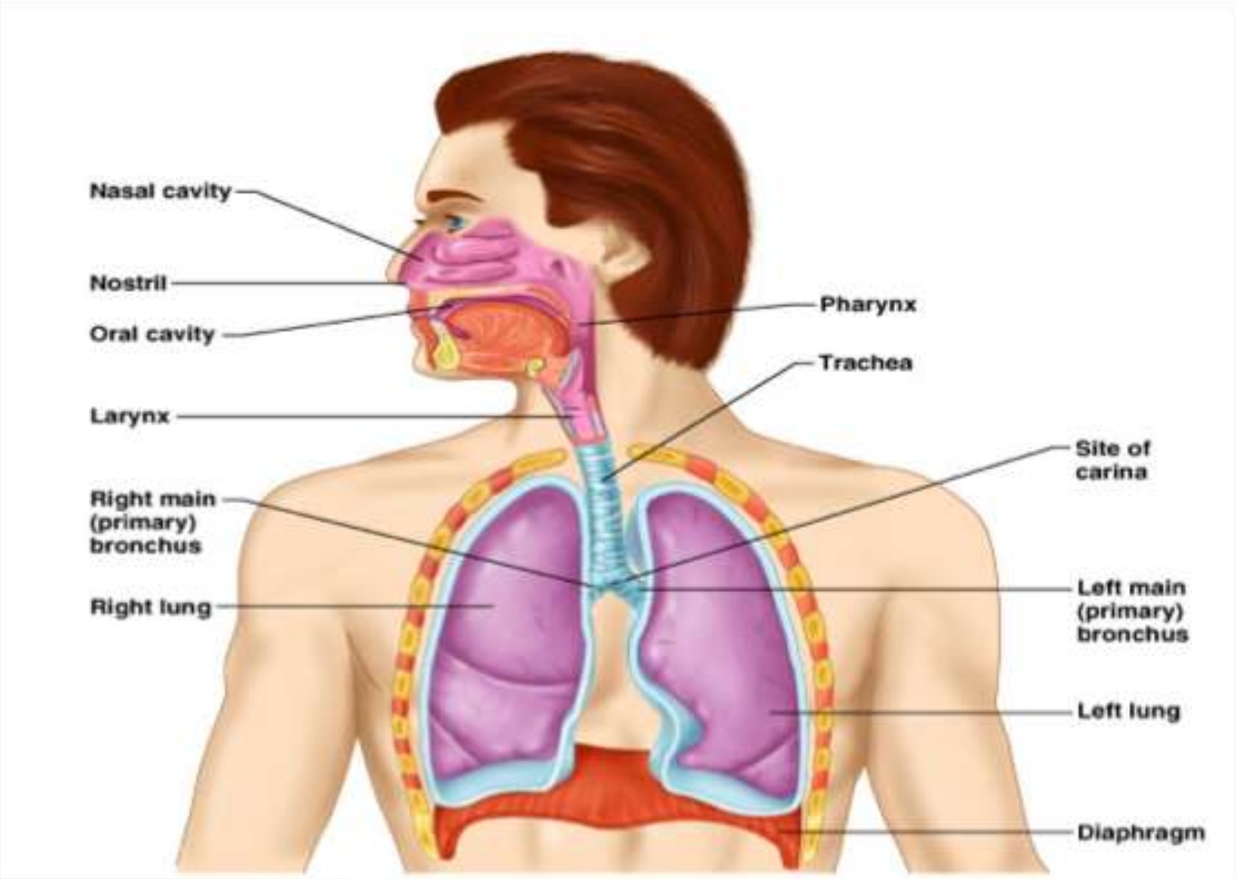
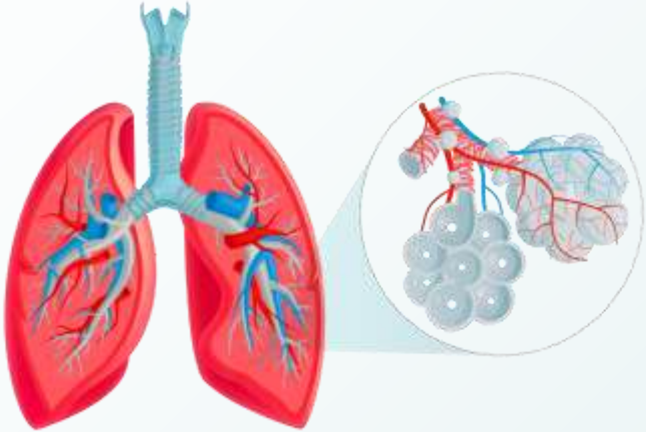
Regulation of Respiration

The Resporetory System



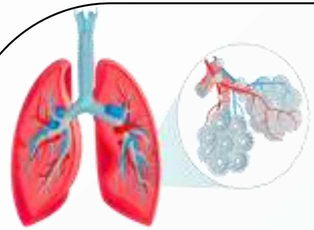
Respiratory Includes

- Pulmonary ventilation
  - Air moves in and out of lungs
  - Continuous replacement of gases in alveoli (air sacs)
- External respiration
  - Gas exchange between blood and air at alveoli
  - O_2 (oxygen) in air diffuses into blood
  - CO_2 (carbon dioxide) in blood diffuses into air
- Transport of respiratory gases
  - Between the lungs and the cells of the body
  - Performed by the cardiovascular system
  - Blood is the transporting fluid
- Internal respiration
  - Gas exchange in capillaries between blood and tissue cells
  - O_2 in blood diffuses into tissues
  - CO_2 waste in tissues diffuses into blood



INTRODUCTION

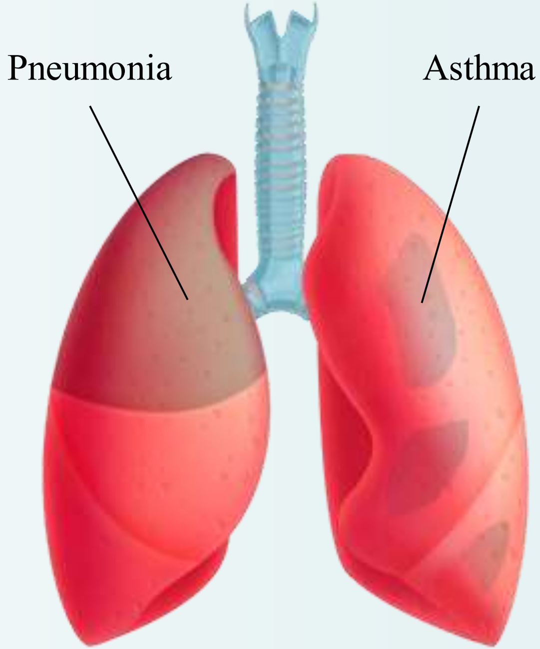
A. The respiratory system consists of tubes that filter incoming air and transport it into the microscopic alveoli where gases are exchanged.

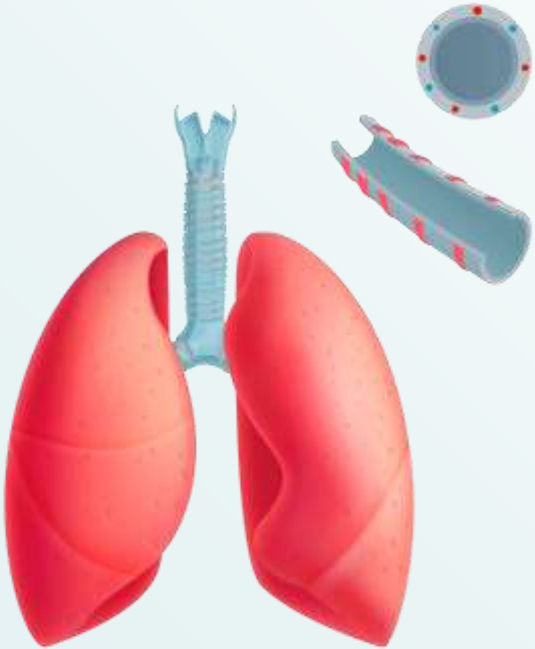


INTRODUCTION

B. The entire process of exchanging gases between the atmosphere and body cells is called respiration and consists of the following:
ventilation, gas exchange between blood and lungs, gas transport in the bloodstream, gas exchange between the blood and body cells, and cellular respiration.

The Respiratory Organs



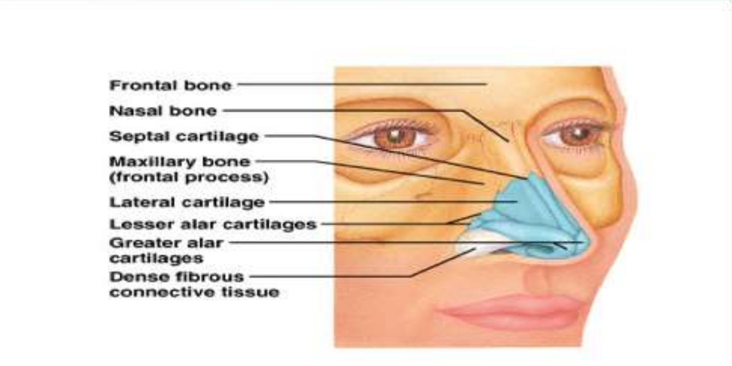


✶Organs of the Respiratory System ✶

A. The organs of the respiratory tract can be divided into two groups: the upper respiratory tract (nose, nasal cavity, sinuses, and pharynx), and the lower respiratory tract (larynx, trachea, bronchial tree, and lungs)

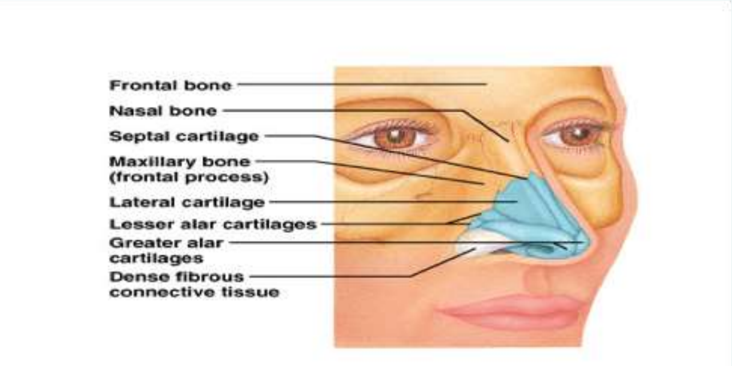
B. Nose

1. The nose, supported by bone and cartilage, provides an entrance for air in which air is filtered by coarse hairs inside the nostrils.



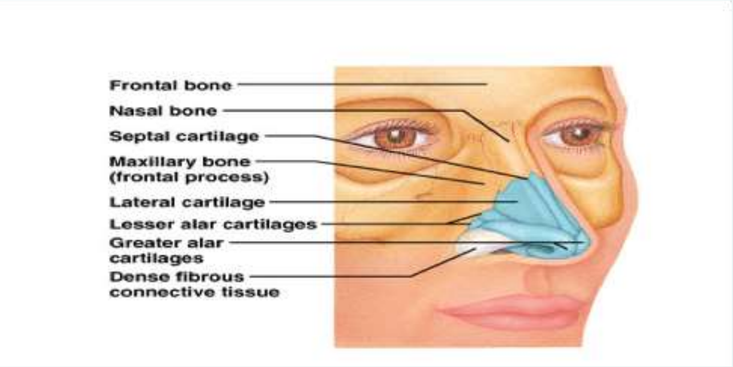
E. Pharynx

1. The pharynx is a common passageway for air and food.
2. The pharynx aids in producing sounds for speech.



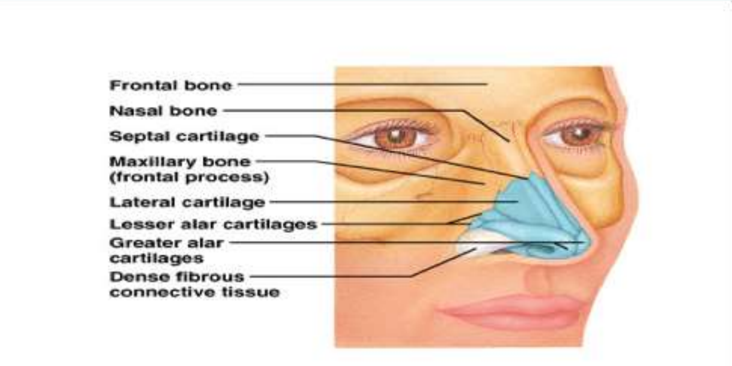
F. Larynx

1. The larynx is an enlargement in the airway superior to the trachea and inferior to the pharynx.
2. It helps keep particles from entering the trachea and also houses the vocal cords.
3. The larynx is composed of a framework of muscles and cartilage bound by elastic tissue.



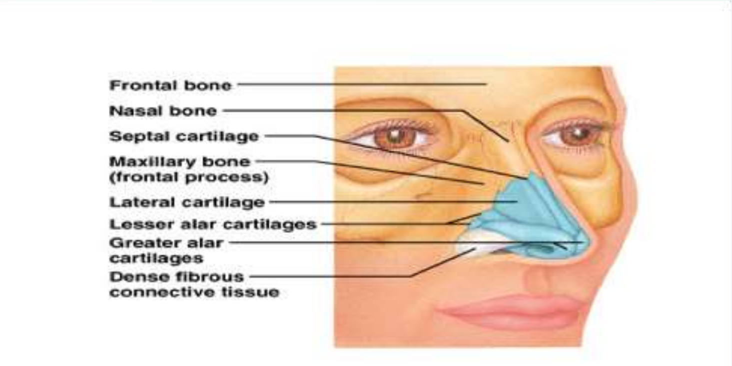
G. Trachea

1. The trachea extends downward anterior to the esophagus and into thoracic cavity, where it splits
and left bronchi.
the into right
2. The inner wall of the trachea is lined with ciliated mucous membrane with many goblet cells that serve to trap incoming particles.
3. The tracheal wall is supported by 20 incomplete cartilaginous rings.



H. Bronchial Tree

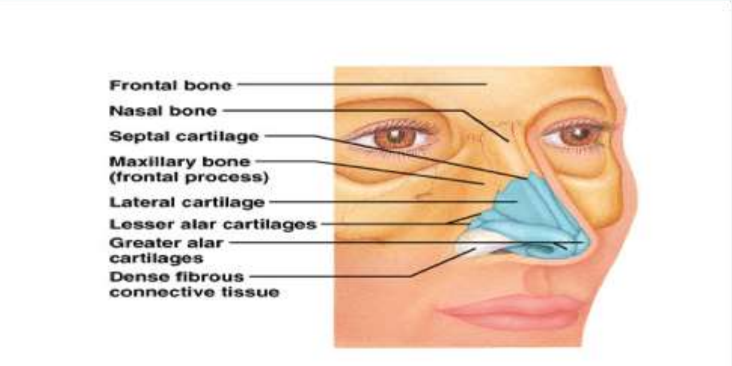
1. The bronchial tree consists of branched tubes leading from the trachea to the alveoli.
2. The bronchial tree begins with the two primary bronchi, each leading lung.



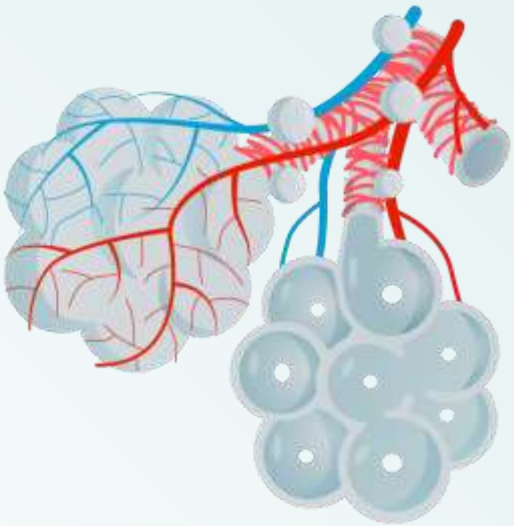
3. The branches of the bronchial tree from the trachea are right and left primary bronchi; these further subdivide until bronchioles give rise to

alveolar ducts which terminate in alveoli.

4. It is through the thin epithelial cells of the alveoli that gas exchange between the blood and air occurs.



REGULATION OF BREATHING



REGULATION OF BREATHING

-The motor neurons that stimulate the respiratory muscles are controlled by two major descending pathways: one that controls voluntary breathing and another that controls involuntary breathing. The unconscious rhythmic control of breathing is influenced by sensory feedback from receptors sensitive to the $P(CO_2)$, pH, and $P(O_2)$ of arterial blood.

-Inspiration and expiration are produced by the contraction and relaxation of skeletal muscles in response to activity in somatic motor neurons in the spinal cord. The activity of these motor neurons is controlled, in turn, by descending tracts from neurons in the respiratory control centers in the medulla oblongata and from neurons in the cerebral cortex.

Brain Stem Respiratory Centers
Medulla Oblongata and Pons

-The somatic motor neurons that stimulate the respiratory muscles have their cell bodies in the gray matter of the spinal cord.

-The motoneurons of the phrenic nerve, stimulating the diaphragm, have cell bodies in the cervical level of the spinal cord those that innervate the respiratory muscles of the rib cage and abdomen have cell bodies in the thoracolumbar region of the cord.

-These spinal motoneurons are regulated, either directly or via spinal interneurons, by descending fibers from the brain.

-The respiratory rhythm is generated by a loose aggregation of neurons in the ventrolateral region of the medulla oblongata, which forms the rhythmicity center for the control of automatic breathing. four types of neurons have been identified that fire at different stages of inspiration.

-These send axons that stimulate the spinal motoneurons of the phrenic nerve to the diaphragm, causing inspiration.

-There is also a ventral respiratory group of neurons in the medulla that contains both I and E neurons. The inspiratory neurons located here stimulate spinal interneurons, which in turn activate the spinal motoneurons of respiration. There is also a region of densely packed expiratory neurons in the ventral respiratory group

-These E neurons inhibit the motoneurons of the phrenic nerve during expiration. The activity of the I and E neurons varies in a reciprocal way to produce a rhythmic pattern of breathing.

-There is evidence that the rhythmicity of I and E neurons may be driven by the cyclic activity of particular pacemaker neurons within the rhythmicity center of the medulla.

-These pacemaker neurons display spontaneous, cyclic changes in the membrane potential, somewhat like the pacemaker cells of the heart

-One area(the apneustic center)appears to promote inspiration by stimulating the I neurons in the medulla. The other area(the pneumotaxic center)seems to antagonize the apneustic center and inhibit inspiration.

Chemoreceptors:

The automatic control of breathing is also influenced by input from chemoreceptors, which are collectively sensitive to changes in the pH of brain interstitial fluid and cerebrospinal fluid, and in the PCO2 , pH, and PO2 of the blood. There are two groups of chemoreceptors that respond to changes in blood PCO2 ,pH, and PO2 .These are the central chemoreceptors in the medulla oblongata and the peripheral chemoreceptors.

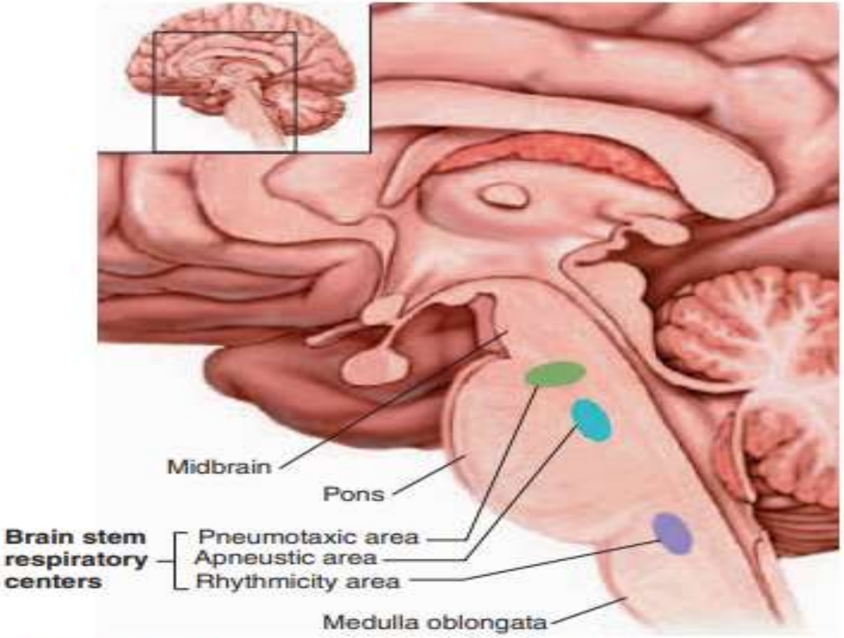


Figure 16.24 **Approximate locations of the brain stem respiratory centers.** The rhythmicity center in the medulla oblongata directly controls breathing, but it receives input from the control centers in the pons and from chemoreceptors.

-These are the central chemoreceptors in the medulla oblongata and the peripheral chemoreceptors.

-The peripheral chemoreceptors are contained within small nodules associated with the aorta and the carotid arteries, and they receive blood from these critical arteries via small arterial branches.

-The aortic bodies, located around the aortic arch, and the carotid bodies, located in each common carotid artery at the point where it branches into the internal and external carotid arteries.

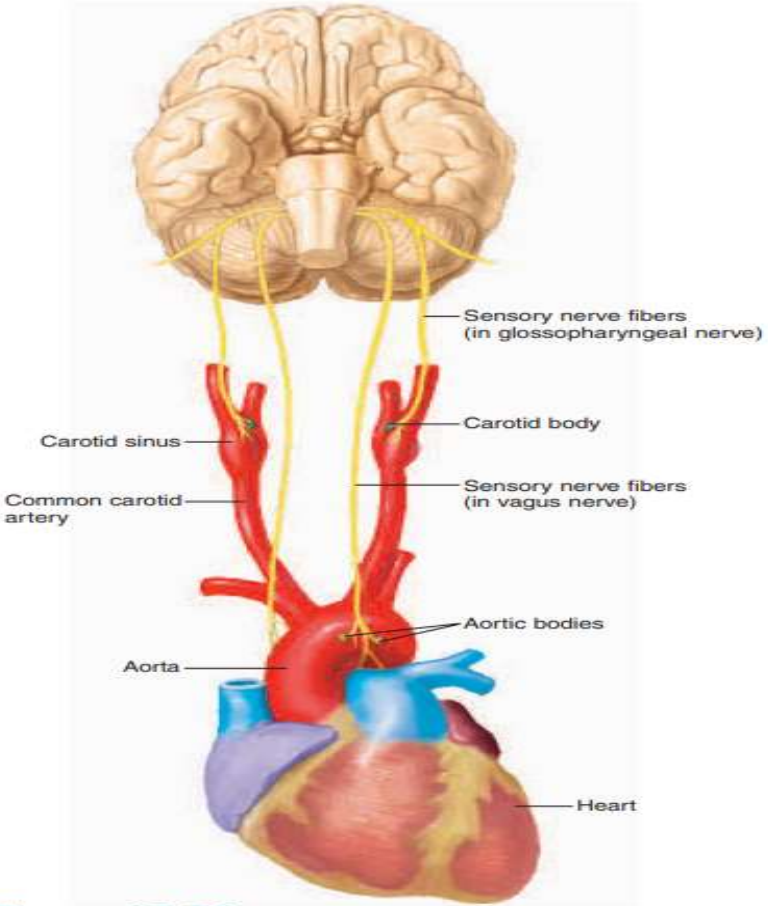


Figure 16.25 **Sensory input from the aortic and carotid bodies.** The peripheral chemoreceptors (aortic and carotid bodies) regulate the brain stem respiratory centers by means of sensory nerve stimulation.

Effects of Blood PCO_2 and pH on Ventilation

Chemoreceptor input to the brain stem modifies the rate and depth of breathing so that, under normal conditions, arterial PCO_2,pH, and PO_2 remain relatively constant. If hypoventilation(inadequate ventilation) occurs, PCO_2quickly rises and pH falls. The fall in pH is due to the fact that carbon dioxide can combine with water to form carbonic acid, which, as a weak acid, can release H^+ into the solution.

-The oxygen content of the blood decreases much more slowly because of the large “reservoir” of oxygen attached to hemoglobin. During hyperventilation, conversely, blood PCO2 quickly falls and pH rises because of the excessive elimination of carbonic acid. The oxygen content of blood, on the other hand, is not significantly increased by hyperventilation (because hemoglobin in arterial blood is 97% saturated with oxygen even during normal ventilation). For these reasons, the blood PCO2 and pH are more immediately affected by changes in ventilation than is the oxygen content.

Chemoreceptors in the Medulla

-The chemoreceptors most sensitive to changes in the arterial PCO2 are located on the ventrolateral surface of the medulla oblongata, near the exit of the ninth and tenth cranial nerves.

-These chemoreceptor neurons are anatomically separate from, but synoptically communicate with, the neurons of the rhythmicity center in the medulla. An increase in arterial PCO2 causes a rise in the H + concentration of the blood as a result of increased carbonic acid concentration

-Carbon dioxide in the arterial blood can cross the blood-brain barrier and, through the formation of carbonic acid, can lower the pH of cerebrospinal fluid . This lower pH then stimulates the central chemoreceptors to increase ventilation when there is a rise in the arterial PCO2.

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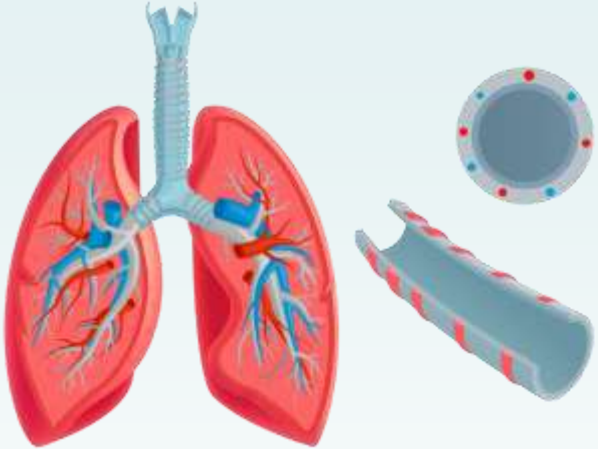
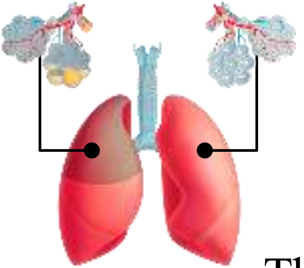


Effects of Blood PO2 on Ventilation

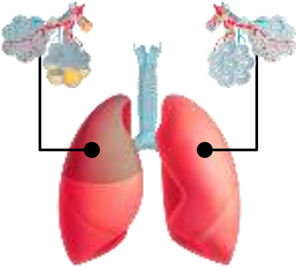
Under normal conditions, blood PO2 affects breathing only indirectly, by influencing the chemoreceptor sensitivity to changes in PCO2 .Chemoreceptor sensitivity to PCO2 is augmented by a low PO2 .



Effects of Pulmonary Receptors on Ventilation

-The lungs contain various types of receptors that influence the brain stem respiratory control centers via sensory fibers in the vagus nerves. Unmyelinated C fibers are sensory neurons in the lungs that can be stimulated by capsaicin, the chemical in hot peppers that creates the Burning sensation.

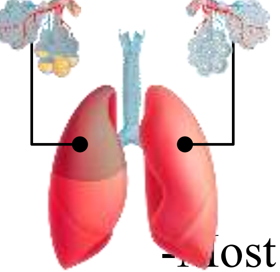
-These receptors produce an initial apnea, followed by rapid, shallow breathing when a person eats these peppers or inhales pepper spray. Irritant receptors in the wall of the larynx, and receptors in the lungs identified as rapidly adapting receptors, can cause a person to cough in response to components of smoke and smog, and to inhaled particulates.



HEMOGLOBIN AND OXYGEN TRANSPORT

-Deoxyhemoglobin eoxyhemoglobin loads with oxygen to form oxyhemoglobin in the pulmonary capillaries, and a portion of the oxyhemoglobin unloads its oxygen in the capillaries of the systemic circulation. The bond strength between hemoglobin and oxygen, and thus the extent of unloading, is changed under different conditions.

-If the lungs are functioning properly, blood leaving in the pulmonary veins and traveling in the systemic arteries has a PO2 of about 100 mmHg, indicating a plasma oxygen concentration of about 0.3 ml O 2 per 100 ml blood. The total oxygen content of the blood, however, cannot be derived if only the PO2 of plasma is known. The total oxygen content depends not only on the PO2 but also on the hemoglobin concentration

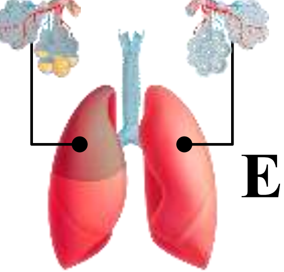


Hemoglobin

-Most of the oxygen in the blood is contained within the red blood cells, where it is chemically bonded to hemoglobin. Each hemoglobin molecule oxyhemoglobin dissociates to release oxygen to the tissues, the heme iron is still in the reduced (Fe^{2+}) form and the hemoglobin is called deoxyhemoglobin, reduced or hemoglobin.

The Oxyhemoglobin Dissociation Curve

-Blood in the systemic arteries, at a PO_2 of 100 mmHg, has a percent oxyhemoglobin saturation of 97% (which means that 97% of the hemoglobin is in the form of oxyhemoglobin). This blood is delivered to the systemic capillaries, where oxygen diffuses into the cells and is consumed in aerobic respiration. Blood leaving in the systemic veins is thus reduced in oxygen



Effect of pH and Temperature on Oxygen Transport

-In addition to changes in PO2 ,the loading and unloading reactions are influenced by changes in the affinity of hemoglobin for oxygen. Such changes ensure that active skeletal muscles will receive more oxygen from the blood than they do at rest. This occurs as a result of the lowered pH and increased temperature in exercising muscles.

- The affinity is decreased when the pH is lowered and increased when the pH is raised; this is called the Bohr effect. When the affinity of hemoglobin for oxygen is reduced, there is slightly less loading of the blood with oxygen in the lungs but greater unloading of oxygen in the tissues. the Bohr effect helps to provide more oxygen to the tissues when their carbon dioxide output is increased by a faster metabolism

Effect of 2,3-DPG on Oxygen Transport

- Mature red blood cells lack both nuclei and mitochondria. Without mitochondria they cannot respire aerobically; the very cells that carry oxygen are the only cells in the body that cannot use it! Red blood cells, therefore, must obtain energy through the anaerobic metabolism of glucose.

- At a certain point in the glycolytic pathway, a “side reaction” occurs in the red blood cells that results in a unique product— **2,3-diphosphoglyceric acid (2,3-DPG).**

- An increased concentration of 2,3-DPG in red blood cells thus increases oxygen unloading.

- **Anemia**
- When the total blood hemoglobin concentration falls below normal in anemia, each red blood cell produces increased amounts of 2,3-DPG.

- If the hemoglobin concentration were reduced by half, you might expect that the tissues would receive only half the normal amount of oxygen

- **Fetal Hemoglobin**
- The effects of 2,3-DPG are also important in the transfer of oxygen from maternal to fetal blood. In an adult, hemoglobin molecules are composed of two alpha and two beta chains.

- Normal **adult hemoglobin** in the mother **(hemoglobin A)** is able to bind to 2,3-DPG. **Fetal hemoglobin,** or **hemoglobin F,** by contrast, cannot bind to 2,3-DPG, and thus has a higher affinity for oxygen than does hemoglobin A.

Inherited Defects in Hemoglobin Structure and Function

- A number of hemoglobin diseases are produced by congenital (inherited) defects in the protein part of hemoglobin.

- **Sickle- cell anemia – a disease** is caused by an abnormal form of hemoglobin called hemoglobin S.

- **Thalassemia** is any of a family of hemoglobin diseases found predominantly among people of Mediterranean ancestry. In alpha thalassemia, there is decreased synthesis of the alpha chains of hemoglobin, whereas in beta thalassemia the synthesis of the beta chains is impaired. Beta thalassemia can be caused by over 200 different point mutations in DNA, as well as by rare DNA deletions.

Muscle Myoglobin

- **myoglobin** is a red pigment found exclusively in striated muscle cells. In particular, slow-twitch, aerobically respiring skeletal fibers and cardiac muscle cells are rich in myoglobin.

- Myoglobin is similar to hemoglobin, but it has one heme rather than four; therefore, it can combine with only one molecule of oxygen.

- Myoglobin may also have an oxygen-storage function, which is of particular importance in the heart.

- During diastole, when the coronary blood flow is greatest, myoglobin can load up with oxygen. This stored oxygen can then be released during systole, when the coronary arteries are squeezed closed by the contracting myocardium.

Carbon dioxide

- is carried by the blood in three forms:

(1) as dissolved CO_2 in the plasma—carbon dioxide is about 21 times more soluble than oxygen in water, and about one-tenth of the total blood CO_2 is dissolved in plasma.

(2) as carbaminohemoglobin—about one-fifth of the total blood CO_2 is carried attached to an amino acid in hemoglobin (carbaminohemoglobin should not be confused with carboxyhemoglobin, which is a combination of hemoglobin and carbon monoxide)

(3) as bicarbonate ion, which accounts for most of the CO carried by the blood.

The Chloride Shift

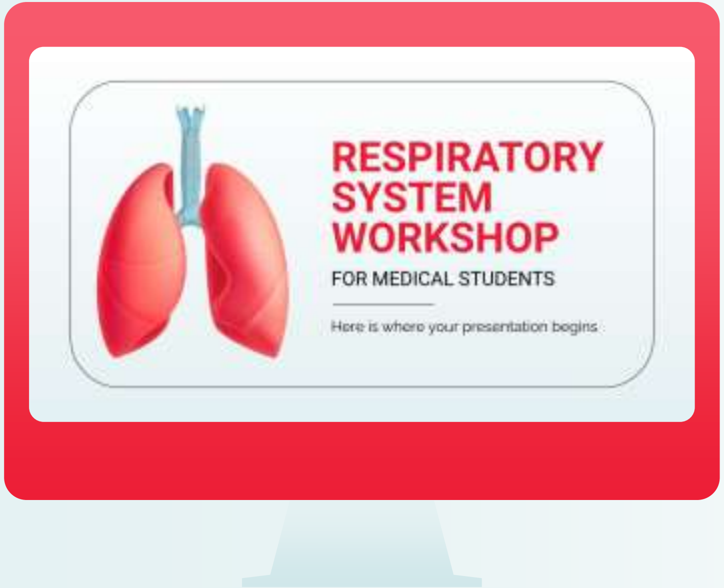
- As a result of catalysis by carbonic anhydrase within the red blood cells, large amounts of carbonic acid are produced as blood passes through the systemic capillaries.

- The hydrogen ions (H^+) released by the dissociation of carbonic acid are largely buffered by their combination with deoxyhemoglobin within the red blood cells.

The Reverse Chloride Shift

- Carbon dioxide is released from the blood as it travels through the pulmonary capillaries.
- A “reverse chloride shift” occurs during this time, and carbonic acid is transformed into CO_2 and H_2O.
- The CO_2 is eliminated in the exhaled air.
- Sources of carbon dioxide in blood include:

(1) dissolved CO_2
(2) carbaminohemoglobin
(3) bicarbonate (HCO_3).



Principles of Acid-Base Balance

- The blood plasma within arteries normally has a pH between 7.35 and 7.45, with an average of 7.40.

- Carbon dioxide is produced by tissue cells through aerobic cell respiration and is transported by the blood to the lungs, where it can be exhaled. carbonic acid can be reconverted to carbon dioxide, which is a gas.

- Because it can be converted to a gas, carbonic acid is referred to as a volatile acid, and its concentration in the blood is controlled by the lungs through proper ventilation (breathing).

- All other acids in the blood— including lactic acid, fatty acids, ketone bodies, and so on— are nonvolatile acids.

- Under normal conditions, the H+ released by nonvolatile metabolic acids does not affect the blood pH because these hydrogen ions are bound to molecules that functions buffers.

Principles of Acid-Base Balance

- A fall in blood pH below 7.35 is called acidosis because the pH is to the acid side of normal.

- Acidosis does not mean acidic (pH less than 7); a blood pH of 7.2, for example, represents serious acidosis. Similarly, a rise in blood pH above 7.45 is called alkalosis.

- Both of these conditions are categorized into respiratory and metabolic components of acid-base balance.

- Respiratory acidosis is caused by inadequate ventilation (hypoventilation), which results in a rise in the plasma concentration of carbon dioxide, and thus carbonic acid.
- Respiratory alkalosis, by contrast, is caused by excessive ventilation (hyperventilation).
- Metabolic acidosis can result from excessive production of nonvolatile acids. It can also result from the loss of bicarbonate, in which case there would not be sufficient free bicarbonate to buffer the non-volatile acids. Metabolic alkalosis, by contrast, can be caused by either

Ventilation and Acid-Base Balance

- In terms of acid-base regulation, the acid-base balance of the blood is divided into the respiratory component and the metabolic component.
- The respiratory component refers to the carbon dioxide concentration of the blood, as measured by its PCO2.

- As implied by its name, the respiratory component is regulated by the respiratory system.
- Ventilation is normally adjusted to keep pace with the metabolic rate, so that the arterial PCO2 remains in the normal range.

- In hypoventilation, the ventilation is insufficient to “blow off” carbon dioxide and maintain a normal PCO2. Indeed, hypoventilation can be operationally defined as an abnormally high arterial P .

Ventilation and Acid-Base Balance

- In hyperventilation, conversely, the rate of ventilation is
- greater than the rate of CO2 production.
- Arterial PCO2, therefore, decreases, so that less carbonic acid is formed than under normal conditions. The depletion of carbonic acid raises the pH of the blood, and respiratory alkalosis occurs.
- Hyperventilation can cause dizziness because it also raises the pH of cerebrospinal fluid (CSF).
- A change in blood pH, produced by alterations in either the respiratory or metabolic component of acid-base balance, can be partially compensated for by a change in the other component.

References: Human physiology, Stuart Ira Fox.

Fundamentals of anatomy and physiology, Martini.