Eight and 12 week courses of cyclophosphamide in nephrotic syndrome

Sir,—We read with great interest the report on cyclophosphamide treatment of steroid dependent nephrotic syndrome recently published in this journal by Ueda et al.1 Surprisingly the authors could not find any difference in the number of patients who remained in sustained remission after treatment with cyclophosphamide for either eight or 12 weeks, contrary to our previous finding.2 We would like to comment on the conclusions of this study, as we find considerable differences in the treatment procedures used in their study and ours, in addition to the age differences in patients described by the authors.

Most notable is the difference in the initial treatment of nephrosis. All of our patients were treated initially according to the standard treatment protocol of the Arbeitsgemeinschaft für Pädiatrische Nephrologie (APN), that is, 60 mg/m²/day continuously for four weeks, followed by treatment on alternate days with 40 mg/m²/48 hours prednisone. In contrast, the duration of the initial treatment of patients in the study by Ueda et al was significantly longer, that is, four weeks of continuous steroid administration, followed by three to four months' treatment with tapered down prednisone dose (reduction of 5 to 10 mg/m² every two weeks). Thus the total amount of prednisone in the initial treatment was 2240 mg/m² in the APN study, but about 4620 mg/m² in the study of Ueda et al. It has been shown recently that the intensity of the initial treatment is a critical factor in the outcome and prognosis of steroid sensitive nephrotic syndrome—that is, the longer and more intensive the initial treatment is, the lower the number of patients who relapse, and the number of relapses and frequent relapers.3 We therefore would assume that the patients of Ueda and his colleagues represent a highly selective group, who suffer from a more severe nephrotic syndrome than the patients treated by the APN protocol, and where steroid dependency could not be prevented by any intensive initial treatment. Otherwise it could not be explained why the cumulative percentage of sustained remission rates after eight or 12 weeks' cyclophosphamide were only 24% or 25%, respectively, which is lower than all other published results of cytotoxic drug treatment for steroid dependent nephrotic syndrome.4-9 We therefore strongly suggest that the differences in the results of the two studies are due to the selection of patients who were treated with cyclophosphamide. The longer duration of the trial (five years Ueda et al v 2 years in the APN study) and the higher number of patients in the study by Ueda et al seem to play only a minor part in these results (see table) as all but one of the patients of Ueda et al relapsed within two years after treatment with cyclophosphamide. Therefore our study was sufficient to judge the effectiveness of cyclophosphamide treatment, which was later confirmed in a five year evaluation of APN study groups.10

In summary, we cannot agree with the general conclusion of Ueda et al that the effect of an eight week course of cyclophosphamide appears to be the same as that of a 12 week course in children with steroid dependent minimal change nephrotic syndrome. This is probably only true for such a small number of patients who were as intensively treated initially as in the study of Ueda et al. For those who were treated less intensively, by the authors of this brief communication the detailed series of Ueda et al. 3-5

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Characteristics of steroid dependent patients in study groups

<table>
<thead>
<tr>
<th>Ueda et al</th>
<th>APN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:female</td>
<td>28:13</td>
</tr>
<tr>
<td>Mean age at onset of nephrosis (years)</td>
<td>6:40</td>
</tr>
<tr>
<td>Mean steroid dose for initial treatment (mg/m²)</td>
<td>4620</td>
</tr>
<tr>
<td>Mean duration of nephrosis before cyclophosphamide (months)</td>
<td>7:80</td>
</tr>
<tr>
<td>Mean duration of nephrosis before cyclophosphamide (months)</td>
<td>19:20</td>
</tr>
<tr>
<td>No. of relapses (12) or (6) months before entry</td>
<td>5:11 (12) 4:5 (12) 4:4 (6) 4:8 (6)</td>
</tr>
<tr>
<td>Total cumulative dose of prednisone before the relapse (mg)</td>
<td>18:50</td>
</tr>
<tr>
<td>No. of patients with relapse after cyclophosphamide/total patients</td>
<td>3:41</td>
</tr>
<tr>
<td>Cumulative % of sustained remission</td>
<td>24:52 6:18 2:18 24</td>
</tr>
</tbody>
</table>

Acute wheezy bronchitis—lumping and splitting

Sir,—Mertola and colleagues have carried out a very comprehensive and worthwhile study on the association between viral infection and wheezing in childhood.1 However, their terminology 'wheezy bronchitis' as an appropriate diagnostic term for their study population should be reconsidered. It is an emotive term, and its definition far from clear.


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