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Topochemical Examinations of the Lungs of the Rat after Combined Administration of Serpasil and Deslanatoside. I. Histochemical Examinations

Badania topochemiczne płuc szczura po skojarzonym podawaniu Serpasilu i Deslanatosidu. I. Badania histochemiczne

Топохимические исследования легких крыс после сопряженного применения Серпасила и Десланатозида. I. Гистохимические исследования

Serpasil and Lanatoside are drugs commonly used in medical practice. Serpasil in used in arterial hypertension (3). Lanatoside is used in circulatory failure, in atrial fibrillation, in circulatory failure with tachycardia, i.e. in diseases which may result from high blood pressure (1).

All somatic changes evidencing themselves with concrete pathologic symptoms are usually preceded by changes on the enzymatic — functional level of the tissue. Hence it was expedient to examine the activity of enzymes taking part in gaseous exchange present in lymphatic tissue of the lungs, as well as the level of catecholamines after administration of both drugs.

MATERIAL AND METHODS

Examinations were carried out on female white Wistar rats, sexually mature, with body weight ca 160 g. They were under observation in spring months and fed with the standard LSM feed. The animals were divided into 4 experimental groups.

Group I — rats which were not given any drugs.

Group II — rats which were given Serpasil in the dose of 0.5 mg/kg body weight for 5 days.

Group III — rats which were given Serpasil in the dose of 0.25 mg/kg body weight for 5 days.

Group IV — rats which were given Serpasil in the dose of 0.25 mg/kg body weight, Lanatoside in the dose of 0.4 mg/kg body weight.

Serpasil was produced by CIBA and Lanatoside by POLFA Warsaw. The drugs were administered by intraperitoneal route.

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After 5 days of the drugs administration the animals were killed by decapitation and their pulmonary tissue was collected for examinations. The material was fixed in Baker's liquid (fluid) (13) and in mixture of 5% $K_2CH_2O_4$ and 5% $K_2CH_2O_7$. Fixed material was segmented on freezing microtome. There was determined activity of acid, alkaline phosphatase according to Hillarp's and Hökfelt's method (6). On the unifixed material there was determined succinate dehydrogenase (SDh) and lactate dehydrogenase (LDh) (6).

STUDY RESULTS

Succinate dehydrogenase (SDh EC.1.3.99.1)

Group I. Reaction to succinate dehydrogenase was made evident in columnar epithelium and in mascular elements of bronchi and bronchioles. In the wall of pulmonary parenchyma vessels the activity of the enzyme was very weak and occurred only in muscular cells. A delicate reaction occurred im some cells of pulmonary alveoli, while in the site where lymphatic tissue accumulated in the bronchial region the reaction was much stronger (Fig. 1).

Group II. In this group reaction to dehydrogenase was clearly stronger, especially in columnar epithelium and in Reisessen's membrane in bronchi. Stronger reaction also occurred in the lymphatic tissue around bronchi, as well as in the wall of pulmonary alveoli (Fig. 2).

Group III. In all the animals of the group there was observed a decrease of the activity of the enzyme in epithelium and in cells of interalveolar septa. Reaction was similar to that of control group.

Group IV. In this experimental group reaction was slighthy weaker than in control group and the strongest reaction occurred in muscles and epithellum of bronchi and bronchioles.

Lactate dehydrogenase (LDh EC.1.1.1.27)

Group I. In animals, which were not given any drugs there was observed strong activity of lactate dehydrogenase in the wall of blood vessels, in epithelium, in muscular membrane of bronchi and bronchioles. The strongest reaction was observed in epithelium. In pulmonary parenchyma reaction occurred in cells of interalveolar septa lining the lumen of pulmonary alveolus (Fig. 3).

Group II. In the lungs of animals from this group there was observed an increase of activity of the examined enzyme. Very strong reaction occurred in epithelium and muscular membrane of bronchi.

Group III. Activity of the enzyme in lungs was weaker in both foregoing groups, there was especially evident decrease of its activity in muscular membrane of bronchi and in the walls of vessels (Fig. 4).

Group IV. Like in group III activity of the enzyme was weak. Only in few places there were present agglomerates of cells with strongly expressed reaction.

Alkaline phosphatase (Al Ph EC.3.1.31)

Group I. Active enzyme occurred in lungs of all the examined animals, strongly showing itself in the wall of blood vessels and in epithelium of bronchi (Fig. 5). In pulmonary parenchyma, only in few places a delicate reaction occurred.

Group II. In the group of animals receiving the biggest dose of Serpasil there was observed a considerable decrease of activity of the enzyme in columnar cells of bronchial epithelium and in pulmonary parenchyma. Endothelium of blood vessels contained active enzyme similar in quantity to the control group.

Group III. In this group there was observed a clear increase of activity of the enzyme in blood vessels. In the respiratory tract strong reaction occurred in columnar cells of epithelium, in its parabasic part. In interalveolar septa cells with active enzyme appeared (Fig. 6).

Group IV. In comparison with the control group there was observed an increase of activity of the enzyme. In bronchial epithelium at the basis of cells and on their surface there were present very large quantities of the reaction product. Active enzyme with greater intensity in interalveolar septa, and focally appeared sites of accumulated lymphatic tissue with very strongly expressed reaction.

Acid phosphatase (Ac Ph E.C.3.1.3.2)

Group I. In most of the animals the activity of acid phosphatase in bronchi and bronchioles was little. In interalveolar septa there occurred few cells with active enzyme. There were sporadically found accumulations of macrophages in interalveolar septa and an agglomerate of lymphatic tissue in the lower part of bronchi, where enzymatic reaction was more strongly expressed (Fig. 7).

Group II. The activity of acid phosphatase was slightly stronger than in the control group. In some places there was observed widening of interalveolar septa with more numerous cells with active enzyme.

Group III. Reaction to acid phosphatase in this experimental group was much weaker, only in interalveolar septa were found few cells with active enzyme present.

Group IV. In this group reaction was approximately like in the control group, but it should be noted, that focal accumulation of cells with strong activity of the enzyme was found here in some places.

Catecholamines

Group I. Catecholamines were present in pulmonary parenchyma and bronchi. Greater quantities of manifested amines were observed in some cells of respiratory epithelium (Fig. 8).

Group II. In lungs of all the animals after a large dose of Serpasil there was observed a considerable decrease of catecholamines. Only in few places of pulmonary parenchyma there wese observed agglomerates of cells containing stained alveoli with amines (Fig. 9).

Group III. Stained picture of amines let believe that their number was slightly smaller than in the control. In pulmonary parenchyma, only focally, there was observed a stronger reaction.

Group IV. In regard to the present stained reaction the content of amines was estimated to be approximal to the control, however, their distribution was irregular, there occurred sites with big accumulation of catecholamines and sites with their minimum number.

DISCUSSION

While analyzing obtained results there was considered side effect of Serpasil and Lanatoside on lungs. These drugs can be used together. Both these drugs are characterized by fairly small toxicity, though some papers show severe respiratory complications in patients with previous pulmonary insufficiency (7).

The first stage consisted in checking whether the most active morphological elements of the lungs in the respiratory process exhibit histoenzymatic changes of enzyme essential in respiratory processes.

It was observed, that with a greater dose of Serpasil enzymatic activity of succinic and lactic dehydrogenase increased. The highest activity was shown by these enzymes in the epithelium of bronchi and bronchioles and in some cells of pulmonary alveolus. Klika (5) examining histochemistry of the lungs states that granular cells of the pulmonary alveolus, epithelium of the bronchi and bronchioles, having a common developmental route are characterized by the highest level of these enzymes of the whole lung tissue, and consequently by the greatest biochemical involvement in metabolism of the lungs. Klika claims that intensification of breathing is associated with an increase of glandular activity of alveoli and of bronchial and bronchiolal epithelium, which he regards as glandular elements in the lungs. The observed decrease of enzymatic activity after combined administration of Serpasil and Lanatoside may suggest a slight respiratory failure. This correlates with Wasyluk's (12) suggestions about a possibility of respiratory insufficiency occurrence.

An increase of Al Ph activity after combined administration of Serpasil and

Lanatoside observed in this study suggests increase of transport through cellular membranes of undamaged pulmonary parenchyma and also possible regeneration processes (9).

Pragłowski (9) explained increase of Al Ph activity in the lungs after electric stroke with exclusion of some areas of pulmonary parenchyma caused by necrosis. The focally observed, in pulmonary parenchyma, considerable increase of Ac Ph activity after a large dose of Serpasil and after combined administration of Serpasil and Lanatoside would indicate an increased phagocytosis in pulmonary parenchyma. Acid phosphatase with great activity occurs in granular pneumocyts, macrophages, in bronchiolal epithelium and in lymphatic tissue at bifurcations of bronchi (2, 4). Foci with very great Ac Ph activity could not be considered, according to Brundelet, normal pictures. It should rather be assumed that these areas were damaged to some extent. While examining cells which acquired phagocytary capacity Mustakallio (8) observed an increase of Ac Ph activity and dehydrogenases activity.

The above described changes in pulmonary biochemical activity are confirmed by decreased level of catecholamines. Effect of Serpasil on a decrease of blood pressure takes place by a decrease in the number of catecholamines, like after roserpine (10, 11).

Summing up, it may be stated, that administration of large doses of Serpasil causes considerable changes in activity of enzymes responsible for respiratory processes, but after combined administration of Serpasil and Lanatoside differences in activity of enzymes are slight, as compared with control group. It should be emphasized that time of drug administration in this study was short.

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EXPLANATION TO FIGURES

Fig. 1. Group I. Pulmonary parenchyma. Reaction to succinic dehydrogenase. Magn. ca 200 ×.
Fig. 2. Group II. Pulmonary parenchyma. Reaction to succinic dehydrogenase. Magn. ca 200 ×.
Fig. 3. Group I. Pulmonary parenchyma. Reaction to lactic dehydrogenase. Magn. ca 200 ×.
Fig. 4. Group II. Pulmonary parenchyma. Reaction to lactic dehydrogenase. Magn. ca 200 ×.
Fig. 5. Group I. Pulmonary parenchyma. Reaction to alkaline phosphatase. Magn. ca 200 ×.
Fig. 6. Group III. Pulmonary parenchyma. Reaction to alkaline phosphatase. Magn. ca 200 ×.
Fig. 7. Group I. Pulmonary parenchyma. Reaction to acid phosphatase. Magn. ca 200 ×.
Fig. 8. Group I. Pulmonary parenchyma. Catecholamines. Magn. ca 200 ×.
Fig. 9. Group II. Pulmonary parenchyma. Catecholamines. Magn. ca 200 ×.

STRESZCZENIE

Badano wpływ Serpasilu i Deslanatosidu na aktywność enzymów biorących udział w wymianie gazowej oraz występujących w tkance limfatycznej płuc, a także sprawdzano obecność amin katecholowych. Oba te leki aktualnie są często stosowane: Serpasil — w celu obniżenia ciśnienia tętniczego, Deslanatosid — w niewydolności krążenia. Z przeprowadzonych obserwacji wynika, że podawanie dużych dawek Serpasilu wpływa na znaczne zmiany w aktywności enzymów odpowiedzialnych za procesy oddechowe, ale w skojarzonym podawaniu z Deslanatosidem różnice w aktywności enzymów są niewielkie. Po Serpasilu obserwowano również zmniejszoną ilość amin katecholowych. Należy zwrócić uwagę na znaczny wzrost aktywności fosfatazy kwaśnej.

РЕЗЮМЕ

В данной работе представлено результаты исследования влияния Серпасила и Десланатосида на активность энзимов участвующих в газообмене и выступающих в лимфатической ткани легких. Исследовано также наличие катехоловых аминов. Эти два препарата часто применяются: Серпасиль — для понижения артериального давления; Десланатосид — при недостаточности кровообращения. На основе наблюдений определено, что применение больших доз Серпасила значительно изменяет активность энзимов, участвующих в дыхательных процессах, а подан с Деслантосидом не вызывает больших разниц в активности энзимов. Серпасиль значительно уменьшает количество катехоловых аминов, и повышает активность кислой фосфатазы.

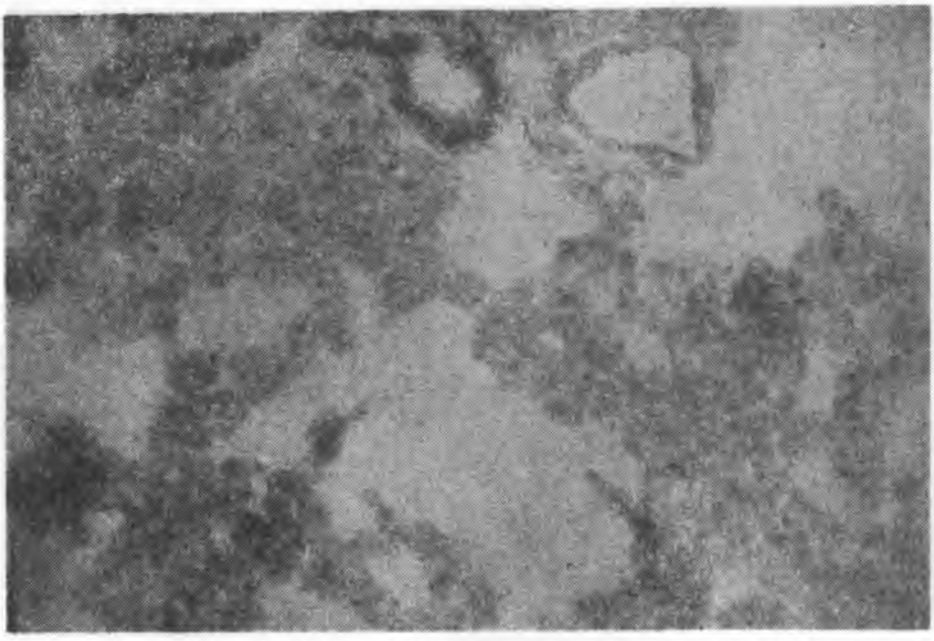

Fig. 1

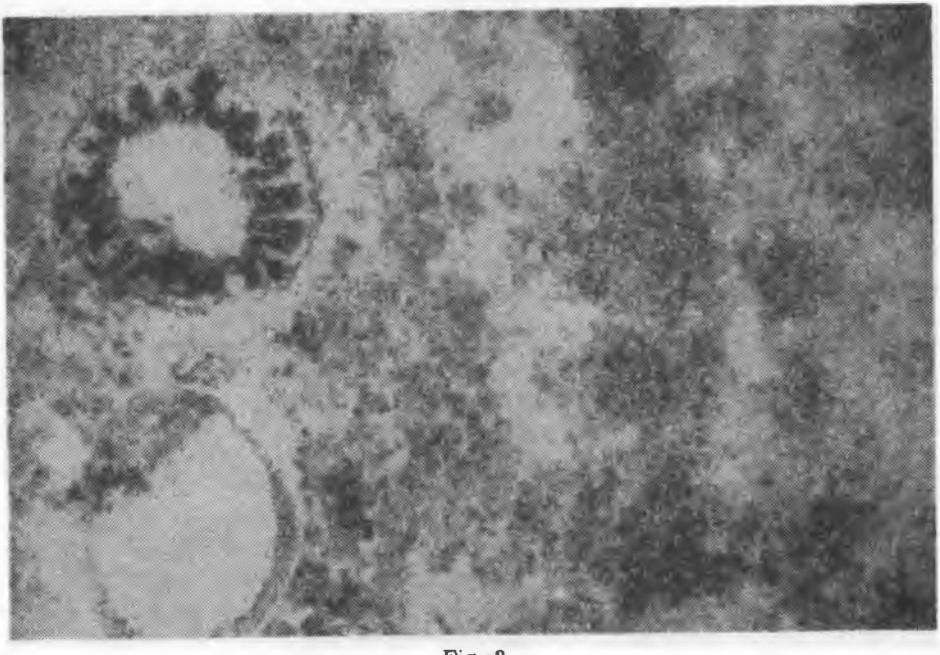

Fig. 2

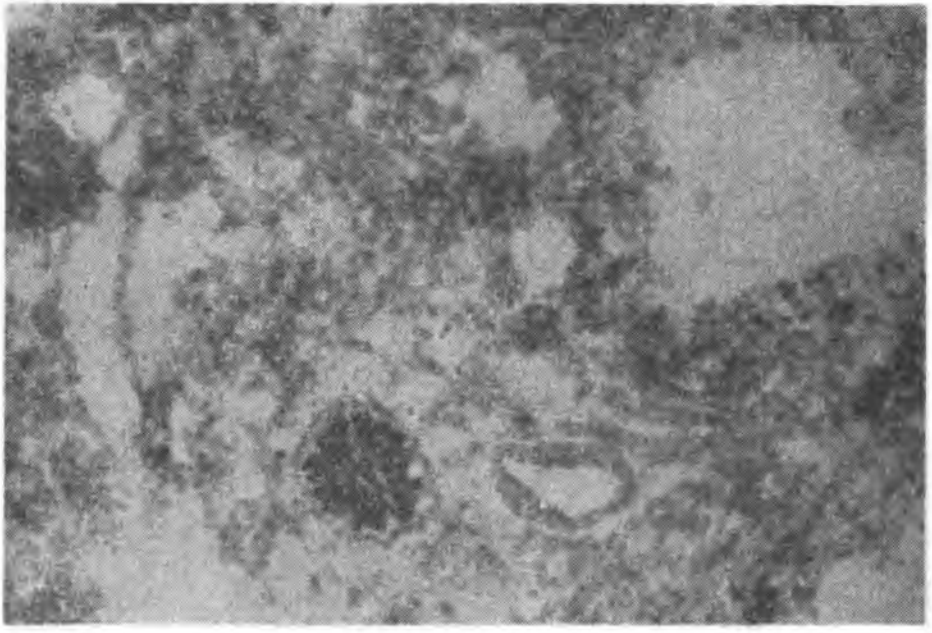

Fig. 3

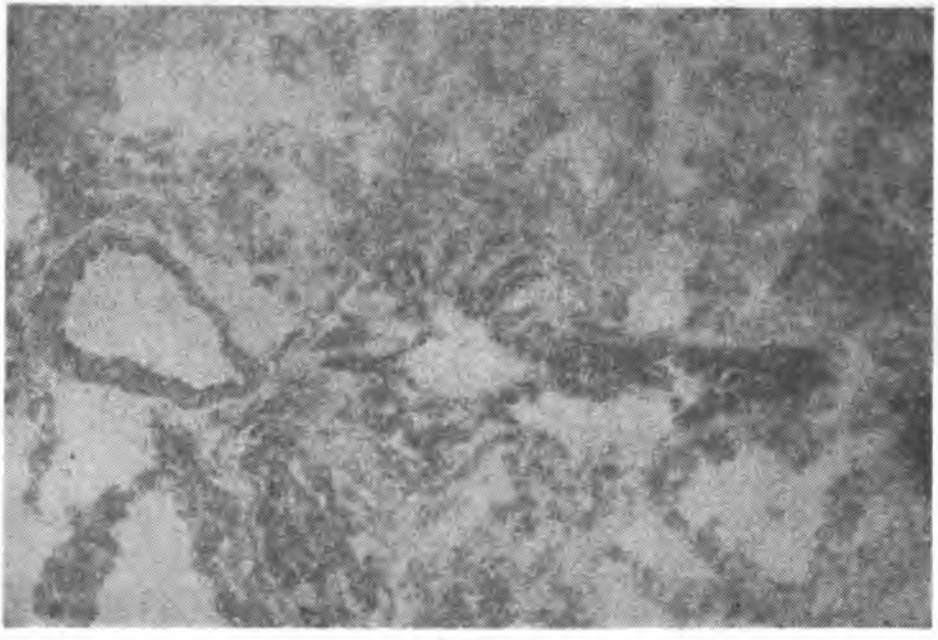

Fig. 4

Fig. 5

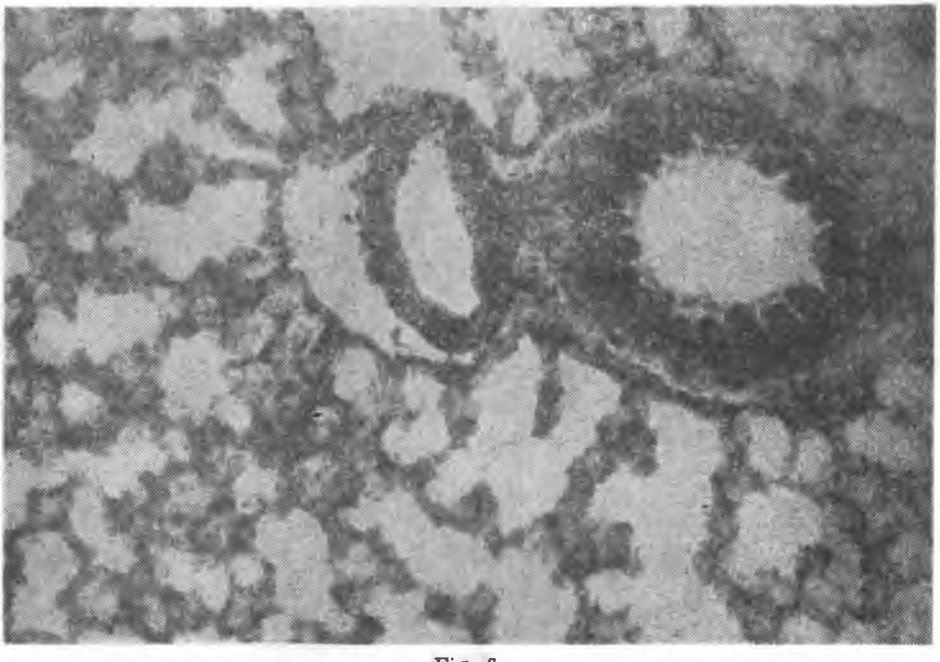

Fig. 6

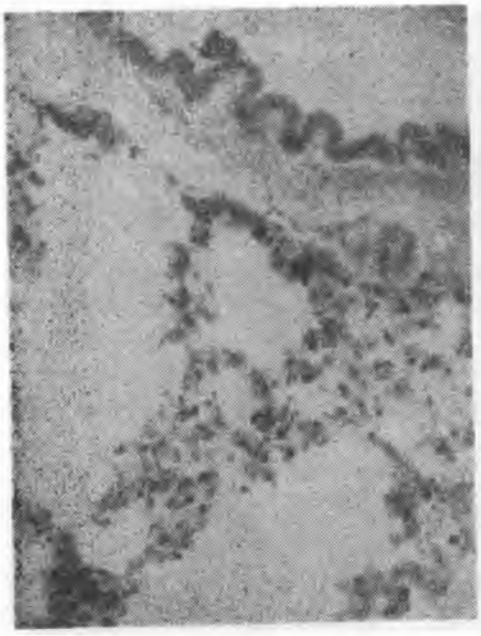

Fig. 7

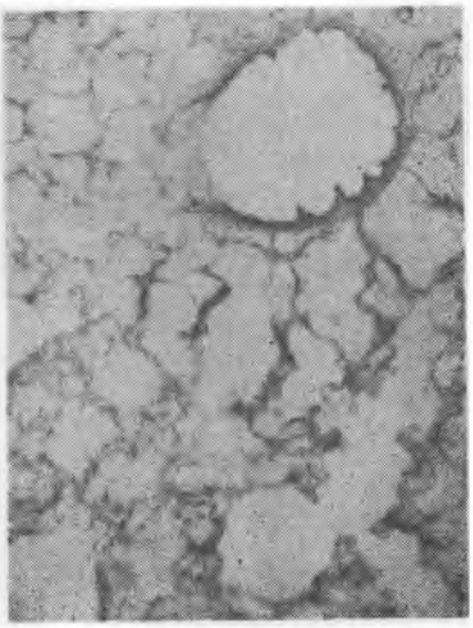

Fig. 8

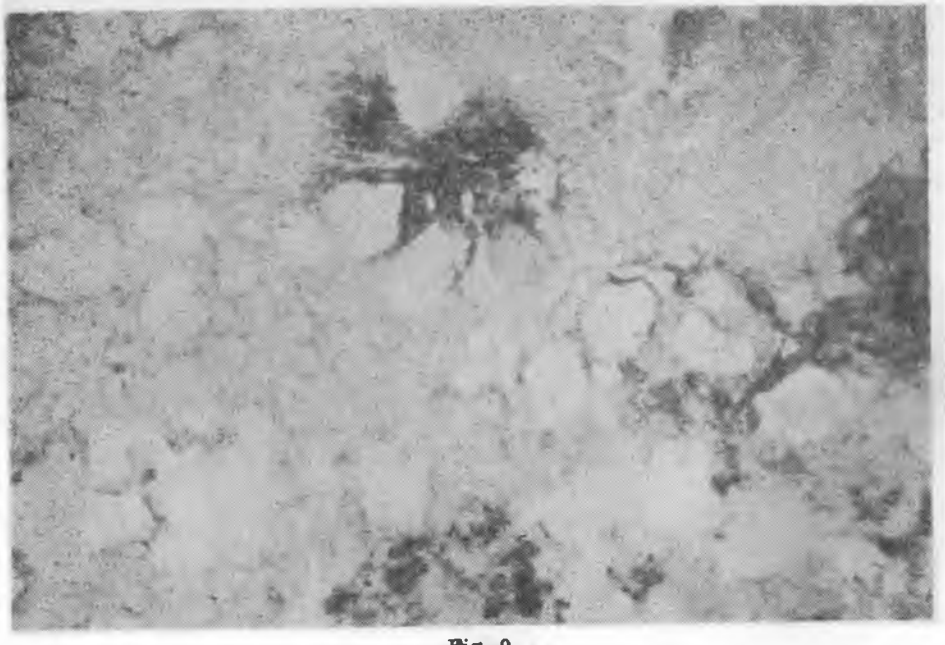

Fig. 9