immunoglobulin (IVlg) has been attributed to blockade of the receptors on the cell surface of macrophages and monocytes for the Fc region of IgG (Fc/R) resulting in antibody dependent cellular cytotoxicity (ADCC) inhibition.1 This is supported by the findings that IVlg slows the clearance of red cells coated with anti-D immunoglobulin and treatment with anti-D raises the platelet count in D-positive patients with immune thrombocytopenic purpura with or without a spleen. Patients with Guillain–Barré syndrome or chronic inflammatory demyelinating polyneuropathy may improve after plasma exchange, infusion of fresh frozen plasma, or after treatment with IVlg.2 Monocytes and macrophages play an important part in the pathogenesis of Guillain–Barré syndrome and chronic inflammatory demyelinating polyneuropathy.3 Inflammatory cells are present in the nerves from the earliest stages of Guillain–Barré syndrome. Demyelination occurs in close proximity to these cells and degenerated myelin is largely restricted to nerve fibres invaded by macrophages.4 To investigate if blockade of FcγR on invading macrophages by anti-D immunoglobulin results in improvement in chronic inflammatory demyelinating polyneuropathy, anti-D immunoglobulin was given to a D-positive patient with chronic inflammatory demyelinating polyneuropathy who had never had spontaneous remissions and who in a double blind crossover study had responded to IVlg and not to albumin. Response to anti-D immunoglobulin was compared with that after IVlg.

The ethics committee of the Academic Medical Centre and with the informed consent of the patient he received 26 μg/kg bodyweight/day intravenously on three consecutive days (total dose 3 mg/kg) of human anti-D immunoglobulin (Rheuman Berna IV). Haemoglobin fell from 10.5 mmol/l on day 1 to 7.5 mmol/l on day 8 and the packed cell volume from 0.50 to 0.34. Haemoglobin decreased from 1.3 g/l to values below 0.1 g/l on day 3. From day 8 onwards these values slowly increased. Bilirubin increased from 6 μmol/l to 27 μmol/l on day 3. The erythrocyte direct anti-antibody became strongly positive with a titre of 1:256 on day 3.

After two weeks muscle strength, electrophysiological variables, and walking distance had not changed and treatment with 0.4 μg/kg bodyweight IVlg on five consecutive days was started. Muscle strength and walking distance improved. Most changes in electrophysiological measurements were in the direction of improvement.

The non-blind design has probably not influenced the results. The patient was very much in favour of this experimental treatment because of its convenience. The results of measurements of muscle strength during the first week after anti-D immunoglobulin treatment did not differ much. Moreover, electrophysiological testing, which cannot be influenced by the patient, showed changes in the direction of deterioration rather than improvement.

The anti-D immunoglobulin dosage was not too low. The same or lower dosage is effective in rats. The strongly positive anti-D-Fc receptor blocking antibodies produced in the course of immunisation.5

This patient with chronic inflammatory demyelinating polyneuropathy responded to IVlg and to albumin. From this finding we conclude that either improvement after IVlg in chronic inflammatory demyelinating polyneuropathy and immune thrombocytopenic purpura is based on a common mechanism but that this influences a pathogenic pathway in immune thrombocytopenic purpura which is not involved in chronic inflammatory demyelinating polyneuropathy or that IVlg has a different action in the two diseases.

Nitric oxide production in bacterial meningitis

Bacterial meningitis of adults is still a serious disease with the mortality from pneumococcal meningitis being as high as 30%. Intracranial complications such as cerebrovascular involvement, brain oedema, and increased intracranial pressure may lead to irreversible neuronal damage. The pathophysiological mechanisms of bacterial meningitis are still unknown in detail. Experimental studies of bacterial meningitis indicate that several mediators including cytokines, platelet activating factor, endotoxin, and reactive oxygen species are involved in the pathophysiology. Recently, we have shown that nitric oxide (NO) is involved as a mediator of cerebrovascular changes and brain oedema in the early phase of pneumococcal meningitis in the rat.1 Nitric oxide, which is produced from L-arginine by NO-synthases (NOS) plays a part in the pathophysiology of a variety of CNS disorders including cerebral ischaemia and seizures and in inflammatory processes.2 During inflammation, large amounts of NO and superoxide radical are thought to be produced by polymorphonuclear leucocytes, macrophages, and blood vessels. We investigated NO production in serial CSF samples from six patients with bacterial meningitis (Table 1). Production of NO was assessed by measuring nitrite, a stable metabolic product of NO. Nitrite determinations were made on 50 μl aliquots of CSF samples mixed with 200 μl of Griess reagent. The absorbance was read at 543 nm after 10 minutes of reaction and nitrite concentration was determined with reference to a standard curve from concentrations of 1 μM to

White blood cell count (WBC) and nitrite concentration in CSF of six patients with bacterial meningitis

<table>
<thead>
<tr>
<th>Patient age/sex</th>
<th>Days after onset of disease</th>
<th>CSF WBC (cells/μl)</th>
<th>Bacteria cultured from CSF</th>
<th>CSF nitrite (μmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18/F</td>
<td>1</td>
<td>3370</td>
<td>Neisseria meningitidis</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1953</td>
<td>Streptococcus pneumoniae</td>
<td>36</td>
</tr>
<tr>
<td>34/M</td>
<td>4</td>
<td>163</td>
<td>Strepococcus pneumoniae</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>1120</td>
<td>—</td>
<td>33</td>
</tr>
<tr>
<td>18/M</td>
<td>3</td>
<td>2730</td>
<td>Neisseria meningitidis</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>140</td>
<td>Haemophilus influenzae</td>
<td>25</td>
</tr>
<tr>
<td>59/F</td>
<td>1</td>
<td>1900</td>
<td>Streptococcus pneumoniae</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>61</td>
<td>—</td>
<td>42</td>
</tr>
<tr>
<td>67/F</td>
<td>2</td>
<td>491</td>
<td>Streptococcus pneumoniae</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>222</td>
<td>—</td>
<td>49</td>
</tr>
<tr>
<td>60/M</td>
<td>1</td>
<td>9000</td>
<td>Strepococcus bovis</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>9813</td>
<td>—</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>336</td>
<td>—</td>
<td>24</td>
</tr>
</tbody>
</table>

CSF nitrite concentrations in controls ranged from 20 nmol/l to 33 nmol/l (median: 24 nmol/l). *CSF was obtained from ventricular drainage.

We thank Professor Ph Rümke and Dr P Aalbersberg for the anti-D immunoglobulin (Primmed), Professor B Ongerboer de Visser for electrophysiological studies, and Dr E S Louwense for measuring muscle strength.

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5 Peters IB, Berek ALL. Further evaluation of anti-D immunoglobulin: anid Bloodbank.

[Further references and details are present in the original text, but have been omitted for brevity.]
1 mM sodium nitrite. Immediately after lumbar puncture CSF was centrifuged and stored. All samples were investigated simultaneously. Each sample was measured twice and the mean value was calculated. Samples of CSF from seven patients with non-inflammatory neurological disorders served as controls.

Compared with controls nitrite concentrations were raised in the first CSF sample of all six patients who had not received antibiotics at that time (table). In all patients the nitrite concentrations in CSF dropped after the onset of antibiotic treatment. Five patients made a complete recovery, one patient died due to septic shock (patient 5). Our data correspond with the findings published by Visser et al who found increased nitrite concentrations in the CSF of patients with meningococcal meningitis. Follow up investigations were not done in that study. Possible sources of NO during meningitis are bacteria, polymorphonuclear leucocytes, macrophages, neurons, and vascular smooth muscle cells. We recently showed that primary cultures of cerebral endothelial cells and astrocytes of the rat can be stimulated by pneumococci to release NO, presumably via the inducible NOS (unpublished data). Further studies are required to investigate whether nitrite concentrations in CSF are associated with the clinical course of the disease and thus could have a predictive role.

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