

Respiratory Failure: Hypoxemia, Hypercapnia and Hypoxia

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The inspiration of oxygen and expiration of carbon dioxide are vital functions of the human body. A decrease in PO_2 and increase in PCO_2 can alter many normal physiologic processes, and may eventually be fatal. The human body has various reflex mechanisms to manage such changes. Understanding of these reflexes and identification and management of any impairment in them is essential in the management of many respiratory and renal diseases.



Partial Pressure of Gases

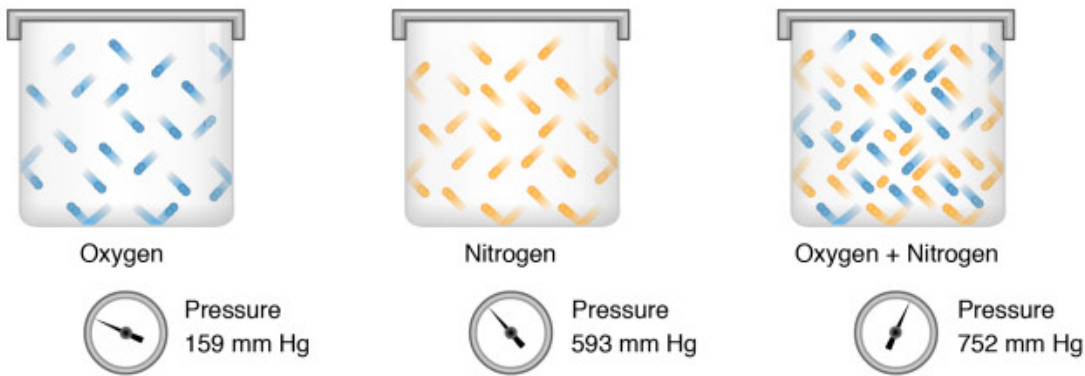


Image: "Partial Pressure is the Force Exerted by a Gas. The Sum of the Partial Pressures of all the Gases in a Mixture Equals the Total Pressure." by OpenStax. License: [CC-BY 3.0](https://creativecommons.org/licenses/by/3.0/)

Atmospheric dry air is a mixture of many gases. At sea level, this air has a pressure of **760 mm Hg**. The partial pressure that each gas contributes to this atmospheric pressure is based on the percentage of gas in the air.

$$P_{\text{gas}} = F_{\text{gas}} \times P_{\text{atm}}$$

- P_{gas} = Partial pressure of gas
- F_{gas} = Fraction of gas in air
- P_{atm} = Atmospheric pressure

Taking the above formula, the PO_2 will be:

$$PO_2 = 0.21 \times 760 \text{ mm Hg}$$

$$PO_2 = 160 \text{ mm Hg}$$

PCO_2 is very low in the atmospheric dry air, and hence, is considered to have a **partial pressure of 0 mm Hg**. As the air is inspired, it is warmed to 37°C and completely humidified. The gases in the air have a slightly lower partial pressure, owing to the addition of water vapors. This air has not yet participated in gas exchange. In the alveoli, where gas exchange occurs, PO_2 decreases and PCO_2 increases considerably.

Site of air	PO_2 (mm Hg)	PCO_2 (mm Hg)
Atmosphere	160	0
Trachea (humidified)	150	0
Alveoli	100	40

In an ideal system, **PO_2 and PCO_2 of the alveolar and pulmonary capillary compartments are roughly the same**. As some of the blood shunts through the lungs, the PO_2 of the systemic arterial blood is slightly lower than that of the pulmonary capillaries.

Site of blood	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)
Pulmonary arteries	40	46
Pulmonary capillaries	100	40
Systemic arteries	95	40

Alveolar-Arterial Gradient

The difference between **PO_2 of alveoli and PO_2 of arterial blood** is referred to as alveolar-arterial gradient (A-a gradient).

$$\text{A-a gradient} = P_A\text{O}_2 - P_a\text{O}_2$$

$P_A\text{O}_2$ = Alveolar PO_2 (calculated from the alveolar gas equation)

$P_a\text{O}_2$ = Arterial PO_2 (measured in arterial blood)

In a normal healthy non-smoker's system, A-a gradient is 5–10 mm Hg.

Alveolar Gas Equation

Arterial PO_2 ($P_a\text{O}_2$) is measured from an arterial blood sample. Unlike $P_a\text{O}_2$, alveolar PO_2 ($P_A\text{O}_2$) cannot be measured directly by taking an air sample from alveoli. Instead, an equation is used to estimate $P_A\text{O}_2$.

$$P_A\text{O}_2 = P_I\text{O}_2 - \frac{P_a\text{CO}_2}{R} + \left[P_a\text{CO}_2 * F_I\text{O}_2 * \frac{1 - R}{R} \right]$$

$P_A\text{O}_2$ = Alveolar partial pressure of oxygen

$P_I\text{O}_2$ = Partial pressure of inspired oxygen

$P_a\text{CO}_2$ = Arterial partial pressure of carbon dioxide

$F_I\text{O}_2$ = Fraction of inspired gas that is oxygen

R = Respiratory exchange ratio

The above equation can be simplified when $F_{I\text{O}_2} < 1$

$$P_A\text{O}_2 = P_I\text{O}_2 - \frac{P_a\text{CO}_2}{R}$$

Alveolar PCO_2

Alveolar PCO_2 **depends on two factors:**

- Alveolar ventilation
- Metabolic rate

Alveolar ventilation has an **inverse** relationship with $P_A\text{CO}_2$.

- Hyperventilation decreases $P_A\text{CO}_2$ as deoxygenated air clears away faster. If ventilation is doubled, $P_A\text{CO}_2$ halves.
- Hypoventilation increases $P_A\text{CO}_2$ as deoxygenated air remains in alveoli for a longer time. If ventilation is halved, $P_A\text{CO}_2$ doubles.

Metabolic rate has a **direct** relationship with $P_A\text{CO}_2$.

- Increased metabolic rate increases $P_A\text{CO}_2$.
- Decreased metabolic rate decreases $P_A\text{CO}_2$.

The body compensates for these changes in $P_A\text{CO}_2$ by altering alveolar ventilation. In other words, to keep $P_A\text{CO}_2$ constant, the **body matches metabolic rate with equivalent changes in alveolar ventilation**. For example, during exercise (increased metabolism), the respiratory rate also increases to expel the increased $P_A\text{CO}_2$.

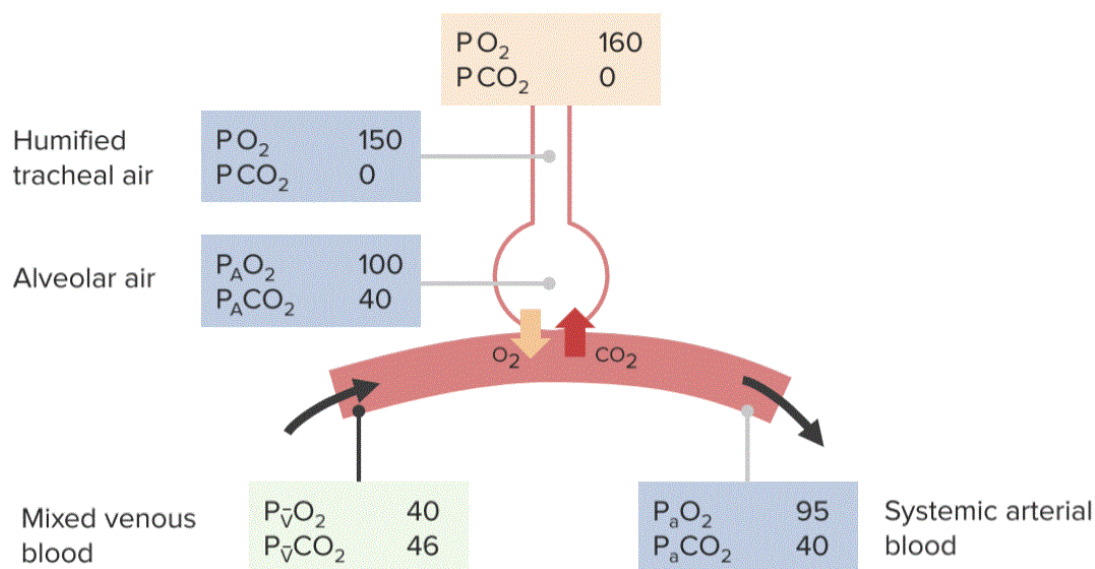
Alveolar PO₂

Alveolar PO₂ (P_AO₂) depends on P_ACO₂, and therefore, on alveolar ventilation.

- Hyperventilation decreases P_ACO₂, leaving more space for oxygen (increased P_AO₂).
- Hypoventilation increases P_ACO₂, decreasing space for oxygen (increased P_AO₂).

Arterial-Venous Gradient

The difference between PO₂ of arterial blood and PO₂ of venous blood is referred to as arterial-venous gradient (a-v gradient). The arterial-venous gradient is highly dependent on the rate of metabolism. At higher metabolic rates, more O₂ is produced. Hence, the a-v gradient is high during exercise and in trained athletes.



"Overview Arterial-venous and Alveolar-arterial Oxygen Gradients" Image created by Lecturio

Tissue Hypoxia — Deprivation of Oxygen Supply

Hypoxia is a state of the body or a region of the body when it is **deprived of adequate oxygen supply**. It results from the failure of oxygen delivery to cells.

Etiology of Hypoxia

Tissue hypoxia has many diverse reasons. The mechanisms behind these causes can be summarized as follows:

- **General ischemia**
- **Localized ischemia**
- **Anemia**
- **Carbon monoxide poisoning**
- **Hypoxemia**

Generalized ischemia results from a low cardiac output. Many heart diseases could contribute towards it. Localized ischemia, on the other hand, is caused by vascular dysfunction, as in cases of peripheral vascular disease and gangrenes.



[Image](#): "Cyanosis of the hand in someone with low oxygen saturation." by James Heilman. License: [CC BY-SA 3.0](#)

Anemia decreases the capacity of **blood** to carry oxygen as lesser hemoglobin is available to bind to oxygen. This leads to a decreased supply of oxygen throughout the body.

Carbon monoxide binds to hemoglobin and keeps it from carrying oxygen. The binding of carbon monoxide to hemoglobin is 100 times stronger than that of oxygen to hemoglobin. Additionally, it keeps the already bound oxygen from releasing at tissues.

Hypoxemia refers to a decreased oxygen level in the blood (specifically arterial blood), as opposed to hypoxia which refers to the decreased oxygen level in tissues, organs and/or the body. Hypoxemia would eventually lead to hypoxia, but, as mentioned above, it is only one of the many causes of hypoxia.

Body's Response to Hypoxia

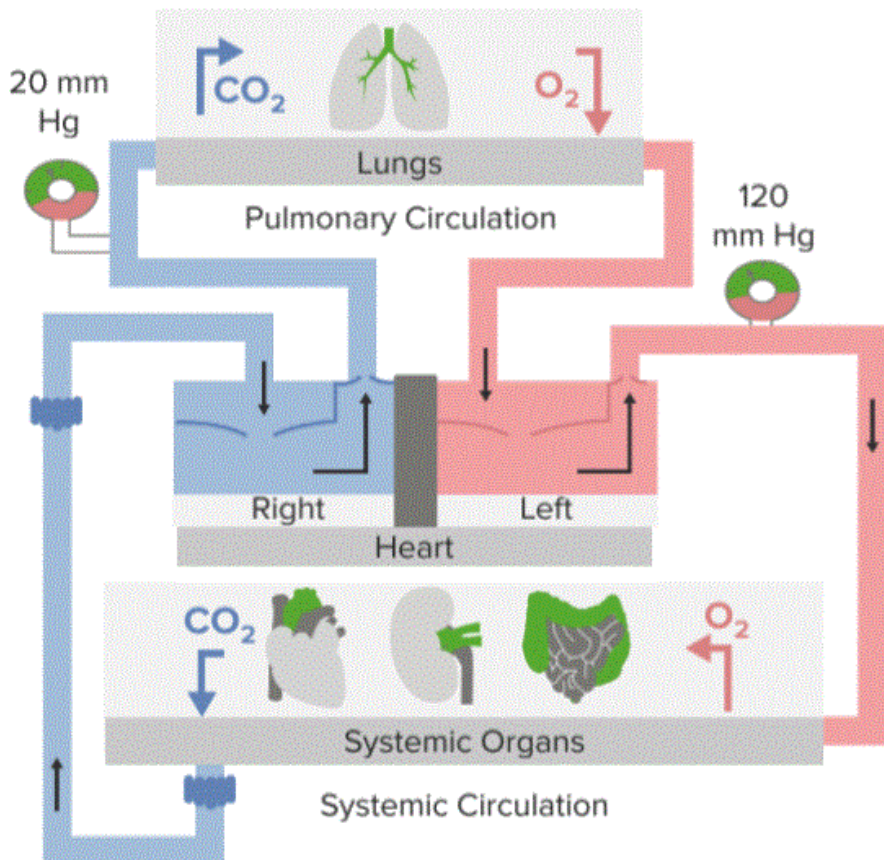
The body has various compensatory mechanisms set in place to combat hypoxia. The immediate response includes:

- Shifting respiratory reactions from aerobic to anaerobic reactions, leading to lactic acid build-up
- Increasing ventilation in response to lower PO_2
- Systemic vasodilation to improve tissue perfusion
- Pulmonary vasoconstriction to shunt blood towards better-ventilated regions

If hypoxia remains for a longer duration (over 2 weeks), interstitial cells in the peritubular capillary bed of the renal cortex secrete erythropoietin. Erythropoietin will primarily target erythrocyte progenitors to induce the production of red blood cells. This improves the oxygen supply. Therefore, **erythrocytosis** is considered to be an **important clinical sign** of chronic hypoxia.

Hypoxemia — Decreased Blood Oxygen

Air is inhaled into the alveoli where oxygen diffuses into the blood through the walls of the alveoli and capillaries. Hypoxemia, i.e. **decreased oxygen in the blood**, occurs due to dysfunction at any stage in this process.



"Hypoxemia. Low Arterial Partial Pressure of O₂" Image created by Lecturio

Hypoventilation or Low P_{iO_2}

The very first stage of respiration is inhaling an adequate amount of oxygen.

- In hypobaric conditions, the atmospheric pressure of air is lower, and hence, the constituent gases, including oxygen, have lower partial pressure.
- In closed compartments, oxygen is limited. Over time, its consumption can lead to decreased F_{iO_2} .
- Hypoventilation causes decreased $P_{A}O_2$.

Diffusional Impairment

The exchange of gases (O_2 & CO_2) between the alveoli and blood occurs by simple diffusion.

- **Thicker alveolar or capillary wall** impairs diffusion of gases.
- **Pulmonary fibrosis** thickens the walls of the [lungs](#). Fluid in the lungs can decrease the diffusion capacity.
- The measurement of the uptake of CO in mL/min/mm Hg is called the diffusing capacity of the lung (**DLCO**).

Right-to-left Shunt

Some pathological shunts can skip the pulmonary circulation.

- **Cardiac defects** allow the mixing of deoxygenated blood with oxygenated blood.

- **Uncorrected left-to-right shunts** can progress to the right-to-left shunt. This phenomenon is known as **Eisenmenger syndrome**.

V/Q Inequality

The gas exchange across the alveolar-capillary barrier could either be diffusion-limited or perfusion-limited. **The diffusion-limited gas exchange** occurs when net diffusion into pulmonary capillary depends on a magnitude of A-a gradient. If the gradient is high, more oxygen will diffuse. **The perfusion-limited gas exchange** occurs when the gas exchange is limited by blood flow through pulmonary capillaries. People with heart diseases (reduced cardiac output) experience a perfusion-limited gas exchange.

Ideally, the **ventilation-perfusion ratio (V/Q) should be 1**. Physiologically, the apex of a lung is poorly perfused (decreased blood flow) and highly ventilated. The V/Q ratio is high and signifies that oxygen does not get a chance to properly diffuse from alveoli to blood. In contrast, the base of a lung is highly perfused (increased blood flow) and normally ventilated. The V/Q ratio is low and signifies that enough oxygen is not available to properly oxygenate the blood.

Hypercapnia — Increased Carbon Dioxide in Blood

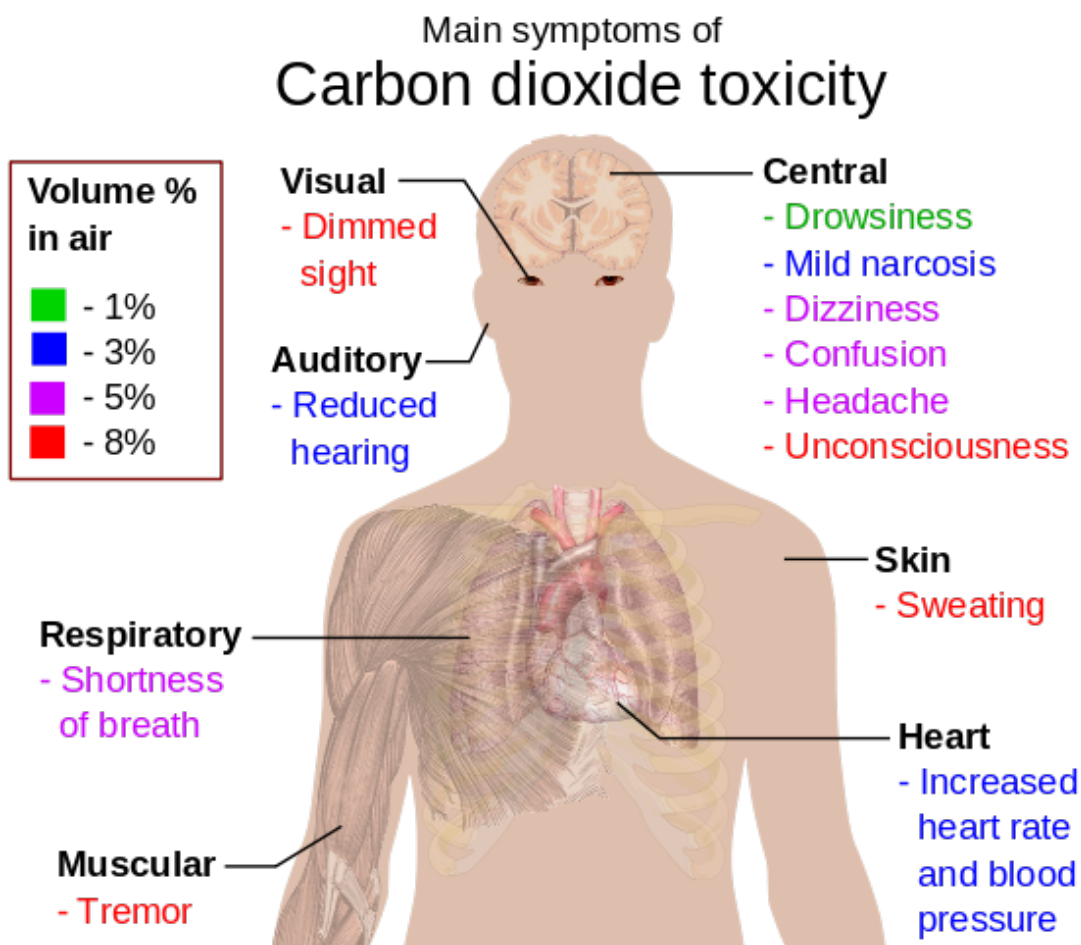


Image: "Main Symptoms of Carbon Dioxide Toxicity" by Mikael Häggström. License: Public Domain

Hypercapnia refers to an **increased carbon dioxide level in the blood**. Hypercapnia occurs when enough carbon dioxide is not being expelled from the body.

- $P_a\text{CO}_2$ directly depends on $P_A\text{CO}_2$. Expulsion of CO_2 from the alveoli is important to maintain a concentration gradient between alveoli and blood and facilitate the diffusion of CO_2 across the alveolar-capillary barrier.
- Poor ventilation decreases the V/Q ratio, stopping the adequate off-loading of CO_2 from erythrocytes.
- A higher metabolism produces more CO_2 . Without proper reflex, this can lead to hypercapnia.

References

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