Respiratory system:

 Respiration is a complex process by which living organisms exchange O_2 & CO_2 between organism and the environment. It is important in obtaining energy by oxidation of food substances. The obtained energy is stored in form of high energy phosphate compounds like ATP. It includes many processes:

1- External respiration: exchange of air between the external environment and pulmonary alveoli.

2- Exchange of gases between the alveolar air and the blood flowing along the pulmonary capillaries.

3- Transport of gases by the blood.

4- Exchange of gases between the tissue cells and blood in the tissue capillaries.

5- Internal respiration: consumption of O_2 by the cells and production of CO_2.

Functions of respiratory system:

 In addition to the main function of respiratory system which is **gas exchange** between organism & environment, resp. system can perform other **non respiratory functions** include the following:

1- **Protective** function: against some microorganisms by preventing them from entering the body or by removing them from respiratory surface. These are done by:

 Ciliary activity moves the superficial liquid lining layer continuously toward the pharynx.

 Neutrophils, lymphocytes & alveolar macrophages are present in alveoli defense against bacteria & viruses.

 Lungs synthesize immunoglobulin IgA for its own defense.

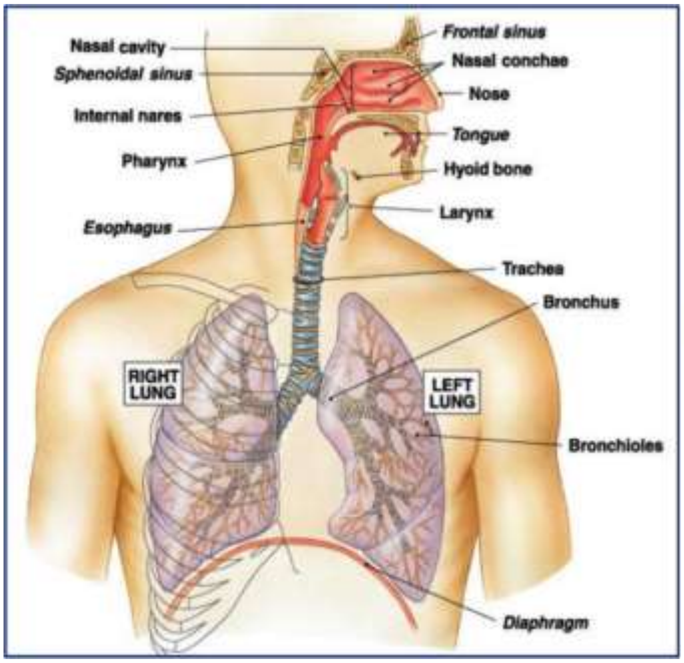
2- **Acid –Base balance**: respiratory system can alter blood PH by changing blood CO_2 level so as to keep pH normal.This is done through the chemoreceptors and respiratory center integrations.

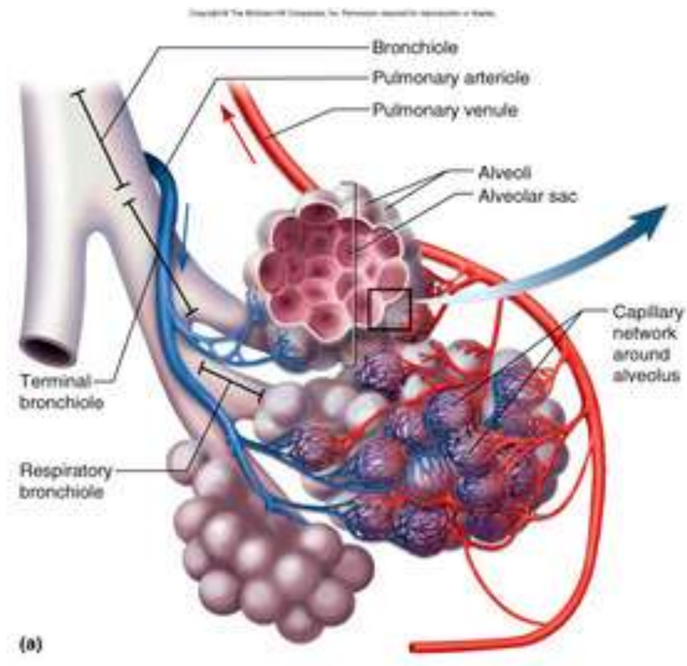
3- **Olfaction**: the sensation of smell.

4- **Metabolic** functions of the lungs: these functions include:

 Regulation of blood pressure: endothelial cells of pulmonary capillary secrete an enzyme called ***angiotensin converting enzyme(ACE***), which converts angiotensin I to active angiotensin II, a potent vasoconstrictor.

 Lungs synthesize hormones like ***serotonin***, ***histamine***, ***prostaglandin E2, F2 and G2*** & release them to circulation under various circumstances such as histamine, bradykinin and prostaglandins are released during asthma attack .Heparin histamine, serotonin & prostaglandinsE2and F2 are released during anaphylactic shock.





Respiratory airways

1- Upper respiratory airways

 Have several physiological functions in addition to air conduction, such as swallowing, conditioning of air (warming and humidification) before its passage to the trachea and defense mechanism.

 Upper respiratory airways include many parts: the external nose, nasal cavity and pharynx.

- **Nose**: Mucous membrane of nose is lined by ciliated columnar epithelium

2- Lower reparatory airways
 Consists of larynx, trachea, bronchi & bronchioles, alveolar ducts & alveoli in lungs.
 Trachea is a tube extends from the larynx to the bifurcation in the mediastinum.
- It is lined with „**C" shaped** rings of cartilage, which prevent the collapse of the tube when the air pressure is reduced during inspiration (otherwise breathing would be impossible).
- The dorsal surface of the trachea has no cartilage, but instead has smooth muscles, which contract to reduce the size of the trachea, (e.g. during coughing or an asthma attack).Smooth muscles relax during swallowing (food passing down the esophagus)and also to expand the trachea during exercise (so air breathed in faster).

Tracheobronchial Tree

 Trachea the first generation respiratory passageway is divided into right & left main bronchi, which are the second generation respiratory passageway.

 Bronchus in turn is divided into small branches: the bronchioles inside the lung.

 Bronchioles are further divided into very small bronchioles: the respiratory bronchioles.

 There are 20- 25 generations before reaching finally to the alveolar alveoli.

 The inner surface of trachea (bronchi & bronchioles) is lined with mucus secreting cells (mucus traps foreign particles, e.g. dust and parasites) & ciliated cells carrying the mucus to the nose

 Conducting zone extend from trachea to terminal bronchioles which are ciliated for removal of debris. It is incapable of gas exchange but they work as a passageway for air movement. It constitutes the anatomical dead space.

 Respiratory zone extends from the respiratory bronchioles to the alveoli. It is a site for gas exchange.

Pulmonary ventilation

 Means inflow and outflow of air between the atmosphere and the lung alveoli.

 Air moves from the region of a high pressure to one of a lower pressure.

 A pressure difference is established by the mechanics of pulmonary ventilation: **inspiration** and **expiration**.

 The muscles cause the lungs to expand and contract.

 Lungs can be expanded and contracted in two ways:

- **Downward and upward movement of the diaphragm** to lengthen or shorten the chest cavity.

- **Elevation and depression of the ribs** to increase and decrease the anterior-posterior diameter of the chest cavity.

 Normal quiet breathing is accomplished by the movement of the diaphragm.

Inspiration

 Inspiration is an active process.

 The dome shaped **diaphragm** flattens as it contracts. This increases the height of the thoracic cavity.

 The **external intercostal** muscles contract to raise the ribs .This increases circumference of thoracic cavity

 During deep or forced inspiration, additional muscles are recruited: **scalene**, **sternocleidomastoid** and **pectoralis minor**.

 Intrapleural pressure becomes more negative (-2.5 − -6)mmHg ,due to increase thoracic volume ,as compare to the atmospheric pressure, therefore air flows into the lung.

Expiration

 Quiet expiration in healthy people is a passive process(no muscle contraction)

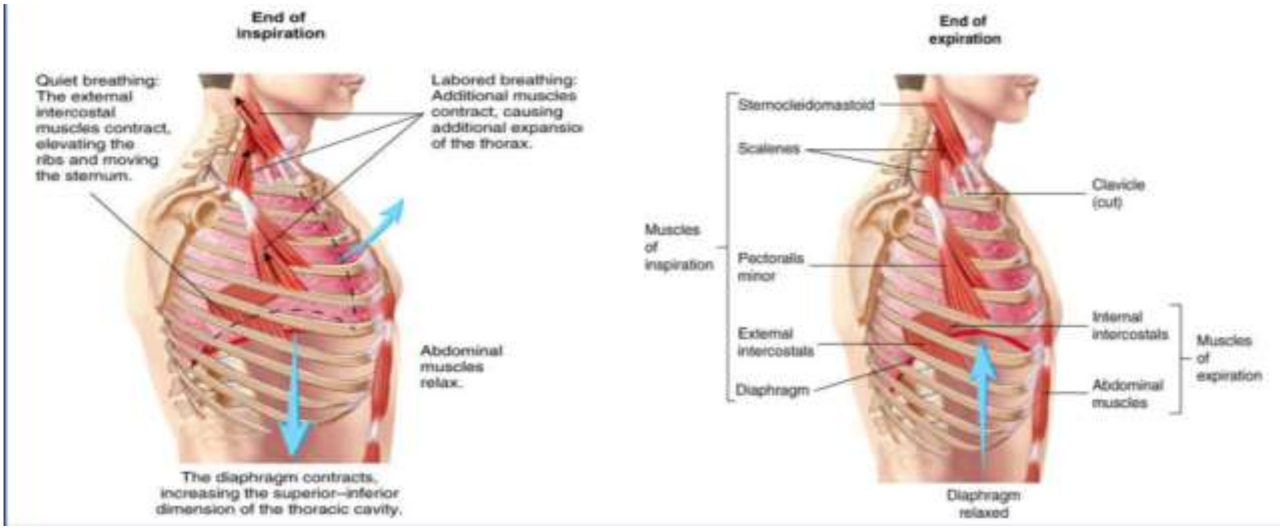
 Inspiratory muscles relax

 Relaxing diaphragm moves superiorly (up).

 Elastic fibers in lung recoil

□ Volumes of thorax and lungs decrease simultaneously, increasing the pressure to slightly positive so the air flows out of the lungs.

□ Expiration during the exercise or lung diseases becomes active process requiring use of accessory muscles like internal intercostal muscles and abdominal muscles.



Basic concepts of air movement and pressure

Pulmonary pressure

□ lungs have tendency to collapse due to their elastic structures, therefore they collapse like a balloon to expel air through trachea when there is no force to keep it inflated.

□ **Pleural pressure** is pressure of fluid in the thin space between lung and chest wall .

- During inspiration: pleural pressure decreases because thoracic volume increases according to Boyle's law.

- During expiration: pleural pressure increases because thoracic volume decreases.

□ **Alveolar pressure**: is the pressure of the air inside alveoli.

- If glottis is open, no air moves into or out of lungs .Pressure in all parts of respiratory tree & all the ways to alveoli is equal to atmospheric pressure.

- During inspiration alveolar pressure falls as compare to the atmospheric pressure.

- During expiration, alveolar pressure slightly ↑ to force inspired air out of lung during 2-3 sec. of expiration.

□ **Transpulmonary pressure** is the differences between the alveolar pressure and pleural pressure.

- Pressure differences between alveoli & pressure on outer surface of lung measures the elastic force of Lung that tends to collapse lung, which is known as **recoil** pressure.

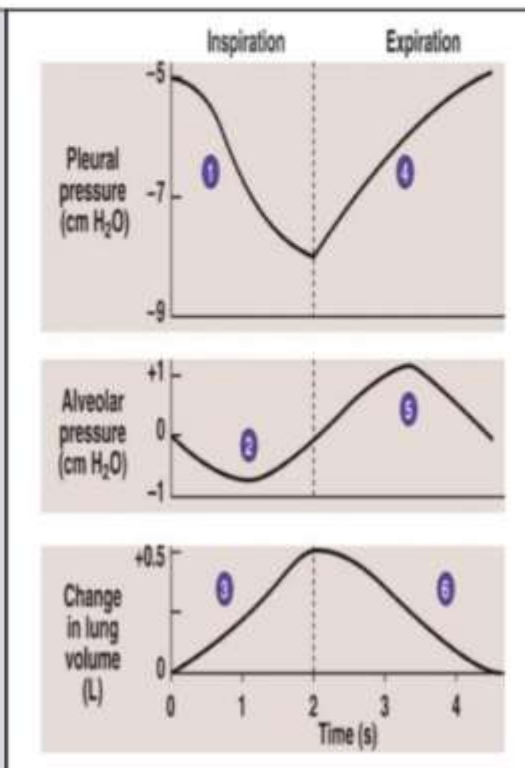
□ **Atmospheric pressure** is the pressure exerted by the weight of the air in the atmosphere.

Table :Gas laws	
Description	Importance
Boyle's law: The pressure of a gas is inversely proportional to its volume at a given volume.	When alveolar volume increases, pleural pressure decreases below atmospheric pressures causing airflow into the lungs ,and vice versa when alveolar volume decreases
Dalton's law: The partial pressure of a gas in a mixture of gases is the percentage of the gas in the mixture times the total pressure of the mixture of gas.	The greater the difference in partial pressure between 2 points, the greater the rate of gas movement.
Henry's law: The concentration of a gas dissolved in a liquid is equal to the partial pressure of the gas over the liquid times the solubility coefficient of the gas.	A small amount of the gases in air dissolves in the fluid lining the alveoli (CO_2 is 24times more soluble than O_2, therefore CO_2exits through the respiratory membrane more readily than O_2 enters).

1-Pleural pressure ↓because thoracic volume ↑

2- As inspiration begins alveolar pressure ↓below the atmospheric pressure because the decreased pleural pressure causes alveolar volume to ↑

3-Air flows into the lungs because the alveolar pressure is lower than atmospheric pressure.



4- Pleural pressure ↑because thoracic volume ↓.

5-As expiration begins alveolar pressure ↑below the atmospheric pressure because the increased pleural pressure causes alveolar volume to ↓

6-Air flows out of the lungs because the alveolar pressure is greater than atmospheric pressure.

Pressures and volumes changes during the respiratory cycle.

Work of breathing

 Pressure volume work performed in moving air into & out of lungs. Most of it performed during inspiration.

 Work of breathing must overcome three sources of resistance encountered during inspiration :

1- Airway resistance is generated between air molecules & walls of conducting airways.

2- Compliance work: work performed to overcome elastic recoil of lungs. It accounts for the largest proportion of total work of breathing.

Pathophysiology note: Airway diameter can be reduced(& ↑ed airway resistance) e.g., airway diameters are reduced by smooth muscle contraction & excess inflammatory secretions in obstructive airway diseases such as asthma & chronic bronchitis .As a result work caused by airway resistance increases

Pharmacology note: Many drugs affect large airway diameter by affecting bronchial smooth muscles tone .For example β2 –adrenergic agonists such as albuterol which stimulates bronchodilation .Other classes of drugs prevent bronchoconstriction or inhibit inflammation e.g., steroids.

Pathology note: In emphysema compliance work is reduced because destruction of lung tissues & loss of elastic tissues of lung, but in pulmonary fibrosis, compliance work is ↑ed because fibrotic tissues require more work to expand.

3- Tissues resistance: is generated as pleural surfaces slide over each other during respiratory cycle .It accounts for a small portion (5%) of the total work of breathing.

Pulmonary compliance

The ease with which the lungs and thoracic wall can be expanded.(extent to which lung will expand for each unit increase in transpulmonary pressure. Compliant lungs are easy to distend.

 Compliance is determined by (2 factors in which compliance related: elasticity of the lungs and surface tension in the alveoli):

- **Elastic force** which is caused by **elastic tissues** of the lungs (elastin and collagen fibers).It represents **one third** of the total lung elasticity.

- Elastic force caused by **surface tension** of the fluid that lines the inside wall of the alveoli (caused by air fluid interface).It represents **two thirds** of the total lung elasticity.

Compliance is decreased with any condition that:

1. destroys the lung tissue (emphysema)

2 fills the lungs with fluid (pneumonia)

3. produces a deficiency of surfactant (premature birth, near-drowning)

4. interferes with lung expansion (pneumothorax)

Pulmonary surfactant

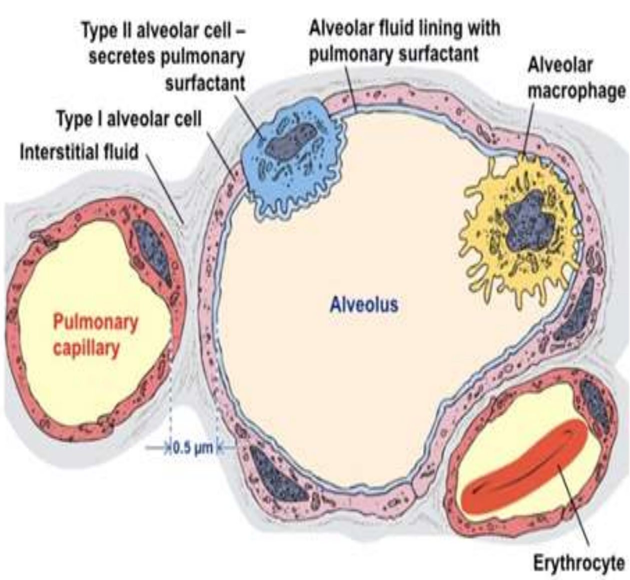
- It is an essential lipid-protein complex formed by type II alveolar cells.
- Surfactant is present when the lungs are fully developed.
- **Function:** Surfactant decreases surface tension which:
  - increases pulmonary compliance (reducing the effort needed to expand the lungs)
  - reduces tendency for alveoli to collapse
- This will helps lungs fill with air and keeps air sacs (alveoli) from deflating.

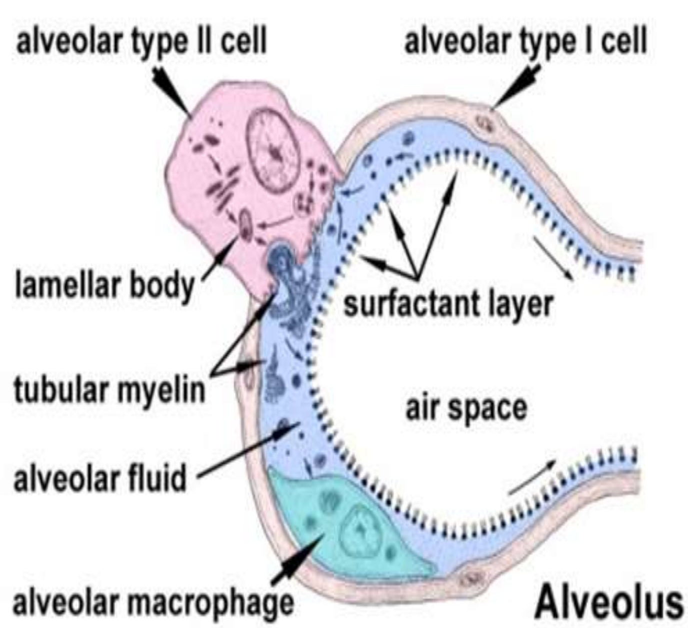
 Surfactant production is decreased by the effect of smoking, histamine and hypoxia while its production increases by hormonal effect (insulin, thyroid hormone and glucocorticoid hormone).

Walls of alveoli are coated with a thin film of water & this creates a potential problem. Water molecules, including those on alveolar walls, are more attracted to each other than to air, & this attraction creates a force called surface tension. This surface tension ↑es as water molecules come closer together, which is what happens when we exhale & our alveoli become smaller (like air leaving a balloon). Potentially, surface tension could cause alveoli to collapse and, in addition, would make it more difficult to 're-expand' the alveoli (when you inhaled). Both of these would represent serious problems: if alveoli collapsed they would contain no air & no oxygen to diffuse into blood &, if 're-expansion' was more difficult, inhalation would be very, very difficult if not impossible. Fortunately, our alveoli do not collapse & inhalation is relatively easy because the lungs produce a substance called surfactant that reduces surface tension.

Respiratory Distress Syndrome (RDS)

- It is a problem often seen in premature babies (whose lungs have not yet fully developed).
- The condition makes it hard for the baby to breathe.
- The disease is mainly caused by a lack of surfactant.





Gas exchange

 Gas exchange across the respiratory membrane occurs by diffusion.

 Respiratory gases diffuse from area of high partial pressure to area of low pressure.

 Partial pressure: is the pressure of each gas alone, which is used to express the concentration of the gas.

- Partial pressure of O_2 and CO_2 are designed as PO_2 and PCO_2respectively

- Partial pressure of a gas is calculated by multiplying its fractional concentration by the total pressure, for example the percentage of O_2 is 21% of total pressure 760 mmHg (atmospheric pressure), therefore PO_2 is 160 mmHg

 Atmospheric air ,alveolar air and expired air have different concentrations of gases because:

1- Air is humidified before it reaches the alveoli.

2- A constant diffusion of O_2 from the alveoli into the blood, while CO_2 is constantly diffusing from the pulmonary blood to the alveoli.

3- The alveolar air is only partially replaced by atmospheric air.

 There are about 300 millions alveoli in the two lungs.

 The alveolar walls are thin ,within them is a solid network of interconnecting capillaries, and blood flows in the alveolar walls as a sheet

 Gas exchange occurs through the membrane of all the terminal portions of the lungs (not only the alveoli).These membranes are known the respiratory membrane or the pulmonary membrane.

 Factors affecting the rate of diffusion through the respiratory membrane

1- The thickness of the membrane.

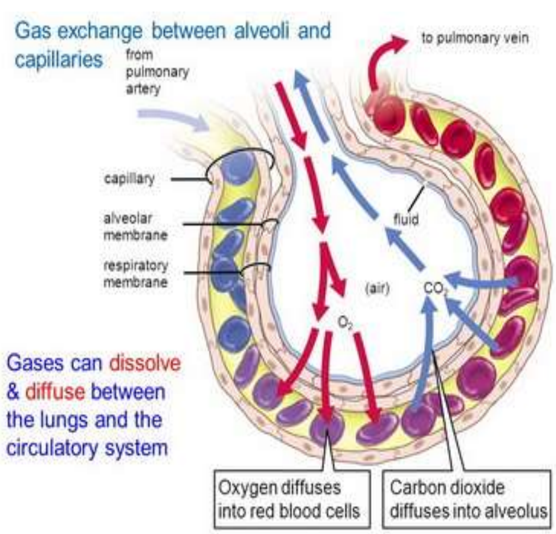
2- The surface area of the membrane.

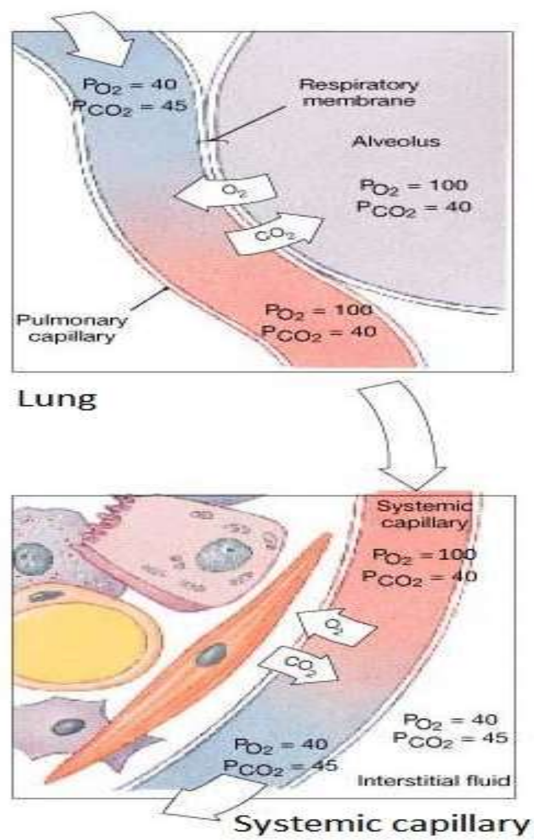
3- The diffusion coefficient of the gas in the substance of the membrane.

4- The pressure differences between the two sides of the membrane.

Exchange of gases: **Partial Pressures of O2 and CO2in the body** (P = partial pressure):

- Alveoli
  - PO2 = 100 mm Hg
  - PCO2 = 40 mm Hg
- Alveolar capillaries
  - Entering the alveolar capillaries
    - PO2 = 40 mm Hg
    - PCO2 = 45 mm Hg
  - Leaving the alveolar capillaries
    - PO2 = 100 mm Hg
    - PCO2 = 40 mm Hg
  - Entering the systemic capillaries
    - PO2 = 100 mm Hg
    - PCO2 = 40 mm Hg
  - Body cells (resting conditions)
    - PO2 = 40 mm Hg
    - PCO2 = 45 mm Hg
  - Leaving the systemic capillaries
    - PO2 = 40 mm Hg
    - PCO2 = 45 mm Hg





How are oxygen transported in the blood?

- Oxygen is carried in blood:

  1 - bound to hemoglobin (98.5% of all oxygen in the blood)
  2 - dissolved in the plasma (1.5%)

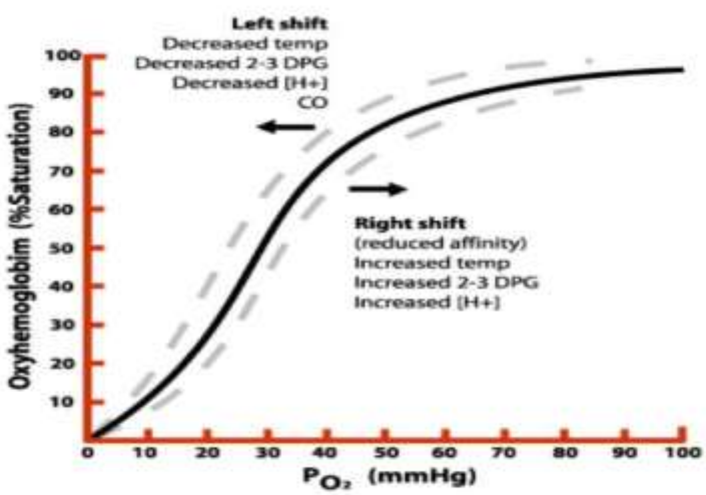
Because almost all oxygen in the blood is transported by hemoglobin, the relationship between the concentration (partial pressure) of oxygen and hemoglobin saturation (the % of hemoglobin molecules carrying oxygen) is an important one.

Hemoglobin saturation:

- extent to which the hemoglobin in blood is combined with O2
- depends on PO2 of the blood:
- The relationship between oxygen levels and hemoglobin saturation is indicated by the **oxygen-hemoglobin dissociation (saturation) curve**.
- at high partial pressures of O2 (above 40 mm Hg), Hb saturation remains rather high (75 - 80%).
- 40 mm Hg is the typical partial pressure of oxygen in cells of the body.
- under resting conditions, 20 - 25% of Hb molecules give up oxygen in the systemic capillaries. This is significant because it means that you have a substantial reserve of oxygen.
- When you do become more active, partial pressures of oxygen in your (active) cells may drop well below 40 mm Hg.
- as oxygen levels decline, hemoglobin saturation also declines - and declines precipitously. This means that blood (hemoglobin) 'unloads' lots of oxygen to active cells - cells that, of course, need more oxygen.

What is the oxygen dissociation curve?

- ❖ It is a graph that plots the proportion of Hb in its oxygen saturated form on vertical axis against partial pressure of oxygen on the horizontal axis.
- ❖ At high partial pressures of oxygen, Hb binds to oxygen to form oxyhaemoglobin. All RBC are in form of oxyhaemoglobin when blood is fully saturated with oxygen.
- ❖ At low partial pressures of oxygen (e.g. within tissues that are deprived of oxygen), oxyhaemoglobin releases oxygen to form Hb.



Which factors affect the oxygen dissociation curve?

The oxygen dissociation curve can be shifted right or left by a variety of factors.
A **right** shift indicates decreased oxygen affinity of Hb allowing more oxygen to be available to tissues.
A **left** shift indicates increased oxygen affinity of Hb allowing less oxygen to be available to tissues.

pH:

- A ↓ in pH shifts the curve to the right.
- an ↑in pH shifts the curve to the left.
- This occurs because a higher H + conc. causes an alteration in amino acid residues that stabilises deoxyhaemoglobin that has a lower affinity for oxygen. This rightwards shift is referred to as the **Bohr** effect.

Carbon dioxide (CO2):

- A ↓ in CO2 shifts the curve to the left,
- an ↑ in CO2 shifts the curve to the right.
- CO2 affects the curve in two ways. **Firstly**, accumulation of CO2 causes carbamino compounds to be generated, which bind to oxygen and form carbaminohaemoglobin that stabilizes deoxyhaemoglobin. **Secondly**, accumulation of CO2 causes an increase in H+ ion conc and a decrease in pH, which will shift the curve to the right.

Temperature:

- An ↑ in temperature shifts the curve to the right,
- a ↓ in temperature shifts the curve to the left.
- Increasing the temperature denatures the bond between oxygen and Hb, which increases the amount of oxygen and Hb and decreases the conc of oxyhaemoglobin.
- Temperature does not have a dramatic effect but the effects are noticeable in cases of hypothermia and hyperthermia.

Organic phosphates:

- 2,3-Diphosphoglycerate (2,3-DPG) is the main primary organic phosphate.
- An increase in 2,3-DPG shifts the curve to the right,
- a decrease in 2,3-DPG shifts the curve to the left.
- 2,3-DPG binds to haemoglobin and rearranges it, which decreases its affinity for oxygen.

How does carbon monoxide affect the curve?

CO interferes with oxygen transport function of blood by combining with Hb to form carboxyhaemoglobin (COHb). CO has approximately 240 times the affinity for Hb that oxygen does and for that reason even small amounts of CO can tie up a large proportion of Hb in the blood making it unavailable for oxygen carriage. If this happens PO2 of blood & Hb conc. will be normal but oxygen conc. will be grossly reduced. The presence of COHb also causes oxygen dissociation curve to be shifted to the left, interfering with unloading of oxygen.

How does methaemoglobin affect the curve?

Methaemoglobin is an abnormal form of haemoglobin in which the normal ferrous form is converted to the ferric state. Methaemoglobinaemia causes a left shift in the curve as methaemoglobin does not unload oxygen from haemoglobin.

What is the Bohr effect in exercise physiology?

with EXERCISE the oxygen-hemoglobin curve shifts to the RIGHT. This is because of four factors:
1) The decrease in pH (from the muscle cells getting more acidic)
2) An increase in muscle temperature (from muscle contraction)
3) An increase in the partial pressure of carbon dioxide (from the working muscles)
4) An increase of a byproduct molecule from glycolysis known as 2,3-BPG.

This shifting of the curve to the RIGHT (from these 4 factors) is referred to as the Bohr effect. Christian Bohr is the scientist who first explain this occurence from aerobic exercise.

Fetal haemoglobin

Fetal haemoglobin (HbF) is the main oxygen transport protein in the human fetus during the last 7 months of development. It persists in the newborn until roughly 6 months of age. HbF has different globin chains to adult haemoglobin (Hb). Whereas adult haemoglobin is composed of two alpha and two beta subunits, fetal haemoglobin is composed of two alpha and two gamma subunits. This change in the globin chain results in a greater affinity for oxygen and allows the fetus to extract blood from the maternal circulation. This increased affinity for oxygen means that the oxygen dissociation curve for fetal haemoglobin is shifted to the left of that of adult haemoglobin.

Carbon dioxide - transported from the body cells back to the lungs as:

1 - bicarbonate (HCO3) - 60%

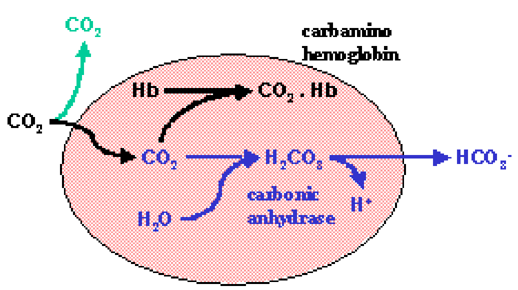
- formed when CO2 (released by cells making ATP) combines with H2O (due to the enzyme in red blood cells called carbonic anhydrase) as shown in the diagram below

2 - carbaminohemoglobin - 30%

- formed when CO2 combines with hemoglobin (hemoglobin molecules that have given up their oxygen)

3 - dissolved in the plasma - 10%

Carbon dioxide transport



Control of Respiration

❖ The medulla (in brainstem): controls automatic breathing
❖ Apneustic center (in the pons (in brain stem) - promote inspiration
❖ Pneumotaxic center (in the pons- in brainstem) - inhibits inspiration

The rhythmicity center of the medulla:

- controls automatic breathing
- consists of interacting neurons that fire either during inspiration (I neurons) or expiration (E neurons)
  - I neurons - stimulate neurons that innervate respiratory muscles (to bring about inspiration)

- E neurons - inhibit I neurons (to 'shut down' the I neurons & bring about expiration)

Apneustic center (located in the pons) - stimulate I neurons (to promote inspiration)

Pneumotaxic center (also located in the pons) - inhibits apneustic center & inhibits inspiration

Factors involved in increasing respiratory rate

- Chemoreceptors - located in aorta & carotid arteries (peripheral chemoreceptors) & in the medulla (central chemoreceptors)
- Chemoreceptors (stimulated more by increased CO2 levels than by decreased O2 levels) > stimulate Rhythmicity Area > Result = increased rate of respiration

Heavy exercise ==> greatly increases respiratory rate

Mechanism?

- NOT increased CO2
- Possible factors:
  - reflexes originating from body movements (proprioceptors)
  - epinephrine release (during exercise)
- impulses from the cerebral cortex (may simultaneously stimulate rhythmicity area & motor neurons)