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# Low levels of active T-RFC in the blood of multiple sclerosis patients

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There is no doubt that immune factors play a role in multiple sclerosis (MS). However, the full meaning of immune mechanisms in the sense of the pathogenesis of the disease is still unknown. It seems that the most acceptable explanation of the cause of MS is a predisposition to infection in childhood and a maladaptive immune response *(10)*. Characteristics of the humoral immune response within the central nervous system are well known and have been studied extensively. In the cerebrospinal fluid (CFS) of MS patients, elevated immunoglobulins (G, A), oligoclonal IgG and pleocytosis could be regularly found *(6)*. The most interesting finding is the presence of oligoclonal immunoglobulins, whose full meaning is still unclear. Contrary to the above, there is not much data about the role of cellular immunity in the pathogenesis and clinical course of MS.

The aim of this work was to evaluate the dynamics of lymphocyte subpopulations in the clinical course of the disease. MS was diagnosed after the criteria of Allison and Millar *(1)*. According to the stage of the disease, 29 MS patients were divided into two groups: *a.* 11 patients with active disease (beginning and exacerbation), and *b.* 18 patients with stable disease (remission). The patients' ages with active disease were from 18 to 47 years (median: 28 years) and the duration of the disease had been from a few months to 7 years (median: 1 year). The eighteen patients classified in the group with stable disease were between 25 and 67 years of age (median: 40 years) and the duration of disease had been from 3 to 26 years (median: 10 years). The control group, matched for age and sex with the group of MS patients, consists of 37 healthy persons (students, laboratory staff and neurotics). The age was in the range of 20 to 64 years.

All MS patients were treated by ACTH (one or two injections monthly). Immunological tests were performed 1 to 2 weeks after ACTH administration. The total T-RFC (rosette forming cells) and EAC-RFC were detected according to the method of Holm et al. *(3)*. The details of the method for the detection of active T-RFC are described elsewhere in this issue *(8)*. A lymphocyte with 3 or more sheep erythrocytes attached, was considered a rosette-forming lymphocyte. The relative and absolute concentration of cells forming rosettes was determined.

There was no significant difference comparing the relative and absolute numbers of active T, total T and B lymphocytes between age-matched controls and MS patients. However, some differences were noticed when groups of the active and stable form of the disease were compared. As Figure 1 indicates, the percentage of active T lymphocytes was much lower in the group of patients with active disease than in stable disease or control groups. The percentage of total T and B lymphocytes was similar in all groups. The absolute number of RFC (Figure 2) shows almost the same changes as those indicated in the relative numbers of cells. Again, the difference was significant for active T lymphocytes only. In spite of the much lower number of total T-RFC in active disease than in the control, the difference is not significant.

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Other immunological tests showed significant elevation of IgM in the blood and immunoglobulins (G, A) in the CSF of MS patients. The humoral immune response to viruses, detected by the level of antibodies in the blood, was almost the same in MS patients and controls (other neurological diseases).

There is a controversy in the literature about the changes in the level of total T lymphocytes. Some authors found their number reduced in active disease *(7)*, but others could not confirm these findings *(5)*. In many papers the age of the control patients was not declared, which may be the reason for different results. We agreed with the suggestion of Symington et al. *(10)* that the control group needs to be carefully matched for variables such as age and sex, which was done in our experiments. Recently, attention has been focused on the role of active T lymphocytes as a subpopulation of the total T lymphocytes. They are also thought to be an immunocompetent T-surveillance cell. The fact that the level of active T lymphocytes was decreased in the blood of MS patients may be a sign of deficiency in the cell mediated immunity. The lower number of total T lymphocytes in the acute phase of the disease is in line with the above presumption.

Data accumulated in the last few years better clarify the role of cell mediated immunity in the clinical course of MS. Profound changes in the functional properties of lymphocytes were found in the blood and CSF. The reactivity of peripheral blood lymphocytes to PHA and PWM is reduced *(9)*. Antel et al. *(2)* found that nonspecific T-suppressor cell activity in MS patients is subnormal during attack and rises as remission commences. Some irregularities similar to the ones described above were seen in the CSF of MS patients. Elevated total T, but decreased active T and B lymphocytes were found in MS patients *(4, 6)*. Furthermore, the response of CSF lymphocytes from MS patients to stimulation with PHA, ConA, or PWM is reduced *(6)*. Taking into account all these facts, as well as our results, it could be concluded that aberration in the functions of cell me-

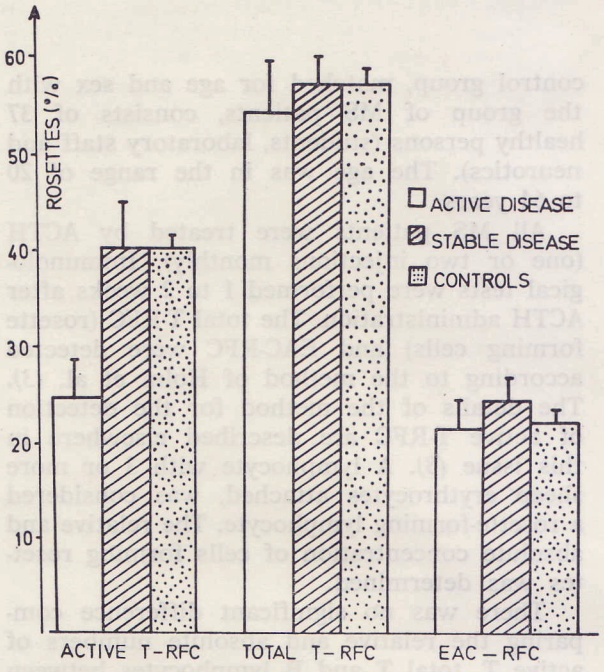


Figure 1. *Percentage of RFC (mean ± s.e.m.) in the blood of MS patients and controls. (Levels of significance for active T-RFC: control vs. active disease — $p < 0.001$; stable disease vs. active disease — $p < 0.01$).*

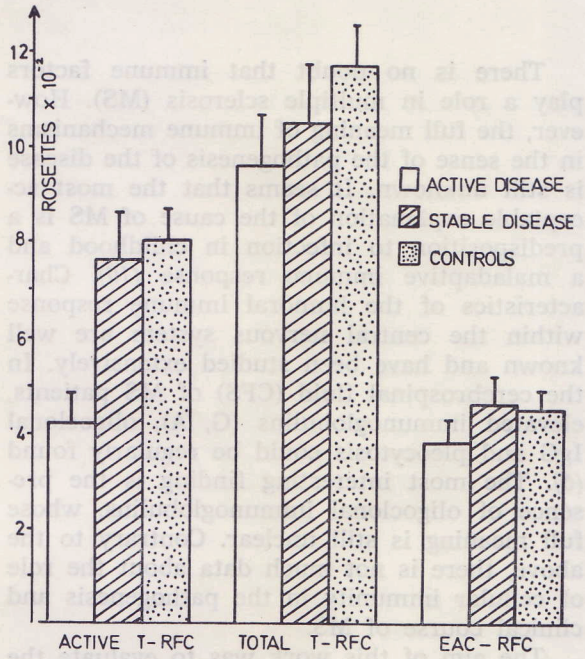


Figure 2. *Average number of RFC (mean ± s.e.m.) in the blood of MS patients and controls. (Levels of significance for active T-RFC: control vs. active disease — $p < 0.01$; stable disease vs. active disease — $p < 0.05$).*

diated immunity in MS patients exists. Consequently, it is difficult to accept that all of these changes are secondary to the central nervous system lesions.

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