HYPOXIA

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Jan Cendelín, 2017

Hypoxia = lack of O_2 in the tissues

Hypoxemia = lack of O_2 in the blood

Asphyxia = lack of O_2 + accumulation of CO_2

Hypercapnia = $\uparrow PaCO_2$

Hypocapnia = $\downarrow PaCO_2$

Oxygen delivery:

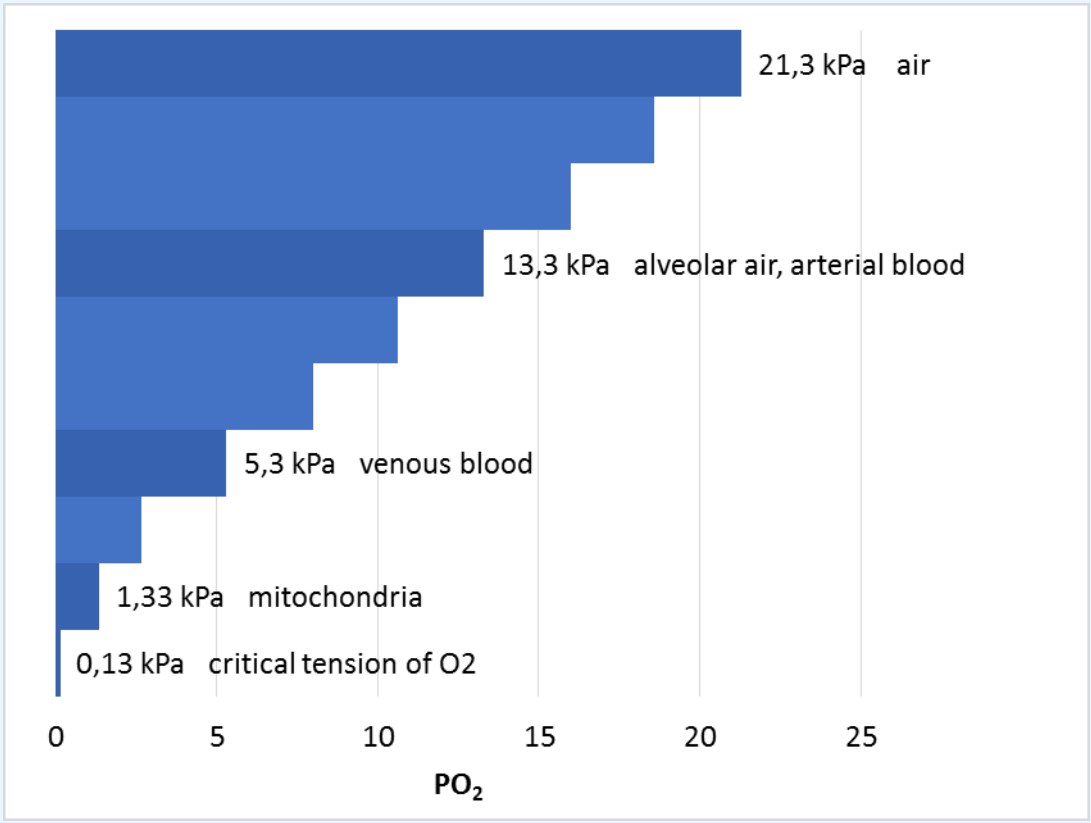
- atmosphere (air composition, pressure), respiratory system, circulation, blood (hemoglobin)

O_2 consumption: 200 - 250 ml/min

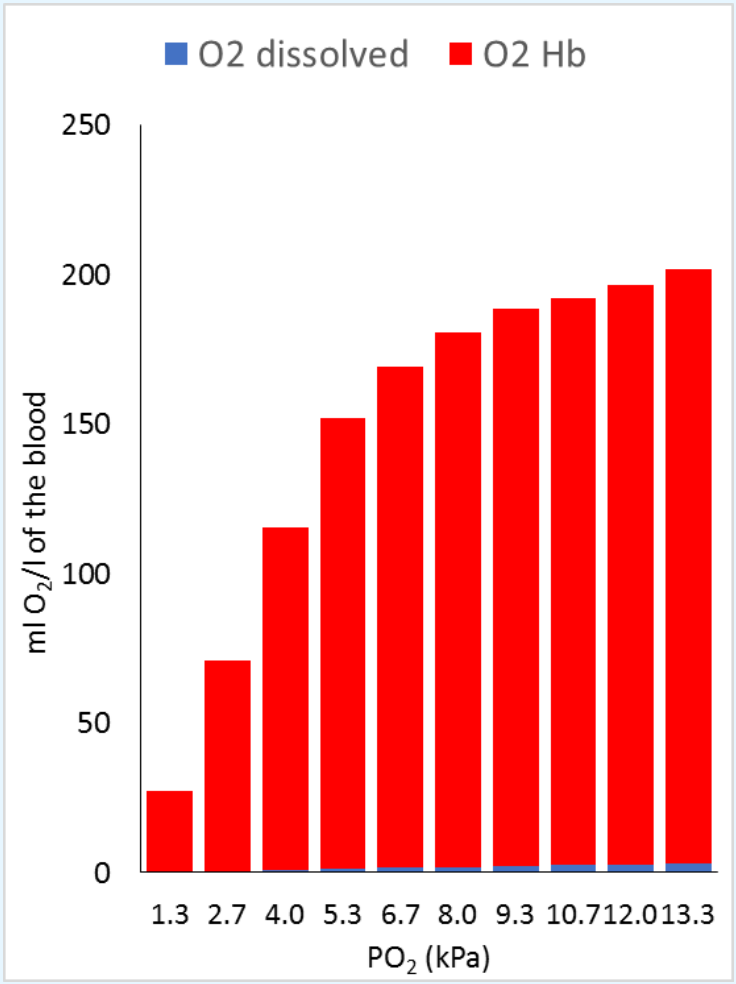
- ATP production in the mitochondria, oxidative processes

O_2 reserve for some 5 min: the lungs, blood, myoglobin in the muscles

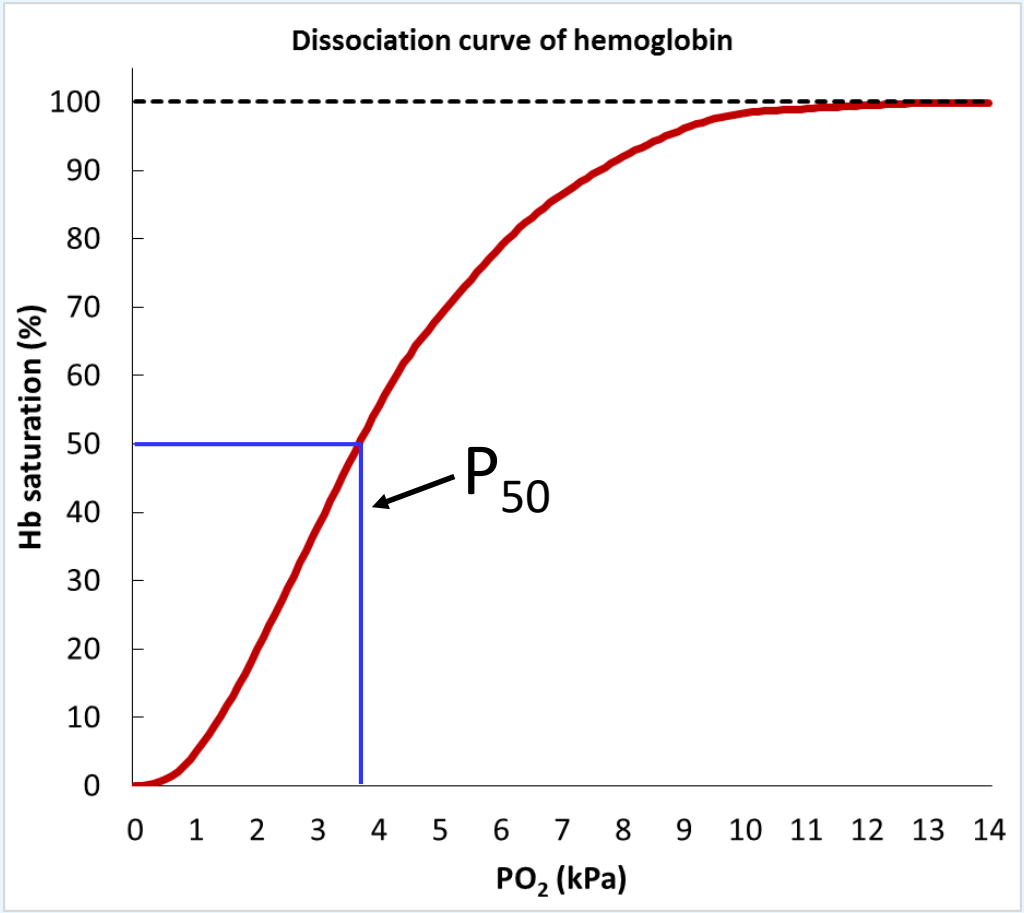
O_2 gradient between from the atmosphere to mitochondria



O_2 content in 1 l of the blood in in dependence on PO_2

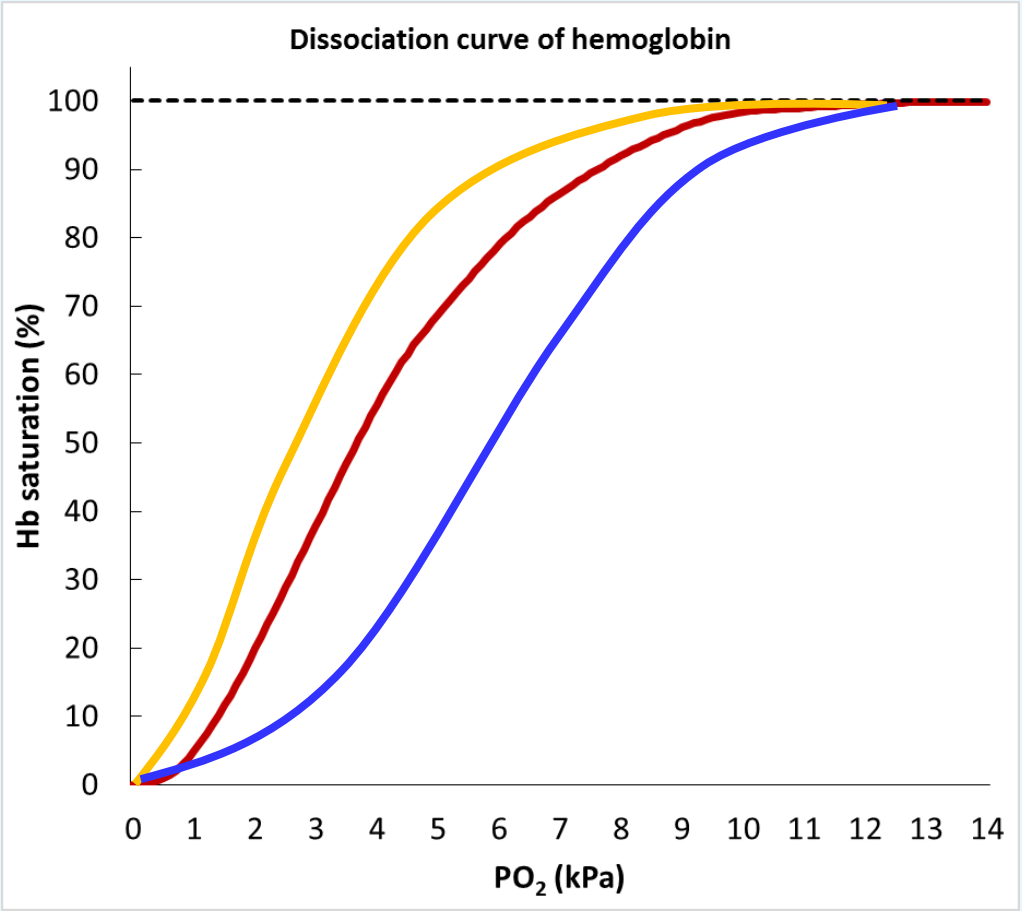


1 g HbO_2 → 1,34 - 1,39 ml O_2


Dissociation curve of hemoglobin
Hb saturation (%)
100
90
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
PO2 (kPa)
P50

Shift to the left:

- ↑ pH
- ↓ CO_2
- ↓ temperature
- ↓ 2,3-DPG



Shift to the right:

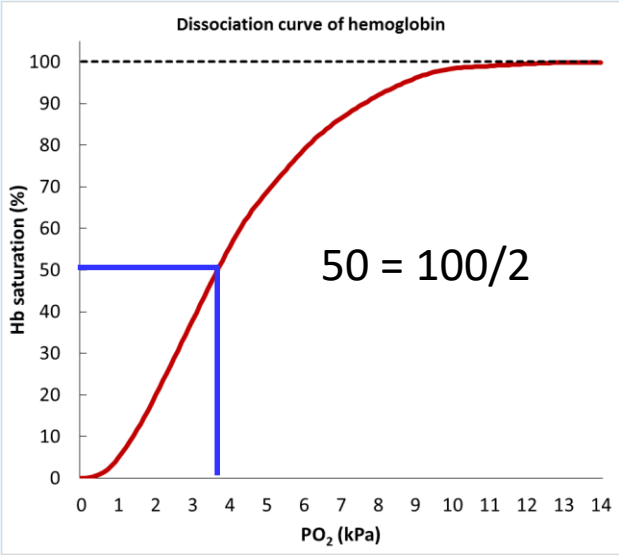
- ↓ pH
- ↑ CO_2
- ↑ temperature
- ↑ 2,3-DPG

CYANOSIS

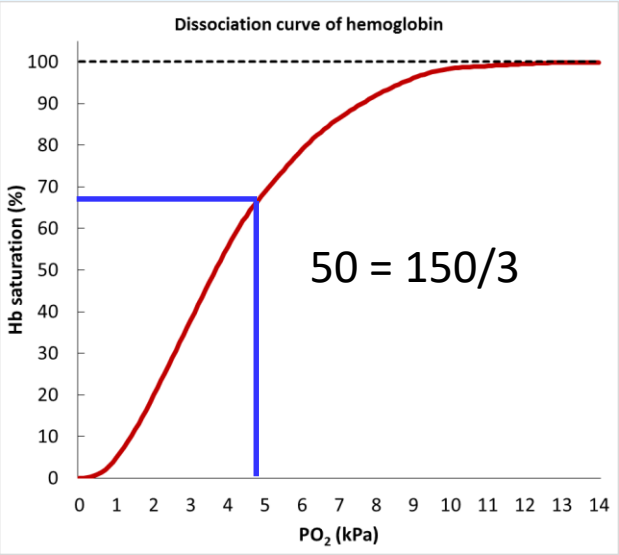
= blue or purple color of the mucous membranes and skin caused by reduced hemoglobin

- If reduced hemoglobin > 50 g/l
- It depends on:
  - hemoglobin saturation with O_2
  - total hemoglobin concentration → easy in the presence of polycythemia (polyglobulia)
    → less probable in anemia

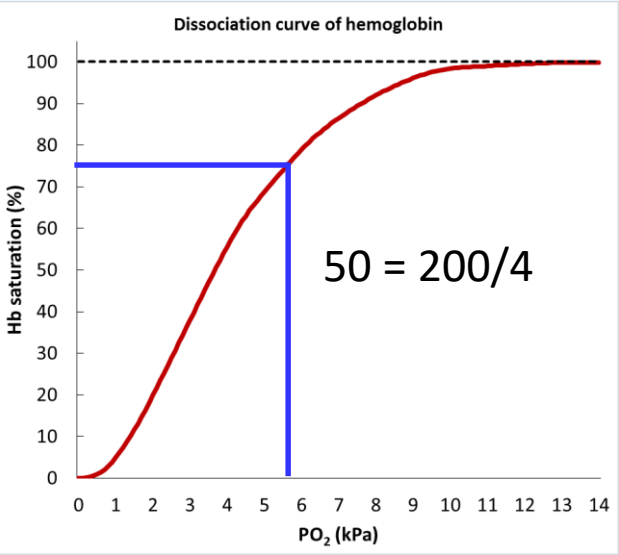
Anemia



Normal RBC



Polyglobulia



CYANOSIS

- **Peripheral**
  - restricted on some part of the body
  - blood stagnation (e.g. disorders of the veins)
- **Central**
  - whole body, more marked on mucous membranes
  - hypoxic hypoxia – respiratory disorders, right-left shunts

TYPES OF HYPOXIA

- Hypoxic
- Transport, anemic
- Circulatory
- Histotoxic

Hypoxic hypoxia

= hypoxia with decreased PaO_2

→ decreased hemoglobin saturation

→ decreased O_2 in the blood

→ decreased PvO_2 – higher O_2 extraction in the tissues

Affects the whole organism.

Causes:

- Low partial pressure of O2 in the air
  - high altitude, breathing in a restricted space, increased content of other gasses in the air
- Ventilation disorders
  - obstructive and restrictive disorders
- Disorders of diffusion in the lungs
  - restrictive disorders (↓ diffusion area), emphysema, pulmonary edema, pneumonia, ARDS
- Disorders of lung perfusion
  - pulmonary embolism, changes of ventilation/perfusion ratio
- Heart defects with right-left shunt + A-V shunts in the lungs

Hypoxic hypoxia

Manifestations: - depend on the cause and mechanism of hypoxia development

- Central cyanosis
- Dyspnea
- Fatigue, reduced fitness
- Disorders of organ function (the brain)
- Lactate acidosis (rather while performing simultaneous muscle activity)

Respiratory insufficiency

Partial, type 1

- Hypoxia without hypercapnia (even with hypocapnia)

Global, type 2

- Hypoxia + hypercapnia
- Ventilation disorders

$PaCO_2$ depends namely on lung ventilation.
Due to its good solubility, CO_2 is less affected by diffusion disorders than O_2.

Manifest – changes of respiratory gasses also during resting
Latent – respiratory gasses normal in rest but changed during physical activity

Transport (anemic) hypoxia

= hypoxia due to reduced capacity of the blood do bind O_2

→ normal PaO_2

→ normal hemoglobin saturation (if it is capable of O_2 binding)

→ reduced amount of O_2 in the blood

Affects the whole organism.

Causes:

- Anemia – lack of hemoglobin
- CO intoxication
- Methemoglobinemia = nitrate intoxication

Manifestations:

- Pallor in anemia, red skin in CO intoxication, cyanosis with grey shade in methemoglobinemia
- Fatigue, dyspnea, tachycardia, palpitation, functional heart murmur
- In severe cases (e.g. CO intoxication, severe anemia) organ disorders, disturbance of consciousness, death

Circulatory hypoxia

= hypoxia due to reduced blood perfusion of the tissues

→ normal PaO_2

→ normal hemoglobin saturation

→ normal O_2 content in the blood

→ usually reduced PvO_2 (↑ extraction of O_2 in the tissues)

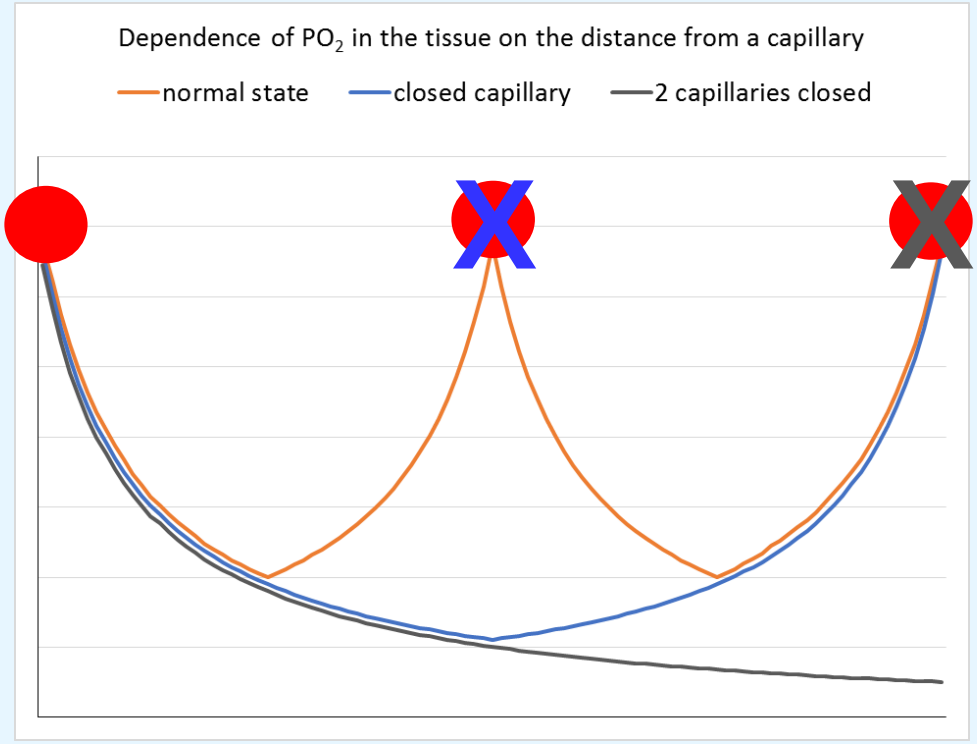
Globally or locally.

Causes:

- Ischemic
  - arterial occlusion
  - left heart failure
  - shock
- Stagnation
  - vein occlusion
  - right heart failure

Manifestation:

- Pain
- Pallor (ischemia)
- Cyanosis (stagnation)
- Organ affection



Reduced filling of circulation leads to collapse of some capillaries.

Histotoxic hypoxia

= hypoxia due to inability of the cells to use oxygen (mitochondria, cytochromoxidase)

→ normal PaO_2

→ normal hemoglobin saturation

→ normal O_2 content in the arterial blood

→ increased O_2 content in the venous blood

Usually global.

Causes:

- Cyanide intoxication
- Cobalt intoxication

Manifestation:

- No cyanosis, rather red skin (oxygenated blood in the veins)

Compensatory responses to hypoxia

- Activation of various reactions in individual types of hypoxia
  - It depends on PaO_2 and O_2 oxygen content in the arterial blood

    → activation of peripheral (aortal and carotic bodies, kidney, vessels, erythrocytes) and central chemoreceptors (respiratory center)

    → sympathetic activation, respiratory center activity influencing, erythropoietin production, vasomotor activity, 2,3-DPG production

- Local or global level
- Different efficiency in individual types of hypoxia
- Can complicate the state.

Compensatory responses to hypoxia

Local reactions:

- Vasodilation - induced by decreased PaO_2 or increased $PaCO_2$
  - ↑ blood flow

  But: generalized vasodilation → drop of peripheral resistance – a factor of shock pathogenesis

  But: In the lungs, hypoxia induces vasoconstriction → pulmonary hypertension

- Hb dissociation curve shift to the right → decreased affinity of Hb to O_2 → release O_2

- Anaerobic metabolism → lactate acidosis

- VEGF (vascular endothelial growth factor) expression → new vessels

- p53 expression → reduction of cell proliferation

Compensatory responses to hypoxia

Systemic reactions:

- Hyperkinetic circulation
  - acute reactions
  - sympathetic activation
  - efficient in the transport type of hypoxia

- Increased ventilation
  - acute reaction
  - ineffective in the anemia, efficient in reduced PO_2 in the air

  → hypocapnia → respiratory alkalosis

- Erythropoietin (kidneys, liver)
  - long-term response
  - polyglobulia, correction of the anemia
  - mainly in the hypoxic or circulatory type of hypoxia