le coma dépassé
(death by neurological criteria)

Lori Shutter, MD
lori.shutter@uc.edu
Director, NSICU/Neurocritical Program
Assoc. Professor, Clinical Neurosurgery & Neurology
University of Cincinnati Medical Center
Life is pleasant.  
Death is peaceful.  
It’s the transition that’s troublesome.  

Isaac Asimov
Historical Perspective

Moses Maimonides, a 12th century rabbi – physician, argued that a decapitated person was immediately dead, even in presence of movement.

18th & 19th centuries: general fear of incorrect determination of death

Mechanical ventilators in 1950s
- Mollaret & Goulon: ‘le coma dépassé’, 1959

Harvard Ad Hoc Committee

President’s Commission: ‘*Defining Death*’, 1981.
- Uniform Determination of Death Act
Historical Perspective

Uniform Determination of Death Act adopted as federal legislation by most states

- Set *legal ground* for determining death by brain criteria but *no medical criteria* for the determination

---

To embody these conclusions in statutory form the Commission worked with the three organizations which had proposed model legislation on the subject, the American Bar Association, the American Medical Association, and the National Conference of Commissioners on Uniform State Laws. These groups have now endorsed the following statute, in place of their previous proposals:

**Uniform Determination of Death Act**

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.

The Commission recommends the adoption of this statute in all jurisdictions in the United States.
Legal Perspective

Ohio code 2108.30 enacted Nov 1981

“An individual is dead if he has sustained either irreversible cessation of circulatory and respiratory functions or irreversible cessation of all functions of the brain, including the brain stem, as determined in accordance with accepted medical standards.

A physician who makes a determination of death in accordance with this section and accepted medical standards or any person who acts in good faith in reliance on a determination of death made by a physician is not liable for damages in any civil action or subject to prosecution in any criminal proceeding for his acts or the acts of others based on that determination.

Institutions determine their local policy
Philosophical Perspective

Dying is an active process. Death is an event.

Definitions

- **Whole-brain death**: loss of all brain function – cortex, pituitary & brainstem
- **Higher brain death**: introduced in 1975 ‘consciousness & cognition are essential to life’
- **Brainstem death**: loss of arousal pathways and inability to maintain physiological systems
Religious Perspective

Christianity
- Catholicism, Aug 2000: brain death is consistent with teachings of the church
- Protestants: universal acceptance

Judaism
- Accepted by all Reform & Conservative Jews
- Orthodox Jews are split

Islam accepted in early 1990s

Hindu acceptance in 1993
Guidelines for Determination of Brain Death


New AAN practice parameter released June 7, 2010. Why?

- Considerable practice variation: prerequisites, lowest acceptable core temperature, and number of required examinations, others.¹
- Chart audits show deficiencies in documentation.²
- Desire to address 5 key questions

Key Questions

1. Are there patients who fulfill the clinical criteria of brain death who recover brain function?
   No

2. What is an adequate observation period to ensure that cessation of neurologic function is permanent?
   Insufficient evidence to determine

3. Are complex motor movements that falsely suggest retained brain function sometimes observed in brain death?
   Yes: facial myokymia; transient bilateral finger tremor; repetitive leg movements; ocular microtremor; cyclical constriction / dilatation in light-fixed pupils (‘hippus’); retained plantar reflexes (flexion or “stimulation induced undulating toe flexion”)

Wijdicks, Evidence-based guideline update. Neurology 2010
Key Questions

4. What is the comparative safety of techniques for determining apnea?
   
   Apnea testing is safe but insufficient data to compare different techniques

5. 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.

Wijdicks, Evidence-based guideline update. Neurology 2010
Exam Prerequisites

Irreversible loss of clinical brain function
  – Proximate cause is known by clinical or neuroimaging evidence of an acute CNS catastrophe that is compatible with clinical diagnosis of brain death

Exclusion of complicating medical conditions that may confound clinical assessment
  – No severe electrolyte, acid-base, or endocrine disturbance

No drug intoxication, poisoning, or recent CNS depressants

Achieve normal systolic BP (≥ 100 mm Hg)

Core temperature ≥32°C (90°F)
  – >36°C for apnea test

*Report of the Quality Standards Subcommittee of the American Academy of Neurology, 1995*
Brain Death Examination

Perform one neurologic examination (sufficient to pronounce brain death in most US states).

- Some US state statutes require two examinations

Sufficient time period has passed since onset of the brain insult to exclude possibility of recovery

- “usually several hours”

All physicians are allowed to determine brain death in most US states.

- It is reasonable that physicians determining brain death should demonstrate competency in this examination. Neurologists, neurosurgeons, and intensivists may have specialized expertise. Requirements of their involvement are based on state and hospital regulations.
Brain Death Examination

Bilateral pupil response
Oculocephalic reflex (Doll’s Eyes)
Corneal reflex
Vestibulo-ocular reflex
  – Elevate or lower HOB 30°, clear ear canal.
  – Irrigate both tympanic membranes with ≥ 50 mL of ice water and observe for 1 minute after each ear irrigation.

Cough / Gag reflex
Cerebral motor response to central pain
Assess for spontaneous breathing

AAN Practice Parameter 1995; 2010
Examination of Brainstem Reflexes

Pupils
- Size: midposition (4-5 mm), round, oval, or irregular
- No response to bright light

Ocular movement
- No oculocephalic reflex – Doll’s eyes (test only if no C-spine injury suspected)
- Caloric testing:
  • HOB at 30° and otoscopic exam of TM to assure no obstruction
  • Observed for 1 min after irrigation with 50 ml ice cold water and wait 5 min before testing other side

Examination of Brainstem Reflexes

Facial sensation and facial motor response
- No corneal reflex
- No grimacing to painful stimuli

Pharyngeal and tracheal reflexes
- No gag
- No cough to bronchial suctioning

Response to Pain

No cerebral motor response in any extremity to painful stimuli

- Supraorbital nerve
- Trapezius squeeze
- Sternal rub
- TMJ pressure
- Axillary squeeze
Assess for Spontaneous Breathing

“Apnea” Test

Prerequisites

- Core temp \( \geq 36.5{}^\circ\text{C} \left(97{}^\circ\text{F}\right) \)
- SBP \( \geq 90 \text{ mmHg} \) \( \left(100 \text{ mm Hg in 2010}\right) \)
- Euvolemia
- Normal pCO2
- Normal pO2

*Report of the Quality Standards Subcommittee of the American Academy of Neurology, 1995*
Determination of Apnea

Preoxygenate at 100% FiO2 for at least 10 min

Draw a baseline ABG, PCO$_2$ must be $\sim$ 40

Disconnect ventilator, and deliver O$_2$ by catheter at 6 – 8 L/min at carina

Watch abdomen and chest wall for respiratory movements 8-10 min

- Any movement must produce adequate tidal volumes

Brain Death Examination

Apnea Test

– Duration varies, usually 5 -10 minutes.
  • General rule: after 2 minutes off ventilator the PCO₂ will increase by 5, then for every additional minute the PCO₂ will increase by 2.

– Draw post-test ABG and reconnect the ventilator.

– The patient has no CNS respiratory drive if PCO₂ > 60mm Hg.
  • Adjust criteria for known CO₂ retention.

– During test if patient becomes hemodynamically unstable, stop testing, draw ABG and reconnect the ventilator. Test is indeterminate if PCO₂ < 60mm Hg.
  • Consider confirmatory studies.

\[
\begin{align*}
\text{Sample 1} & : \quad 61 - 40 = 21 \\
& \quad 21 - 5 = 16 / 2 = 8 \\
& \quad (2 \text{ min}) + (8 \text{ min}) \\
& \quad \text{Total} = 10 \text{ min}
\end{align*}
\]

\[
\begin{align*}
\text{Sample 2} & : \quad 61 - 46 = 15 \\
& \quad 15 - 5 = 10 / 2 = 5 \\
& \quad (2 \text{ min}) + (5 \text{ min}) \\
& \quad \text{Total} = 7 \text{ min}
\end{align*}
\]

AAN Practice Parameter 1995; 2010
Complications of Apnea Testing
Complications of Apnea Testing

Complications of apnea testing
- Hypotension
- Hypoxia
- Cardiac arrhythmias

Factors associated with complications
- pH < 7.3 or > 7.5
- Plasma Na <120 or >170
- Serum potassium <3.0 or >6.0
- Calcium <8.0 or >10.5
- Pretest hypotension or administration of vasopressors

If apnea test is aborted and pCO2 is not ≥60, an ancillary test must be performed
Apnea testing with CPAP

Levesque et al

- 20 adults 3 different groups
  - 6 L/min O2 by cannula into ETT
  - T-piece system with 12 L/min O2
  - CPAP with 10 cm H20
- No change in pCO2 change
- Less hypoxia with CPAP

Critical Care Medicine, 2006
Brain Death Declaration

Brain death criteria are met if there is no response to any component of the examination.

Confirmatory tests are typically **NOT** necessary.

- Recommended if unable to assess all cranial nerves or unable to perform apnea test.
- Options are: CBF, EEG, TCD, EP, CTA, MRI/MRA
- Barbiturate levels are required in setting of barbiturate coma.
Documentation Worksheet

Developed to improve documentation and assist in exam performance.

Physician(s) can document separately on worksheet ALL of the following:

- Absence of each brain stem reflex tested
- Absence of motor response to pain
- Absence of respiration with PCO2 > 60 mm Hg
- Date, time of death*, and signature.

  • *Time of death is the time the arterial PCO2 reached the target value.

Worksheet is placed in medical record.
Normal SBP
No hypothermia
No reversible confounders
No response to pain
No brainstem response
Apnea

<table>
<thead>
<tr>
<th>Vital Statistics</th>
<th>Date</th>
<th>Time</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Systolic BP greater than or equal to 90 mm Hg.</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>b. Body Temperature greater than or equal to 96.5°F</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>c. Toxicology Results (document even if negative)</td>
<td>Negative</td>
<td></td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>d. Pentobarbital Level</td>
<td>NA</td>
<td>Result</td>
<td>mcg/mL</td>
<td>NA</td>
</tr>
<tr>
<td>e. Mydriatic Drugs Used</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>f. Neuromuscular Blocking Agents Used</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>g. Any Residual Neuromuscular Blockade</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cerebral Responsibility</th>
<th>Date</th>
<th>Time</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Response to central painful stimulation <strong>at any three</strong> locations (i.e. sternal rub, supra-orbital pain, TMJ pressure, nares reflex, anterior axillary fold pressure, upper trapezius squeeze)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brainstem Responsivity</th>
<th>Date</th>
<th>Time</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Pupillary Reaction</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>b. Pupil Size (constricted, mid-size, dilated)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>c. Corneal Reflexes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>d. Oculocephalic Reflex</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>e. Oculovertical Reflex</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>f. Gag Reflex</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>g. Cough Reflex</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>h. Spontaneous breathing (pre-apnea ABG, post-apnea ABG)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Arterial Blood Gas at beginning of test</td>
<td>PaO₂, PaCO₂, pH</td>
<td>PaO₂, PaCO₂, pH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial Blood Gas at end of test</td>
<td>PaO₂, PaCO₂, pH</td>
<td>PaO₂, PaCO₂, pH</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Two service physician signatures

Print First Physician
Name
Service

Print Second Physician
Name
Service

Refer patient to LifeCenter Organ Donor Network, 513-558-5000
What if...?
18 yo AAM brought to ED by EMS with a self-inflicted GSW to the head through the orbits
<table>
<thead>
<tr>
<th>Medical Examiner's Case</th>
<th>Yes No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Probable Cause of Coma</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vital Statistics</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Systolic BP greater than or equal to 90 mm Hg</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>b. Body Temperature greater than or equal to 96.5°F</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>c. Toxicology Results (document even if negative)</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>d. Pentobarbital Level</td>
<td>NA</td>
<td>Result</td>
</tr>
<tr>
<td>e. Mydriatic Drugs Used</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>f. Neuromuscular Blocking Agents Used</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>g. Any Residual Neuromuscular Blockade</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cerebral Responsibility</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Response to central painful stimulation at any three locations (i.e. sternal rub, supra-orbital pain, TMJ pressure, nares reflex, anterior auxiliary fold pressure, upper trapezius squeeze)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brainstem Responsivity</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Pupillary Reaction</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>b. Pupil Size (constricted, mid-size, dilated)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>c. Corneal Reflexes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>d. Oculocephalic Reflex</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>e. Oculovestibular Reflex</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>f. Gag Reflex</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>g. Cough Reflex</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>h. Spontaneous breathing (pre-apnea ABG, post-apnea ABG)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

| Arterial Blood Gas at beginning of test | | |
| PaO₂ | PaCO₂ | pH |
| PaO₂ | PaCO₂ | pH |

| Arterial Blood Gas at end of test | | |
| PaO₂ | PaCO₂ | pH |
| PaO₂ | PaCO₂ | pH |

| Two service physician signatures | | |

Refer patient to LifeCenter Organ Donor Network, 513-558-5000

UC Neuroscience Institute
Confirmatory Testing

Not mandatory
Desirable in patients in whom specific components of clinical testing cannot be reliably performed or evaluated
Any of the suggested confirmatory tests may produce similar results in patients with catastrophic brain damage who do not (yet) fulfill the clinical criteria of brain death.

### Table 2. Confirmatory Testing for a Determination of Brain Death

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral angiography</td>
<td>The contrast medium should be injected under high pressure in both anterior and posterior circulation. No intracerebral filling should be detected at the level of entry of the carotid or vertebral artery to the skull. The external carotid circulation should be patent. The filling of the superior longitudinal sinus may be delayed.</td>
</tr>
<tr>
<td>Electroencephalography</td>
<td>A minimum of eight scalp electrodes should be used. Interelectrode impedance should be between 100 and 10,000 Ω. The integrity of the entire recording system should be tested. The distance between electrodes should be at least 10 cm. The sensitivity should be increased to at least 2 μV for 30 minutes with inclusion of appropriate calibrations. The high-frequency filter setting should not be set below 30 Hz, and the low-frequency setting should not be above 1 Hz. Electroencephalography should demonstrate a lack of reactivity to intense somatosensory or audiovisual stimuli.</td>
</tr>
<tr>
<td>Transcranial Doppler ultrasonography</td>
<td>There should be bilateral insonation. The probe should be placed at the temporal bone above the zygomatic arch or the vertebrobasilar arteries through the suboccipital transcranial window. The abnormalities should include a lack of diastolic or reverberating flow and documentation of small systolic peaks in early systole. A finding of a complete absence of flow may not be reliable owing to inadequate trans temporal windows for insonation.</td>
</tr>
<tr>
<td>Cerebral scintigraphy (technetium Tc 99m hexametazime)</td>
<td>The isotope should be injected within 30 minutes after its reconstitution. A static image of 500,000 counts should be obtained at several time points: immediately, between 30 and 60 minutes later, and at 2 hours. A correct intravenous injection may be confirmed with additional images of the liver demonstrating uptake (optional).</td>
</tr>
</tbody>
</table>
Cerebral Angiography

Injection of contrast in both the anterior and the posterior circulation.

No intracranial flow of carotid or vertebral circulation

External carotid flow patent

False negatives if brain death as a result of cellular toxicity and not edematous swelling
Electroencephalography (EEG)

**Test Parameters**
- Minimum of 30 minutes
- 16- or 18- channel
- Sensitivity = 2µV/mm

Finding c/w brain death: electrocerebral silence (ECS)
- Can not detect subcortical function

Sensitive to drug effects, sedation, hypothermia, toxic or metabolic factors, and artifacts
Diagnostic uncertainty in 20%
Transcranial Dopplers (TCD)

Bilateral insonation with assessment of at least one artery on each side
- Intracranial: MCA, Vertebrals
- Extracranial: ICA
Perform twice with 30 min interval between testing

Findings:
- Oscillating flow or low amplitude (<50 cm/s), brief (<200ms) spikes in early systole without diastolic flow
- Absent intracranial flow (with known temporal windows)

Sensitivities: 70-100%
Specificity 97-100%
Single Photon-Emission Computed Tomography (SPECT)

Hollow skull phenomenon

Munari et al
- SPECT in 20 patients
- No false positive results
- 95% diagnosis confirmed initially
- 100% after 48 hours

Early false negative results may delay diagnosis

Crit Care Med, 2005
Future Possibilities for Confirmatory Tests

CTA
- Prospective observational study of 27 confirmed BD patients
- Sensitivity 89%
- Higher false negatives in other studies: sensitivities 52-70%

CT Perfusion
MRA

Escudero et al. Neurocrit Care, 2009
Can I call it?

Triple flexion
Babinski sign
Preserved DTRs
Abdominal and cremasteric reflexes
Sweating
Blushing
Respiratory-like movements without significant TV
  – Shoulder elevation / adduction
  – Back arching
  – Intercostal expansion
Head turning

Spontaneous movements or with painful stimuli (if no full decerebrate or decorticate response considered to be at spinal level):
  – Brief slow movements of upper limbs
More complex movements (Lazarus signs) come from spinal cord
  – Stretching of the arms, followed by crossing or touching of the arms on the chest, and finally falling of the arms alongside the torso.
Communication: ‘to hear what isn’t being said’
Communication Tips: Staff

Respect!!!
Work as a team
Recognize others skills and limitations
Phone / hallway etiquette
Listen for the unspoken needs
Share knowledge
Develop a system & use it
Communication Tips: Family

Empathy & respect
Listen for the meaning, not just the words
Observe body language of others
Monitor your body language
Talk at a 4th grade level
Prepare family for what lies ahead
  – Set expectations
Never fear speaking the truth
  – Acknowledge that things are not going well
Communication: 4 Stages of Brain Death

“Things looks very bad, but we are doing everything we can”

“Despite our best efforts, things are worse”

“There is no sign of brain function left, but we need to confirm this with some tests”

“I’m sorry, but your family member has died”

– We are keeping his/her body on machines so it will stay warm while you say goodbye.
Communication Tips

Organize your thoughts ahead of time
- Practice your explanation
- Adapt to the situation (no ‘canned’ speeches)
- Be comfortable with the word ‘death’

Be patient / Embrace silence
- Don’t do all the talking
- Don’t rush the explanation, answer all questions
- Understanding brain death is associated with higher donation rates
Communication Tips

Don’t send mixed messages
- We are supporting organs, not life.
- Do not examine the patient after declaration.
- It is acceptable to be sad.
  “Grief teaches the steadiest minds to waver”

Use all hospital supportive resources
- Chaplains / priests, ODA, Social work, OPO

Set time limits for continued organ support
Communication: Organ Donation

Never introduce the topic
  – LifeCenter should be involved early and available to speak with the family once declared.

If family brings up topic
  – Support their good intentions and let them know the people that can help with that decision are available.

Remember an open casket is possible after donation & autopsy
Questions?
References

The University Hospital, Health Alliance Policy # II-312, Determination of Death; 1985
Ex cudero et al. Diagnosing brain death by CT perfusion and multislice CTA. *Neurocrit Care* 11:261-271; 2009.