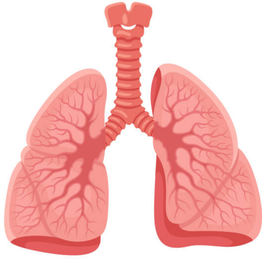

UNIT 5

RESPIRATORY PHYSIOLOGY

Structure

5.1 Introduction

Expected Learning Outcomes

5.2 Overview of Respiration

5.3 Human Respiratory System

Structure and Function of Lungs

5.4 Pulmonary Circulation

5.5 Mechanics of Breathing

Pulmonary Ventilation

Inspiration and Expiration in Lungs

5.6 Mechanism of Gas Exchange between Alveoli and Tissue

External Respiration and Internal Respiration

5.7 Transport of O_2 and CO_2 in Blood

5.8 Regulation of Respiration

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5.1 INTRODUCTION

You have studied about the circulatory system of human body in unit 4. The main function of circulatory system is to transport oxygen (O_2) and removal of carbon dioxide (CO_2) from the body cells. The oxygen we inhale is essential for our survival. You know our body needs oxygen to work properly. Most cells in human body meet bulk of their energy requirement from chemical reactions involving oxygen. In turn, they produce CO_2, the major end product of these reactions. Since, CO_2 is harmful for the body so it has to be eliminated. You are aware that lung is the main organ that exchanges gases between body cells and the blood capillaries.

In this unit, you will learn about the organs of respiratory system, mechanism of respiration, transport of oxygen and carbon dioxide, gaseous exchange between blood capillaries and fluid medium, and regulation of respiration in the body.

Expected Learning Outcomes

After studying this unit, you should be able to:

- identify the components of respiratory system;
- explain the anatomy of lungs;
- discuss the mechanics of ventilation;
- describe pathways to exchange gases between alveoli, blood vessel and tissues;
- define the inspiration and expiration; and
- describe the regulation of respiration.

5.2 OVERVIEW OF RESPIRATION

You studied in the last Block 1 that circulatory system plays an important role in transportation of nutrient-rich and oxygenated blood to each cell of the body and removal of cellular waste material (CO_2, urea and uric acid etc.) from the body. The gaseous exchange in human body, however is a continuous process. Since most of the cells of a complex human body are not in direct contact with the external environment due to skin, GIT & respiratory lining, they have developed specialized respiratory system e.g. lungs & associated structures to carry out the function of O_2 supply to the body cells and in turn, removal of CO_2 produced by cellular metabolism.

The respiratory system can be divided into parts based on its function (Fig. 5.1).

1. **Breathing (ventilation).** The process of movement of air into the lungs during inspiration and out of the lungs during expiration is called ventilation. .

2. **Exchange of gases (Exchange I):** The gaseous exchange take place between alveoli of lungs and blood capillaries. The circulatory system helps to transport and exchange the gases and other nutrients with the cells. This is called External Respiration.

3. **Internal respiration (Exchange II).** It is the cellular respiration in which O_2 gas is utilized by the cells and CO_2 is released as a by-product. The CO_2 is carried by the systematic transport to human heart and then transported to the lungs through pulmonary circulation finally reaching alveoli for removal.

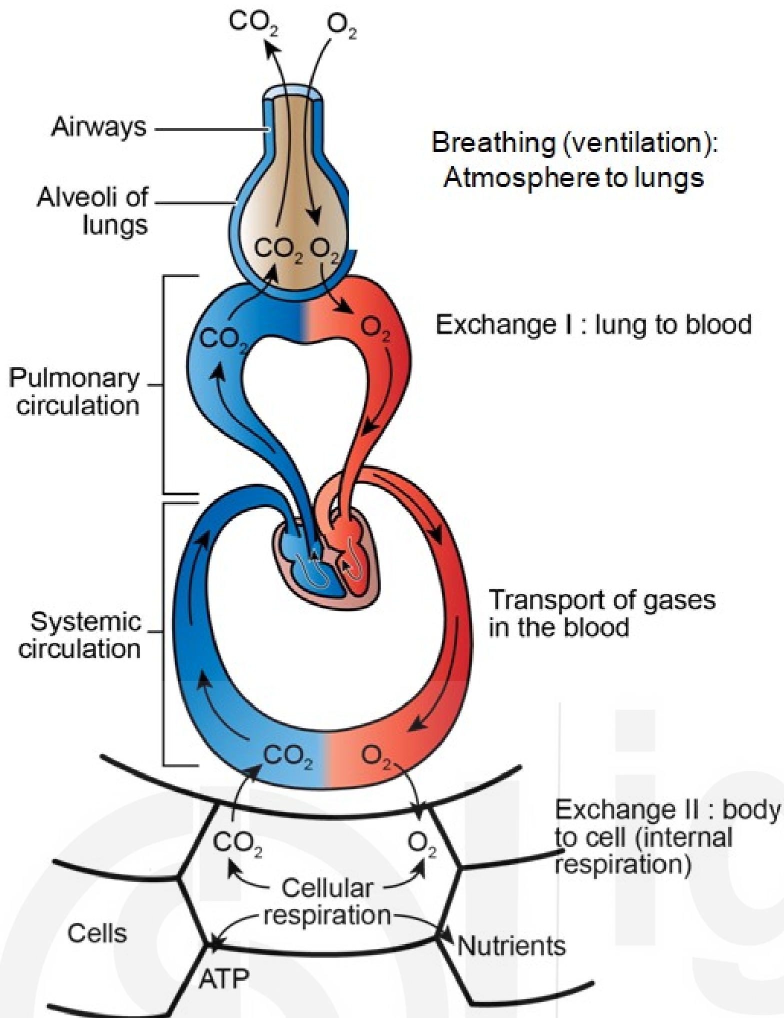


Fig. 5.1: Overview of external and internal respiration.

SAQ 1

Fill in the blanks:

i) The movement of air into the lungs refers to.................................

ii) The gaseous exchange between lungs and blood capillaries is called ....

iii) The cellular respiration occurs between ....

5.3 HUMAN RESPIRATORY SYSTEM

The organization of respiratory system can be categorised on (1) structural and (2) functional basis.

The structural classification of respiratory system:

(a) **The upper respiratory system** which includes the nose, nasal cavity, pharynx & associated structures and,

(b) **The lower respiratory system** which comprises the larynx, trachea, bronchi & lungs.

The functional classification of respiratory system:

(a) The conducting zone consists of a series of highly branched hollow air passages or tubes that become smaller in diameter & more numerous at each branching. These conduct air from the nose and mouth to the lungs and therefore known as **conducting zone.** The nasal passage also warms, moistens and cleanses the incoming air. The zone includes nose, nasal cavity, pharynx, larynx, trachea, bronchi, and bronchioles. The air flows down from the nasal cavity to the pharynx, larynx and then trachea, bronchi and ultimately to the lungs.

(b) The respiratory zone: - It is the actual site of respiratory gas exchange within the lungs. It comprises millions (approx. 300 million) of air-filled, tiny blind sacs known as **alveoli.** These are richly supplied with the blood vessels. This zone also includes the respiratory bronchioles and alveolar ducts which lead to alveolar sacs (atrium) & finally terminate into alveoli.

The respiratory system consists of the following structures beginning from nose and the nasal cavity (Fig. 5.2). The nasal cavity leads to the **pharynx** which opens through the larynx region into the trachea. **Larynx** is a cartilaginous box which contains vocal cords. It helps in sound production and hence known as the sound box. It is air passageway amid pharynx and trachea. **Trachea** is a hollow tube extending from larynx to the bronchi of lungs. It allows the passage of air. Hence, it is the main airways to the lungs; hence it is known as windpipe. It is supported with cartilaginous rings which prevent its collapse. Trachea divides at the level of 5th thoracic vertebra into a right and left primary bronchi. Primary bronchi diverge into smaller and narrow branches until they reach in tiny air sacs structure called alveoli.

Watch youtube videos:

1. Lung introduction 01 Meet the lungs

https://www.youtube.com/watch?v=S4_79i2lJPY

2. How to draw diagram of human Respiratory system easily - step by step

https://www.youtube.com/watch?v=IwY_qWg9R5A

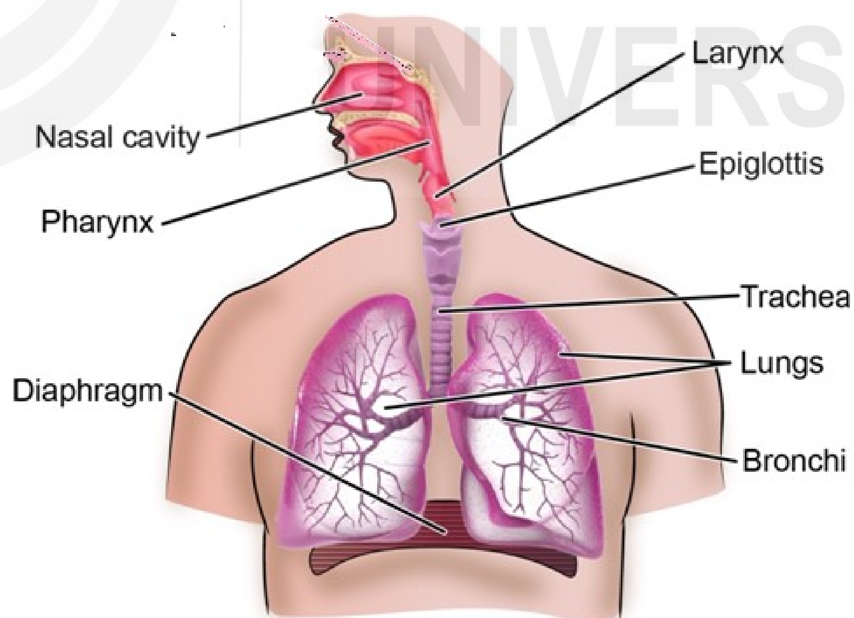


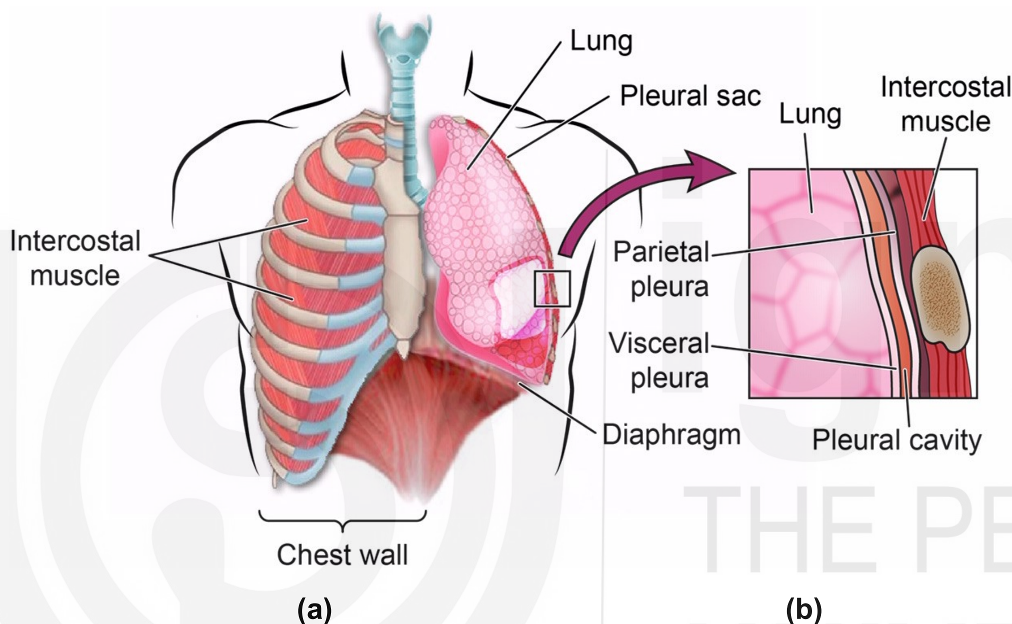
Fig. 5.2: The human respiratory system span from the nasal cavity to the diaphragm.

Let us understand the gross anatomy of the Lung.

5.3.1 Structure of Lung

Lung is the main central organ of the respiratory system for gaseous exchange. Human body has two lungs located in the thoracic cavity. Each lung is a pyramid-shaped structure and attached to the trachea through the right and left bronchi; on the inferior surface. Located below the lungs is a muscular **diaphragm**. The diaphragm is a dome-shaped muscle located at the base of the lungs and thoracic cavity.

The lungs are externally covered by a double-layered serous membrane called the pleura. The pleura consists of two layers called the **parietal pleura** and the **visceral pleura (Fig.5.3)**. Amid these two layers, there is a space called pleural cavity filled with the pleural fluid. The pleural fluid serves as a lubricant that helps in the slight motion of lungs and holds two pleurae together.



Fig, 5.3 a)The lungs with their protective chest wall. b) section of chest cavity wall showing visceral and parietal pleura and pleural cavity.

Each lung is are divided into lobes. The right lung has three lobes: superior, middle and inferior) while left lungs contains two lobes: superior and inferior (Fig.5.4). Each lobe is further divided into many bronchopulmonary segments (each receiving air through a tertiary bronchus), which are further divided into pulmonary lobules (each with its own terminal bronchiole). Each lobe is richly supplied with the blood vessels, lymphatic vessels, and nerves.

The two lungs have all the components of the bronchial tree beyond the primary bronchi; respiratory bronchioles, alveolar ducts, alveolar sacs (atrium) & finally alveoli. Trachea branch into two primary bronchi, and each **bronchus** undergoes repeated divisions to form the secondary and tertiary bronchi and bronchioles ending up in very thin terminal bronchioles. These structural respiratory organs form a clear pathway for the gaseous exchange of O_2 and CO_2.

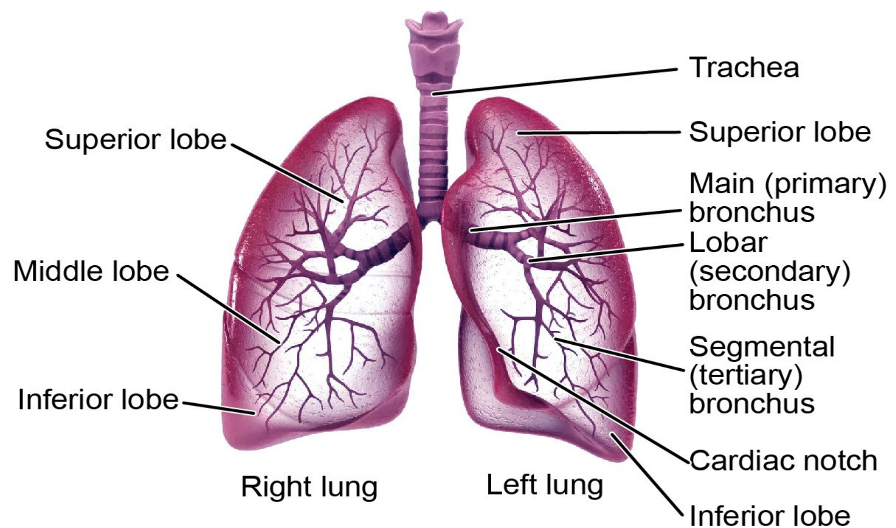
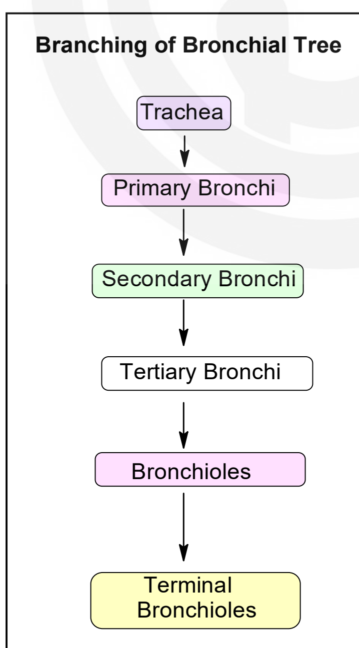


Fig. 5.4: Anatomy of Lungs.

Like trachea; primary, secondary and tertiary bronchi; and initial bronchioles are also supported by incomplete cartilaginous rings. Look at the Fig. 5.5 which shows the structure of terminal bronchiole and alveolar sac. Each bronchiole gives rise to a number of very thin, irregular-walled and vascularised bag-like structures called alveoli (alveolar sac). An alveolar sac is the respiratory tree consisting of a cluster of alveoli responsible for the gas exchange with blood. You can consider a branch of alveoli similar to the root of plants. We can say that an alveolus is the functional part of lungs where exchange of O_2 and CO_2 takes place between blood and alveoli at molecular level. Alveoli sacs are closely supplied with the blood capillaries that connect to large blood vessels.



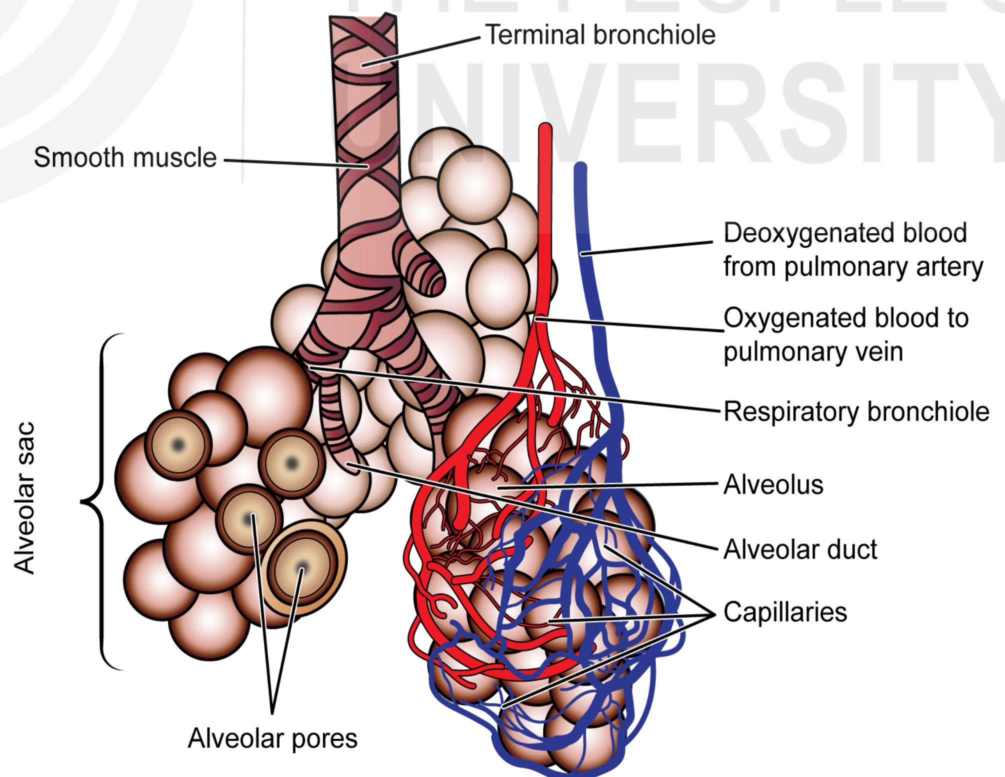


Fig. 5.5: Structure of alveoli and alveolar sac.

SAQ 2

Fill in the blanks with appropriate words from the text.

i) The pharynx receives air from ....

ii) ....is the sound box of the body.

iii) The windpipe of lungs is....................

iv) The nutrient blood supply of the lungs is provided by ....,

v) ....is the functional part of the lung.

5.4 PULMOANRY CIRCULATION

The lungs are perfused by two circulations the **pulmonary & bronchial circulation** differing in their size, origin and function. Pulmonary circulation is the pathway of blood vessels between heart and lungs. **It** consists of a **pulmonary trunk** arising from the right atrium. It divides into a **left pulmonary artery** entering the left lung & a **right pulmonary artery** supplying the right lung (Fig.5.6). These arteries carry deoxygenated or venous blood to the lungs for oxygenation. The pulmonary arteries are the only arteries in the body that carry deoxygenated blood. The pulmonary arteries, in turn, branch profusely along with the bronchi & finally drain in**to the pulmonary capillary networks** surrounding the alveoli. The oxygenated blood, on the other hand, returns to the left atrium of the heart *via* four **pulmonary veins**.

Bronchial arteries, which arise from the aorta, deliver oxygenated blood to the lung tissues perfusing the muscular walls of bronchi & bronchioles, **except the alveoli, which are supplied by the pulmonary circulation.** Some systemic venous blood is drained from the lungs by the **tiny bronchial veins,** but because of multiple connections or **anastomoses** between the two circulations, most venous blood returns to the heart *via* the pulmonary veins.

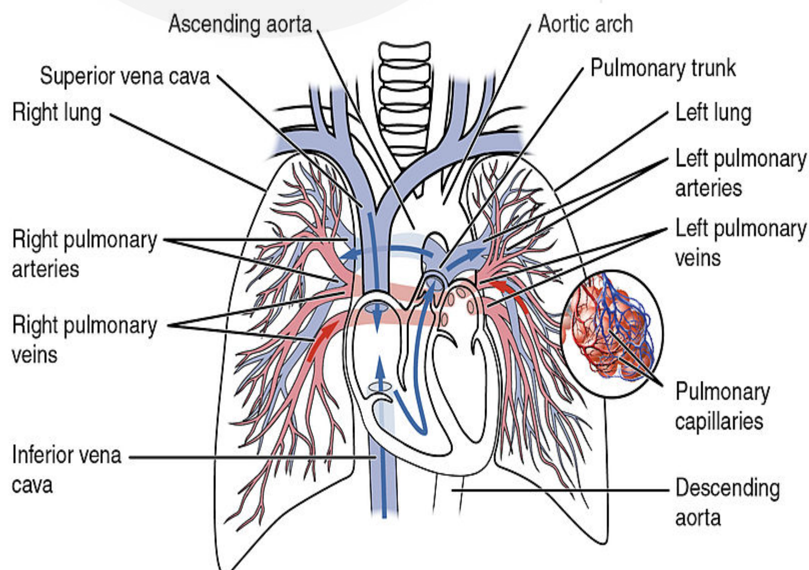


Fig. 5.6: Pulmonary circulation.(Image source: https://commons.wikimedia.org/wiki/File:2119_Pulmonary_Circuit.jpg)

SAQ 3

Name the arteries which perfuse the lungs.

5.5 MECHANICS OF BREATHING

Breathing or Ventilation, is the process of gas movement (oxygen and carbon dioxide) through a series of passages between the atmosphere and the lungs. A healthy human breathing rate is about 10 to 18 breaths per minute. The air moves through the passages because of pressure gradients that are produced by contraction of the diaphragm and thoracic muscles. Before we begin to describe the breathing process, we must understand the concepts of atmosphere pressure, intrapleural pressure & alveolar pressure (or intrapulmonary pressure).

Pulmonary ventilation is a completely mechanical process of breathing. Lungs, airways and respiratory muscles are involved in ventilation. It is dependent on volume changes occurring in the thoracic cavity and consists of two sub-processes - **inspiration (inhalation)** and **expiration (exhalation)** which occur by bulk flow of air.

A rule which regulates the entire process of pulmonary ventilation is that the volume changes lead to pressure changes, which, in turn, lead to the flow of gases to equalize the pressure. The relationship between the pressure & volume of gases is given by **Boyle's Law** which states that at constant temperature, the pressure of a gas in inversely proportional to its volume *i.e.* $P_1V_1=P_2V_2$.

The amount of pleural fluid in the pleural cavity should remain minimal for the negative intrapleural pressure.

Excessive amount of fluid accumulating in the intrapleural space produces a positive pressure.

Pulmonary ventilation involves three different pressures (Fig.5.7):

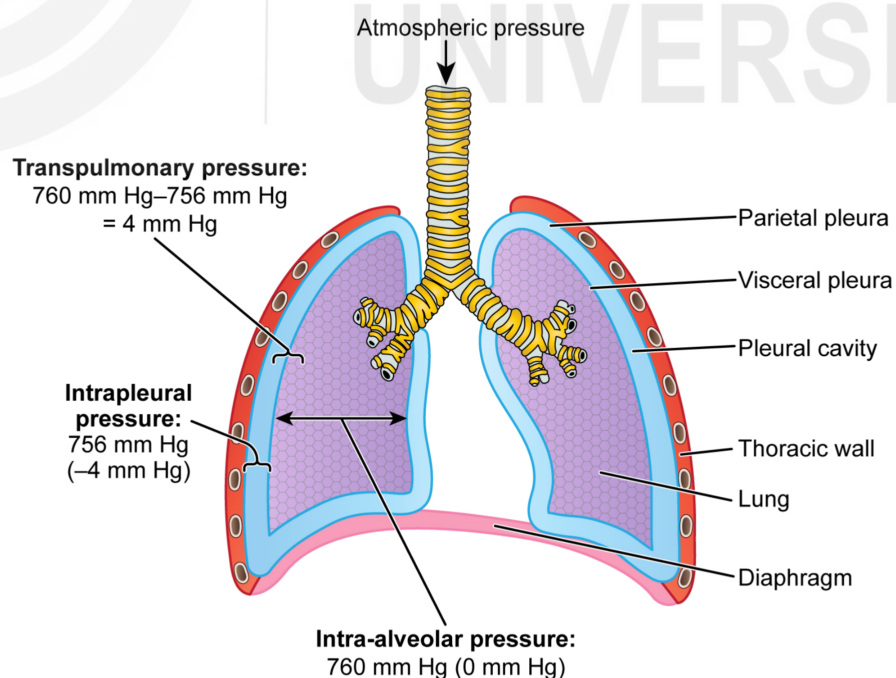


Fig. 5.7: Intrapulmonary and Intrapleural Pressure Relationships.

1. Atmospheric pressure is the pressure exerted by the gases present in the air, surrounding the body. It is calculated by adding the partial pressures of all the gases primarily nitrogen, oxygen with very small quantities of water vapour, CO_2, and inert gases *viz.* argon in the air. At sea level, atmospheric pressure is equal to 760 mm Hg (the pressure exerted by a column of mercury 760mm high).

2. Intrapulmonary (alveolar) pressure is the pressure within the alveoli of the lungs. It changes w.r.t. different phases of breathing but always equilibrates itself with the atmospheric pressure eventually.

3. Intrapleural Pressure – The pressure within the pleural cavity is known as intrapleural pressure. It also fluctuates with different phases of breathing. However, **it is always sub-atmospheric** (lower than atmospheric pressure)

Intra-alveolar pressure changes during the different phases of the cycle. It equalizes at 760 mm Hg but does not remain at 760 mm Hg. **The question is "why the intrapleural pressure is always sub-atmospheric?**

An analogy may help answer this question and also illustrate the mechanism. Imagine two balloons of different size, one inside the other & the space between the two is filled with water. The inner, smaller balloon is open at the top and communicates freely with the atmospheric air. Therefore, it contains air at atmospheric pressure. There are two opposing forces which act upon the wall of the inner balloon (1) the inner air pressure and (2) the water pressure surrounding it. Initially these two pressures are equal and hence there is no tension in the wall of the inner balloon. Now, when we enlarge the outer balloon by pulling it in all directions; the inner balloon also expands by an almost equal amount and its walls become highly stretched and taut.

We can apply the same analogy to the lungs (air-filled inner balloon), thoracic cage (outer balloon) and intrapleural fluid (the water between the balloons). At rest, *i.e.* when there is no respiratory muscle contraction, elastic forces in the tissues of the thoracic cage tend to pull it away from the outer surface of the lungs. **This causes a drop in the intrapleural fluid pressure below that of the alveolar air pressure.** This pressure difference forces the lungs to distend causing stretching virtually to the same degree as the thoracic cage of their elastic walls. The tendency for the lungs to recoil as a result of stretch is balanced by the difference between the alveolar air pressure & intrapleural fluid pressure.

The lungs can be expanded & contracted in two ways: (i) By downward or upward movement of diaphragm to lengthen or shorten the thoracic cavity & (ii) By elevation or depression of ribs to increase or decrease antero-posterior diameter of the thoracic cavity.

Now let us proceed to understand inspiration & expiration process in respiration.

5.5.1 Inspiration and Expiration

Inspiration is the active phase of ventilation. It is the process of inhalation of air into the lungs. During this process, the lung expands to increase their

volume. The first step in a normal quiet inspiration involves contraction of the **main muscles of inspiration, i.e. the diaphragm and external intercostals** (Fig.5.8a).

The diaphragm accounts for 75% of air that enters the lungs during this process.

In strenuous breathing, on the other hand, the diaphragm may descend 10 cm producing a pressure difference of 100 mmHg & the inhalation of 2-3 liters of air.

(i) Diaphragm: The most important muscle of inhalation is the diaphragm which is the primary driver of inhalation. Diaphragm is a dome-shaped skeletal muscle forming the floor of the thoracic cavity. During inspiration, this dome-shaped diaphragm contracts causing it to flatten & move inferiorly downwards. This increases the superior-inferior or vertical dimension (height) of the thoracic cavity. During normal quiet inspiration, the diaphragm descends about 1cm, providing a pressure difference of 1-3 mm & the inhalation of about 500 mL of air.

(ii) External Intercostal muscles: The next most important muscles of inhalation are the external intercostal inserted on ribs. When they contract, they elevate the ribs & the rib cage moves outwards & upwards, increasing the antero-posterior & lateral diameters (horizontal dimension) of the chest cavity.

The atmospheric air consists primarily of N_2, O_2 with very small quantities of water vapour, Co_2 & inert gases *viz.* argon. Therefore, the sum of the partial pressure of all these gases constitutes the atmospheric pressure or barometric pressure. It varies in different parts of the world as a result of differences in altitude, but at sea level it is 760 mm Hg. Since air contains about 21% (20.9%) of oxygen, therefore, the partial pressure of oxygen (pO_2) in inspired air is 0.209 X 760=158.8 mm Hg. at sea level, while that of CO_2 is 0.0004 x 760=0.3 mm Hg.

Contraction of these muscles is responsible for about 25% of the air that enters the lungs during normal quiet inspiration.

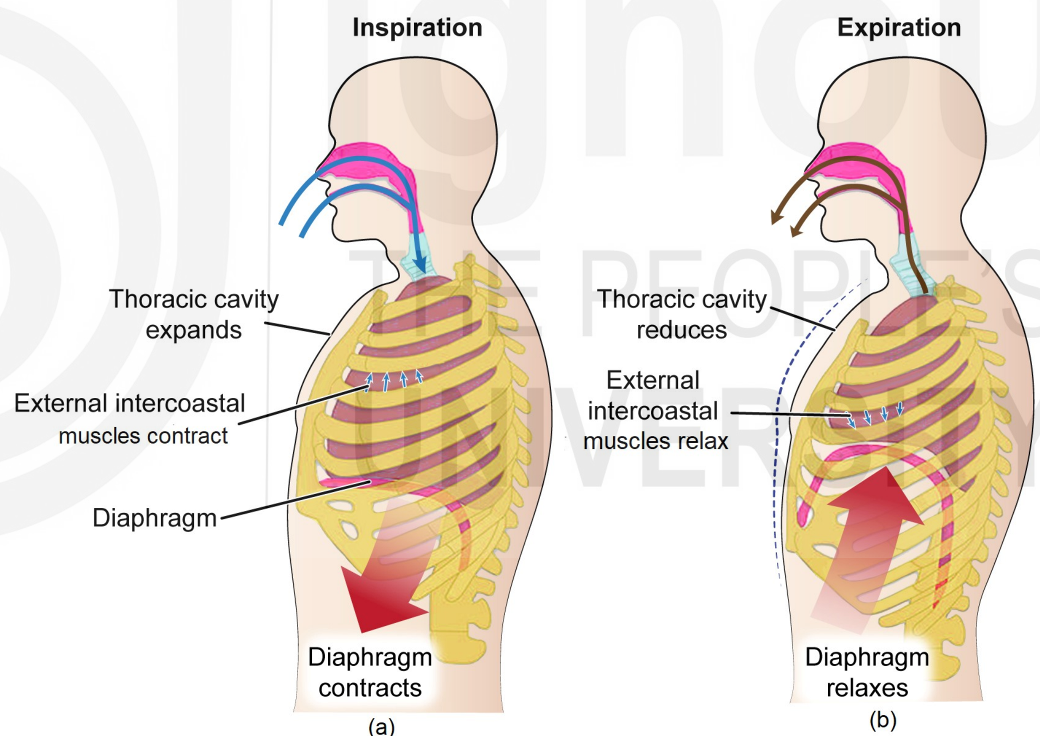


Fig. 5.8: Inspiration and expiration of air.

<u>**Expiration (Exhalation)**</u>:

Expiration is a process of breathing cycle to letting out of air from the lungs. It starts when the external intercostal muscles and the diaphragm relax and thoracic cavity reduces (See Fig. 5.8b). As the diaphragm relaxes, it moves upwards due to its elasticity & resumes its dome-shaped structure & when external intercostals contract, the rib cage moves downwards & inwards (depress). These movements decrease the vertical, lateral & anteroposterior diameter of the thoracic cavity.

Thus, **normal quiet expiration in healthy individuals is a passive process**, because it does not involve any muscular contractions, instead it results from elastic recoil of the chest wall & lungs. Two inwardly directed forces contribute to elastic recoil; (1) The recoil of elastic fibres of the stretched tissues during inhalation & (2) The inward pull of surface tension due to thin film of alveolar fluid.

SAQ 4

Define the following terms

i) Expiration

ii) Inspiration

5.6 MECHANISM OF GAS EXCHANGE BETWEEN ALVEOLI AND TISSUES

You learnt in the previous section that gas exchange process occurs at two level in the body:

1. External Respiration (Pulmonary gas exchange). It occurs between lungs and blood in the pulmonary capillaries (Fig.5.9). The oxygen (O_2) is picked up by the alveoli while carbon dioxide (CO_2) is removed from the alveoli.

2. Internal Respiration (Systemic Gas Exchange): It occurs between systemic capillaries and the tissues/cells. The O_2 is delivered to the tissues and in turn, CO_2 is picked up.

Let us discuss one by one.

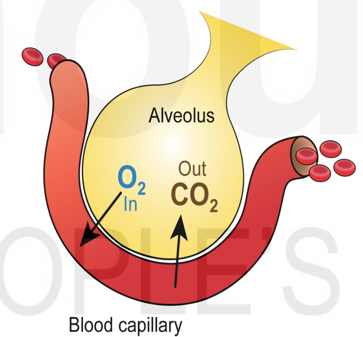


Fig. 5.9: Gas exchange between alveoli and blood capillaries

5.6.1 External Respiration (Pulmonary gas exchange)

External respiration, the process of gas (CO_2) exchange between lungs and blood in the Pulmonary capillaries, is also called pulmonary gas exchange. It involves the transport of oxygen from the outside environment to the alveoli and then to the pulmonary capillaries, while transport of carbon dioxide from the pulmonary capillaries to the alveoli and then outside the body. The movement of oxygen (O_2) in the alveolar air of the lungs to blood in pulmonary capillaries & the diffusion of CO_2 in the opposite direction takes place by diffusion. During external respiration, the deoxygenated blood (dark red in colour) flowing through the lungs is converted to oxygenated blood (scarlet red) & then returned to the left side of the heart for distribution by systemic arteries to all body tissues (Fig.5.10a).

Look at Fig. 5.10(b) shows the difference in partial pressure (p) of oxygen (pO_2) and carbon dioxide (pCO_2) between the alveoli and the blood in the pulmonary capillaries drives the external respiration. Since the blood flowing through the pulmonary capillaries is separated from the alveolar air by a very thin barrier with a huge surface area, the difference in the partial pressures of O_2 & CO_2 on the two sides of the respiratory membrane results in the net

diffusion of O_2 into the blood and of CO_2 into the alveoli (Fig. 5.10). This diffusion continues till the alveolar and capillary partial pressures become equal. As a result, CO_2 is removed and blood is replenished with O_2. The capillary has a high pCO_2 (45 mm Hg) and low pO_2 (40 mm Hg). On the contrary, alveoli air has high pO_2 (104 mm Hg), and low pCO_2 (40 mm Hg). Thus, the partial pressure difference of oxygen about 64 mm Hg (104 - 40 mm Hg), while the partial pressure difference of CO_2 is about 5 mm Hg (45 - 40 mm Hg).

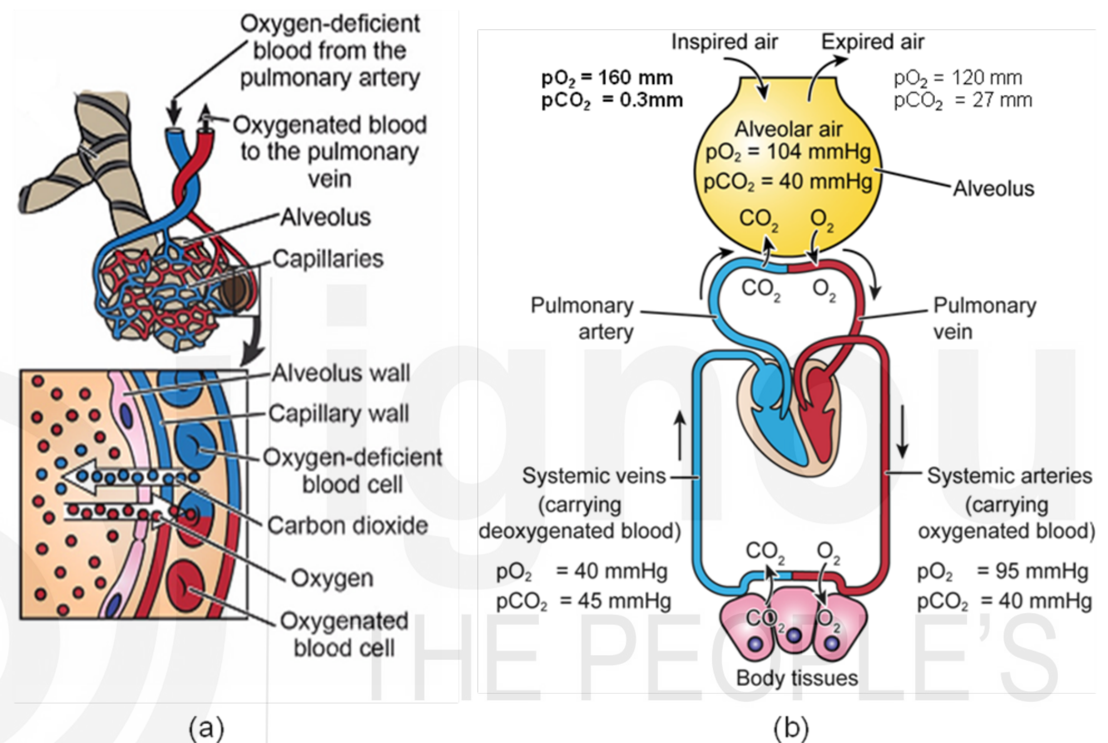


Fig. 5.10: (a) In external respiration, oxygen diffuses across the respiratory membrane from the alveolus to the capillary; (b) The exchange of respiratory gases in alveoli in lungs and tissues cells.

In a normal healthy person, the rates at which O_2 & CO_2 diffuse are so rapid & the blood flow through the capillaries is so slow that complete equilibrium is usually reached in 0.25 seconds, about one-third the time a red blood cell takes to pass through these capillaries. Look at Fig. 5.10. We can observe that the pO_2 in the alveolar air is only 104 mm Hg as opposed to 160 mmHg of inspired air & that of pCO_2 is 40 mmHg (*vs*. 0.3 mm Hg. in expired air). This raises the question that why the pO_2 of alveolar air & inspired air and pCO_2 of expired air is not identical?

The answer is that it is because approximately 150 mL of inspired (& expired) atmospheric air, during each breath, is not utilized for gas exchange in the alveoli. Instead it remains in the air ways (*viz*. pharynx, trachea, bronchii etc. - the conducting portions of respiratory system). That is why it is known as **dead space**. Therefore, pO_2 of alveolar air is lower than the inspired air and that of CO_2 (40 mm Hg) is higher than the expired air (pCO_2=0.3 mm Hg).

5.6.2 Internal Respiration (Systemic Gas Exchange)

In this process, the left ventricle pumps oxygenated blood into the aorta and through the systemic arteries to the systemic capillaries. The exchange of O_2 and CO_2 between systemic capillaries and tissues/cells is called **internal respiration or systemic gas exchange.** The pO_2 of blood in systemic arteries is higher (95 mm Hg) than the pCO_2 in tissue cells (40 mm Hg at rest) because the cells constantly use O_2 to produce ATP. Due to this pressure difference, O_2 diffuses out of the capillaries into tissue cells & blood pO_2 drops to 40 mm Hg by the time blood leaves systemic capillaries.

On the other hand, metabolic reactions occurring within cells/tissues are constantly producing CO_2, therefore, the pCO_2 of cells (45 mm Hg at rest) is higher than that of systemic capillary blood (40 mm Hg). Consequently, CO_2 diffuses from tissues/cells, through interstitial fluid, into systemic capillaries until the pCO_2 in the blood increases to 45 mm Hg. This deoxygenated venous blood returns to the heart & is then pumped to the lungs, where the entire cycle is repeated again. (See Fig. 5.10b).

SAQ 5

Fill in the blanks with appropriate words from the text.

i) .... determines the direction of movement of respiratory gases:

ii) ....laws states that the quantity of gas that will dissolve in a liquid is proportional to the partial pressure of the gas & its solubility:

iii) The PO_2 of blood in systemic capillaries is ....than the PO_2 in tissue cells ....Hg at rest.

iv) The exchange of O_2 and CO_2 between systemic capillaries and tissues/cells is called......................................

5.7 TRANSPORT OF O_2 and CO_2 IN BLOOD

You know oxygen is essential for life as well as proper functioning of cells. Most cells in human body meet bulk of their energy requirement from chemical reactions involving oxygen. In turn, they produce Carbon dioxide (CO_2), the major end product of these reactions. Since CO_2 is harmful for the body so it has to be eliminated. Les us understand how O_2 and CO_2 gases transport in the body.

5.7.1 Transport of Oxygen in Blood

The oxygen can be transported by the blood in **two** forms – 1) in physically dissolved form and 2) in combination with the Haemoglobin.

The amount of oxygen which can be dissolved in blood is directly proportional to the pO_2 of blood. But since O_2 is poorly soluble in water, only 1.5% (3 mL) of O_2 is carried in the physically dissolved form by 1 litre of arterial blood at the

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normal alveolar & arterial O_2 of 100 mm Hg. On the other hand, **98.5% (197 mL) of O_2 is carried by the red blood cells in the bound form to haemoglobin. Thus, the major amount of O_2 is transported in combination with haemoglobin.** Moreover, the biconcave disc shape of the erythrocyte and small dimensions also have adaptive value, facilitating rapid diffusion of O_2 & CO_2 throughout the cell interior.

However, the most outstanding physiological characteristic of RBCs, which makes it the most suitable candidate for transport of O_2, is the presence of the iron-containing protein, the **haemoglobin**, constituting approximately one-third of the total cell weight. Haemoglobin is an oligomeric protein made up of 4 polypeptide chains; 2α and 2β (globin molecule) & each polypeptide chain is associated with a non-proteinaceous or prosthetic part - the haem molecule with a non-covalent linkage (Fig. 5.11).

Fig. 5.11: Chemical structure of haeme group; b) Schematic representative of a single subunit of haemoglobin.

Each haem molecule associates with the single atom of iron (in Fe^{2+} form) in the centre which holds the O_2 molecule. The iron in hemoglobin gives blood its red color. In other words, a single haemoglobin molecule has 4 globin molecules associated with 4 haem molecules & 4 iron atoms. As a result, each haemoglobin molecule can combine with 4 molecules of O_2 in an easily reversible reaction, to form **oxyhaemoglobin.** The equation for this reaction, in terms of single polypeptide chain, can be written as:

$$\underset{\text{Deoxyhaemoblobin}}{\mathbf{Hb + O_2}} \xrightarrow[\text{tissue}]{\text{lungs}} \underset{\text{Oxyhaemoglobin}}{\mathbf{Hb\text{-}O_2}}$$

(The haemoglobin molecule that is not combined with O_2 is known as **reduced or deoxyhaemoglobin.**)

As the number of sites on each haemoglobin molecule which can bind with O_2 is limited (4), there are the maximum number of oxygen molecules present that can be combined with the Hb molecule at any given time. When all the iron atoms in Hb are combined with O_2, the Hb molecule is said to be **fully saturated** however, if it is bound to either 1, 2 or 3 O_2, then it is considered

partially saturated. Thus, **the percentage saturation of Hb** is a measure of the fraction of the Hb molecules combined with O_2.

Observe Fig. 5.12. A curve is plotted between pO_2 on x-axis & percent saturation of Hb on Y-axis. This illustration denoting relationship between the percent saturation of Hb & O_2 is called an **oxy-haemoglobin dissociation curve**. Note that when pO_2 is high (e.g., as in pulmonary capillaries – 104 mm Hg), Hb binds with large amounts of O_2 and reaches almost 100% saturation, whereas at low pO_2 (e.g., in tissue capillaries), O_2 is released or unloaded from the Hb for utilization by the tissues. This is the basis for O_2 transport from lungs to the tissues.

We can see from this S-shaped curve that it has a steep slope between 10-60 mm Hg and then flattens out (plateau) between 70-100 mm Hg. Under normal resting conditions, Hb cycles between 75% & 98% saturation with O_2 in its function as O_2 carrier. In pulmonary capillaries, where pO_2 is high (104 mm Hg), Hb is 98% saturated whereas in tissue capillaries, where the pO_2 is lower (40 mm Hg), Hb is still 75% saturated with O_2. This is the basis for earlier statement that only 25% of the available O_2 unloads from Hb and is used by tissues/cells under resting conditions. However, O_2 saturation of Hb drops to 35% at 20 mm Hg *i.e.*, between 40 & 20 mm Hg, large amount of O_2 is released in response to only small decrease in pO_2. In active tissues, *viz.* contracting muscles, pO_2 may fall below 40 mm Hg, but still a large percentage of O_2 is released from Hb providing more O_2 for active metabolism.

Another factor besides the factors mentioned here is **fetal haemoglobin (Hb-F)** which affects the percentage saturation curve of Hb. It has higher affinity for O_2 than the 4 factors discussed here, because it binds with BPG less strongly. When pO_2 is low, it can carry up to **30% more oxygen** than the maternal Hb-A. As the maternal blood enters the placenta, O_2 is readily transferred to the fetal blood.

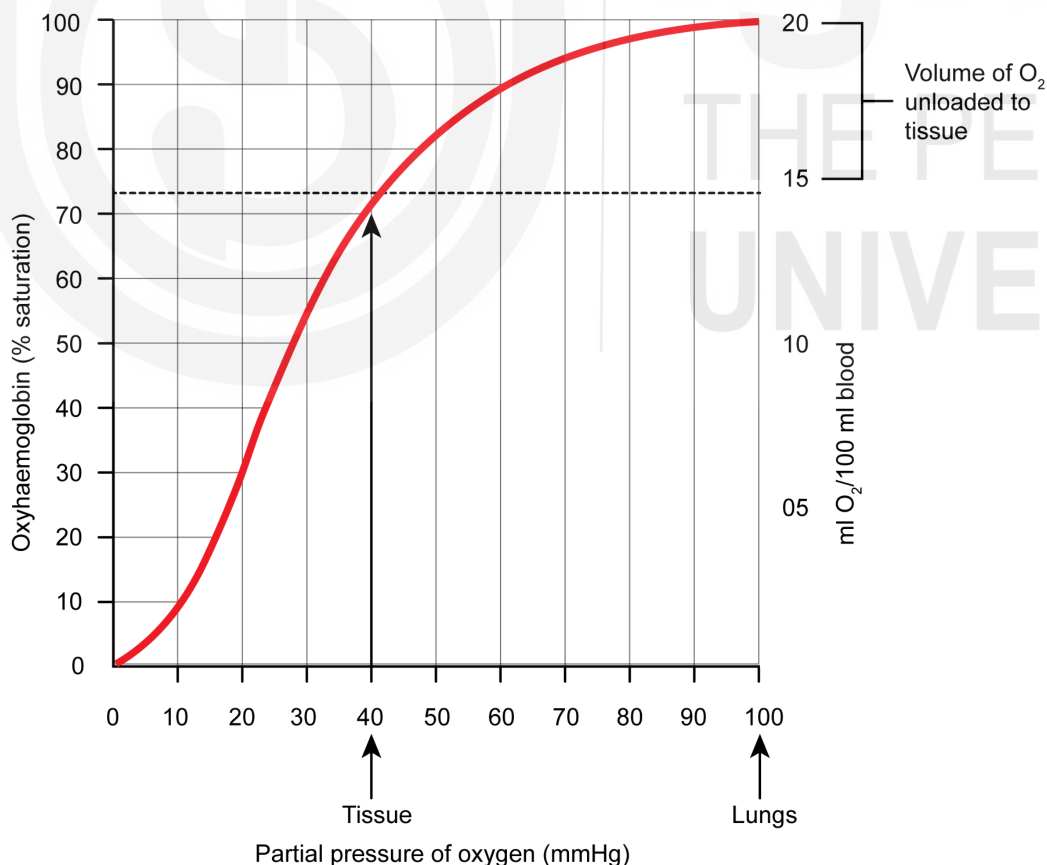


Fig. 5.12: Oxy-haemoglobin dissociation curve.

The oxy-haemoglobin dissociation curve is **sigmoidal in shape** because Hb has relatively low affinity for binding to first 1or 2 O_2 molecules, but once they are bound, the Hb molecule changes shape and therefore binding of subsequent O_2 molecules is greatly enhanced. Same is true for the dissociation of O_2 molecules from Hb.

The most important factors that influence the haemoglobin saturation at a given pO_2 are **pH, pCO_2, amount of BPG (2,3-biphosphoglyceric acid) in**

the blood & temperature. All these factors influence the affinity of Hb for O_2 by modifying its 3-dimensional structure. Generally speaking, an **increase in H^+ concentration (Bohr Effect), pCO_2, BPG levels in blood & temperature decreases the affinity of haemoglobin for O_2 causing the curve to shift to right**. This facilitates the unloading of O_2 from the Hb in blood.

5.7.2 Transport of CO_2 in Blood

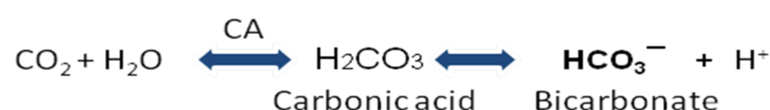
Each 100 mL of deoxygenated blood contains equivalent of 53 mL of gaseous CO_2 under normal resting conditions. Blood carries carbon dioxide from tissue to the lungs in three ways: dissolved form, as carbamino compounds and as bound form to hemoglobin and in the form of bicarbonate ions. We shall look at each of these mechanisms one by one.

1. Dissolved in plasma: The smallest percentage about 5-7% of the CO_2 is transported in blood plasma in physically dissolved form. The CO_2, when reaches lungs, it diffuses into alveolar air and is exhaled.

2. As carbamino compounds: A slightly higher percentage i.e. about 23% of transported CO_2 is carried within RBCs in combination with the amino groups of amino acids and proteins in blood to form **carbamino compounds**. Since the most prevalent protein in blood is Hb (Other plasma proteins are only about ¼th of that of Hb), most of the CO_2 transported in this manner is bound to Hb. The CO_2 binds to terminal amino acids in the 2α and 2β globin chains (& not to haem molecule) of Hb molecule forming **carbamino haemoglobin (Hb-CO_2)** as shown in the following equation:

The formation of Hb-CO_2 is affected by pCO_2 *e.g.,* pCO_2 is relatively high in tissue capillaries, which promotes the formation of Hb-CO_2 whereas in pulmonary capillaries, it is low & therefore CO_2 readily splits apart from globin & enters the alveoli by diffusion.

3. As Bicarbonate ions in plasma: The greatest percentage (70%) of CO_2 molecules is transported in blood plasma as a part of **bicarbonate buffer system.** Look at Fig. 5.13. When CO_2 diffuses into the red blood cells (RBCs), it combines with water forming carbonic acid (H_2CO_3). This reaction is catalyzed by carbonic anhydrase (CA) enzyme of RBCs. However, carbonic acid is highly unstable & immediately dissociates into hydrogen ions & bicarbonate ions, as follows:



This CA enzyme reversibly catalyzes the conversion of CO_2 & H_2O to HCO_3^- + H^+. The H^+ released during the reaction binds to Hb triggering the Bohr's Effect. Thus, O_2 release is enhanced by CO_2 loading (as HCO_3^-). Hence,

bicarbonate buffer system causes a little change in pH of blood by formation of H^+. This is the main advantage of bicarbonate buffer system in blood.

After formation of HCO_3^-, these ions quickly diffuse from the RBCs into the plasma, from where they are carried to the lungs. To maintain the ionic balance, chloride ions (Cl^-), in turn, move from the plasma into the RBCs. This process of ionic exchange is known as **chloride shift (or Hamburger shift)**. The net effect of these reactions is that CO_2 is removed from tissues/cells & transported in blood plasma as HCO_3^-. However, in the pulmonary capillaries of lungs the process is reversed & CO_2 is exhaled.

The amount of CO_2 that can be transported in the blood is influenced by the percentage saturation of Hb with O_2. The lower the amount of oxyhemoglobin, the higher is the CO_2 carrying capacity of the blood, a relationship known as **Haldane effect**. Thus, we can say that just as an increase in CO_2 in blood causes O_2 to split from Hb, in a similar manner binding of O_2 to Hb, causes release of CO_2 from the blood. In this way, Haldane effect enhances the amount of CO_2 released from the blood in lungs (where pO_2 is high) & the pickup of CO_2 in the tissues (where pO_2 is low).

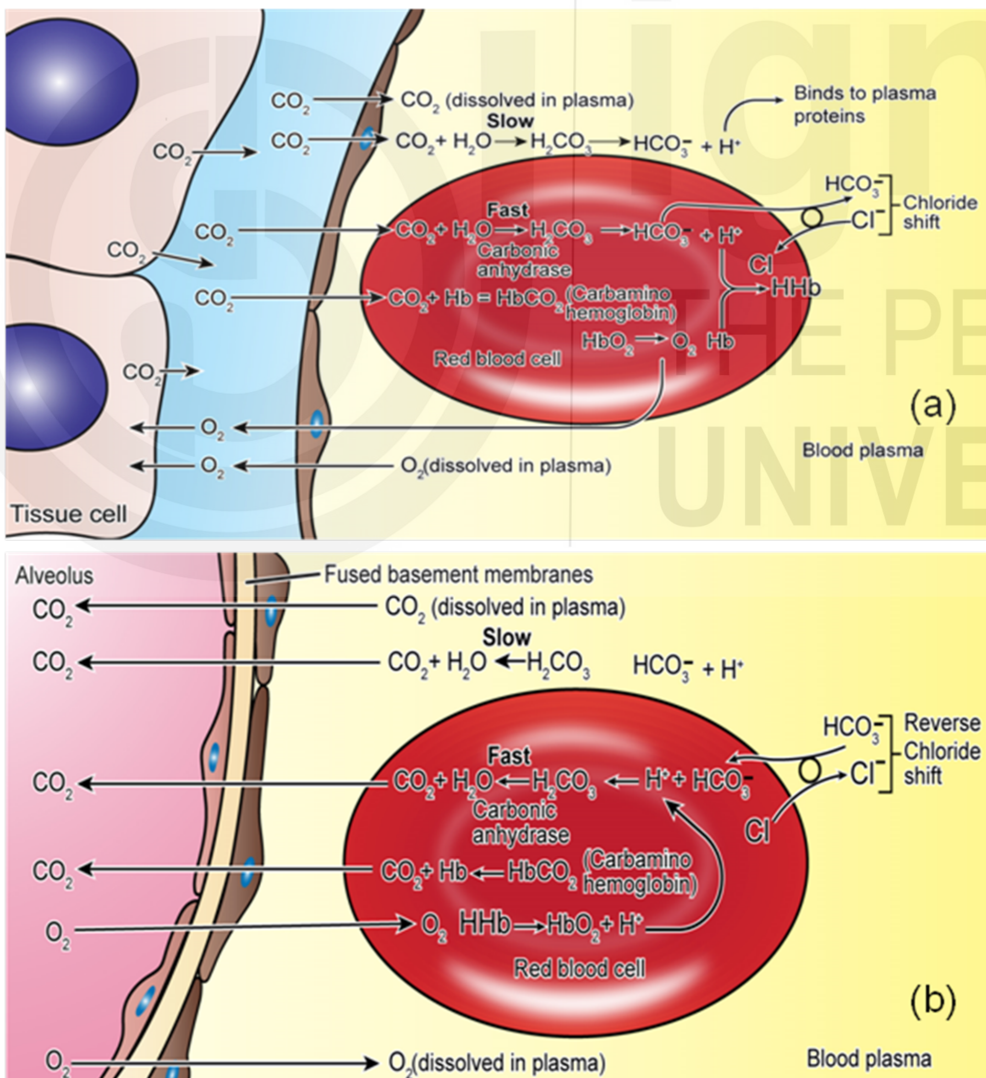


Fig. 5.13: (a) Oxygen release and CO_2 pickup at the tissues b) oxygen pickup and CO_2 release in the lungs.

SAQ 6

Fill in the blanks:

i) RBC facilitates rapid diffusion of O_2 & CO_2 throughout the cell interior due its **....................**

ii) The process of ionic exchange of HCO_3^- and Cl^- move between blood plasma and RBCs is known as **..................**

iii) The lower the amount of oxyhemoglobin, the higher is the CO_2 carrying capacity of the blood, a relationship known as **.....................**

iv) The higher percentage of CO_2 in transported in blood by **..........................**

v) The haemoglobin that is not bound with oxygen is called ....

vi) One haemoglobin molecule can combine with ....molecules of O_2.

5.8 REGULATION OF RESPIRATION

The basic process of respiration changes with metabolic demand e.g., at rest body cells use about 200 mL of O_2 each minute while during strenuous exercise, it can increase by 15-30 fold in normal healthy adults & several times more (up to 30 fold) in endurance-trained athletes. Therefore, regulation of respiration assumes great importance.

Respiration is regulated by two types of mechanisms - the nervous mechanism and chemical mechanism.

Nervous regulation: Nervous system regulates the rate of alveolar ventilation in response to altered level of pO_2 and pCO_2 during physical exercise and other stress conditions. This control mechanism operates through a widely dispersed group of neurons known as **"respiratory centre",** located bilaterally in the reticular substance of medulla oblongata & pons in the brain stem. Therefore, medulla has inspiration-expiration centre to regulate respiration process.

Nervous system has 3 major areas on the basis of their functions (Fig. 5.14):

1. **The medullary rhythmicity area** in the medulla oblongata (controls the basic rhythm of respiration). It is further made up of two groups of neurons :a) Dorsal Respiratory Group of neurons / DRG or **Inspiratory Area** and b) Ventral Respiratory Group/ VRG or **Expiratory Area**

2. **The pneumotaxic area** in the upper pons (by transmitting **inhibitory** impulses prevents overinflation of lungs).

3. **The apneustic area** in the lower pons(sends **stimulatory** impulses to Inspiratory Area and in turn inhibits expiration).

The function of the medullary rhythmicity area is to control the basic rhythm of respiration. It is the **inspiratory area which plays a more fundamental role** in the control of respiration. The excitement of its neurons generates nerve impulses for about 2 seconds. The neuronal activity seems to result from an inherent intrinsic excitability of inspiratory neurons themselves; therefore, they are thought to be **pacemaker neurons.** These impulses stimulate the inspiratory muscles causing their contraction and bring about **Inspiration** for 2 seconds. Then the neuronal signal suddenly comes to halt for 3 seconds bringing about **Expiration**. This is the basic rhythm of respiration.

The neurons of the **expiratory area** remain dormant during normal quiet respiration as expiration is passive. However, during forceful breathing they become active & send nerve Impulses. Impulses from the expiratory area cause contraction of the intercostal & abdominal muscles bringing about forceful expiration.

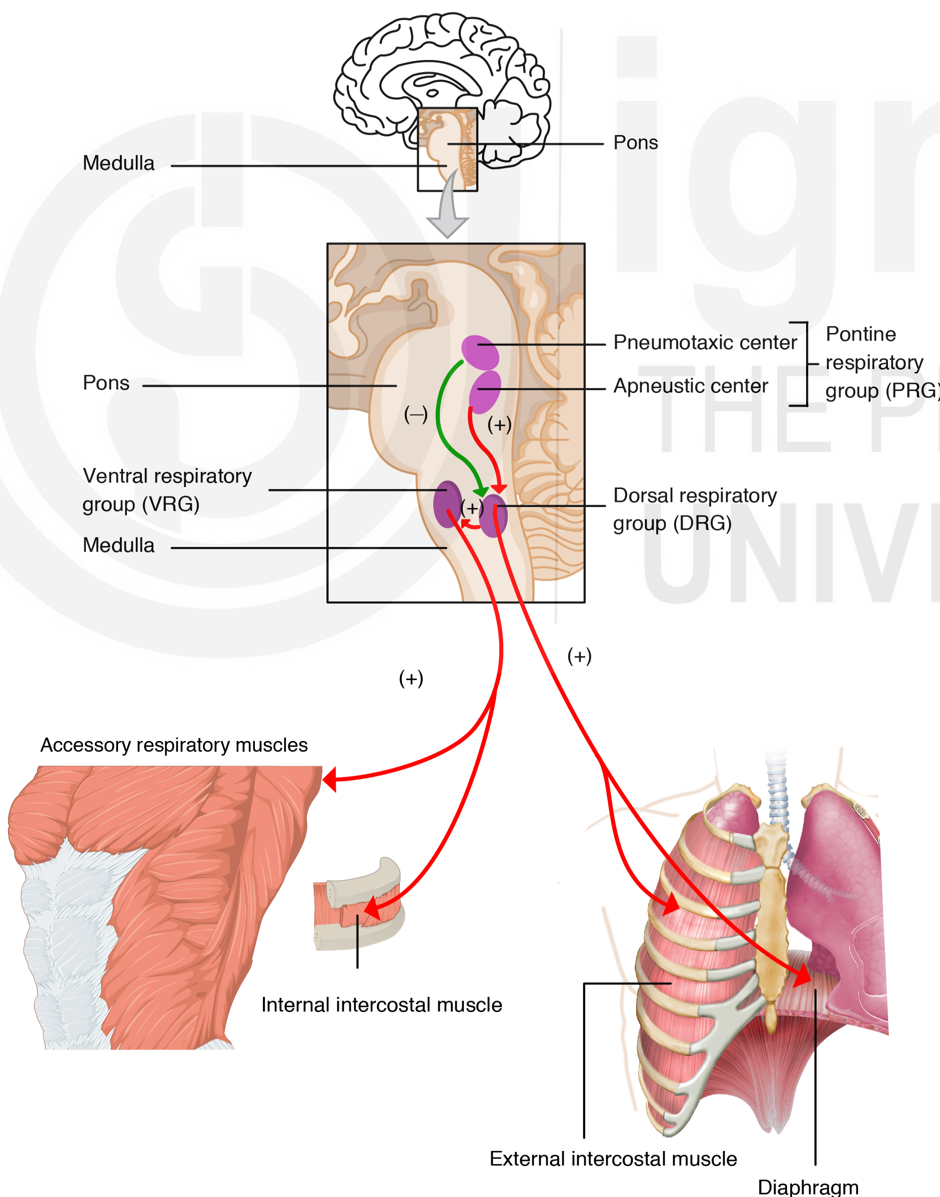


Fig. 5.14: Overview of regulation of Respiratory system (Image courtesy: Anatomy & Physiology, http://cnx.org/content/col11496/1.6/

Chemical regulation

The sensors detecting chemical fluctuations are known as **chemoreceptors**. There are two types of chemoreceptors found in the body:

(1) **The central chemoreceptors** located bilaterally & ventrally in the reticular substance of medullary region of brain, are highly sensitive to changes in either blood CO_2 or H^+ concentration. It has excitatory effects on the Inspiratory Area ,increasing both the rate and depth of Inspiratory signal. And,

(2) **The peripheral chemoreceptors** found in the aortic arch & common carotid arteries, are more sensitive to pO_2 in the blood.

Other factors which influence respiration include; Inflation reflex/Herring-Breuer reflex (mechanical regulation of respiration), pulmonary irritant reflex, hypothalamic controls, cortical controls, temperature, pain, blood pressure & proprioreceptor stimulation etc.

SAQ 7

Name the center which directly stimulates inhalation?

5.9 SUMMARY

So far, you have learned that:

- Breathing facilitates the supply of oxygen to our body cells for the production of energy in the form of ATP and also for the removal of carbon dioxide which is a waste by-product during the process of respiration.
- Respiratory organs ensure the entry of oxygen in our body and in turn, removal of carbon dioxide. The path of air from the nose to the lungs is termed as respiratory tract. Respiratory tract is further divided as an Upper Respiratory Tract and a Lower Respiratory Tract. Upper respiratory tract consists of Nostrils, Nasal cavities, Pharynx, Epiglottis, and Larynx while Lower respiratory tract includes the Trachea, Bronchi, Bronchioles, and the Lungs.
- The entire process of respiration includes pulmonary ventilation, external respiration, transport of gases, internal respiration, and cellular respiration. Respiration mainly comprises two processes: external respiration and internal respiration which is aided by the cardiovascular system. External respiration is the exchange of respiratory gases between the alveolar air & blood in the pulmonary capillaries. Oxygen diffuses from the alveolar air of the lungs to blood in pulmonary capillaries & carbon dioxide in the opposite direction, because of differences in their partial pressures.

- Internal respiration on the other hand, is the gas exchange between the systemic blood capillaries & tissues or cells. Internal Respiration is the cellular Respiration by which oxygen is delivered to the cells to start the set of metabolic reaction for energy production and the carbon dioxide gas is produced as a metabolic product. During this process, oxygen is delivered to the tissues/cells by the systemic capillaries whereas carbon dioxide enters the blood. It is also dictated by the partial pressure gradient.

- **Inspiration** occurs when the diaphragm & external intercostal muscles contract, increasing both the vertical & horizontal dimensions (volumes) of the thoracic cavity while e**xpiration** is largely passive & occurs by relaxation of both the inspiratory muscles & elastic recoil of the lungs. Here, the intrapulmonary (alveolar) pressure exceeds the atmospheric pressure, causing the gases to flow out from the lungs.

- Molecular oxygen is carried in two forms: Physically dissolved in plasma & in chemical combination with haemoglobin molecules in RBCs. The amount of oxygen bound to haemoglobin depends on pO_2 which is depicted in the form of a sigmoidal **oxy-haemoglobin dissociation curve.** The additional factors which affect this relationship are pCO_2 of blood, blood pH, the presence of BPG & temperature.

- **Carbon dioxide** is carried in the blood in three main forms: Physically dissolved in plasma (5-7%); as carbamino compounds bound to haemoglobin (10%) & as bicarbonate ions in plasma (85%).

- The regulation of respiration is brought about by several mechanisms: **Neural mechanism**: It operates through a widely dispersed group of neurons in the **respiratory centre; Chemical regulation:** Important chemical factors modifying respiratory rate & depth are arterial levels of CO_2, O_2 and H^+.

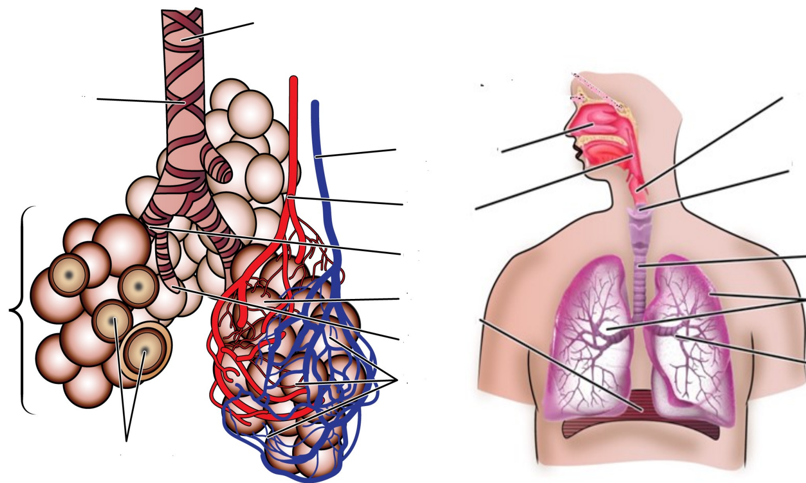
- The chemoreceptors located in the medullary region of brain (**central chemoreceptors)** as well as aortic arch & common carotid arteries **(peripheral chemoreceptors)** also regulate respiration**.**

5.10 TERMINAL QUESTIONS

1. Give an overview of respiration.
2. What are the components of human respiratory system.
3. Explain the structure of lungs, Bronchi and tracheobronchial tree.
4. Explain the pulmonary ventilation.
5. Differentiate between inspiration and expiration
6. Explain the role of partial pressure of gaseous in pulmonary gas exchange and systematic gas exchange?
7. Discuss the mechanism of oxygen and CO_2 transport of in blood with suitable diagram.

8. What is the "respiratory control centre". How does it bring about regulation of respiration?

9. Label the following diagram:



5.11 ANSWERS

Self Assessment Questions

1.
   i. breathing
   ii. external respiration
   iii. blood capillaries and body cells

2. i) Nasal cavity
   ii) Larynx
   iii) Tracheae .
   iv) Bronchial arteries
   v) Alveoli

3. Bronchial arteries

4. i) **Expiration** means letting out of air from the lungs. It starts during the contraction of inspiratory muscles ceases & these muscles relax.
   ii) **Inspiration** means inhalation of air into the lungs.

5. i) The partial pressure gradient of oxygen
   ii) Henry's law
   iii) (95mm Hg), (40mm Hg at rest)
   (iv) Systemic gas exchange

6. i) Biconcave disc shape.
   ii) Chloride shift

iii) Haldane effect.

iv) Bicarbonate buffer system .

v) Deoxyhemoglobin.

vi) 4 molecules of O_2.

7. Medulla oblongata & pons in brain

Terminal Questions

1. Refer to section 5.2.
2. Refer to section 5.3
3. Refer to section 5.3.1
4. Refer to section 5.4
5. Refer to subsection 5.5.1
6. Refer to section 5.6
7. Refer to section 5.7
8. Refer section 5.8
9. Refer to Fig. 5.5 & 5.2

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