Matters arising

HLA typing and T-cell subpopulations in multiple sclerosis

Sir: Recently Hughes and co-workers¹ have reported in this journal an association between the presence of HLA-DR2 and low CD8+ cells in multiple sclerosis patients and their cohabiting relatives. This finding was obtained from two partially different series of multiple sclerosis patients, relatives and unrelated healthy controls whose blood lymphocyte subpopulations were serially determined for several months. With a very similar protocol we have followed up 46 multiple sclerosis patients for 18 months²⁻⁴ and, in agreement with Hughes' group^{5,6} and other investigators^{7,8} we found that chronic progressive multiple sclerosis patients have significantly less CD8+ lymphocytes or high CD4/CD8 ratios.

Now we have concluded the HLA typing of 38 out of 46 multiple sclerosis patients originally included in that study. Our results, which are summarized in the table, are at variance with the results obtained by Hughes from a lower number of patients. HLA-DR2 positive subjects do not differ from negative ones with respect to lymphocyte subset mean percentages.

DR2 is the most frequently found HLA phenotype in caucasian multiple sclerosis patients. HLA-A3 and -B7 are also reported to be more represented in multiple sclerosis subjects than in the normal population. On the contrary HLA-B12 phenotype is negatively associated with the disease, almost in Italians.⁹ Consequently we correlated the presence or absence of these HLA phenotypes to lymphocyte subpopulation numbers. The results, similarly to what we found for HLA-DR2, were negative for a significant association (data not shown).

Our conclusion is that HLA-DR2 and reduced CD8+ cells are independently associated with multiple sclerosis.

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Compston replies

Dr Zaffaroni and colleagues report that there is no difference in percentage of circulating CD8 cells in 11 HLA DR2 positive and 27 DR2 negative patients with multiple sclerosis. They comment that this finding contrasts with our demonstration of an association between HLA DR2 and periodic reductions in CD8 cells, irrespective of clinical status. There are important differences between the protocols used in these two studies which prevent comparison of the results. First, it is not clear whether the value quoted by the Italians for each lymphocyte subpopulation in DR2 positive and negative patients is a mean based on single or serial observations in individuals. Secondly, our main observation related to the prevalence of periodic reductions in CD8 cells and not the absolute numerical value. Thirdly, we compared affected and unaffected individuals whereas Dr Zaffaroni and colleagues have restricted their analysis to patients with multiple sclerosis in all of whom low percentages of CD8 cells are to be expected (as they themselves point out) irrespective of HLA phenotype.

Unexplained chronic subarachnoid bleeding and a slowly progressive neurological syndrome

Sir: Superficial haemosiderosis of the central nervous system has been postulated to be the explanation for the development of a slowly progressive clinical syndrome in a 9 year old child.¹ The authors record supporting evidence including the presence of methaemoglobin and haemosiderin-containing macrophages in the CSF. These findings together with two reports of patients so diagnosed in life, may lead to increased recognition of the clinical syndrome in patients presenting with the suggestive combination of anosmia, nerve deafness and long tract signs, as suggested in our own report of 2 such cases diagnosed at necropsy.²

Dr Zwartz and colleagues note that the deposition of iron-containing pigment in the central nervous system results in gliosis and loss of neurons, but do not refer to the main pathological consequence of haemosiderosis, namely neuroaxonal

Table

	CD3%	CD4%	CD8%	CD4/CD8
HLA DR2+ (n = 11)	74.2 ± 5.9	48.3 ± 8.9	30.4 ± 8.4	1.70 ± 0.6
HLA DR2- (n = 27)	74.6 ± 6.2	47.8 ± 7.1	30.3 ± 7.4	1.75 ± 0.6
t value	0.20	1.98	0.02	0.19
p value	0.83	0.84	0.97	0.19