CHAPTER VIII

RESPIRATORY SYSTEM

Definition: Respiration is the process by which oxygen from the lungs is carried by the blood to the tissues; and carbon dioxide formed in the tissues by metabolic activity is carried by the blood to the lungs and is expired out.

The process of respiration involves four stages, viz.

I. Ventilation means the passage of air in and out of lungs during inspiration and expiration respectively.

II. Intrapulmonary gas-mixing or distribution of oxygen-rich inspired air with the air already present in the lungs.

III. Diffusion which means gas-transfer across the alveolo-capillary membrane due to tension gradient.

IV. Perfusion means flow of adequate quantity of blood through the lungs so that the diffused gases are carried away.

Throughout the body, the function of an organ is reflected in its structure, this is true of the lung in particular.

8.1. STRUCTURE OF THE RESPIRATORY TRACT (Fig. 242)

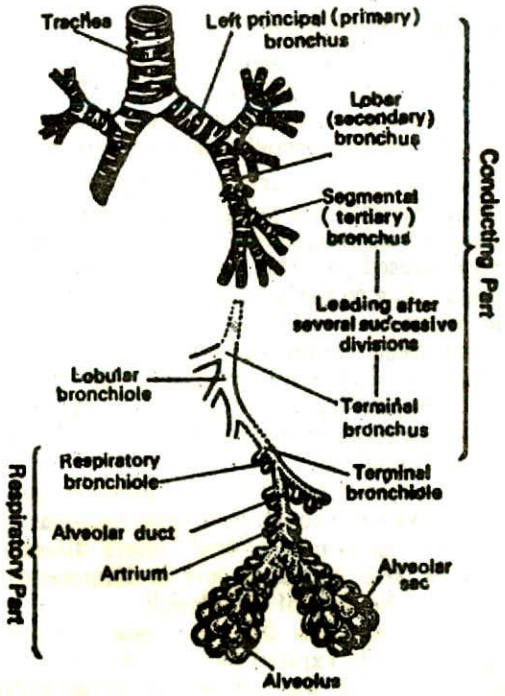


Fig. 242. Oversimplified diagrammatic representation of broncho-pulmonary structure depicting the gross architecture of the conducting and respiratory parts of the trachea and lung at segmental levels.

I. Upper respiratory tract extends from the upper nares to the vocal cord.

II. Lower respiratory tract extends from the vocal cord to the alveoli.

The trachea (windpipe) is a cartilaginous and membranous tube, about 10 or 11 cm long. It is not quite cylindrical, being flattened posteriorly, its external diameter from side to side is about 2 cm in the adult male and 1·5 cm in the adult female. It is kept patent by incomplete C-shaped rings of cartilage on its antero-lateral wall, which keeps air tubes open. There is plenty of sero-mucous glands in the submucous coat innervated by the vagi. Mucous gland along with goblet cells traps dust in the inspired air and air is moistened by contact with moist lining of serous glands. The cilia beat spontaneously at the rate of 20 times per minute and by their movement drive out mucus-trapped foreign particles and bacteria towards the mouth from the respiratory passage, the velocity of movement being 24 mm per minute. The ciliary movement is independent of nerves but dependent in the presence of atmospheric oxygen in the respiratory tube.

Functions of the Respiratory tract

The infolding of nasal mucous membrane over the turbinates offers an area of contact approximately 160 sq cm for the atmospheric air flowing through the nose. The inspiratory air is modified during its passage through the nose as described below :

I. Filtering effect—It is cleared of dust particles :

(a) Large dust particles are caught by the hairs at the nostrils.

(b) Air can flow uninterruptedly through the zigzag passage of the nasal cavity caused by the turbinates but smaller particles suspended in the air due to their momentum are precipitated on the surface of the mucous membrane of the nose and are caught in mucus. This has been described as 'turbulent precipitation' and particles upto the size of 6 μm are caught in this way and are moved towards pharynx by cilliary action of the nasal epithelium when they are expectorated or swallowed. This size is smaller than the size of red blood cells.

(c) Particles between 1 and 5 μm in diameter get precipitated on the wall of the smaller bronchioles (gravitational precipitation) where they evoke fibrotic reaction ('coal-miners' disease).

(d) Particles of size 1 μm or less in diameter diffuse into the alveoli and adhere to the wall of the alveoli

(e) Particles smaller than 0·5 μm remain suspended in the alveolar air and are usually expired out. This size of the particles of cigarette smoke is about 0·3 μm Most of them diffuse into the alveoli where about $\frac{1}{3}$rd gets caught in the alveolar fluid the remainder is expired out. Entrapped particles in the alveoli are removed by macrophages or provoke growth of fibrous tissue in the alveolar septa.

An excess of particles provokes fibrous tissue reaction causing permanent disability.

Role of Ciliated Epithelium

The cilia of trachea and bronchi beat towards the pharynx and propel the mucus with the entangled foreign particles with a velocity of one centimetre per minute towards the pharynx. They thus help materially to keep the respiratory passages free from foreign particles.

II. Air conditioning effect :

The inspired air is brought to near about body temperature and is humidified before it is permitted to enter the deeper air passages Cold and dry air coming in direct contact with the lungs such as after tracheotomy will cause serious lung crusting and infection.

It has been estimated that the inspired air is brought to within 3% of body temperature during its passage through the nose and it is almost completely saturated with water vapour before it is delivered to the lungs

Cough Reflex

'Cough' is a protective reflex by means of which respiratory passages are kept free from foreign matter. Patients in whom cough reflex is lost, get drowned in their own secretion. An instrument called 'Cofulator' has been designed to stimulate cough reflex in these patients.

Sensory stimulus necessary for this reflex is either physical or chemical irritation of the respiratory tract. The larynx and the area of bifurcation of the trachea are most sensitive areas. The afferent fibres run in the vagus to the medulla.

At the commencement of the act a deep inspiration is taken, the epiglottis is then closed and the vocal cord closes the laryngeal opening tightly thus entrapping about 2·5 liters of air into the lungs.

The addominal muscles then contract forcefully pushing firmly the diaphragm against the distended lungs. Internal intercostal and other expiratory muscles contract forcefully causing the pressure within the lungs to rise to about 100 mm Hg or more. The epiglottis and vocal cord then open suddenly and thus the lung air under pressure comes out with explosive violence with a velocity of about 160 km or 100 miles per hour. This act thus helps in clearing out the obnoxious irritating agents from the respiratory passages.

Sneeze Reflex

It is very much like cough reflex but here the zone of afferent stimulus is in the nose and the afferent pathway is in the trigeminal nerve. A large volume of air is drawn into the lungs and the uvula is depressed so that the expired air passes mostly through the nose and partly through the mouth.

Respiratory Units (Fig. 243)

Respiratory units consist of the (i) respiratory bronchioles, (ii) alveolar ducts, (iii) respiratory atrium and (iv) pulmonary alveoli, the walls of these being so thin that gas exchange (Fig 243) may take place between the air contained in these tubules and the capillaries on their wall.

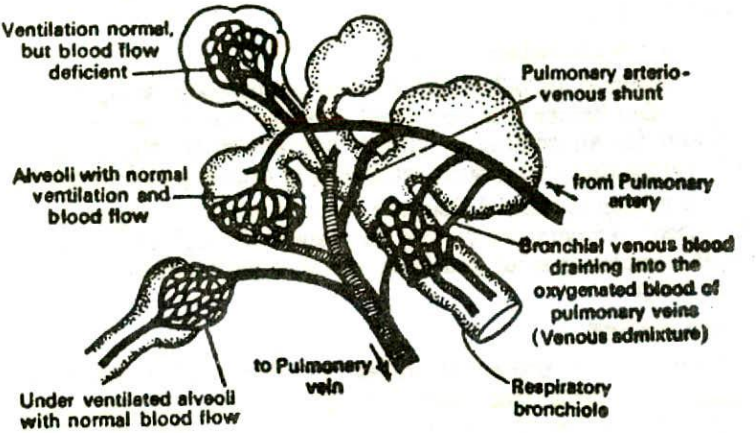


Fig. 243. Schematic representation of ventilation and perfusion (blood flow) of a primary respiratory lobule.

Each *terminal* bronchiole opens into a thin-walled respiratory bronchiole of equal diameter which communicates with some alveoli situated on its wall. However, for the most part each respiratory bronchiole opens into several alveolar ducts, these latter open into dilated spaces called (pulmonary) *atrium* which again communicate with many pulmonary alveoli. Each alveolus is a thin-walled sac filled with air measuring from 75 to 300 μm in diameter. The capillaries of the pulmonary blood vessels ramify around the walls of the alveoli. The alveolar tissue (parenchyma) contains fibres of elastin and collagen and the fluid lining the alveoli has suface tension. As a result the lung is elastic and is held expanded by keeping the pressure around it (intrapleural pressure) lower than alveolar preasure.

Broncho-Pulmonary Anastomosis

On the wall of the respiratory bronchioles the venous blood from the bronchial circulation via the bronchial arteries which arise from the aorta, drains directly into the arterial blood of pulmonary veins. Venous admixture also takes place by direct shunts between the branches of pulmonary artery and pulmonary vein.

Pulmonary Alveoli (Fig. 244)

Pulmonary alveoli are polygonal in shape and are packed so tightly that some have no distinct separate walls and communicate with adjacent alveoli by minute pores. They are lined by a thin layer of squamous epithelium which is separated from the endothelium of the pulmonary capillaries by a homogeneous basal lamina which together with small amount of connective tissue constitutes *interalveolar* septa. Scattered in between the alveolar epithelial cells are found isolated cuboidal cells or *great alveolar cells* which are characterised by microvilli on their free surface. The cytoplasm of these cells contains rough-surfaced endoplasmic reticulum and characteristic multilamellar bodies which secrete a substance called *surfactant*. Surfactant (a layer of phospholipid) has got the unique property of reducing surface tension of *intra-aveolar* fluid and thus helps in keeping the alveoli open and prevents their collapse.

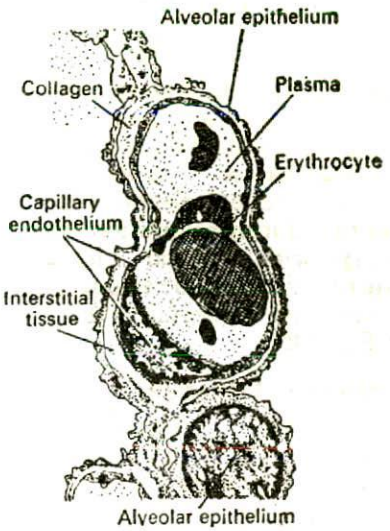


Fig. 244 Diagrammatic representation of electron micrograph showing a pulmonary capillary in the alveolar air with very thin blood-gas barrier.

Functions of respiration :

(1) **Gas transfer :** Transfer of O_2 from the alveoli to the venous blood and CO_2 in the opposite direction.

(2) **Regulation of PCO_2 of blood :** The most important function of respiration is to keep the arterial PCO_2 at 40 mmHg which is essential for many vital functions of the body.

(3) **Regulation pH of blood :** By the reversible reaction $H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ (See chapter on acid-base equilibrium).

(4) **Excretion of certain volatile gases,** e.g. chloroform, ether, ammonia, etc.

(5) **Pumping action :** The rhythmic movement of the diaphragm and chest wall causes rhythmic alteration of pressure in the abdomen and chest cavity. This assists in drawing blood from the lower part of the body to the abdomen and then to chest and thus helps in maintaining venous inflow to the heart.

8.2. PLEURAL CAVITY AND INTRAPLEURAL PRESSURE

The lungs are convered by visceral pleura which is reflected over the inner aspect of the chest wall enclosing a potential cavity between its two layers known as *pleural cavity*. The two layers, parietal and visceral, are kept moist and lubricated by a few millilitres of a muco-polysaccharide containing fluid in the interpleural space so that during respiration the lungs with visceral pleura surrounding it glide smoothly over the *parietal pleura* (Fig. 245).

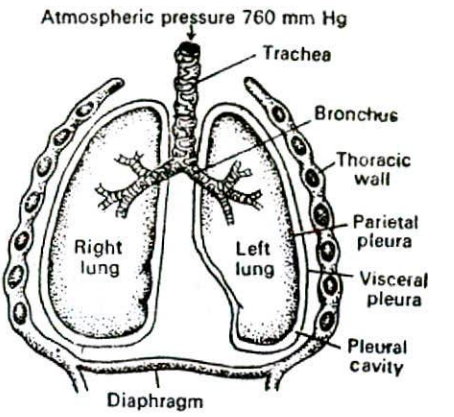


Fig. 245. Diagrammatic representation of pleural cavity. Note that intrapulmonary pressure is same as atmospheric pressure in the resting state.

Intrapleural Pressure

Normal intrapleural pressure, that is pressure in the pleural cavity is negative and amounts to −2·5 mmHg at the end expiratory position. This means that the lungs are not completely collapsed and that alveoli remain partially inflated even after complete expiration.

The factors responsible for negative intrapleural pressure are :

(*a*) *Elastic recoil :*

Due to presence of elastic fibres the lung tissue has a continuous tendency to recoil away from the chest wall. The tendency naturally increases during inspiration with inflation of the alveoli.

(*b*) *Surface tension of the intra-alveolar fluid :*

Due to intramolecular attraction of the surface layer of the fluid lining the alveoli, they have got a tendency to collapse. This collapsing force of the millions of the alveoli produces a summated effect resulting in tendency of the whole lung to recoil away from the chest wall.

In fact about two-thirds of the recoil tendency of the lungs are attributable to the surface tension phenomenon.

Surface tension at the fluid-air interface within the alveoli and the role of surfactant

It was observed by von Neergaard that the pressure required to inflate the air-filled lungs was higher than when it was filled with normal saline. Alveoli are minute spherical bodies, not necessarily of the equal size, lined by the thin layer of fluid and filled with air. The surface tension at the liquid air interface is high and prevents

its expansion whereas in lungs filled with physiological saline the surface tension is absent so that they expand readily.

In a spherical bubble the tension of its wall T tends to collapse the bubble whereas the pressure of air within (P) tends to expand it The relationship between these two opposing forces in equilibrium is given by the equation $P = 2 \times \frac{T}{r}$, where r is the radius of the bubble Naturally, large bubbles (alveoli in this context) have got lower tension than smaller ones and if communication exists between the two the smaller bubbles (alveoli) will empty into the larger ones.

Further as the alveoli become smaller during expiration the surface tension (T) increases and tends to collapse the alveoli. This is prevented by surfactant because of its surface tension-reducing properties.

Alveolar surfactant is a *lipoprotein* with *dipalmityl lecithin* as an important component. It is secreted by the lamellar bodies of the great alveolar cells lining the alveoli. This substance forms a lining for the interior of the alveoli and increases their surface tension during expansion, i e inspiration and decreases their surface tension during expiration.

Surfactant, therefore, not only prevents collapse of the alveoli during expiration but also prevents emptying of smaller alveoli into larger ones, thus ensuring stabilishing effect on the respiratory process.

Pressure changes in the pleural cavity and its relation to volume changes in the lungs

Pressure changes in the pleural cavity and volume changes in the lungs has already been mentioned that the intrathoracic pressure (intrapleural pressure) at the resting stage is slightly negative $-2{\cdot}5$ mmHg. With the enlargement of the thoracic cage in all its diameters during inspiration the intrapleural pressure becomes still more negative and at the end of inspiration in quiet breathing becomes about -6 mmHg. This inspiratory increase in negative pressure in the pleural cavity is reflected in the pressure within the lungs (intrapulmonary) pressure which normally is '0' at rest but falls to about -2 mmHg at the end of inspiration. Air, therefore, rushes in from the atmosphere to the lungs causing inflation of the lungs during inspiration. Negative intrapleural pressure is thus primarily responsible for inspiratory inflow of air into the lungs. It is also responsible for keeping the patency of the airways.

Expiration is usually a passive process due to relaxation of the inspiratory muscles. The intrapleural pressure rises to its resting value with the diminution in size of the the thoracic cage, the lung collapses and the intrapulmonary pressure rises above the

atmospheric pressure till at the end-expiratory resting stage it becomes equal to the atmosphere.

In forced inspiration and expiration the pressure variations in pleura and the lungs are considerably exaggerated. In forced expiration with closed glottis the intrapulmonary pressure may go up to +40 mmHg. It is possible to record intrapleural pressure with a fine polythene tube attached to a thin-walled balloon lying in the lower third of the oesophagus. The diagram shows intrapleural pressure tracing synchronus with volume tracing during respiratory cycle in a normal subject (Fig. 246).

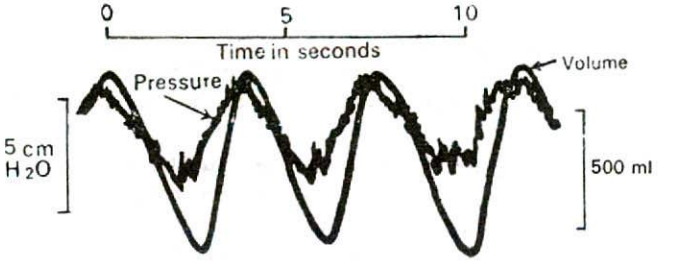


Fig. 246. A simultaneous tracing of tidal volume and intraoesophagcal pressure in a normal resting subject. (After McIlroy, Marshall and Christie's Clinical Science)

Note the time lag between volume tracing and pressure tracing The pressure change occurs fraction of a second earlier than volume changes.

The undulations on the pressure tracing with intraoesophageal balloon is due to prssure variations resulting from heart beat.

8.3. MECHANICS OF BREATHING

The expansion of the lungs during inspiration follows the enlargement of the thoracic cavity in all its diameters by the contraction of the respiratory muscles. These are :

1. Diaphragm :

A dome-shaped muscle separating the abdominal wall from the thoracic cavity, with vertically running fibres at the periphery and horizontally running fibres at the centre ending in the central tendon. It is innervated by *phrenic nerves* (C_3, C_4 and C_5). The muscle is attached behind to fixed structures like vertebrae and in front to sternum and to mobile structures like the lower ribs at the sides. Inspiration commences by contraction of the diaphragm—the central tendon of which moves downwards increasing the vertical diameter of the chest. At the same time the lower ribs are moved somewhat upwards increasing the lateral and antero-posterior diameter of the chest. The descent of diaphragm is accompanied by

displacement of abdominal contents downwards associated with relaxation of the abdominal muscles. It has been estimated that during *quiet breathing* the diaphragm is displaced downwards by

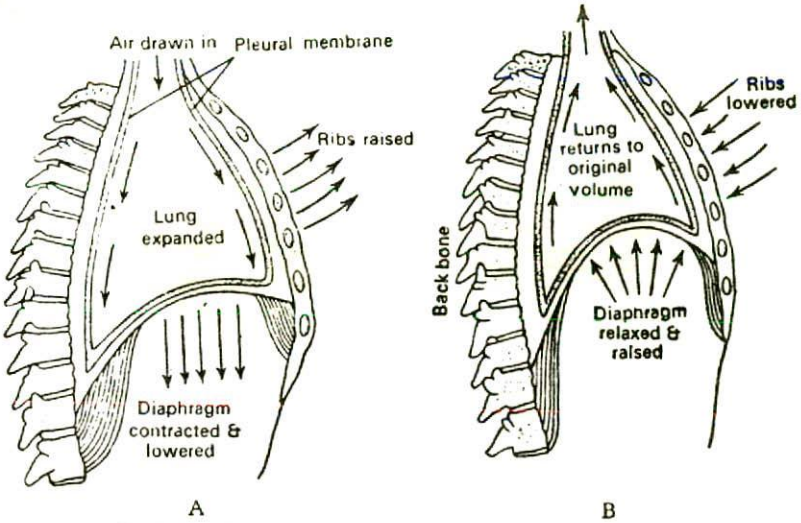


Fig. 247. Position of the diaphragm (from the side) during active inhalation of air (inspiration) in A and passive inhalation of air (expiration) in B.

about 1·5 cm and the area of the diaphragm being 350 sq cm the whole volume of inspired air during a single quiet breathing 500 ml can be accommodated by downward movement of the diaphragm only (Fig. 247). During expiration the diaphragm relaxes, its dome moves upwards aided by contraction of the abdominal muscles pushing the diaphragm upwards. This results in expultion of air from the lungs during expiration (Fig 248).

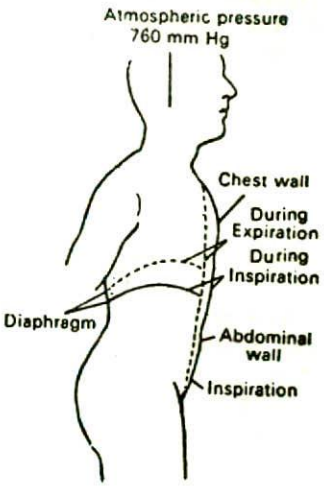


Fig. 248. Diagram shows the changes in position of the abdominal wall and the diaphragm.

2 Intercostal muscles :

The normal breathing is predominantly diaphragmatic. The relative proportions between diaphragmatic and intercostal contribution perhaps vary with different age groups and among different individuals. For example, the infant's ribs are commonly horizontal. Both the

external and intercostal groups of muscle fibres originate and insert on adjacent ribs.

The muscle fibres of the *external* intercostal group run forwards and downwards and those of the *internal* intercostal group run backwards and downwards from rib to rib (Fig 249). The cephalid motion of the ribs indicates that the upper ribs are fixed

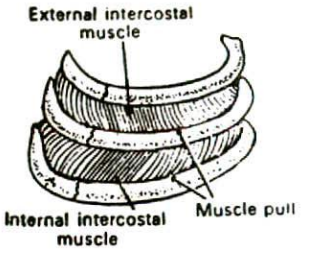


Fig. 249. Diagram showing action of external and internal intercostal muscles during respiration.

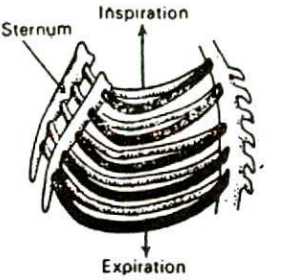


Fig. 250. Schematic representation of the positions of ribs and the sternum.

relative to the lower ones. When the contraction of the abdominal muscle fibres fixes the lower ribs during cough or forced inspiration the rib cage moves downwards. These intercostal muscle fibres are innervated by intercostal nerves (T_1 to T_{11}). Electromyographic studies depict that the intercostal muscles become active during quiet inspiration, forced inspiration and forced expiration. Normal quiet expiration is due to passive relaxation of the intercostal muscles and is not attended with any electrical variation.

3. Motion of the Ribs :

The ribs are almost semicircular bones which articulate with the vertebrae at one end and with the sternum or costal cartilages at the other.

(1) During inspiration the sternum is elevated and pushed forwards due to the elevation of the shaft of the ribs of which the sternal ends are lower than the vertebral ends during expiration. This is caused due to the contraction of internal intercostal muscles and results in an increase in the antero-posterior diameter of the chest. Depression of the shaft of the ribs during expiration causes the opposite effect (Fig. 250).

(2) Rib motion includes the rotation of the ribs around an axis joining two points of attachment at the vertebrae and the sternum (bucket handle motion). This rotation causes an increase in transverse diameter of the thorax. The changes in position of the diaphragm and thorax during inspiration and

expiration are represented diagrammatically in the model as in Fig. 251.

During expiration both intercostal muscles which are responsible for movement of the ribs and sternum described above relax, the size of the thorax decreases in antero-posterior and in transverse diameter the lung volume consequently decreases.

The rib motion is not equal throughout the thorax. The upper ribs are more nearly horizontal than the lower ribs and are arcs of smaller circles. In inspiration the lower ribs are affected by displacement of all the superior ribs. Their motion is, somehow, the sum of the narrowing of many interspaces rather than only the adjacent one. Due to such differences, the changes in the lateral diameter of the thorax are greater in the lower chest than in the upper chest.

The contribution of costal motion to breathing depends on the force of intercostal contraction and on the position of the ribs prior to the intercostal contraction.

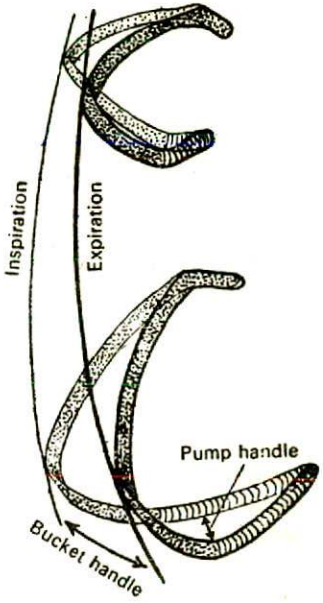


Fig. 251. Diagram shows two kinds of movements of the ribs in respiration ; (i) pump handle in which the anterior end of the downward sloping rib is raised ; and (ii) bucket handle in which the middle of the rib is moved upwards and outwards about an anterior-posterior axis.

Accessory Muscles of Respiration

During forced inspiration and expiration many other muscles besides the diaphragm and intercostal muscles come into play to assist respiration. Most important of this group are the scalenes and sterno-cleido-mastoids of the anterior neck muscles which stabilise the first ribs and upper sternum during forced inspiration. The abdominal muscles contract violently during forced expiration and thus act as accessory muscles. During violent respiratory effort even the platysma and all other muscles of the trunk take part in respiration.

8.4. RESISTANCE TO BREATHING

The air as it enters the lungs meets with two types of resistances, viz.

(1) Elastic resistance

Elastic resistance is exerted by the elastic tissue of the lung parenchyma and surface tension of intra-alveolar fluid. Elastic

tissues of the lungs obey Hooke's law which means that change in volume of lungs is directly proportional to the force applied that is to intrapleural pressure. Lung compliance has been defined as the change in lung volume in litre per cm change of H_2O pressure. This is measured under static conditions to avoid frictional resistance to air flow which occurs during movement of air. After a known volume of air has been inspired and respiratory movement is 'zero'—the change in intrapleural pressure is noted. The change in lung volume (ΔV) divided by change in pressure (ΔP) is the measure of the lung compliance or stretchability. Normal value ranges from 0 09 to 0 26 litre/cm H_2O. Diminution in the lung compliance indicates increased rigidity of the lung, i.e. diminished elesticity as may happen in congestion, fibrosis, emphysema and in various other conditions.

(2) Viscous or non-elastic Resistance :

This is the resistance offered to the air flow into the lungs due to friction between moving column of air and the branching bronchial tubes which get narrower and narrower at each branching (airway resistance) and also the frictional resistance between the muscle fasciculi of the chest wall and tissuss Unlike the elestic resistance which is to be measured only when air flow is 'zero,' frictional resistance comes into play during air flow and can be measured only during active air flow. It is also to be noted that the flow of air in the bronchial system is turbulent and the turbulency increases during broncho-constriction. Turbulency is responsible for increase in viscous resistance—the relationship between the 'resistance' and 'rate of flow', i.e. velocity is given below :

The relationship between frictional resistance (R) and velocity (V) of air flow is given by the formula: $R = K \times V$ where K is a density dependent constant and 'V' is the velocity of air flow. Note that if the velocity of air-flow is doubled the resistance increases 4 times. Typical asthma patients breaths slowly and any attempt to breath rapidly increases their distress.

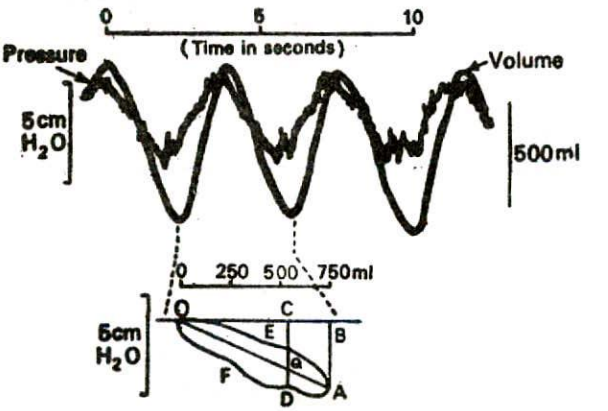


Fig. 252. The intrapleural pressure is recorded by an intraoesophageal ballon. Note that (i) the fall in intrapleural pressure occurs fraction of a second earlier than change in volume (i.e. inspiration). (ii) The small waves on the pressure tracing are due to variation of intrapleural pressure from heart beat. (After McIlroy, Marshall & Christie's Clinical Science).

The diagram (Fig. 252) has been constructed by integration of the volume of air moved with that of intrapleural pressure from moment to moment during one respiratory cycle. The data have been obtained from previous diagram (Fig. 246).

Line AO of the 'ellipse' OFAE represents elastic resistance. The elliptical nature of the pressure-volume curve is due to frictional resistance to air flow. The area OFAB is the total work of inspiration. The area OAB is work done against elastic forces. Area OFA is work against viscous resistance during inspiration.

The energy OAB stored in the lungs during inspiration is available to do the work OAE necessary to overcome the frictional resistance during expiration The pressure exerted against 'viscous' or non-elastic resistance (DQ) is obtained by substracting the elastic pressure (CQ) from the total pressure (CD) exerted at any point of the respiratory cycle. At the point C this is $CD - CQ = DQ$.

Work of Lungs

It can be calculated that the lungs perform work of the order of 0·4 kg-m per minute during quiet breathing of which 60% is spent to overcome the elastic resistance and about 40% is spent to overcome the non-elastic or viscous resistance.

8.5. PULMONARY VOLUMES AND CAPACITIES (SPIROMETRY)

Ventilation (the business of getting gas to and from the lung alveoli) constitutes the first part of respiratory process and ventilation has the dimensions of both volume and time. Ventilation occurs as a result of a pressure difference between the alveolar and oral ends of the airways. Ventilation can be measured with a spirometer which

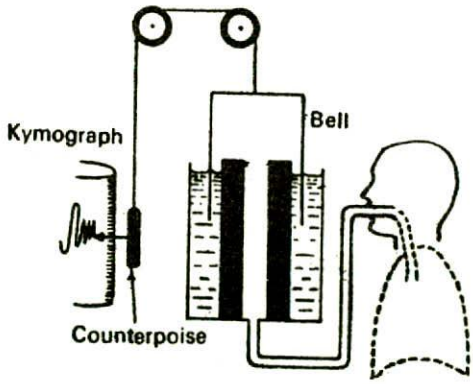


Fig. 253. Recording spirometer. Inspiration causes the spirometric bell to descend and the writing lever to move upwards on the chart. The chart is calibrated so that measurements of lung volume change can be made.

consists of an inverted belljar over a double-walled chamber with water in-between the two walls as shown in Fig. 253. The belljar is attached to counter weight and to a writing point which writes over a moving kymograplic (recording) drum. The subject breaths in and out from the air enclosed on the surface of water below the belljar and the respiratory movement can be recorded on the moving drum and its various componets may be analysed.

Normal ventilation in an adult (75 kg) is about 6 litres per minute with a respiratory rate of 12 breaths per minute and a tidal volume of 500 ml. In a resting day-old infant about 2 5 kg, normal ventilation is about 500 ml per minute at a respiratory rate of 33 breaths per minute and a tidal volume of 15 ml. Thus an adult ventilates about 100 ml/minute/kg body weight whereas an infant ventilates two times more than adult's breaths.

Pulmonary ventilation = Tidal volume × Respiratory rate

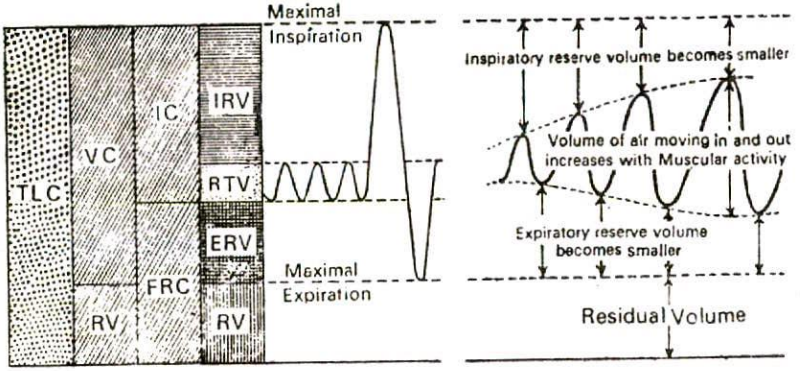


Fig. 254. A schematic representation of the subdivisions of lung volumes and capacities obtained by a spirometer.

Air in lunge may be subdived (Fig 254) at different points into four different volumes and four different capacities. These are defined below :

LUNG VOLUMES

1. Tidal oVlume (TV = 500 ml)

The TV (or Resting Tidal Volume, RTV) is the volume of air breathed in and out during quiet respiration (about 500 ml)

Respiratory Minute Volume (RMV) :

By definition RMV can be obtained by multiplying tidal volume by repiratory rate per minute and is approximately equal to 500 ml × 12 = 6 litres/minute The value of ccurse may vary widely and is increased considerably during exercise when both the tidal volume as well as respiratory rate are increased. At rapid rates of breath-

ing a person usually cannot sustain a tidal volume more than about one-half of his vital capacity.

2. Inspiratory Reserve Volume (IRV) :

The IRV of air that can be breathed in by maximum inspiratory effort after an ordinary inspiration. It amounts to 2·0 to 3·3 litres.

3. Expiratory Reserve Volume ERV) :

The ERV of air that can be breathed out by maximum expiratory effort after an ordinary expiration (about 1 litre).

4. Residual Volume (RV) :

The RV is the amount of air which remains in the lungs after maximal expiration. It can only be expelled out from the lungs by opening the chest and allowing the lungs to collapse (average 1·2 litres).

The volume of air which enters the alveoli with each breath is equal to the TV *minus* the dead space volume.

LUNG CAPACITIES

I. Inspiratory Capacity (IC) :

Maximum volume of air that can be inspired from the end-expiratory position, i e. TV + IRV = about 3·5 litres.

II. Functional Residual Capacity (FRC) :

Volume of air remaining in the lungs after a quiet expirationi e. RV + ERV (about 2·2 litres).

III. Total Lung Capacity (TLC) :

Volume of air that the lung can hold after a maximum possible inspiration, i.e. IC + FRC (about 5·7 litres .

IV. Vital Capacity (VC) :

It is the volume of air that can be breathed out by maximal expiratory effort after a maximum inspiration. By definition it amounts to IC + ERV = (3·5 + 1) litres = 4·5 litres.

The exact amount of vital capacity depends on age, sex and size of the individual. It also shows a racial variation. Best correlation is obtained between height in cm and vital capacity. Thus predicted vital capacity in adult male = height in cm × 20 ml and in females height in cm × 16 ml. The above figures were obtained from observations based on 100 medical students of alcutta.

Europeans have got a higher vital capacity and the empirical formula : height in cm × 25 ml in case of men and height in cm × 20 ml in case of women may be used for calculation of their predicted vital capacity. Observed vital capacity may show a variation of 10% from the predicted vital capacity in normal subjects. Vital capacity diminishes with age and is always lower by more than 10% in old people. Vital capacity is higher by 30 to 40% in the athletes compared to the subjects with sedentary

disposition. Vital capacity is less in supine position than in standing position because the intra-thoracic blood volume diminishes in standing posture, and the diaphragm can move downwards more easily than in supine position. Vital capacity diminishes in conditions associated with weakness of the muscles of respiration, or when the movment of the thoracic cage is restricted or in space occupying defects of the chest. Increased rigidity of the lungs (diminished compliance) as may occur during pulmonary congestion, emphysema, chronic asthma or bronchitis will also cause diminished vital capacity

Significance of vital capacity as a respiratory function test is indeed limited because it is a static test for lung function. However, day-to-day assesment of vital capacity say in a patient with paralysis of respiratory muscles (respiratory polimyelitis) is of prognostic significance.

Maximum Breathing Capacity (MBC), now-a-days called Maximum Ventilation Volume (MVV) :

The subject is allowed to breath into a Douglas bag (Fig. 255) through a valve and is instructed to breath as quickly and as deeply as possible for 12 seconds The volume of expired air collected into the Douglas bag multiplied by 5 will give his/her value of MBC per minute (*ambient temperature and pressure saturated with water vapour*, ATPS which is equal to about 140 liters per minute. The value depends upon the degree of motivation of the subject and upon the efficiency of the muscles of respiration. It measures also the 'bellows action' of the lungs and depends on its elasticity. It is a test simple to perform and a reliable **'respiratory function test'.**

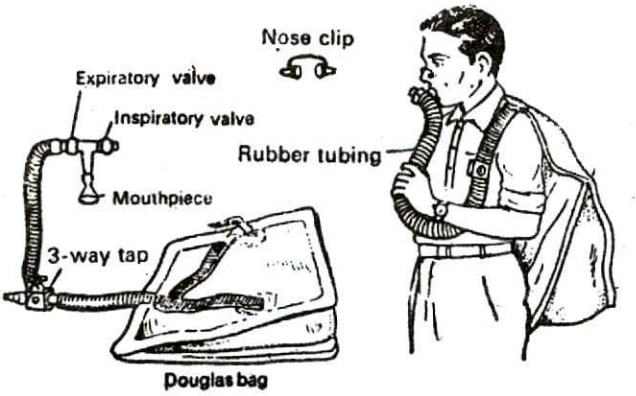


Fig. 255. The collection of expired air in man using a mouthpiece. A nose clip is applied and breathing takes place through the mouth.

Instead of Douglas bag—the test can also be performed in a slow moving Spirometer calibrated for the rate of respiration horizontally

and the volume of respiration vertically. Remarkable reduction in the MBC occurs in diseases like emphysema where both the rate as well as the depth of respiration decrease.

The abbreviations those are commonly used in the spirometric measurements are given in the Table below :

Terms	Symbols	Descriptions
Vital capacity	VC	Maximal volume of air exhaled after forced inspiration (includes TV, IRV and ERV).
Tidal volume	TV	Volume of air inhaled or exhaled during quiet breathing
Inspiratory reserve volume	IRV	Maximal air that can be inhaled after a quiet inspiration.
Expiratory reserve volume	ERV	Maximal air that can be breathed out after quiet expiration.
Residual volume	RV	Volume of air remaining in lungs after full expiration.
Inspiratory vital capacity	IVC	Maximal volume of air inhaled after full expiration.
Forced expiratory volume, per time interval in seconds	FEV_t	Volume of air exhaled in a given period during a complete forced expiration (FVC).
Maximal expiratory flow rate	MEFR	Volume of air exhaled per second measured between 230 ml and 1,200 ml volumes of the forced expiratory Spirogram.
Maximal mid-expiratory flow	MMEF	Volume of air per second exhaled during middle half of expired volume of forced expiratory spirogram.
Maximal voluntary ventilation	MVV	Maximum breathing capacity--litre/minute. Subject can breathe with maximal voluntary effort (actual measurement for twelve seconds).

Forced Expiratory Volume (FEV)

The determination of maximum breathing capacity (MBC) is an exacting procedure and it is the often not possible to perform it

on debiliated patients. Useful information regarding respiratory status of a patient can be obtained by analysis of a single forced expiration after a maximum inspiration on a rapidly moving hymograph. A normal subject can expire 80% ormore of his vital capacity in the first second, Patients with *obst uctive* disease of lung will expire proportionately much less within the first second of expiration (Fig, 256).

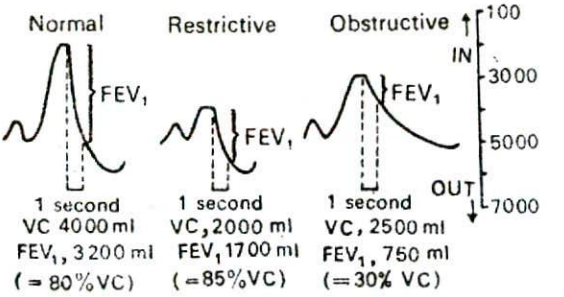


Fig. 256. A schematic recordings of three diagrams of forced expiratory spirograms. Expiration is down and inspiration up and tracings are to be read from left to right. After a deep inspiration the subjects breathed out as forcibly and as rapidly accordidg their ability. The total volume expired is the forced vital capacity and the volume expired in the first second is the forced expired volume is one second (FEV_1) The *restrictive* record was obtained from a subject with scoliosis. The *obstructive* record was obtained from a patient with emphysema Although the vital capacity is reduced remarkably in the 'restrictive' subject, the proportion of the vital capacity expired in the first second is normal (unlike that in the obstructive patient. (After Campbell and Dickinson's Clinical Physiology and also Bell, Davidson and Esmlie-Smith's Text book of Physiology and Biochemistry)

Breathing Reserve (BR) :

Breathing Reserve = MBV (maximum breathing capacity) – RMV (respiratory minute valume) = about 136 litres/minute. When the breathing reserve falls to 60 to 70% of MBC dysponea will result.

Functional Residual Capacity (FRC)

During quiet breathing the pulmonary ventilation is achieved almost entirely by muscles of inspiration The end-expiratory position of the lungs represents the 'resting position' during which all the muscles relaxed. As mentioned earlier the volume of air remaining in the lungs at this level represents 'functional residual capacity' and measures about 2300 ml in an adult male. It provides the air in the alveoli to aerate the blood between the two consecutive respiratory acts, thus preventing marked rise all in the concentration O_2 and CO_2 in the intervals of respiration. Functional residual capacity (FRC) and functional residual volume (FRV) increase in all conditions associated with overdistension of the lungs, e.g in Emphysema. Quantititive measurement of residual

volume and functional residual capacity is not possible by Spirometsy. Some of the special techniques employed for this purpose is described below :

I. N_2-wash-out technique

The man inspires pure O_2 (N_2 free) and expires into a Douglas bag for a 7-minute period. During this period all the N_2 present in his lungs is washed away by inspired O_2. The total volume of expired air in the Douglas bag can be determined by a gas-meter. The volume of expired air multiplied by N_2% gives the quantity of N_2 washed off from the depth of the lungs. Since the lung air contains about 80% of N_2—the volume of functional residual air can be easily calculated.

Example :

Suppose the volume of expired air over the 7-minute period = 50,000 ml and the concentration of nitrogen in the collected gas is 4%

Total quantity of N_2 washed off from lungs $50{,}000 \times 0{\cdot}04$ = 2000 ml. Therefore the functional residual capacity

$$= \frac{2000 \times 100}{80} = 2500 \text{ ml.}$$

II. Body Plethysmograph (Fig. 257) :

It is simply as air-tight tank in which the subject is placed. He inspires the air within the tank and then expires forcefully against a manometer. The expiratory pressure is recorded. The rise of pressure within the chest decreases the volume of gas in the lungs (Boyle's law) and the volume of the chest also decreases. Thus the subject's body occupies less space within the Plethysmograph. A volume recorder records the amount of the reduction which is equal to the degree of compression of gases in the lungs which together with pressure recorded will give the volume of gas in the lungs. Inspiratory capacity is then recorded and deducted from the former value to give functional residual volume (FRV).

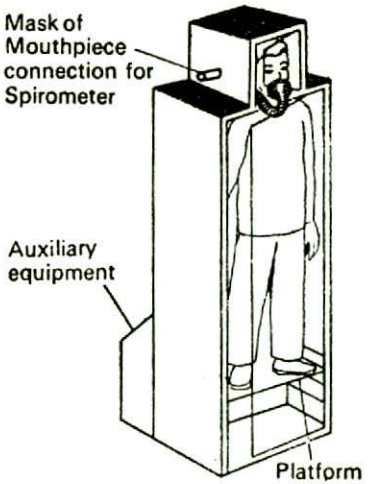


Fig. 257. Body plethysmograph which is an air-tight box fitted with divices for measuring different parameter of 'lung volume, airway resistance and pulmonary blood flow.

8.6. RESPIRATORY DEAD SPACE

The respiratory tract is so designed that during inspira ion its upper part upto the level of terminal bronchiole is filled with atmospheric air. The first part of the expired air, therefore, is also atmospheric air from the non-resp ratory part of the lungs, the second part is a mixture in which the percentage of atmospheric air gradually decreases and that of the alveolar air from the respiratory part ot the lungs gradually increases and the last part of the expired air is pure alveolar air.

Definition : The air which remains confined in the upper respiratory tract with each inspiration and is not available for gaseous interchange constitutes what is known as 'dead space air'.

Anatomical 'dead space' can be measured by making a plaster cast ot airways from the mouth to the terminal bronchioles in the dead space and measuring its volume. It amounts roughly to 150 ml.

Functions of anatomical dead space : (i) Inspired air is saturated by water vapour before it reaches the alveoli of the lungs. (ii) Removes the particulate matter in sizes more than 2·0 μm from the inspired air before it is delivered to the alveoli. But the particles about 2·0 μm entering the alveoli, are removed by lymphatics.

Factors influencing the anatomical dead space : (i) Reflex bronchocontraction due to stimulation of the parasympathetic nerves diminishes the anatomical dead space. (ii) Adrenaline dilates the lower airways by relaxing smooth muscles and upper airways by vasoconstriction which shrink the nasal mucosa.

Physiological dead space : In anideal lung all the alveoli are evenly ventilated and adequately perfused with exactly the required amount of blood. But such an ideal condition is seldom obtained. In fact, in normal subjects the apical alveoli are ventilated adequarly but have got a poor blood supply. Most of the ventilation in these aveoli, therefore, is wasted and produced partial dead space effect. In diseased conditions the situation may be worse—there may be many alveoli which are hyperventilated but have very poor blood flow. These are, therefore, partially dead space areas. Measurement of dead space in these cases will give a value much higher than anatomical dead space and constitutes what is known as physiological dead space. In normal subjects the volumes are very nearly the same. In some disease of the lungs the physiological dead space may amount to 1 to 2 litres producing great respiratory insufficiency. The normal ratio of dead space to tidal volume is in the range 0·2 to 0·35 during breathing at rest. This ratio increases with age but decreases on exercise.

According to *Fowler's method*, physiological dead is space measured with the volume of conducting airways down to the level where rapid dilution of inspired gas occurs with gas already in the lungs. But

Bohr's method measures the volume of the lungs which does not eliminate CO_2.

Measurement of Total Dead Space (Anatomical and Physiological)

This can be done provided a sample of alveolar air is first collected and its CO_2 content is determined by the method to be described subsequently and the partial pressure of CO_2 in the alveolar air (P_ACO_2) is calculated. Expired air is a mixture of dead space air which is practically CO_2 free and of the perfused alveoli. Its CO_2 tension (P_ECO_2) will always be lower than that of P_ACO_2. If V_D represents the 'dead space volume,' V_T represents the tidal volume. The ratio of the dead space volume to tidal volume is given by the equation.

$$\frac{V_D}{V_T} = (P_ACO_2 - P_ECO_2)/P_ACO_2$$

If $P_ACO_2 = 40$ mm Hg and $P_ECO_2 = 30$ mm Hg

$$\frac{V_D}{V_T} = \frac{40-30}{40} = \frac{10}{40} = 0{\cdot}25$$

In other wards ¼th of the tidal ventilation will remain in the dead space. The inspired air is humidified, brought to the body temperature and filtered during its passage through the dead space. The anatomical dead space can be reduced by 50% by tracheostomy, which is beneficial for patients with weak respiration and diminished tidal volume.

Nitrogen-meter method

The subject takes a deep breath of oxygen and then expires through a N_2-meter which records graphically the percentage of N_2 in the expired air from moment to moment. The first part of expired air contains 'zero' % of N_2 because it is pure O_2 from dead space. The second part of the curve shows rising N_2 concentration because it is a mixture of O_2 from the dead space and N_2 from

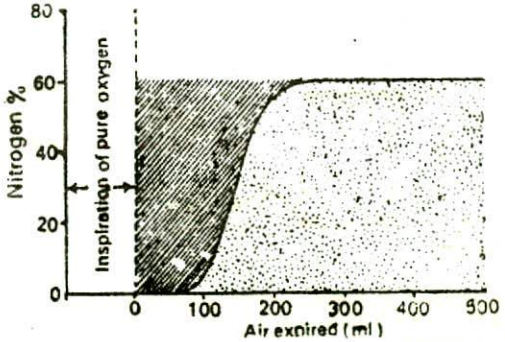


Fig. 258. Continuons tracing of the changes in nitrogen concentration in the expired air following a previous inspiration of pure O_2. This record can be used in calculating dead space.

alveolar air. In the last part of the tracing the N_2 percentage levels off and remains more or loss steady because it is pure alveolar air and in an ideal lung all the alveoli are contrcting sychronously unloading their N_2 content in the expired air at a uniform rate. In Fig. 258 the steady N_2 level is shown to be at 60%.

If the total volume of expired air be 500 ml and the dotted area represents the alveolar air and the hatched area be dead space air :

$$\text{the dead space} = \frac{\text{Area of hatching} \times \text{Total air expired}}{\text{Area of dots} + \text{Area of hatching}}$$

Let us assume that the area of dots = 70 sq. cm and the area of hatching = 30 sq. cm. Since the total volume of expired air = 500 ml, the dead space air $= \frac{30}{30+70} \times 500$ or 150 ml.

8.7. INTRAPULMONARY GAS-MIXING OR EVEN DISTRIBUTION OF INSPIRED AIR

The inspired air enters the alveoli in the form of a cone. At the time of phase reversal, vibrations are set up in the wall of the alveoli due to elastic recoil and cause the inspired air to be evently distribumd throughout the mass of alveolar air so that gaseous interchangement may taken place satistactorily. In diseased conditions associated with loss of elasticity there occurs an uneven distribution of inspired air which may lead to impairment of respiration.

Methods of detectation of uneven ventilation :

(1) Uneven ventilation can be detected with N_2 meter described on page 385. In a subject with ideal lungs the N_2 concentration in the expired air soon reaches a steady level and in the example cited it was 60% after the dead space air was cleared off. Patients with alveoli not contracting synchronously due to loss of elasticity in

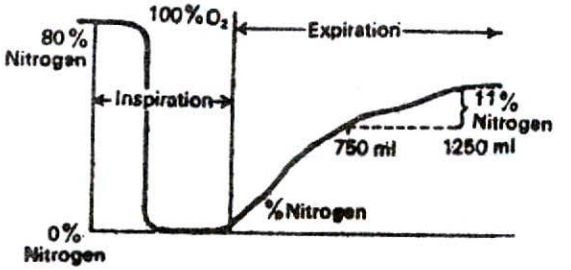


Fig. 259. A schematic graphical representation of N_2 meter record in an abnormal subject measuring the single breath. The increase in nitrogen concentration is measured for a 500 ml sample of the alveolar gas (between 750 ml and 1250 ml of expired gas).

many of them will show a rising phase of N_2 concentration in the expired air instead of a horizontal line. The difference in N_2

concentration between expired volume of 750 ml and 1250 ml should not exceed 1% in normal subjects whereas in emphysema patients the difference is much higher between these two levels of expired ventilation. This is shown in Fig. 259.

(2) It was mentioned previously that breathing pure O_2 for a 7-minute period washes off all the N_2 from the alveolar air and that advantage is taken of this fact in estimation of FRV of the lungs. In a patient with uneven ventilation—N_2 remains confined here and therein the diseased alveoli which have lost their elasticity to varying degree. In such cases, even after O_2 breathing for a 7-minute period, the air on forced expiration will contain 2% or more of N_2 indicating defective intrapulmonary gas-mixing.

8.8. ALVEOLAR AIR

Alveolar air represents the air located in the respiratory part of the lungs which takes part in gas exchange with the blood in the pulmonary capillaries. Alveolar air, therefore, is a physiological quantity and does not represent the air located strictly in the anatomical alveoli. It measures about 3000 ml and is the most important part of the air in the respiratory system since it is primarily responsible for oxygenation of venous blood and unloading the venous blood of adequate quantities of CO_2. With a tidal volume of 500 ml about 350 ml of oxygen-rich atmospheric air mixes with the alveolar air to replenish the oxygen lost from alveolar air by absorbtion with the venous blood.

Method of collection of alveolar air

A sample of alveolar air can be collected by Haldane and Priestley's method (Fig. 260). A tube, about 1·22 m (4 feet) long, is taken. It is

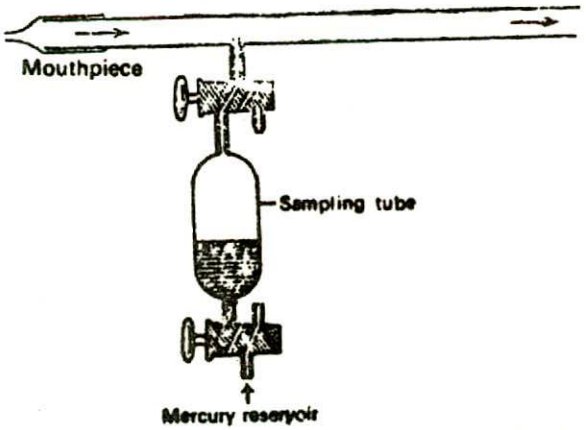


Fig. 260. Diagram shows apparatus for collection on alveolar air as designed by Haldane and Priestley.

fitted with a mouthpiece at one end. A side tube is attached very near to the mouthpiece and is attached to a sampling tube. Through the mouthpiece, the subject makes forcible expiration twice—at first (1) after normal inspiration and then (2) after normal expiration. This is necessary because the alveolar air varies slightly in composition in different phases of respiration. Through the sampling tube, two samples of air are drawn in from the last part of the expired air, while the subject closes the mouthpiece with his tongue at the end of expiration.

A second method of automatic collection of alveolar air has been described by Otis and Rahn and is shown in the diagram (Fig. 261). During inspiration the end expiratory air of the *previous* expiration from the neighbourhood is drawn into the balloon by

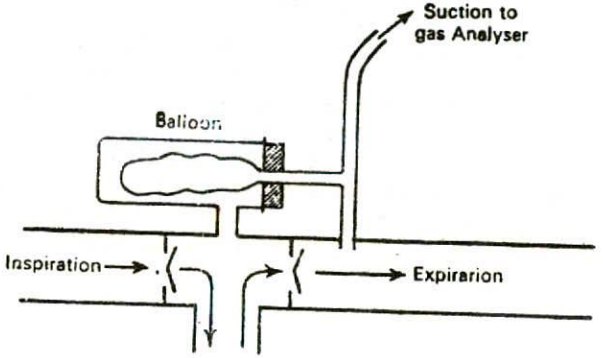


Fig. 261. Diagram shows combined respiratory valve and Otis-Rahn alveolar air sampler.

movement of the expiratory valve. During expiration the balloon is compressed so that no dead space air may contaminate the alveolar air collected into the balloon.

Method of analysis of alveolar air

The classical method is to analyse alveolar air with Llyod's modification of Haldane's gas-analysis apparatus, which is used for analysis of respiratory gases. A measured quantity of air is admitted in the apparatus and its volume is accurately noted. The gas is then passed over caustic potash solution and its volume is noted again. The diminution in volume is due to absorption of CO_2 and from the difference between the original reading and the second reading the percentage of CO_2 in the alveolar air may be calculated. The gas is now passed through alkaline pyrogallol solution which absorbs oxygen. From the reduction in volume the percentage of O_2 in the alveolar air can be calculated.

Composition of alveolar air

The composition of inspired air, normal expired air and alveolar air and also the tension of different gases are shown in the table below.

COMPOSITION OF GASES IN INSPIRED AIR, EXPIRED AIR AND ALVEOLAR AIR

Gases	Inspired air	Expired air	Alveolar air
Oxygen	20·94 vol %	16·4 vol %	14·2 vol %
Carbon dioxide	0·04 „ „	4·0 „ „	5·5 „ „
Nitrogen	79·02 „ „	79·6 „ „	80·3 „ „

The increase in the percentage of nitrogen in the expired air is not real but relative. This is because the volume of the expired air is slightly less than that of inspired air, which is caused by the fact that the amount of CO_2 evolved is less than the amount of oxygen absorbed. Consequently, in the percentage composition, nitrogen shows a relative rise.

Further the composition of expired air varies depending on metabolic activity so that the composition of the alveolar air is kept as constant as possible.

PARTIAL PRESSURE OF GASES IN INSPIRED AIR, EXPIRED AIR AND ALVEOLAR AIR

In a gas mixture, the pressure exerted by a particular gas is directly proportional to the percentage composition of the same gas in the mixture. Supposing in a mixture, oxygen constitutes 20%, then oxygen will exert 20% (i.e. one-fifth) of the total pressure. The following table shows the partial pressures of the various gases :

Barometer 760 mm Hg	Partial Pressure		
Gases	Inspired air	Expired air	Alveolar air
Oxygen	158·25 mmHg	116·2 mmHg	101·2 mmHg
Carbon dioxide	0·30 „ „	28·5 „ „	40·0 „ „
Nitrogen	596·45 „ „	568·3 „ „	571·8 „ „
Water vapour	5·00 „ „	47·0 „ „	47·0 „ „
Total	760·00 mm Hg	760·0 mm Hg	760·0 mm Hg

It will be noted that the alveolar air differs in composition from that of the inspired (atmospheric) air. The reasons for this difference are :

(i) Only a part of the alveolar air is replaced by inspired air as explained previously.

(ii) There is continuous absorption of O_2 from the alveolar air by pulmonary venous blood—the alveolar air, therefore, is poorer in oxygen.

(iii) CO_2 is added continuously to the alveolar air by the pulmonary venous blood—the alveolar air, therefore, is richer in CO_2.

(iv) The inspired air is dry but gets saturated with water vapour during its passage through the respiratory tract. Since some of the space in the alveoli is now occupied by water vapour—the space available for other gases is diminished.

Expired air

It has been noted that part of the expired air ('dead space' air) is atmospheric air rich in O_2 and poor in CO_2. As expiration progresses the expired air becomes a mixture of 'dead space' air and alveolar air and that the last part of the expired air is pure alveolar air. The expired air, therefore, is richer in O_2 but poorer in CO_2 as compared to alveolar air.

Method of collection of Expired air

Expired air is collected in a Douglas bag (Fig. 255) over a certain period of time. The sample of air is taken out from the side tube and analysed with the help Llyod's modification of *Haldane gas analysis apparatus.*

Tension of gases in the alveolar air

In the steady state the total tension of gases including water vapour in the alveoli is equal to the ambient barometric pressure. At sea-level the barometric pressure is 760 mmHg. The alveolar air is saturated with water vapour which exerts a tension of 47 mmHg at body temperature irrespective of the barometric pressure. With these data in view it is possible to calculate tension of O_2 and CO_2 in the alveolar air provided the percentage composition of these gases in the alveolar air is known according to the 'law of partial pressure', which states that the tension of a particular gas in a gas mixture is proportional to its percentage composition.

Thus in atmosphere the pressure of O_2 is roughly $\frac{1}{5}$th of 1 atmosphere = 153 mm Hg approximately. The atmospheric air, however, is dry. In calculation of tension of gases in the alveolar air, the pressure of water vapour (47 mm Hg) is to be deducted from the total pressure of gases in the alveoli which amounts to 760 mm Hg at sea-level.

Thus total pressure in the alveoli = 760 mm Hg
Pressure of H_2O vapour = 47 mm Hg
The pressure of $O_2 + CO_2 + N_2$ = 713 mm Hg
Percentage of O_2 in the alveolar air = 14·2 vol %
Tension of O_2 in the alveolar air = 14·2% of 713
= 101 mmHg (approximately)

Similarly tension of CO_2 in the alveolar air 5·5% of 713 = 39·2 mm Hg or 40 mm Hg (approx.) of the 4 gases present in alveoli ($O_2 + CO_2 + N_2 + H_2O$ vapour) the N_2 and H_2O vapour are neither taken into the blood stream nor added to alveolar air and as such the sum of partial pressure of these gases is constant in the alveoli. This, of course, means that the sum of partial pressure of O_2 and CO_2 is constant in the alveoli under steady state of metabolism and amounts roughly to 140 mm Hg at sea-level. A subject, therefore, can alter the PO_2 of his alveolar air only at

the expense of this alveolar PCO_2 which is rather limited because the alveolar PCO_2 cannot be reduced from normal 40 mm Hg to below 24 mm Hg.

Method of measurement of alveolar and arterial PCO_2

Diffusion of CO_2 is so rapid that alveolar PCO_2 is always equal to arterial PCO_2. Arterial PCO_2 can be measured by direct electrochemical method using a CO_2-sensitive electrode through an arterial puncture needle.

Indirect bloodless method has also be evolved by Campbell *et. a.* and gives reliable result. An anaesthetic bag is filled with about 1 litre of O_2 and the subject breaths and re-breaths into this bag for 1½ minutes. During this period there occurs an almost perfect 'lung bag' equilibrium so that the PCO_2 of the bag air is almost equal to PCO_2 of the alveolar air. However to get an accurate result—the subject takes rest for at least 2 minutes and then re-breaths into the bag once again for 20 seconds during which period there occurs fine adjustment between the mixed venous PCO_2 (P_vCO_2) and the bag air. Recirculation of the blood and consequent higher PCO_2 value is avoided by keeping the second rebreathing period limited to 20 seconds. After the end of the experiment the gas in the bag is analysed and its PCO_2 is calculated. This is equal to mixed venous PCO_2. The arterial PCO_2 is always 6 mmHg lower than the venous PCO_2.

Effect of Voluntary Hyperpnoea on Alveolar air

Hyperpnoea flushes out the alveoli with air so that the CO_2 content and CO_2 tension of the alveolar air and so of the arterial blood is diminished. This causes depression of respiration and may lead to temporary apnoea. During the depressed respiratory phase CO_2 builds up again till the alveolar PCO_2 attains its normal value and breathing is resumed. The alveolar PO_2 rises in the early phase when the PCO_2 is depressed but this has no effect on arterial saturation, which is normally 95% saturated.

Effects of Voluntary Apnoea on Alveolar air

After normal inspiration breath can be held for 30 to 50 seconds This is normal 'breath-holding time'.

During breath-holding time the percentage of CO_2 and PCO_2 in the alveolar air gradually rises and the percentage of O_2 and PO_2 in the alveolar air gradually falls.

At the breaking point the O_2 content of the alveolar air is about 8% (PO_2 = 57 mm Hg) and its CO_2 content is about 7% (PCO_2 = 50 mm Hg). It will be noted that during apnoea there occurs a more significant fall in percentage and tension of oxygen in the alveolar air than rise of CO_2 content and tension.

This is due to different shape of the dissociation curves of the

two gases, so that removal of a given quantity of oxygen from blood will cause a more significant fall in oxygen tension than elevation of CO_2 tension when the same volume of CO_2 is added.

Further CO_2 being highly soluble most of it gets dissolved in body fluids and less is available for elevation of alveolar PCO_2. Here the two stimuli of O_2 lack and CO_2 excess interact with each other in stimulation of respiration.

Inhalation of O_2 before voluntary apnoea will prolong the breath-holding time by 15 to 20 seconds. This is due to

(1) Absence of O_2 lack stimulus during breath-holding period.

(2) The sensitivity of respiratory centre to CO_2 excess is less in the absence of oxygen lack.

Voluntary hyperapnoea before breath holding will wash off CO_2 from the alveolar air and the breath-holding time will be increasd considerably so that the subject may develop cynosis due to O_2 lack before the alveolar PCO_2 rises sufficiently to stimulate the respiration. This shows that CO_2 excess plays a more significant role in stimulating respiration than oxygen lack.

If a gas mixture with CO_2 and O_2 in quantities similar to that at the termination of the breath-holding time is re-breathed by a person at the time of breaking point he can hold his breath for a further period in spite of diminished oxygen and elevated CO_2 in the lungs. This indicates other factors besides O_2 lack and CO_2 excess play an important role in precipitating respiratory movement.

During the period of apnoea a larger volume of O_2 is removed than the volume of CO_2 added to the lungs. This causes a sense of discomfort and distress. Further, holding the chest in a fixed position stimulates afferents from the respiratory muscles which are obviated by the re-breathing experiment cited above. The afferent stimuli orginating in the chest muscles, therefore, constitute the third important factor in determining the breaking point after breath-holding.

Effects of High Altitude on Alveolar Oxygen

At high altitude the barometric pressure falls and so the tension of gases in the inspired air and also in the alveolar air falls. Water vapour exerts a tension of 47 mmHg at all altitudes and CO_2 is continuously exerted from the body into the respiratory alveoli. As a result of this adverse combination the PO_2 of the avleolar air falls at high altitude. Further the fall of alveolar PO_2 is disproportionately low because of extremely low O_2 tension of tissues, O_2 is absorbed very quickly from the alveoli. The formula for calculating alveolar PO_2 at different altitudes is :

$$\text{Alveolar } PO_2 = \frac{PB - PCO_2 - 47}{5} - PO_2 \text{ loss } (PO_2 \text{ loss is the}$$

oxygen pressure decrease caused by oxygen uptake into the blood and the value 47 is the vapour pressure of water).

There occurs a slight fall in alveolar PCO_2 due to hyperventilation but this cannot compensate for O_2 deficit at high altitude. The following table gives alveolar PCO_2 and PO_2 at diferent altitudes along with barometric pressure (*PB*) and percentage saturation of arterial blood with oxygen.

Altitude	*PB* (mmHg)	P_ACO_2 (mmHg)	P_AO_2 (mmHg)	Saturation of arterial blood with oxygen (%)
0	760	40	104	97%
3 km or 10,000 feet	523	36	67	90%
6 km or 20,000 feet	349	24	40	70%
12 km or 40,000 feet	141	24	8	5%
15 km or 50,000 feet	87	24	1	1%

It may be noted that an altitude of 15 km or 50,000 feet the barometric pressure is only 87 mmHg. This, therefore, is the total pressure of gases and water vapour in the alveoli, the latter accounts for 47 mm Hg leaving only $(87-47)=40$ mm Hg for O_2, N_2 and CO_2. Since PCO_2 is 24 mm Hg, only 16 mm Hg of pressure is distributed between N_2 and O_2 present in the ratio of aproximately 4 : 1. That being so on theoretical ground, one would expect that the alveolar PO_2 at this altitude would be about 3 mm Hg. But due to increased uptake of O_2 by grossly anoxic tissues at this altitude the alveolar PO_2 falls to 1 mm Hg only. Even if pure O_2 is inhaled and all the N_2 in the alveoli is replaced by it—the PO_2 in alveoli would be increased to 16 mm Hg only. Oxygen, therefore, must be administered under pressure to sustain life at this altitude.

Factors controlling alveolar PCO_2

Two important factors are :

(i) Metabolic rate, i.e. production of CO_2 in the body. The higher metabolic rate the greater will be the P_ACO_2.

(ii) Alveolar ventilation—the greater the alveolar ventilation the lower will be the P_ACO_2 and the higher will be P_AO_2.

Alveolar PO_2 and Venous Admixture

There is normally a difference between pulmonary capaillary PO_2 (PcO_2) and arterial PO_2. Alveolar PO_2 which normally is in near equilibrium with pulmonary end-capillary PO_2, therefore, is higher than arterial PO_2. The difference is explained by the fact that under normal conditions some blood passes from the venous side to the arterial side avoiding the lungs and without being exposed to alveolar O_2. For example, the Thebesian veins draing directly into the left heart, the bronchopulmonary anastomosis already mentioned. It has been estimated that about 6% of venous blood

pumped by the right heart by-passes the lungs altogether and thus reduces the PO_2 of the pulmonary venous blood. This is called **shunt effect** and by definition it is **anatomical shunt**—contributing to venous admixture.

Physiological Shunt

Even under physiological conditions the millions of alveoli of the lungs are not adequately ventilated and some of them may be completely non-ventilated. Blood flowing through the non-ventilated alveoli will not be oxygenated at all and so will contribute to venous admixture effect. Similarly venous blood flowing through poorly ventilated alveoli will not be adequately oxygenated and thus will produce the same effect as noted above. It is possible that both hypoventilated and hyperventilated alveoli may be present in the same lung but because of the fact that normally ventilated alveoli can effect almost complete saturation of haemoglobin with oxygen—the defective oxygenation of venous blood perfused through hypoventilated alveoli cannot be compensated by perfusion of hyperventilated alveoli. From quantitative aspect, therefore, physiological shunt is larger than anatomical shunt. It is the commonest cause of hypoxia in respiratory diseases.

The concept of anatomical and physiological shunts is analogous to the concept of anatomical and physiological dead space.

Normally alveolar ventilation is about 4 litres/minute and about 5 litres of blood (cardiac output) is perfused through the alveoli per minute. The average ventilation/perfusion ratio for the whole lungs, therefore, is $\frac{4}{5}$ or 0·8.

Increase in physiological dead space is due to absence or diminution of blood flow through well-ventilated alveoli—the condition, therefore, is attended with increase in ventilation/perfusion ratio. The reverse is true in increase in 'shunt' or venous admixture effect when the ratio of ventilation to perfusion is decreased.

8.9. DIFFUSION

Diffusion means movement of a substance from an area of high concentration to an area of low concentration. In the present context the diffusion of O_2 from alveoli to pulmonary capillaries and of CO_2 in the reverse direction is to be considered. N_2 being metabolically inert may be left out of discussion.

The following points are to be noted in this connection :

(1) Gases in the alveoli are dissolved in small quantity of alveolar fluid and are in equilibrium with partial pressure of the respective gases in alveolar air.

(2) Gases in the blood of pulmonary capillaries are also dissolved in water of the plasma where these exert a tension.

The average values of tension of O_2 and CO_2 in these two areas are given below :

	PO_2	PCO_2
Alveoli	100 mm Hg	40 mmHg
Venous blood	40 mm Hg	46 mmHg

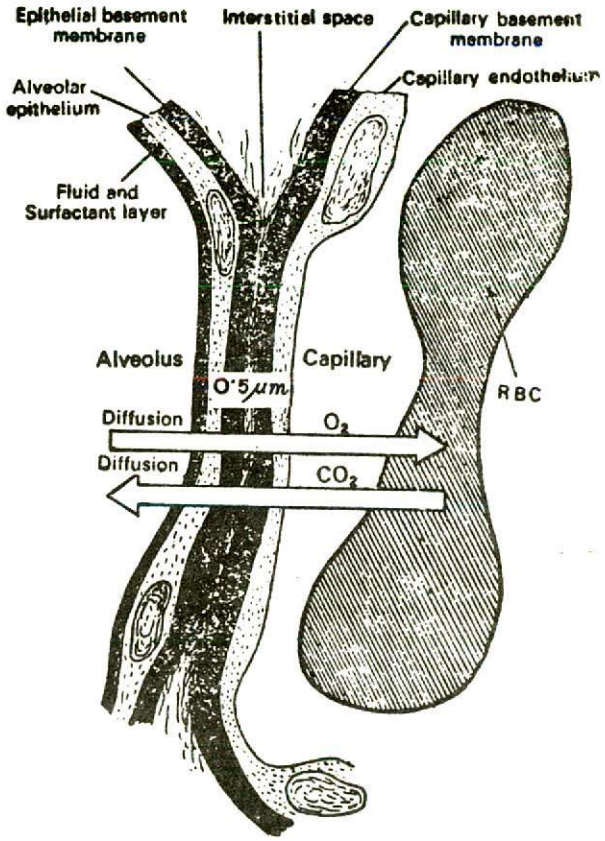


Fig. 262. Diagrammatic representation of alveolo-capillary membrane showing the O_2 diffusion from the surfactant layer→alveolar epithelial cell cytoplasm→capillary basement membrane→endothelial cell cytoplasm→plasma. The CO_2 diffuses reversely.

Diffusion, therefore, takes place in the direction shown by the arrows through the alveolo-capillary membrane (Fig. 262) which consists of

(1) Alveolar epithelium—thin epithelial cells together with its basement membrane.
(2) Thin interstitial space between (1) above and (3) below.
(3) Capillary endothelium together with its membrane.

The alveolo-capillary membrane consisting of all these layers is very thin—the average thickness being about 0·5 μm. This membrane is freely permeable to respiratory gases and thus ensure rapid diffusion of O_2 and CO_2 through them in the direction shown by the arrows from the point of high pressure to the point of low pressure.

The total surface area of the alveolo-capillary membrane is approximately 70 sq. metres in an adult, indicating the large area available for diffusion. The total amount of blood in the lungs at any moment is about 150 ml. This small quantity of blood spread over this large area naturally facilitates diffusion. Further the diameter of the pulmonary capillaries is about 8 μm—the red blood cell membrane, therefore, touches the capillary wall during their passage through the lungs and the gas molecules get almost direct access to the RBC without passing through significant layer of plasma—a fact which also accelerates the process.

Factors controlling Diffusion

Rate of diffusion of a gas between two given points depends not only on the tension gradient between the points but also on the distance between the two points, the surface area available for diffusion, the temperature and the characteristic properties of the gas itself. The most important properties of a particular gas which determines its rate of diffusion are :

(i) ***Solubility :***

Solubility of a gas in water is indicated by its solubility co-efficient which may ba defined as ml of gas (STPD) dissolved in 1 ml of water per atmosphere of pressure. When a liquid is exposed to a mixture of gases at a particular temperature—the pressure exerted by an individual component of gas will be related to its percentage composition (law of partial pressure), and the quantity dissolved in the fluid will be regulated by it. The pressure of the dissolved gas in the fluid will be same as the partial pressure of the same gas in the atmosphere to which it is exposed and with which it is in tension equilibrium. The solubility co-efficients of important gases at 0°C and 1 atmosphere of pressure are the following :

$O_2 = 0·024$	$CO = 0·018$	Helium 0·008
$CO_2 = 0·57$	$N_2 = 0·012$	

This means that N_2 is half as soluble in water as O_2 under standardised condition of temperature and pressure. Undoubtedly, CO_2 is most highly soluble of all the respiratory gasses.

(ii) ***Molecular weight :***

The second important property which determines the rate of diffusion is the molecular weight of the gas. The rate of diffusion of a gas at a particular temperature and pressure gradient is inversely related to the molecular weight (MW) of the gas and directly

related to other factors, such as temperarure. Tension gradient remaining constant the rate of diffusion of a gas $\propto \frac{S}{\sqrt{MW}}$ where S is the solubility coefficient and MW is the molecular weight.

The diffusion coefficient of a gas has been defined as the volume in ml of a gas which will diffuse 0·001 mm distance over a sq. cm of surface per minute at a pressure of 1 atmosphere. A more practical way of consideration of the problem is to assume the diffusion coefficient of O_2 to be 1 and compare it with those of other gases of respiratory importance as given below :

O_2	=	1·0
CO_2	=	20·3
N_2	=	0·53
CO_2	=	0·81
Helium	=	0·95

Pulmonary diffusing capacity for O_2 (DO_2)

DO_2 is the ratio of O_2 transfer in millilitres per minute (VO_2) from the alveolar gas to the capillaries divided by the pressure in mmHg required for this transfer.

$$DO_2 = VO_2/(P_AO_2 - P_oO_2)$$

PoO_2 indicates the average pressure of O_2 in the pulmonary capillary which changes from moment to moment due to gas transfer in a non-linear manner and to obtain an accurate figure involves mathematical calculation and measurements of complicated nature.

For all practical purposes, therefore, CO diffusing capacity is measured and the result is multiplied by 1·23. The affinity of haemoglobin for CO is so great that with small concentration all the CO remains combined with haemoglobin so that the *PCO* of plasma is practically 'zero'.

The above equation, therefore, is simplified to :

$$DCO = \frac{VCO}{P_ACO}$$ and these can be measured with a CO analyser.

In a normal person DO_2 at rest is approximately 15 to 20 ml of O_2/minute/mm Hg pressure difference between alveolar air and mean capillary PO_2.

This may be increased from 3 to 4 times during muscular exercise due to increase in the surface area for diffusion from opening up of new capillaries and alveoli and dilatation of the existing capillaries.

In various diseases, e g. interstitial fibrosis, pulmonary collagenosis —there occurs an increase in resistance to diffusion of O_2 from alveoli to the capillaries. These diseases together constitutes alveolo-capillary block syndrome.

Diffusion of CO_2

CO_2 is much more soluble than O_2 and its diffusibility is at least 20 times higher than that of O_2. An alveolo-arterial PCO_2

difference never occurs and in alveolo-capillary block syndrome retention of CO_2 in the blood does not occur but hypoxia is always prominent.

8.10. PERFUSION

The term 'perfusion' simply means blood flow and in the context of respiration it means blood flow through the lungs. It is approximately equal to 5 litres/minute. Since the alveolar ventilation is about 4 litres/minute the ratio $\frac{\text{alveolar ventilation}}{\text{perfusion}}$ = 0·8 for the whole lung.

Since the pulmonary circulation is a low pressure system in the erect posture the blood flow through the apex is much less than that in the base of the lungs due to effect of gravity. Since there occurs no remarkable change in ventilation from base to apex of the lungs the ventilation/perfusion ratio ($\dot{V}_A/Q$) is high (about 3·3) at the apex and is low (about 0·6) at the base. The apical alveoli, therefore, receive more air than blood (dead space effect) and some ventilation is wasted. The alveoli at the base of the lungs receive more blood than air (shunt effect) and some blood remains unsaturated with oxygen. In the supine posture this regional difference due to effect of gravity is lost and is replaced by low $\dot{V}_A/Q$ ratio in the posterior part and a high $\dot{V}_A/Q$ ratio in the anterior part.

8.11. OXYGEN TRANSPORT

The O_2 content of the arterial and venous blood and relevant data are given in the following table :

	O_2 content	Oxy-Hb	O_2 in Sol	PO_2
Arterial blood	19·3	19	0·3	100 mm Hg
Mixed venous blood	14·2	14	0·2	40 mm Hg

It will be seen that about 98% of oxygen is present in the blood in chemical combination with haemoglobin and only 0·3 ml in arterial blood (about 2%) is in physical solution in water of the plasma. However, this small quantity in physical solution is responsible for tension of oxygen in the plasma. It is the oxygen tension in the blood which is responsible for transfer of this gas from alveolar air to the venous blood across the alveolo-capillary membrane and also for transfer of this gas from arterial blood to the tissue fluid across the capillary membrane. Further, it is the tension of oxygen in plasma which controls the amount of oxy-haemoglobin present in the blood.

Haemoglobin is remarkable in that it can combine with oxygen forming a loose chemical compound known as oxyhaemoglobin

which differs from oxide of haemoglobin known as methaemoglobin in the fact that the O_2 in methaemoglobin is firmly fixed with the haemoglobin molecule.

The amount O_2 of the haemoglobin will combine with forming oxyhaemoglobin is dependent upon the tension of oxygen in the medium where haemoglobin is placed. If the O_2 tension is high a large amount of oxyhaemoglobin will be formed whereas in a medium of low O_2 tension the oxyhaemoglobin will break down liberating O_2, itself being converted into reduced haemoglobin.

O_2 capacity, O_2 content and percentage saturation of haemoglobin :

1 gram of haemoglobin when fully saturated will combine with 1·34 ml of O_2.* Since the blood contains approximately 15 grams of Hb per 100 ml—the oxygen content of the blood when fully saturated will be about $15 \times 1{\cdot}34 = 20$ ml. This is called O_2 capacity of the blood. Naturally the O_2 capacity depends upon the amount of haemoglobin in blood.

Oxygen content of the blood is usually determined by Van Slyke's manometric appratus in which 1 ml of blood is treated anaerobically with potassium ferricynide solution in the chember of the apparatus. The pressure exerted by the liberated oxygen after absorption of CO_2 on a manometer attached with the apparatus is noted and is used for calculation of the oxygen content.

If the blood is first agitated with air so that the Hb gets fully saturated with O_2 the result will indicate O_2 capacity. Percentage saturation of Hb with $O_2 = \dfrac{O_2 \text{ content}}{O_2 \text{ capacity}} \times 100.$

Example :

Thus, if in a particular sample of blood the O_2 content = 19 volume % and the O_2 capacity = 20 volume %

The percentage saturation of Hb = $\dfrac{19}{20} \times 100 = 95\%$. If in another sample of blood the O_2 content is 15 volume % and capacity is 20 volume %. The saturation of Hb will be 75%. If the same blood contained 10 volume of O_2 per 100 ml the saturation would be 50%.

Dissociation curve for haemoglobin.

The curve is constructed by placing blood in containers provided with stopcock at either end (called 'tonometer') and filled with oxygen of known tension. After equilibriation the percentage saturation of haemoglobin in the tonometer is determined and plotted against different oxygen tension.

About 5 ml of blood is put in tonometer of 250 ml capacicy and rotated for 20 minutes in horizontal position in a water bath at 37·5°C. The percentage saturation of haemoglobin at different tensions for human blood is as follows :

*Incidentally, the most accurate method of estimating haemoglobin content of blood is to determine the oxygen capacity and divide the result by 1·34.

Oxygen tension (PO_2)	Percentage saturation of haemoglobin
10 mm Hg	15%
20 mm Hg	40%
30 mm Hg	60%
40 mm Hg	75%
50 mm Hg	85%
60 mm Hg	90%
70 mm Hg	95%

The dissociation curve for O_2 (Fig. 263) is obtained by plotting the percentage saturation of Hb against PO_2.

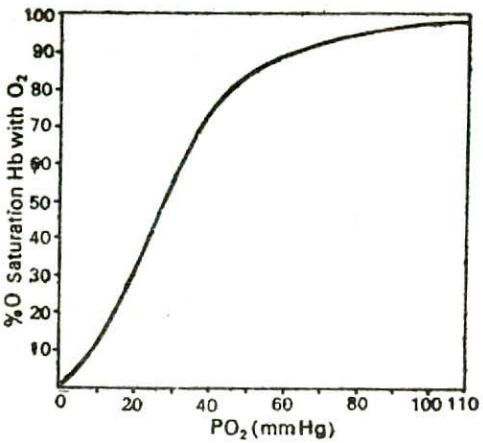


Fig. 263. Oxygen haemoglobin dissociation curve at 40 mmHg, CO_2 tension, pH 7·4, temperature 38°C. (after modification from Comroe JH Jr and others : The Lung : Clinical Physiology and Pulmonary Function Tests and Ganong's Review of Medical Physiology).

Nature of the curve :

The curve shows a steep rise in percentage saturation of haemoglobin with O_2 between 0 and 40 mm Hg O_2 tension.

No significant increase in percentage saturation of Hb occurs between O_2 tension of 60 mm Hg (90% saturation) and 100 mm Hg (100% saturation).

The first part of the curve (between PO_2 zero and 40 mm Hg) is nearly vertical the last part of the curve (from PO_2 60 mm Hg to 100 mm Hg) is almost horizontal and the whole curve is sigmoid in shape.

Explanation of the sigmoid shape of the curve :

Each molecule of globin consists of 4 polypeptide chains to each of which is attached a molecule of haem with Fe^{2+} capable of combining with one molecule of oxygen. As soon as one of the molecules of haem combines with O_2 the other three molecules in the

same polypeptide complex of the globin acquires a great affinity for O_2 and rapidly combines with it. This rapid oxygenation of haemoglobin in the initial phase of its exposure to O_2 is known as **allosteric activation** and explains the sharp rise in the dissociation curve in the lower range of O_2 tension and also the gradual levelling off of the curve at higher range as the haemoglobin reaches the near saturation point.

Factors influencing the shape of the urve :

I. Bohr effect (Fig. 264) : In presence high of PCO_2—the curve is deviated to the right, which means CO_2 favours dissociation of oxy-haemoglobin and release of O_2. This reaction is most pronounced in the middle range of the curve at about PO_2 40 mm Hg and is helpful in release of O_2 in the tissues where the PCO_2 is igh and PO_2 is about 40 mm Hg at rest.

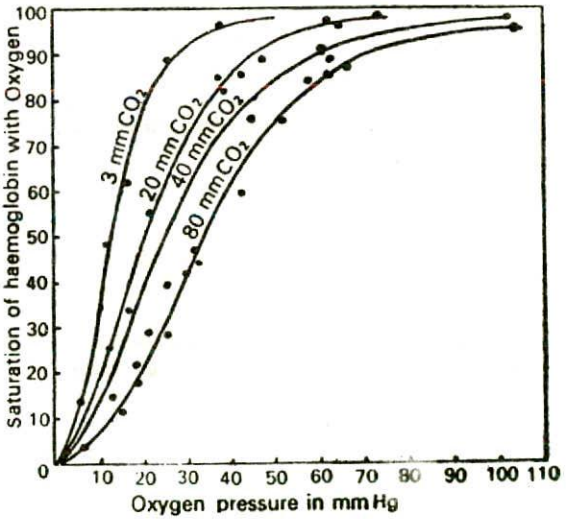


Fig. 264. Oxygen dissociation curves of human blood exposed to partial pressure of 3 mm Hg, 20 mm Hg, 40 mm Hg and 80 mm Hg at carbon dioxide tension showing Bohr effect The percentage saturation was measured by Van Slyke's apparatus and Adar ettal (1924), *Journal of Biological Chemistry*

II. Increased cH, i.e. acidity in the blood shifts the dissociation curve to the right. During exercise lactic acid and other organic acids produed in the active tissures favour release of oxygen from Oxy-Hb.

It is known that increased CO_2 is the cause of increased cH. Effect of CO_2 on shifting the dissociation curve to the right, therefore, s perhaps non-specific in nature.

III. Increased temperature shifts the dissociation curve to the

right (Fig 265). This phenomenon also favours release of oxygen in the active tissues with increased blood flow and metabolic activity leading to rise in temperature.

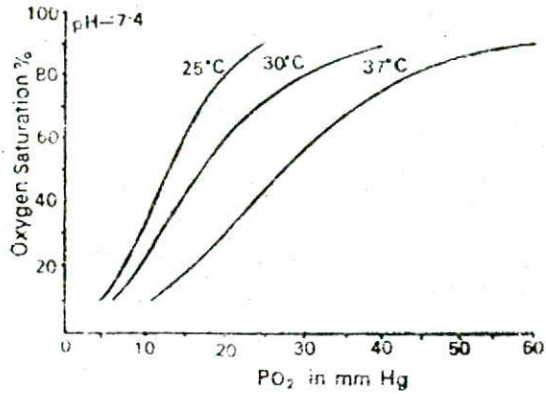


Fig. 265. The effect of temperature on the oxygen dissociation curve of Oxy-Hb of human blood at pH 7·4 (from data P. Astrup, K. Engel, J. N. Severinghaus & E. Munson (1965), *Scandinavian Journal of Clinical and Laboratory Investigation*.

IV. DPG (2, 3-diphosphoglycerate) is formed within the RBC by glycolytic cycle. The reduced haemoglobin molecule can hold tightly one molecule of DPG between its β-chains and thus reduces the affinity of haemoglobin for oxygen and favours its release in the tissues.

The synthesis of DPG is stimulated in anaemia and also during acclimatization to high altitude anoxia. It appears that DPG has an important role to play in O_2 transport in the body but the mystry has not yet been solved.

Recent researches have shown that perhaps DPG favours the dissociation of HbO_2 to Hb and O_2 ($HbO_2 \rightleftharpoons Hb + O_2$) and shifts the dissociation curve to the right. The altitude anoxia and consequent alkalaemia favour this reaction.

Advantages of the sigmoid shape of the urve :

(1) The shape of the curve is such that at normal alveolar PO_2—the haemoglobin of the blood leaving the lungs is almost completely saturated. Any further increase in alveolar PO_2 under normal circumstances, e.g. O_2 inhalation is of no advantage in so far as percentage saturation of haemoglobin is concerned.

(2) The flat upper part of the curve indicates that relatively little reduction in percentage saturation of haemoglobin occurs unless the oxygen tension of the alveolar air falls below 60 mm Hg. Due to fall in barometric pressure—this level of alveolar PO_2 is attained at an altitude of 3 km or 10,000 feet. It is obvious, therefore, that the effect of oxygen lack on the body will not be

manifested till one ascends to an altitude higher than 3 km or 10,000 feet.

(3) The steep slope of the oxygen dissociation curve at lower range of oxygen tension indicates that there occurs rapid breakdown of Oxy-Hb and consequent release of O_2 in the oxygen tension (40 mm Hg to 20 mm Hg) prevailing in the tissue.

(4) Increase CO_2, cH, temperature and DPG all favour rapid release of oxygen in the tissues during activity.

Velocity of the reaction

In the lungs the time taken for 50% saturation of the haemoglobin is only 0·07 second. Since the RBC takes 0·5 second to pass a lung capillary enough time is available for complete oxygenation of haemoglobin.

In the tissues the reverse reaction $HbO_2 \rightleftarrows Hb + O_2$ takes place much more quickly, time taken for 50% desaturation of haemoglobin being only 0·035 second.

Delivery of O_2 in the tissues in anaemia :

The table below gives approximate relevant values of oxygen in blood in normal subjects and in a patient with anaemia (Hb content of blood = 7·5 grams bf or 50% of normal).

Hb content	Arterial blood		Mixed Venous blood		Arterio-venous O_2 content difference
(gram, %)	O_2 content	% saturation	O_2 content	% saturation	
15	20	98%	15	75	5
7·5	10	98%	6	30	4

The first line of compensation is, therefore, effected by drawing upon the reserve volume of O_2 from the mixed venous blood as a result of which the venous blood gets more unsaturated. However, in spite of the greater coefficient of O_2 utilisation the tissues fail to get adequate amount of O_2 as shown in the last column.

$$\text{Coefficient of } O_2 \text{ utilisation} = (\%) = \frac{\text{Arterio-venous } O_2 \text{ content difference}}{\text{Arterial } O_2 \text{ content}} \times 100$$

$$\text{Normal value} = \frac{5}{20} \times 100 = 25\%$$

$$\text{In Anaemia} = \frac{4}{10} \times 100 = 40\%$$

Due to increased quantity of 2, 3-DPG within the RBC in anaemia—the dissociation curve shifts to the right which favours release of oxygen in the tissues. The third method of compensation is increased cardiac output which ensures increased blood flow (and oxygen supply) to the tissues.

Oxygen Exchange in the Lungs (Fig. 266)

The tension of O_2 in the alveolar air is 100 mm Hg and that of the dissolved O_2 in the plasma of the mixed venous blood in only 40 mm Hg.

Due to the tension gradient O_2 diffuses rapidly from the alveolar air to the mixed venous blood increasing the quantity and also tension of O_2 in the plasma in the venous blood. Rise of O_2 tension of the mixed venous blood is followed by rapid increase in O_2 saturation of the haemoglobin. The oxygenated blood leaves the pulmonary capillaries in tension equilibrium with alveolar air, that is, with O_2 tension of 100 mm Hg and with haemoglobin 98% saturated with oxygen.

(1) The gaseous composition of blood is different in different veins of the body. O_2 content of blood of veins draining metabolically active tissues (e.g. muscles, heart) is low whereas the O_2 content of blood of veins from skin and brain is rather high. The term mixed venous blood indicates sample of venous blood from the right heart or pulmonary artery.

(2) The actual gas exchange in the lungs takes place between the gases dissloved in alveolar fluid and plasma water.

Oxygen transport in the tissues (Fig. 266):

Oxygen tension in the tissue fluid is low and is about 40 mm Hg during 'rest'. The arterial blood enters the tissue capillaries with an oxygen tension of 100 mm Hg and with haemoglobin 98%

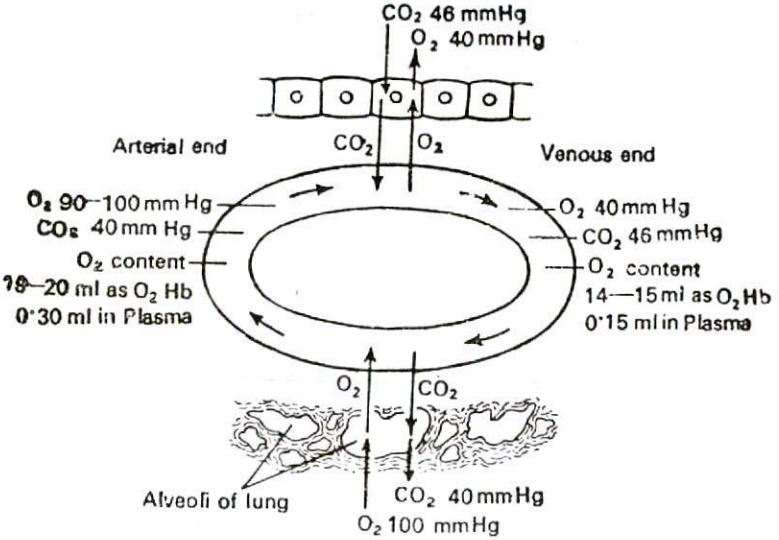


Fig. 266. Carriage of O_2 in the tissues and in the lungs.

saturated with oxygen. So the O_2 diffuses from the plasma to the tissue fluid due to tension gradient between the two fluids. As O_2 diffuses the amount of O_2 in solution decreases and the tension of O_2 in the arterial blood falls. This results in desaturation of haemoglobin which gives oxygen firstly to the plasma from where it goes to the tissue space—the guiding force being the tension gradient. It has already been mentioned that the reaction is very

rapid and so the blood leaves the tissues with oxygen in tension equilibrium with tissue fluid that is 40 mm Hg and consequent 75% saturation of haemoglobin with oxygen.

COMPOSITION OF OXYGEN AND CARBON DIOXIDE IN VENOUS BLOOD AND ARTERIAL BLOOD

Gases	Venous blood		Arterial blood	
	Total vol %	In simple solution vol %	Total vol %	In simple solution vol %
Oxygen	14·0	0·1	19·0	0·30
Carbon dioxide	52·1	2·7	48·3	2·40

TENSION OF GASES IN VENOUS BLOOD AND ARTERIAL BLOOD

Gases	Venous blood	Arterial blood
Oxygen	40 mm Hg	90 mm to 100 mm Hg
Carbon dioxide	46 „ „	40 „ „

8·12. CARBON DIOXIDE TRANSPORT

CO_2 content and tension of blood :

Arterial blood contains about 48 volume of CO_2 and venous blood 52 volume of CO_2 per 100 ml, tension of CO_2 being 40 mm Hg and 46 mm Hg in the arterial and venous blood respectively.

CO_2 is carried in blood in (i) physical solution and (ii) as chemical compounds. The table below summarises the situation.

	Arterial Blood			Venous Blood		
	RBC	Plasma	Whole	RBC	Plasma	Whole
In solution	0·8	1·6	2·4	0·9	1·8	2·7
as Bicarbonate	9·8	33·1	42·9	10·5	35·2	45·7
as Carbamino compound	2·0	1·0	3·0	2·6	1·1	3·7
	12·6	35·7	48·3	14·0	38·1	52·1

Both the corpuscles and plasma carry CO_2, the former carries about one-fourth of the total.

I. CO_2 in physical solution :

Roughly about 5% of CO_2 is carried in physical solution in blood. In solution CO_2 exists mostly as H_2CO_3 according to the following equation

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

Since the reaction is reversible it is clear that H_2CO_3 always remains in equilibrium with small amount of molecular O_2 gas which is responsible for CO_2 tension of blood.

The ingress of CO_2 into the blood in the tissue capillaries is not accompanied by any significant in H^+ concentration because of the

effective 'buffering' action of the blood and of haemoglobin in particular. The buffering property of haemoglobin is due to imidaxole group of histadine linked with haem which contains an ionisable H^+ ion. On oxygenation, histadine parts with its H^+ ion thus actsas an acid. On reduction the H^+ ion is mostly linked with N and thus acts as a weaker acid. Reduced Hb, therefore, is potentially H^+ ion acceptor. 1 m Mol of reduced Hb can accept 0·7 m Mol of H^+ ion without any change of blood reaction. It has been suggested that the H^+ of the $-NH_2$ radical of haem linked valine is also oxylablle like that of histadine and thus confers upon haemoglobin its remarkable buffering property. This explains why venous blood with reduced Hb contains more CO_2 than arterial blood at a given Pco_2 and the dissociation curve of CO_2 for venous blood is situated at higher level.

II. **CO_2 as Bicarbonate :**

From the table (page 405) it is clear that more than 80% of the CO_2 is carried as bicarbonate in the blood and that the major fraction of the carbonate is present in plasma. However, most of the bicarbonates found in plasma are primarily formed within the RBC and then shifted to plasma.

Machanism of formation of CO_2

We have seen that hydration of CO_2 occurs in the blood and the mechanism can be represented as $CO_2 + H_2O \rightleftharpoons H^+ + HCO_3$ Further the H^+ is buffered by reduced Hb within the RBC and by plasma buffers outside the RBC. The reaction can be represented $(H^+ + HCO_3^- + HbO_2 \rightleftharpoons HHb + HCO_3^- + O_2$ (liberated in the tissues) HHb represents H ion buffered by reduced Hb).

The negatively charged HCO_3^- left over in the reaction is neutralised by available bases in the blood. The most abundant available base in plasma being Na^+ the HCO_3^- in the plasma combines with Na^+ to form $NaHCO_3$. The most abundant base within the RBC being K^+, $KHCO_3$ is formed in that location The reaction $H_2O + CO_2 \rightleftharpoons H^+ + HCO_3^-$ is accelerated tremendously due to presence of a specific enzyme carbonic anhydrase* within the RBC.

Concentration of HCO_3^- within the RBC, therefore, becomes very high within a short time and attains a level much higher than that in the plasma. Now since the red cell membrane is impermeable to positively charged ions some HCO_3^- from within the RBC migrates into plasma and some Cl^- from the plasma migrates within

*Carbonic anhydrase is an enzyme with mol wt of 30,000 and containing one atom of Zn per molecule. It is found in the RBC, in renal tubules, in gastro-intestinal mucosa, pancreas, salivary glands, liver, brain and many other tissues. It is inhibited by heavy metals, cynide, sulphonamide and certain other drugs. Acetazolamide (Diamox) is a particular type of sulphonamide which inhibits this enzyme in the kidneys and thereby promotes dieresis.

the RBC in exchange of HCO_3^-. This is alled 'chloride shift' phenomenon (Fig 267) and was discovered by cumburger in 1927. Thus the concentration of HCO_3^- in plasma becomes higher due to migration of this ion from within the RBC according to the law of Donan's equilibrium •

1. CO_2 transport in the tissues

Tension of CO_2 in the tissue fluid is 46 mm Hg (at rest) and that in arterial end of the capillary is 40 mm Hg. CO_2, therefore, diffuses from the tissue space to the capillary due to tension gradient.

It may be recalled that the coefficient of diffusion of CO_2 is very high and in spite of the rather low tension gradient rapid and complete diffusion of CO_2 occurs till tension equilibrium is established.

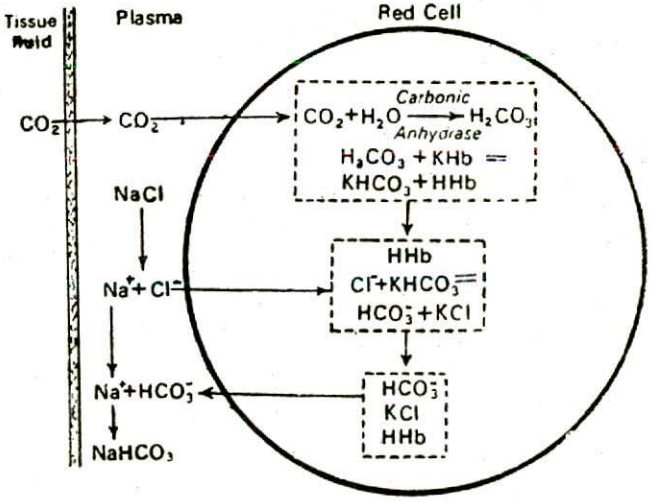


Fig. 267. Schematic representation showing the steps of chloride shift.

The H^+ ion and HCO_3^- ion formed are disposed off as follows :

$$H^+ + NaPr \rightleftharpoons Na^+ + HPr$$
$$Na^+ + HCO_3^- \rightleftharpoons NaHCO_3$$

•To be more accurate, the changes may be explained as follows : The concentration of HCO_3^- ion disproportionately increases in the red cells and the ionic balance between the plasma and corpuscles is disturbed. Depending upon the peculiar property of the red cell membrane, HCO_3^- ion comes out of the cells and chlorine ion moves into the cell till the balance is restored. The ionic interchanges can be explained easily on the principle of Donan equilibrium. The balance of anions and cations between plasma and corpuscles is maintained according to the following equations :

$$\frac{HCO_3^- \text{ (cells)}}{HCO_3^- \text{ (plasma)}} = \frac{Cl^- \text{ (cells)}}{Cl^- \text{ (plasma)}} = \frac{H^+ \text{(plasma)}}{H^+ \text{(cells)}}.$$

Whenever this ratio is disturbed, ionic interchanges will take place till the proper balance is restored. Chloride shift takes place according to this principle.

$$CO_2 + NH_2\text{-}Pr \rightleftharpoons Pr\text{-}NHCOO^- + H^+$$
(carbamino)

$$H^+ + Na_2HPO_4 \rightleftharpoons NaH_2PO_4 + Na^+$$

$$Na^+ + HCO_3^- \rightleftharpoons NaHCO_3$$

When equilibrium is established the plasma changes may be summarised :

1. Some free molecular CO_2 in solution—which is responsible for CO_2 tension.
2. Some CO_2 in solution in H_2O as H_2CO_3
3. Some CO_2 buffered as $NaHCO_3$.
4. Some CO_2 as carbaminoprotein.

Since formation of H_2CO_3 is accompanied by formation of almost equivalent quantities of $NaHCO_3$ the ratio $\frac{H_2CO_3}{NaHCO_3}$ is but little disturbed and the pH of the blood remains almost unaffected.

II. In the RBC

CO_2 diffuses rapidly and the reaction $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ takes place 13,000 times quicker than in plasma because of the presence of the specific enzyme carbonic anhydrase.

III. Carriage of CO_2 as carbamino compound :

(i) CO_2 combines directly with free amino group of the globin and forms carbamino compounds which may be represented as follows :

$$Hb - NH_2 + CO_2 \rightleftharpoons Hb - NHCOO + H^+$$

This occurs (i) independent of carbonic anhydrase and therefore the reaction is not inhibited by cynides.

(ii) CO_2 is not initially changed to H_2CO_3.

(iii) At a very rapid rate in the tissues where haemoglobin is desaturated. Carbaminocompounds are also formed by direct union of CO_2 with plasma proteins but since the concentration of haemoglobin within the RBC is high a larger fraction of carbamino compounds are carried within the RBC than in the plasma.

Further an increase in PCO_2 does not increase the formation of carbamino compounds since increase PCO_2 means increased H^+ concentration which leads to formation $Hb\,NH_3^+$. This does not react with CO_2 directly.

Oxygenation of haemoglobin inhibits carbamino compound formation because Oxy-haemoglobin by virtue of its greater acidity liberates H^+ which blocks carbamino compound fromation. Reduced Hb, on the other hand, favours formation of carbino compound.

In the tissues Oxy-Hb is also being converted simultaneously to reduced Hb which is a weaker acid in comparison with the former and has got a weaker hold on the base (K) available within the RBC. If Oxy-Hb is represented symbolically by HbO_2 its 'salt' with K (potassium) may be symbolised as $KHbO_2$. With the ingress of CO_2 and reaction Oxy-Hb the following changes occur.

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^- + KHbO_2$$
$$\rightleftharpoons HHb + KHCO_3 + O_2 \text{ (liberated)}$$

The $KHCO_3$, of course, ionises to $K^+ + HCO_3^-$. Large quantities of carbamino-haemoglobin are also formed which ionises liberating H^+ which are neutralised by imidazole group of histadine and β-amino group of valine of the globin polypeptide chains.

As already explained the HCO_3^- from within the RBC is exchanged for Cl^- of the plasma according to the law of Donan's equilibrium (chloride shift). The chloride shift mechanism prevents accumulation of large amount of HCO_3^- within the RBC and thus prevents shifting of its pH to the alkaline side.

In the lungs (Fig. 268):

CO_2 diffuses from plasma ($PO_2 = 46$ mm Hg) to the alveolar

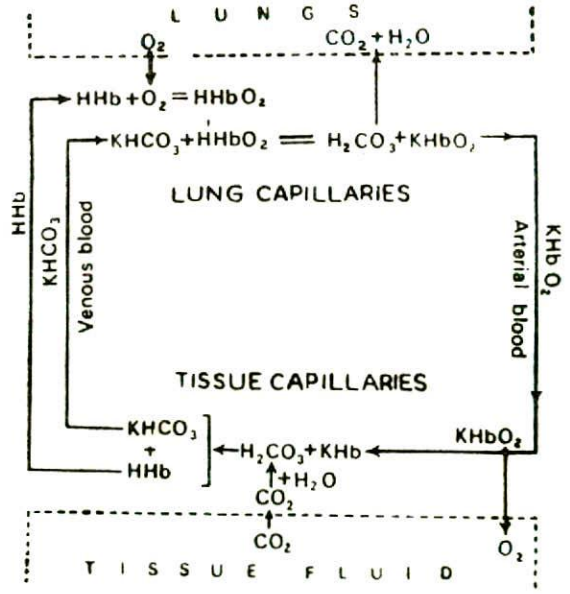


Fig. 268. Schematic representation showing inter relation between carriages of O_2 and of CO_2.

air ($PO_2 = 40$ mm Hg) and so the H_2CO_3 breaks down liberating further amount of CO_2. Simultaneously oxy-haemoglobin is formed

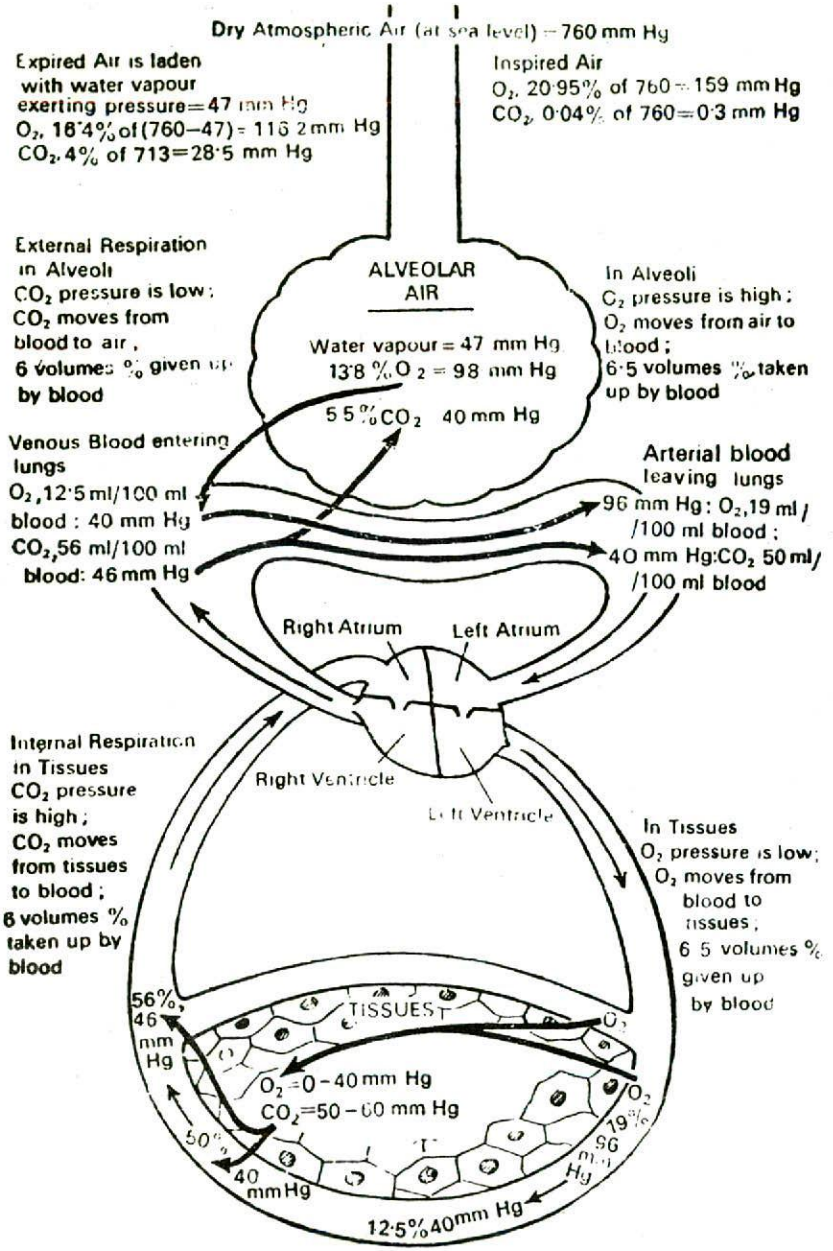


Fig. 269. Schematic representation of mechanism of gas transfer in the lung.

which being a stronger acid snatches off K within the RBC from its combination with acid ions and form $KHbO_2$. Reversed chloride shift occurs and the HCO_3^- ion enters the RBC and is broken down liberating further amount of CO_2 which passes from RBC to plasma and then to the lungs.

$$KHHb + HCO_3^- + O_2 \rightleftharpoons H_2CO_3 + KHbO_2$$
$$H_2CO_3 \rightleftharpoons H_2O + CO_2$$
(CA)

Oxygenation of haemoglobin also breaks down carbamino compound liberating further quantity of CO_2.

The mechanism of gas transfer between the lungs→blood→tissues →venous blood and back to the lungs has been summarised in the diagram (Fig. 269).

Carbon dioxide dissociation curves

With a comparative study of the CO_2 contents of reduced blood, oxygenated blood, bicarbonate solution and warer, under different pressures of CO_2, important facts have been known regarding the behaviour of CO_2 of blood under different physiological conditions.

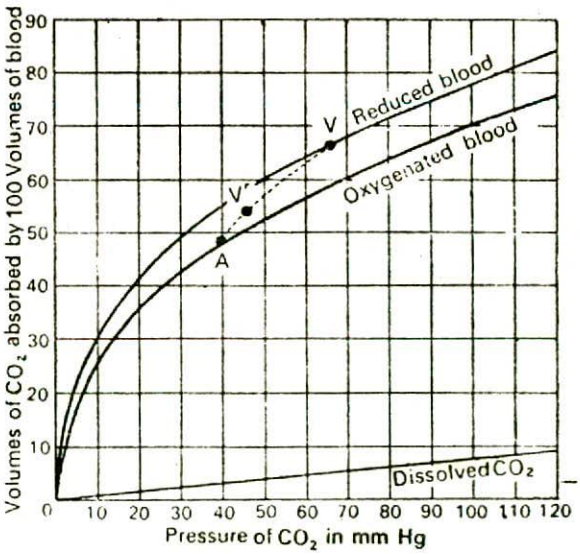


Fig. 270. CO_2 dissociation curves of blood. Continuous curves: *upper* - curve of reduced blood. *Lower*—curve of oxygenated blood. A = arterial point (CO_2 40 mm Hg). V = fully reduced point (CO_2—64 mm Hg). V' = mixed venous point (CO_2—46 mm Hg). Straight line: dissolved CO_2, i.e., CO_2 in physical solution.

The results when plotted in the form of curves, constitute the CO_2 *dissociation curves* (Fig. (270). The following facts are seen: (1) In a vacuum, CO_2 content of blood is nil. (2) At any given CO_2 tension,

reduced blood takes up larger amount of CO_2 than oxygenated blood. So that in the body, reduction of blood in the tissue capillaries increases the degree of CO_2 uptake from the tissues. (3) Oxygenation of blood causes evolution of CO_2. This happens in lungs. (4) As the CO_2 tension is increased, the total amount of CO_2 taken up by blood also rises. As the CO_2 tension falls, CO_2 content also diminishes.

8.13. CONTROL OF RESPIRSTION

The normal rate of respiration in an adult is 14 to 18 per minute with a tidal volume of about 500 ml. The rate and depth of respiration (pulmonary ventilation per minute) is adjusted according to requirement of the body. For instance during muscular exercise metabolic activities are increased and the demand for oxygen by the working muscles is increased. At the same time a large amount of carbon dioxide is produced by the muscles and it becomes necessary to eliminate it. Thus in muscular exercise the respiration is increased both in rate and depth. In fact the increase in minute ventilation is directly proportional to the magnitude of muscular exercise. n the other hand, respiration is depressed during sleep when the metabolic rate is low. Since the rate and depth of respiration can be accurately adjusted to metabolic needs of the body there must be an efficient mechanism for its regulation.

Like other physiological functions of the body the act of respiration, too, is controlled by a special group of nerve cells in the brain stem, which constitutes the 'respiratory centre'. The activity of this centre is controlled by many factors which may be classified under two headings, viz.

I. Nervous factors and II. Chemical factors.

Respiratory entre

Respiratory centre consists of a widely scattered group of nerve cells in the reticular formation of the pons and medulla (Fig 271) which may be divided into 3 major areas :—

(1) Pneumotaxic area—located in the upper pons. It controls the activity of the two lower centres. Section at 'M' produces apneustic type of respiration characterised by prolonged inspiratory

cramps. It has subsequently been established that section of vagal afferents together with section at 'M' is necessary for typical apneustic respiration.

(2) Apneustic area located in the lower pons—so named because when isolated from the influence of 'pneumotaxic centre it leads to apneustic type of respiration mentioned above. Section at 'N' leads to gasping type of respiration from the medullary respiratory centre isolated from the influence of other parts of respiratory centre.

(3) Section at 'O' produces stoppage of respiration because the connection between the medullary respiratory centre and the motoneurones of the phrenic and intercostal nerves are severed.

Medullary respiratory centre located near the lower part of the floor of the fourth ventricle (Fig. 272) consists of two parts.

(1) Inspiratory centre —ventromedially placed and (2) Expiratory centre—dorsolaterally placed.

The above conclusions were based on stimulation experiments. Subsequent careful studies with microelectrodes confirmed the existence of two sets of neurones (viz inspiratory and expiratory) but they are comingled with each other, so that all the inspiratory or expiratory neurones are not collected together to form a 'centre' in the way it is usually understood. However for the sake of simplicity in description existance of such centres bilaterally may be postutated.

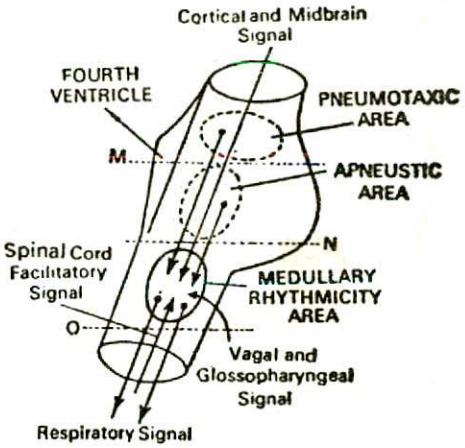


Fig. 271. The three parts of respiratory centre located in the brain stem (after Guyton).

(a) It has been further postulated that inspiratory centre of one side has got connec ion with inspiratory centre of opposite side. Same type of connection exists between the expiratory centres of two sides. So that stimulation of inspiratory centre of one side will have excite-inspiratory effect on the contralateral side. Same remark is true for expiratory centre.

(b) Second postulation is that homolateral inspiratory and expiratory centres have got 'to-and-fro' connection and reciprocally inhibits the activity of each other, so that stimulation of the inspiratory centre is attended simultaneously with inhibito-expiratory effect, though the neurophysiological basis for this connection between inspiratory and expiratory centres has not been established.

(c) The third postulation is that the medullary respiratory neurones have got an intrinsic rhythmicity of their own. If the medullary respiratory centre are isolated from impulses of higher

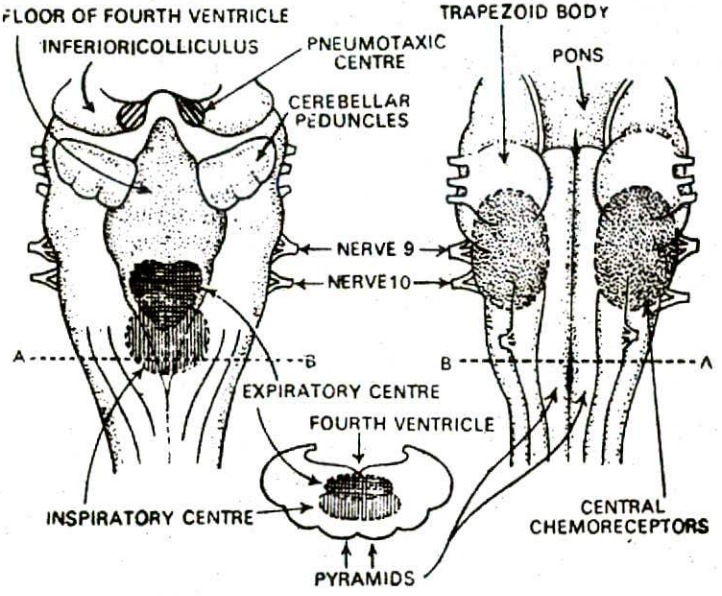


Fig. 272. Diagram of the medulla and pons in the cat's brain stem showing areas involved in control of respiration after electrical stimulation with microelectrodes connected to an amplifire (after Pitts and Burns).

parts by rostral transection 'gasping' type of respiration occurs (hence the name 'gasping centre'). Further transection more caudally will cause complete isolation of the medullary centres which nevertheless exhibits some spontaneous rhythmic discharge at least in the inspiratory nerve calls. The inspiratory centres, therefore, have got a basic rhythmicity of their own (c. f. cardiac muscle). This area, however, by itself is not capable of giving a normal smooth type of respiration. The exact mechanism by which

normal rhythmic respiration is maintained is not yet properly understood. It is probable that normal respiration occurs due to co-ordinated activity of the 3 parts of the respiratory centres mentioned above.

Machanism of rhythmic respiration (Fig. 273)

Inspiration commences by discharge of impulses from apneustic centre to the inspiratory centre. Apneustic centre at the same time sends impulses to the pneumotaxic centre of upper pons. This centre sends excitatory impulses to the expiratory centre which inhibits the inspiratory centre. The inspiratory centre at the same time receives inhibitory impulses from the vagal stretch afferents

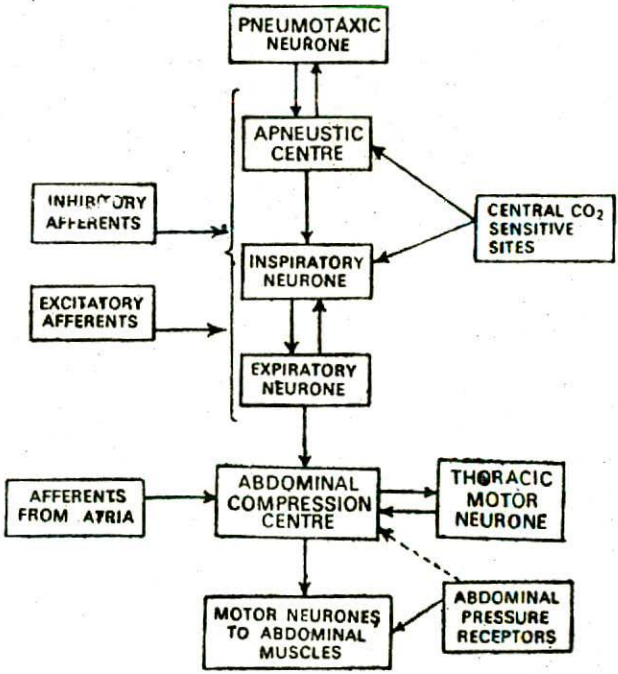


Fig. 273. Schematic representation of respiratory mechanism in the brainstem of a cat.

stimulated by lung inflation during inspiration. Being influenced by the double negative 'feedback' mechanism—the activity of the nerve cells of the inspiratory centre stops and expiration commences passively. The cycle is repeated automatically at the end of expiration because the vagal stretch afferents are no longer active and

the reciprocal inhibition of inspiratory centre from expiratory centre comes to an end after the stoppage of activity of the expiratory centre (Fig. 274).

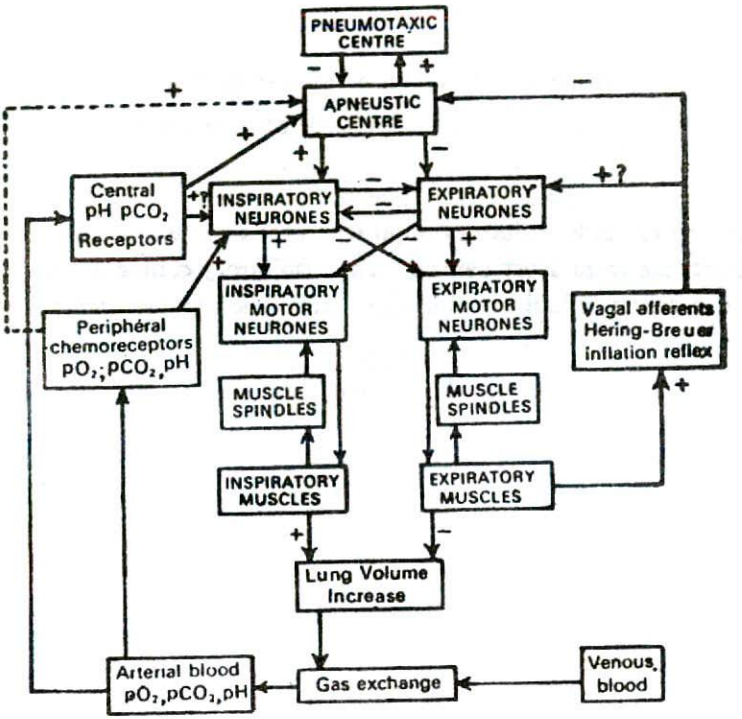


Fig. 274. Diagram depiting major mechanism concerned with the control of respiration and the regulation of alveoria-ventilation.

Reflex effect on activity of abdominal muscles

In the standing position the abdominal muscles are active during expiration but in a resting person in supine position the abdominal muscles are inactive throughout the respiratory cycle.

1. During rapid breathing, e.g. exercise, the abdominal muscles become active during early expiration.

2. Positive intrapulmonary pressure elicits reflex contraction of abdominal muscle. The respon e is abolished by vagotomy. Positive intrapulmonary pressure elicits contraction of abdominal muscles in a closed chest dog but fails to do so if the chest is opened though in this case the the lung distension is greater. The afferent fibres responsible for contraction of abdominal muscles, therefore, are separate from those concerned in Hering-Breure Reflex.

the reciprocal inhibition of inspiratory centre from expiratory centre comes to an end after the stoppage of activity of the expiratory centre (Fig. 275).

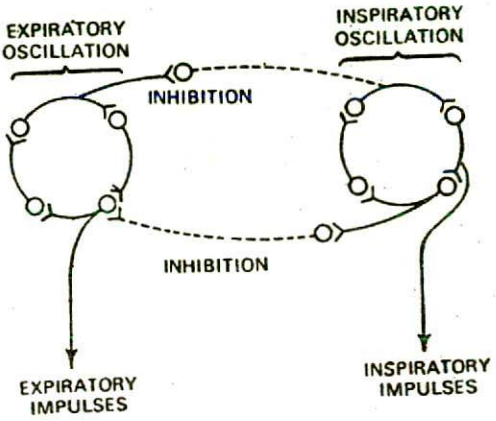


Fig. 275. Diagram depiting the dotted inter-neuronal connection between the expiratory and inspiratory centres responsible for alternate excitation and inhibition of inspiratory and expiratory centres.

Role of abdominal muscles (Fig. 276)

During normal respiration the abdominal muscles are inactive. They become active during

(1) exercise and other conditions leading to hyperpnoea (increase in rate and depth of respiration).

(2) positive pressure breathing (for example during anaesthesia when a pump is attached to an intra-tracheal tube).

(3) diminution in blood volume in certain low pressure areas of circulatory system.

The atrial mechanoreceptors (and probably receptors in other parts of circulatory system) normally maintain reflexy the tone of the abdominal muscles. The afferent fibres run in the vagus and are separate from those concerned in Hering-Breuer reflexes. Centre for these reflexes is a group of nerve cells separate from those of respiratory centre and has been named as abdominal compression centre (ACC). This centre is influenced by the adjoining respiratory centre in reflexes (1) and (2) and in reflexes from the sino-aortic zone, but is affected directly by reflexes from low pressure areas of cardio-vascular system. Amongst the latter the atrial mechanoreceptors have been extensively studied. Fall in pressure in the atria causes increased tonicity of abdominal muscles thereby diminishing the blood volume

in the capacitance vessels of the abdomen and increasing the blood volume in the atria. Rise in atrial pressure has got opposite effect.

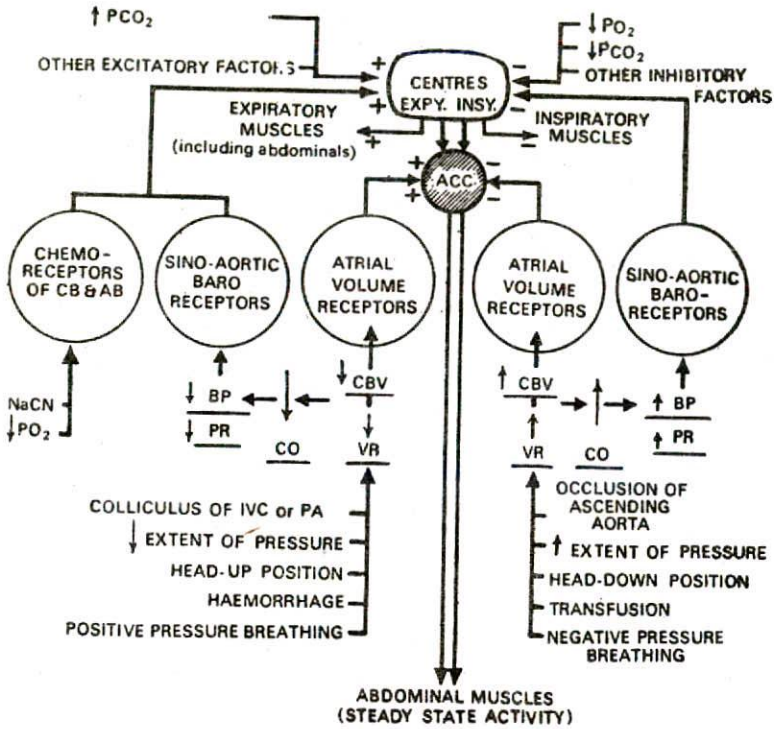


Fig. 276. Schematic representation of main factors and mechanisms concerned with altering the level of activity of abdominal muscles in respiratory to cardiorespiratory changes. The left side of the diagram depicts excitatory influences which affect the action of abdominal muscles either through the respiratory centre or more directly. The right side illustrates inhibitory changes which promote a decrease in the activity of abdominal muscles. EXPY = expiratory centre; INSY = inspiratory centre; ACC = abdominal compression centre (abdominal muscle tonus centre); BP = (arterial) blood pressure; PR = peripheral resistance; CO = cardiac output; CBV = central blood volume; VR = venous return; IVC = inferior vena cava (postcaval vein); PA = pulmonary artery; —, inhibitory effect, + excitatory effect (after Best and Taylor's Physiological Basis of Medical Practice, 9th edn.)

The existence of ACC (abdominal muscle tonus centre) separates from respiratory centre but acting in collaboration with it makes it probable that the activity of the abdominal muscles in respiration is in part determined by reflexes through this centre. This centre, like respiratory centre, is sensitive to P_{O_2}.

Besides respiration the ACC also reflexly modifies the tone of the abdominal muscles in such a way that the intrathoracic blood volume remains unaltered and an effective cardiac output is maintained.

I. NERVOUS CONTROL OF RESPIRATION

The Hering-Breuer Reflexes :

These reflexes prevent overdistension of the lungs during inspiration and collapse of the lungs during expiration. The former reflex is known as Hering-Breuer *inflation* reflex and the latter is Hering-Breuer *deflation* reflex.

1. Inflation reflex :

The receptors for these reflexes are 'stretch receptors' located in the lungs, mainly the bronchi and bronchioles. They are stimulated during inspiration when the lungs become stretched. The afferent impulses travel in the vagi and are relayed in 'tractus solitarius' before they reach the respiratory centre where they exert an inspiration-inhibiting effect The inspiration is thus cut off in time and expiration commences (Fig. 277).

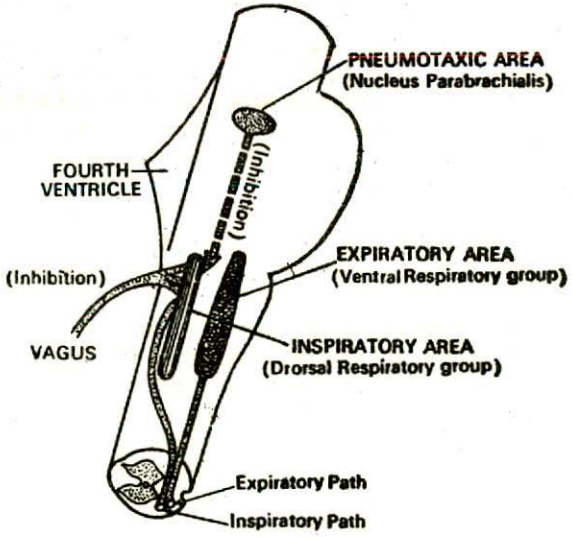


Fig. 277, Oversimplified diagram showing organisation of the respiratory centre.

Section of the vagi abolishes the inflation reflex when the inspiration gets unduely prolonged and the chest is held up in inspiratory position at a time when no air is entering the lungs.

II. Deflation reflex :

The respectors may be described as compression respectors located probably in the alveolar septa. They are stimulated during expiration and reflexly inhabits expiration and reciprocally stimulates inspiration. The afferent fibres are carried in the vagi. The

deflation is thus mediated by a separate set of receptors and carried by a separate set of fibres in the vagi.

It may be mentioned that during normal expiration the stretch receptors become unstretched resulting in cessation of inhibitory impulses to the inspiratory centre. Since this centre is tonically active inspiration commences as soon as inspiration-inhibiting impulses resulting from lung inflation ceases.

The inspiration-exciting effect of 'deflation reflex' becomes obvious in condition, such as, pneumothorax, hydrothorax, etc. where the degree of collapse of the lungs is more severe and results in stimulation of the respiratory process.

The physiological effect of Hering-Breuer reflexes is to maintain the extent of lung inflation so that the tidal volume tends to fall within a useful range. Indirectly the respiration rate is also adjusted so as to maintain adequet level of pulmonary and alveolar ventilation.

Impulses from ascending tracts of the spinal cord (Fig. 278)

It has been mentioned that the respiratory centre consists of a specialised group of cells in the reticular formation. The cells of the reticular formation receive impulses from the collaterals of the ascending tracts. It is believed that those sensory impulses from different parts of the body play an important facilitatory role in maintaining normal respiration. In a patient with depressed respiratory centre respiration may be stimulated by peripheral stimulus of any kind, such as slapping the skin. In fact, it is the practice to slap the new-born baby to establish the first respiratory cycle of life.

Stimulation of any afferent nerve causes reflex alteration in breathing, pain fibres are specially potent in this respect. Stimulation of cold fibres such as application of cold water on the face has got well-known excitatory effect on respiration. Heat receptors located on the skin and in the hypothalamus are stimulated by warm blood during exercise and fever and produce hyperventilation. Muscular proprioceptors send afferent impulses to the respiratary centre and markedly stimulate respiration during muscular exercise. Proprioceptors of the respiratory muscle profoundly modify the respiratory movement of the next cycle.

Rise in pressure in right atrium and the great veins reflexly augments respiration during muscular exercise and cardiac failure.

Glossopharyngeal nerve contains afferent fibres which inhibit respiration during second stage of deglutition.

Hiccough is due to reflex spasm of the diaphragm associated with spasm of the laryngeal muscles arising from irritation of sensory nerve endings of the gastrointestinal tract.

Stimulation of somatic sensory nerves of the nose inhibits respiration and may cause reflex sneezing.

Coughing is a reflex phenomenon caused by irritation of the mucous membrane of the respiratory tract. It is an important protective reflex in which the irritant material is got rid off from the respiratory tract. At the beginning of the act a deep inspiration is

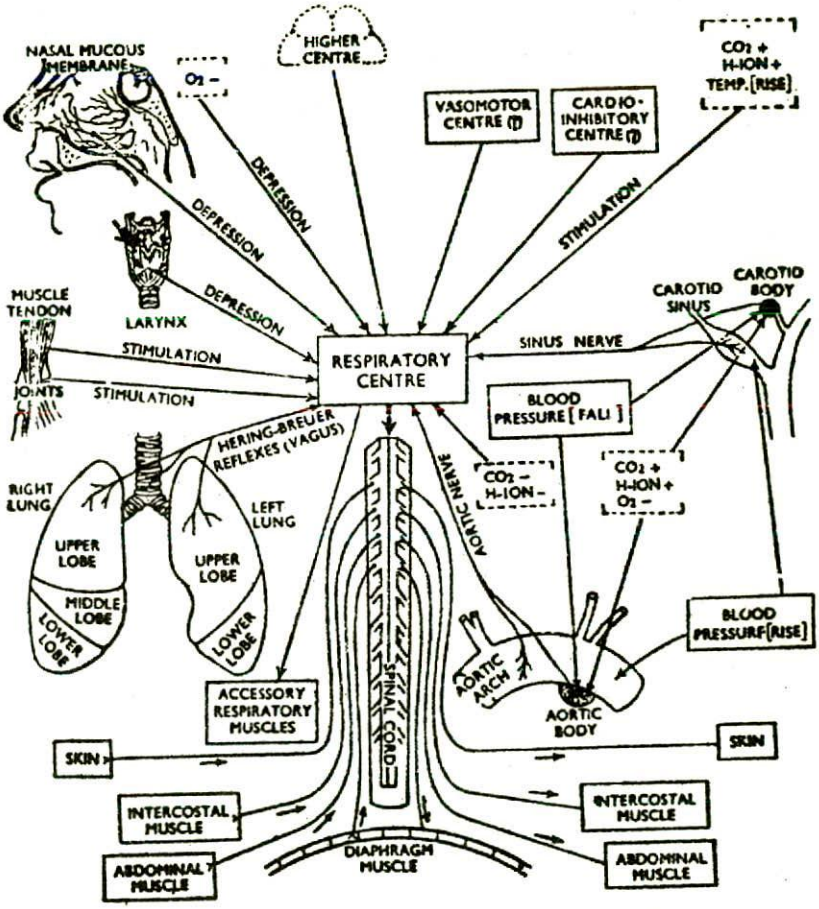


Fig. 278. Schematic representation of regulation of the respiratory centre. + means excess ; – means less.

taken, the glottis is then closed and violent expiratory effort is made against a closed glottis causing great rise in intrathoracic pressure. The glottis is then opened suddenly causing expulsion of the 'cough'—the droplets are ejected with the velocity of a jet plane.

Reflexes from sino-aortic zone

A sudden rise of pressure in this area causes reflex slowing in the rate and amplitude of breathing. If the pressure rise is considerable

in experimental animals, apnoea may result (adrenaline apnoea). If the rise in blood pressure is maintained for some time an 'escape' occurs and respiration commences again. This is due to (i) adaptation of the receptors and (ii) rise in Pco_2 during apnoea stimulating respiratory centre.

Fall in blood pressure stimulates respiration reflexly through the chemoreceptors of the sino-aortic zone.

The reflex slowing of respiration during the rise of blood pressure depresses the 'pump' effect on the abdominal venous reservoirs so that less blood enters the heart and cardiac output is also depressed. Fall of blood pressure is associated with hurried respiration so that more blood is pumped from the abdomen to the thorax which causes an increase of cardiac output. The important role played by abdominal muscles in these responses can be easily understood and is controlled by 'abdominal compression centre' under the influence of respiratory centre.

Distension of Pulmonary Vascular Bed

In experiments where the pulmonary vascular bed was completely isolated but for its nerve supply—distension of the vessels caused rapid shallow breathing.

This was abolished by vagotomy proving its reflex nature. This explains rapid shallow breathing in patients suffering from pulmonary cogestion.

II. CHEMICAL CONTROL OF RESPIRATION

The three most important chemical factors which affect respiration are

(i) CO_2 content of the blood or to be more precise tension of CO_2 (Pco_2) in the arterial blood.

(ii) pH of blood

(iii) O_2 tension (Po_2) of the arterial blood.

CO_2 and Respiration

Haldane and Smith demonstrated the effect of rising concentration of CO_2 in inspired air on respiration by making a subject rebreath his own expired air. They noticed that with an increase in concentration of CO_2 in the inspired air the pulmonary ventilation increased remarkably and that respiration increased both in rate and in depth Atmospheric air normally contains a negligible amount of CO_2 (0·03%). The concentration of CO_2 in the inspired air may be increased up to 1% without any noticable effect on pulmonary ventilation (respiratoay minute volume, RMV). If 4% of CO_2 is inhaled, the RMV in approximately doubled and the subject becomes conscious of his respiration. At concentrations above 6% the cardiac and respiratory functions are depressed and subjective symptoms like confusion and headache occurs. In fact the RMV does not increase significantly when more than 10% CO_2 is inhaled.

About 20% CO_2 in inspired air produce depression of respiration associated with convulsive seizures.

The RMV and alveolar P_{CO_2} (P_{A,CO_2}) are interdependent upon each other and further P_{A,CO_2} increases as the CO_2 of the inspired air increases. In the experiments of Haldane and Smith the alveolar P_{CO_2} was increased gradually by making the subjects rebreath his own expired air over a period of time. It was demonstrated that within the physiological range increase in P_{A,CO_2} is attended with a linear increase in the RMV.

The purpose of this respiratory stimulent effect of CO_2 will be obvious by looking at the simple model shown below. 'A' is a compressible bulb represents the lungs with a tube attached to it (the airways). Fig. 279 shows that 'A' is filled with some quantity of smoke (CO_2).

There is also a device fitted at 'A' through which smoke can be injected. It will be understood that if more and more smoke is injected into the bulb and at the same time the bulb is pumped more and more vigourously the amount of smoke injected in will be equal to the amount of smoke ejected out of the bulb and the concentration of smoke within the bulb will not rise, provided the amount of smoke injected is not excessive.

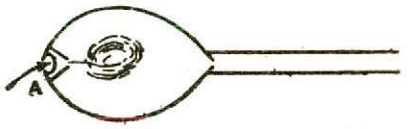


Fig. 279

Increased P_{A,CO_2} stimulates respiration and thereby drives out increasing amount of CO_2 from the lungs with each expiration so that an attempt is made to keep the P_{A,CO_2} at its resting level. This compensation, of course, fails when the concentration of CO_2 in the inspired air exceeds 5%. The table illustrates the point.

EFFECT OF GRADUAL INCREASE IN CO_2 CONTENT OF INSPIRED AIR

CO_2 % in inspired air	Average depth of respiration	Average rate of respiration per minute	CO_2 % in alveolar air
0·04	673 ml	14	5·6
0·79	739 ml	14	5·5
2·02	864 ml	15	5·6
3·07	1216 ml	15	5·5
5·14	1771 ml	19	6·2
6·02	2104 ml	27	6·6

Site of action of CO_2

The powerful stimulant action of CO_2 on respiration has been well established. CO_2-sensitive cells (chemoreceptors) are located in two places, viz. (1) centrally in the medulla and (2) peripherally in the carotid and aortic bodies.

(1) Central Chemoreceptors :

These cells are located bilaterally on the ventral aspect of the

medulla and are placed superficially anterior to the point of entry of the glossopharyngeal and vagous nerves. They are highly sensitive to CO_2 change and to change in pH of the blood and also of cerebrospinal fluid (CSF). Rise in P_{CO_2} or fall in pH stimulates these chemoreceptors primarily which again stimulates secondarily the cells of the respiratory centre increasing the volume and frequency of respiration.

In an elaborate series of experiments Pappenheimer and his co-workers perfused the ventriculo-cisternal systemts of goats with HCO_3^- solution of different concentration and measured their ventilatory response to CO_2. They concluded that CO_2 acts as a respiratory stimulus by increasing [H^+] in the interstitial fluid of the chemoreceptor cells scattered in the vicinity of the capillaries of bulbar reticular formation. These cells are not placed superficially and do not come in direct contact with the CSF.

Mode of action :

CO_2 by itself has little direct stimulant action on respiration. The most potent source of stimulation is rise in H^+ concentration which occurs whenever there is a rise in P_{CO_2} according to the equation $CO_2+H_2O \rightleftharpoons H^+ + HCO_3^-$. H^+ cannot diffuse easily from blood to the brain or to CSF but CO_2 can diffuse freely in either direction. A rise in H^+ concentration of the blood, therefore, will have a delayed access to the chemoreceptor cells whereas a rise in CO_2 concentration of the blood will be followed very soon by rise in CO_2 concentration of the CSF and tissue fluid in the brain. The H^+ liberated in CSF by dissociation of $H_2CO_3^-$ will have immediate and direct access to the medullary chemoreceptors with consequent stimulation of respiration. The H^+ liberated in brain tissues will be 'buffered' in the first instance by the acid-base buffers of the brain and its action on the chemoreceptors will consequently be delayed (Fig. 280). It may be noted that there is no significant amount of 'buffers' in the CSF.

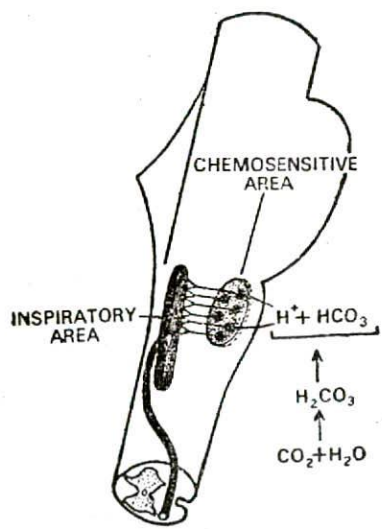


Fig. 280. Stimulation of inspiratory area by the chemosensitive area located bilaterally in the area lying only a few microns beneath the ventral medullary surface. Note that hydrogenions stimulate the chemosensitive area, which mainly CO_2 in the fluid gives rise to the hydrogen ions.

The initial-stimulating effect of CO_2 on respiration declines after a few minutes This is due to the fact that HCO_3^- is transported activity from the blood to the CSF and thus the H^+ of the CSF is neutralised to a considerable extent. This explains the diminution of stimulant effect on respiration of CO_2 which is prompt at the onset but declines to about one-fifth of the original effect after about 2 days.

From the quantitative point of view CO_2 is more potent a respiratory stimulant than H^+ and further the action of both these factors is very conspicuous in the neighbourhood of their normal value. Thus the respiratory stimulant effect of CO_2 is most prominent in the neighbourhood of P_{CO_2} range of 40 to 45 mm Hg and that of H^+ in the range of pH 7·45 to 7 35.

(2) Peripheral Chemoreceptors :

Chemoreceptor cells are located in carotid and aortic bodies and reflexly stimulate respiration when the concentration of CO_2 of the blood flowing through them is increased. Arguments have been raised regarding the relative importance of the central *versus* peripheral chemoreceptors in normal respiratory drive. It appears that the central receptors are more important in this respect—the peripheral receptors playing a secondary supporting role in conditions of emergency. In animals after chronic denervation of the carotid and aortic bodies the resting minute volume (RMV) of respiration falls to 80% of normal and consequently the arterial P_{CO_2} rises by 10 mmHg.

It is, therefore, reasonable to conclude that 80% of the resting respiratory drive of respiration is due to central chemoreceptors and 20% due to peripheral chemoreceptors.

Oxygen tension and breathing :

This has been studied by making the subject breath O_2 and N_2 mixture containing different proportion of oxygen. Normal atmospheric air contains 20·93% of O_2. The amount of oxygen in the inspired gas mixture can be reduced to about 12% in many individuals without any appreciable change in ventilation. However at levels of 10% of O_2 in the inspired air the respiration is stimulated with simultaneous reduction of P_{A,CO_2} as a result of hyperventilation. The low P_{A,CO_2} has a depressant action on respiration It is clear, therefore, that respiration-stimulating effect of O_2 lack will be enhanced if suitable measures are taken to prevent the fall of P_{A,CO_2} by adding appropriate amount of CO_2 to the inspired air.

Further a subject breathing low concentration of O_2 will have a low P_{A,O_2}, a condition analogous to the situation of a subject at high altitude where the low P_{A,O_2} is due to fall in barometric pressure. It can be calculated that the P_{A,O_2} of a subject at 5·5 km 18,000 feet is the same as that of a subject at sea level breathing 10·5% of O_2. In both the resultant hyperventilation will lead to fall in P_{A,CO_2} and alkalosis, which is corrected later by the kidneys. It is

known that fall in P_{A,CO_2} by 4 mm Hg. causes apnoea and alkalosis depresses respiration. The respiration under these condi ions is maintained entirely by O_2 lack or a re-adjustment of sensitivity of respiratory centre to CO_2. In acute exposure to high altitud respiratory drive is maintained by O_2 lack only whereas in persons residing at high altitude for some time the respiratory centre becomes sensitive to low P_{CO_2}.

Mode of action of oxygen lack

The respiration stimulating effect of O_2 lack is seen only in intact animals. In an animal with denervated carotid sinus O_2 lack will depress breathing. It has been proved by various workers and is an universally accepted fact that direct action of O_2 lack on respiratory centre is depression of respiration—the respiration-stimulating effect of O_2 lack is a reflex one through the sino-aortic chemoreceptors. The discharge of impulses from the chemoreceptor cells increases with the fall in oxygen tension of the arterial blood—the maximum effect is observed between arterial P_{O_2} of 60 mmHg and 30 mmHg. This is range in which percentage saturation of blood with oxygen falls almost perpendicularly (dissociation curve) and consciousness is lost very soon.

The carotid and aortic bodies are most highly vascular structures in the body. Consequently, the arterio-venous oxygen content difference is very low. In hypotension with blood pressure near about 60 mmHg the blood flow through these structures becomes very slow and sluggish and the arterio-venous O_2 content difference becomes high indicating low P_{O_2} within the chemoreceptor cells. Under these conditions there occurs reflex stimulation of respiration (and also vasoconstriction) which tends to restore the blood pressure to near normal value.

In conclusion it may be said that under normal conditions the level of pulmonary ventilation is controlled by three chemical agencies, viz.

(1) Rise in arterial P_{CO_2}.
(2) Fall in arterial P_{O_2}.
(3) Increase in arterial cH.

Any one of these factors may play a major role in driving respiration. It seems that above a certain range approximately 75 mmHg. P_{O_2} of inspired air) O_2 lack has no eflect on respiration, similarly below a certain range approximately 33 mmHg P_{CO_2})—CO_2 has no effect on respiration. Under ordinary circumstances the effect of above three factors are additive but one of three factors is enough to augment ventilation in the absence of other two. For example in metabolic acidosis there is great increase in H^+ concentration of the blood, the P_{O_2} being normal and P_{CO_2} below normal. However, the RMV is greatly augmented in this condition.

8.13. VENTILATION DURING EXERCISE

I. Chemical factors

It has been postulated that the three chemical factors, viz. O_2 lack, CO_2 excess and increased H^+ ion concentration play an important role in augmenting the ventilation during muscular exercise. However, it has not been possible to demonstrate any significant alteration in *arterial* Pco_2, Po_2 or cH in muscular exercise which means that the chemical factors have got little role in initiating or maintaining the hyperventilation of exercise. On the other hand, it has also been observed that inhalation of O_2 during muscular exercise reduces the RMV significantly. This can only be explained on the presumption that hypoxic drive is certainly a factor in exercise hyperventilation, even though the *arterial* Po_2 does not fall below its normal value. This is due to change in sensitivity of the afterial chemoreceptors to Po_2 and it has been suggested that these become hypersensitive to normal cH and Pco_2 as well.

II. Nervous factors

1. Cerebral Cortex :

During transmission of impulses to the muscles involved in exercise the pyramidal tract gives collaterals to the respiratory centre as well as to the vasomotor and cardiac centre, which are specialised parts of the reticular formation. This explains the anticipatory rise in RMV—actually before the exercise commences. It has been shown that at the commencement of exercise the alveolar ventilation may rise to a level so as to reduce the alveolar Pco_2. Very soon, however, large amounts of CO_2 formed by the exercising muscles restore the alveolar Pco_2 to normal level, and the alveolar ventilation is stabilised according to the alveolar Pco_2.

2. Proprioceptive impulses from the muscles :

In an anaesthesised person passive movement of the limbs increases the RMV. It is reasonable to conclude, therefore, that during muscular exercise proprioceptive impulses from the muscles and the body acts on the respiratory centre and augments respiration.

The nervous factore, viz direct stimulation from cerebral cortex and reflex proprioceptive stimulation from the muscles perhaps, play more important role in initiating and maintaining the appropriate level of ventilation during exercise so that the muscles get an adequate supply of O_2 and the excessive CO_2 and lactic acid formed are disposed off. Any slight deviation from the appropriate level is rectified by the chemical factors. Rise in body and blood temperature during exercise also stimulates respiration through tha hypothalamus.

8.14. PERIODIC BREATHING

This means periods of hyperventilation followed by apnoea repeated in succession. Two types of periodic breathing have been described :

(1) Cheyne-Stokes breathing in which the periode of apnoea is followed by a phase of gradually rising ventilation followed by gradual fall and the cycle is repeated, each phase lasting about 30 seconds.

(2) Biot's breathing consisting of runs of several normal respiration followed by apnoea.

Cheyne-Stokes breathing sometimes occurs in normal children or adults during sleep or at high altitude. Diseases in which Cheyne-Stokes breathing occus are

(i) Elevated intracranial pressure from any cause, e.g. brain tumour, meningitis, etc.

(ii) Anoxia from heart failure or pulmonary disease.

(iii) Uraemia and other toxic conditions in which the respiratory centres are depressed.

Mechanism of Cheyne-Stokes breathing

Cheynes-Stokes breathing is associated with rise of blood pressure sometimes in the apnoic phase and sometimes later. Rise of intracranial pressure causes anoxia of respiratory centre as well as vasomotor centre, the former is depressed and the latter is stimulated, the depression of respiratory centre is followed by apnoea.

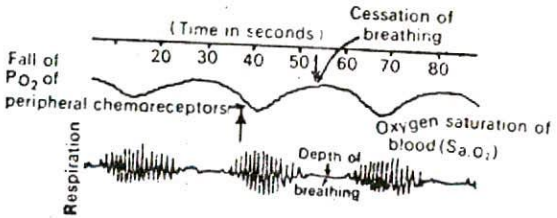


Fig 281. Periodic 'Cheyne-Stokes breathing. When the O_2 saturation of the blood ($Sa_{,}o_2$) and therefore the Po_2 of the peripheral chemoreceptors falls at the level (↓) the respiration is stimulated the $Sa_{,}o_2$ rises and respiration diminishes or ceases (↑). (After R. Hegglin and Bell-Davidson-Smith's *Physiology and Biochemistry*).

Elevation of BP due to stimulation of VMC is followed by relief of anoxia of the brain and so the hyperpnoic phase follows (Fig. 281). The hyperpnoea is attended with washing off of the CO_2 from the lungs and the relief of anoxia of the brain causes fall in blood pressure with consequent anoxia of brain and the whole cycle starts again.

In Cheyne-Stokes breathing the respiratory centre is less sensitive to CO_2. Arterial Pco_2 of 40 mmHg produces augmentation of ventilation to only about 50% of the expected

value. Anoxic stimulation of ventilation reflexly through the sino-aortic zone perhaps plays a role but denervation ot the sino-aortic area does not abolish the Chenye-Stokes type of respiration.

Administration of O_2 improves metabolism of nerve cells of the respiratory centreand administration ot CO_2 stimulates respiratory centre. So both the procedures abolish the abnormal type of breathing.

8.15. ANOXIA (HYPOXIA)

Definition : Anoxia is a condition characterised by inadequate or decreased supply of oxygen to the lungs because of extrinsic reasons. The term 'hypoxia' is more appropriate and is used synonymously with anoxia.

Classification :

I. Anoxic type of anoxia or arterial hypoxia

This type is characterised by *low oxygen tension* in the arterial blood.

II. Anaemic type of anoxia

This type is characterised by *low oxygen content* of the blood due to diminished quantity of haemoglobin or non-functionating haemoglobin.

III. Stagnant anoxia or Hypokinetic hypoxia

This type is characterised by *decreased rate of blood flow* through the tissue. The oxygen content and tension of the arterial blood is normal but that of the venous blood is abnormally low due to sluggish circulation.

IV. Histotoxic Anoxia

This means inability of the tissues to utilise oxygen and occurs in cynide poisoning.

Anoxaemia is a term which means diminished oxygen in the blood.

VI Anoxic anoxia or Arterial hypoxia

The main cause is diminished Po_2 of the arterial blood which, of course, results in diminished saturation of haemoglobin with oxygen. The total oxygen content of the arterial blood, therefore, is lower than normal, since the O_2 tension in the tssues is normally low (40 mm Hg) it may be that in spite of diminished Po_2, the arterial blood may unload its normal quota of oxygen to the tissues resulting in lower Po_2 and low oxygen saturation of haemoglobin in the venous blood than would occur normally.

Example :

	Arterial Blood			Venous Blood		
	Po_2 (mmHg)	O_2 content (vol%)	O_2 sat. of Hb	Po_2 (mmHg)	O_2 content (vol%)	O_2 sat. of Hb
Normal	100	19·3	95%	40	15	75%
Arterial hypoxia	60	17·2	90%	30	12	60%

O_2 content of the mixed venous blood is reduced from 15 volume % to 12 volume %. The final value of O_2 in the mixed venous blood, of course, depends on degree of anoxia.

Causes of arterial hypoxia

1. Diminished O_2 tension in the inspired air, e.g. may occur due to

(i) Admixture with foreign gases like CO or CH_4, etc. at the the bottom of the mines.

(ii) High al itude dùe to low barometric pressure—the partial pressure of O_2 in the alveoli is diminished.

2. Diseased conditions in which the ventilation/perfusion ratio (normal 0.8) is disturbed. This may be due to ineffective ventilation (dead space effect), e.g. in advanced pulmonary emphysema, asthma, obstruction of air passages, or due to venous-admixture effect as may occur in pneumònia or septal defect of the heart.

3. Diseased conditions in which there occurs defective diffusion across the alveolo-capillary membrane, e.g. pulmonary oedema or alveolo-capillary block syndrome.

Anaemic Hypoxia

The characteristic feature of this type of hypoxia is diminished quantity of *functionating* haemoglobin in blood. The oxygen content of blood, therefore, is diminished proportionately to the reduction of haemoglobin but the oxygen tension of blood and percentage saturation of haemoglobin with oxygen is normal.

Causes ;—1. Anaemia from any causes.

2. CO poisoning—here a large amount of haemoglobin remains combined with CO and as such is not available for oxygen carriage.

3. Altered haemoglobin—e.g. methaemoglobin found after poisoning with chlorates, nitrites, ferriaynides and acetanilid etc.

Anaemic hypoxia, if of moderately severe intensity, is attended with increased cardiac output, that is increased blood flow through the tissues so as to compensate to some extent for the diminished O_2 content of blood.

Stagnant Anoxia or Hypokinetic anoxia

The characteristic feature of this condition is diminished blood flow through the tissues due to sluggish circulation. The cardiac

output is low but the O_2 content and tension of the arterial blood is normal. Due to sluggish circulation after the tissues abstract normal amount of O_2 they need—the venous blood is considerably reduced, with its Po_2 much less than normal. Consequently, the Po_2 of the tissue fluid and tissues in general is reduced which has got a damaging influence on the tissues.

Myocardial infaraction is an example of localised hypoxia resulting in loss of function which leads to generalised hypoxia and worsening of the ischaemia of the heart.

Causes of stagnant or hypokinetic anoxia

(a) Congestive cardiac failure, (b) haemorrhage, (c) shock and (d) obstruction to venous return.

Histotoxic Anoxia

This type of anoxia is due to poisoning with cynides or sulphide in which the respiratory enzymes are inhibited and so the tissues cannot utilise O_2 of the blood which contains adequate amount of O_2 at normal tension.

Altitude Anoxia

Anoxia at high altitude is due to low barometric pressure. The percentage composition of atmospheric air in so far as O_2 and N_2 concentration is concerned is same at all altitude but due to fall in barometric pressure at high altitude there occurs a disproportionate fall in Po_2 of the alveolar air and consequent percentage saturation of haemoglobin with oxygen. The effect of high altitude on alveolar oxygen and arterial blood has been discussed in detail in Page 394 and will be discussed again 425xxiv.

Respiratory changes in hypoxia acute and chronic at high altitude

Anoxia of gradual onset occurs in mountaineering and the respiratory responses of a subject to such type of anoxia differs to some extent depending on whether the subject is conditioned for high altitude atmosphere (acclimatised subject) or ascending to high altitude for the first time and is unacclimatised for the high altitude environment.

Respiration in altitude anoxia in unacclimatised subjects :

Breathing 14% O_2 in N_2 (simulated altitude 3 km or 10,000 feet) produces practically no change in respiration. When the oxygen in the inspired air is brought down to 10% (simulated altitude about 5·5 km or 18,000 feet) there occurs 8% increase in ventilation over the resting value. Respiration is doubled when the respired air contains 8% oxygen in nitrogen. Anoxia, therefore, is not so effective a stimulant to respiration as is excess of CO_2.

Anoxic stimulation occurs reflexly through the chemoreceptors of the sino-aortic area. The anoxic hyperventilation, however, is

associated with fall in alveolar and arterial P_{O_2} and with $[H^+]$ in blood, and also in the c. s. f. and interstitial fluid of the brain, which bath the CO_2-sensitive chemoreceptor cells which form part of the respiratory centre complex of the brain stem. This causes depression of respiration.

However, if the anoxic stimulus is sufficiently intense the chemoreceptor reflexes from the sino-aortic area assumes a prepotent role in maintaining hyperventilation in spite of the fall in P_{O_2} and $[H^+]$ resulting from anoxic hyperventilation.

Further, it has been proved that the chemoreceptor cells of the respiratory centre become hypersensitive to CO_2 and $[H^+]$ in presence of oxygen deficiency. This is shown in the accompanying

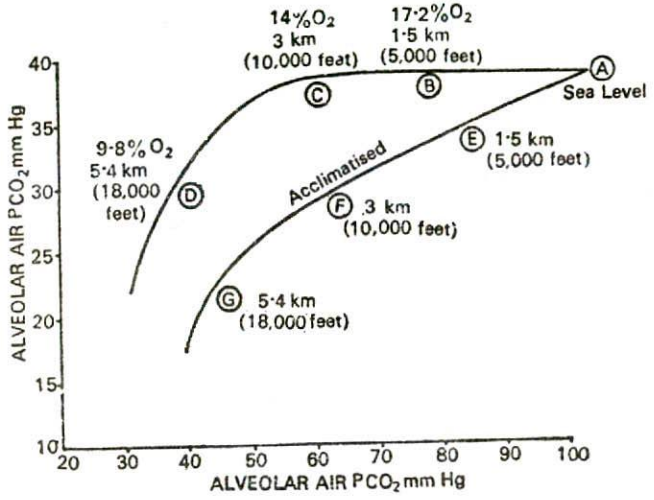


Fig. 282. The alveolar air gas tensions of subjects exposed to chronic and acute anoxia.

diagram (Fig. 282) which indicates that the respiratory stimulant effect of CO_2 is significantly greater when the alveolar P_{O_2} is maintained at a steady value of 40 mm Hg than when it is kept at its normal value of 100 mm Hg. The slope of $\dot{V}/P_{O_2}$ line increases as the alveolar P_{O_2} is lowered. Anoxia, therefore, increases the sensitivity of respiratory chemoreceptors to CO_2 and $[H^+]$.

Respiration in subjects exposed to anoxia of long duration (acclimatised subjects):

The above discussion applies to person exposed to anoxia for the first time (acute anoxia). The respiratory pattern of subjects exposed to anoxia for a long time or who are permanent residents of high altitudes (acclimatised subjects) is shown by the lower curve in the

same diagram. As can be seen from the diagram the alveolar P_{CO_2} value of an acclimatised subject begins to fall from an altitude of 1·5 km or 5000 feet upwards and is always lower than that of an unacclimatised subject. Thus at an altitude of 5·4 km or 18,000 feet the alveolar P_{CO_2} value of an acclimatised subject is only 22 mm Hg as compared to 30 mm Hg of an unacclimatised subject. This, of course, is due to the fact that the acclimatised subjects can and do hyperventilate more than his unacclimatised friend in spite of the consequent fall in alveolar P_{CO_2}. The alveolar P_{O_2} rises consequently with obvious advantage for better oxygenation of venous blood.

It has been pointed out in page 424 that the $[H^+]$ of the blood and c. s. f. depends on the ratio of $\frac{P_{CO_2}}{[HCO_3^-]}$ and that CO_2 being highly soluble and diffusible the changes in P_{CO_2} of the blood is more or less the same as that in the c. s. f. But the $[HCO_3^-]$ in the c. s. f. is controlled independently and that active transport of HCO_3^- occurs from the c. s. f. to blood in anoxis so that the fall in $[HCO_3^-]$ is always more marked in the c. s. f. than in the blood in cases of low arterial and c. s f. P_{CO_2} Thus $[H^+]$ of the c. s. f. and interstitial fluid of the brain is quickly brought back to normal level so that the chemoreceptors of the brain stem influencing the respiratory centre can function properly in spite of the fall in P_{CO_2} of alveolar air and arterial blood Thus 4 subjects were studied at an altitude of about 3·8 km or 12 500 feet. In 24 hours the P_{CO_2} of the arterial blood fell on an average from 40 to 30 mm Hg and the pH increased form 7·43 to 7·48. The P_{CO_2} of the c. s. f. fell to the same extent, i. e. by 10 mm Hg but there was no increase in pH of the c. s. f. This was due to remarkable fall in $[HCO_3^-]$ of the c. s. f. to the extent of 5 mEq/litre compared to about 2 mEq/litre in blood. The stabilisation of $[H^+]$ in the c. s. f. and tissue fluid of the brain was thus acheived by active transport of $[HCO_3^-]$ from the c. s. f. to the cerebral capillaries. The sensitivity of the bulbar chemoreceptors acting on the respiratory centre was thus unaffected in spite of fall in P_{CO_2} of the c. s. f. and brain.

It may be summarised, therefore, that during acclimatisation the low P_{CO_2} of the c. s. f. and interstitial fluid of the brain resulting from anoxic hyperventilation is counteracted by active secretion $[HCO_3^-]$ from the c. s. f. and tissue fluid of the brain to the blood so that the $[H^+]$ of the c. s. f. and brain remains unaltered and that the activity of the respiratory chemoreceptors are not depressed. After some time, however, kidneys also play an important role in adjustment of pH of the blood and c. s. f. by excreting urine with high pH value. The advantage of this hyperventilation is obvious, because it enables to maintain high alveolar P_{O_2} and ensures more effective oxygenation of venous blood.

In residents of high altitude—the lung volume is increased so

that the lungs can hold more air. Further the alveolar wall is stretched out facilitating gaseous interchange. More pulmonary capillaries open up increasing the surface area for diffusion.

Oxygen therapy in anoxia or hypoxia

Three methods are commonly employed in administration of oxygen. These are :

(i) Nasal catheter—it is possible to raise the alveolar Po_2 from its normal value 100 mm Hg to 600 mm Hg by this method.

(ii) Oxygen tent—the patient is put in an atmosphere enriched with oxygen. The alveolar Po_2 usually go upto about 300 mm Hg.

(iii) Oxygen mask—either pure oxygen on high concentration of oxygen is breathed through a mask. Sometimes a specially designed mask (B. L B. mask) is used in which part of the oxygen in the expired air is utilised for rebreathing.

In altitude anoxia or hypoxia due to presence of foreign gases in the atmosphere at high concentration administration of pure O_2 is of great value and offers absolute protection except when the altitude is very high and O_2 must be delivered through a pressure mask.

In hypoxia due to alveolar hypoventilation breathing 100 per cent O_2 can increase the alveolar concentration of oxygen 5 times the normal value and thus is extremely beneficial.

In alveolo-capillary block syndrome—oxygen therapy is extremely beneficial because the rise in concentration of oxygen in the alveoli raises the diffusion gradient and thereby facilitates diffusion of oxygen across the diffusing membrane.

In anaemic anoxia—the functionating haemoglobin is low but the oxygen saturation of functionating haemoglobin is normal and Po_2 of plasma is normal. Oxygen therapy, therefore, is of limited benefit because only the O_2 in solution can be increased by O_2 therapy, the O_2 content is but little affected.

In hypokinetic hypoxia—the O_2 content and tension of arterial blood leaving the lung is normal and so O_2 inhalation is of limited value. However, the normal amount of O_2 in solution in arterial blood is 0·3 ml per 100 ml. This can be increased to 1·8 volume of O_2 per ml of blood when the alveolar Po_2 is raised to 600 mmHg by O_2 inhalation. This means only an increase of about 10% of O_2 content at high pressure and may mean the difference between life and death.

In histotoxic anoxia – the enzymes are paralysed so that the tissues fail to pick up oxygen from blood therapy, therefore, are of no avail.

Danger of oxygen therapy in anoxia or hypoxia

In patients suffering from chronic hypoxia—the respiration is maintained by reflex stimulation of the sino-aortic bodies and the sensitivity of the chemoreceptors to CO_2 is diminished. Sudden

relief of hypoxia by oxygen therapy may produce hypoventilation with hypercapnia or hypercarbia and unconsciousness which may lead to death.

8.16. DYSPNOEA

Dyspnoea means difficulty in breathing associated with a sense of distress. It is to be differentiated from hyperpnoea which simply means hyperventilation, as occurs in muscular exercise, and is usually not associated with sense of distress, unless, of course, the exercise very severe.

The factores responsible for dyspnoea may be classified into three categories, viz :

I. Alteration in chemical composition of blood

(i) Hypoxia
(ii) Hypercapnia or Hypercarbia
(iii) Increased H-ion concentration.

II. Excessive work of the respiratory muscles to inflate and deflate the lungs so as to provide adequate ventilation

(i) Diminished lung compliance, e.g. in congestion, fibrosis, etc.
(ii) Abnormalities in chest wall and diaphragm.
(iii) To provide increased demand for O_2 in diseases associated with high metabolic rate.

III. Psychogenic dyspnoea :

Due to impulses from higher centres.

1. Dyspnoea due to alteration in chemical composition of blood :

(i) O_2 lack from causes enlisted under 'arterial hypoxia in page 425iv.

(ii) Hypokinetic anoxia interferes with transport of respiratory gases due to sluggish circulation, as occurs in cardiac failure.

(iii) Anaemic anoxia, if severe, will lead to O_2-lack in the body.

(iv) Factors affecting diffusion of gases across the alveolo-capillary membrane (alveolo-capillary block syndrome)

Stimulation of respiration leading to dyspnoea by the factors mentioned above occurs reflexly via the sino-aortic mechanism. It is believed that the Hering-Breuer reflex also becomes overactive in these conditions, which also augments respiratory rate and supplements the discomfort of dyspnoea.

(v) The CO_2 excess and respiratory acidosis occurs in alveolar hypoventilation associated with decrease in vebtilation/perfusion ratio. The causes (i) to (iv) listed above are usually not associated with CO_2 tention because CO_2 diffuses at least 20 times more rapidly than O_2.

(vi) Metabolic acidosis will also produce dyspnoea by

stimulating respiratory centre both directly as well as reflexly in the same way as CO_2 excess.

2. Excessive work of the respiratory muscles :

(i) (a) Obstruction of the larynx or bronchi as in diphtheria or asthma will produce dyspnoea due to excessive work of the respiratory muscles to overcome the resistance offered by the resistance. (b) O_2 lack and CO_2 excess due to hypoventilation will also add to the discomfort of dyspnoea by reflex and direct effect on respiratory centre

(ii) Reduced distensibility of the lungs as occurs in oedema, congestion, fibrosis, and inflammation of the lungs. Due to diminished distensibility of the lungs, i.e. diminished compliance, the respiratory muscles are to work hard to maintain an adequate ventilation through the rigid alveoli. The Hering-Breuer reflex is said to be overactive in these cases and so accelerate the rate of respiration.

Applied physiology

Dyspnoea on exertion or even at rest in advanced cases, is the commonest symptom of heart disease, e. g. mitral stenosis It has been proved to be not due to arterial hypoxia or hyperkapnia. Engorgment of pulmonary capillaries leading to diminised distensibility of lungs is the prime cause of cardiac dyspnoea. When pulmonary oedema supervenes, anoxia will complicate the picture. It has been mentoined elsewhere that distension of pulmonary capillaries causes rapid shallow breathing.

(iii) Conditions which cause limitation of movement of the diaphragm or chest wall will lead to distressed breathing resulting from undue effort of the muscles of respiration. In emphysema, for instance, the elasticity of the lungs is lost and the chest is held up in inspiratory position during rest. The diaphragm is fixed in an elevated position. Inspiration can, therefore, be effected only by unusual effort of the inspiratory muscles. Expiration is also effected by active contraction of the muscles of expiration.

(iv) In diseases associated with high metabolic rate, e g thyrotoxicosis there is an increased demand for O_2 in the tissues and also an increased demand for elimination of CO_2. This demand is increased during muscular effort. In such patients the respiratory muscles are to work more to meet the increased demand for oxygen and such these patients are liable to be dyspnoea on slight exertion.

In severe diabetic acidosis. Kussmaul breathing, or air hunger may be observed in comatose subject.

3. Psychogenic or Emotional dyspnoea :

Many persons of neurotic disposition are apprehensive that they may not be able to get sufficient quantity of air if they enter a overcrowded room. These persons develope 'air hunger' on entering

a croweded room, e.g. cinema hall and sometimes hyperventilates to such an extent that they develope alkalosis and tetany in a crowded place or rather 'stuffy' atmosphere.

8.17. DYSBARISM (CAISSON DISEASE)

(Compressed Air Sickness)

Divers, who work under water, generally work in caissons. A caisson is a steel chamber, filled with compressed air in which the divers are placed and sunk in deep waters Thus, the workers are exposed to air at high pressure. At the outset, there may not be much discomfort. Temporary dizziness, noises in the airs, frequency of micturition, slowing of respiration and slowing of pulse rate may occur. But when the subject comes out of the chamber and returns to normal atmospheric pressure (i. e., during **rapid decompression**) serious effects appear which may set in immediately or after some time. In milder cases, a sensation of pain is felt. It is felt especially in the joints, so that the subject adopts an attitude of flexion.

In severe cases there may be—(a) Cyanosis. (b) Small running pulse showing circulatory failure. (c) Paralysis, usally of the legs. (d) Unconsciousness, which may lead to death. The phenomenon is explained as follows :

The air being breathed under high pressure, the amounts of oxygen and nitrogen, carried in physical solution in plasma, are much more than normal. When the pressure is reduced during decompression, this extra amount can no more be held in physical solution and the gases come out in the form of bubbles. The oxygen is rapidly used up by the tissues and does not cause much harm. But the nitrogen bubbles cannot be disposed of in this way and may block the capillaries in any locality (causing **gas embolism**). It may accumulate in the heart and be frothed up in the blood stream This prevents the cardiac action and leads to circulatory failure. The pain is due to local gas embolism. The unconsciousness and paralysis are due to bubbles of nitrogen in the nervous system. Nitrogen being about five times more soluble in fats than in water and the nervous system being especially rich in lipids (especially the medullary sheaths), bubbles of nitrogen evolve in the central nervous system and are particularly prominent at the junction of white and gray matter. So that the nervous system is very easily affected in dysbarism (Caisson disease).

The *percentage reduction* of pressure is more important than absolute reduction. Thus a sudden reduction to less than 45% of original pressuae in which the subject was placed will lead to dysbarism. Thus a diver originally exposed to a pressure of 8 atmospheres can be subjected to quick decompression of 4 atmospheres without any harmful effect. After some time the preseure may be

reduced to 2 atmospheres and then after equilibriation at this pressure can be brought back to 1 atmosphere.

Obviously dysbarism may occur in rapid ascents to high altitude. About 9 km or 30,000 feet is the critical altitude where symptoms of dysbarism are first felt because the barometric pressure here (226 mm Hg) is less than 45% of that at sea level. This can be avoided by inhalation of pure O_2 before the flight so that the system gets practically N_2-free. Oxygen inhalation is to be continued during the flight.

The pressure within the Russian space-ships is kept at about 1 atmosphere in a hamatically sealed cabin containing N_2 and O_2 in the same proportion as these are present in the atmosphere. The space-ships move through perfect vacuum and any leak in the cabin either in the door or in the wall will cause dysbarism. In fact two Russian astronauts lost their lives due to this cause because they failed to lock the cabin door properly during their return journey.

In order to prevent the occurrence of this disease, decompression should be very gradual and if symptoms have already appeared, the subject should be immediately exposed to compressed air.

8 18. ASPHYXIA

Definition. Improper aeration of blood, if continued for some time in an intact animal, produces a series of pathological manifestations and ultimately death. These manifestations are collectively called asphyxia.

Classifications. Asphyxia may be—(1) general—such as, by occlusion of the trachea, pneumothorax, etc., or (2) local - as by ligature of blood vessels supp ying a particular locality.

Essential Conditions of Asphyxia. (1) There must be both CO_2

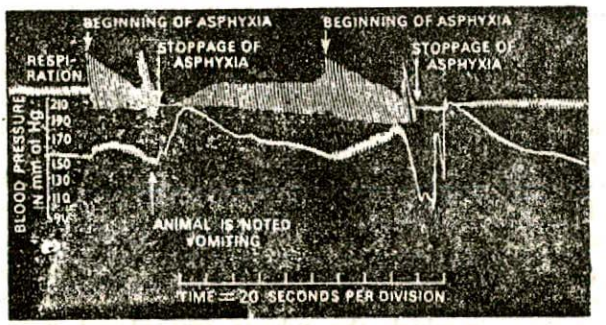


Fig. 283. The tracing shows the increase of blood pressure in intact animal during artificial asphyxiation of an anaesthetised cat (after Mukherjee et al. Ind. Jour. Physiol. & Allied Sci.).

excess as well as O_2 lack. (2) Animal must be intact (if the sino-aortic nerves are cut, typicall asphyxia will not be obtained). (3) The improper aeration must be continued Fig. 283).

The phenomenon of asphyxia has been divided into three stages, each stage showing characteristic features. The whole phenomenon—fram the onset to death—takes about 5 minutes. The stages, their manifestations and their causes are given below :

Stages	Manifestations	Causes
First stage or stage of phyperpnoea Duration— 1 minute	Rate and depth of respiration increase. At first, both inspiration and expiration increase and the animal becomes dyspnoeic. Then expiratory movements become more pronounced than inspiration. This feature marks the end of the first stage.	The stimulation is due to CO_2 excess only. Although O_2 lack is occurring, yet it is not low enough to exert its effect.
Second stage or stage of expiratory convulsion or stage of central excitation Duration— 1-2 minutes	In the experimental animal the stage of hyperpnoea is followed by unconsciousness Expiration becomes still more pronounced and with each expiration almost the whole body enters into convulsion. All signs of central excitation appear, e.g widespread vasoconstr ction causing systemic rise of blood pressure (Fig. 283), constriction of pupils, exaggeration of reflexes, etc. Saliva is often secreted, vomiting may occur (Fig. 283). The heart rate and intestinal movements may be increased or diminished according to the relative predominance of sympathetic or parasympathetic stimulation and so on.	1. Further accumul tion of CO_2. 2. O_2 lack is, by this time, more pronounced and is enough to stimulate the respiratory centre reflexly through the sino-aortic nerves. 3. Due to convulsions, lactic acid enters the blood stream and produces acidosis. These three factors combine together to stimulate respiration as well as the other nerve centres. Hence, maximum excitation is seen in this stage.

Stages	Manifestations	Causes
Third stage or stage of slow deep inspiration or stage of central depression Duration— 2-3 minutes	Expiratory convulsions cease and are replaced by slow deep inspirations. Inspiration becomes spasmodic and with each inspiration the animal stretches itself out, opens its mouth widely as if gasping for breath. Signs of central depression appear, viz., pupils dilate, reflexes abolished, vasodilatation, fall of blood pressure, etc. The interval between the successive inspiration becomes gradually longer, the animal takes a few gasping breaths and at the end of 4-5 minutes dies.	This stage is due to the direct effect of O_2 lack on the respiratory centre. Although all the factors that were operating in the second stage are also present here, yet they fail to excite any further; because, the nerve centres are exhausted. Hence, O_2 lack is now exerting its direct depressant effect on the respiratory centre.

8 19 HYPERPNOEA

The term **hyperpnoea** means increased breathing. Any rise in the quantity of air breathed per minute is called *hyperpnoea*. Causes of hyperpnoea may be—(1) voluntary, (2) impulses from the cerebral cortex to the respiratory centres, e.g. emotion, (3) impulses from the hypothalamus, (4) reflexly by the stimulation of nerves of general sensation (pain, heat, cold, etc.) in the skin, (5) all conditions where metabolic rate is very high demanding more oxygen supply and producing more CO_2 for elimination, for instance muscular exercise, (6) factors causing dyspnoea (vide page 425xi) will evidently cause hyperpnoea.

Voluntary hyperpnoea, being of special interest, is discussed in detail below :

Effects of voluntary hyperpnoea

When a person, at bodily and mental rest, goes on breathing deeply and quickly (causing overventilation) for about 3 minutes and then stops, the following changes are found to take place. (1) **Breathing remains suspended** for a period (Apnoea). This is due to the washing-out of excess CO_2, and consequent reduction of CO_2 in the arterial blood. After this period of apnoea, *periodic breathing* (alternate breathing and apnoea) may follow for some time and then normal breathing is restored. (2) **Alkalosis**—due to washing out of excess CO_2, blood becomes more alkaline. (3) **Increased excretion of alkaline urine containing bicarbonates.** This is due to failure of the renal tubular cells to provide sufficient H^+ due to

washing-out of excess CO_2. Normally secretion of H^+ and absorption of HCO_3^- are interdependent. In the absence of secretion of H^+, HCO_3^- and Na^+ are eliminated in the urine. (4) Presence of Keto acids in the urine (5) Skin vessels are constricted and the skin is white and cold. (6) Increase in cardiac output and a slight rise of blood pressure. (7) Dizziness and paraesthesiae of the extremities. The consciousness may be dulled. The development of the cerebral symptoms is due to anoxia which causes cerebral vasoconstriction. (8) Tetany (may be due to alkalosis). This is due to failure of renal tubular cells to secrete H^+. As a result NH_3 manufactured by the renal distal tubular cells cannot form ammonium salts. Keto acids as such are eliminated in the urine.

8.20. ORTHOPNOEA

With severe congestive cardiac failure dyspnoea occurs even at rest. The patient feels more comfortable in the sitting positon than when lying down. This condition is called orthopnoea The subject passes the whole day and night, being propped up by pillows or sleeping on an orthopnoeic table. Many theories have been advanced to explain the relative comfort in upright position. Some of the theories are as follows : (1) Removal of the weight of the enlarged liver and other abdominal viscera and thus facilitating the descent of the diaphragm (2) In the sitting position there is greater drainage of blood from the medulla and consequently better blood flow through the respiratory centre. (3) The vital capacity in the upright position is about 25% more than in the recumbent position. (4) Better drainage of blood from the lungs and consequent relief of the pulmonary congestion. This increases the distensibility of the lungs and thus renders the Hering-Breuer reflex less sensitive.

8.21. CYANOSIS

Cyanosis is a clinical condition in which the skin and mucous membranes assume a bluish colour. It may be local or general. When general, it is best seen at the lips, nose, cheeks, ears, hands and feet. It is caused by an alteration in the character of blood circulating in the capillaries. Hence, when blood is pressed out of the part, cyanosis temporarily disappears.

It depends upon the absolute amount of reduced haemoglobin present in the blood. It may also be due to the presence of other haemoglobin derivatives having a darker colour (e. g. methaemoglobin and sulphaemoglobin). At least 5 grams of reduced haemoglobin must be present (i.e., 5×1.34 ml $= 6.7$ ml of oxygen should be less per 100 ml of blood) before cyanosis can be produced. Consequently, in an anaemic subject containing less than 5 grams of haemoglobin (i.e., below 33% Hb) cyanosis is not possible.

Factors causing Cyanosis

1. Inadequate oxygenation of bloood in the lungs, i.e. (a) Less O_2 in the air as in high altitude. (b) Diseases of the lungs. (c) Collapse of the lungs. (d) Obstruction of the trachea and bronchus. (e) Heart failure. (f) CO poisoning, etc.

2. Admixture of venous and arterial blood. This takes place in certain congenital heart diseases, where there is direct communication between right and left sides of the heart. [Patent interventricular septum, patent foramen ovale.]

3. Greater reduction of oxyhaemoglobin—(a) Local chilling. (b) Venous obstruction. This will retard the local circulation and allow more time for greater reduction of haemoglobin. (c) High metabolic rate and thereby higher degree of oxygen utilisation of a part occur.

8.22. ARTIFICIAL RESPIRATION OR RESUSCITATION

Indication : In any condition where respiration fails but heart continues to beat, application of artificial respiration is indicated.

Principle : The purpose of giving artificial respiration is as follows :

1. By maintaining the gaseous interchange, the vitality of the nerve centres, as well as that of the heart, is maintained Artificial respiration also helps to maintain circulation. It is expected that after some time, the respiratory centres will start functioning spontaneously.

2. During artificial respiration, the alternate inflation and deflation of lungs reflexly stimulate the respiratory centres, and thus help them to take up their own spontaneous rhythm.

METHODS OF ARTIFICIAL RESPIRATION

I. *Manual Methods*

Schafer's Method (Fig. 284). The subject is laid in prone position and a small pillow is placed underneath the chest and epigastrium. The head is turned to one side. The operator kneels down by the side of the subject facing towards his head Two hands are placed on the two sides of the lower part of the chest and then the operator slowly puts his body weight leaning forwards and pressing upon the loins of the subject. Intra-abdominal pressure rises, the disphragm is pushed up and air is forced out of the lungs. After this the operator releases the pressure and comes back to his original erect position. The abdominal pressure falls, diaphragm descends and air is drawn in. These movements are repeated about twelve times a minute (roughly the normal rate of respiration). By this means it is possible to have a total pulmonary ventilation of 6,500 ml per

minute, and this amount is sufficient for complete aeration of blood. The advantage of this method is that the patient being in the prone position, mucus or saliva comes out of the mouth and cannot obstruct his airways.

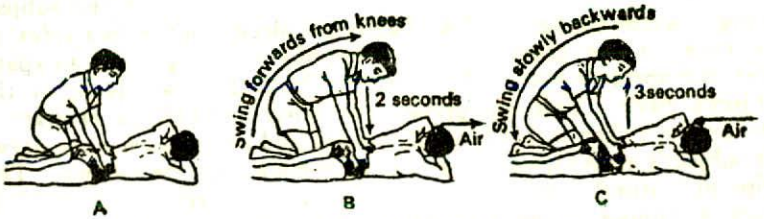


Fig. 284. Schafer's manual method for artificial respiration.

A = Laying casualty's face downwards with head turned to one side, arms bent and forehead resting on his hands with neck extended and kneeling to one side of casualty's hips facing his head ; and placing hands flat on the small of casualty's back just above the top of pelvic bones, thumbs almost touched each other in the midline, fingers being spread over the loins and pointing towards the ground. B = Sitting on heels and swinging body slowly forward from knees being kept arms straight and hands in place all the time only applying gentle pressure by the body weight. Forcing air out of the lungs (*expiration*) to be maintained this position for two seconds counting 'one, two'. C = Relaxing the pressure by swinging quietly and gradually backwards on to heels allowing inspiration and counting three, four, five' in three seconds before swinging forwards again to first movement being kept arms straight and hands in place all the time.

Until the last few years Schafer's prone pressure mathod of artificially inflating the lungs was most widely practised. But now-a days either back-pressure-arm-lift method or Holger Nielson's method or the mouth-to-mouth method is practiced preferably.

Sylvester's method : The subject is placed in supine position. The operator stands or kneels at the head end and holds the two arms of the subject. The operator then raises the subjects hands above his head and then folds the hands back upon the chest, compressing the chest wall at the same time. Such movements alternately increase and decrease the thoracic cavity, thus drawing in and pushing out air from the lungs. This method is most commonly used in the operation theatre or in other accidents. The tongue should be kept pulled out and the mucus from the mouth cavity should be wiped out from time to time, The rate is same as in Schafer's method. In drowning cases, the water in the lungs must, at first, be driven out, by holding the subject upside down or revolving the subject by holding his legs. After this the subject should be given artificial ventilation. Respiratory level and volume during the artificial method has been presented in Fig. 287C.

Holger-Nielsen Method (Fig. 285). The subject is placed in the prone position with the arms abducted at the shoulders and elbows remaining flexed. The face is turned to one side and rests on the hands. The mouth is cleaned after wiping out mucus fluid, etc. from it The operator kneels down in front of the subject facing towards the head Two hands are placed on the two sides of the back of the chest with the thumbs and fingers spread apart. Then the operator puts his body weight leaning forwards upon the subject's back. This compresses the chest and helps in expiration. The operator then makes himself straight and at the same time draws the subject's arms forwards by holding them above the elbows This helps in natural inspiration. This process is repeated about 10 12 times a minute. The respiratory level and volume during this artificial method have been presented in Fig 287B

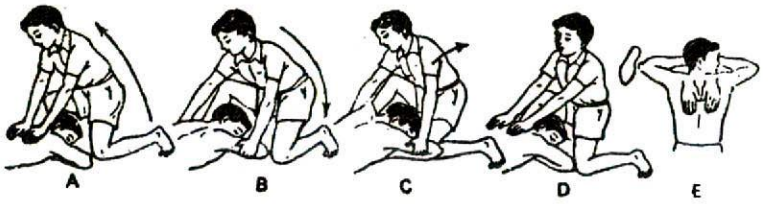


Fig. 285. Back-pressure-arm-lift method or Holger-Nielsen's manual method for artificial respiration.

A = Rocking forward quietly with arms straight and applying light pressure to back by weight of the upper part of body only counting for two seconds, 'one, two' (*expiration*) B = Rocking back with arms straight releasing pressure gradually and sliding hands to elbows of casualty counting three' for one second C = Raising and pulling casualty's arms until tension being felt for two seconds counting 'four, five' causing *inspiration*. D = Placing hands over casualty's shoulder blading with thumbs being touched in the midline and arms straight. Then lving casualty's arms down and placing hands on his back as in figure A for one second counting 'six'. E = Position of casualty and operator – laying casualty with face downwards and turning to one side, arms bent and forehead rested on his hands being nose and mouth unobstructed and neck extended ; and kneeling at his head being placed one knee near casualty's head and one foot alongside his elbow and hands being placed over casualty's shoulder blades with thumbs touching in the midline and fingers spreading out and being kept arms straight. [If arms being injured placing them by the sides of body doing the complete procedure but inserting hands under casualty's shoulders and raising them for inspiration. If arms and chest both injured duarm to be raised and lowered by inserting hands under casualty's shoulders.]

Mouth-to-mouth method (Fig. 286). The subject is laid in the supine position with extended head. The operator sits by the side of the subject's head. The operator holds the lower jaw of the subject by one thumb and index-finger and clamps the nostrils with the other thumb and index-finer. The operator then keeps his mouth over the subject's mouth and exhales forcibly which causes inflation of the lungs and thorax. The operator then takes off his mouth and the process is repeated 10-20 times per minute. It is a positive-

pressure breathing. The respiratory level and volume during this artificial method have been presented in Fig. 287A.

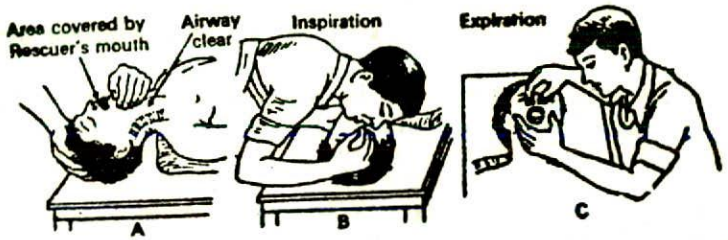


Fig. 286. Schematic representation of mouth-to-mouth artificial ventilation. A = The patient is laid flat on his back on the table (or on ground higher than that on which rescuer stands and under the patient's shoulders some soft article is placed so that the patient's head falls well back. Standing (or kneeling) opposite to the patient's head the rescuer presses with one hand on the crown of the patient's head gently so that the head is fully extened. Other hand is placed on the patient's jaw so that the jaw is drawn well forward. B = Breathing in deeply the rescuer's mouth is placed over the patient's mouth whilst pinching the patient's nose to block the nasal orifice. The rescuer breaths out forcibly into the patient's lungs. [When the patient is child or baby the rescuer should breathe delicately.] C = The patient expires passively and the jaw is kept drawn well forward so that the patient's air passage is alwas kept patent.

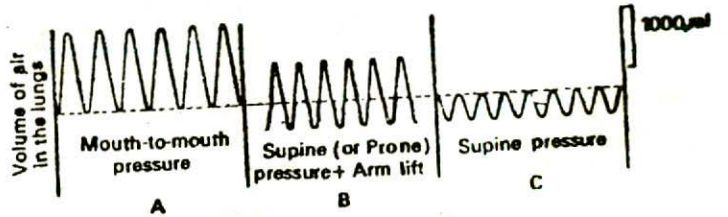


Fig. 287. Graphical representation of pressure of amount of gas during some artificial ventilation showing cessation of respiration in the dotted line.

Eve's Rocking Method. The patient is tied on a stretcher. The head and feet are alternately tilted through an angle of 45°. Eight or nine movements are carried out per minute, 7 seconds for each movement—4 seconds head down and 3 seconds feet down. When the head is down, the weight of the abdominal viscera presses against the diaphragm, so that air is pushed out of the lungs (*expiration*). When the feet are down, diaphragm descends and air is drawn into the lungs (*inspiration*). This method is useful aboard ship when a hammock can be used

II. *Instrumental Method*

Instead of a human operator, machineries are used. The advantage is that it can be carried on for good length of time, whereas the human operator is likely to be fatigued. The machines generally work on two principles: (1) Negative-pressure breathing by

alternately compressing and relaxing the chest wall and (2) Positive-pressure breathing by introducing air or oxygen directly into the lungs—intermittently or continuously.

Some of the methods working on the first principle are as follows :

Drinker's Method (Fig. 288). In this method the patient is placed in an airtight chamber, the head remaining outside. By mechanically driven pumps, the pressure in the chamber is alternately lowered and raised. When the pressure is lowered the chest swells up and air is drawn into the lungs When the pressure is raised chest becomes compressed and air is pushed out. In this way, artificial ventilation may be continued for any length of time. These methods are very useful in cases where prolonged artificial respiration is necessary, such as in morphine poisoning, in paralysis of the respiratory muscles, as in poliomyelitis, pneumothorax and etc. [The so-called iron lungs is an instrument working on this principle.]

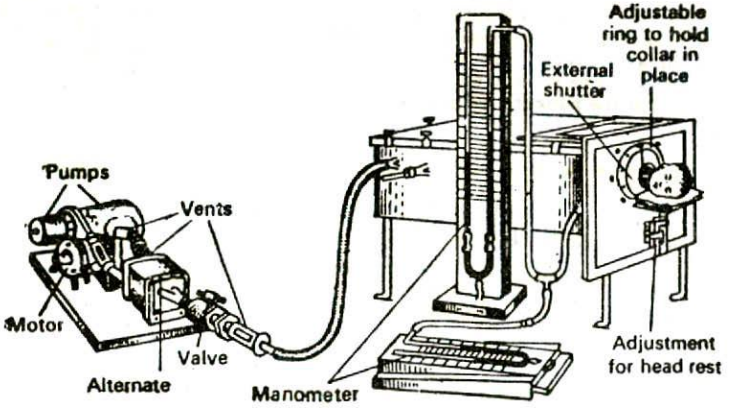


Fig. 288. Drinker's respiration (so-called iron lungs) (after Best & Taylor.)

Bragg-Paul's Method A rubber bag is wrapped round the chest wall of the subject By suitable pumps, pressure in the bag is alternately raised and lowered thus compressing and relaxing the chest wall alternately. In this way respiration is carried out

Some of the methods working on the second principle are as follows :

Continuous Insufflation Method. This method is used in subjects who are to undergo operation requiring opening of the thorax. It is obvious that none of the above methods are applicable here. A thin flexible tube is inserted in the trachea as far as its bifurcation and a constant stream of oxygen (with or without 5% CO_2) is allowed to pass into the lungs, so that lungs remain slightly distended. In this way it is possible to maintain respiration without any movement of the subject.

Intermittent I ıflation Method. This methed is adopted to maintain the respiration of animals during experiments. Various types of apparatus have been designed for this purpose. In the simplest method. a cannula is introduced and tied to the trachea. Warm moist air is driven into the lungs from a rhythmically acting pump. After each blast, the lung collapses and air is expelled through a side tube in the cannula. When artificial gas mixtures are used, a very elaborate apparatus is required.

Tank respirator (Fig. 289 A) : In tank respirator the patient's body is placed inside the tank and his head is protruded through a flexible but airtight collar. Opposite to the patient's head there is a motor-driven leather diaphragm that moves back and forth with sufficient excursion to raise and lower the pressure within the tank. Inward movement of leather diaphragm gets to produce positive pressure around the body and causes expiration ; and outword movement of leather diaphragm produces negative pressur and causes inspiration. In this condition, positive pressure that causes expiration rises to 0 to +5 cm water and the negative pressure that causes inspiration falls to −10 to −20 cm water.

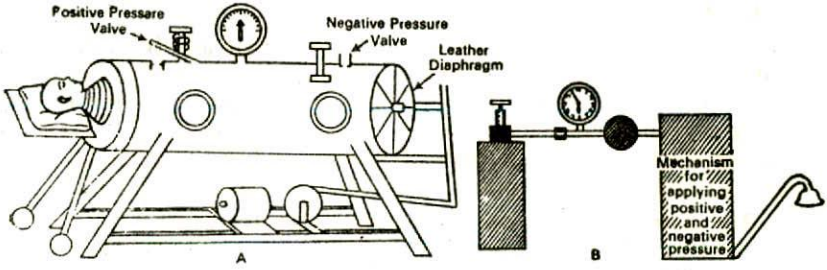


Fig. 289 (after Guyton)

Resuscitator (Fig 289 B). This apparatus forces air through the mask that fits over the patient's face into the lungs of the patient during the positive pressure cycle and then either allows air to flow out the lungs during the remainder of the cycle or pulls the air out by negative pressure. Resuscitator commonly has safety valve which prevents the positive pressure from rising normally about +14 mm Hg and the negative pressure from falling below −9 mm Hg.

In the new-born Baby. Artificial respiration is necessary for those newly born babies, whose respiration is delayed. The methods and principles followed in such cases are as follows : (1) Holding the baby upside dowa (to allow more blood to go to the brain) and putting on the back (reflex stimulation). (2) Alternately putting the child in warm and cold water (reflex stimulation). In the maternity hospitals various other methods are employed wotking on these principles. (3) Pumping CO_2 through the nostrils or mouth into the lungs of the child. This is usually done by forcibly blowing

through the mouth of the child after closing its nostrils. This is supposed to raise the CO_2 tension of blood and stimulate respiratory centres. Mouth-to-mouth resuscitation is quite effective in infants.

8.23. ACCLIMATISATION

(Compensatory changes at moderately high altitude)

The term acclimatisation means the adjustment of the human body to suit the climate at a higher altitude. When the ascent is slow and to a moderate height (betwesn 3000 and 4250 metres or 10,000 and 14200 feet) as in mountaineering, various compensatory processes are mobilised to combat the injurious, effects and the subject is ultimately adapted to the rarefied atmosphere. Some of the changes are *immediate* and others are a little *delayed.*

CHANGES IN ACCLIMATISATION

Changes in the bone marrow. The red marrow proliferates as a result of anoxia. The yellow marrow may be transfomed into red marrow.

I. *Respiration :*

(a) Changes in pulmonary ventilation has already been discussed in detail in page 425vii where it has been shown that the respiratory centre becomes hypersensitive to P_{CO_2} due to long continued anoxia. It has further been shown that in chronic acclimatisation, e.g. in persons residing at high altitude the hypersensitiveness of the respiratory chemoreceptors are more marked than in acute acclimatisation.

Barometric pressure is 440 mm Hg at an altitude of 4260 metres (14,200 feet). So the O_2 pressure in the alveoli is 14% of (440 − 47 =) 393 mm Hg i.e. about 56 mm Hg.

Other changes in respiratory system are listed below :

Vital capacity of lungs increases in those people who live at higher altitude for long.

Diffusing capacity for O_2 through the alveolo-capillary membrane increases. The factors responsible for this change are :

(i) Expansion and dilatation of pulmonary capillaries,
(ii) Increased blood volume,
(iii) Increased lung volume,
(iv) Elevated pulmonary arterial pressure,
(v) The apical part of the lungs which is normally underperfused is adequately perfused during anoxic acclimatisation.

II. *Circulation :*

The right heart hypertrophies so that blood can be effectively pumped through the expanded capillary bed of the lung.

There occurs temporary increase in cardic output. Blood flow through the heart, brain, muscles and other organs is increased at

the expense of blood flow through the skin and kidneys. The blood capillaries of animals exposed to anoxia for a long time get dilated to accommodate the extra blood which is brought in more intimate contact with the tissues.

III. ***Blood :***

2, 3-DPG content of RBC increases.

In acclimatisation the haemoglobin content of the blood increases due to anoxia, the PCV rises and also the blood volume increases often as much as 20 to 30 percent resulting in total increase of circulating haemoglobin by 50 to 90%

IV. ***Cellular acclimatisation :***

Mitochondria and certain cellular oxidative enzyme systems increase in animals exposed to anoxia for a long time. It is presumed that in human beings too intracellular enzyme systems develop in such a way that oxygen can be utilised more effectively.

V. ***Changes in urine :***

Kidneys excrete alkaline urine. Urea content is more and ammonium salts, less. In other words, the ammonia coefficient falls. There is less excretion of acid in the urine. These are attempts to combat alkalosis resulting from hyperventilation.

Natural acclimatisation of natives residing at high altitnde

Natural acclimatisation occurs in natives born and brought up at high altitude. Heighest altitude at which permament acclimatisation

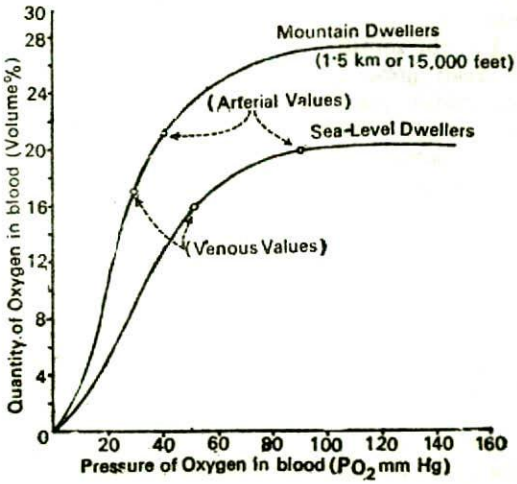


Fig. 289. Oxygen-dissociation curves for blood of high-altitude and sea-level dwellers, showing the respective arterial Po_2 and venous Po_2 and oxygen contents as recorded in their native surroundings (from PAHO Scientific Publication and after Guyton's ***Medical Physiology***).

is possible is perhaps about 5,500 metres or 18,000 feet (Peruvian Andes). The natives of these places have got a short body structure with a large-sized chest giving a high ratio to ventilatory capacity to body mass. The right heart is usually hypertrophied with rather high pressure in the pulmonary artery so as to fill up effectively the expanded pulmonary capillary system.

The mechanism of O_2 transfer in these natives is also highly effacious and has been compared with that of an unacclimatised subject in the accompanying diagram (Fig. 289):

The dissociation curve for the person residing at high altitude shows:

(1) low Po_2 (40 mm Hg) of the arterial blood compared to 100 mm Hg of the person at sea-level.

(2) In spite of the low pressure—the O_2 content of the arterial blood is higher than that of the person at sea-level because of high haemoglobin content.

(3) Venous Po_2 of the high altitude natives is only 10 mm Hg lower than those of the sea-level dwellers despite the low arterial Po_2. The fact is that the oxygen consumption of the high landers is usually higher in comparison to that of sea-level residents there cannot be any doubt the tissues of the naturally acclimatised person can utilise oxygen more effectively.

In Peruvian Andes coal mines are situated at an altitude of about 5800 metres or 19,000 feet whereas the workers in the mine live with their families in a township at an altitude of about 5,500 metres or 18,000 feet. It has not been possible to persuade the workers to live permanently at about 5,800 metres or 19,000 feet in neighbourhood of the mines. They complain that at that altitude they do not keep good health and that they cannot sleep well at night, do not relish their food and that they develop also sexual weekness. About 5,500 metres or 18,000 feet altitude may be taken to be the limit of human tolerance and the altitude where permanent acclimatisation is possible. The natives born and brought up here are supirior to the best acclimatised low landers in the following respects:

The chest-size is increased where as body-size is somewhat decreased giving a high ratio of ventilatory capacity to body mass.*

The right heart of these persons is considerably hypertrophied to provide a high head of pressure in the pulmonary arteries so that blood can circulate through a greatly expanded pulmonary capillary system.

The RBC count and so the haemoglobin content and oxygen capacity of the blood is high so that even though the arterial Po_2 is low the O_2 content of the arterial blood is higher than those living at lower altitudes.

*The same has been observed in Tensing Norgay and other mountaineer Sherpas of Himalayan Mountaining Institute.

The O_2 content of the mixed venous blood is also higher though its percentage saturation is only slightly less than those living at lower altitude.

In all probability acclimatisation also occurs at cellular level the exact nature of which is not properly understood. It is, however, known that the power to utilise oxygen in the natives of high altitude is higher and that the efficiency of muscular work of these persons is by no means less than those living at sea-level.

Acute mountain sickness :

Sometimes a well-acclimatised mountaineer may develop acute illness due to failure of compensatory adjustments to high altitude. The following effects are noticed—(1) The red cell mass and PCV are elevated considerably. (2) Pulmonary arterial pressure becomes very high and the right heart failure supervenes. The peripheral arterial pressure begins to fall and death occurs due to acute pulmonary oedema which aggravates the anoxic situation. Most of the patients recovers if brought promptly to a lower altitude and oxygen is administered.

Maj. Joyal, a veteran mountaineer, and the founder principal of the Himalayan Mountaineering Institute at Darjeeling died of acute sickness described above.

8.24. MOUNTAINEERING

Mr. Tenzing Norgay's ascent of Everest (about 8,825 metres or 29,028 feet) along with Mr. Edmund Hillary provided a great impetus to mountaineering and it was to commemorate this signal success, a special institute named as Himalayan Mountaineering Institute was established in Darjeeling in 1954. With the setting up of this institute mountain-climbing in India has become a source for scientific studies. Physiologists have studied different physiological changes which occur at hight altitude. The heights at which symptoms of altitude sickness actually start or physiological changes which manifest themselves are not common to all men. Generally within 3,050 metres (10,000 feet) there is no additional O_2 necessary. It has however been noticed that in most cases breathing becomes laboured at about 3 600 metres (12,000 feet). At about 5,500 metres (18,000 feet), there is definite panting and other symptoms of altitude sickness or mountain sickness appear and additional O_2 is necessary. It is not possible to maintain steady acclimatisation beyond 5,500 metres or 18,000 feet and often deterioration occurs at an altitude of about 6,600 metres or 22,000 feet and pure O_2 must be inhaled continuously.

It has been observed in the aptitude tests of flyers that acclimatisation is easiest between the ages of 30 and 40 years. In these ages there is increased of general efficiency, better circulation and less vesolability.

Mere physiological adaptation is not enough, phychological adaptation plays a vital part. Mental make-up, loss of sleep,

deteriorating physical condition and the rarefied atmosphere are contributory factors. Beside these there are nutritional problems, namely total intake of calories, the fluid balance, etc. have to be taken into account. The effect of extreme cold is another very important factor in mountaineering. Abrupt changes in weather cause abnormalities in regulation of circulation and of body temperature. Sometimes this stress along with exertion of mountain-climbing causes fatal circulatory crisis. The mountaineers who succumbed during ascent developed headache, nausea, vomiting, difficulty in breathing, pain in the chest, rapid pulse, high body temperature, ultimately loss of consciousness, etc.

8.25. ATMOSPHERE

(High Attitude Physiology)

The atmosphere surrounding the earth may be divided into four layers according to their physical characteristics :—

I. **Troposphere** is the lowest and the most dense layer in direct contact with the surface of the earth and extending upwards for about 5 miles on the equatorial region and 10 miles over the poles. About 50% of the weight of the atmosphere is due to weight of the air in the first 3·5 miles in the troposphere. The density of air in this region ensures easy respiration, and also helpful in aeroplane flight and acts as a protective layer for ultraviolet and other radiations from space. Further, most of the meteors are burnt into ashes by friction with this dense layer.

Tremendous amount of heat is generated during takeoff and landing of the spaceships due to friction and special devices are employed for temperature regulation during journey of spaceships through this layer.

The troposphere contains minute particles of dust and also water vapour in varying proportions which condense to form cloud. Rain, storms and thunderstorms are characteristically located in troposphere only. The atmosphere gets colder and colder as one ascends higher and higher so that at the upper level of troposphere or the lower level of stratosphere the temperature is about −50°C.

2. **Stratosphere** commences where the troposphere end and extends for about 50 miles.

Stratosphere is isothermal—the average temperature being −55°C and is free from any air turbulance. This region is ideally suited for aeroplane flight.

3. **Inosphere** extends for a distance of about 200 miles above the stratosphere. This layer is so called because molecules of gases here exist in an ionised state due to action of ultraviolet light. The temperature of the particles is about 3000°C and they move with tremendous velocity. The particles however are so few that a spacecraft moving through this zone do not come in contact with

them and the temperature of the craft is regulated by radiation it receives from the sun and the heat it re-radiates into the space. This layer is rich in ozone and is responsible for reflection of shortwave radio to distant places. This is the most important layer in protecting us from the baneful effect of cosmic rays.

4. Exosphere is the atmosphere extending for about 600 miles above inosphere and merging imperceptably into the space.

The problems which an aviater have to face are disscussed below :

I. Anoxia :

Alveolar Po_2 at different altitudes due to low barometric pressure has been discussed in page 394. It has also been shown that above an altitude about 3 km or 10,000 feet the alveolar Po_2 falls rapidly accompanied with desaturated of arterial blood with oxygen. At an altitude of about 12 km or 40,000 feet the arterial blood is only 5% saturated with oxygen. The fall in alveolar Po_2 is due to factors which may be enumerated again (1) fall in inspired air Po_2 dependent on fall in barometric pressure. (2) Occupation of alveolar space by N_2 which is an inert gas and enters the alveoli in quantities about 4 times that of oxygen during each inspiration. (3) CO_2 which is produced metabolically and exerts a tension of 24 mm Hg at high altitude due to hyperpnoea. (4) Water vapour which exerts a tension of 47 mm Hg at all altitudes. It will be seen, therefore, that the $Pco_2 + P_{H_2O}$ amount to 71 mm Hg and is always to be deducted from the total available gas pressure in the alveoli which is equal to the ambient barometric pressure. The gas pressure remaining after deduction will be distributed to O_2 and N_2 of which about only 14% will be Po_2 and the remaining P_{N_2}. Nitrogen in the alveolar air (but not the CO_2 or H_2O vapour) can be replaced by O_2 by oxygen inhalation and thereby the alveolar Po_2 can be increased at any altitude to the approximate value of combind $Po_2 + P_{N_2}$ of the alveolar air at that altitude. The table below gives the barometric pressure, the values of alveolar Po_2 and arterial O_2 saturation at different altitudes with and without inhalation of oxygen.

Altitude (feet)	Bar. Pr. (mm Hg)	Alveolar O_2 Tension (mmHg)		Art. O_2 Sat.(vol%)	
		without O_2	with O_2	without O_2	with O_2
0	760	104	673	97	100
3 km or 10,000	523	67	436	90	100
6 km or 20,000	349	40	262	70	100
9 km or 30,000	226	21	139	20	99
12 km or 40,000	141	8	58	5	87
15 km or 50,000	87	1	16	1	15

The figure 290 shows the value of arterial oxygen saturation at different altitudes (1) without oxygen (left hand) and (2) with O_2 right hand curves.

The data and the curve indicate that inhalation of pure O_2 will keep the arterial blood 90% saturated with oxygen upto an altitude of 11·7 km or 39,000 feet. It then falls rapidly so that at an altitude

of 14 km or 47,000 feet the arterial blood is only 50% saturated in spite of O_2 inhalation. 50% arterial saturation is the point where consciousness is soon lost. Without oxygen this limit is reached at 7 km or 23,000 feet. The rule in aviation, therefore, is that with supply of pure oxygen one can ascend upto an altitude about 12 km or 40,000 feet. Above that point a pressurised cabin will be necessary.

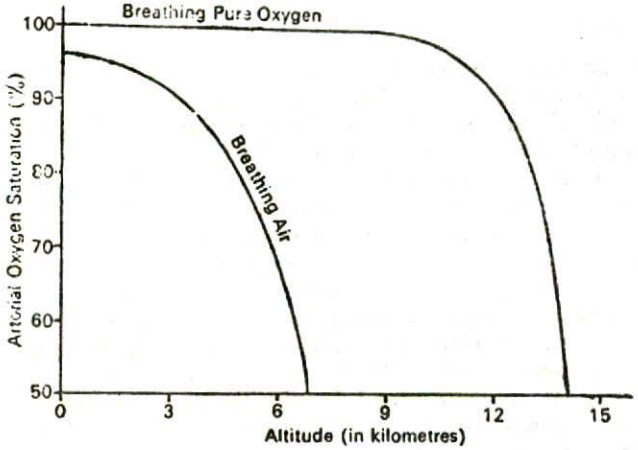


Fig. 230. Effect of low atmospheric pressure on arterial oxygen saturation when breathing pure oxygen on the alvedar Po_2 at different altitudes.

Radiation Hazards :

About 20% of the sun's rays are filtered by the atmosphere before hey reach the earth. Brightness of the sun increases, therefore, by $\frac{1}{5}$th at the upper atmosphere and from above the earth appears less distinct for 2 reasons :

(1) One is looking at a less bright object from a more bright area.

(2) Reflection of light from the atmosphere blocks the vision of the horizon.

It has already been mentioned that most of the UV radiations and cosmic rays are absorbed by the upper atmosphere.

The cosmic particles consist mostly of electrons and protons and are aggregated in two zones, viz. Van Allen's inner belt and outer belt respectively. The inner belt extends at an altitude from 300 to 3000 miles (about 480 to 4825 km) around the equator and consists mostly of high energy protons and electrons and since its energy level is high it is not possible to protect a spacecraft from its penetrating effect.

The outer belt is situated between 6000 and 20,000 miles (7650 and 32200 km) around the equator and consists almost entirely of electrons.

These belts are to be avoided during space travel. For orbiting round the earth the space craft should be kept below at altitude of 300 miles or 480 km that is the inner radiation belt (Fig. 290A) of Van Allen. For interplanatory travel—the spaceship should leave the earth through the polar escape route

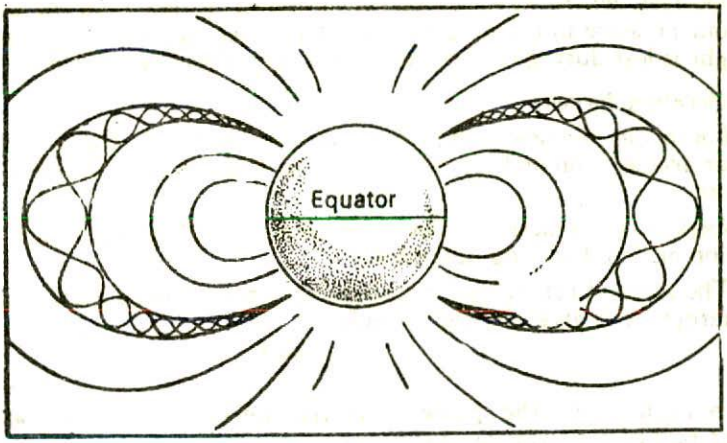


Fig. 290A. Diagrammatic representation of the hazardous radiation belts of Van Allen around the earth.

Dysbarism at high altitude (Decompression sickness)

The problem of sudden decompression has been discussed in detail in page 425xxiv and it has been pointed out there that dysbarism is more common in Caisson workers during rapid decompression than in aviators. It may occur in aviators during rapid ascent to an altitude of 9 km or 30,000 feet in an unpressurised aircraft. Since now-a-days pressurised planes are always used especially during high altitude flight decompression sickness ordinarily should not occur in aviators unless the aircraft is damaged leading to sudden failure of cabin pressure at an altitude of about 9 km or 30,000 feet. Parachute jumping from that altitude or above may also cause decompression sickness and the aviators usually wash off the N_2 in their system as much as possible by taking several deep breaths of oxygen, before the jump. In fact, now-a-days parachute jump is also effected in a sealed capsule with adequate oxygen to prevent dysbarism.

Explosive decompression

Sudden decompression from sea-level pressure to low barometric pressure of an altitude of 15 km or 50,000 feet or over do not cause any damage to the system and with little practice human

beings can tolerate this explosive decompression without much discomfort. Air in the cavities, e.g. the middle ear is expelled through the eustachian tube, the air in the colon is expanded and is expelled out as flatus, air in the stomach is belched out, air in lungs excapes through the open glottis. Subsequent X ray examination of the chest reveals partial atelaectasis in some parts of the lungs in a few subjects.

Boiling of body fluids occurs on exposure to an altitude of 63,000 feet where the barometric pressure is less than the water vapour pressure in the lungs (47 mm Hg). About 2% of the body weight is lost during the 3-minute time the subject remains alive.

Acceleratory forces

Linear acceleration :—At the commencement of flight simple linear acceleration and the termination of flight linear deceleration occurs.

Angular acceleration :—During turning on plane or 'loop' formation or dive bombing operation.

The force of centrifugal acceleratory force (F) during turning of an aeroplane is given by the formula :

$$F = \frac{mv^2}{r}$$

where m mass of the plane, v is the velocity of turning and r is the radius of curvature of the turn.

It may be noted that the force of angular acceleration increases with the square of the velocity, i.e. if the velocity is doubled the force will increase 4 times. The force also varies directly as the sharpness of the turn ($1/r$)

Acceleratory force—'G' unit :

When a man is sitting on his chair the intensity of the force exerted on his seat by the weight of his body resulting from the pull of gravity called 1 'G'. If the force with which he presses against his seat becomes 4 times his normal weight such as during pullout from a dive—the force acting on his seat and body is equal to 4 G.

During outside loop formation the pilot is to be held down to his seat by belt and a force of negative G acts upon his body from foot to head direction. The magnitude of this force may be -1G or -2G, etc. depending on its intensity.

Effect of centrifugal acceleratory forces

I. **Circulamion** :—Blood by virtue of its fluid nature can be easily translocated along the long axis of the body. When the human body is subjected to positive 'G' force acting from head to foot direction—the blood is translocated to lower parts of the body resulting in rise of pressure of veins of the lower limb and stagnation of blood in that situation. When the centrifugal acceleratory force is $+4$G or over the venous pressure in the lower limbs in the

standing position is approximately 400 mm Hg and stagnation of the blood in the lower parts of the body results in fall of inflow to the heart followed by diminished cardiac output and consequently the blood pressure falls to a very low level. The accompanying diagram (Fig. 290B) shows the relationship between the 'G' force and blood pressure. It may be seen that with a force of +4G acting on the body the systemic blood pressure falls to 40 mm Hg. This causes at first retinal anaemia leading to 'blackout' followed almost immediately by cerebral anaemia leading to unconsciousness. Such a situation is faced by pilots during 'pullout' of the dive bombing operations and can be avoided by adopting appropriate posture (knee and hip bent position) and by wearing proper type of suits called anti-G suits which maintains a firm pressure on the lower limbs and abdomen preventing accumulation of blood in these areas. However with the release from '4G' forces, as happens normally during dive bombing the consciousness is soon regained and the vision is restored to normal. Mental confusion persists for some time during which the plane may go out of control.

Extremely high positive acceleratory forces, e.g. +20G lasting for fraction of a second will cause fracture of vertebrae.

Since negetive G forces act from foot to head direction blood is translocated towards the brain and as shown in Fig. 290B the blood pressure at the heart level may be as 400 mm Hg with a force of −12G acting for few seconds This causes extreme bradycardia from baroreceptor reflexes. Rupture of the subarachnoid vessels in spite of severe hypertension occurs much less frequently than expected because translocation of c.s.f. also occurs towards the head region which buffers the effect of hypertension on cerebral blood vessels. Extreme congestion of the blood vessels of the eye with temporary 'redout' is a common feature. Mental confusion is lik[illegible] for some time after the negative G forces have ceased to ac

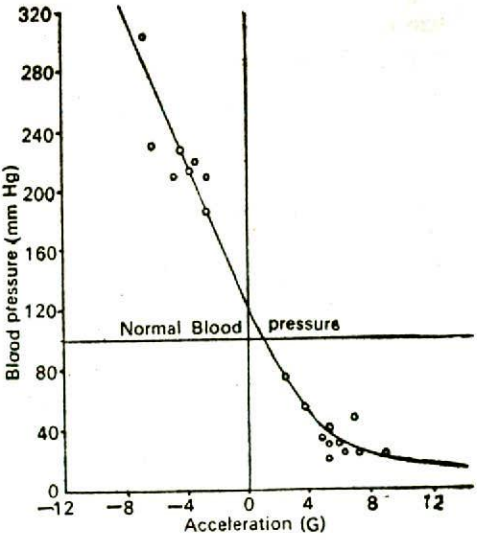


Fig. 290B. Effect of angular acceleratory forces on arterial pressure measured of the heart (from Armstrong Principles and Practice of Aviation Medicine).

Transverse G forces acting through the antero-posterior axis of the body will not produce any ill effect ordinarily. Thus a force of 15G to 25G acting for many seconds or a force of 100G acting for fraction of a second can be tolerated easily. When very large acceleratory forces are to be faced the astronauts should place himself in a semi-reclining or lying position.

Protection of body against centrifugal acceleratory forces

I. Posture—If the aviator compresses his abdominal muscles to an extreme degree and then leans forwards with the knees flexed and drawn up pooling of blood in the large vessels of the abdomen and legs can be prevented to some extent and onset of blackout delayed.

II. 'Anti-G' suit prevents pooling of blood to lower part of the body. Theoretically, a pilot with a suit of water can withstand large acceleratory forces both positive and negative because the movement of water in the suits will counterbalance almost exactly the movement of blood. Suits have been devised which prevents pooling of blood to the lower part of the body by applying positive pressure to the legs and abdomen.

It has been said that the Germans lost the last Great war because they failed to devise appropriate 'anti-G' suits.

Effect of linear acceleratory forces on the body

The problem of toleration of tremendous linear acceleratory forces develops during blast-off acceleration and landing deceleration of the spaceships. A force of about +9G develops during the first stage booster and +8G during the second stage. It is not possible for human body to withstand these acceleratory forces in the standing position. Astronauts, therefore, assume a semi-reclining position transverse to the direction of acceleration. It is possible to tolerate this force for as long as 5 minutes or longer the G force acts through the transverse axis of the body.

Deceleration during landing poses another difficulty. It must be accomplished much more slowly from high velocities and deceleration should commence at a distance of 10,000 miles (about 16,000 km) for a space craft travelling at a speed of 100 Mach (a speed possible in interplanetary space travel).

Sense of position and equilibrium

The utricle and saccule and the 3 pairs of semicircular canals are primarily concerned in perception of the sense of position of the head in relation to space and trunk and also in angular rotation of the head in difference direction. These organs reflexly adjusts posture and equilibrium by altering the position of the body in relation to the position of the head through their elaborate connection with vestibular nuclei, flocculonodular lobe of the cerebellum and the red nucleus, reticular formation and medial longitudinal fasciculus. These organs have been described elsewhere.

The sensory epithelium of the utricle and saccule is known as macula and consists of rows of sensory hair cells embedded in gelatenous mass and pulled by calcareous particles in different directions depending on different position of the head. They are, therefore, typical gravity receptors and fail to function in zero-G state. Further, they are not stimulated unless the head leans forwards by at least 10 degrees or backwards by 25 degrees. These respectors, therefore, are very inefficient and their evolution lags far behind the requirement of rapid change in position demanded by modern aircrafts. Aircrafts, therefore, are provided with appropriate instruments to keep the aviator informed about the rapid ascent and descent, during flight. This is, of course, more important during night flight.

The sensory epithelium of the semicircular canals is simulated during angular rotation of the head due to inertia of the endolymph. They, however, are stimulated at the beginning and at the termination of rotatory movement and remain inactive during rotation. Further, the rotational movement must exceed 2° per second per secand to stimulate effectively the semicircular canal mechanism. These organs, therefore, are also very inefficient organs for perception of rotatory movement demanded by modern aircraft manoevers. The aviator again must depend on his instruments for proper appreciation of this movement during flight.

Parachute Jump :

When a aviator jumps with a parachute he falls with an accelerated velocity of 16 feet per second per second. However as his velocity of fall increases the air resistance also increases because the atmosphere becomes denser and denser. After about 12 seconds the deceleratory forces due to atmosphere counter balances the acceleratory forces due to gravity and by the time the aviator has fallen by about 4·25 km or 1400 feet, he acquires a constant rate of fall, of about 55 metres or 175 feet per second. This is called terminal velocity (Fig 290C).

By this time either the parachute opens spontaneously or is opened voluntary by the aviator by pulling on the ripcord. With usual size parachute the terminal velocity is reduced to about 6 m or 20 feet per second and the force of impact with the ground is reduced to $\frac{1}{81}$th without the parachute. This force of impact is actually the same as experienced by one jumping from an hight of 7 feet and in untrained subjects is severe enough to cause fracture of the leg bones and the pelvis.

An aviator jumping from a very high altitude will certainly be unconscious immediately after fall due to acute anoxia and will regain his consciousness when he has decended to an altitude of about 7 km or 23,000 feet. His mental confusion will persists for a few seconds but if he is provided with a parachute with automatic opening device he will have safe landing on the earth.

Another hazard of parachute landing is injury from the damaged plane. Usually the tail-end of the plane hits the head of jumper causing serious injury. To avoid this hazard now-a-days pilots of military planes are provided with a device so that they enclose themselves in a sealed capsule filled with oxygen. The capsule is fitted with the seat of the pilot which is ejected upwards by pressing a lever so that the pilot lands safely after the damaged plane has cleared off and also is protected from anoxia and cold.

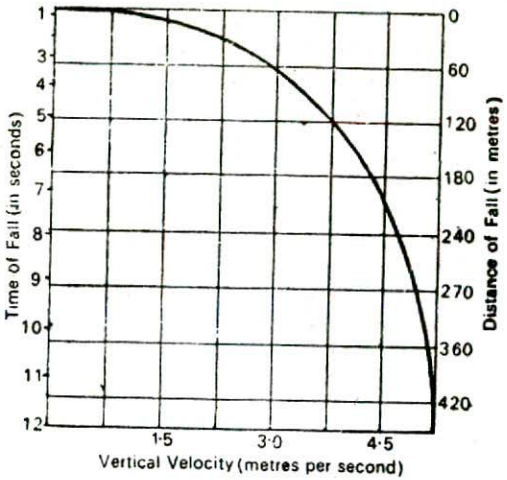


Fig. 290C. Velocity of fall of a human body from a high altitude, showing the attainment of a terminal velocity. Deceleratory forces associated with Parachute Jump (from Armstrong's Principles and Practice of Aviation Medicine—The Williams Co. 1943).

Weightlessness in space (zero-G state)

An astronaut in an orbiting sattelite experiences weightlessness because a component of the force applied to his spaceship is utilised to counteract the effect of gravity and another component is used to keep the spaceship in the orbit. Weightlessness may also occur in journey to the moon or other planets because there exists in space an area where the gravitational pull of the earth is counterbalanced by that of the moon or other planets acting in opposite direction. An astronaut in weightless state simply floats in his cabin and it becomes a problem for him to take food or to dispose his excreta in the desired way because these substances like the astronaut himself have got a tendency to float and move in any direction because they has no weight. It is an engineering problems to device means by which the astronaut may keep himself steady and can work for control of the spaceships.

Biological problems of 'zero-G' state are :

(1) Translocation of body fluids within the body because absence of gravity causes loss of hydrostatic pressure.

(2) Loss of muscle tone—which is normally reflexly maintained by gravity receptors This, of course, diminishes strength of muscular contraction and results in clumsy and often useless voluntary movement.

Prolonged stay in space results in

(1) diminished maximmuum cardiac output.
(2) decreased capacity to do work.
(3) decreased PCV.
(4) decreased blood volume.
(5) Osteoporosis—due to decalcification.

The changes are most marked during the first week of stay in space and fortunately is not progressive. These changes can be seen in any patient with prolonged stay in bed. These changes can be avoided to a considerable extent by vigourous exercise programme during space journey.

8 26. UNDERWATER PHYSIOLOGY

It is known that the hydrostatic pressure of water increases by 1 atmosphere for each 33 feet or about 10 metres increase in depth of water so that a person submarged to a depth of 10 metres will be exposed to a pressure of 2 atmospheres (atmospheric pressure + hydrostatic pressure). Similarly a diver at a depth of 66 feet or about 20 metres will be exposed to a pressure of 3 atmospheres and one at 100 feet or 30 metres depth to 4 atmospheres, in this case 1 atmospheric pressure is due to air and the rest due to water.

The gases in his lungs, gastrointestinal tract, air sinuses, etc. which were originally at 1 atmospheric pressure will be compressed in accordance with Boyle's law. According to this law, if the volume of a given mass of gas is reduced, the molecules are brought closer together and the rate of bombardment upon a unit surface increases, the increase becoming manifest as a rise in pressure For instance at a depth of 10 metres below the sea the volume of air in his lungs will be half that at sea-level. The respiratory gases will, therefore, be at high pressure in the lungs, in the blood and in the tissues with undesirable side effects. The three gases of primary concern in respiration are N_2, O_2 and CO_2. Helium is sometimes used in place of nitrogen in respiratory gas mixture. The effect on body of these gases under high pressure are as follows :

Nitrogen : A diver beneath the sea breaths compressed air—the pressure of which must be equal to the atmospheric pressure *plus* the hydrostatic pressure of the column of water below which the diver is working. Nitrogen, if breathed at high pressure for some hours, leads to varying degrees of 'narcosis' which increases as the depth increases and so the pressure of the gas increases. At greater depths there occur mental confusion and muscular weakness, till at a depth of 300 feet (about 90 metres) or more (10 atm) the diver becomes comatose.

The mechanism of nitrogen narcosis is perhaps due to interference with transmission of nerve impulses in the brain and nerve tissues in general which are exceedingly rich in lipids. Since nitrogen is highly soluble in lipids the nerve tissues get saturated with nitrogen which interferes with excitability and transmission of nerve impulses.

Oxygen : High pressure of oxygen has got deletorious effect on nervous system. Breathing oxygen at a pressure of 2280 mm Hg (3 atm) will lead to convulsion and coma in most persons within an hour. At lower Po_2 numbness and pins-and-needle sensations, restlessness and irritability, muscular twitching, nausea are common symptoms. Muscular exercise greatly accelerates the appearance of toxic symptoms in divers exposed to high Po_2.* Fig. (290D) shows the tolerence curve of persons doing moderate amount of work at different depths breathing pure oxygen. The curve shows that the time limit for safety is 23 minutes at 12 m or 40 feet, 45 minutes at 9 m or 30 feet, and $1\frac{1}{2}$ hour at 6 m or 20 feet depth. However, the toleration curve is a rough guide only because of great interindividul and intraindividual variation.

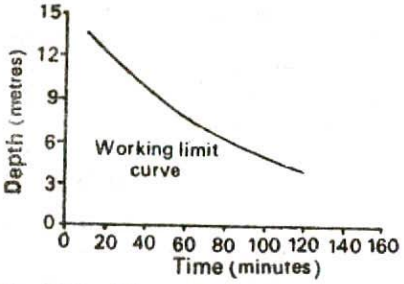


Fig. 290D. The oxygen tolerance curve, depicting the length of time that a subject can remain without danger at different depths when breathing pure oxygen (after Guyton).

Chronic oxygen poisoning may occur by inhaling pure O_2 at *normal* atmospheric pressure—and is characterised by congestion and oedema of respiratory passages. The epithelium of the bronchi and alveoli are damaged by direct contact with 100% oxygen for more than 12 hours at a stretch. The lung tissues are damaged locally due to disruption of some of the essential elements. The damage in this case is limited to lung tissue and respiratory passage epithelium—the brain and other tissues are protected by haemoglobin which buffers oxygen. When the Po_2 rises above 2 atmospheres —the haemoglobin buffer mechanism fails—the Po_2 of all the tissues rises and acute poisoning symptoms with convulsions and coma precipitated.

*During the last Great War elaborate experiments were done to perfect respiratory gas mixtures for divers operating for "human torpedoes", 'x-crafts' and 'frogmen' (Fig. 290E). It was soon realised that pure oxygen can be used only for very shallow diving. It was further observed that diluting the oxygen with nitrogen will allow the divers to work at a depth double that was possible with the use of oxygen only.

Mechanism of oxygen poisoning :

Oxygen at high pressure inactivates enzymes containing –SH groups in the Kerbs tricarboxylic acid cycle. Conversion of pyruvic acid to acetyl co-enzyme A and of α-ketoglutaric acid to succinyl-CoA requires lipoic acid as a co-factor, which contains to–SH

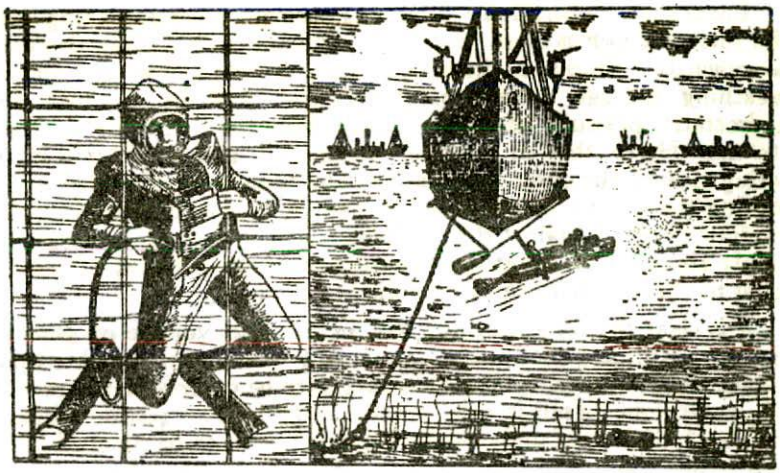


Fig. 290E

groups. Oxygen at high tension inactivates the lipoic acid complex and thus prevents the formation of high energy phosphate bond from oxidation of pyruvic acid via the Krebs cycle.

Carbon dioxide : The P_{CO_2} in the alveoli depends solely on metabolic activity and is independent of the depth of dive. Thus if the tidal volume is adequate and the design of the diving gear is perfect CO_2 should not accumulate in the body. In certain types of respiratory apparatus, however, the expired CO_2 accumulates and is rebreathed by the diver. If the P_{CO_2} rises to about 80 mm Hg in the breathing apparatus compensatory hyperpnoea developes and the blood P_{CO_2} is kept near normal. Any further rise in P_{CO_2} of the respiratory apparatus cannot be compensated for by hyperpnoea and alveolar and blood P_{CO_2} begins to rise. This results in depression of respiration, lethergy, finally coma and death from respiratory acidosi

Helium is often used as a substitute for N_2 by the deep sea divers because of the following advantages :

(1) Unlike N_2 it exhibits no narcotic effect even at depths below 650 feet (about 200 metres).

(2) Because of its low density it offers comparatively little airway resistance and as such is easier to breath

(3) Because of its low atomic weight it diffuses more rapidly than nitrogen through the body tissues and also is removed more quickly from the body during decompression after a long dive.

(4) Helium is less soluble than N_2 in the body fluids which reduces the quantity of bubbles than can form in the tissues of the diver during decompression after a long dive.

Underwater respiration—Breathing through tubes extending upto the surface becomes more and more difficult as the diver descends downwards. Thus at a distance of only 5 feet below the surface breathing through a tube becomes very difficult because the hydrostatic pressure of water at this depth will be higher than 100 mm Hg so that an external pressure of about 860 mm Hg is acting around the chest of the diver. The pressure at the inlet of the tube on the surface of water is 760 mm Hg. It is difficult to make respiratory effort against this gradient. It is, therefore, necessary to supply air or other breathing mixture through tubes at a pressure equal to the external pressure applied to the body.

It is clear that at a depth of say 33 feet the volume of gases in the lungs will be ½ that of the normal and to maintain adequate tidal volume double the amount of tidal level is to be pumped in to prevent CO_2 retention. Thus if tidal volume is 0·5 litre at rest on surface, at a depth of 33 feet under water 1 litre of air is to be pumped in at each stroke. Since in the situation under discussion the environmental pressure around the diver is 2 atmospheres the partial pressure of the gases in the alveoli will also be approximately doubled. The blood gas tension will initially remain unchanged since blood is incompressible. The alveolar Po_{O_2} will, therefore, be higher than that of the venous blood coming to the lungs and CO_2 will diffuse from the lungs to the blood. To prevent the accumulation of CO_2 hyperventilation will be necessary, before and during the diving operation. Oxygen, with much Po_2 in the lungs will always pass from the lungs to the blood. However, during rapid ascent there is a chance of Po_2 being lower in the lungs than in the blood and so oxygen may diffuse in the reverse direction (i.e. from blood to lungs) producing acute anoxia and unconsciousness.

Associated hazards are those affecting the circulation and blood pressure. At a depth of 33 feet the absolute systolic blood pressure will be (1520+120=)1640 mm Hg. In order to see clearly under water it is necessary to wear a face mask. If goggles only are worn the blood pressure in the blood vessels of the eye will be greater than that of the pressure of air trapped in the goggles and conjunctival haemorrhage will occur. At greater depths the eyes may bulge out with serious injuries unless masks are worn so that the environmental pressure outside the eyeball counteracts the high level of *absolute* blood pressure in the orbital and retinal blood vessels.

A mixture of 98% helium and 2% oxygen has been found useful

for divers working at depths between 400 and 1000 feet. At this range of great pressure nitrogen is poisonous and only 1 to 2% O_2 in the breathing mixture is enough to maintain sufficient oxygen tension in the alveoli. In spite of the advantages of helium noted above, at this high concentration it changes the quality of the voice and makes it high pitched and squeaky and speech communication becomes difficult, particularly on telephone with the surface. Temporary inhalation of nitrogen is helpful in restoring the quality of the voice. Aquanauts may come out of especially designed underwater craft and work for long period at the ocean floor. Helium under pressure conducts the body heat rapidly and as such maintenance of body temperature is an additional problem under these conditions.

Squeeze occurs during rapid descent when volume of all the gases in the body becomes greatly reduced due to increased pressure outside the body. 'Squeeze' affects the lungs very adversely and even if a diver commences to dive with a full inspiration his chest begins to cave in at a depth of about 100 feet. The only way to avoid it is to breath additional volume of air during descent.

During rapid ascent there is risk of overexpansion of the lungs and if the glottis kept closed the pressure of air in the lungs may go up to such an extent as to cause rupture of the pulmonary capillaries This may be followed by air embolism and depth

Decompression sickness has already been described in page 425xxxi. It has been pointed out that release of nitrogen bubbles dissolved in body fluids and especially in the nerve tissues are responsible for the symptoms which may in some instances be very severe and lead to death. The only means by which decompression sickness can be avoided is slow and gradual decompression, remembering that in cases of prolonged dive under the sea most of the nitrogen remains in solution in fats and lipids and is released very slowly on decompression. Obviously the time required for decompression depends on two factors, viz. :

(i) The depth to which the diver has descended.
(ii) The time he has been exposed to the heavy atmosphere.

Decompression tables have been prepared by U. S. Navy to control the process. For instance a diver who has worked at a depth of 190 feet for 1 hour will need decompression in different stages lasting 3 hours.

SCUBA diving : SCUBA (self-contained underwater breathing apparatus) or aqua-lung is now popularly used by professionals as well as sport divers. The hazards of decompression sickness and inert gas narcosis occur. Unconsciousness and collapse may also supervenne. Lung rupture and consequent air embolism may ensue if the divers ascend without exhailing. Under these circumstances the much expansion of volume of gas in the lungs

causes the alveolar walls to tear and as a result air escapes into the pulmonary veins and thence to the cerebral and coronary circulation.

Scuba works on 'open-circuit' principle which means that the expired air is expelled into the sea water. 'Close-circuit' apparatus has also been developed where the O_2 of the expired air is used over and over again after removal of the CO_2 by CO_2 absorbent They resemble the anaesthetic Boyle's apparatus without the anaesthetic gas. The limitation of the close-circuit system is intolerance to pure oxygen. The safe rule is *not more than 30 minutes at 30 feet depth with oxygen alone.*

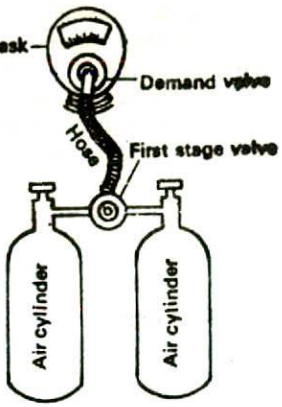


Fig. 290F. The SCUBA apparatus or *Aqua-lung*.

In Fig. 290F, air cylinders are made of special alloy and are light but can withstand light pressure of compressed air.

First stage valve reduces the pressure from the tank to a constant flow pressure level.

Inspiratory and expiratory demand value which allows air to be inspired with very slight negative pressure and then to be expelled into the sea.

Mask and a tube system with minimum dead space.

Shallow water black-out is generally happened in relatively shallow water, viz. swimming pool where the victim becomes unconsciousness during ascent from a breath-hold dive. As he ascends the ambient pressure falls, and the alveolar, therefore, arterial, Po_2 becomes so slow that the subject loses consciousness. The subject can stay submerged for a long time until the arterial Po_2 falls to a low level and stimulates breathing. A diver may hyperventilate before a dive to reduce the ventilatory dive caused by CO_2 accumulation.

8.27. ROLE OF PROSTAGLANDINS ON RESPIRATORY SYSTEM

PGE_1 and PGE_2 relax human bronchiolar smooth muscle and increase pulmonary blood flow, while $PGF_{2\alpha}$ contracts bronchiolar smooth muscle and inhibits the bronchodilating effect of isoproterenol This has led to the hypothesis that palmonary synthesis and release of PGE may be clinically sign ficant in producing increased pulmonary blood flow in response to hypoxia. Furthermore, certain states of bronchial asthma may be caused by a reduced PGE

PGF ratio, leading to bronchial vasoconstriction. The mechanism whereby PGE produces bronchial dilatation differs from that of isoproterenol since PGE is devoid of β-adrenergic stimulation. Theoretically, PGE's could be very useful in the treatment of asthma since they are metabolised by the lung and would not have the cardiovascular side effects associated with β-adrenergic stimulants.

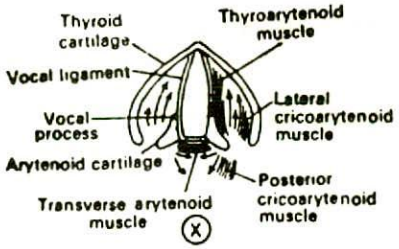
8 28. VOCALISATION

Two seperate processes are involved in vocalisation, viz. :
I. Phonation. II. Articulation.
The whole process is dominated and co-ordinated by speech centre in the cerebral cortex, damage to which will lead to permanent aphasia.

Phonation is due to vibration of vocal cords which are folds stretched along the lateral wall of the larynx between thyroid and arytenoid cartilages. These are positioned by and their tension is regulated by the intrinsic muscles of the larynx.

The relevant intrinsic muscles (Fig. 291X) and their mode of action are :

(1) *Thyroarytenoid muscle* is made of many small slips of muscle fibres controlled seperately by different nerve fibres. The contraction of these muscles fibres independently of each other are responsible for control of shape of vocal cord, thick or thin or with sharp and blunt edge during phonation of different types (Fig 292Y).



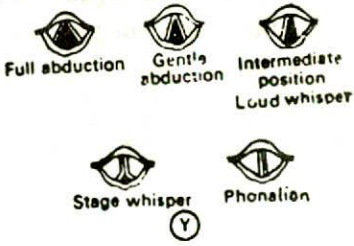


Fig. 291X. Diagrammatic representation of the basic structure of the larynx showing that each vocal cord is stretched between the thyroid cartilage and an arytenoid cartilage which helps phonation.

Fig. 291Y. Some of positions and shapes of the vocal cords during different types of phonation.

(2) *Posterior crico-arytenoid muscle* pulls the aretenoid cartilages away from thyroid cartilage and thereby stretches the vocal cords increasing their tension.

(3) The *transverse arytenoid muscle* pulls the arytenoid cartilages together and thus draws the vocal cords towards each other.

(4) The *lateral crico-arytenoid muscle* pulls the arytenoid cartilage forwards and increases the gap between the vocal cords to allow easy respiration.

The vocal cords vibrate laterally because the pressure of air from below pushes the vocal cords apart. The rapid flow of air between their margin creates a 'negative pressure' which approximates the cords towards each other. The cycle is then repeated.

Changes in frequency of vibration of vocal cords are effected by

(i) alteration in *tension of the cords*

and (ii) alteration in *thickness* of the vibrating edge.

Tension of the vocal cords is regulated by intrinsic laryngeal muscles described above, e.g. posterior crico-arytenoid and transverse arytenoid muscles which increase and lateral crico-arytenoid muscles which decrease the tension of the vocal cords.

Thickness of the vibrating edge is regulated by the muscle fibres of the thyro-arytenoid muscles. It has been mentioned that groups of muscle fibres in this muscle may contract independent of each other—one group producing thin edge and the other group producing thick edge of the vocal cords.

Extrinsic muscles of the larynx also has got a role to play. Elevation of the larynx increases the tension and depression of the larynx decreases the tension of the vocal cords.

Articulation and Resonance :

The three major organs for *articulation* are :

(i) lips, (ii) tongue and (iii) soft palate.

The *buccal cavity*, the *nose* and *nasal sinuses*, the *pharynx* and the *chest cavity*—they all act as *resonators* and determine the quality of the voice. Thus if the nose is blocked due to cold—the quality of voice is appreciably altered.