Chapter **3**

RESPIRATION

Body needs oxygen to oxidise the food nutrients and derive energy. In this process carbon dioxide is produced in the body, which is toxic and must be removed quickly and efficiently. The oxygen utilization & carbon dioxide production takes place within the mitochondrion of cells of the various tissues. The transport of O_2 and CO_2 to and from the cells of various tissue is done by the blood. But the actual uptake of oxygen from the air and discharge of CO_2 into the environment takes place at the level of lungs. This exchange of O_2 and CO_2 between the organism and the environment is defined as respiration. Air is moved in and out of the lungs by their bellows action (ventilation). It is then distributed within each lung, so that alveoli are adequately ventilated and also perfused by the blood.

Oxygen and carbon dioxide are then exchanged between the gas mixture in the alveoli and the blood in the pulmonary capillaries (gas transfer). The gases are then transported in the blood to the tissue.

Organisation of The Respiratory System

The respiratory system in mammals includes the tissues and organs associated with pulmonary ventilation and pulmonary respiration (air passages) lungs and musculoskeletal system.

The respiratory passage is composed of the nasal passages, pharynx, bronchi, bronchioles and alveoli of the lungs (other parts of passage).

Nasal cavities : The nasal cavities are lined with a mucous - secreting, pseudostratified ciliated epithelium. The mucus and the cilia trap the particulate matter contained within the air. Thus the air passing through the basal cavities is filtered, warmed and moistened. The nasal cavity is also the site of receptors for the sense of smell.

Pharynx : Pharynx is a common passage way for the respiratory and digestive system. The pharynx ensures that the food or liquid does not enter the respiratory system during swallowing.

Larynx : The larynx serves as a valve for the respiratory passageway separating the upper respiratory system from the lower respiratory system.

Trachea : Air passes through the nasal cavities pharynx into the trachea or wind pipe, which is a tubular structure. The trachea is surrounded by three-quarter rings of cartilage, except on the side next to the esophagus. Here the cartilage is replaced by connective tissue which is less rigid and permits easier passage of food down the esophagus.

The upper end of the trachea is modified to form the larynx or voice box, which contains the vocal cords. The opening between the pharynx and the larynx is the glottis, guarded by a flap of fibre cartilage, the epiglottis. The muscles of the larynx can vary the shape and size of the glottis and close it altogether. The action of these muscles are important in phonation as well as in preventing objects from the respiratory passage way.

The Lungs : The trachea divides into-two branches, the bronchus. Each bronchus enters a lung and divides into smaller and smaller branches, the bronchioles. The bronchi have rings of cartilage and the larger bronchioles have plates of cartilage that hold them open. The small bronchioles lack cartilage but have highly developed smooth muscle, circularly arranged.

Each terminal bronchiole leads into a small sac, formed by a grape like cluster of microscopic sacs called alveoli.

Each inspiration draws air down this system of passages to its destination in the alveoli where the gas exchange occurs. Microscopically, the alveoli are composed of a single layer of epithelial cells, covered by a thin layer of elastic connective tissue.

The alveoli are surrounded by capillaries that arise from branches of the pulmonary artery and feed into the branches of the pulmonary vein. The membranes separating the air in the alveoli from the blood in the capillaries are thin.

The other set of structures associated with respiration (skeletal and muscular) consists of ribs, intercostal muscles, diaphragm and accessory muscles.

Mechanism of Respiration

The Flow of Air in and out of the Lungs

In order to reach the alveoli, fresh atmospheric air must flow along an extensive system of large and small tubes. However, gases flow from one region to another only if a pressure differences exists. The lungs themselves contain elastic fibres in the connective tissue that binds the air sacs together, but they contain no muscle. The lungs cannot pump air into and out of it. Any such pumping mechanism would necessitate thick muscular walls to the lungs, which would impede the rapid exchange of gases.

Role of Respiratory Muscles

The lungs and the heart lie in an air tight cavity, the thoracic cavity. This is bounded by the sternum in front, the spinal column behind and the ribs that connect them. The thoracic cavity is closed off above by the dome shaped diaphragm.

Inspiration

During inspiration, the thoracic cavity increase in size in all three dimensions. Contractions of the skeletal muscles of the diaphragm flattens the dome of the diaphragm, increasing the thoracic cavity from top to bottom. The contraction of the external intercostal muscles connecting the ribs, also increase in the size of the thoracic cavity. This increase in the volume of the thoracic cavity results in a negative pressure, forcing the air to enter through the only passage available, namely the lungs.

Expiration

Expiration is a decrease in size of the thorax and lungs with air outflow. As the air fills the lungs, the elastic fibres in the connective tissue are stretched and develop tension. The muscles of the diaphragm and the external intercostal muscles also relax during expiration, thereby decreasing the volume of the thoracic cavity and increasing the pressure inside it. The positive pressure inside forces the air out of the lungs, up the trachea and out through the nasal cavities.

Expiration is a purely passive process in contrast to inspiration, which is an active process requiring energy expenditure for the contraction of muscles.

Pulmonary Blood Vessels

The pulmonary artery carries blood from the right ventricles of the heart. It divides into right and left branches which pass into the respective lungs. These arteries arborize, following the pattern of the bronchi and supply the gross structure of the lung and alveoli.

The air in the alveolus is separated from blood in the capillary by (1) the alveolar wall, (2) the capillary wall and in some cases (3) an interstitial layer between the alveolar and capillary walls. Drainage is from the capillaries into small veins that ultimately unites to form the pulmonary veins that empty into the left auricle.

Respiration Rate

Respiration occurs at a relatively fixed frequency in various species of domestic animals. The respiratory rates in cycles per minute for domestic species is given in table 1.

Table 1 : Respiratory rates of domestic animals (cycles/min.)

Species	No/min	Species	No/min
Horse	8-16	Dog	10-30
Ox	10-30	Cat	20-30
Sheep	12-20	Chicken	15-30
Goat	12-20	Buffalo	16-30
Dairy Cow	18-28	Camel	16-30
Pig	8-18		

The respiratory rate at rest varies considerably among animals of the same species. Faster rates are normally found in young animals.

The respiratory rate is increased along with tidal volume by almost any respiratory stimulus such as exercise.

Lung Volumes and Capacities

Tidal volume : Tidal volume is the amount of air which flows in and out of the lungs with each respiration, during quiet breathing. This volume may be considered as the average volume inspired or expired during a single respiratory cycle. Tidal volume of different species of animals is given in table 2.

Table 2 : Tidal volume of different species.

Species	Tidal Volume (range)	Species	Tidal Volume (range)
Horse	1.75-12 Litres	Dog	175 ml.
Cow	1.9-7 Litres	Goat	310 ml.
Sheep	280 ml.	Pig	200 ml.
Cat	36.6-47.2 ml.		

With maximal inspiration and expiration, this value can be increased several folds.

Vital Capacity : Vital capacity is the largest possible respiratory volume. It is the volume of air which flows during the deepest possible inspiration.

Inspiratory Reserve Volume : The extra air that can be taken in after a normal inspiration is known as inspiratory reserve volume.

Expiratory Reserve Volume : The extra air that can be forced out after a quick expiration is the expiratory reserve volume.

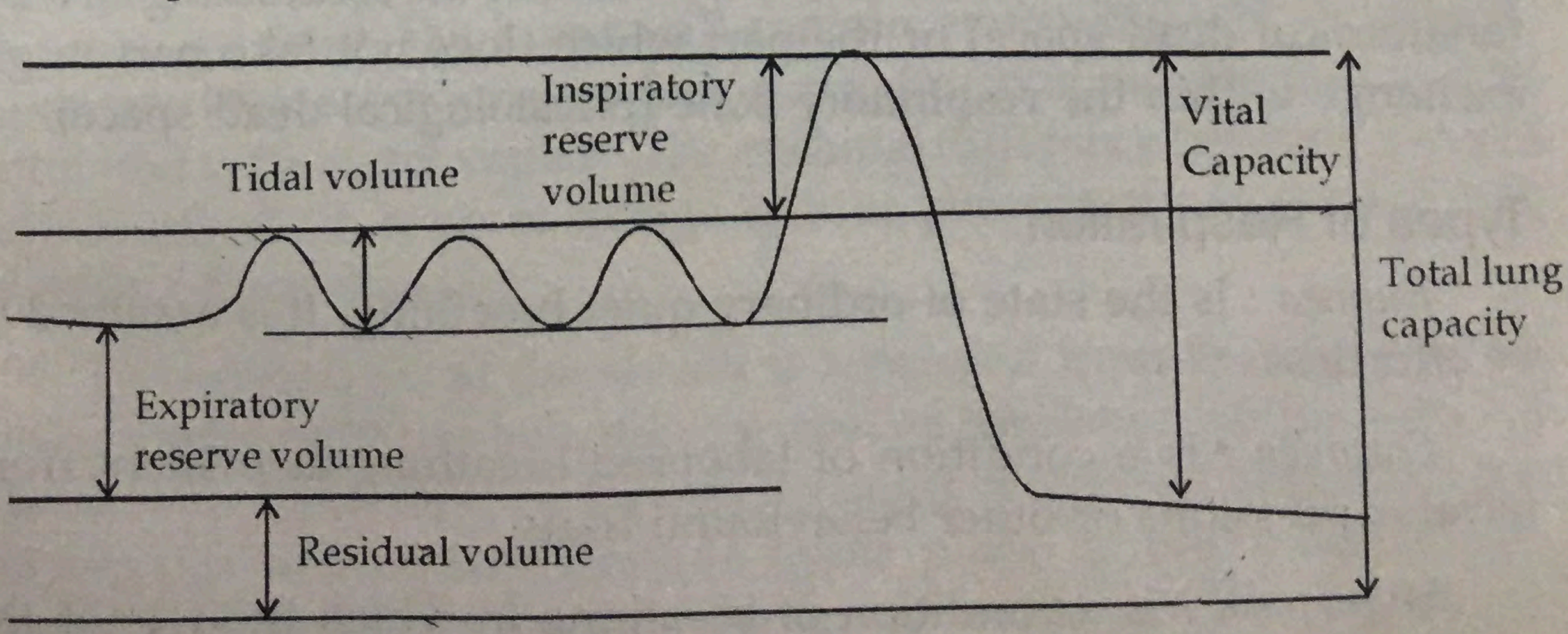


Figure : Lung Volumes

Residual Volume : Residual volume is the volume of air left in the lung after all of the expiratory reserve volume has been forced out. Residual air cannot be expelled by exhaling but only by collapsing the lungs by injections of air into the intrapleural spaces.

Total Lung Capacity : Total lung capacity is the residual air plus the vital capacity.

Respiratory Volumes of Horse

Inspiratory reserve volume	6 Litres
Tidal volume	6 Litres
Expiratory reserve volume	12 Litres
Residual volume	12 Litres
Total lung capacity	36 Litres

Minute Volume is the volume of air entering the lungs per minute.

Minute volume = Respiratory rate × Tidal volume.

How to Determine Whether A Young is Born Dead or Alive .

From its lung : Lungs of a living animal or an animal which was born alive, will contain the minimal volume, hence will float in water. The lungs of the fetus or animal born dead are solid, because there in no air within them and will sink in water. This is sometimes a useful test in determining whether or not a new born animal has taken a breath following birth.

Respiratory dead space : Respiratory dead space may be defined as the volume of gas that is inspired or expired but takes no part in the gas exchange. This may be due to the volume of the conducting airways (anatomical dead space) or the part which does not take part in gas exchange within the respiratory zone (physiological dead space).

Types of Respiration

Eupnea : Is the state of ordinary quiet breathing. It is assumed to be effortless.

Dyspnea : Is a condition of laboured breathing as evident from facial expressions or other behavioural traits.

Hyperpnea : Is a condition of breathing in which the rate or the depth, or both, are increased.

Polypnea : Is a rapid shallow panting type of respiration. The predominant change is an increase of respiratory frequency. Polypnea occurs during heat stress in goat, sheep, dog etc and is a physiological mechanism to dissipate excess heat from the body during heat stress.

Apnea : signifies cessation of breathing.

Morphological Adaptations and Pigment Synthesis

Domestic animals acclimated to high altitudes have increased vital capacity and pulmonary ventilation. Most birds and mammals at high altitudes synthesize more haemoglobin than at sea level.

Oxygen Consumption

Oxygen consumption of domestic animals

Species	Body weight (kg)	Oxygen consumption (ml. O_2/ gm wet wt/hr.)
Sheep	46.8	0.250
Cow	300.0	0.124
Cat	3.0	0.446
Dog	20.0	0.360

Rate of oxygen consumption is influenced by activity, temperature, nutrition, body size, stage in life cycle, season and time of the day.

Exchange of Gases

Normal atmospheric air has a composition of roughly 79 percent nitrogen, 20 percent oxygen and a variable amount of carbon dioxide, rare gases and water vapour making up the remaining one percent. Air expired from the lungs will contain approximately 79 percent nitrogen, 16 percent oxygen, four percent carbon dioxide and will be saturated with water vapour. The essential difference between expired and inspired air is an exchange of four percent of oxygen for four percent carbon dioxide.

The expired air in the alveoli is separated from the blood in the pulmonary capillaries by a thin membrane consisting of the epithelial lining of the alveoli and the endothelial lining of the capillaries. Diffusion of oxygen and carbon dioxide takes place across this alveolar membrane which results in a change of 'venous blood' to 'arterial blood'.

The rate of gas exchange is influenced by several factors including the permeability of the membrane, the area of surface in contact, the relative partial pressure of gases in blood and alveoli, and the volume of blood exposed to the alveoli.

Oxygen is taken up by the venous blood and carbon dioxide is released by it to be carried to the external environment along with the expired air. The oxygen taken up by the blood is transported in the form of a combined oxygen haemoglobin complex.

Oxygen Dissociation Curves

The amount of oxygen that can be taken up by a sample of blood or by aqueous solution of haemoglobin at varying oxygen pressures, can be plotted on a standard graph paper with the percentage of haemoglobin saturation as the ordinate and the oxygen pressure in millimetres mercury as the abscissa.

The curves are basically similar over a wide range of animal species. The dissociation curve of O_2 from Hb is somewhat sigmoid in shape. The curve clearly shows that the actual amount of oxygen combining with Hb is a function of partial pressure of oxygen. The movement of carbon dioxide into and out of the blood is of importance to determine the combining capacity of oxygen with haemoglobin at a given pressure. The pH, temperature and the concentration of 2,3-biphosphoglycerate affect the oxygen-hemoglobin dissociation curve. The decrease in O_2 affinity of hemoglobin when the pH of blood falls is called the Bohr effect.

A dusky bluish discoloration of the tissue due to a higher concentration of reduced hemoglobin is called cyanosis.

The Binding Equilibria of Haemoglobin

Haemoglobin binds oxygen in a characteristic manner in order to function as a carrier of oxygen in the erythrocyte, from the oxygen rich gas phase of the lung to the oxygen-poor peripheral tissues.

Because of the ability of the haemoglobin to bind oxygen, whole blood can absorb some 21 ml of gasèous oxygen per 100 ml, whereas blood plasma alone can absorb only about 0.3 ml of oxygen by physical solution.

A plot of percent saturation of haemoglobin against oxygen partial pressure is sigmoidal. The sigmoidal oxygen binding curve of haemoglobin means that haemoglobin has relatively low affinity for binding the first one or two oxygen molecules but once they are bound, the binding of the subsequent oxygen molecules is greatly enhanced. Conversely, the loss of one oxygen molecule from fully oxygenated haemoglobin causes the rest to dissociate more readily when the oxygen pressure is decreased.

Effect of pH

The position of the haemoglobin oxygen equilibrium is also affected by the pH. The higher the pH of the haemoglobin solution at a given partial pressure of oxygen, the greater the percent saturation with oxygen. This reversible effect results because when haemoglobin is oxygenated, it ionizes, to set free one protein according to the equation.

$$HHb^+ + O_2 \rightarrow HbO_2 + H^+$$

in which HHb^+ is a protonated subunit of a deoxyhemoglobin molecule. Since this reaction is freely reversible, increasing the concentration will cause the equilibrium to shift to the left, toward decreased saturation whereas decreasing the concentration will cause the equilibrium to shift to the right, toward increased saturation. This effect of pH on the oxygen-haemoglobin equilibrium is called the **Bohr effect**.

The partial pressure of oxygen and the pH are the two most important factors regulating the function of haemoglobin in the transport of oxygen. In the lungs, where the partial pressure of oxygen is high (about 100 mm Hg) and the pH also relatively high, haemoglobin tends to become almost maximally saturated with oxygen, about 96 percent. In the interior of the peripheral tissues, where the oxygen tension is low (about 45 mm Hg) and the pH also low (due to the high concentration of CO_2 formed as the end product of respiration) the haemoglobin binds oxygen less strongly and will thus unload some of its oxygen to the respiring cell mass, until the haemoglobin is only about 65 percent saturated. Haemoglobin thus cycles between 65 and 96 percent saturation with oxygen, in its function as oxygen carrier.

Control of Respiration

Breathing is regulated by the complex actions of the various muscles of the respiration. The muscles of the chest, diaphragm, thorax and those within the lungs function in an integrated manner. The rhythm of inspiratory and expiratory movements depends upon both extrinsic and intrinsic mechanisms for control.

The intrinsic or chemical control of respiration ensures that respiration is adequate to meet the needs of the body.

The extrinsic respiratory controls monitor the distension and collapse of the lungs during respiration.

Respiratory Center

Within the pons there are two paired respiratory centres, the **pneumotaxic centres** and the **apneustic centres**, which influence respiratory rate and rhythm. Within the medulla there are two additional centres, the inspiratory center and the expiratory center.

Many aspects of the act of breathing are integrated at the cord level, but the origin of the rhythmicity and the setting of the limits of the tidal volume and respiratory frequency are dependent upon the neuronal pools in the medulla oblongata.

The information from the peripheral receptors, chemosensitive areas in the brain and from higher nervous centres including the cerebral cortex is synthesized by the respiratory centres. The respiratory centres send out efferent impulses via the phrenic and intercostal nerves setting the breathing pattern.

The cranial nerves and the upper part of the brain above pons does not regulate respiration, as the animal continues to breathe regularly even if these areas or nerves are cut or damaged.

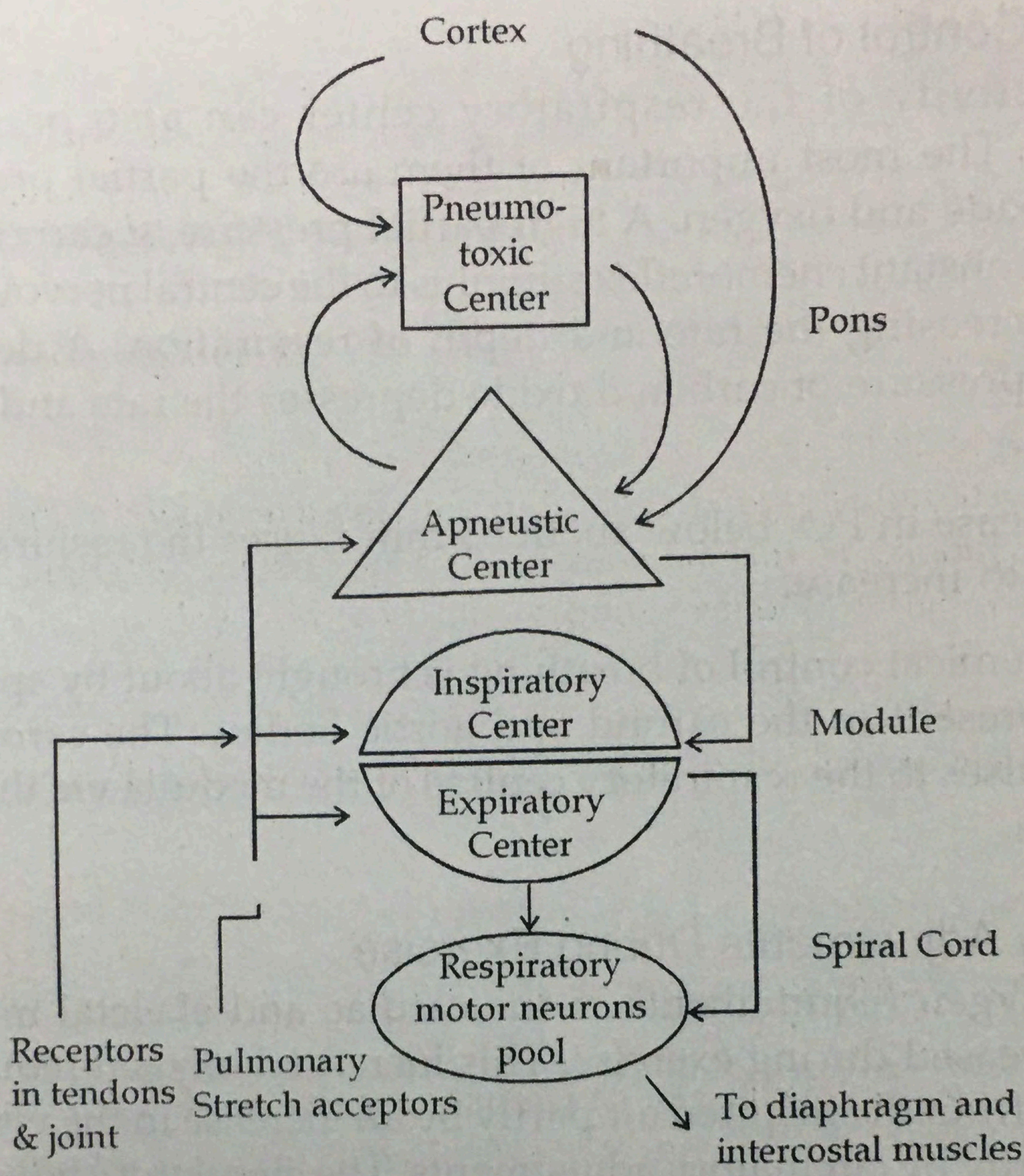
Apneustic and Pneumotaxic Center

The apneustic center the pneumotaxic center lies in the pons. The pneumotaxic center sends periodic inhibiting response which converts the continuing discharge activity of the inspiratory center into a rhythmic pattern.

Inspiratory and Expiratory Centres

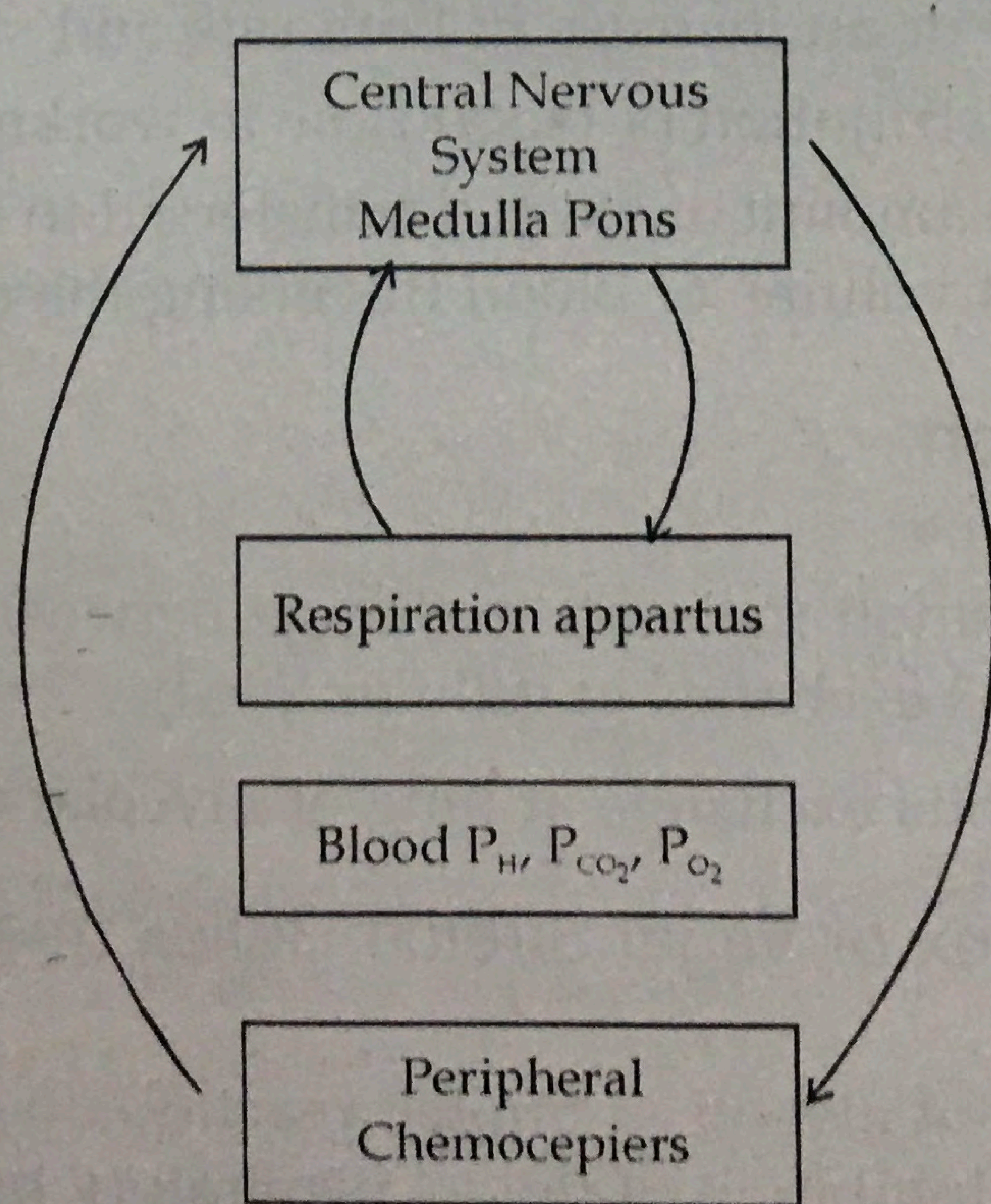
Both the inspiratory and expiratory centres lie in the medulla. Inspiratory stimulus when stimulated causes deep inspiration, due to contraction of the muscles of the thorax, and the diaphragm. Expiratory center when stimulated, causes the cessation of inspiration and the contraction of the expiratory muscles follow.

The pneumotaxic center, the inspiratory center and the expiratory center make up a feedback circuit between the medulla and the pons.



Central Control of Respiration in Mammals

Role of Vagus (Hering Breuer reflex) : The vagus nerve carries apparent impulses that originate in receptors in the lung tissue which are sensitive to stretch.



Chemical Control of Breathing

The activity of the respiratory center can also be modified chemically. The most important of them are the partial pressures of carbon dioxide and oxygen. A high partial pressure of carbon dioxide provides a constant chemoreflex stimulus to the central nervous system, thereby, increasing the rate and depth of respiration. A decrease in the partial pressure of carbon dioxide depresses the rate and depth of respiration.

A decrease in PO_2 below about 65 mm causes the respiration rate and depth to increase.

The chemical control of breathing is brought about by specialized receptors present in the carotid and aortic bodies. The carotid body sends impulses to the respiratory centres of the medulla via the carotid sinus nerve.

Circulatory Adjustments During Exercise

The oxygen requirements of the cardiac and skeletal muscles is greatly increased during exercise. This increased oxygen requirement is obtained from the inspired air partly by an increase in the ventilation rate and partly by circulatory adjustments. The circulatory adjustments are as follows :

(i) Increase in blood flow which occurs through an increase in cardiac output and blood pressure. The cardiac output can increase as a result of an increase in heart rate or an increase in stroke volume or an increase in both rate and stroke volume.

(ii) Preferential distribution of blood flow to working muscles.

(iii) Increase in the amount of oxygen transferred to the active tissues from each unit volume of blood traversing the capillary beds.

Types of Respiration

Respiration is of two types.

1. Internal respiration (gaseous exchange between cells and fluid medium i.e. gas exchange at cellular level).
2. External (gaseous exchange at lung or alveolar level).

Herring Breur Reflex or Vagal Stretch Reflex (mechanoreceptor reflex)

Excess inflation of alveoli → Stretch reaction on alveolar wall → Impulse to brain → Inhibition of dorsal inspiratory neurons.

Vagus nerve can inhibit inspiratory center to cause expiration hence it is known as vagal stretch reflex.

Factors Affecting Diffusion of Gases

Rate of diffusion of gas (D) $\alpha = \dfrac{\Delta P X A X S}{d X \sqrt{M}}$

ΔP = Difference in partial pressure

A = Cross sectional area

S = Solubility of gas

d = Distance of diffusion or thickness of tissue

M = Molecular weight of gas

Diffusion coefficient (D_c) of different gases assuming D_c of oxygen is about 1

O_2	≈	1.0	N_2	=	0.53
CO_2	=	20.3	He	=	0.95
CO	=	0.81			

Transport of O_2 in Blood and Tissue Fluid

1- Transport of O_2

Mainly takes place via two methods

i. In combination with Hb (in the form of HbO_2) - About 97%

ii. In dissolved form (as physical solution)- about 3%

i. In combination with Hb – About 97%

- Each gram of Hb binds with 1.34 ml of O_2.
- (1.39 ml when Hb is chemically pure, but impurities such as methaemoglobin reduce this so if Hb is 100% saturated 15 gm Hb of 100 ml of blood combines with 20.1 ml of O_2 (15 X 1.34)
- Systemic arterial blood is 97% saturated, so about 19.4 ml (20.1 X 0.97) O_2 per 100 ml of blood.
- On passing through tissue capillaries the amount of O_2 in blood is reduced to 14.4 ml (Hb is 75% saturated).

Thus under normal conditions about 5 ml (19.4-14.4) of O_2 are transported form lung to the tissue by each 100 ml of blood flow.

ii. In dissolved form

- Amount of dissolved oxygen is linear function of PO_2.
- At normal arterial PO_2 of 95 mmHg about 0.29 ml O_2 dissolved in 100ml of blood.
- At 40 mmHg in the tissue capillary about 0.12 ml O_2 dissolved in 100ml of blood.
- It means 0.17 ml (0.29-0.12) of O_2 is normally transported in the dissolved state of the tissue by each 100 ml of the arterial blood.
- During strenuous exercise, when Hb release of O_2 to the tissue increases about 3 times, the relative quantity of O_2 transported in dissolved state falls to 1.5%.

Respiratory Centers in Brain

Unlike many centers, it is not a collection of circumscribed nuclei but it consists of regions within the medulla and pons (brain stem) associated with specific functions related to respiration.

Respiratory center is located in medulla. It is divided in 4 major collections of neurons :

1. Dorsal respiratory group (DRG)
2. Ventral respiratory group (VRG)
3. Pneumotaxic center
4. Apneuestic center

Name of respiratory center	Location	Functions
Dorsal respiratory group	Dorsal portion of medulla	• Mainly causes inspiration and generate basic rhythm of berating • Inputs form peripheral chemo-receptors to this center are relayed via vegal and glossopharyngeal nerve and output is relayed via phrenic nerve to diaphragm.
Ventral respiratory group	Ventro-lateral portion of medulla	• Mainly causes expiration • Related with both inspiratory and expiratory activity but mainly causes expiration.

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		• Its inspiratory anu expiratory neurons become active during exercise.
Pneumotaxic center	Rostral pons or dorsally in superior pons	• Control rate and depth of breathing • Its primary function is to limit inspiration, therefore, it regulates inspiratory volume and respiratory rate (It control the 'switch-off' point of the inspiratory ramp, thus controlling the duration of the filling phase of the lung cycle). • It has a secondary effect of increasing the rate of breathing (because of limitation of inspiration and shorting of expiration). • It limits the duration of inspiration and increases frequency of respiratory rate. • It transmits signals to inspiratory area.
Apneuestic center	Caudal pons	• Least understood and believed to be associated with deep inspiration. • Perhaps complementary breaths (sighs) are results of activity of this center.

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