

The Respiratory System

The respiratory system is responsible for maintaining the balance between bringing oxygen and eliminating CO₂ (Gas exchange).

The respiratory process

1. External respiration (external environment – blood)

This process occurs at the level of the lungs.

O₂ moves from the alveolar air into the blood, while CO₂ moves from the blood into the alveoli to be eliminated.

2. Internal respiration (blood – tissues)

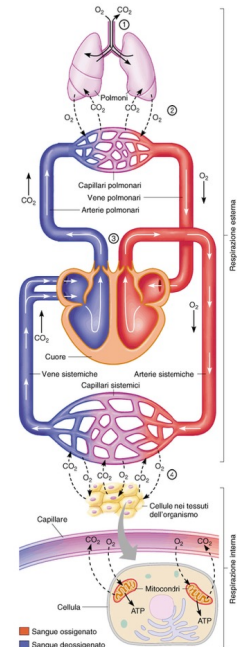
This process occurs at the tissue level.

O₂ moves from the blood to the cells, while CO₂ produced by cellular metabolism enters the blood.

3. Cellular respiration

It occurs inside the mitochondria

represents the metabolic process by which cells use O₂ to produce ATP.



Respiration is not simply the act of inhaling and exhaling.

In reality, it includes a series of integrated events.

We can distinguish:

1. External respiration

This process occurs at the level of the lungs.

Here, oxygen moves from the alveolar air into the blood, while carbon dioxide moves from the blood into the alveoli to be eliminated.

Therefore, external respiration refers to the exchange between the external environment and the blood.

2. Internal respiration

This process occurs at the tissue level.

In this case, oxygen moves from the blood to the cells, while CO₂ produced by cellular metabolism enters the blood.

So here, the exchange occurs between blood and tissues.

3. Cellular respiration

This is a different concept altogether.

It occurs inside the mitochondria and represents the metabolic process by which cells use oxygen to produce ATP.

In other words:

the respiratory system brings oxygen in;

the cardiovascular system distributes it;

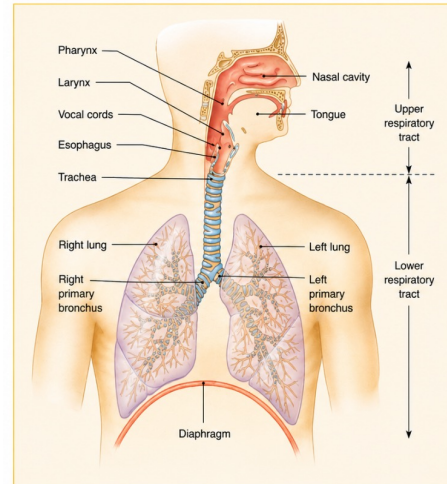
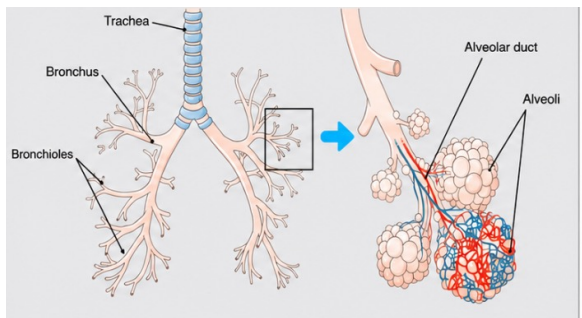
the cells use it to generate energy.

These three levels are strictly interconnected.

If one of these processes is impaired, the entire homeostasis of the organism is affected.

The respiratory system form a functional point of view

- **conducting airways**
- **respiratory portion**



From a functional point of view, the respiratory system can be divided into:
conducting airways
respiratory portion

The conducting airways include:
nasal cavities;
pharynx;
larynx;
trachea;
bronchi;
bronchioles.

These structures are not primarily responsible for gas exchange.
Their functions are:
conducting air
filtering it
humidifying it
warming it

The true functional region for gas exchange is represented by the terminal respiratory region, namely:
respiratory bronchioles
alveolar ducts
alveoli

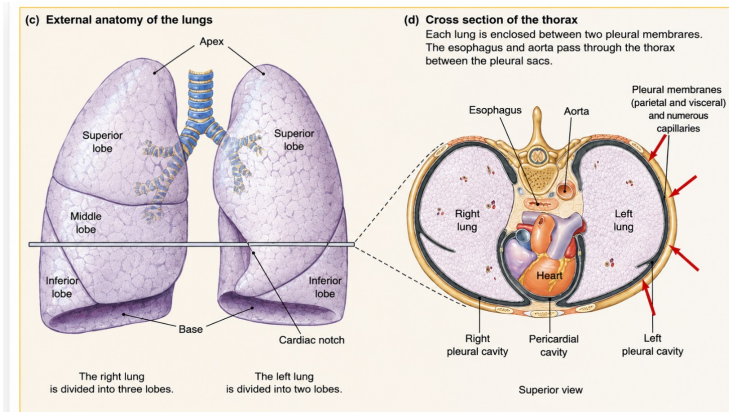
This is where oxygen and carbon dioxide transfer occurs.

This distinction is extremely important in physiology because each segment has specific structural and functional characteristics.

Recalling the respiratory system anatomy

Bronchial tree :
Tree-like
organization

In the terminal
region:
alveoli



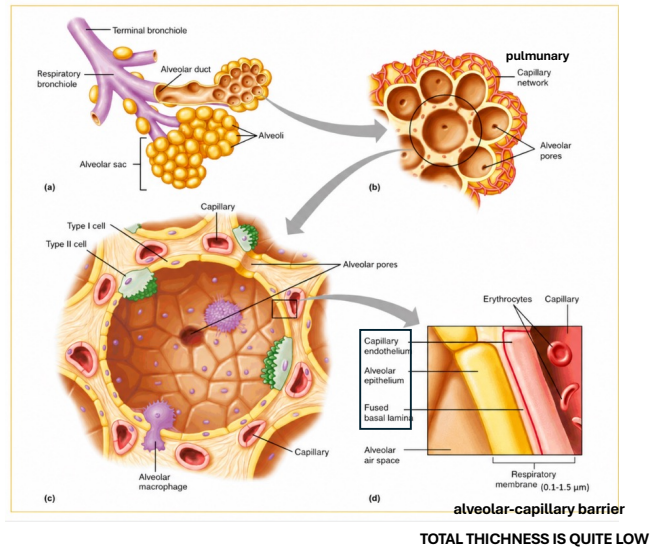
Air enters through the nasal cavities or the mouth, passes through the pharynx and then the larynx. From there it reaches the trachea, which bifurcates into the right and left primary bronchi.

The bronchi progressively branch into smaller structures:
secondary bronchi;
tertiary bronchi;
bronchioles;
terminal bronchioles.

This tree-like organization is called the bronchial tree.
As we move toward the periphery:
the diameter of the airways decreases;
the overall surface area greatly increases;
cartilage progressively disappears;
smooth muscle becomes more important.

In the terminal region of the bronchioles the lungs organize alveoli, which represent the fundamental functional unit for gas exchange.

Alveoli and Alveolar ducts



The most important region is the alveolar region.

Alveoli are small sac-like structures with extremely thin walls. They are specifically designed to maximize gas exchange. Alveoli are not isolated, they are organized into clusters and communicate with structures called alveolar ducts.

Alveolar ducts have a dual function:
they conduct air toward the alveoli
they distribute airflow among the different respiratory units

Structurally, the alveolar wall is extremely thin in order to minimize diffusion distance.

Remember:
the thinner the barrier;
the more efficient gas exchange will be.

The alveolar wall is in extremely close contact with the pulmonary capillary network. This creates the so-called respiratory membrane or alveolar-capillary barrier.

The alveolar-capillary membrane represents the crucial site for gas exchange. It is composed of:
alveolar epithelium;
fused basement membranes;
capillary endothelium.

Its total thickness is extremely small, on the order of only a few micrometers. This allows very rapid gas diffusion.

Oxygen diffuses:
from the alveolus;
into the blood.

Carbon dioxide diffuses instead:

from the blood;

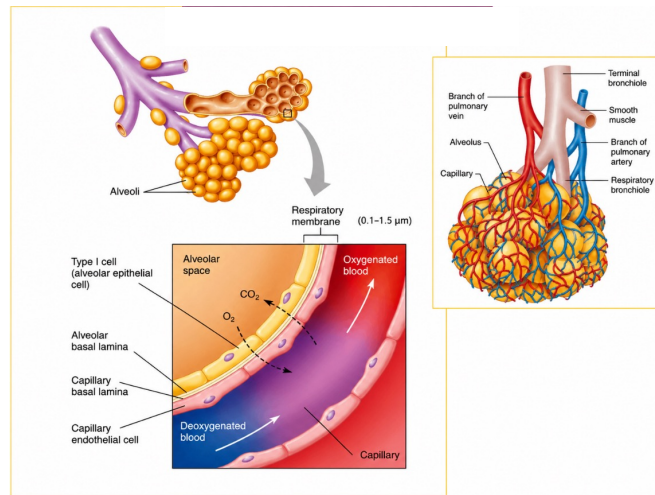
into the alveolus.

All of this occurs through simple passive diffusion, following partial pressure gradients.

There are no pumps for oxygen.

Gas movement depends exclusively on pressure differences.

Alveolar surface area available for gas exchange



One of the most extraordinary aspects of the lungs is the enormous surface area available for gas exchange. Our respiratory system contains approximately 300 million alveoli. Overall, the total exchange surface is extremely large: approximately 70–100 square meters. This means that the respiratory surface is comparable to the size of an apartment.

Why is such a large surface necessary?

Because gas exchange must be extremely rapid and efficient.

According to Fick's law:

diffusion rate increases as the available surface area increases;

diffusion increases when the barrier is thinner;

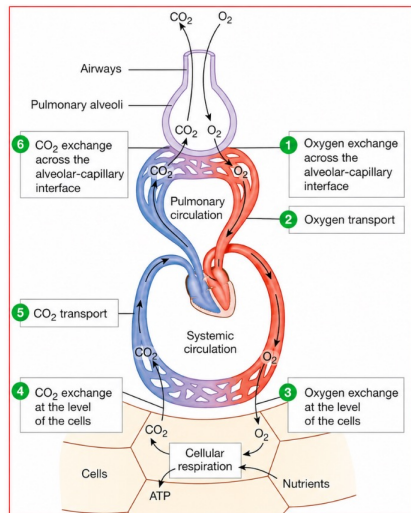
diffusion increases when the concentration gradient is greater.

Therefore, the lungs are structurally optimized to maximize all of these parameters.

Diseases that destroy alveolar surface area, such as emphysema, severely impair gas exchange because they reduce the available exchange surface.

Gas Exchange and Fick's Law

How quickly O₂ diffuses from the alveoli into the pulmonary capillaries



$$V = \frac{A \times \Delta C \times D_s}{\Delta x}$$

Labels for the equation:

- V : Volume of gas diffusing
- A : Surface area available for exchange
- ΔC : Difference in the gas partial pressure between the alveolus and the blood
- D_s : Gas diffusion coefficient
- Δx : Thickness of the alveolar-capillary membrane

Indeed, according to Fick's law we have that:
 diffusion rate increases as the available surface area increases;
 diffusion increases when the barrier is thinner;
 diffusion increases when the pressure gradient is greater.

Application of the Fick's law to the respiratory system

The entire process is based on simple diffusion.
 This means that gases move spontaneously from an area where their concentration — or partial pressure — is higher toward an area where it is lower.

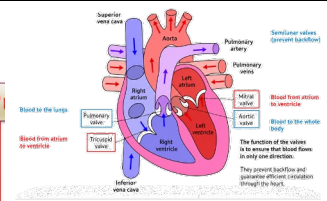
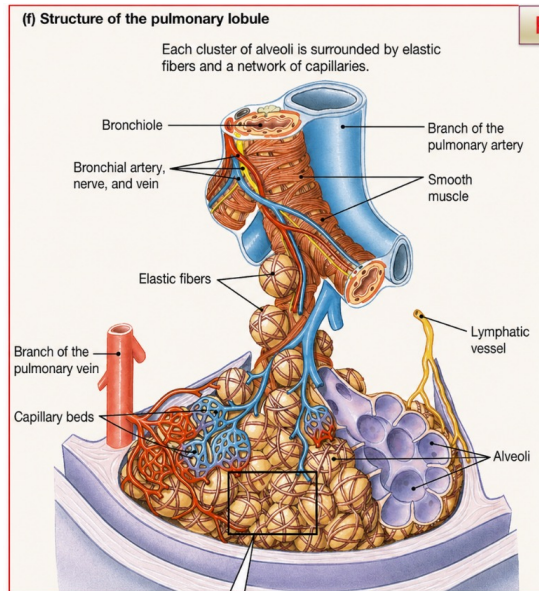
In the lungs:
 oxygen moves from the alveoli into the blood
 carbon dioxide moves from the blood into the alveoli.

At the tissues, the opposite happens:
 oxygen leaves the blood and enters the cells;
 carbon dioxide produced by metabolism enters the bloodstream.

This process follows Fick's law.
 Fick's law tells us that diffusion becomes more efficient when:
 the surface area is large
 the membrane is thin
 and the pressure gradient is high.

And the lungs are perfectly designed for this:
 millions of alveoli create a huge exchange surface;
 and the respiratory membrane is extremely thin.

Pulmonary circulation



Pulmonary circulation is a low-pressure, low-resistance circuit.

Venous blood coming from the right ventricle reaches the lungs through the pulmonary arteries.

This blood is poor in oxygen and rich in carbon dioxide.

At the level of the alveolar capillaries, gas exchange occurs:

the blood becomes oxygenated;
carbon dioxide is eliminated.

The oxygenated blood then returns to the left side of the heart through the pulmonary veins.

It is important to emphasize that in pulmonary circulation:

arteries carry oxygen-poor blood;
veins carry oxygen-rich blood.

Therefore, the distinction between artery and vein depends on the direction of blood flow relative to the heart, not on oxygen content.

The extremely close relationship between alveoli and capillaries is essential. Ventilation and perfusion must be properly matched.

If an alveolus is ventilated but not perfused, or perfused but not ventilated, gas exchange becomes inefficient.

Fundamental physical laws to understand gas exchange

1. Dalton's law

Dalton's law states that, in a mixture of gases, each gas exerts its own partial pressure independently of the others.

Gas	P_{gas} dry air (atm)	P_{gas} humid air 100%
Nitrogen (N ₂)	593 mm Hg	575 mm Hg
Oxygen (O ₂)	160 mm Hg	154 mm Hg
Carbon dioxide (CO ₂)	0.25 mm Hg	0.24 mm Hg
Water vapor	0 mm Hg	23.8 mm Hg

The total atmospheric pressure is equal to the sum of the partial pressures of the individual gases.

Why is this concept so important ?

Because gases diffuse according to partial pressure gradients.

To understand gas exchange, we must introduce some fundamental physical laws.

The first is **Dalton's law**.

Dalton's law states that, in a mixture of gases, each gas exerts its own partial pressure independently of the others.

Atmospheric air is a mixture composed mainly of:

nitrogen;

oxygen;

small amounts of carbon dioxide and other gases.

The total atmospheric pressure is equal to the sum of the partial pressures of the individual gases.

For example:

oxygen represents about 21% of atmospheric air;

therefore its partial pressure will be approximately 21% of the total atmospheric pressure.

Why is this concept so important?

Because gases diffuse according to partial pressure gradients.

Oxygen moves:

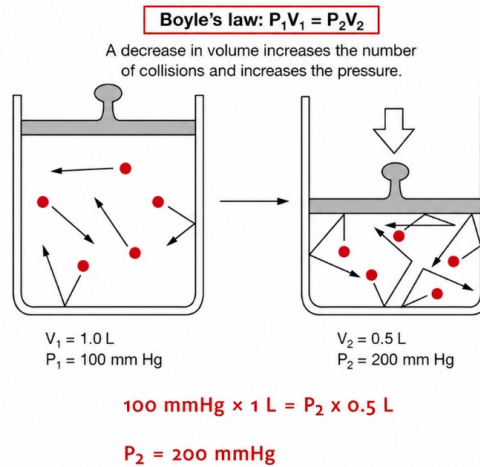
from regions where its partial pressure is higher;

toward regions where its partial pressure is lower.

This is the physical basis of respiratory gas exchange.

2. Boyle's law

Describes the relationship between pressure and volume.
At constant temperature: **pressure** and **volume** are inversely proportional.



The second fundamental law is **Boyle's law**.

Boyle's law describes the relationship between pressure and volume.

At constant temperature:

pressure and volume are inversely proportional.

This means:

if volume increases, pressure decreases;

if volume decreases, pressure increases.

This law is fundamental for understanding pulmonary ventilation.

When the thoracic cavity expands:

lung volume increases;

intrapulmonary pressure decreases;

air flows into the lungs.

When thoracic volume decreases instead:

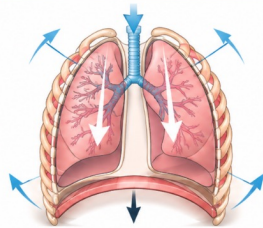
intrapulmonary pressure increases;

air flows out.

Therefore, breathing occurs through pressure changes generated by volume changes.

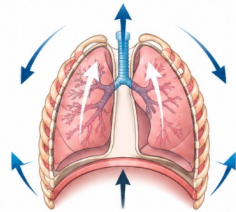
The Boyle's law is fundamental for understanding pulmonary ventilation

When the thoracic cavity expands:



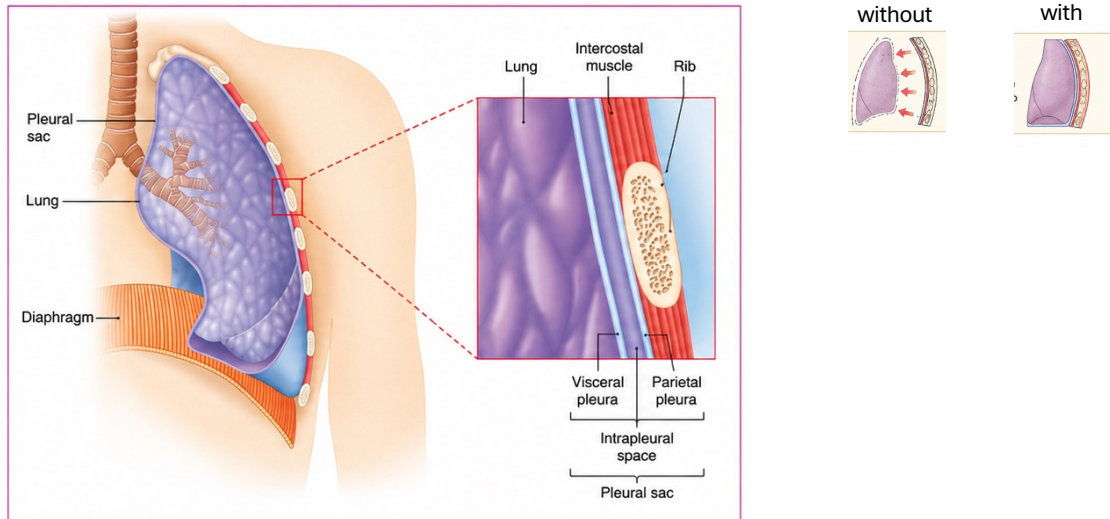
- Lung volume ↑
- Intrapulmonary pressure ↓
- Air flows **INTO** the lungs

When the thoracic cavity decreases instead:



- Lung volume ↓
- Intrapulmonary pressure ↑
- Air flows **OUT** of the lungs

The Pleura



The lungs are covered by the pleura, a thin membrane that protects them and helps them during breathing.

The pleura is made up of two layers:

Visceral pleura: directly adheres to the lungs.

Parietal pleura: lines the inside of the chest wall.

Between the two layers there is a very small space called the **pleural cavity**, which contains a fluid that reduces friction when we breathe.

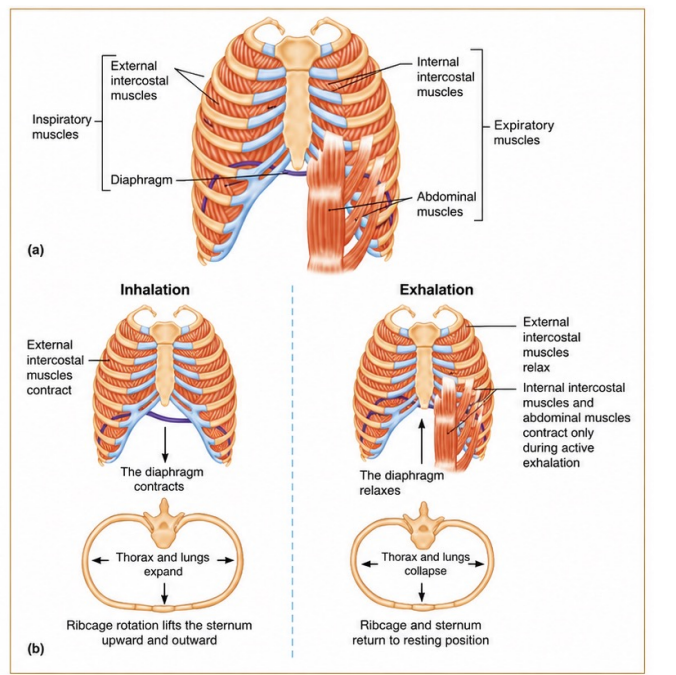
The respiration cycle

Muscles involved

Inspiration

Expiration

2 group of muscles for those



The respiratory cycle includes two phases:
inspiration;
expiration.

Inspiration

Inspiration is an active process.

During inspiration, the following muscles contract:

the diaphragm;
the external intercostal muscles.

The diaphragm moves downward, increasing the vertical diameter of the thoracic cavity.

The external intercostals elevate the ribs, increasing:

the anteroposterior diameter;
the lateral diameter.

The increase in thoracic volume causes:

an increase in lung volume;
a decrease in alveolar pressure.

Because alveolar pressure becomes lower than atmospheric pressure, air enters the lungs.

Expiration

Quiet expiration is predominantly passive.

It occurs thanks to the elastic recoil of the lungs and thoracic cage.

When the inspiratory muscles relax:

thoracic volume decreases;
alveolar pressure increases;
air is expelled.

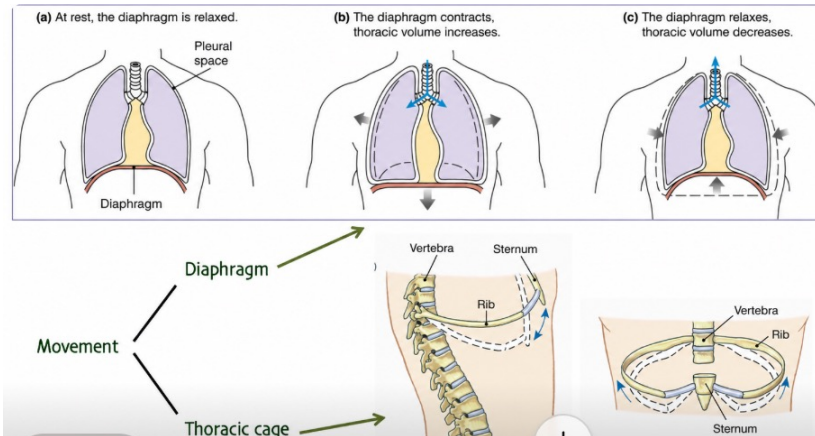
During forced expiration, additional muscles are involved:

abdominal muscles;
internal intercostal muscles.

These muscles further increase intrathoracic pressure, facilitating air expulsion.

The respiration cycle

The mechanics



In normal breathing, expiration is mostly passive, due to the elastic recoil of the lungs and the relaxation of the diaphragm. During forced breathing, other muscles are also involved.

In quiet breathing, the main muscle that drives both inspiration and, indirectly, expiration is the diaphragm.

Inspiration: the diaphragm contracts and moves downward → the volume of the thoracic cavity increases → air enters the lungs.

Expiration: the diaphragm relaxes and moves upward → the thoracic volume decreases → air leaves the lungs.

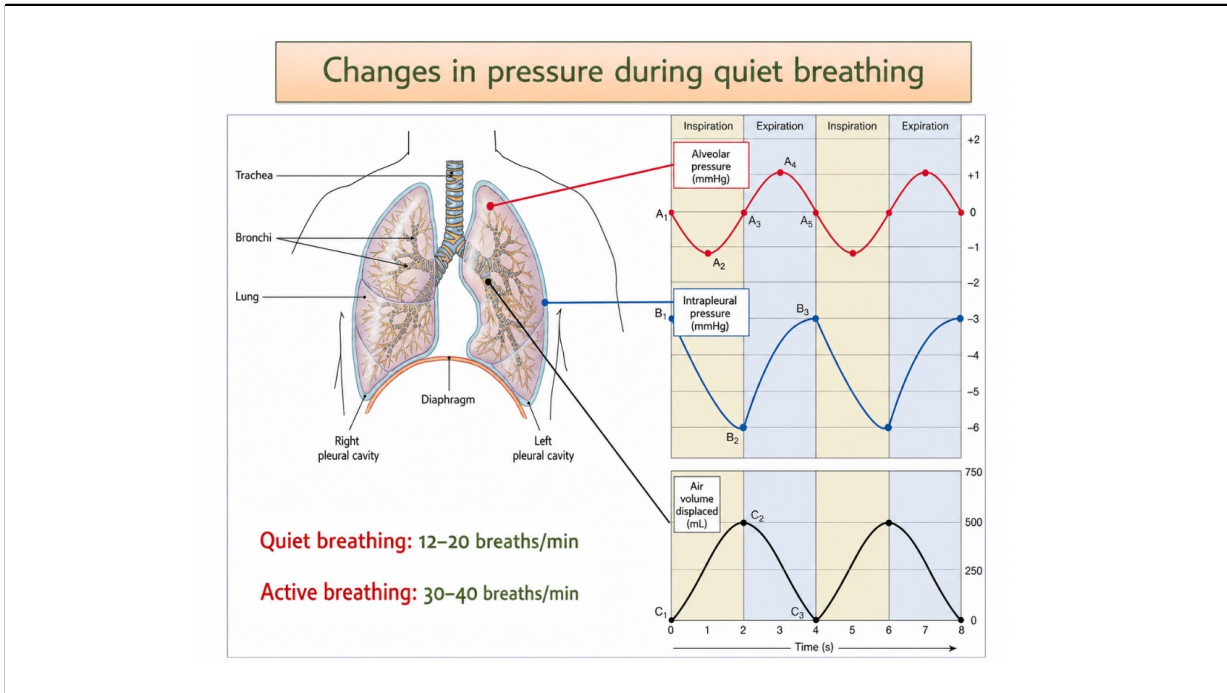
In normal breathing, expiration is mostly passive, due to the elastic recoil of the lungs and the relaxation of the diaphragm.

During forced breathing, other muscles are also involved:

forced inspiration: external intercostals, sternocleidomastoid, and scalene muscles;

forced expiration: abdominal muscles and internal intercostals.

So, the diaphragm is the main muscle of respiration, especially for inspiration.



This slide summarizes the pressure changes that occur during a normal respiratory cycle. Several pressures are involved in pulmonary ventilation.

Atmospheric pressure

Atmospheric pressure represents the pressure of the external environment. Under normal conditions at sea level, it is considered constant.

Intrapulmonary pressure

Also called alveolar pressure, this is the pressure inside the alveoli. Small fluctuations in intrapulmonary pressure are sufficient to generate airflow.

During inspiration:

alveolar pressure becomes slightly negative relative to atmospheric pressure; air enters.

During expiration:

alveolar pressure becomes slightly positive; air exits.

Intrapleural pressure

The intrapleural pressure is the pressure inside the pleural cavity. Under physiological conditions, it is always negative.

Why intrapleural pressure is negative?

The **lungs** are elastic, they naturally tend to recoil slightly inward.



The **thoracic cage** tends to expand outward.

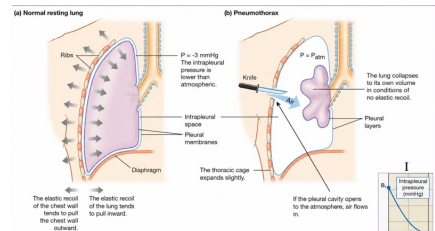
as a result

Generation of "**vacuum**" in the pleural space

- keeps the lungs attached to the thoracic wall



Air can enter the pleuric space



Why is it negative? Because:

The lungs are elastic, so they naturally tend to recoil slightly inward.

The thoracic cage, on the other hand, tends to expand outward.

These two opposite forces create a kind of "vacuum" in the pleural space.

This vacuum keeps the lungs attached to the thoracic wall.

So, when the chest moves, the lungs move together with it.

If this vacuum disappears, as in pneumothorax, the lung separates from the thoracic wall and collapses."

The lungs are elastic, so they naturally tend to recoil slightly inward. The rib cage, on the other hand, tends to expand outward. These two opposing forces create a sort of "vacuum" within the pleural space. This vacuum keeps the lungs attached to the chest wall. As a result, when the thorax moves, the lungs move with it. If this vacuum disappears, as in pneumothorax, the lung detaches from the chest wall and collapses.

How to evaluate the respiratory function? The spirometry

For Air in – Air out detection

Tidal volume

A small volume of air moved during a quiet breathing

Inspiratory reserve volume

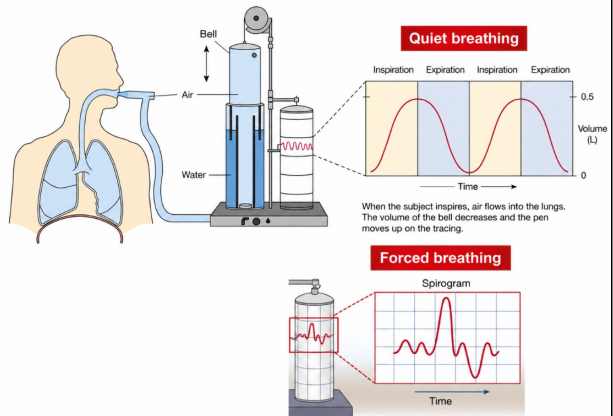
additional amount of air that can be inhaled after a normal inspiration.

Expiratory reserve volume

This is the additional amount of air that can be exhaled after a normal expiration.

Residual volume

Even after maximal expiration, some air always remains inside the lungs – it prevents alveolar collapse.



To evaluate respiratory function, we can measure pulmonary volumes using spirometry. Spirometry is one of the most important functional tests in respiratory physiology. It measures the amount of air moving into and out of the lungs. During quiet breathing, we move a relatively small volume of air called tidal volume. However, the lungs contain several additional volumes.

Inspiratory reserve volume

This is the additional amount of air that can be inhaled after a normal inspiration.

Expiratory reserve volume

This is the additional amount of air that can be exhaled after a normal expiration.

Residual volume

Even after maximal expiration, some air always remains inside the lungs. This residual volume prevents alveolar collapse.

Spirometry allows us to assess lung function and identify obstructive or restrictive respiratory disorders.

For example:

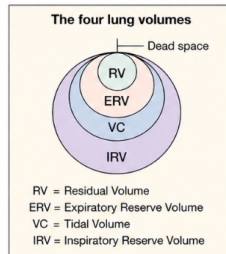
obstructive diseases mainly impair airflow;

restrictive diseases reduce lung expansion

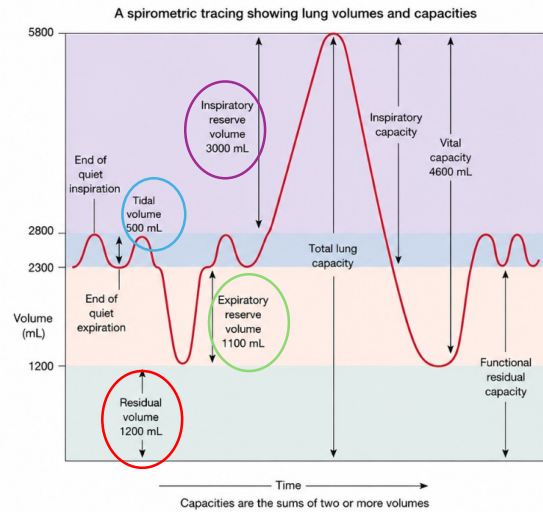
The instrument records:

- the volume of air that comes out
- the time needed to expel it

It generates a graph volume x time



Lung volumes		Males	Females	
Vital capacity	IRV	3000 mL	1900 mL	Inspiratory capacity
	VC	500 mL	500 mL	
	ERV	1100 mL	700 mL	
Residual volume (RV)		1200 mL	1100 mL	Functional residual capacity
Total lung capacity		5800 mL	4200 mL	



Pulmonary capacities are combinations of different pulmonary volumes.

Understanding these capacities helps us evaluate how efficiently the respiratory system works.

Inspiratory capacity

This is the maximum amount of air that can be inspired after a normal expiration.

It is equal to:

tidal volume;

plus inspiratory reserve volume.

Functional residual capacity

This is the amount of air remaining in the lungs after a normal expiration.

This volume is physiologically very important because it prevents large fluctuations in alveolar gas composition.

Vital capacity

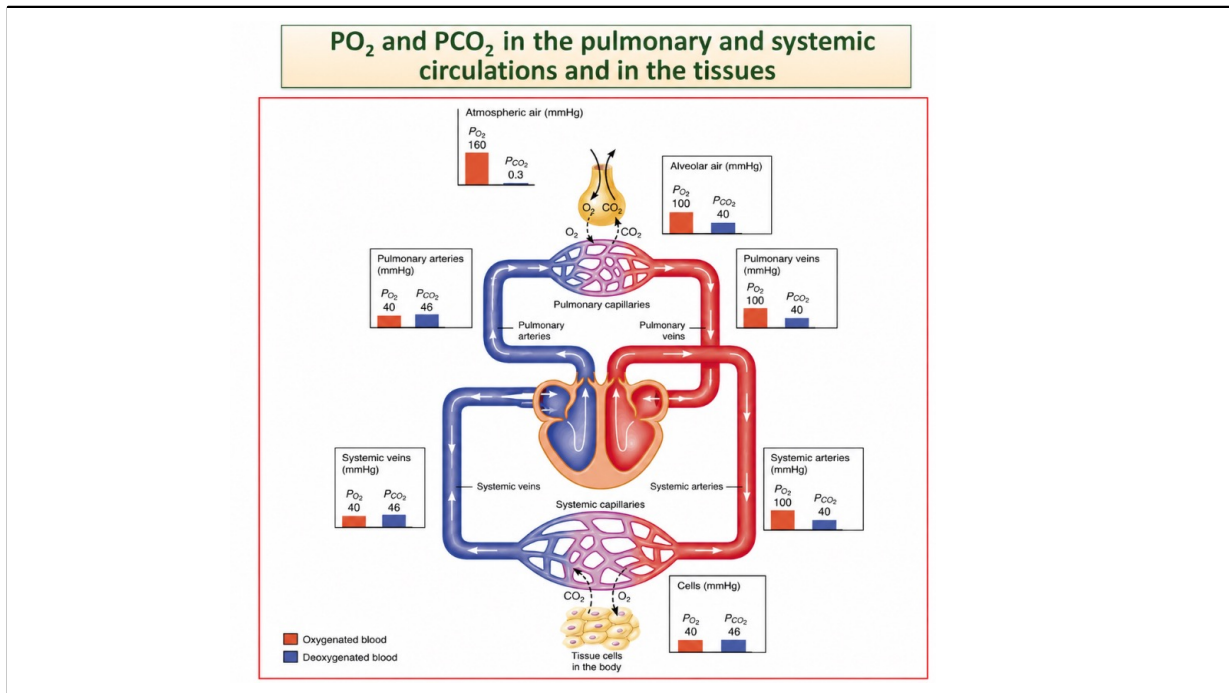
Vital capacity represents the maximum amount of air that can be exhaled after a maximal inspiration.

It reflects the functional capacity of the respiratory system.

Total lung capacity

This is the total amount of air the lungs can contain after maximal inspiration.

These parameters are fundamental in clinical physiology because many respiratory diseases alter pulmonary volumes and capacities in characteristic ways.



This slide shows how oxygen and carbon dioxide pressures change throughout the body.

In the alveoli:

oxygen pressure is high
carbon dioxide pressure is low.

In venous blood arriving from tissues:

oxygen is low because cells consumed it
carbon dioxide is high because cells continuously produce it.
So oxygen diffuses into the blood, while carbon dioxide diffuses into the alveoli.

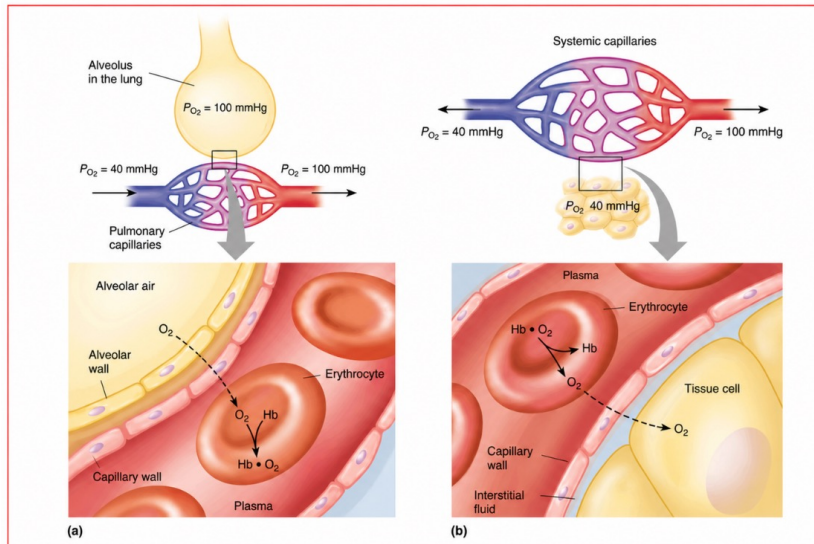
At the tissues, the situation reverses:

oxygen leaves the blood;
carbon dioxide enters it.

So respiration is really driven by continuous pressure gradients between:

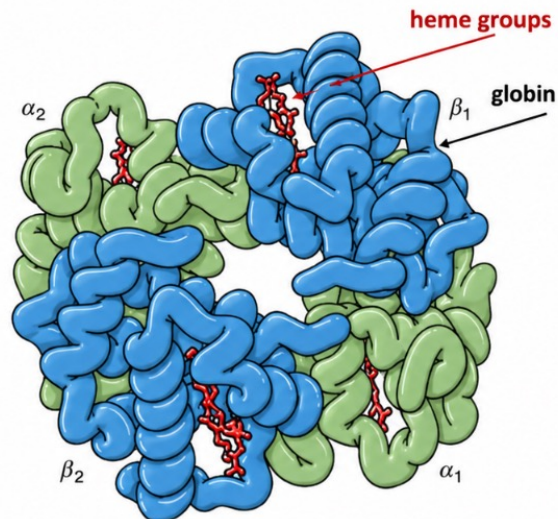
alveoli and blood;
blood and tissues.

Oxygen exchange at the alveolar and cellular level



Additional image of the gas exchange at alveolar and cellular level

O₂ is transported bound to hemoglobin inside red blood cells



Most oxygen in blood is not dissolved freely in plasma.

Almost all oxygen is transported bound to hemoglobin inside red blood cells.

Hemoglobin is made of four subunits:

two alpha chains;

and two beta chains.

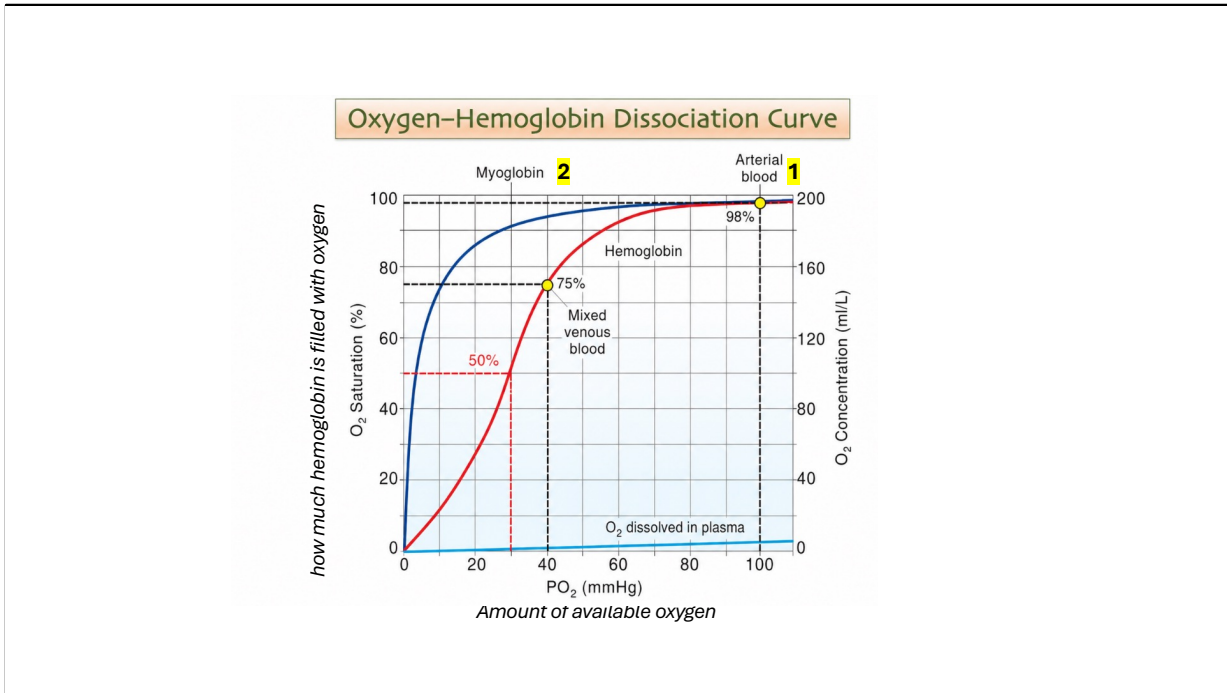
Each subunit contains a heme group with an iron atom.

This iron is in the ferrous form, Fe²⁺, and can reversibly bind oxygen.

Since each hemoglobin has four heme groups, one molecule can carry up to four oxygen molecules.

The key point is that this binding is reversible.

Hemoglobin must bind oxygen efficiently in the lungs and release it efficiently in the tissues.



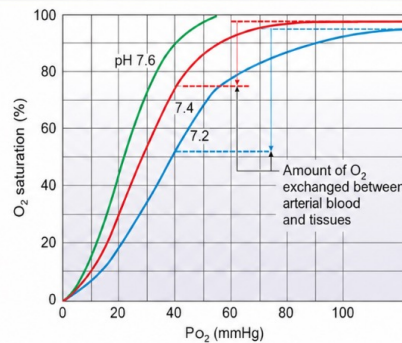
This graph shows the relationship between oxygen pressure and hemoglobin saturation. Notice the sigmoid shape of the curve. This shape is due to cooperative binding. When one oxygen molecule binds hemoglobin, the affinity for the next oxygen molecule increases.

In the lungs:
 PO₂ is high;
 hemoglobin becomes almost fully saturated.

In the tissues:
 PO₂ is lower;
 hemoglobin releases oxygen.

Why is the curve S-shaped?
 When hemoglobin binds one oxygen molecule, it becomes easier to bind the next ones.
 Called as cooperative behavior.

Physical factors that modify the binding of O₂ to hemoglobin: CO₂ and pH



Decreases in pH (and therefore increases in H⁺) or increases in PCO₂ reduce the affinity for O₂. Increase in CO₂

- **Bohr effect:** In the *lungs*, CO₂ moves from the blood into the alveoli; this favors the binding of O₂ to Hb; in the *tissues*, blood takes up CO₂, and Hb more easily releases O₂ (affinity decreases).
- **Bohr effect (Bohr shift)** allows a greater exchange of O₂ between arterial blood and tissues, and between venous blood and alveoli.

Hemoglobin affinity for oxygen is not constant.

It changes depending on the environment.

An increase in:

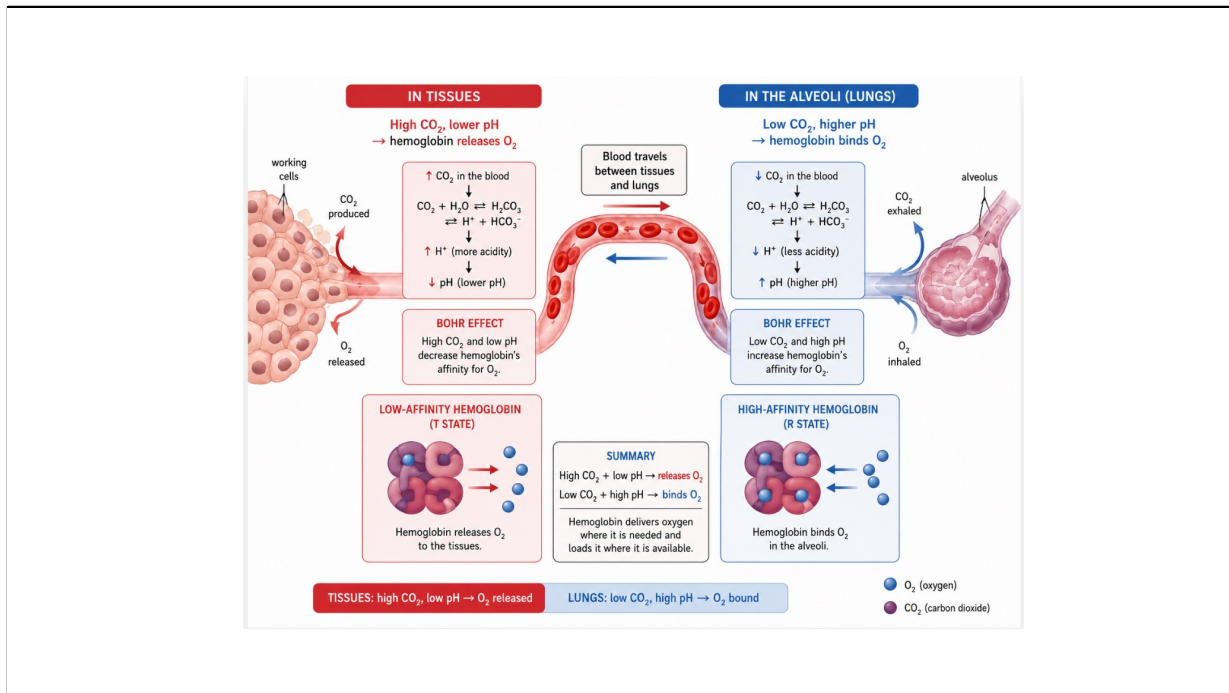
carbon dioxide; or hydrogen ions, meaning lower pH, reduces hemoglobin affinity for oxygen.

This shifts the curve to the right. And this is actually useful.

Why?

Because metabolically active tissues produce more CO₂, more H⁺ and become more acidic.

Under these conditions, hemoglobin releases oxygen more easily exactly where tissues need it.



This slide illustrates the Bohr effect, the mechanism that regulates the binding between hemoglobin and oxygen according to CO₂ levels and pH.

At the tissue level, cells produce large amounts of CO₂. CO₂ diffuses into the blood and red blood cells, where it encounters water and, thanks to the enzyme carbonic anhydrase, is converted into carbonic acid. Carbonic acid then dissociates into H⁺ ions and bicarbonate. The increase in H⁺ ions makes the blood more acidic and lowers the pH. Under these conditions, hemoglobin decreases its affinity for oxygen and therefore releases O₂ to the tissues. This corresponds to the T state, the low-affinity form of hemoglobin. In this way, oxygen is mainly delivered to the most metabolically active tissues, where CO₂ production is greatest.

In the pulmonary alveoli, the opposite process occurs. CO₂ is eliminated during exhalation, H⁺ ion concentration decreases, and pH rises. As a result, hemoglobin increases its affinity for oxygen and binds O₂ in the alveoli. This corresponds to the R state, the high-affinity form of hemoglobin.

In summary:

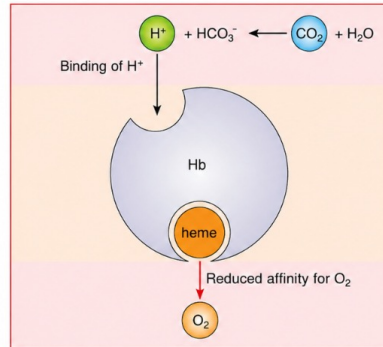
high CO₂ and low pH promote oxygen release in the tissues;

low CO₂ and high pH promote oxygen binding in the lungs.

In this way, hemoglobin delivers oxygen where it is needed and reloads it in the lungs.

Molecular model of the Bohr effect

Binding with H^+ decreases the affinity of the heme group for O_2 , so it is released more easily



- When blood reaches the tissues, a fraction of oxyhemoglobin (HbO_2) releases O_2 and becomes deoxyhemoglobin. This form has a higher affinity for protons (H^+), which helps to buffer their concentration, limiting the drop in pH.
- When venous blood returns from the tissues to the lungs, deoxyhemoglobin is converted into oxyhemoglobin, which has a lower affinity for H^+ . These are released, react with bicarbonate, and form CO_2 , which is then exhaled.

Carbon Dioxide Transport and the Haldane Effect

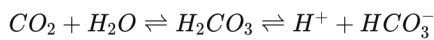
1. Tissue cells continuously produce CO₂

Cellular respiration produces carbon dioxide as a waste product.

CO₂ moves:

- from the cells
- into the blood
- especially into red blood cells.

2. In the blood CO₂ reacts with water



This forms:

•carbonic acid (*by anhydrase enzyme of red blood cells*)

•which then dissociates into:

- H⁺
- bicarbonate (HCO₃⁻)

Bicarbonate is the main form in which CO₂ is transported in the blood.

3. Problem: H⁺ ions acidify the blood

If too many H⁺ ions remain free:

- the pH decreases
- the blood becomes too acidic.

4. Here deoxyhemoglobin comes into play

Deoxyhemoglobin is hemoglobin that has already released oxygen to the tissues.

When it loses O₂:

- it changes its conformation slightly
- and binds H⁺ more easily.

So it **acts like a "sponge" for H⁺ ions.**

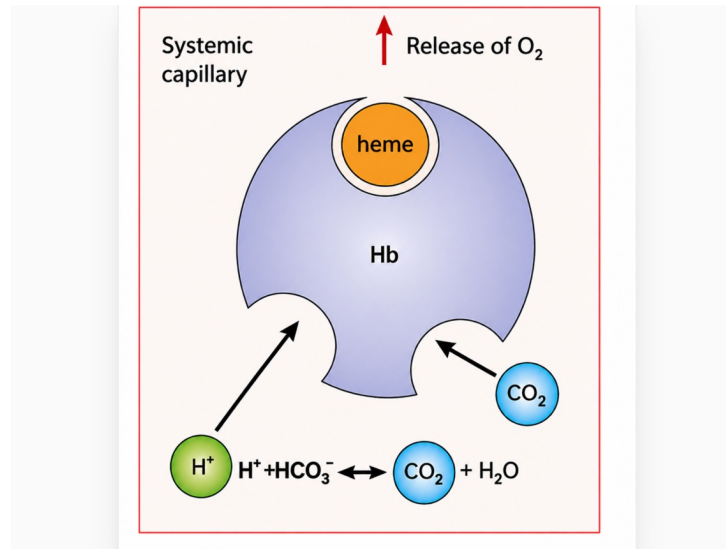
5. By binding H⁺, the reaction continues

If deoxyhemoglobin removes H⁺ ions:

- the concentration of free H⁺ decreases
- the chemical equilibrium shifts to the right
- therefore more CO₂ is converted into:
 - H⁺
 - bicarbonate.

This follows the Le Chatelier's principle.

The Haldane effect describes how oxygenation influences CO₂ transport.
Deoxygenated hemoglobin binds carbon dioxide more easily.



Carbon dioxide is transported in blood in three forms:

dissolved in plasma, bound to proteins and hemoglobin and mainly as bicarbonate ions.

Most CO₂ is converted into bicarbonate inside red blood cells. The Haldane effect describes how oxygenation influences CO₂ transport.

Deoxygenated hemoglobin binds carbon dioxide more easily.

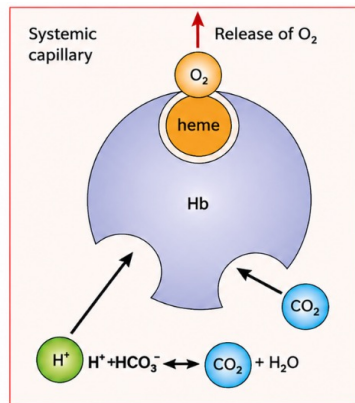
So at the tissues:

hemoglobin releases oxygen and binds more CO₂.

In the lungs:

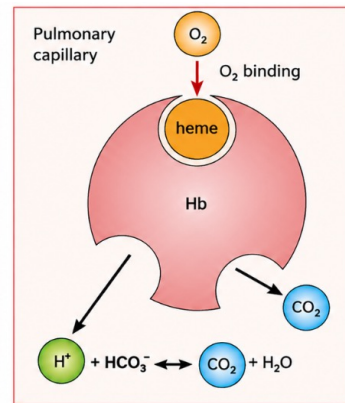
oxygen binds hemoglobin and CO₂ is released.

Relationship Between Bohr and Haldane Effects



Tissues

Low PO_2 promotes CO_2 binding to Hb;
the Bohr effect promotes O_2 release



Lungs

High PO_2 promotes CO_2 release from Hb;
the reverse Bohr effect promotes O_2 binding

This slide connects the Bohr and Haldane effects together.

At the tissues:

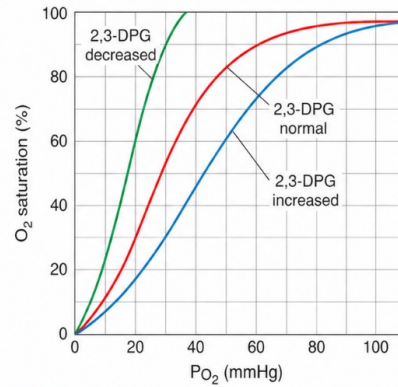
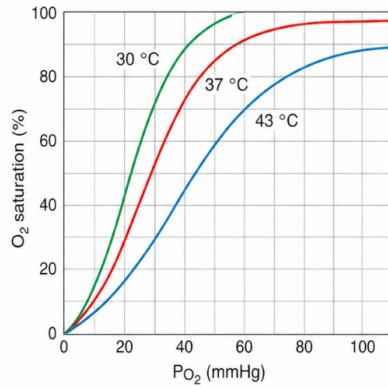
low oxygen promotes oxygen release and favors carbon dioxide binding.

At the lungs:

high oxygen promotes oxygen binding and facilitates carbon dioxide release.

So these two mechanisms work together to maximize oxygen delivery and carbon dioxide elimination.

Physical factors that modify the binding of O₂ to hemoglobin: temperature and 2,3-diphosphoglycerate



Chemical factors

- ✓ 2,3-diphosphoglycerate (DPG), an intermediate product of anaerobic glycolysis: [DPG] increases in hypoxic conditions (low oxygen, emphysema, anemia) and with an increase in pH
- ✓ ATP
- ✓ GTP

Other factors also influence hemoglobin affinity for oxygen.

Two important ones are:

Temperature

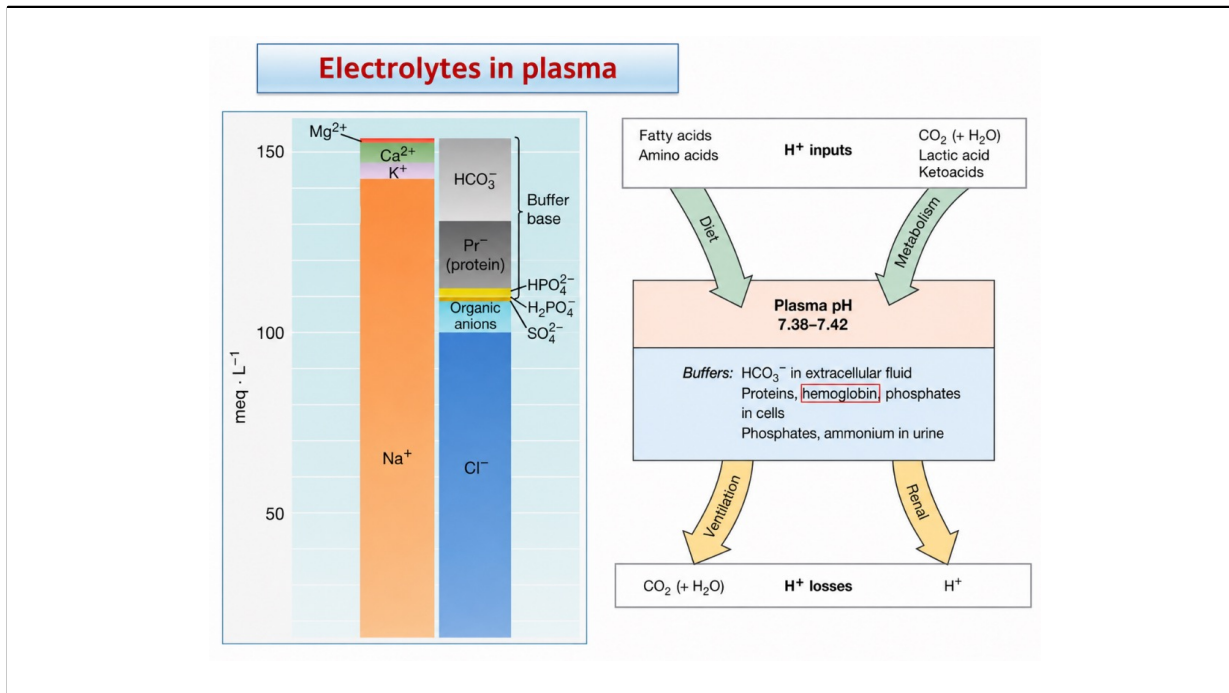
An increase in temperature shifts the dissociation curve to the right.

This means oxygen is released more easily.

Again, this is useful because active tissues produce heat.

2,3-BPG, ATP and GTP

These molecules act as allosteric regulators of Hemoglobin: they bind to hemoglobin at sites different from the oxygen-binding site and modify its conformation.



Blood chemistry is tightly regulated. The plasma contains several important electrolytes (see the graph for reference). Among them, bicarbonate is particularly important for acid–base balance. The bicarbonate buffering system helps stabilize blood pH.

When hydrogen ion concentration increases bicarbonate can buffer excess acidity. This is essential because cellular function is extremely sensitive to pH changes.

Maintaining blood pH within a narrow range is absolutely critical for life. Normal blood pH is around 7.4. Even small deviations can alter enzyme activity, membrane function and protein structure.

Severe acidosis or alkalosis can become life-threatening.

Respiration and Acid–Base Balance

- The concentration of HCO_3^- in plasma is on average 24 mEq/L, about 600,000 times greater than that of H^+ . The HCO_3^- ions present in plasma buffer the H^+ ions coming from non-respiratory sources



- According to the law of mass action, any change in CO_2 , H^+ , and HCO_3^- will shift the reaction until a new equilibrium is reached
- The HCO_3^- ion acts as a buffer only when it binds to H^+ . Therefore, an increase in PCO_2 leads to an increase in H^+ ions (acidosis)

Hypoventilation (+ CO_2) → acidosis

Hyperventilation (- CO_2) → alkalosis

Respiration and acid–base balance are strictly interconnected.

Carbon dioxide reacts with water to form carbonic acid. This reaction generates hydrogen ions.

So:

increased CO_2 leads to increased acidity;

decreased CO_2 reduces acidity.

This explains why:

hypoventilation causes respiratory acidosis

hyperventilation causes respiratory alkalosis

The lungs therefore help regulate pH simply by controlling how much CO_2 is eliminated.

Neural Control of Breathing

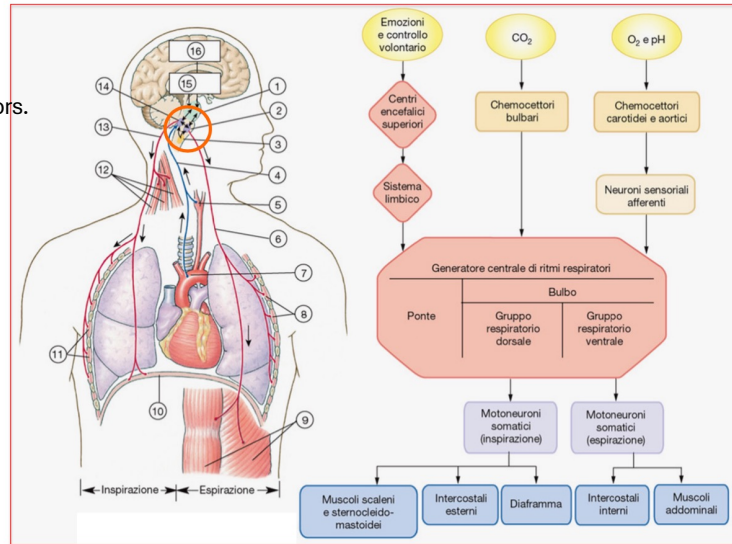
Breathing is regulated by integrating:

- voluntary control from the cortex;
- automatic control from the brainstem;
- sensory information from chemoreceptors.

Chemoreceptors detect:

carbon dioxide;
oxygen;
and pH levels.

If CO_2 increases:
respiratory centers stimulate ventilation;
breathing becomes faster and deeper.



Breathing is regulated by integrating voluntary control from the cortex, automatic control from the brainstem and sensory information from chemoreceptors.

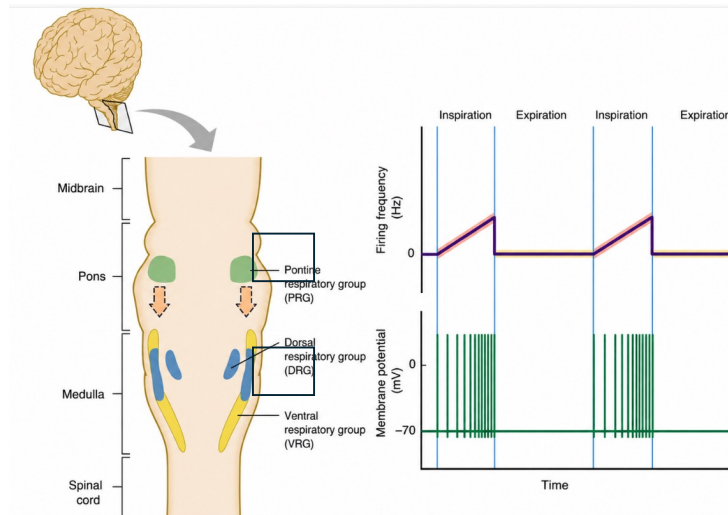
Chemoreceptors detect:

carbon dioxide
oxygen
and pH levels.

Among these, CO_2 is the most important regulator under normal conditions. If CO_2 increases the respiratory centers stimulate ventilation so that breathing becomes faster and deeper. This allows the body to eliminate excess CO_2 and restore homeostasis.

Neural Control of Breathing

Inspiratory neurons



This slide explains how the brain automatically controls respiration.

The control of breathing takes place in the brainstem, especially in the pons and the medulla. Here we find groups of neurons called respiratory centers, which automatically generate the respiratory rhythm without requiring conscious effort.

In the medulla, we find the dorsal respiratory group, or DRG, which is the main inspiratory center. These neurons send signals to the diaphragm and inspiratory muscles, initiating inspiration.

Also in the medulla, there is the ventral respiratory group, or VRG, which becomes active mainly during forced breathing, for example during physical exercise, coughing, or major respiratory effort.

In the pons, we find the pontine respiratory group, or PRG, whose role is to modulate and smooth the respiratory rhythm. Looking at the graphs on the right, we can observe the activity of inspiratory neurons over time.

The upper graph represents the frequency of action potentials. During inspiration, the neurons progressively increase their activity: this means they send more and more nerve impulses to the diaphragm, which therefore contracts more strongly.

At the end of inspiration, neuronal activity abruptly stops. At this point, the diaphragm relaxes and expiration begins.

In the lower graph, we instead see the individual action potentials of the neuron. During inspiration, the neurons fire many closely spaced impulses, whereas during expiration they remain almost silent.

Therefore, the main message of this slide is that breathing is automatically controlled by neuronal circuits in the brainstem: when inspiratory neurons become active, we inhale; when they stop firing, we exhale.