Gas Exchange

External Respiration

Respiration is the transport of oxygen to the cells within tissues and the transport of carbon dioxide in the opposite direction

External Respiration

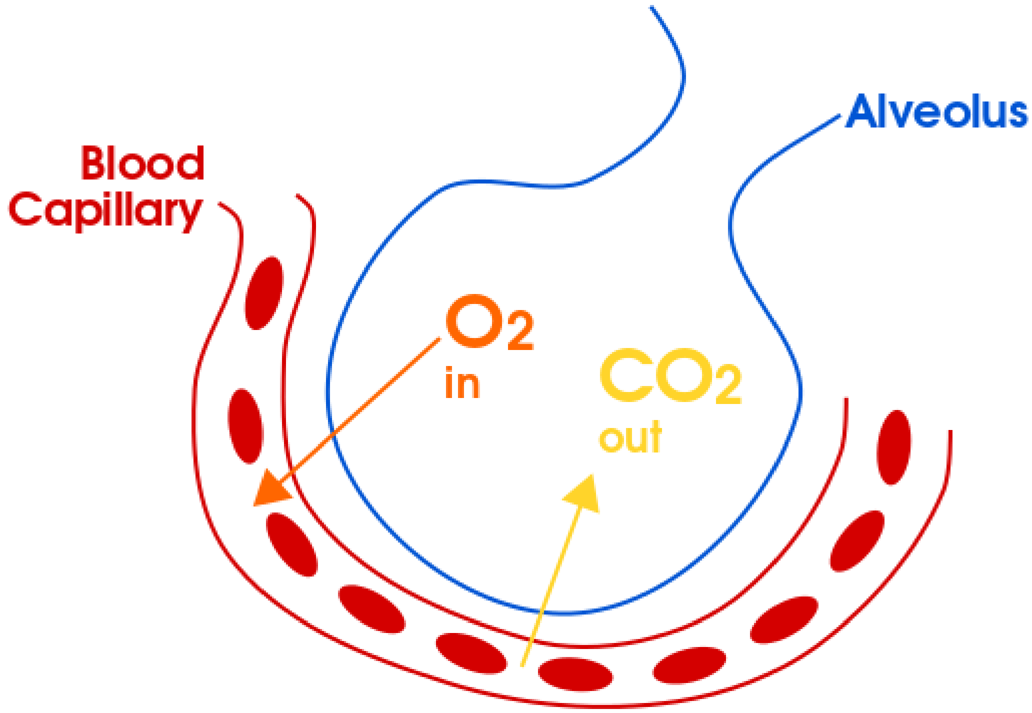
External respiration is the formal term for gas exchange. It describes both the bulk flow of air into and out of the lungs and the transfer of oxygen and carbon dioxide into the bloodstream through diffusion. While the bulk flow of air from the external environment happens due to pressure changes in the lungs, the mechanisms of alveolar gas exchange are more complicated. The primary three components of external respiration are the surface area of the alveolar membrane, the partial pressure gradients of the gasses, and the matching of perfusion and ventilation.

Surface Area

The alveoli have a very high surface area to volume ratio that allows for efficient gas exchange. The alveoli are covered with a high density of capillaries that provide many sites for gas exchange. The walls of the alveolar membrane are thin and covered with a fluid, extra-cellular matrix that provides a surface for gas molecules in the air of the lungs to diffuse into, from which they can then diffuse into the capillaries.

Partial Pressure Gradients

Partial pressure gradients (differences in partial pressure) allow the loading of oxygen into the bloodstream and the unloading of carbon dioxide out of the bloodstream. These two processes occur at the same time.



Gas exchange in the alveolus: External respiration is a result of partial pressure gradients, alveolar surface area, and ventilation and perfusion matching. This illustration shows gas exchange in the alveolus. The drawing shows the blood stream wrapped around alveolus, with oxygen being delivered by the blood to the alveolus and carbon dioxide from the alveolus as the blood flows through it. This is external respiration, a result of partial pressure gradients, alveolar surface area, and ventilation and perfusion matching.

Oxygen has a partial pressure gradient of about 60 mmHg (100 mmHg in alveolar air and 40 mmHg in deoxygenated blood) and diffuses rapidly from the alveolar air into the capillary.

Equilibrium between the alveolar air and capillaries is reached quickly, within the first third of the length of the capillary within a third of a second. The partial pressure of oxygen in the oxygenated blood of the capillary after oxygen loading is about 100 mmHg. The process is similar in carbon dioxide. The partial pressure gradient for carbon dioxide is much smaller compared to oxygen, being only 5 mmHg (45 mmHg in deoxygenated blood and 40 mmHg in alveolar air).

Based on Henry's law, the greater solubility of carbon dioxide in blood compared to oxygen means that diffusion will still occur very rapidly despite the lower partial pressure gradient. Equilibrium between the alveolar air and the capillaries for carbon dioxide is reached within the first half of the length of the capillaries within half a second. The partial pressure of carbon dioxide in the blood leaving the capillaries is 40 mmHg.

Ventilation and Perfusion Matching

The exchange of gas and blood supply to the lungs must be balanced in order to facilitate efficient external respiration. While a severe ventilation–perfusion mismatch indicates severe lung disease, minor imbalances can be corrected by maintaining air flow that is proportional to capillary blood flow, which maintains the balance of ventilation and perfusion.

Perfusion in the capillaries adjusts to changes in PAO2. Constriction in the airways (such as from the bronchospasms in an asthma attack) lead to decreased PAO2 because the flow of air into the lungs is slowed. In response, the arteries being supplied by the constricted airway undergo vasoconstriction, reducing the flow of blood into those alveoli so that the perfusion doesn't become much greater relative to the decreased ventilation (a type of ventilation–perfusion mismatch called a shunt). Alternatively, breathing in higher concentrations of oxygen from an oxygen tank will cause vasodilation and increased blood perfusion in the capillaries.

Ventilation adjusts from changes in PACO2. When airflow becomes higher relative to perfusion, PACO2 decreases, so the bronchioles will constrict in order to maintain to the balance between airflow (ventilation) and perfusion. When airflow is reduced, PACO2 increases, so the bronchioles will dilate in order to maintain the balance.

Internal Respiration

Cellular respiration is the metabolic process by which an organism obtains energy through the reaction of oxygen with glucose.

Internal respiration refers to two distinct processes. The first is the exchange of gasses between the bloodstream and the tissues. The second is the process of cellular respiration, from which cells utilize oxygen to perform basic metabolic functions.

Gas Exchange with Tissues

Gas exchange occurs in the alveoli so that oxygen is loaded into the bloodstream and carbon dioxide is unloaded from the bloodstream. Afterwards, oxygen is brought to the left side of the heart via the pulmonary vein, which pumps it into systemic circulation. Red blood cells carry the oxygen into the capillaries of the tissues of the body. Oxygen diffuses into the cells of the tissues, while carbon dioxide diffuses out of the cells of the tissues and into the bloodstream.

The factors that influence tissue gas exchange are similar to the factors of alveolar gas exchange, and include partial pressure gradients between the blood and the tissues, the blood perfusion of those tissues, and the surface areas of those tissues. Each of those factors generally an increase gas exchange as those factors are increased (i.e., more oxygen diffusion in tissues with more blood perfusion). Regarding the partial pressure gradients in systemic capillaries, they have a PaO2 of 100mmHg and a PaCO2 of 40mmHG within the capillary and a PaO2 of 40 mmHg and PaCO2 of 45 mmHg inside issue cells, which allows gas exchange to occur.

Cellular Respiration

Cellular respiration is the metabolic process by which an organism obtains energy through the reaction of oxygen with glucose to produce water, carbon dioxide and ATP, which is the functional source of energy for the cell. The oxygen supply for cellular respiration comes from the external respiration of the respiratory system.

Cellular respiration includes three major steps, and occurs mainly in the cytoplasm of the cell and within the mitochondria of the cell. The net formula for cellular respiration is:

Glycolysis: The breakdown of glucose into pyruvate, ATP, H2O, and heat.

Krebs Cycle: Produces NADH from pyruvate.

Oxidative Phosphorylation: Produces ATP from NADH, oxygen, and H+. The oxygen plays the role of electron receptor in an electron transport chain to produce ATP.

The net formula for cellular respiration is:

Glucose+6 Oxygen→6 Carbon Dioxide+6Water+38 ATP

The carbon dioxide waste is the result of the carbon from glucose ($C_6H_{12}O_6$) being broken down to produce the pyruvate and NADH intermediates needed to produce ATP at the end of respiration. The energy stored in ATP can then be used to drive processes that require energy, including biosynthesis, locomotion, or transportation of molecules across cell membranes. Cellular respiration can occur anaerobically without oxygen, such as through lactic acid fermentation. Human cells may use lactic acid fermentation in muscle tissue during strenuous exercise when there isn't enough oxygen to power the tissues. This process is very inefficient compared to aerobic respiration, as without oxidative phosphorylation, the cell cannot produce nearly as much ATP (2 ATP compared to 38 during cellular respiration).

Oxygen Transport

Hemoglobin is the primary transporter of oxygen with an oxygen binding capacity between 1.36 and 1.37 ml O_2 per gram Hgb.

Hemoglobin

About 98.5% of the oxygen in a sample of arterial blood in a healthy human breathing air at sea-level pressure is bound to the hemoglobin in blood (Hb). Hemoglobin is a protein found in red blood cells (also called erythrocytes).

There are roughly 270 million hemoglobin molecules in a single red blood cell, and each contains 4 hem groups. The function of Hb is to provide a binding site for oxygen to carry oxygen throughout the bloodstream to the systemic tissues for cellular respiration.

About 1.5% of oxygen is physically dissolved in the other blood liquids and not connected to Hgb. It has an oxygen binding capacity between 1.36 and 1.37 ml O_2 per gram Hb.

Factors affecting on the Hb saturation

Hb saturation is determined by

1-partial pressures of oxygen

-High partial pressure of O_2 – lungs – Hb is 98% saturated

- Low partial pressures of oxygen – tissues – Hb is only 75% saturated

2-Low pH (carbonic acid, lactic acid)

3-High temperature

4-High 2,3 diphosphoglycerate concentration (DPG)

5-High partial pressure of carbon dioxide

These conditions(2,3,4 and 5) decrease Hb's affinity for oxygen,

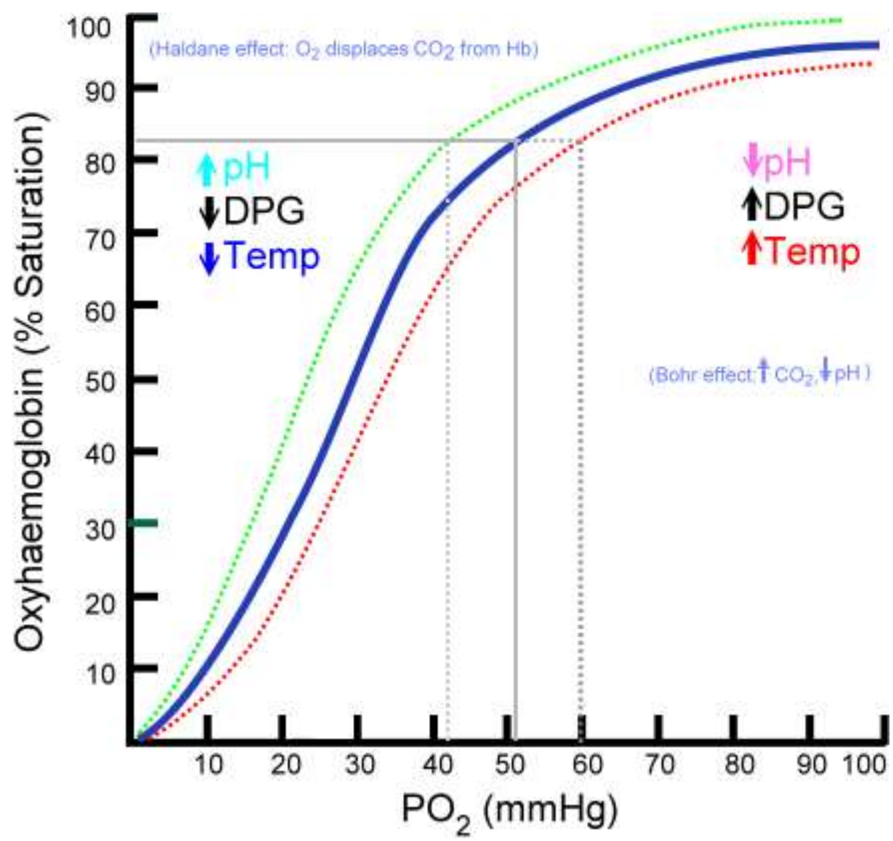
releasing more oxygen to active cells.

Oxyhemoglobin Dissociation Curve

The percentage of oxygen that is saturated in the hemoglobin of blood is generally represented by a curve that shows the relationship between PaO_2 and O_2 saturation. Saturation of O_2 in hemoglobin is an indicator for how much O_2 is able to reach the tissues of the body. Higher PaO_2 means higher saturation of oxygen in blood. Under normal conditions the PaO_2 in systemic blood is equal to 50%, about 26.6 mmHg,; this is called the $P50$.

The curve starts to plateau at PaO_2 higher than 60 mmHg, meaning that increases in PaO_2 after that point won't significantly increase saturation. This also means that the approximate carrying capacity for oxygen in hemoglobin has been reached and excess oxygen won't go into hemoglobin. The carrying capacity can be increased if more hemoglobin is added to the system, such as through greater red blood cell generation in high altitude, or from blood transfusions. The lower areas of the curve show saturation when oxygen is unloaded into the tissues. This is a graph of the oxyhaemoglobin dissociation curve. The oxygen–hemoglobin dissociation curve plots the percent hemoglobin saturation (y-axis) against the partial pressure of oxygen in the blood (x-axis). The graph shows three colored curves: the blue curve is the standard curve, while the red and green curves are right and leftward shifts respectively.

The oxyhaemoglobin dissociation curve: The oxygen–hemoglobin dissociation curve plots the percent hemoglobin saturation (y-axis) against the partial pressure of oxygen in the blood (PO2). The blue curve is standard curve, while the red and green curves are right and leftward shifts respectively. The oxyhemoglobin dissociation curve can shift in response to a variety of factors. A change in the P50 of the curve is a sign that the dissociation curve as a whole has shifted. Shifts indicate a change in affinity for oxygen's binding to hemoglobin, which changes the ability of oxygen to bind to hemoglobin and stay bound to it (i.e., not be released from it).



The oxyhaemoglobin dissociation curve: The oxygen–hemoglobin dissociation curve plots the percent hemoglobin saturation (y-axis) against the partial pressure of oxygen in the blood (PO2). The blue curve is standard curve, while the red and green curves are right and leftward shifts respectively

Rightward shifts indicate a decreased affinity for the binding of hemoglobin, so that less oxygen binds to hemoglobin, and more oxygen is unloaded from it into the tissues. The curve shifts right during decreased blood pH (called the Bohr effect), increased temperature, and during exercise among other things.

Anemia (a disorder marked by a decreased red blood cell count and less hemoglobin) also causes a rightward shift, but also changes the shape of the curve so that it moves downward as well as a result of the reduced levels of hemoglobin.

Leftward shifts indicate an increased affinity for the binding of hemoglobin, so that more oxygen binds to hemoglobin, but less oxygen is unloaded from it into the tissues. Causes of leftward shifts include increased blood pH, decreased temperature, and carbon monoxide exposure. Carbon monoxide binds to hemoglobin in place of oxygen, so that less oxygen reaches the tissues; this can be fatal if severe enough.

Carbon Dioxide Transport

CO2 is carried in blood in three different ways: dissolved in plasma, bound to hemoglobin, or as a bicarbonate ion.

Carbon Dioxide Transport

Carbon dioxide is the product of cellular respiration, and is transported from the cells of tissues in the body to the alveoli of the lungs through the bloodstream. Carbon dioxide is carried in the blood through three different ways.

Dissolved in the Plasma

About 5% of carbon dioxide is transported in the plasma of the blood as dissolved CO2 molecules that aren't bound to anything else. Carbon dioxide has a much higher solubility than oxygen, which explains why a relatively greater amount of carbon dioxide is dissolved in the plasma compared to oxygen.

Bound to Hemoglobin

This is a color picture of the structure of hemoglobin. It depicts hemoglobin as a tetramer of alpha (red) and beta (blue) subunits with iron-containing hem groups (green). Structure of human hemoglobin: Hemoglobin is a tetramer of alpha (red) and beta (blue) subunits with iron containing hem groups (green). While oxygen binds to the iron content in the hem of hemoglobin, carbon dioxide can bind to the amino acid chains on hemoglobin. When carbon dioxide clings to hemoglobin it forms carbanimohemoglobin.

About 10% of carbon dioxide in the human body is transported this way. Carbanimohemoglobin gives red blood cells a bluish color, which is one of the reasons why the veins that carry deoxygenated blood appear to be blue. A property of hemoglobin called the Haldane effect states that deoxygenated blood has an increased capacity to carry carbon dioxide, while oxygenated blood has a decreased capacity to carry carbon dioxide. This property means that hemoglobin will primarily carry oxygen in systemic circulation until it unloads that oxygen and is able to carry a relatively higher amount of carbon dioxide. This is due to deoxygenated blood's increased capacity to carry carbon dioxide, and from the carbon dioxide loaded from the tissues during tissue gas exchange.

Bicarbonate Ions

The majority (85%) of carbon dioxide travels in the blood stream as bicarbonate ions. The reaction that describes the formation of bicarbonate ions in the blood is:

$CO2 + H2O \rightarrow H2CO3 \rightarrow H+ + HCO3–$

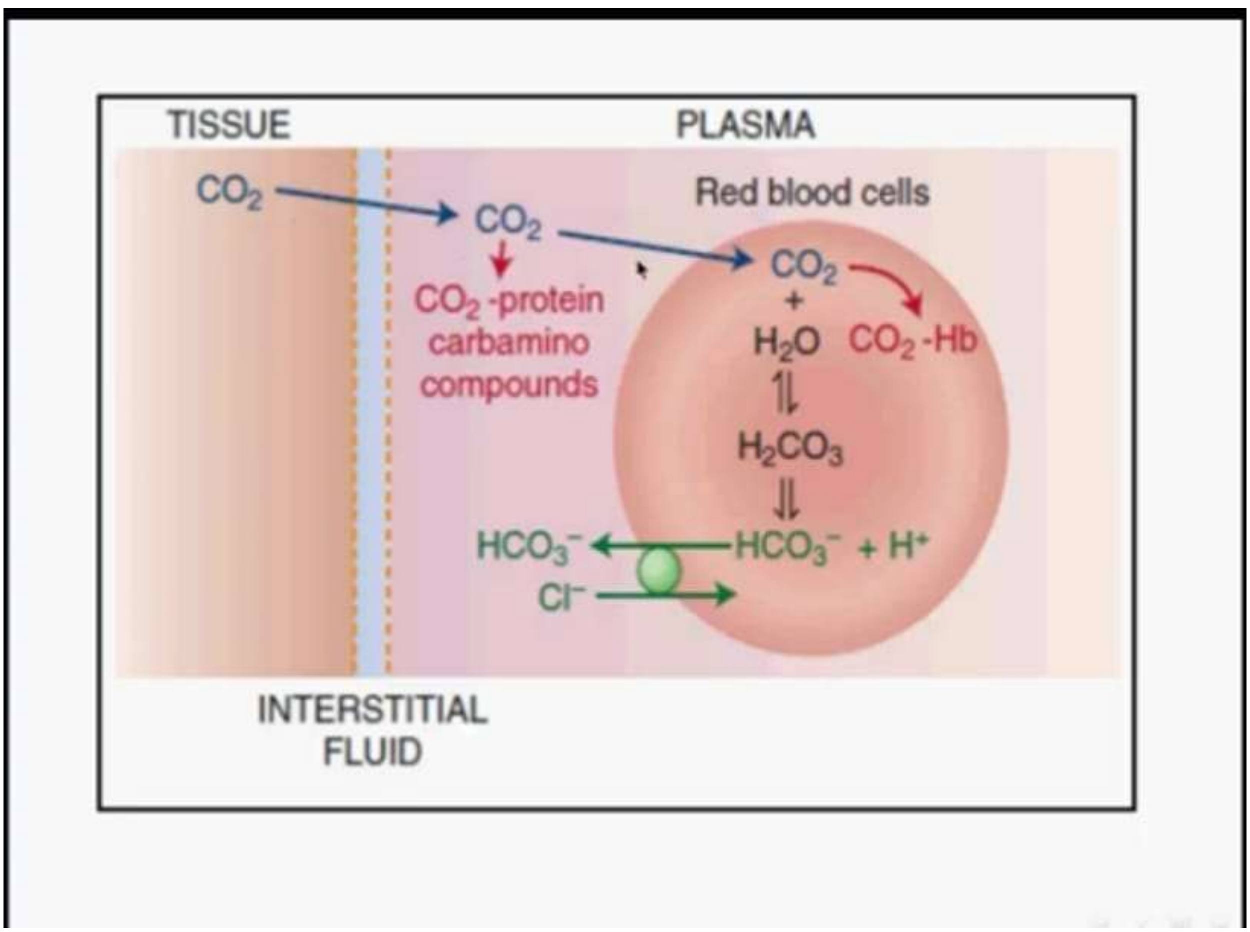
This means that carbon dioxide reacts with water to form carbonic acid, which dissociates in solution to form hydrogen ions and bicarbonate ions. The main implication of this process is that the pH of blood becomes a way of determining the amount of carbon dioxide in blood. This is because if carbon dioxide increases in the body, it will manifest as increased concentrations of bicarbonate and increased concentrations of hydrogen ions that reduce blood pH and make the blood more acidic.

Conversely, if carbon dioxide levels are reduced, there will be less bicarbonate and less hydrogen ion dissolved in the blood, so pH will increase and blood will become more basic. Bicarbonate ions act as a buffer for the pH of blood so that blood pH will be neutral as long as bicarbonate and hydrogen ions are balanced.

This connection explains how ventilation rate and blood chemistry are related, as hyperventilation will cause alkalosis, and hypoventilation will cause acidosis, due to the changes in carbon dioxide levels that they cause. Bicarbonate is also carried in the fluids of tissues besides the blood vessels, especially in the duodenum and intestine, so problems in those organs can cause a respiratory system response.

Transport to the Alveoli

After carbon dioxide travels through the bloodstream to the capillaries covering the alveoli of the lungs through any of the 3 methods listed above, it must return to dissolved carbon dioxide form in order to diffuse across the capillary into the alveolus. Dissolved carbon dioxide is already able to diffuse into the alveolus, while hemoglobin-bound carbon dioxide is unloaded into the plasma. For carbon dioxide stored in bicarbonate, it undergoes a reaction reversal. Bicarbonate ions dissolved in the plasma enter the red blood cells by diffusing across a chloride ion gradient (replacing chloride inside the cell), and combining with hydrogen to form carbonic acid. Next, the action of carbonic anhydrase breaks carbonic acid down into carbon dioxide in water, which leaves the cell by diffusion. The dissolved carbon dioxide is then able to diffuse into the alveolus.



Chloride (Cl^-) ion shift