LETTERS TO

THE EDITOR

Lack of association between macrocytosis and multiple sclerosis

An increase in red cell diameter in patients with multiple sclerosis (MS) compared with normal controls was described by Plum and Fog in 1959. Interest in this subject has been reawakened by reports indicating that patients with MS had mild but significant macrocytosis compared with an age- and sex-matched control neurological group. The cause of the macrocytosis is unknown, but some observations have suggested a possible disturbance in vitamin B12 metabolism, binding or transport. We have compared haematological records of patients with definite MS with those of an individually matched neurological control group.

This study was based on a population of 154 consecutive patients, who satisfied the Poser criteria for clinically or laboratory definite MS. Patients with possible MS were not included. The mean (SD) disease duration was 8-4 (7-9) years. The mean Kurzke Expanded Disability Status Scale (EDSS) was 2-9 (1-9). All patients provided blood samples before specific therapy was started.

The control group consisted of 154 patients with miscellaneous neurological and psychiatric disorders which included cerebral, cerebrovascular lesions, headache, mechanical cord and nerve root lesions, trigeminal neuralgia, vestibular disease, and anxiety disturbances. Patients with subacute combined degeneration and reticular patients were excluded on the basis of a possible vitamin B12 or folate deficiency.

Red cell counts, haemoglobin (Hgb), haematocrit (Hct) and mean cell volume (MCV) were measured using the Coulter Blood Counter. Demographic and haematological characteristics of the MS patients and of the control group are shown in table 1.

No significant differences between the two groups were found in any of the measures considered (two tailed Student's t test), nor was any difference observed when comparing MS female and male patients with their respective sexes in the controls. The mean reference value for MCV of our laboratory is 90 fl (range 80 to 99 fl). Forty three MS patients showed a value higher than the mean of laboratory range compared with 40 control subjects. This difference was not significant. Only one patient in each group had an MCV higher than the normal laboratory range. No linear correlation was found between haematological measures and disease duration (Pearson Product Moment Correlation Coefficient). Twenty six patients had an MS history of less than 1 year. This clinical subgroup did not show any significant difference in MCV when compared with neurological controls or with MS patients who had a longer disease duration.

Our results obtained in a relatively large population do not support previous findings of a significant association between MS and macrocytosis. In spite of recent evidence which indicates macrocytosis as an early phenomenon in the course of the disease we did not observe any macrocytosis in the clinical subgroup of patients with short disease duration (< 1 year). Since our study did not differ from previous ones either in the clinical design or in the characteristics of the neurological control group other possible explanations which may account for these discordant findings must be considered. Plum and Fog suggested that the Price-Jones curve in MS patients was similar to that seen in pernicious anaemia (A). Further, in more, PA is reported to have geographic, racial and genetic distribution similar to MS. In particular Najim Al-Din et al observed that MS and PA share the same HLA pattern (HLA A3-B7-DR2).

However, MS patients from Central and Southern Italy are more likely to show HLA DR4 and DR5 instead of HLA DR2. The lack of association therefore between MS and rapid progressive disability may be attributed to the fact that the genetic background of our population is different from that of previous studies.

Alternatively macrocytosis may be due to an associated deficiency, a coincidental finding rather than a deficit specifically related to the disease.

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The IMAO-B MDL 72.974 A in Parkinson's disease

The IMAO-B inhibitor seleagine has been reported to potentiate levodopa treatment and to prevent the progression of disability in early Parkinson's disease. MDL 72.974 A is a new potent, selective, enzyme-activated irreversible inhibitor of MAO type B. Five patients in stage III-IV Parkinson's disease with motor oscillations and dyskinesias were studied. Mean (SD) age at onset was 46 (6) years, duration of the disease was 6 (2) years. All patients exhibited a significant improvement in their motor performance in response to levodopa therapy (mean (SD) daily dose, 750 (200) mg plus a dopa-decarboxylase inhibitor. Motor disability was evaluated using the motor scale of the UPDRS.

The baseline score (at the time of maximal disability without treatment) and the treated score (at time of maximal clinical improvement) were recorded. In all patients all regular drugs were withheld 18 hours before evaluation of motor response to a single suprapharmacological morning dose of levodopa [160 (20) mg] (mean of 2 tests). During the test, Parkinsonian disability was rated before and 15, 30, 45, 60, 90, 120, 150, 180, 240 minutes after drug administration. Patients then received MDL 72.974 A (4 mg) once a day in addition to levodopa and other regular anti-Parkinsonian drugs (anticholinergic and dopamine agonists) for 3 weeks. No modification of doses was allowed during this period. At the end of the period, the motor response to the same suprapharmacological dose of levodopa plus MDL 72.974 A was assessed (mean of 2 tests) under the same conditions as described above. The effects (delay of onset, duration of action, improvement in motor disability score, dyskinesia score) of levodopa alone and of MDL 72.974 A administered simultaneously with levodopa were compared.

After the 3 weeks of combined treatment, the baseline motor score disability was significantly improved (table). A significant prolongation of the duration of "on" response with MDL 72.974 A (4 mg) plus levodopa was observed on the acute challenge study, after 3 weeks of sustained treatment (table). Such differences were not observed when the dose of MDL 72.974 A was of 1 mg (not shown). Dyskinesias were similar in intensity to those experienced with levodopa alone but the duration was longer. Adverse effects consisted of postural hypotension (n = 3), transient facial flush (n = 1), dry mouth (n = 2), gastralgia (n = 1). No haematological or biochemical changes occurred.

Table: Effect of a single oral dose of levodopa without or with MDL 72.974 A (4 mg) on Parkinsonian disability

<table>
<thead>
<tr>
<th>Motor disability score</th>
<th>Response timings (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levodopa</td>
<td>Baseline</td>
</tr>
<tr>
<td>38.5 (20.1)</td>
<td>12.9 (5.6)</td>
</tr>
<tr>
<td>Levodopa + MDL 72.974 A</td>
<td>32.0 (16.8)*</td>
</tr>
</tbody>
</table>

Table: Demographic and haematological characteristic in MS and neurological controls

<table>
<thead>
<tr>
<th>Multiple Sclerosis (N = 154)</th>
<th>Neurological Controls (N = 154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age (years)</td>
<td>Mean (SD) age (years)</td>
</tr>
<tr>
<td>35-9 (11-2)</td>
<td>35-9 (11-6)</td>
</tr>
<tr>
<td>Sex ratio</td>
<td></td>
</tr>
<tr>
<td>Male:Female</td>
<td>Male:Female</td>
</tr>
<tr>
<td>50:104</td>
<td>50:104</td>
</tr>
<tr>
<td>Red cell count (&gt;10)</td>
<td></td>
</tr>
<tr>
<td>4-70 (0-45)</td>
<td>4-68 (0-46)</td>
</tr>
<tr>
<td>Hgb (g/dl)</td>
<td></td>
</tr>
<tr>
<td>129 (147)</td>
<td>139 (11)</td>
</tr>
<tr>
<td>Hct</td>
<td></td>
</tr>
<tr>
<td>40-60 (3-80)</td>
<td>40-30 (4)</td>
</tr>
<tr>
<td>MCV (8)</td>
<td></td>
</tr>
<tr>
<td>86-57 (6-4)</td>
<td>86-56 (6-2)</td>
</tr>
</tbody>
</table>

* p < 0.05.
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