SHORT REPORT

HLA antigens in chronic inflammatory demyelinating polyneuropathy

D J Feeney, J D Pollard, J G McLeod, G J Stewart, T J Doran

Abstract
HLA typing of 71 patients with chronic inflammatory demyelinating polyneuropathy (CIDP) showed an overall increase in frequencies of HLA-A3, -B7, -DR2 as well as concomitantly decreased frequencies of HLA-44 and DR7. The strongest associations were seen with HLA-DR2, -DR7 and -B44 in CIDP overall, although they did not reach statistical significance.

It is generally considered that acute inflammatory neuropathy (Guillain-Barre syndrome, GBS) and chronic inflammatory neuropathy (CIDP) are variants of the same disease and it has been proposed that genetically determined host factors may govern the chronicity of the pathological process. Further evidence for genetic factors in the pathogenesis of CIDP include the demonstration of an association with the M3 allele of the alpha-1-antitrypsin system (PiM3) and possibly Gm haplotypes on chromosome 14.

As the earlier studies of HLA antigens and CIDP were performed on small numbers of patients, we have examined the HLA class I and II antigen frequencies on a larger group of 71 patients.

Patients and methods
HLA-A and -B antigens were determined in 71 patients who satisfied the diagnostic criteria for CIDP. Fifty six of these were also investigated for HLA-DR/-DRw and -DQ. CIDP patients were further divided into chronic relapsing (CR) and non-relapsing (CRN) subgroups. Most of the patients have been described earlier and this study includes those reported in the earlier, smaller series.

Control populations consisted of 2,516 normal healthy blood donors and hospital staff typed for HLA-A and -B locus antigens. One thousand and fifty eight of these were also typed for HLA-D. Three hundred and fifteen and 322 were satisfactorily typed for DRw and DQ respectively.

Typing for HLA-A and -B antigens was carried out by the standard NIH microlymophocytotoxicity test. HLA-DR/DRw/DQ antigens were typed by the standard procedure of the Seventh International Histocompatibility workshop. All typing sera were standardised against International Histocompatibility Workshop sera. Phenotype frequencies were compared by the chi-square test using Yates' correction factor for continuity. Correction for multiple comparisons was applied where appropriate.

Results
Results are summarised in tables 1–3. HLA typing revealed non-significant frequency increases of HLA-A3 (p = 0.239) -B7 (p = 0.150), -DR2 (p = 0.104) and an overall decrease of -B44/B12 (p = 0.069) and -DR7 (p = 0.060) frequencies in both chronic relapsing (CR) and non-relapsing (CRN) subgroups of CIDP. No change was seen in the frequencies of HLA-A30/31 or -B8 in either group. The frequency of HLA-DR2 was raised in both subgroups although it fell short of statistical significance (p = 0.104). It is well recognised that HLA-B7 and -DR2 are in linkage disequilibrium in the normal population. We have observed a non statistically significant increase in the frequency of HLA-B7 and -DR2 in this patient cohort and would therefore expect a corresponding increase in the co-incidence of the B7-DR2 supertype. In the current data, this co-occurrence of B7 and DR2 appears to be much greater than would be seen normally (table 3).

Discussion
This report represents the largest number of patients so far studied for HLA associations in CIDP. It does not confirm earlier observations of a borderline increase in frequency of HLA-B8/-DRw or -Aw 30/31. This work suggests that there may be an association with -DR2, although the findings do not reach statistical significance after applying the correction for multiple comparisons and would need to be confirmed in another cohort. The difference between our findings and those of the earlier studies are probably explained by the smaller number of patients in the first reports. Since CIDP has been regarded as the peri-
### Table 1 Antigen frequencies

<table>
<thead>
<tr>
<th>HLA-A Locus</th>
<th>ANTIgen</th>
<th>CIDP Total</th>
<th>CIDP-CR</th>
<th>CIDP-CN1</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>0.3622</td>
<td>0.3542</td>
<td>0.3913</td>
<td>0.3373</td>
<td>0.3705</td>
</tr>
<tr>
<td>A2</td>
<td>0.4507</td>
<td>0.4583</td>
<td>0.4348</td>
<td>0.4901</td>
<td>0.4675</td>
</tr>
<tr>
<td>A3</td>
<td>0.3380</td>
<td>0.3333</td>
<td>0.3478</td>
<td>0.2677</td>
<td>0.2699</td>
</tr>
<tr>
<td>A11</td>
<td>0.1127</td>
<td>0.1250</td>
<td>0.0870</td>
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<td>0.2677</td>
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<tr>
<td>A23(9)</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0299</td>
<td>0.0316</td>
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<tr>
<td>A26(9)</td>
<td>0.2113</td>
<td>0.2083</td>
<td>0.2174</td>
<td>0.1480</td>
<td>0.1516</td>
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<tr>
<td>A26(10)</td>
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<td>0.0208</td>
<td>0.0870</td>
<td>0.0603</td>
<td>0.0680</td>
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<tr>
<td>A28(19)</td>
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<td>0.0832</td>
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<td>A30(19)</td>
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<td>0.0832</td>
<td>0.0435</td>
<td>0.0434</td>
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<tr>
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<td>0.0624</td>
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<td>Aw33(19)</td>
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<td>0.0000</td>
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<tr>
<td>Aw34(10)</td>
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<tr>
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</tr>
<tr>
<td>Aw43</td>
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<td>n = 48</td>
<td>n = 23</td>
<td>n = 2516</td>
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### Table 2 Antigen frequencies

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<th>HLA-B Locus</th>
<th>ANTIgen</th>
<th>CIDP Total</th>
<th>CIDP-CR</th>
<th>CIDP-CN1</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
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<td>B7</td>
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<td>0.5333</td>
<td>0.3913</td>
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<td>B8</td>
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<td>B14</td>
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<td>0.0783</td>
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<td>0.0731</td>
</tr>
<tr>
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<td>0.0262</td>
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<td>0.0330</td>
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<tr>
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<td>0.0208</td>
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<td>0.0000</td>
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<td>Bw44(12)</td>
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<td>0.2893</td>
<td>0.2893</td>
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<td>Bw45(12)</td>
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<td>0.0000</td>
<td>0.0000</td>
<td>0.0123</td>
<td>0.0123</td>
</tr>
<tr>
<td>Bw46</td>
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<td>0.0000</td>
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<td>Bw47</td>
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<td>0.0000</td>
<td>0.0103</td>
<td>0.0103</td>
</tr>
<tr>
<td>Bw48</td>
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<tr>
<td>Bw49(21)</td>
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<tr>
<td>Bw50</td>
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<tr>
<td>Bw51(5)</td>
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<tr>
<td>Bw52(9)</td>
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<td>Bw53</td>
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<td>Bw55(22)</td>
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<td>Bw60(40)</td>
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<td>Bw61(40)</td>
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<td>0.0435</td>
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<td>0.0175</td>
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<td>Bw62(15)</td>
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<td>0.1740</td>
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<td>0.1165</td>
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<td>Bw63</td>
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<tr>
<td>Bw71(70)</td>
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<td>0.0000</td>
<td>0.0009</td>
<td>0.0009</td>
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<tr>
<td>Bw72(70)</td>
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<td>0.0000</td>
<td>0.0009</td>
<td>0.0009</td>
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<tr>
<td>Bw73</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

*p = 0.239  
^p = 0.150  
^p = 0.069

There are no references in the text provided.
Table 3  Co-occurrence of HLA Antigens

<table>
<thead>
<tr>
<th></th>
<th>CIDP</th>
<th>Controls*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of DR2 in B7 individuals</td>
<td>80%</td>
<td>48-3%</td>
</tr>
<tr>
<td>Frequency of B7 in DR2 individuals</td>
<td>62%</td>
<td>31-7%</td>
</tr>
</tbody>
</table>

*Ninth Histocompatibility Workshop 1984.

In the current study, both clinical subgroups of CIDP displayed a tendency for raised frequencies of HLA-B7 and -DR2 and decreased frequencies of HLA-44 (B12).

These results suggest that there may be genetic similarities between peripheral and central demyelinating disorders mapping to chromosome 6 genes, or linked genes. Involvement of common HLA alleles in CIDP and MS would support our earlier observation in the alpha-1-antitrypsin (Pi) system, but clearly, large multicentre studies are required to resolve this issue.

Alpha-1-antitrypsin genes are known to be in linkage with genes that code for constant regions of IgG heavy chains (Gm), and in turn, these Gm genes interact with HLA genes to influence the immune response to disease. It is therefore appropriate to examine the possibility that HLA, Pi and Gm gene system interactions may be involved in CIDP and these studies are now planned.

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21 Feeney DJ. An investigation of major histocompatibility complex and Gm genetics in rheumatoid arthritis. Perth, Western Australia: University of Western Australia, 1982; pp34. (Thesis).