The 2023 AAN/AAP/CNS/SCCM Pediatric and Adult Brain Death/Death by Neurologic Criteria Consensus Practice Guideline

A Comparison With the 2010 and 2011 Guidelines

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Abstract

In collaboration with the American Academy of Pediatrics, Child Neurology Society, and Society for Critical Care Medicine, the American Academy of Neurology formulated an updated, evidence-informed consensus-based guideline for pediatric and adult brain death/death by neurologic criteria (BD/DNC) determination. In comparison with the prior guidelines, the revisions and additions in this guideline, which are summarized in this review, are intended to (1) ensure recommendations are conservative, yet practical, and emphasize circumstances in which BD/DNC determination should be delayed or deferred, so as to minimize the risk of a false-positive BD/DNC determination; and (2) provide guidance about aspects of BD/DNC determination that clinicians find challenging and/or controversial. We hope that clinicians throughout the United States will use this information to revise their hospital BD/DNC determination policies to conform to the standardized process for BD/DNC determination described in the new guideline, to ensure that every BD/DNC evaluation is consistent and accurate.

Introduction

In collaboration with the American Academy of Pediatrics (AAP), Child Neurology Society (CNS), and Society for Critical Care Medicine (SCCM), the American Academy of Neurology (AAN) formulated an updated, evidence-informed consensus-based guideline for pediatric and adult brain death/death by neurologic criteria (BD/DNC) determination. The 2023 guideline, which builds on the minimum standards for BD/DNC determination established in the World Brain Death Project (WBDP) through international expert consensus, is based on multidisciplinary expertise from US adult and pediatric neurologists, intensivists, and neurosurgeons. It replaces the 2010 AAN guideline for adult BD/DNC determination and the 2011 AAP, CNS, and SCCM guideline for pediatric BD/DNC determination (hereafter referred to as "the prior guidelines"), which were preceded by the 1995 AAN guideline for adult BD/DNC determination and the 1987 guideline for pediatric BD/DNC determination published by the Task Force for the Determination of Brain Death in Children, respectively.

Although the prior pediatric and adult guidelines were very similar, there were a few notable differences. The publication of a single guideline with recommendations for both pediatric and adult BD/DNC determination represents successful achievement of one of the goals outlined at a 2016 multisociety summit organized by the AAN to improve public trust in BD/DNC determination. In the 2023 guideline, recommendations for both pediatric and adult BD/DNC determination are largely identical, but because of physiologic differences between children and adults, and historical considerations, the 2023 guideline includes some age-specific guidance.

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In addition to synthesizing guidance for BD/DNC determination regardless of age, the 2023 guideline expands upon and updates prior recommendations on (1) the prerequisites for BD/DNC determination, (2) examinations/examiners, (3) apnea testing, (4) ancillary testing, and (5) communication about BD/DNC and BD/DNC declaration. 1,3,4 It also addresses aspects of BD/ DNC determination that were not covered in the prior guidelines, including BD/DNC evaluation after treatment with interventions to lower elevated intracranial pressure (ICP) or, in the setting of primary infratentorial injury, preserved neuroendocrine function, targeted temperature management (TTM), extracorporeal membrane oxygenation (ECMO), or pregnancy; requirements for advanced practice providers (APPs) to perform BD/DNC evaluations; absence of obligation to obtain consent to initiate BD/DNC evaluation; and information to include in hospital BD/DNC determination policies about management of disagreements with families. The intent of these changes and additions is to (1) ensure the recommendations are conservative, yet practical, and emphasize the circumstances in which BD/DNC determination should be delayed or deferred, so as to minimize the risk of a false-positive BD/DNC determination, and (2) provide guidance about aspects of BD/DNC determination that clinicians find challenging and/or controversial.

The credibility of BD/DNC determination requires every evaluation to be consistent and accurate (i.e., there can be no false-positive BD/DNC determinations), and the Uniform Determination of Death Act (UDDA) requires determinations of death to be made in accordance with accepted medical standards.9 To facilitate this, hospital BD/DNC determination policies must conform to standardized guidelines established by relevant national medical societies. Reviews of US hospital BD/DNC determination policies after publication of the prior guidelines demonstrated variability in the exclusion of confounding conditions, examinations/ examiners, apnea testing, and ancillary testing. 10,11 To promote consistency between US hospital BD/DNC determination policies and the 2023 guideline, we herein review differences between the 2023 guideline and prior guidelines and highlight new topics. We hope that clinicians throughout the United States will use this information to revise their hospital BD/DNC determination policies to conform to the standardized process for BD/DNC determination described in the 2023 guideline so that every BD/DNC evaluation performed in every hospital by every clinician is consistent and accurate.

Differences Between the 2023 Guideline and the Prior Guidelines

Terminology

There are 3 notable differences between terminology in the 2023 guideline and the prior guidelines. Although these differences do not affect the process or accuracy of BD/DNC determination, they warrant mention. First, like the WBDP, the 2023 guideline uses the term brain death/death by neurologic

criteria" (or "BD/DNC") in lieu of the term "brain death," to both embrace the colloquial terminology and emphasize the equivalence to death by cardiopulmonary criteria. Lecond, the 2023 guideline uses the term "permanent" rather than "irreversible" to describe the severity of brain injury necessary for BD/DNC determination; "permanent" is defined as "(1) will not resume spontaneously and (2) medical interventions will not be used to attempt restoration of function. An extensive discussion of the rationale to use the term "permanent" in this context can be found elsewhere. Finally, the 2023 guideline interprets the UDDA, which requires "loss of all functions of the entire brain, including the brainstem" as "loss of function of the brain as a whole, including the brainstem, resulting in coma, brainstem areflexia and apnea in the setting of an adequate stimulus. The setting of an adequate stimulus.

Prerequisites for BD/DNC Determination

Table 1 provides a detailed comparison of the guidance about prerequisites for performance of a BD/DNC evaluation included in the 2023 guideline and prior guidelines. Age-specific guidance is italicized. There are new recommendations (bold text) about the etiology of brain injury, observation period after brain injury and before initiating BD/DNC evaluation, severity of brain injury, neuroimaging results, temperature, blood pressure, exclusion of intoxication, exclusion of pharmacologic paralysis, laboratory parameters, and other considerations.

The 2023 guideline requires *both* a minimum systolic blood pressure (SBP) *and* a mean arterial pressure (MAP), whereas the prior guidelines required *either* a minimum SBP *or* MAP. 1,3,4 Because blood pressure is age-dependent, the 2023 guideline requires SBP \geq 100 mm Hg and MAP \geq 75 mm Hg in adults and both SBP and MAP \geq 5th percentile for age in children. For patients who have a baseline blood pressure that varies significantly from their age-based normal blood pressure, the 2023 guideline recommends targeting SBP and MAP that approximate the known chronic baseline blood pressure.

To exclude intoxication, the 2023 guideline provides a pharmacokinetic table for common drugs that can depress the CNS and recommends ensuring serum drug levels are within the therapeutic or subtherapeutic range, when able, with specific mention that the pentobarbital level (if administered) must be < 5 μ g/mL or below the lower limit of detection for the laboratory.

In addition, although the 2023 guideline acknowledges that there is no scientific rationale to identify acceptable electrolyte or metabolic thresholds for BD/DNC determination, it includes a table with ranges of values that warrant correction and/or performance of ancillary testing.

Examinations/Examiners

Table 2 compares the guidance in the 2023 guideline and prior guidelines about the examinations/examiners for BD/DNC determination. Age-specific guidance is italicized. There are new recommendations (bold text)

Component	American Academy of Neurology, American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Determination ^{1*}	2010 American Academy of Neurology Guideline for Adult BD/DNC Determination ³	2011 American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric BD/DNC Determination ⁴
Age	•>37 weeks corrected gestational age	• ≥18 years	• >37 weeks gestational age and <18 years
Etiology of brain injury	Establish the presence of a catastrophic, permanent brain injury caused by an identified mechanism known to lead to BD/DNC in the absence of confounders Do not perform a BD/DNC evaluation if there is any evidence of consciousness, preservation of any brainstem reflex, motor movements mediated by the brain/brainstem, or spontaneous breathing Conduct further diagnostic evaluation and do not evaluate for BD/DNC if a patient is comatose, is apneic, and has no brainstem reflexes, but there is no identified mechanism of brain injury known to lead to BD/DNC	Establish the cause of coma through history, examination, neuroimaging, and laboratory tests Exclude mimicking conditions	Establish the presence of irreversible coma due to a known diagnosis Exclude mimicking conditions
Observation period after brain injury and before initiating the BD/ DNC evaluation	Observe for at least 48 h after acute brain injury before initiating BD/DNC evaluation in patients younger than 24 mo Observe for at least 24 h after hypoxic ischemic brain injury before initiating BD/DNC evaluation in patients 24 mo or older Observe for a sufficient amount of time (based on the pathophysiology of the brain injury) after brain injury before initiating BD/DNC evaluation to ensure that there is no potential for recovery Observe for a sufficient amount of time (based on the pathophysiology of the brain injury and the findings on neuroimaging) after medical or surgical interventions to treat elevated intracranial pressure before initiating BD/DNC evaluation to ensure that there is no potential for recovery	X (There is insufficient evidence to determine the minimally acceptable observation period to ensure irreversible loss of function of the brain)	Observe for at least 24 h after birth Observe for 24-48 h or longer after hypoxic ischemic brain injury or other severe acute brain injury if there are concerns or inconsistencies in the examination
Severity of brain injury	Establish that brain injury is permanent (function is lost and will not resume spontaneously and medical interventions will not be used to attempt to restore function)	• Establish that brain injury is irreversible	Establish that brain injury is irreversible
Neuroimaging results	Ensure that neuroimaging is consistent with the mechanism and severity of brain injury Ensure that neuroimaging shows evidence of catastrophic supratentorial injury before BD/DNC evaluation in patients with primary posterior fossa injury	X	Ensure that neuroimaging demonstrates evidence of an acute central nervous system injury consistent with the profound loss of brain function
Temperature	Core temperature >36°C Wait at least 24 h after rewarming to 36°C before BD/DNC evaluation if core body temperature has been ≤35.5°C	• Core temperature >36°C	Core temperature >35°C

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Blood pressure	• Ensure that systolic blood pressure is ≥100 mm Hg and mean arterial pressure is ≥75 mm Hg (only the mean arterial pressure goal is applicable on venoarterial extracorporeal membrane oxygenation) in adults • Ensure that systolic and mean arterial pressure are ≥5 th percentile for age (only the mean arterial pressure goal is applicable on venoarterial extracorporeal membrane oxygenation) in children • Target a systolic and mean arterial pressure that approximates the known chronic baseline for patients who have a baseline blood pressure that varies significantly from their age-based normal	• Ensure that systolic blood pressure is ≥100 mm Hg	• Ensure that systolic or mean arterial blood pressure are ≥ 5 th percentile for age
Exclude intoxication	Exclude intoxication by any substance that can depress the central nervous system by Ensuring blood and urine drug screen are negative (if clinically indicated); Ensuring the serum level is therapeutic or subtherapeutic and not considered to contribute to the neurologic state; Waiting at least 5 half-lives, taking hepatic or renal dysfunction, body mass index, body temperature (hypothermia), and age into consideration (pharmacokinetic table provided for common drugs that depress the central nervous system) Ensure the pentobarbital level is <5ug/mL or below the lower limit of detection for the laboratory (if administered) Ensure the blood alcohol level is <80mg/dL	Exclude intoxication by any substance that can depress the central nervous system by History Drug screen Ensuring the serum level is below the therapeutic range Waiting at least 5 half-lives, taking hepatic or renal dysfunction into consideration Ensure blood alcohol level is <80mg/dL	Exclude intoxication by any substance that can depress the central nervous system (alcohol, antiepileptics, barbiturates, intravenous/inhaled anesthetics, opioids, sedatives) by Ensuring the serum level is in the low to mid-therapeutic range Waiting several half-lives (tables for elimination half-life provided) Exclude alcohol intoxication by checking the blood alcohol level
Exclude pharmacologic paralysis	Exclude pharmacologic paralysis, if administered or suspected, through the use of a train-of-four stimulator or demonstration of deep tendon reflexes	Ensure the presence of 4 twitches on train-of-four with maximum ulnar stimulation	Evaluate nerve function with a nerve stimulator
Laboratory parameters	Exclude severe metabolic, acid- base, or endocrine disturbance (table of laboratory derangements that may confound the BD/DNC evaluation provided) Evidence of neuroendocrine function does not preclude BD/ DNC evaluation	Exclude severe electrolyte, acid- base, or endocrine disturbance	Identify and treat reversible causes of coma that interfere with the clinical evaluation including severe electrolyte derangements, hyperglycemia or hypoglycemia, severe pH disturbances, severe hepatic or renal dysfunction, and inborn errors of metabolism
Other considerations	Pregnancy is not a contraindication for BD/DNC evaluation	X	Χ

about the number of examinations/examiners, qualifications of examiners, observation period between examinations, and components of the examinations.

The most notable update in the 2023 guideline regarding examinations/examiners is the recommendation that clinicians must perform a minimum of one examination in

Component	American Academy of Neurology, American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Determination ^{1*}	2010 American Academy of Neurology Guideline for Adult BD/DNC Determination ³	2011 American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric BD/DNC Determination ⁴
No. examinations/examiners	Minimum of 1 in adults, but a second independent examination may decrease the risk of a false-positive determination due to diagnostic error 2 in pediatrics	•1	• 2 (the first determines the criteria are met and the second confirms irreversibility)
Qualifications of examiners			
Requirements for physicians	Attending physicians who are appropriately credentialed members of a hospitals' medical staff and adequately trained and competent in performance of BD/DNC evaluation in children/adults, as applicable, in accordance with local laws and institutional standards Trainees must be directly supervised by an attending physician, as described above, in settings where local laws and institutional standards do not allow them to perform BD/DNC evaluations independently	All physicians are legally allowed to perform BD/DNC evaluations in most states, but some states or hospitals require examiners to have certain expertise	Attending physicians must specialize in pediatric critical care, pediatric neurology, neonatology, pediatric anesthesiology with critical care training, pediatric neurosurgery, or pediatric trauma surgery and be qualified and competent to perform BD/DNC evaluations Adult attending physicians should have appropriate neurologic and critical care training for pediatric BD/DNC determination
Requirements for advanced practice providers	Advanced practice providers who work in settings where local laws and institutional standards allow them to perform BD/DNC evaluations independently must be appropriately credentialed and adequately trained and competent in BD/DNC determination in children/adults, as applicable Advanced practice providers who work in settings where local laws and institutional standards do not allow them to perform BD/DNC evaluations independently must be directly supervised by an attending physician, as described above	X	X
Demonstration of Competence	Clinicians performing BD/DNC evaluations should demonstrate competence by such means as completion of a supervised BD/DNC evaluation in a clinical environment Supplementary education can include completion of a well-designed online or in-person training course	It is reasonable to require all physicians performing BD/DNC evaluations be intimately familiar with the criteria for BD/DNC determination and demonstrate competence in the evaluation	Trainees should be encouraged to learn how to properly perform BD/ DNC evaluations by observing and participating in the examination process with experienced attending physicians
Avoidance of conflicts of interest	Clinicians involved with surgical recovery of organ for transplantation must not be involved with BD/DNC determination	X	Examiners should have no conflicts of interest related to BD/DNC determination
Observation period between examinations	 In consideration of the stipulated observation period in the 2011 guidelines, a minimum of 12 h should separate the 2 examinations in pediatric patients 	• N/A	• 12 h (>30 days-18 years old) • 24 h (≤30 days old)
Components of examination	Assess for unresponsiveness to visual/auditory/tactile stimulation Assess for the absence of motor response (other than spinal	Assess for unresponsiveness to noxious stimulation Assess for the absence of motor response of face/extremities (other than spinal reflexes)	Assess for unresponsiveness to noxious stimulation Assess for the absence of motor response of face/extremities

Table 2 Examinations/Examiners (continued)

2023 American Academy of Neurology, American Academy of Pediatrics, American Academy of Pediatrics, Child Neurology Society, and Society 2010 Child Neurology Society, and Society American Academy of Neurology of Critical Care Medicine Guideline of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Guideline for Adult BD/DNC for Pediatric BD/DNC Component Determination¹ Determination³ Determination⁴ reflexes, which are described in · Assess for the absence of pupillary Assess for the absence of pupillary detail in a table) of face/extremities reflexes reflexes Assess for the absence of pupillary • Assess for the absence of · Assess for the absence of reflexes oculocephalic and oculovestibular oculovestibular reflexes Assess for the absence of reflexes · Assess for the absence of corneal oculocephalic reflexes unless • Assess for the absence of corneal reflexes Assess for the absence of gag and there is concern for cervical • Assess for the absence of gag and spine/skull base integrity cough reflexes Assess for the absence of sucking · Assess for the absence of cough reflexes oculovestibular reflexes if the and rooting reflexes oculocephalic reflexes are absent or not assessed because of concern for cervical spine/skull base integrity (if there is concern for cervical spine/ skull base integrity, BD/DNC determination can still be made without ancillary testing if oculovestibular reflexes are absent) · Assess for the absence of corneal reflexes • Assess for the absence of gag and cough reflexes Assess for the absence of sucking and rooting reflexes (<6 mo old) All elements of the BD/DNC examination that can be assessed must be assessed and findings must be consistent with BD/DNC (a patient does not meet criteria for BD/DNC if any component is inconsistent with BD/DNC)

adults, but a second clinician may perform a separate and independent examination because performance of 2 independent examinations may decrease the risk of a falsepositive BD/DNC determination because of diagnostic error. This differs from the guidance about the number of examinations/examiners in both the 2010 AAN guideline for adult BD/DNC determination and the WBDP, both of which only require one examination/examiner (although the WBDP suggests, rather than recommends, that a single examination is the minimum standard for BD/DNC determination in adults).2,3 However, it is in accordance with the BD/DNC determination guidelines in most other countries around the world. A 2020 review found that 93% (57/61) BD/DNC determination guidelines that provided information about the number of examiners required ≥2 examiners and 86% (44/53) BD/ DNC determination guidelines that provided information about the number of examinations required ≥2 examinations. 13

In children, similar to the 2011 AAP, CNS, and SCCM guideline, the 2023 guideline recommends 2 clinicians perform independent examinations. ^{1,4} In consideration of the WBDP's recommendation for consideration of an interexamination

observation period and the stipulated interexamination observation period in prior guidelines (1987: 48 hours for patients aged 7 days to 2 months, 24 hours for patients aged 2 months to 1 year, and 12 hours for patients older than 1 year; 2011: 24 hours for patients aged 30 days or younger and 12 hours for patients older than 30 days to 18 years), the 2023 guideline indicates that the interval between the examinations should be 12 hours for all children, independent of age. 1,2,4,6 Dissimilar to the prior pediatric guidelines, the 2023 guideline does not recommend use of ancillary testing to shorten the interexamination observation period.

In addition, the 2023 guideline includes a table of spinal reflexes (reproduced from the WBDP) and a table that summarizes how to perform each examination component, responses consistent with BD/DNC, and clinical considerations for each examination component (adapted from the WBDP).^{1,2}

Apnea Testing

Table 3 summarizes the guidance in the 2023 guideline and prior guidelines on apnea testing, including the number of tests, prerequisites, contraindications, techniques, targets, and reasons to abort testing (bold text indicates new

^{*} Italicized text indicates age-specific guidance. Bold text indicates new recommendations.

Component	American Academy of Neurology, American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Determination ^{1*}	2010 American Academy of Neurology Guideline for Adult BD/DNC Determination ³	2011 American Academy of Pediatrics, Child Neurology Society, and Society of Critica Care Medicine Guideline for Pediatric BD/DNC Determination ⁴
Number of apnea tests	At least 1 in adults (after the final neurologic examination) 2 in pediatric patients (after each neurologic examination)	•1	• 2
Prerequisites	Ensure the patient is not hypoxemic/ hypotensive/hypovolemic	• Ensure the patient is not hypoxemic/ hypotensive/hypovolemic	• Ensure the patient is not hypoxemic/ hypotensive/hypovolemic
Contraindications	High risk of cardiopulmonary decompensation	Prior evidence of carbon dioxide retention (severe obesity or chronic obstructive pulmonary disease)	High cervical spine injury High risk of cardiopulmonary decompensation (e.g., high oxygen requirement or ventilator settings)
Technique	 Ensure that the patient has an invasive arterial catheter whenever possible Ensure PaCO₂ 35-45 mm Hg unless the patient is known to be hypercarbic at baseline (target the chronic baseline PaCO₂ if the patient is known to be hypercarbic and the baseline PaCO₂ is known or the estimated chronic baseline if the baseline PaCO₂ is unknown) Ensure arterial pH 7.35-7.45 Preoxygenate for at least 10 minutes with 100% oxygen on the ventilator (and through the membrane lung, for patients on extracorporeal membrane oxygenation) to PaO₂ >200 mm Hg Provide apneic oxygenation by Discontinuing intermittent mandatory ventilation and placing an insufflation catheter that is <70% of the diameter of the endotracheal tube/tracheostomy through the endotracheal tube/tracheostomy just above the level of the carina and delivering 100% oxygen at 4-6 L/min (adults only); or Stopping intermittent mandatory ventilation and delivering 100% oxygen using continuous positive airway pressure on the ventilator; or Discontinuing intermittent mandatory ventilating resuscitation bag with a functioning positive endexpiratory pressure valve; or Titrating exogenous carbon dioxide into the extracorporeal membrane oxygenation circuit or adjusting the sweep gas flow rate to 0.2-1 L/min (for patients on extracorporeal membrane oxygenation) 	 Preoxygenate for at least 10 minutes with 100% oxygen to PaO₂ >200 mm Hg 	Ensure that the patient has an invasive arterial catheter whenever possible Ensure normalization of the pH and PaCO ₂ , measured by arterial blood gas analysis Preoxygenate for 5-10 minutes with 100% oxygen Discontinue intermittent mandatory ventilation Provide apneic oxygenation by attaching a T-piece or self-inflating bag valve system such as a Mapleson circuit to the endotracheal tube or using continuous positive airway pressure if needed
Apnea testing target	PaCO ₂ ≥60 mm Hg and ≥20 mm Hg above the pre-apnea test baseline level and arterial pH <7.3, in patients known to not have chronic hypercarbia or patients known/suspected to have chronic hypercarbia whose baseline PaCO ₂ is not known (sample from both the distal arterial line and extracorporeal membrane circuit postoxgenator for patients on venoarterial extracorporeal membrane oxygenation) PaCO ₂ ≥60 mm Hg and ≥20 mm Hg above the chronic elevated premorbid baseline level and arterial pH <7.3, in	• PaCO ₂ ≥60 mm Hg or ≥20 mm Hg above baseline normal PaCO ₂	• PaCO ₂ ≥60 mm Hg and ≥20 mm Hg above baseline

Component	2023 American Academy of Neurology, American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Determination ^{1*}	2010 American Academy of Neurology Guideline for Adult BD/DNC Determination ³	2011 American Academy of Pediatrics, Child Neurology Society, and Society of Critica Care Medicine Guideline for Pediatric BD/DNC Determination ⁴
	hypercarbia whose baseline PaCO ₂ is known (sample from both the distal arterial line and extracorporeal membrane circuit postoxgenator for patients on venoarterial extracorporeal membrane oxygenation)		
Reasons to abort testing	≥1 breath (the patient does not meet criteria for BD/DNC) Systolic blood pressure <100 mm Hg or mean arterial pressure <75 mm Hg in adults or <5 th percentile for age in children despite titration of vasopressors, inotropes, and/or intravenous fluids Progressive decrease in oxygen saturation <85% Cardiac arrhythmia with hemodynamic instability	Respiration (abdominal or chest excursions or a brief gasp) Systolic blood pressure <90 mm Hg Oxygen saturation <85% for >30 seconds	 Respiratory effort Hemodynamic instability Oxygen saturation <85% PaCO₂ ≥60 mmHg cannot be achieved

^{*} Italicized text indicates age-specific guidance. Bold text indicates new recommendations.

recommendations and italicized text indicates age-specific guidance). The 2023 guideline requires clinicians to perform at least one apnea test after the final examination in adults and 2 apnea tests, one after each examination, in children; the prior guidelines required one apnea test in adults and 2 in children.

The most notable change to the apnea testing recommendations in the 2023 guideline is the target: (1) PaCO₂ ≥60 mm Hg and ≥20 mm Hg above the pre-apnea test baseline level *and* arterial pH < 7.3 in patients known to not have chronic hypercarbia or patients known/suspected to have chronic hypercarbia whose baseline PaCO2 is not known or (2) $PaCO_2 \ge 60 \text{ mm Hg } and \ge 20 \text{ mm Hg above the}$ chronic elevated premorbid baseline level and arterial pH < 7.3 in patients known to have chronic hypercarbia whose baseline PaCO₂ is known. This differs from the 2010 AAN guideline for adult BD/DNC determination (which recommended a target $PaCO_2$ of ≥ 60 mm Hg $or \geq 20$ mm Hg above baseline normal PaCO2) and the 2011 AAP, CNS, and SCCM guideline for pediatric BD/DNC determination (which recommended a target PaCO₂ of ≥60 mm Hg and ≥20 mm Hg above baseline), both of which did not include a pH target.^{3,4} However, it is similar to the apnea testing target included in the WBDP (pH < 7.3 and PaCO₂ \geq 60 mm Hg, unless the patient has preexisting hypercapnia, in which case the target should be ≥ 20 mm Hg above baseline if known).² Although very few BD/DNC determination guidelines around the world include a pH target for apnea testing, the rationale to do so is based on the understanding that the combination of hypercarbia and secondary acidosis should

stimulate functional medullary chemoreceptors to prompt respiration. 1,13

The 2023 guideline also includes a table with detailed guidance for performance of apnea testing which addresses prerequisites, preparatory steps, techniques to provide apneic oxygenation, cardiopulmonary monitoring during testing, instructions for performance of arterial blood gases, targets, and reasons to abort testing prematurely.¹

Ancillary Testing

Table 4 compares recommendations about ancillary testing in the 2023 guideline and prior guidelines. ^{1,3,4} There are new recommendations (bold text) about ancillary testing caveats, indications, and acceptable vs unacceptable tests. Age-specific guidance is italicized. The most notable change is the designation of EEG as an unacceptable test for all patients; it was previously considered acceptable for both pediatric and adult BD/DNC determination. This designation is consistent with WBDP guidance that EEG no longer be used as an ancillary test for adult BD/DNC determination. ² The decision to denote EEG as an unacceptable ancillary test is based on concern that while it assesses function of the cerebral hemispheres, it does not evaluate brainstem function, which is problematic given that ancillary testing is often performed because of inability to fully assess brainstem function. ¹

The 2023 guideline also includes a table that summarizes the diagnostic criteria, advantages, disadvantages, sensitivity/ specificity, and comments about acceptable ancillary tests, which is adapted from the WBDP. 1,2

Table 4 Ancillary Testing 2023 American Academy of Neurology, American Academy of Pediatrics, Child 2011 Neurology Society, and Society of 2010 American Academy of Pediatrics, Child Neurology Society, and Society of Critical Critical Care Medicine Guideline for American Academy of Neurology Pediatric and Adult BD/DNC Guideline for Adult BD/DNC Care Medicine Guideline for Pediatric BD/ Component Determination¹ Determination³ DNC Determination⁴ • Only perform ancillary testing to assist • There is the potential for disparities • Ancillary testing is not a substitute for **Caveats** with BD/DNC determination if the between tests and for false-positive neurologic examination examination or apnea testing cannot results All portions of the neurologic examination be completed or the findings cannot be • In lieu of ordering ancillary tests, clinicians that can be completed should be interpreted adequately may decide to defer BD/DNC completed and documented before Do not use ancillary testing to assist determination if clinical findings are ancillary testing is performed with BD/DNC determination · If the results of ancillary testing are unreliable o In the setting of hypothermia; equivocal or there is concern about its o In the setting of high levels of validity, BD/DNC cannot be declared so medications that depress the central the patient should be observed until BD/ nervous system; DNC can be declared based on the o Solely because of the presence of an examination and apnea testing, or a open fontanelle, skull fracture, skull follow-up ancillary test can be performed defect, or cerebrospinal fluid (a waiting period of 24 h is recommended diversion device; or before clinical re-evaluation or repeat o To avoid performing otherwise testable ancillary testing) elements of the BD/DNC evaluation The neurologic examination(s) and apnea test(s) need to be performed to the fullest extent possible and findings must be consistent with BD/DNC before ancillary testing is performed If any findings on the examination(s)/ apnea test(s) are consistent with brain-mediated activity, ancillary testing must not be performed because the patient does not meet criteria for BD/DNC • Inability to exclude intoxication by any **Indications** • Inability to correct metabolic • Inability to complete the examination derangements adequately, but the because of an underlying medical substance that can depress the central neurologic examination(s)/apnea condition nervous system test(s) are consistent with BD/DNC • Uncertainty about the reliability of part(s) • Inability to complete the examination · Inability to perform components of the of the neurologic examination because of an underlying medical • Inability to perform the apnea test examination because of an underlying medical condition (e.g., fracture of the • Uncertainty about the reliability of part(s) cervical spine/skull base/orbit, severe of the neurologic examination facial injury/abnormality, injury to the Inability to perform the apnea test cervical spine) • Desire to reduce the interexamination • Inability to interpret whether examination observation period Desire to allow family members to better findings such as limb movements are spinally mediated comprehend BD/DNC determination · Inability to perform or complete the apnea test because of concern about the risk of cardiopulmonary decompensation or hypoxemia, hypotension, or a cardiac arrhythmia with hemodynamic instability before reaching the arterial pH and PaCO₂ targets • Knowledge/suspicion of chronic hypercarbia without knowledge of the chronic baseline PaCO₂ Acceptable tests • 4-vessel catheter angiography · 4-vessel catheter angiography • 4-vessel catheter angiography • Radionuclide cerebral blood flow scan Electroencephalography Electroencephalography • Radionuclide cerebral blood flow scan • Transcranial Doppler ultrasonography (in • Radionuclide cerebral blood flow scan adults only) Transcranial Doppler ultrasonography Unacceptable Electroencephalography • Transcranial Doppler ultrasonography • Computed tomography angiography • Auditory-evoked potentials • Magnetic resonance angiography Computed tomography angiography tests · Somatosensory-evoked potentials · Magnetic resonance imaging Computed tomography perfusion Computed tomography angiography Somatosensory-evoked potentials Magnetic resonance angiography • Magnetic resonance angiography Bispectral index · Magnetic resonance imaging • Magnetic resonance imaging · Somatosensory-evoked potentials

^{*} Italicized text indicates age-specific guidance. Bold text indicates new recommendations.

Component	American Academy of Neurology, American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric and Adult BD/DNC Determination ^{1*}	2010 American Academy of Neurology Guideline for Adult BD/DNC Determination ³	2011 American Academy of Pediatrics, Child Neurology Society, and Society of Critical Care Medicine Guideline for Pediatric BD/DNC Determination ⁴
Communication before initiating the BD/DNC evaluation	Make a reasonable attempt to inform families about the intent to perform BD/DNC evaluation Provide emotional support and guidance Ensure communication is clear, concise, and supportive Use simple terminology that families can understand Permit families to be present during the neurologic examination and apnea test Inform families about the potential for spinal reflexes and the fact that these movements do not preclude BD/DNC determination	Inform families about the intent to perform BD/DNC evaluation	Provide support and guidance for families as they face difficult end-of-life decisions and attempt to understand what has happened to their child Ensure communication is clear, concise, and supportive Inform families that once death has occurred, continuation of medical therapies, including ventilator support, is no longer an option unless organ donation is planned Permit families to be present during the evaluation to help them understand that their child has died
Need for consent to initiate the BD/DNC evaluation	No obligation to obtain consent before BD/DNC evaluation unless otherwise stipulated by institutional policy/state law or regulations	X	X
Time of death	Document the time of death as the time the arterial blood gas results from the final apnea test (if >1 is performed) demonstrate that the arterial pH and PaCO ₂ are consistent with BD/DNC criteria (for patients who meet clinical criteria for BD/DNC) Document the time of death as the time an attending clinician (e.g., nuclear medicine physician or angiographer) documents in the medical record that the ancillary test results are consistent with BD/DNC (if ancillary testing is required and performed)	Document the time of death as the time the arterial blood gas results demonstrate that the PaCO ₂ is consistent with BD/DNC criteria (for patients who meet clinical criteria for BD/DNC) Document the time of death as the time the ancillary test has been officially interpreted if apnea testing is not completed	Document the time of death as the time after completion of the second examination and apnea test
Steps after death	Provide families with a reasonable but limited amount of time with the deceased patient before discontinuation of organ support, the length of which is based on the judgment of the attending clinician of record in accordance with the institution's policy Educate families and discuss risks and benefits to the fetus of continuing maternal organ support for pregnant patients (in conjunction with clinicians knowledgeable in maternal-fetal medicine, child neurology, and neonatology, as needed)	Contact an organ procurement organization, in accordance with federal and state laws	Give families adequate time to grieve with the child after death is declared
Information to include in hospital BD/DNC determination policies about management of disagreements with families	Include a process to resolve disagreements with families who do not agree with the medical team's plan to initiate BD/DNC evaluation and/or termination of organ support after BD/DNC determination Include consideration of providing a reasonable period to accommodate families after death	X	X

* Bold text indicates new recommendations.

Communication About BD/DNC and BD/DNC Declaration

Finally, Table 5 presents the recommendations on communication about BD/DNC and BD/DNC declaration included in the 2023 guideline and prior guidelines. ^{1,3,4} There are new recommendations (bold text) about communication before initiating BD/DNC evaluation, need for consent to initiate BD/DNC evaluation, time of death, steps after death, and information to include in hospital BD/DNC determination policies about management of disagreements with families. Additional information about guidance on these new topics is addressed below.

New Topics in the 2023 Guideline

BD/DNC Determination After Interventions to Lower Elevated ICP

The prior guidelines and the WBDP do not address BD/DNC determination after interventions to lower elevated ICP, but questions have been raised about BD/DNC determination in this situation. The 2023 guideline indicates that after medical or surgical interventions to treat elevated ICP, clinicians must wait a sufficient amount of time to ensure there is no recovery of brain function before initiating BD/DNC evaluation as determined based on the pathophysiology of brain injury and the neuroimaging findings. In the pathophysiology of brain injury and the neuroimaging findings.

BD/DNC Determination in the Setting of Primary Infratentorial Injury

The UDDA requires that there be "loss of all functions of the entire brain, including the brainstem" for BD/DNC determination, but the prior guidelines did not address BD/ DNC determination in the setting of primary infratentorial injury. 3,4,9 Review of BD/DNC determination guidelines in other countries demonstrated that BD/DNC determination in the setting of primary infratentorial injury is infrequently addressed and guidance is inconsistent and sometimes ambiguous. 13,15 However, a meta-analysis that included 3,602 BD/DNC determinations demonstrated that the mean prevalence of primary infratentorial brain injury leading to BD/DNC was 6% (range of 2%-16% across studies). 16 The authors identified 38 cases of isolated brainstem death (cases in which the clinical evaluation was consistent with BD/DNC, but ancillary testing demonstrated cerebral blood flow or electrical activity); 28 of these patients ultimately had loss of cerebral blood flow and/or electrical activity, consistent with whole-brain death. To guide BD/DNC determination in regions that follow the whole-brain concept of BD/DNC, the WBDP suggests that in the setting of isolated brainstem pathology (primary infratentorial injury±supratentorial signs of intracranial hypertension on neuroimaging), ancillary testing be used to assess for the absence of cerebral blood flow even if the examination and apnea test are consistent with BD/DNC.²

To meet the UDDA's requirement (interpreted by the 2023 guideline as "loss of function of the brain as a whole, including the brainstem, resulting in coma, brainstem areflexia and apnea in the setting of an adequate stimulus"), the 2023 guideline recommends that clinicians ensure a primary infratentorial injury has also led to catastrophic supratentorial injury, as demonstrated by conventional neuro-imaging, before initiating a BD/DNC evaluation. ^{1,9}

The Effect of Preserved Neuroendocrine Function on BD/DNC Determination

Because the UDDA requires that there be "loss of all functions of the entire brain, including the brainstem" for BD/DNC determination, some argue that BD/DNC determination requires loss of neuroendocrine function.^{9,17} The 1995 AAN guideline for adult BD/DNC determination specifically noted that BD/DNC determination does not require the absence of diabetes insipidus.⁵ In a section on the need to exclude confounding conditions before the BD/DNC evaluation, the 2010 AAN guideline for adult BD/DNC determination mentioned that (1) there should be no severe endocrine disturbance at the time of BD/DNC evaluation, but (2) hypotension due to hypovolemia secondary to diabetes insipidus is common after BD/DNC.³ Neither the 1987 guideline nor the 2011 guideline for pediatric BD/DNC determination addresses neuroendocrine function. 4,6 Both the WBDP and a 2019 AAN position statement state that neuroendocrine function does not preclude BD/DNC determination.2,18

As previously noted, the 2023 guideline interprets the UDDA's requirement as "loss of function of the brain as a whole, including the brainstem, resulting in coma, brainstem areflexia and apnea in the setting of an adequate stimulus." As such, the 2023 guideline recommends that clinicians may initiate a BD/DNC evaluation and declare BD/DNC despite evidence of neuroendocrine function.

BD/DNC Determination After Treatment With TTM

While the prior guidelines recommended a minimum core temperature for BD/DNC evaluation to address the fact that hypothermia may suppress brain function, they did not stipulate an observation period once the temperature has normalized to exclude the potential for recovery of neurologic function.^{3,4} Review of BD/DNC determination guidelines from around the world demonstrated that only 3% (2/78) clearly indicated the amount of time to observe a patient who was hypothermic (because of the use of TTM or other etiologies) after rewarming; both advised waiting 24 hours.¹³ The WBDP also recommends delaying BD/DNC evaluation for 24 hours after the temperature has normalized and consideration of use of a cerebral blood flow study, in addition to examination and apnea testing, if medications or drugs that could depress the CNS were previously administered.2

The 2023 guideline recommends that for patients whose core temperature has been $\leq 35.5^{\circ}$ C, clinicians (1) should wait a minimum of 24 hours after rewarming to $\geq 36^{\circ}$ C before BD/DNC evaluation and (2) must not use ancillary testing to bypass this observation period. 1

BD/DNC Determination on ECMO

Although one-third of adult and pediatric deaths on ECMO are BD/DNC declarations, the prior guidelines did not address BD/DNC determination on ECMO.^{3,4,19,20} Review of BD/DNC determination guidelines in other countries around the world demonstrated that only 3% (2/78) provided guidance about BD/DNC determination on ECMO.¹³ The WBDP includes recommendations about BD/DNC determination on ECMO, and these were used as the basis for guidance on this topic in the 2023 guideline. 1,2 The 2023 guideline recommends that when performing apnea testing for patients on ECMO, preoxygenation should be provided through both the membrane lung and the ventilator.1 To achieve an adequate rise in PaCO2, exogenous carbon dioxide can be added to the ECMO circuit and/or the sweep gas flow rate can be titrated down to 0.2-1 L/min. For patients on venoarterial ECMO, arterial blood should be sampled from both the distal arterial line and the ECMO circuit post-oxygenator, and values from both locations must meet the pH and PaCO₂ targets for BD/DNC determination.

BD/DNC Determination During Pregnancy

The 2010 AAN guideline for adult BD/DNC determination did not address BD/DNC determination during pregnancy, and a 2016 review of US hospital BD/DNC determination policies found that 3% (8/317) did not allow BD/DNC determination if the fetus was potentially viable; of policies that allowed BD/DNC determination in pregnant persons, 99% (305/309) did not include guidance about who was responsible for making decisions for the fetus and 94% (289/ 309) did not provide guidance about fetal management after maternal BD/DNC declaration. 3,21 Similarly, review of BD/ DNC determination guidelines in other countries around the world demonstrated that only 1% (1/78) mentioned the need to consider pregnancy before discontinuation of organ support after BD/DNC declaration. 13 The WBDP (1) recommends the decision about whether to continue organ support after maternal BD/DNC declaration for the sake of the fetus be made after multidisciplinary discussion with the decedent's family about potential fetal outcome, taking into consideration the decedent's advance directives or expressed wishes, and (2) provides detailed guidance about prevention and management of maternal systemic complications if the decision is made to continue organ support for the sake of the fetus.2

The 2023 guideline notes that pregnancy is not a contraindication to BD/DNC evaluation and that after BD/DNC determination in a pregnant person, there should be a multidisciplinary discussion (including the clinicians involved in the care of the decedent and clinicians knowledgeable in maternal-fetal medicine, child neurology, and neonatology) with the surrogate decision-makers about the risks and benefits to the fetus of continuing maternal organ support. The AAN provides additional guidance about BD/DNC determination in pregnancy in a 2019 position statement. See the decedent and clinicians knowledges and provides about BD/DNC determination in pregnancy in a 2019 position statement.

Requirements for Advanced Practice Providers to Perform BD/DNC Evaluations

The prior guidelines only addressed physician qualifications to perform BD/DNC evaluations, but a review of US hospital BD/DNC determination policies found that 2% (8/342) indicated that APPs could perform BD/DNC evaluations. ^{3,4,10} The 2023 guideline recommends that (1) in settings where acute and critical care APPs are performing BD/DNC evaluations independently in accordance with local laws and hospital policies, they must be appropriately credentialed and adequately trained and be competent in BD/DNC evaluation in children or adults, as applicable, and (2) in settings where APPs are not permitted to perform BD/DNC evaluations independently in accordance with local laws and hospital policies, they must be directly supervised by an attending clinician who is an appropriately credentialed member of the hospitals' medical staff and is adequately trained and competent in BD/ DNC evaluation in children or adults, as applicable.¹

The Absence of Obligation to Obtain Consent to Initiate BD/DNC Evaluation

Prior guidelines did not address the need for consent to initiate the BD/DNC evaluation, but the WBDP and a 2019 AAN position statement note that while reasonable efforts should be made to notify a patient's family of the intent to perform a BD/DNC evaluation, there is no obligation to obtain consent.^{2-4,18} The 2023 guideline reiterates this recommendation.¹

Information to Include in Hospital BD/DNC Determination Policies About Management of Disagreements With Families About BD/DNC Determination

Prior guidelines did not address management of disagreements with families about BD/DNC determination, but surveys demonstrate that half of pediatric and adult clinicians involved in BD/DNC determination have dealt with disagreements with families about performance of a BD/DNC evaluation or discontinuation of organ support after BD/DNC determination. A review of US hospital BD/DNC determination policies found that three-quarters do not address management of disagreements with families about BD/DNC determination. The WBDP provides a number of recommendations about management of disagreements with families about BD/DNC determination including notation in hospital BD/DNC determination policies about (1) indications to accommodate objections and (2) the interventions that can be (a) initiated, (b)

continued, or (c) withheld after BD/DNC determination.² A 2019 AAN position statement discusses management of disagreements with families about BD/DNC determination and encourages clinicians to ensure hospital BD/DNC determination policies address management of objections including the conditions and time frame for accommodation, as appropriate.¹⁸

The 2023 guideline recommends that hospital BD/DNC determination policies include (1) a process to resolve disagreements with families who object to the plan to initiate BD/DNC evaluation and/or terminate organ support after BD/DNC determination and (2) consideration of provision of a reasonable period to accommodate families.¹

Conclusion

The UDDA requires that determinations of death be made in accordance with accepted medical standards. With the retirement of the 2010 AAN guideline for adult BD/DNC determination and the 2011 AAP, CNS, and SCCM guideline for pediatric BD/DNC determination, because there are no other nationally recognized guidelines for BD/DNC determination in the United States, the 2023 AAN, AAP, CNS, and SCCM guideline for pediatric and adult BD/DNC determination will now be the accepted medical standard for BD/DNC determination. ^{1,8} It is thus the responsibility of clinicians involved in BD/DNC determination in the United States to coordinate with hospital administrators, legal teams, and ethicists, as appropriate, to update their hospital policies on BD/DNC determination to conform to the 2023 guideline. ⁹

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