We noted a marked diminution of absolute B cell numbers, as Silverman also found. Before infusion, the absolute B cell number was 750 (SD 200-1200) and after six hours 238/μl (65-494). This is clinically important as it temporarily interrupts antibody production. The immunomodulation caused by the megadose intravenous methylprednisolone was only transitory and the T subset of the B-cell level returned to their initial levels 24 hours after the infusions. Because methylprednisolone is rapidly excreted (half life: 10-30 minutes), the dose was repeated in one day, and thus its effect diminishes rapidly. Several authorities have noted a significant decrease in the IgG, IgA, C3, C4, and immune complex concentrations after methyl- prednisolone pulse therapy. The levels of these indices of humoral immune response were normal in our patients: IgG 12-5 (SD 3-633) ± 116 (2-986) g/l; IgA 2-3 (1-4-2) ± 1 (1-1) g/l; IgM 1-99 (0-48-17) ± 1 (0-32) g/l; C3 0-93 (0-12-1) ± 0-23 (g/l); C4 0-27 (0-13-0-24) (g/l) and were unchanged during the methylprednisolone pulse therapy.

The immune complex concentration was normal before the infusion: mean 210-6 ng/ml (124-300). Following infusion, the numbers of complexes increased significantly. The patients who developed proteinuria also showed this increase. These values were not influenced by the infusions.

Thus, in summary, despite the brief immunomodulation the megadose steroid treatment is of great clinical importance in the treatment of active rheumatoid arthritis resistant to other drugs. Decreased suppressor cell activity and consequently high T4/T8 ratio are usually found in the active clinical state of rheumatoid arthritis. 3 11 12


Response criteria for slow acting antirheumatic drugs

Sir: I applaud Scott and his colleagues for putting one of the recommendations of the consensus meeting 2 into practice by attempting to derive simple and standardized criteria to define response to second line treatment. 2 The approach used does have some problems, however, and I would like to offer some possible modifications for consideration.

To select parameters on the basis of percentage change after treatment with respect to baseline results is misleading. The normal results for articular index, pain, and morning stiffness are all zero. A normal articular erythema sedimentation rate is below 10 mm/h but is dependent on age and sex. The other indices investigated all have finite normal ranges and these need to be taken into account in calculating the percentage change. For example, a measurement with an upper limit of normal of 100 units might be said to have improved 100% if a result of 120 falls to <10—that is, to normal, but by Scott's method it has only improved by 20%. It is apparent that had C reactive protein been included it would have shown a higher percentage improvement, whereas plasma viscosity would have fared badly. Despite this, however, the measures selected are similar to those identified by several sophisticated statistical methods 4 and would also be the choice based on common sense, reflecting several aspects of active rheumatoid disease which might be expected to improve with successful second line treatment.

If we apply the Scott criteria to two patients A and B we can see a particular problem with the approach (table 1). The response scores for the two patients are clearly misleading, and this has resulted primarily from the fact that the response criteria do not take into account the initial disease activity. After treatment patient A has fewer tender joints than patient B and has had a greater reduction in ESR and duration of morning stiffness, but patient B has a greater response.

As second line treatment does not 'cure' rheumatoid arthritis a positive response to treatment will fall somewhere between the predicting disease state and care criteria to list of all signs and symptoms. It is therefore more reasonable to have several grades of response or even a scale of response, but it needs to take the initial disease state into consideration. Use of the same simple measures used by Scott in a scale response also has its problems. If we assume that the four variables are all equally important then we need to know what particular ESR, pain, stiffness, and articular index results mate with one another so that standardised results can be determined and readily combined. For example, let us suppose that clinical data suggest the approximate equivalents shown in table 1. (These are based on actual data generated in patients not to be refined.) If we apply these criteria to patients A and B in table 1 we see the scores are:

Patient A before: 5+6+3+5=19
after: 2+4+1+2=9
response: 19—9=10

Patient B before: 2+4+1+2=9
after: 1+2+1+3=7
response: 9—7=2

The response achieved in patient B is now seen in a more sensible light. There is some response, but because the score before treatment was the same as for patient A after treatment it is perhaps not surprising that the gain for patient B is less. This approach provides three pieces of information about each patient—the initial and final disease activity and the difference between these. These three, derived from a simple scale of response, provide more useful information and, with refinement, might be of practical importance.

Table 1 Application of Scott's criteria to two patients

<table>
<thead>
<tr>
<th>Patient A</th>
<th>Patient B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td><strong>ESR</strong> (mm/h)</td>
<td>65</td>
</tr>
<tr>
<td>Pain (cm)</td>
<td>6</td>
</tr>
<tr>
<td>Stiffness (min)</td>
<td>60</td>
</tr>
<tr>
<td>Articular index</td>
<td>18</td>
</tr>
<tr>
<td>Overall response</td>
<td>0</td>
</tr>
</tbody>
</table>

*ESR—erythrocye sedimentation rate.
Table 2 Approximate standardisation of results for different measures

<table>
<thead>
<tr>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR* (mm/h)</td>
<td>&lt;16</td>
<td>16-25</td>
<td>26-35</td>
<td>36-45</td>
<td>46-55</td>
<td>56-65</td>
<td>66-75</td>
<td>76-85</td>
<td>86-95</td>
<td>96-105</td>
</tr>
<tr>
<td>Pain (cm)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Spontaneous (min)</td>
<td>1-40</td>
<td>41-80</td>
<td>81-120</td>
<td>121-160</td>
<td>161-200</td>
<td>201-240</td>
<td>241-280</td>
<td>281-320</td>
<td>321-360</td>
<td>&gt;361</td>
</tr>
<tr>
<td>Articular index</td>
<td>0</td>
<td>1-4</td>
<td>5-8</td>
<td>9-12</td>
<td>13-16</td>
<td>17-20</td>
<td>21-24</td>
<td>25-28</td>
<td>29-32</td>
<td>33-36</td>
</tr>
</tbody>
</table>

*ESR = erythrocyte sedimentation rate.


Sir: We agree with Scott et al.1 about the need for an acceptable index to measure response to treatment in rheumatoid arthritis. We have developed an algorithm with this in mind, based on a tree diagram, using a synovitis score, erythrocyte sedimentation rate (ESR), C reactive protein score, Ritchie score, and morning stiffness score, which scores on a scale of 1-7. It has been extensively validated, is easy to use, and forms part of our routine clinical practice. It has the ability to stratify patients for disease activity before treatment and subse-

quent analysis of their response. In a published trial of combination treatment in rheumatoid arthritis2 it identified a significantly better outcome and rate of response to such treat-
ment. The three of the four measures used by Dr Scott et al are incorporated into our algorithm (ESR, Ritchie index, morning stiffness). The fourth, visual analogue pain score, measures a similar facet of disease to the Ritchie index, as shown when substitution of the pain score for the Ritchie index produced a 90% agreement in our activity index scores (Jones P W et al, unpublished data). Unfortunately, the authors seem to have achieved their conclusions by evaluating a group of patients not representa-
tive of the spectrum of rheumatoid disease.

The suggested response criteria are an oversimplification of reporting response to therapy with clear shortcomings. They do not provide a measure of disease activity at outset nor are they sensitive to change. For example, a patient may show a fall in ESR from 60 to 40 mm/h, improvement in morning stiffness from two hours to one hour, reduction in pain by 30%, and a fall in Ritchie index of 20 to 10. This patient has shown a clear response to a drug, albeit partial, but the use of the suggested criteria would fail to show this, so the treatment would be deemed ineffective. In this situation the addition of a second drug rather than a change of treatment may produce further improvement.3

Use of percentage change in a measure of the response criteria is erroneous. It is not surprising that variables such as ESR and morning stiffness show large percentage changes as their normal values are low, whereas a parameter such as joint size when reverting from abnormal to normal can only improve by a small percentage. To include a disease measure within a response matrix it should have the following properties: validity, reversibility, sensitivity, reproducibility, and ease of use. Measures fulfilling these criteria should not duplicate the same dimensions of disease. Unfortunately, many of the measures available in rheumatology do not fulfill these stringent criteria. Continuing research and development of methods to measure rheuma-
toid disease is therefore important.

An activity index to score rheumatoid disease is clearly needed. Unfortunately, the response criteria as quoted are too simplistic to be meaningful. Development of a severity index, composed of irreversible components of the disease, that would complement an activity score of reversible components, would provide a basis to evaluate long term outcome and treatment in rheuma-
toid patients.

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Trauma and seronegative spondyloarthropathy: rapid joint destruction triggered by physical injury in HLA-B7

Sir: Several cases of HLA-B27 positive patients who developed peripheral arthritis immediately after injury have been reported in the last few years.\(^1\)\(^-\)\(^4\)

The role of trauma in the initiation of seronegative spondyloarthropathy has been discussed.\(^1\)\(^-\)\(^3\)\(^,\)\(^5\) Trauma may alter or release antigens, or both, from connective tissue,\(^2\)\(^,\)\(^3\)\(^,\)\(^6\) and may lead in predisposed subjects to the development of an autoimmune reaction. This predisposition was associated with HLA-B27 in all reported cases.\(^1\)\(^,\)\(^4\)

A new case of peripheral arthritis triggered by physical injury is reported here. Unlike previously reported cases of peripheral arthritis precipitated by trauma this patient was B27 negative, but had the cross-reactive antigen B7. No other precipitating factors were identified. After two different injuries the same patient developed arthritis, which caused rapid deterioration in two different joints.

In May 1985, after a minor injury to his left elbow, a 48 year old man developed arthritis of the same joint, without fever, diarrhoea, or urethritis. Arthrocentesis yielded a yellow, turbid fluid, whose culture proved negative. He was treated with anti-inflammatory drugs and intra-articular corticosteroids, but joint effusion persisted and flexus deformation developed in two months. In July 1989 his left knee was slightly swollen and painful. Intra-articular corticosteroids were given, with a bad response. Blood examination showed: erythrocyte sedimentation rate 29 mm/1st h, white cell count 6 x 10\(^9\)/1, haemoglobin 130 g/l, and C-reactive protein 24 mg/l. Arthrocentesis yielded a turbid fluid, with no growth on culture. The joint fluid was clear. Intra-articular corticosteroids were given, with a bad response. Blood examination showed: erythrocyte sedimentation rate 29 mm/1st h, white cell count 6 x 10\(^9\)/1, haemoglobin 130 g/l, and C-reactive protein 24 mg/l. Arthrocentesis yielded a turbid fluid, with no growth on culture. The joint fluid was clear.

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Response criteria for slow acting antirheumatic drugs.

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