**PATHOPHYSIOLOGY OF RESPIRATORY SYSTEM**

Each stage of the breathing (external respiration, transport of gases in blood, internal respiration) may be disturbed separately or together, and this makes impossible normal ensuring of the organism by the due amount of oxygen and removal of carbon dioxide. The pathological state in which due saturation of the blood by oxygen and removal of carbon dioxide are not ensured, is called respiratory insufficiency. The cases in which the normal content of the gases in the blood is maintained owing to the strenuous activity of the respiratory system and heart, are also classified as respiratory insufficiency is increased heart activity.

 Since function of the external respiration apparatus and activity of the blood circulation system are closely connected, one of the main compensatory changes under conditions of respiratory insufficiency.

 The main clinical symptoms of the respiratory insufficiency are dyspnea and cyanosis. In severe cases edema is observed as a result of heart failure.

 The respiratory insufficiency may be acute (attacks of bronchial asthma pneumothorax) and chronic. 3 stages of the chronic respiratory insufficiency are distinguished:

1. dyspnea is observed during physical work;
2. in the resting state need of the organism for oxygen is satisfied owing to compensatory mechanisms, and slight physical work causes dyspnea;
3. dyspnea and cyanosis are observed even in the resting state.

So, in the first period of the respiratory insufficiency the reserve potentials of the external respiration are limited, whereas in the severe forms the compensatory resources of the organism are completely exhausted; hypoxemia and hypercapnia come into being. In response to the decreased pulmonary ventilation and alveolar hypoxia, the pressure in pulmonary arteries is increased by reflex way. As a result of overstrain of the right ventricle myocardium and dystrophic changes in it caused by hypoxia, gradually right ventricular failure and congestion in the greater circulation develop; pulmonary heart comes into being.

 According to the etiologic factors and developmental mechanisms the following groups of the respiratory insufficiency are distinguished:

1. connected with disturbances in the pulmonary ventilation;
2. connected with disturbances in the alveolar diffusion;
3. not connected immediately with the pulmonary pathology (disorders in the activity of the respiratory center, decreased partial pressure of the oxygen, anemias, etc.).

To have an idea about the pulmonary ventilation the pulmonary volumes (tidal inspiratory and expiratory reserve, residual volumes) and capacities (inspiratory, functional residual, vital, total lung capacities) as well as pulmonary and alveolar ventilation are determined. Besides, the following indices characterize different aspects of the functional state of the respiratory system:

1. Maximal pulmonary ventilation (*MV*)-is the volume of the air that is inspired and expired per minute under condition of maximal strain of the respiratory system (normally- 80-200 *l/min*). It is determined in the condition of 50 maximal deep inspirations per minute.

2. Diffusion capacity of lungs (*DCL*)- is the ability of the alveolar capillary membrane to let in and out the gases. It reflects the volume of the gas that is able to pass through the membrane per minute when the pressure difference between its two sides is 1mm Hg. Normally the diffusion capacity of lungs for oxygen is 15-20ml/mm Hg per minute. It is calculated by the following formula:

1. Ventilation-perfusion ratio (*VA/Q*)-reflects conformity between activity of the lungs and functional state of the lesser circulation. Normally ventilation-perfusion ratio is 0.8, but it is widely changed in norm, as well as in pathology.

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1. Tiffeneau's index (TI):

*TI= Intensive vital capacity in the first second* x *100%*

*Vital capacity*

Normally Tiffeneau’s index is about 80%. In bronchial asthma it is decreased (40% and less).

*TI= 2.8l x 100% =80%*

*3.5l*

Changes in pulmonary ventilation are divided into three groups: alveolar hyperventilation, alveolar hypoventilation and uneven ventilation.

Alveolar hyperventilation is characterized by increased vital capacity, minute respiratory volume and maximal pulmonary ventilation. In healthy organism these changes are observed in the period of increased need for oxygen and disappear in resting state. Pathological hyperventilation is observed in the following cases:

1. pathological processes accompanied by increased excitability of the respiratory center (cerebral hemorrhage, tumor of the brain);
2. pathological states causing hypoxemia (anemia, high altitude sickness, mountain sickness);
3. arterial hypertension;
4. compensatory hyperventilation caused by decreased respiratory surface of lungs (pulmonary edema, pneumonia).

Protracted hyperventilation results in decreased carbon dioxide content in the blood and respiratory alkalosis.

 Hypoventilation accompanies the following cases:

1. a number of pulmonary diseases ;
2. deformation of chest (kyphosis, scoliosis);
3. pathological processes in respiratory muscles;
4. hypofunction of respiratory center;
5. increased intracranial pressure;
6. disorders in cerebral circulation.

 Uneven ventilation is observed when alveoli participate in breathing unequally. Usually it is not accompanied by hypercapnia, but in severe cases may result in hypoxemia. The following factors cause uneven ventilation:

1. decreased elasticity of lungs ( pulmonary emphysema );
2. disturbed bronchial conduction ( bronchial asthma);
3. accumulation of exudate in alveoli.

Various forms of respiratory insufficiency differ from one another by mechanism of the disturbances in ventilation. The following factors play a part in etiology and pathogenesis of respiratory deficiency:

Decreased atmospheric pressure and changes in the composition of the inspired air.

Disorders in the control mechanisms of the pulmonary ventilation (changes in the nerve centers):

1. lesions of the brain (inflammation, tumor, circulatory disorders, edema);
2. some forms of neurosis and psychosis;
3. decreased excitability of the respiratory center resulted from protracted severe hypoxia (decreased atmospheric pressure, circulatory disorders, carbon monoxide poisoning, anemias);
4. influence of the narcotic and toxic substances on the respiratory center.

Disturbed function of the respiratory muscles, lesion to their nerves (in poliomyelitis, myositis, myasthenia, polynevritis, tetanus, botulism).

Thoracodiaphragmatic disturbances, that is, limited excursion of lungs and diaphragm caused by deformation of chest (damage to ribs and vertebrae, ossification of costal cartilages), pleuritis, pleural adhesion, ascites, meteorism, severe obesity, violent pain (intercostal neuralgia, dry pleurisy). In paralysis of phrenic nerve paradoxical breathing is observed, that is, in the period of inspiration diaphragm rises and limits the possibilities of the lungs to expand; during the expiration they come down.

Disturbances in functions of the upper respiratory tract caused by inflammatory diseases and obstruction (complete or partial) of their lumen (rhinitis, polyp, twist of nasal septum, damage to ciliated epithelium).

Disturbances in functions of larynx and trachea. Their stenosis and partial obstruction by foreign bodies are accompanied by stenotic (rare and deep) breathing, whereas complete obstruction of their lumen causes asphyxia.

Disturbances in functions of bronchi-frequently are caused by inflammatory processes (bronchitis) or allergic reactions (bronchial asthma). Lumina of bronchioles are narrowed, the sputum accumulated in bronchi and bronchioles makes difficult the pulmonary ventilation. Attacks of bronchial asthma promote decrease of elasticity of lungs, development of emphysema.

Disturbances in functions of pulmonary alveoli- are observed in pneumonia, emphysema, pneumosclerosis, atelectasis, etc. In pneumonia part of alveoli is obstructed by exudate, alveolar ventilation is decreased and gaseous exchange is weakened.

 In emphysema elasticity of alveolar walls is decreased, interalveolar septa are atrophied, their epithelial cells are replaced by connective tissue, blood flow in the most of pulmonary capillaries is ceased, vital capacity decreases 20-60%. As a result of decreased pulmonary elasticity expiration becomes difficult (expiratory dyspnea). Damage to alveolar walls, obliteration of capillaries and uneven ventilation result in hypercapnia and hypoxemia.

 Atelectasis (pulmonary collapse) is caused by squeezing of pulmonary tissue (accumulation of fluid in the pleural cavity, pneumothorax, tumors), obstruction of lumina of bronchi, disturbed synthesis of surfactant. Collapsed alveoli do not participate in ventilation.

9. Diseases and lesions of pleura. Accumulation of fluid (exudative pleurisy, hydrothorax, hemothorax) or air (pneumothorax) in the pleural cavity may cause atelectasis. In cases of considerable (1.5-2 liters) accumulation of fluid in the pleural cavity clearly marked disorders of gaseous exchange occur as a result of crowding of the mediastinum to the opposite side and compression of the other lung with resultant circulatory disturbances. Circulatory disturbances result from diminished aspirating action of the thorax and displacement of the heart which hinders the blood inflow from the veins. Pain also limits the respiratory movements.

 Pneumothorax develops as a result of entrance of air into pleural cavity by the following ways:

1. traumatic injury (penetrating wound) to the chest;
2. injury to pulmonary tissue (tuberculosis, abscess, emphysema, gangrene);
3. artificial administration of air into pleural cavity in tuberculosis when it is necessary to exclude the affected lung from respiration, compress it and thereby hasten cicatrisation of the cavernous focus.

 Three forms of the pneumothorax are distinguished:

1. Closed pneumothorax-has no opening through the chest wall; it may result from sudden and very sharp elevation of intrathoracic pressure;
2. Open pneumothorax-the outside air freely enters the pleural cavity and leaves it through an opening during inhalations and exhalations; the air may compress the lung on the healthy side, owing to which the volume of inhaled air is sharply reduced and severe dyspnea and circulatory disturbances develop. In the opening is large, paradoxical breathing may be observed: during inspiration the volume of lung on the side of pneumothorax is decreased whereas during expiration it is increased (part of air from the healthy lung enters the collapsed lung).
3. Valvular pneumothorax-the orifice opens during inhalations and air is pumped into the pleural cavity until the pressure of the air in it equals that of the atmospheric air.

Obstructive and restrictive types of ventilation insufficiency are distinguished. Obstructive type is connected with narrowing of the respiratory tracts (squeezing of the trachea and bronchi by tumors, bronchitis, bronchiectasia). It causes decreased adaptability of the respiratory system to the additional functional strain: increased respiration rate, rapid inspiration and expiration become impossible.

 Restrictive type of respiratory disturbances is connected with decreased ability of lungs to expand and contract. This type is observed in pulmonary diseases (pneumosclerosis); as well as in lesions of pleura (hydrothorax and pneumothorax) deformities of the chest (ossification of costal cartilages, kyphoscoliosis, etc.). In these cases the vital capacity is decreased (breathing becomes superficial), but respiration rate may be increased according to needs of the organism.

 Mechanism of respiratory insufficiency connected with the following factors is also based on the disturbances in the ventilation:

1. increased ratio of pulmonary residual volume to the tidal volume (emphysema);
2. increase of the anatomic dead space (a large cavern, abscess, bronchiectasia).

Since the diffusion coefficient of carbon dioxide is 20 times that of oxygen, in diseases of the respiratory system its diffusion is changed comparatively less than that of oxygen. Alveolar diffusion is disturbed in the following cases:

1. decreased partial pressure of the oxygen in the alveolar air (decreased amount of O2 in inspired air, disturbed pulmonary ventilation );
2. decreased total surface area of alveoli (pulmonary edema, pneumonia, atelectasis squeezing of lungs by tumors, exudate, air );
3. thickening of the alveolar and capillary membranes (interstitial edema, formation of hyaline membranes in alveoli).

Diffusion of gases through pulmonary membranes depends considerably on the pulmonary blood flow.

Under the conditions of the decreased pulmonary blood circulation efficiency of the respiration also is decreased. In respiratory insufficiency connected with circulatory disorders (thromboembolism of the pulmonary artery) dispite the fact that ventilation in the injured area of the lungs is continued, it does not participate in ventilation. The blood passing through this area is not enriched by O2.

When circulation rate in pulmonary capillaries is increased, erythrocytes cannot take sufficient amount of oxygen.

To elucidate relations between the activity of lungs and state of pulmonary circulation, ventilation-perfusion ratio is determined. Some pathological reflexes cause disparity between ventilation and perfusion: decreased pO2 in alveoli causes rapid rise of pressure in pulmonary arteries (Euler-Lillestrand reflex); at the same time blood flow is increased in the area of lungs where pO2 is reduced (Rossier-Boulman reflex). This strengthens unevenness of the blood flow and ventilation.

Changes in the gaseous composition of the blood include hypoxemia, hypercapnia and hypocapnia.

Hypoxemia, that is, insufficient oxygen in the blood (pO2 in arterial blood < 90-80 mm Hg) occurs in severe anemias, after considerable loss of blood, in marked functional disorders in the hematopoietic system. Hypoxemia results in cyanosis and hypoxia in tissues.

Hypercapnia (pCO2 in arterial blood > 40-45 mm Hg) results from decreased excitability of the respiratory center and diseases of the external respiration apparatus. Hypercapnia causes increase in activity of the respiratory center and accelerates pulmonary ventilation, promoting this way excretion of the carbon dioxide.

 Hypocapnia results from excessive excretion of carbon dioxide from the organism. Its main cause is decreased pO2 in the inspired air which causes reflex activation of the respiratory system.

 Disturbances in the respiratory rhythm are observed in dyspnea, pathological forms of respiration, asphyxia, respiratory defence reflexes.

 Dyspnea is laboured (difficult) breathing characterized by disturbances in the rhythm and strength of the respiratory movements. It is observed in states in which physiological needs of the organism for oxygen are increased or the oxygen that enters the organism through lungs does not satisfy its needs. In dyspnea the regulation of respiration is disturbed; respiration may be accelerated or decelerated, shallow or deep. Dyspnea is usually accompanied by distressing sensation of lack of air.

 The main causes of dyspnea are the following:

1. humoral factors (changes in gaseous composition and pH of the blood, accumulation of underoxidized metabolites);
2. stimulation of the respiratory center by impulse coming from receptors of the respiratory system;
3. influence of the central nervous system (especially of the cerebral cortex) on the respiratory center (in the states of fear, agitation, hysteria).

 The following types of dyspnea are distinguished:

1. inspiratory dyspnea (long and difficult inhalations)-is connected with stenosis in the upper respiratory tracts and trachea (tumors, diphtheria, laryngeal edema), laryngospasm, foreign bodies in the respiratory tracts;
2. expiratory dyspnea (long and laboured exhalations) – is observed in diseases that are accompanied by decreased elasticity of lungs (emphysema), spasm and obstruction of bronchioles by mucus (bronchial asthma);
3. mixed dyspnea (both respiratory phases are difficult).

Pathological forms of respiration include Kussmaul’s respiration, periodic respiration (Biot’s respiration and Cheyne-Stokes respiration) and agonal respiration.

 Long respiratory movements followed by long pauses characterize Kussmaul’s respiration. It is accompanied by noise. Kussmaul’s respiration may occur in diabetic coma, uremia, eclampsia, etc.

 Biot’s respiration is characterized by pauses in ordinary respiration, that is, a series of respiratory movements are followed by a long pause, after which there is a new series of respiration movements, etc. It is observed in meningitis, encephalitis, some cases of poisoning, heat stroke.

 Cheyne-Stokes respiration is characterized by increasingly greater respiratory movements which reach their maximum and then gradually decrease, the respiration unnoticeably becoming shallow and ending in a pause which lasts up to 30 seconds; after the pause the same phenomena recur. It occurs in extreme cases of oxygen deficiency, for instance, in severe pulmonary insufficiency, chronic nephritis, decompensated heart diseases, cerebral lesions (sclerosis, hemorrhages, embolisms, tumors), increased intracranial pressure and mountain sickness.

 Periodic respiration, Cheyne-Stokes respiration in particular, is based on oxygen deficiency and reduced, excitability of the respiratory center which reacts weakly to the usual carbon dioxide concentration in the blood. During suspension of respiration carbon dioxide accumulates in the blood with the result that respiration is resumed, the excess carbon dioxide is eliminated from the blood and respiration is suspended again. Inspiration of oxygen and carbon dioxide mixture eliminates periodic respiration.

 Agonal respiration is observed in the period of death struggle (agony) terminal pause. At first weak, then strong inspirations reach maximum, gradually their intensity decreases and respiration stops. This is deep convulsive breathing characterized by participation of skeletal muscles, especially those that do not take part in ordinary respiration (the muscles of mouth, neck, etc.); the head is thrown back, the mouth is widely open. The agonal respiration is resulted from sharp excitation of the bulbar respiratory center, which is deprived of the regulating influence of the higher part of the brain.

 Apnea, that is, rather long respiratory pauses or suspensions of respiration, may occur after excessive pulmonary ventilation as a result of sharp decrease in carbon dioxide in the blood. It may arise also by reflex way, for instance, in response to stimulation of the different vagus nerve fibers. Apnea in the newborns also is due to carbon dioxide deficiency in their blood.

 Asphyxia is the most severe form of the acute respiratory insufficiency- the organism does not receive oxygen, and carbon dioxide does not abandon it.

 The main etiologic factors of asphyxia are the following:

1. squeezing of the respiratory tracts (strangulation);
2. occlusion of the respiratory tracts by tumor or foreign bodies;
3. getting of the fluid into the respiratory tracts (amniotic water in fetus) and lungs (in drowned persons);
4. laryngeal or pulmonary edema;
5. paralysis of the respiratory muscles;
6. paralysis of the respiratory center;
7. sharp decrease of oxygen in air;
8. disturbances in transport of oxygen into tissues (acute loss of blood, poisoning by carbon monoxide);
9. disturbance in tissue respiration (poisoning by cyanides).

 Experimentally asphyxia may be produced by compression of the trachea or administration of various suspensions into the respiratory tract of animals.

 Asphyxia presents characteristic picture of respiratory, blood pressure and cardiac disturbances. Mechanism of changes in asphyxia is connected with hypoxia, hypercapnia, acidosis which cause also reflex action. Acidosis is connected with hypercapnia and increased amount of underoxidized metabolites.

 4 stages are distinguished in the development of the asphyxia:

1. inspiratory dyspnea - elevated blood pressure and increased heart rate;
2. expiratory dyspnea - decreased heart rate;
3. preterminal pause (respiratory standstill from several second to 1-2 minutes) - decrease of arterial pressure, loss of consciousness;
4. terminal respiration - changes at this stage are due to exhaustion of the nerve centers: extinction of reflexes, dilatation of the pupils, relaxation of muscles, drop in arterial pressure, decreased heart rate; the period ends in a few terminal respiratory movements and respiratory paralysis.

 The terminal respiratory movements are governed by the lower weakly excitable parts of the spinal cord, which take over the function of the paralyzed respiratory center.

 In man acute asphyxia lasts 3-4 minutes. Cardiac contractions continue some time after respiratory standstill, and it is still possible to revive the organism before complete cardiac arrest.

 Respiratory defence reflexes include coughing and sneezing. Coughing arises reflexly during irritation (by mucus, foreign matter or any other cause) of the air passages (mainly that of the mucosa of the trachea and bronchi) and sneezing- from that of nasal mucosa. Both coughing center and sneezing center are localized in the medulla oblongata.

 In coughing afferent impulses passing from the respiratory passages (mainly through the vagus nerves) to the medulla oblongata cause the following sequence of events. About 2.5 liters of air is inspired. The epiglottis closes, and the vocal cords shut tightly to entrap the air within the lungs. The abdominal muscles and expiratory muscles (internal intercostals) contract forcefully, the pressure in the lungs rises. The vocal cords and epiglottis suddenly open widely so that air under pressure in the lungs explodes outward. The rapidly moving air carries with it any foreign matter that is present in the bronchi or trachea.

 Sometimes coughing arises as a result of stimuli originating in the pleura, peritoneum, posterior wall of esophagus, liver, spleen and directly in the central nervous system, for instance, in the cerebral cortex (encephalitis, hysteria). In these cases coughing is of no defence importance. Also, the violent coughing, by causing elevated pressure in the thoracic cavity, weakens its aspirating force. The outflow of blood through veins to the right heart may be impeded; the venous pressure drops and the cardiac contractions become weaker. Delivery of blood to the left auricle is hindered as a result of increased pressure in the alveoli and compression of the pulmonary capillaries and veins. Therefore, the blood flow is disturbed not only in the lesser circulation, but also in the greater circulation. Protracted coughing results in frequent changes of the pressure in lungs; alveolar septa are damaged, elasticity of lungs is decreased and emphysema develops.

 Yawning is deep breath when the rima vocalis is abruptly open, then effort is continued in inspiration when the rima vocalis is closed and once again when it is open. It is believed that yawning is directed to expanding of physiological atelectasis, volume of which is increased in the state of fatigue and sleepiness.

The main factors causing disturbances in the transport of oxygen from lungs to tissues are the following:

1. anemia;
2. cardiovascular insufficiency (decreased circulation rate);
3. weakened dissociation of the oxyhemoglobin;
4. insufficiency in the external respiration.

 Tissue (internal) respiration, that is, absorption of oxygen from the blood, its assimilation by cells and discharge of carbon dioxide into the blood, may be disturbed under influence of exogenous and endogenous factors. The exogenous causes include all the substances that affect the oxidative processes in the tissues by influencing the organs from without:

1. phosphorus-depresses the oxidative processes in the tissues by combining with oxygen;
2. arsenic;
3. cyanide compounds-inactivate cytochrome oxidase and this way disturb oxidation processes in tissues;
4. narcotics-decrease activity of dehydrases in cells;
5. some bacterial toxins.

 The endogenous causes are all the factors which, arising within the organism, disturb the oxidative processes in tissues:

1. dysfunction of certain endocrine glands - in hypothyrosis, hypofunction of hypophysis and sexual glands the oxidative processes in tissues are depressed; adrenaline, insulin and other hormones exert direct or indirect influence on tissue respiration;
2. malignant tumors, avitaminoses, infectious processes, severe cardiovascular disorders-cause disturbances in tissue respiration both in individual organs and in all of the organism’s tissues;
3. dysfunction of the nervous system-trophic ulcers of the neurogenic origin;
4. anemia-carbonic acid is accumulated in tissues and acidosis develops.

 Hypoxia (oxygen deficiency)-is typical pathological process connected with insufficient oxygen supply of tissues or inadequate utilization of oxygen by tissues.

 All types of hypoxia are divided into two groups:

1. Exogenous hypoxia-is connected with decreased partial pressure of the oxygen in the inspired air.
2. Endogenous hypoxia-is connected with diseases of the organism.

 Exogenous hypoxia may be hypobaric or normobaric. It is observed in the following cases:

1. mountain sickness, high altitude sickness, etc.;
2. in badly ventilated mines and wells;
3. faulty oxygen supply systems of diving suits, flying apparatuses, submarines, resuscitation apparatus, intratracheal narcosis apparatuses.

 In experiment the exogenous hypoxia is reproduced by keeping the animal in the chamber where the inert gases are added to the air or by using the rarefied air in the altitude chamber.

 Exogenous hypoxia causes hypoxemia, hypercapnia, acidosis, disturbances in the electrolytic balance.

 The following forms of the endogenous hypoxia are distinguished:

1. respiratory (pulmonary) hypoxia-is connected with disturbed gaseous exchange in the pulmonary alveoli (weak alveolar ventilation, impeded diffusion of the oxygen through alveolar-capillary membranes, disturbed proportionality between pulmonary ventilation and diffusion, increased number of arteriovenous anastomoses);
2. circulatory (cardiovascular) hypoxia-is resulted from disturbed cardiovascular system activity and decreased circulating blood volume (decompensated heart diseases, myocardial infarction, cardiac tamponade, cardiosclerosis, shock, severe infectious diseases, allergic reactions, etc.); ischemia and venous hyperemia in certain organ or tissue causes local hypoxia;
3. hemic (blood) hypoxia-develops as a result of decreased oxygen capacity (anemia, hydremia, carboxyhemoglobinemia, poisoning with oxidizing substances), changes in ability of hemoglobin to combine with oxygen;
4. histotoxic (tissue) hypoxia-develops as a result of decreased ability of tissues to take the oxygen (cyanide poisoning, hypothyroidism, hypofunction of hypophysis and sexual glands, avitominoses);
5. mixed types of hypoxia.
6. Hypoxia of load and substratum type of hypoxia are also distinguished.

 In the processes of adaptation of the organism to the state of hypoxia compensatory reactions of the respiratory and cardiovascular systems, blood and tissues play a great part:

1. respiratory compensatory mechanisms: increased alveolar ventilation (deep and frequent breathing) as a result of irritation of the vascular reflexogenic zones and brain stem;
2. hemodynamic compensatory mechanisms: reflex tachycardia, mobilization of the blood from depots, redistribution of the circulating blood;
3. hematogenic compensatory mechanisms: increased oxygen capacity (as a result of increased number of erythrocytes and content of hemoglobin in the blood) and rapid dissociation of oxyhemoglobin (resulted from acidosis and decreased pO2 ) as a result of which tissues take more oxygen;
4. tissue compensatory mechanisms: more active absorption of oxygen from the blood and predominance of the anaerobic glycolysis in the metabolic processes; in the adaptation of tissues to hypoxia great is role of activation of the hypothalamohypophyseal system and hypersecretion of glucocorticoids.

In severe and long states of hypoxia the organism’s adaptive possibilities are exhausted and the decompensated stage of hypoxia sets in. At this stage a number of functional and morphological changes occur in tissues and organs intensity of which depends on the functional state of the cells and properties of the metabolism.

 The most severe changes occur in the central nervous system (in cerebral cortex, then in brain stem, spinal cord). Hypoxia in brain cause, at first, excitation (euphoria), and then inhibition, sleepiness, headache, ataxia.

 The second (after brain cells) for its sensibility to hypoxia is the cardiac muscle. Hypoxia causes tachycardia, weakness in myocardium’s mechanical capacity for work, decreased stroke volume. In severe cases tachycardia is replaced by bradycardia; arrhythmia, pallor, coldness in extremities, cold sweat are observed, syncope occurs. In the first periods of hypoxia arterial pressure is increased, then decreased rapidly (as a result of disturbances in activity of the vasomotor center and decreased stroke volume).

 In acute hypoxia breathing becomes superficial and frequent; pulmonary ventilation is disturbed, sometimes periodic respiration of Cheyne-Stokes type is observed.

 In severe hypoxia motor activity of the stomach and intestine is weakened, secretion of the digestive juices is decreased.

 Hypoxia causes changes in the metabolism. Disturbances in the process of biological oxidation are the first. ATP in cells as decreased, products of its breakdown are increased. Accumulation of acid metabolites cause metabolic acidosis. Negative nitrogen balance, changes in the electrolyte metabolism, disturbances in synthesis of mediators are observed.

 The tissues with low sensibility to hypoxia (bones, cartilages) may continue their vital activity under conditions of oxygen deficiency for a long time.