How We Will Diagnose Brain Death

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Brain Death in Children Summary

1. Is not death of the brain
   • Not an anatomic diagnosis
2. Is the permanent cessation of brain function
   • Is a functional diagnosis
3. Remains a clinical determination that is remarkably consistent around the world
4. Unnecessarily complicated in pediatrics
5. Need to understand if any difference exists between no flow and some flow
Historical Advances Influencing Brain Death
A Definition of Irreversible Coma

Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death

Via Wijdicks, Brain Death, 2011
“from ancient times, when the respiration and heart stopped, the brain would die in a few minutes”

“in those times, the heart was considered to be central organ of the body”

“this is no longer valid when modern resuscitative and supportive measures are used”

“characteristics of a permanently nonfunctioning brain”

“no discernable central nervous system activity”
Dying, Death and the Brain

Death of the person

versus

Death of the human organism

versus

Death of its parts
Cranial Vault
Most common herniation sequence
Its All About the Brainstem

Cerebrum

Cerebellum

Brainstem

Fish (Zebrafish, Danio rerio)

Amphibian (Bullfrog, Rana catesbeiana)

Reptile (American Crocodile, Crocodylus acutus)

Bird (Goose, Anser anser domesticus)

Mammal (Brown Rat, Rattus norvegicus)

Primate (Rhesus monkey, Macaca mulatta)

Human (Homo sapiens)

E Wijdicks, with thanks
Reticular Activating System
Brainstem Control of Consciousness
Whole Brain or Brainstem?
Cessation of Brain Function

1976: Conference of Medical Royal Colleges of the United Kingdom
E Wijdicks, with thanks
Brainstem death is the infratentorial consequence of a supratentorial catastrophe
Brainstem Death? Whole Brain Death?
Moving away from misleading anatomical terms
Cessation of all Brain Function

1. Consciousness
   - cognition
   - awareness/ receptivity
   - interaction with environment
2. Central motor function/response
3. Central sensory function/response
4. Respiratory drive
5. Brainstem reflexes including airway control
The work of the organism, is expressed in it’s commerce with the surrounding world:
1. Receptivity to stimuli & signals
2. Drive to act
3. Ability to act
Moderate to Severe Ischemic Changes after Clinical Brain Death

n=41

Wijdicks, Pheifer Neurology 2008
Neurological Determination of Death/Brain Death

1. Unresponsive coma with a known proximate cause and absence of reversible conditions
2. Absence of centrally-mediated motor responses
3. Absent brainstem reflexes & the capacity to breathe

Brain Death Determination
Variable and Inconsistent?

Variability in brain death determination practices in children.
   Mejia and Pollack JAMA 1995

Brain death worldwide. Accepted fact but no global consensus in diagnostic criteria.
   Wijdicks, Neurology, 2002

Variability among hospital policies for determining brain death in adults.
   Powner et al, CCM, 2004

Variability of hospital based brain death guidelines in Canada.
   Hornby et al, Can J Anes, 2006
Brain Death Internationally

Differences in procedures for diagnosis of brain death in adults and children:

• apnea testing
• observation time
• age related criteria
• required expertise of physicians
• provisions for anoxic BD
• confirmatory lab tests
• legal standards
Brain arrest: the neurological determination of death and organ donor management in Canada
2003 Canadian Hospital-based Brain Death Document Survey

Brainstem Reflexes

Pediatric (n=11) vs. Adult (n=26)

Hornby et al, Can J Anes, 2006
Brain Death Internationally
Very Consistent Clinical Fundamentals

1. Deep unresponsive coma
2. Established cause
3. Absence of reversible conditions
4. Absence of confounding/confusing conditions
5. Absence of:
   a) motor responses
   b) brainstem reflexes
   c) capacity to breathe
International guideline development for the determination of death

Sam D. Shemie
Laura Hornby
Andrew Baker
Jeanne Teitelbaum
Sylvia Torrance
Kimberly Young
Alexander M. Capron
James L. Bernat
Luc Noel
and The International Guidelines for Determination of Death phase 1 participants, in collaboration with the World Health Organization
Catastrophic brain injury (CBI) with potential to evolve to brain death

Mechanical ventilation (may occur prior to CBI) and neuro-protective interventions

Continuing deterioration despite intervention, with potential to evolve to brain death

Cessation of brain function

Cessation of brain function with no possibility to resume by any means

Biological events after death
# Death after Cessation of Brain Function

**Table 2** Minimum acceptable clinical standards and additional testing beyond minimum clinical standard.

<table>
<thead>
<tr>
<th>Description</th>
<th>Minimum Acceptable Clinical Standard</th>
<th>Additional Testing Beyond Minimum Standard</th>
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| N-1         | **Catastrophic brain injury:** continuing deterioration and progressive loss of brain function despite intervention** | 1. Established etiology and/or structural lesion capable of causing death by neurological criteria  
2. Reduced consciousness (as measured by GCS 3–5 or FOUR score)  
3. Evidence for progressing loss of brainstem function | 1. Neuroimaging that explains the severity of brain injury  
2. Repetition of clinical exams with trends  
3. Demonstration of elevated intracranial pressure (ICP) by monitoring |
| N-2         | **Cessation of brain function** | 1. Coma (excluding spinal cord mediated reflexes)  
2. Absence of brainstem reflexes:  
   - Pupils mid-position or greater and absent pupillary light reflex (fixed dilated pupils)  
   - Corneal  
   - Gag/pharyngeal  
   - Cough/tracheal  
   - Vestibulo-ocular (‘cold caloric’)  
   - Loss of central drive to breathe  
   NB: performance of apnoea testing should be reserved as the last test of brainstem function | None: cessation of brain function is a clinical determination |
| N-3         | **Cessation of brain function with no possibility to resume** | 1. Preconditions fulfilled  
2. Confounding conditions excluded or addressed  
3. Refractory to all applied interventions  
4. Intervention not available or indicated | 1. Repetition of the minimum clinical standard examination  
2. Ancillary laboratory tests e.g.  
   - Demonstration of brain blood flow or perfusion to be absent  
   - Refractory intracranial hypertension as measured by ICP monitoring  
   - Transcranial Doppler consistent with absent net flow velocity |

Data from UNOS/OPTN and Sheehy et al 2003; 349:667-74

Stephen Ashwal, with thanks
Brain Death Internationally

Differences in procedures for diagnosis of brain death in adults and children:

- apnea testing
- observation time
- age related criteria
- required expertise of physicians
- provisions for anoxic BD
- confirmatory lab tests
- legal standards

Hornby, Shemie et al, Can J Anes, 2006
Wijdicks, NEUROLOGY 2002;58:20–25
Age Related Observation Periods

- Newborn <30 days: 24 hours
- 30 days-18 years: 12 hours

Ancillary tests

- CBF or EEG if uncertainty
Brain Death in Children: Why Does It Have to Be So Complicated?

The clinical diagnosis of brain death should be based on a straightforward premise. After a known and untreatable catastrophic brain injury and after every

Why do these recommendations vary so widely on age considerations? Likely because of the lack of evidence and lack of detailed understanding of age-specific neuro-
Brain Death in Canadian PICUs: Demographics, Timing, and Irreversibility

- Multi-center medical record review of determination of brain death in 4 Canadian PICUs
  - before national guidelines implemented
- All deaths screened for study eligibility
  - term newborn to < 18 years
  - minimum of 1 brain death exam performed

Joffe, Shemie et al Ped Crit Care Med, 2013
Results

- n=135
- median age: 7 years (2 weeks - 17 yrs)
  - 19 cases < 1 yr old
- major causes of death
  - 44% traumatic brain injury
  - 19% cardiac/respiratory arrest
  - 10% meningitis
  - 6% intracranial hemorrhage
- 2nd exam corroborated 1st > 99% cases
  - necessity of second exam?
Patients wrongly certified dead

Patients in five English hospitals have been incorrectly diagnosed as being dead over the past five years, the BBC has discovered.

The information was obtained under the Freedom of Information Act by the Donal MacIntyre programme.

In each case the mistake was later realised, the programme reports.
Dramatic Diagnostic Errors
There is no such thing as “reversible brain death”

*If the exam is done properly*

1. Inexperienced physicians
2. Misjudgement of confounders
3. Incomplete clinical testing
4. Misinterpretation of confirmatory tests
Appendix 5: Checklist for adults and children 1 year and older

Minimum clinical criteria
a. Deep unresponsive coma with the following established etiology
   Yes □ No □
b. Confounding factors precluding the diagnosis?
c. Temperature (core) __________
d. Brainstem reflexes:
   - Bilateral absence of motor responses (excluding spinal reflexes)
     Yes □ No □
   - Absent cough
     Yes □ No □
   - Absent gag
     Yes □ No □
   - Bilateral absence of corneal responses
     Yes □ No □
   - Bilateral absence of vestibulo-ocular responses
     Yes □ No □
   - Bilateral absence of pupillary response to light (pupils ≥ mid-size)
     Yes □ No □
e. Apnea
   At completion of apnea test: pH ______ PaCO₂ ______ mm Hg
   Yes □ No □
   PaCO₂ ≥ 20 mm Hg above the pre-apnea test level
   Yes □ No □

Ancillary tests
Ancillary tests, as defined by determination of the absence of Intracerebral blood flow, should be performed when any of the minimum clinical criteria cannot be established or unresolved confounding factors exist.

Ancillary testing has been performed
Yes □ No □
Date: ___________ Time: ___________

Absence of Intracerebral blood flow has been demonstrated by
- Cerebral radiocontrast angiography □
- Radionuclide angiography □
- Other ___________

Declaration and documentation
The first and second physicians’ determinations may be performed concurrently. If performed at different times, a full clinical examination including the apnea test must be performed, without any fixed examination interval, regardless of the primary etiology.

This patient fulfills the criteria for neurological determination of death
Physician (print name): __________________________ Signature: __________________________
Date: ___________ Time: ___________

Standard end-of-life care
Is this patient medically eligible for organ or tissue donation?
Yes □ No □
Has the option for organ or tissue donation been offered?
Yes □ No □
Has consent been obtained for donation?
Yes □ No □

Shemie et al, CMAJ, 2006
Complete and irreversible loss of all clinical functions of the brain.

= BRAIN ARREST

Minimum International Standard
= loss of function based on clinical evaluation
Death after Cessation of Brain Function

Minimum Acceptable International Clinical Standard

1. Clear and proximate cause
   - beware if brain imaging is normal
2. Preconditions fulfilled
3. Confounding conditions excluded or addressed
4. Refractory to all applied treatments
5. Unresponsive coma
6. Absent brainstem reflexes
7. Loss of central drive to breathe
Brain Blood Flow
Limitations to Brain Blood Flow Testing
False Positives

1. Majority of clinical brain death has no blood flow
2. Presence of some residual brain blood flow of unclear significance
3. Validity of various blood flow tests unresolved
4. Distinction between relevant and irrelevant flow on imaging tests is not clarified
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Neurological Determination of Death Instructional Video

Neurological Determination of Death: Instructional Video

open access

http://www.organsandtissues.ca/english/ndd/index.htm

www.blood.ca
END
Movements in Brain Death: A Systematic Review

Gustavo Saposnik, Vincenzo S. Basile, G. Bryan Young