Brain Death

January 29, 2017 by Josh Farkas

CONTENTS

- Brain death basics (#brain_death_basics)
- Clinical findings in brain death (#clinical_findings_in_brain_death)
- Clinical context (#clinical_context)
- Diagnosis of brain death (#diagnosis_of_brain_death)
  - (1) Initial suspicion (#dx_step_1 = clinical_suspicion)
  - (2) Evaluate for confounders (#dx_step_2 = exclude_confounders)
  - (3) Dedicated neurologic examination (#dx_step_3 = dedicated_neuro_exam)
  - (4) Apnea test (#dx_step_4 = apnea_test)
  - (5) Confirmatory test PRN (#dx_step_5 = confirmatory_test_PRN)
- If brain death is confirmed:
  - Immediate next steps (#immediate_steps_if_brain_death_is_confirmed)
  - Ongoing supportive care (#management_of_the_brain_dead_patient_with_potential_for_organ_donation)
- Podcast (#podcast)
- Questions & discussion (#questions & discussion)
- Pitfalls (#pitfalls)

brain death basics

(back to contents/sitemap)

definition of brain death

- Defined as irreversible cessation of all cerebral and brainstem functioning.
- Legally recognized as equivalent to cardiopulmonary death in the United States.
physiology of brain death

- The final common pathway of brain death is shown below.
- Regardless of the initial injury, eventually brain death occurs via a spiral of progressive intracranial hypertension, tissue damage, and edema. This is essentially an intracranial compartment syndrome.

![Final common pathway of brain death](image)

clinical findings in brain death

key findings

- Absence of all cranial nerve function.
- Coma (for example no response to pain)
- EEG (if attached) that is completely flat (no activity).
- No respiratory drive (patient doesn’t over-breathe the ventilator).

strange phenomena can be observed in brain death

- Brain dysfunction may lead to the disinhibition of spinal cord reflexes (which are normally suppressed). This may lead to some strange movements, which are often misinterpreted as volitional. For example:
  - Triple flexion is the most common movement encountered. Stimulation of feet causes flexion at the ankles, knees, and hips. This may appear to be a withdrawal, but it’s just a reflex.
  - Neck flexion may stimulate raising of an arm or flexion of a finger.
  - Very slow turning of the head to one side.
  - Myokymia (localized quivering of a muscle; may involve facial or ocular muscles).
  - Lazarus sign (flexion at waist).

clinical context

(1) common causes of brain death (if present, these support the diagnosis of brain death)

- Traumatic brain injury
- Intracranial hemorrhage
- Anoxic brain injury
- Severe meningoencephalitis
- Cerebral edema from fulminant hepatic failure

(2) potential mimics of brain death
- Fulminant Guillain-Barre syndrome
- Hypothermia
- Variety of drug intoxications, for example:
  - Tricyclics
  - Lidocaine
  - Baclofen
  - Sedatives, especially barbiturates
  - Paralytics
  - Anticholinergics
  - Bupropion
- High C-spine injury
- Locked-in syndrome
  (\(\ast\) = full recovery is possible)

### diagnosis of brain death

The following is a general approach to diagnosing brain death.

- If at any point the patient shows evidence of cerebral activity, then brain death is excluded.
  - It's much easier to **exclude** brain death than to prove it.
- Most hospitals have a brain death protocol, which must be followed precisely with complete documentation.

#### dx step 1 = clinical suspicion

**initial suspicion:** Consider brain death in any patient with catastrophic brain injury and a bedside exam consistent with brain death:

- Unresponsiveness to pain
- No cranial nerve function:
  - No pupillary or corneal reflex
  - No oculocephalic reflex (doll's eyes)
  - No cough reflex (when suctioning endotracheal tube)
- No respiratory drive (not over-breathe the ventilator)

**rapid informal apnea test**
- If safe, decrease the respiratory rate on the ventilator to a very low rate (e.g. 4 breaths/min).
- Observe end tidal CO2 and respiratory effort for ~5 minutes:
  - If the patient makes any respiratory effort, then brain death is excluded.
  - If the etCO2 rises and the patient makes no spontaneous respiratory effort, this predicts apnea on a formal apnea test.

**is it worthwhile to pursue a formal brain death diagnosis?**
- Potential reasons to pursue formal diagnosis might include:
  - Required prior to organ donation.
  - May resolve confusion regarding goals of care and/or issues with surrogate decision-makers.
  - Reassures the family that nothing further can be done (the family may wish to pursue this testing).
  - Avoids future criticism or legal issues regarding premature withdrawal of life-sustaining therapy.
- Potential reasons *not* to pursue a formal diagnosis of brain death:
  - The patient is obviously moribund (without any potential for organ donation).
  - There is no confusion regarding goals of care.
  - Comfort-directed care is clearly appropriate, so brain death declaration wouldn't affect management.

---

**dx step 2 = exclude confounders**

**exclude common confounding factors:**
- Temperature must be normal (>35°C).
- Blood pressure must be adequate.
- Glucose and chemistries must be relatively normal.
- All sedatives and paralytics must be discontinued (for >4-5 half-lives).

**consider less common confounders:**
- Fulminant Guillain-Barre syndrome.
- Drug intoxication (e.g. tricyclics, lidocaine, baclofen, sedatives, paralytics, anticholinergics, bupropion).
- High C-spine injury.
- Locked-in syndrome.

---

**dx step 3 = dedicated neuro exam**

*This examination generally must be performed by two different clinicians.*

**clinical examination for brain death**
- Confirm coma off sedation (no response to pain in any extremity, above eyes, at the temporal-mandibular joint).
- Complete cranial nerve exam must be negative:
  - No pupillary or corneal reflex.
  - No oculocephalic reflex (doll's eyes).
  - No oculovestibular reflex (cold caloric).
  - No gag reflex (tested by suctioning the back of the throat with a Yankauer catheter).
  - No cough reflex (tested by in-line suctioning of an endotracheal tube).
dx step 4 = apnea test

prerequisites

- Patient must be stable enough to tolerate apnea (e.g. not severely hypoxemic or acidic).
- CO2 is normal or at the patient's known baseline (in cases of COPD). If the patient has evidence of chronic CO2 retention without a known baseline CO2, the apnea test can't be done.

prior to the test

- Patient is pre-oxygenated with 100% FiO2 for 10 minutes.

induction of apnea
The goal is to stop ventilating the patient but to provide \textit{apneic oxygenation} and some continuous positive pressure to prevent de-recruitment.

There are various ways of accomplishing this:

(a) Simply keep the patient on the ventilator on a CPAP mode with no backup rate. Some authors have reported this, but most ventilators won't allow the patient to be apneic without kicking into a backup ventilation mode (Solek-Pastuszka 2016 [https://www.ncbi.nlm.nih.gov/pubmed/27742325]).

(b) A nice way to achieve this might be to use a flow-inflating bag to provide oxygen and CPAP (video above).

(Traditionally, the apnea test was accomplished by inserting a cannula to deliver oxygen \textit{into the endotracheal tube}. This strategy has a risk of causing pneumothorax, so it's not recommended) (Gorton 2016 [https://www.ncbi.nlm.nih.gov/pubmed/27460062]).

Observe for respiratory effort or clinical deterioration. If there is any respiratory effort then the patient isn't brain dead — reconnect to the ventilator immediately and resume supportive care.

Abort the apnea test if the patient develops significant desaturation (<85%) or hemodynamic instability.

Perform an ABG after 10 minutes of apnea, then place the patient back on ventilator support.

- A positive test typically requires PaCO2 to increase >60mm and/or ~20 mm above baseline.
- Some protocols may allow for etCO2 to be used in place of an ABG.

If PaCO2 doesn't increase sufficiently, the test may be repeated following pre-oxygenation and performed over 15 minutes.

\textbf{dx step 5 = confirmatory test PRN}

\textbf{confirmatory test is required if any of the following criteria cannot be satisfied:}

1. There is a clear cause of catastrophic brain injury which is consistent with brain death.
2. There are no potentially confounding factors, such as:
   - Sedative accumulation or poisoning with unknown agent.
   - Interference with neurologic exam: C-spine injury, facial or skull-base trauma, eye pathology.
   - Known focal brainstem pathology (patient might have locked-in syndrome).
3. An apnea test can be completed successfully (e.g. the patient is stable enough to tolerate apnea).

\textbf{the most useful confirmatory test is cerebral scintigraphy:}
Radiolabeled dye is injected into a peripheral vein. If there is perfusion to the brain, the dye will be taken up in brain tissue.

In brain death, lack of brain perfusion causes an “empty skull sign” (image below).

A cerebral scintigraphy which shows lack of blood flow to the brain (based on an official interpretation by a radiologist) is extremely solid evidence of brain death.

Early in the process of brain death, there may be a small amount of perfusion remaining. In this case, a repeat test in 6-12 hours may show lack of flow.

More on cerebral scintigraphy [here](https://emcrit.org/pulmcrit/brain-death-flow-scan/).

**Radiolabeled dye**

- **Flow scan indicated If:**
  - Examination & clinical context consistent with brain death
  - Confounding factor(s) make it impossible to pronounce death based on clinical examination and apnea test

- **Radionuclide flow scan**
  - Normal flow
  - Reduced flow (e.g., some patches of flow within the brainstem or thalamus)
  - No flow

- **Possible impending brain death**
  - Continue support
  - Repeat scan in 12-24 hours

- **Patient is brain dead**
  - Continue support
  - Search for alternative cause of coma (e.g., MRI scan, toxicological evaluation)

---

**Flatline EEG supports a diagnosis of brain death**

- EEG isn’t generally ordered as a confirmatory test, but some patients may already be attached to video EEG monitoring (e.g. after anoxic brain injury).
- A persistently flatline EEG for 24-48hr after anoxia without any medications on board indicates a terrible prognosis (e.g. brain death or persistent unconsciousness).
- Note that a flatline EEG can be found in the absence of brain death in some situations (e.g. drug intoxication). Therefore, by itself the flatline EEG is less powerful evidence supporting brain death than the flow scan.

---

**Immediate steps if brain death is confirmed**

- The family should be informed that the patient has died (with appropriate explanation of brain death).
- Do not discuss organ donation with the family; this should be done by a separate organ procurement team.

---

**Management of the brain dead patient with potential for organ donation**

Ongoing high-quality supportive care is required to maximize organ function. Optimal management of the donor may increase the likelihood of successful allograft function and favorable long-term outcomes for organ recipients.

**General resuscitative principles**
Overall, the general principles of management of the donor are similar as for any patient receiving high-quality supportive care. Resuscitation may be tailored slightly to favor preserving function of the organs for donation. Long-term consequences of interventions don't exist (e.g. C. difficile infection due to broad-spectrum antibiotics, myopathy due to high-dose steroid).

**corticosteroid**

- Reasons to give steroid:
  - (a) Brain death can cause pituitary deficiency, promoting hemodynamic instability.
  - (b) Steroid may reduce inflammation, thereby improving graft organ functionality.
- Large doses are commonly used (e.g. 1,000 mg IV methylprednisolone daily).

**management of diabetes insipidus**

- Diabetes insipidus commonly occurs, but not always (it is possible to be brain dead and still have a functioning hypothalamus). If it occurs, it should be treated with a goal of bringing the sodium back to a fairly normal value (hyponatremia may impair liver function).
- Diagnosis:
  - In the context of brain death, diabetes insipidus may be strongly suspected on the basis of copious dilute urine production.
  - The differential diagnosis may include polyuria due to hyperglycemia, hypothermia, or medications.
  - If doubt exists, the diagnosis of diabetes insipidus may be established by labs showing hyponatremia and ongoing production of hypotonic urine (urine osmolarity < 200 mOsm/L or urine specific gravity <1.005). However, treatment shouldn't be delayed while waiting for these studies to return.
- Tx option #1 = desmopressin.
  - IV desmopressin 2-4 micrograms q6hr-q8hr.
  - Advantage = easy to do, doesn't tie up an intravenous line.
  - Disadvantage = if hyponatremia occurs, DDAVP will take hours to wear off.
- Tx option #2 = vasopressin infusion.
  - Very low doses of vasopressin are sufficient to reverse diabetes insipidus (e.g. 0.01 units/minute or lower). These doses won't necessarily have much effect on hemodynamics.
  - Useful for patients who are hypotensive (in which cases higher doses are generally given, e.g. ~0.04 units/minute).
  - Advantage = titratable (so it can be turned off if hyponatremia or low urine output occurs), may help support blood pressure in hypotension.
  - Disadvantage = slightly more work than DDAVP (ongoing IV infusion).

**preservation of lung function**

- Expert management probably has the greatest impact on lung procurement, compared to other organs.
- Avoid subclavian central line (pneumothorax won't have time to heal, potentially making it more problematic).
- Bronchoscopy is required to evaluate candidacy for lung donation. Avoid performing bronchoalveolar lavage if possible (or, if mandatory, use the lowest volume of saline possible).
- Use of airway pressure release ventilation (APRV) has been shown to improve candidacy for lung donation (https://www.ncbi.nlm.nih.gov/pubmed/21422364).
- Avoid volume overload.

**improvement in cardiac function**

- Myocardial stunning and systolic heart failure are common following brain death. With supportive care, these often improve over time.
- Supportive care principles are similar to other patients with cardiogenic shock.
- Thyroid hormone supplementation may assist in cardiac recovery.
  - Following brain death, a sick-euthyroid state frequently occurs (with elevated levels of inactive reverse-T3, low levels of active T3, and normal levels of T4). Exogenous thyroid hormone has commonly been used in efforts to improve cardiac function and candidacy for heart donation. No high-level evidence supports this practice, which remains controversial. Consensus guidelines recommend consideration of thyroid hormone supplementation in patients with hemodynamic instability (25978154).
  - If thyroid hormone is given, either thyroxine (T4) or triiodothyronine (T3) may be used. Triiodothyronine (T3) may be a bit more effective, but it is less widely available in IV form. Commonly used doses are:
Thyroxine (T4): 20 ug IV bolus followed by 10 ug/hour IV maintenance infusion.
Triiodothyronine (T3): 4 ug IV bolus followed by 3 ug/hr IV maintenance infusion (if unavailable, liothyronine has excellent oral bioavailability)

temperature management

- Brain death may lead to spontaneous development of hypothermia.
- Temperature should be monitored. External warming may be necessary to avoid hypothermia.

empiric antibiotics

- Broad-spectrum antibiotics are often administered (e.g. piperacillin-tazobactam).

To download the episode:
Right Click Here and Choose Save-As

Going further:

- In a severely neurologically injured patient, avoid any long-acting sedative (ideally, only propofol or dexmedetomidine would be used). This facilitates an unclouded neurologic examination.
- Failure to consider a diagnosis of brain death. For example, if a patient is brain dead following anoxic brain injury, there is no role for therapeutic hypothermia or neuroprognostication: the patient is dead.
- Brain dead patients may produce a variety of spinal reflexes (e.g. triple flexion). These shouldn't be mistaken as indicating that the patient is alive.
- Be extremely cautious about declaring brain death in patients with poisoning or brain dysfunction of unclear etiology (otherwise this may happen).
- EEG can be flatline due to medication effects, so be careful about using EEG as a confirmatory test.
• **Organ donation in the Emergency Department** ([https://emcrit.org/emcrit/organ-donation-brain-death/](https://emcrit.org/emcrit/organ-donation-brain-death/)) (Scott Weingart, EMCrit RACC)
• **Brain death** ([https://wikem.org/wiki/Brain_death](https://wikem.org/wiki/Brain_death)) (WikEM)
• **Brain death imaging** ([https://radiopaedia.org/articles/brain-death-2](https://radiopaedia.org/articles/brain-death-2)) (Radeopaedia)

---

The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.