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CHANGES IN ACTIVITY OF ADENOSINE DEAMINASE AND ANTIOXIDATIVE ENZYMES IN PATIENTS WITH DUST DISEASES OF THE LUNGS

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Morphological, biochemical, and clinical manifestations of the pneumoconioses give indirect proof that immune mechanisms are involved in the development of this disease. Despite many attempts to discover antigenic changes characteristic of pneumoconioses in the lungs and other changes which can be regarded as probable specific manifestations of immune mechanisms in the development of this pathology, we have as yet no integral picture of the disturbances of the immune system [1]. Further investigations into this problem are accordingly indicated.

Enzymic disturbances of purine metabolism in immunodeficiency states were first discovered in 1972 [11]. One of the key enzymes of purine metabolism is adenosine deaminase (ADA), which is widely distributed in human and animal tissues [5]. Its principal substrates are adenosine and deoxyadenosine. Normally ADA decomposes purines and is involved in the formation of hypoxanthine, a source for purine resynthesis. It is now known that a decrease in ADA activity accompanies many primary and secondary immunodeficiency states. Highest ADA activity in man is observed in lymphoid tissue, erythrocytes, and tissues of the gastrointestinal tract, where ADA activity is necessary for the utilization of alimentary purines, taken in with the food. Maximal ADA activity is found in cortisone-sensitive thymocytes. Some increase in ADA activity is observed in the lymphocytes of persons "developing" an immune response [10].

Recently the important role of active forms of oxygen (AFO) in the development of dust diseases of the lungs has been discovered. The main sources of AFO in the body are phagocytic cells, platelets, eosinophils, and endotheliocytes. AFO play a dual role in the function of aerobic organisms. They are responsible for realization of the mechanism of the bactericidal effect, and for the formation of biologically active substances (prostaglandins, leukotrienes); they are also

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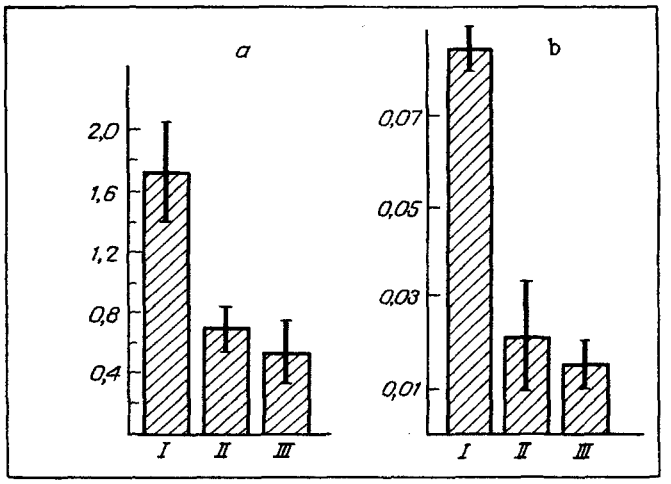

Fig. 1. Changes in ADA activity of lymphocytes (a) and erythrocytes (b) in patients with pneumoconiosis and chronic dust bronchitis. Ordinate, ADA activity (in nmoles/min/10^7 cells at 37°C). Here and in Fig. 2: I) normal individuals, II) patients with chronic dust bronchitis, III) patients with pneumoconiosis.

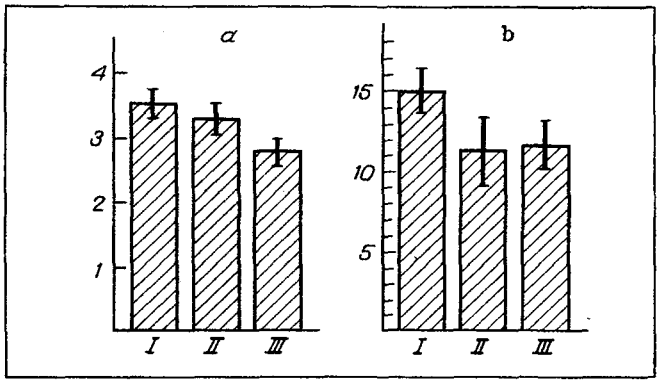

Fig. 2. SOD (a) and catalase (b) activity in patients with pneumoconiosis, chronic dust bronchitis, and healthy individuals. Ordinate, on left — activity (in conventional units); right — catalase activity (in conventional units).

involved in collagen metabolism and they affect expression of receptors [2, 6, 9]. However, high reactivity of AFO in some cases leads to the transformation of biologically important compounds, accompanied by loss of their functional activity. In the healthy organism there is a powerful system of antiradical defense, which appears during evolutionary development and eliminates an excess of free radicals. The system of defense against AFO includes antioxidative enzymes: superoxide dismutase (SOD), catalase, and glutathione peroxidase, as well as nonenzymic components, namely glutathione, ascorbic acid, α-tocopherol, certain amino acids, and ceruloplasmin [6, 8, 9, 12].

The information given above convinced us of the desirability of undertaking a simultaneous study of activity of ADA, an enzyme of purine metabolism, and of antioxidative enzymes (SOD and catalase) in patients with occupational dust diseases of the lungs.

The aim of this investigation was to study activity of ADA, SOD, and catalase as characteristic of the state of the immune and antioxidative systems in lymphocytes and whole blood from patients who had worked for between 11 and 20 years in an atmosphere containing a high concentration of dust, and suffering from chronic dust bronchitis and pneumoconiosis, and for comparison, with the corresponding parameters for healthy individuals.

TABLE 1. Individual Characteristics of Antiradical Defense and Purine Metabolism in Patients with Dust Diseases of the Lungs

Serial No.	Diagnosis	SOD	Catalase	ADA of lymphocyte	ADA of erythrocytes
		Conventional units		nmoles/min	
1	Silicosis	2,8	9,4	0,49	0,012
2	»	3,0	12,8	0,52	0,018
3	»	2,9	12,8	0,35	0,039
4	»	2,5	11,9	0,52	0,013
5	»	2,6	10,4	0,48	0,016
6	»	2,8	12,8	0,57	0,019
7	»	2,7	10,6	0,47	0,017
8	»	2,9	12,5	0,58	0,015
9	»	3,0	12,0	0,59	0,013
10	»	2,8	11,7	0,57	0,018
11	»	—	—	1,1	—
12	»	—	—	1,0	—
13	»	—	—	1,1	—
14	CDB	3,3	14,4	0,83	0,009
15	»	3,2	13,2	0,78	0,027
16	»	3,5	9,4	0,45	0,016
17	»	2,9	10,2	0,61	0,043
18	»	3,1	9,4	0,84	0,02
19	»	3,3	12,8	0,67	0,026
20	»	3,2	12,5	0,77	0,021
21	»	3,1	10,0	0,62	0,019
22	»	3,3	11,2	0,67	0,023
23	»	3,4	10,1	0,65	0,021
	Healthy individuals	3,5	15±1	1,7±0,3	0,08±0,005

Legend. CDB) Chronic dust bronchitis.

ADA activity is independent of age and sex [15], and individual fluctuations do not exceed 25% [13]. We obtained similar data in relation to antioxidative enzymes.

EXPERIMENTAL METHOD

Lymphocytes were isolated from peripheral blood by Boyüm's method [7] and washed 3 times with 50 mM potassium-phosphate buffer, pH 7.4. Erythrocytes also were washed 3 times with potassium-phosphate buffer. To measure ADA activity we used an extract obtained by freezing and thawing the cell suspension 4 times. Measurements of ADA activity were carried out at 265 nm on an LKB-4050 spectrophotometer, in 50 mM potassium-phosphate buffer, pH 7.4, containing 43 μM adenosine/ml. The unit of ADA activity corresponds to the quantity of substrate (adenosine) converted during 1 min by 10^7 cells at 37°C [3]. Activity of catalase and SOD was determined in whole blood at room temperature, by the traditional methods [4, 14].

EXPERIMENTAL RESULTS

The results of investigation of ADA activity are given in Fig. 1. It will be clear from Fig. 1a that ADA activity of the lymphocytes in patients with pneumoconiosis and chronic dust bronchitis was depressed on average by 3 and 2.5 times respectively compared with activity of the enzyme in healthy individuals. ADA activity of the erythrocytes also was depressed: fivefold in patients with pneumoconiosis and 3.7-fold in patients with chronic dust bronchitis. A marked decrease in ADA activity of both types of cells was found in 80% of patients studied, and ADA activity in 20% of patients was a little below the lower limit of normal.

Activity of the antioxidative enzymes was lower than in normal individuals: SOD, which inactivates superoxide radicals, was on average 24% lower in patients with pneumoconiosis and 11% lower in patients with chronic dust bronchitis; activity of catalase, which inactivates H_2O_2, was on average 22% lower in patients with pneumoconiosis and 25% lower in patients with chronic dust bronchitis (Fig. 2). As will be clear from Fig. 2, the degree of depression of catalase activity was virtually identical in patients with the two diseases, whereas SOD activity was depressed rather more in patients with pneumoconiosis.

Some reduction of SOD and catalase activity in the patients tested indicates weakening of functional activity of antiradical defense.

The results relating to weakening of ADA activity in lymphocytes and erythrocytes of the patients of the groups studied indicate that during prolonged work in a dusty atmosphere disturbances of purine metabolism arise, similar to those observed during the onset of secondary immunodeficiency states. We have not found any such results described in Soviet or other publications.

Together with other data, the results described above can be used to determine increased risk groups during work in a dusty atmosphere. Work in a dusty atmosphere, with depression of ADA activity of the lymphocytes below unity, can be taken as dangerous.

The individual characteristics of the enzyme activity studied are given in Table 1.

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