Clinical Diagnosis of Prolonged States of Impaired Consciousness in Adults

EELCO F. M. WIJDICKS, MD, AND RONALD E. CRANFORD, MD

A prolonged state of impaired consciousness is a devastating consequence of severe structural brain injury but fortunately is uncommon. Patients may be diagnosed as being in a persistent vegetative state, having akinetic mutism, or being in a minimally conscious state. These conditions can be distinguished from each other by a comprehensive clinical neurologic examination. Recovery is determined by age, cause, and time in such state. For patients diagnosed as being in a permanent (irreversible) vegetative state, hope for a clinically meaningful recovery is unrealistic after 1 year. Prolonged survival is possible only with meticulous care and aggressive medical intervention to prevent and treat systemic complications.


CT = computed tomography; EEG = electroencephalogram; MCS = minimally conscious state; MRT = magnetic resonance imaging; PET = positron emission tomography; PVS = persistent vegetative state

Coma, a disorder of awareness and arousal, occurs when brain injury interrupts the neuronal networks that bring consciousness into being. Awakening from coma can be dramatic and instantaneous, as in a treated hypoglycemic coma, or endlessly slow, as in severe structural brain injury. When improvement does not occur for several months, this condition is called a persistent vegetative state (PVS). However, PVS is not common, and other lesser states of impaired consciousness occur more frequently.

The assessment of prolonged states of impaired consciousness is primarily a matter of clinical judgment by physicians competent in neurologic diagnoses. Such assessment requires an experienced neurologist who can perform a thorough and comprehensive clinical neurologic examination and then can carefully interpret neuroimaging and electrophysiologic studies before making a final diagnosis.

CLASSIFICATION OF PROLONGED STATES OF IMPAIRED CONSCIOUSNESS

Crippling neurologic disease of the brain is hard to classify. What term should be used for an unconscious patient who spontaneously opens his or her eyes, displays a muted pseudobulbar grimace, fails to communicate, grunts—unless a tracheostomy prevents such a sound—and manifests only vegetative symptoms, such as changes in pulse, frequency of breathing, and blood pressure, in response to pain stimulus? Terms have been discarded because they failed to capture the essence of this state, namely, a totally unconscious state with only retained autonomic function.

Kretschmer1 introduced the term Das apallische Syndrom in 1940 (Figure 1), and the connotation is still used in a few European countries. Kretschmer coined the term to be phonetically similar to apraxic, agnostic, and aphasic and related the abnormality to a lesion of the pallium, the mantle of gray matter forming the cortex. Other terms include coma vigile,2 La stupor hypertonique post-comateuse,3 and Vie Vegetative,4 and most recently wakeful unconscious state,5 none of which are still in use.

One of the first attempts to define this syndrome clinicopathologically (“neocortical death”) came from the Institute of Neurological Sciences in Glasgow but applied only to patients after cardiac arrest.6 Neurosurgeon Jennett and neurologist Plum proposed the term persistent vegetative state and described clinical features clearly different from other less severely affected disabling neurologic states (Figure 2).7 These patients emerge from coma with opening of their eyes—primarily due to brainstem function—but with absent awareness largely because of thalamic and neocortex dysfunction. A PVS can be described as a state of “wakeful unconsciousness,” “eyes open unconsciousness,” or “being awake but unaware.”

In their 1972 communication, Jennett and Plum7 wrote that the word vegetative itself is not obscure: vegetate is defined in the Oxford English Dictionary as “to live a merely physical life, devoid of intellectual activity or social intercourse,” and vegetative is used to describe “an organic body capable of growth and development but devoid of sensation and thought.”

The term persistent vegetative state was coined to emphasize the “vegetative or non cognitive components of the nervous system.” Plum mentioned that “the term persistent autonomic state could have been employed almost equally well,” but the term was “less flexible” and “would have been less understood by the patient’s family.” The term persistent vegetative state became cemented in the medical vernacular but unfortunately in layman’s jargon was changed to the disrespectful term a vegetable.
STATES OF IMPAIRED CONSCIOUSNESS

FIGURE 1. Article by Kretschmer that defined the term Das apallische Syndrom (aplastic syndrome).

CLINICAL FEATURES OF A PVS

A comprehensive review by a multisociety task force codified the neurologic condition of a persistent and permanent vegetative state. The task force report was endorsed by 5 major organizations, including the American Academy of Neurology and American Neurological Association. The criteria for the diagnosis of a PVS are listed in Table 1. A diagnostic neurologic examination for the purpose of establishing the diagnosis of a PVS is typically postponed until at least 1 month has passed since the patient has had impaired consciousness. This task force recommended the use of the term permanent vegetative state (in preference to persistent) in which irreversibility is virtually certain. The term permanent—a prognostic rather than diagnostic qualifier—could be applied after 12 months have passed following a head injury or 6 months following brain damage from other causes.

A full neurologic examination cannot be performed reliably if the patient has recent evidence of bacteremia or early sepsis, if the patient is fatigued from a recent transport or bodily hygiene ritual, or if sedative agents are being used; the latter are a staple of modern intensive care units and have an often underappreciated cumulative effect. Family members or nursing staff who report that the patient has had periods of awareness should be taken seriously, and they should demonstrate what they interpret as a meaningful or voluntary response.

Patients in a PVS usually have minimal hemodynamic support. Many patients have had the trachea intubated in the initial phases of coma to protect the airway or support insufficient respiratory drive, but after a few weeks breathing becomes regular through a tracheostomy with only need for oxygen to ensure adequate gas exchange. Decannulation is often performed later.

When a patient is in a PVS, his or her eyes may open wide when the patient is touched, but visual pursuit is absent or very brief and not reproducible. A visual orienting reflex may occur, but, for example, placing the front page of a newspaper or optokinet tape right before the patient and moving it sideways should not elicit persistent visual scanning, tracking, or an optokinetic nystagmus. When large objects are placed before the patient or a person suddenly and closely approaches the patient, the patient may briefly turn the eyes and suggest target focusing, but the response extinguishes quickly. The patient sometimes has a disconjugate gaze, and brief nystagmoid jerks are seen, but the eyes typically move back and forth without fixation. However, tracking occasionally appears later without other signs of improvement. Blinking to threat may occur only rarely. Response to sound is often present and is complex, and many patients may show a startle response. Consistently looking toward the origin of sound (eg, handclap) is not compatible with the diagnosis of a PVS. The startle response may be myoclonus (early in the clinical course) or eye closure, head flexion, and a decorticate response (later in the clinical course). These responses do not require cortical feedback loops and do not imply intact hearing. A pain stimulus produces inconsistent “grimacing” or no response. More often it causes an increasing pulse rate, tachypnea, and pathologic limb flexion or extension. Facial expression may change when the patient is moved or touched. Snout (when the patient is kissed, a snout reflex may be elicited), glabella, palmo-mental, and corneomandibular reflexes may be elicited easily. Yawning and teeth grinding may remain as primitive brainstem reflexes. After the tracheostomy has been “corked” or removed, patients do not talk but may make sounds with different vowels; they may moan, groan, or squeal spontaneously. In extremely exceptional cases, patients may speak single words at random. Swallowing of saliva occurs, but the coordinated stages of oropharyngeal passage are impaired and lead to aspiration if challenged.
When ice chips are placed inside the patient’s mouth, primitive chewing movements may be observed, and an involuntary swallowing-gag reflex may occur. It is more likely that any food placed in the patient’s mouth will be inhaled with the next breath. In some patients, a tongue depressor may cause forceful biting with the ability to lift the head up (called bulldog reflex by Bricolo). Episodic screaming resembling rage has been reported but is highly unusual.

The patient’s muscle tone is increased and leads to back arching. Most patients are in a decorticate position with arms flexed and legs extended. Motor response is absent or no better than pathologic flexion or extension responses. These motor responses may be muted because of overriding spasticity and early contractures. Immobility causes acrocyanosis. Tendon reflexes are difficult to elicit because of these contractures, including a Babinski sign in patients with equinovarus. The jaw reflex is brisk. Grasp reflexes are common in some patients, thumbs become buried in balled fists or may wedge between ring and middle finger. Fumbling movements may occur after the patient touches bed linen, but they are nonpurposeful. Male patients may seem to touch their genitalia often, and erections occur frequently during rapid eye movement sleep but do not occur in the wake part of the cycle. Spontaneous non-directed choreiform movements of the head, trunk, and limbs, sudden catatonic postures resembling salutes, extreme opisthotonos (arc-en-cercle), and sudden half sitting position may occur in patients in a PVS; none of these movements are responsive to neuroleptic agents, benzodiazepines, dopaminergic drugs, and electroconvulsive therapy and could persist for months. Dysautonomic features such as increased bronchial secretions, hypertensive surges, tachycardia, and tachypnea may accompany these catatonic manifestations.

In patients in a PVS, circadian sleep-wake cycles are preserved but, in some patients, may be markedly diminished with the patient’s eyes primarily closed with brief episodes of opening. Isono et al found more brainstem lesions in such patients. Sleep-wake cycles are preserved possibly because of retained tonically active mesencephalon synapsing through sympathetic tracts to the pineal gland and involving serotonin, norepinephrine, and melatonin.

**OTHER DISORDERS OF PROLONGED IMPAIRED CONSCIOUSNESS**

When patients do not fulfill the criteria of a vegetative state, the Aspen Neurobehavioral Conference Workgroup suggested recognizing a possibly more common condition of severe disability with minimal awareness. They suggested the term minimally conscious state (MCS). An MCS is estimated to be 10 times more common than a PVS. The definition of an MCS is not based on prospective data, and little is known about the chances of improvement. Immediately after the term was introduced, concerns were voiced with frank rejection by some, and others thought MCS was decidedly undefined. The authors claim that the distinction of an MCS from vegetative state is a partial presence of awareness and is “important for prognosis, treatment decisions, resource allocation, and medicolegal judgments.” Nonetheless, acceptance of this condition in the neurologic community has been rapid, with recognition of its existence. However, as the working group acknowledged, important data on incidence and prevalence, an accurate diagnosis, course of recovery, and potential for treatment remain largely unknown. The proposed criteria for an MCS are shown in Table 2. This set of criteria describes patients with some interactive communi-
acknowledged characteristics, but there is a continuum and overlap with MCS. The descriptive term akinetic mutism is problematic for 2 reasons. First, most patients with akinetic mutism are not akinetic, and many may move in response to pain stimulus. Second, a few patients are mute; many can speak occasional words that signal some understanding. Patients rapidly localize a pain stimulus and may mouth or groan in response to moving or salient stimuli. Pain stimuli may provoke no response or a decorticate posture.

In contrast, a far less common state of impaired consciousness is akinetic mutism.21,22 The syndrome has fairly recognizable characteristics, but there is a continuum and overlap with MCS. The descriptive term akinetic mutism is problematic for 2 reasons. First, most patients with akinetic mutism are not akinetic, and many may move in response to pain stimulus. Second, a few patients are mute; many can utter only a single word. In the original description of akinetic mutism by Cairns et al,28 the clinical picture is described as follows:

The patient sleeps more than normally, but he is easily roused. In the fully developed state he makes no sound and lies inert, except that his eyes regard the observer steadily, or follow the movement of objects, and they may be diverted by sound. Despite his steady gaze, which seems to give promise of speech, the patient is quite mute, or he answers only in whispered monosyllables. Often-repeated commands may be carried out in a feeble, slow, and incomplete manner; but usually there are no movements of voluntary character; no restless movements, struggling, or evidence of negativism.

Cairns et al28 noted fluctuations and episodes in which the patient responded with some speech and purposeful movements.

The main clinical features of akinetic mutism are an abulic emotionless state, unresponsiveness, and tracking of movement in the hospital room or intensive care unit. (The ability of the patient to follow the examiner in the room or suddenly be prompted by a person entering the room has been compared to hypermetamorphosis, a phenomenon observed in monkeys after the temporal lobes have been removed. These animals seem to respond to movement, rather than objects.) Pain stimuli may provoke no response or a decorticate posture.

There is reasonable consensus among neuroscientists that akinetic mutism can be caused by bilateral lesions of the cingulate gyrus. The role of the anterior cingulate cortex is important and explains most of the symptoms. The anterior cingulate cortex is involved in executive functions but also affects vocalization and, because of the connections between the cingulate cortex and supplementary motor area, reduces initiation of movement.29 Akinetic mutism is rare and is possibly unrecognized by physicians. Other lesions affecting the diencephalic structures, such as the thalamus, basal ganglia, or even mesencephalic structures involving the reticular activating system, have been described.21 Akinetic mutism has been described in aneurysmal subarachnoid hemorrhage associated with bifrontal lesions,22,23 hypothalamic lesions and obstructive hydrocephalus,31 and an infiltrative astrocytoma in the fornix.27

Very few physicians confuse a PVS with brain death.10 In the latter, patients are apneic and often need vasoactive drugs to maintain normal blood pressure in addition to vasopressin to maintain normal intravascular volume. Clinical criteria for brain death have been published previously and are summarized in Table 3.32 When the brain is dead, the entire brain and brainstem are dead, and the person is legally dead. Throughout the world, legal rulings have permitted the use of neurologic criteria for death.31

### TABLE 1. Criteria for the Diagnosis of a Persistent Vegetative State

| 1. No evidence of awareness of themselves or their environment; they are incapable of interacting with others |
| 2. No evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli |
| 3. No evidence of language comprehension or expression |
| 4. Intermittent wakefulness manifested by the presence of sleep-wake cycles |
| 5. Sufficiently preserved hypothalamic and brainstem autonomic functions to survive if given medical and nursing care |
| 6. Bowel and bladder incontinence |
| 7. Variably preserved cranial nerve (pupillary, oculocephalic, corneal, vestibulo-ocular, and gag) and spinal reflexes |

Data from The Multi-Society Task Force on PVS.9

### TABLE 2. Criteria for a Minimally Conscious State

To diagnose a minimally conscious state, limited but clearly discernible evidence of self- or environmental awareness must be demonstrated on a reproducible or sustained basis by 1 or more of the following behaviors

1. Follows simple commands
2. Gestural or verbal yes/no responses (regardless of accuracy)
3. Intelligible verbalization
4. Purposeful behavior, including movements or affective behaviors that occur in contingent relationship to relevant environmental stimuli and are not due to reflexive activity. Some examples of qualifying purposeful behavior are:
   - Appropriate smiling or crying in response to the linguistic or visual content of emotional but not to neutral topics or stimuli
   - Vocalizations or gestures that occur in direct response to the linguistic content of questions
   - Reaching for objects that demonstrates a clear relationship between object location and direction of reach
   - Touching or holding objects in a manner that accommodates the size and shape of the object
   - Pursuit eye movement of sustained fixation that occurs in direct response to moving or salient stimuli

Data from Giacino et al.18
A review of causes of coma or mimicking neurologic states is beyond the scope of this article. However, in a patient with impaired consciousness, reversible medical conditions such as acute metabolic encephalopathies (electrolyte abnormalities and acute endocrinopathies), drug-induced coma, and hypothermia should be excluded. A locked-in syndrome could be mistaken for a PVS. In this condition, the patient is fully aware but is unable to move except for opening eyes, blinking, and vertical eye movements in response to physician requests. The pathologic substrate is commonly a destruction of the base of the pons, sparing the ascending reticular activating system in the tegmentum.

**Pathology**

A PVS is expected only when destructive injury occurs in critical areas that control awareness. The pathologic changes can be classified into traumatic or nontraumatic injury, although overlap may occur (eg, anoxic-ischemic injury due to cardiac arrest or shock in multitraumatized patients). The most frequently reported pathologic substrate of PVS in traumatic cases is diffuse axonal injury, with a variable contribution of superimposed ischemic lesions. Bilateral thalamic damage is a fairly constant feature and suggests that the thalamic reticular nucleus is operational in arousal.

When autopsy cases of patients in a PVS are compared to those in an MCS or other severely disabled cases, injury in a PVS is more severe. These findings include more frequent thalamic lesions and multiple localizations of axonal injury (eg, corpus callosum, rostral brainstem). Although overlap was considerable, Jennett et al reported that the combinations of ischemic damage, thalamic injury, or white matter axonal injury were not found in severely disabled patients but only in those in a PVS. Anoxic-ischemic injury causing a PVS usually affects the entire cortical mantle, not only all territories (the parieto-occipital more often than the frontotemporal region) but also throughout the full thickness replacing neurons and nerve fibers with gliosis, lipid phagocytes, and collagen. Cavities in the caudate and lentiform nucleus are common. In the autopsy of Karen Ann Quinlan (cerebral injury associated with cardiopulmonary arrest and ingestion of sedatives and alcohol), cortical thinning was found, as well as areas of cortical sparing with the thalamic, caudate nucleus, and putamen regions most notably affected. The prominence of thalamic lesions was remarkable, again pointing toward this important structure for awareness. Purkinje cells and granular layers in the cerebellum are commonly affected after anoxic-ischemic injury, and cystic softening in periaqueductal gray matter and the dorsolateral brainstem is a common post-traumatic finding. An example of cortical thinning is shown in Figure 3.

<table>
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<tr>
<th>TABLE 3. Clinical Criteria for Brain Death</th>
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<td>Coma</td>
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<td>Absence of motor responses</td>
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<td>Absence of pupillary responses to light and pupils at midposition with respect to dilatation (4-6 mm)</td>
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<td>Absence of corneal reflexes</td>
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<td>Absence of caloric responses</td>
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<td>Absence of gag reflex</td>
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<tr>
<td>Absence of coughing in response to tracheal suctioning</td>
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<td>Absence of respiratory drive at PaCO2, that is 60 mm Hg or 20 mm Hg above normal baseline values</td>
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FIGURE 3. Macroscopic specimen of the brain of a 23-year-old man who had been in a permanent vegetative state for 10 years after surviving massive brain edema due to Reye syndrome but died of bronchopneumonia. Brain weight is 370 g (similar to brain weight at birth). Top, Gross picture of brain in situ, showing marked atrophy of both frontoparietal areas. Middle, Gross picture of whole removed brain, left-sided perspective with marked frontal atrophy. Bottom, Coronal section of brain with marked cortical atrophy and hydrocephalus ex vacuo.

component of auditory-evoked potential) and event-related potentials precludes the development of an MCS or PVS.\(^{46}\)

With anoxic-ischemic injury and traumatic injury as predominant causes of a vegetative state, one should expect these lesions on neuroimaging studies. Diffuse laminar cortical necrosis and traumatic rotational force lesions in the corpus callosum and dorsal brainstem are prevalent but are seen only on magnetic resonance imaging (MRI). On computed tomography (CT), diffuse atrophy and bilateral thalamic lesions are common in both conditions.\(^{35}\) Regardless of the underlying cause, patients who survive a few months in a PVS show pronounced reduction in white matter volume on serial CT scans with more obvious concomitant enlargement of the ventricular system.\(^{9}\) Secondary axotomy and transneuronal degeneration are possible mechanisms for this progressive loss of brain tissue (Figure 4).

There have been sporadic studies of brain physiology in patients in a PVS.\(^{47-49}\) The data have been used to support lack of awareness and may be comforting for those questioning the validity of a comprehensive neurologic examination. These studies may provide insight into the cortical disconnection, but their value for prognostication is unproved. The most interesting are the positron emission tomography (PET) studies, and very preliminary studies in selected patients have been published. One study of 5 patients in a PVS quantified cerebral metabolism and found that the resting rates are less than 50%.\(^{14}\) (This decline has been speculatively compared to an anesthetized brain.) Topographic differences have been found in patients with near-normal cortex metabolism but with profound abnormal thalamic and mesencephalic function. PET studies have also documented that the most severe abnormalities are in the frontal and temporoparietal region, disconnecting this region from the thalamus.\(^{47-49}\) A multimodality study using PET and functional MRI in patients in a vegetative state for 1 month (several days to weeks) found lack of activation of the temporoparietal area.\(^{50}\)

Coleman et al\(^{51}\) recently used PET and EEG in PVS and MCS in a small study of patients. A weak but statistically significant correlation was found between EEG power spectrum and glucose metabolism in an MCS that was not evident in a PVS. This lack of “neurometabolic coupling” was considered distinctive between the 2 disorders of impaired consciousness.\(^{51}\)

In an attempt to further distinguish an MCS from a PVS, functional MRI studies have been performed.\(^{52}\) A functional MRI scan involves T2-weighted images with grading echo pulse sequence changes of oxyhemoglobin in the perfused area, which is considered evidence of neuronal activation. The study is of interest but shows the difficulties in carving out the boundaries of an MCS. In that study, both patients had focal neurologic abnormalities but could identify objects visually, follow 1-step commands, and occasionally speak a single word. None of these tasks were observed consistently. Passive simulation tests were performed and included light touch of both hands and an auditory narrative of familial events presented by a family member. The functional MRI showed evidence of activation of superior middle temporal gyri to passive listening. Because of activation of the occipital cortical regions, the authors further speculated that activation of these regions
while the patient listened to the narrative content might imply an “imaginal representation of the person speaking.”

The data revealed that the remaining brain physiology in a patient in an MCS, as tested by functional MRI, could be different from that in a patient in a PVS. Both patients in MCS underwent a resting PET with fluorodeoxyglucose that showed approximately 40% of normal regional cerebral metabolic rates, rates comparable to those found in earlier studies of patients in PVS.

**Management**

Long-term management of PVS requires a temporary tracheostomy for more-appropriate pulmonary toilet, permanent gastrostomy for nutrition, and meticulous skin care. Physical therapy could possibly reduce the chance of contractures when coma duration is brief. Permanent contractures occur after the first year a patient is in a coma and cannot be prevented. Hypertonic bladder requires catheterization and anticholinergic agents to improve bladder emptying and reduce a vesicourethral reflux and urinary tract infections. Medical management is complex and often punctuated by treatment of intercurrent infections and skin breakdown, some of which become life threatening if not treated aggressively.

The frustration in seeing a patient “lying in a coma” often fosters a strong desire to “do something,” but specific therapy is not available. A recent Cochrane evaluation of sensory stimulation programs (with an enormous burden on family members and a brutal schedule, cycles of 20 minutes repeated every hour for 6 days a week) found no evidence of effect. Besides flawed study designs, there was lack of blinded assessment. Mackay et al treated 17 comatose patients with “coma stimulation” and compared the results with 21 patients recruited from 10 different hospitals and claimed shortening of coma duration. Kater found improved cognitive scores with his stimulation program, but none of these scores have been used widely or have been validated.

Most recently, in a study by Davis and Gimenez, stable patients were subjected to an intensive program of auditory stimuli that consisted of music, taped familiar voices, bells and claps, and radio or television. Effect was measured using complicated scales or combined eye and motor responses. Safety was monitored by simultaneous recording of effect on blood pressure and intracranial pressure. This therapy was proved ineffective.

Wilson et al reported on 24 patients in a PVS with multimodal stimulation (subjecting patients not only to sound but also to favorite perfume, food, clothes, and toys or pictures associated with hobbies). Effect was measured by time spent with eyes open and presence of spontaneous movement interpreted as signs of improved arousal. Significant differences in responses were found between multimodal and unimodal stimulation. This study lacked proper neurologic assessment and details surrounding brain injury.

Thalamic stimulators have been implanted in an attempt to increase output of the reticular formation. The patients were treated within 3 months of traumatic head injury. In the series by Yamamoto et al, 8 of 21 patients improved in awareness. In the series by Cohadon and Richer, 13 of 25 patients “improved to some degree of consciousness.” In both these studies, proof of effect could not be distinguished from spontaneous recovery.

In summary, these stimulation studies, based on the premise to provide “sensory input to the damaged reticular activating system promoting reorganization of undamaged neurons or regeneration,” should be considered flawed and...
States, and traces of awareness were found in a survey conducted in the United Kingdom and in the United States. In a vegetative state from age 24 to 71 years until her death survival (30-40 years) has been reported. (One woman was medical intervention with each complication. Long-term survival beyond 3 years for a patient in such a state has not been reported. Only a few patients, an estimated 10 primarily young patients, have been reported to recover to some degree. All “improved” patients remained in a severely disabled state fully dependent on care, were bedbound or wheelchair bound, and needed permanent gastrostomy and urinary catheter. Predictive factors for recovery have not been identified. However, there seems to be a strong correlation between the development of progressive and severe atrophy of the cerebral hemispheres on CT as confirmatory evidence of the irreversibility of the underlying condition, both in MCS and PVS (R.E.C., personal observation).

Mortality from untreated infections or overwhelming sepsis is extremely high in the first 3 years. (The Multi-Society Task Force on PVS noted a 70% mortality in 3 years and an 84% mortality in 5 years.) Prolonged survival can be achieved only with meticulous care and aggressive medical intervention with each complication. Long-term survival (30-40 years) has been reported. (One woman was in a vegetative state from age 24 to 71 years until her death (R.E.C., personal observation).

The reliability of the diagnosis of a PVS has been surveyed in the United Kingdom and in the United States, and traces of awareness were found in a considerable proportion of patients deemed to be in a PVS. Inaccuracy (or overdiagnosis) was more likely in patients presumably identified as in a PVS within 3 months of injury and with trauma. Improvement soon after admission following the initial insult, insufficient observation by the examining physician, or pharmacological agents depressing consciousness are plausible explanations. In contrast, patients who reside in long-term facilities may not have been diagnosed as being in a vegetative state; indistinct terms (eg, severe brain injury, static encephalopathy, or even comatose) may be used, and, far more importantly, families may not have been informed about the permanent nature of the brain injury. Failure to recognize (or under-diagnosis of) specific unconscious states has not been systematically studied. It may well be frequent.

The media are replete with so-called miracle awakenings, some of which are only temporary. Apart from being incorrect, the press coverage of these cases is hyperbolic. These cases often involve the sudden appearance of communicative speech in patients in a prior MCS who were not in a PVS.

OUTCOME

As alluded to previously, a permanent vegetative state can be diagnosed 6 to 12 months after the initial devastating injury. Permanent in this context means irreversible. Hope for a clinically meaningful recovery is unrealistic, with recovery extremely rare and not better than a severely disabled fully dependent state of living. Recovery beyond 3 years for a patient in such a state has not been reported. Only a few patients, an estimated 10 primarily young patients, have been reported to recover to some degree. All “improved” patients remained in a severely disabled state fully dependent on care, were bedbound or wheelchair bound, and needed permanent gastrostomy and urinary catheter. Predictive factors for recovery have not been identified. However, there seems to be a strong correlation between the development of progressive and severe atrophy of the cerebral hemispheres on CT as confirmatory evidence of the irreversibility of the underlying condition, both in MCS and PVS (R.E.C., personal observation).

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CONCLUSIONS

Prolonged states of impaired consciousness are uncommon because most patients improve within 3 to 6 months, and many die. The diagnosis of prolonged states of impaired consciousness is primarily clinical with less emphasis at present on static and functional neuroimaging and electrodiagnostic studies, which have not achieved sufficient validity and specific recognizable patterns. After stimulation, absence of operational modular networks on functional MRI and markedly depressed EEG in a patient in a PVS after cardiac arrest are other results that could confirm a clinical diagnosis but are nonspecific. These tests confirm clinical examination findings of a human being with no awareness of the damage done and no awareness of any discomfort. From a clinical standpoint, eye movements are the most critical physical sign. Response to approaching objects distinguishes between a PVS (visual tracking absent or very inconsistent), akinetic mutism (no consistent tracking but spontaneous focusing on moving objects), and an MCS (visual tracking almost always present).

The recent case of Terri Schiavo in Florida has generated not only controversies about the need for prolonged care but also, more remarkably, a dispute about her neurologic condition. Unprecedented in this case was a major focus on distinguishing a permanent vegetative state from an MCS. Far more surprising, being in an MCS was considered by some an opportunity for therapeutic intervention and the approach to take despite Schiavo’s unchanged catastrophic neurologic state for 15 years. Seven of the 8 board-certified neurologists who examined Schiavo diagnosed her as being in a permanent vegetative state; the credentials and testimony of the eighth neurologist who testified in court that Schiavo was not in a permanent vegetative state were completely discredited by the trial court judge, George Greer. Further details including legal proceedings will be published.
According to these neurologists, including the court-appointed expert, Schiavo demonstrated the typical clinical features of a permanent vegetative state. Her EEGs were markedly suppressed or showed no electrical activity, as seen on EEGs of patients with the most severe forms of encephalopathy after cardiac resuscitation. Follow-up CT scans showed profound atrophy of the cerebral cortex. The postmortem evaluation by the chief medical examiner of Pinellas County, Florida, and a consultant neuropathologist found massive, irreversible damage of the cerebral hemispheres, consistent with the clinical diagnosis of a permanent vegetative state. In fact, at autopsy, Schiavo’s brain weighed only 615 g, less than half the weight of a brain from a healthy person and more than 25% less than the weight of the brain of Quinlan (835 g), who was in a permanent vegetative state for 10 years. The impressive microscopic features of Schiavo’s brain included widespread laminar necrosis with predominance in the parieto-occipital regions, thalami, basal ganglia, and hippocampi.

The dispute about Schiavo’s existence continued after her death, with her grave marker showing 2 dates. The day she died 15 years later as the day “at peace.”

To epitomize, for most of us, an irreversible prolonged condition, in which patients are unconscious and permanently disconnected from outside stimuli and thus unaware of sound, touch, light, and pain, is considered unacceptable; for some of us, it is even close or equivalent to death. Important position papers on withholding or withdrawing life-prolonging medical treatment have been published, and they have defined mechanical ventilation, nutrition, and hydration as life-prolonging medical treatments. A proxy early in the hospital course could decide on withdrawal of hydration and nutrition.

For some families, there may be incredulity at the wide open eyes and gazed look while no interaction is registered, and they may need years to accept the irreversibility of the condition. Others may follow their guiding religious principles or moral values and wish to continue the maintenance of life in any circumstance.

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