

Bioethics for clinicians:

24. Brain death

Neil M. Lazar,* Sam Shemie,† George C. Webster,‡
Bernard M. Dickens§

Abstract

BRAIN DEATH IS DEFINED AS THE COMPLETE AND IRREVERSIBLE absence of all brain function. It is diagnosed by means of rigorous testing at the bedside. The advent of neurologic or brain death criteria to establish the death of a person was a significant departure from the traditional way of defining death and remains ethically challenging to some. We review the ethical, cultural, religious and legal issues surrounding brain death and outline an approach to establishing a diagnosis of brain death in clinical practice.

Mr. S. is a 35-year-old man who has a sudden, excruciating headache and collapses in his chair at dinner. At the emergency department a CT scan reveals a subarachnoid hemorrhage. Mr. S is admitted to the intensive care unit for monitoring and supportive measures aimed at controlling the intracranial pressure. The next morning he is noted to be nonresponsive, with nonreactive, mid-position pupils.

A 3½-year-old boy is playing near the backyard pool under supervision of his babysitter. The caretaker goes into the house to answer the telephone. Upon returning, she discovers the child face down in the pool. The paramedic team arrives and finds the child's vital signs are absent. Basic life support is started, and the boy is taken to a local general hospital. He is resuscitated with intubation, ventilation and intravenous epinephrine injection. The minimum documented duration of absent vital signs is 30 minutes. The boy is transferred to a pediatric hospital. He is comatose and unresponsive, with spontaneous breathing, reactive pupils and intermittent generalized seizures. He is treated with phenytoin and phenobarbital.

What is brain death?

Brain death is defined as the absence of all brain function demonstrated by profound coma, apnea and absence of all brain-stem reflexes.^{1,2} The clinical diagnosis was first described in the medical literature in 1959³ and was put into practice in the next decade with the use of specific clinical criteria.^{4,5} In most cases brain death can be diagnosed at the bedside. Common causes include trauma, intracranial hemorrhage, hypoxia due to resuscitation after cardiac arrest, drug overdose or near drowning, primary brain tumour, meningitis, homicide and suicide.

Why is the issue of brain death important?

Ethics

“Brain death” as a criterion for determining the death of a person is a social formulation, perhaps justifiable in the context of organ donation and transplantation. It implies a notion of irreversibly lost personhood. The diagnosis uncovers cultural and religious diversity in a pluralistic society and challenges public trust in the medical community.

Social formulation

For centuries, determining the death of another person was seen to be a rather

Review

Synthèse

*Associate Professor, Faculty of Medicine and Joint Centre for Bioethics, University Health Network and University of Toronto, Toronto, Ont.; †Assistant Professor, Faculty of Medicine, Hospital for Sick Children and University of Toronto, Toronto, Ont.; ‡Assistant Professor, Faculty of Medicine, Adjunct Professor, Department of Philosophy, University of Manitoba, and Clinical Ethicist, Health Care Ethics Service, St. Boniface General Hospital Winnipeg, Man.; §Professor, Faculty of Law, Faculty of Medicine and Joint Centre for Bioethics, University of Toronto, Toronto, Ont.

This article has been peer reviewed.

CMAJ 2001;164(6):833-6

This series began in the July 15, 1996, issue and can be found on CMAJ's Web site (www.cma.ca/cmaj/series/bioethic.htm).

Series editor: Dr. Peter A. Singer, University of Toronto Joint Centre for Bioethics, 88 College St., Toronto ON M5G 1L4; fax 416 978-1911; peter.singer@utoronto.ca

straightforward matter. The cessation of cardiac and respiratory functions was thought to be sufficient to conclude that a person had died. The advent of neurologic or brain death criteria to establish the death of a person was a significant departure from the traditional way of defining death and remains ethically challenging. However, regardless of which criteria are used, agreement about when death occurs is not simply an agreement about medical or biological criteria for death but is also a “social formulation.”⁶ On this point, Karen Gervais noted “that even in pre-technological culture, the choice of the traditional cardiopulmonary criteria was a choice, an imposition of values on biological data. It was a choice based on a decision concerning significant function, that is, a decision concerning what is so essentially significant to the nature of the human being that its irreversible cessation constitutes human death.”⁷

Personhood

Conceptually, death of the whole brain is seen to be a significant threshold separating one who is living from one who is dead. Notwithstanding the fact that cardiac and respiratory function can be maintained by artificial means in a person who is brain dead, those who accept a whole-brain definition of death argue that those brain functions necessary for the integrated functioning of the person are irreversibly lost. Without artificial support, the person would not be able to spontaneously sustain those necessary functions.

Some have argued that the whole-brain definition of death should be amended to incorporate people in a persistent vegetative state; that is, those who have experienced the irreversible loss of so-called higher brain functions. Proponents of this higher-brain definition of death argue that consciousness and the capacity to relate to other people and the wider world is a defining characteristic of human beings. In this view, the death of that part of the brain responsible for consciousness and interaction with the world is equivalent to the death of the person. Although the whole-brain definition of death has gained wide acceptance, the higher-brain definition has not. Concern about the implications of this higher-brain definition of death can be found in the early work of the US President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research:⁸

[T]he implication of the personhood and personal identity arguments is that Karen Quinlan, who retains brainstem function and breathes spontaneously, is just as dead as a corpse in the traditional sense. The Commission rejects this conclusion and the further implication that such patients could be buried or otherwise treated as dead persons.

Cultural and religious diversity

Understanding, defining and determining brain death continue to be ethically challenging and complex undertak-

ings in many cultures. Various cultural and religious groups (e.g., some First Nations and Asian cultures, and Orthodox Judaism) do not accept that death has occurred until all vital functions have ceased. Furthermore, in the clinical setting, some families simply may not accept that a relative is dead. Many experience a certain discomfort when they view a person who is brain dead but who appears to be alive because the body is being sustained by life support.

Trust

The enduring public ambivalence toward organ donation and retrieval may be rooted in the experience of witnessing a person declared brain dead who is sustained on life support. This concern may not only be about accurately determining death, but may also reflect fears that death will be declared prematurely for the sake of organ and tissue retrieval. The importance of this ambivalence should not be underestimated by clinicians caring for the critically ill or by those involved in the procurement of tissue and organs.

Law

The law approaches death as an event rather than a process, and as a matter of status rather than as a medical condition. Death marks the time when legal consequences arise, notably distribution of a person’s estate under a will or intestacy, and lawful disposal of bodily remains. The law sets the criteria by which death is measured, although physicians determine whether the legal criteria of death are satisfied.

The law recognizes a person as living even when the legal indicators of life — heartbeat and respiration — are being artificially maintained. That is, a person on a ventilator is considered living. However, when a body of someone who is brain dead is being artificially preserved to maintain tissue quality for organ retrieval, different legal criteria may be applicable. In some jurisdictions in North America and elsewhere, various criteria of whole-brain death have been formulated. In Manitoba, for instance, the Vital Statistics Act provides that “the death of a person takes place at the time at which irreversible cessation of all of that person’s brain function occurs.”⁹ In other jurisdictions, medical decision-making procedures are recognized. For instance, the Human Tissue Gift Act in Ontario provides that, “for the purposes of a post mortem transplant, the fact of death shall be determined by at least two physicians in accordance with accepted medical practice.”¹⁰

This opens the way to the accommodation of medical brain death criteria. The Human Tissue Gift Act in Ontario states that “no physician who has had any association with the proposed recipient that might influence his/her judgement shall take part in the determination of the fact of death of the donor ... nor can a physician who took any part in the determination of the fact of death of the donor participate in any way in the transplant procedures.”^{11,12}

Persistent vegetative state is not death. However, courts may be prepared to authorize withdrawal of artificial nutrition and hydration of a patient who has been in such a state for 6 months or more and who shows no evidence of improvement in order that the person may be allowed to die according to conventional tests of death.¹³ With appropriate consent, the person's death may be managed to allow organ retrieval for transplantation, although it should be clear that death is permitted as a legitimate end for the patient and not simply as a convenience for others.

Policy

Many national neurological and neurosurgical societies have drafted policies and practice guidelines for the declaration of brain death.¹⁴⁻¹⁷ Very few differences are apparent, and there is consistent emphasis on apnea testing and bedside assessment of brain function as the preferred method of establishing the diagnosis of brain death. Routine confirmatory testing with electroencephalography or cerebral angiography has fallen into disfavor. Other electrophysiological tests showing promise have not been sufficiently validated and are technically challenging both to perform and to interpret.

These policies and practice guidelines apply equally to adults and children over 2 months of age. Brain death in infants less than 2 months of age is approached differently in most policies and usually includes apnea testing, repeated bedside testing of brain functions, electroencephalography and tests of cerebral perfusion.¹⁸

How should I approach the issue of brain death in practice?

Physicians who participate in the declaration of brain death should be experienced in the relevant clinical criteria and diagnostic procedures.¹⁷ For the purposes of organ dona-

tion, 2 qualified physicians, neither of whom has had any significant association with the potential recipient, must do the declaration. No physician who takes part in the determination of the fact of death of the donor shall participate in any way in the transplant procedures.

Clinical criteria for the declaration of brain death include cerebral unresponsiveness secondary to an identifiable cause. Reversible conditions such as hypothermia (temperature below 32.2°C), and the influence of central nervous system depressants and muscle relaxants need to be ruled out. Cerebral unresponsiveness can be determined at the bedside using a variety of stimuli. In particular, there should be no motor response within the cranial nerve distribution to stimuli applied to any part of the body. Spinal cord reflexes may still be present in some cases. Seizures or decorticate/decerebrate posturing rule out a diagnosis of brain death. Determining the irreversibility of coma may require a period of observation between 2 and 24 hours, depending on the cause of the coma.

All brain-stem reflexes must be absent when tested with appropriate stimuli at the bedside. These include pupillary, oculocephalic (doll's eyes), oculovestibular (cold caloric), corneal, gag, cough and respiratory reflexes. During apnea testing, no spontaneous respiration should be evident upon disconnection of the ventilator for a period long enough to allow the partial pressure of carbon dioxide in arterial blood (PaCO₂) to rise above 60 mm Hg and the pH to fall below 7.28. Starting from a normal PaCO₂ and a normal body temperature, the PaCO₂ usually increases to at least 60 mm Hg within 8 to 10 minutes after dis-

connection of the ventilator. Oxygenation is maintained by pre-oxygenation of the patient and the use of low-flow oxygen (usually 5 to 6 L/min) delivered through a catheter placed in the trachea at the level of the carina.

If aspects of the clinical examination cannot be completed at the bedside, usually for technical reasons (anatomic issues or physiologic instability), supportive diag-

Establishing a diagnosis of brain death

- A physician experienced in the relevant clinical criteria and diagnostic procedures is required to declare brain death.
- For the purposes of organ donation, 2 physicians are required to declare brain death. Neither physician can have had any significant association with the potential recipient, nor can they participate in any way in the transplant procedures.
- All brain-stem reflexes (pupillary, oculocephalic [doll's eyes], oculovestibular [cold caloric], corneal, gag, cough and respiratory) must be absent when tested with appropriate stimuli at the bedside.
- Motor responses within the cranial nerve distribution must be absent when tested with stimuli applied to any part of the body. Spinal cord reflexes may still be present in some cases. Seizures or decorticate/decerebrate posturing rule out a diagnosis of brain death.
- Reversible conditions such as hypothermia (temperature < 32.2°C), and the influence of central nervous system depressants and muscle relaxants must be ruled out.
- Determining the irreversibility of coma may require a period of observation between 2 and 24 hours, depending on the cause of the coma.
- During apnea testing, no spontaneous respiration should be evident upon disconnection of the ventilator for a period long enough to allow the partial pressure of carbon dioxide in arterial blood to rise above 60 mm Hg and the pH to fall below 7.28 (usually 10 minutes).
- If aspects of the clinical examination cannot be completed at the bedside, supportive diagnostic procedures (e.g., radionuclide scanning or 4-vessel cerebral angiography to rule out intracranial blood flow) can be considered to support the diagnosis.

nostic procedures can be considered. Absence of intracranial blood flow, as determined by cerebral radionuclide scanning or 4-vessel cerebral angiography, is strongly supportive of a diagnosis of brain death. Electroencephalography has proven to be unreliable as a supportive test for brain death and is no longer included in most practice guidelines. Brain-stem evoked potentials, transcranial doppler, other imaging tests such as MRI and the atropine test are all currently under investigation to determine their role in supporting a diagnosis of brain death.

Once brain death has been diagnosed according to the clinical criteria¹⁷ outlined above, physicians and families must realize that brain death equals the death of the patient. Families should be told in no uncertain terms that the patient has died. Issues for the family to consider at this time include organ or tissue donation, autopsy examination and funeral arrangements.^{19,20} Life support should be removed unless organ donation is being considered. If there is conflict regarding the diagnosis of brain death that cannot be resolved by the clinicians and the family at the bedside, the coroner may be called in to evaluate the case and possibly complete the medical certificate of death.

Two possible exceptions to this approach have been discussed in the literature. The first is the unusual circumstance of an apparently brain dead patient who is pregnant at the time of diagnosis. A small number of such cases have been described in the literature,²¹ some with attempts made to maintain the pregnancy until viability of the fetus. No consensus has been reached as to when this should be attempted, although at least one author has proposed that the pregnancy be at least 24 weeks' gestation at the time of diagnosis of brain death in the mother.²²

Another exception might be based on religious objections to the acceptance of brain death as a criterion for declaring death. New York State adopted a religious exception to brain death in 1987, and New Jersey in 1991. Regardless, maintenance of normal cardiovascular homeostasis for more than a few days under these circumstances would be unlikely, and traditional cardiovascular death criteria would soon be met.

In clinical practice, distinguishing between brain death and persistent vegetative state is not difficult. In a persistent vegetative state, spontaneous respiration is always present, cardiovascular stability is usually present, and sleep-wake cycles may be present. Brain death is diagnosed after a shorter period of observation (between 2 and 24 hours), whereas a persistent vegetative state is usually not certain until the patient has been observed for a few months.

The cases

Mr. S. probably has progressed to clinical brain death. His doctors will have to perform a formal evaluation at the bedside to determine this status. A careful review of the medication record fails to reveal any sedative or neuromuscular-blocking drugs administered. The patient is not hypothermic. No stimulation evokes a response except for

spinal reflexes of the lower extremities. All brain-stem reflexes are negative when tested with adequate stimuli. His family is informed of the results of these tests and is asked whether Mr. S. was in favour of organ donation. The family agrees to consider organ donation. Mr. S. is formally declared brain dead by 2 qualified physicians. Nine other patients benefit from transplants of his organs.

The condition of the boy deteriorates over the ensuing 48 hours, with signs of brain-stem herniation, including fixed and dilated pupils, diabetes insipidus and impaired thermoregulation. A CT scan of the head shows severe cerebral edema consistent with hypoxic-ischemic injury. Examination by 2 independent specialists on 2 separate occasions confirms the clinical diagnosis of brain death. The family is counseled on multiple occasions regarding the diagnosis of brain death and consents to organ donation. Seven patients benefit from transplants of the child's organs.

Contributors: Neil Lazar was the principal author; Sam Shemie, George Webster and Bernard Dickens provided input and contributed to the writing and revising of the article.

Competing interests: None declared.

References

1. Taylor RM. Reexamining the definition and criteria of death. *Semin Neurol* 1997;17:265-70.
2. Setzer N. Brain death: physiologic definitions. *Crit Care Clin* 1985;1:375-96.
3. Wertheimer P, Jouviet M, Descotes J. À propos du diagnostic de la mort du système nerveux dans les comas avec arrêt respiratoire traités par respiration artificielle. *Presse Med* 1959;67:87-8.
4. A definition of irreversible coma. *JAMA* 1968;205:37-340.
5. Spoor MT, Sutherland FR. The evolution of the concept of brain death. *Ann R Coll Physicians Surg Can* 1995;28:30-2.
6. Capron A. Legal issues in pronouncing death. In: Reich WT, editor. *Encyclopedia of bioethics*. Rev ed. New York: Simon & Schuster Macmillan; 1995. p. 534-9.
7. Gervais KG. Death, definition and determination: philosophical and theological perspectives. In: Reich WT, editor. *Encyclopedia of bioethics*. Rev ed. New York: Simon & Schuster Macmillan; 1995. p. 540-8.
8. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Defining death: a report on the medical, legal and ethical issues in the determination of death*. Washington: The Commission; 1981.
9. *Vital Statistics Act*, RSM 1987, ch V-60, s 2.
10. *Human Tissue Gift Act*, RSO 1990, ch H-20, s 7(1).
11. *Human Tissue Gift Act*, RSO 1990, ch H-20, s 7(2).
12. *Human Tissue Gift Act*, RSO 1990, ch H-20, s 7(3).
13. *Airedale National Health Service Trust v. Bland*, [1993] 1 A.C. 789 (House of Lords, England).
14. Medical consultants on the diagnosis of death to the President's Commission: guidelines for the determination of death. *JAMA* 1981;246:2184-5.
15. Practice parameters for determining brain death in adults. *Neurology* 1995;45:1012-4.
16. Criteria for the diagnosis of brain stem death. *J R Coll Physicians Lond* 1995;29:381-2.
17. Canadian Neurocritical Group. Guidelines for the diagnosis of brain death. *Can J Neurol Sci* 1999;26:64-6.
18. Task Force for the Determination of Brain Death in Children. Guidelines for the determination of brain death in children. *Arch Neurol* 1987;44:587-8.
19. Waisel DB, Truong RD. The end-of-life sequence. *Anesthesiology* 1997;87:676-86.
20. Jennett B. Brain stem death defines death in law. *BMJ* 1999;318:1755.
21. Field DR, Gates EA, Creasy RK, Jonson AR, Laros RK. Maternal brain death during pregnancy: medical and ethical issues. *JAMA* 1988;260:816-22.
22. Dillon WP, Lee RV, Tronlone MJ, Buckwald S, Foote RJ. Life support and maternal brain death during pregnancy. *JAMA* 1982;248:1089-91.

Reprint requests to: Dr. Neil M. Lazar, Associate Professor, Faculty of Medicine and Joint Centre for Bioethics, University Health Network and University of Toronto, Rm. 10EN-214, 200 Elizabeth St., Toronto ON M5G 2C4; neil.lazar@uhn.on.ca