CHAPTER 22

COMA IN CHILDHOOD

Thomas K. Koch

Coma is not a disease but rather a state of central nervous system (CNS) depression or dysfunction that can result from a variety of life-threatening conditions. In most circumstances, the initial evaluation will indicate the site of the anatomic disruption and possibly suggest the likely etiology, allowing for the immediate institution of appropriate therapy. This initial therapy is often life-saving, and it is imperative for the physician or other health care personnel to clearly understand the evaluation of the comatose patient and properly interpret the findings.

Coma is a state of unconsciousness from which the patient cannot be aroused ("unarousable unresponsiveness"). There is no speech, the eyes do not open, and the extremities do not move to command nor do they appropriately ward off noxious stimuli. Reflexive posturing movements may be retained. Other states of altered consciousness include stupor, obtundation, and lethargy. **Stupor** is similar to coma except that the patient is arousable only with vigorous stimulation, and when the stimulation ceases, the patient immediately returns to an unresponsive state. **Obtundation** is similar to stupor except that the patient can be aroused with stimulation and is able to maintain the aroused state after removal of the stimulus. **Lethargy** is a sleepy state from which the patient can easily be aroused and maintained awake but there is a tendency to desire sleep.

ANATOMY OF CONSCIOUSNESS

Consciousness requires both arousal and awareness. Arousal is simply wakefulness, which is clinically manifested by spontaneous or stimulus-induced eye opening. Activation of the reticular activating system (RAS), which spans the paramedial brain stem from the level of the midbrain to the pons, results in arousal. Awareness is the ability to recognize oneself and the environment. Awareness allows for the accomplishment of goal-directed or purposeful tasks and implies the integrity of the cerebral hemispheres. With a compromise of either one or both of these structures, the patient will be rendered comatose. A chronic condition resulting from severe bilateral cortical injury, distinct from coma by virtue of intact arousal but without awareness, has been termed the "persistent vegetative state."

PATHOPHYSIOLOGY OF COMA

The pathophysiologic mechanisms responsible for the production of coma can be considered in three broad categories: a structural lesion, a diffuse encephalopathy, and

seizures. After the emergency management and stabilization of the patient, the goal in evaluating the comatose patient is to arrive at the correct etiologic category so that further diagnostic and therapeutic measures can proceed in a timely fashion.

Structural lesions (brain tumors, abscesses, hematomas, and so forth) can be either supratentorial or infratentorial. Supratentorial lesions produce coma by brain stem compression either through central downward or uncal herniation, while infratentorial lesions can cause either intrinsic brain stem damage or extrinsic compression of the brain stem. Head trauma is one of the most important causes of mass lesions leading to coma in children. Given a history of closed head trauma, it is imperative to evaluate the patient for intra- and/or extra-axial hematomas. Severe brain swelling, termed "malignant hyperemia," can occur in children after severe head trauma without a mass lesion and is believed to be secondary to cerebral vasocongestion and frequently associated with a poor outcome. The "shaken baby syndrome" needs to be considered in any child with head trauma and a suspected history of child abuse.

Diffuse encephalopathies usually produce disturbances of brain function that are symmetric, although hypoglycemia, hepatic encephalopathy, and hyperosmolar nonketotic hyperglycemia may be exceptions. Diffuse encephalopathies can be caused by subarachnoid hemorrhage, meningoencephalitis, and metabolic disturbances. Common causes of metabolic coma include hypoxic ischemia, hypoglycemia, toxin/drug ingestion, hepatic failure, Reye syndrome, adrenal failure, and myxedema. A characteristic feature of diffuse metabolic encephalopathies is the preservation of the pupillary light reflex despite depression of more caudal brain stem functions. Notable exceptions to this include glutethimide intoxication, high-dose barbiturates, atropine, profound hypothermia, and anoxia. In children, miotic pupils are often seen in drug intoxication and are unusual in trauma-related coma.

Seizures and the postictal state can present as unconsciousness. Although seizures usually are accompanied by more overt clinical motor manifestations, manifestations of convulsive phenomena can, on occasion, be subtle or absent. If there is significant clinical suspicion to consider seizures as an etiology of unresponsiveness, then an immediate electroencephalogram (EEG) is necessary. A prolonged postictal confusional state lasting hours to days can follow status epilepticus and can occur in patients with a chronic encephalopathy (see Chapter 10).

Clinical Findings

A careful **history** focussed on the time of development of the comatose state is crucial in the early evaluation, decision making concerning etiology, and treatment. An acute onset usually suggests a vascular etiology such as stroke or hemorrhage. A subacute onset is more commonly observed in patients with brain tumors or abscesses, hydrocephalus, chronic subdural hematomas, and metabolic coma.

The **general examination** can provide important clues regarding the etiology of the coma. Immediate attention must be directed to vital functions. In addition to patency of the airway and respiration, blood pressure and heart rate require careful monitoring. An elevation of blood pressure can be indicative of increased intracranial pressure or posterior fossa mass lesions. The funduscopic examination may show papilledema, indicating increased intracranial pressure. Retinal hemorrhages imply trauma, acute hypertension, or increased intracranial pressure. The head, ears, and nose should be checked for hemotympanum, Battle sign (swelling and ecchymoses over the mastoid bone behind the ear), raccoon eyes, and cerebrospinal fluid (CSF) leakage from the nose or ears, all of which are indicative of a basilar skull fracture. A stiff neck implies

meningeal irritation from infection, the presence of subarachnoid blood or cerebellar tonsillar herniation, and though this is an important sign, it may not be present in deep coma or in infants or toddlers.

The neurologic examination of the comatose patient is comprised of five simple tests of cortical and brain stem integrity, including the level of consciousness, respiratory pattern, pupillary reflexes, extraocular motility, and motor response to stimulation. The patient's responses to these tests correlates with specific levels of brain function and anatomic integrity. The pattern of responses and corresponding levels of anatomic involvement can lead to the correct pathophysiologic etiology (see Table 22.1).

The **level of consciousness** is best assessed by the ease and degree of arousal. Eye opening indicates an intact brain stem RAS and can occur spontaneously or only in response to either verbal or painful stimulation. In the truly comatose patient, there is no arousal despite the degree of noxious stimulation.

A normal **respiratory pattern** indicates brain stem integrity. Cheyne-Stokes, or periodic respiration, in which there is an alternating pattern between hyperventilation and apnea, can be seen with bilateral cortical or upper brain stem (thalamus/upper midbrain) damage. True hyperventilation can be seen with acid-base abnormalities or midbrain damage causing central neurogenic hyperventilation. Ataxic or irregular breathing suggests pontomedullary dysfunction.

The **pupillary reflexes** are the single most important feature in the examination of the comatose patient. Symmetric pupils 3 to 4 mm in diameter that are directly and consensually responsive to light indicate midbrain integrity. As mentioned earlier, most forms of metabolic coma preserve the pupillary light reflex. Midposition, fixed pupils indicate midbrain failure and usually imply severe, often irreversible, brain stem injury. They are commonly referred to as the "pupils of death." Fixed, dilated pupils (greater than 7 mm in diameter) usually result from third nerve compression or anticholinergic or sympathomimetic drug intoxication. Pinpoint pupils (1 to 1.5 mm in diameter) usually indicate pontine disruption or opioid intoxication. Pupillary asymmetry (anisocoria) greater than 1 mm with a dissimilar response to light usually implies focal midbrain or third nerve involvement and can be the first sign of the uncal herniation syndrome.

Extraocular motility is an important part of the assessment of brain stem integrity beginning at the pontomedullary junction with vestibular nerve input, and synapses in the pontine gaze center from the sixth nerve nucleus, ascending the medial longitudinal fasciculus and finally terminating in the midbrain third nerve nucleus. This pathway can be tested on a reflex level using oculocephalic (doll's eyes) or oculovestibular response (caloric stimulation). To perform the oculocephalic reflex, the patient's eyes are opened and the head is rotated from side to side. If full conjugate gaze is elicited, then the midbrain and pons are intact, and this essentially excludes a brain stem lesion. If the maneuver is negative (eyes remain straight ahead within the head during rotation), then a stronger stimulus is required. Cold water calorics should be performed after one is certain that the tympanic membrane is normally intact. To perform this maneuver, the head is placed in midline at 30 degrees of elevation. Approximately 30 to 50 ml of ice water is injected into the ear canal. If the midbrain and pons are intact, there will be tonic deviation of both eyes towards the side of the cold water irrigation. If only the ipsilateral eye abducts without the contralateral eye adducting, then the patient has an internuclear ophthalmoplegia (INO) indicating a normally functioning pons but abnormal function of the medial longitudinal fasciculus (MLF) and/or midbrain. No response with either eye indicates pontine dysfunction or metabolic abnormality.

The **motor response** to painful stimulation (supraorbital, sternal, or nail-bed compression) can be either a purposeful withdrawal, abnormal posturing, or flaccidity/

TABLE 22.1 Anatomic Stages of Coma

	EARLY DIENCEPHALIC	LATE DIENCEPHALIC	MIDBRAIN	PONTOMEDULLARY
Respiratory Pattern	Normal	Cheyne-Stokes respiration	Cheyne-Stokes respiration or hyperventilation	Ataxic
Pupillary Response	Small, reactive	Small, reactive	Midposition, fixed	Fixed
Extraocular Motility	Intact (Doll's eyes/caloric stimulation)	Intact (Doll's eyes/caloric stimulation)	Internuclear ophthalmoplegia	Absent
Motor Response	Withdrawal	Decorticate	Decerebrate	Flaccid

unresponsiveness. Posturing is either decorticate (flexion of the upper and extension of the lower extremities) or decerebrate (extension of all extremities). Decorticate posturing can be seen with thalamic dysfunction, while decerebrate posturing indicates midbrain damage. Patients with pontine or medullary dysfunction usually are flaccid without a response to painful stimuli.

Stages of Coma

The highest level of coma is the **early diencephalic stage,** which is characterized by an intact brain stem but without cerebral hemispheric function. All brain stem reflexes are intact. The **late diencephalic stage** is characterized by the loss of thalamic function. While the pupillary reflexes and extraocular motility are intact, Cheyne-Stokes respiration and decorticate posturing are seen. The **midbrain stage** indicates damage to the midbrain and all rostral structures; the pupils are fixed and in midposition, oculomotor function is characterized by internuclear ophthalmoplegia, and decerebrate posturing is present with either Cheyne-Stokes respiration or central neurogenic hyperventilation. The **pontomedullary stage** indicates total brain stem dysfunction with fixed pupils, ophthalmoplegia, an absent motor response, and absent or inadequate respirations (see Figure 22.1).

Causes of Coma

It is common practice to grade the severity of coma by using the pediatric Glasgow Coma Scale (Table 7.1). This is a helpful way of quantifying coma in order to serially follow the patient, but it does not replace the initial neurologic examination. In the evaluation of comatose patients, it is essential to decide whether the coma is the result of structural lesion, metabolic abnormality, or seizures. If the patient has a structural lesion, then immediate neurosurgical intervention is often necessary after neuroimaging studies have been performed. In contrast, metabolic disorders require appropriate laboratory testing and expedient medical management. The condition of the comatose patient who has a structural lesion or metabolic abnormality can often be deduced from the pattern of response to four essential neurologic parameters: respiratory pattern, pupillary reflex, extraocular motility, and motor response to stimulation.

Structural lesions causing coma can be either supratentorial or infratentorial in location. **Supratentorial lesions** tend to cause dysfunction from the sequential loss of brain or brain stem function in a rostral-caudal fashion with the predictable progression of the clinical stages of coma from early diencephalic to late diencephalic and midbrain to pontomedullary stages. This pattern is suggestive of a central downward herniation syndrome. Supratentorial lesions may cause unilateral herniation of the medial portion of the temporal lobe to produce an uncal herniation syndrome. This results in direct asymmetric pressure being exerted on the midbrain. Initial presentation is characterized by ipsilateral pupillary dilation with a diminished response to light. A complete pattern of midbrain dysfunction with bilateral pupillary dysfunction, extraocular abnormalities, decerebrate posturing, and abnormalities of respiratory drive can rapidly develop. The uncal herniation syndrome must be recognized early and treated aggressively with agents to decrease intracranial pressure and neurosurgical intervention; otherwise, irreversible brain stem damage occurs with death of the patient. **Infratentorial lesions** tend to present with the sudden onset of focal brain stem signs, indicating midbrain or pontomedullary dysfunction. Midposition nonreactive pupils are seen with midbrain lesions, while pinpoint pupils are seen with pontine hemorrhage

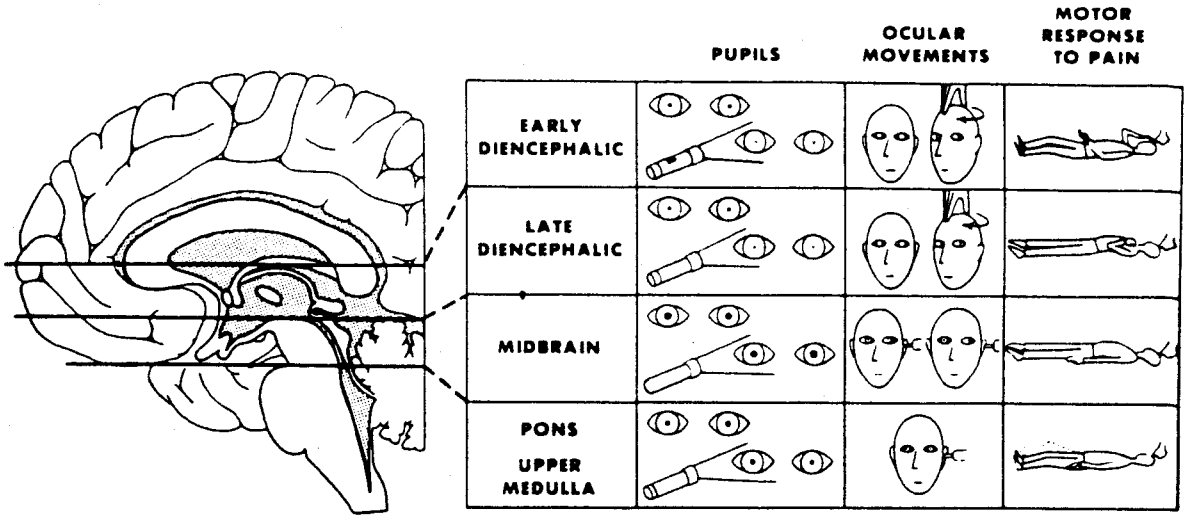

FIGURE 22.1 The signs and symptoms of different anatomic levels of brain involvement in coma. (Adapted and reproduced with permission from Plum F, Posner JB. *The Diagnosis of Stupor and Coma*, 3rd ed. Philadelphia: F.A. Davis, 1980.)

and less often in pontine infarction, cerebellar hemorrhage, or cerebellar infarction. Either dysconjugate eye movements with an internuclear ophthalmoplegia or conjugate gaze deviation away from the side of the lesion and toward a hemiparesis are highly suggestive of an infratentorial lesion.

Clinical features characteristic of a **metabolic coma** include a mixed pattern of brain stem dysfunction, which does not correspond to anatomic stages of coma (early diencephalic, late diencephalic, midbrain, or pontomedullary); pupils that usually remain reactive to light despite depressed respiration (exceptions to this include glutethimide toxicity, deep barbiturate coma, acute anoxia, hypothermia, and anticholinergic [large pupils] or opioids [pinpoint pupils]); symmetric motor responses to painful stimulation (exceptions noted above); gradual onset rather than sudden loss of consciousness; and the presence of asterixis, myoclonus, or tremor. Most causes of metabolic coma are associated with a metabolic acidosis. A respiratory alkalosis can occur with hepatic encephalopathy, sepsis, and salicylate intoxication. A respiratory acidosis is seen with sedative drug intoxication and a pulmonary encephalopathy. Common causes of metabolic coma include hypoxic-ischemic encephalopathy, hypoglycemia, hepatic dysfunction, inborn errors of metabolism, renal failure, pulmonary failure, hypothermia, hyperthermia, drugs/toxins, disordered osmolality, and infection (see Table 22.2).

Hypoxic ischemia in children is most commonly caused, following resuscitation, by cardiac arrest, sudden infant death syndrome, and drowning. The prognosis is dependent upon the duration of hypoxic ischemia, the immediate signs of brain or brain stem dysfunction, and the rapidity of their normalization. The early absence of pupillary reflexes and extraocular motility is a poor prognostic sign. In adults, the lack of pupillary reflexes on initial examination is incompatible with a good recovery. Within 24 hours, pupillary reflexes, extraocular motility, and at least some motor posturing should be present for an eventually good recovery. Neurologic residuae following severe hypoxic ischemia can include spasticity, ataxia, movement disorders, seizures, short-term memory loss, and mental retardation. Severe hypoxic ischemia can result in a persistent vegetative state.

TABLE 22.2 Common Causes of Metabolic Coma

Anoxic ischemia	Pulmonary failure
Hypoglycemia	Hypothermia/hyperthermia
Hepatic dysfunction Reye structure Hepatic failure	Drugs/toxins
Inborn errors of metabolism Urea cycle defects Organic acidemias Aminoacidurias	Disordered osmolality Hypo-osmolar states Hyperosmolar states
Renal failure	Infections

Hypoglycemia in children can result from inadequate glycogen stores, ketotic hypoglycemia, or in children older than 6 years of age, an islet cell adenoma. Initial symptoms include perspiration, excitation, restlessness, and tachycardia. Somnolence then develops with eventual progression to coma. The symptoms poorly correlate with the serum glucose concentration. Hypoglycemic coma can persist for up to 90 minutes without incurring irreversible brain damage. Symptoms frequently resolve following glucose administration; however, more severe hypoglycemia can result in permanent residuae similar to hypoxic ischemia.

Hepatic dysfunction leading to coma in children includes Reye syndrome and hepatic failure. Reye syndrome is characterized by acute hepatic failure with fatty degeneration and associated encephalopathy with coma, seizures, and increased intracranial pressure. It has been associated with a preceding viral infection and salicylate use. The prognosis is best correlated with the severity of the cerebral edema and management of the intracranial pressure. Acute hepatic failure can be seen with acetaminophen overdose or hepatitis. Frequently hepatic coma is accompanied by a respiratory alkalosis, which is a helpful laboratory sign. The prognosis is dependent upon the etiology of the underlying liver disorder.

Inborn errors of metabolism frequently present with an altered state of consciousness and seizures. Urea cycle defects tend to present in early infancy with an elevated serum ammonia concentration. Organic acidemias and aminoacidurias often present with episodic bouts of coma in association with acidosis, an anion gap, and ketosis. They are similar in their acute presentation to Reye syndrome. This is especially true for methylmalonic acidemia, propionic aciduria, systemic carnitine deficiency, and medium-chain acyl-CoA dehydrogenase deficiency (see Chapter 3).

Renal failure can lead to a uremic encephalopathy with myoclonus, seizures, tetany, and unconsciousness. Acute renal failure can also cause systemic hypertension leading to hypertensive encephalopathy. There is poor correlation between blood urea nitrogen (BUN) and mental status.

Pulmonary failure can cause an encephalopathy by CO_2 narcosis. Features include headache, tremor, myoclonus, and asterixis. In patients with chronic pulmonary failure, rapid correction of the $PaCO_2$ can lead to myoclonus, seizures, and coma. The pathogenesis of this condition appears to be due to rapid shifts in the CSF acid-base balance.

Hypothermia and hyperthermia can both cause an alteration in consciousness. Cognitive slowing begins to occur below temperatures of 93°F (34°C). Hypothermia rarely causes motor posturing with decortication or decerebration and does not disrupt extraocular motility. Recovery is usually complete. An encephalopathy with hyperthermia occurs with temperatures greater than 107.6°F (42°C). Brain stem reflexes are not disrupted, but seizures can occur. Permanent neurologic residuae are common and are frequently manifested as ataxia, hemiparesis, and dementia.

Disordered osmolality occurs in patients with a serum osmolality of less than 260 mOsm/kg or greater than 330 to 350 mOsm/kg. The clinical features of hypo-osmolar states include altered consciousness, increased intracranial pressure, and seizures. The rapid correction of hyponatremia can lead to central pontine myelinolysis. Clinically, the features of hyper-osmolar states include altered mentation, tremor, myoclonus, and focal deficits. Brain stem function is normal. Seizures can occur during rehydration. With hyperglycemic hyperosmolality, focal seizures are common and do not respond well to conventional anticonvulsant medication.

Toxin or drug-induced coma is a common cause of metabolic coma in childhood. Sedative/hypnotic drugs are most frequently responsible, and while a careful review of the history is essential, urinary toxicology screens are crucial for an accurate diagnosis. While the ingestion of drugs or toxins may have been accidental, careful consideration must be given to potential child endangerment. The preservation of pupillary reflexes with associated loss of extraocular motility is characteristic of a drug-induced coma. Lead exposure and toxicity in young children (<5 years) can produce coma, seizures, and increased intracranial pressure. In older children, lead produces a more typical peripheral motor neuropathy and anemia.

Infection with either bacterial or viral agents can lead to a meningeal irritation with neck stiffness, Kernig and/or Brudzinki sign. These signs may not be present before the age of 2 years. Increased intracranial pressure is a frequent complication of bacterial meningitis, and a full fontanel is an important clinical sign of increased pressure in a febrile and irritable infant.

Management

The **initial management** of the comatose patient requires careful attention to vital functions: **airway, breathing,** and **circulation.** Protection of the airway is imperative, and if it appears that the patient cannot maintain an adequate airway or ventilatory drive, then intubation and ventilatory support should be immediately carried out. The next step is to establish reliable intravenous access, and while this is being done, serum glucose and electrolytes must be determined. These steps should be followed by the intravenous administration of glucose at a dosage of 1 g/kg body weight. Given clinical suspicion or lacking a reliable history, nalaxone (Narcan) should also be administered at 0.1 mg/kg body weight.

General supportive management proceeds after the patient has been stabilized and there has been careful assessment of the clinical history, thorough physical examination, and all metabolic studies have been completed. Laboratory studies should include blood sugar, blood gases, complete blood count, electrolytes, BUN, creatinine, osmolality, liver function studies, urinalysis, toxicology screen, and CSF examination (one must be certain to exclude an intracranial mass lesion before the lumbar puncture). If a mass lesion is suspected as the cause of coma, then an emergency computerized tomographic (CT) or magnetic resonance imaging (MRI) head scan must be performed. If seizures are suspected, an appropriately performed EEG must be completed, and

anticonvulsant therapy may be required. Patients in coma require careful medical management in an intensive care unit with appropriate supportive care. If infection is considered at any time as a major cause of coma, then the patient requires an immediate lumbar puncture and broad-spectrum antibiotic coverage is administered. Continued patient care depends upon the results of the studies obtained.

Brain Death

The criteria for brain death require documentation of the irreversible cessation of all levels of cortical and brain stem function. Reversible disorders that need to be excluded prior to declaring a patient brain-dead include: reversible metabolic derangements, such as hypoglycemia, drug or toxin overdose, hypothermia (temperature <32.3°C), and hypotension. Guidelines for the determination of brain death in children have been published that emphasize the importance of the history and the clinical examination. The physical examination must demonstrate an absence of all cortical and brain stem function (see Table 22.3).

The patient must be unresponsive with unreactive pupils, absent inducible eye movements by cold water caloric stimulation, absent corneal reflexes, absent gag reflex, no motor response to pain, and be apneic in the presence of a maximum CO_2 drive to ventilation (CO_2 greater than 60 mm Hg). Age-related observation periods have been established. For children over age 1 year, two examinations are recommended 12 to 24 hours apart. Between ages 2 months and 1 year, two examinations and EEGs 24 hours apart or one examination and an EEG and radionuclide angiogram are recommended. For infants ages 7 days to 2 months, two examinations and EEGs separated by 48 hours

Table 22.3 Guidelines for Determination of Brain Death in Children

A. History: Determine the cause of coma to eliminate remediable or reversible conditions.

B. Physical examination criteria
   1. Coma and apnea
   2. Absence of brain stem function
      a. Midposition or fully dilated pupils
      b. Absence of spontaneous oculocephalic (Doll's eyes) and caloric-induced eye movements
      c. Absence of movement of bulbar musculature and 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 the spinal cord level
   5. Examination should remain consistent for brain death throughout predetermined period of observation.

C. Observation period according to age
   1. 7 days–2 mo: two examinations and EEGs 48 hr apart
   2. 2 mo–1 yr: two examinations and EEGs 24 hr apart or one examination and an initial EEG showing ECS (*) combined with a radionuclide angiogram showing no CBF (†), or both
   3. > 1 yr: two examinations 12 to 24 hr apart; EEG and isotope angiography optional

*ECS, electrocerebral silence.
†CBF, cerebral blood flow.

are recommended. When an EEG is performed to demonstrate electrocerebral silence (ECS), it should be carried out over a period of 30 minutes using standardized techniques for brain death determinations. Since the standard 10-cm electrode separation may not be possible in small children, the interelectrode distance should be decreased proportionally to the patient's head size. There should be insufficient patient drug concentrations to suppress the EEG. Techniques to document a lack of blood flow to the brain, such as cerebral radionuclide angiography and contrast angiography, can offer helpful confirmatory evidence of brain death in children over age 2 months. The value of such techniques for children younger than 2 months is under investigation.

References

Ashwal S, Schneider S. Brain death in infants and children. In: Berg BO, ed. *Neurologic Aspects of Pediatrics.* Boston: Butterworth-Heinemann, 1992; 31:639–659.

Caronna J, Simon RP. The comatose patient: a diagnostic approach and treatment. *Int Anesthesiol Clin* 1979; 17:3–18.

Edwards R, Simon RP. In: Baker AB, Joynt RJ, eds. *Clinical Neurology*, Vol. 2. Philadelphia: Harper & Row, 1979; 2:1–14.

Fisher CM. The neurologic examination of the comatose patient. *Acta Neurol Scand* 1969; 45(suppl 36):1–56.

Guidelines for the determination of death in children. *Pediatrics* 1987; 80:298–300.

Levy DE, Bates D, Caronna JJ, et al. Prognosis in nontraumatic coma. *Ann Intern Med* 1981; 94:293–301.

Levy DE, Caronna JJ, Singer BH, et al. Predicting outcome from hypoxic-ischemic coma. *JAMA* 1985; 253:1420–1426.

Plum F, Posner J. *The Diagnosis of Stupor and Coma*, 3rd ed. Philadelphia: F.A. Davis, 1980.

Simon RP. Coma in children. In: Berg BO, ed. *Neurologic Aspects of Pediatrics.* Boston: Butterworth-Heinemann, 1992; 30:627–638.

Simon RP. Stupor and coma. In: Mills J, Ho MT, Salber PR, et al, eds. *Current Emergency Diagnosis and Treatment.* Los Altos: Lange Medical Publications, 1983: 73–88.