Physiology of Respiration

Lec.1&2 ***2nd year*** ***Dr.Mahir Al-Talah***

Pulmonary Ventilation

The goals of respiration are to provide O_2 to the tissues and remove CO_2 to achieve these goals, respiration can be divided into four major functions:-

(1) Pulmonary ventilation*: Which means the inflow and outflow of air between the atmosphere and the lung alveoli.*

(2) Diffusion of oxygen and carbon dioxide *between the alveoli and the blood.*

(3) Transport of oxygen and carbon dioxide *in the blood and body fluids to and from the body's tissue cells.*

(4) Regulation of ventilation *and other facets of respiration.*

Ventilation and the exchange of gases (oxygen and carbon dioxide) between the air and blood are collectively called ***external respiration****.*

Gas exchange between the blood and other tissues and oxygen utilization by the tissues are collectively known as ***internal respiration****.*

Structure of the Respiratory System

The air passages of the respiratory system are divided into two functional zones.

The ***respiratory zone*** *is the region where gas exchange occurs, and it therefore includes the respiratory bronchioles (because they contain separate outpouchings of alveoli) and the terminal alveolar sacs.*

The ***conducting zone*** *includes all of the anatomical structures through which air passes before reaching the respiratory zone.The conducting zone of the respiratory system, in summary,consists of the mouth, nose, pharynx, larynx, trachea, primary bronchi, and all successive branchings of the bronchioles up to and including the terminal bronchioles. In addition to conducting air into the respiratory zone, these structures serve additional functions: warming and humidification of the inspired air and filtration and cleaning.*

Regardless of the temperature and humidity of the ambient air, when the inspired air reaches the respiratory zone it is at a temperature of 37°C (body temperature), and it is saturated with water vapor as it flows over the warm, wet mucous membranes that line the respiratory airways. This ensures that a constant internal body temperature will be maintained and that delicate lung tissue will be protected from desiccation. Mucus secreted by cells of the conducting zone structures serves to trap small particles in the inspired air and thereby performs a filtration function. This mucus is moved along at a rate of 1 to 2 centimeters per minute by cilia projecting from the tops of epithelial cells that line the conducting zone. There are about 300 cilia per cell that beat in a coordinated fashion to move mucus toward the pharynx, where it can either be swallowed or expectorated. As a result of this filtration function, particles larger than about 6 μm do not normally enter the respiratory zone of the lungs.

Muscles that cause lung expansion and contraction.

The lungs can be expanded and contracted in two ways:

(1) By downward and upward movement of the diaphragm to lengthen or shorten the chest cavity.

(2) By elevation and depression of the ribs to increase and decrease the anteroposterior diameter of the chest cavity.

Normal quiet breathing *is accomplished almost entirely by the first method, that is, by movement of the diaphragm. During inspiration, contraction of the diaphragm pulls the lower surfaces of the lungs downward. Then, during expiration, the diaphragm simply relaxes, and the elastic recoil of the lungs, chest wall, and abdominal structures compresses the lungs and expels the air.*

During heavy breathing*, however, the elastic forces are not powerful enough to cause the necessary rapid expiration, so that extra force is achieved mainly by contraction of the abdominal muscles, which pushes the abdominal contents upward against the bottom of the diaphragm, thereby compressing the lungs.*

The second method for expanding the lungs is to raise the rib cage. This expands the lungs because, in the natural resting position, the ribs slant downward, thus allowing the sternum to fall backward toward the vertebral column. But when the rib cage is elevated, the ribs project almost directly forward, so that the sternum also moves forward, away from the spine, making the anteroposterior thickness of the chest about 20 per cent greater during maximum inspiration than during expiration. Therefore,all the muscles that elevate the chest cage are classified as muscles of inspiration, and those muscles that depress the chest cage are classified as muscles of expiration. The most important muscles that raise the rib cage are the external intercostals, but other muscles help also.

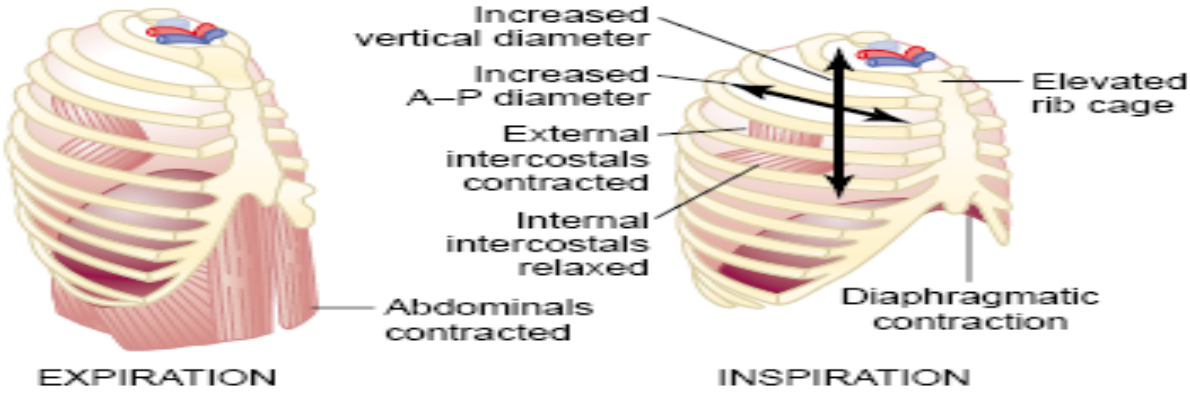


Figure 37–1

Contraction and expansion of the thoracic cage during expiration and inspiration, demonstrating diaphragmatic contraction, function of the intercostal muscles, and elevation and depression of the rib cage.

Movement of air to the lungs and the pressures that cause the movement:

The lung is an elastic structure that collapses like a balloon and expels all its air through the trachea whenever there is no force to keep it inflated. Also, there are no attachments between the lung and the walls of the chest cage, except where it is suspended at its hilum from the mediastinum. Instead, the lung "floats" in the thoracic cavity, surrounded by a thin layer of pleural fluid that lubricates movement of the lungs within the cavity. Further, continual suction of excess fluid into lymphatic channels maintains a slight suction between the visceral surface of the lung pleura and the parietal pleural surface of the thoracic cavity. Therefore, the lungs are held to the thoracic wall as if glued there, except that they are well lubricated and can slide freely as the chest expands and contracts.

Pulmonary pressures:

(A)Pleural pressure

Pleural pressure is the pressure of the fluid in the thin space between the lung pleura and the chest wall pleura. This is normally a slight suction, which means a slightly negative pressure. The normal pleural pressure at the beginning of inspiration is about –5 centimeters of water.

(B)Alveolar pressure

Alveolar pressure is the pressure of the air inside the lung alveoli. When the glottis is open and no air is flowing into or out of the lungs, the pressures in all parts of the respiratory tree, all the way to the alveoli, are equal to atmospheric pressure, which is considered to be zero reference pressure in the airways—that is, 0 centimeters water pressure. To cause inward flow of air into the alveoli during inspiration, the pressure in the alveoli must fall to a value slightly below atmospheric pressure (below 0).

(C)Transpulmonary pressure

The transpulmonary pressure is the difference between the alveolar pressure and the pleural pressure. It is the pressure difference between that in the alveoli and that on the outer surfaces of the lungs, and it is a measure of

the elastic forces in the lungs that tend to collapse the lungs at each instant of respiration, called the recoil pressure.

Physical Factors Influencing Pulmonary Ventilation

The lungs are stretched during inspiration and recoil passively during expiration. The inspiratory muscles consume energy to enlarge the thorax. Energy is also used to overcome various factors that hinder air passage and pulmonary ventilation.

Airway Resistance

The major nonelastic source of resistance to gas flow is friction, or drag, encountered in the respiratory passageways. The relationship between gas flow (F), pressure (P), and resistance (R) is given by the following equation:

$$F=\Delta P/R$$

The amount of gas flowing into and out of the alveoli is directly proportional to ΔP, the difference in pressure, or the pressure gradient, between the external atmosphere and the alveoli. Normally, very small differences in pressure produce large changes in the volume of gas flow. The average pressure gradient during normal quiet breathing is 2 mm Hg or less, and yet it is sufficient to move 500 ml of air in and out of the lungs with each breath.

But, as the equation also indicates, gas flow changes inversely with resistance. That is, gas flow decreases as resistance increases. However, as a rule, airway resistance is insignificant for two reasons:

1. Airway diameters in the first part of the conducting zone are huge, relative to the low viscosity of air.

2. As the airways get progressively smaller, there are progressively more branches. As a result, although individual bronchioles are tiny, there are an enormous number of them in parallel, so the total cross-sectional area is huge.

Alveolar Surface Tension

At any gas-liquid boundary, the molecules of the liquid are more strongly attracted to each other than to the gas molecules. This unequal attraction produces a state of tension at the liquid surface, called surface tension, that (1) draws the liquid molecules closer together and reduces their contact with the dissimilar gas molecules, and (2) resists any force that tends to increase the surface area of the liquid.

Water is composed of highly polar molecules and has a very high surface tension. Because water is the major component of the liquid film that coats the alveolar walls, it is always acting to reduce the alveoli to their smallest possible size. If the film was pure water, the alveoli would collapse between breaths. But the alveolar film contains **surfactant**, *a detergent-like complex of lipids and proteins produced by the type II alveolar cells. Surfactant decreases the cohesiveness of water molecules, much the way a laundry detergent reduces the attraction of water for water, allowing water to interact with and pass through fabric. As a result, the surface tension of alveolar fluid is reduced, and less energy is needed to overcome those forces to expand the lungs and discourage alveolar collapse. Breaths that are deeper than normal stimulate type II cells to secrete more surfactant.*

Compliance of the lungs

Healthy lungs are unbelievably stretchy, and this distensibility is referred to as lung compliance.

Lung compliance is determined largely by two factors: (1) distensibility of the lung tissue, and (2) alveolar surface tension. Because lung distensibility is generally high and alveolar surface tension is kept low by surfactant, the lungs of healthy people tend to have high compliance, which favors efficient ventilation.

Lung compliance is diminished by a decrease in the natural resilience of the lungs. Chronic inflammation, or infections such as tuberculosis, can cause nonelastic scar tissue to replace normal lung tissue (fibrosis).

Another factor that can decrease lung compliance is a decrease in production of surfactant. The lower the lung compliance, the more energy is needed just to breathe.

Since the lungs are contained within the thoracic cavity, we also need to consider the compliance (distensibility) of the thoracic wall. Factors that decrease the compliance of the thoracic wall hinder the expansion of the lungs. The total compliance of the respiratory system is comprised of lung compliance and thoracic wall compliance.

Pulmonary volumes and capacities

Recording changes in pulmonary volume—spirometry

A simple method for studying pulmonary ventilation is to record the volume movement of air into and out of the lungs, a process called spirometry. spirometr consists of a drum inverted over a chamber of water, with the drum counterbalanced by a weight. In the drum is a breathing gas, usually air or oxygen; a tube connects the mouth with the gas chamber. When one breathes into and out of the chamber, the drum rises and falls, and an appropriate recording is made on a moving sheet of paper.

(A)Pulmonary volumes

The four pulmonary lung volumes that, when added together, equal the maximum volume to which the lungs can be expanded. The significance of each of these volumes is the following:

1. ***The tidal volume*** *is the volume of air inspired or expired with each normal breath; it amounts to about 500 milliliters in the adult male.*
2. ***The inspiratory reserve volume*** *is the extra volume of air that can be inspired over and above the normal tidal volume when the person inspires with full force; it is usually equal to about 3000 milliliters.*
3. ***The expiratory reserve volume*** *is the maximum extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration; this normally amounts to about 1100 milliliters.*
4. ***The residual volume*** *is the volume of air remaining in the lungs after the most forceful expiration; this volume averages about 1200 milliliters*

(B)Pulmonary capacities

In describing events in the pulmonary cycle, it is sometimes desirable to consider two or more of the volumes together. Such combinations are called pulmonary capacities. The important pulmonary capacities, which can be described as follows:

1. ***The inspiratory capacity*** *equals the tidal volume plus the inspiratory reserve volume. This is the amount of air (about 3500 milliliters) a person can breathe in, beginning at the normal expiratory level and distending the lungs to the maximum amount.*
2. ***The functional residual capacity*** *equals the expiratory reserve volume plus the residual volume. This is the amount of air that remains in the lungs at the end of normal expiration (about 2300 milliliters).*
3. ***The vital capacity*** *equals inspiratory reserve volume plus the tidal volume plus the expiratory reserve volume. This is the maximum amount of air a person can expel from the lungs after first filling the lungs to their maximum extent and then expiring to the maximum extent (about 4600 milliliters).*
4. ***The total lung capacity*** *is the maximum volume to which the lungs can be expanded with the greatest possible effort (about 5800 milliliters); it is equal to the vital capacity plus the residual volume.*

All pulmonary volumes and capacities are about 20 to 25 per cent less in women than in men, and they are greater in large and athletic people than in small and asthenic people.

Dead Space

Some of the inspired air fills the conducting respiratory passageways and never contributes to gas exchange in the alveoli. The volume of these conducting zone conduits, which make up the anatomical dead space, typically amounts to about 150 ml. This means that if TV is 500 ml, only 350 ml of it is involved in alveolar ventilation. The remaining 150 ml of the tidal breath is in the anatomical dead space.

If some alveoli cease to act in gas exchange (due to alveolar collapse or obstruction by mucus, for example), the alveolar dead space is added to the anatomical dead space, and the sum of the nonuseful volumes is referred to as total dead space.

Pulmonary Function Tests

Because the various lung volumes and capacities are often abnormal in people with pulmonary disorders, they are routinely measured in such patients. Spirometry is most useful for evaluating losses in respiratory function and for following the course of certain respiratory diseases. Although it cannot provide a specific diagnosis, it can distinguish between obstructive pulmonary disease involving increased airway resistance (such as chronic

bronchitis) and restrictive disorders involving a reduction in total lung capacity resulting from structural or functional changes in the lungs (due to diseases such as tuberculosis, or to fibrosis due to exposure to certain environmental agents such as asbestos). Increases in TLC, FRC, and RV may occur as a result of hyperinflation of the lungs in obstructive disease, whereas VC, TLC, FRC, and RV are reduced in restrictive diseases, which limit lung expansion.

More information can be obtained about a patient's ventilation status by assessing the rate at which gas moves into and out of the lungs. The minute ventilation is the total amount of gas that flows into or out of the respiratory tract in 1 minute. During normal quiet breathing, the minute ventilation in healthy people is about 6 L/min (500 ml per breath multiplied by 12 breaths per minute). During vigorous exercise, the minute ventilation may reach 200 L/min.

Two other useful tests are FVC and FEV. FVC, or forced vital capacity, measures the amount of gas expelled when a subject takes a deep breath and then forcefully exhales maximally and as rapidly as possible. FEV, or forced expiratory volume, determines the amount of air expelled during specific time intervals of the FVC test. For example, the volume exhaled during the first second is FEV1. Those with healthy lungs can exhale about 80% of the FVC within 1 second. Those with obstructive pulmonary disease exhale considerably less than 80% of the FVC within 1 second, while those with restrictive disease can exhale 80% or more of FVC in 1 second even though their FVC is reduced.

Nonrespiratory Air Movements

Many processes other than breathing move air into or out of the lungs, and these processes may modify the normal respiratory rhythm. Most of these nonrespiratory air movements result from reflex activity, but some are produced voluntarily. The most common of these movements are;

Cough reflex

The bronchi and trachea are so sensitive to light touch that very slight amount of foreign matter or other causes of irritation initiate the cough reflex. The larynx and carina (the point where the trachea divides into the bronchi) are especially sensitive, and the terminal bronchioles and even the alveoli are sensitive to corrosive chemical stimuli such as sulfur dioxide gas or chlorine gas. Afferent nerve impulses pass from the respiratory passages mainly through the vagus nerves to the medulla of the brain. There, an automatic sequence of events is triggered by the neuronal circuits of the medulla, causing the following effect.

***1.** About 2.5 liters of air are rapidly inspired.*

***2.** The epiglottis closes, and the vocal cords shut tightly to entrap the air within the lungs.*

***3.** The abdominal muscles contract forcefully, pushing against the diaphragm while other expiratory muscles, such as the internal intercostals, also contract forcefully. Consequently, the pressure in the lungs rises rapidly to as much as 100 mm Hg or more.*

***4.** The vocal cords and the epiglottis suddenly open widely, so that air under this high pressure in the lungs explodes outward. Indeed, sometimes this air is expelled at velocities ranging from 75 to 100 miles per hour. Importantly, the strong compression of the lungs collapses the bronchi and trachea by causing their noncartilaginous parts to invaginate inward, so that the exploding air actually passes through bronchial and tracheal slits. The rapidly moving air usually carries with it any foreign matter that is present in the bronchi or trachea.*

Sneeze reflex

The sneeze reflex is like the cough reflex, except that it applies to the nasal passageways instead of the lower respiratory passages. The initiating stimulus of the sneeze reflex is irritation in the nasal passageways; the afferent impulses pass in the fifth cranial nerve to the medulla, where the reflex is triggered. A series of reactions similar to those for the cough reflex takes place; however, the uvula is depressed, so that large amounts of air pass rapidly through the nose, thus helping to clear the nasal passages of foreign matter.

Vocalization

Speech involves not only the respiratory system but also:

(1) Specific speech nervous control centers in the cerebral cortex
(2) Respiratory control centers of the brain
(3) The articulation and resonance structures of the mouth and nasal cavities.
Speech is composed of two mechanical functions:
(1) Phonation, which is achieved by the larynx
(2) Articulation, which is achieved by the structures of the mouth.

Phonation.

The larynx is especially adapted to act as a vibrator. The vibrating element is the vocal folds, commonly called the vocal cords. The vocal cords protrude from the lateral walls of the larynx toward the center of the glottis; they are stretched and positioned by several specific muscles of the larynx itself.
During normal breathing, the cords are wide open to allow easy passage of air. During phonation, the cords move together so that passage of air between them will cause vibration. The pitch of the vibration is determined mainly by the degree of stretch of the cords, but also by how tightly the cords are approximated to one another and by the mass of their edges.

Articulation and resonance.

The three major organs of articulation are the lips, tongue, and soft palate. The resonators include the mouth, the nose and associated nasal sinuses, the pharynx, and even the chest cavity. For instance, the function of the nasal resonators is demonstrated by the change in voice quality when a person has a severe cold that blocks the air passages to these resonators.

Hiccups *; sudden inspiration resulting from spasm of diaphragm,believed to be initiated by irritation of diaphragm or phrenic nerve ,sound occure when inspired air hits vocal fold of closing glottis.*

Yawn *; very deep inspiration,taken with jaws wide open ,ventilates all alveoli(not the case in normal quite breathing).*

Thank you……...

Physiology of Respiration *Lec - [3&4]*

Gas Exchanges between the Blood, Lungs, and Tissues.

*During **external respiration** oxygen enters and carbon dioxide leaves the blood in the lungs .At the body tissues, where the process is called **internal respiration**, the same gases move in opposite directions by the same mechanism(**diffusion**.) To understand these processes, we must examine some of the physical properties of gases and consider the composition of alveolar gas.*

Basic Properties of Gases

*Two gas laws provide most of the information we need—**Dalton's law** of partial pressures reveals how a gas behaves when it is part of a mixture of gases, and **Henry's law** will help us understand movement of gases into and out of solution.*

Dalton's Law of Partial Pressures

Dalton's law of partial pressures states that the total pressure exerted by a mixture of gases is the sum of the pressures exerted independently by each gas in the mixture .Further, the pressure exerted by each gas—its partial pressure—is directly proportional to the percentage of that gas in the gas mixture.
Nitrogen makes up about 79 %of air, and the partial pressure of nitrogen [PN2]is 78.6 %× 760 mm Hg, or 597

mm Hg .Oxygen gas, which accounts for nearly 21 % of the atmosphere, has a partial pressure[PO2] of 159 mm Hg(20.9 %× 760 mm Hg) .Thus, nitrogen and oxygen together contribute about 99 %of the total atmospheric pressure.

Air also contains 0.04 %carbon dioxide, up to 0.5 %water vapor, and insignificant amounts of inert gases(such as argon and helium).

TABLE 22.4 Comparison of Gas Partial Pressures and Approximate Percentages in the Atmosphere and in the Alveoli

	ATMOSPHERE (SEA LEVEL)		ALVEOLI	
GAS	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)	APPROXIMATE PERCENTAGE	PARTIAL PRESSURE (mm Hg)
N_2	78.6	597	74.9	569
O_2	20.9	159	13.7	104
CO_2	0.04	0.3	5.2	40
H_2O	0.46	3.7	6.2	47
	100.0%	760	100.0%	760

At high altitudes, where the atmosphere is less influenced by gravity, partial pressures decline in direct proportion to the decrease in atmospheric pressure .For example, at 10,000 feet above sea level where the atmospheric pressure is 523 mm Hg, PO2 is 110 mm Hg .Moving in the opposite direction, atmospheric pressure increases by 1 atm(760 mm Hg) for each 33 feet of descent(in water) below sea level .

Thus, at 99 feet below sea level, the total pressure exerted on the body is equivalent to 4 atm, or 3040 mm Hg, and the partial pressure exerted by each component gas is also quadrupled.

Henry's.Law

According to Henry's law, when a mixture of gases is in contact with a liquid, each gas will dissolve in the liquid in proportion to its partial pressure.Thus the greater the concentration of a particular gas in the gas phase, the more and the faster that gas will go into solution in the liquid. At equilibrium, the gas partial pressures in the two phases are the same .If, however, the partial pressure of one of the gases later becomes greater in the liquid than in the adjacent gas phase, some of the dissolved gas molecules will reenter the gaseous phase.

So the direction and amount of movement of each gas is determined by its partial pressure in the two phases . This flexible situation is exactly what occurs when gases are exchanged in the lungs and tissues.

How much of a gas will dissolve in a liquid at any given partial pressure also depends on the solubility of the gas in the liquid and on the temperature of the liquid .The gases in air have very different solubilities in water(and in plasma) .Carbon dioxide is most soluble .Oxygen is only 1⁄20 as soluble as CO2, and N2 is only half as soluble as O2 .Thus, at a given partial pressure, much more CO2 than O2 dissolves in water, and practically no N2 goes into solution .The effect of increasing the liquid's temperature is to decrease gas solubility .Think of club soda, which is produced by forcing CO2 gas to dissolve in water under high pressure.

If you take the cap off a refrigerated bottle of club soda and allow it to stand at room temperature, in just a few minutes you will have plain water—all the CO2 gas will have escaped from solution.

Hyperbaric oxygen chambers [Hyperbaric oxygen therapy involves breathing pure oxygen in a pressurized room.] provide clinical applications of Henry's law .These chambers contain O2 gas at pressures higher than 1 atm and are used to force greater-than-normal amounts of O2 into the blood of patients suffering from carbon monoxide poisoning or tissue damage following radiation therapy .Hyperbaric therapy is also used to treat individuals with gas gangrene, because the anaerobic bacteria causing this infection cannot live in the presence of high O2 levels .

Composition of Alveolar Gas

The gaseous makeup of the atmosphere is quite different from that in the alveoli .The atmosphere is almost entirely O2 and N2; the alveoli contain more CO2 and water vapor and much less O2.

These differences reflect the effects of [1] gas exchanges occurring in the lungs(O2 diffuses from the alveoli into the pulmonary blood and CO2 diffuses in the opposite direction),[2] humidification of air by conducting passages, and[3] the mixing of alveolar gas that occurs with each breath .

Because only 500 ml of air is inspired with each tidal inspiration, gas in the alveoli is actually a mixture of newly inspired gases and gases remaining in the respiratory passageways between breaths.

The alveolar partial pressures of O2 and CO2 are easily changed by increasing breathing depth and rate .A high AVR brings more O2 into the alveoli, increasing alveolar PO2, and rapidly eliminates CO2 from the lungs.

External Respiration :Pulmonary Gas Exchange

During external respiration, dark red blood flowing through the pulmonary circuit is transformed into the scarlet river that is returned to the heart for distribution by systemic arteries to all body tissues .Although this color change is due to O2 uptake and binding to hemoglobin in red blood cells(RBCs), CO2 exchange (unloading) is occurring equally fast.

The following three factors influence the movement of oxygen and carbon dioxide across the respiratory membrane :

1 . Partial pressure gradients and gas solubilities.

2 . Matching of alveolar ventilation and pulmonary blood perfusion.

3 . Structural characteristics of the respiratory membrane.

Partial Pressure Gradients and Gas Solubilities

Because the PO2 of venous blood in the pulmonary arteries is only 40 mm Hg, as opposed to a PO2 of approximately 104 mm Hg in the alveoli, a steep oxygen partial pressure gradient exists, and O2 diffuses rapidly from the alveoli into the pulmonary capillary blood .Equilibrium—that is, a PO2 of 104 mm Hg on both sides of the respiratory membrane—usually occurs in 0.25 second, which is about one-third the time a red blood cell is in a pulmonary capillary .

The lesson here is that the blood can flow through the pulmonary capillaries three times as quickly and still be adequately oxygenated .Carbon dioxide moves in the opposite direction along a much gentler partial pressure gradient of about 5 mm Hg(45 mm Hg to 40 mm Hg)until equilibrium occurs at 40 mm Hg .

Carbon dioxide is then expelled gradually from the alveoli during expiration .Even though the O2 pressure gradient for oxygen diffusion is much steeper than the CO2 gradient, equal amounts of these gases are exchanged because CO2 is 20 times more soluble in plasma and alveolar fluid than O2.

Ventilation-PerfusionCoupling;

For gas exchange to be efficient, there must be a close match, or coupling, between ventilation(the amount of gas reaching the alveoli) and perfusion (the blood flow in pulmonary capillaries) In alveoli where ventilation is inadequate, PO2 is low .As a result, the terminal arterioles constrict, and blood is redirected to respiratory areas where PO2 is high and oxygen pickup may be more efficient .

In alveoli where ventilation is maximal, pulmonary arterioles dilate, increasing blood flow into the associated pulmonary capillaries .Notice that the autoregulatory mechanism controlling pulmonary vascular muscle is the opposite of the mechanism controlling most arterioles in the systemic circulation.

While changes in alveolar PO2 affect the diameter of pulmonary blood vessels(arterioles), changes in alveolar PCO2 cause changes in the diameters of the bronchioles .Passageways servicing areas where alveolar CO2 levels are high dilate, allowing CO2 to be eliminated from the body more rapidly, while those serving areas where PCO2 is low constrict

As a result of modifications made by these two systems, alveolar ventilation and pulmonary perfusion are synchronized .Poor alveolar ventilation results in low oxygen and high carbon dioxide levels in the alveoli; consequently, the pulmonary arterioles constrict and the airways dilate, bringing air flow and blood flow into closer physiological match .

High PO2 and low PCO2 in the alveoli cause respiratory passageways serving the alveoli to constrict, and promote flushing of blood into the pulmonary capillaries .Although these homeostatic mechanisms provide appropriate conditions for efficient gas exchange, they never completely balance ventilation and perfusion in every alveolus because (1) gravity causes regional variations in both blood and air flow in the lungs, and(2) the occasional alveolar duct plugged with mucus creates unventilated areas .

These factors, together with the shunting of blood from bronchial veins, account for the slight drop in PO2 from alveolar air (104 mm Hg) to pulmonary venous blood(100 mm Hg).

Thickness and Surface Area of the Respiratory Membrane

In healthy lungs, the respiratory membrane is only 0.5 to 1 mm thick, and gas exchange is usually very efficient.

Internal Respiration:

Capillary Gas Exchange in the Body Tissues

In internal respiration, the partial pressure and diffusion gradients are reversed from the situation described for external respiration and pulmonary gas exchange. However, the factors promoting gas exchanges between the systemic capillaries and the tissue cells are essentially identical to those acting in the lungs. Tissue cells continuously use O2 for their metabolic activities and produce CO2. Because PO2 in the tissues is always

lower than that in the systemic arterial blood (40 mm Hg versus 100 mm Hg), O2 moves rapidly from the blood into the tissues until equilibrium is reached, and CO2 moves quickly along its pressure gradient into the blood. As a result, venous blood draining the tissue capillary beds and returning to the heart has a PO2 of 40 mm Hg and a PCO2 of 45 mm Hg.

In summary, the gas exchanges that occur between the blood and the alveoli and between the blood and the tissue cells take place by simple diffusion driven by the partial pressure gradients of O2 and CO2 that exist on the opposite sides of the exchange membranes.

Thank you……!!!!

Physiology of Respiration ***Lec - [5]***

Carbon Dioxide Transport

Normally active body cells produce about 200 ml of CO2 each minute—exactly the amount excreted by the lungs .Blood transports CO2 from the tissue cells to the lungs in three forms :

1. ***Dissolved in plasma*** ***(7–10 .)%*** *The smallest amount of CO2 is transported simply dissolved in plasma.*

2. ***Chemically bound to hemoglobin*** ***(just over 20%)*** *In this form, CO2 is carried in the RBCs as carbaminohemoglobin.Because carbon dioxide binds directly to the amino acids of globin (and not to the heme), carbon dioxide transport in RBCs does not compete with the oxyhemoglobin transport mechanism.*

CO2 loading and unloading to and from Hb are directly influenced by the PCO2 and the degree of Hb oxygenation .Carbon dioxide rapidly dissociates from hemoglobin in the lungs, where the PCO2 of alveolar air is lower than that in blood .Carbon dioxide is loaded in the tissues, where the PCO2 is higher than that in the blood .

Deoxygenated hemoglobin combines more readily with carbon dioxide than does oxygenated hemoglobin .

3. ***As bicarbonate ion in plasma*** ***(about 70 .)%*** *Most carbon dioxide molecules entering the plasma quickly enter the RBCs, where most of the reactions that prepare carbon dioxide for transport as bicarbonate ions (HCO3–)in plasma occur.*

when CO2 diffuses into the RBCs, it combines with water, forming carbonic acid (H2CO3). H2CO3 is unstable and quickly dissociates into hydrogen ions and bicarbonate ions :

$$\underset{\text{carbon dioxide}}{CO_2} + \underset{\text{water}}{H_2O} \rightleftharpoons \underset{\text{carbonic acid}}{H_2CO_3} \rightleftharpoons \underset{\text{hydrogen ion}}{H^+} + \underset{\text{bicarbonate ion}}{HCO_3^-}$$

Although this reaction also occurs in plasma, it is thousands of times faster in RBCs because they (and not plasma) contain carbonic anhydrase(, an enzyme that reversibly catalyzes the conversion of carbon dioxide and water to carbonic acid .Hydrogen ions released during the reaction)as well as CO2 itself (bind to Hb, triggering the Bohr effect; thus, O2 release is enhanced by CO2 loading .Because of the buffering effect of Hb, the liberated H+ causes little change in pH under resting conditions .Hence, blood becomes only slightly more acidic (the pH declines from 7.4 to 7.34)as it passes through the tissues.

Once generated, HCO3– moves quickly from the RBCs into the plasma, where it is carried to

the lungs .

To counterbalance the rapid outrush of these anions from the RBCs, chloride ions(Cl–)move from the plasma into the RBCs .This ion exchange process, called the chloride shift, occurs via facilitated diffusion through an RBC membrane protein.

In the lungs, the process is reversed .As blood moves through the pulmonary capillaries, its PCO2 declines from 45 mm Hg to 40 mm Hg .For this to occur, CO2 must first be freed from its "bicarbonate housing."

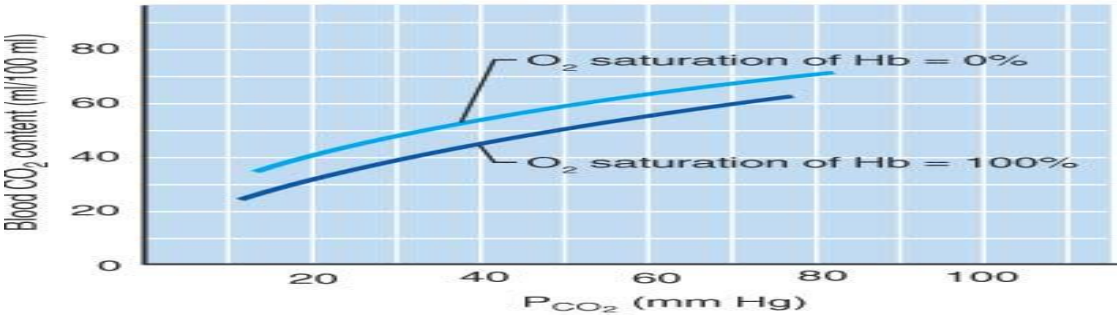
HCO3– reenters the RBCs (and Cl– moves into the plasma)and binds with H+ to form carbonic acid, which is then split by carbonic anhydrase to release CO2 and water .

This CO2, along with that released from hemoglobin and from solution in plasma, then diffuses along its partial pressure gradient from the blood into the alveoli.

The Haldane Effect

The amount of carbon dioxide transported in blood is markedly affected by the degree of oxygenation of the blood .The lower the PO2 and the lower the extent of Hb saturation with oxygen, the more CO2 that can be carried in the blood .

*This phenomenon, called the **Haldane effect**, reflects the greater ability of reduced hemoglobin to form carbaminohemoglobin and to buffer H+ by combining with it .As CO2 enters the systemic bloodstream, it causes more oxygen to dissociate from Hb [Bohr effect], which allows more CO2 to combine with Hb and more HCO3– to be formed (**Haldane effect**).*



In the pulmonary circulation the situation is reversed—uptake of O2 facilitates release of CO2 .

As Hb becomes saturated with O2, the H+ released combines with HCO3–, helping to unload CO2 from the pulmonary blood .

The Haldane effect encourages CO2 exchange in both the tissues and lungs.

Influence of CO2 on Blood pH:

Typically, the H+ released during carbonic acid dissociation is buffered by Hb or other proteins within the RBCs or in plasma.

The HCO3– generated in the red blood cells diffuses into the plasma, where it acts as the alkaline reserve part of the blood's carbonic acid–bicarbonate buffer system .

The carbonic acid–bicarbonate buffer system is very important in resisting shifts in blood Ph; .

For example, if the hydrogen ion concentration in blood begins to rise, excess H+ is removed by combining with HCO3– to form carbonic acid a weak acid that dissociates very little at either physiological or acidic pH .

If H+ concentration drops below desirable levels in blood, carbonic acid dissociates, releasing hydrogen ions and lowering the pH again.

Changes in respiratory rate or depth can produce dramatic changes in blood pH by altering the amount of carbonic acid in the blood .

Slow, shallow breathing allows CO2 to accumulate in the blood .As a result, carbonic acid levels increase and blood pH drops .
Conversely, rapid, deep breathing quickly flushes CO2 out of the blood, reducing carbonic acid levels and increasing blood pH .Thus, respiratory ventilation can provide a fast-acting system to adjust blood pH [and PCO2] when it is disturbed by metabolic factors .

The end……

Physiology of Respiration *Lec - [6]*

Control of Respiration

Neural Mechanisms and Generation of Breathing Rhythm

Although our tidelike breathing seems so beautifully simple, its control is fairly complex, involving neurons in the reticular formation of the medulla and pons.

Medullary Respiratory Centers

*Clustered neurons in two areas of the medulla oblongata appear to be critically important in respiration. These are (**1**) the dorsal respiratory group (DRG), located dorsally near the root of cranial nerve IX, and (**2**) the ventral respiratory group (VRG), a network of neurons that extends in the ventral brain stem from the spinal cord to the pons-medulla junction. The VRG appears to be a rhythm-generating and integrative center.*
It contains groups of neurons that fire during inspiration and others that fire during expiration in a dance of mutual inhibition.
When its inspiratory neurons fire, a burst of impulses travels along the phrenic and intercostal nerves to excite the diaphragm and external intercostal muscles, respectively. As a result, the thorax expands and air rushes into the lungs.
When the VRG's expiratory neurons fire, the output stops, and expiration occurs passively as the inspiratory muscles relax and the lungs recoil. This cyclic on/off activity of the inspiratory and expiratory neurons repeats continuously and produces a respiratory rate of 12–18 breaths per minute, with inspiratory phases lasting about 2 seconds followed by expiratory phases lasting about 3 seconds. This normal respiratory rate and rhythm is referred to as eupnea.
During severe hypoxia, VRG networks generate gasping (perhaps in a last-ditch effort to restore O2 to the brain). When a certain cluster of VRG neurons is completely suppressed, as by an overdose of morphine, or alcohol, respiration stops completely.

Until recently, it was thought that the DRG acts as an inspiratory center, performing many of the tasks now known to be performed by the VRG. We now know that in almost all mammals including humans, the DRG integrates input from peripheral stretch and chemoreceptors and communicates this information to the VRG.

Pontine Respiratory Centers

Although the VRG generates the basic respiratory rhythm, the pontine respiratory centers influence and modify the activity of medullary neurons. For example, pontine centers appear to smooth out the transitions from inspiration to expiration, and vice versa; and when lesions are made in its superior region, inspirations become very prolonged, a phenomenon called apneustic breathing.
*The pontine respiratory group [formerly called the **pneumotaxic center**] and other pontine centers transmit impulses to the VRG of the medulla. This modifies and fine-tunes the breathing rhythms generated by the VRG during certain activities such as vocalization, sleep, and exercise. The pontine respiratory centers, like the DRG, receive input from higher brain centers*

and from various sensory receptors in the periphery.

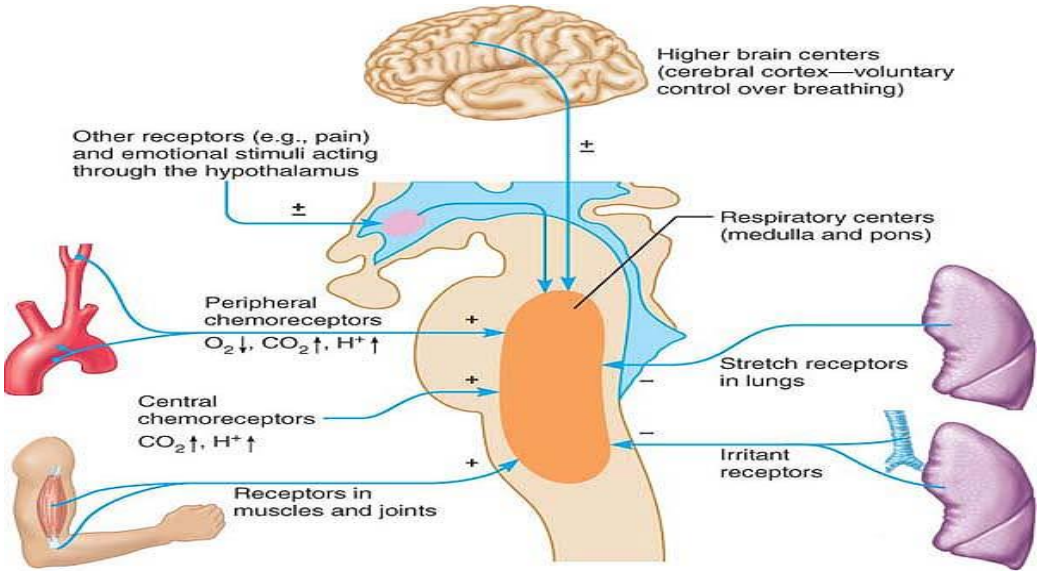
Genesis of the Respiratory Rhythm

Although there is little question that breathing is rhythmic, we still cannot fully explain the origin of its rhythm. One hypothesis is that there are pacemaker neurons, which have intrinsic (automatic) rhythmicity like the pacemaker cells found in the heart. Though pacemaker activity has been demonstrated in rostral VRG neurons in newborns, no such activity has been found in adults. This leads us to the second (and most popular) hypothesis: Normal respiratory rhythm is a result of reciprocal inhibition of interconnected neuronal networks in the medulla. Rather than a single set of pacemaker neurons, there are two sets that inhibit each other and so cycle their activity to generate the rhythm.

Factors Influencing Breathing Rate and Depth

Inspiratory depth is determined by how actively the respiratory center stimulates the motor neurons serving the respiratory muscles. The greater the stimulation, the greater the number of motor units excited and the greater the force of respiratory muscle contractions. Respiratory rate is determined by how long the inspiratory center is active or how quickly it is switched off.

Depth and rate of breathing can be modified in response to changing body demands. The respiratory centers in the medulla and pons are sensitive to both excitatory and inhibitory stimuli.



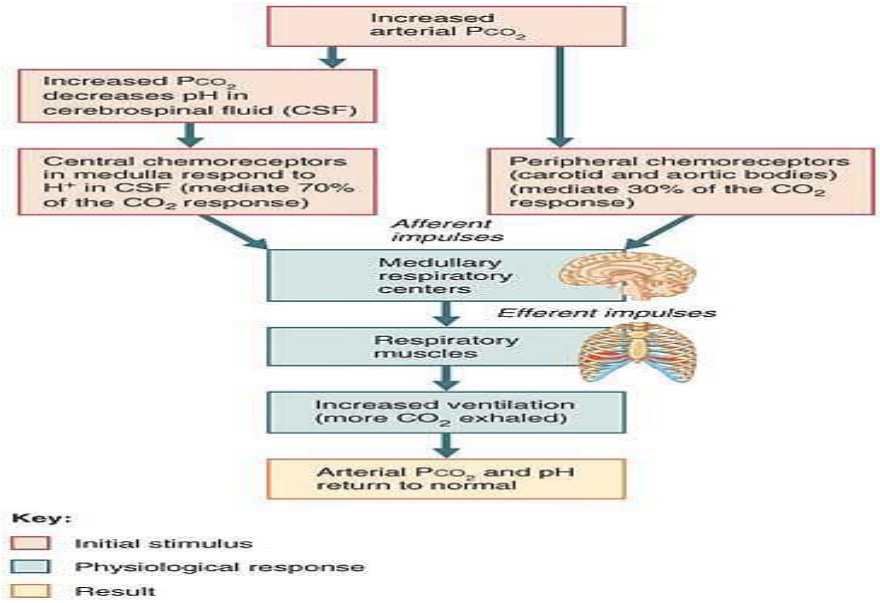
Neural and chemical influences on brain stem respiratory centers. Excitatory influences (+) increase the frequency of impulses sent to the muscles of respiration and recruit additional motor units, resulting in deeper, faster breathing. Inhibitory influences (–) have the reverse effect. In some cases, the impulses may be excitatory or inhibitory (±), depending on which receptors or brain regions are activated. The cerebral cortex also directly innervates respiratory muscle motor neurons.

Chemical Factors

Among the factors that influence breathing rate and depth, the most important are changing levels of CO2, O2, and H+ in arterial blood. Sensors responding to such chemical fluctuations, called chemoreceptors, are found in two major body locations. The central chemoreceptors are located bilaterally in the ventrolateral medulla. The peripheral chemoreceptors are found in

the aortic arch and carotid arteries.

Influence of PCO2 *Of all the chemicals influencing respiration, CO2 is the most potent and the most closely controlled. Normally, arterial PCO2 is 40 mm Hg and is maintained within ±3 mm Hg of this level by an exquisitely sensitive homeostatic mechanism that is mediated mainly by the effect that rising CO2 levels have on the central chemoreceptors of the brain stem. CO2 diffuses easily from the blood into the cerebrospinal fluid, where it is hydrated and forms carbonic acid. As the acid dissociates, H+ is liberated. This is the same reaction that occurs when CO2 enters RBCs. Unlike RBCs or plasma, however, cerebrospinal fluid contains virtually no proteins that can buffer the added H+. Thus, as PCO2 levels rise, a condition referred to as hypercapnia, the cerebrospinal fluid pH drops, exciting the central chemoreceptors, which make abundant synapses with the respiratory regulatory centers. As a result, the depth and rate of breathing are increased. This enhanced alveolar ventilation quickly flushes CO2 out of the blood, increasing blood pH. An elevation of only 5 mm Hg in arterial PCO2 results in a doubling of alveolar ventilation, even when arterial O2 levels and pH are unchanged. When PO2 and pH are below normal, the response to elevated PCO2 is even greater. Increased ventilation is normally self-limiting, ending when homeostatic blood PCO2 levels are restored.*



Notice that while rising CO_2 levels act as the initial stimulus, it is rising H^+ levels that prod the central chemoreceptors into activity. In the final analysis, control of breathing during rest is aimed primarily at regulating the H^+ concentration in the brain.

HOMEOSTATIC IMBALANCE

Hyperventilation is an increase in the rate and depth of breathing that exceeds the body's need to remove CO2. A person experiencing an anxiety attack may hyperventilate involuntarily to the point where he or she becomes dizzy or faints. This happens because low CO2 levels in the blood (hypocapnia) cause cerebral blood vessels to constrict, reducing brain perfusion and producing cerebral ischemia. Earlier symptoms of hyperventilation are tingling and involuntary muscle spasms (tetany) in the hands and face caused by blood Ca2+ levels falling as pH rises. Such attacks may be averted by breathing into a paper bag because then the air being inspired is expired air, rich in carbon dioxide, which causes carbon dioxide to be retained in the blood.

When PCO2 is abnormally low, respiration is inhibited and becomes slow and shallow. In fact, periods of apnea (breathing cessation) may occur until arterial PCO2 rises and again stimulates respiration.

Sometimes swimmers voluntarily hyperventilate so that they can hold their breath longer during swim meets. This is incredibly dangerous for the following reasons. Blood O2 content rarely drops much below 60% of normal during regular breath-holding, because as PO2 drops, PCO2 rises enough to make breathing unavoidable. However, strenuous hyperventilation can lower PCO2 so much that a lag period occurs before it rebounds enough to stimulate respiration again. This lag may allow oxygen levels to fall well below 50 mm Hg, causing the swimmer to black out (and perhaps drown) before he or she has the urge to breathe.

Physiology of Respiration *Lec - [7&8]*

Factors Influencing Breathing Rate and Depth

Chemical Factors :-

Influence of PCO2 …. see lecture 6.

Influence of PO2 *Cells sensitive to arterial O2 levels are found in the peripheral chemoreceptors, that is, in the aortic bodies of the aortic arch and in the carotid bodies at the bifurcation of the common carotid arteries. Those in the carotid bodies are the main oxygen sensors.*

Under normal conditions, the effect of declining PO2 on ventilation is slight and mostly limited to enhancing the sensitivity of peripheral receptors to increased PCO2. Arterial PO2 must drop substantially, to at least 60 mm Hg, before O2 levels become a major stimulus for increased ventilation. Remember, there is a huge reservoir of O2 bound to Hb, and Hb remains almost entirely saturated unless or until the PO2 of alveolar gas and arterial blood falls below 60 mm Hg. The central chemoreceptors then begin to suffer from O2 starvation, and their activity is depressed. At the same time, the peripheral chemoreceptors become excited and stimulate the respiratory centers to increase ventilation, even if PCO2 is normal. Thus, the peripheral chemoreceptor system can maintain ventilation when alveolar O2 levels are low even though brain stem centers are depressed by hypoxia.

HOMEOSTATIC IMBALANCE

In people who retain CO2 because of pulmonary disease (e.g., emphysema and chronic bronchitis), arterial PCO2 is chronically elevated and, as a result, chemoreceptors adapt to this chemical stimulus. In such cases, a declining PO2 acting on the oxygen-sensitive peripheral chemoreceptors provides the principal respiratory stimulus, the hypoxic drive. Thus, gas mixtures administered to such patients during respiratory distress are only slightly enriched with O2 because inspiration of pure oxygen would slow their breathing, further elevating their PCO2.

Influence of Arterial pH *Changes in arterial pH can modify respiratory rate and rhythm even when CO2 and O2 levels are normal.*

Because little H+ diffuses from the blood into the cerebrospinal fluid, the direct effect of arterial H+ concentration on central chemoreceptors is insignificant compared to the effect of H+ generated by elevations in PCO2. The increased ventilation that occurs in response to falling arterial pH is mediated through the peripheral chemoreceptors. Although changes in PCO2 and H+ concentration are interrelated, they are distinct stimuli. A drop in blood pH may reflect CO2 retention, but it may also result from metabolic causes, such

as accumulation of lactic acid during exercise or of fatty acid metabolites (ketone bodies) in patients with poorly controlled diabetes mellitus.
Regardless of cause, as arterial pH declines, respiratory system controls attempt to compensate and raise the pH by eliminating CO2 (and carbonic acid) from the blood; thus, respiratory rate and depth increase.

Summary of Interactions of PCO2, PO2, and Arterial pH

1. *Rising CO2 levels are the most powerful respiratory stimulant.*
As CO2 is hydrated in cerebrospinal fluid, liberated H+ acts directly on the central chemoreceptors, causing a reflexive increase in breathing rate and depth. Low PCO2 levels depress respiration.

2. *Under normal conditions, blood PO2 affects breathing only indirectly by influencing chemoreceptor sensitivity to changes in PCO2. Low PO2 augments PCO2 effects; high PO2 levels diminish the effectiveness of CO2 stimulation.*

3. *When arterial PO2 falls below 60 mm Hg, it becomes the major stimulus for respiration, and ventilation is increased via reflexes initiated by the peripheral chemoreceptors. This may increase O2 loading into the blood, but it also causes hypocapnia (low PCO2 blood levels) and an increase in blood pH, both of which inhibit respiration.*

4. *Changes in arterial pH resulting from CO2 retention or metabolic factors act indirectly through the peripheral chemoreceptors to promote changes in ventilation, which in turn modify arterial PCO2 and pH. Arterial pH does not influence the central chemoreceptors directly.*

Influence of Higher Brain Centers

Hypothalamic Controls

Acting through the hypothalamus and the rest of the limbic system, strong emotions and pain send signals to the respiratory centers, modifying respiratory rate and depth. For example, have you ever touched something cold and clammy and gasped? That response was mediated through the hypothalamus. So too is the breath holding that occurs when we are angry and the increased respiratory rate that occurs when we are excited.
A rise in body temperature acts to increase the respiratory rate, while a drop in body temperature produces the opposite effect; and sudden chilling of the body (can cause cessation of breathing (apnea)—or at the very least, gasping.

Cortical Controls

Although breathing is normally regulated involuntarily by the brain stem respiratory centers, we can also exert conscious (volitional) control over the rate and depth of our breathing—choosing to hold our breath or to take an extra deep breath, for example. During voluntary control, the cerebral motor cortex sends signals to the motor neurons that stimulate the respiratory muscles, bypassing the medullary centers. Our ability to voluntarily hold our breath is limited, however, because the brain stem respiratory centers automatically reinitiate breathing when the blood concentration of CO2 reaches critical levels. That explains why drowning victims typically have water in their lungs.

Pulmonary Irritant Reflexes

The lungs contain receptors that respond to an enormous variety of irritants. When activated, these receptors communicate with the respiratory centers via vagal nerve afferents.
Accumulated mucus, inhaled debris such as dust, or noxious fumes stimulate receptors in the bronchioles that promote reflex constriction of those air passages. The same irritants stimulate a cough when present in the trachea or bronchi, and a sneeze when present in the nasal cavity.

The Inflation Reflex

The visceral pleurae and conducting passages in the lungs contain numerous stretch receptors that are vigorously stimulated when the lungs are inflated. These receptors signal the medullary respiratory centers via afferent fibers of the vagus nerves, sending inhibitory impulses that end inspiration and allow expiration to occur. As the lungs recoil, the stretch receptors become quiet, and inspiration is initiated once again. This reflex, called the ***inflation reflex****, or* ***Hering-Breuer reflex*** *(her'ing broy'er), is thought to be more a protective response (to prevent excessive stretching of the lungs) than a normal regulatory mechanism.*

Respiratory Adjustments

Adjustments During Exercise

Respiratory adjustments during exercise are geared both to intensity and duration of the exercise. Working muscles consume tremendous amounts of O2 and produce large amounts of CO2; thus, ventilation can increase 10- to 20-fold during vigorous exercise. This increase in ventilation in response to metabolic needs is called ***hyperpnea****.*

It differs from hyperventilation in that the respiratory changes in hyperpnea do not lead to significant changes in blood O2 and CO2 levels. By contrast, hyperventilation is excessive ventilation, and is characterized ***by low PCO2 and alkalosis.***

Exercise-enhanced ventilation does not appear to be prompted by rising PCO2 and declining PO2 and pH in the blood for two reasons.

First*, ventilation increases abruptly as exercise begins, followed by a gradual increase, and then a steady state of ventilation. When exercise stops, there is an initial small but abrupt decline in ventilation rate, followed by a gradual decrease to the pre-exercise value.*

Second, *although venous levels change, arterial PCO2 and PO2 levels remain surprisingly constant during exercise. In fact, PCO2 may decline to below normal and PO2 may rise slightly because of the efficiency of the respiratory adjustments. Our present understanding of the mechanisms that produce these observations is sketchy, but the most accepted explanation is as follows.*

The abrupt increase in ventilation that occurs as exercise begins reflects interaction of three neural factors:

1. *Psychological stimuli (our conscious anticipation of exercise.)*
2. *Simultaneous cortical motor activation of skeletal muscles and respiratory centers.*
3. *Excitatory impulses reaching respiratory centers from proprioceptors in moving muscles, tendons, and joints.*

The subsequent gradual increase and then plateauing of respiration probably reflect the rate of CO2 delivery to the lungs (the "CO2 flow"). The small but abrupt decrease in ventilation that occurs as exercise ends reflects the shutting off of the three neural factors listed above. The subsequent gradual decline to baseline ventilation likely reflects a decline in the CO2 flow that occurs as the oxygen debt is being repaid. The rise in lactic acid levels that contributes to O2 debt is not a result of inadequate respiratory function, because alveolar ventilation and pulmonary perfusion are as well matched during exercise as during rest (hemoglobin remains fully saturated). Rather, it reflects cardiac output limitations or inability of the skeletal muscles to further increase their oxygen consumption. In light of this fact, the practice of inhaling pure O2 by mask, used by some football players to replenish their "oxygen-starved" bodies as

quickly as possible, is useless. The panting athlete does have an O2 deficit, but inspiring extra oxygen will not help, because the shortage is in the muscles—not the lungs.

Adjustments at High Altitude

Most people live between sea level and an altitude of approximately 2400 m (8000 feet). In this range, differences in atmospheric pressure are not great enough to cause healthy people any problems when they spend brief periods in the higher-altitude areas. However, when you travel quickly from sea level to elevations above 8000 ft, where air density and PO2 are lower, your body responds with symptoms of ***acute mountain sickness*** *(**AMS**)—headaches, shortness of breath, nausea, and dizziness. In severe cases of AMS, lethal pulmonary and cerebral edema may occur.*

When you move on a long-term basis from sea level to the mountains, your body begins to make respiratory and hematopoietic adjustments via an adaptive response called ***acclimatization****.*

As already explained, decreases in arterial PO2 cause the peripheral chemoreceptors to become more responsive to increases in PCO2, and a substantial decline in PO2 directly stimulates the peripheral chemoreceptors.

As a result, ventilation increases as the brain attempts to restore gas exchange to previous levels.

Within a few days, the minute respiratory volume stabilizes at a level 2–3 L/min higher than the sea level rate. Because increased ventilation also reduces arterial CO2 levels, the PCO2 of individuals living at high altitudes is typically below 40 mm Hg (its value at sea level).

Because less O2 is available to be loaded, high-altitude conditions always result in lower-than-normal hemoglobin saturation levels.

For example*, at about 19,000 ft above sea level, O2 saturation of arterial blood is only 67% (compared to nearly 98% at sea level).*

But Hb unloads only 20–25% of its oxygen at sea level, which means that even at the reduced saturations at high altitudes, the O2 needs of the tissues are still met adequately under resting conditions.

Additionally, at high altitudes hemoglobin's affinity for O2 is reduced because of increases in BPG concentration, with the result that more O2 is released to the tissues during each circulatory round.

Although the tissues in a person at high altitude receive adequate oxygen under normal conditions, problems arise when all-out efforts are demanded of the cardiovascular and respiratory systems.

Unless one is fully acclimatized, such conditions almost guarantee that body tissues will become severely hypoxic.

When blood O2 levels decline, the kidneys accelerate production of erythropoietin, which stimulates bone marrow production of RBCs. This phase of acclimatization, which occurs slowly, provides long-term compensation for living at high altitudes.

The end