The Exchange of Gases Between the Atmosphere and the Blood

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Anatomical Considerations

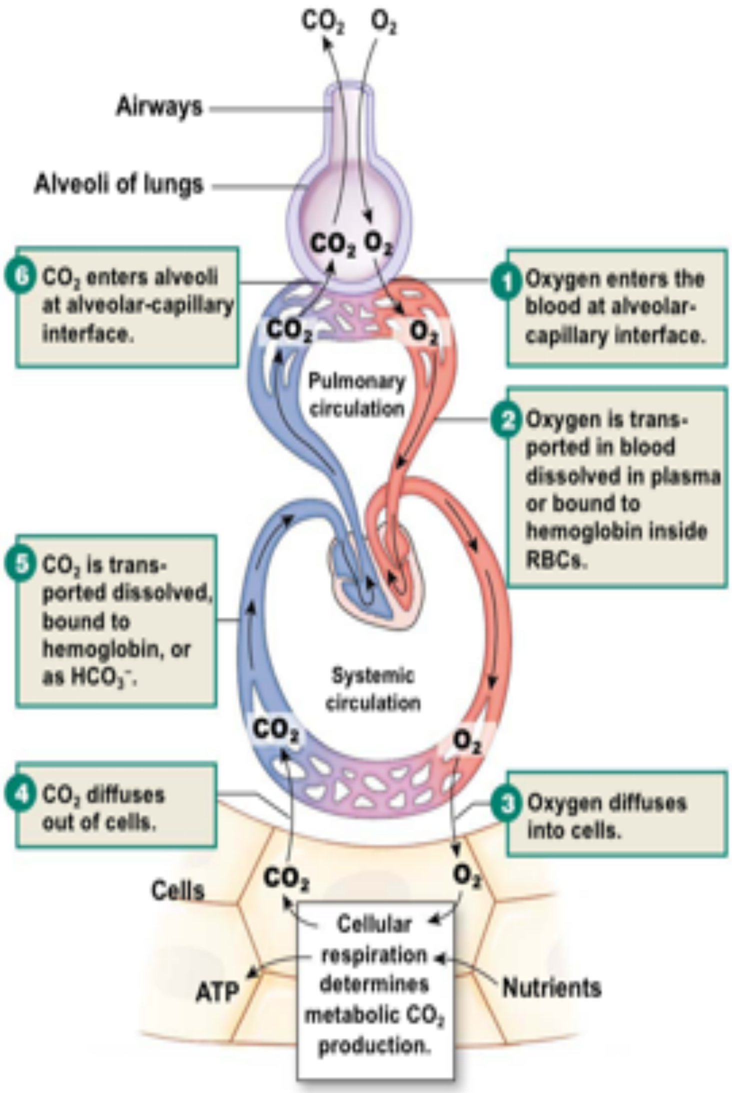
- Review of anatomy and bronchi
- 75% of breathing is from the diaphragm / 25% is from the intercostal muscles
- Breathing In
    - Ribs go up and out / Diaphragm goes down ➡ increases size of cavity
    - This creates a negative pressure which sucks air in
- Breathing Out
    - Ribs go down and in / Diaphragm goes up ➡ decreases size of cavity
    - This creates a negative pressure that blows air out
    - Breathing out is a passive recoil process that relaxes the intercostal muscles and the diaphragm
- Pleural membranes
    - The parietal pleura is adhered to the cavity and the diaphragm. When they move, they pull the pleura with it expanding the cavity.
    - The visceral pleura is connected to the parietal pleura with surfactant and the two membranes move together.
- Respiratory bronchiole
    - This is after the terminal bronchi and the first place that the walls are thin enough to transport O_2.
    - This is the start of the respiratory zone
    - 21% O_2 enters the respiratory bronchiole and 16% O_2 exists it
    - 0.4% CO_2 enters the respiratory bronchiole and 4% CO_2 exists it

Sensors

- To avoid hypoxia (low O_2) and hypercapnia (high CO_2), the body responds to three regulated variables
    - Oxygen
        - Arterial oxygen delivery to the cells is needed to support cellular respiration
    - Carbon dioxide
        - CO2 is produced as a waste product during the citric acid cycle
        - Excretion of CO2 is essential
            - High levels of CO2 depresses the CNS
            - High levels of CO2 causes acidosis
    - pH
        - Maintaining pH is essential to homeostasis

Causes of Low Alveolar P_{O_2}

- Inspired air has abnormally low oxygen content
    - Fractional Concentrations of Gases in the Air
        - N_2 79%
        - O_2 21%
        - CO_2 .04%
- Alveolar ventilation is inadequate (hypoventilation)
    - Decreased lung compliance
    - Increased airway resistance
    - CNS depression
        - *Alcohol poisoning*
        - *Drug overdose*

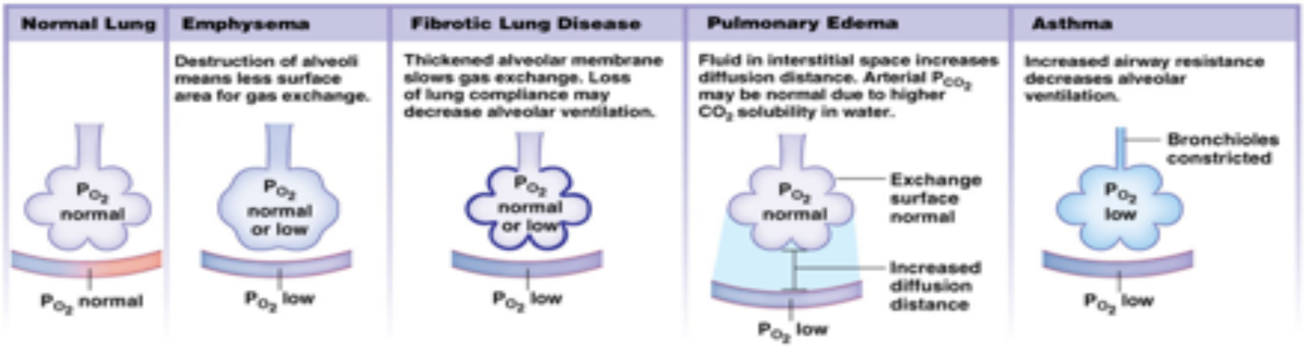


Diffusion and Solubility

- Constants
    - Surface area
    - Barrier permeability
    - Diffusion distance
- Concentration gradient
    - Primary factor affecting gas exchange

Gas Exchange

- Pathological changes
    - Decrease in amount of alveolar surface area - Emphysema
    - Increase in thickness of alveolar membrane - Fibrotic lung diseases
    - Increase in diffusion distance between alveoli and blood - Pulmonary edema



Gas Exchange Diagram

Gas Exchange Diagram

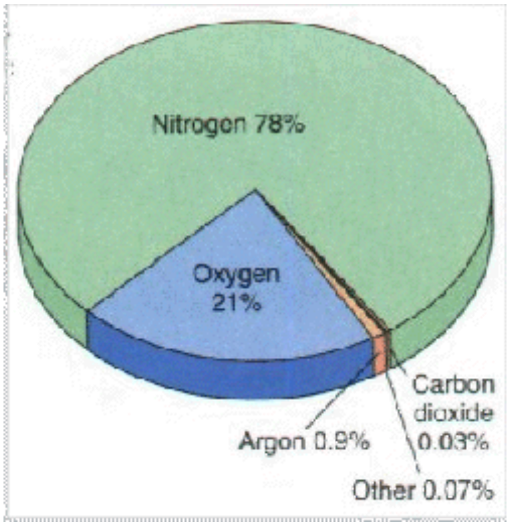
Fractional Concentrations of Gases in the Air

- N_2 79%
- O_2 21%
- CO_2 .04%

Partial Pressure of Gases in the Air

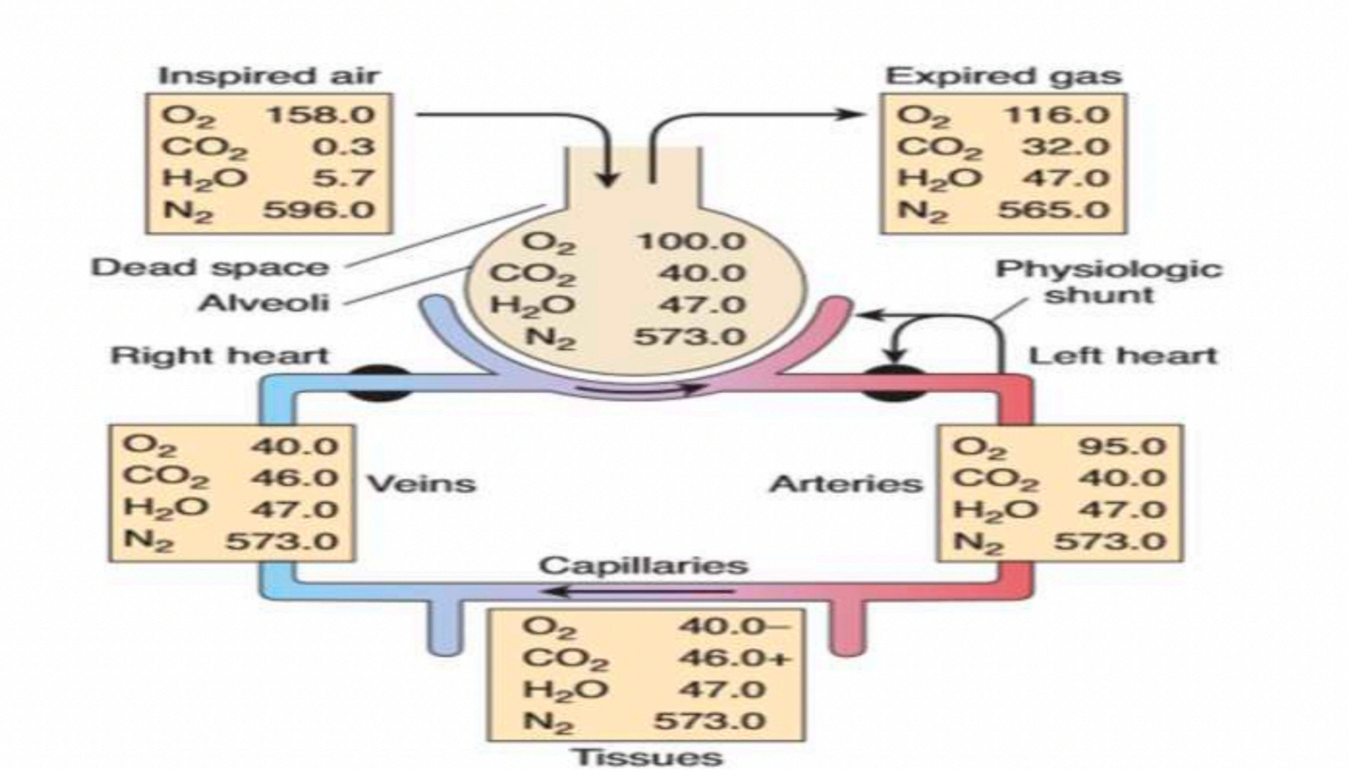
- In clinical setting, the concentration of a gas is usually expressed as a "Partial Pressure"
- The Partial Pressure of a gas (P_{gas}) is equal to the fractional concentration of that gas times the total pressure of the gas mixture.
- Normal Values
  - P_{N_2} = 79% x 760 mm Hg = 600 mm Hg
  - P_{O_2} = 21% X 760 mm Hg = 160 mm Hg
  - P_{CO_2} = .04% x 760 mm Hg = .3 mm Hg

    Note: 760 mm Hg is the atmospheric pressure at sea level.



Partial Pressures in mm Hg of Gases in Various Areas of the Body

Gas	Atmosphere	Trachea Mixture of In & Out Air	Alveoli	Arterial	Venous	Tissue
Nitrogen	596	564	573	573	573	573
Oxygen	158	149	100	95	40	40
CO_2	0.3	0.3	40	40	46	46
Water Vapor	5.7	47	47	47	47	47
Total	760	760	760	755	706	70



Notes about Partial Pressures of O_2 and CO_2

- The O_2 in the air is 160 mm Hg and in the alveoli is 100 mm Hg
- The CO_2 in the air is very low but goes up dramatically in the alveoli
- The alveoli O_2 & CO_2 are the Arterial Blood Gases (ABG's)
- How is it possible that there is more O_2 content in the air we exhale compared to the air in the alveoli?

Partial Pressure of Gases in the Alveoli of the Lungs

- The Effect of Water Vapor Pressure
  - As air is inhaled it becomes warmed to body temperature and completely saturated with water.
  - The amount of water that the air contains (called the "water vapor pressure") is directly proportional to the temperature of the air.
    - Consider: a pan of water covered by a bell jar, which traps the water vapor rising from the pan of water
  - At body temperature, the air will have a water vapor pressure = 47 mm Hg
  - The water vapor acts to "dilute" the contribution of other gases to the total pressure in the lungs (which is still equal to the atmospheric pressure)
  - As a result, the total pressure in the lungs is effectively "diluted" or reduced to
    Total Pressure in the Lungs = 760 – 47 + 713 mm Hg

Partial Pressure of Gases in the Alveoli of the Lungs

- The Concentration of O_2 in the Alveoli of the Lungs
    - As the O_2 in the alveoli diffuses into the bloodstream, the fractional concentration of O_2 (PA_{O_2}) falls to 14%
    - Normal Value PA_{O_2} = 14% x 713 mm Hg = 100 m Hg
- The Concentration of CO_2 in the Alveoli of the Lungs
    - As the CO_2 in the bloodstream enters the alveoli of the lungs, the fractional concentration of CO_2 (PA_{CO_2}) rises to 5.5%
    - Normal Value PA_{CO_2} = 5.5% x 713 mm Hg = 40 mm Hg
- There is no significant differences in the concentration of gases in the alveoli of the lungs between inhalation and exhalation. This is because the gain on O_2 and loss of CO_2 during each breath is small compared to the total volume of air in the lungs (about 2L), which is made-up mostly of N_2 (about 80%)

Partial Pressure of Gases in the Exhaled Air

- Exhaled air is actually a mixture of the air that was down the alveoli and the air that was up in the throat and trachea bronchial tree (i.e. the Dead Space)
- Normal Values
    - PE_{O_2} = 116 mm Hg
    - PE_{CO_2} = 27 mm Hg
    - PE_{H_2O} = 47 mm Hg
    - PE_{N_2} = 570 mm Hg

Partial Pressure of Gases <u>Dissolved in the Blood Plasma</u> (the Blood Gases)

- The ABG values are normally the same as the partial pressure of gases in the alveoli of the lungs

Gas Laws and Air Composition

- Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure.
- In natural systems, gases are normally present as a mixture of different types of molecules.
    - For example, the atmosphere consists of oxygen, nitrogen, carbon dioxide, and other gaseous molecules, and this gaseous mixture exerts a certain pressure referred to as atmospheric pressure
- **Partial pressure** (P_x) is the pressure of a single type of gas in a mixture of gases.
    - For example, in the atmosphere, oxygen exerts a partial pressure, and nitrogen exerts another partial pressure, independent of the partial pressure of oxygen.
- **Total pressure** is the sum of all the partial pressures of a gaseous mixture.
- **Dalton's law** describes the behavior of nonreactive gases in a gaseous mixture and states that a specific gas type in a mixture exerts its own pressure; thus, the total pressure exerted by a mixture of gases is the sum of the partial pressures of the gases in the mixture.

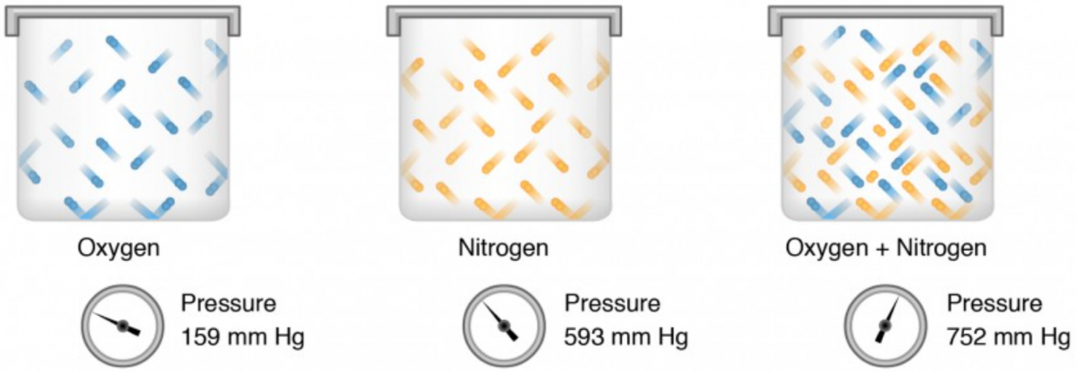


Figure 1. Partial pressure is the force exerted by a gas. The sum of the partial pressures of all the gases in a mixture equals the total pressure.

- Partial pressure is extremely important in predicting the movement of gases.
- A gas will move from an area where its partial pressure is higher to an area where its partial pressure is lower.
- In addition, the greater the partial pressure difference between the two areas, the more rapid is the movement of gases.

Solubility of Gases in Liquids

- Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure.
- **Henry's law** describes the behavior of gases when they come into contact with a liquid, such as blood.
- Henry's law states that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas.
  - The greater the partial pressure of the gas, the greater the number of gas molecules that will dissolve in the liquid.
  - The concentration of the gas in a liquid is also dependent on the solubility of the gas in the liquid.
  - For example, although nitrogen is present in the atmosphere, very little nitrogen dissolves into the blood, because the solubility of nitrogen in blood is very low. The exception to this occurs in scuba divers; the composition of the compressed air that divers breathe causes nitrogen to have a higher partial pressure than normal, causing it to dissolve in the blood in greater amounts than normal. Too much nitrogen in the bloodstream results in a serious condition that can be fatal if not corrected. Gas molecules establish an equilibrium between those molecules dissolved in liquid and those in air.

The composition of air in the atmosphere and in the alveoli differs. In both cases, the relative concentration of gases is nitrogen > oxygen > water vapor > carbon dioxide. The amount of water vapor present in alveolar air is greater than that in atmospheric air

(Table 2). Recall that the respiratory system works to humidify incoming air, thereby causing the air present in the alveoli to have a greater amount of water vapor than atmospheric air. In addition, alveolar air contains a greater amount of carbon dioxide and less oxygen than atmospheric air. This is no surprise, as gas exchange removes oxygen from and adds carbon dioxide to alveolar air. Both deep and forced breathing cause the alveolar air composition to be changed more rapidly than during quiet breathing. As a result, the partial pressures of oxygen and carbon dioxide change, affecting the diffusion process that moves these materials across the membrane. This will cause oxygen to enter and carbon dioxide to leave the blood more quickly.

Ventilation and Perfusion

Two important aspects of gas exchange in the lung are ventilation and perfusion. **Ventilation** is the movement of air into and out of the lungs, and perfusion is the flow of blood in the pulmonary capillaries. For gas exchange to be efficient, the volumes involved in ventilation and perfusion should be compatible. However, factors such as regional gravity effects on blood, blocked alveolar ducts, or disease can cause ventilation and perfusion to be imbalanced.

The partial pressure of oxygen in alveolar air is about 104 mm Hg, whereas the partial pressure of the oxygenated pulmonary venous blood is about 100 mm Hg. When ventilation is sufficient, oxygen enters the alveoli at a high rate, and the partial pressure of oxygen in the alveoli remains high. In contrast, when ventilation is insufficient, the partial pressure of oxygen in the alveoli drops. Without the large difference in partial pressure between the alveoli and the blood, oxygen does not diffuse efficiently across the respiratory membrane. The body has mechanisms that counteract this problem. In cases when ventilation is not sufficient for an alveolus, the body redirects blood flow to alveoli that are receiving sufficient ventilation. This is achieved by constricting the pulmonary arterioles that serves the dysfunctional alveolus, which redirects blood to other alveoli that have sufficient ventilation. At the same time, the pulmonary arterioles that serve alveoli receiving sufficient ventilation vasodilate, which brings in greater blood flow. Factors such as carbon dioxide, oxygen, and pH levels can all serve as stimuli for adjusting blood flow in the capillary networks associated with the alveoli.

Ventilation is regulated by the diameter of the airways, whereas perfusion is regulated by the diameter of the blood vessels. The diameter of the bronchioles is sensitive to the partial pressure of carbon dioxide in the alveoli. A greater partial pressure of carbon dioxide in the alveoli causes the bronchioles to increase their diameter as will a decreased level of oxygen in the blood supply, allowing carbon dioxide to be exhaled from the body at a greater rate. As mentioned above, a greater partial pressure of oxygen in the alveoli causes the pulmonary arterioles to dilate, increasing blood flow.

External Respiration

The pulmonary artery carries deoxygenated blood into the lungs from the heart, where it branches and eventually becomes the capillary network composed of pulmonary capillaries. These pulmonary capillaries create the respiratory membrane with the alveoli. As the blood is pumped through this capillary network, gas exchange occurs. Although a small amount of the oxygen is able to dissolve directly into plasma from the alveoli, most of the oxygen is picked up by erythrocytes (red blood cells) and binds to a protein called hemoglobin, a process described later in this chapter. Oxygenated hemoglobin is red, causing the overall appearance of bright red oxygenated blood, which returns to the heart through the pulmonary veins. Carbon dioxide is released in the opposite direction of oxygen, from the blood to the alveoli. Some of the carbon dioxide is returned on hemoglobin, but can also be dissolved in plasma or is present as a converted form, also explained in greater detail later in this chapter.

External respiration occurs as a function of partial pressure differences in oxygen and carbon dioxide between the alveoli and the blood in the pulmonary capillaries.

Although the solubility of oxygen in blood is not high, there is a drastic difference in the partial pressure of oxygen in the alveoli versus in the blood of the pulmonary capillaries. This difference is about 64 mm Hg: The partial pressure of oxygen in the alveoli is about 104 mm Hg, whereas its partial pressure in the blood of the capillary is about 40 mm Hg. This large difference in partial pressure creates a very strong pressure gradient that causes oxygen to rapidly cross the respiratory membrane from the alveoli into the blood.

The partial pressure of carbon dioxide is also different between the alveolar air and the blood of the capillary. However, the partial pressure difference is less than that of oxygen, about 5 mm Hg. The partial pressure of carbon dioxide in the blood of the capillary is about 45 mm Hg, whereas its partial pressure in the alveoli is about 40 mm Hg. However, the solubility of carbon dioxide is much greater than that of oxygen—by a factor of about 20—in both blood and alveolar fluids. As a result, the relative concentrations of oxygen and carbon dioxide that diffuse across the respiratory membrane are similar.

Internal Respiration

Internal respiration is gas exchange that occurs at the level of body tissues (Figure 3). Similar to external respiration, internal respiration also occurs as simple diffusion due to a partial pressure gradient. However, the partial pressure gradients are opposite of those present at the respiratory membrane. The partial pressure of oxygen in tissues is low, about 40 mm Hg, because oxygen is continuously used for cellular respiration. In contrast, the partial pressure of oxygen in the blood is about 100 mm Hg. This creates a pressure gradient that causes oxygen to dissociate from hemoglobin, diffuse out of the blood, cross the interstitial space, and enter the tissue. Hemoglobin that has little oxygen bound to it loses much of its brightness, so that blood returning to the heart is more burgundy in color.

Considering that cellular respiration continuously produces carbon dioxide, the partial pressure of carbon dioxide is lower in the blood than it is in the tissue, causing carbon dioxide to diffuse out of the tissue, cross the interstitial fluid, and enter the blood. It is then carried back to the lungs either bound to hemoglobin, dissolved in plasma, or in a converted form. By the time blood returns to the heart, the partial pressure of oxygen has returned to about 40 mm Hg, and the partial pressure of carbon dioxide has returned to about 45 mm Hg. The blood is then pumped back to the lungs to be oxygenated once again during external respiration.

Brief Explanation of Gas Exchange

- In order for CO_2 and O_2 to increase and decrease in the alveoli, it needs Hemoglobin (Hb) to help transport it.
    - Hb contains a 4 protein chain each with an Fe atom and the Fe easily combines with O_2.
    - The Hb affinity for O_2 will change depending on need.
    - The only way that the Hb knows when to pick up or dump O_2 or CO_2 is based upon the partial pressure.
- Because of Partial Pressure, the molecules will always diffuse from areas of high concentration to areas of low concentration.
    - Partial pressure will determine when O_2 and CO_2 needs to diffuse
    - Example – The O_2 partial pressure at sea level outside the body is 160 mm Hg. (760 mm Hg x 21%). When that pressure reaches the lungs and dead space it is decreased to 104 mm Hg. And as the blood enters the right ventricle it is decreased to 40 mm Hg because it has been used up by the body.

Brief Explanation of Gas Exchange

- This difference in pressure makes it easy for gases to diffuse down the concentration gradient.

Outside 160 mm Hg >>> Lungs O_2 rich 104 mm Hg >>> Lungs O_2 poor 40 mm Hg

Diffused gases will always diffuse down their partial pressure gradients

- This is why it is harder to breath at high altitudes. The concentration of O_2 in the air is still 21%, but the pressure has greatly decreased which makes it much harder to diffuse.
- Hemoglobin (Hb) makes it all possible. The globin in hemoglobin is a protein and when proteins bind to stuff they change their shape, which makes it much easier for O_2 to connect with it.
    - There are 4 binding sites on each Hb molecule. Once 1 O_2 has connected to it, it tends to attract 3 more O_2 molecules to complete it. This is called cooperativity.
    - Now that the Hb has bound to 4 oxygens, it is called Oxyhemoglobin – HbO_2.
- When the blood leaves the lungs, it is fully saturated and it travels in the plasma to the tissues.
- After the O_2 has moved along the gradient, it is quickly decreased to about 40 mm Hg, which is O_2 poor.
- All of this metabolic activity in the tissues created CO_2 as a waste product and heat.
- The CO_2 and heat triggers the need for more O_2 by lowering Hb affinity for it.
- The CO_2 can also bind to Hb and when it does it changes the shape of the Hb molecular shape. This change allows the Hb to pick up more CO_2 and pick up less O2.
- The spike in CO_2 from the tissues actually makes the blood more acidic. Now because of the acidity, the CO_2 and the H_2O combines and makes carbonic acid.
    - The carbonic acid breaks down into bicarbonate and Hydrogen ions. These ions change the shape of the Hb again and makes it with less affinity for O_2 and more affinity for CO_2.
- The Hb is now maxed out with CO_2 and as it moves to the alveoli, the CO_2 is dropped off along the gradient.

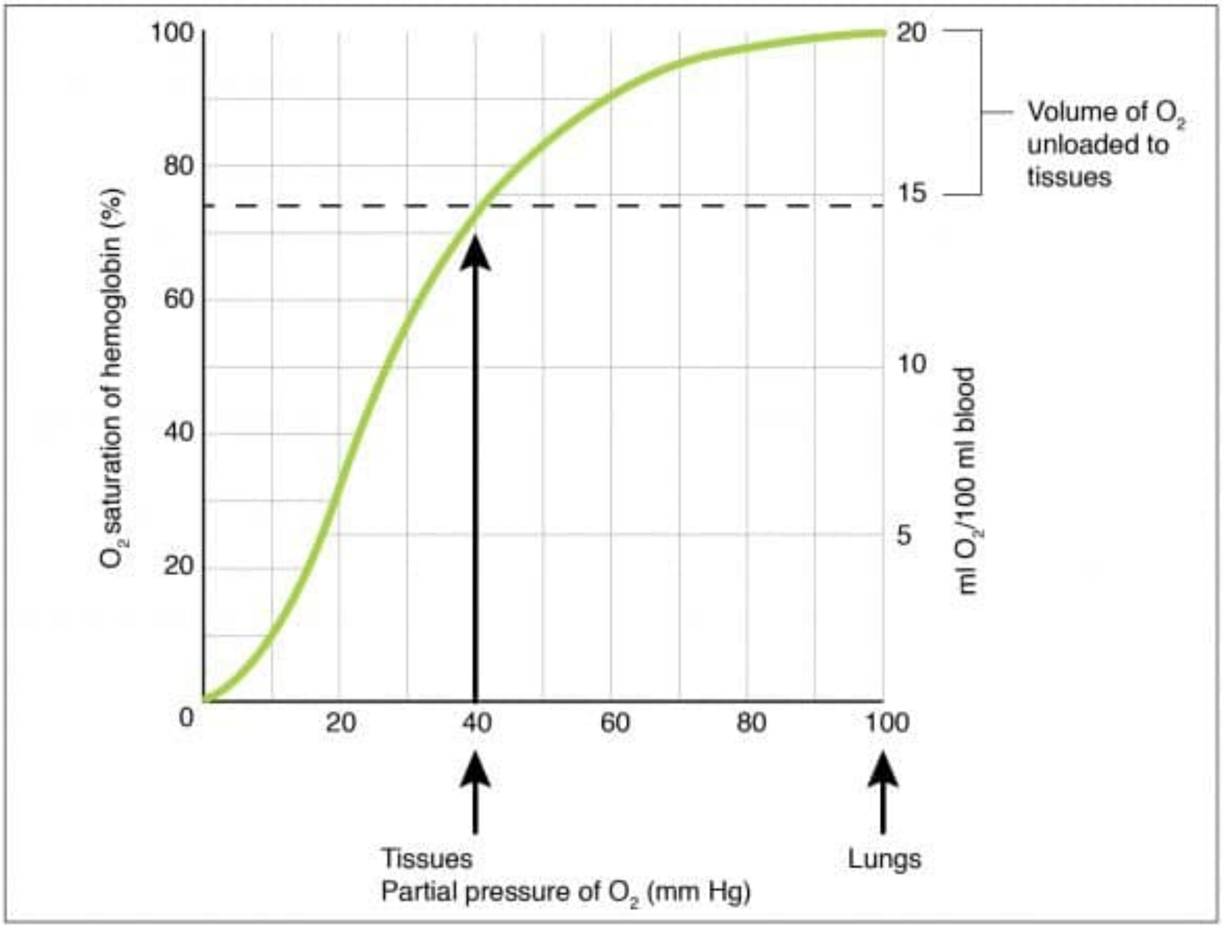
The Transport of Oxygen

- Oxygen enters the bloodstream via the lungs, where it diffuses across the alveolar epithelium and pulmonary capillary endothelium to reach the pulmonary circulation.
- Once the oxygen has entered the pulmonary circulation, it is carried in the blood to target tissues in two distinct forms:
    - Bound to hemoglobin (around 98% of total blood oxygen content)
    - Directly dissolved in the plasma (only around 2% of total blood oxygen content)

Hemoglobin

- Hemoglobin is made up of four subunits.
    - Each subunit is formed of a globin polypeptide chain and an associated hem group. Each iron atom, and therefore each subunit, can reversibly associate with a single oxygen molecule.
- There are a variety of structurally distinct subunits that combine to form different types of hemoglobin.
    - Normal adult hemoglobin makes up about 97% of adult hemoglobin and is comprised of 2 α and 2 β subunits.
    - Fetal hemoglobin has a different subunit make-up.
- Each hemoglobin subunit can bind a single oxygen molecule**,** so each hemoglobin molecule can associate with between 0 and 4 oxygen molecules at any one time.
- When an oxygen molecule binds to a hem group, a change occurs in the related globin chain structure. As the globin chains are closely linked, a change in the shape of one subunit is also transmitted to the other subunits. Oxygen binding to one haemoglobin subunit acts to **increase the remaining subunits' affinity for oxygen**. Deoxygenated haemoglobin exists in a 'tense' (T) conformation, with a low affinity for oxygen. As oxygen begins to bind to haem groups, the haemoglobin moves into a 'relaxed' (R) state, allowing further oxygen molecules to bind more easily. This process is referred to as co-operativity.[2]

This co-operativity between the subunits results in the characteristic **sigmoidal oxygen-haemoglobin dissociation curve** shown in Figure 2.



(a) Partial pressure of oxygen and hemoglobin saturation

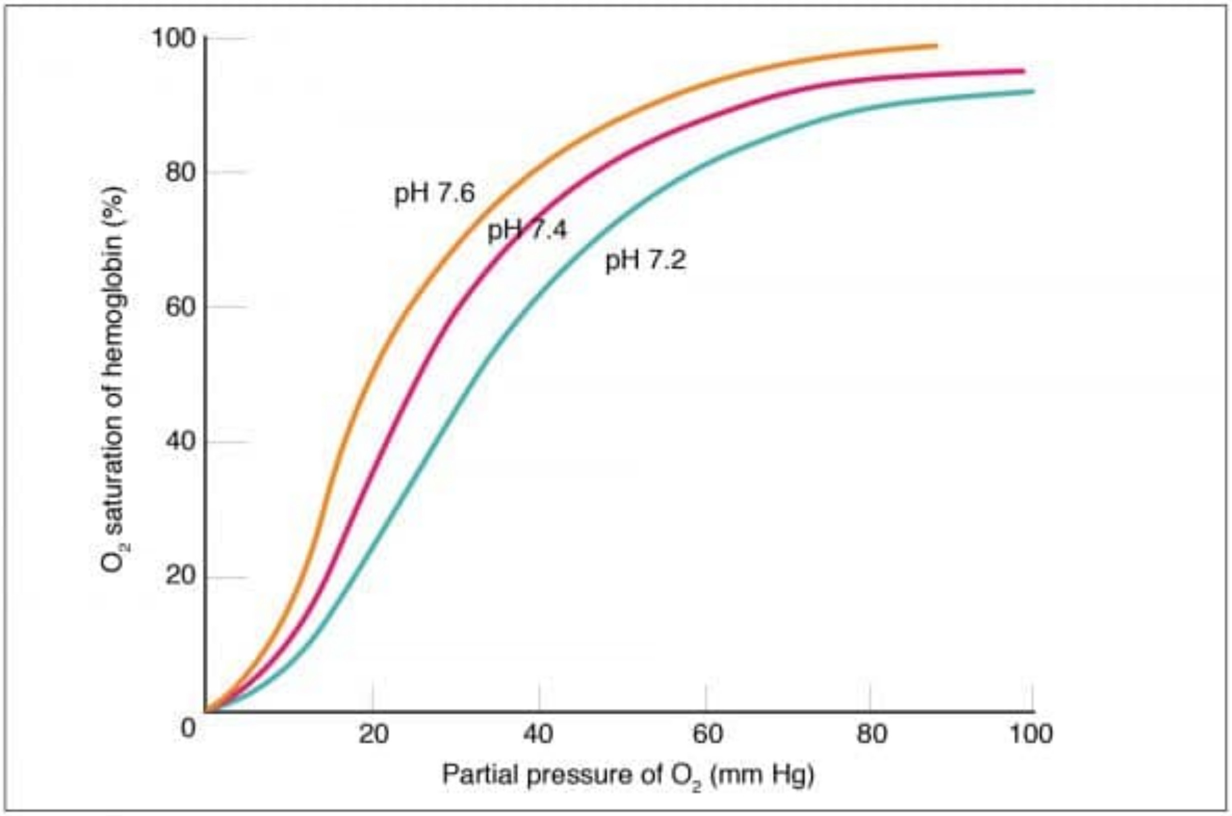
Haemoglobin-oxygen affinity

As shown by the oxygen-haemoglobin dissociation curve above, the amount of oxygen bound to haemoglobin (the oxygen saturation) is affected by the **partial pressure of oxygen** (PaO_2) in the blood. However, this relationship and the shape of the curve are not constant, as the affinity of haemoglobin for oxygen is affected by the **physiological environment**.

Some important factors which affect **haemoglobin-oxygen affinity** are discussed below.

pH

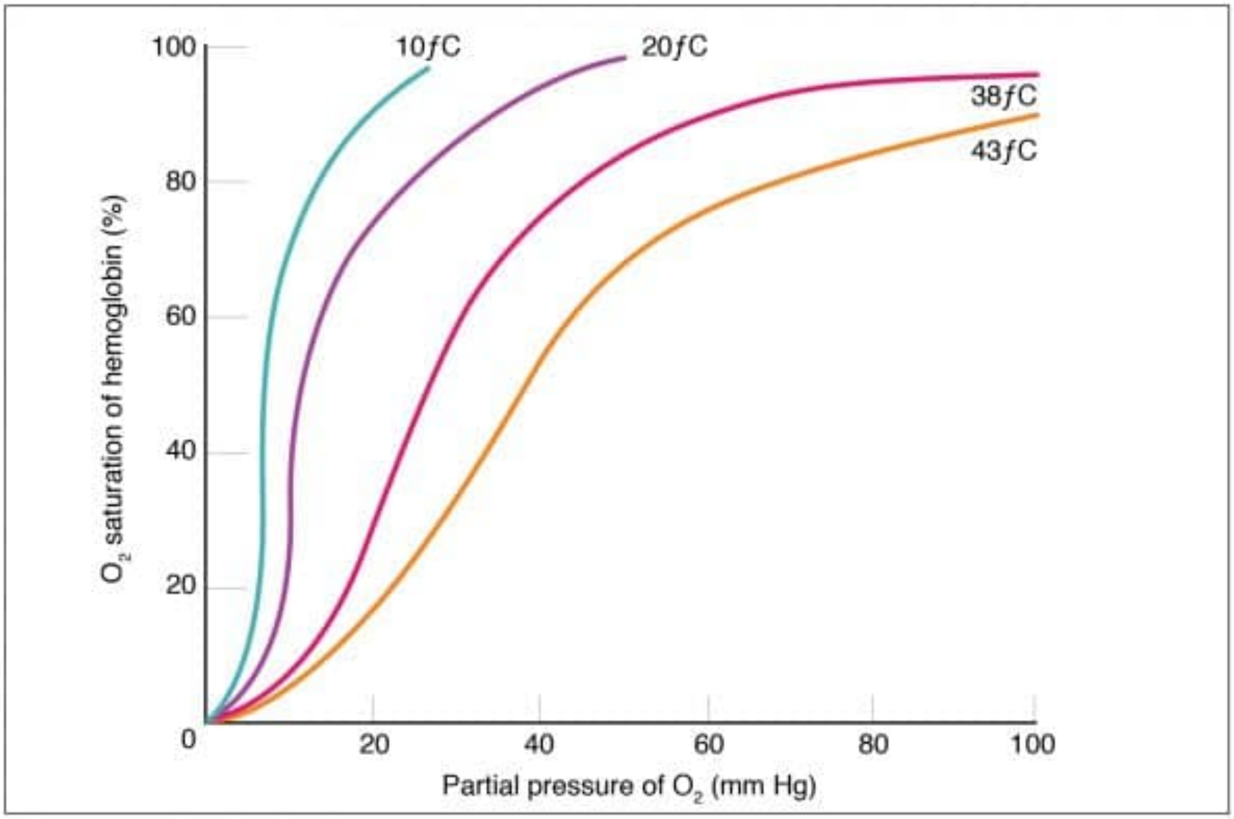
Low pH, a feature of tissues with high metabolic activity, **reduces the affinity** of haemoglobin for oxygen, **shifting the curve to the right**. The reduced affinity means that **more oxygen is offloaded in metabolically active tissues**, where the oxygen requirement is highest. The reduction of haemoglobin-oxygen affinity at low pH is known as the **Bohr effect**.



(b) Effect of pH

Temperature

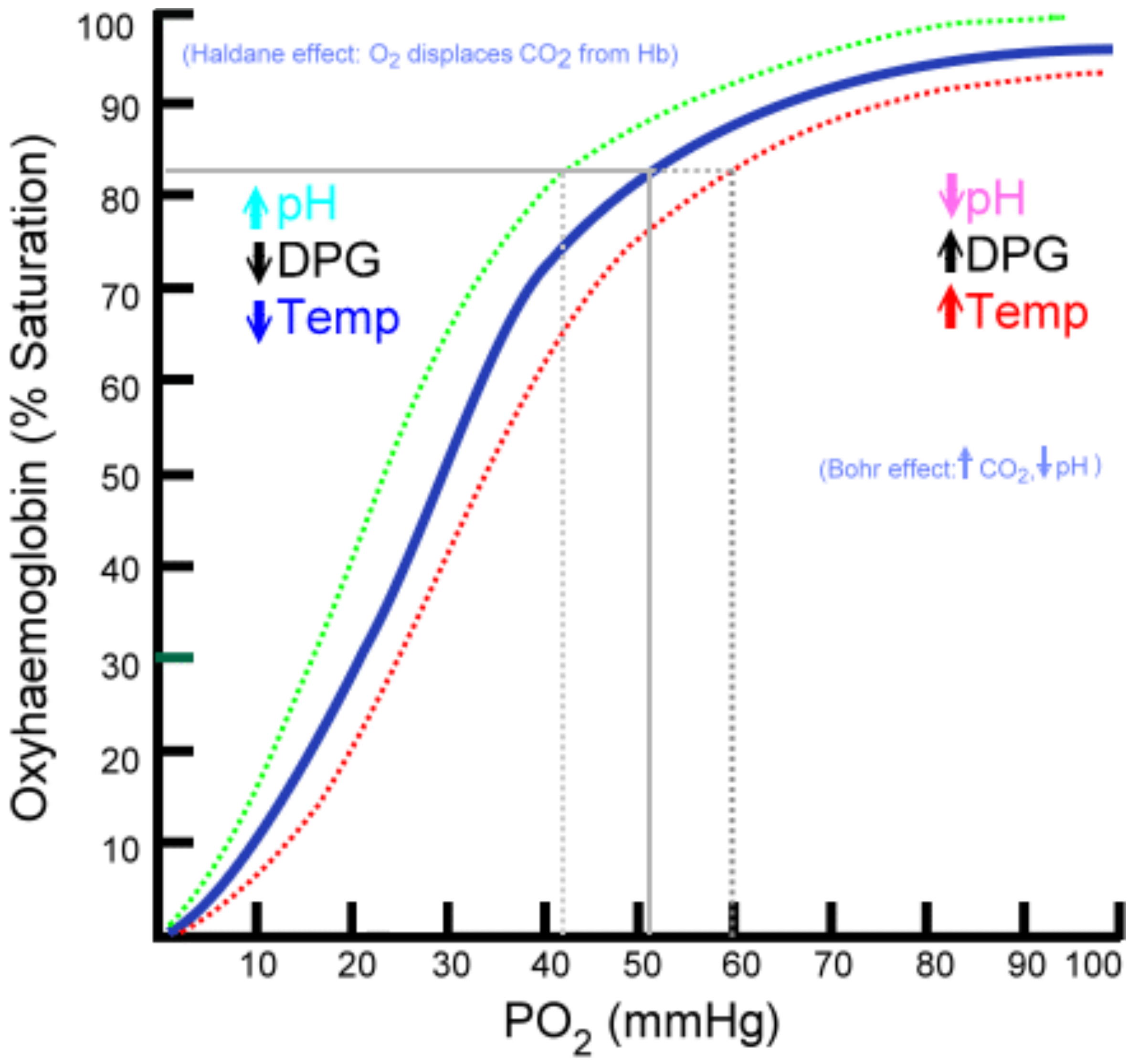
Increased temperature **reduces** haemoglobin's affinity for oxygen, **shifting the curve to the right**. This has an important effect during exercise when active muscle rises in temperature and therefore triggers increased oxygen offloading.



(c) Effect of temperature

2,3-DPG

2,3- diphosphoglycerate is an intermediate product of **glycolysis**, found in red blood cells. 2,3-DPG **reduces the affinity** of haemoglobin for oxygen, **shifting the curve to the right**. Increased 2,3-DPG is found in **anaemia** and at **altitude**, which is important in the prevention of tissue hypoxia.[2]



- The Total O_2 Content in the Blood (Volume %)
  - At PA_{O_2} = 100 mm Hg

$$\frac{.5\ \text{ml}\ O_2\ \text{dissolved in the plasma}}{100\ \text{ml whole blood}} + \frac{19.5\ \text{ml}\ O_2\ \text{carried by the RBC's}}{100\ \text{ml whole blood}}$$

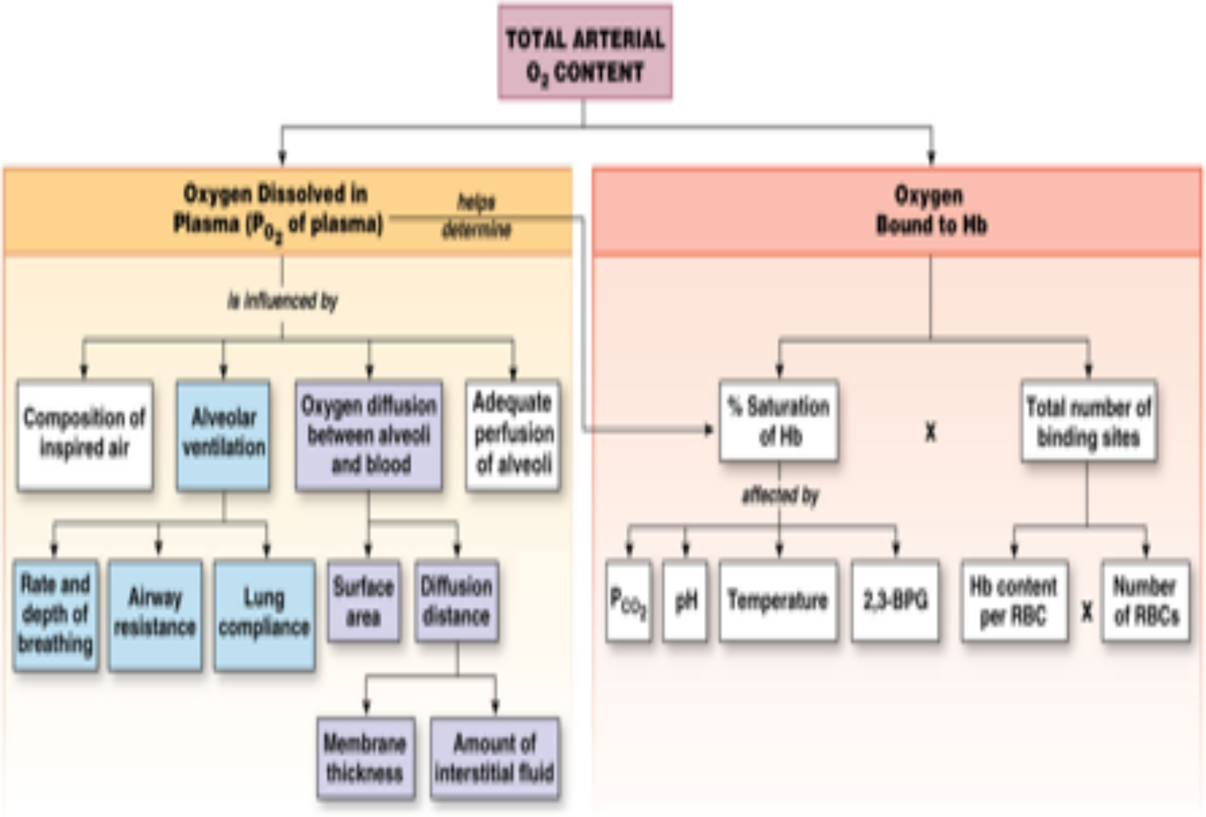
$$= \frac{20\ \text{ml}\ O2}{100\ \text{ml whole blood}} = 20\ \text{ml}\ \%$$

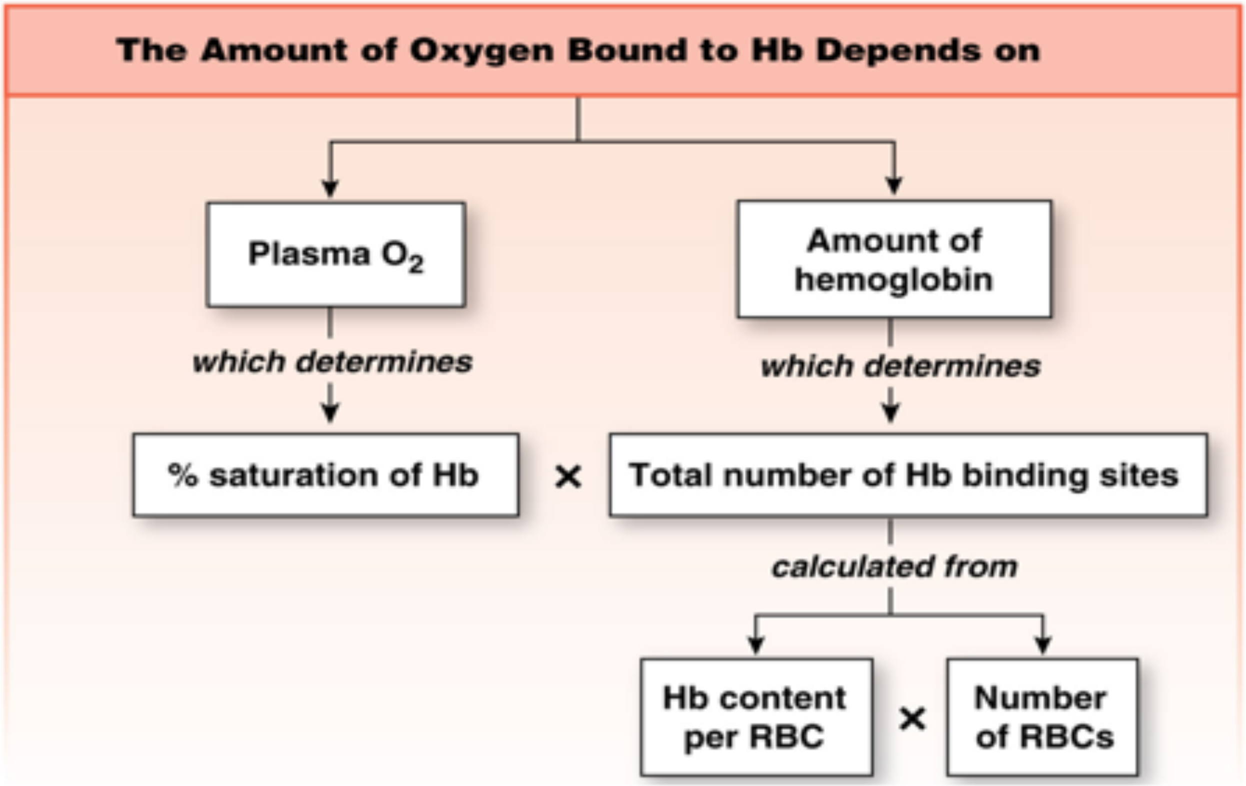
- At PV_{O_2} = 40 mm Hg

$$\frac{.1\ \text{ml } O_2 \text{ dissolved in the plasma}}{100\ \text{ml whole blood}} + \frac{15\ \text{ml } O_2 \text{ carried by the RBC's}}{100\ \text{ml whole blood}}$$

$$= \frac{15.1\ \text{ml } O2}{100\ \text{ml whole blood}} = 15.1\ \text{ml } \%$$

Note: This represents a sufficient reserve of O2 in the venous blood to sustain the person for about 4 minutes without breathing.





Factors that affect the loading-up / unloading of O_2 by the RBC's (The Bohr Effect)

- In The Tissues

  Local ↑ CO_2 ➡ ↓ Affinity between Hb & O_2 ➡ Unloading of O_2 by the RBC's
  Local ↑ H ➡ ↓ Affinity between Hb & O_2 ➡ Unloading of O_2 by the RBC's
  Local ↑ Temperature ➡ ↓ Affinity between Hb & O_2 ➡ Unloading of O_2 by the RBC's

Clinical Considerations – Hypoxia

- A deficiency of O2 reaching the tissue cells
- Types of Hypoxia
  - Hypoxic Hypoxia
    - Low PAO_2 causing a ↓ O_2 content in the blood
    - Associated with any respiratory problems producing a state of hypoventilation
    - Examples
      - Pulmonary Diseases such a bronchial asthma, emphysema, and tuberculosis
      - Breathing at high altitude (where the PAO_2 is low)
      - Hypoventilation caused by a depression of the Respiratory Reflex Center (example – barbiturate sedative overdose)

Clinical Considerations – Hypoxia

- Anemic Hypoxia
  - Low Hemoglobin content / RBC count available to carry O_2 in the blood
  - Examples
    - Hemorrhage
    - Pernicious anemia
    - Sickle cell anemia

      Abnormal Hb – S has ↓ affinity for O_2
    - Carbon monoxide (CO) poisoning

      Hb – CO ➡ Hb-CO (Carbonmonoxy-Hemoglobin)
- Ischemic Hypoxia
  - Decreased O_2 delivery as a result of a ↓ Blood Flow
  - Examples:
    - Acute hypotension (shock)
    - Heart failure
    - Thrombosis / Embolism ➡ ↓ Blood Flow
- Histotoxic Hypoxia
  - O_2 can not be biochemically utilized in cellular respiration by tissue cells due to poisoning
  - Example: cyanide poisoning

Carbon Dioxide Transport

- Percentages
  - Dissolved: 7%
  - Converted to bicarbonate ion: 70%
  - Carbonic anhydrase and chloride shift
  - Bound to hemoglobin: 23%
- Hemoglobin also binds H^+
- Hb and CO_2: carbaminohemoglobin

- The amount of CO_2 dissolved in the blood plasma
  - The amount of CO_2 dissolved in the plasma is directly proportional to the partial pressure of CO_2 (Henry's Law)
  - At $PACO_2$ = 40 mm Hg

    Approximately $\frac{2.5\text{ ml } CO_2 \text{ dissolved in plasma}}{100\text{ ml whole blood}}$
  - At $PVCO_2$ = 46 mm Hg

    Approximately $\frac{3\text{ ml } CO_2 \text{ dissolved in plasma}}{100\text{ ml whole blood}}$

- The amount of CO_2 carried by the RBC's
  - CO_2 can reversibly bind to the Hemoglobin in the RBC's

    $Hb = CO_2 \leftrightarrow Hb\text{-}CO_2$ (carbamino-hemoglobin)
  - The amount of CO_2 carried by the RBC's is also directly proportional to the partial pressure of CO_2

The Transport of CO_2 - continued

- At $PACO_2$ = 40 mm Hg
  Approximately $\frac{2.5 \text{ ml } CO_2 \text{ dissolved in plasma}}{100 \text{ ml whole blood}}$
- At $PVCO_2$ = 46 mm Hg
  Approximately $\frac{4 \text{ ml } CO_2 \text{ dissolved in plasma}}{100 \text{ ml whole blood}}$
- The amount of CO_2 dissolved in the plasma as HCO_3
  HCO_3 – bicarbonate ion
  - CO_2 can reversibly react with H_2O to form H_2CO_3
    HCO_3 = carbonic acid
  - The amount of CO_2 dissolved in the plasma as HCO_3 is also directionally proportional to the partial pressure of CO_2
    At $PACO_2$ = 40 mm Hg
    Approximately $\frac{44 \text{ ml } CO_2 \text{ dissolved as } HCO_3}{100 \text{ ml whole blood}}$
    At $PVCO_2$ = 46 mm Hg
    Approximately $\frac{47 \text{ ml } CO_2 \text{ dissolved as } HCO_3}{100 \text{ ml whole blood}}$

Question: Do you think the pH of the systemic venous blood is lower than the pH of systemic arterial blood? $pH_A = 7.4$ $pH_V = 7.36$

- The Total CO_2 Content in the Blood (Volume %)
  - At $PACO_2$ = 40 mg Hg
    2.5 ml CO_2 dissolved + 2.5 ml CO_2 carried + 44 ml CO_2 at HCO_3
    in plasma by RBC's

    $$= \frac{49 \text{ ml } CO_2}{100 \text{ ml whole blood}} = 49 \text{ ml } \%$$

  - At $PVCO_2$ = 46 mg Hg
    3 ml CO_2 dissolved + 4 ml CO_2 carried + 47 ml CO_2 at HCO_3
    in plasma by RBC's

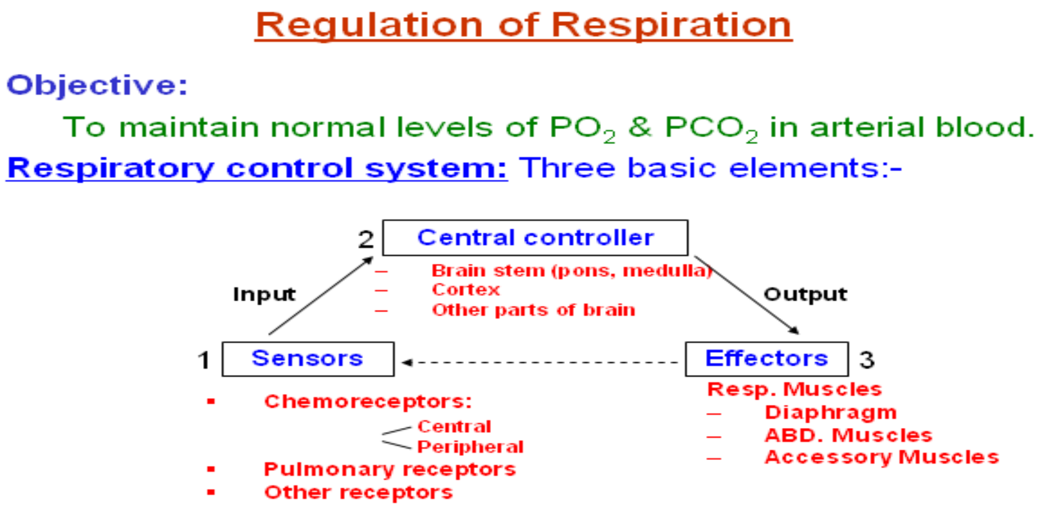
    $$= \frac{54 \text{ ml } CO_2}{100 \text{ ml whole blood}} = 54 \text{ ml } \%$$

Control of Respiration: Medullary Respiratory Centers

- The dorsal respiratory group or inspiratory center
  - Appears to be the pacesetting respiratory center
  - Excites the inspiratory muscles and sets breath rates (12-15 breaths/minute)
  - Becomes dormant during expiration
- The ventral respiratory group is involved in forced inspiration and expiration

Depth and Rate of Breathing: Higher Brain Centers

- Hypothalamic controls act through the limbic system to modify rate and depth of respiration
    - Example: breath holding that occurs in anger
- A rise in body temperature acts to increase respiratory rate
- Cortical controls are direct signals from the cerebral motor cortex that bypass medullary controls
    - Examples: voluntary breath holding, taking a deep breath



Regulation of Respiration

Objective:

To maintain normal levels of PO_2 & PCO_2 in arterial blood.

Respiratory control system: Three basic elements:-

Hyperventilation

- Increase in the rate and depth of breathing that exceeds the bodies need to remove CO2
- Occurs when low CO2 levels in the blood cause cerebral blood vessels to constrict which produces cerebral ischemia

Hypoventilation

- Hypoventilation – slow and shallow breathing due to abnormally low P_{CO2} levels
    - Apnea (breathing cessation) may occur until P_{CO2} levels rise

Respiratory Adjustments: Exercise

- Respiratory adjustments are geared to both the intensity and duration of exercise
- During vigorous exercise:
    - Ventilation can increase 20 fold
    - Breathing becomes deeper and more vigorous, but respiratory rate may not be significantly changed (hyperpnea)
- As exercise begins
    - Ventilation increases abruptly, rises slowly, and reaches a steady state
- When exercise stops
    - Ventilation declines suddenly, then gradually decreases to normal

Respiratory Adjustments: Exercise

- Neural factors bring about the above changes, including:
  - Psychic stimuli
  - Cortical motor activation
  - Excitatory impulses from proprioceptors in muscles

Respiratory Adjustments: High Altitude

- The body responds to quick movement to high altitude (above 8000 ft) with symptoms of acute mountain sickness – headache, shortness of breath, nausea, and dizziness
- Acclimatization – respiratory and hematopoietic adjustments to altitude
- The higher the altitude, the lower the atmospheric pressure
- Consider: the P_{O_2} at 30,000 (Mt. Everest)
  - P_{O_2} = 21% x 226 mm Hg = 47 mm Hg
  - The P_{O_2} remains 21% at 30,000 ft., however the atmospheric pressure is only 226 mm Hg (less than 1/3 the atmospheric pressure at sea level)
- Question: What do you think happens to the atmospheric pressure as you descend <u>below</u> sea level?

The bottle above was sealed at 14,000 feet on the left. In the middle picture, the bottle was crushed by atmospheric pressure at 9,000 feet. The picture on the right shows the effect of atmospheric pressure at sea level.

Chronic Obstructive Pulmonary Disease (COPD)

- Exemplified by chronic bronchitis and obstructive emphysema
- Patients have a history of:
  - Smoking
  - Dyspnea, where labored breathing occurs and gets progressively worse
  - Coughing and frequent pulmonary infections
- COPD victims develop respiratory failure accompanied by hypoxemia, carbon dioxide retention, and respiratory acidosis

Arterial Blood Gas Analysis

ABG Parameter			ABG result
pH	>7.45	Alkalaemia	
	7.36-44	Normal	
	<7.35	Acidaemia	
pCO2	>45	High	
	35-45	Normal	
	<35	Low	
HCO3	>26	High	
	24+/- 2	Normal	
	<22	Low	
AG	> 16	High	
	12+/-4	Normal	
	< 8	Low	
Glucose	>10	High	
	< 2	Low	
Gap: Gap	$\frac{\Delta AG}{\Delta HCO_3} = \frac{AG - 12}{24 - HCO_3}$		
Lactate	**<1.9**	Normal	
	>2.0	High	
pO2	80-100	Normal	
	< 80	Hypoxia	

Calculation and interpretation

pH	pCO2	Interpretation
↓	↓	Metabolic acidosis
↑	↑	Metabolic alkalosis
↑	↓	Respiratory alkalosis
↓	↑	Respiratory acidosis

Corrected standard AG for albumin

$\frac{\text{Albumin}}{4} + 1.5 \times \text{Phosphate}$

Anion Gap calculation

$\{[Na^{+}] - [Cl^{-} + HCO_{3}]\} = 12+/-4$

Corrected Na+ for AG in hyperglycemia

Corrected Na+ = Na + $\frac{\text{Glucose} - 5}{3}$

Gap: Gap calculation for metabolic acidosis

<0.4	Low or Normal AG metabolic acidosis
0.4-0.8	Normal + high AG metabolic acidosis
0.8-2.0	Pure high metabolic acidosis
>2.0	Metabolic acidosis with metabolic alkalosis/respiratory acidosis

PAO2 = [713 x FiO2] – [pCO2 x 1.25]

A-a gradient = PAO2 – PaO2 = $\frac{\textbf{Age}}{\textbf{4}} + 4$

Compensation rules for				
	Metabolic acidosis		**Metabolic alkalosis**	
Expected PCO2	1.5 X [HCO3] + 8 (+/- 2)		0.7 X [HCO3] + 20 (+/- 5)	
	Respiratory acidosis		**Respiratory alkalosis**	
	Acute	Chronic	Acute	Chronic
Expected HCO3	$24 + \frac{pCO2 - 40}{10} \times 1$	$24 + \frac{pCO2 - 40}{10} \times 4$	$24 - \frac{40 - pCO2}{10} \times 2$	$24 - \frac{40 - pCO2}{10} \times 5$