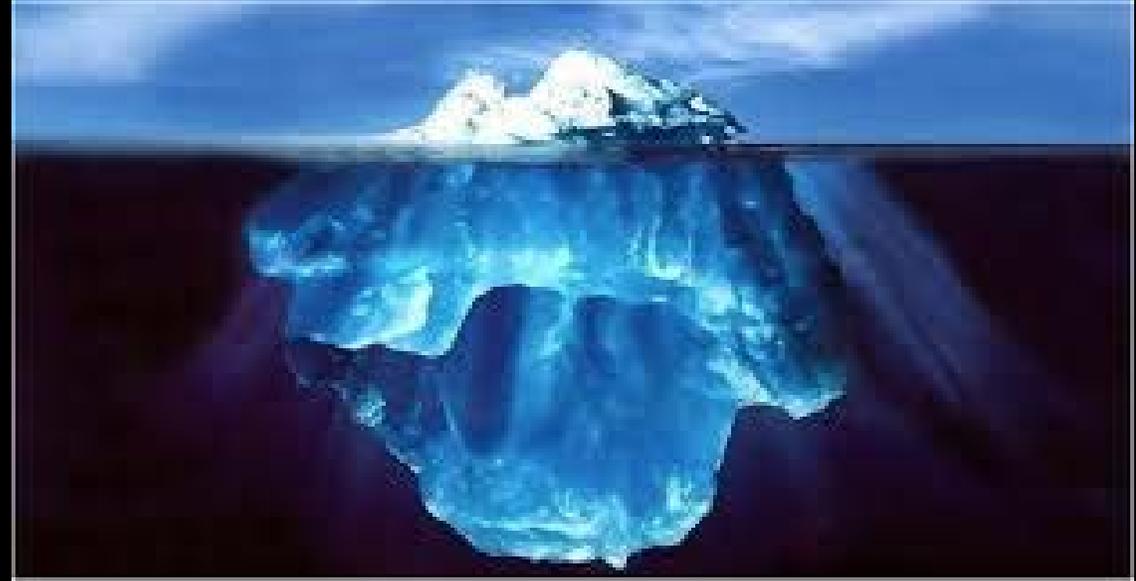


# Navigating the Uncharted and Frozen Waters: Declaring Brain Death in the Post-Hypothermia Patient



**11 MAY 2019**

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# Relevant Disclosures

- Associate Medical Director, Organ Donor Management, LODN
- Executive Committee, Neurocritical Care Society



# 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



# The burning question(s)

In the absence of organ donation, what is gained by declaring a human being dead by neurologic criteria?

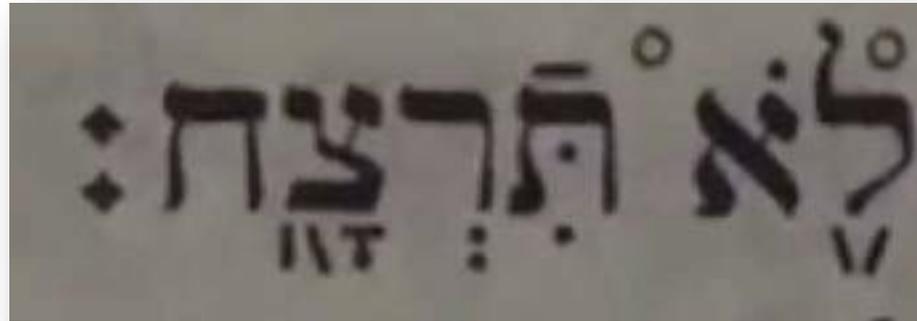
Does brain death actually reflect a cogent understanding of biology or philosophy?

# Organ donation is serious business

“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 man continued in satisfactory condition today with the heart of a 25-year-old girl pumping his blood after the medical breakthrough Sunday of a human heart transplant.

Louis Washkansky, 55, a Lithuanian-born businessman, was in the critical postoperative period of what Grootes Shuur Hospital called the first successful human heart transplant.

Heart specialists around the world were waiting to see if Washkansky's body would accept or reject the heart of Denise Ann Darvall, an accounting machine operator killed in a car crash.

"The longer Washkansky goes on, the better," said Dr. Jacobus G. Burger, medical supervisor of the hospital, "although that does not mean the heart will not be rejected later. The body could decide in 5 or 10 years' time that it doesn't want this heart."

Washkansky had a tracheotomy—a breathing tube inserted in his throat—and could not speak although he was reported fully conscious Sunday afternoon after the five-hour operation.

He was being fed anticoagulants to prevent blood clotting. Dr. Berger said that without the transplant Washkansky would have been dead within a few days because his heart's muscle was worn down.

The landmark operation was supervised by Dr. Jan. H. Louw, the hospital's chief surgeon, with Prof. Chris Barnard performing the main surgery.

Surgeons removed the heart from Miss Darvall's body first and kept it going by a mechanical pump while they took out Washkansky's damaged heart. They then transplanted the girl's heart into the man's chest and started it beating with jolts from electrodes.

"It was like turning the ignition switch of a car," said Dr. Louw.

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

"It sounds to me like a damn good job—scientifically valid," said Dr. Norman E. Shumway, head of the cardiovascular surgery division at the Stanford Medical Center.

He said his staff is ready to perform the same operation when the right combination of

dying patient and donor—whose heart must be taken no later than half an hour after death—occurs at Stanford.

Dr. Shumway predicted that within 10 years doctors will be transplanting hearts with the same frequency they now transplant kidneys. About 600 persons throughout the world were living with transplanted kidneys as of last February.

Dr. Michael DeBakey, who led the development of the heart pump, said "in Houston the transplant 'certainly would be a great achievement if they're able to overcome the rejection.'" Dr. Kenneth Sell of the U.S. Naval Medical Research Institute said there was "quite a definite chance" Washkansky might survive two years or more since several dogs which have received heart transplants are still alive two years afterward.

One abortive heart transplant effort was made in 1964 at the University of Mississippi. Surgeons there kept a patient alive despite a failing heart in a long but futile wait for a suitable human donor. In desperation they finally transplanted the heart of a chimpanzee, which failed after one hour.



1967 first heart transplant by Barnard:

Denise Darvall, the donor, was **NOT** brain dead

# We owe her memory the knowledge of her name

## Denise Darvall



She died violently, hit by a car...

But her heart beats on in his body



And her kidney keeps him alive

Because her head had been badly crushed when she was hit by a car, Denise Ann Darvall (*left*) was doomed to death. But the accident left most of her internal organs intact. Her father authorized the removal not only of her heart, but of her kidneys as well. One kidney was dispatched to a hospital 20 miles away. There, in what has become in only 13 years a fairly commonplace operation, it was transplanted to 10-year-old Jonathan Van Wyk, who was dying of kidney failure. He is shown (*bottom*), smiling, after surgery. Also smiling is Louis Washkansky (*above, right*), who has just been told he has a new heart. He is aware of hazards ahead. To keep the body from rejecting the foreign tissue, for instance, potent drugs will be used to suppress the body's immunological defenses, rendering him vulnerable to infection. Washkansky has an added handicap: diabetes. But his old heart had degenerated to the point of uselessness, and it was good just to feel alive again.

"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."

# Historical Background-

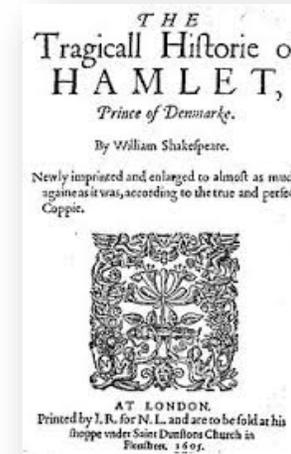
## Harvard Ad Hoc Committee – 1968

**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”
- The American Academy of Neurology 1995 / 2010 practice parameters delineate medical standards

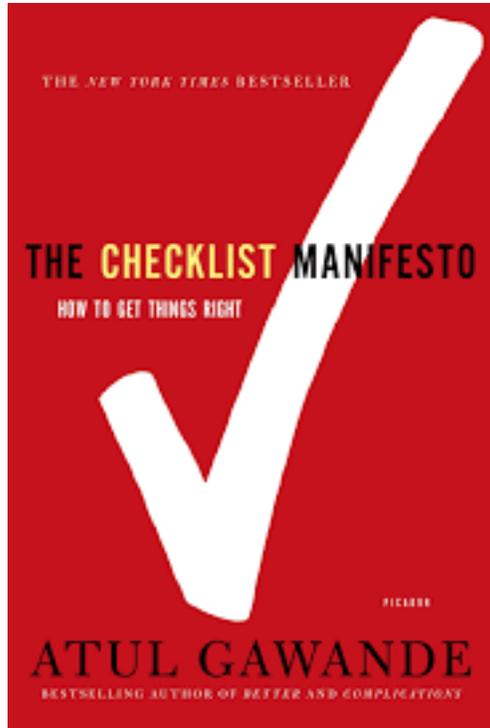


## Neurology®

**Evidence-based guideline update: Determining brain death in adults : Report of the Quality Standards Subcommittee of the American Academy of Neurology**  
Eelco F.M. Wijdicks, Panayiotis N. Varelas, Gary S. Gronseth, et al.  
*Neurology* 2010;74:1911  
DOI 10.1212/WNL.0b013e3181e242a8

This information is current as of December 21, 2012

# Brain death and flight operations...



## APPENDIX 2

### 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  $< 10 \mu\text{g/mL}$ )
- No evidence of residual paralytics (electrical stimulation if paralytics used).
- Absence of severe acid-base, electrolyte, endocrine abnormality
- Normothermia or mild hypothermia (core temperature  $> 36^\circ\text{C}$ )
- Systolic blood pressure  $\geq 100 \text{ mm Hg}$
- No spontaneous respirations

#### Examination (all must be checked)

- Pupils nonreactive to bright light
- Corneal reflex absent
- Oculocephalic reflex absent (tested only if C-spine integrity ensured)
- Oculovestibular reflex absent
- No facial movement to noxious stimuli at supraorbital nerve, temporomandibular joint
- Gag reflex absent
- Cough reflex absent to tracheal suctioning
- Absence of motor response to noxious stimuli in all 4 limbs (spinally mediated reflexes are permissible)

#### Apnea testing (all must be checked)

- Patient is hemodynamically stable
- Ventilator adjusted to provide normocarbica ( $\text{PaCO}_2$  34–45 mm Hg)
- Patient preoxygenated with 100%  $\text{FiO}_2$  for  $> 10$  minutes to  $\text{PaO}_2 > 200 \text{ mm Hg}$
- 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  $\text{H}_2\text{O}$
- Disconnect ventilator
- Spontaneous respirations absent
- Arterial blood gas drawn at 8–10 minutes, patient reconnected to ventilator
- $\text{PCO}_2 \geq 60 \text{ mm Hg}$ , or 20 mm Hg rise from normal baseline value
- OR:
- Apnea test aborted

# Closer examination reveals the issues...

## APPENDIX 2

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# 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.”

# The media plays a different card

HOME » NEWS » HEALTH » HEALTH NEWS

## 'Miracle recovery' of teen declared brain dead by four doctors

A teenager who was declared brain dead by four doctors has made a "miracle" recovery after his parents asked for another medical opinion just moments before his life support machine



Steven Thorpe with Julia Piper, the GP who helped to save his life Photo: NEWSTEAM

**FAKE NEWS**

Tuesday, 30 April 2013

## "Brain Dead" Brit Escapes Death Sentence of Organ Harvesting Doctors

Written by Dave Bohon

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<https://www.thenewamerican.com/culture/faith-and-morals/item/15244-brain-dead-brit-escapes-death-sentence-of-organ-harvesting-doctors>

<http://www.telegraph.co.uk/news/health/news/g223408/Miracle-recovery-of-teen-declared-brain-dead-by-four-doctors.html>

# Numbers that keep me up at night:

Of donors who had **absent brainstem reflexes**

60%

**Normal or minimally injured brainstem** reported at  
autopsy

## Conclusions that keep me up at night:

The predictive accuracy of absent brainstem reflexes in confirming irreversible brainstem injury is unknown

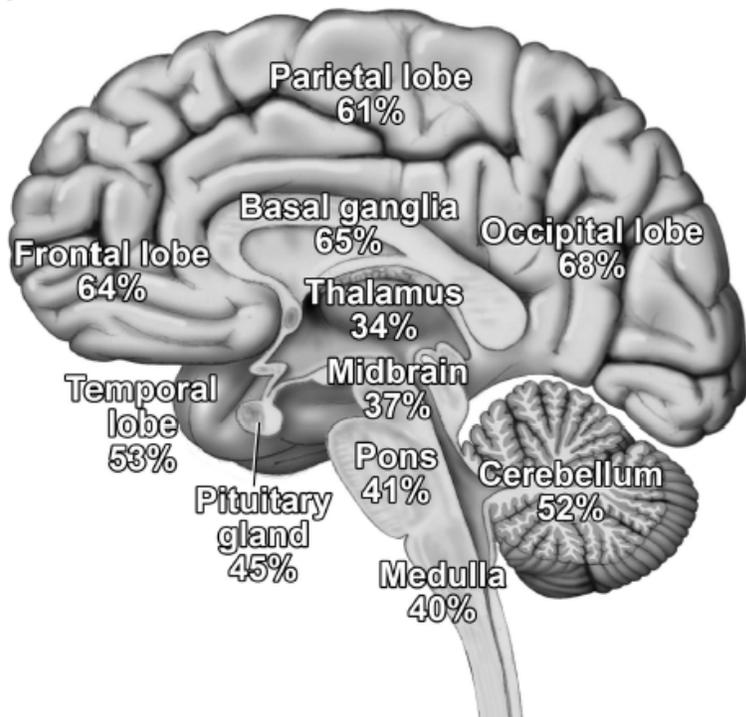


HURT ME  
WITH THE TRUTH  
BUT,  
NEVER COMFORT ME  
WITH A LIE.

# Insult to injury: it's all about a threshold

1 - x% = NORMAL

**Figure 2** Percentage of moderate to severe neuronal ischemic changes in 41 autopsies of patients who fulfilled the clinical criteria of brain death



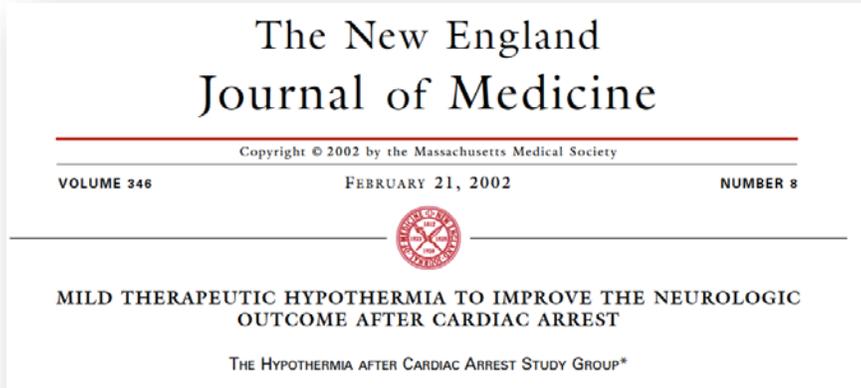
Neuropathology of brain death in the modern transplant era



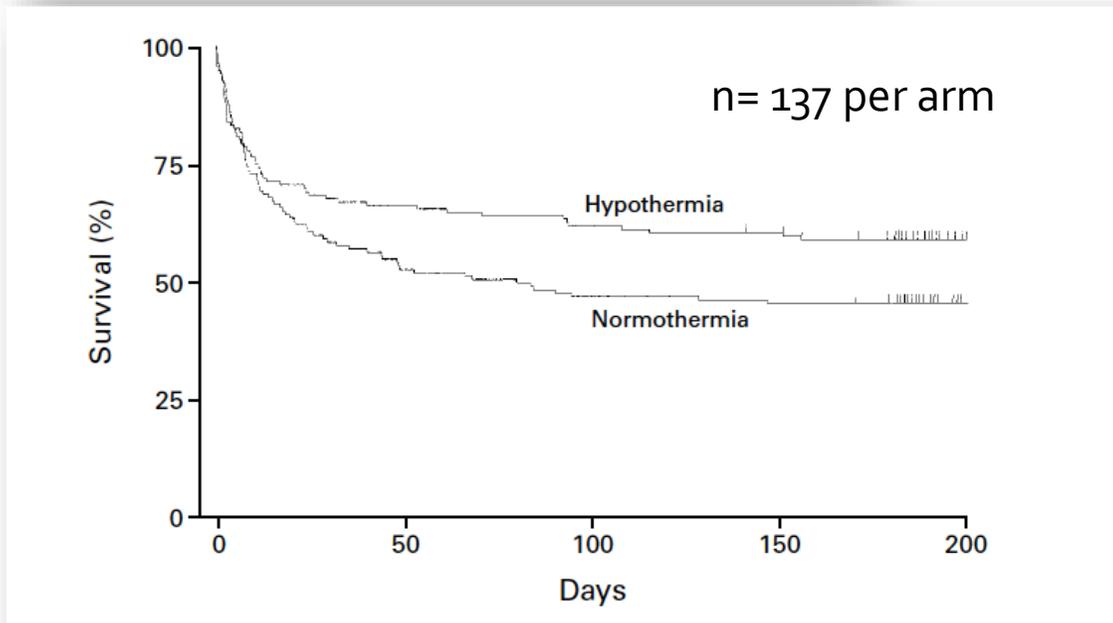
“Although neuronal loss is widespread, total brain necrosis is not observed.”

“... the diagnosis of brain death therefore should be based on clinical assessment alone.”

# Adding to storm: Therapeutic Hypothermia



33°



NNT = 7

# Creates a massive knowledge gap

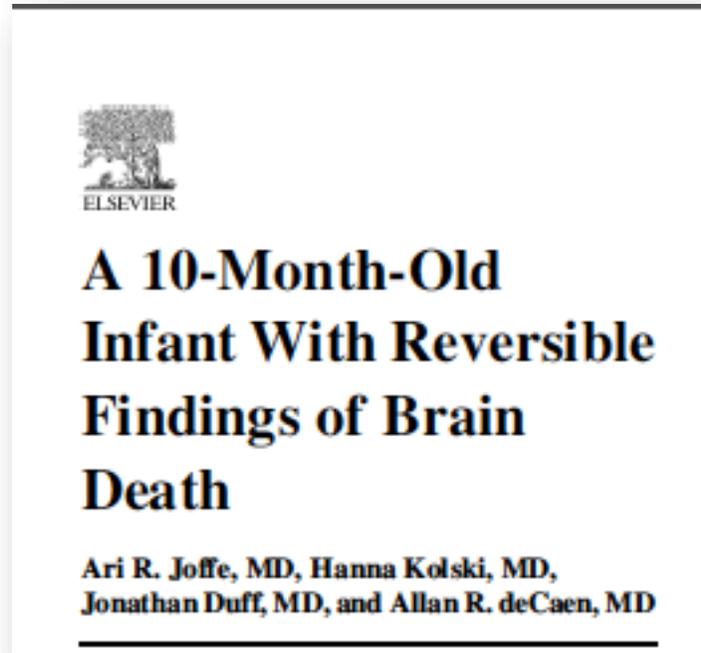
Therapeutic Hypothermia has **unpredictable effects** on GABA agents [benzodiazepines, propofol, barbiturates]:

- 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



378 PEDIATRIC NEUROLOGY Vol. 41 No. 5

**57 hrs** after BD  
declaration

## Case Report

Reversible brain death after cardiopulmonary arrest and induced hypothermia\*

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

**26 hrs** after BD  
declaration

Crit Care Med 2011 Vol. 39, No. 6

# 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



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

Ari R. Joffe, MD, Hanna Kolski, MD,  
Jonathan Duff, MD, and Allan R. deCaen, MD

2009

## Reversible brain death after cardiopulmonary arrest and induced hypothermia\*

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

# 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

Table 1. Timing and description of important events

Hours	
0	Return of spontaneous circulation
2	Initial examination in intensive care unit: no eye opening, no response to pain, pupils 3 mm nonreactive, multifocal myoclonus
7	Head computed tomography scan suggests diffuse cerebral edema consistent with global hypoxic-ischemic injury
16 <sup>a</sup>	Therapeutic hypothermia initiated with surface cooling and cold saline infusion
50 <sup>a</sup>	Rewarming initiated and propofol and fentanyl infusion stopped
56 <sup>a</sup>	Examination: no eye opening, no response to pain, sluggishly reactive 2-mm pupils, no corneal reflexes, intact cough reflex and gag reflex, spontaneous respirations present
72 <sup>a</sup>	First clinical examination consistent with brain death
78 <sup>a</sup>	Second clinical examination consistent with brain death
78 <sup>a</sup>	10-min apnea test with rise in pCO <sub>2</sub> from 41 to 108 mm Hg
98 <sup>a</sup>	Patient taken to operating room for organ procurement: noted cough, bilateral corneal reflex, and respirations
106	Repeat electroencephalogram shows no discernible cerebral electrical activity
145	Loss of remaining brainstem function, clinical examination again consistent with brain death
171	Somatosensory-evoked potential shows absence of P17 and N20 responses
194	Magnetic resonance image shows diffuse cerebral and cerebellar edema, transtentorial and cerebellar herniation
200	Nuclear cerebral blood flow study confirms absence of cerebral blood flow
202	Termination of mechanical ventilation, patient pronounced dead by cardiopulmonary criteria

# Case 2 discussion: (1) pulmccm.org

Dec  
26  
2011

## First report of transiently reversible brain death after induced hypothermia (Crit Care Med)

 Critical Care, Neurology Critical Care

 3 Comments

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

^ | v · Reply · Share ›



Adam Webb → Matt Hoffman · 6 years ago



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.

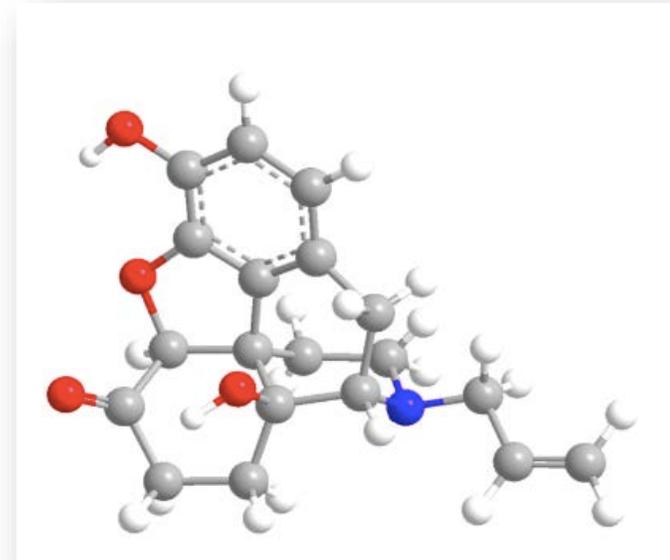
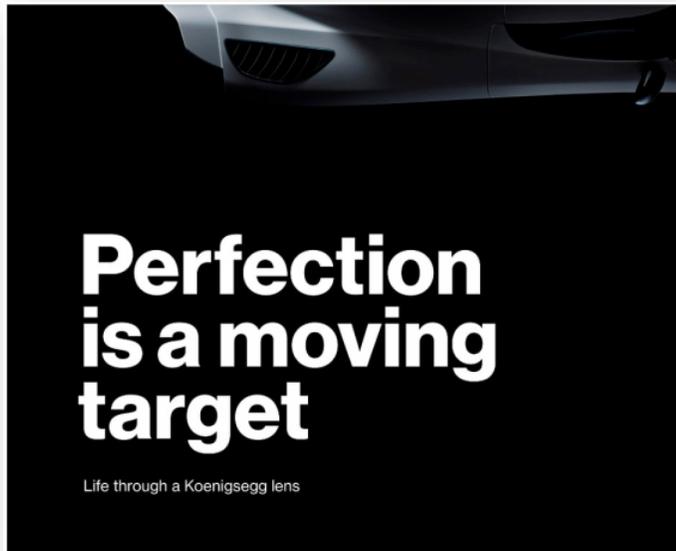
Confirmatory testing should be done in any patient who cannot undergo full clinical brain death testing (i.e. too unstable for an apnea test) or in a patient in whom you cannot completely exclude confounding factors (i.e. has been on a barbiturate infusion for ICP).

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.

^ | v · Reply · Share ›

# $T_{1/2}$ in the ICU



	Fentanyl	Oxycodone	Versed	Heroin
$T_{1/2}$ (hrs)	2 -4  (> 10 days = 3 days)	3 -6	2 - 7	2*

# Another curve ball: ECMO / MCS

- ECMO sweep turned down, FiO<sub>2</sub> increased to 1.0 for apnea testing
- Sudden rise in PaCO<sub>2</sub>
- Hypercapnic hyperoxic apnea test does not verify irreversible cessation of the medullary respiratory rhythm centers

**Determining Brain Death After  
Therapeutic Hypothermia on  
Nonpulsatile Continuous-Flow  
Mechanical Circulatory  
Support Devices**

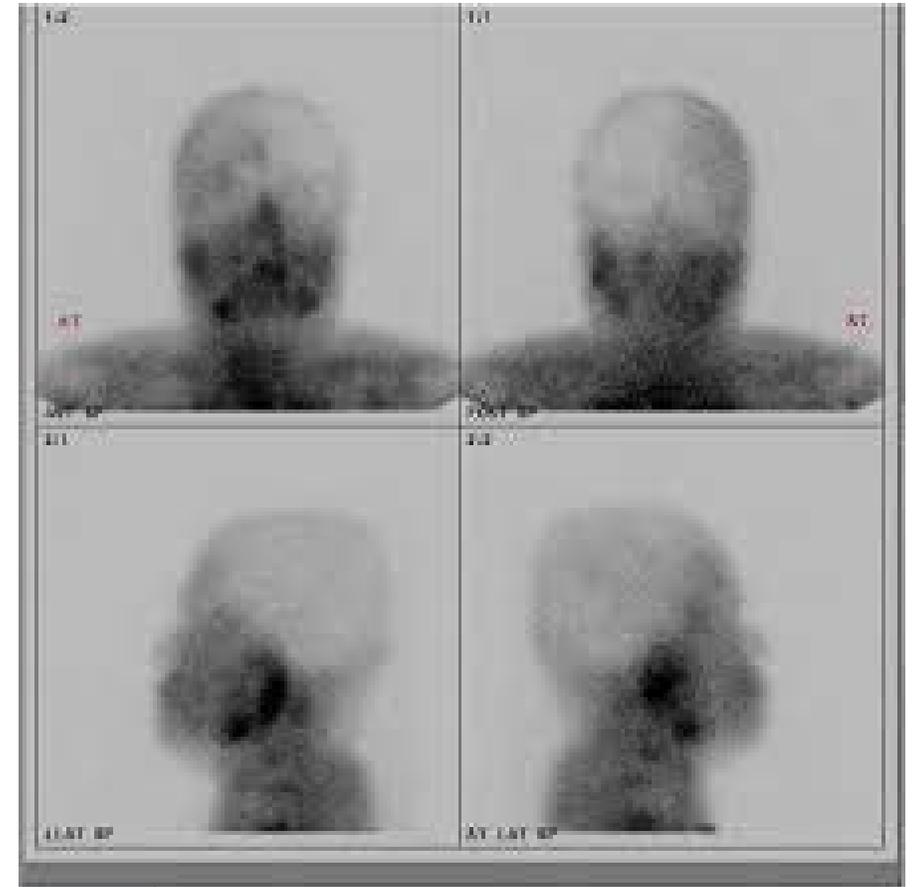
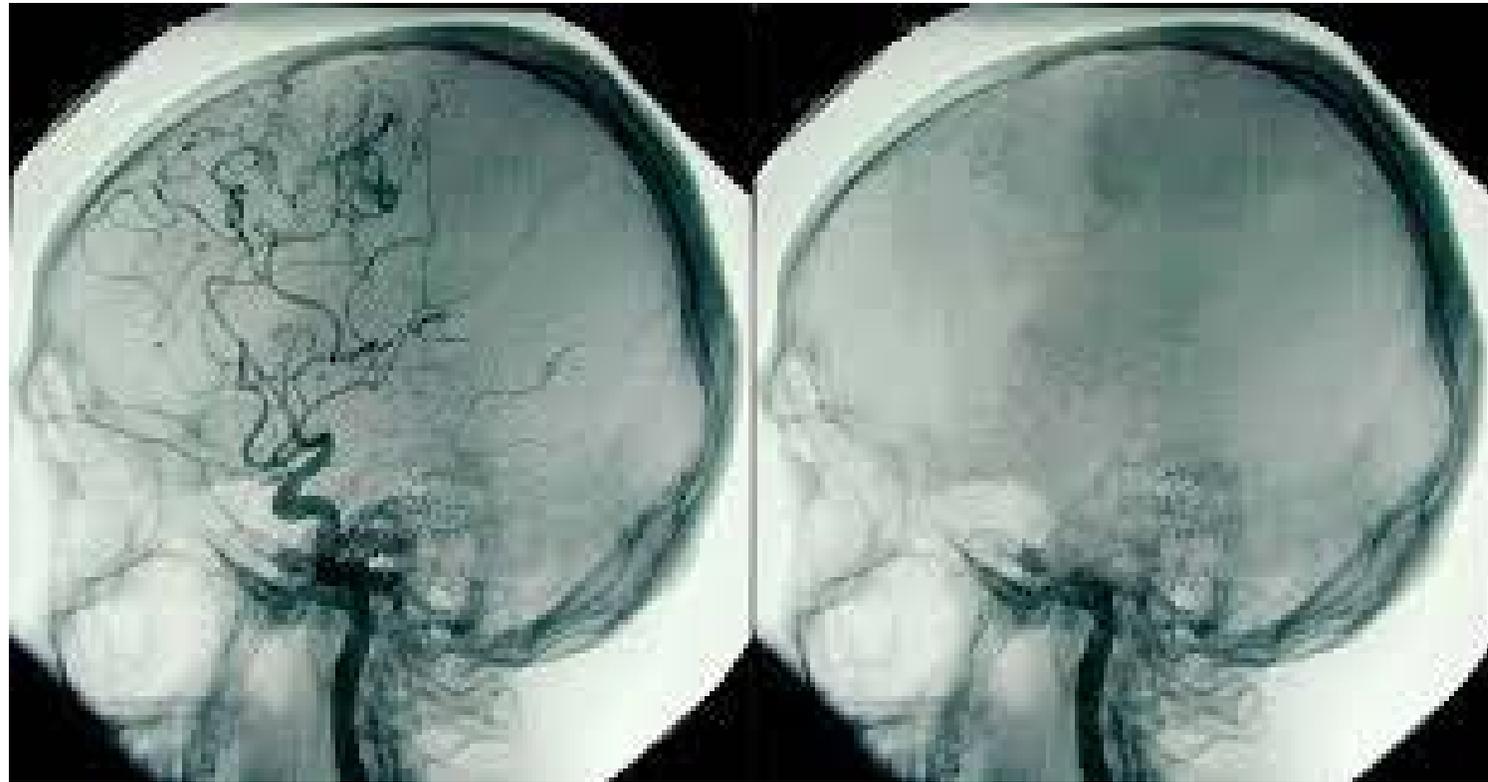


# How do we move forward now?

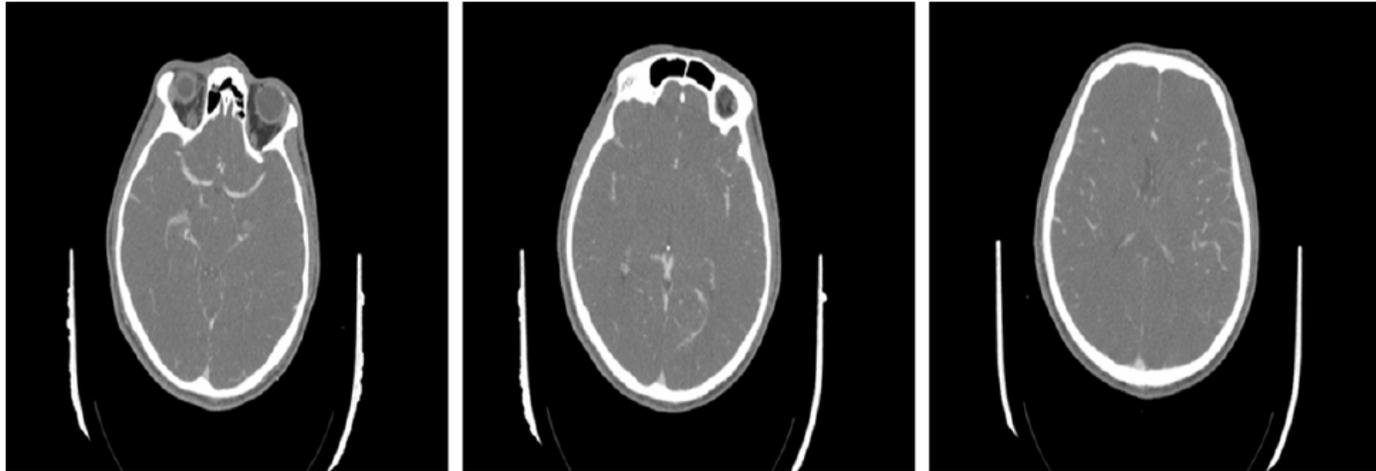
Patients who undergo therapeutic hypothermia (33°) ought to be considered to have a confounding condition for clinical brain death testing anytime within 48 - 72 hours of rewarming

- 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



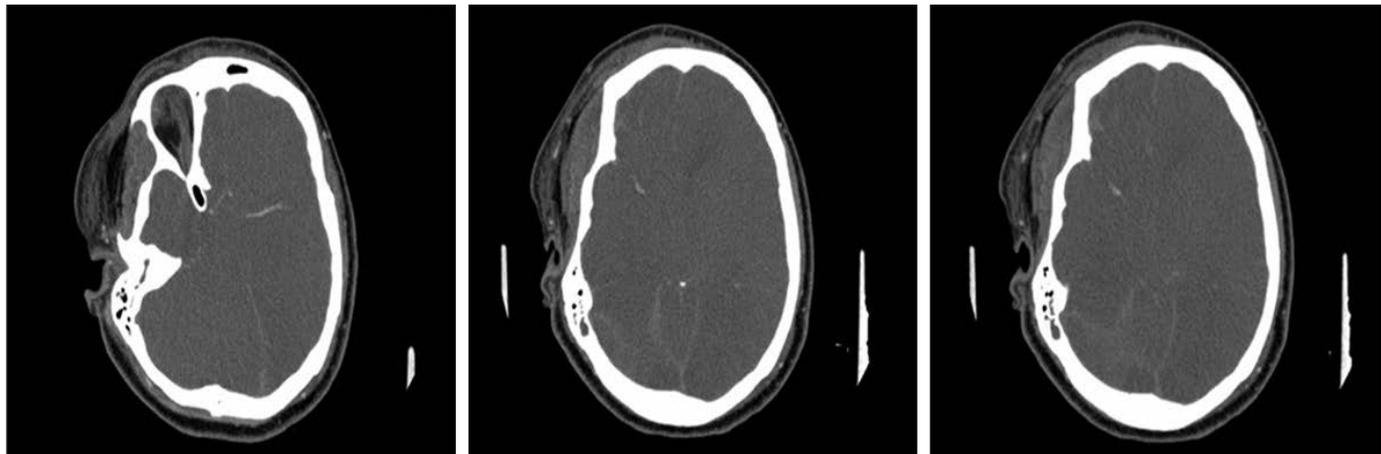
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*Original Article*

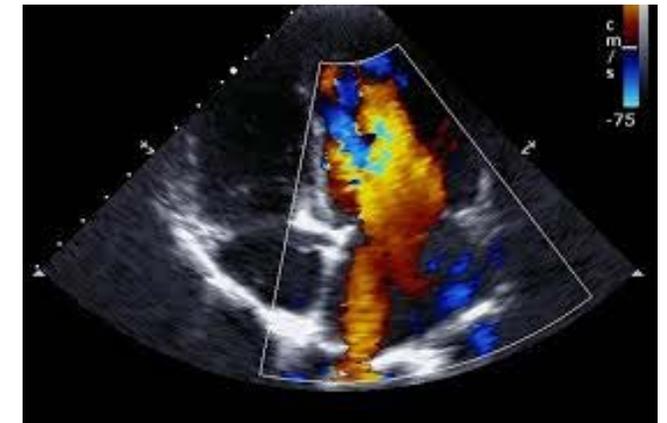
**Confirming the brain death diagnosis using brain CT angiography: experience in Tokat State Hospital**

Kayhan Karakuş<sup>1\*</sup>, Seden Demirci<sup>2\*</sup>, Aysun Yakut Cengiz<sup>1\*</sup>, Mehmet Haydar Atalar<sup>3\*</sup>

Int J Clin Exp Med 2014;7(7):1747-1751



(+)



# There are no participation trophies in brain death testing

## Computed tomography (CT) angiography for confirmation of the clinical diagnosis of brain death (Review)

Taylor T, Dineen RA, Gardiner DC, Buss CH, Howatson A, Pace NL

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

85% = a solid B

[good enough for the Dean's list?]

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

[it] may be useful ... assuming clinicians are aware of the relatively low overall sensitivity

# 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.

Table 2 Pitfalls of confirmatory tests

### Cerebral angiogram

Image variability with injection of arch or selective arteries

Image variability with injection and/or push technique

No guidelines for interpretation

### Transcranial Doppler ultrasonographic scan

Technical difficulties and skill-dependent

Normal in anoxic-ischemic injury

### EEG

Artifacts in intensive care settings

Information from mostly cortex

### Somatosensory evoked potentials

Absent in comatose patients without brain death

### CT angiogram

Interpretation difficulties

Retained blood flow in 20% of cases

Possibility to miss slow flow states because of rapid acquisition of images

### Nuclear brain scan

Areas of perfusion in thalamus in patients with anoxic injury or skull defect

# Root cause analysis of why this matters...

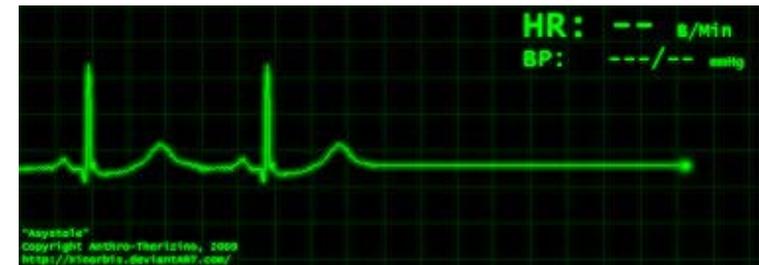
## Role of brain death and the dead-donor rule in the ethics of organ transplantation

Robert D. Truog, MD, FCCM; Walter M. Robinson, MD, MPH

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



# 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



# Questions

