

The vegetative state: guidance on diagnosis and management

A report of a working party of the Royal College of Physicians

Clin Med
2003;3:249–54

1 INTRODUCTION

Background

1.1 This guidance has been compiled to replace the recommendations published by the Royal College of Physicians in 1996,¹ in response to requests for clarification from the Official Solicitor. The guidance applies primarily to adult patients and older children in whom it is possible to apply the criteria for diagnosis discussed below.

Wakefulness without awareness

1.2 Consciousness is an ambiguous term, encompassing both wakefulness and awareness. This distinction is crucial to the concept of the vegetative state, in which wakefulness recovers after brain injury without recovery of awareness.^{2–5}

Definitions

The vegetative state

1.3 A patient in the vegetative state (VS) appears at times to be wakeful, with cycles of eye closure and eye opening resembling those of sleep and waking. However, close observation reveals no sign of awareness or of a ‘functioning mind’: specifically, there is no evidence that the patient can perceive the environment or his/her own body, communicate with others, or form intentions. As a rule, the patient can breathe spontaneously and has a stable circulation. The state may be a transient stage in the recovery from coma or it may persist until death. The vegetative state can follow a variety of severe insults to the brain, most commonly traumatic or hypoxic-ischaemic brain injuries.

1.4 The terms ‘wakefulness’ and ‘awareness’ require further clarification.

Wakefulness

1.5 Wakefulness refers to a state in which the eyes are open and there is a degree of motor arousal; it

contrasts with sleep, a state of eye closure and motor quiescence. There are degrees of wakefulness. Wakefulness is normally associated with conscious awareness, but the VS indicates that wakefulness and awareness can be dissociated. This can occur because the brain systems controlling wakefulness, in the upper brainstem and thalamus, are largely distinct from those which mediate awareness.⁶

Awareness

1.6 Awareness refers to the ability to have, and the having of, experience of any kind. We are typically aware of our surroundings and of bodily sensations, but the contents of awareness can also include our memories, thoughts, emotions and intentions. Although understanding of the brain mechanisms of awareness is incomplete, structures in the cerebral hemispheres clearly play a key role. Awareness is not a single indivisible capacity: brain damage can selectively impair some aspects of awareness, leaving others intact. Many brain processes, including some in the cerebral cortex, occur in the absence of awareness.

1.7 There is no simple single clinical sign or laboratory test of awareness. Its presence must be deduced from a range of behaviours which indicate that an individual can perceive self and surroundings, form intentions and communicate. As our techniques of assessment are fallible, we can never exclude the possibility of some awareness with complete certainty: this leaves open the possibility that some extremely simple forms of awareness may survive in the VS, including the experience of pain, although the available evidence suggests that this is not the case.^{5,7,8}

The persistent vegetative state

1.8 This refers arbitrarily to a VS which has continued for four weeks or more. (In the previous version of these recommendations this was referred to as the ‘continuing vegetative state’ to distinguish it more clearly from the permanent vegetative state: we have reverted here to the more widely used term but have avoided the ambiguous abbreviation ‘PVS’.)

The permanent vegetative state

1.9 When the VS is deemed permanent, a prediction is being made: that awareness will never recover. This prediction cannot be made with absolute certainty. However, as discussed below in para 2.8, the chances of regaining awareness diminish considerably as the time spent in the VS increases.

2 CRITERIA FOR DIAGNOSIS OF THE VEGETATIVE STATE

Preconditions

2.1 The following preconditions must apply before diagnosis of the VS can be considered.

- 1 The cause of the condition should be established as far as is possible. It may be due to acute cerebral injury, degenerative conditions, metabolic disorders, infections or developmental malformations.
- 2 The possibility that the persisting effects of sedative, anaesthetic or neuromuscular blocking drugs are responsible in whole or part should be considered. Drugs may have been the original cause of an acute cerebral injury, usually hypoxic, but their continuing direct effects must be excluded either by the passage of time or by appropriate laboratory tests.
- 3 The possibility that continuing metabolic disturbance is responsible for the clinical features must be considered and excluded. Metabolic disturbances may of course occur during the course of a VS.
- 4 The possibility that there is a treatable structural cause should be excluded by brain imaging.

Clinical criteria

2.2 The following criteria are usually met.

- 1 The key requirement for diagnosis is that there must be no evidence of awareness of self or environment at any time; no response to visual, auditory, tactile or noxious stimuli of a kind suggesting volition or conscious purpose; no evidence of language comprehension or meaningful expression. These are all necessary conditions for the diagnosis.
- 2 There are typically cycles of eye closure and eye opening giving the appearance of a sleep-wake cycle.
- 3 Hypothalamic and brainstem function are usually sufficiently preserved to ensure the maintenance of respiration and circulation.

2.3 Criteria 2 and 3 are usually satisfied by patients in the vegetative state but, unlike the first criterion, they are not obligatory (thus, for example, a patient with cerebral injuries sufficient to cause the vegetative state might, incidentally, have third nerve

palsies preventing eye opening, or injuries to the chest or medulla affecting respiratory function).

Clinical features

2.4 It may be helpful to fill out the clinical picture by describing compatible clinical features which occur commonly, features which are compatible with the diagnosis but atypical, and features which are incompatible with the diagnosis.

- 1 *Compatible features* As well as showing signs of a cycle of sleep and wakefulness, patients in the vegetative state may make a range of spontaneous movements including chewing, teeth grinding, swallowing, roving eye movements and purposeless limb movements; they may make facial movements such as smiles or grimaces, shed tears, or make grunting or groaning sounds for no discernible reason (it would be unusual for a patient to display the entire range of movements). They may react to a number of stimuli: brainstem reflexes (pupillary, oculocephalic (doll's eye), corneal, oculovestibular (caloric) and gag) can be present; various stimuli, usually noxious or noisy, can both excite a generalised arousal response, with quickening of respiration, grimaces or limb movements, and cause the extensor or flexor withdrawal of a limb; patients' eyes may turn fleetingly to follow a moving object or towards a loud sound. Grasp reflexes may be present.
- 2 *Compatible but atypical features* It is unusual for patients in a VS to follow a moving target for more than a fraction of a second, to fixate a target or to react to visual menace. However, all these behaviours have been described in patients whose clinical features are in all other respects typical of the VS.⁵ Patients have also been described in whom isolated fragments of behaviour, such as the utterance of a single inappropriate word, occur in what otherwise appears to be a VS.^{5,9} These features appear to reflect the survival of 'islands' of cortex which are no longer part of the coherent thalamo-cortical system required to generate awareness.⁶ Epileptic seizures occur occasionally.⁵ Features of these kinds should prompt careful reassessment of the diagnosis, but they do not in themselves negate the diagnosis of the VS.
- 3 *Incompatible features* Evidence of discriminative perception, purposeful actions and communicative acts is incompatible with the diagnosis of the VS. Thus a smile in response to the arrival of a friend or relative, an attempt to reach out for an object or the appropriate use of language would all indicate the presence of a 'functioning mind' and the recovery of awareness, although such recovery is sometimes very limited.

Differential diagnosis (Tables 1 and 2)

2.5 The VS must be distinguished from minimally conscious (or 'low awareness') states, states of life-long severe disability

with preserved awareness, the locked-in syndrome, coma, and death confirmed by brainstem death testing.

- *Minimally conscious state (MCS)* The terms ‘minimally conscious’, ‘minimally responsive’ or ‘low awareness’ state refer to the condition of patients who show minimal but definite evidence of awareness despite profound cognitive impairment.¹⁰ Patients emerging from the VS often enter the MCS, which may be the end point of their improvement, or a staging post on the way to further recovery.
- *People with life-long severe disabilities* Some people with severe intellectual disabilities, commonly accompanied by severe physical disabilities, have limited capacity to respond to the outside world; but those close to them are clear that they do communicate and are aware, and may indeed have a rich internal life. Such people should not be classed as vegetative.
- *Locked-in syndrome* Locked-in syndrome results from

brainstem pathology which disrupts the voluntary control of movement without abolishing either wakefulness or awareness. Patients who are ‘locked in’ are substantially paralysed but conscious, and can communicate using movements of the eyes or eyelids.

- *Coma* Coma is a state of unconsciousness in which the eyes are closed and sleep–wake cycles absent. Coma is usually transient, lasting for hours or days; the VS is one possible outcome.
- *Death confirmed by brainstem death testing* This implies the irreversible loss of all brainstem functions: it is followed by cardiac arrest, usually within hours or days, despite intensive care.

2.6 The above distinctions are made primarily on clinical grounds. Brain imaging with computed tomography (CT) or magnetic resonance imaging (MRI) often helps to clarify the cause of these clinical syndromes, but the findings on imaging are not specific. Cerebral atrophy is commonly seen in patients in the VS.

2.7 Sophisticated techniques used to assess cortical function – positron emission tomography (PET), electroencephalography (EEG), magnetoencephalography (MEG) and evoked potential (EP) studies – can be used to shed light on the physiology of the VS, but are not yet routine diagnostic tools. Their use is not required for diagnosis of the VS, which remains essentially clinical.

Table 1. Glasgow Coma Scale (GCS).

E Eye opening	M Motor function	V Verbal
1 None	1 None	1 None
2 To pain	2 Extends to pain	2 Grunts
3 To sound	3 Abn flexion to pain	3 Inapprop words
4 Spontaneously	4 Normal flexion to pain	4 Confused
	5 Localises pain	5 Oriented
	6 Normal	

Table 2. The differential diagnosis of the vegetative state.

Condition	Vegetative state	Minimally conscious state	Locked-in syndrome	Coma	Death confirmed by brainstem tests
Awareness	Absent	Present	Present	Absent	Absent
Sleep–wake cycle	Present	Present	Present	Absent	Absent
Response to noxious stimuli	+/-	Present	Present (in eyes only)	+/-	Absent
Glasgow Coma Scale score	E4, M1–4, V1–2	E4, M1–5, V1–4	E4, M1, V1	E1–2, M1–4, V1–2	E1, M1–3, V1
Motor function	No purposeful movement	Some consistent or inconsistent verbal or purposeful motor behaviour	Volitional vertical eye movements or eyeblink preserved	No purposeful movement	None or only reflex spinal movement
Respiratory function	Typically preserved	Typically preserved	Typically preserved	Variable	Absent
EEG activity	Typically slow wave activity	Insufficient data	Typically normal	Typically slow wave activity	Typically absent
Cerebral metabolism (PET)	Severely reduced	Insufficient data	Mildly reduced	Moderately to severely reduced	Severely reduced or absent
Prognosis	Variable: if permanent, continued vegetative state or death	Variable	Depends on cause but full recovery unlikely	Recovery, vegetative state or death within weeks	Already dead

NB: as explained in the text, EEG and measures of cerebral metabolism are not *required* to make these clinical diagnoses. EEG = electroencephalography; PET = positron emission tomography.

The time course

2.8 The prognosis of patients in the persistent VS is influenced by age, the underlying cause of the VS and its current duration. People in a VS one month after trauma stand a slightly better than even chance of regaining awareness; in cases of the VS due to non-traumatic causes, fewer than one-fifth of people in a VS at one month recover awareness. The chances of regaining awareness fall as time passes. Beyond one year following trauma, and beyond six months in non-traumatic cases, the chances of regaining consciousness are extremely low. In the very small number of well documented cases, recovery has usually been to a state of exceptionally severe disability.³ Patients in the persistent VS should therefore be observed for 12 months after head injury (traumatic brain injury) and six months after other causes before the VS is judged to be 'permanent'.

3 MANAGEMENT OF THE VEGETATIVE STATE

Medical care

3.1 Patients in the VS require a high quality of nursing care to avoid the preventable complications of their highly dependent state. Standard measures include adequate nutrition, often via a percutaneous endoscopic gastrostomy (PEG) tube, good skin care, passive joint exercises to minimise contractures, suction where necessary to help avoid aspiration, careful management of the doubly incontinent bladder and bowel, and attention to oral and dental hygiene. Until there is firm scientific evidence that treatment, in terms of specific medical, physiotherapeutic or rehabilitative activities, improves the outcome of patients in a VS, the use of these measures is a matter of clinical judgement. The medical and nursing staff must keep the relatives and carers well informed throughout the course of the VS.

Assessment

3.2 Both the initial diagnosis of the VS and the subsequent diagnosis of the permanent VS should be made with great care. There is evidence that the VS has been diagnosed in error.^{11,12} The explanations for misdiagnosis include confusion about the meaning of the term, inadequate observation in suboptimal circumstances, 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.

3.3 Thus, when the diagnosis of the permanent VS is being considered, it is essential that the patient should be examined by at least two doctors who are both experienced in assessing disorders of consciousness. They should take into account the views of the medical staff, other clinical staff (including clinical neuropsychologists, occupational therapists and physiotherapists with expertise in assessing disorders of consciousness),

carers and relatives about the patient's reactions and responses. They should undertake their clinical assessments separately and write the details of their assessments and their conclusions in the notes. They should consider the results of the investigations which have been performed to clarify the cause of the condition. As the patient's physical position can affect responsiveness, it may be valuable to assess the patient in more than one position. It may be helpful for nursing staff and relatives to be present during the examination.

Re-assessment

3.4 There is no urgency in making the diagnosis of the permanent VS. If there is any uncertainty in the mind of the assessor, the diagnosis should not be made and the patient should be reassessed after an interval. Structured observation may help to reveal signs of awareness in doubtful cases.¹³⁻¹⁵ The key consideration in making the diagnosis is whether the patient might be aware to some degree: it is always important to seek the views of nursing staff, relatives and carers on this issue.

Final definitive diagnosis and decisions concerning life support

3.5 When the diagnosis of a permanent VS has been made by establishing the cause of the syndrome so far as possible, by confirming the patient's clinical state and by the passage of time, recovery cannot reasonably be expected, and further therapy is futile. It merely prolongs an insentient life for the patient, and a hopeless vigil entailing major emotional costs for relatives and carers.

3.6 In these circumstances, the clinical team, with the help of colleagues when required, should review the evidence formally. When the diagnosis of a permanent VS is considered definite, it should be discussed sensitively with relatives, who should then be given time to consider the implications, including the possibility of withdrawing artificial means of administering nutrition and hydration. At present, in England and Wales, the courts require that the decision to withdraw nutrition and hydration should be referred to them before any action is taken. In Scotland, although the court does not require that it be involved prior to any action being taken, as a result of the Lord Advocate's advice following the Law Hospital case,¹⁶ it would be prudent for a doctor to seek the authority of the Court of Session in order to guarantee that the Lord Advocate would not initiate a criminal prosecution.

3.7 A decision to withdraw other life-sustaining medication, such as insulin for diabetes, may also need to be referred because the legal position is uncertain. By contrast, decisions not to intervene with cardio-pulmonary resuscitation, antibiotics, dialysis or insulin can be taken clinically, in the best interests of the patient, after full discussion with those concerned.

3.8 Where a patient has made a valid and applicable advance

Box 1. Checklist for the diagnosis of the permanent vegetative state.

The diagnosis of the permanent vegetative state requires prolonged observation, experience in the assessment of disorders of consciousness, and discussion with relatives and with medical and paramedical staff. It cannot be made by following a simple protocol. However, we hope that this checklist will be of some practical help by highlighting the key steps on the way to the diagnosis.

- 1 In cases due to head injury, has at least one year elapsed since the onset?
or,
- 2 In cases due to other causes, have at least six months elapsed since the onset?
- 3 Has the cause been established? (It should be established 'as far as possible'.)
- 4 Have effects of drugs been excluded?
- 5 Have effects of metabolic disturbance been excluded?
- 6 Has the possibility of a treatable structural cause been excluded by brain imaging?
- 7 Have two doctors, who are experienced in the assessment of disorders of consciousness, independently confirmed that there is no evidence of:
 - awareness of self or environment
 - purposeful movement
 - any attempt to communicate?
- 8 Do medical staff, nursing staff and other therapists agree?
- 9 Do family and friends agree?*
- 10 In case of doubt, has an expert clinical neuropsychological assessment been carried out?

Where the answer is 'yes' to all these questions, the diagnosis of the permanent vegetative state is confirmed.

First assessing doctor: Name Qualifications Signature Date	Second assessing doctor: Name Qualifications Signature Date
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*Sometimes, even when all other members of the family and friends of the patient are in agreement, one individual may be unable to agree with the general conclusion that the patient lacks awareness. Any evidence of awareness should be examined very seriously, but in these circumstances the continuing disagreement of one individual with the conclusion of health professionals and others close to the patient is not a bar to the diagnosis of the permanent vegetative state.

directive indicating their refusal of continuing treatment, this must be respected. If not, efforts should be made to establish what the patient's views and preferences might have been, to help to make a decision in his or her best interests.

3.9 As indicated earlier, one cannot ever be certain that a patient in the VS is wholly unaware, although the available evidence supports this supposition. In view of this small but undeniable element of uncertainty, it is reasonable to administer sedation when hydration and nutrition are withdrawn to eliminate the possibility of suffering, however remote. The normal standards of palliative care should be observed to ensure the dignity of the death.

A note on children and young persons (0–18 years)

3.10 Formal diagnosis of the permanent vegetative state in children in the UK is rare. However, there is evidence to suggest that older children (older than circa 10 years) behave clinically and prognostically in a similar fashion to adults. For younger children, in whom survival may be poorer than in older children, greater account must be taken of the child's potentially evolving developmental capabilities. For reasons of this kind, the diagnosis can seldom be made unequivocally under the age

of one year. However, there seems no reason why the guidance contained in this document should not be applied to children over the age of ten years, and it can be used with appropriate caution in children between one and ten years.

3.11 Where withdrawal or withholding of life-sustaining treatment is being contemplated in children, clinicians should refer to guidance from professional regulatory bodies.^{17–19}

This guidance has been endorsed by the Royal College of Physicians of Edinburgh and the Royal College of Physicians and Surgeons of Glasgow. Readers will find the editorial by McLean in 2001 provides a helpful summary of the current medico-legal position, including differences between Scotland and England/Wales.²⁰ In Scotland, local advice should be sought from the Central Legal Office of the NHS in the Scottish Executive.

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