

## Editorial

### Persistent vegetative state

A recent meeting held at the Royal College of Physicians, London in March 1995 provided a timely re-evaluation of many aspects of the persistent vegetative state, a syndrome which, although affecting relatively few patients, raises immense clinical, ethical, and social dilemmas. Organised by the Centre of Medical Law and Ethics, King's College, London on behalf of the EC BIOMED 1 programme, and the Royal Hospital for Neuro-disability, London it provided an opportunity for a forum of international experts in the field to present data and debate many of these dilemmas in an attempt to reach a consensus view. The mere fact that by the end of the two days some 21 different terms had been used for various low level states of cerebral function, many of which are undoubtedly identical, indicates the difficulty with even providing an acceptable definition for the syndrome.

Some 20 years after Jennett and Plum<sup>1</sup> originally suggested the term persistent vegetative state for patients who are awake but unaware, Jennett reviewed two recently published consensus statements defining the features necessary to diagnose persistent vegetative state. One was prepared by the American Neurological Association<sup>2</sup> and the other by a Multi-Society Task Force<sup>3,4</sup> representing the five major United States Neurological and Neurosurgical Societies. The Task Force define the vegetative state as one in which patients lack any awareness of the self and the environment, resulting in an inability to interact with others. They make no purposeful or voluntary responses to visual, auditory, tactile, or noxious stimuli, and have no evidence of language comprehension or expression. Sleep-wake cycles are preserved, as are hypothalamic and autonomic brain stem functions. Although cranial nerve and spinal reflexes may be retained to a variable degree, there is usually incontinence of both urine and faeces. These patients may make spontaneous movements of the face, trunk, or limbs—for example, grunting, chewing, or facial grimacing—but these must be non-purposeful. The diagnosis is not tenable if there is any degree of sustained visual pursuit, persistent visual fixation, or voluntary movement. To the trained clinical neurologist or neurosurgeon this definition does not seem at first sight to present any major diagnostic problem, but some words of caution are necessary. Great care is required with the bedside assessment of a patient with severe brain dysfunction given the normally expected fluctuations in arousal and awareness levels, and the necessity to differentiate persistent vegetative state from other states. In particular it is important to recognise the "locked in"

syndrome in which the patients are aware of themselves and their environment but are unable to respond due to lost motor function and speech. These reports and the meeting also reiterated Jennett and Plum's emphasis on abandoning at least some of the terms sometimes applied to these patients such as the apallic syndrome, neocortical necrosis, akinetic mutism, and prolonged coma, terms which merely lead to confusion rather than enlightenment.

Another facet of the persistent vegetative state in which difficulties are encountered is with its incidence, prevalence, and rate of recovery. Here there is confusion due to inconsistencies in the definition of persistent vegetative state. For example, the American Neurological Association definition requires that the patient should have been in a vegetative state for one month before diagnosing persistent vegetative state. The Task Force, however, requires one month only for non-acute cases, whereas acute cases are included in the definition so long as they have been in the vegetative state within one month of the insult. Consequently by their definition patients will be included if they have only been in the vegetative state for a few days after emerging from coma, despite an apparent high rate of recovery. This inevitably leads to the debate as to when does the vegetative state become persistent. At the meeting this was neatly side stepped by the consensus view that the word "persistent" in persistent-vegetative state should be abandoned. Although this may be valid when rates of recovery are considered, and will not seem so "final" to anxious relatives, it will inevitably lead to increasing rather than decreasing difficulties when making comparisons between different centres for estimates of the incidence of vegetative patients and of rates of recovery. It will, however, require publication of several authoritative statements in the future approving this view before "persistent" is permanently dropped. Similarly the introduction of new terms such as "postcoma unawareness", because it has fewer negative connotations than persistent vegetative state, will do little to further understanding about the subject.

An interesting dichotomy emerges between the rates of recovery of awareness in patients in a persistent vegetative state due to acute head trauma compared with those in a persistent vegetative state due to non-traumatic insults such as hypoxic-ischaemic encephalopathy, stroke, hypoglycaemia, a tumour, intracranial infection, or haemorrhage. If patients with acute head trauma are in a persistent vegetative state at three months after the

cerebral insult then within one year some improvement will be shown by about one third, of whom one fifth will be severely disabled. The outcome for the non-traumatic cases is far worse, with only about 7% improving, usually with severe disability. Such data led the Task Force to conclude that in traumatic cases the vegetative state was permanent after one year, but in non-traumatic cases permanence was to be expected after three months. Despite the occasional claim of patients recovering beyond these time periods the degree of disability is usually very severe. The ethical and social implications of such a conclusion are still fervently debated, however, and in the United Kingdom the courts do not accept an unequivocal poor outcome at three months as indicating a final state. Before artificial nutrition can be withdrawn from a patient in the persistent vegetative state approval from the courts has to be obtained in the United Kingdom.

The variability in outcome for patients in a persistent vegetative state has inevitably led to a consideration of a variety of measures which may assist improved prediction. These have largely centred on neurophysiological measures such as sensory evoked potentials and the EEG. To date the results, as exemplified by those reported by Professor J-M Guérit (Belgium), in patients in a persistent vegetative state seem to be very variable and of little value in predicting outcome. These results, however, raise the interesting and possibly disturbing spectre of subpopulations of patients lurking within the clinically defined persistent vegetative state population. The value of an original and theoretically plausible neurophysiological measure, eye blink habituation, in predicting outcome was reported by Professor PW Schönle and Dr D Schwall (Germany). Because eye blink habituation can be consistently elicited in non-brain damaged subjects, can be obtained at the bedside, and eye blink responses are present in severely brain damaged patients whereas other head or limb movements are impaired, it offers the potential to become a test of functioning of higher integrative CNS activity. Recording the frequency of blinking by clinical observation to repetitive visual, acoustic, or tactile stimuli prospectively in 13 patients, suggested that patients with a favourable outcome showed early learning with evidence of blink habituation, whereas patients with a less favourable outcome were able to react to stimuli but did not habituate. The patients studied, however, were either in a comatose or a vegetative state, clinical states which were combined in the data analysis. This was the situation with many of the studies reported at the meeting, and although probably reflecting the difficulty most centres have in acquiring a sufficiently large cohort of patients in a "pure" persistent vegetative state, it complicates the problem of understanding the condition.

Do these data indicate a window of opportunity in which therapeutic intervention may alter the outcome? Several speakers considered this issue, describing the possible roles for sensory stimulation, brainstem electrical stimulation, and drug treatment. Sensory stimulation, as pointed out by one of the leading proponents of the field, Dr MD Dimancescu (United States), has a long and venerable history dating from Hippocrates who wrote "the patient in a state of coma should be spoken to in a loud voice, splashed with cold water and exposed to bright light". Is the result of regular, sequentially applied, multi-modality sensory stimulation, however, likely to provide any material benefits other than those accrued by the relatives and nursing and paramedical staff who feel themselves involved in an apparently active mode of treatment as opposed to one which is inherently passive? Although

there may be theoretical justification for such programmes at a neuronal level—for example, inducing synaptic sprouting or enhancing the recruitment of undamaged neurons—controlled prospective studies are still lacking. It may well be that because of the emotive atmosphere surrounding the patient in a persistent vegetative state few relatives would agree to the patient being entered into such a study, preferring instead to demand a full programme of sensory stimulation. The methodology for evaluating the effects of rehabilitative treatments has advanced considerably in the past few years, however, and it should now be possible to devise studies which will not only satisfy the understandable anxieties of the relatives, but will also ensure that patients are not denied access to a potentially beneficial form of treatment.

Another form of treatment of interest but awaiting scientific evaluation is that of brainstem stimulation. In an exhaustive study of 20 patients in a persistent vegetative state given pulsed electrical stimulation via implanted electrodes in the mesencephalic reticular formation or of the median thalamic complex, Professor T Tsubokaw (Japan) reported evidence from both neurophysiological studies and cerebral blood flow of improvement in most patients. How these outcomes manifested themselves at a behavioural level was less impressive. The role of post-acute pharmacotherapy is currently largely at the theoretical rather than the practical level. Based on animal experiments likely candidates worthy of trial in patients in a persistent vegetative state would seem to be cholinergic and catecholaminergic drugs.

Dr K Andrews (London) reported several general conclusions regarding the management of patients with persistent vegetative state which had been reached at a workshop held before this meeting. These were as follows:

- A neurorehabilitation specialist should be involved with the patient's care as soon as possible after the cerebral insult.
- There should be an early introduction of the principles of neurodisability management.
- It is important that a planned programme is negotiated with the patient's family at an early stage based on explanation and involvement.
- All categories of patients should be given the opportunity to receive assessment and a planned programme.
- There should be provision of an identified and organised interdisciplinary continuum of care.

As a "Patients Charter" for the vegetative patient this would seem admirable, but it leaves a great deal unstated, including problems of definition, duration of any therapeutic regime, the outcome to be expected, and consideration of when it is ethically justifiable to withdraw life sustaining treatment. These and many other medical and ethical considerations of crucial importance to patients, their relatives, and all those concerned with care of the vegetative patient remain unanswered. It was encouraging that the participants at the meeting recognised these many deficiencies, and were anxious to consider them.

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- 1 Jennett B, Plum F. Persistent vegetative state after brain injury: a syndrome in search of a name. *Lancet* 1972;i:734-7.
- 2 American Neurological Association committee on ethical affairs. Persistent vegetative state: report of the American Neurological Association committee on ethical affairs. *Ann Neurol* 1993;33:386-90.
- 3 Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (first part). *N Engl J Med* 1994;330:1499-508.
- 4 Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (second part). *N Engl J Med* 1994;330:1572-9.