

Clinical Practice Title: Determination of Brain Death/Death by Neurologic Criteria (Adult)	
Clinical Practice Owner (CCG) / Author:	Contact Information
Neuroscience CCG	Name: Douglas Franz, MD
Mohamed Teleb, MD	email: douglas.franz@bannerhealth.com

Brief Description of Clinical Practice
All adults (≥18 years) with suspected irreversible brain injuries will be evaluated using confirmatory diagnostic testing to determine irreversible cessation of all functions of the entire brain (brain death).

Reviewed History			
Reviewed by (name/group):	Original Date:	Revision Date:	Review Date:
Neuroscience CCG	February 24, 2016	May 4, 2021	
Editorial Board	April 6, 2016	June 9, 2021	
Critical Care CCG	April 27, 2016	June 16, 2021	
ED CCG	N/A	June 16, 2021	
Hospital Medicine CCG	N/A	June 16, 2021	
Surgery CCG	N/A	July 16, 2021	
Trauma System Steering Council	N/A	June 17, 2021	
Risk	N/A	November 5, 2021	
Legal	N/A	November 5, 2021	
Donor Network of AZ	N/A	November 12, 2021	
CNO	May 2016	February 7, 2022	
CMO	April 28, 2016	April 28, 2022	

Clinical Leadership Team (CLT) Resources		
CLT	Original Approval Date: May 26, 2016	Revision Approval Date: June 22, 2022
Go-Live	Original Go-live Date:	Revision Go-live Date:
Toolkit link: https://collaboration.bannerhealth.com/clinical/CareMgmt/BHCorp_CM/nscg/deathdeter/Implement/Forms/AllItems.aspx		

Associated Documents		
Type	Number	Name
Policy	5981	Brain Death Declaration
Protocol		

Determination of Brain Death/Death by Neurologic Criteria (Adult)

PRACTICE APPROACH

Expected Clinical Practice

PRACTICE STATEMENT

All adults (≥ 18 years) with suspected irreversible brain injuries will be evaluated using confirmatory diagnostic testing to determine irreversible cessation of all functions of the entire brain (brain death/ death by neurologic criteria).

RATIONALE

In 1981 as the result of a Presidential Commission, the Uniform Determination of Death Act (UDDA) proposed a legal definition of death 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 brain stem, is dead. A determination of death must be made with accepted medical standards” (JAMA, 1981).

All states have adopted the UDDA, although some states have added specific amendments. An evidence-based protocol and physician documentation is required to ensure proper diagnosis and to meet legal standards. Though organ donation is typically considered for those undergoing brain death testing, declaration should happen regardless if patient has organ donation options or not.

Brain death/death by neurologic criteria (BD/DNC) confirmation requires a bedside physical examination demonstrating absence of all brainstem reflexes, coma or unresponsiveness to noxious stimuli including no purposeful or reflexic motor responses derived from brain function, and a lack of spontaneous breathing (via apnea testing) (Wijdicks, 1995; 2010; Greer, et al, 2020). In clinical contexts where apnea testing is not safe or feasible, confirmatory diagnostic studies are indicated to determine BD/DNC (Wijdicks, 1995; 2010). Using these approaches to BD/DNC diagnosis, no cases of recovered function in adults has been published in the medical literature (Wijdicks, 2010; Lustbader, et al, 2011).

Only one full exam with apnea testing is needed; more than one exam can lead to decreased organ donation rates. There is no published history of a second exam showing reversibility when the first was performed appropriately according to accepted criteria as stated above (Wijdicks, 2010). Despite this evidence, the number of exams and specific requirements should comply with your states department of health recommendations and BD/DNC laws. There may be times when two independent examinations help facilitate family interactions.

CLINICAL APPROACH

The clinical methodology will consist of determining the appropriate Physician/Provider–type as well as prerequisites to the determination of BD/DNC, neurologic exam documentation requirements, apnea testing and ancillary diagnostic testing.

Provider Responsibility and Determination

Brain death should be determined by a neurologist, neurosurgeon, or critical care specialist/trauma surgeon with adequate specific experience and knowledge. It is recommended that physicians have completed either a BD/DNC simulation or an online certification. All clinicians performing these evaluations should be attending physicians. Integration of trainees and advanced practice providers is determined by the appropriate department (Neurology, Neurosurgery, Critical Care, Trauma), with attending physician oversight and ultimate responsibility for the determination. For facilities without these specialists (Neurology, Neurosurgery, Critical Care, Trauma), an online course or real-time support and guidance from a Banner Health Telemedicine-approved resource is suggested.

For potential organ donors: It is recognized that there may be a potential conflict of interest if a physician involved with declaration of BD/DNC is also involved with care of a transplant recipient. In those situations, another physician not involved with care of a transplant recipient should be asked to do the BD/DNC examination.

Prerequisites

- Clinicians should ensure that a patient has sustained a catastrophic, irreversible brain injury by an identified mechanism that is known to lead to BD/DNC before initiating a BD/DNC evaluation. If a patient is comatose with lack of brainstem reflexes and apnea, and there is not an identified mechanism of brain injury that is known to lead to BD/DNC, the patient requires further diagnostic evaluation and should not undergo evaluation for BD/DNC. Neuroimaging that has been performed after sufficient time has elapsed from the onset of the brain injury should show findings consistent with a mechanism of catastrophic injury known to lead to BD/DNC.
- There is no evidence to support a specific observation period between brain injury and performance of the BD/DNC evaluation; however, patients with hypoxic-ischemic brain injury and patients with prior hypothermia should have their exam delayed at least 24 hours after the injury and rewarming to $\geq 36^{\circ}$ C. See flow chart below for further BD/DNC declaration guidance in therapeutic hypothermia patients.
- Central nervous system (CNS) drug depressants must be excluded as potential causes. Drug screens, alcohol level (≤ 80 mg/dL), and if possible plasma drug levels below the therapeutic range (e.g. pentobarbital level) should be considered when indicated. Alternatively, when a history of CNS depressant exposure is present, one can wait five half-lives before clinical examination to ensure no contribution from that drug. Caution should be used, however, if renal or hepatic dysfunction is present or if hypothermia has been used, as these conditions that might delay drug metabolism. See flow chart below for further BD/DNC declaration guidance in therapeutic hypothermia patients.
- There should be no evidence of neuromuscular blockade (defined by train-of-four testing with four twitches, or if train-of-four is not available, the presence of deep tendon reflexes) after previous use of paralytic agents before BD/DNC examination.
- Severe (as by physician judgment) electrolyte disturbances, acid-base, and endocrine disorders should not be present. If metabolic derangements cannot be adequately corrected, physicians may proceed with clinical BD/DNC evaluation and if consistent with BD/DNC confirm with ancillary testing.
- Normothermia or near-normothermia ($\geq 36^{\circ}$ C) should be established using warming blankets if needed.
- Normotension as defined by systolic blood pressure ≥ 100 mm Hg and MAP ≥ 75 mm Hg must be present, using pressor therapy and/or fluids when needed. If the patient has a chronic condition with a baseline blood pressure that varies significantly from their age-based normal range, clinicians should target a blood pressure that approximates the known chronic baseline for that individual patient.
- In cases where two examinations are required by law, a qualified Physician conducting the initial exam may not conduct the second exam (in 6 US states: California, Connecticut, Florida, Iowa, Kentucky and Louisiana). The second evaluation must be performed by another qualified Physician. There is no physiological reason to require an observation period between these 2 evaluations.

Neurologic Exam Documentation Requirements

- Not responsive to visual, auditory and tactile stimulation
- No motor response must be present to noxious stimuli applied to the head/face, trunk, and limbs excluding spinal reflexes (e.g. triple flexion)
- No evidence of eye opening or movement must be present to noxious stimuli applied to head/face, trunk and limbs
- Pupillary responses to bright light bilaterally must be absent. Constricted pupils < 2 mm suggest narcotic or unopposed sympathetic input and should not be considered consistent with BD/DNC.
- Absence of eye movements with oculoccephalic reflex testing (vertically and horizontally), excepting conditions where testing is unsafe such as an immobilized spine or compromised skull base integrity.
- Absence of eye movements with bilateral oculovestibular reflex testing (“cold caloric testing”)
 - Place Head of Bed at 30 degrees from horizontal
 - Check ear canals for obstruction and ensure intact tympanic membrane
 - Gently hold eyelids open
 - Instill 50 mL of ice water into one of the external canals and observe for deviation for one minute
 - Wait five minutes before testing other ear canal with same procedure
- Absence of facial movements or grimacing with noxious stimulation
- Absence of corneal reflexes
- Absence of pharyngeal (gag) reflex and tracheal ¹(cough) reflex to pharyngeal stimulation and deep tracheal suctioning
- Absence of respirations (not breathing above ventilator set rate)

- Presence of other spinal reflexes does not negate BD/DNC exam such as: Triple flexion, Babinski, Lazarus (looks like Moro reflex), Undulating toe (flexion/extension), Finger flexor movement (thumbs up sign), Semi-rhythmic facial spasm (due to denervated seventh nerve), Sweating, flushing, tachycardia, blood pressure swings, Opisthotonus, Tonic neck flexion. If it is unclear whether limb movements are spinally mediated, an ancillary test is required before declaring BD/DNC.
- If components of the neurologic examination cannot be obtained in an accurate or reliable manner, clinicians must perform ancillary testing to complete BD/DNC determination, In cases where oculocephalic reflexes may not be safely tested, ancillary testing is not required if oculovestibular reflexes are absent and all other criteria are satisfied.

Apnea Testing

Clinicians must perform at least 1 apnea test after the final BD/DNC neurological exam. Apnea testing is meant to document an absence of breathing in response to a CO₂ challenge as documented by a PaCO₂ level \geq 60 mm Hg and an increase from baseline of \geq 20 mmHg by arterial blood gas and clinical observation documenting no respiratory movements and a pH $<$ 7.30. Apnea testing can be performed by several methods.

- The most common method is to let the CO₂ rise while being disconnected from the ventilator but oxygenated by a catheter
- Alternative oxygenation methods include
 - Deliver 100% oxygen via continuous positive airway pressure (CPAP) at 10 cm H₂O while still connected to the ventilator
 - Use a T-piece tube with a CPAP valve at the outflow end
 - Deliver 100% oxygen via flow-inflating resuscitation bag with a functioning peek end expiratory pressure (PEEP) valve. The level of PEEP is often set to the same PEEP as the ventilator before disconnection.

Patients with chronic CO₂ retention, including conditions such as chronic obstructive pulmonary disease (COPD), obstructive sleep apnea, or severe obesity may have diminished responses to increasing PaCO₂ utilized in the apnea testing. If the patient's chronic baseline PaCO₂ is known, apnea testing may proceed if that patient is at that baseline PaCO₂ before testing. An estimated baseline may be used for baseline PaCO₂ when needed, but ancillary testing is required for BD/DNC declaration if apnea is present.

Prerequisites to apnea testing include eucapnia (PaCO₂ 35 – 45 mm Hg), normothermia (\geq 36° C), neutral pH (7.35 – 7.45), and lack of hypoxia and hypovolemia. Ventilator settings can be adjusted to achieve target PaCO₂ prior to apnea testing. Hypoxia and hypotension can prevent completion of apnea testing, requiring an additional ancillary test as below.

Pressors or fluids boluses may be used to ensure systolic blood pressure \geq 100 mmHg and MAP \geq 75 mm Hg as stated above. An arterial line is recommended for monitoring blood pressure and drawing ABGs but is not required.

Traditional Apnea Testing Protocol

- Connect pulse oximetry device if not in place.
- If ventilator adjustments are made, wait 30 minutes before repeating ABG to confirm PaCO₂ 35 – 45 mm Hg and pH 7.35 – 7.45.
- Patient maintains oxygenation with PEEP of 5 cm water
- Pre-oxygenate with 100% FiO₂ for more than 10 minutes (goal PaO₂ $>$ 200 mm Hg)
- Draw ABG immediately before disconnecting ventilator to establish baseline PaCO₂, PaO₂, and pH levels.
- Obtain a sterile suction catheter $<$ 70% of the diameter of the ETT/trach. Tape the hole used to apply suction. Connect catheter to the wall oxygen using suction tubing. Turn on oxygen to provide 6L/min.
- Expose the chest to monitor for respirations
- Disconnect ventilator
- Insert suction catheter until resistance is met and pull back 2 cm to the level of the carina.
- Spontaneous respirations are absent during the entirety of testing.
- Abort if
 - spontaneous respiratory effort is observed
 - SBP \leq 100 mm Hg or MAP \leq 75 mm Hg
 - Progressive decrease in oxygen saturation below 85%
 - cardiac arrhythmia with hemodynamic instability is present.
- If test aborted, draw ABG
- Reconnect ventilator using previous ventilator settings and 100% FiO₂
- Recommend drawing ABG at 8 – 10 minutes, although earlier and more frequent draws may be considered.

- If the pH and PaCO₂ criteria are not reached, and the patient did not experience hemodynamic instability or hypoxemia during apnea testing, apnea testing can continue beyond a 10-minute timeframe with repeat ABG testing at least every 2 minutes.
- Reconnect ventilator using previous ventilator settings and 100% FiO₂ when test completed
- If the test was aborted but the patient did not desaturate and maintained hemodynamic stability, apnea testing can be repeated for a longer period after again pre-oxygenating and re-establishing normal PaCO₂ and pH levels.
- If the patient become hypoxemic during the apnea test and the pH and PaCO₂ level criteria were not reached, clinicians should repeat the apnea test using alternative oxygenation methods as described above to maintain functional residual capacity.
- If the patient develops a cardiac arrhythmia with hemodynamic instability during the apnea test and the pH and PaCO₂ level criteria were not reached, clinicians should repeat the BD/DNC evaluation when apnea testing can be safely completed or perform an ancillary test.
- Apnea testing is considered consistent with BD/DNC if
 - No respirations occur AND
 - Arterial pH level is < 7.30 AND
 - PaCO₂ level is ≥ 60 mm Hg and ≥ 20 mm Hg above the patient's pre-apnea test baseline level or their chronic baseline level, whichever is greater.

Considerations for Determination of Brain Death in Patients Receiving Extracorporeal Membrane Oxygenation (ECMO) Therapy

(These criteria are in addition to the general BD/DNC criteria.)

- Apnea testing may be performed on ECMO. The same general considerations apply that the patient be normothermic and without cardiovascular or metabolic instability. The patient must not have metabolic alkalosis or be under the influence of sedative medication and neuromuscular blocking agents.
- Increase oxygenator sweep gas FiO₂ to 1.0. Decrease oxygenator sweep flow to 0.2 to 1L/min allow PaCO₂ to rise to greater than 60 mm Hg. Alternatively, exogenous CO₂ may be used.
- When PaCO₂ on arterial blood gas is greater than 60 mm Hg, disconnect the patient from ventilator and place on a T-piece oxygen set up. The setup is as follows: blue tubing connected to a tandem oxygen set up for humidity with two oxygen flow meters set at 12L/min and both entrainment devices set at 100% FiO₂. The blue tubing is connected to a T-Piece adapter that is placed on the ET tube followed by another six-inch piece of blue tubing (one section) connected to the distal end of the T-piece (this acts as a reservoir for oxygen).
- Physician should observe the patient carefully for any evidence of spontaneous respiratory efforts
- If at any time in the process the patient becomes unstable they should be placed back on mechanical ventilator support.
- When drawing ABGs, patients on VA ECMO require samples from the distal arterial line and the ECMO circuit post oxygenator. The PaCO₂ and pH levels from both samples must meet criteria for BD/DNC. Patients on VV ECMO only require ABGs from the distal arterial line.
- Draw ABG at 10 minutes or earlier . At the physician's discretion and if the patient is stable, the apnea test can continue for up to 10 minutes. Apnea test is consistent with BD/DNC if there is no spontaneous respiratory effort with PaCO₂ greater than 60 mm Hg for at least 5 minutes.
- The apnea test is consistent with BD/DNC if there is no spontaneous respiratory effort with PaCO₂ greater than or equal to 60 mm Hg for at least 5 minutes.

Ancillary Diagnostic Testing

This testing is required only when apnea testing cannot be performed or completed due to clinical factors (such as hemodynamic instability, hypoxia) to confirm a BD/DNC diagnosis. Neurological examinations and apnea test need to be performed to the fullest extent possible and must be consistent with BD/DNC.

The following conditions may interfere with the clinical diagnosis of BD/DNC, so that the diagnosis cannot be made with certainty on clinical grounds alone. Confirmatory tests may be considered in the following circumstances

- Severe facial trauma impairing elements of the exam
- Cervical spine fractures impairing elements of the exam
- Preexisting pupillary abnormalities or other cranial nerve abnormalities that impair the exam
- Sleep apnea or severe pulmonary disease resulting in chronic retention of PaCO₂ when baseline PaCO₂ is unknown.

Only one test consistent with BD/DNC required. Preferred tests include

- Catheter cerebral angiography
- Cerebral perfusion scintigraphy (nuclear perfusion scan)

Alternative testing if above cannot be performed

- Transcranial Doppler (TCD), 2 exams at least 30 minutes apart

TCD testing is reliable only if reliable signal is found. TCD also requires bilateral anterior (temporal window) and posterior (suboccipital window) insonation which can be technically difficult. It should be noted that CT and MR cerebral angiograms are not considered reliable enough for BD/DNC confirmation testing, nor is CT-perfusion imaging.

Note that EEG is no longer considered a valid test for Brain Death confirmation.

Discontinuation of Somatic Support after Brain Death Confirmation

It is recommended that somatic support is discontinued within 48 hours after brain death declaration. When conflicts exist between a family decision and clinical context, consider legal, ethical and administrative input.

“There will be times that a need to vary from the clinical practice will exist based on individual patient variability and clinical evaluation, documentation in the medical record may be needed to account for this difference.”

REFERENCES

- Greer, DM., Shemie, SD., Lewis, A., et al. Determination of brain death/death by neurologic criteria: The world brain death project. *JAMA*. 2020; 342:1078-1097.
- Guidelines for the determination of brain death: report of the medical consultants on the diagnosis of death to the President's commission for the study of ethical problems in medicine and biochemical and behavioral research. *JAMA*. 1981; 246:2184-2186.
- Lustbader D., O'Hara, D., Wijdicks, EFM., et al. Second brain death examination may negatively affect organ donation. *Neurology*. 2011; 76:119-124.
- Migdady, I., Stephens, RS., Price, C., et al. The use of apnea test and brain death determination in patients on extracorporeal membrane oxygenation: A systematic review. *J Thorac Cardiovasc Surg*. 2021; 162:867-877.
- Weiner, J., Sheer, C. How should clinicians respond when patients' loved ones do not see "brain death" as death? *AMA J Ethics*. 2020; 22:E995-1003.
- Wijdicks, EFM. Determining brain death in adults. *Neurology*. 1995; 45:1003-1011.
- Wijdicks, EFM., Varelas, PN., Gronseth, GS., Greer, DM. Evidence-based guideline update: Determining brain death in adults. *Neurology*. 2010; 74:1911-1918.

KEYWORDS AND KEYWORD PHRASES

Apnea testing
Brain death
Clinical Practice
Critical Care
Neurology
Neurosurgery
Organ donation
Trauma

Figure. Flow Diagram for Determination of Brain Death/Death by Neurologic Criteria in Persons Treated With Therapeutic Hypothermia

