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Features of the Mechanism of Development and Course of Pneumonia When Exposed to Pesticides

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Subject of inquiry: 4995 people living in Buvayda district in Fergana region, 223 cats of males and females 2,2 - 4,5 kg by mass.
Aim of inquiry: The aim of presented work is to study the features of mecha- nism of the development and course of experimental pneumonia against a back- ground of body intoxication by pesticide of OPC - antio group.
Methods of inquiry: the technique of sampling complex study of common morbidity rate, physiological, morphological, electrophysiological, biochemical, statistical.

Key words: pesticide, pneumonia, organophosphorus compound (OPC) - antio, respiratory diseases, hemodynamics, microcirculation, metabolism.

The results achieved: the work has been first carried out complex experimental and clinical study in laboratory animals (cats) with pneu- monia models and spread of respiratory diseases in children, especially, pneumonia in areas of intensive pesticide use. It has been established that mechanism of the development and pneumonia course against a background of body intoxication by OPC- antio is associated, first of all, with disorders of central respiratory regulation and also function of respiratory muscles to a considerable degree and its biome- chanics. It has been first demonstrated, that the specific feature of external respira- tion in mechanism of the development and experimental pneumonia course is the decrease of respiratory volume at the expense of elevation of resistive and elastic respiratory resistance and increase of its respiratory rate mainly at the expense of prolongation of expiration phase. Disorders of microcirculation and hemodynamics in lungs have been shown an important link of particularity of acute pneumoniaagainst a background of body intoxication by high doses of OPC- antio, effecting on clinical course and outcome, It has been established that leading cause of the and economy of external respiration falling under the tissue hypoxia are disorders of regular respiration and function of respiratory muscles lipid peroxida- tion, metabolic acidosis, disturbance of phospholipid compound of lung paren- chyma, and also restriction of oxygen diffusion from air into blood and from blood into tissue, First presented, that the occurrence of acute pneumonia and respiratory diseases were noted more frequently in those cotton grown regions where pesti- cides were used larger in comparison with cattle-breeding regions.

Practical value: the development of fundamentally new approach to correc- tion and prevention of respiration disorders, metabolism and tissue hypoxia. It has been demonstrated that elevation of body resistance to severe is possible under the increase of oxygen consumption mainly at the expense of condition im- proving to diffuse it from blood into tissue. It has been established that in order to achieve the positive result contacted with pesticides, it is necessary to reduce si- multaneously the degree of metabolic acidosis, POL inhibition in biological mem- branes and normalization of phospholipid compound of tissues. It has been first shown that antioxidant lonol (Dibunol) can be used equally with common used an- tidotes additionally to traditional therapy. These data have been applied to set up principally a new approach for prediction and mode of treatment pneumonia for people living in areas ofintensive pesticide use.

Degree of embed and economical effectivity: Theoretical approaches and methods developed in thesis have been used in research work of department nor- mal and pathological physiology in Samarkand State Medical Institute and in work of departments of normal, pathological physiology and pathologic anatomy in TMA.

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All over the world, there is a steady upward trend in respiratory diseases (A.G. Chuchalin, 2020; A.M. Ubaydullaev, Sh.U. Ismoilov, 2000; M.M. Ilkovich, A.N. Kokosov, 2005). In Uzbekistan, respiratory diseases rank first, and pain has increased 2.5 times over the past 5 years, especially bronchial asthma - 1.8 times and chronic nonspecific lung diseases (CNLD) - 1.3 times (A.M. .Ubaidullaev, I.V. Liverko, 2003). A special role in the pathogenesis of COPD is given to local changes, which are characterized by the predominance of degenerative-dystrophic processes in the mucous membranes of the respiratory tract, which in turn depend on the characteristics of local blood circulation, its nervous and humoral regulation. In the pathogenesis of inflammatory diseases of the bronchopulmonary system, one of the leading links is the activation of free radical oxidation, which can cause damage to lung structures (S.A.Syurin et al., 1995; I.I.Logovinenko, 1997; V.N. Rakitsky, T.V. Yudina, 2006; L.V. Khripach and others, 2006; V. Cottinetal., 1996).

Purpose of the study. The purpose of this work is a comprehensive study of the features of the mechanism of development and course of experimental pneumonia against the background of organism poisoning with a pesticide from the FOS-antio group.

Pneumonia is one of the frequent complications of a chemical disease that occurs in 27-60% of cases of acute poisoning, with a mortality rate of up to 50.0% in acute exotoxicoses (EA Luzhnikov, 1982; LN Zimina, 1984). In modern conditions, the widespread use of pesticides leads to a decrease in the adaptive capabilities of the body, which can contribute to the frequent spread of inflammatory lung diseases. However, the pathogenetic mechanisms of the development of pneumonia, in particular, pathomorphological features and features of violation of the neurohumoral regulation of respiration, when exposed to pesticides, have not been studied. Therefore, our department has been studying for a long time (doctor of medical sciences Ya.K. Kurambaev) the pathogenetic mechanisms of the development of pneumonia under pesticide load in the experiment and the frequency of inflammatory respiratory diseases in cotton-growing and livestock farms of our Republic in comparative terms.

Materials and methods. Acute experimental pneumonia was modeled in 200 outbred cats according to the method (J.Korpas, Z.Tomory, 1972). To assess the effect of FOP antio in high doses (42.6 mg/kg) when administered orally in cats of both sexes, a pneumotachometric study of the function of external respiration, an electrophysiological, ultrasonic-Doppler method for recording pulmonary hemodynamics were performed (Matsievsky D.D., 19 ...) blood gas composition and acid-base balance (COR) using an Astrup-Siggard-Andersen micrometer on the Radiometer device (Denmark). Determined PO_2, pCO_2, pH blood pH. The content of bound and solution oxygen was determined by calculation. The activity of the LPO process was determined by the accumulation of its products that react with thiobarbituric acid in the blood (Gavrilov VV et al., 1987).

Acute experimental pneumonia was modeled in more than 200 outbred cats by introducing 0.3 ml of resinous turpentine into the lumen of the trachea using a catheter, which penetrated the alveoli through the bronchi and caused an aseptic inflammatory process. The focus of pneumonia was formed within 24 hours, at the later stages of the disease bacterial pneumonia developed, the etiological factor of which was the saprophytic and conditionally pathogenic microflora of the respiratory tract.

Resined turpentine, unlike ordinary turpentine, is devoid of toxic properties. Morphological changes in the lungs that occur in this model of acute pneumonia did not differ significantly from those in spontaneous pneumonia (I.Korpas, Z.Tomory, 1972). The degree of prevalence of the inflammatory process was assessed preliminary when examining the lung during thoracotomy, and finally - during a morphological study.

Poisoning of animals with antio (formation) by Sandoz was carried out at a dose of 1/5 LD_{50} (acute experiments), the duration of the experiments ranged from 3-4 hours to 5-7 days. Histological sections were stained with hematoxylin and eosin, picrofuchsin-fuxelin and Sudan III according to Goldman.

In addition, in order to elucidate the mechanisms of the effect of pesticides on the course of pneumonia, the functions of external respiration were studied, the electrical activity of the respiratory muscles was recorded, the state of the pulmonary and systemic circulation, the activity of lipid peroxidation processes, as well as an assessment of the incidence of the population in cotton-growing and livestock areas of the Republic.

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Morphologically, the initial signs of inflammation against the background of antio poisoning, as in non-poisoned control animals, were detected 12-24 hours after the administration of: tarred turpentine. However, in poisoned animals, the processes of alteration and exudation were of a deeper nature than in groups of animals not exposed to antio. The bronchial epithelium was swollen, in some places separated from the basement membrane.

Lymphohistiocytic accumulations were located around the bronchi and vessels in the form of clutches, the bronchial lumens were narrowed and filled with mucopurulent and hemorrhagic exudate. Free erythrocytes were seen in the cavities of the alveoli. Further, attention was drawn to the swelling of alveolocytes, a decrease in the lumen of the alveoli and distelectasis. Along with this, the presence of extensive foci of parenchyma lysis was noted. In the walls of the alveoli - small multiple diffusely scattered focal lymphoid cell infiltrates. However, there are no general alveolar-macrophage reactions.

In general, it seemed that the combined effect of antio and turpentine creates conditions for the action of secondary damaging factors that can deepen the pathology and expand the range of morphological changes characteristic of pneumonia in the phase of their acute course.

Inhalation of a hypoxic gas mixture (10% O2 in N2) against this background caused a further increase in pulmonary ventilation (Fig. 1). Usually, hypoxia causes an increase in the activity of inspiratory neurons and a decrease in the activity of expiratory neurons.

It was found that the development and course of pneumonia against the background of poisoning with FOS antio (formation) is accompanied, first of all, by a violation of the central regulation of respiration, apparently directly affecting the neural structures of the respiratory center, as well as to a large extent by disrupting the work of the respiratory muscles and its biomechanics. A specific feature of the violation of external respiration in this case is a decrease in tidal volume due to an increase in resistive and elastic resistance of breathing and an increase in its frequency, mainly due to a lengthening of the expiratory phase. The established disorders of the processes of microcirculation and hemodynamics in the lungs are characteristic. It has been shown that disorders in the regulation of respiration and the work of the respiratory muscles, caused by the activation of LPO, metabolic acidosis, a violation of the phospholipid composition of the lung parenchyma, as well as the restriction of oxygen diffusion from air to blood and from blood to tissues, are the leading causes of a decrease in the efficiency and economy of external respiration in conditions of tissue hypoxia.

The disorders of respiration and gas exchange noted above, as well as the restructuring of the volumetric and temporal structure of the respiratory cycle under conditions of severe OPC intoxication, could be due mainly to three factors: shifts in humoral stimuli - respiratory gas tension and blood pH, changes in the regulation of respiration and the function of the respiratory muscles and, finally, impaired ventilation sensitivity to these stimuli.

Changes in the tension of respiratory gases and blood pH in acute intoxication with FOS. Changes in the most important regulators of respiration - the tension of respiratory gases and blood pH - in acute poisoning with the pesticide antio from the FOS group, despite the maintenance of normal values of lung ventilation and normoxia in arterial blood, significant metabolic acidosis develops.

This can be considered as evidence of impaired tissue respiration. At the same time, the reaction from the blood buffer systems leads to a deficiency of bases, which causes the development of uncompensated metabolic acidosis. Thus, under the influence of antio (FOS) on the body of cats anesthetized with pentobarbital, there are profound respiratory disorders that are incompatible with life. Moreover, the animals die within 2-3 hours after the administration of the drug. At the same time, there is evidence in the literature that FOS has an ambiguous effect on animals under anesthesia and non-anesthetized animals. So, in animals under anesthesia under the influence of FOS, there is a decrease in blood pressure, respiratory depression. In non-anesthetized animals, opposite effects are observed - stimulation of respiration, an increase in blood pressure.

The second feature is that in non-anesthetized animals, gas exchange in the lungs under conditions of toxic acute poisoning is also disturbed.

The main signs of its impairment in experimental pneumonia against the background of antio poisoning are a decrease in the pH of the "oxygen effect of the respiratory cycle" (oxygen consumption per respiratory cycle) and a decrease in the efficiency of blood oxygenation in the lungs, leading to an increase

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in shunting of mixed venous blood into the arterial bed. An analysis of the data obtained allows us to state that these disorders are only partially due to the restructuring of external respiration. Their main reason is the pronounced limitation of the diffusion of oxygen from the air into the blood.

Development of tissue hypoxia.

Of fundamental importance, in our opinion, is the established fact of the development of hypoxia in the lungs, as, indeed, in other organs, according to the principle of a "vicious circle". Precisely because of the presence of such a vicious circle, the initial mismatch of oxygen delivery to tissues in response to metabolic demand leads to the development of a number of interrelated processes, which, ultimately, further reduce oxygen transport. In turn, the restriction of the delivery of this gas increases hypoxia and causes an even greater decrease in the amount of O2 delivered to the tissues. If there were no effective mechanisms to compensate for hypoxia, then due to the development of a vicious circle, even a moderate hypoxic effect would lead to the death of the organism. However, under real conditions, under severe intoxication with FOS, the anesthetized animals die from histotoxic hypoxia. At the same time, it was precisely the force of the development of tissue hypoxia in a vicious circle that, even in non-anesthetized animals, the state of the oxygen regime of the body turned out to be extremely unstable.

The main thing, from our point of view, is the stages of development of tissue hypoxia, presented in the form of a diagram (Fig. 3.). They include: a mismatch in oxygen delivery to its request and a decrease in tissue pO2 as a result, restriction of tissue respiration and a compensatory increase in the aerobic phase of glycolysis, leading to the accumulation of organic acids in the blood, primarily lactic acid, and the development of decompensated metabolic acidosis; activation of lipid peroxidation (LPO) processes; in the development of interstitial edema.

Ultimately, these changes limit the diffusion of oxygen from the blood to the tissues. The reality of these processes has been proven by direct changes in the experiment. In our experiments, when using experimental models, a significant decrease in this indicator was recorded, which indicates a pronounced discrepancy between the amount of oxygen delivered to tissues per unit time and the oxygen demand.

Along with metabolic acidosis, in the word severe toxic hypoxia, activation of lipid peroxidation (LPO) processes in peripheral blood was found. The activation mechanism (LPO) during hypoxia requires a separate, more detailed study. Within the framework of this work, it can be assumed that the main of them, apparently, is the increase in the formation of free radicals under the influence of pronounced acidosis and the activation of lipid peroxidation due to an excess of reduced forms of electron carriers in the respiratory chain.

In addition, one of the possible mechanisms for the activation of lipid peroxidation was directly during hypoxia; obviously, spatial and temporal heterogeneity of oxygen tension in the blood and tissues can be.

Lipid peroxidation in the membranes of the pulmonary vessels, an excess of its products in the tissue of the lungs of the blood, as well as acidosis, damage the endothelium of the capillaries. This vascular damage leads to the development of interstitial edema of lung tissue in the focus of inflammation and activation of BAS.

Along with a pronounced interstitial edema in the lungs in the focus of inflammation after preliminary intoxication with FOS, note frequent and complete microcirculation disorders, multiple microatelectases with infiltration of the interalveolar septa, in some places uneven expansion of the lumen of the alveoli by depletion and rupture of the interalveolar septa, as well as desquamation of the alveolar epithelium, spasm of the small bronchi other. In addition to the fact that such a significant damage to the respiratory zone of the lungs leads to a violation of external respiration and gas exchange, it limits the diffusion of oxygen from the blood into tissues.

Unfortunately, there are still reliable ways to change the rate of oxygen diffusion from the blood into the lung tissue in vivo. Nevertheless, the diffusion capacity of the lungs, the membrane components of which reflect the diffusion of oxygen through the lung parenchyma, can be characterized to a certain extent and the conditions for the diffusion of oxygen from the blood into the tissues of the lungs.

Violation of the biomechanics of respiration.

- The development of tissue hypoxia, accompanying energy deficiency, metabolic acidosis and lung damage, disrupt the synthesis of phospholipids. At the same time, increased lipid peroxidation,

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increased activity of phospholipases and a number of other factors inherent in hypoxia accelerate the processes of their destruction in the surfactant and parenchyma. Changes in the phospholipid composition of the lung lead to at least two important results:

- violation of the ultraarchitectonic properties of the pulmonary surfactant and a decrease in the diffusion capacity of the lungs. The first of them reduces the extensibility of the lungs, increases the energy consumption for breathing, leads to a functional restructuring of the volume-time organization of the respiratory cycle and external respiration in general. Limiting the diffusion of oxygen from the air into the blood reduces the efficiency of blood oxygenation in the lungs.

- in conditions of natural respiration, in addition to the elastic, respiratory muscles also need to overcome additional resistance arising from friction and turbulence of the gas flow.

Consequently, the data obtained indicate that during hypoxia, not only elastic, but also active resistance to breathing increases.

At the same time, studies conducted by B.T. Shakarov (1996) under our guidance and guidance of prof. S.A. Blinova indicate that FOS antio causes significant changes in the APUD system of the lungs.

In particular, in acute poisoning with antio in doses of 1/10 LD5ol in the lungs, hemodynamic disturbances are observed in the form of edema of the walls of the intrapulmonary bronchi, the accumulation of edematous fluid in the alveoli, associated with increased release of serotonin and other biologically active substances by lung apudocytes. These changes can contribute to the predominance of the exudative component of the inflammatory reaction and cause severe pneumonia.

Thus, in the mechanisms of a severe course of pneumonia under conditions of pesticide use, in addition to the above changes in the central regulation of respiration and other changes, changes in local endocrine cells - apudocytes of the bronchopulmonary system also play a certain role.

In clinical terms, a comparative study of the incidence in two districts of our Republic: in cotton-growing Buvayda, where pesticides are used, and in livestock breeding - Nurata, where pesticides are not used, showed that the incidence rate of children under the age of 4 years, according to the application rate, is almost 1.5 times higher. in the Buvayda district compared with the control - Nurata.

The excess of morbidity levels was observed in the following classes and nosological forms: rickets, malnutrition, diseases of the blood and hematopoietic organs, diseases of the nervous system and sensory organs, including conjunctivitis and otitis, respiratory diseases, including 3-5 times more common pneumonia, SARS, bronchitis, and diseases of the digestive system. At the same time, infectious and parasitic diseases, including intestinal infections in most cases, were more often recorded in the livestock region than in the cotton region. Differences in morbidity levels are statistically significant ($p<0.05$), with the exception of the class “diseases of the endocrine system, digestive disorders, metabolic and immune system disorders”.

Consequently, the conducted experimental clinical studies have shown that under the influence of pesticides, inflammatory processes in the lungs are more severe with a predominance of alterative and exudative processes, which, apparently, associated with a violation of the central regulation of respiration, activation of lipid peroxidation, metabolic acidosis, changes in the APUD system, and other changes that contribute to the development of hypoxia.

These same changes seem to be the reason for the frequent spread of inflammatory diseases and respiratory infection in cotton-growing areas, compared with livestock areas, which differ in the degree of application of territorial loads of pesticides.

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