

SERUM HUMORAL FACTORS CAUSING THE ALTERED PHYSIOLOGICAL STATE OF THE PERIPHERAL BLOOD LYMPHOCYTES IN SCHIZOPHRENIA

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Statistically significant correlation was found between the relative percentage of cells responding to stimulation by phytohemagglutinin (PHA) by DNA synthesis in cultures of lymphocytes from patients with schizophrenia and also in the percentage of lymphocytes no longer responding to PHA stimulation by DNA synthesis in cultures of white blood cells from healthy donors as a result of the cultivation of those cells in medium containing 20% blood serum from patients with schizophrenia. Similar correlation was found between the relative percentage of adhesive lymphocytes in cultures of white blood cells from patients with schizophrenia and in the percentage of adhesive lymphocytes in cultures of white blood cells from healthy donors as a result of their cultivation in medium containing 20% blood serum of schizophrenic patients. The results confirm the hypothesis that the altered physiological state of the peripheral blood lymphocytes of patients with schizophrenia is due to factors present in the blood serum of such patients.

KEY WORDS: schizophrenia; lymphocyte; serum factors.

To test the validity of the hypothesis that the altered physiological state of the peripheral blood lymphocytes of patients with schizophrenia is due to the action of factors present in the blood serum of such patients on these cells [3], it was necessary not only to reproduce this state of the patients' lymphocytes in model experiments but also to demonstrate that this activity of the blood serum of patients with schizophrenia is dependent on the degree of change in the functional state of their lymphocytes. Ability to reproduce the altered state of the peripheral blood lymphocytes of schizophrenics has been demonstrated in the course of so-called cross experiments [1].

The object of this investigation was to study the relationship between the activity of the blood serum of schizophrenics and the physiological state of their blood lymphocytes.

EXPERIMENTAL METHOD

Peripheral blood lymphocytes and blood serum from 13 patients with different forms of schizophrenia (continuous and intermittent forms) were investigated. Lymphocytes and blood serum from 13 healthy donors were used as the control. Blood was obtained after admission of the patient to hospital and before medical treatment began or 2 weeks or more after treatment had ended. The patients were aged 22-43 years: 6 men (mean age 31 years) and 7 women (mean age 33 years). The donors were healthy persons aged 22-37 years: 7 men (mean age 29 years) and 6 women (mean age 32 years).

White blood cells and serum were obtained by the method described previously [1, 8]. DNA synthesis was stimulated by the addition of phytohemagglutinin P (PHA-P; Difco) to the medium up to a final concentration of 40 µg/ml; the cell concentration in the cultures was 10⁶ cells/ml. DNA synthesis in the nuclei of the lymphocytes was judged by their DNA content (cytophotometry after preliminary staining of the cells by Feulgen's method). The methods of preparation of the culture media, of cultivating the statistical analysis of the results

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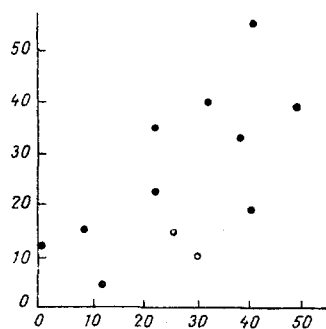


Fig. 1

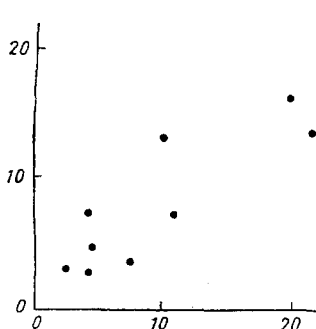


Fig. 2

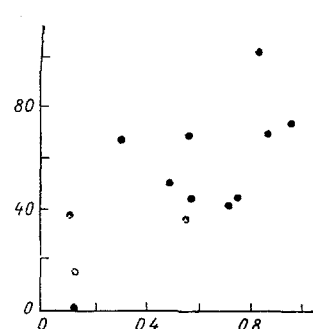


Fig. 3

Fig. 1. Response of healthy donors' lymphocytes to stimulation with PHA during culture in medium containing 20% blood serum of patients with schizophrenia. Ordinate, percentage of healthy donor's lymphocytes cultivated in medium with 20% blood serum of a given patient and responding to stimulation by DNA synthesis; abscissa, percentage of lymphocytes of schizophrenic patient responding to stimulation by DNA synthesis.

Fig. 2. Changes in percentage of adhesive cells in cultures of healthy donors' lymphocytes grown in medium containing 20% blood serum of schizophrenic patients. Ordinate, percentage of adhesive lymphocytes of healthy donor grown in medium containing 20% blood serum of schizophrenic patient; abscissa, percentage of adhesive lymphocytes in culture of lymphocytes of schizophrenic patient.

Fig. 3. Correlation between antithymic activity of blood serum of schizophrenic patient and percentage of healthy donors' cells no longer responding to stimulation by DNA synthesis after cultivation in medium containing 20% serum of schizophrenic patient. Ordinate, percentage of healthy donor's cells no longer responding to stimulation by DNA synthesis after cultivation in medium containing 20% schizophrenic blood serum; abscissa, cytotoxic index of blood serum of schizophrenic patient.

were all described previously [1, 8]. In a parallel series of cultures the content of adhesive lymphocytes was determined [7].

To study one of the correlations mentioned above data for the cytotoxic index of schizophrenic blood serum, generously provided by G. I. Kolyaskina and T. M. Maznina (Laboratory of General Pathophysiology, Institute of Psychiatry, Academy of Medical Sciences of the USSR) were used. The cytotoxic index was determined by the method described by Luria and Domashneva [5].

EXPERIMENTAL RESULTS

The study of correlation between the ability of lymphocytes from a patient with schizophrenia to respond in tissue culture to stimulation with PHA by DNA synthesis and the ability of the serum of that patient to inhibit the response of healthy donors' lymphocytes to PHA revealed direct linear correlation between the parameters studied ($r = 0.62$; $P < 0.05$; $n = 12$). The blood serum of those patients whose lymphocytes responded weakly to PHA stimulation thus very strongly inhibited the response of lymphocytes of healthy donors to PHA. Conversely, in those cases when the response of the lymphocytes of schizophrenics to stimulation differed negligibly from the response of healthy donors' lymphocytes, their serum inhibited the response of the donors' lymphocytes to PHA only feebly (Fig. 1).

Cultivation of healthy donors' lymphocytes in medium containing 20% blood serum of schizophrenic patients increased the percentage of adhesive cells in those cultures. The tests showed that the ability of blood serum of schizophrenic patients to increase the percentage of adhesive cells in cultures of healthy donors' blood correlated well ($r = 0.96$; $P < 0.01$; $n = 9$) with the percentage of adhesive lymphocytes in their peripheral blood (Fig. 2).

The study of correlation between the level of antithymic activity of the blood serum of schizophrenic patients and the ability of the lymphocytes of these patients to respond to stimulation with PHA by DNA synthesis also revealed direct linear correlation between the two parameters ($y = 16.8 + 60.6x$; $r = 0.69$; $P < 0.01$; $n = 13$). Consequently, lymphocytes of schizophrenic patients whose blood serum possessed high antithymic activity responded to stimulation with PHA much less strongly than lymphocytes of patients whose blood serum had low antithymic activity (Fig. 3).

The results of these experiments confirm reliably that the direct cause of the change in the physiological states of the lymphocytes of patients with schizophrenia is the presence of factors in the patients' blood serum, for the intensity of the changes in the physiological state of the lymphocytes of healthy donors induced by the patients' blood serum correlated directly with the character of the physiological state of the patients' lymphocytes. This conclusion is in good agreement with the many data pointing to the presence of a membranotropic factor [3, 4, 6] and of other biologically active compounds [2, 5] in the blood serum of schizophrenic patients.

Analysis of the third of the correlations cited in this paper, confirming the validity of the conclusion deduced above, suggests that the serum factor modifying the physiological state of the lymphocytes in schizophrenia is immunological in nature. The increase in the percentage of adhesive cells in cultures of healthy donors' lymphocytes observed in the experiments (Fig. 2) and the reduced response of these cells to stimulation can be attributed to their injury by the blood serum of the schizophrenic patients.

The increase in the adhesive properties of the donors' lymphocytes observed experimentally suggests that the decrease in proliferative activity of these cells produced by the blood serum of schizophrenics was caused directly by a change in the properties of the cell membrane of the lymphocytes. The properties of the cell membrane are known to determine to a substantial degree the DNA transcription processes in the cell and its proliferative activity [9, 10, 11]. The postulated ability of schizophrenic blood serum to change the course of biosynthesis of a highly important macromolecular cell component may prove to be an important factor in the discussion of the pathogenetic role of contact between the serum factor (or, more probably, the membranotropic factor of the blood serum) with the brain neurons of patients with schizophrenia.

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