Determination of Brain Death / Death by Neurologic Criteria

PURPOSE

To describe [ENTER CENTER NAME]'s policy governing determination of death by brain criteria in adult and pediatric patients.

POLICY STATEMENT

Brain death, or Death by Neurologic Criteria (BD/DNC) is a clinical diagnosis which can be made when there is complete and permanent cessation of all brain function. Clinicians must ascertain that a patient has sustained a catastrophic, permanent brain injury caused by an identified mechanism that is known to lead to BD/DNC before initiating a BD/DNC evaluation.

Clinicians should conduct further diagnostic evaluation and not undertake evaluation for BD/DNC if a patient is comatose, apneic and has absent brainstem reflexes, and there is not an identified mechanism of brain injury that is known to lead to BD/DNC. Clinicians should determine that neuroimaging is consistent with the mechanism and severity of brain injury.

The diagnosis of BD/DNC should be based on the clinical evaluation and ancillary testing should only be used when the clinical evaluation, including the neurologic examination and apnea test, cannot be completed in their entirety, or if the interpretation of the evaluation is confounded. If ancillary testing is used, the clinical evaluation must always be fully completed, and if any signs of brain function are detected, the patient does not meet BD/DNC criteria and ancillary testing is not indicated.

An individual with permanent cessation of all brain function, including the brain stem, is dead. The observation period after brain injury and before initiation of the BD/DNC evaluation is essential to ensure permanence of the brain injury and exclude the possibility of recovery of brain function. In general, the observation period is at the discretion of the clinical team and should be based on the pathophysiology of the brain injury. In certain circumstances, an observation period of longer duration is needed, such as in patients treated with therapeutic hypothermia after cardiac arrest.

As such, we recommend that after cardiac arrest, BD/DNC testing should be delayed for at least 24 hours, or if they undergo therapeutic hypothermia, 24 hours post-rewarming (>36°C). For all other brain injuries, the observation period is at the discretion of the clinical team based on the pathophysiology of the brain injury. For infants and children younger than 24 months, clinicians

should wait at least 48 hours after the acute brain injury before beginning the evaluation for BD/DNC. In the case of additional cardiac arrest requiring CPR, the waiting period does not need to be reset.
Clinicians may initiate a BD/DNC evaluation and determine a patient BD/DNC despite evidence of neuroendocrine function.

BD/DNC determination should be performed in an Intensive Care Unit (ICU) setting where resources and subsequent discussions and care are most appropriate.

BD/DNC determination should be undertaken with the utmost of care and attention to meticulous technique and should not be rushed or require off-hours determination.

APPLICATION

Adults: aged 18 years and older for adults.
Pediatric patients: 37 weeks corrected gestational age to 17 years and 364 days.

EXCEPTIONS

Children younger than age 37 weeks corrected gestational age cannot be determined to be BD/DNC.

PROCEDURE

1. Federal law requires that the primary team notify the local organ procurement organization as soon as they recognize a non-survivable catastrophic brain injury with potential for BD/DNC. They should not wait until after a determination has been made.

2. Prerequisites
   - 2.1. The presence of sedative drugs, hypothermia, shock, or other potential conditions that may depress brain function must be excluded or corrected prior to proceeding with the BD/DNC evaluation. Even in situations in which it is clear that confounding cannot be completely eliminated, and ancillary testing will be needed, the clinical examination must still be completed to the fullest extent possible, and if signs of brain function are present, the patient is not dead and ancillary testing is not indicated. The following clinical criteria must be observed:

     - 2.1.1. Clinical and neuroimaging evidence of acute Central Nervous System (CNS) catastrophe that is compatible with cerebral circulatory arrest and permanent loss of all brain function. To note, in rare patients, neuroimaging may not be possible, but the clinical determination of BD/DNC can still be made with confidence, such as with severe traumatic brain injury with brain herniation.

     - 2.1.2. The condition must be felt to be permanent with the highest confidence.

     - 2.1.3. Body temperature must be 96.8°F (36°C) or higher. If the patient has been hypothermic ≤35.5˚C (either spontaneously or therapeutically), the temperature must be maintained ≥36°C for at least 24 hours prior to BD/DNC testing.

2.1.4. Screen to exclude other sedative drugs where clinically indicated, such as drug administration recently in doses to cause impairment of consciousness and affect brainstem function. If a patient had a positive toxicology screen on admission, a repeat should be performed prior to BD/DNC determination. Ensure the alcohol blood level, if clinically indicated, is ≤80mg/dL If barbiturates are present on serum toxicology testing or were used therapeutically for control of intracranial pressure or seizures, serum levels should not be supratherapeutic (or otherwise felt to be confounding) at the time of the clinical examination. Allow at least five half-lives for all CNS depressing medications or intoxicants to pass, and longer if there is renal or hepatic dysfunction or if the patient is obese or was hypothermic. Account for age-dependent metabolism of potentially depressing medications in infants and young children and older patients. If the patient received pentobarbital, the level must be <5mcg/mL or below the lower limit of detection prior to evaluation. Consultation with clinical pharmacy may help with calculating drug clearance for known received medications based on dosages received and the individual's metabolism.

2.1.5. In adults, absence of hypotension, that is, SBP ≥100mmHg AND MAP ≥75mmHg (vasopressors may be used). In children, clinicians should maintain SBP and MAP ≥5th percentile for age.

2.1.6. If an individual has baseline blood pressure that varies significantly from their age-based normal range, clinicians should target a SBP and MAP that approximates the known chronic baseline for that individual patient.

2.1.7. The presence of deep tendon reflexes (DTRs) or muscle twitch on Train-of-four (TOF) stimulation indicates that the patient is no longer paralyzed and clinical testing may ensue.

2.1.8. No severe electrolyte, severe acid-base or severe endocrine derangements that may affect neurologic examination. A complete metabolic panel should be obtained within 24hrs of BD/DNC testing (see Tables). To note, if a potential confounder is detected, but there is no intention to correct (e.g. elevated BUN in a patient who will not receive dialysis), and the confounder will not auto-correct, clinical determination may still proceed, but ancillary testing is needed.

2.1.9. In cases where there is either high clinical suspicion or imaging confirmation of a cervical spine injury, ancillary testing must be performed in addition to clinical examination to the fullest extent possible.

2.1.10. Even if ancillary testing is deemed necessary, **the clinical examination should still be performed to the fullest extent possible**, and if signs of brain function are present, the patient is not brain dead and ancillary testing should not be performed.

2.1.11. After medical or surgical interventions to treat elevated intracranial pressure, clinicians must wait a sufficient amount of time to ensure there is no recovery of brain function before initiating the BD/DNC evaluation. This observation period must be based on the pathophysiology of the brain injury leading to the neurologic state of the patient and the findings on neuroimaging.

2.1.12. For adults supported by venoarterial (VA) ECMO, clinicians should target a MAP ≥75mmHg; and for children supported by VA ECMO, clinicians should target MAP ≥5th percentile for age.

3. Clinical criteria

3.1. In adults, at least one clinical exam is required. In instances which two examinations are required, the clinical examination must be performed by two different attending physicians with appropriate training and expertise. Optimally, the two attendings are blinded to the results of the other's testing. In adults, when two exams are performed, no specific period is required between the exams. Physicians involved in the recovery of organs may not perform the clinical examinations intended to assess death by brain criteria. An attending neurologist or neurosurgeon must perform one of the examinations.

3.2. In children, 2 clinicians must each perform a separate and independent examination for BD/DNC, and a minimum interval of 12 hours should separate the examinations.

3.3. A trainee or APP may perform the examination under direct observation of the attending physician to ensure meticulous and proper technique. Both attendings must be appropriately credentialed members of the hospital's medical staff and be adequately trained and competent in the evaluation of BD/DNC. The following criteria are assessed:

3.3.1. Coma with completely unresponsiveness to all noxious stimulation.

3.3.2. Absence of all brainstem reflexes.

3.3.3. Apnea in the setting of an appropriate CO_2 and pH challenge (See apnea testing below).

3.4. Evaluation of unresponsiveness

3.4.1. The patient should be completely comatose with no cerebrally-mediated responses, including withdrawal, seizures, or posturing (decerebrate or decorticate, spontaneously or to noxious stimulation (including sternal rub, nailbed pressure, as well as cranial noxious stimuli such as supraorbital notch pressure, nasal "tickle" and pressure on the TMJ). Spinally-mediated reflexes may be present, including deep tendon reflexes, Babinski sign, triple flexion, and various "Lazarus" signs as described in the literature.

3.4.2. Motor and sensory examination in the extremities requires deep noxious stimulation at multiple locations on each limb. Deep nailbed pressure should be applied distally, and proximal stimulation should include pinching medially above the knee and above the elbow. Corporal stimulation includes a sternal rub and trapezius pinch.

3.4.3. If it is unclear whether observed limb movements are spinally mediated, determination of BD/DNC should include an ancillary test.

3.5. Evaluation of brainstem reflexes

3.5.1. The pupils should be mid-position to dilated (typically 2-7mm) in the absence of mydriatics and unreactive to bright light or noxious stimulation. It is recommended that a magnifying glass be used to ensure the absence of reactivity. Automated pupillometry may be used as an adjunct method but has not been validated in BD/DNC determination. Please note that automated pupillometers automatically check for pupillary reaction a second time if the first attempt shows no reactivity, a built-in safeguard. If reactivity is seen with pupillometry, the examiner should reevaluate based on standard methods. Note: small pupils (<2mm) should alert to the possibility of opiate intoxication;

3.5.2. Eye movements: There should be no spontaneous eye movements, and there should be no movement of either eye on testing the oculocephalic and oculovestibular reflexes.

3.5.2.1. Oculocephalic testing should not be performed if cervical spine fracture or instability is present or suspected, but oculovestibular reflex testing should still be performed. The oculocephalic response is tested by rapid rotation of the head to either side and up and down (brisk neck flexion). The oculocephalic test is the only portion of the BD/DNC evaluation that may be omitted, and the patient can still be determined BD/DNC on clinical grounds alone, so long as the oculovestibular test can be performed.

3.5.2.2. Oculovestibular reflex should be performed after the integrity of the tympanic membranes has been ensured. It is elicited by instilling ice water into each external auditory canal with the head of the bed elevated 30 degrees. Sixty seconds of constant exposure to ice water in each ear should be used, with concomitant observation for any eye movements for the entire time. Both ears should be tested (separately), and there should be a 5-minute delay before testing the contralateral ear to allow the endolymph of the tested ear to re-equilibrate to normal temperature.

3.5.3. Corneal Reflex: There is no blinking or eye movement when the cornea is adequately stimulated (use a cotton-tipped applicator with adequate pressure) at the appropriate location (adjacent to the iris, taking care not to damage the cornea).

3.5.4. Gag Reflex: There is no gag or cough reflex when each side of the posterior pharynx is stimulated with a tongue depressor or suction device.

3.5.5. Cough Reflex: There is no cough in response to deep tracheal suctioning to the level of the carina.

3.5.6. The presence of deep tendon or other spinally-mediated reflexes does not preclude the diagnosis of death by brain criteria.

3.5.7. There should be no spontaneous respirations above the set rate on the ventilator.

3.5.8. In infants younger than six months, clinicians performing the BD/DNC neurologic examination must determine that there is no sucking or rooting reflex.

4. Apnea

4.1. Apnea may be demonstrated by the absence of spontaneous respirations in the presence of an adequate CO_2 and pH challenge. The apnea test is a clinical bedside test to determine the response of the medullary brainstem respiratory center to a CO_2 and acidosis stimulus. A lack of respiratory effort to hypercarbia indicates loss of function of the most caudal part of the brainstem. An attending physician, respiratory therapy and ICU nurse must be present during the entire test. It is recommended to inform the laboratory services of the planned apnea testing to ensure expedited ABG results. Apnea testing should only be performed after the two neurologic examinations are consistent with BD/DNC and should be performed after the second examination. In children, two apnea tests are performed, one after each neurological examination. An arterial line should be placed if possible, to facilitate the drawing of blood gas samples and to continuously monitor the blood pressure.

4.2. Apnea Procedure

4.2.1. Apnea Prerequisites

4.2.1.1. Before attempting apnea testing, clinicians must ensure that the patient's risk of cardiopulmonary decompensation during apnea testing is assessed and is acceptable. Specifically, clinicians must ensure that the patient is not hypoxemic, hypotensive, or hypovolemic before starting the apnea test.

4.2.1.2. Core temperature should be at least 36°C (96.8°F).

4.2.1.3. Again ensure that the patient has not recently received any sedative or paralytic agents prior to apnea testing.

4.2.1.4. The patient should be hemodynamically stable (minimum SBP 100mmHg, minimum MAP 75mmHg). It is recommended to establish an SBP >120 for adult patients prior to the test to ensure safe performance and completion, as the patient's blood pressure may drop during the test due to acidosis. This

may be achieved with the use of fluid boluses and/or vasopressors, as needed.

4.2.1.5. The patient should be pre-oxygenated for at least 10 mins to a PaO_2>200 mmHg.

4.2.1.6. A baseline ABG should show that the =pH is 7.35-7.45, and the $PaCO_2$ is 35-45mmHg

4.2.1.7. If the patient has a history of known CO_2 retention at baseline ($PaCO_2$ greater than 45mmHg), the goal $PaCO_2$ during apnea testing should also be ≥20 mmHg above a baseline known value (in addition to ≥60mmHg). If CO_2 retention is suspected, but the baseline pCO_2 is not known, apnea testing should still be performed, but ancillary testing is also required.

4.2.2. Equipment and Personnel

4.2.2.1. Suction catheter of appropriate size (<70% of the diameter of the ET tube) with connecting tubing;

4.2.2.2. Sterile gloves;

4.2.2.3. Oxygen or suction connecting tubing;

4.2.2.4. Oxygen flow meter with nipple;

4.2.2.5. Mapleson breathing system;

4.2.2.6. ABG kits;

4.2.2.7. Cardiac monitor, pulse oximeter; and

4.2.2.8. Nursing and respiratory therapy personnel with appropriate expertise must be present during the procedure.

4.2.3. Suction the patient according to the standard procedure.

4.2.4. Pre-oxygenate the patient with 100% oxygen on present means of respiratory support for 10-30 minutes and check a baseline ABG. Ensure that the patient is not on a PEEP of >5 since higher PEEP requirements may suggest difficulty with apnea testing (although apnea testing is still possible). (To note, the patient may be at higher risk of decompensation if PEEP is >5 or unable to achieve target PaO_2.) The starting $PaCO_2$ should be 35-45mmHg, the pH 7.35-7.45 and the PaO_2 of ≥200mm Hg. The $PaCO_2$ will be allowed to rise and the pH to drop while the undraped thorax and abdomen are observed carefully for signs of spontaneous respirations.

4.2.5. In adults, disconnect the patient from the ventilator (if possible) and note the time the test is started. To note, modern ventilators are susceptible to auto-cycling

due to high sensitivity. Thus, condensation in the tubing, or even the patient's heartbeat, can trigger a delivered breath from the ventilator. Disconnection removes any question of whether the breath is patient-initiated or not.

4.2.6. In adults, insert an endotracheal suction catheter into the endotracheal or tracheostomy tube to approximately the level of the carina. Care must be taken not to intubate a mainstem bronchus; the tip of the catheter should be estimated to be at, or a few millimeters below, the tip of the endotracheal or tracheostomy tube.

4.2.7. Attach the aspirator manifold of the catheter to the oxygen flow meter via the oxygen connecting tubing.

4.2.8. Set the flow meter to 4-6L/min. A higher flow rate may cause CO_2 washout and potentially barotrauma. Continuously monitor oxygen saturation by pulse oximeter.

4.2.9. In children (or adults), apnea testing can be accomplished via (1) stopping intermittent mandatory ventilation and delivering 100% oxygen via CPAP on the ventilator or (2) stopping intermittent mandatory ventilation and disconnecting the ventilator from the patient's ETT/tracheostomy and delivering 100% oxygen via a flow-inflating resuscitation bag with a functioning PEEP valve.

4.2.10. An ABG should be drawn at approximately 5, 8 and 10 minutes of elapsed time (and longer if needed) to establish that the $PaCO_2$ has reached ≥60mmHg AND ≥20mmHg rise above the patient's pre-AT baseline. Testing for a period longer than 10 minutes may be required if the $PaCO_2$ is below 60mmHg at the end of this test, but the patient was hemodynamically stable. If this is required, the patient must again be preoxygenated to a PaO_2 ≥200mmHg, pH normalized, and normocapnia reestablished ($PaCO_2$ 35-45mmHg).

4.2.11. Apnea testing should be aborted if:

4.2.11.1. SBP less than 100mmHg or MAP less than 75mmHg in adults, or SBP or MAP $<5^{th}$ percentile for age in children

4.2.11.2. progressive oxygen desaturation to less than 85%

4.2.11.3. any respirations are observed

4.2.11.4. cardiac arrhythmia with hemodynamic instability. If the patient develops a decrease in blood pressure or oxygen saturation and the need to abort the apnea test appears imminent, clinicians should obtain an ABG before placing the patient back on the ventilator. Reconnect the patient to ventilatory support after 10 hyperventilating breaths with the resuscitation bag using 100% oxygen. This will ensure rapid correction of respiratory acidosis.

4.2.11.5. If there is no respiratory effort after an arterial $PaCO_2$ ≥60mmHg has been achieved, AND $PaCO_2$ rise ≥20mmHg above baseline, AND the pH is <7.30, the patient meets BD/DNC criteria. The time of death is the time the ABG is officially reported in the EMR.

4.2.11.6. If the patient experienced hypoxemia during apnea testing and the pH and $PaCO_2$ level criteria were not reached, clinicians should either repeat the apnea test using an alternative apneic oxygenation method that maintains functional residual capacity, for example CPAP via a flow-inflating resuscitation bag. Repeat the apnea test when it can be safely completed or perform an ancillary test.

4.2.11.7. Document test results in the medical record using the appropriate checklist and form. Include vital signs, ABG values, SaO2, clinical observations and personnel performing the test.

4.2.12. Clinicians should adhere to the following protocol for apnea testing on ECMO:

4.2.12.1. Preoxygenate by using 100% FIO_2 on the ventilator and through the membrane lung.

4.2.12.2. For adults supported by VA ECMO, clinicians should target a MAP ≥75mmHg; and for children supported by VA ECMO, clinicians should target MAP ≥5^{th} percentile for age.

4.2.12.3. To achieve an adequate increase in $PaCO_2$ level, either titrate exogenous CO_2 into the ECMO circuit or adjust the sweep gas flow rate to 0.2-1L/min.

4.2.12.4. Sample ABGs from both the patient's distal arterial line and the ECMO circuit post oxygenator for patients on VA ECMO. $PaCO_2$ and pH levels from both locations are required to meet BD/DNC criteria for the apnea test to be consistent with BD/DNC. This ensures that, independent of the mixing point, the $PaCO_2$ and pH levels in the cerebral circulation meet BD/DNC criteria. For patients on venovenous ECMO, sample ABGs only from the patient's distal arterial line.

4.2.12.5. Avoid hypotension during apnea testing on ECMO by increasing ECMO flows, intravenous fluid administration, or vasopressor/ionotropic support.

5. <u>Ancillary Tests</u>

5.1. An ancillary test should only be performed in the setting that the clinical examination cannot be fully or safely performed, or confounding is present that cannot be corrected. These tests must be officially interpreted by an attending radiologist (digital subtraction angiogram), nuclear medicine specialist (radionuclide study) or attending neurologist (TCD).

5.2. Clinicians must not use ancillary tests to assist in the diagnosis of BD/DNC in the setting of hypothermia or high levels of sedating medications or to avoid performing otherwise testable elements of the BD/DNC assessment.

5.3. If any findings on the BD/DNC neurologic examinations or apnea test are consistent with brain-mediated activity, the patient does not meet criteria for BD/DNC, and ancillary testing must not be performed.

5.4. An ancillary test should be performed if:

5.4.1. apnea testing cannot be completed due to pulmonary or hemodynamic instability

5.4.2. concern for C-spine or skull base integrity

5.4.3. facial or eye trauma or edema hindering clinical examination of brainstem function

5.4.4. confirmed cervical spine injury or severe peripheral neuropathy that limit the adequate assessment of extremity movement or spontaneous respirations

5.4.5. neurological examination findings that maybe difficult to interpret, such as limb movement that may or may not be spinally-mediated

5.4.6. metabolic derangements that are unable to be adequately corrected

5.5. Ancillary tests include:

5.5.1. Four vessel conventional cerebral digital subtraction angiography by hand injection under pressure demonstrating absence of intracerebral filling; the extracranial circulation will still fill, but the intracranial circulation, for both carotid and vertebral arteries, will arrest at the entry point (dural ring).

5.5.2. Nuclear medicine (NM) study demonstrating absence of cerebral blood flow and perfusion, measured by lack of uptake of tracer. SPECT or anterior and lateral Planar views are required to ensure the brainstem has no uptake of tracer.

5.5.3. Transcranial doppler must demonstrate sharp systolic spikes and zero or reversible flow during diastole; absence of flow signal may be due to the patient's anatomy, low flow or operator error, and may not be used for BD/DNC determination. Anterior and posterior circulations must be tested bilaterally twice, 30 minutes apart. Transcranial doppler has not be validated in children for BD/DNC and should not be used as an ancillary test in this age group.

5.5.4. Any of these three ancillary tests may be repeated in 24 hours if the result is equivocal, provided that all criteria continue to be met and a clinical determination still cannot be performed.

5.5.5. Note that MR-angiography and CT-angiography have ***not*** been validated as reliable ancillary tests for the declaration of BD/DNC and if performed for other reasons, any results suggestive of no cerebral blood flow should ***not*** be used to determine BD/DNC .

5.5.6. Note that EEG is not a valid ancillary test in BD/DNC.

6. Time of death

6.1. The time of death should be recorded as the time the ABG with the appropriate CO_2 and pH values are reported in the electronic medical record. If ancillary testing is used, the time of death should be when the attending radiologist or neurologist signs the results of the test.

7. Family Communication

7.1. Note that a family's permission is not required to perform BD/DNC testing, but it is recommended that they be informed that evaluation for BD/DNC will be taking place. It is recommended to explain to the family what the clinical examination and apnea testing involve, and that if testing confirms the lack of brain function, the patient will be legally declared dead. Sometimes it may be helpful to have the family present during the clinical determination, including the apnea test, so that they may better understand the process and the severity and permanence of brain injury. If any spinal-mediated reflexes or automatisms are observed, families should be informed early on that these are not reflective of brain function, but rather arise from the spinal cord. Explaining to families the meaning of BD/DNC is important to assist them in preparing for the patient's passing. Families also do not have to consent to have the ventilator removed after brain-death is confirmed since the patient is already medically and legally deceased. However, it is left to the discretion of the attending physician in charge of the patient's care to decide what a reasonable amount of time is allowed for the family to come to terms with the diagnosis prior to removal of the ventilator. In situations in which the family refuses to accept the diagnosis of BD/DNC, the clinical team should discuss with the ethics committee, hospital legal and hospital administration.

8. BD/DNC in Pregnancy

8.1. Patients who are pregnant can develop catastrophic, permanent brain injuries and may be determined to meet BD/DNC criteria. In these situations, the fetus may still be viable. Continued organ support in a pregnant person after BD/DNC determination may lead to the delivery of a viable newborn. The ethical analysis of whether to continue organ support in a pregnant person determined BD/DNC should largely focus on the welfare of the fetus.

8.2. Pregnancy in and of itself is not a contraindication to BD/DNC evaluation. Clinicians should assess and diagnose pregnant persons with catastrophic, permanent brain injuries for BD/DNC.

8.3. Following the determination of BD/DNC in a pregnant person, the clinicians providing care, assisted by clinicians knowledgeable in maternal-fetal medicine, child neurology,

and neonatology, as needed, should educate and discuss with surrogate decision makers the risks and benefits to the fetus of continuing maternal organ support.

9. BD/DNC in Primary Posterior Fossa Injury

9.1. Patients with primary posterior fossa injury may be clinically comatose with brainstem areflexia and apnea; however, they may retain some cortical function. To avoid determining BD/DNC in patients with primary posterior fossa injury and retained supratentorial function, clinicians should ensure that the posterior fossa process has also led to catastrophic ***supratentorial*** injury as demonstrated on a conventional neuroimaging study before initiating the BD/DNC evaluation.

[END]

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