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Pediatric vegetative state: Epidemiological and clinical issues

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1. Introduction

The vegetative state (VS), a state of wakefulness without awareness, has been well recognized in children despite the fact that little descriptive information has been published [3,14,21,38]. This review will focus on our current understanding of VS from a pediatric and medical perspective. Information concerning etiology, epidemiology, clinical course, and most importantly, potential for recovery of consciousness and function as well as long-term survival of these patients will be discussed. Much of the information contained in this review is based on the deliberations of the Multi-Society Task Force on the Persistent Vegetative State [38].

2. Clinical aspects

The Multi-Society Task Force on PVS established both a definition and criteria for the diagnosis of VS [38]. These were based in large part on the original description of VS by Jennett and Plum in 1972 [21], on material from other organizations that published position statements on VS, and by the deliberations of the Task Force.

2.1. Definition

The *vegetative state can be described as a condition of complete unawareness of the self and the environment accompanied by sleep-wake cycles with either complete or partial preservation of hypothalamic and brain stem autonomic functions* [38].

Most authorities now recommend not using the term *persistent*. Originally the term was used to describe the previous condition of the patient. It has also been used to imply the irreversible nature of VS. Rather it is recommended that the term *permanent* be used to imply an irreversible state. Thus, a VS patient would become permanently vegetative when the diagnosis of irreversibility is established to a high degree of clinical certainty, ie, when the chance of regaining consciousness becomes extremely unlikely. Based on data collected by the Task Force, probabilities for recovery from VS for children who have suffered traumatic and non-traumatic brain injuries can now be estimated and are reviewed in the section on potential for recovery. This information can be used by physicians and families or surrogates so that a clear understanding of the prognosis is understood. Such information is helpful in ultimately defining and determining the level of care that such children should receive.

2.2. Criteria

The Task Force established the following criteria for adults and children to diagnose the VS [38]. Patients in VS show all of the following characteristics:

- No evidence of awareness of themselves or their environment; they are incapable of interacting with others.
- No evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli.

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– No evidence of language comprehension or expression.
– Intermittent wakefulness manifested by the presence of sleep-wake cycles.
– Sufficiently preserved hypothalamic and brain stem autonomic functions to survive if given medical and nursing care.
– Bowel and bladder incontinence.
– Variably preserved cranial nerve (pupillary, oculocephalic, corneal, vestibulo-ocular, gag) and spinal reflexes.

2.3. Clinical features of patients in a vegetative state

Children in a VS lack any evidence of self-awareness or recognition of external stimuli. Rather than being in a state of "eyes-closed" coma they remain unconscious but have irregular periods of wakefulness alternating with periods of sleeping. Vegetative patients demonstrate a variety of sounds, emotional expressions, and body movements and they may smile or shed tears. They have inconsistent head and eye turning movements to sounds and inconsistent non-purposeful trunk and limb movements. Perhaps, of most importance and most easy to objectively examine, is the fact that they do not have evidence of sustained visual fixation nor do they demonstrate sustained visual tracking.

Hypothalamic and brain stem autonomic functions are preserved in the majority of children in VS. Many children maintain adequate respiratory function although they previously required ventilatory support or tracheostomy. In the majority of infants and children in VS, chewing and swallowing are impaired and in about 50% of children gastrostomies are required for nutritional support [5].

2.4. Related conditions

Table 1 lists several of the major neurological conditions that the clinician must be aware of and capable of differentiating from VS. This table was modified from the report issued by the Multi-Society Task Force on PVS [38] and a recent report by the Aspen Group on the Minimally Conscious State [17]. The three principal serious neurological conditions in which there may be overlap of clinical findings on examination that must be differentiated from VS include:

1. **Coma** is a state of deep, unarousable, sustained pathologic unconsciousness with the eyes closed which results from dysfunction of the ascending reticular activating system either in the brain stem or both cerebral hemispheres [28]. Coma usually requires the period of unconsciousness to persist for at least one hour to distinguish coma from syncope, concussion, or other states of transient unconsciousness. The term unconsciousness implies global or total unawareness and applies equally to patients in either coma or a VS. Patients in coma are unconscious because they lack both wakefulness and awareness. In contrast, patients in a VS are unconscious because, although they have retained wakefulness, they lack awareness.
2. **Brain death** describes the permanent absence of all brain functions, including those of the brain stem [4]. Brain dead patients are irreversibly comatose, apneic, and have absent brain stem reflexes including the loss of all cranial nerve functions. The appearance of brain death can be imitated by deep anesthesia, sedative overdose, or severe hypothermia. Patients who are brain dead differ from patients who are in a VS as these latter patients have preserved sleep/wake cycles, brain stem functions and some degree of respiratory drive. Guidelines for the diagnosis of brain death infants and children are now well established and brain death can be diagnosed in the newborn infant as well [4].
3. **Minimally Conscious State** The minimally conscious state is a condition of severely altered consciousness in which minimal but definite behavioral evidence of self or environmental awareness is demonstrated [17]. To make the diagnosis of MCS, limited but clearly discernible evidence of self or environmental awareness must be demonstrated on a reproducible or sustained basis by one or more of the following behaviors: (1) following simple commands; (2) Gestural or verbal yes/no responses; (3) intelligible verbalization; and (4) purposeful behaviors [5,17].

3. Epidemiology

It is difficult to obtain accurate data regarding the prevalence of the number of children or adults in a VS. Previously published data have estimated that there are approximately 4,000 to 10,000 children in VS in the United States [38]. Based on previously published estimates from many countries and available world wide population data, it is possible to estimate the average number as well as the range of the number of children

Table 1
PVS and related conditions in children

Condition	Self-awareness	Experiences suffering	Sleep-wake cycles	Motor function	Respiratory function	EEG	Prognosis for neurologic recovery
PVS	Absent	No	Intact	No purposeful movement	Normal or mildly depressed	Polymorphic delta/theta	Depends on etiology: a) Acute traumatic/non-traumatic b) Degenerative/metabolic c) Developmental malformations
COMA	Absent	No	Absent	No purposeful movement	Variably depressed	Polymorphic delta/theta	Usually evolves to recovery, PVS, or death in 2 to 4 weeks
Brain death	Absent	No	Absent	None or only reflex spinal movements	Absent	electro-cerebral silence	None
Minimally conscious state	Present	Yes	Intact	Some purposeful movements	Normal or mildly depressed	Polymorphic delta/theta	Depends on etiology: a) Acute traumatic/non-traumatic b) Degenerative/metabolic c) Developmental malformations

This table is adapted from the report of the Multi-Society Task Force on PVS [38] and from the report on the Minimally Conscious State [17].

and adults in a VS (Table 2). For children less than 15 years of age, the estimated average number of children worldwide in a VS is approximately 93,000 (range 11,365 to 151,536); for the United States it is lower than previous estimates (average 3,000; range 367 to 4,897). As the neurological insults occurring in children are different from adults, the risk for developing VS also differs. Based on the available literature for the common severe insults causing acute brain injury in children, an approximate risk for the development of VS can be estimated (Table 3). A study of 847 children in VS includes some epidemiological data concerning the incidence of VS in children as a function of age, sex and etiology (Table 4) [7]. Overall, the incidence of VS spans all age groups. Acute traumatic and non-traumatic injuries to the nervous system accounts for approximately 30% of cases. Perinatal insults (17.7%), chromosomal disorders or congenital malformations (13.0%) and infections (10.3%) occur less frequently. As clinical experience suggests, in a number of patients (28%), no specific cause can be determined.

4. Etiology and clinical course

The etiology of the VS in children can be classified into three broad groups of disorders including (1) acute traumatic and non-traumatic brain injuries; (2) metabolic and degenerative disorders affecting the nervous system; and (3) developmental malformations (Table 5). The clinical course resulting in VS depends on the particular underlying disease process. Establishing the etiology of the VS is important, as it will enable the clinician to assess the likelihood of it becoming persistent as well as estimate the chance for clinical recovery or survival.

4.1. Acute traumatic and non-traumatic injuries

The most common causes of acute brain injury leading to the VS in children are head trauma and hypoxic-ischemic encephalopathies. Severe traumatic brain injury in children is usually due to non-accidental trauma but also occurs after motor vehicle accidents particularly when infant restraints have not been used, when a child riding a bicycle is struck by a car or when the victim is a pedestrian. Hypoxic-ischemic injuries following cardiorespiratory arrest occur at birth, after episodes of near miss sudden infant death syndrome, near-drowning, and other unexplained acute life threatening episodes.

The clinical course after an acute injury is similar to that described in adults [18]. It usually begins with eyes-closed coma for several days to weeks followed by the appearance of sleep/wake cycles. In a clinical study of the evolution of the VS in children, Gillies and Seshia retrospectively determined that the average transition from eyes-closed coma to the VS was 8.6 ± 1.7 days in 17 children ages 1 month to 6 years [18]. Other responses such as decorticate and decerebrate posturing (1.7 ± 0.3 days), roving eye movements (1.8 ± 0.7 days), and eye blinking (3.3 ± 1.1 days) appeared earlier than sleep-wake cycles.

4.2. Metabolic and degenerative disorders

The progression of many metabolic and degenerative nervous system disorders in children may result

Table 2
Worldwide prevalence of patients in a vegetative state

Region	Total population	Average # of VS patients	Low estimate of # of VS patients	High estimate of # of VS patients
Children (<15 years)				
World	1,894,200,000	92,816	11,365	151,536
United States	61,215,000	3,000	367	4,897
North America	67,830,000	3,324	407	5,426
Latin America	172,800,000	8,467	1,037	13,824
Europe	123,590,000	6,056	742	9,887
Asia	1,149,000,000	56,301	6,894	91,920
Africa	361,620,000	17,719	2,170	28,930
Adults (>15 years)				
World	4,419,800,000	216,570	26,519	353,584
United States	230,285,000	11,284	1,382	18,423
North America	255,170,000	12,503	1,531	20,414
Latin America	367,200,000	17,993	2,203	29,376
Europe	603,410,000	29,567	3,620	48,273
Asia	2,681,000,000	131,369	16,086	214,480
Africa	499,380,000	24,470	2,996	39,950
Total				
World	6,314,000,000	309,386	37,884	505,120
United States	291,500,000	14,284	1,749	23,320
North America	323,000,000	15,827	1,938	25,840
Latin America	540,000,000	26,460	3,240	43,200
Europe	727,000,000	35,623	4,362	58,160
Asia	3,830,000,000	187,670	22,980	306,400
Africa	861,000,000	42,189	5,166	68,880

Population data obtained from http://www.prb.org/datafind/datafinder.htm Children defined as age <15 years and adults as age >15 years. Prevalence rates are based on previously published data as summarized in Ashwal, 1994. Overall the average prevalence of VS patients was 49 per million with the low estimate being 6 per million and the high estimate being 80 per million.

Table 3
Risk of PVS from acute severe brain injury in children

Disease	Risk of developing PVS
Severe traumatic brain injury	5–10%
Cardiorespiratory arrest	
In hospital	15%
Out of hospital	60–70%
Near drowning	20–45%
Central nervous system infections	5–10%
Hemorrhagic shock encephalopathy	80%
Strangulation	50%
Sudden infant death syndrome	40%

Estimates in this table are for children who suffer very severe acute traumatic or non-traumatic brain injury and are based on available pediatric literature [3].

in an irreversible VS. In contrast to patients who become vegetative within several weeks after an acute injury, patients with metabolic or degenerative diseases slowly evolve to a VS over several months or years. In children, metabolic diseases involving sphingolipid metabolism, adrenoleukodystrophy, the neuronal ceroid lipofuscinoses, organic acidurias, or the mitochondrial encephalopathies can result in VS. Frequently the neurological condition of such patients plateau and they remain in VS for prolonged periods rather than continuing to deteriorate. Once the VS is discernable for one to two months in such patients, recovery is not expected.

4.3. Developmental malformations

The term *developmental vegetative state* can be applied to those infants and children who are in a VS due to severe congenital central nervous system malformations such as anencephaly or hydranencephaly (Table 6). The diagnosis of the VS in infants and children poses several unique problems because of the immaturity of the developing brain and the potential influences of developmental plasticity on the acquisition of some degree of cognition.

In the newborn period, the only congenital malformation in which the diagnosis of the VS can be made with certainty is anencephaly. Infants with anencephaly have the complete absence of the cerebral cortex and thus are unable to develop conscious awareness [37].

Table 4
Epidemiological factors reported in 847 children in PVS

	# of pts in PVS	
	Number of patients	Percent of total
Age (yrs)		
<1	193	22.7
1< 2	112	13.2
2–6	191	22.6
7–18	201	23.7
19+	150	17.7
Sex		
Male	447	52.8
Female	400	47.2
Etiology		
Trauma	124	14.6
Non-traumatic	138	16.3
Infection	87	10.3
Perinatal	150	17.7
Chromosomal/developmental	110	13.0
Miscellaneous	238	28.1

Adapted from Ashwal et al. [7].

Newborn infants with other malformations such as hydranencephaly have minimal cerebral cortical tissue and usually remain in a VS. However, because the brain is developing, some of these infants may show limited awareness of the environment and demonstrate minimal purposeful activity within the first several months of life [33]. Substantial neurological improvement beyond a profound and severe disability in such children is extremely unlikely. Other infants with less extensive malformations (such as certain forms of holoprosencephaly or lissencephaly) may appear vegetative as infants but ultimately develop evidence of awareness and responsiveness. These infants generally continue to have very severe disabilities.

The concept of the VS does not apply to preterm infants because of developmental immaturity and to a lesser extent, the lack of consistently recognizable sleep-wake cycles which may be present in the preterm infant but are better developed at term and are clearly present by three months of age [3]. Newborns and young infants have a limited degree of social awareness and a variety of responses that may be tenuous, inconsistent, and unsustained. Thus it is very difficult to assess by examination the presence of sustained and reproducible abnormalities on examination. By three months, these responses are more sustained and consistently elicitable.

Table 5
Etiologies of PVS in children

Acute traumatic and non-traumatic injuries
Traumatic
1. Non-accidental injury (ie child abuse)
2. Motor vehicle accidents
3. Birth injury
4. Gunshot wounds and other forms of direct cerebral injury

Non-traumatic
1. Hypoxic-ischemic encephalopathy
   a. Cardiorespiratory arrest (e.g. Sudden Infant Death Syndrome)
   b. Perinatal asphyxia
   c. Near drowning
   d. Suffocation/strangulation
2. Cerebrovascular
   a. Cerebral hemorrhage
   b. Cerebral infarction
3. CNS infection
   a. Bacterial meningitis
   b. Viral meningoencephalitis
   3. Brain abscess
5. CNS tumors

Degenerative and metabolic disorders
1. Ganglioside storage diseases
2. Adrenoleukodystrophy
3. Neuronal ceroid lipofuscinoses
4. Organic acidurias
5. Mitochondrial encephalopathies
6. Gray matter degenerative disorders

Developmental malformations
1. Anencephaly
2. Hydranencephaly
3. Lissencephaly
4. Holoprosencephaly
5. Encephaloceles
6. Schizencephaly
7. Congenital hydrocephalus
8. Severe microcephaly

Adopted from the Multi-Society Task Force on PVS [38].

5. Neurodiagnostic studies in children with VS

5.1. Electroencephalography

Electroencephalograms (EEGs) of children in a VS show variable and non-specific abnormalities [3]. Likewise, specific EEG abnormalities that are predictive of the evolution from coma to the vegetative state have not been reported in children. In most children in a vegetative state, EEGs show diffuse generalized polymorphic delta or theta activity and little difference can be observed during sleep compared to wakefulness. The EEG also appears more discontinuous and of lower voltage compared to that seen in adult patients with VS.

Once children remain in VS, the EEG abnormalities persist. In those patients who begin to show recovery of consciousness from the vegetative state, one

Table 6
Incidence of recovery of consciousness and function in children in PVS one month after traumatic and non-traumatic brain injury

	Outcome at 3, 6, and 12 months as a percentage of children diagnosed PVS 1 month after insult			Functional recovery of those patients who recovered consciousness by 12 months	
	3 mos (% pts)	6 mos (% pts)	12 mos (% pts)	Recovery	(% pts)
Traumatic ($n = 106$)					
Dead	4	9	9	Severe disability	35
VS	72	40	29	Moderate disability	16
Recovered consciousness	24	51	62	Good recovery	11
Total	100%	100%	100%		62%
Non-traumatic ($n = 45$)					
Dead	20	22	22	Severe disability	7
VS	69	67	65	Moderate disability	0
Recovered consciousness	11	13	13	Good recovery	6
Total	100%	100%	100%		13%

This table was adapted from the Multi-Society Task Force on PVS [38].

may observe decreased delta and theta activity and the reappearance of non-reactive alpha rhythms. However, this phenomenon is inconsistent and unreliable in predicting the potential for future recovery [3]. In rare instances the EEG in children in VS has been reported to be isoelectric. It is also unusual to see paroxysmal epileptiform EEG activity in the infant or child in a VS and the incidence of clinical seizure activity in these children is extremely low.

5.2. Somatosensory and brain stem evoked responses

Evoked response testing may be useful in trying to assess the risk for vegetative outcome in infants and children who present in post-traumatic or post-anoxic coma [3,11,16,30,32,39]. Of the modalities available, somatosensory evoked responses (SERs) are the most sensitive and reliable [3]. Bilateral absence of the SER, one week after the insult, is usually highly predictive of the failure to regain consciousness with the outcome being death or survival in a VS. Patients with absent SERs, however, may recover modest cognitive activity and are more likely to do so from traumatic than anoxic coma. In such patients return of the SER may precede or coincide with clinical improvement. In contrast, patients with normal SERs may become and remain vegetative. In contrast to SERs, the BAER is of very limited value. Numerous studies have shown preservation of the BAER when the SER is absent in children who remain vegetative or die [3]. Multimodal evoked response testing, in which combinations of somatosensory, brain stem, and visual evoked responses have been used, is also useful in predicting either a poor or vegetative neurological outcome although not with complete accuracy [3].

5.3. Neuroimaging studies

Neuroimaging studies (e.g., computed tomography or magnetic resonance imaging scans) of infants and children in a VS usually demonstrate diffuse or multifocal cerebral disease involving the gray and white matter, a phenomena which reflects our current understanding of the neuropathology of the disorder [1]. Early in life, imaging studies may detect the presence of major central nervous system malformations consistent with the diagnosis of VS for which there is little hope of recovery. In the majority of patients with traumatic and non-traumatic brain injury, serial imaging studies usually demonstrate progressive atrophy. This provides objective evidence that there is little chance for future improvement. In those patients who are vegetative yet who show no significant abnormalities on neuroimaging studies, one must be cautious about the future. These patients may have a better chance for recovering consciousness, as there is no obvious evidence of serious structural nervous system disease. Additional studies including evoked response testing and measurements of cerebral metabolic activity may be helpful to determine the potential for recovery. Some VS children with cerebral atrophy on neuroimaging studies will also show pontine atrophy, a finding associated with impaired brain stem function and presumably a poorer chance for survival [27].

5.4. Cerebral metabolism

Adult patients in a VS have a 50% to 60% decrease in the cerebral glucose metabolic rate as measured by positron emission tomography (PET) [24,26]. PET scanning has only been reported in one child in VS [23]. In this patient, the cerebral glucose metabolic rate was decreased substantially on repeated studies performed over a one-year period. Serial examinations of brain metabolic activity may potentially be of great value in providing objective criteria confirming the clinical diagnosis of VS, particularly in infants and children. However, this will require further evaluation because of the low rates of brain metabolic activity and blood flow in the young infant which increase with development and shift to regions of higher cortical function [13]. Thus, in young infants and children it may be difficult to determine whether depressed rates of cerebral glucose metabolism or blood flow are normal for age or whether they reflect a severely injured brain. In addition, many patients are treated with anticonvulsants or other medications which have the potential to decrease cerebral metabolic activity and it is unknown whether these pharmacologic effects are greater in children than adults after nervous system injury.

5.5. Magnetic resonance spectroscopy

Proton and phosphorous magnetic resonance spectroscopy (MRS) offer potential as objective instruments to detect severe brain injury in infants and children. Depletion of cerebral energy metabolites as demonstrated by phosphorous MRS correlates well with poor outcome due to neonatal asphyxia [10]. The presence of reduced amounts of N-acetyl aspartate and increased lactate correlate with severe neurologic injury in many forms of acute childhood injury that may result in the VS [20]. Data from adults on MRS in VS patients have been reported [29]. Our own experience of using proton MRS in children in a VS, has shown severe spectroscopic abnormalities but no consistent spectral signature that is diagnostic [8].

5.6. Intracranial pressure and cerebral blood flow

It is clear from previous studies that monitoring intracranial and cerebral perfusion pressure is useful in predicting death but not in determining whether a particular child will make a good recovery or remain vegetative or moderately or severely disabled [36]. Likewise, measurement of cerebral blood flow during the first several days after an insult is of limited predictive value although children who do evolve into a VS will have reduced flow compared to those who recover completely [9]. However, once a patient is in a VS, CBF is likely to be reduced. This has been demonstrated in adults using either PET or single photon emission computed tomography (SPECT) [12,31]. Such studies examining this phenomenon in children have not yet been done and it is unlikely that they will have sufficient validity or specificity to predict long-term outcome.

6. Prognosis for recovery

Recovery from VS can be considered in terms of *recovery of consciousness* and *recovery of function* [38]. Prognosis depends on the underlying nature of the brain disease causing the VS.

6.1. Acute traumatic and non-traumatic injuries in children

6.1.1. Traumatic injuries

Recovery of awareness from a post-traumatic VS appears to be somewhat better in children compared to adults. The Multi-Society Task Force on PVS has collected data (Table 6) on the potential for recovery from a VS after severe traumatic brain injury in adults and children [38]. Of 106 children vegetative one month after severe head injury, 24% regained awareness by three months. At one year, 29% remained in a VS, 9% had died, and 62% recovered consciousness. Late recoveries after 12 months were not reported although a recent study by Kriel and coinvestigators found that 2 of 40 children with traumatic brain injury began to recover after one year in VS [22]. One patient had limited language function and was described as "able to express wants and needs." The other child had no language but was socially responsive and smiled in response to a voice or face. It is not clear whether this patient actually regained consciousness. In this study, 8 of 9 patients in VS for less than three months recovered to a severe disability; the remaining patient was moderately disabled. In the 15 patients in VS for 3 to 6 months, 12 recovered to a severe disability and 3 to a moderate disability and in those 5 patients in VS for 6 to 12 months 3 were severely and 2 moderately disabled. No good recoveries were reported in this series of 40 children who were in posttraumatic VS for 3 months. This data can be compared to the Multi-Society Task Force report where it was observed that of the 62% of

Table 7
Probabilities for recovery of consciousness and function at 12 months in children in PVS after traumatic and non-traumatic brain injury

	Traumatic PVS ($n = 106$)	Non-traumatic PVS ($n = 45$)
1. Outcome probabilities at 12 months for patients who remain in PVS for 3 months		
Dead (%)	14	3
PVS ((%)	30	94
Severe (%)	24	3
Mod/good (%)	32	0
2. Outcome probabilities at 12 months for patients who remain in PVS for 6 months		
Dead (%)	14	0
PVS ((%)	54	97
Severe (%)	21	3
Mod/good (%)	11	0

Modified from the Multi-Society Task Force on PVS [38]. This table gives estimates of the probabilities for recovery of consciousness and recovery of function from PVS in children after traumatic and non-traumatic brain injury. Severe = recovery to a severe disability; Mod/Good, recovery to a moderate disability or to a good recovery.

children who did recover consciousness from a post-traumatic VS, recovery of function were as follows: good recovery (11%), recovery to a moderate disability (16%), and recovery to a severe disability (35%).

Only one other study has provided data on recovery after TBI in children who were in a VS one month after injury [19]. At 19 months post injury, 84% of children (total $n = 82$) had recovered consciousness and 16% of these children became independent in daily activities. Less than 5% of children recovered consciousness beyond 9 months after injury.

6.1.2. Non-traumatic injuries

Children in non-traumatic VS have a much poorer potential for recovery than from traumatic VS. Data collected by the Multi-Society Task Force on PVS showed that only 11% of children regained awareness by three months after injury [38]. At one year most children remained in a VS (65%) or died (22%); only 13% showed recovery and this was usually to a severe disability. Good or moderate functional recovery is extremely unlikely but may occur in children vegetative from a non-traumatic brain insult. In most of the patients who show recovery, awareness can usually be detected within two months of injury. Kriel and coinvestigator also reported in their recent studies that 3 of 13 children in post-anoxic VS for longer than 12 months (i.e. 370, 480, and 840 days) showed recovery of consciousness [22]. These patients recovered to a severe disability, only demonstrating a "social smile" and it is unclear whether this reflected recovery of consciousness or a patterned subcortical behavioral response.

Additional data on post-hypoxic VS ($n = 55$) found that only 55% recovered consciousness by 19 months and only 4% became independent [19]. Less than 5% recovered beyond 9 months after injury. Children in a VS due to hypoxia ischemia also had a higher incidence of seizures and complications such as pneumonia, gastrointestinal complications and heterotopic calcifications.

6.2. Degenerative and metabolic disorders

Children in a VS due to degenerative or metabolic diseases have no possibility of recovering because these diseases are progressive or reach a clinical plateau in their terminal stages. In some children who are not vegetative but severely disabled an intercurrent illness may cause patients to appear vegetative. As the illness improves the child may recover to his/her previous state of limited cognition.

6.3. Developmental malformations

Infants and children with congenital brain malformations severe enough to cause a developmental VS are unlikely to acquire awareness. Anencephaly is the only malformation in which the prognosis for no recovery can be made at birth [37]. Other malformations diagnosed at birth may result in a vegetative outcome and if confirmed by clinical examination at three to six months of age, the prognosis for any improvement is extraordinarily small. The majority of infants with such malformations who recover consciousness have extremely limited awareness and minimal functional capacities.

6.4. Probability for recovery

The Multi-Society Task Force on PVS has estimated the probability for recovery of consciousness and function from traumatic and non-traumatic VS in adults and children who were vegetative one month after an acute injury (Table 7) [38]. Outcome probabilities at 12 months were determined for patients who remained vegetative at 3 and 6 months. Functional recovery was determined for two possible outcomes: 1) good recovery or recovery to a moderate disability and 2) recovery to a severe disability. Based on these probabilities, the following statements can be made:

1. After 3 months, children in post-traumatic VS, have a 56% chance of recovering consciousness in contrast to only 3% in children in non-traumatic VS. Of those children who recover, the probability for recovering to a severe disability is 24% and of making a moderate or good recovery 32%.
2. After 6 months, children in post-traumatic VS, have a 31% chance of recovering consciousness in contrast to only 3% of children in non-traumatic VS. However, the chance of making a moderate or good recovery is now much less (i.e. 11%); recovery to a severe disability is more likely (21%).
3. VS could thus be judged to be permanent 12 months after traumatic brain injury and 3 months after non-traumatic injury in children. The chance for recovery after this time period seems to be exceedingly rare and almost always to a severe disability.

7. Survival

Both adults and children in VS have shortened life spans despite preservation of brain stem and autonomic functions. In adults, long-term studies have shown that about 82% of patients will die within three years and 95% within five years of onset of VS. About 10% of adults who are in a VS will survive five to ten years and only 4% beyond that time [38].

As noted in Table 6, 91% of children vegetative one month after traumatic brain injury were alive at one year; of those children in VS from non-traumatic injury, 78% survived. In infants and children in a VS, estimates of survival based on the clinical experience of child neurologists for different age groups recently has been published [6]. These estimates range from 4.1 ($\pm$ 0.7) years for infants to 7.4 ($\pm$ 1.8) years in children 7 to 18 years of age. A large population based study examining 847 children and adults considered to be in VS found approximately the same duration of survival for older children but a much shortened median life expectancy in children under age one year [7]. The life span of infants and children in a VS appeared to be an age dependent phenomena. For example, the median survival time of children less than one year of age was 2.6 ($\pm$ 0.3) years in contrast to children age 2 to 6 years where it was 5.2 ($\pm$ 0.4) years. There is also likely to be some relation between certain etiologies of the VS and survival times. For the data available it appears that children in a VS from non-traumatic injury (8.6 yrs) and chromosomal disorders (8.2 yrs) have a longer life expectancy than children in whom the VS is due to perinatal disorders (4.1 $\pm$ 0.6 yrs), traumatic brain injury (3.0 $\pm$ 0.3 yrs), or infection (2.6 $\pm$ 0.3 yrs). This does not appear to be due to any interdependency between age and etiology. The reasons for these limited differences remain unclear. One possible explanation is that the shortened life spans observed in the perinatal or infection groups may be due to a greater degree of permanent brain stem or hypothalamic injury which causes greater immobility, an increased risk for aspiration, and an overall poorer nutritional status which renders these patients more susceptible to infection or cardiorespiratory arrest.

Life span does not appear to be affected by the residential location of a child in VS. There were no differences reported in life span in those children living at home (4.5 $\pm$ 0.7 yrs) compared to those living in an institution (5.2 $\pm$ 0.7 yrs); life expectancy of children living in a skilled nursing facility or private hospital setting was somewhat shortened (3.2 $\pm$ 0.7 yrs). Although there is no definite reason to explain these limited differences in life expectancy, our experience suggests that the associated medical problems of VS patients are similar irrespective of facility. In cases where there are more serious acute or chronic medical problems, additional home nursing care is frequently provided to families or the incidence of hospital readmissions is increased; if patients are in institutions or skilled nursing facilities their care levels are upgraded to meet their specific needs.

Additional data have been reported concerning life expectancy of children in a permanent vegetative state [35] as well as comparing life-expectancy of children in a VS compared to a MCS [34]. Some data are also available regarding the costs of care of children in a VS in the United States [15].

There are no data concerning extraordinary long survival (ie, greater than 15 years) for children in VS.

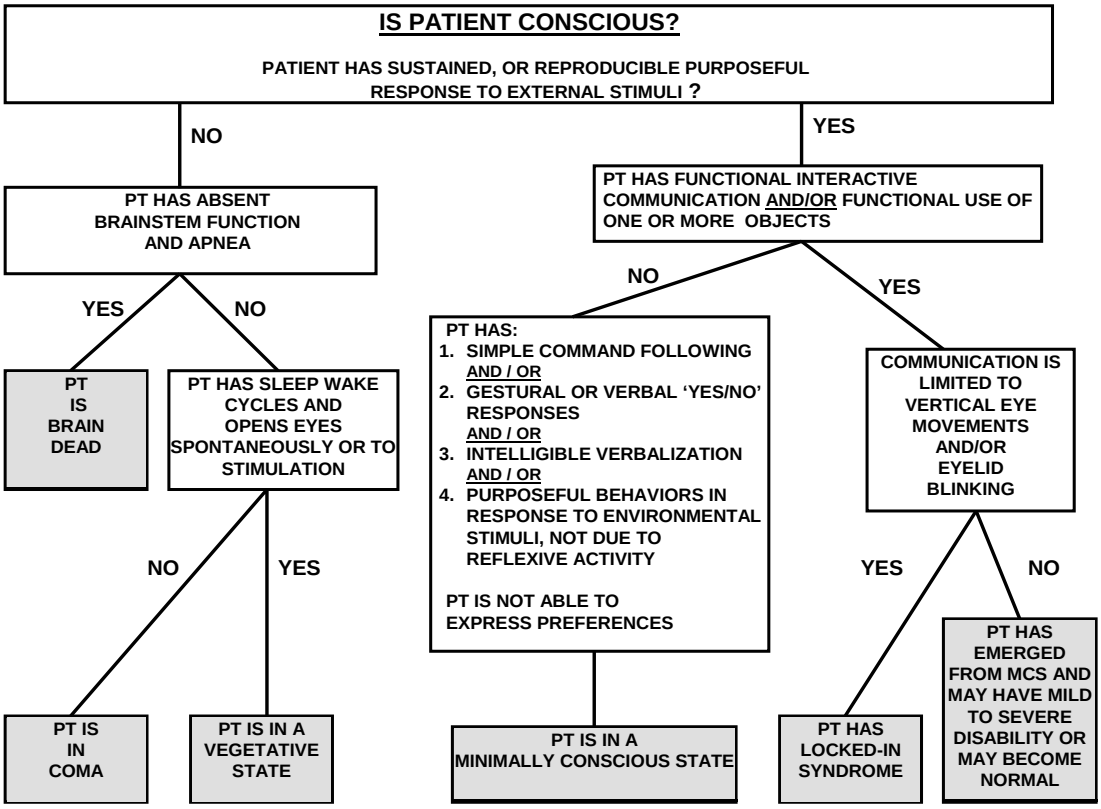

Fig. 1. An approach to evaluating the unconscious child. If the patient has no evidence of sustained or reproducible purposeful responses to external stimuli, then the patient is deemed unconscious. Further examination to determine if the patient is in coma, the VS, or brain death is required. The diagnosis of brain death can be confirmed based on well-established criteria. If the patient has sleep-wake cycles and appears "awake but unaware", the diagnosis of the VS can be made. If the patient does not have sleep wake cycles, the patient is considered to be in coma. If the patient has evidence of sustained or reproducible purposeful responses to external stimuli, then the patient would be considered to be conscious and one must differentiate between the MCS, the locked-in syndrome, some degree of disability, or normal.

Rare cases of prolonged survival for periods up to 10 to 20 years were reported in the survey of child neurologists [6]. The Multi-Society Task Force on PVS has estimated that the probability of an individual patient having such prolonged survival is less than 1 in 15,000 to 75,000 [38].

8. Medical treatment

Children in a VS require careful medical treatment and nursing care. Preventive care including daily range of motion exercises, skin care and frequent patient repositioning help to maintain the personal hygiene and dignity of the pediatric patient. Gastrostomies are necessary in about half the children to maintain adequate nutrition and hydration. Pulmonary care may reduce the need for antibiotic treatment for episodes of recurrent aspiration pneumonia. As urinary tract infections are common, intermittent catheterization or use of incontinent diapers can reduce this risk.

Physicians and families or surrogates must attempt to define the level of medical treatment in children in VS. These include: 1) high-technology treatments, such as assisted ventilation, dialysis, and cardiopulmonary resuscitation; 2) commonly ordered treatments, including medications and supplemental oxygen; 3) hydration and nutrition; and 4) nursing care. After the appropriate level of treatment is identified and agreed upon by those responsible for the care of a child in VS, physicians should write explicit orders indicating which treatments can be administered and which should be withheld. At all times, the child's hygiene and dignity should be maintained.

8.1. Withdrawal of artificial nutrition and hydration

Death due to the withdrawal of artificial nutrition and hydration in infants and children in a VS usually

occurs within 3 to 10 days [2]. The immediate cause of death is dehydration and electrolyte imbalance, rather than starvation. It is rare, however, for pediatricians or child neurologists to recommend discontinuation of fluids and nutrition in infants and children in a vegetative state [25]. A survey by the Child Neurology Society Ethics Committee found that 75% of members never recommend withholding of fluid and nutrition from such patients [6]. This attitude appears to be changing as organizations are more clearly defining in position papers the fact that it is ethically acceptable to withdraw fluids and nutrition in patients in VS [40].

9. Concluding statement

Much has been learned about VS in infants and children over the past decade. We now have a satisfactory definition and clinical criteria to diagnose this condition and we can differentiate VS into three broad categories of disease. Although epidemiological data concerning the incidence and prevalence of VS are limited, there is reasonably good information concerning the prognosis for recovery of consciousness and function and of life expectancy. There are essentially no well-controlled prospective studies of "coma-stimulation" protocols in children to assess whether any such treatments are of value. There is also an emerging consensus about the need to define the level of care for children in VS, to preserve their hygiene and dignity and also to consider limiting care and withholding/withdrawing treatment once it is clear that improvement will not occur. Additional clinical research is needed to resolve unanswered medical issues concerning the diagnosis and prognosis of VS in children. A paradigm on how to evaluate significantly impaired patient to determine if they are in a VS or other condition is presented in Fig. 1.

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