Understanding Clinical Brain Death

A Practical Approach

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Disclosures

I have no disclosures pertaining to this presentation.

Learning Objectives

- Understand the history of clinical brain death and its nuances in the critical care setting today

- Practically apply concepts regarding brain death testing and its role in the trauma patient

Brain Death

- Brain death accounts for nearly 2% of deaths in the United States, and is often a result of traumatic brain injury

- "**Irreversibility**" is an important operative term in discussing brain death, also known as death by neurological criteria
  - This is different from "coma" when discussing the topic with patient families
  - Also different from "vegetative state" or "minimally responsive state"

The History of Brain Death

- Herophilus of Chalcedon (ca. 300 B.C.) hypothesized that the brain transmitted motor impulses from the soul to the extremities.
- Aristotle felt the heart was the center of the human being and that the brain served to cool the blood
- Galen (ca. 160 AD) discovered the cranial nerves and found that cognition was affected by brain injury
- Thomas Willis (1664) delineated much of modern neuroanatomy, in *Cerebri Anatome*
- 1960, CPR developed and supported by American Heart Association

The Harvard Criteria (1968)

- Dr. Henry Beecher was an anesthesiologist and prominent medical ethicist who chaired the Harvard Ad Hoc Committee to Examine the Definition of Brain Death
- They determined the following criteria for brain death
  - Unreceptivity and unresponsivity
  - No movements or breathing
  - No reflexes
  - Flat EEG
    - All of these tests shall be repeated at least 24 hours with no change
    - Exclusion of hypothermia (below 90°F) or CNS depressants

Harvard Medical School Center for Bioethics, 2017

The Collaborative Study (NIH, 1977)

- Aimed to determine prospectively which neurological criteria were most associated with cardiac arrest within 3 months in comatose patients who continued to receive cardiopulmonary support.

- Needed two criteria, unresponsive coma and apnea, and then changes in neurological exam and EEG would be followed over time.

- In 503 cases, 87% died from cardiac standstill. However, if the criteria were apnea, coma, and isoelectric EEG, **only patients with intoxication improved**

Uniform Determination of Death Act
(US Uniform Law Commission, 1980)

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 President's Commission (1981)

- Heard philosophical, political, and religious testimony, as well as expert witnesses in five pertinent medical disciplines

- Goals were to develop criteria that
  - Eliminated error in classifying a living person as dead
  - Allowed as few errors as possible in classifying a dead person as alive
  - Allowed a determination to be made without unreasonable delay
  - Were explicit, adaptable, and accessible to verification

- It was here that **apnea testing** as we know it today was defined, and it was the first set of guidelines to include shock as a confounder.

The President's Commission

- Final criteria:
  - Unreceptive and unresponsive coma
  - Absent pupillary, corneal, oculocephalic, oculovestibular, oropharyngeal reflexes
  - Apnea with $PaCO_2$ greater than 60 mmHg
  - Absence of posturing or seizures
  - Irreversibility demonstrated by establishing cause and excluding reversible conditions
  - Period of observation determined by clinical judgment
  - Use of cerebral blood flow tests when brainstem reflexes are not testable, sufficient cause cannot be established, or to shorten period of observation.

- The commission was careful not to equate persistent vegetative state (PVS) with death, hence its emphasis on the brainstem in the formulated statement.

American Academy of Neurology Guidelines

- Reviewed in 1995 and then 2010, the latest iteration distilled evidence-based from expert opinion-based guidelines

- AAN found that
  - No recoveries in adults had been reported since the adoption of the AAN 1995 guidelines
  - The apnea test was safe using the apneic-oxygenation method
  - Confirmatory tests were less reliable and useful than had been suggested and should be used sparingly
  - Adequate documentation could be facilitated with a checklist

American Academy of Neurology Guidelines

- 1 exam is sufficient
- Acute CNS catastrophe 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 or poisoining
- Core temperature >= 32° C
- Coma or unresponsiveness
- Absence of brainstem reflexes
  - Pupils
  - Ocular movement

Etiologies of Brain Death

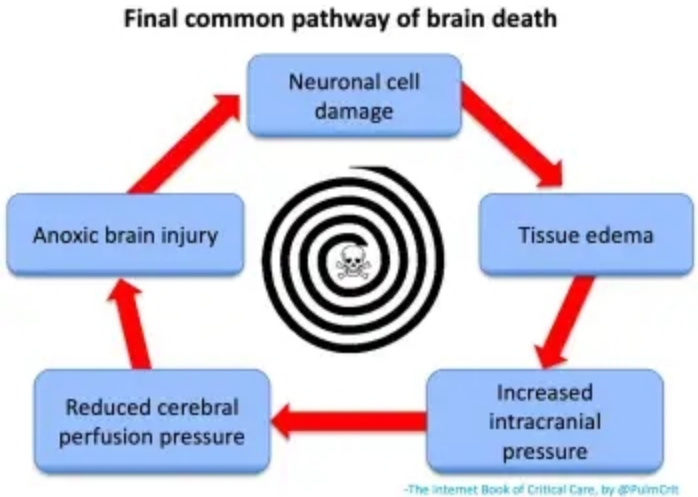
CPP = MAP - ICP

- Brain edema
  - Pons damage can alter respiratory drive
  - Medulla oblongata damage can obliterate the respiratory drive altogether
  - Control of vasomotor tone by the medulla oblongata can be lost, resulting in hypotension
  - Importantly, once cerebral blood flow stops in an apneic patient with absent brainstem reflexes and no confounders, it does not return.
  - We do not really see “respirator brain” anymore, because that degree of necrosis involves very prolonged cardiopulmonary support without cerebral perfusion

- Diffuse anoxic brain injury (least common)
  - Post-cardiac arrest
  - Exsanguination

Pathophysiology of Brain Death

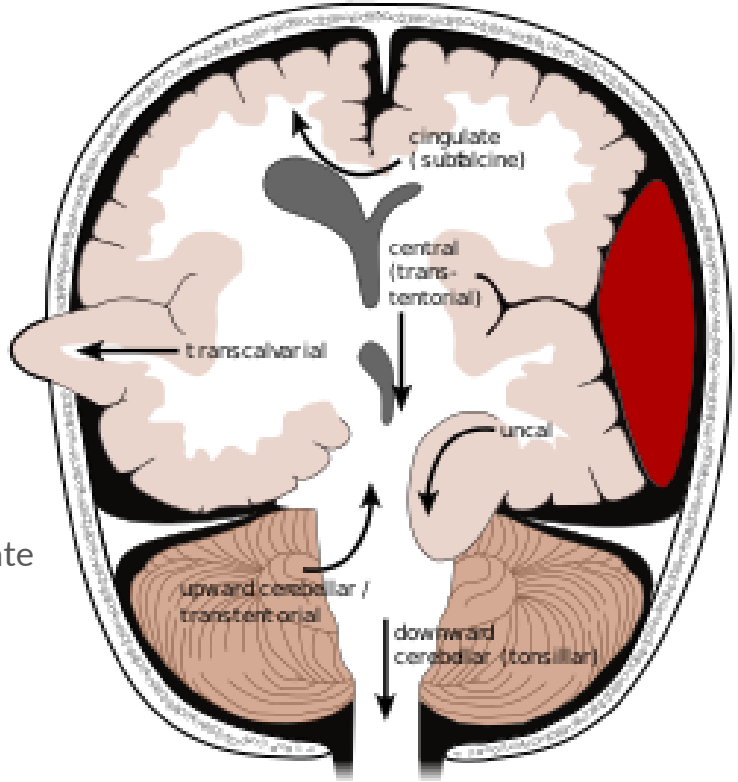
CPP = MAP - ICP

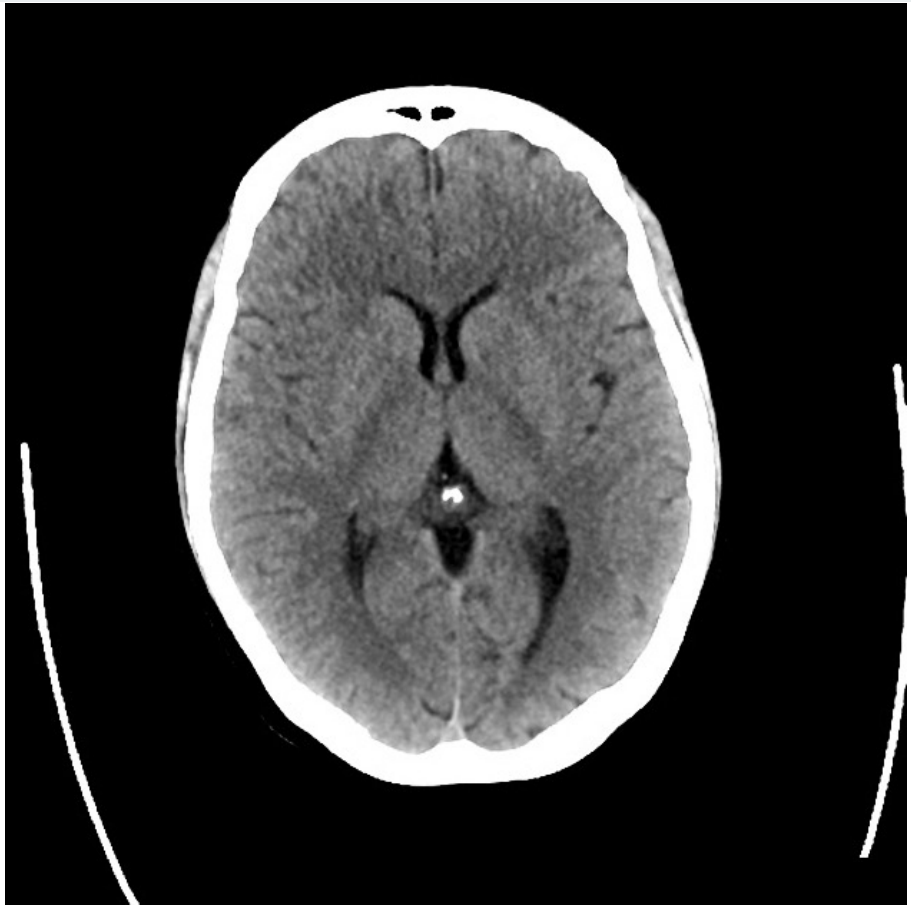


Neuroanatomy

Brainstem

- Midbrain
  - Responsible for motor function
  - Relays information for vision and hearing
- Pons
  - Wakefulness and consciousness
  - Damage can result in comatose or “locked-in” state
- Medulla oblongata
  - Lowest structure in brainstem
  - Most responsible for respiratory drive
  - Vasomotor input





Images courtesy of radiopaedia.org

Brain Death Criteria Checklist

Prerequisites

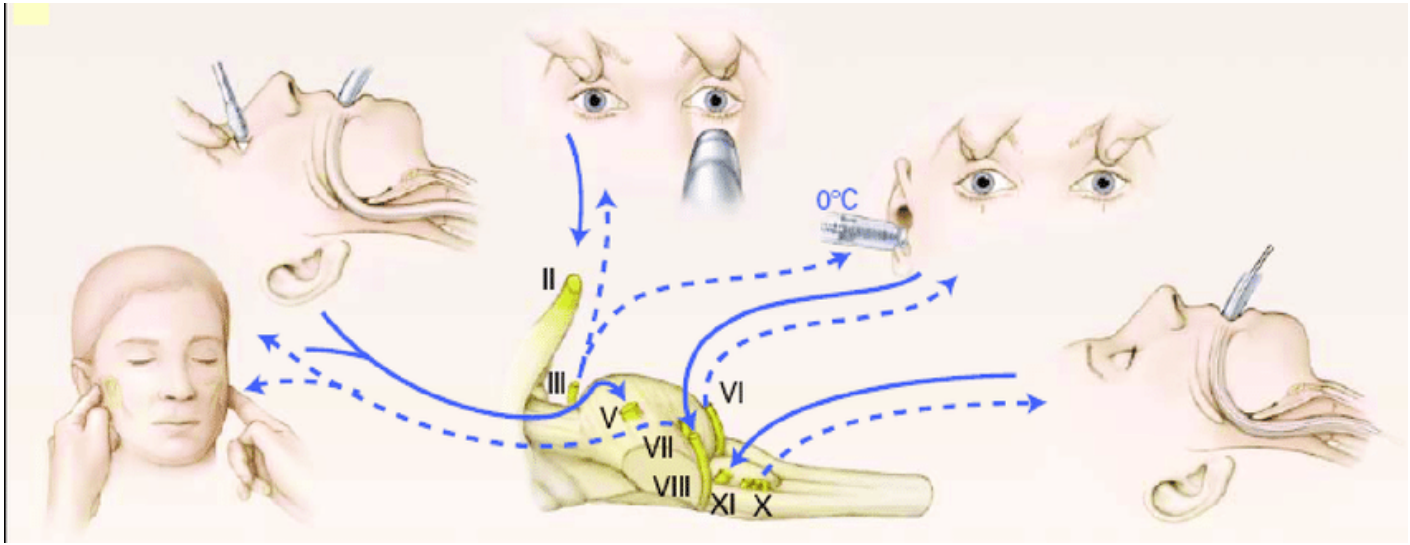
- Coma, irreversible and cause known
- Neuroimaging explains coma
- Sedative drug effect absent
- No residual neuromuscular blockade
- Absence of severe acid-base, electrolyte, or endocrine abnormality
- Normal or near-normal temperature (core temperature >= 36°C
- Systolic blood pressure >= 100 mmHg
- No spontaneous respirations

Brain Death Criteria Checklist

Examination

1) Pupils nonreactive to bright light
2) Corneal reflex absent
3) Eyes immobile, oculocephalic reflex absent (only test if C-spine integrity ensured)
4) Oculovestibular reflex absent
5) No facial movement to noxious stimuli at supraorbital nerve, TMJ, and nailbed compression
6) Gag reflex absent
7) Cough reflex absent
8) No motor response to noxious stimuli in all four limbs (spinal reflexes are permissible)

Brainstem reflexes



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Spinal Reflexes

- Present in 13-75% of brain death cases
- Toe flexion/extension triggered by plantar tactile stimulation
- Triple flexion reflex = flexion of thigh, leg, and foot triggered by plantar tactile stimulation
- Pronator extension reflex
- Quadriceps flexion by local noxious stimuli
- Repetitive twitching of facial muscles
- “Lazarus sign” = bilateral arm flexion, shoulder adduction, hand raising to chest/neck, triggered by head flexion and sternal rub
- Myoclonus
- Muscle fasciculations

Brain Death Criteria Checklist

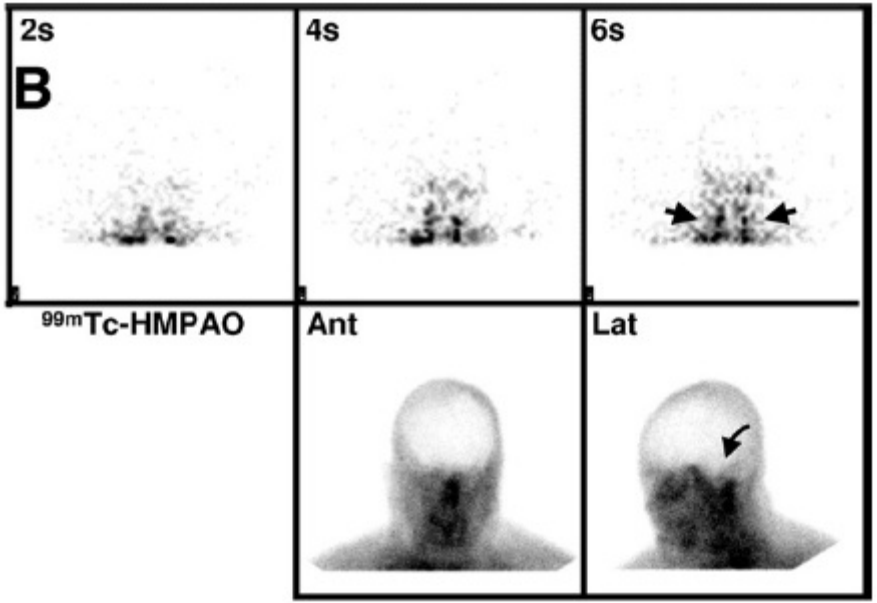
Apnea Testing

1) Patient is hemodynamically stable with SBP >=100 mmHg
2) Ventilator adjusted to provide normocarbia (PaCO2 35-45 mmHg)
3) Patient pre-oxygenated with 100% FiO2 for > 10 minutes to PaO2 > 200 mmHg
4) Patient maintains oxygenation with PEEP of 5 cm water
5) Disconnect ventilator
6) Provide oxygen via an insufflation catheter
7) Spontaneous respirations absent
8) ABG drawn at 8-10 minutes, patient reconnected to ventilator
9) **Document time of death when PaCO2 >= 60 mmHg or 20 mmHg rise from normal baseline value**

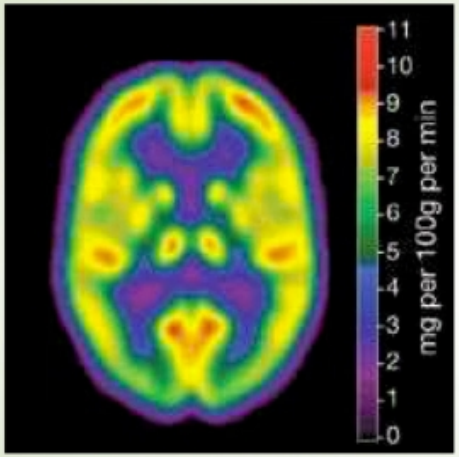
Or, apnea test aborted and confirmatory ancillary test (EEG or blood flow study)

Ancillary Testing

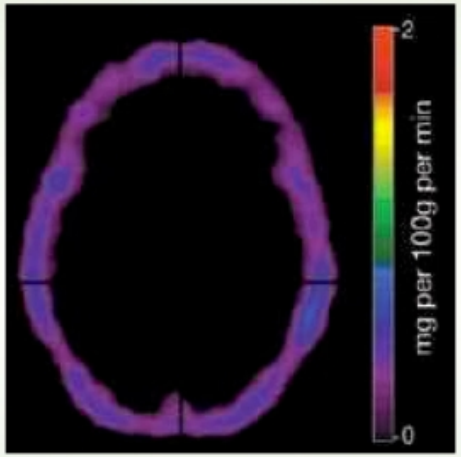
- Cerebral Angiography
- Electroencephalogram (EEG)
- Transcranial Doppler Ultrasonographic Scan
- Somatosensory Evoked Potentials
- CT Angiogram
- Radionuclide perfusion scintigraphy
    - (Nuclear Brain Scan)



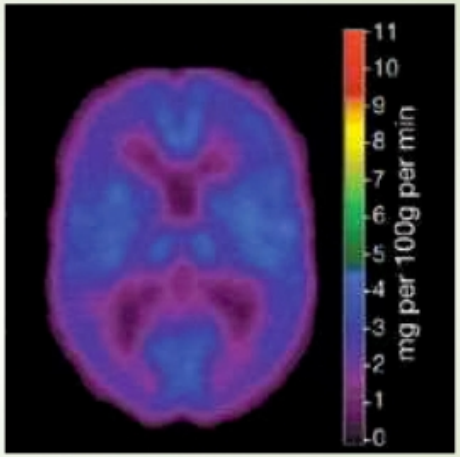
Courtesy of nucmedresource.com



HEALTHY CONTROL



BRAIN DEAD



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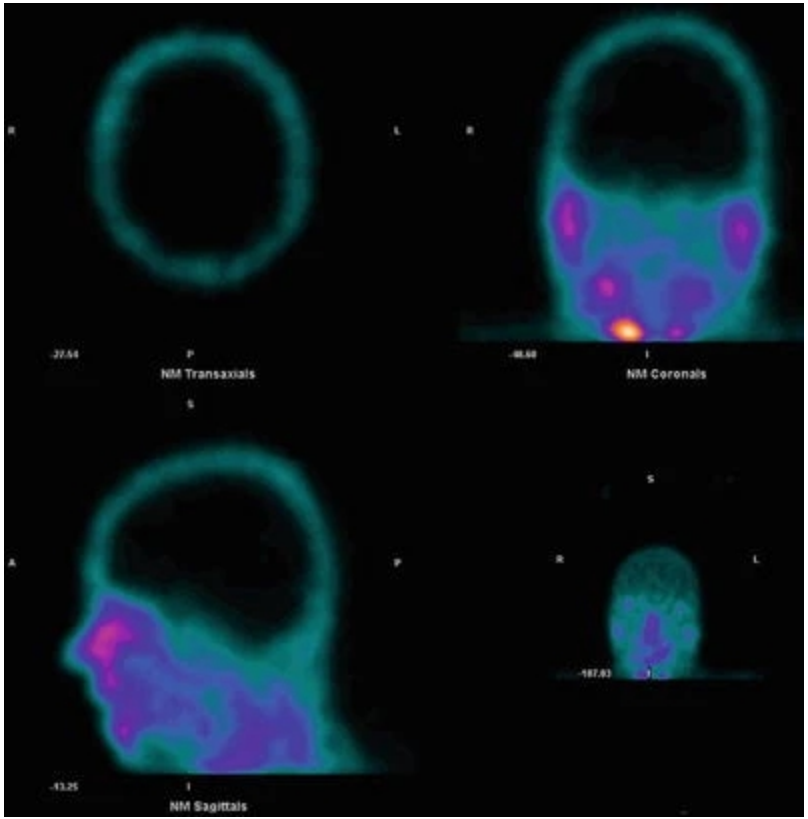

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Trauma Considerations

- Traumatic injuries that preclude an adequate clinical neurological exam should warrant consideration of ancillary testing for brain death
  - High cervical spine injuries
  - Eye/globe/orbit injuries
  - Tympanic membrane rupture

- Possible intoxication, if neuroimaging does not explain coma (urine drug screen is commonly used but may be inadequate), warrants a similar approach

Religious and Cultural Considerations

- Differences in belief about when life ends in different religions
- Approaches to organ donation can be different in different cultures and religions
- Islamic organizations have taken different approaches
    - 3rd International Conference of Islamic Jurists upheld brain death as death
    - Organization of Islamic Conferences' Islamic Fiqh Academy maintains a circulatory definition
- In Judaism, life begins and ends with breathing
    - Orthodox Jewish teachings do not believe in brain death as death
    - Influences in state legislation in New York and New Jersey

Worldwide Survey (2020)

- Reviewed 136 corresponding countries contacts (42% of the world)
- High variability in brain death criteria protocols
  - 83 countries had protocols (78 of these had unique protocols)
  - 53 countries did not
- Apnea test was a requirement in 91% of protocols
- Ancillary test was deemed necessary in 22% of protocols

Practices and Perceptions

- International study by Patel PV et al. in 2015 showed 22% of low-income vs. 97% of high-income countries had an institutional protocol for brain death determination
- Countries with an organ transplant network were more likely to have a brain death provision

- In 2006, a study of the United States top 50 Neurology and Neurosurgery institutions showed notable variability, both between institutions and states
    - A common requirement was found in that the physician declaring brain death should not be an organ procurement team member

Closing Thoughts

30 % decrease in brain death declaration in the past decade. Why?

- Some physicians do not perform brain death testing unless organ donation is a possibility
- Some ICU directors do not admit “dead” patients
- Some communities object to organ donation and also brain death testing
- Craniotomies and craniectomies are being done that decrease ICP to preclude swelling that would lead to a brain death testing clinical scenario

- **More patients are having early withdrawal of support in catastrophic brain injuries**

Closing Thoughts

- Traumatic brain injury can lead to death by neurological criteria - irreversible
- Neuroimaging should almost always explain neurological condition
- When in doubt, wait, wait, wait
- The clinical neurological exam for brainstem reflexes should always precede brain death testing
- Apnea testing is the gold standard for brain death testing, but cervical spine injuries and chronic CO_2 retainers should not undergo it
- Ancillary testing has a role, but is often fraught with caveats
- People of different backgrounds and cultural practices may have differing views on brain death and organ donation

Questions?

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