Guidelines for Brain Death in Children: Toolkit

These guidelines and toolkit are based upon the available literature and consensus opinion of a panel of national experts, and may differ from individual state laws or statutes, as well as individual hospital policies and procedures. Please review all relevant hospital and state policies and regulations when utilizing the Society of Critical Care Medicine guideline and toolkit in the assessment and declaration of brain death in children. Please use the Alt + Left Arrow to return to previous view.

Tab 1: Index

1. **Revised pediatric guidelines for determination of brain death in children:**
   [http://pediatrics.aappublications.org/content/early/2011/08/24/peds.2011-1511](http://pediatrics.aappublications.org/content/early/2011/08/24/peds.2011-1511)

**Endorsing organizations:**

American Academy of Pediatrics:
   - Section on Critical Care
   - Section on Neurology
American Association of Critical Care Nurses
Child Neurology Society
National Association of Pediatric Nurse Practitioners
Society of Critical Care Medicine
Society for Pediatric Anesthesia
Society of Pediatric Neuroradiology
World Federation of Pediatric Intensive and Critical Care Societies
2. Guideline summary
   a. Examination criteria
   b. Apnea testing
   c. Observation period
   d. Ancillary studies
   e. Algorithm for examination (Algorithm)
   f. Special populations
      i. Neonates
      ii. Teenage patients (PEDIATRIC TRAUMA PATIENTS)

3. Teaching materials
   a. PowerPoint slide set
   b. Neurologic examination
      i. Examination
      ii. How to perform oculocephalic (doll's eye) testing
      iii. How to perform oculovestibular (cold water caloric) testing
      iv. How to perform an apnea test (Apnea)

4. Documentation
   b. Sample notes formats:
      i. Note template in Word (Note_template)
      ii. Electronic medical record (EMR) version (EMR_sample)

5. Other materials
   a. Drug elimination table (Drug_elimination)
   b. Perfusion scan (Scan)

Please use the Alt + Left Arrow to return to previous view.
Tab 2: Guideline Summary

Examination criteria

- Appropriate patients for testing
  
  Age >37 weeks gestational age to 18 years of age
  
  Temperature >35°C
  
  Normotensive without volume depletion
    
    Blood pressure measured by indwelling arterial catheter is preferable.
    
    Hypotension is defined as systolic blood pressure or mean arterial pressure <2 standard deviations below normal values for age norms.
  
  Metabolic disturbances capable of causing coma should be identified and corrected.
  
  Patient should have a known irreversible cause of coma. Drug intoxication, neurotoxins, and chemical exposures should be considered in cases where a cause of coma has not been identified.
  
  Medications can interfere with the neurologic examination; sedatives, analgesics, antiepileptics, and neuromuscular blocking agents require adequate time for drug clearance (Drug elimination).
    
    Stop all such medications and allow adequate time for drug metabolism.
    
    Organ system dysfunction and hypothermia can alter drug metabolism.
    
    Obtain blood or plasma levels to confirm drug levels are in the low to mid-therapeutic range.
    
    If elevated levels are noted, an ancillary test can be performed.
    
    Initial exam should be deferred for at least 24 hours after trauma or resuscitation event.

- Two examinations are performed by two different attending physicians.

- Observation period
  
  Examinations are separated by an observation period.
    
    Term newborns (>37 weeks gestational age) to 30 days: **24 hours**
    
    Children >30 days to 18 years: **12 hours**
  
  Reduction of the observation periods is acceptable using an accepted ancillary (Ancillary) study.
    
    When an ancillary study is used to decrease the observation interval, two examinations and two apnea tests are recommended.
    
    One examination (or all components that can be completed safely) and an apnea test should be completed before the ancillary study, and the second examination (or all components that can be completed safely) and an apnea test should be completed after the ancillary study.
The second examination can occur at any time following the ancillary study in children of all ages.

- Spinal reflexes may remain intact and do not preclude a determination of brain death.
- Presence of diabetes insipidus does not preclude a determination of brain death.
- Death is declared after the second neurologic examination and apnea test confirming an unchanged and irreversible condition.

**Apnea testing** (see Apnea test for detailed explanation)

- An apnea test should be performed with both exams. Both apnea tests may be performed by the same physician. The physician performing the apnea test should be trained in ventilator management.
  The arterial PaCO$_2$ should increase $\geq$20 mm Hg above baseline and reach at least 60 mm Hg, with the patient demonstrating no respiratory effort.
  If unable to perform safely or to complete the apnea test, an ancillary test should be performed.

**Ancillary studies** (for more detail, see [Ancillary](#))

- Ancillary testing is not required to make a determination of brain death.
- Ancillary testing is indicated in the following situations:
  - Unable to safely perform or to complete apnea testing
  - Unable to perform all components of the neurologic examination
  - Uncertainty exists about the neurologic examination results
  - A medication effect may be present that interferes with neurologic testing
- Ancillary testing may be used to reduce the intra-examination observation period.
- If ancillary tests are utilized, a second clinical examination of neurologic function and apnea testing should be performed.
- Accepted ancillary tests:
  - Electroencephalogram (EEG) — ~30 minutes of monitoring is needed
  - Radionuclide cerebral blood flow ("perfusion") study
- Studies that have not been validated as ancillary tests:
  - Transcranial Doppler sonography
  - Computed tomography (CT) angiography
  - Magnetic resonance imaging (MRI) angiography

**Special populations**

- Infants at 37 weeks estimated gestational age to 30 days of age
It is important to carefully and repeatedly examine term newborns with particular attention to examination of brainstem reflexes and apnea testing. Assessment of neurologic function in the term newborn may be unreliable immediately after an acute catastrophic neurologic injury or cardiopulmonary arrest. A period of at least 24 hours is recommended before evaluating the term newborn for brain death. The observation period between examinations should be 24 hours for term newborns (37 weeks) to 30 days of age.

Ancillary studies in newborns are less sensitive than in older children. No data are available to determine brain death in infants < 37 weeks EGA.

- **Teenage patients (Older Pediatric Trauma Patients?)**
  
  Variability exists for the age designation of pediatric trauma patients. In some states, the age of the pediatric trauma patient is defined as <14 years of age.
  
  If the pediatric trauma patient is cared for in the pediatric intensive care unit, the pediatric guidelines should be followed.
  
  If the older pediatric trauma patient is cared for in an adult intensive care unit, the adult brain death guidelines should be followed.
Tab 3: Brain death determination

Educational media:
- PowerPoint slide set

Exam basics:
- Order of exam – There is no set order, but it is more efficient to test one ear for oculovestibular function at the beginning and the other at the end, so that the first ear tested has had time to warm back to body temperature.
- **Spontaneous movement** – NO spontaneous movement, even posturing, is seen in a brain-dead patient, though spinal reflexes may be present.
- **Response to pain**
  Method:
  - Trapezius squeeze, supraorbital pressure, earlobe pinching, or sternal rub
  - Observe for localization
  In brain death, there will be NO movement, excluding spinal cord events such as reflex withdrawal or spinal myoclonus.
  - FYI --Do not be misled by testing for pain response on the foot as the patient may have an intact triple-flexion response, which is a spinal arc, and could be misinterpreted as localization.
- **Test cranial nerves**
  - **Corneal reflex**
    Method:
    - Hold the eyelid open
    - Touch the cornea with gauze, tissue, or the tip of a swab
    - Observe for eyelid (eyelash) movement
    - Repeat on other eye
    In brain death, there will be NO movement.
    Tests cranial nerves V and VII
  - **Facial grimace**
    Method:
    - Apply a noxious stimulus to the face using supraorbital ridge pressure or a swab inserted into the nares with upward pressure against the turbinates.
    - Observe face for grimace.
    In brain death, there will be NO grimace
    Tests cranial nerves V and VII
Pupillary response to light
In brain death, there is no response to light.
  Pupils may be mid-position to dilated, but fixed.
  Pupils need not be equal or dilated.
Tests cranial nerves II and III

Cough and gag
Stimulate the posterior pharynx
Suction the patient to depth of carina using an endotracheal suction catheter
Tests cranial nerves IX and X

Oculocephalic test (doll’s eye reflex)
Contraindications
  Presence of cervical collar
Physiology
  Tests the extraocular muscle movements controlled by cranial nerves III and VI
Method
  Hold the eyelids open.
  The examiner moves the patient’s head from side to side forcefully and quickly.
In brain death, the eyes always point in the direction of the nose and do not lag behind or move.

FYI
Even someone who is blind will have doll’s eye reflex if the brainstem is intact.
The phenomena of the doll’s eye reflex is based on old-fashioned dolls that had porcelain heads and wooden eyeballs. The wooden eyeballs would lag behind in movement when the porcelain head was turned due to inertia. Modern dolls (eg, Barbie) have eyes painted on the head.
A positive doll’s eye reflex is normal; negative is indicative of brainstem dysfunction.

Oculovestibular test (“cold water calorics”)
Note: this test may be substituted for occulocephalic testing in the patient with cervical spine injury.
  - Contraindications
    - Ruptured tympanic membrane
Otorrhea

Materials needed:
- Container of ice water
- 20-60 mL syringe
- IV tubing or 16- to 20-gauge IV catheter (needle removed)
- Emesis basin and/or absorbent pad

Method:
- Place absorbent pad under the patient’s head.
- Elevate the head of the bed to 30° so that the lateral semicircular canal is vertical.
- Have someone hold the eyelids open so that the pupils can be observed.
- Fill the syringe with ice water and attach the IV tubing or catheter.
- Instill 40-60 mL of ice water into the external auditory meatus while observing for eye movement.
- Allow at least a 5-minute interval before testing the other ear.

Interpretation
- Any nystagmus is not consistent with brain death.

Physiology:
- Ice water cools the endolymph in the semicircular canal.
- Tests cranial nerves III, VI, and VIII
- C-O-W-S: cold opposite, warm same. When cold fluid is instilled into the ear canal, the fast phase of nystagmus will be to the side opposite from the ear tested; in the comatose patient, the fast phase of nystagmus will be absent, as this is controlled by the cerebrum. Cold water instillation in the ear canal of a comatose patient will result in deviation of the eyes toward the ear being irrigated. When brainstem function is absent, no nystagmus will be observed.

- Apnea test

Contraindications
- Patients with high cervical spine injury
- Patients requiring high levels of respiratory support

Prior to the apnea test:
- Normalize PaCO₂; confirm with arterial blood gas measurements.
In a child with chronic lung disease, the child’s baseline PaCO$_2$ should be used.

Confirm core temperature $\geq 35^\circ$C.

Normalize blood pressure.

Pre-oxygenate with 100% oxygen for 5-10 minutes.

Ensure correction of metabolic parameters and clearance of sedating pharmacologic agents. Ensure there is no recent use of neuromuscular blocking agents. Train-of- may be needed to confirm absence of neuromuscular blockade.

Performing the apnea test:

Methods of administering oxygen ($FIO_2 = 1.0$) while not ventilating patient:

- T-piece connection providing O2.
- Flow-inflating anesthesia bag with positive end-expiratory pressure titrated to the desired level.
- Low-flow endotracheal tube insufflation with 100% O2. Caution: use of tracheal insufflation may be associated with CO2 washout and barotrauma and is not recommended in the pediatric guidelines.
- Use of continuous positive airway pressure via the ventilator is not recommended as apnea may not be appreciated if the ventilator reverts to an assist mode when apnea is sensed.

Monitor by direct visualization for any spontaneous respiratory effect

- In line end tidal CO2 monitoring can be used to measure any respiratory effort resulting in CO2 excursion

Arterial blood gas measures should be obtained every 3-5 minutes until apnea criteria are met (increase in PaCO$_2 \geq 20$ mm Hg AND PaCO$_2 \geq 60$ mm Hg).

Any spontaneous respiratory effort is NOT consistent with brain death.

FYI

In patients without significant pulmonary disease or injury, apneic oxygenation will permit the arterial oxygen saturation to remain high or change minimally. Despite no active ventilation, gas exchange continues to take place in the alveoli, with oxygen diffusing out of the alveoli and CO$_2$ diffusing into them. If the respiratory quotient is assumed to be 0.8, then for every 1 mL of oxygen consumed, 0.8 mL of CO$_2$ will be produced. As a result, there is a net entrainment of oxygen (the only gas being provided to the patient) down the tracheobronchial tree.
CO₂ rises ~4 mm Hg for every minute of apnea. The rate may be lower in the setting of brain death due to the loss of brain metabolism. At this rate, it will take at least 5 minutes of apnea for the pCO₂ to rise by 20 mm Hg; often it requires 7-9 minutes. Therefore, one may choose to draw a blood gas at minute 5-6 of apnea, and continue the apnea observation while awaiting the results, so that another may be drawn every 2 - 3 minutes until the apnea criteria have been met.

Termination of apnea test:
Draw arterial blood gas to verify appropriate CO₂ change from baseline.
Place patient back on ventilator support.
Document test result.
Abort the apnea test and obtain ancillary testing if hemodynamic instability occurs or if unable to maintain SaO₂ ≥85%.

Ancillary testing
- Tests not required unless clinical examination or apnea test cannot be completed.
- Ancillary tests may not be used in lieu of clinical neurologic examination; rather, ancillary testing should be followed by a confirmatory clinical examination.
- Ancillary tests may be used to decrease the observation period. There is no specific recommendation on when the second clinical examination can be performed after the ancillary study to make a determination of death.
- If ancillary testing supports the diagnosis of brain death, then a second exam and apnea test should be performed, but repeat ancillary testing is not necessary.
- If the ancillary test is equivocal, then a 24-hour waiting period is recommended before retesting.
- Imaging studies such as CT or MRI scans are not considered ancillary studies to make a determination of brain death.
- Accepted ancillary studies
  - Both EEG and cerebral blood flow have similar confirmatory value.
  - Ancillary studies are less sensitive in newborns.
  - “Gold standard” = four-vessel cerebral angiography
    - Requires moving patient to angiography suite
    - May be used in the presence of high-dose barbiturate therapy
    - May be difficult to perform in smaller infants and children
  - Cerebral blood flow study
    - Commonly used with good experience in pediatric patients
May be used in the presence of high-dose barbiturate therapy
Standards established by Society of Nuclear Medicine and Molecular Imaging
         and the American College of Radiology
Example: no accumulation of tracer in non-perfused cranial vault, while scalp and
         facial structures are perfused

EEG
Standards established by American Electroencephalographic Society
Low to mid-therapeutic barbiturates levels should not preclude use of EEG

- Ancillary studies not yet validated and with little to no experience in children:
  Transcranial Doppler
  CT angiography
  CT perfusion with spin labeling
  Nasopharyngeal somatosensory evoked potential studies
  MRI + magnetic resonance angiography
  Perfusion MRI
Algorithm for Determination of Brain Death Comatose Child
(37 weeks gestational age to 18 years of age)

Does Neurologic Examination Satisfy Clinical Criteria For Brain Death?
A. Physiologic parameters have been normalized:
   1. Normothermic: Core Temp > 35°C (95°F)
   2. Normotensive for age without volume depletion
B. Coma: No purposeful response to external stimuli (exclude spinal reflexes)
C. Examination reveals absent brainstem reflexes: Pupillary, corneal, vestibule-ocular (Caloric), gag.
D. Apnea: No spontaneous respirations with a measured PaCO$_2$ ≥ to 60 mmHg and ≥ 20 mm Hg above the baseline PaCO$_2$

NO
A. Continue observation and management
B. Consider diagnostic studies: baseline EEG, and imaging studies

YES

Toxic, drug or metabolic disorders have been excluded?

NO
A. Await results of metabolic studies and drug screen
B. Continued observation and reexamination

YES

Patient Can Be Declared Brain Dead (by age-related observation periods*)
A. Newborn 37 weeks gestation to 30 days: Examinations 24 hours apart remain unchanged with persistence of coma, absent brainstem reflexes and apnea. Ancillary testing with EEG or CBF studies should be considered if there is any concern about the validity of the examination.
B. 31 days to 18 years: Examinations 12 hours apart remain unchanged. Ancillary testing with EEG or CBF studies should be considered if there is any concern about the validity of the examination.

*Ancillary studies (EEG & CBF) are not required but can be used when (i) components of the examination or apnea testing cannot be safely completed; (ii) there is uncertainty about the examination; (iii) if a medication effect may interfere with evaluation or (iv) to reduce the observation period.
# Brain Death Examination for Infants and Children

Two physicians must perform independent examinations separated by specified intervals

<table>
<thead>
<tr>
<th>Age of Patient</th>
<th>Timing of first examination</th>
<th>Examination interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Term newborn (≥27 weeks gestational age) and up to 30 days old</td>
<td>☐ First exam may be performed 24 hours after birth OR 24 hours following cardiopulmonary resuscitation or other severe brain injury</td>
<td>☐ At least 24 hours&lt;br&gt;☐ Interval shortened because ancillary study (section 4) is consistent with brain death</td>
</tr>
<tr>
<td>☐ 31 days to 18 years old</td>
<td>☐ First exam may be performed 24 hours following cardiopulmonary resuscitation or other severe brain injury</td>
<td>☐ At least 12 hours OR&lt;br&gt;☐ Interval shortened because ancillary study (section 4) is consistent with brain death</td>
</tr>
</tbody>
</table>

## Section 1. PREREQUISITES for brain death examination and apnea test

### A. IRREVERSIBLE AND IDENTIFIABLE Cause of Coma (Please check)
- ☐ Traumatic brain injury
- ☐ Anoxic brain injury
- ☐ Known metabolic disorder
- ☐ Other (Specify) ________________

### B. Correction of contributing factors that can interfere with the neurologic examination

- ☐ Core Body Temp is ≥95°F (≥35°C)
- ☐ BP or MAP in acceptable range for age (BP should not be less than 2 standard deviations below age appropriate norm)
- ☐ Sedative/analgesic drug effect excluded as a contributing factor
- ☐ Metabolic intoxication excluded as a contributing factor
- ☐ Neuromuscular blockade excluded as a contributing factor

If ALL prerequisites are marked YES, then proceed to section 2; if not, then defer examination. *See Section 4.

## Section 2. PHYSICAL EXAMINATION

**NOTE: Spinal cord reflexes are acceptable**

<table>
<thead>
<tr>
<th>Spinal cord reflexes are acceptable</th>
<th>Examination One</th>
<th>Examination Two</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Flaccid tone, patient unresponsive to deep painful stimuli</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>b. Pupils are midposition or fully dilated; light reflexes are absent</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>c. Corneal, cough, gag reflexes are absent</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>Sucking and rooting reflexes are absent (in neonates and infants)</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>d. Oculovestibular reflexes are absent</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>e. Spontaneous respiratory effort while on mechanical ventilation is absent</td>
<td>☐ Yes ☐ No</td>
<td>☐ Yes ☐ No</td>
</tr>
</tbody>
</table>

*Explain any exam element that could not be performed:_______________*

## Section 3. APNEA TEST

<table>
<thead>
<tr>
<th>Apnea test is contraindicated or could not be completed due to:_______________</th>
<th>Ancillary study (EEG or radionuclide CBF) was performed. (See Section 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Exam 1: No spontaneous respiratory efforts were observed despite final PaCO₂ ≥ 60 mm Hg and a ≥ 20 mm Hg increase above baseline.</td>
<td>Pre PaCO₂: __________&lt;br&gt;Apnea duration: ______ minutes&lt;br&gt;Post PaCO₂: __________</td>
</tr>
<tr>
<td>☐ Exam 2: No spontaneous respiratory efforts were observed despite final PaCO₂ ≥ 60 mm Hg and a ≥ 20 mm Hg increase above baseline.</td>
<td>Pre PaCO₂: __________&lt;br&gt;Apnea duration: ______ minutes&lt;br&gt;Post PaCO₂: __________</td>
</tr>
</tbody>
</table>
Section 4. ANCILLARY TESTING is required when:
(1) components of the examination or apnea testing cannot be completed;
(2) if there is uncertainty about the results of the neurologic examination; or
(3) if a medication effect may be present.
Ancillary testing may be performed to reduce the inter-examination period however a second neurologic examination is required.

- [ ] Electroencephalogram (EEG) report documents electrocerebral silence
- [ ] Cerebral Blood Flow (CBF) study report documents no cerebral perfusion

☐ Yes  ☐ No

Section 5. SIGNATURES

Examiner One
I certify that my examination is consistent with cessation of function of the brain and brainstem. Confirmatory exam to follow.

(Printed Name) _______________________________ (Signature) _______________________________

(Specialty) ____________________________ (Pager/ID #) _______ (Date) _______ (Time) _______

Examiner Two
I certify that my examination and/or ancillary test report confirms unchanged and irreversible cessation of function of the brain and brainstem.
Date/Time of death: _______________________________

(Printed Name) _______________________________ (Signature) _______________________________

(Specialty) ____________________________ (Pager/ID #) _______ (Date) _______ (Time) _______


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### Medications Administered to Critically Ill Pediatric Patients and Recommendations for Time Interval after Discontinuation until Testing

<table>
<thead>
<tr>
<th>Medication</th>
<th>Infants/Children Elimination Half-Life</th>
<th>Neonates Elimination Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous induction, anesthetic, and sedative agents</td>
<td></td>
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</tr>
<tr>
<td>Thiopental</td>
<td>Adults: 3-11.5 hrs (shorter half-life in children)</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>2.5 hrs</td>
<td></td>
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<tr>
<td>Etomidate</td>
<td>2.6-3.5 hrs</td>
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<tr>
<td>Midazolam</td>
<td>2.9-4.5 hrs</td>
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<tr>
<td>Propofol</td>
<td>2-8 mins, terminal half-life 200 mins (range, 300-700 mins)</td>
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<tr>
<td>Demedetomidine</td>
<td>Terminal half-life 85-159 mins (79-81)</td>
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<tr>
<td>Antiepileptic drugs</td>
<td></td>
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<tr>
<td>Phenoobarbital</td>
<td>Infants: 20–133 hrs; children: 37–73 hrs</td>
<td></td>
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<tr>
<td>Phenobarbital</td>
<td>25 hrs</td>
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<tr>
<td>Phenytoin</td>
<td>11–55 hrs</td>
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<tr>
<td>Diazepam</td>
<td>1 month to 2 yrs: 40–50 hrs</td>
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<tr>
<td>Lorazepam</td>
<td>2-12 yrs: 15–21 hrs</td>
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<tr>
<td>Clonazepam</td>
<td>Infants: 40.2 hrs (range, 18–73 hrs)</td>
<td></td>
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<tr>
<td>Valproic acid</td>
<td>Children: 2–14 yrs; mean 9 hrs; range, 3.5–20 hrs</td>
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<tr>
<td>Levitinacetam</td>
<td>Children 4–12 yrs: 5 hrs</td>
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<tr>
<td>Intravenous narcotics</td>
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<tr>
<td>Morphine Sulfate</td>
<td>Infants 1–3 months: 6.2 hrs (5–10 hrs)</td>
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<td></td>
<td>6 months to 2 yrs: 2.9 hrs (1.4–7.8 hrs)</td>
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<tr>
<td></td>
<td>Children: 1–2 yrs</td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>Infants &lt;3 months: 8.2–10.7 hrs (range, 4.9–31.7 hrs); infants 3–18 months: 2.3 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children 5–8 yrs: 3 hrs</td>
<td></td>
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<tr>
<td>Fentanyl</td>
<td>Infants 5 to 4.5 yrs: 24 hrs (mean); 0.5–14 yrs: 21 hrs (range, 11–36 hrs for long-term infusion)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children 2–8 yrs: 97 ± 42 mins</td>
<td></td>
</tr>
<tr>
<td>Sufentanil</td>
<td></td>
<td></td>
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<tr>
<td>Muscle relaxants</td>
<td></td>
<td></td>
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<tr>
<td>Succinylcholine</td>
<td>5–16 mins; prolonged duration of action in patients with pseudocholinesterase deficiency or mutation</td>
<td></td>
</tr>
<tr>
<td>Pancuronium</td>
<td>1.0 hrs</td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>41 mins</td>
<td></td>
</tr>
<tr>
<td>Atracurium</td>
<td>17 mins</td>
<td></td>
</tr>
<tr>
<td>Rocuronium</td>
<td>3–12 months: 1.3 ± 0.5 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 to &lt;3 yrs: 1.1 ± 0.6 hrs</td>
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<tr>
<td></td>
<td>3 to &lt;8 yrs: 0.8 ± 0.3 hrs</td>
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<tr>
<td></td>
<td>Adults: 1.4–2.4 hrs</td>
<td></td>
</tr>
</tbody>
</table>

*Elimination half-life does not guarantee therapeutic drug levels for longer-acting medications or medications with active metabolites. Drug levels should be obtained to ensure that levels are in a low to midtherapeutic range before neurologic examination to determine brain death. In some instances, this may require waiting several half-lives and rechecking serum levels of the medication before conducting the brain death examination. Modified from Ashwal and Schneider (57). Metabolism of pharmacologic agents may be affected by organ dysfunction and hypothermia. Physicians should be aware of total amounts of administered medication that can affect drug metabolism and levels.*

Example of Electronic Medical Record Documentation for Determination of Pediatric Brain Death

### Pediatric Brain Death Examination Documentation 12/10/2014 7:27 PM

**Exam Sequence: 0043199**

**Note:** For use with patients 21 weeks postconception to 15 years of age. The patient must be examined in the hospital during treatment of potentially reversible anomalies. Determination of brain death in infants and children must be made by two attending physicians.

The examining physician will note each applicable component of the exam and where applicable, document supporting information or examination data. All boxes must be completed.

Have reasonable efforts been made to notify the patient's parents/legal guardian that a determination of brain death will soon be completed? [YES] [NO] [321119]

<table>
<thead>
<tr>
<th>Age of Patient</th>
<th>Timing of First Exam</th>
<th>Interval after First Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn (21 weeks to 28 days)</td>
<td>First exam may be performed 24 hours after birth or following postpartum resuscitation or other severe brain injury</td>
<td>At least 24 hours</td>
</tr>
<tr>
<td>29 days to 1 year</td>
<td>First exam may be performed 24 hours after birth or following postpartum resuscitation or other severe brain injury</td>
<td>At least 12 hours</td>
</tr>
<tr>
<td>2 years to 18 years</td>
<td>First exam may be performed 24 hours after birth or following postpartum resuscitation or other severe brain injury</td>
<td>At least 6 hours</td>
</tr>
</tbody>
</table>

### I. PREREQUISITES for Brain Death Examination

#### A. IRREVERSIBLE AND IDENTIFIABLE Cause of Coma:

[Definition of cause of coma]

#### B. Correcting contributing factors that can interfere with neuro exam

<table>
<thead>
<tr>
<th>Exam</th>
<th>Exam Date/Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Core body temp &lt; 96°F (35°C) for a minimum of 24 hours, preferably longer</td>
<td>12/10/2014 7:33 PM</td>
</tr>
<tr>
<td>2. Hypertension or MAP &gt; acceptable range based on age</td>
<td>12/10/2014 7:33 PM</td>
</tr>
<tr>
<td>3. Sedation or analgesics used in an acceptable range</td>
<td>12/10/2014 7:33 PM</td>
</tr>
<tr>
<td>4. Metabolic derangement excluded as a contributing factor</td>
<td>12/10/2014 7:33 PM</td>
</tr>
<tr>
<td>5. Neurologic blockade excluded as a contributing factor</td>
<td>12/10/2014 7:33 PM</td>
</tr>
</tbody>
</table>

If ALL prerequisites are marked YES, then proceed to Section II (Physical Exam), or if confounding variable(s) present, proceed to Section IV (Ancillary Study).

### II. Physical Exam (Please check)

1. Fetal cord reflexes acceptable
2. Anorectal, cough, gag reflexes are absent
3. Occult vesical reflexes are absent
4. Spontaneous respiratory effort is absent

Questions to be answered:

- **APNEA Test**
  - May be performed by same physician for both exams.
  - Preoxygenate patient with 100% oxygen for 5 minutes. Once preoxygenated, change mechanical ventilation to continuous positive pressure ventilation or a biphasic circuit while observing for any spontaneous respiratory movements. 
  - PaCO2 must be allowed to rise to 60 mm Hg and >20 torr over baseline PaCO2. If no respiratory effort is noted at PaCO2 >60 Torr and >20 torr above baseline, documentation of apnea consistent with neurologic death noted. The patient is placed back on mechanical ventilation. Once the patient is stable, the examination is continued with a repeat clinical examination or ancillary testing.

- **OF**
  - Apnea test is contraindicated or could not be performed to completion because of [WH PED DDC APNEA EXCLUSION: 3043199]. Ancillary study was therefore performed to document brain death (Section IV).

### III. Ancillary testing to document brain death

- **EEG**
  - Electroencephalogram (EEG) report documents electrophysiological silence.
- **CBF**
  - Cerebral Blood Flow (CBF) study report documents no cerebral perfusion

If all elements of the Physical Exam are complete, proceed to Section II (Apnea Test). If an element of the Physical Exam cannot be performed, proceed to Section IV (Ancillary Study).
Electronic Medical Record Sample Note

(Information in "{ }" are included as drop down lists for selection; see next page for list contents. *** used to allow for free text entry)

Neurological Function Exam - {PICU INITIAL/CONFIRMATORY}

The irreversible and identifiable cause of coma include: {PICU CAUSE OF COMA}.

The following criteria have been evaluated:
- Core Body Temp > 35 degrees Celsius: {YES/NO}
- Systolic BP or MAP in acceptable range: {YES/NO}
- Sedative/analgesic drug effect excluded as a contributing factor: {YES/NO}
  - Phenobarbital: {PICU PHENOBARBITOL}
  - Pentobarbital: {PICU PENTOBARBITAL}
- Metabolic intoxication excluded as a contributing factor: {YES/NO}
- Neuromuscular blockers excluded as a contributing factor: {YES/NO}

Exam:

Cortical Function:

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous movement is absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response to voice is absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facial grimace in response to painful stimuli is absent</td>
<td></td>
<td></td>
</tr>
</tbody>
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Brainstem Function:

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils are midposition or fully dilated and light reflexes are absent</td>
<td></td>
<td></td>
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<td>Corneal, cough, gag reflexes are absent</td>
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</tr>
<tr>
<td>Sucking and rooting reflexes are absent (in neonates and infants)</td>
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Ancillary Tests (not required in any age group, but may decrease exam interval): {PICU ANCILLARY TEST}.

This exam demonstrates irreversible cessation of all activity in the cerebral hemispheres and brainstem.  {PICU NEURO EXAM DISPOSITION}.

Signature_____________________________  Date/Time ______________________
<table>
<thead>
<tr>
<th>EMR choice descriptor</th>
<th>Choices</th>
</tr>
</thead>
</table>
| {PICU INITIAL/CONFIRMATORY} | • Initial  
• Confirmatory |
| {PICU CAUSE OF COMA} | • Traumatic brain injury  
• Anoxic brain injury  
• Known metabolic disorder  
• *** |
| {PICU PHENOBARBITOL} | • Not used in this patient  
• Level = *** at ***  
• *** |
| {PICU PENTOBARBITAL} | • Not used in this patient  
• Level = *** at ***  
• *** |
| {OCULO-VESTIBULAR RESPONSE} | • Absent  
• Absent left (unable to test right)  
• Absent right (unable to test left)  
• Unable to test due to CSF leak  
• *** |
| {PICU OCULOCEPHALIC RESPONSE} | • No response (negative)  
• N/A - unable to perform secondary to spine immobilization or facial injuries  
• *** |
| {PICU RESPIRATORY DRIVE} | • Not yet performed  
• N/A - unable to test secondary to concurrent cardiopulmonary dysfunction  
• Absent as evidenced by an apnea test. Pretest pCO2 was ***. Patient was pre-oxygenated with FiO2 = 1.0 for several minutes. Patient was then placed on CPAP (no breaths) via ETT. After *** minutes, a blood gas was drawn. Pulse oximetry and hemodynamics were stable throughout. Blood gas result: pH ***, pCO2 ***, pO2 ***; indicating a pCO2 increase of *** mm Hg  
• Apnea test being performed by another physician, see additional note |
| {PICU ANCILLARY TEST} | • Not indicated at this time  
• EEG: {PICU EEG}  
• Cerebral Perfusion Study: {PICU CEREBRAL PERFUSION STUDY} |
| {PICU EEG} | • Ordered  
• In progress  
• Pending reading  
• Electrocerebral silence  
• *** |
| {PICU CEREBRAL PERFUSION STUDY} | • Ordered  
• Absent cerebral blood flow  
• *** |
| {PICU NEURO EXAM DISPOSITION} | • A confirmatory exam will be performed in approximately 24 hours by a second physician, given the child’s age is less than 31 days  
• A confirmatory exam will be performed in approximately 12 hours by a second physician, given the child’s age is greater than or equal to 31 days  
• An ancillary test is planned, a confirmatory test will be performed in *** hours  
• Results discussed with family  
• Time of death *** |
Neurological Function Exam - PICU

**INITIAL**

Name: 
Hospital #: 
Room/Bed: 
DOB: 
Age: 
MRN: 
Attending Provider: 
Admission Date: 

The irreversible and identifiable cause of coma include:

- Traumatic brain injury
- Anoxic brain injury
- Known metabolic disorder

The following criteria have been evaluated:

- Core Body Temp >35°C:
  - Yes
  - No
- Systolic BP or MAP in acceptable range:
  - Yes
  - No
- Sedative/analgesic drug effect excluded as a contributing factor:
  - Yes
  - No
- Phenobarbital:
  - Not used in this patient
  - Level *** at ***
- Pentobarbital:
  - Not used in this patient
  - Level *** at ***
- Metabolic intoxication excluded as a contributing factor:
  - Yes
  - No
- Neuromuscular blockers excluded as a contributing factor:
  - Yes
  - No
Exam:

Cortical Function:

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Oculovestibular response:

- Absent
- Absent left (unable to test right)
- Absent right (unable to test left)
- Unable to test due to CSF leak

Oculocephalic response (doll's eye):

- No response (negative)
- N/A - unable to perform secondary to spine immobilization or facial injuries

Respiratory drive:

- Not yet performed
- N/A unable to test secondary to concurrent cardiopulmonary dysfunction

Absent as evidenced by an apnea test. Pretest pCO₂ was ***. Patient was pre-oxygenated with FIO₂ = 1.0 for several minutes. Patient was then placed on CPAP (no breaths) via ETT. After *** minutes, a blood gas was drawn. Pulse oximetry and hemodynamics were stable throughout. Blood gas result: pH ***, pCO₂ ***, pO₂ ***, indicating a pCO₂ increase of *** mm Hg
Apnea test being performed by another physician, see additional note
***

Ancillary Tests (not required in any age group, but may decrease exam interval):

Not indicated at this time

EEG:
- Ordered
- In progress
- Pending reading
- Electrocerebral silence
  ***

Cerebral Perfusion Study:
- Ordered
- Absent cerebral blood flow
  ***

This exam demonstrates irreversible cessation of all activity in the cerebral hemispheres and brainstem.

- A confirmatory exam will be performed in approximately 24 hours by a second physician; given the child's age is less than 31 days
- A confirmatory exam will be performed in approximately 12 hours by a second physician, given the child's age is 31 days or greater

An ancillary test is planned
- A confirmatory test will be performed in *** hours
- Results discussed with family.
- Time of death ***

Attending performing exam:
BRAIN DEATH

Jana Stockwell, MD, FCCM
Circulatory death:
- Cessation of cardiac activity

Brain death: Irreversible cessation of all functions of the entire brain, including the brain stem
First introduced in a 1968 report authored by a special committee of the Harvard Medical School.

Adopted in 1980, with modifications, by the President's Commission for the Study of Ethical Problems in Medicine and Biomedical Research, as a recommendation for state legislatures and courts.

The "brain death" standard was employed in the legislation known as the Uniform Determination of Death Act, which has been enacted by a large number of jurisdictions and the standard has been endorsed by the American Bar Association.

In 1987, the 1st pediatric guidelines were published.

Revised in 2011 for children 37 weeks to 18 years.

Endorsed by:
- Society of Critical Care Medicine
- Section on Critical Care, AAP
- Section on Neurology, AAP
- Child Neurology Society
- Many others
American College of Critical Care Medicine formed a multidisciplinary committee

Goal: review the neonatal and pediatric literature from 1987 & update recommendations

Evidence weighed using Grading of Recommendations Assessment, Development and Evaluation (GRADE) classification system
ANATOMY OF HUMAN BRAIN – 3 REGIONS

- Cerebrum
  - Controls memory, consciousness, and higher mental functioning

- Cerebellum
  - Controls various muscle functions

- Brain stem consisting of the midbrain, pons, and medulla, which extends downwards to become the spinal cord
  - Controls respiration and various basic reflexes (e.g., swallow and gag)
Deep coma
- Non-responsive to most external stimuli
- Have a dysfunctional cerebrum but, by virtue of the brain stem remaining intact, are capable of spontaneous breathing and heartbeat

PVS – persistent vegetative state
- Eyes may move
- May have sleep-wake cycles
Heart
- Needs O₂ to survive and without O₂ will stop beating
- Not controlled by the brain but it is autonomous

Breathing
- Controlled by vagus nerve, located in the brain stem
- Main stimulant for vagus nerve is \( \uparrow \text{CO}_2 \) in the blood
  - Causes the diaphragm & chest muscles to expand
  - Spontaneous breathing can not occur after brain stem death

With artificial ventilation, the heart may continue to beat for a period of time after brain stem death.

Time lag between brain death and circulatory death in the unsupported patient is generally ~2-10 days, but much longer in those with fully supported organ function.
<table>
<thead>
<tr>
<th>Waiting period before initial brain death examination</th>
<th>Not specified</th>
<th>24 hrs after CPR or severe acute brain injury is suggested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core body temp</td>
<td>Not specified</td>
<td>35°C (95°F)</td>
</tr>
<tr>
<td># of clinical exams</td>
<td>2; 1 if ancillary testing confirms in 2 mos-1 year age group</td>
<td>2, even if ancillary testing done</td>
</tr>
<tr>
<td># of examiners</td>
<td>Not specified</td>
<td>2 different attendings</td>
</tr>
<tr>
<td>Observation interval</td>
<td>7d-2m: 48 hrs 2m-12m: 24 hrs &gt;1yr: 12 hrs, 24 if HIE</td>
<td>37 weeks-30d: 24 hrs 31d-18yr: 12 hrs</td>
</tr>
<tr>
<td>Decreased observation time</td>
<td>In age &gt;1yr, if cerebral blood flow or EEG consistent with dx</td>
<td>Permitted in either age group if cerebral blood flow or EEG consistent with dx</td>
</tr>
<tr>
<td></td>
<td>1987</td>
<td>2011</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Apnea testing</td>
<td>Required, but not specified how many</td>
<td>2 required unless clinically contraindicated</td>
</tr>
<tr>
<td>Final pCO₂ threshold</td>
<td>Not specified</td>
<td>≥60 mmHg &amp; ≥20 mmHg above baseline</td>
</tr>
<tr>
<td>Ancillary study</td>
<td>7d-2m: 2 EEGs separated by 48hrs 2m-1y: 2 EEGs separated by 24h, or a cerebral blood flow study instead of 2(^{nd}) &gt;1y: none</td>
<td>Required only if unable to complete exam and apnea test</td>
</tr>
<tr>
<td>Time of death</td>
<td>Not specified</td>
<td>Time of 2(^{nd}) exam &amp; apnea test or ancillary study</td>
</tr>
</tbody>
</table>
 INITIAL REQUIREMENTS

- Clinical or radiographic evidence of an acute catastrophic cerebral event consistent w/ dx of brain death
- Exclusion of conditions that confound clinical evidence (i.e.-metabolic)
- Confirmation of absence of drug intoxication or poisoning
  - Barbiturates, NMB’s, etc.
- Core body temp >35°C
Cerebral motor response to pain
- Supraorbital ridge, the nail beds, trapezius
- Motor responses may occur spontaneously during apnea testing (spinal reflexes)
- Spinal reflex responses occur more often in young
- If patient had paralytic, then test w/ train-of-four

Spinal arcs are intact!
- Triple flexion response of legs
- Round, oval, or irregularly shaped
- Midsize (3-6 mm), but may be totally dilated
- Absent pupillary light reflex
  - Although drugs can influence pupillary size, the light reflex remains intact only in the absence of brain death
  - IV atropine does not markedly affect reactivity, but does affect size
  - Topical administration of drugs and eye trauma may influence pupillary size and reactivity
  - Pre-existing ocular anatomic abnormalities may also confound pupillary assessment in brain death
  - Paralytics do not affect pupillary size or response
  - Dilated pupils suggest anticholinergic drugs (TCAs, neuroleptics) or sympathomimetic drugs (cocaine, amphetamines, theophylline)
- Oculocephalic reflex = doll’s eyes
  - Not based on Barbie type dolls with painted eyes
  - But on old fashioned type dolls with wooden eyes in porcelain heads

- Vestibulo-ocular = cold caloric test
Contraindication
- Presence of cervical collar – oculovestibular testing ("cold calorics") may still be done

Physiology
- Tests the extraocular muscle movements controlled by cranial nerves III and VI

Method
- Hold the eyelids open
- Examiner moves the patient’s head from side to side forcefully and quickly
In brain death, the eyes always point in the direction of the nose and do not lag behind or move.

FYI

Even someone who is blind will have doll’s eye reflex if the brainstem is intact.
Example: Head turned abruptly to right

- Negative doll’s eyes
  - Eyes continue to point straight forward despite head turn
  - Equates to brainstem dysfunction

- Positive doll’s eyes
  - You have them!
Contraindication:
- Ruptured tympanic membrane
- Otorrhea

Method:
- Elevate the HOB 30° to properly orient the semi-circular canal
- Irrigate tympanic membrane with 40-60 mL iced water. Do 1 ear at beginning of exam and 1 at end to allow endolymph temp to equilibrate
- Observe patient for 1 minute after each ear irrigation, with a 5 minute wait between testing of each ear
- Ice water cools the endolymph in the semicircular canal
- Tests cranial nerves III, VI, and VIII
- C-O-W-S: cold opposite, warm same. When cold fluid is instilled into the ear canal, the fast phase of nystagmus will be to the side opposite from the ear tested
  - In the comatose patient, the fast phase of nystagmus will be absent, as this is controlled by the cerebrum. Cold water instillation in the ear canal of a comatose patient will result in tonic deviation of the eyes toward the ear being irrigated.
  - In the brain dead patient, no nystagmus will be observed
Movement only of eye on side of stimulus
  - Internuclear ophthalmoplegia
  - Suggests brainstem structural lesion

Tonic deviation of both eyes
  - Coma

No eye movement
  - Brainstem injury / brain death
  - Facial trauma involving the auditory canal and petrous bone can also inhibit these reflexes
Corneal reflexes are absent in brain death

- Corneal reflexes - tested by using a cotton-tipped swab
- Grimacing in response to pain can be tested by applying deep pressure to the nail beds, supraorbital ridge, TMJ, or swab in nose
- Severe facial trauma can inhibit interpretation of facial brain stem reflexes
Both gag and cough reflexes are absent in patients with brain death

- Gag reflex can be evaluated by stimulating the posterior pharynx with a tongue blade, but the results can be difficult to evaluate in orally intubated patients
- Cough reflex can be tested by using suction catheter deep, past end of endotracheal tube
Contraindications:
- Patients with high cervical spine injury
- Patients requiring high levels of respiratory support

Goal:
- \( \text{paCO}_2 \) levels \( \geq 60 \) mmHg
- \( \geq 20 \) mmHg over baseline
- In a child with chronic lung disease, the child’s baseline \( \text{PaCO}_2 \) should be used
- Pre-oxygenate with 100% oxygen several minutes
- Allow baseline PaCO$_2$ to be ~40 mmHg
- Place patient on T-piece or flow inflating bag
  - Titration of PEEP via a flow inflating bag may assist in preventing alveolar collapse and derecruitment
  - Use of CPAP via the ventilator is not recommended as apnea may not be appreciated if the ventilator reverts to an assist mode when apnea is sensed
- Observe for respiratory effort for ~6-10 minutes
- CO₂ rises ~4 mm Hg every minute of apnea
  - The rate may be lower in the setting of brain death due to the loss of brain metabolism
- At this rate, it will take at least 5 minutes of apnea for the pCO₂ to rise by 20 mm Hg; often it requires 7-9 minutes
- Therefore, one may choose to draw an arterial blood gas at minute 5-6 of apnea, and continue the apnea observation while awaiting the results. Repeat gas every 2 minutes until the apnea criteria have been met or the test must be aborted.
- Abort testing if the SpO₂ falls below 85% or there is hemodynamic instability
In patients without significant pulmonary disease or injury, apneic oxygenation will permit the arterial oxygen saturation to remain high or change minimally.

Despite no active ventilation, gas exchange continues to take place in the alveoli, with oxygen diffusing out of the alveoli and CO$_2$ diffusing into them.
If the respiratory quotient is assumed to be 0.8, then for every 1 mL of oxygen consumed, 0.8 mL of CO$_2$ will be produced.

As a result, there is a net entrainment of oxygen (the only gas being provided to the patient) down the tracheobronchial tree.
CONFIRMATORY TESTING

- **Gold standard: 4 vessel angiography**
  - Rarely done
- **Cerebral blood flow = perfusion scan**

**EEG**
- Standards established by American Electroencephalographic Society
- Low to mid-therapeutic barbiturates levels should not preclude use of EEG
- Say “dead”, not “brain dead”
- Say “artificial or mechanical ventilation”, not “life support”
- Time of death = time of second examination, including apnea and/or ancillary test completion. When a patient meets all criteria for brain death, they are legally dead.
  - NOT when ventilator removed
  - NOT when heart beat ceases
- State law and local institutional policies should be reviewed and followed.
- Ask staff not talk to the patient as if he’s still alive