Brain death

DR SAJAD AHMAD TAK (DNB SCHOLAR)

REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

Brain Death/Death by Neurologic Criteria Determination

By Ariane Lewis, MD; Matthew P. Kirschen, MD, PhD

ABSTRACT

PURPOSE OF REVIEW: This article describes the prerequisites for brain death/death by neurologic criteria (BD/DNC), clinical evaluation for BD/DNC (including apnea testing), use of ancillary testing, and challenges associated with BD/DNC determination in adult and pediatric patients.

RECENT FINDINGS: Although death determination should be consistent among physicians and across hospitals, states, and countries to ensure that someone who is declared dead in one place would not be considered alive elsewhere, variability exists in the prerequisites, clinical evaluation, apnea testing, and use of ancillary testing to evaluate for BD/DNC. Confusion also exists about performance of an evaluation for BD/DNC in challenging clinical scenarios, such as for a patient who is on extracorporeal membrane oxygenation or a patient who was treated with therapeutic hypothermia. This prompted the creation of the World Brain Death Project, which published an international consensus statement on BD/DNC that has been endorsed by five world federations and 27 medical societies from across the globe.

SUMMARY: The World Brain Death Project consensus statement is intended to provide guidance for professional societies and countries to revise or develop their own protocols on BD/DNC, taking into consideration local laws, culture, and resource availability; however, it does not replace local medical standards. To that end, pending publication of an updated guideline on determination of BD/DNC across the lifespan, the currently accepted medical standards for BD/DNC in the United States are the 2010 American Academy of Neurology standard for determination of BD/DNC in adults and the 2011 Society of Critical Care Medicine/American Academy of Pediatrics/Child Neurology Society standard for determination of BD/DNC in infants and children.

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REVIEW Open Access

Brain death: a clinical overview

William Spears[1], Asim Mian[2] and David Greer[1*]

Abstract

Brain death, also commonly referred to as death by neurologic criteria, has been considered a legal definition of death for decades. Its determination involves many considerations and subtleties. In this review, we discuss the philosophy and history of brain death, its clinical determination, and special considerations. We discuss performance of the main clinical components of the brain death exam: assessment of coma, cranial nerves, motor testing, and apnea testing. We also discuss common ancillary tests, including advantages and pitfalls. Special discussion is given to extracorporeal membrane oxygenation, target temperature management, and determination of brain death in pediatric populations. Lastly, we discuss existing controversies and future directions in the field.

Keywords: Brain death, Death by neurologic criteria, Brainstem death, ECMO, Targeted temperature management, Pediatrics

History of brain death

Preceding the 1950s, the concept of death revolved around cessation of cardiorespiratory function. It naturally followed that cessation of brain function occurred after the loss of respiration and circulation, and indeed loss of brain activity was considered a critical component of death.

In the years that followed, the development of advanced live support measures including cardiopulmonary resuscitation (CPR) and positive pressure ventilation (PPV) brought this interdependence and the traditional definition of death into question. In 1959, the concept of brain death/death by neurologic criteria (BD/DNC) was first theorized as "le coma dépassé", by Mollaret and Goulon, who described an apneic, comatose patient without brainstem reflexes or electroencephalographic (EEG) activity [1]. Neurologists began to postulate that neurologic function was equally or more vital than cardiopulmonary function, and began a process to define death neurologically, independent of other essential organ functions. In 1968, a group of Harvard faculty proposed the first clinical definition as the Harvard Brain Death Criteria, which consisted of clinical and EEG criteria [2]. In 1980, the Uniform Determination of Death Act established a legal basis for a neurologic determination of death in the U.S., and adult guidelines were put forth in the 1995 (and revised 2010) American Academy of Neurology (AAN) guidelines on the determination of BD/DNC. In 1987, the American Academy of Pediatrics task force on brain death in children published guidelines for the pediatric population [3], which was updated in 2011 [4, 5].

What does brain death mean?

First, what does the term "brain death" truly mean? This is perhaps best understood by exploring the evolution and controversy of the idea. In fact, one of the salient remaining debates in the field involves the terminology of brain death, sometimes also referred to as "whole brain death", or "brainstem death". In order to promote a broad understanding by lay persons, scientists, and legal powers, most experts advocate for use of the term BD/DNC [6].

Proponents of the idea of neurologic criteria to diagnose brain death argue that the body is more than the sum of its parts, and that death is equated to loss of the whole person [7]. For example, most would not argue

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Determination of Brain Death/Death by Neurologic Criteria
The World Brain Death Project

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IMPORTANCE There are inconsistencies in concept, criteria, practice, and documentation of brain death/death by neurologic criteria (BD/DNC) both internationally and within countries.

OBJECTIVE To formulate a consensus statement of recommendations on determination of BD/DNC based on review of the literature and expert opinion of a large multidisciplinary, international panel.

PROCESS Relevant international professional societies were recruited to develop recommendations regarding determination of BD/DNC. Literature searches of the Cochrane, Embase, and MEDLINE databases included January 1, 1992, through April 2020 identified pertinent articles for review. Because of the lack of high-quality data from randomized clinical trials or large observational studies, recommendations were formulated based on consensus of contributors and medical societies that represented relevant disciplines, including critical care, neurology, and neurosurgery.

EVIDENCE SYNTHESIS Based on review of the literature and consensus from a large multidisciplinary, international panel, minimum clinical criteria needed to determine BD/DNC in various circumstances were developed.

RECOMMENDATIONS Prior to evaluating a patient for BD/DNC, the patient should have an established neurologic diagnosis that can lead to the complete and irreversible loss of all brain function, and conditions that may confound the clinical examination and diseases that may mimic BD/DNC should be excluded. Determination of BD/DNC can be done with a clinical examination that demonstrates coma, brainstem areflexia, and apnea. This is seen when (1) there is no evidence of arousal or awareness to maximal external stimulation, including noxious visual, auditory, and tactile stimulation; (2) pupils are fixed in a midsize or dilated position and are nonreactive to light; (3) corneal, oculocephalic, and oculovestibular reflexes are absent; (4) there is no facial movement to noxious stimulation; (5) the gag reflex is absent to bilateral posterior pharyngeal stimulation; (6) the cough reflex is absent to deep tracheal suctioning; (7) there is no brain-mediated motor response to noxious stimulation of the limbs; and (8) spontaneous respirations are not observed when apnea test targets reach pH <7.30 and $Paco_2$ ≥60 mm Hg. If the clinical examination cannot be completed, ancillary testing may be considered with blood flow studies or electrophysiologic testing. Special consideration is needed for children, for persons receiving extracorporeal membrane oxygenation, and for those receiving therapeutic hypothermia, as well as for factors such as religious, societal, and cultural perspectives; legal requirements; and resource availability.

CONCLUSIONS AND RELEVANCE This report provides recommendations for the minimum clinical standards for determination of brain death/death by neurologic criteria in adults and children with clear guidance for various clinical circumstances. The recommendations have widespread international society endorsement and can serve to guide professional societies and countries in the revision or development of protocols and procedures for determination of brain death/death by neurologic criteria, leading to greater consistency within and between countries.

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History

- Before 1950 , the concept of death revolved around irreversible cessation of cardiorespiratory function.

cessation of brain function

- **In 1959,** the concept of brain death/death by neurologic criteria (BD/ DNC) was first theorized as “le coma dépassé”,

(By Mollaret and Goulon.).

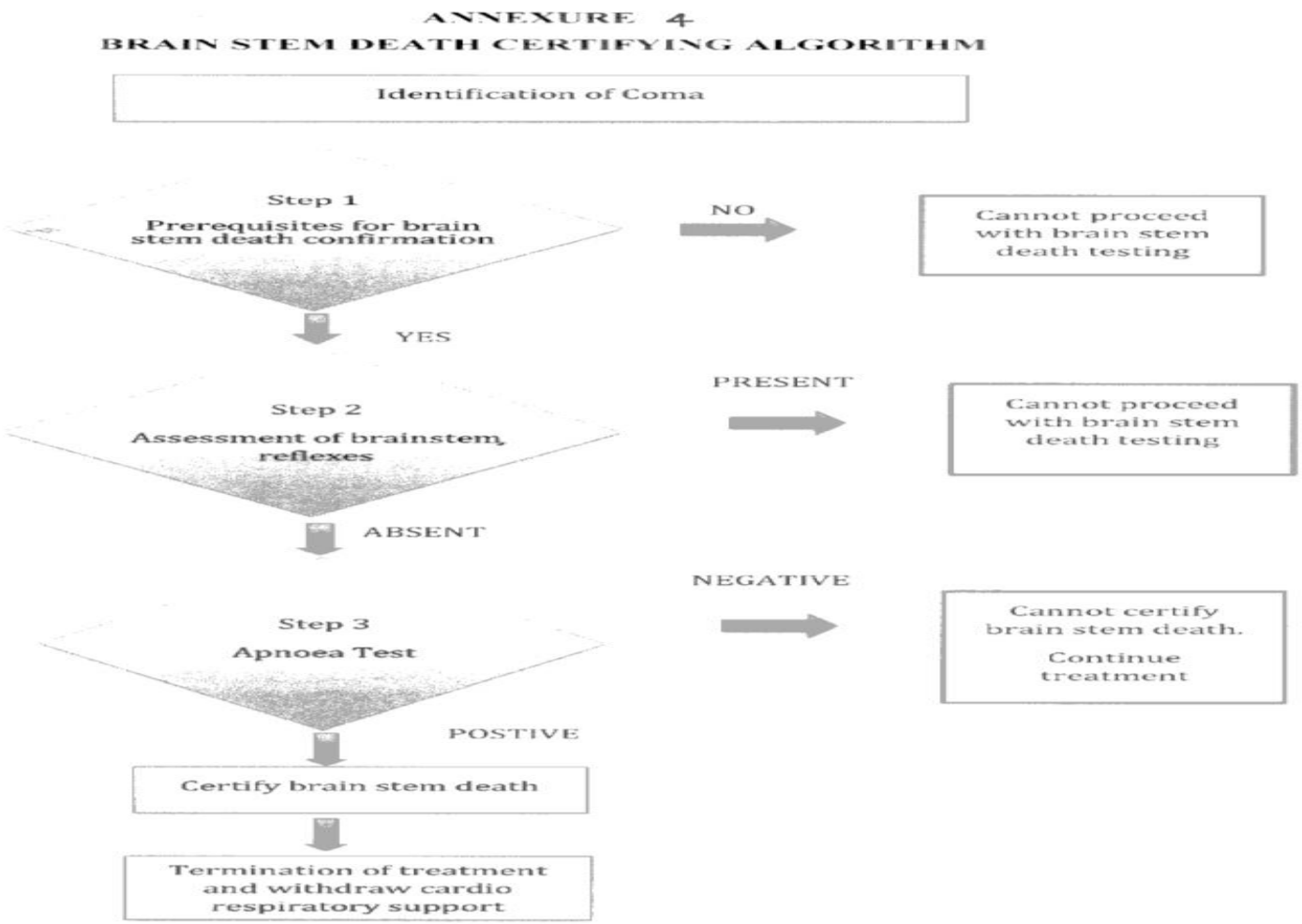
- **In 1968,** ……..first clinical defnition as the Harvard Brain Death Criteria, which consisted of clinical and EEG criteria .

- **1981**…. the Uniform Determination of Death Act.
- The American Academy of Neurology (AAN) published a standard for BD/DNC in adults in 1995 and updated it in 2010.
- The Task Force for Determination of Brain Death in Children published a standard for BD/DNC in infants and children in **1987**;
- This was updated in 2011 by the Society of Critical Care Medicine (SCCM), American Academy of Pediatrics (AAP), and Child Neurology Society (CNS).

Indian perspective

- **Transplantation of Human Organs (THO) act was passed by Indian parliament in 1994, which legalized the Brainstem death.**
- Even after 25 yrs , …no uniform guidelines exist for the procedure.
- Four physicians are required,(including a neurologist or neurosurgeon).
- Two clinical assessments atleast 6 hrs apart .

Algorithm (kerala)



- **The WORLD BRAIN DEATH PROJECT … ..to formulate a consensus statement of recommendations on BD/DNC….**

- **Published …august 2020.**

- **BD/DNC** is defined as the complete and permanent loss of brain function as defined by unresponsive coma with loss of capacity for consciousness , brainstem reflexes and the ability to breathe independently.

Concepts of BD/DNC

- Three formulations;
- Whole brain death (advocated by USA and WBDP)
- Brainstem death (advocated by UK and india)
- Higher brain death.

PREREQUISITES FOR BRAIN DEATH/DEATH BY NEUROLOGIC CRITERIA

Component	AAN 2010	SCC/AAP 2011	World brain death project .
Etiology	**Establish cause of irreversible coma by history,exam, brain imaging etc.** (eg; hypoxic ischemic brain injury,stroke,meningitis,traumatic brain injury etc **Exclude mimics** (fulminant GBS, botulism, high cervical cord injury)	do	Do
Observation period before ist examination.	Not mentioned (no specific time limit)	**24 to 48 hrs** after cpr or severe brain injury. 24hr after birth	24 hrs after resuciated cardiac arrest and after rewarming in therapeutic hypothermia or birth asphyxia

	AAN 2010	SCC/AAP ..2011	WBDP
irreversibility	Establish that brain injury is irreversible	Do Neuroimaging should demonstrate evidence of an acute central nervous system injury consistent with the profound loss of brain function	do Suggested to ensure neuroimaging evidence of intracranial hypertension is present or intracranial pressure measurements equal or exceed mean arterial pressure
Temperature	>36 °C (96.8 °F)	>35 °C (95 °F)	≥36 °C (96.8 °F)
Blood pressure	Systolic blood pressure ≥100 mm Hg	Systolic or mean arterial blood pressure should not be less than 2 standard deviations below age-appropriate norms	Systolic blood pressure ≥100 mm Hg or mean arterial pressure ≥60 mm Hg in adults and age-appropriate in pediatric patients

	AAN 2010	SSC/AAP 2011	WBDP
Exclude intoxication	Exclude Drug or intoxicant by history, drug screen, ensuring serum level is below the therapeutic range, and waiting at least 5 half-lives, taking hepatic or renal dysfunction into consideration. Ensure blood alcohol level is below 0.08%	do (eg; (alcohol, antiepileptic drugs, barbiturates, IV/inhaled anesthetics, opioids, sedatives)	Do
Exclude pharmacologic paralysis	Ensure presence of four twitches with maximum ulnar stimulation	Evaluate nerve function with a nerve stimulator	Exclude pharmacologic paralysis with a peripheral nerve stimulator/train-offour or by demonstrating presence of deep tendon reflexes
Laboratory parameters	exclude severe electrolyte, acidbase, and endocrine	do	do

2. Clinical examination /tests

TABLE 12-3 **Clinical Examination/Examiner Specifications for Brain Death/Death by Neurologic Criteria**

Component	2010 American Academy of Neurology Medical Standards for BD/DNC in Adults[10]	2011 Society of Critical Care Medicine, American Academy of Pediatrics, and Child Neurology Society Standards for BD/DNC in Infants and Children[12]	World Brain Death Project[2]
Number of examiners	One	Two	One
Qualifications of examiners	Not stated	Attending physicians who are qualified and competent to perform the brain death examination Specialty of pediatric critical care, pediatric neurology, neonatology, pediatric anesthesiology with critical care training, pediatric neurosurgery, or pediatric trauma surgery 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	Practitioners who have completed training, are licensed to independently practice medicine, and are trained in determination of BD/DNC, counseling families at end of life, and managing devastating brain injuries Pediatric patients should be evaluated by experienced pediatric clinicians with specialty in neonatology, neurosurgery, pediatric critical care, pediatric neurointensive care, pediatric neurology, or trauma surgery
Number of examinations	One	Two	One in adults and two in pediatric patients
Observation period between examinations	Not stated	12 hours (>30 days-18 years of age) 24 hours (37 weeks estimated gestational age to 30 days)	If two examinations are performed, an observation period between examinations is unnecessary
Components of clinical examination	Assessment for unresponsiveness	Assessment for unresponsiveness	Assessment for unresponsiveness
	Assessment for absence of motor response of face/extremities	Assessment for absence of motor response of face/extremities	Assessment of absence of motor response of face/extremities
	Assessment for absence of pupillary light reflex	Assessment for absence of pupillary light reflex	Assessment for absence of pupillary light reflex
	Assessment for absence of oculocephalic and oculovestibular reflexes	Assessment for absence of oculovestibular reflex	Assessment for absence of oculocephalic and oculovestibular reflexes
	Assessment for absence of corneal reflex	Assessment for absence of corneal reflex	Assessment for absence of corneal reflex
	Assessment for absence of gag and cough reflexes	Assessment for absence of gag and cough reflexes Assessment for absence of sucking and rooting reflexes (neonates and infants)	Assessment for absence of gag and cough reflexes Assessment for absence of sucking and rooting reflexes (neonates)

BD/DNC = brain death/death by neurologic criteria.

pupillary light refex

- Naked eye and flash light
- A magnifying glass or quantitative pupillometry is strongly recommended.
- **absence of ipsilateral and contraleral pupillary response , with pupils fixed in a** mid-sized or dilated position (4-6mm).
- very small pupils (<2 mm) should alert the practitioner to a possible confounder, e.g. from opiate intoxication or isolated brainstem injury.

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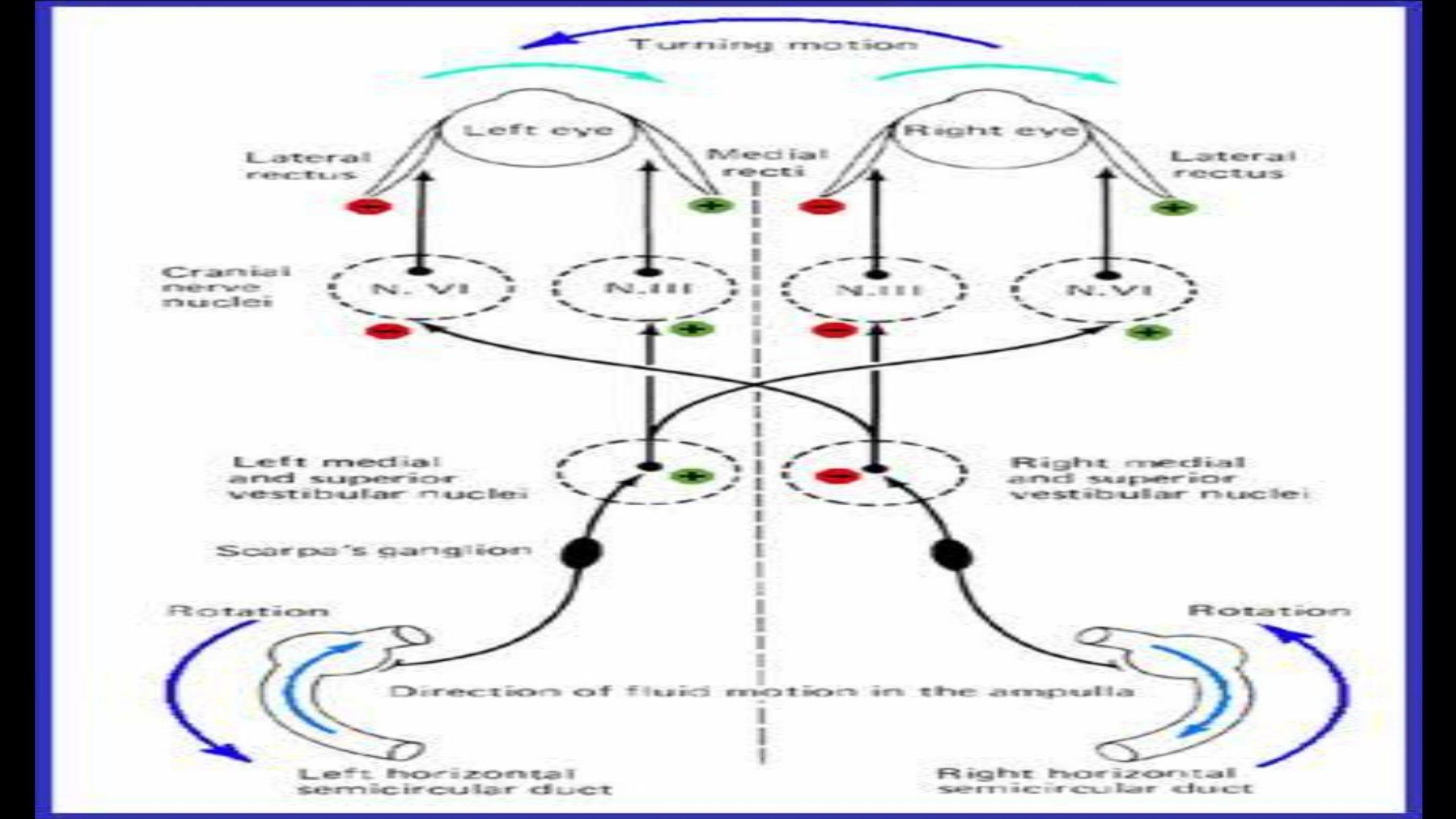
Quick Concepts

Oculocephalic Reflex Testing During Brain Death Examination

3. Oculocephalic (OCR) and oculovestibular (OVR) reflexes
   A. Test
      - OCR: Rotate the head briskly horizontally to both sides. There should be no movement of the eyes relative to head movement. Testing vertically is optional
      - OVR: Examine the auditory canal for patency and an intact tympanic membrane. Elevate the head to 30° to place the horizontal semicircular canals in the correct vertical position. Irrigate with at least 30 mL of ice water for at least 60 seconds using a syringe or a syringe attached to a catheter placed inside the canal. Test both sides separately, with a 5-minute interval between to allow the endolymph temperature to equilibrate
   B. Response consistent with BD/DNC
      - There should be absence of extraocular movements. Detection of any extraocular movements is not compatible with BD/DNC


Turning motion
Left eye
Right eye
Lateral rectus
Medial recti
Lateral rectus
Cranial nerve nuclei
N. VI
N.III
N.III
N.VI
Left medial and superior vestibular nuclei
Right medial and superior vestibular nuclei
Scarpa's ganglion
Rotation
Rotation
Direction of fluid motion in the ampulla
Left horizontal semicircular duct
Right horizontal semicircular duct

5. Motor responses of the face and limbs
   A. Test
      - Apply deep pressure to all of the following:
        i. the condyles at the level of the temporomandibular joints
        ii. the supraorbital notch bilaterally
        iii. the sternal notch
        iv. all 4 extremities, both proximally and distally
      - Insert a cotton swab on a stick in each nostril to perform "nasal tickle" testing

B. Response consistent with BD/DNC

- Noxious stimuli should not produce grimacing, facial muscle movement, or a motor response of the limbs other than spinally mediated reflexes
- Noxious stimuli above the foramen magnum should not produce any movement in the face or body. Noxious stimuli below the foramen magnum should not produce any movement in the face but may elicit spinally mediated peripheral motor reflexes

6. Gag and cough reflexes
   A. Test
      - Gag reflex: stimulate the posterior pharyngeal wall bilaterally with a tongue depressor or suction catheter
      - Cough reflex: stimulate the tracheobronchial wall to the level of the carina with deep endotracheal placement of a suction catheter
   B. Response consistent with BD/DNC
      - Absence of gag and cough
   C. Considerations
      - The efferent limb for the cough reflex includes the phrenic nerve, which may be injured in persons with high cervical cord injuries, so ancillary testing is recommended in this setting

3. Apnea test

Apnea test

- **Contraindications.**
- Prior evidence of carbon dioxide retention (severe obesity or chronic obstructive pulmonary disease).
- High cervical spine injury.
- Chronic hypoxemia due to cyanotic heart disease.

- **Technique:**

- Preoxygenate for at least 10 minutes with 100% oxygen to PaO2 >200 mm Hg
- Ensure PaCO2 35-45 mm Hg
- Reduce ventilator frequency to 10 breaths per minute
- Reduce positive end-expiratory pressure to 5 cm H2O Disconnect the ventilator Preserve oxygenation with an insufflation catheter placed through the endotracheal tube delivering 100% oxygen at 6 L/min Use T-piece circuit or continuous positive airway pressure (CPAP), if needed

- Disconnect the ventilator
- Preserve oxygenation with an insufflation catheter placed through the endotracheal tube delivering 100% oxygen at 6 L/min .
- Use T-piece circuit or continuous positive airway pressure (CPAP), if needed

- Apnea testing target:

- pH <7.3
- PaCO2 ≥60 mm Hg ,unless the patient has preexisting hypercapnia, in which case target

  should be ≥20 mm Hg above baseline, if known

- **Reasons to abort testing:**
- Spontaneous respirations witnessed
- Systolic blood pressure <100 mm Hg or mean arterial pressure <60 mm Hg
- Sustained oxygen desaturation <85%.
- Unstable arrhythmia

Apnea Testing in Brain Death

An Animation

Fernando Goldenberg
Jeffrey Frank
Agnieszka Ardelt
Dale Mertes

Summary of BD/DNC

- Establish cause of irreversible brain injury (irreversible coma)
- Excluding confounding factors
- Absent brainstem reflexes
- Apnea

TABLE 12-5 **Ancillary Testing for Brain Death/Death by Neurologic Criteria**

Component	2010 American Academy of Neurology Medical Standards for BD/DNC in Adults[10]	2011 Society of Critical Care Medicine, American Academy of Pediatrics, and Child Neurology Society Standards for BD/DNC in Infants and Children[12]	World Brain Death Project[2]
Indications	Components of the examination cannot be completed because of the underlying medical condition Uncertainty about the reliability of parts of the neurologic examination Apnea test cannot be performed	Components of the examination cannot be completed because of the underlying medical condition Uncertainty about the reliability of parts of the neurologic examination Apnea test cannot be performed Medication effect may be present Reduce interexamination observation period May be helpful for social reasons, allowing family members to better comprehend the diagnosis of BD/DNC	Components of the examination cannot be completed because of the underlying medical condition Uncertainty regarding interpretation of spinal-mediated motor reflexes High cervical spine injury Uncertainty about drug elimination Severe metabolic, acid-base, or endocrine derangements that cannot be corrected and are judged to potentially be contributing to loss of brain function The whole-brain death formulation is being followed and there is isolated brainstem pathology Law/regional guidance mandates ancillary testing
Acceptable tests	Four-vessel catheter angiography EEG Radionuclide cerebral blood flow scan Transcranial Doppler	Four-vessel catheter angiography EEG Radionuclide cerebral blood flow scan	Four-vessel catheter angiography Radionuclide cerebral blood flow scan Transcranial Doppler (adults only) EEG only if mandated by regional law or policy or if craniovascular impedance has been affected by open skull fracture, decompressive craniectomy, or an open fontanelle/sutures, in which case it should be performed in conjunction with somatosensory and brainstem auditory evoked potentials

BD/DNC = brain death/death by neurologic criteria; EEG = electroencephalography.

EEG criteria

- **Electro cerebral inactivity (ECI):** defined as absence over all regions of head of identifiable electrical activity of cerebral origin,whether spontaneous or induced by physiological stimuli.

- Working definition; ..absence of non artifactual electrical activity with a peak to peak amplitude above 2uVwhen recording from scalp electrode pairs that were 10cm or further apart.

Requirements

- **Electrodes and montages**

French guidelines…minimum of 8 electrodes

AAN ….atleast 16 channels.

Midline electrodes (Fz,Cz, Pz) should be included (detect low voltage activity , less artefacts).

- 2. **Interelectrode impedence:**
- 10 to 10,000 ohms.
- Needle electrodes (high impedence) and electrode caps (short circuit) should be avoided .

3. **EEG RECORDING :**

sensitivity ….maximum 2uV/mm.

High frequency filters (low pass) …not below 30Hz

Low frequency filters ……not above 1hz.

- **Timing** :
- Atleast 30 minutes.

- Integrity of entire recording system should be tested.

- Auditory and bilateral somatosensory stimuli (touch and pain) …repeatedly applied and be clearly marked.

- AAN…1 EEG is sufficient
- French and European …..2 EEG.

- **Evaluation of extrcerebral potentials:**

  ACNS (American clinical neurophysiology society) recommend ;

- ECG monitoring
- Continous video recording ….to identify any artifact in EEG.
- Respiration artefact must be documented with specific notations.
- Additional monitor ….for other artifacts from pt .or local environment (a pair of elctrodes on dorsum of hand)

Table 1. Tests of Brain Blood Flow

Test	Diagnostic criteria	Advantages	Disadvantages	Sensitivity/ specificity, %	Comments
Digital subtraction angiography/conventional 4-vessel angiography	Absence of contrast within the intracranial arterial vessels	• Reference standard for ancillary tests	• Requires transport to imaging suite • Invasive (requires technical skills) • Kidney susceptibility to contrast • Stasis filling–false negative	100/ 100[a,41,42]	• Persistence of flow does not contradict comprehensive competent clinical diagnosis • Equipment and operator dependence limits practical use; still used as calibration standard
Radionuclide angiography	Absence of radiologic activity upon imaging of the intracranial vault	• Can be performed at bedside • No kidney susceptibility to contrast	• Limited evaluation of brainstem • Limited availability	98.5/ 56[43]	• Persistence of flow does not contradict comprehensive competent clinical diagnosis
Radionuclide perfusion scintigraphy	Absence of radiologic activity indicating metabolic uptake upon imaging of the intracranial vault	• Can be performed at bedside (planar imaging)	• Limited availability • Planar imaging may limit brainstem evaluation • SPECT requires patient transport to scanner	Planar: 77.8/ 100; SPECT: 88.4/100[a,44]	• Uptake of isotope indicates metabolic activity
Transcranial Doppler ultrasound	Biphasic (oscillating) flow or small systolic spikes on initial assessment of intracranial arterial supply, confirmed or proceeding to absent flow velocity signal on second assessment	• Easily performed at bedside • No contrast required • Can assess carotid and basilar circulations	• Operator expertise required • 10% of patients have no acoustic windows	90/98[45]	• Persistence of flow does not contradict comprehensive competent clinical diagnosis
Computed tomography angiography	No opacification of intracranial arterial circulation, or deep veins	• Widely available • Relatively quick to perform	• Requires transport to imaging suite • Kidney susceptibility to contrast • Stasis filling–false negative	52-97/ 100[a,46-65]	• Persistence of flow does not contradict comprehensive competent clinical diagnosis • Limited consensus on required diagnostic criteria • Small number of studies with lack of reference standard • Not currently validated against above accepted tests
Magnetic resonance angiography	No visualization of intracranial arterial circulation	• Not affected by stasis filling • Visualization improved by gadolinium	• Requires transport to imaging suite • Specialized critical care equipment required in scanner • Time of flight imaging affected by hematoma	93-100[66-69]/ 100[a,66,67]	• Persistence of flow does not contradict comprehensive competent clinical diagnosis • Small number of studies with lack of reference standard • Uncertainty about risks of nephrogenic systemic fibrosis[70] • Not currently validated against above accepted tests

Abbreviations: BD/DNC, brain death/death by neurologic criteria; SPECT, single-photon emission computed tomography.

[a] Specificity is assumed on basis of experimental data but should be interpreted with caution[71] given the limitation of studies that reported only on clinically confirmed BD/DNC.

Table 2. Tests of Electrophysiological Function

Test	Diagnostic criteria	Advantages	Disadvantages	Sensitivity/ specificity, %	Comments
EEG	No detectable electrical activity (≥2 μV) over a 30-min period	• Noninvasive • Can be performed at bedside	• Predominantly cortical assessment • Electromagnetic environmental noise can erroneously suggest cerebral electrical activity • Confounded by sedation, hypothermia, toxic states, metabolic disorders	53-80. 4/97[41,72]	Concerns on confounding and interobserver variability limit use; may be more specific used in conjunction with multimodality evoked potential testing
Somatosensory evoked potentials	Bilateral absence of any electrical transmission through the brainstem and cerebrum in the setting of an intact signal in the brachial plexus and spinal cord	• Noninvasive • Can be performed at bedside • Less susceptible to sedation than EEG	• Confounded by cervical spinal cord injury, isolated brainstem lesions, sedation, hypothermia	100/78[73]	Limited specificity as isolated test; may be helpful as component of multimodality evoked potential testing, used in conjunction with EEG
Auditory evoked potentials	Bilateral absence of waveforms through the brainstem to auditory cortex	• Noninvasive • Can be performed at bedside • Less susceptible to sedation than EEG	• Confounded by sedation, profound hypothermia, isolated eighth cranial nerve or brainstem lesions • Limited to auditory cortex		Not useful as isolated test; may be helpful as component of multimodality testing
Visual evoked potentials	Bilateral absence of waveforms through brainstem to visual cortex with preserved electroretinogram	• Noninvasive • Can be performed at bedside • Less susceptible to sedation or hypothermia than EEG	• Confounded by sedation, retinal or optic nerve lesions • Limited to visual cortex		Not useful as isolated test; may be helpful as component of multimodality evoked potential testing

Abbreviation: EEG, electroencephalography.

Figure 1. Checklist for Determination of Brain Death

Prerequisites (all must be checked)

- ☐ Coma, irreversible and cause known.
- ☐ Neuroimaging explains coma.
- ☐ CNS depressant drug effect absent (if indicated toxicology screen; if barbiturates given, serum level <10 µg/mL).
- ☐ No evidence of residual paralytics (electrical stimulation if paralytics used).
- ☐ Absence of severe acid-base, electrolyte, endocrine abnormality.
- ☐ Normothermia or mild hypothermia (core temperature >36°C).
- ☐ Systolic blood pressure ≥100 mm Hg.
- ☐ No spontaneous respirations.

Examination (all must be checked)

- ☐ Pupils nonreactive to bright light.
- ☐ Corneal reflex absent.
- ☐ Oculocephalic reflex absent (tested only if C-spine integrity ensured).
- ☐ Oculovestibular reflex absent.
- ☐ No facial movement to noxious stimuli at supraorbital nerve, temporomandibular joint.
- ☐ Gag reflex absent.
- ☐ Cough reflex absent to tracheal suctioning.
- ☐ Absence of motor response to noxious stimuli in all four limbs (spinally mediated reflexes are permissible).

Apnea testing (all must be checked)

- ☐ Patient is hemodynamically stable.
- ☐ Ventilator adjusted to provide normocarbia ($PaCO_2$ 35–45 mm Hg).
- ☐ Patient preoxygenated with 100% FiO_2 for >10 minutes to PaO_2>200 mm Hg.
- ☐ Patient well-oxygenated with a positive end-expiratory pressure (PEEP) of 5 cm of water.
- ☐ Provide oxygen via a suction catheter to the level of the carina at 6 L/min or attach T-piece with continuous positive airway pressure (CPAP) at 10 cm H_2O.
- ☐ Disconnect ventilator.
- ☐ Spontaneous respirations absent.
- ☐ Arterial blood gas drawn at 8–10 minutes, patient reconnected to ventilator.
- ☐ PCO_2 ≥60 mm Hg, or 20 mm Hg rise from normal baseline value.

OR:

- ☐ Apnea test aborted.

Ancillary testing (only one needs to be performed) (to be ordered only if clinical examination cannot be fully performed due to patient factors, or if apnea testing inconclusive or aborted)

- ☐ Cerebral angiogram
- ☐ HMPAO SPECT
- ☐ EEG
- ☐ TCD

Time of death (DD/MM/YY) _____/_____/_____

Name of physician and signature

_____

Copies of this summary and additional companion tools are available at or through AAN Member Services at (800) 879-1960.

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Thankyou