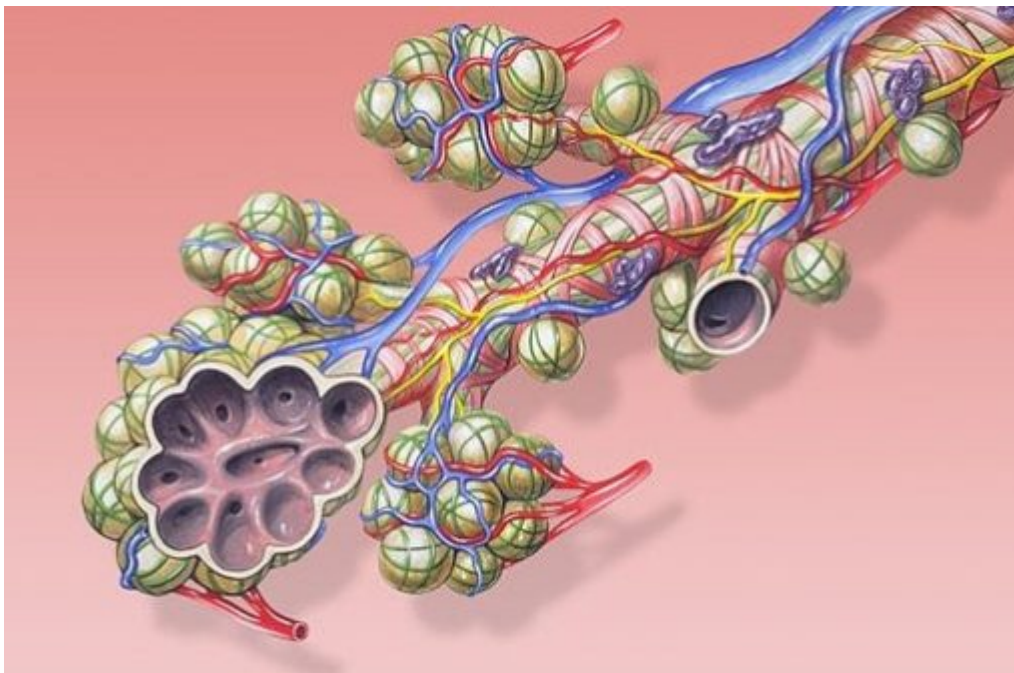


Respiratory Physiology: Airways, Lung Volume, Pulmonary Gas Exchange and more

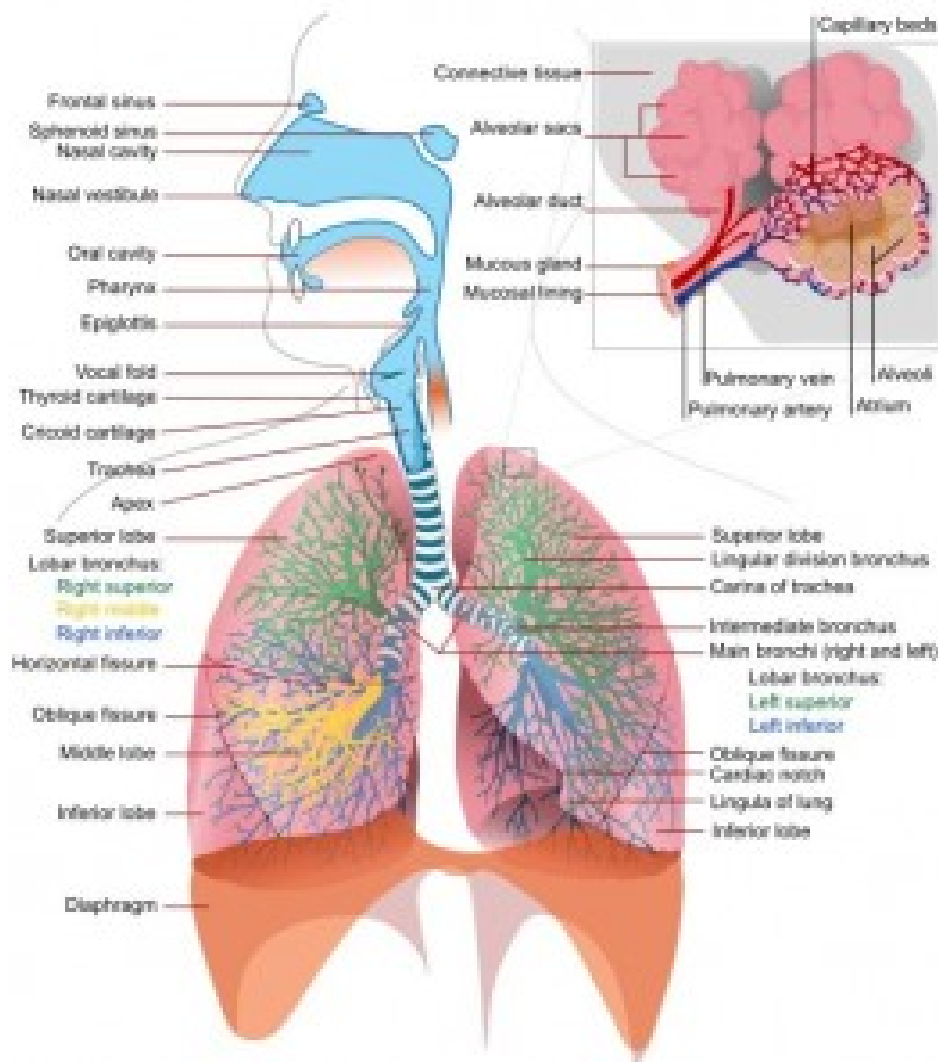
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Breathing is one of the vital functions and is essential to human life. In an emergency, airway management is a top priority. In this article, one can learn how breathing works, what we need it for, and how the body controls it.



Airways

Air flows into our lungs by inhalation. But until it reaches there, it travels through various passageways. Depending on whether we breathe through the nose or mouth, the air enters through the naso- or the oropharynx. Next, it passes through the laryngopharynx and reaches the **trachea**. The trachea is divided into 2 main bronchi, one leading to the right lung and the other to the left. The main bronchi branch out further into the lobar and segmental bronchi and finally become bronchioles. These are divided into **respiratory bronchioli**, where air sacs or **alveoli** are found. Gas exchange takes place here.



[Image:](#) "the respiratory system consists of the airways, the lungs, and the respiratory muscles that mediate the movement of air into and out of the body" by LadyofHats. License: Public Domain

Dead space

There are 16 divisions up to the respiratory bronchioli that result in an area of 0.15 L, which is ventilated but not used for gas exchange. It is called the **anatomic dead space**. With an average breath of 0.5 L and a normal respiratory rate of 15 breaths per minute, the dead space ventilation is 2.25 L/min, which amounts to one-third of the total respiratory minute volume of 7.5 L/min.

The purpose of the dead space is to warm up and moisturize the breathing air. Furthermore, the dead space is equipped with **ciliated epithelium**, which is supposed to keep foreign bodies away from the gas exchange surfaces.

The **functional or physiological dead space** includes the anatomic dead space, as well as the alveoli that are ventilated but not perfused (and thus, not contributing to the gas exchange). However, in a healthy person, these are so few that the functional dead space is more or less equivalent to the anatomic dead space.

Alveolar space

The alveolar space has a volume of about 4 L. Here, the gas exchange by diffusion takes

place. **Fick's law of diffusion** states that the number of diffused particles per unit of time depends on the area available for diffusion. The area of the alveolar space that can be used for diffusion amounts, with its many ramifications, to approx. 80 m² and is sufficient to meet our need for oxygen even during physical labor.

The alveoli are all connected via the **alveolar ducts**. When considering 2 alveoli of different sizes that are connected, the pressure in the alveoli can be described with **Laplace's law**:

$P = 2 \times T/r$ where T = wall tension, and r = radius.

The wall thickness can be neglected in this case, since it is the same with all the alveoli. Also, the surface tension ensures that the wall tension of all alveoli is equal, which brings us to the conclusion that the pressure in the smaller alveolus is greater than the one in the larger alveolus. Consequently, the gas from the smaller alveolus will be emptied into the larger alveolus to compensate for pressure. The smaller alveolus collapses. If this happens in the entire lung, it is called **atelectasis**.

Atelectasis usually occurs in premature babies. They do not yet produce the **surface-active agent (surfactant)** or **anti-atelectasis factor**. Pulmonary surfactant is formed starting in pregnancy week 24 by the type II pneumocytes of the respiratory epithelium. It consists of 90% phospholipids and 10% surfactant proteins.

The surfactant molecules reduce the wall tension T in the alveoli. The smaller the radius of the alveolus, the narrower the surfactant molecules are placed together, reducing the wall tension even more. This way, the pressure is compensated, and the smaller alveoli do not collapse.

Surfactant does not only prevent atelectasis, but it also has immunoregulatory functions. Furthermore, the surfactant prevents excessive water inflow from the capillaries into the alveoli.

Lung Volume and Lung Capacities

Depending on the depth of breathing and the anatomical conditions, different lung volumes can be defined. Lung capacities describe an additive combination of individual volumes. The volumes and capacities are shown in the image below.

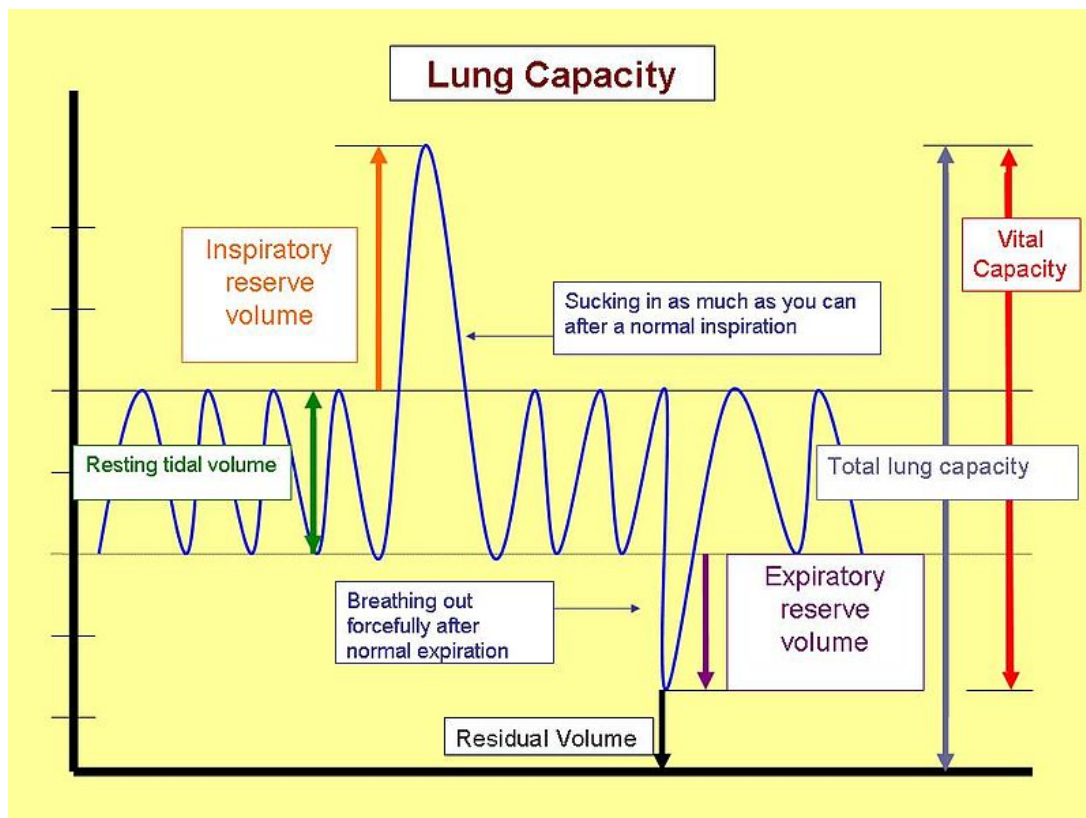


Image: "Lung Capacity" by Stephanie Greenwood. License: [Gemeinfrei](#)

This process starts in the respiratory rest position with normal inspiration. After one and a half cycles, the minimum is reached by maximal exhalation of the patient. Now, the lungs only contain the residual volume (RV), which is divided into collapse volume and minimum volume. Next, a maximal inhale follows and again a maximal exhalation. Then the patient returns to quiet respiration.

The metrological examination of the **lung parameters** has to separate static variables from dynamic variables, which are time-dependent. Using spirometry, which allows for a time-dependent determination of changes in volume, it is possible to determine these parameters.

The **FEV₁/FVC ratio**, which allows determining the **relative forced expiratory volume in 1 s (rFEV₁)**, is an important tool in the differential diagnosis of pulmonary diseases.

The rFEV₁ is calculated as follows:

rFEV₁ = forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC)

The forced expiratory volume in 1 s describes the volume that a patient can exhale after maximum inhalation in 1 s at the maximum possible effort (i.e. forced expiration). It is important to note that this test is highly dependent on the motivation and cooperation of the patient.

Respiratory Mechanics

There has to be a certain pressure difference for the air and respiratory gases to have a directed flow. This pressure difference is achieved during inhalation by increasing the lung volumes using the respiratory muscles. In chest breathing, this is done by the **external intercostal muscles**.

In abdominal breathing, this task is fulfilled by the **diaphragm**. The accessory respiratory

muscles facilitate inspiration. These are the **scalene muscles**, the **sternocleidomastoid muscle**, and the **pectoralis major muscle** when the shoulder girdle is fixed. When we support our arms on our knees after jogging, we instinctively support our breathing.

Exhalation occurs mainly passively. Due to the tension of elastic elements and the surface tension of the alveoli, the lung seeks to contract. Because of the adhesion forces between **lamina visceralis** and **pleura parietalis**, the lungs do not collapse *in situ* but follow the movements of the chest wall. With the relaxation of the previously contracted muscles, the air flows out of the lungs.

The thorax, in turn, seeks to expand, which counteracts the tendency of the lungs to retract. The **resting position** is achieved when the resulting force (F_{result}) of these 2 opposing forces on the overall lung-thorax system is 0, which means that the volume of the lung is equivalent to the functional residual capacity (FRC). FRC is equal to the sum of expiratory reserve volume (ERV) and RV.

Respiratory cycle

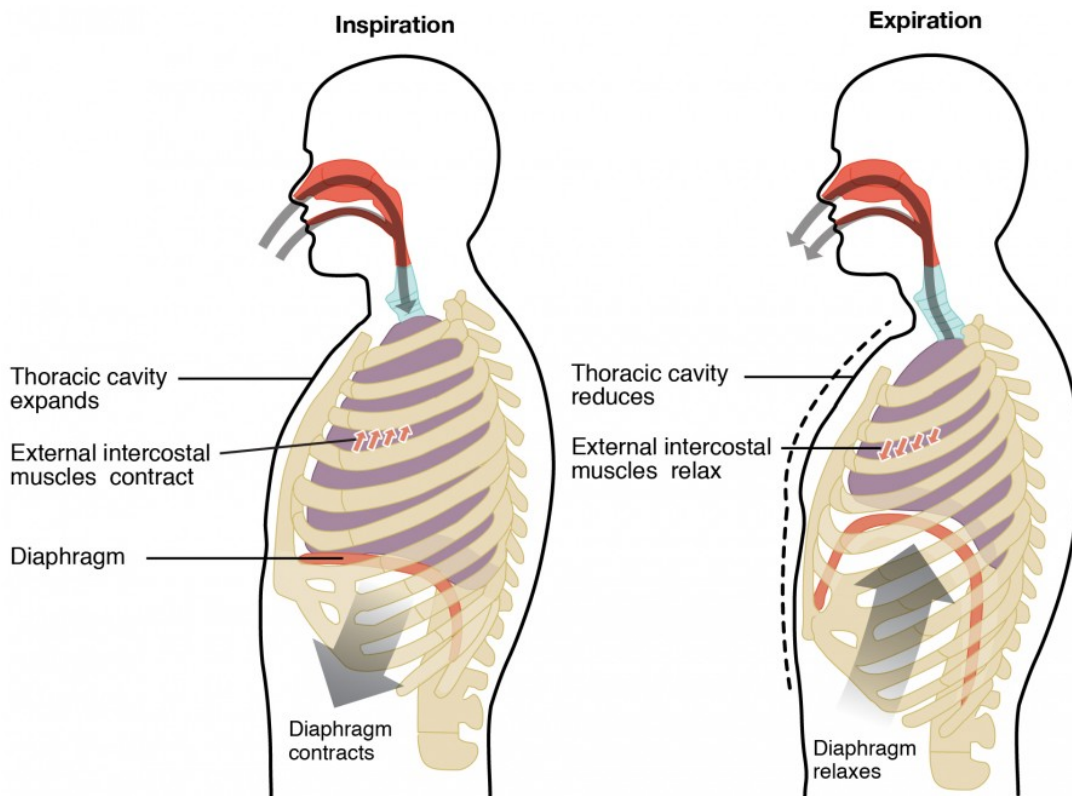


Image: "Inspiration and Expiration" by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

The respiratory cycle can be divided into 4 steps:

1. The thorax rises; the diaphragm contracts.
2. The lungs follow this movement, led by the adhesive forces in the pleural space; air flows into the lungs.
3. The respiratory muscles relax.
4. The lung follows its disposition to collapse as far as the thorax allows; air flows out of it.

Step 1 and 2 describe the **active inspiration** by increasing the thorax, while step 3 and

4 address **passive expiration**.

However, expiration can also be forced. For this, the abdominal press of the **abdominal muscles** is used. If the pressure in the pleural space becomes too large, the airways can collapse because of the decreasing pressure difference. A resistance outside of the chest, like pursed lip breathing, can remedy this.

Compliance and lung hysteresis

Compliance (C) generally describes the elasticity of a system and is defined as:

$C = \Delta V / \Delta p$ = change in volume/change in pressure

Compliance of the lungs is determined by the elastic characteristics of connective tissue and by the surface tension of the alveoli. The compliance of the thorax is influenced by parts of the passive and active locomotor system of the torso, i.e. by the ligaments and muscles.

Plotting volume against transmural pressure yields the **lung hysteresis curve**, whose slope represents compliance. The lung hysteresis of the total respiratory system, i.e. both lung and thorax, is influenced by the intrapulmonary pressure, which is the pressure difference between the alveolar and the atmospheric pressure. It has an S-shaped course. In normal breathing, it behaves approx. linear. Here, the inspiration movement is set against a relatively constant resistance.

Stretching of the chest is dependent on the intrapleural pressure, i.e. the pressure between the intrapleural space and the outer space. Its compliance increases for larger volumes. The hysteresis curve of the thorax, thus, resembles the course of an exponential function.

The difference between intrapulmonary and intrapleural pressure is relevant for the stretching of the lung. Here, compliance and the steepness of the curve decreases with an increase in the filling amount. Thus, the lung hysteresis behaves contrary to the hysteresis of the thorax, which makes the curve of the total system S-shaped.

Pressure change in dynamic respiration

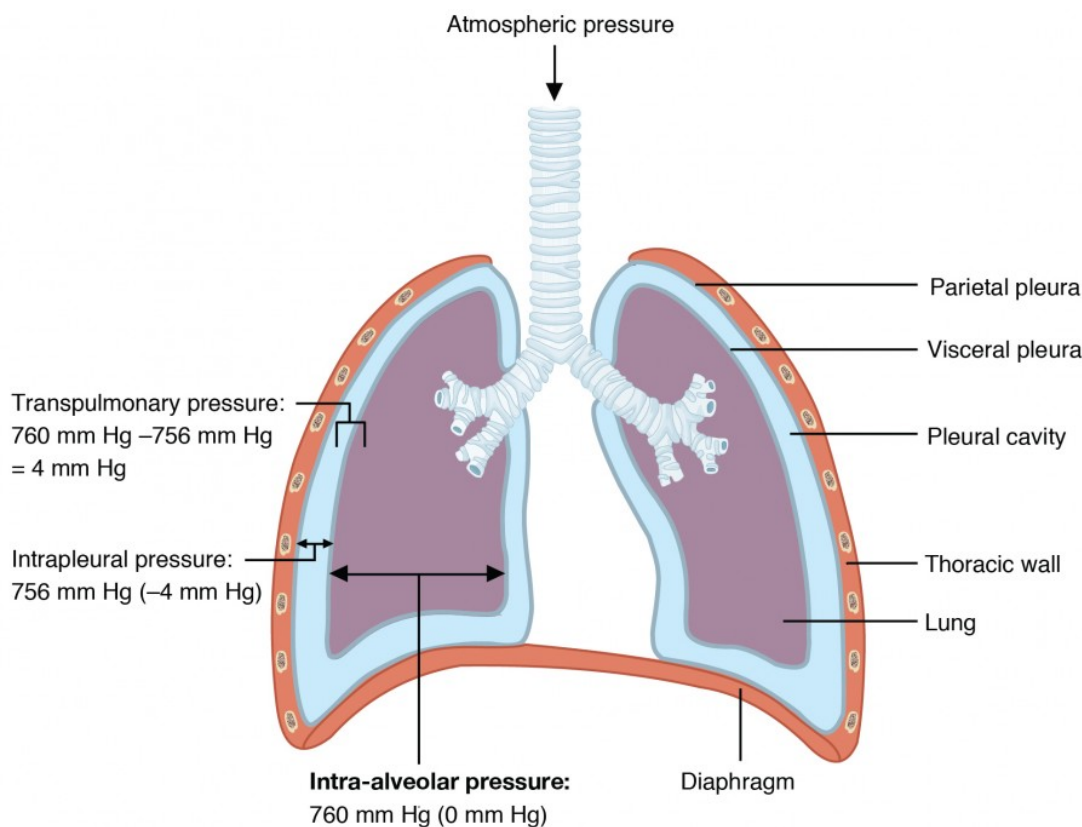


Image: "Intrapulmonary and Intrapleural Pressure Relationships" by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

When resting, the pleural space is affected by the elastic pull of the lung that results in "negative" pressure (suction) called the **intrapleural pressure**. During inspiration, this pressure becomes more negative; during expiration, it becomes more positive.

The **intrapulmonary pressure**, i.e. the pressure difference between alveoli and outside air, remains constant at 0 during the entire respiratory cycle, provided the glottis is opened, and constant pressure equalization can take place.

In dynamic breathing, which corresponds to our regular breathing, the pressure compensation is restricted and, thus, delayed. The air cannot flow into the alveoli fast enough because of the viscous resistance, which is produced by the airways resulting in pressure in the alveolar space that is lower than that of the outside air. The intrapulmonary pressure amounts to $-1 \text{ cm H}_2\text{O}$. During expiration, the reverse is the case, with an intrapulmonary pressure of $1 \text{ cm H}_2\text{O}$.

This change of the intrapulmonary pressure also affects the intrapleural pressure: During dynamic breathing, it reaches its minimum shortly before the end of inspiration. Analogously, the maximal intrapleural pressure can be measured shortly before the end of expiration.

Pulmonary Gas Exchange

The purpose of pulmonary respiration is to supply the body's cells with oxygen and to release carbon dioxide into the surrounding air. The transport of oxygen from the surrounding air to the oxygen-consuming cells follows 4 steps:

1. Convective transport through ventilation
2. Diffusion from the alveoli into the pulmonary capillaries
3. Convective transport through the blood to the capillaries in the peripheral tissue

4. Diffusion from the capillary blood into the tissue

Partial pressures of the respiratory gases

Dalton's law states that each gas in a mixture exerts a partial pressure, which corresponds to its share of the total volume. Consider the partial pressures of the respiratory gases in the alveolar space at standard conditions:

$p_{AO_2} = 100 \text{ mm Hg}$ and $p_{ACO_2} = 40 \text{ mm Hg}$

These partial pressures are influenced by the composition of the outside air but also by the alveolar ventilation. When the ventilation increases, the alveolar partial pressure of oxygen increases, while the partial pressure of carbon dioxide decreases. These pressure changes occur because the breathing air supplies new oxygen, while carbon dioxide is exhaled completely and (almost) does not exist in the atmospheric air.

The venous blood in the pulmonary capillaries flows past the alveoli with an **oxygen partial pressure** of approx. 40 mm Hg and a **carbon dioxide partial pressure** of 46 mm Hg. These pressure differences ensure that the respiratory gases can diffuse through the barrier of the alveolar epithelium, which is a thin layer of **interstitial and capillary endothelium**. Thus, they are the driving force for the pulmonary gas exchange.

The blood leaves the capillaries with an oxygen partial pressure of 100 mm Hg and a carbon dioxide partial pressure of 40 mm Hg. Thus, the partial pressures in the blood have been adjusted to those of the alveolar gas mixture. Out of the contact time of 0.75 s, only 0.25 s are needed to saturate the blood with oxygen completely. In a healthy person, the resting oxygen uptake is, therefore, limited not by diffusion but by perfusion. If less blood flows through the capillaries, less blood will be oxygenated.

In sum, gas exchange is influenced by the driving pressure difference, the area available for diffusion, by perfusion, and the barrier to be overcome.

Ventilation-perfusion ratio

In standard conditions, the ventilation-perfusion ratio equals 1. If an area of the lung is less ventilated, though, e.g., due to a blocked bronchus, the alveolar oxygen partial pressure of the affected alveoli aligns itself with the venous blood which causes vasoconstriction of the vessels in this region (**hypoxic pulmonary vasoconstriction**), also called the **Euler-Liljestrand mechanism**. A portion of the blood is diverted to increase the perfusion of the better-ventilated areas. The ventilation-perfusion ratio of the less ventilated area is **less than 1**.

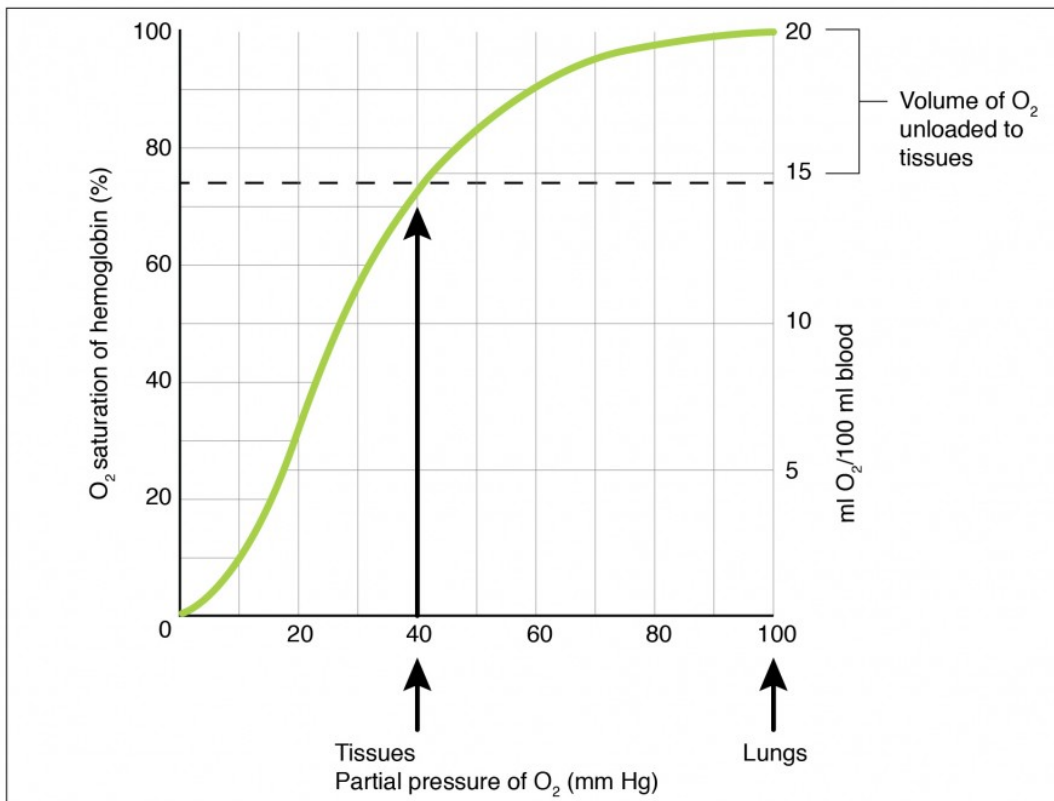
In contrast, if an area of the lung is less perfused, e.g., due to **stenosis**, the alveolar oxygen partial pressure in the affected alveoli rises and is similar to the outside air. The ventilation-perfusion ratio is, therefore, **greater than 1**.

With an **upright upper body**, a physiological ventilation-perfusion imbalance sets in. Due to gravity, perfusion and alveolar ventilation increase from the top down. Thereby, perfusion correlates more strongly with height than ventilation does, as the apex of the lung is supplied with blood only in the systole because of its position above the heart. Therefore, the ventilation-perfusion ratio **at the apex of the lung is higher than the average. At the base of the lung, it is less than 1**.

Respiratory Gas Transport

Hemoglobin, contained in the erythrocytes, is responsible for the transport of oxygen in the blood. It binds the oxygen to its central divalent iron. **Hüfner's number** describes the maximal oxygen binding capacity of 1 g of hemoglobin. It is 1.34 mL. Thus, a healthy adult with 150 gram hemoglobin per liter of blood can transport 0.2 L of oxygen in 1 L of blood.

Oxygen binding curve



(a) Partial pressure of oxygen and hemoglobin saturation

Image: "Oxygen-Hemoglobin Dissociation and Effects of pH and Temperature" by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

The oxygen binding curve shows the relationship between oxygen saturation and oxygen partial pressure in the blood. The tetrameric structure of hemoglobin and the cooperative interactions of its units result in a **sigmoidal plot** of the oxygen binding curve. If oxygen binds to 1 of the 4 subunits, a conformational change of the molecule occurs, which facilitates further oxygen uptake of the remaining units.

The higher the oxygen partial pressure, the greater the affinity of hemoglobin to oxygen and, therefore, the oxygen uptake in the erythrocytes. The sigmoidal path of the oxygen binding curve is necessary for the oxygen to be taken up in the lung and released in the tissue.

Various factors influence the course of the curve: With increasing temperature, the affinity of hemoglobin for oxygen decreases. The same is true for **decreasing pH value (Bohr effect)**, which facilitates the release of oxygen in the tissue because venous blood is more acidic than arterial blood. The same effect is produced by rising carbon dioxide partial pressure in the periphery. Moreover, 2,3-bisphosphoglycerate that is contained in

the erythrocytes can also reduce the oxygen affinity of hemoglobin.

Carbon dioxide transport

Carbon dioxide is mainly transported in the plasma in the form of bicarbonate. For this to happen, CO_2 is first converted to carbonic acid H_2CO_3 by carbonic anhydrase in erythrocytes, which break down immediately to bicarbonate and protons. Then, the bicarbonate leaves the erythrocytes in exchange for chloride ions (**chloride shift** or **Hamburger phenomenon**). A small amount of carbon dioxide is bound to the hemoglobin and transported. The result is **carbaminohemoglobin**.

The carbon dioxide binding curve is approx. linear and dependent on the blood's oxygenation level. Deoxygenated blood has a higher affinity for carbon dioxide (**Haldane effect**).

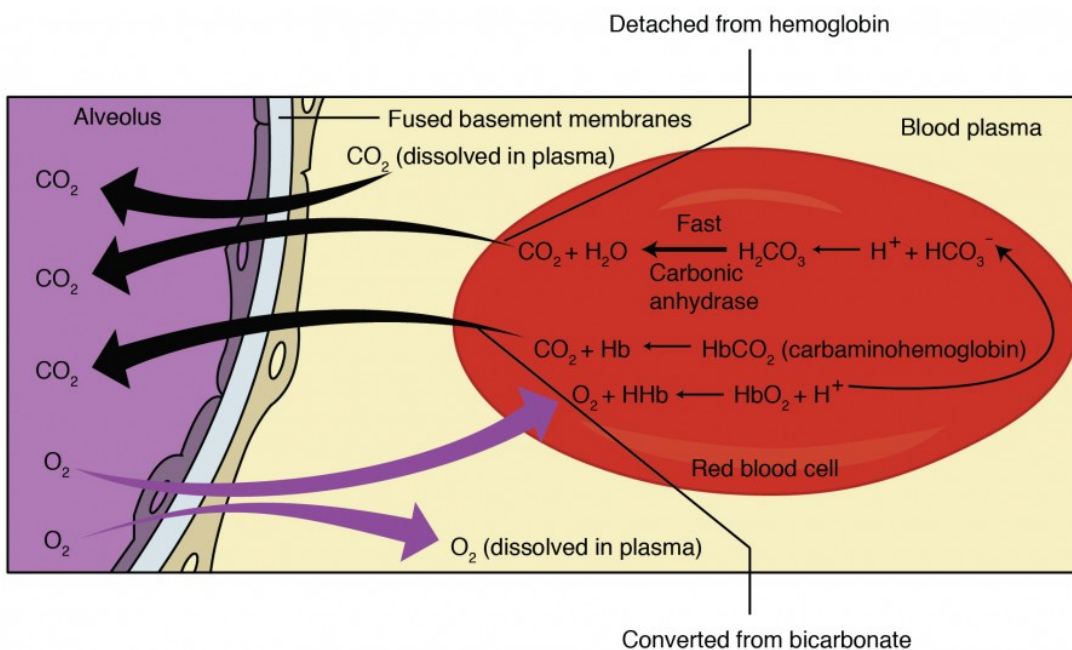


Image: "External Respiration" by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Regulation of Breathing

The respiratory control center is located in the **medulla oblongata** and the **pons**. Three different types of neurons form the **ventral respiratory group**:

- Inspiratory neurons
- Post-inspiratory neurons
- Expiratory neurons

Each of them is active in its respective phase.

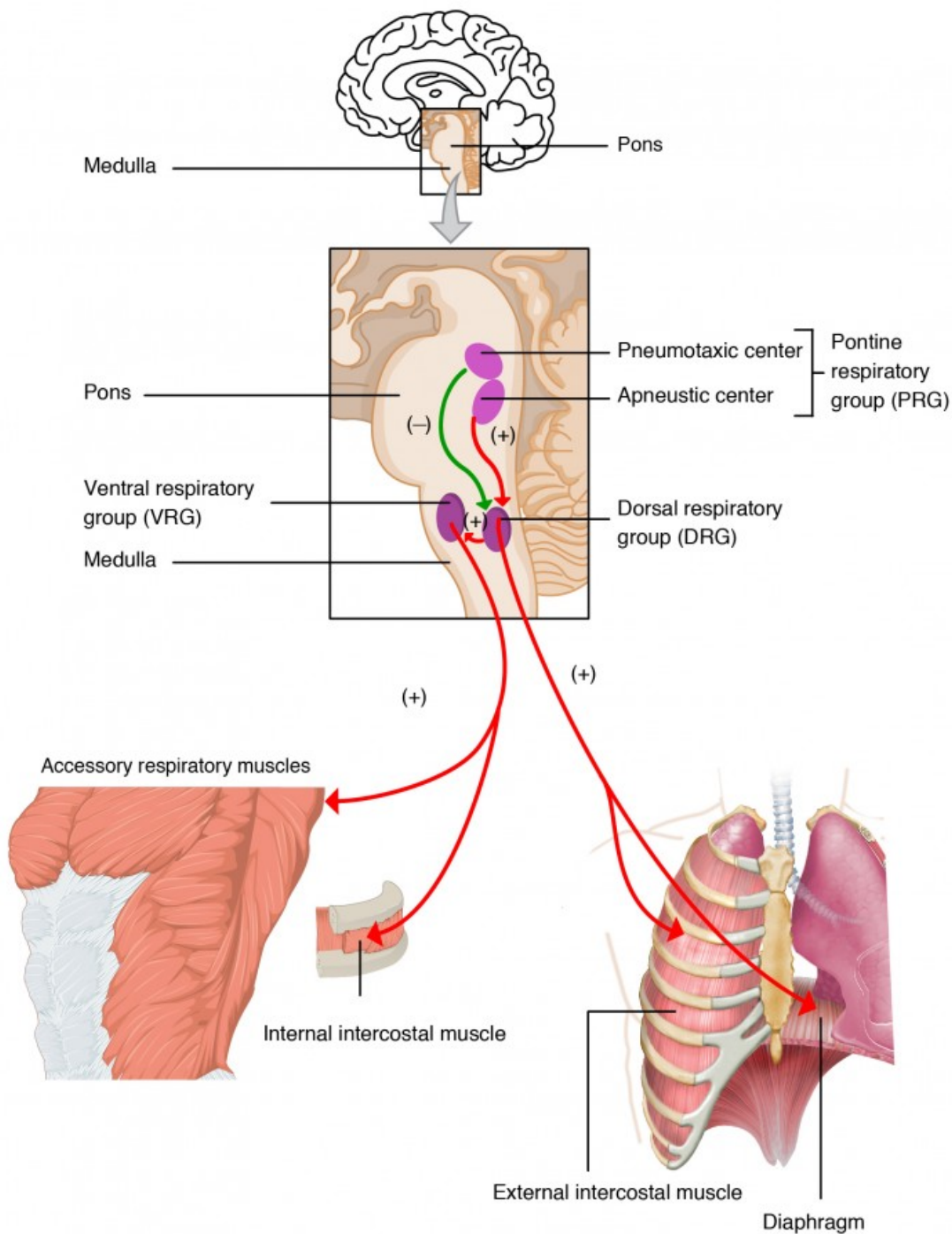


Image: "The medulla oblongata contains the dorsal respiratory group (DRG) and the ventral respiratory group (VRG)." by Phil Schatz. License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

This group is influenced by 2 other modifying groups of neurons: The **pontine respiratory group** has an inhibitory effect, while the **dorsal respiratory group** processes signal from the airways and the cardiovascular system.

Chemosensors serve as afferents; they are located peripherally at the carotid bifurcation, at the aortic arch, and centrally in the brainstem. The peripheral sensors are located in the aortic bodies (glomera). They respond to decreasing oxygen concentrations, decreasing pH-value, or increasing CO₂ levels. The CO₂ partial pressure exerts the strongest stimulus, increasing the respiratory minute volume by up to 80 L/min.

Other influences on the respiratory control center include free nerve endings in the airways, stretch receptors of the bronchial wall, and muscle spindles of the intercostal

muscles. These allow, for example, the sneeze reflex, the **Hering-Breuer reflex**, and the deflation reflex.

Furthermore, breathing is influenced by the autonomic nervous system and the endocrine system. Breathing increases, for example, because of the influence of the sympathetic nervous system.

Review Questions

Solutions can be found below the references.

1. Which of the following statements is true?

- A. Total capacity is the sum of functional residual capacity and inspiratory reserve volume.
- B. Vital capacity is the sum of inspiration capacity and expiratory reserve volume.
- C. Inspiratory reserve volume is the volume that can be inhaled in the resting position.
- D. In a pneumothorax, the lungs collapse to their residual volume.
- E. After maximal exhalation, only the functional residual capacity remains in the lungs.

2. Which of the following statements is true?

- A. The alveolar pressure during inspiration is higher than the environmental pressure.
- B. The alveolar pressure during expiration is lower than the alveolar pressure during inspiration.
- C. The alveolar pressure never exceeds the intrapleural pressure.
- D. The alveolar pressure is always less than the intrapleural pressure.
- E. The intrapleural pressure may exceed the intrapulmonary pressure during forced expiration.

3. A patient has a tidal volume of 0.5 L and a respiratory rate of 15 breaths per minute. The alveolar pressures are: $O_2 = 95$ mm Hg, $CO_2 = 40$ mm Hg. The blood pH value is 7.4. The patient spontaneously doubles his tidal volume and halves his respiratory rate. Which of the following statements are true?

- A. The respiratory minute volume has increased.
- B. Dead space ventilation is unchanged.
- C. Alveolar ventilation has increased.
- D. The alveolar CO_2 pressure is decreased to about half.
- E. The pH value in a blood gas analysis is shifted towards acidosis.

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Correct Answers: 1B,2D,3C

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Notes