Hypoxia

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Hypoxia:

Hypoxia 2:

Hypoxia 3:

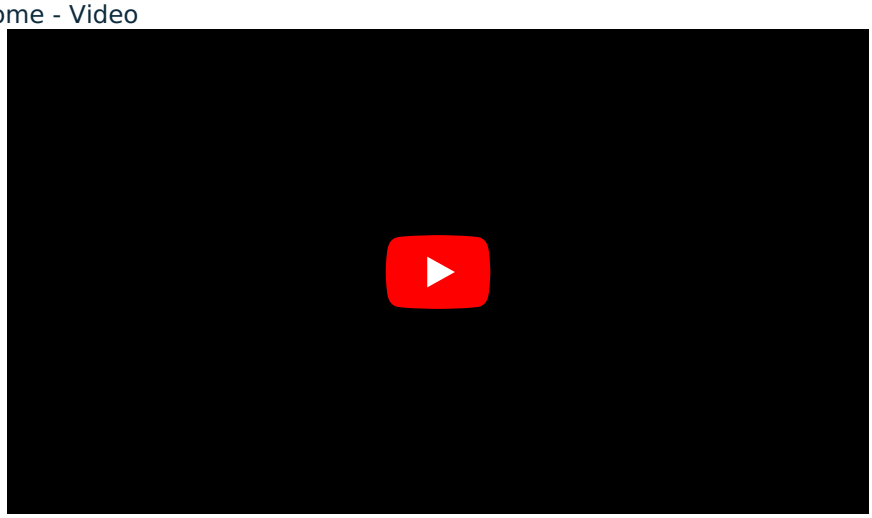
Hypoxia 4:

Hypoxia types:

Hypoxia is the collective name for the lack of oxygen in the whole organism or just its tissues. The term hypoxia has to be distinguished from the term **hypoxemia**, which is a lack of oxygen in the arterial blood. Complete lack of oxygen is also known as **anoxia**. In clinical practice, hypoxia is divided into the following groups according to the place where the oxygen transfer disorder occurs (the so-called **Barcroft scheme**):

1. **hypoxic** hypoxia
2. **anaemic** hypoxia
3. **stagnant** hypoxia
4. **histotoxic** hypoxia

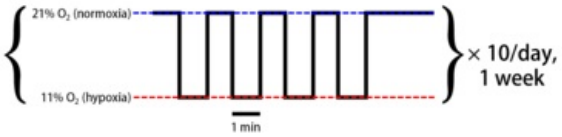
Acute Coronary Syndrome - Video



Causes of Hypoxia

Hypoxia can be caused by:

- Inadequate oxygenation of the blood in the lungs: deficiency of O2 in the atmosphere, hypoventilation (neuromuscular disorder);
- Pulmonary disease: abnormal alveolar ventilation-perfusion ratio;

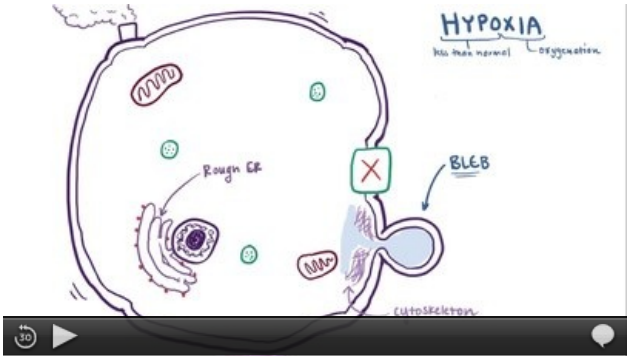


Example of a typical intermittent hypoxia protocol

Hypoxic hypoxia

Hypoxic (or **hypoxemic**) hypoxia is caused by the **low partial pressure of oxygen (pO_2) in the arterial blood.** Hypoxic hypoxia is caused by a disorder in the transfer of oxygen between the lungs and blood. The causes can be:

- low inspiratory oxygen fraction;
- respiratory system disorders;
- arteriovenous shunts.



Hypoxia summary video

The low inspiratory oxygen fraction is due to the low oxygen volume in the environment. Most often it is caused by a stay at high altitudes. The human body is able to withstand altitudes up to **4000 m above sea level** without acclimatization (decrease in pO_2 to 35–40 torr). From **5000 m above sea level,** severe hypoxia occurs and at **6000m above the sea,** the victim becomes unconscious. The complex of symptoms that occur in a person with hypoxia in these conditions is called Acute Mountain Sickness (AHN).

Disability of the respiratory system can be caused by a number of diseases or injuries, such as pneumothorax, asthma, pulmonary emphysema, or cystic fibrosis.

Arteriovenous shunts cause mixing of arterial and venous blood, so there is more deoxy-Hb in the blood flowing to the tissues, which causes cyanosis and an insufficient oxygen concentration gradient for efficient tissue transfer.

Anemic hypoxia

Anemic (or **transport**) hypoxia is caused by **insufficient numbers of functional erythrocytes or hemoglobin**. The basic feature of this type of hypoxia is arterial hypoxemia with normal pO_2 in the environment, the arteriovenous difference is the same. Anemic hypoxia can be caused by decreased erythrocyte number (blood loss, decreased erythropoesis, increased disintegration), decreased hemoglobin concentration with sufficient erythrocytes number (so-called hypochromic anemia), pathological Hb production or eliminating Hb from O_2 binding.

Carbon monoxide poisoning

One of the conditions that can cause Hb elimination is carbon monoxide poisoning. CO has about **210× greater affinity for Hb** than oxygen, the incurred complex is called carbonylhemoglobin (but textbooks often mention carboxyhemoglobin). The formation of carbonylhemoglobin **precludes the binding of O_2 to Hb** in sufficient quantity and thus precludes its diffusion into tissues. The remaining Hb, on the other hand, binds O_2 more strongly, which makes the diffusion even worse. In addition, the partial pressures of other gases in the environment are normal, so chemoreceptors signalling **a lack of oxygen** are not activated. This, together with the fact that CO has no taste or odour, makes poisoning by this gas really dangerous.

CO poisoning is manifested by headaches, nausea, confusion, congestion in the face, vomiting. At higher concentrations, convulsions, unconsciousness, and cherry-coloured mucous membranes occur (carbonylhemoglobin has a bright red colour).

The first aid in poisoning is to take the victim to **fresh air**. The excretion of CO from the blood can be sped up by **breathing pure oxygen** from a bottle or by hyperbaric **oxygen therapy**.

Methemoglobinemia

Another condition is methemoglobinemia, in which **iron in Hb** is oxidized **from Fe^{2+} to Fe^{3+}**. The incurred haemoglobin is referred to as methemoglobin (MetHb). There are rare congenital forms in which, due to a deficiency of the enzyme **diaphorase I** (NADH-methemoglobin reductase), defective Hb accumulates, which is formed in small amounts even under normal conditions.

However, the forms obtained are more common due to a number of **oxidants** or some antibiotics and local anaesthetics. Methemoglobinemia often affects **young children** in areas where drinking water has a higher nitrate content. The child's body is not able to reduce the increased amount of methemoglobin in the long term, and cyanosis is manifested, which is why the disease is nicknamed **"bluing of children"**.

Methemoglobinemia can be treated with **methylene blue**, which (when given in small doses) converts to **leucomethylene blue** in the body, which facilitates the conversion of MetHb to Hb.

Circulatory hypoxia

Circulatory hypoxia is also called **stagnant hypoxia.** It is caused by a general or local circulatory disorder while the composition of the arterial blood is normal (normal pO_2). In the case of a circulatory disorder, the blood flows more slowly in a space, which leads to greater extraction of oxygen and an increase in arteriovenous differences. The cause may be shock, ischemia (decreased blood flow to the tissues), or blood stagnation, caused by the formations of atherosclerotic plaques, embolism, vascular obliteration, or heart failure. Circulatory shock can affect a large number of organs, but mostly circulatory hypoxia acts only locally.

The space where ischemia appears is cold and pale when stagnant, cyanotic. Local circulatory hypoxia often presents with severe pain in the affected area.

Histotoxic hypoxia

Histotoxic hypoxia **occurs when cells are unable to utilize O_2**. This disrupts the gradient of O_2 transfer to the tissues and the oxygenated blood thus enters the veins, which results in a pink discolouration of the skin. Histotoxic hypoxia occurs when poisoned by cyanide, alcohol, cobalt, and other poisons

Cyanide poisoning inhibits cytochrome c oxidase so there's not enough ATP to maintain cellular functions. Cold tolerance is also reduced because heat is generated during *aerobic ATP production*. Cyanide poisoning is treated by serving **methylene blue** to form methemoglobin, which reacts with cyanides to form *non-toxic cyanomethemoglobin*.

Manifestations of hypoxia

- **Phase 1** – Significant respiratory effort, restlessness, sweating, mental disorders, sympathetic predominance (hypertension, tachycardia, arrhythmia).
- **Phase 2** – Cyanosis, hypoxia, and hypercapnia are manifested by their central depressing effect, the predominance of parasympathetic – hypotension, bradycardia.
- **Phase 3** – Significant cyanosis, nerve and heart tissue damage, loss of consciousness, extreme bradycardia, circulatory arrest. Cyanosis is manifested at a concentration of deoxy-Hb greater than *50 g/l*, it does not manifest itself in anaemic hypoxia (little Hb in general, or little free Hb) and histotoxic hypoxia (greater amount of oxy-Hb in the venous blood).
  A significant part of the damage is the loss of the cells' ability to maintain **ionic gradients**.

Response to hypoxia

The cells undergo anaerobic glycolysis (but lactate makes the situation even worse).

- HIF (hypoxia-inducible factor) is expressed.
  - VEGF (vascular endothelial growth factor) – induces the growth of new blood vessels, which should ensure a better supply of hypoxic tissue.
  - p53 (reduction of cell proliferation until stress conditions end).
- Erythropoietin secretion.
- 2,3-DPG – In the absence of oxygen, 2,3-DPG (*diphosphoglycerate*) is formed in the erythrocytes, resulting from a branch from glycolysis. DPG binds preferentially to deoxy-Hb and stabilizes it in a state of low affinity for oxygen, resulting in greater oxygen availability to tissues. This reaction lasts for several hours, under prolonged hypoxic conditions the concentration of 2,3-DPG returns to normal.

References

Related articles

- Newborn hypoxia
- Disorders of acid-base balance

External links

- Hypoxie (Czech wikipedia)
- Hypoxia (medical) (English wikipedia)

Sources

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