Activities of Complement and Acute Phase Proteins in Subjects Exposed to Ozone

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Serum complement activity was studied by the turbidimetric method in workers of a plasticizer shop exposed to ozone. The inhibitory potential (α-1-antitrypsin) decreased, activity of complement component C_3 increased, and the deficit of orosomucoid was augmented with the length of service.

Key Words: *ozone; α-1-antitrypsin; orosomucoid*

Immunotropic factors form the immune status of healthy subjects and determine the specific features of diseases in immunocompromised patients. Clinical and immunological examinations of workers engaged in chemical industry and occupationally exposed to gases irritating the airways revealed some changes in immune homeostasis [9]. Immunological studies showed that these disorders impair nonspecific mechanisms, such as oxidase transport and acute phase proteins and serum protease inhibitors, specifically, α-1-antitrypsin [6].

Ozone effects on man attract now special attention [9,10]. The state of the complement system is a reliable diagnostic and prognostic marker of the organism's status [4]. We investigated the effect of ozone on human serum complement activity and evaluated the levels of acute phase proteins α-1-antitrypsin (AAT) and orosomucoid (OM).

MATERIALS AND METHODS

Clinical and immunological studies were carried out in 158 workers (144 men and 14 women), divided into groups depending on the length of service (1-10 years and more). The reference groups consisted of healthy subjects (n=8) working at the same plant and residents of the town (n=12) in which this petroleum plant was situated. The mean age of workers with the length of service of 1-7 years was 36.5 years, the rest were aged 44.2 years. The immune status was evaluated by serum content of complement components and acute phase proteins measured turbidimetrically [5] at 340 nm with Orion Diagnostica kits. Blood samples were collected from the ulnar vein after overnight fasting. The concentration of ozone in the working zone corresponded to maximally permissible level (0.1 mg/ml).

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RESULTS

Chronic nonspecific pulmonary diseases predominate in the morbidity structure in workers engaged in dialkylphthalates production [1]. High sensitivity of the complement to various factors does not allow us to trace an absolutely unambiguous correlation between visible changes in the respiratory organs and serum complement activity (Table 1), though such a tendency is seen statistically. Analysis of the initial status of subjects exposed to ozone showed the highest complement activity (C_3 and C_4) in subjects working at the plant for at least 6 years. During this period 85% workers developed chronic bronchitis. High serum complement activity in these workers is not surprising, because the concentration of antigen-antibody complexes formed by immunoglobulins G and M [4], the main activators of the classical pathway of complement activation, also increased. Immune complexes can also initiate the alternative pathway. It was shown that C_3 convertase of the alternative pathway activates not only its natural substrate C_3, but also C_4 and C_2 components. Thus,

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both activation pathways function in reality, supplementing and stimulating each other [4].

A high level of complement components detected in just 3% patients without manifest changes in the respiratory organs was apparently caused by other immunological processes. Just a tendency to increase in complement activity (within normal) was observed in subjects working at the plant for 4 years. An increase in the content of C_3 component with the duration of occupational contacts with ozone (almost 4 times higher than in other workers of the plant after 7 years) was a marker of pronounced chronic transformation of bronchopulmonary disease and of inefficiency of cellular mechanisms responsible for detoxication and utilization of foreign antigens.

Proteases released into the bloodstream promoted a compensatory increase in the concentrations of their inhibitors, specifically, AAT. The level of AAT tended to increase in subjects working at the plant for 1-3 years, while after 3 years it gradually decreased (Table 1). Long exposure to ozone (6-7 years and more) decreased serum inhibitory activity in comparison with the control groups. Presumably, relative exhaustion of inhibitory potential of the blood and, as a result, high proteolytic activity of the enzymes destroyed the airway mucosa, leading to chronic bronchitis [8].

It has been previously demonstrated that the concentration of AAT maximally increased in acute bronchitis and acute pneumonia and to a lesser extent in chronic bronchitis, particularly obstructive [2,3,6-8]. Inhibitor deficiency was detected in patients with a concomitant pulmonary emphysema, which developed as a result of this deficiency. Proteinase activities (elastase, cathepsins H, B, and L) were higher in chronic bronchitis than in acute pneumonia and acute bronchitis.

The level of AAT in workers engaged in the plasticizer shop decreased in comparison with the plant and town controls, being at the lower boundary of the normal range (Table 1). No deficit of proteinase inhibitors, including AAT, was detected in the majority of patients with chronic obstructive pulmonary diseases [6-8]. However, activated neutrophils of these patients released elastase in very high concentrations at sites of contact of cell membrane with connective tissue. Therefore, with migration of neutrophils the local concentrations of elastase surpasses the inhibitor capacity. Therefore, activation and migration of cells will always lead to focal connective tissue destruction which cannot be prevented.

The initial status of all subjects exposed to ozone was characterized by specific changes in the immune status. AAT is a natural elastase inhibitor covalently binding the enzyme at a 1:1 ratio, and the resultant complex is utilized by immune system cells [7]. In immune imbalance, normal blood content of AAT does not rule out pathological metabolism of AAT.

In turn, an excess of normal or abnormal metabolites or products of cell reactions representing endogenous toxic substances leads to endogenous intoxication. Laboratory evaluation of the severity of endotoxicosis is sometimes effective [3].

Activity of OM increased and reached the maximum at the end of the first year, being 2.6-fold above the maximal value in plant workers. During subsequent

TABLE 1. Serum Levels of C_3 and C_4 Components and Acute Phase Proteins in Workers of Plastisizer Shop with Different Length of Service (*M±m*)

Group		C_3	C_4	AAT	OM
		g/liter			
Control	in town	1.96±0.09	0.36±0.01	4.21±1.51	0.37±0.09
	at the plant	1.97±0.07	0.44±0.04	3.28±1.29	0.42±0.13
Length of service, years	1	2.01±0.12	0.47±0.02	6.74±1.94	1.12±0.17**
	2	2.26±0.21	0.53±0.05	6.98±1.59	0.40±0.07
	3	2.09±0.09	0.72±0.09*	8.42±1.25**	0.42±0.04
	4	2.57±0.16**	0.71±0.09*	5.00±0.75	0.32±0.11
	5	2.59±0.21*	0.70±0.11	5.24±0.91	0.25±0.09
	6	3.48±0.18**	0.81±0.09**	2.45±0.11	0.20±0.05
	7	3.86±0.98	0.86±0.15	2.15±0.19	0.18±0.07
	8	4.57±0.85*	1.81±0.08**	1.19±0.09**	0.19±0.04*
	9	4.59±0.93*	1.02±0.18*	1.01±0.13**	0.19±0.06
	10	4.66±0.78**	1.12±0.29*	1.07±0.48	0.15±0.04*
	more than 10	5.06±1.19*	1.10±0.36	1.00±0.51	0.12±0.07*

Note. *$p<0.05$, **$p<0.01$ *vs.* plant control.

years OM activity gradually decreased and after 6-year service attained the lower boundary of the normal values (Table 1). The deficit of OM in the blood after 10-year exposure to ozone constituted 40% of normal.

The function of OM is not yet known [2,3]. It binds to the group-specific receptor for asialoglycoproteins on hepatocyte surface, and through a ligand-receptor mechanism is transferred from the bloodflow into the bile by transcytosis. During this process OM can transport some substances from the blood into the bile.

No doubt, changes in blood concentrations of OM, AAT, and complement components indicate their involvement in the mechanisms of glycobiological regulation of blood cell function. The initial immune status and reserve potential play an important role in the immunopathological response to ozone exposure, but this relationship deserves special studies in subjects occupationally exposed to ozone.

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