Hypoxia

Hypoxia is defined as a deficiency in either the delivery or the utilization of oxygen at the tissue level, which can lead to changes in function, metabolism and even structure of the body.

Parameters

Classification, etiology and mechanism of hypoxia

Alterations of metabolism and function in the body

Pathophysiological basis of prevention and treatment

parameters

PO_2

CO_{2max}

CO_2

SO_2

P_{50}

PO_2 partial pressure of oxygen

PO2 is the tension produced by the oxygen molecules physically dissolved in plasma.

Normal PaO_2: 100mmHg

PvO_2: 40mmHg

Determined by PiO2 and pulmonary function

CO_{2max} oxygen binding capacity of hemoglobin

CO_{2max} refers to the maximal amount of oxygen that could be bound by the hemoglobin, which reflects the ability of hemoglobin carrying oxygen.

Normal value: 20ml/dl

Determined by quantity and quality of Hb

CO_2 oxygen content

CO_2 includes oxygen that is bound to hemoglobin and physically dissolved in the blood (0.3ml/dl).

Normal value: CaO_2:19ml/dl

CvO_2:14ml/dl

Determined by PO_2 and CO_2max

The arteriovenous oxygen content difference (CaO_2-CvO_2) reflects the oxygen volume of tissue uptake.

SO_2 oxygen saturation

SO_2 is the percentage of hemoglobin present as oxyhemoglobin .

Normal value: SaO2: 95%

SvO2: 75%

The relation between oxygen partial pressure and oxygen saturation is shown as oxygen dissociation curve (ODC).

An increase in 2,3-diphosphoglyceric acid (2,3-DPG), H^+, PCO_2 and temperature will shift the curve to the right, in turn to the left.

P_{50}

P_{50} means the oxygen partial pressure required to saturate 50% of the hemoglobin, which reflects the affinity of hemoglobin for oxygen.

Normal value P_{50}:26-27mmHg

Classification, etiology, mechanism of hypoxia

- Hypotonic hypoxia
- Hemic hypoxia
- Circulatory hypoxia
- Histogenous hypoxia

Hypotonic hypoxia

hypoxic hypoxia

Hypotonic hypoxia is characterized by the decrease of PaO_2(less than 60mmHg).

Etiology and mechanism

- Decreased PO_2 of inspired air
  - high altitude
- External respiratory dysfunction
  - hypoventilation
  - impaired diffusion
  - partial ventilation-perfusion imbalcance
- Venous-to-arterial shunt
  - congenital heart disease, Tetralogy of Fallot

Characteristics of blood oxygen

$PaO_2\downarrow$, $SaO_2\downarrow$, $CaO_2\downarrow$, CO_{2max} N,
CaO_2-$CvO_2\downarrow$/N

Cyanosis refers to the bluish color of skin, nails, lips and mucous membranes when the deoxyhemoglobin concentration of the blood in the capillaries is more than 5g/dl.

Hemic hypoxia

isotonic hypoxia

Hemic hypoxia refers to the altered affinity of Hb for oxygen or decrease in amount of Hb in the blood.

Etiology and mechanism

Anemia

Carbon monoxide poisoning

CO can react with Hb to form carboxyhemoglobin which can not take up oxygen. So there is a deficiency of Hb that can carry oxygen.

CO can inhibit glycolysis in RBC, which reduces the production of 2,3-DPG and shifts the ODC to the left, decreasing the amount of oxygen released.

Methemoglobinemia

The ferrous state (Fe^{2+}) in Hb may be oxidized to the ferric state (Fe^{3+}) under the action of oxidizers, e.g. nitrite and nitrobenzene, to form methemoglobin ($HbFe^{3+}OH$), which loses the ability to carry oxygen.

Methemoglobin can also make the ODC of normal HbO_2 shift to the left.

Enterogenous cyanosis

when a lot of pickled vegetables containing nitrate are taken, the reabsorbed nitrite reacts with $HbFe^{2+}$ to form $HbFe^{3+}$. The skin appears to coffee color. This phenomenon is called enterogenous cyanosis.

High affinity of Hb for O_2

- Alkaline solution
- Depot blood

Characteristics of blood oxygen

PaO_2 N, SaO_2N, CaO_2 ↓/N, CO_{2max} ↓/N, CaO_2-CvO_2 ↓

CaO_2-CvO_2 is below normal because PO_2 in the capillary is declined rapidly due to reduced CaO_2.

Severe anemia : pallor

CO poisoning : cherry red

Methemoglobinemia: coffee color

Circulatory hypoxia

hypokinetic hypoxia

Circulatory hypoxia refers to inadequate blood flow leading to inadequate oxygenation of the tissues, which is also called hypokinetic hypoxia.

Etiology and mechanism

Tissue ischemia

shock, left heart failure, thrombosis, arterial stenosis

Tissue congestion

shock, right heart failure

Characteristics of blood oxygen

PaO_2N, SaO_2N, CaO_2 N, CO_{2max} N, CaO_2-CvO_2 ↑

Because the blood flows slowly in the capillary due to ischemia or congestion, the tissues will take more oxygen from unit volume blood.

Patient with circulatory hypoxia may appear cyanosis.

Histogenous hypoxia

Histogenous hypoxia refers to the tissue cells can not make use of the oxygen supplied to them, though the amount of oxygen delivered to them is adequate.

Etiology and mechanism

Inhibition of oxidative phosphorylation

- tissue intoxicity

cyanides, sulphuret, rotenone,

(cytochrome oxidase)

Mitochondria injury

bacteriotoxin, radiation, free radical

Absence of Vitamin

Vit B1, Vit B2, Vit PP co-enzyme

Characteristics of blood oxygen

PaO_2 N, SaO_2N, CaO_2 N, CO_{2max} N, CaO_2-CvO_2 ↓

Oxygen content in vein increased because cells utilize less oxygen. The color of skin and mucous membrane are pink red flush.

Alterations of metabolism and function

Respiratory system

Circulatory system

Hematologic system

Central nervous system

Tissues and cells

Respiratory system

Compensatory response

Low PaO_2 stimulates the chemoreceptor in carotid and aortic body, which reflexly causes ventilation to increase.

Injury manifestation

High altitude pulmonary edema

Central respiratory failure

respiratory inhibition, irregular respiratory rhythm and frequency, hypoventilation, e.g. periodic breathing, Cheyne-Stoke respiration, Biot's breathing

Circulatory system

Compensatory response

Increased cardiac output

hyperventilation and pulmonary expansion stimulate lung stretch receptors, which reflexly excite sympathetic nerve.

Pulmonary vasoconstriction

Ca^{2+} influx↑, the action of vasoconstrictive substances and SN

Redistribution of blood

vasodilatation : heart and brain

hypoxia metabolites, lactic acid, adenosine

Ca^{2+} influx↓

vasoconstriction : skin, kidney, gastrointestinal tract

Capillary hyperplasia

HIF→VEGF

Injury manifestation

Pulmonary hypertension

Decreased diastolic and systolic myocardial function

Arrhythmia **Vagus Nerve**

Decreased venous return to heart

severe hypoxia

Hematologic system

Compensatory response

Increase in the amount of RBCs and Hb

More EPO produced and released by kidney

Improved RBC oxygen release capability

More 2,3-DPG produced from glycolysis process

Injury manifestation

Plasma viscosity↑, blood flow resistance ↑, afterload of heart ↑

When PO_2 is low markedly, 2,3-DPG will cause CaO_2 to decrease.

Central nervous system

Acute hypoxia: headache, agitation, poor faculty of memory, inability to make judgment, depress or loss of coordination

Chronic hypoxia: impaired concentration, fatigue, drowsiness

cerebral edema and neuron injury

Tissues and cells

Compensatory response

Enhanced cell capacity for use of oxygen

number and membrane surface of mitochondria↑

activity of succinic dehydrogenase and cyt-oxidase ↑

Enhanced anaerobic glycolysis

ATP↓ and ATP/ADP ↓→phosphofructokinase ↑

Enhanced myoglobin

Low metabolic state

Injury manifestation

Cell membrane injury

Na^+ influx cell swelling

K^+ efflux synthetic disorder

Ca^{2+} influx

phospholipase

Ca^{2+}-dependent protein kinase

Mitochondria injury severe hypoxia

Lysosome injury

Pathophysiological basis of prevention and treatment

Eliminating causes

Oxygen therapy

Hyperbaric oxygen therapy