promise which helps us retain that distinction is "anaemic hypoxia."

In summary, precise definition is important because, as Medalla, et al. say, recognition of different etiologies can result in different patterns of symptoms such as the immediate versus delayed encephalopathies associated with "pure circulatory collapse" versus carbon monoxide poisoning. If we must also be alert to ways in which different etiologies lead to overlapping pathologies and pathologies and pathophysiologies. The terminologies which we have found helpful is stagnant hypoxia, which is divided into the states of ischaemic and oligemic hypoxia, and anaemic hypoxia. While these entities have clearly differing pathophysiological implications, our knowledge of their implications for neuro- psychological symptoms is as yet incomplete. There is a greater chance of completing that side of the story if lesions are identified by standard nomenclature which accurately reflects the underlying pathophysiology.

JEFFREY EVANS
Rehabilitation Psychology and Neuropsychology
Department of Physical Medicine and Rehabilitation,
University of Michigan Hospitals, Ann Arbor, Michigan

WALTER I. SOBOTA
Department of Psychiatry,
Sinai Hospital of Detroit, Detroit, Michigan, USA


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 histo- logical 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.2 It is probably due to either a segmentally restricted lesion of 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 presentations, they described that the authors should have ruled out a possible cervical hydromyelia or syringomyelia with amyotrophy or even a congenital cervical spinal tumour, and familial syringomyelia is well-known.3 For this purpose a myelo–CT 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 had symptoms mimicking SMA. In each case, MRI was the greatest help and was the most straightforward method. In conditions running a more benign course such as monomeric amyotrophy, studies with NMR or metrazamide CT have demonstrated atrophy of the related spinal cord.4

Muscle biopsy findings in the cases of Dr Goutieres et al. were all consistent with "neurogenic fascicular atrophy". In the absence of giant type fibres which are typical for SMA in early infancy, muscle biopsy revealed the presence of denervation, the extent of reinnervation and the chronology of the process, but did not conclusively disclose the precise anatomical localisation of the denervating event. "There is no comment on whether there were any giant type fibres in the muscle biopsies.

KALRIYE YALAZ
HALUK TOPALOGLU
MURAT AKSU
KIVILCIM GUCUYENER
MERAL TOPCU
Department of Paediatric Neurology, Hacettepe University Children's Hospital, 06100, Turkey

Correspondence to: Dr Topaloglu.

Dr Goutieres et al reply:

We appreciate the interest of Dr Yakaz et al in our paper. We do not think that the cases we reported here are consistent with the form described by Darwish et al. In their three patients, muscle atrophy was already present at birth and the condition remained static, in marked contrast with the progressive disease extent with a postnatal onset seen in our patients. We agree that MRI of the cord is desirable but was not available to us at the time we saw these patients. We did not feel it justifiable to perform contrast myelography as the clinical features, clearly indicated anterior horn cell disease. In particular, the absence of sensory changes, diffuse abolition of deep tendon reflexes, normal sphincter function and electromyographic features extending to clinically normal muscles distant from the cervical region, all favour spinal muscular atrophy. The progressive extension of the disease in the form described here, and its occurrence in two siblings born consanguineous parents are also strong arguments against a malformative, vascular or tumoural process. Indeed, the late clinical picture in our patients was very similar to that of the classic types of spinal muscular atrophy. Our aim was to draw attention to an unusual clinical variant rather than describe a new disease entity.

Defining prognosis in medical coma

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

The editorial generally summarizes accurately the international study's results but omits emphasizing a dimension which may have been overlooked. 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 98% of patients who aren't included in the study? Whatever their implications, the results are the same: if they survive are doomed to severe disability? Most Americans are aware of the meaningfulness of probability odds. Given 20:1 odds they might well feel it to be a worthwhile discussion whether they had never won a race, but they certainly would not do so if they risked having to witness and indefatigably support a pinned and crippled being if that was the cost of losing the bet. Dr Bates does not consider that there may be some damaging downside 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 lives 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 1, 3, 5, later that if they continue to receive maximal care, or their loved ones may have a 2% or 5% statistical chance of a good recovery we also tell them that continued survival also brings 95 to 98% of cases 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 deal with the end is not necessary delicate 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 player in this situation, the patient is. Evidence in this country, that is: we physicians are under-filling our responsibility on this critical matter.

Dr Derek Humphry was the author of a small monograph entitled "Final Exit", which offers direct advice on how to commit suicide for those who, for whatever reasons, wish to consider that course as a last resort. It has reached the national bestseller list. The accompanying New York Times news story included comments from bookellers, journalists and potential patients that implied that physicians often overses or 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 misery that accompanies chronic, overwhelming brain damage. This knowledge places them in a position to understand the humane needs in such cases and advise families accordingly.

FRED PLUM
Department of Neurology, and
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 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 insentient 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 environments, 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 ensure that MS patients had already been diagnosed as having MS, but also those who had been symptomatic but not yet recognised as well as those patients whose symptoms of underling 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 overlooks the fact that such studies can at best only be estimates within a cohort and cannot be generalised; epidemiological studies are merely showing anecdotal 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, cutting of a finger using a razor, 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 authors as McDonald and Barnes3 who commented that "A consistent observation in MS is an early breakdown of the blood-brain barrier which is largely repaired over weeks, leading to marked changes in the size of acute lesions" and by compromised discourse, "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, since it is a common experience 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 19864 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 seem to have plagued this study: for reasons which are not explained, symptoms alone are not recognised as exacerbations. Nevertheless, diplopia, paresthesia and vertigo, classic symptoms of MS are quite often unaccompanied by objective evidence of neurolological 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 encountered even 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 solely 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 can only 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, even when subjects to trauma, makes causative assumptions that our study data do not support.

With regard to his comments concerning the validity of trauma as a marker, 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 traumatic events can 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 large numbers of cases. Our study is focused on 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 trauma 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 peripheral inflammatory lesions 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 physiologic factors were not counted erroneously as exacerbations.

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