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The vegetative and minimally conscious states: Consensus-based criteria for establishing diagnosis and prognosis

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Abstract. Disorders of consciousness continue to be the subject of hot debate in healthcare settings, research consortiums, bioethics departments and media forums. There are no standards of care to guide assessment and treatment decisions resulting in wide disparities in daily practice. In response to this problem, expert panels in neurology and neurorehabilitation were convened and charged with developing consensus-based definitions and diagnostic criteria for disorders of consciousness. The Multi-Society Task Force Report on the persistent vegetative state and the Aspen Workgroup statement on the minimally conscious state represent two such initiatives. This paper summarizes the practice recommendations proposed by these groups and discusses their implications for existing and future interventions.

Keywords: Vegetative state, minimally conscious state, rehabilitation, practice guidelines

1. Introduction

A universally-accepted definition of consciousness has eluded philosophers and scientists for more than two thousand years. It should come as no surprise then, that clinicians continue to be perplexed by disorders of consciousness. There are many unsettled questions that complicate the assessment and treatment of patients with severe alterations in consciousness. In the rehabilitation setting, clinicians are faced with questions that often have no clear answers (e.g., *when is one considered conscious, is there a reliable method of measuring consciousness, can purposeful behavior be differentiated from random behavior, is it possible to predict recovery of consciousness*). Plum and Posner recognized the central problem underlying the study of consciousness in their now-classic text, *The Diagnosis of Stupor and Coma*. They noted:

> *"The limits of consciousness are hard to define satisfactorily and we can only infer the self-awareness of others by their appearance and their acts (p. 3) [2]."*

The lack of a direct measure of consciousness is perhaps the root cause of the confusion and controversy associated with disorders of consciousness. Over the last quarter-century, there has been a move toward establishing operational definitions of specific conditions characterized by a disturbance in consciousness. The success of these efforts has been mixed, although recent multidisciplinary initiatives aimed at consensus-building have begun to influence the conduct of research in this area.

The purpose of this paper is to summarize the consensus opinion of the major professional organizations in neurorehabilitation and neurology concerning the diagnosis, prognosis and outcome of patients in VS and MCS. Although all of the recommendations outlined here are not evidence-based, they represent the results of systematic and exhaustive literature reviews. They are intended to facilitate future scientific investigation and multidisciplinary discussion by providing a com-

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mon frame of reference for the examination and treatment of patients with disorders of consciousness. Before reviewing these recommendations, a brief history of the evolution of specific terms is provided.

2. Evolving concepts and terms

The *persistent vegetative state* (*PVS*) is a familiar but poorly understood diagnostic term. PVS was introduced by Jennett and Plum in 1972 to describe patients who exhibit no behavioral signs of self or environmental awareness, but are awake and have sufficient preservation of autonomic functions (e.g., respiration, heart rate, temperature regulation) to sustain survival when appropriate supportive care is provided [1]. In contrast to coma, patients in PVS do not require artifical life support as diencephalic and brain stem structures are sufficiently spared to sustain these functions.

The original intent of the term PVS did not imply permanence or irreversibility but rather an ongoing state of wakeful unconsciousness. Approximately a decade later, Plum and Posner [2] introduced a conceptual shift by suggesting that PVS refers to the vegetative state in its permanent form. Interestingly, this reconceptualization of the term was followed by a 10 year period of scientific quiescence in the study of disorders of consciousness. The silence was broken by two position statements published in the United States in the early 1990's on PVS. After conducting an evidence-based review of the world literature on outcome following PVS, the Multi-Society Task Force (MSTF) on PVS recommended that the term *persistent* VS be applied one month after the onset of VS [3]. Although not stated explicitly, the Task Force report implied that the term, *vegetative state* (VS) should be applied to patients who meet the diagnostic criteria for PVS but are less than one month post-injury. The MSTF also introduced the term *permanent vegetative state* and established temporal cut-offs for permanence based on the cause of injury. The MSTF report was approved by the American Academy of Neurology (AAN), Child Neurology Society, American Neurological Association, American Association of Neurological Surgeons, and American Academy of Pediatrics. The second position statement, published one year later by the American Congress of Rehabilitation Medicine (ACRM), held that PVS should not be diagnosed until 12 months post-injury [4].

In view of the conflicting recommendations proposed by the AAN and ACRM, the Aspen Neurobehavioral Conference, consisting of delegates from neurology, neurosurgery and neurorehabilitation, was convened and charged with developing a consensus statement on diagnosis and prognosis of PVS. In addition to discussing the diagnostic and prognostic criteria for VS, the Aspen workgroup operationally-defined a new condition termed the *minimally conscious state* (*MCS*) [5, 6]. The Aspen statement was subsequently endorsed by the American Academy of Physical Medicine and Rehabilitation, American Association of Neurological Surgeons, American Congress of Rehabilitation Medicine, Brain Injury Association of America and Child Neurology Society, and was recommended as an educational tool by the American Academy of Neurology.

2.1. Vegetative state

Patients in VS demonstrate intermittent wakefulness as evidenced by eye-opening or sleep-wake cycles on EEG, however, they fail to produce any purposeful or voluntary behavior in response to auditory, visual, tactile or noxious stimulation and do not exhibit any sign of language comprehension or expression [5]. There are generalized physiologic responses to pain (e.g., abnormal posturing, tachypnea, diaphoresis) and roving eye movements that may be misinterpreted as visual pursuit unless careful examination is conducted. Cranial nerve functions are variable and there is double incontinence. The Aspen workgroup acknowledged that the diagnosis of VS typically requires serial bedside examination and should not rely solely or neuroimaging or lab studies. The neuropathologic substrate underlying VS varies according to the cause of injury. Neuropathologic profiles include diffuse laminar cortical necrosis (hypoxic-ischemic injury), bilateral involvement of the paramedian thalamic nuclei (cerebrovascular disease) and diffuse axonal injury (traumatic brain injury).

2.2. Persistent and permanent vegetative state

In light of the confusion and controversy surrounding PVS, the Aspen workgroup recommended that the word "persistent" be avoided when describing VS. They went on to recommend that the diagnosis of "vegetative state" be accompanied by specification of the cause of injury and length of time post-onset. For example, an appropriate diagnostic impression would read, "post-traumatic VS of 6 weeks duration." The recommendation to abandon the term *persistent vegetative state* was driven, in part, by empirical data from two different

studies indicating that approximately 50% of patients in VS at one month post-injury will recover consciousness by 12 months [3,7]. The recommendation to record the cause and chronicity of injury was motivated by the fact that both of these variables contribute to outcome and, as such, they represent important prognostic indicators.

2.3. Prognosis in VS

In an effort to refine outcome prediction following VS, the MSTF calculated average probabilities for recovery of consciousness and degree of functional disability at 12 months post-injury based on type of injury (i.e., traumatic v. non-traumatic) and length of VS (i.e., 3 v. 6 months) [3]. Outcome measures included recovery of consciousness and degree of disability according to Glasgow Outcome Scale [8] criteria. The MSTF recommendations were subsequently endorsed by the Aspen workgroup and have achieved broad acceptance in both neurology and neurorehabilitation.

The MSTF report concluded that the probability of recovery of consciousness is approximately 35% for patients who remain in post-traumatic VS at 3 months post-injury. Among this group, roughly 20% will be left with severe disability at one year while the remaining 15% will achieve moderate to good outcomes. In those who fail to recover consciousness by 3 months, 35% will die and the other 30% will remain in VS at 1 year post-injury. Of those still in VS at 6 months, approximately 30% will die, 50% will remain in VS, and 15% will recover consciousness by 12 months.

Outcome probabilities differ significantly for patients in non-traumatic VS, relative to those with traumatic injuries. At 3 months, the probability of subsequent recovery of consciousness in the non-traumatic group falls to less than 10%. Among those patients who fail to recover consciousness by 3 months, approximately half will die during the ensuing 9 months and the other half will remain in VS. The MSTF did not find any cases of recovery after 6 months in the non-traumatic group. The mortality rate drops below 30% after 6 months, however, more than 70% of the survivors will remain in VS.

Informed by the MSTF report, the American Academy of Neurology (AAN) published a practice guideline in 1995 that established parameters for determining when VS should be considered permanent [9]. The temporal parameters for permanent VS in adults and children are shown in Table 1 according to cause of injury.

Table 1
Parameters for establishing when the vegetative state is expected to remain permanent

Etiology	*Temporal Criterion*
Traumatic brain injury	After 12 months
Non-traumatic brain injury	After 3 months
Congenital malformations	After 3 to 6 months
Metabolic disease	After 1 to 3 months
Degenerative disease	After 1 to 3 months
Anencephaly	At birth

It is important to recognize that these parameters are based on probabilities and should not be viewed as absolute. Although rare, recovery of consciousness has been reported after the criteria for permanence have been met [10–12]. A second caveat that should be considered when using the cut-offs for permanence concerns the size of the patient pool from which these criteria were drawn. Although the MSTF collected prognostic data on approximately 600 patients, there were only 53 patients for whom follow up data were available beyond 12 months post-injury. Among this group, long-term outcome data were based on anecdotal reports in 50% of cases. A third confound relates to the age of the studies included in the MSTF's review. Outcome data were culled from studies completed as long as 20 years ago. It is difficult to generalize the results of these earlier studies to the present day as there have been dramatic advances in neurosurgical and medical management over the last two decades. In light of these concerns, the Aspen statement recommended that the term permanent VS be communicated to family members as the point after which recovery of consciousness should be considered highly improbable, as opposed to impossible.

2.4. Minimally conscious state

Neurorehabilitation specialists are acutely aware of the importance of recognizing subtle signs of consciousness in patients who are otherwise unable to initiate purposeful behavior or communicate intelligibly. The Aspen workgroup, as well as other professional groups in the United States and Europe [4,13], distinguished this subgroup of patients from those in VS by their inconsistent capacity to execute limited but clearly discernible behavioral signs of cognitive function. There was broad consensus that a distinct diagnostic term was required to differentiate these patients from those in VS. There was also strong agreement that the term chosen should emphasize that these patients retained at least some capacity for cognitive processing as this might lead to differences in clinical manage-

ment and outcome, relative to those in VS. An earlier term, "minimally responsive state," had been proposed by the ACRM. This term was rejected by the Aspen workgroup because it failed to acknowledge the partial preservation of cognition in these patients [4]. Ultimately, the "*minimally conscious state*(*MCS*)" was selected as it provided descriptive information denoting some degree of conscious awareness. A full description of the clinical features and prognostic aspects of MCS was published by Giacino and colleagues in 2002 [6].

MCS may occur following traumatic, hypoxic-ischemic or vascular lesions. In most cases, MCS represents a transitional state reflecting improvement from coma or VS after acquired brain injury, or decline in consciousness as in neurodegenerative conditions. The most common injury profile following trauma consists of an aggregate of focal lesions, often including contusions, intracranial hemorrhage, ischemia and brain stem damage [14]. Thalamic lesions and severe diffuse axonal injury (i.e., grades II/III) appear to be much less common in MCS relative to VS.

Diagnostic assessment is particularly challenging in MCS as the hallmark of this condition is behavioral inconsistency. Patients in MCS may show clear signs of consciousness on one examination and then fail to produce the same behavior during a second examination conducted minutes, hours or days later. The fluctuation in behavioral responsiveness noted in MCS may account for the alarming rates of misdiagnosis (ranging from 15–43%) [15–17] reported in this population. For this reason, serial assessment is essential.

The diagnosis of MCS requires clearly discernible evidence of 1) simple command-following, or 2) gestural or verbal "yes/no" responses to questions (regardless of accuracy), or 3) episodes of intelligible verbalization (regardless of content), or 4) behaviors that occur in response to specific environmental stimuli and cannot be accounted for by reflexive activity. Typical examples of environmentally-contingent behaviors that meet the requirements of criterion 4 include a) smiling or crying following verbal or visual exposure to emotional but not neutral stimuli, b) vocalizations or gestures triggered by questions or comments presented by a second person, c) reaching for objects with a clear relationship between object location and direction of reach, d) visual pursuit or sustained fixation on objects moved into the field of view and e) touching or grasping objects with attention to the size or shape of the object. Some patients in MCS demonstrate only one of the above criteria while others exhibit all of them. Emergence from MCS occurs when reliable and consistent evidence of either functional communication or functional object use can be documented. At this point, more complex assessment methods are usually required to characterize cognitive functions. Neuropsychological assessment invariably shows significant cognitive impairment during the interval that follows MCS often involving disorientation and confusion.

2.5. Prognosis in MCS

There is very little empirical data available concerning prognosis in MCS. When MCS is diagnosed during the acute stage, there is considerable variability in functional outcome after one year, usually ranging from mild to severe disability. MCS may also represent a permanent outcome. Recent evidence suggests that patients in MCS, as a group, may have a longer course of recovery and may achieve more favorable outcomes by one year post-injury, relative to patients in VS. Giacino and Kalmar [18] retrospectively compared functional outcomes on the Disability Rating Scale (DRS) [19] at 1, 3, 6 and 12 months post-injury in patients diagnosed with VS and MCS on admission to rehabilitation. Patients were separated into two groups based on admitting diagnosis (i.e., VS $=$ 55 and MCS $=$ 49). They were further sub-divided by type of injury (i.e., traumatic v. non-traumatic) to allow for more specific characterization of outcome. Results indicated that the MCS group continued to improve beyond the 6 month mark and attained significantly more favorable outcomes by 12 months post-injury. The difference in outcome between the diagnostic groups was most pronounced in the traumatic MCS subgroup. Table 2 summarizes the degree of residual disability at 12 months for each of the four subgroups.

These findings suggest that establishing an accurate diagnosis is a critical component of outcome prediction in patients with disorders of consciousness. The diagnosis of MCS appears to be associated with a more favorable prognosis for recovery of function, particularly when it is diagnosed early in the course of recovery from traumatic brain injury.

2.6. Implications for treatment

In both VS and MCS, early intervention should focus on maintenance of physical health and prevention of complications. Standard rehabilitative interventions including passive range of motion and stretching exercises, positioning protocols, skin care, bowel and bladder programs, nutritional supplementation and dyspha-

Table 2
Frequency of degree of functional disability at one year post-injury in patients diagnosed with traumatic and non-traumatic VS and MCS (%)

Level of Disability	VS TBI	VS NTBI	MCS TBI	MCS NTBI
None to moderate	4	0	27	0
Moderate to extremely severe	53	33	50	70
Vegetative to extremely vegetative	33	60	0	10
Dead	10	7	0	20

VS TBI = traumatic vegetative state; VS NTBI = non-traumatic vegetative state; MCS TBI = traumatic minimally conscious state; MCS NTBI = non-traumatic minimally conscious state.

gia management are indicated at least until the criteria for permanence are met. In MCS, special attention should be devoted to establishing a functional communication system and facilitating environmental interaction. Assessments should be conducted to determine whether augmentative communication devices and environmental control units are appropriate. Caregivers should be especially sensitive to the potential for language comprehension and should monitor the content of bedside conversations. Interventions for pain management should be routinely implemented given the preserved capacity to perceive pain and experience suffering. When critical decisions concerning changes in level of care and withdrawal of life-sustaining treatment must be made, a professional with expertise in the evaluation and management of patients with severe disturbance in consciousness should be consulted to obtain an additional opinion. In all cases, the patient should be treated with dignity and respect.

3. Conclusion and future directions

The last decade has been witness to numerous advances in basic neuroscience, neurosurgery, neuroradiology, neurology and neurorehabilitation. Accomplishments in these areas have led to the development of more finely-tuned nosologies, novel conceptual models and cutting-edge technologies that have attracted the attention of clinicians and researchers interested in disorders of consciousness. The decade of the nineties will likely be remembered for its role in heightening awareness of disorders of consciousness, it is likely that the next ten years will be recognized for its yield of clinical applications. Armed with better-informed models of brain function (and dysfunction), more effective measurement tools and more sophistocated research methods, a well-defined course of scientific study has been charted [3,6,13]. The success of this endeavor will require cross-cutting, multidisciplinary collaboration among neuroscientists, neurologists and neurorehabilitation professionals. The clinical complexity, cost and emotional toil associated with long-term care and longitudinal research in this population can only be surmounted by pooling the collective resources of all invested parties.

Over the next decade, the care of patients in VS and MCS is likely to be impacted by recent improvements in behavioral assessment methods, neuroimaging techniques and treatment interventions. Neurobehavioral assessment methods with sound psychometric properties are widely available, thus, offering the promise of increased diagnostic and prognostic utility [20–22]. Functional neuroimaging strategies such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI) and magnetic resonance spectroscopy (MRS) are providing new insights into the neural underpinnings of language functions [23–25]. visual processing [26], pain perception [27] and emotional activity [28] of patients in VS and MCS. Brain mapping procedures such as these are also opening new avenues for treatment that employ pharmacologic and electrical stimulation approaches designed to facilitate the activity of damaged and downregulated neural systems.

Perhaps most importantly, clinicians and researchers should remain ever-mindful of the trappings of "therapeutic nihilism." This concept represents the belief that patients with prolonged disorders of consciousness are beyond help, therefore, any effort to intervene is futile and unjustified. In other words, nothing can be done, so nothing should be done. No prophecy was ever more self-fulfilling.

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