CHAPTER 98

BRAIN DEATH IN CHILDREN

STEPHEN ASHWAL, MD

In 1987, guidelines for the determination of brain death in children in the United States were proposed by a task force that represented several major professional medical and legal societies (Table 98-1). These guidelines emphasized the importance of history and clinical examination in determining the etiology of coma so that remedial or reversible conditions were eliminated. In addition, age-related observation periods and the need for specific neurodiagnostic tests were recommended for children younger than 1 year of age. In children older than 1 year, it was recommended that the diagnosis of brain death could be made solely on a clinical basis and that laboratory studies were optional.

Since their publication in 1987, these criteria generally have been accepted. In addition, they have served as explicit guidelines for physicians asked to diagnose brain death in pediatric patients who may be potential organ donors. At the time these guidelines were developed, criteria for term infants younger than 7 days old and preterm infants were excluded because of lack of sufficient data. More recent studies have found that the criteria used in infants under the age of 2 months can also be applied to preterm and term infants.

**Epidemiology**

In the past decade, studies from pediatric intensive care units have reported that the incidence of brain death in older infants and children ranges from 0.65 to 1.2% of admissions. In one study, brain death represented 31.4% of all deaths in children older than 1 month of age and 6.3% of deaths in neonates. During the past several years, researchers at Loma Linda University Children’s Hospital reported that the percentages of brain deaths and overall deaths in their pediatric and neonatal units was 2.1 and 28% respectively.

Brain death most commonly occurs in children younger than 1 year of age and is uncommon in adolescents (Table 98-2). The most frequent cause of brain death in children

**TABLE 98-1. Guidelines for Brain Death Determination in Children**

| A. History: determine the cause of coma to eliminate or exclude reversible conditions
| B. Physical examination criteria
| 1. Coma and apnea
| 2. Absence of brainstem function
| a. Midposition or fully dilated pupils
| b. Absence of spontaneous oculocephalic (doll’s-eye) and caloric-induced eye movements
| c. Absence of movement of bulbar musculature, corneal, gag, cough, sucking, and rooting reflexes
| d. Absence of respiratory effort with standardized testing for apnea
| 3. Patient must not be hypothermic or hypotensive
| 4. Flaccid tone and absence of spontaneous or induced movements, excluding activity mediated at spinal cord level
| 5. Examination should remain consistent for brain death throughout the predetermined period of observation
| C. Observation period according to age
| 1. 7 days to 2 months: two examinations and EEGs 48 hours apart
| 2. 2 months to 1 year: two examinations and EEGs 24 hours apart or one examination and an initial EEG showing ECS combined with a radio-nuclide angiogram showing no CBF, or both
| 3. More than 1 year: two examinations 12 to 24 hours apart; EEG and isotope angiography are optional


CBF = cerebral blood flow; ECS = electrocerebral silence; EEG = electroencephalography.
is traumatic brain injury (usually from child abuse) and, less often, motor vehicle accidents. Asphyxial injury is also common and occurs after near drowning, as a complication of shock, from strangulation or suffocation, or from sudden infant death syndrome (SIDS). Brain death secondary to meningitis may be seen in patients who develop massive cerebral edema with the onset of herniation within 12 to 24 hours of hospitalization. Miscellaneous causes of brain death involve rare metabolic diseases, perioperative central nervous system (CNS) insults, and acute obstructive hydrocephalus.

Declaration and confirmation of brain death in the majority of pediatric patients presenting in coma after a serious CNS injury are usually completed within the first 2 days of hospitalization. Most children are subsequently removed from life support systems or are referred for organ donation within a 2-day period once the diagnosis of brain death is confirmed. Rarely, pediatric patients who are brain dead have been maintained on ventilator support for prolonged periods, but these patients suffer cardiac arrest at an average of 17 days after brain death is suspected. Longer survival (eg, “chronic brain death”) has been reported. There are no reports of children making neurologic recovery if they met adult brain death criteria on examination.

**Clinical Examination**

By definition, all patients who are declared brain dead are comatose and apneic and lack brainstem reflexes. These criteria may not be present on admission in all children; they usually evolve during the first days of hospitalization. Serial examinations are frequently helpful; it is also important to make sure that reversible conditions associated with altered metabolic states, toxin exposure, fluid and electrolyte abnormalities, hypothermia, hypotension, or medication effects have been excluded. Hypothermia occurs in about 50% of children who are comatose after catastrophic brain injuries. Thus, there is a need to rewarm patients before completing the examination and obtaining neurodiagnostic tests.

**Coma**

Assessment of lack of consciousness may be difficult in infants and children. Although there is no absolute way to be certain that a neonate or young infant has lost all conscious awareness and is “unreceptive and unresponsive,” as stated in the original task force criteria, testing by tactile, visual, and auditory stimulation is comparable with that performed in the older child. When attempting to diagnose brain death, even in infants and young children, one is assessing the complete loss of all responsiveness rather than trying to detect subtle conscious behaviors. In most instances, and regardless of the child’s age, the bedside clinical examination can satisfactorily accomplish this goal. Documenting the absence of any form of repetitive, sustained purposeful activity is important, as is differentiating brain death from other states of unconsciousness, such as the vegetative state. If the neurologic examination remains unreliable or if there is uncertainty that the child is unresponsive, confirmatory neurodiagnostic studies, such as electroencephalography (EEG) and measurement of cerebral blood flow (CBF), are required.

**Loss of Brainstem Function**

In preterm and term neonates, one must take into account that several of the cranial nerve responses are not fully developed. For example, the pupillary light reflex is absent before 29 to 30 weeks’ gestation, and the oculocephalic reflex may not be elicitable prior to 32 weeks. Term and preterm infants are difficult to examine because their small size makes it technically difficult to adequately assess cranial nerve function. Assessment of pupillary reactivity can be compromised at the bedside because of difficulty accessing the infant who is in an incubator or because of corneal injury, retinal hemorrhages, and other anatomic factors, such as swelling or partial fusion of the eyelids. Because of the smaller amount of pigmentation and the smaller size of the newborn’s pupils, visualization of changes in the size of the pupil can make assessment of the loss of pupillary reactivity difficult.

Likewise, assessment of ocular motility can be very difficult in intubated infants, and frequently, the examiner

**TABLE 98-2. Age Ranges and Etiologies of Brain-Dead Infants and Children**

<table>
<thead>
<tr>
<th>Age (n = 219)</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 mo</td>
<td>12</td>
</tr>
<tr>
<td>4–12 mo</td>
<td>15</td>
</tr>
<tr>
<td>1–2 yr</td>
<td>17</td>
</tr>
<tr>
<td>2–5 yr</td>
<td>32</td>
</tr>
<tr>
<td>5–10 yr</td>
<td>8</td>
</tr>
<tr>
<td>10–18 yr</td>
<td>10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology (n = 590)</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head injury</td>
<td>30</td>
</tr>
<tr>
<td>Near drowning</td>
<td>9</td>
</tr>
<tr>
<td>CNS infection</td>
<td>16</td>
</tr>
<tr>
<td>Asphyxia</td>
<td>14</td>
</tr>
<tr>
<td>SIDS</td>
<td>5</td>
</tr>
<tr>
<td>Metabolic</td>
<td>5</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>5</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>16</td>
</tr>
</tbody>
</table>


CNS = central nervous system; SIDS = sudden infant death syndrome.
will need assistance, particularly when performing ice-water caloric stimulation. The procedure does not differ substantially when performing this test in newborns versus older children. It is more difficult to adequately assess the caloric response in neonates, as they have small external ear canals; therefore, it is always important to examine both the oculocephalic (doll’s-eye) and the oculovestibular (caloric) reflexes.

Although the corneal reflex is perhaps the easiest brainstem reflex to examine in neonates and infants, it is frequently the least reliable. Contact irritation, dehydration and maceration of the cornea, use of lubricant drops, wearing of eye patches for treatment of hyperbilirubinemia, and use of analgesics frequently affect the tactile surface sensory receptors of the cornea in a negative way. However, it remains important to test for this reflex as its presence indicates preserved brainstem function.

Assessment of lower cranial nerve function is also limited and is usually confined to examination of the gag reflex. There may be a substantial amount of adhesive tape around the face and cheek to secure the endotracheal tube, and this impedes the clinician’s ability to perform this part of the neurologic assessment. When infants are intubated (either by the oral or nasogastric route), testing their gag reflex usually can only be accomplished with stimulation of the endotracheal tube.

**Apnea**

The normal physiologic threshold for apnea (minimum carbon dioxide tension at which respiration begins) for children has been assumed to be the same as adults (pCO₂ > 60 torr). In most studies, there will be a gradual increase in pCO₂ over a 5- to 10-minute period, usually with maintenance of the arterial pO₂ at > 200 torr while supplying 100% tracheal oxygen. Recent reports concerning apnea testing in children have raised questions about (1) the effects of brainstem compressive lesions, (2) potential recovery of brainstem respiratory drive, and (3) the pCO₂ threshold in children. It is important to note that treatment of compressive brainstem lesions might reverse severe neurologic deficits that mimic brain death. Interestingly, a report exists describing the case of a 3-month-old infant who met the 1987 Task Force criteria for pediatric brain death and developed two to three irregular breaths per minute on day 43 of hospitalization. This infant died 71 days after presentation. At issue is whether this should be considered a return of respiratory function and, if so, whether return of irregular breathing is an “improvement” in the absence of other brainstem functions.

The third issue relates to a case report involving a 4-year-old child with a posterior fossa pilocytic astrocytoma who suffered a cardiac arrest. This patient met the clinical criteria for brain death, except for the results of apnea testing, which showed minimal respiratory effort after 9 minutes and 23 seconds, when his pCO₂ measured 91 torr. This child’s spontaneous breathing was insufficient to maintain life, and assisted ventilation was necessary. It was thought that this child’s higher pCO₂ threshold was due to hypoxic-ischemic injury. This case raised questions about whether this was a phenomenon unique to children and whether the current standard of a pCO₂ of 60 torr is correct.

The technique of apnea testing in children is similar to that in adults using apneic oxygenation after disconnecting from the ventilator. Therefore, normalization of the CO₂ tension and core temperature and preoxygenation for 5 to 10 minutes before beginning the apnea challenge are recommended. Careful monitoring of the heart rate and blood pressure during the procedure, while watching the chest cage for movement, is needed. Most studies recommend that pCO₂ levels be determined at 5-minute intervals and continued for 15 minutes if the pCO₂ has not reached 60 torr and if the pO₂ has not fallen below 50 torr. Prolonged bradycardia or development of hypotension during testing is due to irreversible brainstem failure, acidosis, or hypoxemia; at this juncture, the infant should be placed back on the ventilator.

### Neurodiagnostic Testing

**Electroencephalography**

Guidelines for brain death recordings were developed by the American Electroencephalographic Society in 1994. The role of EEG in confirming the diagnosis of brain death in infants, children, and neonates has been described extensively in the literature. Problems with obtaining an EEG in infants and children include shorter interelectrode distances; external artifacts caused by technologies in newborn and pediatric intensive care units; rapid cardiac and respiratory rates of infants and children compared with those seen in adults; shorter distances between the heart and the brain, making the electrocardiographic contribution disproportionately large in children; reduced amplitude of cortical potentials in preterm and term neonates; longer duration of the effect of depressant drugs; greater tendency for suppression burst patterns in infants with neurologic disorders; and the presence of congenital CNS malformations (eg, hydranencephaly) associated with ECS.
It is well recognized that a certain number of brain-dead infants, children, and adults will have persistent EEG activity. Most of these EEG patterns show low-voltage theta or beta activity or intermittent spindle activity. Its persistence in functionally dead brains may continue for days. Data from several studies have found that the initial EEG in brain-dead children is isoelectric in 51 to 100% of patients (mean 83%). In the majority of children who initially have EEG activity, follow-up studies usually show evolution to ECS.

Typically, when the initial EEG in children demonstrates ECS, a repeat EEG will remain isoelectric. However, there have been reported cases of recovery of EEG activity. In these reports, the findings were either inconclusive or the patients had retained some brainstem or cerebral function and, thus, did not meet the clinical criteria for brain death. Since Green and Lauber's report almost 30 years ago of two infants who had return of some EEG activity after an initial ECS recording, there have only been a few additional reports of infants in whom EEG activity returned. Thus, concerns about the return of EEG activity have been overemphasized. In addition, none of these infants recovered. It should be emphasized that ECS may occur soon after a child has had a cardiac arrest. In infants in whom the initial EEG, 8 to 10 hours after cardiac arrest, shows ECS, a repeat study 12 to 24 hours later may show diffuse low-voltage activity. Most of these infants die from associated complications of the acute catastrophic insult; those who survive usually go on to a permanent vegetative or minimally conscious state. Similar observations have been reported in adults.

Overall, the available data in children suggest that demonstration of ECS on the initial EEG is sufficient to support the clinical diagnosis of brain death. However, as previously noted in the 1987 Task Force guidelines, it is not necessary to obtain an EEG in children older than 1 year as long as the neurologic examination remains unchanged for the appropriate observation period.

In children, the most common drugs causing reversible loss of brain electrocortical activity include barbiturates (eg, phenobarbital), benzodiazepines, narcotics, and certain intravenous (thiopental, ketamine, and midazolam) and inhalation (halothane and isoflurane) anesthetics. A recent study in 92 children reported data suggesting that therapeutic levels of phenobarbital (ie, 15 to 40 μg/mL) do not affect the EEG.

### CBF Determination

Neuroimaging techniques can be used to document the absence of CBF. These include cerebral angiography, radionuclide angiography, transcranial Doppler ultrasonography, computed tomography (CT) with contrast injection or xenon inhalation, digital subtraction angiography (DSA), single photon emission computed tomography, and positron emission tomography. Of these, radionuclide angiography remains the most widely used in children because it is portable, relatively sensitive, and easy to perform. Documentation of the absence of CBF confirms brain death and has been reviewed elsewhere in detail.

### Radionuclide Imaging

Studies in children have shown that radionuclide imaging is accurate and reproducible. It has been favorably compared with other methods of detecting the presence or absence of CBF. The absence of CBF in brain death is due primarily to low cerebral perfusion pressure (mean arterial pressure – intracranial pressure [ICP]) and secondarily to release of vasoconstrictors from vascular smooth muscle and brain parenchyma.

A certain percentage of pediatric patients who are brain dead may have CBF early after diagnosis. In studies reported by Drake and colleagues, 15 of 47 brain-dead children had evidence of intact CBF as determined by radionuclide imaging. About two-thirds of the patients who had repeat studies showed loss of CBF 2 to 3 days later. This occurred regardless of whether these patients had ECS or some EEG activity recorded when the first CBF study was obtained. In a more recent report, 5 of 18 clinically brain-dead preterm and term infants retained CBF. Greisen and Pryds also described two suspected brain-dead newborn infants with ECS who had preserved CBF documented by xenon scanning. Overall, it is clear that CBF may be present in infants and children who are clinically brain dead. In most patients, repeat CBF studies 24 to 48 hours later will likely, but not uniformly, document loss of CBF.

### Transcranial Doppler Ultrasonography

Transcranial Doppler ultrasonography has been advocated because it is a portable and noninvasive way to ascertain cerebral circulatory arrest. Reports in pediatric patients since 1983 have validated the specificity and sensitivity of transcranial Doppler ultrasonography. Doppler changes seen in brain-dead patients include loss of diastolic flow, appearance of retrograde diastolic flow, diminution of systolic flow in the anterior cerebral artery with unchanged flow in the common carotid artery, and, finally, the loss of any detectable flow in these vessels.

### Digital Subtraction Angiography

DSA is another technique used to assess the intracranial circulation. This technique can be performed intravenously or by intra-arterial injection. A small amount of nonionic contrast material is injected while DSA of the cerebral vasculature is done, similar to conventional cerebral angiography. This allows visualization of contrast within the major intracranial vessels; lack of such visualization indicates absence of CBF. There are very few reports...
of this technique in children and only one recent case report in a brain-dead neonate. A recent report using intra-
venous DSA in 110 patients with clinical signs of brain
death observed that the initial study documented absent
contrast enhancement in 105 patients. Repeat studies con-
ducted within several hours in the remaining five patients
also confirmed cessation of CBF.

Evoked Responses
Brainstem auditory evoked response (BAER) testing has
been extensively studied as an alternative confirmatory
method. Its portability and noninvasiveness seem ideal,
but several studies have raised doubt as to the BAER’s reli-
ability in determining brain death, particularly in children
younger than 6 months old. More recent studies, however,
have suggested that BAER testing reliably confirms brain
death in children. In one report, almost 90% of 51 brain-
dead children had loss of the BAER (complete loss in 27
patients; loss of waveforms III to VII in 18 patients). It
also was shown that loss of BAER preceded the develop-
ment of ECS. This finding suggested that BAER testing
might be more useful than EEG for earlier laboratory con-
firmation of brain death. However, if testing is performed
too early, a false-positive result may occur.

Somatosensory evoked potentials (SEPs) possibly may
have greater discrimination in the confirmation of brain
death. Recent studies of SEPs in children found that only
62.5% of patients had complete absence of SEPs or just a
cervical cord (but no thalamocortical) response, suggesting
SEPs are of limited use as a confirmatory test in children.

Brain Death in the Newborn
About 550 newborns of a total of 4.9 million live births
may be diagnosed as brain dead. Etiologies of brain death
based on data from 87 newborns younger than 1 month of
age included hypoxic-ischemic encephalopathy (61%),
birth trauma (8%), malformations (6%), cerebral hemor-
rhage (6%), infection (7%), SIDS (7%), nonaccidental
trauma (4%), and metabolic causes (1%).

Preterm and term neonates younger than 7 days of age were
excluded from the 1987 Task Force pediatric brain death guide-
lines. The ability to diagnose brain death in newborns is still
viewed with uncertainty. This is due to the small number of
brain-dead neonates reported in the literature. Several years
after publication of the guidelines, data on 18 brain-dead
neonates were published, and it was suggested that brain death
could be diagnosed in term infants and preterm infants of
greater than 34 weeks gestational age within the first week of life.
Because the newborn has patent sutures and an open
fontanelle, increases in ICP after acute injury are not as signif-
ificant as in older patients. Thus, the usual cascade of events of
herniation from increased ICP and reduced cerebral perfusion
are less likely to occur in newborns. Brain death in newborns
(even those age < 7 d) can be diagnosed, provided the physi-
cian is aware of the limitations of the clinical examination and
laboratory testing. It is important to carefully and repeatedly
examine these infants, with particular attention to examination
of brainstem reflexes and apnea testing. An observation period
of 48 hours is recommended to confirm the diagnosis. If an
EEG is isoelectric or if a CBF study shows no flow, the obser-
vation period can be shortened to 24 hours. Although there are
few cases of preterm infants who become brain dead, it is likely
that the same time frame would be applicable. There have been
few instances of neonates or older infants who showed mini-
mal transient clinical or EEG recovery, but none appears to
have regained meaningful neurologic function, and all died
within brief periods of time.

Because of the significant physiologic and cerebrovascu-
lar differences in the neonatal response to injuries resulting
in brain death, previous studies have observed a much
higher incidence of newborns with EEG activity or cerebral
perfusion. In addition, some newborns with ECS showed
preserved CBF. Conversely, others without CBF showed EEG
activity. In the neonate, even though CBF and mean arter-
ial blood pressures are much lower, increases in ICP after
acute injury are less dramatic. Recent data on 30 newborns
who had EEGs and radionuclide perfusion studies found
that one-third with ECS showed evidence of CBF and 58%
of those with absent CBF had evidence of EEG activity.

Data on 37 of 53 brain-dead newborns in whom EEGs
were performed revealed the following: ECS (n = 21); very
low voltage (n = 13); burst-suppression (n = 1); seizure
activity (n = 1); normal (n = 1). Almost all patients whose
first EEG showed ECS had ECS on the second study, and
most patients who initially did not show ECS on their first
EEG did so on a repeat study. The data suggested that for
confirmation of brain death, only one EEG showing ECS is
necessary, provided the examination remains unchanged.

CBF data have shown that it is absent in 72% of brain-
dead newborns. In some infants who initially had CBF,
repeat studies demonstrated the absence of flow. No signif-
icant differences were observed in the median duration of
brain death in those neonates with CBF (4 days), compared
with those without CBF (3 days). These findings, as well as
those described earlier, emphasize the limitations of both
CBF determinations and EEG findings for confirmation of
brain death in neonates.

Organ Procurement in
Brain-Dead Children
Because brain death is more frequently due to severe asphyx-
ial injury in children than in adults, concerns that similar
injury to other organs would preclude transplantation have
been raised. Inotropic agents to support blood pressure and
cardiac function may also be necessary, particularly if the etiology of brain death was related to a preexisting global asphyxial insult that may have caused hypoxic myocardial injury. Recent data, however, suggest that organ transplantation, including heart transplantation, can be successfully accomplished from pediatric donors. Likewise, although brain-dead child abuse victims have rarely been considered organ donors because of legal issues, many centers now try to obtain surrogate consent. With cooperation from the medical examiner’s office, they have been able to successfully obtain organs from such donors.

The loss of neuroendocrine function must be treated in order to accomplish successful organ donation. Perhaps the most common problem is diabetes insipidus, which can be easily controlled with low-dose vasopressin (3 to 5 U intramuscularly or 0.05 to 0.1 U/kg intravenously, as needed). Some patients may also require supplemental corticosteroid therapy, as impairment of the hypothalamic-pituitary-adrenal axis may occur. Adequate respiratory support to maintain organ function is also important. In addition, treatment and prevention of infection will minimize cardiovascular instability. In most instances, the time available for this type of monitoring and support is relatively short (2 days) before organ donation occurs. Support for the grieving family and for the nursing and other medical staff is extremely important and perhaps is one of the most vital services a physician can provide. The responsibilities of the physician involved in the declaration of brain death must always be clearly demarcated from those physicians interested in organ procurement.

**Summary**

The diagnosis of brain death in pediatric patients is based on the same principles as in adults. Although the neurologic examination is difficult because of the size of the patient, immaturity of certain developmental reflexes being tested, and pathophysiologic differences such as the presence of open sutures and fontanelles in the neonate and infant, the fundamentals of the examination (coma, apnea, and absent brainstem reflexes) allow for accurate diagnosis. It is clear that a certain percentage of infants and children, like adults, will not have “confirmatory” neurodiagnostic testing. As is the case in many other areas of medicine, clinical judgment and serial examinations allow for the establishment of a definitive diagnosis. Better understanding of the pathophysiology of the evolution of brain death in neonates and infants should help decide whether the recommended age-related periods of observation are based on differences in developmental neurophysiology or cerebrovascular regulation. A paradigm for the diagnosis of brain death is given in Figure 98–1.

**Suggested Readings**

Practitioner and Patient Resources

The Compassionate Friends, Inc.
P.O. Box 3696
Oak Brook, IL 60522-3696
Phone: (630) 990-0010 or (877) 969-0010
Fax: (630) 990-0246
http://www.compassionatefriends.org

The mission of The Compassionate Friends is to assist families toward the positive resolution of grief following the death of a child of any age and to provide information to help others be supportive.

The Dougy Center, The National Center for Grieving Children and Families
P.O. Box 86852
Portland, OR 97286
Fax: (503) 777-3097
http://www.dougy.org

The mission of The Dougy Center for Grieving Children is to provide loving support to families and organizations seeking to assist children grieving a death locally, nationally, and internationally by allowing individuals to share their experiences as they move through their healing process.