



Brain Death Declaration Policy and Privileging Criteria

Keck Medical Center of USC

Background



- The President’s Commission report on “guidelines for the determination of death” culminated in a proposal for a legal definition that led to the Uniform Determination of Death Act (UDDA).
- The act reads:
 - “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 within accepted medical standards.”

California Codes

Health and Safety Code



- **7180.** (a) 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 in accordance with accepted medical standards. (b) This article shall be applied and construed to effectuate its general purpose to make uniform the law with respect to the subject of this article among states enacting it. (c) This article may be cited as the Uniform Determination of Death Act.
- **7181.** When an individual is pronounced dead by determining that the individual has sustained an irreversible cessation of all functions of the entire brain, including the brain stem, there shall be independent confirmation by another physician.
- **7182.** When a part of the donor is used for direct transplantation pursuant to the Uniform Anatomical Gift Act (Chapter 3.5 (commencing with Section 7150)) and the death of the donor is determined by determining that the individual has suffered an irreversible cessation of all functions of the entire brain, including the brain stem, there shall be an independent confirmation of the death by another physician. Neither the physician making the determination of death under Section 7155.5 nor the physician making the independent confirmation shall participate in the procedures for removing or transplanting a part.
- **7183.** Complete patient medical records required of a health facility pursuant to regulations adopted by the department in accordance with Section 1275 shall be kept, maintained, and preserved with respect to the requirements of this chapter when an individual is pronounced dead by determining that the individual has sustained an irreversible cessation of all functions of the entire brain, including the brain stem.

Hospital Responsibility



- The California legislature has delegated to hospitals responsibility for brain death determination and declaration “in accordance with accepted medical standards” when there is “irreversible cessation of all functions of the entire brain, including the brain stem”.

Declarant Qualification



- License
 - California Law stipulates that brain death must be declared by two California licensed physicians.
- Neuroscience Affiliation
 - Keck Medical Center of USC policy requires that one of the declarants be a member of one of the neuroscience departments, Neurology or Neurosurgery in order to declare a patient clinically brain dead. The second examiner may be a physician who is an active member of the medical staff who is privileged.
- Privileging Criteria
 - Requires 2 proctored brain death exams (either 1 simulated patient and 1 proctored or 2 proctored brain death exams), review of this presentation and passing a multiple-choice quiz.

Practical Guidance for Determining Brain Death



- Many of the details of the clinical neurological examination to determine brain death cannot be established by evidence-based methods at this time.
- It must be emphasized that this guidance is opinion-based. Alternative protocols may be equally informative.
- The detailed brain death evaluation protocol that follows is intended as a useful tool for clinicians.
- Most US state laws have adopted the Uniform Determination of Death Act (UDDA).



- The UDDA does not define “accepted medical standards”.
- The American Academy of Neurology’s 2010 practice parameter delineated the medical standards for the determination of brain death.
- Considerable practice variation remains.



- To ensure that the cessation of brain function is “irreversible”, physicians must:
 - determine the cause of coma
 - exclude mimicking medical conditions
 - observe the patient for a period of time to exclude the possibility of recovery
 - A minimum of 24 hours is recommended specifically for anoxic brain injury after resuscitated cardiac arrest or re-warming
- To determine “cessation of all functions of the entire brain, including the brain stem”, physicians must:
 - determine the presence of unresponsive coma
 - determine the absence of brainstem reflexes
 - determine the absence of respiratory drive after a CO₂ challenge

Practical Guidance for Determining Brain Death Clinical Evaluation

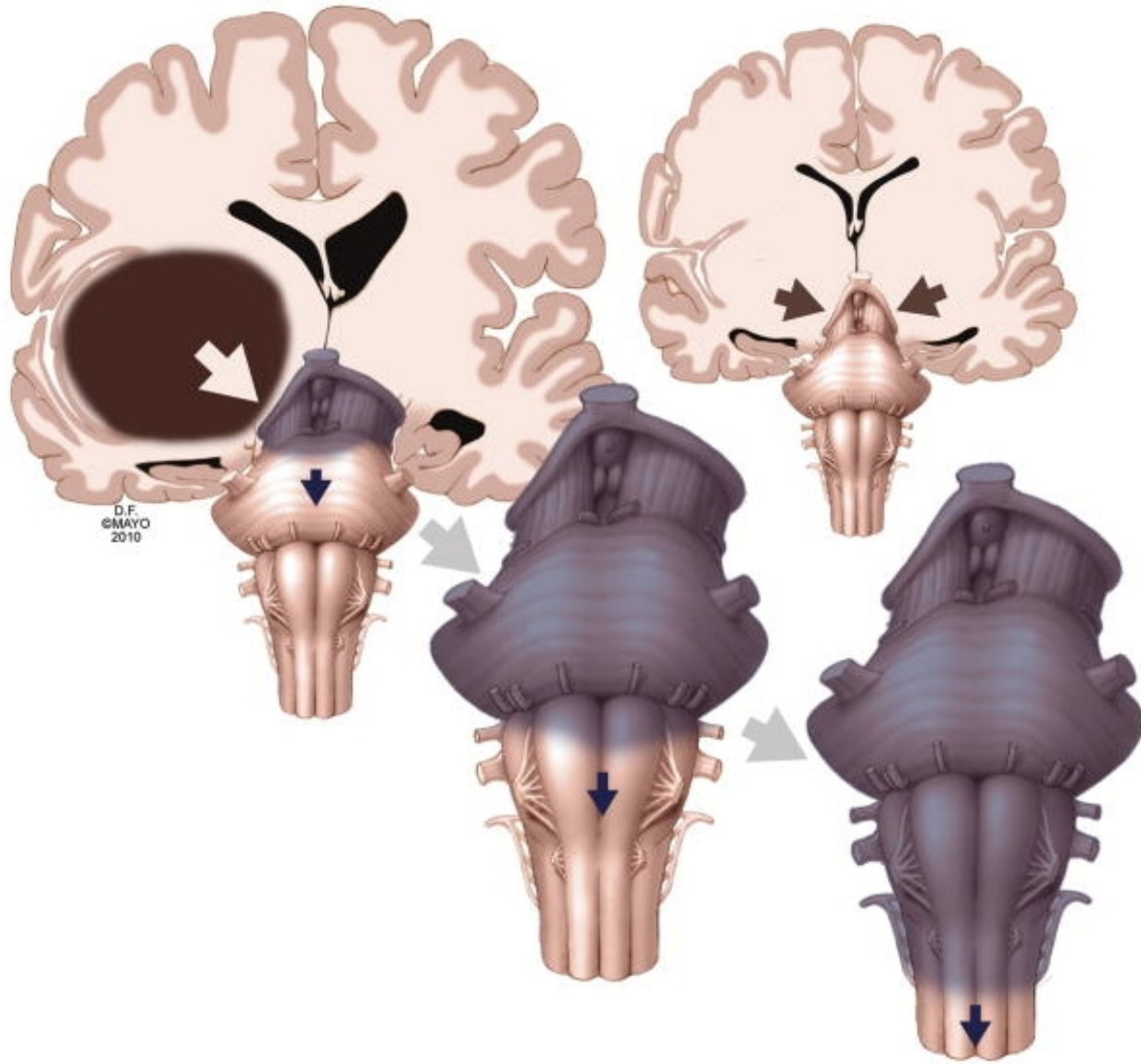


- Establish irreversible and proximate cause of coma
 - The cause of coma can usually be established by history, examination, neuroimaging, and laboratory tests.
 - Exclude the presence of a CNS-depressant drug effect by history, drug screen, calculation of clearance using 5 times the drug's half-life, or drug plasma levels below the therapeutic range.
 - Prior use of hypothermia may delay drug metabolism.

Practical Guidance for Determining Brain Death Clinical Evaluation, continued



- The legal alcohol limit for driving is a practical threshold below which an examination to determine brain death could reasonably proceed.
- There should be no recent administration or continued presence of neuromuscular blocking agents (this can be defined by the presence of a train of four twitches with maximal ulnar nerve stimulation).
- There should be no severe electrolyte, acid-base, or endocrine disturbance (defined by severe acidosis or laboratory values markedly deviated from the norm).



- Typical rostrocaudal progression of brainstem injury from hemispheric lesion.
- Brain death is a result of an acute brain injury, typically progressing from a hemispheric lesion to a brainstem lesion.
- Brainstem injury mostly advances caudally from the mesencephalon to the medulla oblongata and usually all pontine reflexes have disappeared before the medulla oblongata stops functioning.



- Achieve normal core temperature
 - In most patients, a warming blanket is needed to raise the body temperature and maintain a normal or near-normal temperature ($>36^{\circ}\text{C}$). After the initial equilibration of arterial carbon dioxide with mixed central venous carbon dioxide the PaCO_2 rises steeply, but then more slowly when the body metabolism raises PaCO_2 . To avoid delaying an increase in PaCO_2 , normal or near-normal core temperature is preferred during the apnea test.
- Achieve normal systolic blood pressure
 - Hypotension from loss of peripheral vascular tone or hypovolemia (diabetes insipidus) is common; vasopressors or vasopressin are often required. Neurologic examination is usually reliable with a systolic blood pressure ≥ 100 mm Hg or a mean arterial pressure of at least 60 mm Hg



- Perform neurologic examination
 - If a certain period of time has passed since the onset of the brain insult to exclude the possibility of recovery, one neurologic examination should be sufficient to pronounce brain death. However, some US State statutes, such as California, require two examinations.
 - Legally, all physicians are allowed to determine brain death in most US States. Neurologists, neurosurgeons, and intensive care specialists may have specialized expertise. It seems reasonable to require that all physicians making a determination of brain death be intimately familiar with brain death criteria and have demonstrated competence in this complex examination.
 - Some US State or hospital guidelines require the examiner to have certain expertise.

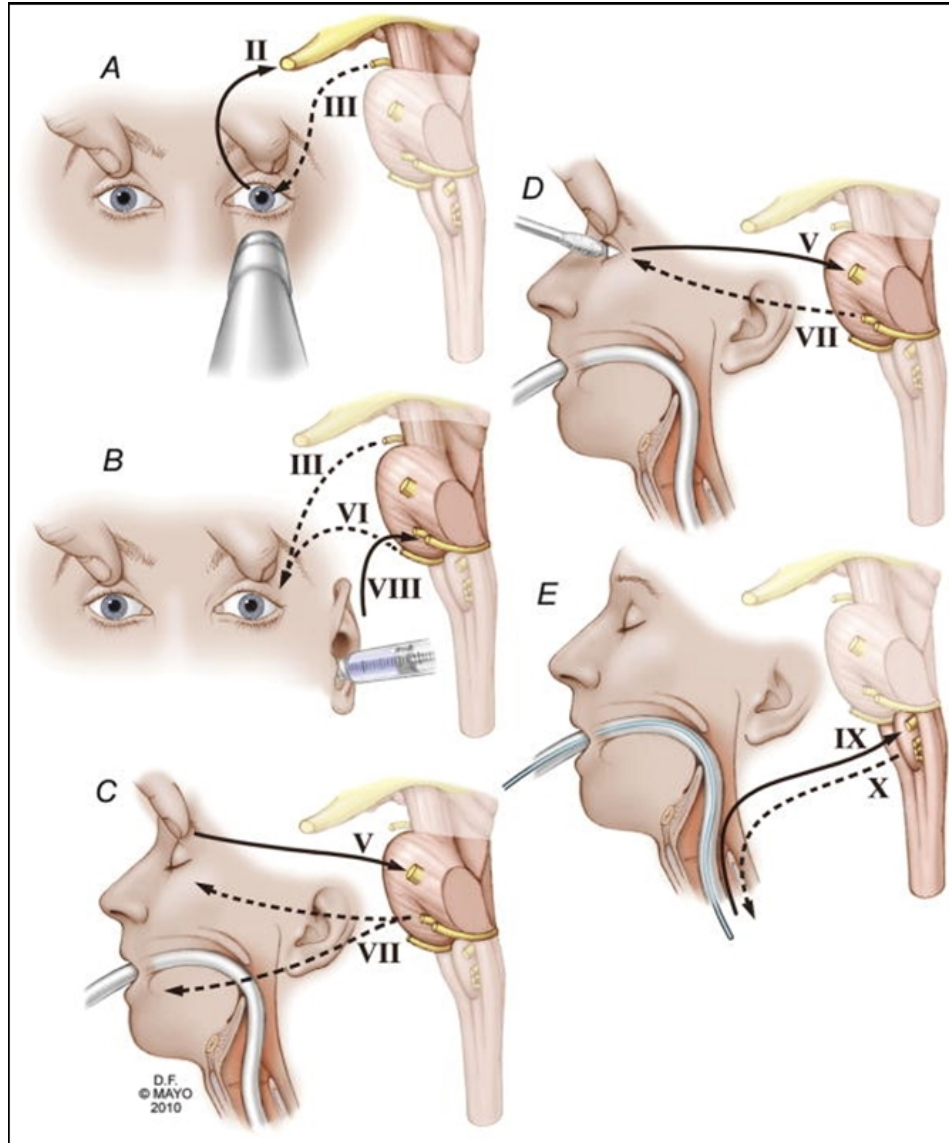
Practical Guidance for Determining Brain Death Neurologic Assessment



- Coma
 - Patients must lack all evidence of responsiveness.
 - Eye opening or eye movement to noxious stimuli is absent. Noxious stimuli should not produce a motor response other than spinally mediated reflexes.
- Absence of brainstem reflexes
 - Absence of pupillary response to a bright light is documented in both eyes.
 - Usually, the pupils are fixed in a midsize or dilated position (4–9 mm). Constricted pupils suggest the possibility of drug intoxication. When uncertainty exists a magnifying glass/pupillometer should be used.



- Absence of corneal reflex
 - Absent corneal reflex is demonstrated by touching the cornea with a piece of tissue paper, a cotton swab, or squirts of water. No eyelid movement should be seen.
- Absence of ocular movements using oculocephalic testing and oculovestibular reflex testing
 - Once the integrity of the cervical spine is ensured, the head is briskly rotated horizontally and vertically. There should be no movement of the eyes relative to head movement. The oculovestibular reflex is tested by irrigating each ear with ice water (caloric testing) after the patency of the external auditory canal is confirmed. The head is elevated to 30 degrees. Each external auditory canal is irrigated (one ear at a time) with approximately 50 cc of ice water. Movement of the eyes should be absent during 1 minute of observation. Both sides are tested, with an interval of several minutes.



Brainstem reflexes, showing the afferent (solid line) and efferent (dotted line) limbs of each reflex arc:

- A. Pupillary light reflex
- B. Oculovestibular reflex
- C. Supraorbital nerve compression;
- D. Corneal reflex
- E. Cough reflex
- F. Gag reflex



Brain Death- Associated Reflexes and Automatisms

<i>Movement</i>	<i>Description</i>	<i>Onset after BD dx</i>	<i>Age, sex (M/F)</i>	<i>Source (no. of subjects)</i>	<i>Automatism or reflex^a</i>
Lazarus sign ^b	Seems to be grasping for endotracheal tube; one or both arms flexed at elbows with hands brought to chin or face and then returned to the bed beside the body; reported spontaneously, during apnea testing, and with neck flexion during transcranial doppler examination	0–2 days	26/67 M/F	Heytens et al. (1) ²⁴ Ropper (5) ¹⁵ de Fretas et al. (4) ²⁰ Urasaki et al. (1) ²¹ Turnel et al. (2) ¹² Jastremski et al. (1) ²³	Automatism and reflex
Undulating toe	Slow flexion/extension movements of toes, spontaneous or elicited by tactile/noxious plantar stimulation	NA	NA	McNair et al. (3) ²⁴ Saposnik et al. (25) ⁸	Automatism and reflex
Unusual facial movements	Flaring of alae nasi	NA	14 M	Rodrigues et al. (1) ²⁸	Automatism
Extensor posturing	Asymmetrical opisthotonus (back arching to left or right spontaneously)	2 days	51 M	Heytens et al. (1) ²⁴	Automatism
Facial myokymia	Intermittent repetitive undulating muscle contractions of left cheek	NA	54 M	Saposnik et al. (1) ¹	Automatism
Spinal myoclonus	Multifocal myoclonus involving lower limbs and abdominal muscles lasting 15 hours, bilateral and asymmetric, causing the body to jump over the bed	6 days	56 M	Fujimoto et al. (1) ²⁹	Automatism
Respiratory-like movements	Both shoulders adduct and slow cough-like movements minutes after respirator removal	35 minutes	67 F	Urasaki et al. (1) ²¹ Ropper (5) ²⁵	Automatism
Hugging-like motion	Sudden hugging-like motion with both arms and flexion of the trunk to 30° for a few seconds	NA	NA	Aranibar (1) ²⁰	Automatism
Decerebrate-type movements	Spontaneous decerebrate type movements in all four extremities	24 hours	35 M	Jastremski et al. (1) ²³	Automatism
Eyelid opening	Left or bilateral eyelid opening with noxious stim to ipsilateral nipple	24 hours	57 M	Friedman (1) ²¹	Reflex
Head turning	Inconsistent extension of both upper extremities at the elbow and wrist after noxious stimulation; head intermittently turns from side to side for 10–30 seconds with passive neck flexion, extension, or sternal rub	4 days	42 M	Christie et al. (1) ²²	Reflex
Decerebrate-like posturing with mechanical ventilation	Symmetric movements lasting 5 seconds in both arms with hyperpronation and forearm extension, wrist flexion, metacarpophalangeal joint extension, and interphalangeal joint flexion synchronously triggered by insufflation of mechanical ventilation and by superficial pressure or noxious stimulation to the arms, thorax, or abdomen	Immediate	30 F, 11-month- old boy	Marti-Fabregas et al. (2) ²³	Reflex
Limb elevation with neck flexion	A rapid jerk raising all four limbs off the bed 0.5–8 inches with passive neck flexion	NA	NA	Ropper (5) ¹⁵	Reflex
Viscero-somatic reflex	Contraction of the abdominal musculature after parietal peritoneum was cut during organ harvest	Immediate	15–61, M and F	Conci et al. (15) ⁹	Reflex
Other studies					
Spinal reflexes and automatisms	31 different reflexes and 4 automatisms in 11% of 235 BD bodies	NA	NA	Spittler et al. (27) ⁵	4 automatisms and 31 reflexes
Spinal reflexes	7 different reflexes in 79% of 63 BD bodies	0–72 hours	NA	Jorgensen (50) ⁴	Reflex
Spinal reflexes	7 different reflexes in almost 75% of 52 bodies	0 hours	NA	Ivan (~39) ⁶	Reflex
Spinal reflexes	6 different reflexes in 13% of 134 bodies	0–72 hours	NA	Dösemeci (18) ⁷	Reflex

Practical Guidance for Determining Brain Death Apnea test: Prerequisites



- Normotension
- Normothermia
- Euvolemia
- Eucapnia (PaCO₂ 35–45 mm Hg)
- Absence of hypoxia
- No prior evidence of CO₂ retention (i.e., chronic obstructive pulmonary disease, severe obesity)

Prerequisites

- ◆ PaCO₂ between 35 mm Hg and 45 mm Hg
- ◆ Systolic blood pressure ≥100 mm Hg with or without vasopressors
- ◆ Administer 100% oxygen for at least 10 minutes (ideal PaO₂ >200 mm Hg with positive end-expiratory pressure ≤5 cm H₂O)
- ◆ Absence of clinical signs of intravascular volume contraction

Steps

- ◆ Disconnect the patient from the ventilator
- ◆ Deliver oxygen at 6 L/min through a catheter advanced through the tracheal tube until close to the carina
- ◆ Look carefully for any respiratory movements while monitoring pulse oximetry and blood pressure
- ◆ Abort and reconnect to the ventilator if evidence of respiratory movements, refractory hypotension (systolic blood pressure <90 mm Hg) or worsening hypoxemia (pulse oximetry <85%)
- ◆ If no respiratory movements after approximately 8 minutes, obtain arterial blood gases
- ◆ Apnea is established if PaCO₂ ≥60 mm Hg (or 20 mm Hg greater than baseline)

PaCO₂ = partial pressure of carbon dioxide, arterial; PaO₂ = partial pressure of oxygen, arterial.



- Adjust vasopressors to a systolic blood pressure greater than/equal to 100 mm Hg or mean blood pressure greater than/equal to 60 mm Hg.
- Preoxygenate for at least 10 minutes with 100% oxygen to a PaO₂ greater than 200 mm Hg.
- Reduce ventilation frequency to 10 breaths per minute to eucapnia.
- Reduce positive end-expiratory pressure (PEEP) to 5 cm H₂O (oxygen desaturation with decreasing PEEP may suggest difficulty with apnea testing).
- If pulse oximetry oxygen saturation remains greater than 95%, obtain a baseline blood gas (partial pressure of oxygen [PaO₂], PaCO₂, pH, bicarbonate, base excess).
- Disconnect the patient from the ventilator.
- Preserve oxygenation (e.g., place an insufflation catheter through the endotracheal tube and close to the level of the carina and deliver 100% O₂ at 6 L/min).
- Look closely for respiratory movements for 8–10 minutes. Respiration is defined as abdominal or chest excursions and may include a brief gasp.



- Abort if systolic blood pressure decreases to less than 90 mm Hg.
- Abort if oxygen saturation measured by pulse oximetry is less than 85% for greater than 30 seconds. Retry procedure with T-piece, continuous positive airway pressure (CPAP) 10 cm H₂O, and 100% O₂ 12 L/minute.
- If no respiratory drive is observed, repeat blood gas (PaO₂, PaCO₂, pH, bicarbonate, base excess) after approximately 8 minutes.
- If respiratory movements are absent and arterial PCO₂ is greater than/equal to 60 mm Hg (or 20 mm Hg increase in arterial PCO₂ over a baseline normal arterial PCO₂), the apnea test result is positive (i.e., supports the clinical diagnosis of brain death).
- If the test is inconclusive but the patient is hemodynamically stable during the procedure, it may be repeated for a longer period of time (10–15 minutes) after the patient is again adequately preoxygenated.



High Cervical Cord Injury

- In the setting of a high cervical cord injury, it is recommended that an apnea test not be performed and ancillary testing is indicated.

Apnea in Patients With ECMO



- It is recommended that the same fundamentals of the BD/DNC concept etiology, prerequisites, minimum clinical criteria, apnea testing targets, and indications for ancillary testing be applied to adults and children receiving ECMO.
- It is recommended that performance of an apnea test be part of BD/DNC testing in persons receiving veno-venous or veno-arterial ECMO, unless contraindicated due to cardiopulmonary instability.
- In persons receiving veno-arterial ECMO for circulatory and respiratory support, it is recommended that the extracorporeal blood flow be maintained during the clinical evaluation and apnea test in order to prevent hemodynamic instability and maintain a mean arterial pressure of at least 60 mm Hg in adults and age-appropriate targets in pediatrics. Veno-arterial ECMO flow rates may be increased to support the MAP if required before or during testing.



- It is recommended that apnea testing in persons receiving ECMO be conducted by delivering 100% oxygen to the lungs via CPAP on the mechanical ventilator, a resuscitation bag with a functioning PEEP valve or oxygen flow via a tracheal cannula.
- It is recognized that some patients may not be mechanically ventilated during ECMO and suspected BD/DNC. Under these conditions, while an apnea test can still be conducted, maintaining oxygenation during the apnea test may be challenging due to the inability to deliver oxygen to the lower airway. Oxygenation will depend on providing 100% oxygen in the sweep gas.
- If oxygenation cannot be maintained appropriately, the test will need to be aborted and ancillary testing will be recruited.



- In the case is of veno-arterial ECMO with intrinsic cardiac output, blood gases should be measured simultaneously from the distal arterial line and post oxygenator ECMO circuit.
- The oxygen in the membrane lung should be maintained at 100% throughout the duration of testing, titrating the sweep gas flow rate to 0.5-1 L /min
- Terminate test immediately if spontaneous respiratory movements are observed or if the person becomes unstable as previously described.
- Restart mechanical ventilation, returning to the prior ECMO sweep gas flow rate when the pH reaches less than 7.30 and PaCO₂ reaches 60 mm Hg or 20 mm Hg above baseline PaCO₂ if there is premorbid hypercapnia.

Ancillary tests



- In clinical practice:
 - Use cerebral angiography (DSA), nuclear medicine cerebral blood flow study (SPECT) or 2 transcranial Doppler (TCD) examinations at least 30 minutes apart, to confirm the absence of blood flow to the brain parenchyma.
 - CT angiography (CTA), and MRI/magnetic resonance angiography (MRA) are currently not validated against accepted studies.
 - EEG along with somatosensory and brainstem auditory evoked potentials is limited in evaluating brainstem function but can be used to confirm the absence of electro-cerebral activity in adults.
 - Ancillary tests can be used when uncertainty exists about the reliability of parts of the neurologic examination or when the apnea test cannot be performed.



- Interpretation of each of these tests requires expertise.
- In adults, ancillary tests are not needed for the clinical diagnosis of brain death and cannot replace a neurologic examination.
- Physicians ordering ancillary tests should appreciate the disparities between tests and the potential for false positives (i.e., the test suggests brain death, but the patient does not meet clinical criteria).
- Rather than ordering ancillary tests, physicians may decide not to proceed with the declaration of brain death if clinical findings are unreliable.
- Because of a high risk of bias and inadequate statistical precision, there is insufficient evidence to determine if any new ancillary tests accurately identify brain death.

Documentation



- The time of brain death is documented in the medical records. Time of death is the time the arterial PCO_2 reaches the target value or at the end of the 2nd brain death exam (after the apnea test has been completed).
- In patients with an aborted apnea test, the time of death is when the ancillary test has been officially interpreted.
- A checklist is filled out, signed, and dated.



- ..braindeath phrase should be used to document examination in Cerner.
- The following attestation should be used:
 - If first exam is not consistent with brain death:
 - “The patient shows signs of brain activity and is not brain dead”.
 - If first exam is consistent with brain death:
 - “While the patient's exam meets clinical criteria for brain death, a repeat evaluation in 2 hours or longer is required by policy prior to declaration of brain death”.
 - After second clinical exam is consistent with brain:
 - “On the basis of the findings recorded above, indicating irreversible loss of function of the entire brain including the brainstem, I hereby certify death by neurologic criteria on date/time”.
- Federal and state law require the physician to contact an organ procurement organization following determination of brain death.



Are there patients who fulfill the clinical criteria of brain death who recover brain function?

- In adults, recovery of neurologic function has not been reported after the clinical diagnosis of brain death has been established using the criteria given in the 1995 AAN practice parameter.



What is an adequate observation period to ensure that cessation of neurologic function is permanent?

- There is insufficient evidence to determine the minimally acceptable observation period to ensure that neurologic functions have ceased irreversibly.
- A minimum of 24 hours is recommended specifically for anoxic brain injury after resuscitated cardiac arrest or re-warming.



Are complex motor movements that falsely suggest retained brain function sometimes observed in brain death?

- For some patients diagnosed as brain dead, complex, non-brain-mediated spontaneous movements can falsely suggest retained brain function. Additionally, ventilator auto-cycling may falsely suggest patient-initiated breathing.



What is the comparative safety of techniques for determining apnea?

- Apneic oxygenation diffusion to determine apnea is safe, but there is insufficient evidence to determine the comparative safety of techniques used for apnea testing.



Are there new ancillary tests that accurately identify patients with brain death?

- Because of a high risk of bias and inadequate statistical precision, there is insufficient evidence to determine if any new ancillary tests accurately identify brain death.

Preservation of Organs After a Determination of Brain Death



- ▶ Systolic blood pressure goal of 90–160 mm Hg; mean arterial blood pressure of 70–90 mm Hg
 - Dopamine 3–5 mcg/kg/min IV (max 20 mcg/kg/min)^a
 - Phenylephrine 40–60 mcg/min IV^a
 - Vasopressin 1–2.5 units/h IV (also to control polyuria)
- ▶ Minimal tidal volume strategy to limit extravascular lung water (and volutrauma in lung donors)
- ▶ Preserve Pao₂/Fio₂ gradient ≥300 mm Hg
- ▶ Colloid solutions to maintain oxygenation and avoid pulmonary edema
- ▶ Treat cardiac arrhythmias, ventricular tachycardia (amiodarone), torsade de pointes (magnesium sulfate, cardioversion)
- ▶ Corticosteroids (15 mg/kg) to stabilize or reduce pulmonary edema
- ▶ Packed red blood cells (Hematocrit ≥30%)
- ▶ Avoid hypernatremia using hypotonic solutions
- ▶ Maintenance of normoglycemia (100–180 mg/dL)
- ▶ Avoid acidosis (sodium bicarbonate)
- ▶ Supplement electrolytes regularly (ie, phosphate, magnesium, potassium)

Fio₂ = fraction of inspired oxygen; IV = intravenous; Pao₂ = partial pressure of arterial oxygen.
^a Low-dose strategy.

Valuable Resources



- www.aan.com/guidelines
- <https://www.neurocriticalcare.org/education/braindeath>