FOREIGN TECHNOLOGY DIVISION

AUTOANTIBODIES AND TUBERCULIN HYPERSENSITIVITY
OF LEUKOCYTES IN SILICOSIS AND SILICOTUBERCULOSIS

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**Abstract**

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AUTOANTIBODIES AND TUBERCULIN HYPERSENSITIVITY OF LEUKOCYTES IN SILICOSIS AND SILICOTUBERCULOSIS

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Frunze

In recent years interest has steadily grown in regard to immunological processes during silicosis and silicotuberculosis. At present there are many investigations which emphasize the importance of autoimmune mechanisms in the pathogenesis of these diseases (V. Ye. Lyubomudrov, 1965; M. I. Kitayev, 1968; E. C. Vigliani, B. Pernis, 1960, 1962; U. Saffiotti, 1960, and others).

The factors which lead to the formation of autoantigens and autoantibodies are very diverse. As the initial link in this process they consider the formation under the influence of quartz of an antigenic structure, following which there is a specific response of immunocompetent cells to the antigenic information which is brought in. It is assumed that quartz, which enters the lungs during respiration, changes the spatial configuration of the protein molecules (C. Clays, 1954; R. Soda, 1961; Czabo, 1967, others). A significant link in this process is the destruction of macrophages, which absorb the quartz dust particles with the...
liberation of endocellular autoantigen from the protoplasm (E. C. Vigliani, B. Pernis, 1962, and others). In this case quartz is also assigned the role of the nonspecific inductor of autoimmunogenesis (P. Gross, 1960; P. D. Byers, E. I. King, 1961).

Subsequent investigations demonstrated with all obviousness the presence of pulmonary autoantibodies in patients with silicosis and silicotuberculosis (M. I. Kitayev, 1965, 1967; N. V. Revnova, 1968, and others). However, their pathogenetic role and clinical significance during these diseases remained definitely unexplained. Therefore there was definite interest in a clinical-immunological study of silicosis and silicotuberculosis in a comparison with immunochemical investigations of pulmonary autoantibodies.

In the present report the results are given from an investigation of antipulmonary autoantibodies in 150 patients with silicosis and silicotuberculosis. At first in the blood of the patients the complement-fixing pulmonary autoantibodies were determined with the help of the Khudomel reaction of the consumption of complement (1960). This reaction is based on the consumption of complement under the interaction of antigen with the appropriate complement-fixing antibodies. The presence of autoantibodies is recorded based on the inhibition of hemolysis during titration of serum complement in a test series, into which antigen has been introduced, in comparison with a control. In this case a difference in two test tubes is evaluated as +, in three test tubes ++, and in four and more test tubes ++++. The reaction is considered negative with the absence of a difference in the degree of hemolysis between the test and the control series or if there is a difference in one test tube.

With the help of this method we studied the presence of autoantibodies to lyophilized pulmonary antigen in 70 patients with silicosis and silicotuberculosis and in persons suspected of having silicosis. In the blood serum of healthy males such
antibodies were revealed in individual cases. In the serum of patients with silicosis and silicotuberculosis the corresponding antibodies are found in 85% of those investigated. The intensity of the reaction was not connected with the severity of the pathological process. These autoantibodies also appeared in persons with early silicotic changes in the lungs and even in the pre-roentgenologic phase of development of the process. Inhibition of hemolysis frequently corresponded to three, four, and more test tubes. The joining of tuberculosis to silicosis did not influence the frequency of appearance and the content of this type of autoantibodies.

In examining these facts it is possible to arrive at the conclusion that pulmonary autoantibodies, exposed by the reaction of consumption of complement, are determined very frequently not only in persons with silicosis and silicotuberculosis, but also in clinically healthy workers in occupations which are hazardous in regard to silicosis. The resulting data make it possible to speak of definite immunological shifts in underground workers in the pre-roentgenologic period of development of the disease.

We could also be convinced of the presence of a solid bond between the complement activity of the blood and allergization of the organism. Together with the progression of the disease the complement titer of the blood was lowered and at the same time there was an increase in the number of reactions with the inhibition of hemolysis. This circumstance seems very conformable if one accepts that the lowering of complement is conditioned by its binding in the organism by an antigen-antibody complex. In the final result all of this testifies to the presence of autosensitization, in the case of silicosis and silicotuberculosis, to the products of tissue breakdown.

In another series of investigations on 80 patients with silicosis and silicotuberculosis we determined the hemaglo...
pulmonary autoantibodies by means of induced hemagglutination in the Boyden method (M. I. Kitayev, 1967). The titer of this type of autoantibodies usually corresponded to the severity of the process taking place in the lungs, and quite frequently became high in patients with stage II silicosis and silicotuberculosis (1:16-1:32).

The appearance of complement-fixing autoantibodies preceded in time the synthesis of agglutination pulmonary autoantibodies. It follows from this that the organism responds to the pathological effect of silica initially by intensification of the synthesis of complement-fixing autoantibodies and only following further progression of the process develops agglutination pulmonary autoantibodies.

Not lacking in interest is the fact that pulmonary autoantibodies bear a nonspecific nature, since they are bound to approximately the same degree with normal pulmonary tissue and that which is infected with silicosis. Still open is the question of the reasons for the fixation of autoantibodies in the blood of healthy pulmonary tissue.

In a special series of investigations we jointly with V. L. Morozov tested sera containing autoantibodies with three antigens, cardiac and renal. In this case it was established that the autoantibodies are bound just as frequently with any of the investigated antigens. With the help of the method of absorption according to P. N. Kasyakov and V. S. Korostelevaya (1959) we were able to show that these reactions are conditioned by the same antigen, displaying a maximum affinity to the common antigen component of pulmonary and renal tissue (M. I. Kitayev, V. L. Morozov, 1969). In the light of these findings there is doubtless interest in the study of the chemical mechanism of autoantibodies. For this with the help of formalinized tissue autoantibodies were adsorbed from the sera. Before and after absorption the content of protein
fractions and the titer of autoantibodies in them were determined. In this case it was established that after extraction of autoantibodies from the sera the level of γ-globulins was statistically lowered (P < 0.05).

These investigations make it possible to assert that the autoantibodies are related to the γ-globulin fractions.

The synthesis of such a type of autoantibodies, bound in the test tube with the antigens of a healthy lung, apparently reflects the immunological reaction of the organism to the products of tissue breakdown, i.e., testifies to the condition of autosensitization.

In addition to autoallergy tuberculin allergy was also studied. Since skin probes do not reflect the specific reactivity of the organism sufficiently fully, then for the evaluation of infectious allergy the reaction of blood neutrophils to tuberculin in vitro was used (V. A. Fradkin, 1967). According to our data, the degree of allergization of blood neutrophils in patients with silicotuberculosis somewhat exceeded that in the case of silicosis (12-14 against 18-20). The difference in the average values of the index of damage to neutrophils between patients with silicosis and silicotuberculosis was significant (P < 0.05).

In the course of the investigations it was cleared up that the intensity of damage to neutrophils depends mainly on the phase of the tuberculosis process and to a lesser degree on the stage of silicosis. The mechanism of this phenomenon is connected with delayed allergy.

Thus, during silicosis and silicotuberculosis we have taking place autoallergy and a tuberculin type of hypersensitivity, manifested in the sensitization of blood leukocytes.