Fig CT myelography shows a tumour mass filling up the intervertebral foramen between the 4th and 5th thoracic vertebrae. The spinal cord, which is seen surrounded by contrast medium (meridizamide), is slightly dislocated but not compressed.

thoracic vertebra and a tumour mass which filled up the corresponding intervertebral foramen (fig). The spinal cord was not compressed but was slightly dislocated to the right. The patient was successfully treated with local radiotherapy. He has been followed so far for over one year, remaining asymptomatic.

The well known classical clinical manifestations of spinal root compression are pain and segmental motor and sensory abnormalities.1 At levels such as the mid-thoracic region the signs may, however, be few and atypical. There is considerable overlapping in the distribution of the muscular and cutaneous innervation supplied by adjacent thoracic spinal nerves. Thus, for instance, section of a single thoracic root does not necessarily produce any detectable sensory disturbance. The paraspinal musculature consists of a number of long and crossing muscles and an injury to one root has little effect upon function.

Although the clinical picture of our patient was unusual, there had been a previous period of segmental pain, most probably due to root irritation. Since the symptom disappeared spontaneously, more detailed examination had been considered unnecessary at that time. It was only the later appearance of local dorsal muscle jerking which led to investigation, and it was the identification of myoclonus which led to the elucidation of the root lesion and the tumour. Myoclonus is a well established condition of spinal lesions1,2,4,5,6,7 but its appearance in the paraspinal muscles is uncommon. Its appearance as the only manifestations of a lesion primarily involving a spinal root also is unusual. In our patient, there were no upper motor neuron signs, myelography and CT examination showed no cord compression, and the SSEPs showed no abnormal latency values at the spinal level. Therefore, the origin of myoclonus was most probably at the nerve root level. Although not likely, the possibility of spinal cord compression cannot, however, be absolutely excluded.

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References

Failure to promote spinal cord regeneration in rats with immunosuppressive treatment

Sir: We have published several reports of minor improvement in central nervous system (CNS) regeneration in rats treated in ways that would alter their immune response. Our most successful regimen consisted of treatment with 75 mg/kg of cyclophosphamide 48 hours after spinal cord transection.1–4 While no clinical return of sensory or motor skills was noted in treated rats, electrophysiology, axoplasmic flow studies, and anatomic studies indicated that some fibres did pass through the area of complete spinal cord transection in treated rats, but not in control rats. We recently found that an earlier axoplasmic flow study indicating some recovery in long-term untreated control rats was a misinterpretation of data.5 Regeneration has been seen only in rats that have been treated in ways thought to suppress their immunologic responsiveness. While all evidence of regenerating long tracts in the spinal cord has been meager, the best results have been found in those rats treated with cyclophosphamide.

The advent of the immunosuppressant cyclosporin, which is reported to be much less toxic and much more successful in inhibiting immunologic responsiveness, led to our testing this new drug in rats with complete spinal cord transection to see if it would facilitate spinal cord long tract regeneration. We compared control rats with a complete spinal cord transection performed at T-9 cord level as described earlier2,4 with rats given one of two immunosuppressive treatments. Control rats received no specific therapy. A cyclophosphamide treated group received
a single intraperitoneal dose of 75 mg/kg cyclophosphamide 48 hours after spinal cord transection. A cyclosporin treated group received daily intraperitoneal injections of 15 mg/kg cyclosporin suspended in ethyl alcohol and fat emulsion (Intralipid) beginning the day of spinal cord transection and continuing for a total of 14 days. Rats were examined and weighed at frequent intervals to determine evidence of drug toxicity.

Four months (±6 days) after spinal cord transection the rats were tested for regeneration by electrophysiologic means. A stimulus of 0-01 to 10 mA for 0-35 ms duration was applied to the corticospinal tract in the high cervical cord.3 Recording electrodes were placed on each of 12 roots, three dorsal and three ventral on each side. A series of 128, 256, or 512 stimulations were applied and a computer of average transients was used to detect an evoked response.

Twenty-one days before planned killing, 50 µl of tritiated proline were injected into each sensory motor cortex.4 An injection of this type results in labelling of the entire corticospinal tract in the spinal cord but no other spinal cord tracts are labelled.4 After completion of electrophysiologic evaluation, the rat was killed by perfusion with 10% formalin fixative. A 10 mm long section of cervical cord above the transection site and a similar length of low thoracic/lumbar cord caudal to the transection site were removed. These segments of spinal cord were solubilized and scintillation counted for the presence of tritium. Radioactivity in each segment was described as disintegrations per minute per millimeter (DPM/mm) cord length because the label was restricted to the longitudinally running corticospinal tract.

Only two of 14 spinal cord transected untreated control rats survived for 4 months. By contrast, nine of 18 spinal cord transected rats treated with cyclosporin and eight of 19 cyclophosphamide treated rats failed to survive. Three of the deaths in the cyclophosphamide treated rats occurred at the time of anaesthesia and/or surgery. All of the nine cyclosporin deaths occurred at times independent of such surgical intervention. Some of the deaths occurred relatively early in the experiment. In the hope of being able to test at least 10 survivors in each group, additional rats were put into the cyclosporin and cyclophosphamide treated groups to compensate for early deaths.

No rat showed electrophysiological evidence of regeneration of long tracts. The DPM/mm in the proximal and distal spinal cord are shown in the table. Seven of the rats had to be dropped from this part of the analysis because of technical problems in performing the evaluation. Five had improper injections into the white matter instead of the cortex of the brain, one had a higher spinal cord transection, and in one case the scintillation vial was broken.

Cyclosporin proved to be more toxic in these paraplegic rats than one would expect from previous reports.7-10 While three of eight deaths in the cyclophosphamide treated group occurred during anaesthesia and surgery for electrophysiologic testing or injection of isotope into the cortex, all nine deaths in the cyclosporin group were due to infections or other unexplained late effects of treatment. All deaths in the cyclophosphamide group were delayed, occurring 16 to 87 days after surgery with a mean of 48 days ±8-2 (R ± SEM). In this study, we found neither electrophysiologic nor axoplasmic flow evidence that any regeneration occurred.

Tritiated proline was injected into the cortex on postoperative day (POD) 91 and label in the corticospinal tract was determined on POD 107-118. The labelling found in the corticospinal tract in the cervical region was variable. A stronger label found in the cervical area of control rats than that found in the cyclophosphamide treatment group (p < 0-025). We believe this represents biologic variability in spite of the statistical difference found. The only alternative hypothesis we can suggest is that a single dose of cyclophosphamide given on (POD) 2 has a long lasting (89 days and later) effect on the metabolism of the neurons. This metabolic effect results in impaired transport of injected labelled proline to the spinal cord axons or in impaired incorporation into cellular proteins which in turn label the corticospinal tract.

In four previous studies, rats treated with 75 mg/kg cyclophosphamide one day after spinal cord transection showed evidence of regeneration. In the first study,2 which used electrical conduction as an endpoint, four of 12 treated rats showed regeneration (p < 0-02 compared to controls). In a second experiment,4 which studied H3 proline transported by regenerated axons, four of 13 rats showed some regeneration (p = 0-03 compared to matched controls). In a third study,5 which searched for regenerated axons using the Fink/Heimer Nauta technique, six of seven rats showed some regeneration (p < 0-02 compared to matched controls). In another study,3 a group of 11 treated rats showed greater transport of tritiated proline presumably via regenerated axons (p < 0-04 compared to matched controls).

In this experiment, both cyclosporin and cyclophosphamide proved toxic and none of the enhancement of CNS regeneration was detected. Data from this experiment do not support our original hypothesis that an immune reaction to CNS tissue plays an important part in the inhibition of CNS long tract regeneration.

### References


### Table: Study groups

<table>
<thead>
<tr>
<th>Control untreated</th>
<th>Cyclophosphamide 1 dose 75 mg/kg</th>
<th>Cyclosporin 15 mg/kg/day for 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths before 4 months/Rats entered</td>
<td>2/14</td>
<td>8/19</td>
</tr>
<tr>
<td>Rats showing conduction via regenerated axons</td>
<td>0/12</td>
<td>0/11</td>
</tr>
<tr>
<td>Rats included in radioisotope study</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>DPM/mm proximal R ± SEM</td>
<td>1046 ± 112</td>
<td>640 ± 107</td>
</tr>
<tr>
<td>DPM/mm distal R ± SEM</td>
<td>144 ± 12.8</td>
<td>96.8 ± 22.2</td>
</tr>
</tbody>
</table>
Matters arising

Reflex path length and clonus frequency

Sir: Iansek, in a recent article on the effects of reflex path length on clonus, noted that Walsh proposed the existence of a central pacemaker as the determinant of clonus frequency. However, we did not use the term "pacemaker" as he stated, nor did we imply such a mechanism. We proposed that clonus is due to the repeated activation of the muscle stretch receptors, and we observed consequent central refractory and excitatory periods. As Iansek noted, the refractory period would not restrict the lower frequency, but only the upper frequency. We disagree with the author's statement that the lower frequency is determined by the reflex delay (alone), which would imply that for any muscle, the lower frequency could not be changed. Although we were unable to lower the frequency of clonus, Rack has demonstrated that it is possible to do so using a different experimental design. The lower frequency depends upon the muscle contraction and relaxation times which are influenced by the inertial load on the muscle, as well as the reflex delay time. We measured the refractory period only in the triceps surae muscle (90–100 ms). This period may differ for other muscle groups with different central stretch reflex organisations, thereby resulting in different maximum clonus frequencies. In order to reach an understanding of clonus, it is essential to consider not only reflex path length but also muscle contraction and relaxation times, muscle load, muscle spindle activity and central excitability, all of which play a role in clonus. The author's conclusion that clonus frequency in spastic muscles is a direct consequence of path length is an oversimplification. The reflex latency time is only one of the peripheral contributing factors which must be integrated with alternation of the stretch reflex refractory and excitatory phases in order for clonus to be manifest.

To summarise, Iansek has not accounted for our findings of refractoriness. It is true that different muscles may have different rates of clonus, but this in no way changes our conclusion that both central and peripheral elements must play a role.

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