A predominantly cervical form of spinal muscular atrophy

We have reservations about the paper by Dr Goutieres et al,1 though not the concept itself. Documenting the clinical and histological findings in five infants, they describe a condition "A predominantly cervical form of spinal muscular atrophy". Cervical spinal muscular atrophy (SMA) is a real entity and has been reported previously.1 It is probably due to defects in the lower cervical segments of the spinal cord resulting in muscle wasting and contractures of the upper extremities and normal lower limbs.

They have not mentioned any necropsy findings. They need other sources of confirmation since they attempt to describe a newly defined clinical condition. In atypical cases, they describe that the authors should have ruled out a possible cervical hydromyelia or syringomyelia with myelotomy or even a congenital cervical spinal tumour, and familial syringomyelia is well-known.4 For this purpose a myelitis-C® or an MRI of the cervical spine should have been done. Imaging spinal areas by MRI has almost revolutionised our concepts. We have seen two children with cervical spinal pathologies, one with a dermoid tumour and one with suspected syringomyelia (unoperated upon as yet, so no tissue diagnosis is available). Both cases were successfully treated by the Ventriculomegaly Centre.

Defining prognosis in medical coma

I appreciated David Bates’ well written editorial, which set the process and limitations of establishing prognoses in patients with medical coma. Since we collaborated on the international non-traumatic coma study,5 perhaps I may make one or two points not strongly emphasised by Dr Bates.

The editorial generally summarises accurately the international study’s results but omits emphasising a dimension which may be of some importance. The study excluded all patients whose coma did not result either from known organ failure, or from known exogenous causes such as a deprivation of oxygen supply or an excess insulin dose. All cases with self-induced coma-causing drug poisoning as well as all cases in which aetiological diagnosis was uncertain were automatically excluded. The reasons are straightforward: nearly all such patients survive intact with intensive care including some with a flat EEG and fixed pupils lasting for a day or more.

I regret that I disagree with Dr Bates in his contention that since only a small number of several thousand patients can reduce the theoretical error of 5% in predicting poor outcome, one cannot make decisions based on unfavourable early signs, however bad they may be. What about the 95% to 99% of survivors? Why, if they survive to demonstrate severe disability? Most Americans are aware of the meaning of probability odds. Given 20:1 odds they might be willing to bet on a horse which had never won a race, but they certainly would not do so if they risked having to witness and indefatigably support a pained and crippled being if that was the cost of losing the bet. Dr Bates does not argue that such a case is damaging the statistical case of severe disability, yet that is what our study would say. It is not a statistical argument, it is damaging a little statistical feature anywhere in his editorial. Many Americans are becoming increasingly apprehensive about being rescued from an early death by critical care measures only to face permanently blighted by intractable pain, severe physical disability, cognitive impairment or some combination of all three. When we advise patients or their families on day 13, 5 or later that if they continue to receive maximal care, they or their loved ones may have a 2% or 5% statistical chance of a good recovery we also tell them that continued survival also implies at least a 50–60% chance of the major permanent disability associated with permanent severe disability. Facing such choices, a few will say, “Please do everything, doctor”. In my own experience, however, most will urge, “please be merciful—he/she couldn’t stand living as a permanent cripple, much less being a hopeless burden on the family”.

The humane decision of who and when to treat and how long to treat is not necessarily delicate, difficult and sometimes painful for the physician; it is an even greater burden for the family. At least by the US Constitution, the doctor is neither the only party nor the major decision in this situation, the patient is. Evidence in this country, is that we physicians are under-fulfilling our responsibility in this critical matter.

In a year, Derek Humphrey was the author of a small monograph entitled “Final Exit”, which offers direct advice on how to commit suicide for those who, for whatever reason wish to consider the option. I have not read the national bestseller list. The accompanying New York Times news story included comments from bookellers, journalists and potential patients that implied that physicians often over ذات and unduly
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 humane needs in such cases and advise families accordingly.

FRED PLUM
Department of Neurology, and Neurosurgery
The New York Hospital-Cornell Medical Center, 525 East 68th Street, New York, NY 10021, USA


Bates replies:
I am grateful to Professor Plum for emphasizing 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 insentient life and the consequent burden on the family. My purpose was rather to emphasize 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. 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 follow the course of the disease at all stages of the disease, starting from the index case to the period of the acute episode. The study would have to be continued to observe the natural history of the disease, including the long-term course of the disease, and the outcome of the disease after the acute episode.

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 overlooks the fact that such studies can at best only be estimates within a cohort and cannot be generalised; epidemiological studies are merely meant for providing aetiological clues but cannot be used to deny possible causal relationships. 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, contusion of the right index finger, 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 Barnes who commented that “A consistent finding in subjective event is a breakdown of the blood-brain barrier which is largely repaired over weeks, leading to marked changes in the size of acute lesions” and byCompston 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, contrary to the common experience of MS patients who have had viral infections. It is not clear why the authors do not consider the aetiological significance of trauma in the MS lesion.

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 changes on neurological examination. It is curious that Sibley et al. used 48 hours’ duration for an exacerbation as opposed to the more generally accepted 24 hours.

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 not uncommonly occur after a series of several exacerbations within a single year.

CHARLES M POSER
Department of Neurology, Harvard Medical School, Boston, MA, USA


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 causative 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, on the annual rates.

Our study tested the hypothesis, advanced by others, that trauma, particularly following a head injury, 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 causes a breach in the blood-brain barrier, a cause new lesions in MS. The anecdotal case reports that form the clinical basis for his belief are selected from large numbers of cases and are due to a 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, all traumas would not be followed by exacerbations, since many new lesions of MS are asymptomatic. 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. 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.

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.
Defining prognosis in medical coma.

F Plum

*J Neural Neurosurg Psychiatry* 1992 55: 523-524
doi: 10.1136/jnnp.55.6.523-b

Updated information and services can be found at:
[http://jnnp.bmj.com/content/55/6/523.3.citation](http://jnnp.bmj.com/content/55/6/523.3.citation)

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
[http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to:
[http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to:
[http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)