

## Features of the Development of Secondary Tissue Hypoxia in Persons of Different Ages

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### Abstract

Oxygen play a key role in the life of the cell. Hypoxia leads to a disorder of the vital activity of the organism as a whole. The aim of the work is the analysis and synthesis of literature data on the development of the respiratory system and study hypoxia in the altitude. The features of the formation of compensatory and adaptive mechanisms are traced. Due to the fact that many disease is accompanied by hypoxia, their further investigation with various pathologies in the clinic and experiment is promising and relevant.

**Keywords:** Hypoxia; Age; Oxygen; Altitude

Extensive literature and the results of our many years of research indicate the significant role of the age factor in the body's response to lack of oxygen. The development of the central nervous system and its higher divisions, which occurs in the process of ontogenesis, causes an increase in sensitivity and a decrease in the body's resistance to hypoxia; along with this, the role of the nervous system in the management of the respiratory system, which changes with age, in the implementation of compensatory reactions, is enhanced.

At each stage of individual development, depending on the oxygen demand of the body and the possibilities of its satisfaction in real conditions, a greater or lesser load falls on one or another link of the respiratory system. At the earliest stages of embryonic ontogeny, changes at the molecular, subcellular, and cellular levels play a predominant role in the adaptation of respiration to the environment [1]. During the development of the embryo and fetus, the appearance, growth and differentiation of its gas transport link - the cardiovascular system and blood - is of primary importance for the functioning of the respiratory system. The fetus, along with this, has specific features of the respiratory function of the blood: the fractional composition of hemoglobin (the main carrier of

oxygen and carbon dioxide) in the fetus differs from the fractional composition of hemoglobin and its oxygen-binding properties in the child [2]. The fetal oxyhemoglobin dissociation curve is shifted to the left [2].

The respiratory system of the fetus becomes complete only after the birth of the child, and with the beginning of the functioning of the lungs, it acquires the ability to carry out direct gas exchange between the blood and the air [3,4].

During the periods of the first and second childhood and at primary school age, a relatively smooth (mainly quantitative) development of the respiratory system occurs. During puberty, along with quantitative changes, more and more pronounced qualitative changes occur in the entire respiratory system, leading to a significant increase in the efficiency and economy of the body's oxygen regimes, and an improvement in the quality of their regulation.

With the growth and development of the body, the power of the respiratory system gradually increases, reaching a maximum level in middle age. From birth to puberty, the rate of oxygen supply to the

lungs, alveoli, its transport by arterial, mixed venous blood and the rate of its consumption by tissues increase. In the process of growth and development of the child, the function of the respiratory system is economized: the volume of air entering the lungs and the volume of circulating blood required to utilize each liter of oxygen become smaller (ventilation and hemodynamic equivalents decrease), the oxygen effect of the respiratory and cardiac cycles increases, increases the efficiency and economy of the oxygen regimes of the body, the range of external disturbances is expanded, under which the correspondence between the rate of oxygen delivery and the oxygen demand of the body is maintained. With an age-related decrease in the intensity of oxidative processes, the development of mechanisms that ensure a more complete utilization of oxygen from the blood and an increase in the use of oxygen from the alveolar air causes an even greater decrease in the intensity of oxygen supply to the lungs and alveoli, its transport by blood. This leads to the fact that the oxygen regimes of the body become more intense with age, the pressure gradients  $PO_2$  (alveolar-venous and arterial-venous) decrease, the partial pressure of oxygen in the alveolar air and its tension in the arterial blood decrease, and the partial pressure carbon dioxide rises.

The revealed patterns apply to the entire life cycle, with the exception of the neonatal period, pubertal and senile ages, which attract special attention of physiologists and doctors [5].

During the period of the first and second childhood, the development of the respiratory system proceeds smoothly, the efficiency and economy of the body's oxygen regimes increase, and the quality of their regulation improves. At puberty, the increase in the efficiency and economy of the body's oxygen regimes and the quality of their regulation seems to be suspended. The restructuring of the nervous and humoral regulation of vital functions taking place at this time in the body is not always sufficiently uniform, the growth and development of the external respiration and circulatory systems, with an increasing need for oxygen in a rapidly growing organism, lead to a deterioration in the quality of regulation of the oxygen regimes of the body: their efficiency decreases, their ventilation and hemodynamic equivalents, the coefficient of oxygen utilization decreases, the boundaries of external disturbances narrow, at which the high quality of regulation of the oxygen regimes of the body is maintained [6]. In middle age, the respiratory system reaches its full development, its function becomes most efficient and economical [7].

In old age, which is the final stage of the life cycle, changes in the respiratory system and oxygen regimes of the body are especially pronounced [8]. The thorax, airways and lungs undergo structural and functional changes, the respiratory rhythm becomes more frequent, the minute volume of breathing increases, the relationship between pulmonary and alveolar ventilation changes, the physiological dead space significantly increases and the share of alveolar ventilation in the minute volume of breathing decreases. Despite the increase in minute volume of respiration, alveolar ventilation decreases, which, along with compaction of the alveolar-capillary membrane, a decrease in the diffusion surface of the alveoli and a deterioration in the process of oxygen diffusion through the alveolar-capillary membranes, leads to an increase in the alveolar-capillary  $PO_2$  gradient, a decrease in tension and oxygen content in the arterial blood and oxygen saturation. The transport of oxygen by the blood undergoes pronounced changes: with aging, not only the oxygen capacity of the blood and the oxygen content in it decrease, but also the function of the cardiovascular system deteriorates significantly, the rate of mass transfer of oxygen by arterial blood decreases, the number of functioning capillaries decreases, the conditions of macro- and microcirculation are disturbed and changes the rate of oxygen delivery to individual cells. A decrease in blood flow velocity, deterioration of microcirculation, a decrease in the oxygen capacity of the blood, arterial blood saturation with oxygen and oxygen content in it, lead to a decrease in the speed and intensity of oxygen delivery to tissues, to a greater uneven distribution of  $PO_2$  in them, which affect on the ability of cells to utilize oxygen [9,10].

In the cardiac and skeletal muscles of old animals, the conditions for oxygen diffusion deteriorate significantly: the distance between functioning capillaries increases, the density of capillaries in the tissue decreases, their length increases, which leads to a decrease in  $PO_2$  in certain areas of the tissues, to a greater uneven distribution [11]. The biochemical properties of the tissue also change. In the muscles, the content of myoglobin decreases, the activity of respiratory enzymes decreases. All this complicates the utilization of oxygen. The intensity of oxygen consumption decreases with aging, the oxygen regimes of the body become less efficient and economical, and, in contrast to what is observed in puberty, more intense.

Arterial hypoxemia, slowing down of systemic blood flow, decrease in hemoglobin content in the blood cause a decrease in the

rate of oxygen delivery to tissues, and microcirculatory disorders - more pronounced than at a young age, uneven supply of oxygen to various parts of tissues and individual cells [12]. Damage of the tissue in cellular, mitochondrial, and molecular levels resulting from a decrease in oxygen delivery, leads to a decrease in the ability of tissues to utilize oxygen, resulting in an increase in critical  $P_{O_2}$  level in tissues [13]. This, along with changes in the neurohumoral mechanisms of respiration regulation, causes significant changes in the oxygen regimes of the body during aging [14].

In this way, in old age, respiratory, circulatory, hemic hypoxia are combined, the intensity of tissue respiration decreases, which explains the peculiarity of hypoxic conditions in this age period.

The level of development of the respiratory system and the nerve formations that control it determines the characteristics of the body's response to oxygen deficiency and the specifics of hypoxic conditions at different stages of ontogenesis [15]. Reflex compensatory reactions to a decrease in  $P_{O_2}$  in children and adolescents differ from similar reactions in adults. In hypoxic hypoxia, their respiratory minute volume and alveolar ventilation increase to a lesser extent than in middle-aged and old people.

A feature of the reaction of external respiration of preschool children to the inhalation of rarefied air is an increase in the respiratory rhythm. When the air is rarefied in the hyperbaric chamber, a pronounced increase in breathing in preschoolers is noted at an "altitude" of 2000 and 3000 m. Similar results were recorded in mountainous conditions, that is, increased breathing is a natural reaction of the child's body to a lack of oxygen in the inhaled air. The respiratory rate at an altitude of 2100 m on the second day of stay increased in children aged 3-8 years and the children's breathing continued to be more frequent on the tenth day of stay at this altitude. At an altitude of 3000 m (the second day of stay), breathing was rapid in all children aged 3-8 years. When the air is rarefied in the hyperbaric chamber and in high altitude, the tidal volume (TO) in preschool children either did not change or decreased. The minute ventilation (MV) in preschool children increased significantly less than in middle-aged people, the rate of oxygen supply to the lungs decreased. The ratio of alveolar ventilation (AV) to MV in children of 4-7 years of age slightly increased when the air was rarefied in the hyperbaric chamber and in the mountains.

Increased breathing is a natural reaction of the body to a lack of oxygen in the inhaled air and during the second childhood [16]. With short-term inhalation of hypoxic mixtures (15.4-11.4% oxygen with nitrogen), in children aged 8-11 years, breathing became more frequent, but in one third of children of this age, its frequency remained the same as normal. The tidal volume during hypoxia in all children of primary school age increased, that is, during the second childhood, the body has the ability to increase the MV not only due to increased respiration, but also due to a slight increase in respiratory volume.

In children of primary school age (8-11 years old), short-term inhalation of a mixture of nitrogen with 15.4-14.7% oxygen caused an increase in pulmonary ventilation by  $30 \pm 1.1\%$  (16-47%), the mean MV was  $7,4 \pm 0.13$  l/min. Short-term inhalation of a hypoxic mixture of 12-11.4% oxygen with nitrogen led to its increase by an average of  $38 \pm 0.9\%$  (22-66%).

Despite the fact that the lack of oxygen in the inhaled air in children causes a smaller increase in MV than in adults, the relative values of MV (per 1 kg of body weight) in them continue to be almost twice as large as in adults (in children when inhaling a mixture with 12-11.4% oxygen, they averaged  $241 \pm 4.9$  ml/min per 1 kg of body weight, while in adults under these conditions -  $162 \pm 4.1$ ).

With an increase in respiratory volume during hypoxia in children aged 8-11 years, the physiological dead respiratory space also increases. If when inhaling a mixture of nitrogen with 15.4-14.7% oxygen, it increased by an average of one third, then when inhaling a mixture with 12-11.4% oxygen, it increased by more than half. Such a sharp increase in the physiological dead respiratory space is due, on the one hand, to an increase in TO, on the other hand, unlike in adults, an increase in the proportion of physiological dead respiratory space in each respiratory volume. The ratio of alveolar ventilation to MV in children of this age during hypoxia becomes less favorable than normal.

In this regard, alveolar ventilation during hypoxia in children aged 8-11 years increased less than the MV: in adults under these conditions, MAV increased by an average of 40%, in children by 18%. The found age differences indicate that the adaptation of external respiration to a lack of oxygen in the inhaled air in

children is less effective than in middle age, although the intensity of ventilation of the alveoli (MAV per 1 kg of body weight) with a decrease in the oxygen content in the inhaled mixture to 11, 4% in children continued to be almost twice as high as in adults.

During puberty, the body's ability to respond to a decrease in  $PO_2$  in the inhaled air by increasing respiration is still preserved, but in adolescents, an increase in tidal volume begins to predominate. At an altitude of 1000-4000 m, the respiratory rate increased only in 40% of adolescents, but in most of them the respiratory rate did not change, the respiratory volume increased, although to a lesser extent than in adults. TV in half of the adolescents, when "ascent" in the hyperbaric chamber, began to increase from a "height" of 1000 m. In adolescents, there was a smaller increase in TV than in adults when inhaling a gas mixture with 10-12% oxygen, and also in the first days of staying in the mountains at altitude of 2000 m. Pulmonary ventilation in adolescents with a lack of oxygen increases less than in adults. This difference was especially pronounced when the air was rarefied in the hyperbaric chamber (up to an "altitude" of 5000 m), although in the mountains at an altitude of 2100 m, the MV increased less significantly in adolescents than in middle-aged people. When "lifting" in the hyperbaric chamber to a "height" of 1000-3000 m, alveolar ventilation in adolescents may not increase. In the mountains at an altitude of 2100 m, during the first days of our stay, we noted some increase in alveolar ventilation (BTPS), but it was significantly less than in middle-aged people. The ventilation equivalent in adolescents in the mountains increased much more than in adults, and the oxygen effect of the respiratory cycle decreased markedly. In the mountains at an altitude of 2100 m, during the first days of our stay, we noted some increase in alveolar ventilation (BTPS), but it was significantly less than in middle-aged people. The ventilation equivalent in adolescents in the mountains increased much more than in adults, and the oxygen effect of the respiratory cycle decreased markedly.

In the elderly, a decrease in  $PO_2$  in the inhaled air deepens respiratory failure. In the mountains at an altitude of 2100 m, they have more than young people, increased minute volume of respiration and physiological dead respiratory space; alveolar ventilation almost did not increase, the oxygen utilization factor and the oxygen effect of the respiratory cycle decreased more noticeably, the ventilation equivalent increased; in other words, in the elderly, breathing during hypoxia became less efficient and less economical [17].

Studies conducted in the mountains have shown that adaptation to prolonged hypoxic exposure in the elderly proceeds more torpidly than in middle-aged people and children. Respiratory rate and minute volume remain high for three weeks in the mountains. In the mountains at an altitude of 2100 m above sea level, non-acclimatized elderly people showed symptoms of mountain sickness with shortness of breath, nocturnal attacks of suffocation, Cheyne-Stokes breathing, nausea, and headache [18].

An important adaptive response of the body to a lack of oxygen in the air is an increase in the mass transfer of oxygen by blood from the alveoli to the tissues, which depends primarily on changes in cardiac activity and hemodynamics [19]. Registration of heart rate at rest, during an orthostatic test and a functional test with a load (10 flexions for 30sec), and then in the Elbrus region showed that on the second day of stay in the mountains (altitude 2100m) at rest in all preschool children age, the pulse increased by 2-30 beats/min. In adults, the increase in heart rate on the second day of stay in the mountains averaged about  $5.1 \pm 1.6$  beats/min. The children's pulse remained frequent during the entire stay in the mountains (18 days). At an altitude of 3000 m above sea level, the heart rate increased. Increased heart rate in children, as evidenced by ECG data, was due to a decrease in diastole time.

An increase in the minute volume of blood was noted on the 6-10th day of stay at this altitude; MV remained high on the 20th day. The systolic volume did not increase, the pulse was rapid.

In children of primary school age, with short-term inhalation of a hypoxic mixture with 15.4-11.4% oxygen, the heart rate increased. MV during inhalation of a hypoxic mixture with 15.4-14.7% oxygen increased in children of this age by an average of 30%.

Inhalation of a mixture with 12-11.4% oxygen did not cause a further increase in the MV in all children. Only in a sixth of the children, the MV continued to increase. Its value in them was 50-60% higher than the MV in normoxia (in adults, when inhaling the same gas mixture, this indicator increased by 10-15%). An increase in systolic volume played a certain role in increasing the MV in children 8-11 years old (unlike preschoolers). When inhaling a gas mixture with 15.4-14.7% oxygen, CO increased by 15% compared to its level during normoxia in children. However, it should be emphasized that although, compared with the norm, CO increased

significantly on average, in those children who had a pronounced increase in heart rate (over 100 beats/min), it remained the same as in the norm, or even slightly decreased, that is, an increase in the MV in these children was achieved in a less economical way.

The blood circulation in children in relation to the supply of tissues with oxygen was significantly less efficient than in adults. This is evidenced by a greater hemodynamic equivalent and a lower oxygen effect of the cardiac cycle. If normally in children 8-11 years old, 1 liter of oxygen was extracted by tissues from  $18.4 \pm 0.80$  liters of circulating blood, then when inhaling a gas mixture with 15.4-14.7% oxygen, from  $23.8 \pm 0.81$  l of blood. The efficiency of blood flow decreased even more markedly with a more severe degree of hypoxia, when each liter of oxygen was extracted by the tissues from  $31.4 \pm 0.9$  liters of blood. The low efficiency of blood flow in relation to the supply of tissues with oxygen is also evidenced by the arteriovenous difference in oxygen decreasing during hypoxia and the coefficient of oxygen utilization from arterial blood. Thus, when inhaling a mixture of nitrogen with 15.4-14.7% oxygen,  $C_{(a-v)O_2}$  in children decreased from  $5.16 \pm 0.05$  to  $4.2 \pm 0.05$  volume %, and the oxygen utilization coefficient decreased accordingly up to 25 and 21%. The oxygen content in arterial blood, especially when inhaling a mixture with 12-11.4% oxygen, decreased by more than 2 vol.% and amounted to  $15.1 \pm 0.2$  (13.9-16.2) vol.%. The oxygen content in the mixed venous blood in children remained virtually unchanged. Under hypoxia, the oxygen effect of the cardiac cycle also significantly decreased.

The reaction of the cardiovascular system to the inhalation of a mixture of nitrogen with 11.5-12.2% oxygen and to the rarefaction of air in the mountains in adolescents is specific.

In adolescents and young men, the increase in heart rate begins at lower altitudes and is more pronounced than in adults. At the "height" of 2000 m in the hyperbaric chamber in adolescents, the pulse quickens by an average of 2-20 beats/min.

At the "height" of 3000 m, the increase reaches 7-30, and at the "height" of 4000 m - 10-30 beats/min. Similar data were obtained during the first days of stay in the mountains at an altitude of 2000 m. The intensity of blood flow, the intensity of oxygen transport by arterial and mixed venous blood, as well as the heart rate and hemodynamic equivalent in adolescents are higher.

Experimental studies conducted on dogs of different ages, breathing nitrogen gas mixtures with different oxygen content (from 20.9 to 5.5%), showed that during puberty (6-7 months), the body of puppies responds to a decrease in oxygen content during inhaled air (as well as adult animals) some increase in heart rate, a persistent increase in the MV (according to Fick), an increase in mean arterial pressure and a decrease in total peripheral resistance. However, unlike adult dogs in puppies during puberty, changes in hemodynamic parameters reached a maximum (152% of the initial level) with less severe hypoxia (7.5% oxygen in the inhaled air) than in middle-aged dogs (5.5% oxygen). The intensity of blood flow (MV per 1 kg of body weight) in puppies during hypoxia was greater.

The reaction of the cardiovascular system to a decrease in  $PO_2$  in the inhaled air in the elderly and senile age is less pronounced at an altitude of 2100 m above sea level, the heart rate in the elderly increased only on the fourth or fifth day of stay in the mountains, its increase in relation to the heart rate at the level the sea is small - 3-8 beats/min. The orthostatic test and dosed physical activity (15 squats per minute) caused a smaller increase in heart rate in old people than in young people, both at normal and at low  $PO_2$  in the inhaled air. However, at an altitude of 2100 m and especially 3000 m above sea level, this increase was large. The minute volume of blood in elderly people at an altitude of 2100 m remained practically unchanged. Its decrease, as well as the decrease in CO, on the second day of stay in the mountains are not statistically significant. Systolic pressure on the second day of stay in the mountains at an altitude of 2100 m did not increase. The increase in systolic pressure by 25-30 mmHg and a higher level of diastolic were noted on the tenth day of stay in the mountains. The blood pressure of the old people was also slightly elevated on the twentieth day of their stay in the mountains.

With a decrease in  $PO_2$  in the inhaled air, a different degree of activation of such important compensatory mechanisms as increased ventilation and blood flow determines the features of changes in the oxygen regimes of the body and the development of hypoxic conditions in different age periods [20]. Large relative (l/min per 1 kg of body weight) values of alveolar ventilation cause higher levels of oxygen partial pressure in the alveolar air and arterial blood in children. At an altitude of 2000-3000 m above



sea level, with an appropriate rarefaction of air in the pressure chamber or inhalation of a mixture with 10-12% oxygen (which corresponds to an altitude of 4000 m), arterial blood oxygen saturation was maintained at a higher level in preschool children than in persons of other age groups.

Less than in adults, the increase in alveolar ventilation and its lower relative value (ml/min per 1 kg of body weight) in adolescents are the cause of a more pronounced decrease in the rate of oxygen supply to the lungs and alveoli, the partial pressure of oxygen in the alveolar air, as well as a more pronounced than in adults and children, reducing arterial oxygen saturation.

In the elderly at an altitude of 2100 m above sea level, with a pronounced increase in the MV, the rate of oxygen supply to the lungs and alveoli decreases more than in adolescents and adults, the level of arterial blood oxygenation is the lowest. Even at such a low altitude as 2100 m, on the second day of their stay in the mountains, the arterial blood of the elderly is only 80-89% saturated with oxygen,  $PO_2$  in it becomes below the critical level. Thus, with the same  $PO_2$  of the ambient air in children and adults, the  $PO_2$  of arterial blood is above the critical level, in the elderly it is lower, and in adolescents it approaches it.

The represented data testify to the unequal severity of arterial hypoxemia in children, adolescents, middle-aged people and the elderly with the same environmental  $PO_2$ . Hypoxia in the elderly is aggravated by the lower oxygen capacity of the blood, which causes a significantly lower oxygen content in arterial blood, a lower rate of mass transfer of oxygen by it.

In persons of different ages with a decrease in  $PO_2$  in the air, the rate of oxygen mass transfer by arterial blood changes unequally. On the second day of stay at an altitude of 2000 m it decreased by 120-60 ml/min in adolescents, and by 170 ml/min in the elderly, compared with that registered previously. After a twenty-day stay in the mountains, due to an increase in the rate of blood flow, oxygen capacity of the blood, and the oxygen content in it, the rate of oxygen mass transfer by arterial blood in children, adolescents and middle-aged people significantly (especially in children) exceeded the normoxic one. And only in old people (although its increase was noted) the rate of mass transfer of oxygen by the blood was less than with normal  $PO_2$ , the environment.

A sharp decrease in  $PO_2$  and the rate of oxygen mass transfer in the blood led to the development of secondary tissue hypoxia in the elderly at an altitude of 2100 m. Their oxygen consumption has decreased. In the first days of his stay in the mountains at an altitude of 2100 m, pronounced symptoms of mountain sickness appeared.

Despite the fact that in adolescents,  $PO_2$  at this height was above 50 mmHg, that is, a critical level for adults, they (like the elderly) were found to have a decrease in the intensity of oxygen consumption and signs of altitude sickness. Both in acute hypoxia and in the first days of stay at an altitude of 2100 m, against the background of little changes in external respiration, we observed a decrease in oxygen consumption by an average of 10%, and with short-term inhalation of a mixture of nitrogen with 11% oxygen - by 31%. However, during a long stay in the mountains, the oxygen consumption exceeded its level in the plains, while the oxygen consumption in adults after its slight increase (by 7%) in the first days returned to normoxic values by the 8-10th day of stay in the mountains. In adolescents the critical level of arterial blood  $PO_2$  is higher than in adults, since the capillary system in tissues and tissue mechanisms of adaptation to oxygen deficiency in them have not yet reached the level of their development in adults. With a lack of oxygen in the inhaled air in adolescents, the oxygen regimes of the body are less effective and less economical than in adults and children. This is evidenced by a comparison of the rate of oxygen supply to the lungs, and especially the rate of its transport by the blood, with the rate of oxygen consumption by the tissues. When nitrogen mixtures with 12-11% oxygen are inhaled by adults, the efficiency of the oxygen regimes of the body increases in comparison with normoxic indicators, although the efficiency decreases. In adolescents under these conditions, the oxygen regimes of the body become the least economical: for the absorption of 1 liter of oxygen by the tissues, the body of a teenager of 12-13 years old needs about 60 liters, a teenager of 14-16 years old needs about 55 liters of air ventilated in the lungs, and about 38 and 35 liters of circulating blood. A significant decrease in the oxygen effect of the respiratory and cardiac cycles testifies to the lower efficiency of the oxygen regimes of the body.

So, in children, the rate of oxygen mass transfer preserved at the normoxic level and the relatively high  $PO_2$  of arterial blood provide compensation for the lack of oxygen in the inhaled air at an altitude

of 2000-3000 m, due to which secondary tissue hypoxia does not develop. Accelerated blood flow and, consequently, oxygen delivery, a relatively high  $PO_2$ , and tenderness of the hematoparenchymal membranes in children cause a faster mass transfer of oxygen to the cells and the removal of carbon dioxide from them. With a long stay in the mountains at altitudes of 2000-3000 m above sea level in children and adolescents, to a greater extent than in adults, the blood flow rate, oxygen capacity of the blood and the oxygen content in it, as well as the rate of its mass transfer by arterial blood, increase. As a result, oxygen tension in the tissues increases, and their ability to utilize oxygen also increases, as evidenced by an increase in the rate of its consumption.

The adaptive mechanisms developed in the process of evolution for supplying the tissues of a growing organism with an excess amount of oxygen - a high intensity of ventilation and blood flow, provide a reserve of oxygen for parenchymal tissues that absorb large amounts of it, maintain a high level of  $PO_2$  in them. The activity of these mechanisms is aimed at ensuring higher normoxic levels of  $PO_2$  in tissues than in adults, which makes it possible to maintain a high intensity of tissue respiration with oxygen utilization mechanisms that have not yet reached full development. The increase in external respiration and blood circulation, which is carried out in children, albeit in the least effective way, with higher ventilation and hemodynamic equivalents, lower oxygen effects of the respiratory and cardiac cycles with a decrease in  $PO_2$  in the inhaled air, serves the same purpose. Among the long-term mechanisms adaptive to hypoxia in children can be attributed to a more significant and earlier than at other ages, an increase in the oxygen capacity of the blood, the number of erythrocytes and hemoglobin content. All these adaptive reactions provide, however, compensation for the lack of oxygen in the inhaled air during the period of the first and second childhood with narrower ranges of  $PO_2$  decrease in the inhaled air. In children and adolescents, the limits of the decrease in  $PO_2$  in the inhaled air, at which the oxygen consumption of the body does not yet decrease, turn out to be narrow. Compensated hypoxia in them earlier turns into severe hypoxia with the onset of decompensation.

At puberty, the maintenance of homeostasis is carried out mainly no longer according to the childish type, however, the body of adolescents has not yet reached the perfection of adult functions and adapts worse to changes in  $PO_2$  in the inhaled air. Less effective

changes in external respiration with lower relative values (per 1 kg of body weight) of MV and AV, lower than in children,  $PO_2$  of alveolar air lead to more pronounced hypoxemia. A greater than in an adult organism, the need of tissues for oxygen and their lower ability to utilize oxygen at low  $PO_2$ , are the cause of the earlier onset of tissue hypoxia, a decrease in oxygen consumption. The body tissues of adolescents, like children, are less able to utilize oxygen. At this age, the arteriovenous difference in oxygen and the coefficient of its use from the blood, which are low under normal  $PO_2$ , decrease under hypoxic conditions. This may be a consequence of insufficient development of cellular, structural and molecular mechanisms, which determine both the intensity of the process of oxidative phosphorylation and changes in the oxygen regimes of the body, which are more pronounced in adolescents than in children.

The regulation of the oxygen regimes of the body during hypoxia in adults is more perfect. In adults, even during hypoxia, they are more effective and economical than in children, adolescents and the elderly [22]. Under altered conditions of oxygen supply in middle-aged people, within certain limits of external perturbations, until the  $PO_2$  of the ambient air falls below 85-74 mm Hg due to the high quality of regulation of the oxygen regimes of the body, the rate of oxygen consumption by tissues is maintained at a level not lower than the normoxic one [23].

Compensation for the lack of oxygen in the inhaled air in the elderly and especially in the elderly is worse, the degree of arterial hypoxemia is higher, secondary tissue hypoxia develops with a smaller decrease in environmental  $PO_2$  than in children and adults [24].

The presented material indicates that the "critical" levels of  $PO_2$  for the body in different age periods, as well as the conditions for the development of secondary tissue hypoxia, are not the same.

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