Navigating the Uncharted and Frozen Waters: Declaring Brain Death in the Post-Hypothermia Patient

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Relevant Disclosures

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What do you do?

- 25 year old female
- OHCA from heroin overdose
- PEA arrest
- Therapeutic hypothermia to 33° for 24 hrs
- Rewarmed to 37°
- Brain death exam and declaration 8 hrs later
In the absence of organ donation, what is gained by declaring a human being dead by neurologic criteria?

Does brain death actually reflect a cogent understanding of biology or philosophy?
“Whoever saves a life, it is considered as if he saved an entire world.”

-- Mishnah Sanhedrin 4:5; Babylonian Talmud Tractate Sanhedrin 37a
Yet we are obligated to balance...

“Thou shalt not kill.”

-- Commandment VI
Exodus, 20:13
Author unknown
Brain Death – the moral authority required

**Brain death** is the total and irreversible loss of all brain function and the circumstance under which the donation of vital organs most commonly takes place.
The dead donor rule gives us moral agency

The dead donor rule requires patients to be declared dead before the removal of life-sustaining organs for transplantation.
In 1967 Death Evolved

First transplanted human heart beats

CAPE TOWN, South Africa (AP) — A South African and continued in satisfactory condition today with the heart of a 25-year-old girl pumping blood after the medical breakthrough Sunday of a human heart transplant.

Louis Washkansky, 25, a Little Rock, Ark., businessman, was in critical postoperative condition at what Greens Hospital called the first successful human heart transplant.

Heart specialists around the world were waiting to see Washkansky’s body recover from death and accept the heart of Denise Darvall, an accounting machine operator killed in a car crash.

“The longer Washkansky goes on, the better,” said Dr. John C. Durig, medical director of the hospital, “although he won’t get better soon.”

The case was followed with intense interest in the United States, where heart disease is the nation’s leading killer.

“It sounds to me like a clean job — scientifically valid,” said Dr. Norman S. Shumway, senior surgeon. "It’s not going to take years to perfect; when it does work, it will work well."

Washkansky had a breathing tube inserted in his throat — and couldn’t speak although he was reported fully conscious Sunday after the five-hour operation. He was being fed intravenously to prevent blood clots. Dr. Berger said that within 10 years doctors will be transplanting hearts with the same frequency they now transplant kidneys.

This week in history:

1967 first heart transplant by Barnard:

Denise Darvall, the donor, was NOT brain dead
“A heart is likely to be in better condition if it is removed while the dying patient still has a heartbeat. However, in an age before there were guidelines on "brain dead" patients, Prof Barnard's rival transplant surgeons in America had been warned that they could be charged with murder if they removed the heart from patients while it was still beating.”
1981 President’s Commission report on “guidelines for the determination of death” culminated in a proposal for a legal definition that led to the Uniform Determination of Death Act (UDDA). The act reads:

- An individual is dead 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

- This is different than European guidelines

- A determination of death must be made within “accepted medical standards.”
  - EEG was suggested, hypothermia was referenced
Brain Death Standards – “Ay, there’s the rub.”

- Most US States have adopted the UDDA
  - Some have amendments
- UDDA does not define “accepted medical standards”
Brain death and flight operations...

APPENDIX 2

Checklist for determination of brain death
Prerequisites (all must be checked)

- Coma, irreversible and cause known
- Neuroimaging excludes coma
- CNS depressant drug effect absent (if indicated toxicology screen if barbiturates, given, serum level < 10 μg/mL)
- No evidence of residual paralytic (electrical stimulation of paralytic muscle)
- Absence of severe acid-base, electrolyte, endocrine abnormality
- Normothermia or mild hypothermia (core temperature > 36°C)
- Systolic blood pressure ≥ 100 mm Hg
- No spontaneous respirations

Examination (all must be checked)

- Pupil unresponsive to bright light
- Contra lateral reflex absent
- Oculocephalic reflex absent (tested only if C-spine integrity ensured)
- Oculocephalic reflex absent
- No facial movement to noxious stimuli at supraorbital nerve, temporomandibular joint
- Gag reflex absent
- Cough reflex absent to cricothyroid sectioning
- Absence of motor response to noxious stimuli in all 4 limbs (spinally innervated reflexes are permissible)

Apnea testing (all must be checked)

- Patient is hemodynamically stable
- Ventilator adjusted to provide normocarbia (PaO₂ 94−45 mm Hg)
- Patient pronogatized with 100% FIO₂ for > 10 minutes to PaO₂ > 200 mm Hg
- Patient well-oxygenated with a PEEP of 5 cm of water
- Provide oxygen via a suction catheter to the level of the carina at 6 L/min or attach T-piece with CPAP at 10 cm H₂O
- Disconnect ventilator
- Spontaneous respirations absent
- Arterial blood gas drawn at 8−10 minutes, patient disconnected to ventilator
- PCO₂ ≥ 60 mm Hg, ≥ 20 mm Hg rise from normal baseline value OR
- Apnea test aborted
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Checklist for determination of brain death

Prerequisites (all must be checked)
- Coma, irreversible and cause known
- Neuroimaging explains coma
- CNS depressant drug effect absent (if indicated toxicology screen;
  if barbiturates given, serum level < 10 µg/mL)
- No evidence of residual paralytics (electrical stimulation if paralytics used).
- Absence of severe acid-base, electrolyte, endocrine abnormality
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Neurology® 2010;74:1911-1918
The question often asked...

Are there any proven cases where patients were declared brain dead and later were restored to a normal life?

- “No. Often the general public views brain death and coma as the same. They are NOT! Brain death is irreversible. Brain death is death.”

http://www.donorrecovery.org/learn/understanding-brain-death/
The media plays a different card


Of donors who had absent brainstem reflexes

60%

Normal or minimally injured brainstem reported at autopsy

Neurology 76:307, 2011
The predictive accuracy of absent brainstem reflexes in confirming irreversible brainstem injury is unknown.
Although neuronal loss is widespread, total brain necrosis is not observed.

... the diagnosis of brain death therefore should be based on clinical assessment alone.
Adding to storm: Therapeutic Hypothermia

The New England Journal of Medicine

MILD THERAPEUTIC HYPOThERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

The Hypothermia after Cardiac Arrest Study Group

NNT = 7

33°

n = 137 per arm
Therapeutic Hypothermia has unpredictable effects on GABA agents [benzodiazepines, propofol, barbiturates]:

- **Pharmacokinetics**
  - What a body does to a drug

- **Pharmacodynamics**
  - What a drug does to a body

\[ T_{1/2} \times 5 ? \]
History is bound to repeat itself

A 10-Month-Old Infant With Reversible Findings of Brain Death

Reversible brain death after cardiopulmonary arrest and induced hypothermia*

Adam C. Webb, MD; Owen B. Samuels, MD

26 hrs after BD declaration

57 hrs after BD declaration
Case 1

- 10 month old male, bathtub drowning
- ROSC after 37 minutes of CPR
- Fulfilled BD criteria at 42 hours post event
- Spontaneously breathing 15 hours later
- Phenobarbital and Midazolam had been used
Case 2

- 55 yom, witnessed respiratory arrest in ED
- ROSC at 20 minutes
- CT with loss of gray / white + edema
- Propofol and fentanyl stopped +50 hrs from ROSC
- BD exam 22 hrs later
- Return of brainstem function in OR 26 hrs after BD exam, 48 hrs after cessation of infusions
First report of transiently reversible brain death after induced hypothermia (Crit Care Med)

Webb and Samuels (Emory neuro-intensivists) report on a brain-injured patient who, after induced hypothermia and rewarming, had absent brainstem function and a confirmatory apnea test. However, in the O.R. for organ donation 24 hours later, brainstem function transiently returned and the surgery had to be aborted. They urge caution to the rest of us in declaring brain death after induced hypothermia. Crit Care Med 2011;39:1538-1542.

For Dr. Webb's personal comments on this experience (or to add your own), click the "Responses" icon in the upper right of this post.
Case 2 discussion (2): Webb weighs in

Apnea testing is part of the clinical brain death exam and is not a confirmatory test.

Confirmatory tests for brain death as stated in the American Academy of Neurology guidelines include EEG showing absence of cerebral cortical electrical activity, Transcranial doppler showing reversal of or absent diastolic cerebral blood flow, conventional cerebral angiography and Nuclear Medicine cerebral blood flow studies. The latter is by far the most common and preferred.

Confirmatory testing should be done in any patient who cannot undergo full clinical brain death testing (i.e. too unstable for an apnea test) or in a patient in whom you cannot completely exclude confounding factors (i.e. has been on a barbiturate infusion for ICP).

We are suggesting in this report that targeted temperature management after cardiac arrest should be considered a confounding factor regardless of if the patient is now normothermic or how long the patient has been off sedatives as we simply cannot predict the effects.

Your point about calling the neuro-ICU team is an important one. First, brain death testing should only be done by those familiar with brain death, protocols and guidelines. Many intensivists are but many are not. This case shows us how difficult brain death determinations can be even when performed by those who do this every day. It is something that for obvious reasons we have to get right every time.
T\(_{1/2}\) in the ICU

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<thead>
<tr>
<th></th>
<th>Fentanyl</th>
<th>Oxycodone</th>
<th>Versed</th>
<th>Heroin</th>
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<tr>
<td>T(_{1/2}) (hrs)</td>
<td>2 - 4</td>
<td>3 - 6</td>
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<td>(&gt; 10 days = 3 days)</td>
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ECMO sweep turned down, FiO₂ increased to 1.0 for apnea testing

Sudden rise in PaCO₂

Hypercapnic hyperoxic apnea test does not verify irreversible cessation of the medullary respiratory rhythm centers
Patients who undergo therapeutic hypothermia (33º) ought to be considered to have a confounding condition for clinical brain death testing anytime within 48 - 72 hours of rewarming

- These patients require confirmatory testing
  - 4 vessel DSA
  - Brain death EEG
  - Nuclear flow study
  - CT-Angiography of brain
  - Transcranial Doppler
Confirmatory Tests: Angio and Tc-99m HMPAO
CT-angiography – beware the confounders

Original Article
Confirming the brain death diagnosis using brain CT angiography: experience in Tokat State Hospital

Kayhan Karakuş, Sedat Demirci, Aysun Tekin Cengiz, Mehmet Haydar Atalar

Available evidence cannot support the use of CT angiography as a mandatory test...

In 100 cases of clinical brain death, CTA correctly identifies 85

85% = a solid B
[good enough for the Dean’s list?]
Can we agree to disagree?

The case against confirmatory tests for determining brain death in adults

One of my core tenets is that “confirmatory” tests for brain death are residua from the earlier days of refining a clinical entity, now known as brain death. These ancillary tests are not accurate, not conclusive, not pertinent, and not warranted. To put it another way, a clinical neurologic examination is worthy all on its own and more than good enough.
We propose that individuals who desire to donate their organs and who are either neurologically devastated or imminently dying should be allowed to donate their organs, without first being declared dead.

We do not support the dead-donor rule.

The concept of brain death... fails to correspond to any coherent biological or philosophical understanding of death.

Crit Care Med 2003; 31:2391–2396
Where does this leave us?

You are on the bleeding edge of life and death and medical ethics by nature of what you do.

You know more about this now than most of the people with whom you will interact.

These are uncharted waters; what a privilege to navigate them.