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**Points of View**

**PERSISTENT VEGETATIVE STATE AFTER BRAIN DAMAGE**

A Syndrome in Search of a Name

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**Summary**

Patients with severe brain damage due to trauma or ischemia may now survive indefinitely. Some never regain recognizable mental function, but recover from sleep-like coma in that they have periods of wakefulness when their eyes are open and move; their responsiveness is limited to primitive postural and reflex movements of the limbs, and they never speak. Such patients are best described as in a persistent vegetative state, which should be clearly distinguished from other conditions associated with prolonged unresponsiveness. What is common to these patients is the absence of function in the cerebral cortex as judged behaviorally; the lesion may be in the cortex itself, in subcortical structures of the hemisphere, or in the brainstem, or in all of these sites. But the exact site and nature of the lesion is unknown to the bedside clinician, and the name for the syndrome should not imply more than is known.

"...if we have a conception for which no name exists, which we use frequently to speak of, it is as wise, I think, to fashion from an accident to give it a name."—Sir William Gowers

New methods of treatment may, by prolonging the lives of patients with conditions which were formerly fatal, result in situations never previously encountered. And new situations call for new names if they are to be accurately understood and discussed. Twenty years ago French commented that patients who sustained brain lesions which deprived them of the ability to perform the intuitive and protective functions necessary for survival rarely lived more than a few days or, exceptionally, two or three weeks. He then described five patients who had survived for many months with profoundly altered consciousness, but he did not suggest a name for their clinical condition. With the development of intensive-care units it has now become almost commonplace for patients to survive with devastating brain damage, usually the result of head trauma, a brain-stem stroke, or a cardiorespiratory crisis associated with hypoxia. Clinical and pathological reports about such cases are beginning to accumulate, whilst the ethical, moral, and social issues are provoking comment both in the health professions and in the community at large. Once part the acute stage these patients are neither unconscious nor in coma in the usual sense of these terms, both of which imply a sleep-like insensibility. There is clearly need for an acceptable term to describe their state, in

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**Clinical Syndrome**

In the first week or so after injury these patients are in deep coma, never opening their eyes, and then they do react to stimuli; they show varying degrees of response in the limbs. However, unless they have bilateral thalamic-peduncular injuries, the survivors begin, within two or three weeks, to open their eyes—first only in response to pain, then to less amusing stimuli. Soon after this they have periods when, without any provocation, they lie flaccid with their eyes open but do not react to stimuli. Such patients are having intensive nursing care; this involves being turned every two or three hours, and the limbs in their casts may never be put out. The eyes are open and may blink to menace, but they are not attentive; although moving movements may briefly seem to follow moving objects, careful observation does not confirm any consistency in this optimistic interpretation. It seems clear that there is wakefulness without awareness.

The examiner response in the limbs is commonly referred to as deceptively rigidity, after Sherrington's description of the limb postures of animals after midbrain transection. It can also begin to wear off after two or three weeks, and although for a time some examiner movements may still occur, a modal stimulus may now provoke a flaccid withdrawal, but only after an abnormally delayed, and the movement itself is rather slow and dysmetric; there may be the form of normal brisk response. A significant group reflex often appears, and this may be provoked by chance touch of the eyelashes to the experimenter observer or helper. If the resulting movement may last as long as it was initiated by the patient and may even be regarded as purposeful or voluntary. Sometimes segments of coordinated movements may be seen such as scratching, or opening the mouth towards a sensory stimulus, and postural alterations in the limbs may be provoked by movements. Chewing and teeth grinding are common and may go on for long periods; liquid and food placed in the mouth may be swallowed.

Greating or grooming may be provoked by sensory stimuli, but most of these patients are silent; they neither speak nor make any meaningful response to spoken words. Shouting, like a nonsense stimulus, may produce a non-specific somatic and vegetative response with eyeopening, gesticulating, altered respiratory patterns, and even some movements of the limbs. Few would dispute that in this condition the cerebral cortex is not active. Two reported patients with extensive mesencephalic lesions has had this disorder for several months after cardiac arrest. However, it is also possible that for the functions of the cortex to be inactivated whether that structure itself is damaged, because, when a critical amount of damage is sustained by the extracerebral activating system either in the brain-stem or in the basal ganglia or subcortical areas, the cortex may continue to function effectively. Patients with head injury also survive in this state frequently prove to have extensive lesions in the white-matter, with almost complete sparing of the cortex and brain-stem,15-16 but others have secondary brainstem compression or extensive ischaemic brain damage in the cortex and subcortical structures. In the first few weeks after injury the electroencephalogram (E.E.G.) may resolve doubts about whether the patient is really "awake"; if there is extensive necrotization of the brainstem will usually be flat, as in the case of Light et al. who had isoelectric records for many weeks. However, this is rare, and there is very little information...
The persistent vegetative state (PVS) was described in the Lancet exactly 30 years ago by Bryan Jennett, a neurosurgeon, and the neuropathologist Fred Plum (Jennett & Plum 1972). Jennett has recently reviewed the subject (Jennett 2002). Sometimes described as a condition of wakefulness without awareness, it can follow a range of severe insults to the brain. Often misdiagnosed, frequently misunderstood, the syndrome provides a useful shorthand for a diverse but distinctive set of clinical phenomena. Although it has withstood the scrutiny of ethicists and lawyers, it assumes a concept of awareness that may not stand the test of time. In this article I will sketch its key features and end by asking how confident we can really be that a patient in the PVS is wakeful, but conscious of nothing.

Many of us will remember our first encounter with a patient in the vegetative state (VS), as the condition is undeniably eerie. At first glance the patient appears to be wide awake, his eyes open. If he is peaceful when you enter the room, he may be aroused by the sound of your entry, opening his eyes if they are closed, quickening his breathing, grimacing or moving his limbs. Once he is calm again, you may notice a range of spontaneous movements: chewing, teeth grinding, swallowing, rapid movements of the eyes, fleeting fixation. More distressingly he may smile, shed tears, grunt, moan or scream without any discernible reason. Yet despite this varied repertoire of behaviours, you will be unable to convince yourself that you can communicate with him, or he with you; beyond his indiscriminate arousal to prominent stimuli and a flick of the eyes towards them, you will see no sign of perception or purposeful action: in short, you will find no convincing evidence of mind.

The PVS is most often the outcome of major head trauma and of hypoxic-ischaemic brain damage resulting, for example, from cardiorespiratory arrest. It can occur as the end stage of neurodegenerative disorders, and a similar state is seen at the start of life in anencephalic infants. Where trauma is the cause, the pathological basis is, as a rule, diffuse axonal injury, with secondary degeneration in the thalamus; hypoxic-ischaemic insults are associated with cortical laminar necrosis or a diffuse leucoencephalopathy; occasionally the thalamus is the principle site of pathology, and combinations of pathology in cerebral cortex, white matter and thalamus are common (Adams et al. 2000) (Figure 1). The anatomical key to the clinical features of the VS is the complete or relative sparing of the brain stem. Thus cardiorespiratory function and the signs of sleep and wakefulness survive, despite the devastation of the cerebral hemispheres and their functions.

Problems of misdiagnosis and misunderstanding have bedevilled the fortunes of the VS. The most common misunderstanding is terminological, a confusion of the vegetative state per se, the persistent vegetative state and the permanent vegetative state. Claiming that a patient is in the VS per se is to claim that he is in the state described above: wakeful but unaware. There is no implication that he will necessarily remain in the VS and, of course, patients in the VS often do regain awareness after a while (The Multi-Society Task Force on PVS 1994) (Table 1). To describe him as being in a persistent VS is simply to state that he has been in the VS for some time, typically 1 month or more. To deem his VS permanent is to predict that he will never regain awareness. All predictions are fallible, but there are good grounds for regarding the chances of regaining awareness after 1 year in the VS as being

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Or when, under ether,
the mind is conscious but
conscious of nothing
T.S. Eliot (1970)
exceedingly slim – around 2%. If recovery occurs at this stage, severe disability is the rule. The chances of regaining awareness after spending a period in the VS are better after traumatic than nontraumatic brain injury, especially in children, and decline as time passes (Table 1).

If these subtleties of terminology are easily misunderstood, there is also good evidence that the VS is often misdiagnosed (Childs et al. 1993; Andrews et al. 1996). Reports from centres specializing in the management of patients with severe brain injury in the US and the UK indicate that around one-third of patients referred in the VS are in fact aware. Explanations for misdiagnosis include uncertainties on the part of medical staff about the criteria for the diagnosis of the VS, inadequate observation in suboptimal circumstances (for example, on a ward round), failure to consult those who see most of the patient (especially family members), and the inherent difficulty of detecting signs of awareness in patients with major perceptual and motor impairments.

Assuming that one can make a confident diagnosis of the VS, how should someone in this state be managed? The standard practice is to provide adequate supportive care over the first few months to allow awareness to recover whenever possible: this involves adequate nutrition, usually via a feeding tube, good skin care, passive joint exercises to minimize contractures, suction where necessary to help avoid aspiration, careful management of the doubly incontinent bladder and bowel, and attention to oral and dental hygiene. These measures set the stage for attempts by relatives and medical staff to re-establish contact with the patient: they must be on the lookout for subtle signs of awareness in a person whose brain damage may make it very difficult for him to express his thoughts and intentions.

With the passage of time in the VS, the chances that it will be permanent gradually rise. Once a year has passed, it is reasonable to ask whether continued hydration and nutrition are still appropriate. In the UK the decision to withdraw these requires a legal ruling, unless the patient has made a clear advance directive in a living will. The decision should of course be made after discussion with the family, but by this stage the family’s feelings will usually be well known. Surveys indicate that the great majority of doctors and lay people would prefer to be allowed to die should they have the bad luck to enter a permanent vegetative state (Jennett 2002).

**Table 1** Prognosis of the vegetative state when patients are seen one month after the brain insult. Reprinted with permission from Elsevier Science (Lancet, 350, 795–9).

<table>
<thead>
<tr>
<th>Outcome States</th>
<th>Percentage in various outcome states</th>
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<tbody>
<tr>
<td></td>
<td>3 months</td>
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<td>Adults (n = 434)</td>
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<tr>
<td>Trauma</td>
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<td>Dead</td>
<td>15</td>
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<tr>
<td>Persistent vegetative state</td>
<td>52</td>
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<tr>
<td>Aware</td>
<td>33</td>
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<td>Non-traumatic (n = 169)</td>
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<tr>
<td>Dead</td>
<td>24</td>
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<tr>
<td>Persistent vegetative state</td>
<td>65</td>
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<td>Aware</td>
<td>11</td>
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<td>Children (n = 106)</td>
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<tr>
<td>Trauma</td>
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<td>Dead</td>
<td>4</td>
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<tr>
<td>Persistent vegetative state</td>
<td>72</td>
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<tr>
<td>Aware</td>
<td>24</td>
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<td>Non-traumatic (n = 45)</td>
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<tr>
<td>Dead</td>
<td>20</td>
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<tr>
<td>Persistent vegetative state</td>
<td>69</td>
</tr>
<tr>
<td>Aware</td>
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Data assembled from all available sources by the American Multi-Society Task Force on persistent vegetative state.

**Some Complexities and Doubts**

How sure can we be that someone with the typical features of the VS is truly unaware? Consider a feature that Jennett regards as characteristic: most patients show some response to painful stimuli. A stimulated limb may withdraw or there may be a generalized movement of all four limbs, sometimes accompanied by facial grimacing and perhaps a groan (Jennett 2002). Can we really be confident that this behaviour is unaccompanied by an experience of pain? Or take the behaviour of a patient described by Ni-
cholas Schiff who was vegetative by all other criteria but whose agitated response to loud noise and attempts at nursing – clenched teeth, rigid extremities and high-pitched screaming – abated in response to soothing voices or music (Jennett 2002): do these responses imply the occurrence of some kind of awareness, or are they, as Schiff and colleagues believe, mere behavioral fragments, reflecting the preservation of critical islands of cortical function?

These are difficult questions. Two approaches might help come up with an answer: first, learning more about brain function in the VS, and how it compares to brain function in manifestly conscious states; second, clarifying the criteria we apply when we attribute consciousness to others.

Work pursuing the first approach has already made some headway. The brain’s global metabolic rate is depressed in the VS to levels 40–60% below normal: these are as low as, or below, levels of brain metabolism under general anaesthesia (Zeman 1997). In some cases functional studies of brain activity in the VS indicate cortical silence: but this is not a consistent result. Cortical evoked potentials can sometimes be obtained. Menon et al. using PET scanning, even demonstrated a face-specific response in visual association cortex in a patient who went on to recover awareness (Menon et al. 1998) (Fig. 2). Laureys et al. (2000) have shown that auditory stimuli activate Brodmann’s areas 41 and 42, involved in early auditory processing in patients with the VS. Adjacent auditory association cortex, was not activated, and there was evidence of functional disconnection of auditory cortices from other related brain regions. Work of this kind indicates that global brain activity is markedly depressed in the VS. Where stimulus-driven cortical activity persists it is usually fragmentary, and fails to give rise to the widespread interactive processing that most contemporary theories, rightly or wrongly, regard as the physical basis for consciousness (Zeman 2001).

The second approach treads on philosophers’ toes. Two lines of thought are worth a mention. One, dualistic, response to our question – whether we can be sure that a patient in the VS is unaware – denies that we ever can be, because, so the thought goes, experience is private and unobservable. Patients in the VS give little evidence of awareness, but we cannot infer that they are unaware. This uncompromising stance has some appeal, but takes us no further. A contrasting, more promising, line of thought, weakens the assumption on which we based our question. It runs like this. Awareness is as awareness does. People in VS can certainly sense what happens around them: at the very least they can be startled, and perhaps they can be soothed. Sensation is a kind of primitive awareness. Don’t waste time worrying when sensation turns into sentience, or when the light of consciousness dawns. Just ask yourself what this kind of awareness would be worth to you. Few of us would choose to have it last.

REFERENCES

Figure 2 Using position emission tomography functional imaging superimposed on an MR brain scan, there are areas of cortical activation (in red) by familiar faces vs. non-face controls in a patient in the persistent vegetative state at the time of imaging: signs of awareness emerged 2 months later. Reprinted with permission from Elsevier Science (Lancet, 352, 200).