EDITORIAL COMMENTARY

Corticosteroids and multiple sclerosis

It is common practice to employ a short course of corticosteroids to treat acute relapses of multiple sclerosis. Two approaches, high dose intravenous methylprednisolone (IVMP) and intramuscular ACTH, have been shown when compared to placebo to shorten the duration of relapses,^{1,2} although there is no evidence that the final outcome is changed. Of these, IVMP has become the more popular, being a shorter course (typically 3–5 days versus 2 weeks), and indeed ACTH is no longer available for use in the United Kingdom. Relatively small studies have suggested equivalence between oral corticosteroids (using various dose regimes) and IVMP in treating multiple sclerosis relapses,³ although the first has not been tested against placebo. In a placebo controlled trial in acute optic neuritis, oral prednisone was not associated with an increased rate of visual recovery, whereas IVMP followed by an oral tapering off period was.⁴

With this incomplete data from controlled trials, it is not surprising that a survey of United Kingdom neurologists (see Tremlett *et al*, this volume, pp 362–5) has disclosed widely variable patterns of corticosteroid prescribing in patients with multiple sclerosis. There was consensus that a short course of steroids is indicated to treat a proportion of multiple sclerosis relapses, and it was clear that IVMP for 3–5 days is widely adopted as the most popular regime. Beyond these facts, no clear pattern emerged. Although most neurologists will occasionally prescribe oral corticosteroids, there was no consensus as to agent (prednisolone, methylprednisolone, and dexamethasone were all used), dose, or duration of treatment. Nor was there any consensus on the need for an oral tapering off period after a course of IVMP or the duration of such a taper if used. Given the lack of evidence for efficacy, and the potential for side effects, it is of concern that corticosteroids were occasionally given in courses exceeding one month and to treat progressive forms of the disease.

The authors suggest that a further large trial would be needed to clarify outstanding issues—for example, the relative merits of IVMP versus oral prednisolone. This may

be true, and as the authors say, an unambiguous demonstration of equivalence will have health economic benefits, given the significant cost of a course of IVMP. On the other hand, a large and expensive trial might demonstrate superiority of IVMP, and result in no change in current practice. It is perhaps more important to consider the wider issue of the limited effect of corticosteroids—of any type—on the overall course of multiple sclerosis. Thus there is no evidence that they affect the outcome of relapses (20% of which result in significant permanent deficits), the frequency of relapses, or the long term risk for disability. It would seem that high priority should be given to the development of more effective treatments for acute relapse, as well as therapies to reduce relapse frequency. Such approaches will need both basic studies to clarify the pathogenetic mechanisms of relapse and remission (still not well understood), and the application of rationally based and novel therapies in well planned clinical trials—for example, the demonstration from MRI that breakdown of the blood-brain barrier is a consistent feature of acute symptomatic lesions suggests that new approaches to stabilise the barrier are worth trying; one such approach would be antiadhesion molecule therapy. With the introduction of interferons, it is now possible to modify relapse frequency, albeit modestly; new agents are needed which more profoundly reduce both the rate and severity of relapses.

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- 4 Beck RW, Cleary PA, Anderson MM Jr, *et al*. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. *N Engl J Med* 1992;326:581–8.