Guidelines for the Determination of Brain Death in Infants and Children: An Update of the 1987 Task Force Recommendations—Executive Summary

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Objective: To review and revise the 1987 pediatric brain death guidelines.
Methods: Relevant literature was reviewed. Recommendations were developed using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system.
Conclusions and Recommendations: (1) Determination of brain death in term newborns, infants, and children is a clinical diagnosis based on the absence of neurologic function with a known irreversible cause of coma. Because of insufficient data in the literature, recommendations for preterm infants <37 weeks gestational age are not included in these guidelines. (2) Hypotension, hypothermia, and metabolic disturbances should be treated and corrected, and medications that can interfere with the neurologic examination and apnea testing should be discontinued allowing for adequate clearance before proceeding with these evaluations. (3) Two examinations including apnea testing with each examination separated by an observation period are required. Examinations should be performed by different attending physicians. Apnea testing may be performed by the same physician. An observation period of 24 hours for term newborns (37 weeks gestational age) to 30 days of age and 12 hours for infants and children (>30 days to 18 years) is recommended. The first examination determines the child has met the accepted neurologic examination criteria for brain death. The second examination confirms brain death based on an unchanged and irreversible condition. Assessment of neurologic function after cardiopulmonary resuscitation or other severe acute brain injuries should be deferred for 24 hours or longer if there are concerns or inconsistencies in the examination. (4) Apnea testing to support the diagnosis of brain death must be performed safely and requires documentation of an arterial $PaCO_2$ 20mmHg above the baseline and ≥60mmHg with no respiratory effort during the testing period. If the apnea test cannot be safely completed, an ancillary study should be performed. (5) Ancillary studies (electroencephalogram and radionuclide cerebral blood flow) are not required to establish brain death and are not a substitute for the neurologic examination. Ancillary studies may be used to assist the clinician in making the diagnosis of brain death (a) when components of the examination or apnea testing cannot be completed safely due to the underlying medical condition of the patient; (b) if there is uncertainty about the results of the neurologic examination; (c) if a medication effect may be present; or (d) to reduce the interexamination observation period. When ancillary studies are used, a second clinical examination and apnea test should be performed, and components that can be completed must remain consistent with brain death. In this instance, the observation interval may be shortened, and the second neurologic examination and apnea test (or all components that are able to be completed safely) can be performed at any time thereafter. (6) Death is declared when these above criteria are fulfilled.

ANN NEUROL 2012;71:573–585

The Pediatric Section of the Society of Critical Care Medicine and the Section on Critical Care of the American Academy of Pediatrics, in conjunction with the Child Neurology Society, formed a multidisciplinary committee of medical and surgical subspecialists under the auspices of the American College of Critical Care Medicine to review and

View this article online at wileyonlinelibrary.com. DOI: 10.1002/ana.23552

Received Dec 6, 2011, and in revised form Dec 6, 2011. Accepted for publication Jan 27, 2012.

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See the Appendix on page 584.

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revise the 1987 guidelines. Its purpose was to review the neonatal and pediatric literature from 1987, including any prior relevant literature, and update recommendations regarding appropriate examination criteria and use of ancillary testing to diagnose brain death in neonates, infants, and children. The committee was also charged with developing a checklist to provide guidance and standardization to determine and document brain death. Uniformity in the determination of brain death should allow physicians to pronounce brain death in pediatric patients in a more precise and orderly manner and ensure that all components of the examination are performed and appropriately documented. The committee believes these revised diagnostic guidelines (Table 1) and a standardized checklist form (Table 2) will assist physicians in determining and documenting brain death in children. This should ensure broader acceptance and utilization of such uniform criteria.

This update affirms the definition of death as stated in the 1987 pediatric guidelines established by multiple organizations as follows: "An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brainstem, is dead. A determination of death must be made in accordance with accepted medical standards."[1]

The committee recognizes that medical judgment of involved pediatric specialists will direct the appropriate course for the medical evaluation and diagnosis of brain death. The committee also recognizes that no national brain death law exists. State statutes and policy may restrict determination of brain death in certain circumstances. Physicians should become familiar with laws and policies in their respective institution. The committee also recognizes that variability exists for the age designation of pediatric trauma patients. In some states, the age of the pediatric trauma patient is defined as <14 years of age. Trauma and intensive care practitioners are encouraged to follow state/local regulations governing the specified age of pediatric trauma patients.

The following is an executive summary of the recommendations produced from this committee. The full report is available in Critical Care Medicine and Pediatrics.[2,3] The committee believes these guidelines to be an important step in protecting the health and safety of all infants and children. These revised clinical guidelines and accompanying checklist are intended to provide an updated framework to promote standardization of the neurologic exam and use of ancillary studies based on the evidence available to the committee at the time of publication.

Recommendations

Term Newborns (37 Weeks Gestational Age) to Children 18 Years of Age

DEFINITION OF BRAIN DEATH AND COMPONENTS OF THE CLINICAL EXAMINATION. Brain death is a clinical diagnosis based on the absence of neurologic function with a known diagnosis that has resulted in irreversible coma. Coma and apnea must coexist to diagnose brain death. A complete neurologic examination that includes the elements outlined in Table 3 is mandatory to determine brain death; all components must be appropriately documented. An algorithm to diagnose brain death in infants and children is provided in the Figure.

PREREQUISITES FOR INITIATING A CLINICAL BRAIN DEATH EVALUATION. Determination of brain death by neurologic examination should be performed in the setting of normal age-appropriate physiologic parameters. Factors potentially influencing the neurologic examination that must be corrected prior to examination and apnea testing include:

- Shock or persistent hypotension. Systolic blood pressure or mean arterial pressure should be in an acceptable range (systolic blood pressure not less than 2 standard deviations below age appropriate norm) based on age. Placement of an indwelling arterial catheter is recommended to ensure that blood pressure remains within a normal range during the process of diagnosing brain death and to accurately measure $PaCO_2$ levels during apnea testing.
- Hypothermia. Hypothermia is known to depress central nervous system function[4–6] and may lead to a false diagnosis of brain death. Hypothermia may alter metabolism and clearance of medications that can interfere with brain death testing. Efforts to adequately rewarm before performing any neurologic examination and maintain temperature during the observation period are essential. A core body temperature of $>35°C$ (95°F) should be achieved and maintained during examination and testing to determine death.
- Severe metabolic disturbances. Severe metabolic disturbances can cause reversible coma and interfere with the clinical evaluation to determine brain death. Reversible conditions such as severe electrolyte imbalances, hyper- or hypoglycemia, severe pH disturbances, severe hepatic or renal dysfunction, or inborn errors of metabolism may cause coma in a neonate, infant, or child.[5,6] These conditions should be identified and treated before evaluation for brain death, especially in situations where the clinical history does not provide a reasonable explanation for the neurologic status of the child.

TABLE 1: Summary Recommendations for the Diagnosis of Brain Death in Neonates, Infants, and Children

Recommendation	Evidence Score	Recommendation Score
1. Determination of brain death in neonates, infants, and children relies on a clinical diagnosis that is based on the absence of neurologic function with a known irreversible cause of coma. Coma and apnea must coexist to diagnose brain death. This diagnosis should be made by physicians who have evaluated the history and completed the neurologic examinations.	High	Strong
2. Prerequisites for initiating a brain death evaluation:		
A. Hypotension, hypothermia, and metabolic disturbances that could affect the neurological examination must be corrected prior to examination for brain death.	High	Strong
B. Sedatives, analgesics, neuromuscular blockers, and anticonvulsant agents should be discontinued for a reasonable time period based on elimination half-life of the pharmacologic agent to ensure they do not affect the neurologic examination. Knowledge of the total amount of each agent (mg/kg) administered since hospital admission may provide useful information concerning the risk of continued medication effects. Blood or plasma levels to confirm that high or supratherapeutic levels of anticonvulsants with sedative effects are not present should be obtained (if available) and repeated as needed or until the levels are in the low to mid therapeutic range.	Moderate	Strong
C. The diagnosis of brain death based on neurologic examination alone should not be made if supratherapeutic or high therapeutic levels of sedative agents are present. When levels are in the low or mid therapeutic range, medication effects sufficient to affect the results of the neurologic examination are unlikely. If uncertainty remains, an ancillary study should be performed.	Moderate	Strong
D. Assessment of neurologic function may be unreliable immediately following cardiopulmonary resuscitation or other severe acute brain injuries, and evaluation for brain death should be deferred for 24 to 48 hours or longer if there are concerns or inconsistencies in the examination.	Moderate	Strong
3. Number of examinations, examiners, and observation periods:		
A. Two examinations including apnea testing with each examination separated by an observation period are required.	Moderate	Strong
B. The examinations should be performed by different attending physicians involved in the care of the child. The apnea test may be performed by the same physician, preferably the attending physician who is managing ventilator care of the child.	Low	Strong
C. Recommended observation periods:	Moderate	Strong
a. 24 hours for neonates (37 weeks gestation to term infants 30 days of age).		
b. 12 hours for infants and children (>30 days to 18 years).		
D. The first examination determines the child has met neurologic examination criteria for brain death. The second examination, performed by a different attending physician, confirms that the child has fulfilled criteria for brain death.	Moderate	Strong
E. Assessment of neurologic function may be unreliable immediately following cardiopulmonary resuscitation or other severe acute brain injuries, and evaluation for brain death should be deferred for 24 to 48 hours or longer if there are concerns or inconsistencies in the examination.	Moderate	Strong

TABLE 1 (Continued)

Recommendation	Evidence Score	Recommendation Score
4. Apnea testing:		
A. Apnea testing must be performed safely and requires documentation of an arterial $PaCO_2$ 20mmHg above the baseline $PaCO_2$ and $\geq$60mmHg with no respiratory effort during the testing period to support the diagnosis of brain death. Some infants and children with chronic respiratory disease or insufficiency may only be responsive to supranormal $PaCO_2$ levels. In this instance, the $PaCO_2$ level should increase to $\geq$20mmHg above the baseline $PaCO_2$ level.	Moderate	Strong
B. If the apnea test cannot be performed due to a medical contraindication or cannot be completed because of hemodynamic instability, desaturation to <85%, or an inability to reach a $PaCO_2$ of $\geq$60mmHg, an ancillary study should be performed.	Moderate	Strong
5. Ancillary studies:		
A. Ancillary studies (EEG and radionuclide CBF) are not required to establish brain death unless the clinical examination or apnea test cannot be completed.	Moderate	Strong
B. Ancillary studies are not a substitute for the neurologic examination.	Moderate	Strong
C. For all age groups, ancillary studies can be used to assist the clinician in making the diagnosis of brain death to reduce the observation period or (i) when components of the examination or apnea testing cannot be completed safely due to the underlying medical condition of the patient; (ii) if there is uncertainty about the results of the neurologic examination; or (iii) if a medication effect may interfere with evaluation of the patient. If the ancillary study supports the diagnosis, the second examination and apnea testing can then be performed. When an ancillary study is used to reduce the observation period, all aspects of the examination and apnea testing should be completed and documented.	Moderate	Strong
D. When an ancillary study is used because there are inherent examination limitations (ie, i to iii in 5C above), then components of the examination done initially should be completed and documented.	High	Strong
E. If the ancillary study is equivocal or if there is concern about the validity of the ancillary study, the patient cannot be pronounced dead. The patient should continue to be observed until brain death can be declared on clinical examination criteria and apnea testing, or a follow-up ancillary study can be performed to assist with the determination of brain death. A waiting period of 24 hours is recommended before further clinical reevaluation or repeat ancillary study is performed. Supportive patient care should continue during this time period.	Moderate	Strong
6. Declaration of death:		
A. Death is declared after confirmation and completion of the second clinical examination and apnea test.	High	Strong
B. When ancillary studies are used, documentation of components from the second clinical examination that can be completed must remain consistent with brain death. All aspects of the clinical examination, including the apnea test, or ancillary studies must be appropriately documented.	High	Strong
C. The clinical examination should be carried out by experienced clinicians who are familiar with infants and children, and have specific training in neurocritical care.	High	Strong

GRADE (Grading of Recommendations Assessment, Development, and Evaluation), a recently developed standardized methodological consensus-based approach, was used to evaluate the evidence and make recommendations for this guideline.
The Evidence Score is based on the strength of the evidence available at the time of publication.
The Recommendation Score is the strength of the recommendations based on available evidence at the time of publication. Please see full publication for scoring guidelines listed in Table 1.
CBF = cerebral blood flow; EEG = electroencephalography.

TABLE 2: Checklist for Documentation of Brain Death

Brain Death Examination for Infants and Children[a]

Age of Patient	Timing of First Examination	Interexamination Interval
Term newborn 37 weeks gestational age and up to 30 days old	☐ First examination may be performed 24 hours after birth OR following cardiopulmonary resuscitation or other severe brain injury	☐ At least 24 hours
		☐ Interval shortened because ancillary study (Section 4) is consistent with brain death
31 days to 18 years old	☐ First examination may be performed 24 hours following cardiopulmonary resuscitation or other severe brain injury	☐ At least 12 hours OR
		☐ Interval shortened because ancillary study (Section 4) is consistent with brain death

Section 1. Prerequisites for Brain Death Examination and Apnea Test

A. Irreversible and Identifiable Cause of Coma (please check)

☐ Traumatic brain injury

☐ Anoxic brain injury

☐ Known metabolic disorder

☐ Other (specify) _____

B. Correction of Contributing Factors That Can Interfere with the Neurologic Examination

	Examination 1		Examination 2	
a. Core body temperature is >95°F (35°C)	☐ Yes	☐ No	☐ Yes	☐ No
b. Systolic blood pressure or MAP in acceptable range (Systolic BP not less than 2 standard deviations below age-appropriate norm) based on age	☐ Yes	☐ No	☐ Yes	☐ No
c. Sedative/analgesic drug effect excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
d. Metabolic intoxication excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
e. Neuromuscular blockade excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No

☐ If ALL prerequisites are marked YES, then proceed to section 2, OR

☐ _____ confounding variable was present. Ancillary study was therefore performed to document brain death (Section 4).

Section 2. Physical Examination (please check); Note: Spinal Cord Reflexes Are Acceptable

	Examination 1, Date/Time: _____		Examination 2, Date/Time: _____	
a. Flaccid tone, patient unresponsive to deep painful stimuli	☐ Yes	☐ No	☐ Yes	☐ No
b. Pupils are midposition or fully dilated and light reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No

TABLE 2 (Continued)

Section 2. Physical Examination (please check); Note: Spinal Cord Reflexes Are Acceptable

	Examination 1, Date/Time: _____		Examination 2, Date/Time: _____	
c. Corneal, cough, gag reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
d. Sucking and rooting reflexes are absent (in neonates and infants)	☐ Yes	☐ No	☐ Yes	☐ No
e. Oculovestibular reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
f. Spontaneous respiratory effort while on mechanical ventilation is absent	☐ Yes	☐ No	☐ Yes	☐ No

☐ The _____ (specify) element of the examination could not be performed because _____.

Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death (Section 4).

Section 3. Apnea Test

	Examination 1, Date/ Time _____	Examination 2, Date/ Time _____
No spontaneous respiratory efforts were observed despite final $PaCO_2$ ≥60mmHg and a ≥20mmHg increase above baseline (Examination 1). No spontaneous respiratory efforts were observed despite final $PaCO_2$ ≥60mmHg and a ≥20mmHg increase above baseline (Examination 2).	Pretest $PaCO_2$: _____ Apnea duration: _____ min Post-test $PaCO_2$: _____	Pretest $PaCO_2$: _____ Apnea duration: _____ min Post-test $PaCO_2$: _____

Apnea test is contraindicated or could not be performed to completion because _____.
Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death (Section 4).

Section 4. Ancillary Testing

Ancillary testing is required (1) when any components of the examination or apnea testing cannot be completed; (2) if there is uncertainty about the results of the neurologic examination; or (3) if a medication effect may be present. Ancillary testing can be performed to reduce the interexamination period; however, a second neurologic examination is required. Components of the neurologic examination that can be performed safely should be completed in close proximity to the ancillary test. Date/time: _____

☐ EEG report documents electrocerebral silence OR ☐ Yes ☐ No

☐ CBF study report documents no cerebral perfusion ☐ Yes ☐ No

Section 5. Signatures

Examiner 1

I certify that my examination is consistent with cessation of function of the brain and brainstem. Confirmatory examination to follow.

Printed name _____

Signature _____

Specialty _____

Pager #/license # _____

Date mm/dd/yyyy _____

Time _____

TABLE 2 (Continued)

Section 5. Signatures
Examiner 2
I certify that my examination ☐ and/or ancillary test report ☐ confirms unchanged and irreversible cessation of function of the brain and brainstem. The patient is declared brain dead at this time.
Date/time of death _____
Printed name _____
Signature _____
Specialty _____
Pager #/license # _____
Date mm/dd/yyyy _____
Time _____

[a]Two physicians must perform independent examinations separated by specified intervals.
BP = blood pressure; CBF = cerebral blood flow; EEG = electroencephalography; MAP = mean arterial pressure.

- Drug intoxications including barbiturates, opioids, sedatives, intravenous and inhalational anesthetics, antiepileptic agents, and alcohols can cause severe central nervous system depression and may alter the clinical examination to the point where they can mimic brain death.[3,4] Testing for these drugs should be performed if there is concern regarding recent ingestion or administration. When available, specific serum levels of medications with sedative properties or side effects should be obtained and documented to be in a low to mid therapeutic range before neurologic examination for brain death testing. Adequate clearance (based on the age of the child, presence of organ dysfunction, total amount of medication administered, elimination half-life of the drug, and any active metabolites) should be allowed prior to the neurologic examination. In some instances, this may require waiting several half-lives and rechecking serum levels of the medication before conducting the brain death examination. If neuromuscular-blocking agents have been used, they should be stopped, and adequate clearance of these agents should be confirmed by use of a nerve stimulator with documentation of neuromuscular junction activity and twitch response. Unusual causes of coma such as neurotoxins and chemical exposure (ie, organophosphates and carbamates) should be considered in rare cases where an etiology for coma has not been established.

Assessment of neurologic function may be unreliable immediately following resuscitation after cardiopulmonary arrest[7–10] or other acute brain injuries, and serial neurologic examinations are necessary to establish or refute the diagnosis of brain death. It is reasonable to defer the neurologic examination to determine brain death for $\geq$24 hours if dictated by the clinical judgment of the treating physician in such circumstances. If there are concerns about the validity of the examination (eg, flaccid tone or absent movements in a patient with high spinal cord injury or severe neuromuscular disease), if specific examination components cannot be performed due to medical contraindications (eg, apnea testing in patients with significant lung injury, hemodynamic instability, or high spinal cord injury), or if examination findings are inconsistent, continued observation and postponing further neurologic examinations until these issues are resolved are warranted to avoid improperly diagnosing brain death. An ancillary study can be pursued to assist with the diagnosis of brain death in situations where certain examination components cannot be completed.

Neuroimaging with either computed tomography (CT) or magnetic resonance imaging (MRI) should demonstrate evidence of an acute central nervous system injury consistent with the profound loss of brain function. It is recognized that early after acute brain injury, imaging findings may not demonstrate significant injury. In such situations, repeat studies are helpful in documenting that an acute severe brain injury has occurred. CT and MRI are not considered ancillary studies and should not be relied upon to make the determination of brain death.

NUMBER OF EXAMINATIONS, EXAMINERS, AND OBSERVATION PERIODS.

Number of Examinations and Examiners. The committee supports the 1987 guidelines recommending performance of 2 examinations separated by an observation period. The committee recommends that different attending physicians involved in the care of the child perform these examinations.

TABLE 3: Neurologic Examination Components to Assess for Brain Death in Neonates, Infants, and Children,[a] Including Apnea Testing

Reversible conditions or conditions that can interfere with the neurologic examination must be excluded prior to brain death testing. See text for discussion.
1. Coma. The patient must exhibit complete loss of consciousness, vocalization, and volitional activity.
Patients must lack all evidence of responsiveness. Eye opening or eye movement to noxious stimuli is absent.
Noxious stimuli should not produce a motor response other than spinally mediated reflexes. The clinical differentiation of spinal responses from retained motor responses associated with brain activity requires expertise.
2. Loss of all brainstem reflexes including:
Midposition or fully dilated pupils that do not respond to light.
Absence of pupillary response to a bright light is documented in both eyes. Usually the pupils are fixed in a midsize or dilated position (4–9mm). When uncertainty exists, a magnifying glass should be used.
Absence of movement of bulbar musculature including facial and oropharyngeal muscles.
Deep pressure on the condyles at the level of the temporomandibular joints and deep pressure at the supraorbital ridge should produce no grimacing or facial muscle movement.
Absent gag, cough, sucking, and rooting reflex.
The pharyngeal or gag reflex is tested after stimulation of the posterior pharynx with a tongue blade or suction device. The tracheal reflex is most reliably tested by examining the cough response to tracheal suctioning. The catheter should be inserted into the trachea and advanced to the level of the carina followed by 1 or 2 suctioning passes.
Absent corneal reflexes.
Absent corneal reflex is demonstrated by touching the cornea with a piece of tissue paper, a cotton swab, or squirts of water. No eyelid movement should be seen. Care should be taken not to damage the cornea during testing.
Absent oculovestibular reflexes.
The oculovestibular reflex is tested by irrigating each ear with ice water (caloric testing) after the patency of the external auditory canal is confirmed. The head is elevated to 30°. Each external auditory canal is irrigated (1 ear at a time) with approximately 10 to 50ml of ice water. Movement of the eyes should be absent during 1 minute of observation. Both sides are tested, with an interval of several minutes.
3. Apnea. The patient must have the complete absence of documented respiratory effort (if feasible) by formal apnea testing demonstrating a $PaCO_2$ $\geq$60mmHg and $\geq$20mmHg increase above baseline.
Normalization of the pH and $PaCO_2$, measured by arterial blood gas analysis, maintenance of core temperature >35°C, normalization of blood pressure appropriate for the age of the child, and correcting for factors that could affect respiratory effort are a prerequisite to testing.
The patient should be preoxygenated using 100% oxygen for 5–10 minutes prior to initiating this test.
Intermittent mandatory mechanical ventilation should be discontinued once the patient is well oxygenated and a normal $PaCO_2$ has been achieved.
The patient's heart rate, blood pressure, and oxygen saturation should be continuously monitored while observing for spontaneous respiratory effort throughout the entire procedure.
Follow-up blood gases should be obtained to monitor the rise in $PaCO_2$ while the patient remains disconnected from mechanical ventilation.
If no respiratory effort is observed from the initiation of the apnea test to the time the measured $PaCO_2$ is $\geq$60mmHg and $\geq$20mmHg above the baseline level, the apnea test is consistent with brain death.
The patient should be placed back on mechanical ventilator support, and medical management should continue until the second neurologic examination and apnea test confirming brain death are completed.
If oxygen saturations fall below 85%, hemodynamic instability limits completion of apnea testing, or a $PaCO_2$ level of $\geq$60mmHg cannot be achieved, the infant or child should be placed back on ventilator support with

TABLE 3 (Continued)

appropriate treatment to restore normal oxygen saturations, arterial CO_2 pressure, and hemodynamic parameters. Another attempt to test for apnea may be performed at a later time, or an ancillary study may be pursued to assist with determination of brain death.
Evidence of any respiratory effort is inconsistent with brain death, and the apnea test should be terminated.
4. Flaccid tone and absence of spontaneous or induced movements, excluding spinal cord events such as reflex withdrawal or spinal myoclonus.
The patient's extremities should be examined to evaluate tone by passive range of motion, assuming that there are no limitations to performing such an examination (eg, previous trauma, etc), and the patient should be observed for any spontaneous or induced movements.
If abnormal movements are present, clinical assessment to determine whether these are spinal cord reflexes should be done.

[a]Criteria adapted from 2010 American Academy of Neurology criteria for brain death determination in adults.[11]

Children being evaluated for brain death may be cared for and evaluated by multiple medical and surgical specialists. The committee recommends that the best interests of the child and family are served if at least 2 different attending physicians participate in diagnosing brain death to ensure that (1) the diagnosis is based on currently established criteria, (2) there are no conflicts of interest in establishing the diagnosis, and (3) there is consensus by at least 2 physicians involved in the care of the child that brain death criteria are met. The committee also believes that because the apnea test is an objective test, it may be performed by the same physician, preferably the attending physician who is managing ventilator care of the child.

Duration of Observation Periods. The committee recommends the observation period between examinations to be 24 hours for neonates (37 weeks gestational age; up to 30 days) and 12 hours for infants and children (>30 days to 18 years). The first examination determines that the child has met neurologic examination criteria for brain death. The second examination confirms brain death based on an unchanged and irreversible condition. Reduction of the observation period and use of ancillary studies are discussed in separate sections of these guidelines.

APNEA TESTING. Apnea testing should be performed with each neurologic examination to determine brain death in all patients unless a medical contraindication exists. Contraindications may include conditions that invalidate the apnea test (such as high cervical spine injury) or raise safety concerns for the patient (high oxygen requirement or ventilator settings). If apnea testing cannot be completed safely, an ancillary study should be performed to assist with the determination of brain death.

Apnea testing in term newborns, infants, and children is conducted similarly as in adults. Normalization of the pH and $PaCO_2$, measured by arterial blood gas analysis, maintenance of core temperature at >35°C, normalization of blood pressure appropriate for the age of the child, and correcting for factors that could affect respiratory effort are prerequisites to testing. The patient must be preoxygenated using 100% oxygen for 5 to 10 minutes prior to initiating this test. The physician(s) performing apnea testing should continuously monitor the patient's heart rate, blood pressure, and oxygen saturation while observing for spontaneous respiratory effort throughout the entire procedure. $PaCO_2$, measured by blood gas analysis, should be allowed to rise to $\geq$20mmHg above the baseline $PaCO_2$ level and $\geq$60mmHg. If no respiratory effort is observed from the initiation of the apnea test to the time the measured $PaCO_2$ is $\geq$60mmHg and $\geq$20mmHg above the baseline level, the apnea test is consistent with brain death. The patient should be placed back on mechanical ventilator support, and medical management should continue until the second neurologic examination and apnea test confirming brain death are completed. If oxygen saturations fall below 85%, hemodynamic instability limits completion of apnea testing, or a $PaCO_2$ level of $\geq$60mmHg cannot be achieved, the infant or child should be placed back on ventilator support with appropriate treatment to restore normal oxygen saturations, CO_2 pressure to normocarbia, and hemodynamic parameters. In this instance, another attempt to test for apnea may be performed at a later time, or an ancillary study may be pursued to assist with determination of brain death. Evidence of any respiratory effort is inconsistent with brain death, indicating that the apnea test should be terminated and the patient placed back on ventilatory support.

ANCILLARY STUDIES. The committee recommends that ancillary studies are not required to establish brain death and should not be viewed as a substitute for the neurologic examination. Ancillary studies may be used to assist the clinician in making the diagnosis of brain death (1) when components of the examination or apnea testing cannot be completed safely due to the underlying medical condition of the patient; (2) if there is

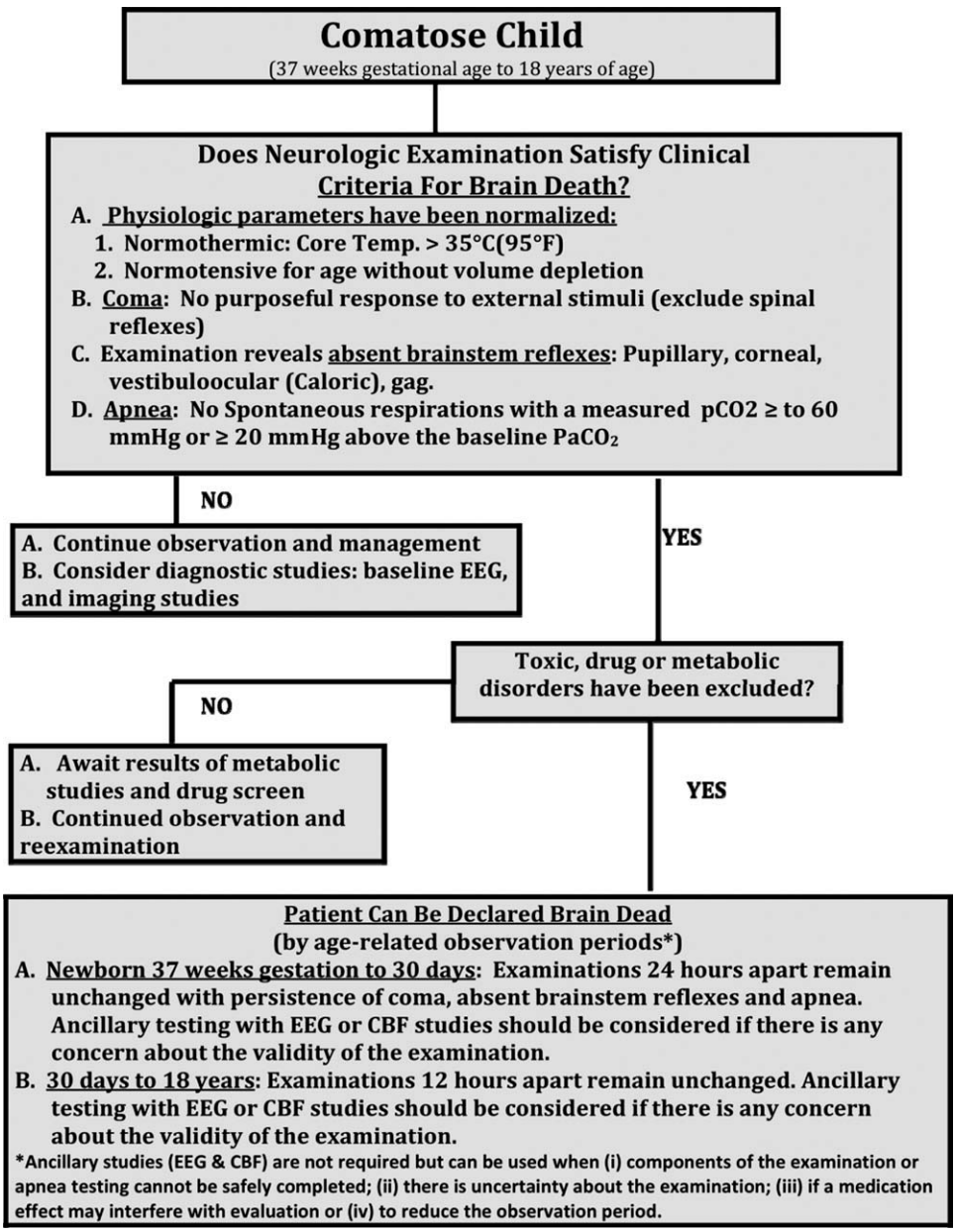

FIGURE: Algorithm to diagnose brain death in infants and children. CBF = cerebral blood flow; EEG = electroencephalography.

uncertainty about the results of the neurologic examination; (3) if a medication effect may be present; or (4) to reduce the interexamination observation period. The term *ancillary study* is preferred to *confirmatory study* because these tests assist the clinician in making the clinical diagnosis of brain death. Ancillary studies may also be helpful for social reasons, allowing family members to better comprehend the diagnosis of brain death.

Four-vessel cerebral angiography is the gold standard for determining absence of cerebral blood flow (CBF). This test can be difficult to perform in infants and small children, may not be readily available at all institutions, and requires moving the patient to the angiography suite. Electroencephalographic documentation of electrocerebral silence and use of radionuclide CBF determinations to document the absence of CBF remain the most widely used methods to support the clinical diagnosis of brain death in infants and children. Both of these ancillary studies remain accepted tests to assist with determination of brain death in infants and children. Radionuclide CBF testing must be performed in accordance with guidelines established by the Society of Nuclear Medicine and the American College of Radiology.[12,13] Electroencephalographic (EEG) testing must be performed in accordance

with standards established by the American Electroencephalographic Society.[14] Interpretation of ancillary studies requires the expertise of appropriately trained and qualified individuals who understand the limitations of these studies to avoid any potential misinterpretation.

Similar to the neurologic examination, hemodynamic and temperature parameters should be normalized prior to obtaining EEG or CBF studies. Pharmacologic agents that could affect the results of testing should be discontinued and levels determined as clinically indicated. Low to mid therapeutic levels of barbiturates should not preclude the use of EEG testing.[15] Evidence suggests that radionuclide CBF study can be utilized in patients with high-dose barbiturate therapy to demonstrate absence of CBF.[16,17] Other ancillary studies such as transcranial Doppler study and newer tests such as CT angiography, CT perfusion using arterial spin labeling, nasopharyngeal somatosensory evoked potential studies, MRI-magnetic resonance angiography, and perfusion MRI have not been studied sufficiently nor validated in infants and children and cannot be recommended as ancillary studies to assist with the determination of brain death in children at this time.

Repeating Ancillary Studies. If the EEG study shows electrical activity or the CBF study shows evidence of flow or cellular uptake, the patient cannot be pronounced dead at that time. The patient should continue to be observed and medically treated until brain death can be declared solely on clinical examination criteria and apnea testing based on recommended observation periods, a follow-up ancillary study can be performed to assist and is consistent with the determination of brain death, or withdrawal of life-sustaining medical therapies is made irrespective of the patient meeting criteria for brain death. A waiting period of 24 hours is recommended before further ancillary testing using radionuclide CBF study is performed to allow adequate clearance of Tc-99m.[12,13] Although no evidence exists for a recommended waiting period between EEG studies, a waiting period of 24 hours is reasonable and recommended before repeating this ancillary study.

Shortening the Observation Period. If an ancillary study, used in conjunction with the first neurologic examination, supports the diagnosis of brain death, the interexamination observation interval can be shortened, and the second neurologic examination and apnea test (or all components that can be completed safely) can be performed and documented at any time thereafter for children of all ages.

Special Considerations for Term Newborns (37 Weeks Gestation) to 30 Days of Age

The ability to diagnose brain death in newborns is still viewed with some doubt, primarily due to the small number of brain-dead neonates reported in the literature[18–20] and uncertainty regarding whether there are intrinsic biological differences in neonatal brain metabolism, blood flow, and response to injury. The Task Force supports that brain death can be diagnosed in term newborns (37 weeks gestation) and older infants, provided the physician is aware of the limitations of the clinical examination and ancillary studies in this age group. It is important to carefully and repeatedly examine term newborns, with particular attention to examination of brainstem reflexes and apnea testing. As with older children, assessment of neurologic function in the term newborn may be unreliable immediately following an acute catastrophic neurologic injury or cardiopulmonary arrest. A period of $\geq$24 hours is recommended before evaluating the term newborn for brain death. Because of insufficient data in the literature, recommendations for preterm infants $<$37 weeks gestational age were not included in these guidelines.

APNEA TESTING. A thorough neurologic examination must be performed in conjunction with the apnea test to make the determination of death in any patient. Data suggest that the $PaCO_2$ threshold of 60mmHg is also valid in the newborn.[21] Apnea testing in the term newborn may be complicated by the following: (1) treatment with 100% oxygen may inhibit the potential recovery of respiratory effort,[22,23] and (2) profound bradycardia may precede hypercarbia and limit this test in neonates. If the apnea test cannot be completed, the examination and apnea test can be attempted at a later time, or an ancillary study may be performed to assist with determination of death. There are no reported cases of any neonate who developed respiratory effort after meeting brain death criteria.

OBSERVATION PERIODS IN TERM NEWBORNS. The committee recommends that the observation period between examinations be 24 hours for term newborns (37 weeks gestational age) to 30 days of age based on data extracted from available literature and clinical experience.

ANCILLARY STUDIES. Available data suggest that ancillary studies in newborns are less sensitive than in older children. Awareness of these limitations would suggest that longer periods of observation and repeated neurologic examinations are needed before making the diagnosis of brain death and also that as in older infants and children, the diagnosis should be made clinically and based on repeated examinations rather than relying exclusively on ancillary studies.

Declaration of Death (for All Age Groups)

Death is declared after the second neurologic examination and apnea test confirm an unchanged and irreversible condition. An algorithm (see Fig) provides recommendations for the process of diagnosing brain death in children. When ancillary studies are used, documentation of components from the second clinical examination that can be completed, including a second apnea test, must remain consistent with brain death. All aspects of the clinical examination, including the apnea test, or ancillary studies must be appropriately documented. A checklist outlining essential examination and testing components is provided in Table 2. This checklist also provides standardized documentation to determine brain death.

Additional Considerations (for All Age Groups)

The implications of diagnosing brain death are of great consequence. Therefore, experienced clinicians who are familiar with neonates, infants, and children and have specific training in neurocritical care should carry out examinations to determine brain death. These physicians must be competent to perform the clinical examination and interpret results from ancillary studies. Qualified clinicians include pediatric intensivists and neonatologists, pediatric neurologists and neurosurgeons, pediatric trauma surgeons, and pediatric anesthesiologists with critical care training. Adult specialists should have appropriate neurologic and critical care training to diagnose brain death when caring for the pediatric patient from birth to 18 years of age. Residents and fellows should be encouraged to learn how to properly perform brain death testing by observing and participating in the clinical examination and testing process performed by experienced attending physicians. It is recommended that both neurologic examinations be performed and documented by an attending physician who is qualified and competent to perform the brain death examination.

Acknowledgments

We thank Dr R. Jaeschke for his direction in the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) evaluation process.

Society of Critical Care Medicine (SCCM) staff support: Laura Kolinski, SCCM; Lynn Retford, SCCM. SCCM Board of Regents: M. Michele Moss, MD, FCCM; Tim Yeh, MD, FCCM. SCCM Facilitator: Lorry Frankel, MD, FCCM.

Potential Conflicts of Interest

Nothing to report.

Appendix

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Endorsements and Approvals

This document has been reviewed and endorsed by the following societies:

- American Academy of Pediatrics (subsections: Section on Critical Care, Section on Neurology)
- American Association of Critical Care Nurses
- Child Neurology Society
- National Association of Pediatric Nurse Practitioners
- Society of Critical Care Medicine
- Society for Pediatric Anesthesia
- Society of Pediatric Neuroradiology
- World Federation of Pediatric Intensive and Critical Care Societies

The American Academy of Neurology affirms the value of this article.

The following subsections of the American Academy of Pediatrics have had the opportunity to review and comment on this document:

- Committee on Bioethics
- Committee on Child Abuse and Neglect
- Committee on Federal Government Affairs
- Committee on Fetus and Newborn
- Committee on Hospital Care
- Committee on Medical Liability and Risk Management
- Committee on Pediatric Emergency Medicine
- Committee on Practice and Ambulatory Medicine
- Committee on State Government Affairs
- Council on Children with Disabilities
- Section on Anesthesiology and Pain Medicine
- Section on Bioethics
- Section on Child Abuse and Neglect
- Section on Emergency Medicine
- Section on Hospital Medicine
- Section on Perinatal Pediatrics
- Section on Neurological Surgery
- Section on Pediatric Surgery

The Pediatric Section of the American Association of Neurosurgeons and the Congress of Neurologic Surgeons have been provided the opportunity to review this document.

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