prolong the lives of those suffering, thereby providing the necessity for self-action by the patient.

Perhaps when we advise patients and families who face difficult decisions, we would be better to heed the available evidence about who will do well and who will do badly rather than withholding recommendations because unduly cautious statisticians choose to neglect the downside effects of their theoretical arguments. Neurologists are in an especially favourable position to understand the human needs in such cases and advise families accordingly.

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Bates replies:
I am grateful to Professor Plum for emphasising the important exclusions in the International Study on Prognosis in Non-traumatic Coma and appreciate his comments relating to the use of unfavourable early signs. I did not intend to suggest that clinical or laboratory indicators of poor outcome were not to be used as part of the process to make decisions in patient management, and I am very conscious of what Professor Plum refers to as the “downside statistical feature” of prolonging an insensible life and the consequent burden on the family. My purpose was rather to emphasise that predictors of poor outcome should not be used as the sole factor in making decisions about life support, though they should be used in discussions with relatives of the patient and with our colleagues in helping to arrive at an appropriate clinical decision.

A prospective study of physical trauma and multiple sclerosis

I read with great interest the article by Sibley et al.1 Because of my own involvement in this particular problem, I wish to make the following comments.

There can be no more difficult task than to conduct epidemiological surveys of multiple sclerosis (MS) because of its unpredictability and symptomatic variability. It is therefore unsuitable for measurements with the yardsticks currently at hand. Indeed, to design an epidemiologically valid study, it would be necessary to match MS patients (not just healthy controls) for age, sex, ethnic origin, duration and geographic sites of residence, living and social-economic environment, duration and severity of disease, type of clinical course, stage of activity, and number and location of lesions using modern imaging techniques such as MRI. It would be necessary to determine whether the lesions had already been diagnosed as having MS, but also those who had been symptomatic but not yet recognised as well as all those patients whose symptoms of underlying MS will not appear until they are subjected to trauma.

Most of these problems are not taken into consideration in Sibley’s article.

It is generally pointed out that the “scientific” evidence of epidemiology and biostatistics overlaps the fact that such studies can at best only be estimates within a cohort and cannot be generalised; epidemiological studies are merely providing aetiological clues but cannot be used to deny possible causal relationships.2 As was pointed out by Schoenberg, “Statistical significance (or lack thereof) does not equal biological significance.”

It is difficult to understand, on the basis of what is already known about the pathogenesis of MS, how trauma such as laceration of the hand, contact with the fingernail, a root canal procedure, or a thorn in the foot can possibly lead to the appearance or recurrence of symptoms of MS. Sibley et al dismiss the alteration of the blood-brain barrier in the genesis of the MS lesion; in doing so they disregard the numerous recent publications which have amply confirmed this fact, including statements by such authorities as McDonald and Barnes3 who commented that “A consistent progression of events is the breakdown of the blood-brain barrier which is largely repaired over weeks, leading to marked changes in the size of acute lesions” and by Committee who wrote, “Blood-brain barrier damage is necessary early in the development of focal demyelination”.

One cannot expect that all, or even most MS patients will have exacerbations following trauma, but an experience of recurrent MS exacerbations for MS patients to have repeated viral infections without changes in the course of their disease.

The relationship between trauma to the head, neck or back that I have supported, is based upon clinical, neuropathological, and experimental evidence which were reviewed in 1986 and based on the obligatory step of the alteration of the blood-brain barrier for the formation of the MS lesion. This has now been amply documented.

Additional problems seemed to have plagued this study: for reasons which are not explained, symptoms alone are not recognised as exacerbations. Nevertheless, diplopia, paresthesiae and vertigo, classic symptoms of MS are quite often unaccompanied by objective evidence of neurologic examination. It is curious that Sibley et al used 48 hours’ duration for an exacerbation as opposed to the more generally accepted 24 hours.5 Finally, it is difficult to draw any conclusions from data given on the basis of mean annual exacerbation rates for the simple reason that exacerbations in MS are never uniformly distributed; periods of complete quiescence lasting several years are not uncommonly occur after a series of several exacerbations within a single year.

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Sibley et al reply:
We age- and sex-matched MS patients with healthy controls only to establish the degree of accident-proneness of MS patients. It probably needs to be clearly restated that the patients were used as their own controls when they were not “at risk”.

Physical trauma had no positive influence on either exacerbation rate or progression of MS in our group of MS patients as a whole, or in various subgroups divided according to sex, age, degree of disability, or duration of disease—all of these data cannot be presented in our paper in the interests of brevity. We have not analysed separately based on sites of residence or socioeconomic factors.

I am sure that Dr. Poser is aware that we have no way of identifying MS patients whose disease has not yet been recognised. His statement that some of them will not have symptoms until subjected to trauma, makes causal assumptions that our study data do not support.

With regard to his comments concerning the validity of statistical methods, we believe that it is common scientific practice to generalise on the basis of data obtained in representative samples of a group. The calculation of annual exacerbation rates was for the convenience of the reader; the chi-square calculations were done on actual exacerbation numbers during periods at risk and not at risk for trauma, not on the annual rates. Our study tested the hypothesis, advanced by others, that trauma, rather than trauma, could cause exacerbations of MS. We are happy to see that Dr. Poser agrees that peripheral trauma, at least, can be dismissed as a cause. He continues to believe, however, that CNS trauma that causes a breach in the blood-brain barrier can cause new lesions in MS. The anecdotal case reports that form the clinical basis for his belief are selected from larger numbers of cases and selected on the basis of the temporal relationship between trauma and exacerbation and cannot be accepted as valid evidence that trauma is a risk factor in MS.

We agree that if trauma were a causative factor that all traumas would not be followed by exacerbations, since many new lesions of MS are symptomatic. However, a study such as ours should have shown a higher proportion of exacerbations when at risk for trauma in 170 patients over a five year period since the frequency of trauma was high.

The Multiple Sclerosis NMR Group at Queen Square has found that in some patients gadolinium leakage may precede other evidence of new lesion formation; they attribute this to inflammation, not to trauma.6 Certainly barrier breakdown due to the perivenular inflammatory lesion is an early event, but we believe that the cause of this inflammatory response is unknown and our data suggest that trauma is not a factor in new lesion formation.

Our decision to define exacerbations on the basis of objective neurological changes only are in keeping with the Schumacher Committee criteria for definition of a relapse.7 The 48 hour minimum duration of new symptoms was an arbitrary departure from the Schumacher criteria to help ensure that fluctuations in symptoms due to fatigue and other physiological factors were not counted erroneously as exacerbations.

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Multiple sclerosis, tropical spastic paraparesis and HTLV-I infection

A course without remissions (s) and relapses was the one clinical feature that distinguished human T-cell lymphotropic virus type-I (HTLV-I) associated tropical spastic paraparesis (TSP) invariably from multiple sclerosis (MS) in the series of cases reported by Rudge et al. We do not consider this to be an absolute rule since we have reported a patient with HTLV-I associated TSP who did indeed manifest such a pattern of illness.

We should perhaps emphasise that our patient was an African, born and raised in Swaziland where the very occurrence of MS is quite uncertain. Also, corticosteroids, if not given, an intervention that might have contributed to the relapsing-remitting course in a case of HTLV-I associated myelopathy described recently by McKendall et al.


Neuropathological features of Alzheimer's disease in non-demented Parkinsonian patients

I was interested to read about the two cases reported by Daniel and Lees. Both of the patients had neuropathological features of Alzheimer's disease and nigral loss but clinically had dopa-responsive Parkinsonian. However, one of the interesting features of their condition that may help distinguish such patients from those with idiopathic Parkinsonian disease is the speed with which they develop involuntary movements related to therapy. In both of their cases the patients developed abnormal movements within 12 and six months of starting oral levodopa. This may relate to their combined pathology of nigral loss with striatal plaques and neurofibrillary tangles. It will therefore be of interest to see if patients who develop early dyskinetic movements with levodopa have similar neuropathology.


This account of the papers presented at a postgraduate course concerning Parkinson's and extrapyramidal syndromes held at Tremizzo, Italy in April of 1990 comprehensively covers the pathophysiology of akinesia and hyperkinesia, the aetiology of Parkinson's disease, the multiple system atrophies and current problems and potential developments in therapy. All but 17 of the 56 contributors are from Italy and thus to a considerable degree the book represents an authoritative Italian statement concerning this important group of movement disorders. It is a most impressive account and the balanced content reflects not only the excellence of the contributors but also the editorial skills of Professors Caraceni and Nappi.

The text is gratefully free of the irritating defects often associated with precipitate publication of proceedings and manages to be both comprehensive and succinct. Particularly impressive is an account of the renaissance of interest in the subthalamic nucleus in the organisation of basal ganglia function by Rondot, the biochemical Parkinsonian syndrome by Gerlach and Reiderer, and Duvoisin's critique of genetic and epidemiological factors. Other impressive surveys cover the neuropsychology of the parkinsonian syndromes, primary autonomic failure, single photon emission computer tomography and the management of late complications of Parkinson's disease. Perhaps because of the rarity of recent device developments the chapter on adrenal medullary implants is not the strongest or most critical but does illustrate the breadth of topics covered. The book is printed in Italy and the chapter on dopa-responsive extrapyramidal disorders is elegantly produced and the print is agreeable to read.
A prospective study of physical trauma and multiple sclerosis.

C M Poser

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