasomotor and cardiac areas in the medulla may have minor effects on respiration.

(Ref. Ganong 22th edition, Page 680)

h. ***Effects of sleep*** : Respiration is less rigorously controlled during sleep than in the waking state, and brief periods of apnea occur in normal sleeping adults. There are variable changes in the ventilatory response to hypoxia. If the Pco_2 falls during the waking state, various stimuli from proprioceptors and the environment maintain respiration, but during sleep, these stimuli are decreased and a decrease in Pco_2 can cause apnea. During REM sleep, breathing is irregular and the CO_2 response is highly variable.

(Ref. Ganong 22th edition, Page 680)

4. **Hormonal eftects on respiration :** Ventilation is increased during the luteal phase of the menstrual cycle and during pregnancy. Experiments with animals indicate that this is due to activation of estrogen-dependent progesterone receptors in the hypothalamus. However, the physiologic significance of this increased ventilation is unknown.

(Ref. Ganong 22th edition, Page 678)

Role of medullary oscillatory circuit

The inspiratory and expiratory neurons complete a circuit between them known as "medullary oscillatory circuit" which play important role for the basic rhythm of respiration.

In the figure there are four inspiratory neurons on left side and four expiratory neuron on right side. Let us first consider inspiratory neuron. If one of the inspiratory neuron excited, it excites the next one, which excites the third one and so forth. This excitation continue around and around the inspiratory

circuit and as it doing so, colateral impulses are transm itted to inspiratory muscles for about 2 sec. In addition it also transmit inhi- bitory impulse to the expiratory net work. But just as soon as inspiratory oscillation ceases, there is no longer inhibition to expiratory net work. So the netural excitability of expiratory net work causes the expiratory oscillation. It continued for about 3 second.

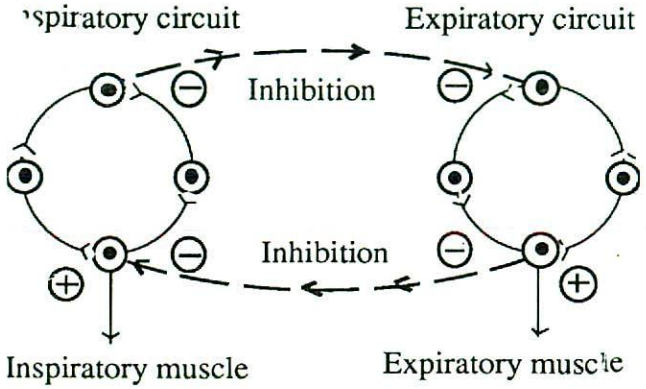


Fig. 7-13. *Medullary Oscillatory circuit.*

During this oscillation excitatory impulses are transmitted to expiratory muscles and inhibitory to the inspiratory network to keep it from oscillation. When the expiratory network stoped it oscillation, the inspiratory network begins to oscillate once again. In this way, medullary oscillatory circuit maintain normal rhythm of respiration.

Hering-Breuer Reflex

The rate and depth of respiration is controlled by the reflex which is transmitted from the stretch receptor of the lungs to the respiratory centre through the vagus nerve is called Hering Breuer reflex.

It has two parts :

1. *Hering Breuer inflation reflex :* When the air is inspired in the lungs, the stretch receptors in the wall of the lung stimulated and sends inhibitory impulse through the vagus nerve into the "tractus solitarius" of brain and then to the respiratory centre and thereby prevent further inflation. This is called Hering-Breuer inflation reflex.
2. *Hering Breuer deflation reflex :* The stretch receptors in the wall of the lung alveoli become unstretched during expiration. The impulses from these receptors ceases, which allows inspiration again and again. This is called Hering-Breuer deflation reflex.

Functions :

i. It is essential for the modification of continuous inspiration into rhythmic inspiration.
ii. It prevents the over distension of the lungs and thus protect it from burst.

Q. **Explain how respiration increases during exercise Or, Regulation of respiration during exercise.**

Ans. The factors that increase the rate and depth of respiration during exercise are summarized below-

a. *Nervous factor or direct stimulation of respiratory centre from motor cortex :* During exercise the brain transmitting impulses to the contracting muscles, also transmit colateral impulses to the respiratory centre. This stimulation of respiratory centre increases the rate of respiration.
b. *Indirect stimulation from proprioceptors* : During exercise, the movement of the limbs and body excites the proprioceptors. This then transmit impulses to the respiratory center which inturn increases the respiration. Beside this, during exercise hypoxia develops in the muscles that elicits afferent nerve signal to the respiratory center to excite respiration.
c. *Chemical factors* : During exercise the Pco_2 increases and Po_2 decreases. This then stimulate chemosensitive area of brain and peripheral chemoreceptor system, which then increase rate of respiration.

(Ref. Guyton & Hall-11th Edition, page 520)

Effects of bilateral section of phrenic nerves

Either the diaphragm or the external intercostal muscles alone can maintain adequate ventilation at rest. Transection of the spinal cord above the third cervical segment is fatal without artificial respiration, but transection below the fifth cervical segment is not, because it leaves the phrenic nerves that innervate the diaphragm intact; the phrenic nerves arise from cervical segments 3-5. Conversely, in patient with bilateral phrenic nerve palsy but intact innervation of their intercostal muscles, respiration is some what labored but adequate to maintain life. The scalen and sternocleidomastoid muscles in the neck are inspiratory muscles that help to elevate the thoracic cage during deep labored respiration.

Q. **What are the effect of transsection of one or two parts in the respiratory centre ?**

Ans.

1. When the medulla is transsected immediately above the medullary rhythmicity area and also immediately below this area basic rhythmicity occurs in at least some of the inspiratory neurons.
2. If the medulla is transsected immediately above the rhythmicity area but this area still connected to the spinal cord respiration occurs in gaps rather than in normal.
3. When the apneustic area is still connected to the medullary rhythmicity area but the pons has been transsected between the apneustic and pneumotaxic area - the pattern of prolonged inspiration and very short expiration occurs which is called apneusis.
4. When the afferent nerve fibres of vagus and of the glossopharyngeal nerves has been transsected - the apneustic pattern becomes specially marked.

5. When the vagus and pneumotaxic centre is transsected - very prolonged inspiration occurs.

Effects of exercise on respiration

Many cardiovascular and respiratory mechanisms must operate in an integrated fashion if the O_2 needs of the active tissue are to be met and the extra CO_2 and heat removed from the body during exercise. Circulatory changes increase muscle blood flow while maintaining adequate circulation in the rest of the body. There is in addition an increase in the extraction of O_2 from the blood in exercising muscles and an increase in ventilation that provides extra O_2, eliminates some of the heat, and excretes extra CO_2.

Changes in ventilation : Durine exercise, the amount of O_2 entering the blood in the lungs is increased because the amount of O_2, added to each unit of blood and the pulmonary blood flow per minute are increased. The Po_2 of blood flowing into the pulmonary capillaries falls from 40 to 25 mm of Hg or less, so that the alveolar capillary Po_2 gradient is increased and more O_2 enters the blood. Blood flow per minute is increased from 5.5 L/min to as much as 20-35 L/min. The total amount of O_2 entering the blood therefore increases from 250 mL/min at rest to values as high as 4000 mL/min. The amount of CO_2 removed from each unit of blood is increased, and CO_2 excretion increases from 200 mL/min to as much as 8000 mL/min. The increase in O_2, uptake is proportionate to work load up to maximum. Above this maximum O_2 consumption levels off and the blood lactate level continues to rise. The lactate comes from muscles in which aerobic resynthesis of energy stores cannot keep pace with their utilization and an *oxygen* debt is being incurred.

There is an abrupt increase in ventilation with the onset of exercise, followed after a brief pause by a further, more gradual increase. With *moderate exercise,* the increase is due mostly to an increase in the depth of respiration; this is accompanied by an increase in the respiratory rate when the exercise is more *strenuous*. There is an abrupt decrease in ventilation when exercise ceases, followed after a brief pause by a more gradual decline to pre-exercise values. The abrupt increase at the start of exercise is presumably due to psychic stimuli and afferent impulses from proprioceptors in muscles, tendons, and joints. The more gradual increase is presumably humoral even though arterial pH, Pco_2, and Po_2 remain constant during moderate exercise. The increase in ventilation is proportionate to the increase in O_2 consumption, but the mechanisms responsible for the stimulation of respiration are still the subject of much debate. The increase in body temperature may play a role. Exercise increases the plasma K^+ level, and this increase may stimulate the peripheral chemoreceptors. In addition, it may be that the sensitivity of the respiratory center to CO_2 is increased or that the respiratory fluctuations in arterial Pco_2 increase so that, even though the mean arterial Pco_2 does not rise, it is CO_2 that is responsible for the increase in ventilation. O_2 also seems to play some role despite the lack of a decrease in arterial Po_2, since during the perfonnance of a given amount of work, the increase in ventilation while breathing 100% O_2 is 10-20% less than the increase while breathing air. Thus, it currently appears that a number of different factors combine to produce the increase in ventilation seen during moderate exercise.

When ***exercise becomes more vigorous***, buffering of the increased amounts of lactic acid that are produced liberates more CO_2, and this further increases ventilation. With increased production of acid, the increases in ventilation and CO_2 production remain proportionate, so alveolar and arterial CO_2 change relatively little (*isocapnic buffering*). Because of the hyperventilation, alveolar Po_2 increases. With further accumulation of lactic acid, the increase in ventilation outstrips CO_2 production and alveolar Pco_2 falls, as does arterial Pco_2. The decline in arterial Pco_2 provides respiratory compensation for the metabolic acidosis produced by the additional lactic acid. The additional increase in ventilation produced by the acidosis is dependent on the carotid bodies and does not occur if they are removed.

The respiratory rate after exercise does not reach basal levels until the ***O_2 debt*** is repaid. This may take as long as 90 minutes. The stimulus to ventilation after exercise is not the arterial Pco_2 which is normal or low, or the arterial Pco_2, which is normal or high, but the elevated arterial H^+ concentration due to the lactic acidemia. The magnitude of the O_2 debt is the amount by which O_2 consumption exceeds basal consumption from the end of exertion until the O_2 consumption has returned to preexercise basal levels. During repayment of the O_2 debt, there is a small rise in the O_2 concentration in muscle myoglobin. ATP and phosphorylcreatine are resynthesizcd, and lactic acid is removed. Eighty percent of the lactic acid is converted to glycogen and 20% is metabolized to CO_2 and H_2O.

Because of the extra CO_2 produced by the buffering of lactic acid during strenuous exercis rises, R rises, reaching 1.5-2.0. After exertion, while debt is being repaid, the R falls to 0.5 or less.

(Ref. Ganong 22th edition, Page-681, 682)

Q. **What are the changes that occurs in respiratory system during exercise?**

Ans. The changes in the body that occurs during excercise is proportional to the intensity of exercise.

A. ***In moderate Excercise :***

1. *Pulmonary ventilation :* Pulmunary ventilation increases. *It is due to* -
   i. The alveolar PCO_2 of the subject rises and a large amount of CO_2 is diffuses to the alveolar air at each instant.
   ii. A rise of body temperature stimulates respiration

itself and also sensitizes the response of respiratory mechanism to the arterial PCO_2.

iii. A slight fall in arterial PO_2 which itself stimulate breathing, also sensitizes the respiratory response to PCO_2.

iv. Breathing is also stimulated by -

a. Reflexes from the moving joints.

b. Impulses from the higher centers.

2. *Oxygen usage :* This is increased. *It is due to* -

i. Breathing : The increase in pulmonary ventilation introduces large amounts of fresh air into the lung.

ii. O_2 Uptake in the lung : Large amount of oxygen are taken up from the lungs by the blood.

iii. Supply of oxygen to the tissues : A great blood supply to the muscle due to increased cardiac out put and redistribution of blood to the systemic circulation.

iv. Removal of oxygen by the tissues : This is effected as follows -

a. Dilatation and increase in the number of patent capillaries in the muscles slows the rate of the blood flow.

b. Low oxygen tension allows oxygen to diffuse more rapidly and to a greater extent.

c. High CO_2 tension and raised tamperature increases the extent and rate of dissociation of oxyhaemoglobin.

3. *Co_2 output :* Large amount of CO_2 is formed in the body, which is eleminated. *It is due to* -

i. Increased formation of CO_2.

ii. This increased CO_2 increase the PCO_2.

iii. Increased PCO_2 increases pulmonary ventilation causes rapid and more elemination of CO_2.

B. ***In severe Exercise :***

1. *Pulmonary ventilation* : Breathing remains much above the resting level for a prolonged period after the exertion is over.

2. *Lactic acid formation* : Lactic acid accumulates in the anoxic muscles and diffuses out into the blood stream and through out the body fluid.

3. *Respiratory quotient* : During the period of exertion first rises above 1 and may reach 1.5 or 2; attained maximum shortly after the end of exercise.

(Ref. Wright's. 13th Edition; page 214-17)

Oxygen debt

During exercise, the amount of O_2 entering the blood in the lungs is increasecd because the amount of O_2 added to each unit of blood and the pulmonary blood flow per minute are increased. The PO_2 of blood flowing into the pulmonary capillaries falls from 40 to 25 mm Hg or less, so that the alveolar-capillary PO_2 gradient is increased and more enters the blood. Blood flow per minute is increased from 5.5 liter/minute to as much as 20-35 liter/minute. The total amount of O_2 entering the blood therefore increases from 250 ml/minute at rest to values as high as 4000 ml/minute. The amount of CO_2 removed from each unit of blood is increased, and CO_2 excretion increases from 200 ml/minute to as much as 8000 ml/minute. The increase in O_2 uptake is proportionate to work load up to a maximum. Above this maximum, O_2 consumption levels off and the blood lactate level continues to rise. The lactate comes from muscles in which aerobic resynthesis of energy stores cannot keep pace with their utilization and an ***oxygen debt*** is being incurred.

(Ganong 22th Edition; page 681)

Respiratory insufficiency

Definition : Respiratory insufficiency means abnormalities in normal function of respiratory system. ***or***

Respiratory insufficiency means any type of abnormalities in normal rate and depth of respiration.

Causes of respiratory insufficiency :

i. Inadequate ventilation.

ii. Reduce gaseous diffusion through respiratory membrane.

iii. Abnormal ventilation- perfusion ratio.

(Ref. Guyton 10th edition)

Physiological basis of respiratory insufficiency

i. Some respiratory diseases result from inadequate ventilation.

ii. Whereas others result from abnormalities of diffusion through the pulmonary membrane or abnormal transport in the blood from the lungs to the tissues.

Diagnosis and treatment : The diagnosis and treatment of most respiratory disorders depend heavily on understanding the basic physiologic principles of respiration and gas exchange.

The therapy is often entirely different for these diseases, so it is no longer satisfactory simply to make a diagnosis of *respiratory insufficiency.*

(Ref. Guyton 10th Edition; page- 484)

Lung function tests

1. *Tests to evaluate the mechanics of the breathing by spirometer :*

a. Vital capacity (Male : 3.2 to 4.6 liter, Female : 2.9 to 4.2 liter)

b. Timed vital capacity or forced expiratory volume-FEV (80% in first hour)

c. Ventilatory boundaries of the lungs : The residual vlume (It is about 1200 ml) could not be determined

by spirometry. But it is estimated by means of nitrogen dilution technique.

2. Peak expiratory flow rate (about 6 to 15 liters/second)
3. *Test to evaluate the alvelolar ventilation :*
   a. Determination of dead spacce volume (In a young adult man *anatomical dead space* is about 150 ml).
   b. Uniform distribution of air measured by nitrometer.
4. *Test evaluating alveloar ventilation & perfusion ratio* (about 0.84) depending on continuous analysis of the carbon dioxide percentage of the expired air by carbondioxide analyser.
5. *Test involving the diffusing capacity :* By method of carbon monooxide diffusion measurement. The test envolving the Po_2 and Pco_2 and the blood by blood gas tensimeter of blood gases analyzer.
6. Measurement of maximum O_2 uptake (about 250 ml/minute).
7. Test to the efficiency of gaseous exchange at alveolar level (about 25 ml/mmHg/min).
8. Measurement of lung compliance (about 200 ml/cm of H_2O pressure).
9. *Test evaluating the pulmonary capillary blood (*about 7 mm Hg) *pressure :* These tests are uaually undertaken prior to removal of the lung or a portion of the lung. Before undertaken this procedure, cardiac catheterization is done and the tip of the catheter is passed through the pulmonary atery into the lung or the portion of the lung to be resected. If the pulmonary pressure is recorded to be normal and there is least chance of pulmonary oedema, the lung resection can be undertaken.
10. *Tests evaluating the functional integrity* of individual lobe of the lung by broncho-spirometer.
11. Bronchography.

(Ref. Ghosh and Sahana 2nd -381 & Concise Medical Physiology 2nd edition, page-190,191)

Tests done in the diagnosis of lungs diseases :

1. *X-ray chest P/A* (posterio-anterior) view & lateral view : For-Pneumonia, Pulmonary fibrosis, Tuberculosis, Sarcoidosis, Carcinoma etc.
2. *Sputum* microscopy and culture.
3. Spirometry
4. Arterial blood gas analysis
5. Bronchoscopy
6. CT Scanning etc.

Define the following

1. *Eupnea* : It means normal breathing.
2. *Tachypnea* : It means rapid breathing than normal.
3. *Bradypnea* : It means slow breathing than normal.
4. *Hypoxia* : It means decreased O_2 in tissue.
5. *Anoxia* : It means total lack of O_2.
6. *Hypoxemia* : It means reduced O_2 in blood.
7. *Hypercapnia* : It means excess CO_2 in blood.
8. *Hypocapnia* : It means depressed CO_2 in blood.
9. *Dyspnoea* : It means difficulty in breathing.
10. *Apnoea* : It means temporary cessation of breathing.
    1. *Voluntary apnoea* : Voluntary breath hold.
    2. *Involuntary apnoea* : During swallowing.

(Ref. Guyton & Hall-11th edition)

Hypoxia

Definition : Hypoxia is O_2 deficiency at the tissue level.

(Ref. Ganong 22th edition, Page 683)

Classification :

Hypoxia is classified in four types :

1. ***Hypoxic hypoxia*** *(anoxic anoxia)* : In this type of hypoxia PO_2 of the arterial blood is reduced.
   Here, O_2 carriage is normal but source of O_2 is less. It is the most common form of hypoxia seen clinically.

   Disoders causing hypoxic hypoxia :
   i. Lung failure (gas exchange failure)
      Pulmonary fibrosis
      Ventilation-perfusion imbalance
   ii. Shunt
   iii. Pump failure (ventilatory failure)
      Fatigue
      Mechenical defects
      Depression of respiratory controller in the brain.
2. ***Anaemic hypoxia*** : In this type of hypoxia the arterial PO_2 is normal but the amount of hemoglobin available to carry O_2 is reduced.
   It occurs due to-
   a. Lack of haemoglobin
   b. CO poisoning
   c. Abnormal Hb due to poisoning with nitrates, nitric oxide and other metals.
3. ***Stagnant or ischaemic hypoxia*** : In this type of hypoxia the blood flow to a tissue is so low that adequate O_2 is not delivered to it despite a normal Po_2 and hemoglobin concentration.
   It occurs due to-
   a. Decreased cardiac output due to heart failure.
   b. Decreased blood flow to the organ.
   c. Impaired venous return, haemorrhage and shock.
4. ***Histotoxic hypoxia*** : In this type of hypoxia, the amount of

O_2 delivered to a tissue is adequate but, because of the action of a toxic agent, the tissue cells can not make use of the O_2 supplied to them.

It occurs due to-

a. Poisoning with potassium cyanide which interferes tissue oxidation by paralysis the enzyme cytocrom oxidase.

b. Narcotics also depressed tissue oxidation by interfere with dehydrogenous system.

(Ref. Ganong 22th edition, Page-683, 684)

Causes of hypoxia

The following is a descriptive classification of the causes of hypoxia :

1. *Inadequate oxygenation of the lungs because of extrinsic reasons :*
   a. Deficiency of oxygen in atmosphere.
   b. Hypoventilation (neuromuscular disorders)
2. *Pulmonary disease :*
   a. Hypoventilation due to increased airway resistance or decreased pulmonary compliance.
   b. Uneven alveolar ventilation-perfusion ratio (including physiologic dead space and phy-siologic shunt)
   c. Diminished respiratory membrane diffusion.
3. *Venous to arterial shunts (right to left cardiac shunt).*
4. *Inadequate transport and delivery of oxygen :*
   a. Anaemia, abnormal hemoglobin.
   b. General circulatory deficicency
   c. Localized circulatory deficiency (Perip-heral, cerebral, coronary vessels)
   d. Tissue edema.
5. *Inadequate tissue capability of using oxygen :*
   a. Poisnoning of cellular enzymes.
   b. Diminished cellular metabolic capacity because of toxicity, vitamin dificiency or other factors.

(Ref. Guyton & Hall-11th Edition, page 530)

Effects of hypoxia

1. *Stagnant hypoxia* : The effects of stagnant hypoxia depend upon the tissue affected. Hypoxia due to slow circulation is a problem in organs such as the kidneys and heart during shock. The liver and possibly the brain are damaged by stagnant hypoxia in congestive heart failure. The blood flow to the lung is normally very large, and it takes prolonged hypotension to produce significant damage. However, ARDS can develop when there is prolonged circulatory collapse.
2. In *hypoxic hypoxia and the other generalized forms of hypoxia*, the brain is affected first. A sudden drop in the inspired Po_2 to less than 20 mm Hg, which occurs, for example, when cabin pressure is suddenly lost in a plane flying above 16,000m, causes loss of consciousness in 10-20 seconds and death in 4-5 minutes.
3. *Anemic hypoxia* : Hypoxia due to anaemia is not severe at rest unless the hemoglobin deficiency is marked, because red blood cell 2,3-DPG increases. However, anemic patients may have considerable difficulty during exercise because of limited ability to increase O_2 delivery to the active tissues.
4. *Less severe hypoxia* causes a variety of mental aberrations not unlike those produced by alcohol: impaired judgement, drowsiness, dulled pain sensibility, excitement, disorientation, loss of time sense, and headache. Other symptoms include anorexia, nausea, vomiting, tachycardia, and, when the *hypoxia is severe*, hypertension.
5. The rate of ventilation is increased in proportion to the severity of the hypoxia of the carotid chemoreceptor cells.

(Ref. Ganong 22th edition, Page 683, 690)

Treatment of hypoxia *:*

1. *Histotoxic Hypoxia* : Hypoxia due to inhibition of tissue oxidative processes is most commonly the result of cyanide poisoning. Cyanide inhibits cytochrome oxidase and possibly other enzymes. Methylene blue or nitrites are used to treat cyanide poisoning. They act by forming methemoglobin, which then reacts with cyanide to form cyanmethemoglobin, a nontoxic compound. The extent of treatment with these compounds is, of course, limited by the amount of methemoglobin that can be safely formed. Hyperbaric oxygenation may also be useful.
2. *Stagnant, anemic, and histotoxic hypoxia* : Adminis tration of oxygen-rich gas mixtures is of very limited value in stagnant, anemic, and histotoxic hypoxia because all that can be accomplished in this way is an increase in the amount of dissolved O_2 in the arterial blood.
3. *Hypoxic hypoxia* : Administration of oxygen-rich gas mixtures is of very limited value in hypoxic hypoxia when it is due to shunting of unoxygenated venous blood past the lungs. In other forms of hypoxic hypoxia, O_2 is of great benefit. Treatment regimes that deliver less than 100% O_2 are of value both acutely and chronically, and administration of O_2 24 hours per day for 2 years in this fashion has been shown to significantly decrease the mortality of chronic obstructive pulmonary disease.

(Ref. Ganong 22th edition, Page-691)

Hypercapnia

Retention of CO_2 in the body (hypercapnia) initially stimulates respiration. Retention of larger amounts produces symptoms due to depression of the central nervous system: confusion, diminished sensory acuity, and, eventually, coma with respiratory depression and death. In patients with these symptoms, the Pco_2 is markedly elevated, there is severe

respiratory acidosis, and the plasma HCO_3^- may exceed 40 meq/L. Large amounts of HCO_3^- are excreted, but more HCO_3^- is reabsorbed, raising the plasma HCO_3^- and partially compensating for the acidosis.

CO_2 is so much more soluble than O_2 that hypercapnia is rarely a problem in patients with pulmonary fibrosis. However, it does occur in ventilation-perfusion inequality and when for any reason alveolar ventilation is inadequate in the various forms of pump failure. It is exacerbated when CO_2 production is increased. For example, in febrile patients there is a 13% increase in CO_2 production for each 1°C rise in temperature, and a high carbohydrate intake increases CO_2 production because of the increase in RQ. Normally, alveolar ventilation increases and the extra CO_2 is expired, but it accumulates when ventilation is compromised.

(Ref. Ganong 22th edition, Page 692)

Hypocapnia

Hypocapnia is the result of hyperventilation. During voluntary hyperventilation, the arterial Pco_2 falls from 40 to as low as 15 mm Hg while the alveolar Po_2 rises to 120-140 mm Hg.

The more chronic effects of hypocapnia are seen in neurotic patients who chronically hyperventilate. Cerebral blood flow may be reduced 30% or more because of the direct constrictor effect of hypocapnia on the cerebral vessels. The cerebral ischemia causes light-headedness, dizziness, and paresthesias. Hypocapnia also increases cardiac output. It has a direct constrictor effect on many peripheral vessels, but it depresses the vasomotor center, so that the blood pressure is usually unchanged or only slightly elevated.

Other consequences of hypocapnia are due to the associated respiratory alkalosis, the blood pH being increased to 7.5 or 7.6. The plasma HCO_3^- level is low, but HCO_3^- reabsorption is decreased because of the inhibition of renal acid secretion by the low Pco_2. The plasma total calcium level does not change, but the plasma Ca^{2+} level falls and hypocapnic individuals develop carpopedal spasm, a positive Chvostek sign, and other signs of tetany.

(Ref. Ganong 22th edition, Page 692)

Cyanosis

Reduced hemoglobin has a dark color, and a dusky bluish discoloration of the tissues, called cyanosis, appears when the reduced hemoglobin concentration of the blood in the capillaries is more than 5 gm/dl. Minimum 5 gm/dl of deoxygenated Hb is necessary for cyanosis.

(Ref. Ganong 22th edition, Page 684)

Sites of cyanosis examination :

i. Nail beds
ii. Mucous membranes
iii. Earlobes
iv. Lips
v. Fingers, where the skin is thin.
vi. Tip of the nose
vii. Tip of the tongue etc.

(Ref. Ganong 22th edition, Page 683)

Its occurance depends upon :

1. Total amount of hemoglobin in blood.
2. Degree of Hb unsaturation.
3. State of capillary circulation.
4. Pigmentation and thickness of the skin.

(Ref. Ganong 22th edition, Page 684)

Types of cyanosis :

a. Central cyanosis : It occurs in the tip of the tongue.
b. Peripheral cyanosis : It occurs in the lips, nose, ear lobules, nail bed etc.

Cyanosis does not occur in-

1. Anemic hypoxia : Because the total hemoglobin content is low.
2. Carbon monoxide poisoning : Because the color of reduced hemoglobin is obscured by the cherry red color of carbon-monoxyhemoglobin.
3. Histotoxic hypoxia : Because the blood gas content is normal.

A discoloration of skin and mucouse membrane similar to cyanosis is produced by high circulating levels of methemoglobin.

(Ref. Ganong 22th edition, Page 684)

Emphysema

The term pulmonary emphysema means excess air in the lungs. But chronic pulmonary emphysema is a complex destructive process of lungs. It is caused by tobacco smoking.

Effect of Empysema :

i. The bronchial obstruction increases airway registance that causes hypoventilation.
ii. Loss of alveolar wall decreases lung diffusing capacity.
iii. Abnormal ventilation-perfusion ratio.
iv. Pulmonary hypertension. Because loss of lung parenchyma also decreases pulmonary capillary.
v. Due to these, the person develop hypoxia and hypercapnia causing death.

Pneumonia

Definition : The term pneumonia describes any inflammatory condition of lung in which the alveoli are usually filled with fluid and blood cells.

Cause : It is caused by bacteria Pneumococci.

Effect :

1. Reduction of the total surface area of respiratory membrane.

2. Decreased ventilation perfusion ratio.
3. Reduced diffusing capacity.

Pulmonary Hypertension

Sustained elevations of pulmonary arterial pressure can occur in infants and adults. In many cases in adults the cause is unknown, but pulmonary arterial pressure elevation can occur in people who inhale cocaine and in people who take dexfenfluramine and related appetite suppresent drugs that increase serotonin. Pressure elevation eventually leads to right heart failure and death.

Treatment : Vasodilators including prostacycline (epopros tenol) is of value.

(Ref. Ganong 22th Edition)

Atelectasis

Atelectasis means collapse of the alveoli, either in a localized area or in an entire lobe, or in an entire lung.

Cause :

1. Obstruction of airways
2. Lack of surfactant in the fluid lining the alveoli.

Asthma

Asthma is characterized by spastic contraction of the bronchioles which causes extremely difficult breathing.

Cause : Hypersensivity of the bronchioles to foreign substances in the air, plant pollens, smog etc.

Effect :

1. Increased air way resistance.
2. Difficulty in expiration but inspiration is normal.
3. Reduced maximum expiratory rate and timed expiratory volume.
4. Increased functional residual capacity and residual volume.

Tuberculosis (lung)

Ans. In tuberculosis, the tubercle bacilli cause a *peculiar tissue reaction in the lungs*, including-

i. Invasion of the infected tissue by macrophages

ii. *Walling off* of the lesion by fibrous tissue to form the so called tubercle. This walling-off process helps to limit further transmission of the tubercle bacilli in the lungs and therefore is part of the protective process against extension of the infection.

iii. However, in about 3 per cent of all people who develop tuberculosis, if untreated, the walling-off process fails and tubercle bacilli spread throughout the lungs, often causing extreme destruction of lung tissue with formation of large abscess cavities.

iv. Thus, tuberculosis in its late stages is characterized by many areas of fibrosis throughout the lungs as well as reduced total amount of functional lung tissue.

These effects cause :

a. Increased *work* on the part of the respiratory muscles to cause pulmonary ventilation and *reduced vital capacity* and *breathing capacity.*

b. *Reduced total respiratory membrane surface area* and *increased thickness of the respiratory membrane*, causing progressively diminished pulmonary diffusing capacity.

c. Abnormal *ventilation-perfusion ratio* in the lungs, further *reducing overall pulmonary diffusion of oxygen* and *carbon dioxide.*

(Ref Guyton & Hall-11th Edition; page 530)

Acclimatisation

The term acclimatisation means the adjustment of the human body to suit the climate at a higer altitude (between 3050-4260 meters).

The five principal means by which acclimatisation comes about are :

1. Increased pulmonary ventilation.
2. Increased haemoglobin in the blood.
3. Increased diffusion capacity of the lungs.
4. Increased vascularity of the tissues and.
5. Increased ability of the cells to utilize oxy-gen despite the low Po_2.

(Ref Guyton & Hall-11th Edition; page 519)

Artificial respiration

Definition : Artificial respiration is a life saving process when normal respiration will ceases with persistance normal heart beat. This must be applied within 8 minutes of ceasation of respiration.

Purposes of artificial respiration :

1. By maintaining the gaseous exchange, the vitality of nerve center is miantained. It is expected that after sometimes respiratory center will start functioning spontaneously.
2. During artificial respiration the alternate inflation and deflation of lungs reflexly stimulate the respiratory center and thus help them to take up their own rhythm.

Types of artificial respiration

There are two types of artificial respiration :

A. *Manual :*
   i. Mouth to mouth method
   ii. Arm lift back pressure method.

B. *Mechanical :*
   i. Tank respiratory method.
   ii. Brag paul method.

Indications of Artificial Respiration :

i. Drawning.

ii. Deep anesthesia during surgical operation.

iii. Carbon monooxide poisoning
iv. Electric shock.
v. Encephalities affecting respiration.

Asphyxia

In asphyxia produced by occlusion of the airway, acute hypercapnia and hypoxia develop together. There is pronounced stimulation of respiration, with violent respiratory efforts. Blood pressure and heart rate rise sharply, catecholamine secretion is increased, and blood pH drops. Eventually the respiratory efforts cease, the blood pressure falls, and the heart slows. Asphyxiated animals can still be revived at this point by artificial respiration, although they are prone to ventricular fibrillation, probably because of the combination of hypoxic myocardial damage and high circulating catecholamine levels. If artificial respiration is not started, cardiac arrest occurs in 4-5 minutes.

(Ref. Ganong 22th edition, Page-692)

Scuba *(self contained under water breathing apparatus)* **diving**

Introduction : Before the 1940s, almost all diving was done using a diving helmet connected to a hose through which air was pumped to the diver from the surface. Then, in 1943, Jacques Cousteau developed and popularized the *self-contained underwater breathing apparatus*, popularly known as the SCUBA apparatus.

The type of SCUBA apparatus used in more than 99 percent of all sports and commercial diving is the open-circuit demand system.

Components :

i. One or more tanks of compressed air or some other breathing mixture
ii. A first-stage *reducing* valve for reducing the very high pressure from the tanks to a low pressure level
iii. Combination inhalation *demand* valve and exhalation valve that allows air to be pulled into the lungs with slight negative pressure of breathing and then to be exhausted into the sea at a pressure level slightly positive to the surrounding water pressure.
iv. A mask and tube system with small *dead space.*

The demand system operates as follows : The first stage reducing valve reduces the pressure from the tanks so that the air delivered to the mask has a pressure slightly greater than the surrounding water pressure. The breathing mixture does not flow continually into the mask. Instead, with each inspiration, slight negative pressure in the demand valve of the mask pulls the diaphragm of the valve open, and this automatically releases air from the tank into the mask and lungs. In this way, only the amount of air needed for inhalation enters the mask. Then, on expiration, the air cannot go back into the tank but instead is expired into the sea.

The most important problem in use of the SCUBA is the limit on the amount of time one can remain beneath the surface ; for instance, only a few minutes are possible at a 200-foot depth. The reason for this is that tremendous airflow from the tanks is required to wash carbon dioxide out of the lungs - the greater the depth, the greater the airflow in terms of *quantity* of air per minute that is required because the *volumes* have been compressed to sizes.

(Ref Guyton & Hall-11th Edition; page-549)

Drowning

Drowning is suffocation by immersion, usually in water. In about 10% of drownings, the first gasp of water after the losing struggle not to breathe triggers *laryngospasm*, and *death* results from asphyxia without any water in the lungs.

In the remaining cases, the glottic muscles eventually relax and fluid enters the lungs. Fresh water is rapidly absorbed, diluting the plasma and causing *intravascular hemolysis*.

Ocean water is markedly hypertonic and draws fluid from the vascular system into the lungs, decreasing plasma volume.

The immediate *goal in the treatment* of drowning is, of course, resuscitation, but long-term treatment must also take into account the circulatory effects of the water in the lungs.

(Ref. Ganong 22th edition, Page-692)

Periodic Breathing

The acute effects of voluntary hyperventilation demonstrate the interaction of the chemical respiratory regulating mechanisms. When a normal individual hyperventilates for 2-3 minutes, then stops and permits respiration to continue without exerting any voluntary control over it, there is a period of *apnea*. This is followed by a few shallow breaths and then by another period of apnea, followed again by a few breaths (*periodic breathing*).

The cycles may last for some time before normal breathing is resumed. The apnea apparently is due to CO_2 lack because it does not occur following hyperventilation with gas mixtures containing 5% CO_2. During the apnea, the alveolar Po_2 falls and the Pco_2 rises. Breathing resumes because of hypoxic stimulation of the carotid and aortic chemoreceptors before the CO_2 level has returned to normal. A few breaths eliminate the hypoxic stimulus, and breathing stops until the alveolar Po_2, falls again. Gradually, however, the Pco_2, returns to normal, and normal breathing resumes.

(Ref. Ganong 22th edition, Page-692)

Cheyne-Stoke respiration

Periodic breathing occurs in various disease states and is often called *Cheyne-Stokes respiration.*

It is seen most commonly in patients with congestive heart failure and uremia, but it occurs also in patients with brain disease and during sleep in some normal individuals.

Some of the patients with *Cheyne-Stokes respiration* have increased sensitivity to CO_2. The increased response is

apparently due to disruption of neural pathways that normally inhibit respiration. In these individuals, CO_2 causes relative hyperventilation, lowering the arterial Pco_2. During the resulting apnea, the arterial Pco_2 again rises to normal, but the respiratory mechenism again overresponds to CO_2. Breathing ceases, and the cycle repeats.

Another cause of periodic breathing in patients with cardiac disease is prolongation of the lung-to-brain circulation time, so that it takes longer for changes in arterial gas tensions to affect the respiratory area in the medulla. When individuals with a slower circulation hyperventilate, they lower the Pco_2 of the blood in their lungs, but it takes longer than normal for the blood with a low Pco_2 to reach the brain. During this time, the Pco_2 in the pulmonary capillary blood continues to be lowered, and when this blood reaches the brain, the low Pco_2 inhibits the respiratory area, producing apnea. In other words, the respiratory control system oscillates because the negative feedback loop from lungs to brain is abnormally long.

(Ref. Ganong 22th edition, Page-693)

Biots breathing

It is characterized by several normal respiration at a time (1-5 or more) followed suddenly by a period of complete cessation of respiration and so on.

(Ref. Guyton 11th Edition)

Condition where found : Is seen in meningitis and other diseased condition like contusion, concussion of brain etc.

Sleep Apnea

Episodes of apnea during sleep can be central in origin, ie, due to failure of discharge in the nerves producing respiration, or they can be due to airway obstruction (*obstructive sleep apnea*).

This can occur at any age and is produced when the pharyngeal muscles relax during sleep. In some cases, failure of the genioglossus muscles to contract during inspiration contributes to the blockage: these muscles pull the tongue forward, and when they do not contract the tongue falls back and obstructs the airway. After several increasingly strong respiratory efforts, the patient wakes up, takes a few normal breaths, and falls back to sleep. Not surprisingly, the apneic episodes are most common during REM sleep, when the muscles are most hypotonic.

The *symptoms* are loud snoring, morning headaches, fatigue, and day time sleepiness.

When severe and prolonged, the condition is said to increase the incidence of pulmonary hypertension, heart failure, myocardial infarction, and stroke. In addition, the incidence of motor vehicle accidents in sleep apnea patients is seven times greater than it is in the general driving population.

(Ref. Ganong 22th edition, Page-693)

Sudden Infant Death Syndrome

It has been argued that sudden infant death syndrome (SIDS) may be a form of sleep apnea. This disorder, in which apparently healthy infants are found dead, often in their cribs, has attracted a great deal of attention. Apneic spells are common in premature infants. However, periods of prolonged apnea do not correlate with the subsequent occurrence of death, and none of the known tests of chemoresponsiveness reliably predict which infants will subsequently have difficulty. Some of the cases appear to be caused by cardiac arrhythmias complicating the congenital long QT syndrome. In addition, there is evidence that the incidence of SIDS is increased in infants of mothers who smoke. It is increased also by sleeping in the prone position and teaching mothers to put their babies down on their backs has led to a significant reduvtion in incidence.

(Ref. Ganong 22th edition, Page-693)

Q. 14. **Short notes on- decompression sickness.**

Ans. Decompression sickness :

I. *Definition* : Decompression sickness (*the bend', caisson disease*) occurs when the diver ascend to the surface too rapidly.

II. *Cause* : It is caused by the release of inert gases, usually nitrogen or helium, which form bubbles in the tissue (both extracellular and intracellular space) as the ambient pressure falls.

Normally at sea level 1 liter of nitrogen is dissolved in the entire body (less than half in the body water and reminder in the fat). Nitrogen is not metabolized in the body - hence it remains dissolved state.

III. *Clinical features* : Symptoms commonly appear 10-30 minutes after the diver resurfaces.

1. Non -neurological or type I bends (due to bubbles in the tissue) :
   a. Skin irritation
   b. Joint pain.
2. Neurological (type 2 bends)
   a. Cortical blindness
   b. Hemiparesis
   c. Sensory disturbances.

   These features are due to bubbles in the blood stream that obstruct the arteries to the brain and spinal cord. If nitrogen bubbles occur in the pulmonary vessels, divers experiences :
   * Retrosternal discomfort
   * Dyspnoea
   * Cough.
3. Long term problem: Aseptic necrosis caused by infraction due to nitrogen bubbles lodging in nutrient arteries supplying bone.

(N.B. Ascent in an airplane is equivalent to ascent from a dive).

Shock-lung syndrome

In severe shock deterioration of the lungs also often leads to

respiratory distress and death several days later- called the shock lung syndrome.

(Ref. Guyton & Hall-11th Edition)

Oxygen toxicity

It is interesting that while O_2 is necessary for life in aerobic organisms, it is also toxic. Indeed, 100% O_2 has been demonstrated to exert toxic effects not only in animals but also in bacteria, fungi, cultured animal cells, and plants.

Cause : The toxicity seems to be due to the production of the superoxide anion (O_2^-), which is a free radical and H_2O_2.

Effects :

i. When 80%-100% O_2 is administered to humans for periods of 8 hours or more, the respiratory passages become irritated, causing substernal distress, nasal congestion, sore throat, and coughing.

ii. Some infants treated with O_2 for respiratory distress syndrome develop a chronic condition characterized by *lung cysts* and *densities* (*bronchopulmonary dysplasia*). There is evidence that this syndrome is a manifestation of O_2 toxicity. Another complication in these infants is *retinopathy* of prematurity (*retrolental fibroplasia*), the formation of opaque vascular tissue in the eyes, which can lead to serious visual defects. The retinal receptors mature from the center to the periphery of the retina, and they use considerable O_2. This causes the retina to become vascularized in an orderly fashion. Oxygen treatment before maturation is complete provides the needed O_2 to the photoreceptors, and consequently the normal vascular pattern fails to develop.

Treament : There is evidence that this condition can be prevented or ameliorated by treatment with *vitamin E*, which exerts an antioxidant effect, and, in animals, by growth hormone inhibitors.

(Ref. Ganong 22th Edition; page 691)

(Q. 00. Write short notes on- acute oxygen posioning)

Hyperbaric oxygen therapy

Administration of 100% O_2 at increased pressure accelerates the onset of O_2 toxicity, with the production not only of tracheobronchial irritation but also of muscle twitching, ringing in the ears, dizziness, convulsions, and coma. The speed with which these symptoms develop is proportionate to the pressure at which the O_2 is administered; eg, at 4 atmospheres, symptoms develop in half the subjects in 30 minutes, whereas at 6 atmospheres, convulsions develop in a few minutes. Administration of other gases at increased pressure also causes central nervous system symptoms. Administration of O_2 at elevated pressures to rats decreases their brain GABA content and their brain, liver, and kidney ATP content.

On the other hand, exposure to 100% O_2 at 2-3 atmospheres can increase dissolved O_2 in arterial blood to the point that arterial O_2 tension is greater than 2000 mm Hg and tissue O_2 tension is 400 mm Hg. If exposure is limited to 5 hours or less at these pressures, O_2 toxicity is not a problem.

Therefore, ***hyperbaric O_2 therapy*** in closed tanks is used to treat diseases in which improved oxygenation of tissues can not be achieved in other ways.

Indication of hyperbaric O_2 therapy : It is of demonstrated value in-

i. Carbon monoxide poisoning
ii. Radiation-induced tissue injury
iii. Gas gangrene
iv. Very severe blood loss anemia
v. Diabetic leg ulcers and other wounds that are slow to heal
vi. Rescue of skin flaps and grafts in which the circulation is marginal.
vii. It is also the primary treatment for decompression sickness and air embolism.

(Ref. Ganong 22th Edition; page 691)

(Q. 00. Short notes on- Hyper baric oxygen therapy)

***Direction** : Write 'T' for true & 'F' for false against each of the following statement.*

Introduction

Q. 01. **There are about .. million alveoli in man**
- T a. 300
- F b. 50
- F c. 100
- F d. 500
- F e. 200

Q. 02. **Breath rate at rest (adult)**
- T a. breathes 12-18 times/minute.
- T b. breathes 6-8 L/min.
- T c. inhales about 250 ml of O_2/minute
- F d. exhales about 150 ml of CO_2/minute.
- F e. ventilates 400 ml of air per breath.

Q. 03. **Functions of nose include**
- T a. warming the air.
- T b. humidifying the air.
- T c. partially filtering the air.
- T d. helping in olfaction.
- T e. conduction of air.

Q. 04. **Non-respiratory functions of the lungs are**
- T a. Synthesis of prostaglandins.
- T b. Activation of angiotensin-I to angiotensin-II.
- T c. Release of histamine.
- F d. Synthesis of 5-hydroxy tryptamine.
- F e. Transport of O_2 and CO_2.

Q. 05. **Non-respiratory function of the lung is**
- T a. Serotonin metabolism
- F b. Dopamine metabolism
- F c. Adrenaline metabolism
- F d. PGE2 production.
- F e. PGI production.

Q. 06. **Lung defence mechanisms include**
- T a. Mucus secretion
- T b. Macrophages
- T c. Lung fluids
- F d. Negative intraplural pressure
- F e. Surfactant.

Q. 07. **Compliance of the lungs**
- T a. in adult is about 200 ml/cm of water transpulmonary pressure.
- T b. is greater in adults than in infants.
- T c. is gteater when filled with nonnal saline than filled with air.
- T d. is greater when they axe expanded with normal tidal volume.
- F e. is greater in recumbent subjects than in standing.

Q. 08. **Compliance of the lung, is decreased in this conditions**
- T a. Fibrosis of lung
- T b. Pulmonary oedema
- T c. Kyphosis
- F d. Emphysema
- F e. All.

Q. 09. **Surfactant**
- T a. is secreted by type II alveolar epithelial cells.
- T b. increases the lung compliance.
- T c. increases in the fetal lungs during the last month of pregnancy.
- F d. increases the surface-tension of the fluid lining alveolar walls.
- F e. causes collapsing of the lungs.

Q. 10. **Surfactant**
- T a. decreases surface tension.
- T b. is formed by type-II alveolar epithelial cell
- T c. lack causes atelectasis.
- T d. is responsible to prevent collapsing tendency of lungs.
- F e. is secreted by type-I alveolar epithelial cell.

Q. 11. **Surfactant**
- T a. Is composed of phospholipids.
- T b. Is composed of dipalmitoyl lecithin.
- T c. Contains protein.
- T d. Decreases surface tension.
- F e. Is secreted by type-I alveolar epithelium.

Q. 12. **The surfactant material lining the lung alveoli**
- T a. Decreases the surface tension of alveolar fluid

T b. Increases the compliance of lungs
T c. Has increasingly less effect, the more lungs are inflated
T d. Is decreased when pulmonary blood flow is interrupted
F e. Is secreted by type-I alveolar epithelium.

Q. 13. **Instability of alveoli does not occur due to**
T a. Interdependence
T b. Fibrous tissue
T c. Surfactant
F d. Elastic tissue of lungs
F e. Due to negative intrapleural pressure.

Q. 14. **Work done in quiet breathing is**
T c. 0.5 Kg-m/min
F a. 0.1 Kg-m/min
F b. 0.2 Kg-m/min
F d. 2.5 Kg-m/min
F e. 1.5 Kg-m/min

Q. 15. **The work of breathing**
T a. increases when the subject exercises.
T b. increases when the subject lies down.
T c. comprises compliance work, tissue resistance work and airway resistance work.
F d. increases when lung compliance increases.
F e. decreases in asthma.

Q. 16. **Increased fetal cortisol just before birth results in**
T a. Fetal lung maturation
F b. Uterine contraction
F c. Release of oxytocin
F d. Placental steroid biogenesis
F e. All.

Q. 17. **Pulmonary wedge pressure is**
T a. Usually 2-3 mm of Hg.
T b. Mesaured in a perosn with right sided heart failure.
T c. Measured by floating a baloon-tipped catheter to right heart.
F d. Measured by a baloon-tipped catherer to left heart.
F e. All.

Q. 18. **Effort during normal respiration is done due to**
T a. Creating negative pleural pressure
F b. Lung elasticity
F c. Respiratory air passages
F d. Alveolar air spaces
F e. None.

Q. 19. **Respiratory quotient of cerebral tissue is**
T a. 0.95-0.99
F b. 0.75 -0.95
F c. 1.0-1.1
F d. 1.1-1.2
F e. 1.95-1.99

Q. 20. **Liver has the maximum O_2 consumption (51 ml/min), the next organ to have the maximum O_2 (ml/min) is :**
T a. Skeletal muscle
F b. Heart
F c. Brain
F d. Kidney
F e. Skin.

Q. 21. **Respiratory minute volume in a normal person**
T a. 6.0 L/min
F b. 1.2 L/min
F c. 2.1 L/min
F d. 4.2 L/min
F e. 4.0 L/min

Q. 22. **The oxygen consumption of human brain is**
T a. 3.5 ml/100 gm brain/min
F b. 1.0 ml/100 gm brain/min
F c. 1.5 ml/100 gm brain/min
F d. 5.0 ml/100 gm brain/min
F e. 0.5 ml/100 gm brain/min

Q. 23. **Oxygen consumption of whole human brain in ml/minute is about**
T a. 49
F b. 29
F c. 35
F d. 61
F e. 39

Q. 24. **Oxygen consumption of renal cortex and inner medulla are ml/100 gm/min respectively**
T a. 9, 4
F b. 9, 0, 4
F c. 4, 9
F d. 9, 4, 1
F e. 0, 4, 6

Pulmonary Circulation

Q. 25. **Pulmonary circulation**
T d. blood flow is about 9% of total blood volume.
T e. vascular resistance is less than that of systemic vascular resistance.
T a. arterial mean pressure is about 15 mml-Ig.
T b. capillary pressure is 7 mmHg.
F c. blood flow is about 4 litres/min.

Q. 26. **Regarding blood pressure in pulmonary circulation**
T a. Pulmonary artery systemic pressure is about 25 mm of Hg.

T b. Pulmonary artery diastolic pressure is about 8 mm of Hg.
T c. Pulmonary capillary pressure is about 7 mm of Hg
T d. Left atrial and pulmonaiy venous pressure are average 2mm of Hg.
F e. Mean pulmonary pressure is about 7 mm of Hg.

Q. 27. **As blood passes through systemic capillaries**
T a. its O_2 dissociation curve shifts to the right.
T b. its ability to deliver O_2 to the tissues is enhanced.
T c. HCO_3 ions pass from red cells to plasma.
F d. pH rises.
F e. Cl^- ion concentration in red cells falls.

Q. 28. **Factors preventing pulmonary edema are**
T a. Normal negativity of the interstitial fluid pressure.
T b. Lymphatic pumping of fluid out of the interstitial spaces.
T c. Decreased colloid osmotic pressure of interstitial fluid.
F d. Increased interstitial fluid pressure
F e. Increased intra alveolar pressure.

Q. 29. **Ventilation perfusion ratio is maximum in**
T a. Apex of lung
F b. Base of lung
F c. Post lobe of lung
F d. Middle lobe of lung
F e. All.

Q. 30. **Rise of pulmonary arterial pressure is caused by**
T a. Hypoxia
F b. Acidosis
F c. Alkalosis
F d. All of the above
F e. Cyanosis.

Q. 31. **When the atmospheric pressure is halved, which of the following is not likely to develop?**
T a. A rise in cerebral blood flow
F b. An increase in pulmonary ventilation
F c. A fall in arterial PO_2
F d. A rise in arterial pH
F e. None.

Q. 32. **In normal adult, the lung is kept dry because of**
T a. Hydrostatic pressure
F b. Osmotic pressure
F c. Surfactant
F d. Tidal volume
F d. None.

Q. 33. **Pulmonary wedge pressure corresponds to**
T a. Left atrial pressure
F b. Right atrial pressure
F c. Right ventricular pressure
F d. None.
F e. Left ventricular pressure

Inspiration & Expiration

Q. 34. **During inspiration**
T a. heart rate is increased.
T b. more energy is expended than during expiration.
T c. venous return is increased.
F d. lung expansion is assisted by surface tension forces in the alveoli.
F e. lung expansion begins when intrapleural pressure fafls below atmospheric pressure.

Q. 35. **During quite inspiration**
T a. The diaphragm contract
T b. The intrapleural pressure becomes more negative
T c. The intra-alveolar pressure is lower than the atmospheric pressure
F d. Intra-abdominal pressure decreases
F e. surfactant deficiency is associated with a more negative intra-alveolar pressure than normal.

Q. 36. **Expiration**
T a. Is driven by elastic recoil of the lungs during quite breathing.
T b. May be accelerated by actively increasing the intra abdominal pressure.
T c. Is associated with a positive intra-alveolar pressure during quite breathing.
F d. Associated with a a positive intrapleural pressure during breathing.
F e. Is an active process.

Q. 37.**Muscle of expiration**
T a. Rectus abdominis.
F b. Diaphragm
F c. Internal intercostal
F d. External intercostal
F e. None.

Q. 38. **Relaxation of bronchial smooth muscle is induced by**
T a. Vasoactive intestinal polypeptide.
F b. Leukotrienes.
F c. Acetylecholine.
F d. Aold air.
F e. Sulfur dioxide.

Q.39. **Bronchial smooth muscle contracts in response to**
T a. parasympathetic stimulation.
T b. inhalation of cold air.
T c. bronchial mucosal irritation.
F d. local beta adrenoceptor stimulation.
F e. circulating noradrenaline.

Q. 40. **During inspiration there is a fall in**
- T a. intrathoracic pressure.
- T b. intra-pleural pressure.
- T c. intrapulmonary pressure.
- F d. intra abdominal pressure.
- F e. dead space volume.

Q. 41. **The intrapleural pressure at the end of deep inspiration is**
- T a. - 4 mm Hg
- F b. + 4 mm Hg
- F c. - 18 mm Hg
- F d. + 18 mm Hg
- F e. - 7 mm Hg

Q. 42. **During the initial part of inspiration, which of the following does not occur?**
- T a. Intrathoracic pressure rises
- F b. Intrapulmonary pressure falls
- F c. Intrabdominal pressure rises
- F d. The partial pressure of O_2 in dead space rises.
- F e. All.

Pulmonary Ventilation

Q. 43. **In normal lungs**
- T a. the tidal volume is about 500 ml.
- F b. the expiratory reserve volume is 1200 ml.
- F c. the tidal volume is the volume of air inspired or expired per minute.
- F d. the functional residual capacity equals the tidal volume plus the expiratory reserve volume.
- F e. the total lung capacity is about 4600 ml.

Q. 44. **The approximate dead space of a normal 70-kg man breathing normal air is**
- T a. 150 ml
- F b. 230 ml
- F c. 180 ml
- F d. 280 ml
- F e. 380 ml.

Q. 45. **Total dead space can be calculated from**
- T a. PCO_2 of expired air
- T b. PCO_2 of alveolar gas
- T c. Tidal volume
- T d. All of the above
- T e. None of the above

Q. 46. **In an normal adult, the ratio of physiological and anatomical dead space is**
- T a. 1 : 1
- F b. 2 : 1
- F c. 1 : 3
- F d. 3 : 1
- T e. 4 : 1

Q. 47. **Respiratory dead space**
- T a. Is about 150 ml in young adult.
- T b. Increases slightly with age.
- T c. Sturates inspired air with water vapour.
- F d. Decreases during deep inspiration.
- F e. Takes part in gaseous exchange.

Q. 48. **Ventilation is increased**
- T a. when plasma CO_2 level is raised.
- T b. during chronic renal failure.
- T c. during muscular exercise.
- T d. at a high altitude.
- F e. during deep sleep.

Q. 49. **At high altitude, there is an increase in**
- T a. arterial pH.
- T b. diffusing capacity of the lung.
- T c. red blood cell count.
- T d. pulmonary ventilation.
- F e. arterial PO_2

Q. 50. **The ventilation-perfusion ratio**
- T a. is increased by hemorrhage.
- T b. is about 0.8
- T c. is more in apex than in base of the lungs in erect posture.
- F d. decreases with increased physiological dead space.
- F e. is decreased in exercise.

Q. 51. **The residual volume is**
- T a. responsible for expansion of the lungs.
- T b. the gas remaining in the lungs at the end of a full expiration.
- T c. greater on average in men than that in women.
- F d. 2000 ml on average in young adult.
- F e. measured directly using a spirometer.

Q. 52. **The approximate amount of gas left in the lungs after maximal forced expiration in a normal woman is**
- T a. 1.1 litre
- F b. 0 litre
- F c. 0.1 litre
- F d. 3.1 litre
- F e. 4.2 litre.

Q. 53. **Functional residual capacity in a male is :**
- T a. 2.2 litres
- F b. 3.8 litres
- F c. 3.3 litres
- F d. 2.8 litres
- F e. 1.2 litres

Q. 54. **Normal functional residual capacity is**
- T a. 2.2 litres
- F b. 0.5 litres

F c. 1.5 litres
F d. 4.0 litres
F e. 1.2 litres

Q. 55. **In advanced age, there is usually a decrease in**
T a. FEV_1
T b. lung elasticity.
T c. resting arterial blood PO_2
F d. residual volume of the lungs.
F e. ratio of lung residual volume to vital capacity.

Q. 56. **Vital capacity is**
T a. TV + IRV + ERV
F b. Tidal volume + Expiratory rserve volume
F c. Tidal volume + inspiratory reserve volume
F d. IRV + ERV
F e. Tidal volume.

Q. 57. **Vital capacity is a measure of**
T a. Tidal volume plus inspiratory reserve volume plus expiratory reserve volume
F b. Tidal volume
F c. Lnspiratory reserve volume plus expiratory reserve volume
F d. Expiratory reserve volume plus reserve volume
F e. None.

Q. 58. **Total vital capacity is decreased but timed vital capacity is normal in**
T a. Scoliosis
F b. Bronchial Asthma
F c. Chronicbronchitis
F d. All the above
F e. None.

Q. 59. **Vital capacity depends on**
T a. Respiratory muscular stregnth
T b. Condition of air way passage
T c. Position of the body
F d. Atmospheric air
F e. Alveolar air.

Q. 60. **Factors mainly responsible for vital capacity are**
T a. air way resistance
T b. strength of respiratory muscle.
T c. elastic recoil tendency of the lungs.
F d. age.
F e. posture.

Q. 61. **Which tends to decrease with increasing age**
T a. Vital capacity
F b. Systolic blood pressure
F c. Pulse pressure
F d. Residual volume
F e. None.

Q. 62. **Which of the following tend to increase in old age**
T a. Residual volume
T b. Systolic BP
T c. Pulse pressure
F d. Vital capacity
F e. All.

Q. 63. **All of following tend to increase in old age except**
F a. Residual volume
F b. Systolic BP
F c. Pulse pressure
F d. None.
T e. Vital capacity

Q. 64. **The instrument used for measuring the vital capacity and FEV is**
T b. Vitalograph
F a. Wright peak flow meter
F c. Carlens catheter
F d. None of the above
F e. All.

Q. 65. **Spirometry measures all of the following except**
F a. Tidal volume
F b. Vital capacity
F c. FEV_1
F e. All
T d. None of the above

Q. 66. **Which of the respiratory volumes cannot be measured by a simple spirometer?**
T a. Functional residual capacity
F b. Vital capacity
F c. Expiratory reserve volume
F d. Inspiratory capacity
F e. Tidal volume

Q. 67. **Spirometer can measure**
T a. Tidal volume
T b. Vital capacity
F c. Expiratory reserve volume
F d. Residual volume
F e. None of the above

Q. 68. **Spirometer cannot measure**
T a. Residual volume
F b. Tidal volume
F c. Vital capacity
F d. Expiratory reserve volume
F e. None of the above

Q. 69. **Closing volume of lung determines**
T a. Small air way resistance
F b. Distensibility of lung
F c. Residual volume
F d. Dead space

F e. None of the above

Q. 70. **Maximum voluntary ventillation (L/min) is**

T a. 210-250
F b. 90-120
F c. 125-170
F d. 170-210
F e. 110-150

Q. 71. **Flow during last stage of expiration decreases because of**

T b. Dynamic compression of airways
F a. Braking by inspiratory muscles
F c. Collapse of alveoli
F d. All
F e. None.

Q. 72. **Total lung capacity is**

T a. 4 - 5 litres
F b. 3 - 4 litres
F c. 6 - 7 litres
F d. 7 - 8 litres
F e. 2 - 3 litres

Q. 73. **Total lung capacity depend on-**

T a. Lung compliance
F b. Size of airway
F c. Closing tidal volume
F d. Residual volume
F e. None.

Q. 74. **Nitrogen washout method used for**

T b. Residual volume
F a. Dead space volume
F c. Tidal volume
F d. All of the above
F d. None of the above.

Q. 75. **The most important substance controlling alveolar ventilation**

T a. CO_2
F b. O_2
F c. H_2O
F d. None of the above
F e. All of the above

Q. 76. **Normal value of FEV_1 in an adult male is**

T a. 80%
F b. 95%
F c. 65%
F d. 55%
F e. 50%

Transport of O_2 & CO_2

Q. 77. **Transport of gases through respiratory membrane is**

T a. simple diffusion.
F b. facilitated diffusion.
F c. osmosis.
F d. active transport.
F e. filtration.

Q. 78. **Factors that affect the net rate of gas diffusion through respiratory membrane are**

T a. pressure difference across the membrane.
T b. cross sectional area of the membrane.
T c. distance through which the gas must diffuse
T d. molecular weight of the gas.
F e. solubility of the gas.

Q. 79. **Diffusion coefficient for different gases in respiration are**

T a. carbondioxide : 20.3
T b. carbon monoxide : 0.81
T c. nitrogen : 0.53
T d. helium : 0.95
F e. oxygen : 2.0

Q.80. **In which of the following diseases would you expect to find an increase in thickness of the respiratory membrane?**

T a. Pulmonary edema
F b. Emphysema
F c. Asthma
F d. Pulmonary artery thrombosis
F e. Skeletal abnormalities of the chest

Q. 81. **Structure through which O_2 must diffuse in passing from alveolar lumen to haemoglobin**

T a. Surfactant containing liquid
T b. Alveolar membrane, basement membrane
T c. Capillary endothelium, plasma and RBC membrane
T d. All of the above
T d. None of the above

Q. 82. **Lung diffusion capacity is measured with**

T a. CO
F b. CO_2
F c. O_2
F d. H_2
F e. H_2O.

Q. 83. **Partial pressures of respiratory gases in alveolor air are**

T a. PCO_2 : 40 mm of Hg
T b. PH_2O : 47 mm of Hg

T c. PN_2 : 569 mm of Hg
F d. PO_2 : 90 mm of Hg
F e. total alveolar pressure : 700 mm of Hg.

Q. 84. **Partial pressure of O_2**
T a. in lung alveoli : 104 mm of Hg.
T b. in aorta : 95 mm of Hg.
T c. arterial end of tissue capillary : 95 mm Hg
T d. venous end of tissue capillany : 40 mm Hg
F e. in cell : 40 mm of Hg.

Q. 85. **Atmospheric pressure (at sea level) is**
T a. 760 mm of Hg
F b. 500 mm of Hg
F c. 770 mm of Hg
F d. 790 mm of Hg
F e. 750 mm of Hg

Q. 86. **PO_2 of alveolar air is**
T a. 104 mm of Hg.
F b. 140 mm of Hg
F c. 120 mm of Hg
F d. 105 mm of Hg
F e. 110 mm of Hg

Q. 87. **The Alveolar PO_2 is**
T a. 104 mm of Hg
F b. 110 mm of Hg
F c. 120 mm of Hg
F d. 150 mm of Hg
F e. 85 mm of Hg

Q. 88. **Arterial PO_2 is reduced in**
T a. Pulmonary hypoventilation
F b. Anaemia
F c. KCN poisoning
F d. CO poisoning
F e. All of the above.

Q. 89. **On the summit of Mt. Everest, where the barometric pressure is about 250 mm Hg, the PO_2 is about**
T a. 50 mmof Hg
F b. 0.1 mm of Hg
F c. 0.5 mm of Hg
F d. 5 mm of Hg
F e. 100 mm of Hg.

Q. 90. **Oxygen toxicity limits exposures to less than ...hours and pressures to .. atmospheres or less respectively:**
T a. 5, 3
F b. 3, 5
F c. 1, 2
F d. 2, 1
F e. 1, 3

Q. 91. **Oxygen affinity decreases in**
T a. Hypoxia
F b. Hypothermia
F c. HbF
F d. Increase in pH
F e. All of the above.

Q. 92. **Decreased O_2 affinity of Hb in blood with decreased pH**
T a. Bhor effect
F b. Haldane effect
F c. Double Haldane effect
F d. Double Bhor effect
F e. All of the above.

Q. 93. **Oxygen affinity is increased by**
T a. Alkalosis
T b. Hypoxia
T c. Increased HbF
F d. Hyperthermia
F e. All of the above

Q. 94. **Increased PO_2 causes**
T a. release of CO_2 due to O_2-haemoglobin formation in the lung.
T b. helps in the entrance of O_2 into the cells.
F c. release of O_2 from blood to the alveolus.
F d. responsible for release of O_2 from the cell.
F e. maintainance of PO_2 in the blood.

Q. 95. **Release of O_2 is increased with**
T a. A fall in tissue PO_2
T b. Any factor which decreases the O_2 affinity for haemoglobin.
T c. An increase in local PCO_2
F d. A decreased temperature
F e. An increase in local pH.

Q. 96. **The state of iron responsible for O_2 transport**
T a. Fe ++
F b. Fe +++
F c. Both
F d. None.
F e. All.

Q. 97. **Arterial O_2 content is reduced in one of following**
T a. Anemic hypoxia
F b. Stagnant hypoxia
F c. Histotoxic hypoxia
F d. Ischemic hypoxia
F e. All.

Q. 98. **Oxygen affinity is increased by**
T a. Alkalosis
T b. Hypoxia
T c. Increased HbF

F d. Hyperthermia
F e. All.

Q. 99. **Carbon monoxide**
T a. has a greater affinity to combine with Hb than does O_2.
T b. can combine with Hb, where O_2 is supposed to bind.
T c. interferes with O_2 transport
F d. loosely combines with CO_2 in the plasma
F e. interferes with CO_2 transport.

Q. 100. **Which of the following diffuses freely from plasma to extracellular space**
T a. CO_2
F b. H_2O
F c. Glucose
F d. Proteins
F e. Amino acid.

Q. 101. **The diffusing capacity for carbon dioxide compared to that for oxygen is**
T a. 20 times
F b. 10 times
F c. 5 times
F d. 15 times
F e. 2 times

Q. 102. **PCO_2 of alveolar air is**
T a. 40 mm of Hg
F b. 104 mm of Hg
F c. 50 mm of Hg
F d. 35 mm of Hg
F e. 45 mm of Hg.

Q. 103. **PCO_2 in venous blood is**
T a. 46 mm of Hg
F b. 40 mm of Hg
F c. 1.3 mm of Hg
F d. 0.3 mm of Hg
F e. 0.7 mm of Hg

Q. 104. **Increased PCO_2 causes**
T a. release of O_2 from Nb
T b. shift of oxhaemoglobin curve to right
F c. shift of oxhaemoglobin curve to left.
F d. release of CO_2
F e. release of H_2

Q. 105. **Increased CO_2 in blood causes**
T a. respiratory acidosis.
T b. raised cerebral blood flow.
T c. raised plasma bicarbonate.
F d. metabolic acidosis.
F e. alkaline urine.

Q. 106. **A rise in arterial PCO_2**
T a. increases cerebral blood flow
T b. increases arterial pressure
T c. increases the plasma bicarbonate level.
T d. causes increased ventilation.
F e. shifts the O_2-Hb dissociation curve to the left.

Q. 107. **Carbon dioxide**
T a. uptake by the blood leads to similar increases in HCO_3^- ion concentration.
T b. stimulates ventilation when breathed at a concentration of 5%.
F c. is canied as carboxyhaernoglobin on the haemoglobin molecule.
F d. uptake by the blood increases its O_2 binding power.
F e. content is greater than O_2 content in arterial blood.

Q. 108. **Carbon dioxide**
T a. Is more soluble than oxygen.
T b. Increases proportionately within body with decreased ventilation.
F c. Can not penetrate the blood brain barrier.
F d. Is irreversibly hydrated by carbonic anbydrase.
F e. Is hydrated before crossing red cell membrane

Q. 109. **CO_2 transport in the blood**
T a. Occurs mainly in the form of HCO_3^-
T b. Is promoted by carbonic anhydrase within the erythrocytes.
F c. Is saturated at a PCO_2 of approximately 6 kpa.
F d. Is promoted by an increase in the O_2 cotent of the blood.
F e. Leads to an increase in plasma Cl^- level.

Q. 110. **CO_2 transported in the blood is**
T a. In carbamino compounds
T b. In dissolved form in plasma
T c. In HCO_3- form
F d. Bound to Cl^-
F e. In carboxyhemoglobin form.

Q. 111. **Most of the CO_2 transported in the blood is**
T a. In HCO_3^-.
F b. In dissolved state
F c. As carbamino compounds formed from plasma proteins.
F d. As carbamino compounds formed from haemoglobin.
F e. In bound form with Cl ion.

Q. 112. **In a normal adult, 24 hour production of CO_2 is about :**
T a. 280 L
F b. 150 L
F c. 330 L

F d. 410 L
F e. 180 L

Q. 113. **In sternuous exercise, PCO_2 (mm of Hg) falls from:**
T a. 40 to 15
F b. 60 to 35
F c. 25 to 10
F d. 35 to 0
F e. 15 to 10

Q. 114. **CO_2 is carried in the blood**
T a. In combination with haemoglobin
T b. In physical solution in plasma
T c. In combination with plasma proteins
T d. Mainly as bicarbonate
F e. None.

Q. 115. **The most importatnt factor in transport of CO_2 as bicarbonate is**
T a. Carbonic anhydrase in RBC
F b. Affinity to Hb
F c. Basic nature of HCO_3
F d. Increased solubility of CO_2
F e. None.

Q. 116. **P_{50} is**
T a. 28-32 mm of Hg.
T b. partial pressure of O_2 at which 50% haemoglobin statura tion occurs.
F c. 40-50 mm of Hg.
F d. 50% haemoglobin staturation with O_2
F e. an indicator of PCO_2

Q. 117. **At high altitude, there is an increase in**
T a. arterial pH.
T b. diffusing capacity of the lung.
T c. red blood cell count.
T d. pulmonary ventilation.
F e. arterial PO_2

Q. 118. **All are true about 2,3 DPG**
T a. High levels in red cells.
T b. Low affinity of O_2 to hemoglobin
T c. Altered binding to fetal hemoglobin
F d. Causes Bohr effect
F e. None.

Q. 119. **Role of 2,3 DPG in hemoglobin**
T a. Unloading oxygen to tissues
F b. Increased affinity for oxygen
F c. Buffering capacity
F d. Osmotic fragility.
F e. None.

Q. 120. **A shift of oxyhaemoglobin dissociation curve to the right**
T a. increases the P_{50}.
T b. occurs if blood temperature rises
T c. favours O_2 delivery to the tissues.
F d. favouis O_2 up take from the lung by alveolar capillary blood
F e. occurs in the pulmonary capillaries

Q. 121. **Oxyhemoglobin dissociation curve is shifted to the right by**
T a. increased 2,3 DPG
T b. increased PCO_2
F c. increased pH
F d. decreased temperature.
F e. increased PO_2

Q. 122. **Oxyhemoglobin dissociation curve is shifted to the left by**
T a. decreased 2,3 DPG
T b. increased pH
T c. fetal haemoglobin.
T d. increased PO_2
F e. increased PCO_2

Q. 123. **Factors affecting oxy-hemoglobin dissociation curve are**
T a. H^+ concentration.
T b. Temperature.
T c. PCO_2
F d. PN_2
F e. PH_2O

Q. 124. **The O_2-Hb dissociation curve shows that**
T a. O_2 saturation of systemic arterial blood is 97%
T b. O_2 saturation in venous blood is 75%.
T c. flat part indicates oxygenation of Hb in the lungs
T d. it is sigmoid in shape.
F e. flat part occurs in the tissues capillaries.

Q. 125. **Oxygen dissociation is increased by**
T a. Hypercapnia
T b. 2,3 DPG increase
T c. Increased temperatures
F d. Metabolic alkalosis
F e. All.

Q. 126. **Oxygen dissociation curve is**
T a. S-shaped
F b. Bell shaped
F c. Normal curve type
F d. Delta shaped
F e. None.

Q. 127. **Oxygen dissociation is increased by**
T a. Hypercapnia

T b. 2,3 DPG increase
T c. Increased temperatures
F d. Metabolic alkalosis
F e. All.

Q. 128. **Oxygen dissociation curve is shifted to the right in**
T a. Fall in pH
T b. Rise in temperature
T c. Increase of 2,3 DPG
F d. Hb F
F e. All.

Q. 129. **Shift to right of O_2 dissociation curve is seen in**
T a. Decreased pH
F b. Increase Pa CO_2
F c. Decreased Pa CO_2
F d. Increased pH
F e. None.

Q. 130. **Haemoglobin unlike myoglobin shows**
T a. Parabolic curve of oxygen association
F b. Positive cooperativity
F c. Cooperative index of 81
F d. Hill's coefficient of 1
F e. None.

Q. 131. **Nernst equation deals with**
T a. Chloride shift
F b. Oxygen uptake
F c. Cellular ATP levels
F d. Plasma bicarbonate level
F e. All.

Q. 132. **In Bohr effect**
T a. O_2 dissociation increases in hypoxia
F b. O_2 dissociation decreases in hypoxia
F c. O_2 dissociation increase with elevated temperature
F d. None.
F e. All of the above

Regulation of Respiration

Q. 133. **The primary stimulus for respiration is a**
T a. Two fold increase in the PCO_2 of inspired air.
F b. Two fold increase in the PO_2 of inspired air
F c. 50% decrease in the PCO_2 of inspired air
F d. 50% increase in the PO_2 of inspired air
F e. 50% decrease in PCO_2 in inspired air.

Q. 134. **Most potent respiratory stimulant is**
T a. Carbondioxide
F b. Oxygen
F c. H^+
F d. K^+
F c. N_2

Q. 135. **The most important substance controlling alveolar ventilation**
T a. CO_2
F b. O_2
F c. H_2O
F d. None of the above
F e. All of the above

Q. 136. **Spontaneous respiration ceases after**
T a. Transection of the brain stem at the
F b. Transection of the brain stem above the pons caudal end of the medulla.
F c. Bilateral vagotomy.
F d. Bilateral vagotomy combined with transection of the brain stem at the superior border of the pons.
F e. Transection of the spinal cord at the level of first thoracic segment.

Q. 137. **J receptor when stimulated causes**
T a. Rise in the frequency of breathing.
T b. Decrease in the depth of inspiration.
F c. Increase in the depth of inspriation.
F d. Fall in the frequency of breathing. acidosis.
F e. Acidosis.

Q. 138. **The main respiratory control neurons**
T a. Send out regular bursts of impulses to inspiraory muscles during qutie respiration.
F b. Send out regular burst of impulses to expiratory muscles during quite respiration.
F c. Are unaffected by the stimulation of pain receptors.
F d. Are located in the pons.
F e. are unaffected by impulses from the cerebral cortex.

Q. 139. **Respiratory centre is composed of**
T a. pneumotaxic center
T b. apneustic center.
T c. Dorsal respiratory group of neuron
T d. ventral respiratory group of neuron
F e. chemotaxic center

Q. 140. **What is not true for respiration centre?**
T a. Sends out regular impulses to expiratory
F b. Situated in the medulla and pons
F c. Sends out regular bursts of impulses to expiratory muscles during quiet respiration muscles during quiet respiration
F d. Is inhibited during swallowing and vomitting
F e. All.

Q. 141. **Stimulation of the proximal end of a cut vagus would be expected to**
T a. inhibit respiration
T b. cause apnea.
F c. increase heart rate

F d. inhibit coughing
F e. raise blood pressure

Q. 142. **Destruction of the pneumotaxic center located in the pons can cause**
T a. Apneustic respiration
F b. Forcefull expiration
F c. accelerated respiration
F d. Apnea
F e. Cheyne-Stokes breathing.

Q. 143. **CO_2 affects respiratory centre via**
T a. CSF H^+ concentration
F b. Carotid body
F c. Inflation and deflation receptors
F d. Aortic body
F e. All.

Q. 144. **What happens when CO_2 in inspired air increases beyond 10% at atmospheric pressure?**
T a. Depression of CNS
T b. Decreased ventilation
T c. Diminished sensory acuity
T d. Confusion, coma and death
T e. All.

Q. 145. **Respiration is stimulated by**
T a. decreased pH of the blood.
T b. decreased concentration of O_2 in the blood.
T c. excess carbondioxide in the blood.
T d. excess hydrogen ions in the blood.
F e. decreased CO_2 in the blood.

Q. 146. **The factors that increase the rate and depth of respiration during exercise are**
T a. direct stimulation of respiratory centre from motor cortex.
T b. indirect stimulation from proprioceptors.
T c. increased PCO_2 stimulating respiratory centre
T d. decreased PO_2 stfmulating respiratory centre.
F e. increased pH stimulating respiratory centre

Q. 147. **Variations in concentration of which of the following component of blood or cerebrospinal fluid do not affect respiration are**
T a. arterial Na^+
F b. arterial HCO_3^-
F c. arterial H^+
F d. ceroborospinal fluid CO_2
F e. ceroborospinal fluid H^+.

Q. 148. **Chemorceptors**
T a. Stimulates ventilation when the arterial PCO_2 increases by 10%
T b. Can lead to an increase in ventilation when the arterial pH falls
T c. In the brain are responsible for the change in arterial PCO_2.
F d. Stimulate ventilation when the arterial PO_2 falls by 10%
F e. In the carotid body provide the main drive to ventila tion under normal circumstances

Q. 149. **The following stimulate the peripheral chemoreceptors**
T a. Hypoxia
T b. Acidosis
T c. Low perfusion pressure.
F d. Hypocapnia
F e. None.

Q. 150. **Chemoreceptor mechanism is not triggered in**
T a. Histotoxic hypoxia.
F b. Anemic hypoxia
F c. Hypoxic hypoxia
F d. Stagnant hypoxia
F e. None.

Q. 151. **In moderate exercise stimulation of respiration is due to**
T a. Joint propioception receptor
F b. Stimulation of J receptor
F c. Stimulation or lung receptor
F d. Stimulation of medullary centre
F e. None.

Q. 152. **All are increased during exercise**
T a. Cardiac output
T b. Venous return
T c. Coronary blood flow
F d. Peripheral vascular resistance
F e. None.

Q. 153. **Moderate exercise tachypnea is due to stimulation of which receptor**
T a. Propioception
F b. J receptor
F c. Lung receptor
F d. Baro-receptor
F e. None.

Q. 154. **At high altitude, there is an increase in**
T a. arterial pH.
T b. diffusing capacity of the lung.
T c. red blood cell count.
T d. pulmonary ventilation.
F e. arterial PO_2

Q. 155. **First compensatory mechanism in high altitude sickness is**
T a. Polycythemia
T b. Hyperventilation

F c. Alkaline urine
F d. Anaemia
F e. Hypoventilation.

Q. 156. **An increase in ventilation occurs in**
T a. Fall in plasma bicarbonate
T b. Fall in pH of CSF
T c. Rise in blood adrenaline level
F d. Sleep
F e. All.

Q. 157. **J receptor stimulation causes**
T a. Apnoea
F b. Tachynoea
F c. Tachycardia
F d. Hypotension
F e. None.

Q. 158. **Which occurs after hyperventillation with 6% CO_2**
T a. Apnea
F b. Continued hyperventilation
F c. Cheyne stoke's breathing
F d. None.
F e. Kussmaul's breathing

Applied

Q. 159. **In heavy exercise extra O_2 is supplied by**
T a. Increased PCO_2.
T b. Linear flow
T c. Open patent arteries
T d. Increased diffusing area
F e. Increased PO_2

Q. 160. **During heavy exercise there are**
T a. Increased metabolic activity
T b. Increased H^+ concetration.
T c. Increased PO_2 concetration.
F d. Decreased PCO_2
F e. Decreased O_2 concetration.

Q. 161. **Cyanosis**
T a. occurs in polycythemic patient.
T b. occurs when reduced Hb is more than 5 gm/dl.
T c. is caused by high level of methhaemoglobin in the blood.
F d. occurs in anaemic patient.
F e. is caused by high level of carboxy haemoglobin in the blood

Q. 162. **Cyanosis is seen if the concentration of methaemoglobin is more than**
T a. 1.5 G%
F b. 2.0 G%
F c. 3.0 G%
F d. 4.0 G%
F e. 5.0 G%

Q. 163. **Obstructive airway disease reduces**
T a. peak expiratory flow rate.
T b. vital capacity
T c. the forced expiratory volume in first second (FEV_1)
F d. the ratio of FEV_1 and VC
F e. residual volume

Q. 164. **In emphysema there are**
T a. abnormal ventilation perfusion ratio.
T b. decreased diffusing capicity.
F c. normal removal of CO_2.
F d. decreased pulmonary vascular resistance.
F e. Increased airway resistance.

Q. 165. **Hypoxia causes**
T a. Headache
T b. Drowsiness
T c. Loss of self control
F d. Decreased heart rate
F e. Decreased RBC count.

Q. 166. **Hypoxia in chronic respiratory failure**
T a. leads to increased formation of erythropoietin
T b. causes pulmonary hypertension.
T c. may lead to right heart failure.
T d. may cause central cyanosis.
F e. may cause peripheral cyanosis.

Q. 167. **In histotoxic hypoxia**
T a. PO_2 is normal in arterial blood.
T b. O_2 from the capillary blood is not extracted any more
T c. PO_2 of venous blood remains high
F d. PCO_2 of venous blood remains high
F e. O_2 content of the blood is low

Q. 168. **In anemic hypoxia**
T a. haemoglobin concentration is reduced.
T b. arterial PO_2 is normal.
T c. decreased PCO_2 in the arterial blood occurs.
F d. decreased PO_2 in arterial blood occurs.
F e. increased 2,3-DPG in the blood is present.

Q. 169. **If the hypoxia is of slower onset, compensatory mechanisms are**
T a. Hyperventilation
T b. Alkalosis.
T c. Polycythenna.
F d. Acidosis.
F e. Hypoventilation.

Q. 170. **The most common form of hypoxia is :**
T a. Hypoxic

F b. Stagnant
F c. Anemic
F d. Histotoxic
F e. None.

Q. 171. **Hypoxia causes vasoconstriction in**
T a. Lungs
F b. Muscle
F c. Liver
F d. Spleen
F e. None.

Q. 172. **All the following type of hypoxia stimulate the peripheral chemoreceptor, except**
T a. Histotoxic hypoxia
F b. Anaemic hypoxia
F c. Stagnant hypoxia
F d. Hypoxic hypoxia
F e. None

Q. 173. **Which of the following type of hypoxia stimulate the peripheral chemoreceptor**
T a. Anaemic hypoxia
T b. Stagnant hypoxia
T c. Hypoxic hypoxia
F d. Histotoxic hypoxia
F e. All.

Q. 174. **Severe hypoxia may produce:**
T a. BP rise
F b. BP fall
F c. Fall followed by BP rise
F d. No change
F e. None

Q. 175. **Hypoxia is characterised by**
T a. Low arterial PO_2
T b. Intense chemoreceptor response
T c. Favourable response to 100% oxygen
T d. All of the above
F e. None

Q. 176. **Arterial O_2 content is reduced in one of following**
T b. Anemic hypoxia
F a. Stagnant hypoxia
F c. Histotoxic hypoxia
F d. Ischemic hypoxia
F e. None.

Q. 177. **Hyperboric oxygenation is useful in**
T a. Congenital heart disease
T b. Gas gangrene
T c. Carbon-monoxide poisoning
F d. Nitrogen toxicity
F e. All.

Q. 178. **Oxygen therapy is not effective in**
T a. Histotoxic hypoxia
F b. Hypoxic hypoxia
F c. Anaemic hypoxia
F d. Ischemic hypoxia
F e. None.

Q. 179. **Oxygen therapy is effective in**
T a. Hypoxic hypoxia
T b. Anaemic hypoxia
T c. Ischemic hypoxia
F d. Histotoxic hypoxia
F e. All.

Q. 180. **In eupnoea there is**
T a. normal rate or depth of breathing
F b. decreased alveolar ventilation
F c. rapid shallow breathing
F d. difficulty in breathing
F e. decreased rate of breathing.

Q. 181. **Stimulation of the proximal end of a cut vagus would be expected to**
T a. inhibit respiration
T b. cause apnea.
F c. increase heart rate
F d. inhibit coughing
F e. raise blood pressure

Q. 182. **Cheyne-Stokes breathing is**
T a. slowly waxing and waning respiration.
T b. most common type of periodic breathing.
F c. due to acute asthma.
F d. normal breathing.
F e. due to high altitude.

Q. 183. **Periodic breathipg**
T a. is characterised by deep breathing for short period followed by shallow or absence of breathing.
T b. is abnormal respiration.
T c. occurs during sleep.
F d. is normal respiration.
F e. is caused occastionally due to tuberculosis.

Q. 184. **Apneusis**
T a. occurs due to lesion through midpons and vagus nerve.
T b. is ceassation of breathing at the inspiration.
F c. is ceassation of breathing at the height of expiration.
F d. is temporary ceassation of breathing.
F e. occurs in periodic breathing.

Q. 185. **CO_2 retention is most likely to occur in**
T a. Ventilatory failure
F b. High mountain

F c. Carbon monoxide poisoning
F d. Pulmunary failure
F e. Hysterical hyperventilation.

Q. 186. **Pulmonary fibrosis would be expected to produce**
T a. Cyanosis
F b. Histotoxic hypoxia
F c. Stagnant hypoxia
F d. Decreased vital capacity
F e. Emphysema.

Q. 187. **Chronic cigarette smoking produces**
T a. Increased carbmonoxyhemoglobin in blood.
T b. Patches of atelectasis
T c. Myocardial ischemia.
T d. Loss of elastic tissue in the lung
F e. increased anatomic dead space

Q. 188. **O_2 delivery to the tissue would be reduced to the greatest extent in**
T a. a patient with carbon monoxide poisoning
F b. A normal subject breathing 100% O_2 on the top of Mt. everest
F c. A normal subjcet running a marathon at sea level.
F d. a person who has ingested cyanide
F e. a patient with moderately severe metabolic acidosis.

Q. 189. **Manifestations of oxygen toxicity are**
T a. Irritation of the respiratory tract
T b. Retrolental fibroplasia
T c. Convulsions
T d. Cystic lungs in infants
F e. Rupture of the alevoli.

Q. 190. **The poison cyanide inhibits the reaction between**
T a. Cytochrome oxidase and molecular oxygen
F b. Cytochrome A and Cytochrome B
F c. Phosphofructokinase and glucose oxidase
F d. Haemoglobin and oxyhaemoglobin
F e. None.

Q. 191. **Death due to cyanide poisoning results from which of the following types of anoxia?**
F a. Anoxic anoxia
F b. Anaemic anoxia
F c. Stagnant anoxta
F d. Histotoxic anoxia
T e. None of the above.

Q. 192. **Cyanide posoning affects ..... function**
T a. Respiratory
F b. Cardiac
F c. Renal
F d. Liver
F e. None.

Q. 193. **Earliest change in high altitude is**
T a. Hyperventillation
F b. Decrease in work capacity
F c. Drowsiness
F d. Polycythemia
F e. None.

Q. 194. **A person ascends to 12,000 feet develops acute breathlessness this is due to**
T a. Carbon dioxide washout
F b. Decreased pulmonary blood flow
F c. Decreased hypoxic stimulation of respiration
F d. Mechanical interference of thorax
F e. None.

Q. 195. **Which of the following occur in high altitude acclimatisation**
T a. Reticulocytosis
T b. Increase serum erythropoletin
T c. Increased serum cortisol
F d. Increased blood glucose
F e. All.

Q. 196. **Which is seen in high altitude**
T a. Respiratory alkalosis
F b. Metabolic alkalosis
F c. Respiratory acidosis
F d. Metabolic acidosis
F e. None.

Q. 197. **Alkalosis accurs whenever pH is above**
T d. 7.40
F a. 7.000
F b. 7.24
F c. 7.36
F e. 6.40

Q. 198. **Metabolic alkalosis associated with prolonged vomiting is due to primarily to loss of**
T a. Chloride
F b. Sodium
F c. Potassium
F d. Hydrogen ion
F e. None.

Q. 199. **Metabolic alkalosis is seen in**
T a. Thiazide diuretics
T b. Prolonged vomiting
T c. Systemic antacid therapy
F d. Ureterosigmoidostomy
F e. All.

Q. 200. **In hypercapnic acidosis**
T a. Cerebral vasodiliation can occur
T b. Plasma bicarbonate rises
T c. May be associated with pickwickian syndrome

F d. Kaussmal breathing may be present
F e. All.

Q. 201. **Respiratory acidosis can cause**
T a. Increased PCO_2 and decreased P^H
F b. Decreased PCO_2 and decreased P^H
F c. Increased PCO_2 and increased P^H
F d. Decreased PCO_2 and increased P^H
F e. None.

Q. 202. **Smoking causes**
T a. Ciliary motility
T b. Cellular hyperplasia
T c. Mucous secretion
T d. All of the above
F e. None.

Q. 203. **In cigarette smoking, surfactant is :**
T a. Decreased
F b. Increased
F c. Increased followed decrease
F d. Unaltered
F c. Decreased followed increase.

Q. 204. **Destruction of lung tissue and defective gaseous exchange causes**
T d. Pulmonary hypertension
T c. Increased red cell number
T a. Prominent P wave
F b. Decreased cerebral blood circulation
F e. None.

Q. 205. **In COPD all are affected**
T a. FEV
T b. Ratio of FEV to vital capacity
T c. None.
F d. FVC
F e. None.