THE VEGETATIVE STATE IN INFANCY AND CHILDHOOD

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LIFE-SUSTAINING TREATMENTS AND VEGETATIVE STATE: Scientific advances and ethical dilemmas
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Introduction

The vegetative state (VS), a state of wakefulness without awareness, is considered by most clinicians to be a "fate worse than death" [1]. The disorder has been well recognized in children despite the fact that little descriptive information has been published [2-4]. This review will focus on our current understanding of VS from a pediatric and medical perspective and is based on the deliberations of the Multi-Society Task Force on the Persistent Vegetative State [3].

Clinical aspects

The Multi-Society Task Force on PVS established a definition and criteria for the diagnosis of VS [3] based on the original description of VS by Jennett and Plum in 1972 [2], material from other organizations and the deliberations of the Task Force.

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 [3].

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 from 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.

Criteria

The Task Force established the following criteria for adults and children to diagnose the VS [3]. Patients in a VS show all of the following characteristics:

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 brain stem 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, gag) and spinal reflexes.

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. They have inconsistent head and eye turning movements to sounds and inconsistent non-purposeful trunk and limb movements. They also do not have sustained visual fixation nor do they demonstrate sustained visual tracking.

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

Epidemiology and Etiology

It is estimated that there are approximately 4,000 to 10,000 children in VS in the United States [3]. Estimates in other countries for adults in VS have been published but no data are available for children. 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 1) [5].. 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. In a fair number of patients (28%), no specific cause can be determined.

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 2). The 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 and/or survival.

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 injury in children is usually due to non-accidental trauma but also occurs after motor vehicle accidents. Hypoxic-ischemic injuries following cardiorespiratory arrest occur at birth, after episodes of near miss sudden infant death syndrome, near-drowning, and other acute life threatening episodes. The clinical course after an acute injury is similar to that described in adults. It begins with eyes-closed coma for several days to weeks followed by the appearance of sleep/wake cycles

Metabolic and degenerative disorders

The progression of many metabolic and degenerative nervous system disorders in children may result in an irreversible VS. 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 condition of 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, recovery is not expected.

Developmental malformations

The term *developmental vegetative state* can be applied to those children who are in a VS due to severe malformations such as anencephaly or hydranencephaly (Table 2) . The diagnosis of the VS in infants and children poses several unique problems because of immaturity of the developing brain and the potential influences of plasticity on acquisition of cognition. In newborns, the only malformation in which the VS can be diagnosed with certainty is anencephaly. Infants with anencephaly have complete absence of the cerebral cortex and are unable to develop conscious awareness [23]. Infants with malformations such as hydranencephaly have minimal cortical tissue and may show limited awareness and minimal

purposeful activity [24]. Infants with less extensive malformations may appear vegetative but may develop awareness and responsiveness. These infants remain severely disabled.

Prognosis for recovery

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

Acute traumatic and non-traumatic injuries in children

Traumatic injuries

Recovery of awareness is better in children compared to adults. The Multi-Society Task Force has collected data (Table 3) on the potential for recovery from a VS after severe traumatic brain injury (TBI) [3]. Of 106 children vegetative one month after severe head injury, 24% regained awareness by three months. Of the 62% of children who did recover consciousness from a post-traumatic VS, recovery of function was: good recovery (11%), recovery to a moderate disability (16%), and recovery to a severe disability (35%).

Non-traumatic injuries

Children in non-traumatic VS have a much poorer potential for recovery than from traumatic VS. Data collected by Task Force showed that only 11% of children regained awareness by three months [3]. At one year most children remained in a VS (65%) or died (22%); only 13% recovered and this was to severe disability. Good or moderate functional recovery is extremely unlikely but may occur in children after a non-traumatic brain insult.

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 plateau. In some children who are not vegetative but severely disabled an intercurrent illness may cause them to appear vegetative. As the illness improves the child may recover to the previous state of limited cognition.

Developmental malformations

Infants and children with congenital brain malformations severe enough to cause a developmental VS are unlikely to acquire awareness. Some malformations diagnosed at birth may result in a vegetative outcome and if confirmed by examination at three to six months, the prognosis for any improvement is extraordinarily small. The majority of such infants who recover consciousness have extremely limited awareness and minimal functional capacities.

Survival of children in a VS

Both adults and children in VS have shortened lifespans despite preservation of brain stem and autonomic functions. As noted in Table 3, 91% of children vegetative one month after TBI 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 [5]. The lifespan of infants and children in a VS appeared to be an age dependent phenomena. For example, the median survival time of children under 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), TBI (3.0 $\pm$ 0.3 yrs), or infection (2.6 $\pm$ 0.3 yrs).

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.60 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.

Conclusions

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 also 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 also needed to resolve unanswered medical issues concerning the diagnosis and prognosis of VS in children.

Table 1. Epidemiological factors reported in 847 children in PVS

Age (yrs)	# 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, 1994 [5].

Table 2. 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. Lisssencephaly
4. Holoprosencephaly
5. Encephaloceles
6. Schizencephaly
7. Congenital hydrocephalus
8. Severe microcephaly

Adapted from the Multi-Society Task Force Report on PVS [3].

Table 3. 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	**6 mos**	**12 mos**	**Recovery**	**(% pts)**
	(% pts)	(% pts)	(% 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 [3].

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