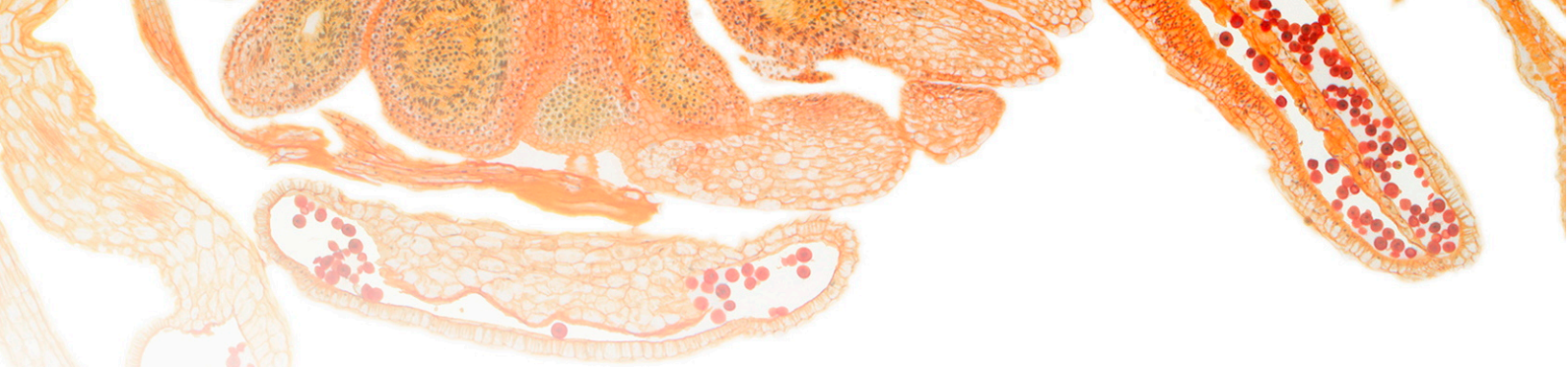

AMA Journal of Ethics®

December 2020, Volume 22, Number 12: E1038-1046

POLICY FORUM: PEER-REVIEWED ARTICLE

What Should We Do About the Mismatch Between the Legal Criteria for Death and How Brain Death Is Diagnosed?

Nathaniel M. Robbins, MD and James L. Bernat, MD

Abstract

Mismatch between whole-brain death criteria embedded in statutes and accepted tests physicians use to diagnose brain death have clinical and ethical implications that could undermine public trust in death pronouncements. We consider merits and drawbacks of 4 ways to address this problem.

To claim one AMA PRA Category 1 Credit™ *for the CME activity associated with this article, you must do the following: (1) read this article in its entirety, (2) answer at least 80 percent of the quiz questions correctly, and (3) complete an evaluation. The quiz, evaluation, and form for claiming* AMA PRA Category 1 Credit™ *are available through the* AMA Ed Hub™.

Legal and Clinical Mismatch

In 1980, the Uniform Determination of Death Act (UDDA) defined death ("brain death") as "irreversible cessation of all functions of the entire brain, including the brain stem … in accordance with accepted medical standards."[1,2] Whole-brain criteria of death have since been adopted in all 50 states.[3] Although the American Academy of Neurology (AAN) and other organizations have outlined "accepted medical standards" for determining brain death (BD) by neurological criteria,[4,5,6] controversy is ongoing because testing pursuant to these standards can only approximate BD as codified in law.[7,8]

Several recent high-profile cases have highlighted this mismatch,[7] although they are not unique.[9] This mismatch has reignited controversy among BD experts,[10] spawned lay misunderstanding,[11] and could threaten public trust in physicians, their BD diagnoses, or BD as a concept. Addressing conceptual, ethical, and practical implications of this mismatch requires that physicians recognize BD as currently defined and the difficulties of assessing function loss "irreversibility" in the "entire brain."[1,2] After discussing these difficulties, we offer 4 solutions for reconciling the mismatch: loosening the whole-brain criterion of death, requiring more stringent testing for diagnosing brain death, acknowledging the incongruence between the concept of death and its bedside determination, and the first 2 solutions in combination.

Irreversible Cessation

One reason for the mismatch between medical and legal standards for determining BD is that accepted medical standards cannot determine irreversible cessation. Function

loss *irreversibility* was recently reaffirmed as a legal requirement for death when a prisoner who was resuscitated after circulatory arrest argued (unsuccessfully and in court) that his life sentence already had been served.[12] Although broad religious, ethical, clinical, and legal consensus exists that death is irreversible and final, in practice, recognizing exactly when life transitions to death is not so easy.[13,14] Circulatory death (CD) is currently diagnosed operationally, based on permanence; the function loss irreversibility criterion is fulfilled and fulfillable only when resuscitation is abandoned or life-sustaining measures are withdrawn.[15] Physicians have always relied on permanent cessation of circulation and respiration to determine death without needing to prove function loss irreversibility—and, as we discuss in relation to BD, proving irreversibility is a problem, because prevailing tests rely on permanent cessation.[15]

Hypoxic brain tissue invariably becomes functionally quiescent before it is irreversibly destroyed.[8] BD examination cross-sectionally evaluates function but cannot distinguish between a "stunned," quiescent brain and an irreversibly damaged brain.[8] The clinical term *ischemic penumbra* refers to a brain that is hypoperfused (ie, deprived of sufficient oxygenated blood) and nonfunctional but potentially salvageable; hypoperfusion is a well-recognized state of perilesional neurons in patients with acute ischemic stroke, one that can confound BD diagnosis.[7,8,16,17,18] Technological advances further blur the line between quiescent and dead brain. For example, it was recently demonstrated that some cellular activity in pig brains can be restored several hours postmortem.[19] Although metabolically active brain cells do not necessarily mean that a brain is living and "proof of demise of every neuron is not required to demonstrate irreversible loss of whole brain function,"[20] cellular restoration is one reason function loss irreversibility is hard to confirm clinically.

The AAN recently defended clinical standards for diagnosing BD in prognostic rather than in conceptual terms, stating that it was "unaware of any cases in which compliant application of the Brain Death Guidelines led to inaccurate determination of death with return of any brain function." [20] Yet confidence in this assertion is limited because accepted standards for diagnosing BD have not been rigorously tested. Patients who meet BD criteria are almost always withdrawn from cardiopulmonary support, which ensures function loss irreversibility.[8] Cardiopulmonary support was continued in Jahi McMath's case, however.[7,8] Independent physicians appropriately declared her to be BD by accepted medical standards, but months later she reportedly demonstrated some preserved brain functions. If some of her brain functions really were preserved, her case seems to illustrate the limited specificity of BD diagnostic tests.[7,8] Despite being controversial,[21] the McMath case is important since opportunities to longitudinally follow a patient after a BD diagnosis are few.[7,8]

Whole Brain Function

In states that have adopted the UDDA, BD determination mandates the "irreversible cessation of all functions of the entire brain, including the brain stem … in accordance with accepted medical standards."[1,2] However, accepted diagnostic tests only enable a physician to examine a patient's motoric responses, which are controlled by the brain stem.[22,24] Clinical examination must demonstrate apnea, cranial nerve areflexia, and unresponsiveness caused by an irreversible pathology, excluding mimicking and potentially reversible conditions.[4,5,23] But "super locked-in patients" with completely destroyed brain stem efferent pathways could appear brain dead, despite preserved consciousness or afferent olfactory and visual pathways, analogous to vegetative patients who demonstrate subclinical awareness when carefully interrogated.[23,25,26,27,28]

Although brain stem destruction damages the reticular activating system, presumably causing unconsciousness, this effect is not currently empirically verifiable.[29,30]

Other examples illustrating the mismatch between accepted medical standards for diagnosing BD and the whole-brain criterion of BD codified in law are patients diagnosed as brain dead per accepted medical standards but who retain neurohormonal functions, such as vasopressin release, which requires an intact neurosecretory hypothalamus.[7,31,32] McMath, for example, reportedly underwent menarche and pubertal development[7] and showed signs of autonomic environmental reactivity.[8,33] Even patients who otherwise meet criteria for BD can have cerebral activity revealed on an electroencephalogram (EEG),[34,35] and though EEG activity does not necessarily indicate "meaningful" brain function, it probably reflects subclinical cognition.[36,37]

Early BD proponents assumed that brain tissue disintegration invariably followed BD diagnosis.[2,9,38,39] Liquefaction can follow total brain infarction eventually, but patients diagnosed as brain dead by current tests often have grossly intact brain tissue at autopsy.[40,41] McMath's magnetic resonance image reportedly showed some areas of preserved brain tissue 9 months after the initial insult.[8,17,33] Other authors note frequent persistence of patients' cerebral electrical activity and blood flow despite a BD diagnosis, particularly following infratentorial injuries.[42] Although preserved brain structure and blood flow do not necessarily imply preserved function, it seems clear that (1) many nonmotoric brain functions, including higher-order and afferent functions, are difficult to interrogate without an intact brain stem; (2) many young brain-dead patients have sustained blood circulation for long periods after a BD diagnosis; and (3) persistent hormonal and autonomic functions seem to contradict a BD diagnosis according to the UDDA's requirement, even when diagnosed appropriately per accepted medical standards.

Saying What We Mean, Meaning What We Say

We and others have argued that "all functions of the entire brain"[1,2] is best interpreted as the functioning of the brain-as-a-whole or the core function of the brain, rather than as the persistence of a single or even each individual brain function.[38,43] Defenders of the functioning of the brain-as-a-whole concept argue that the apparent mismatch posed by persistent hypothalamic or autonomic activity, for example, stems from misinterpreting "all functions of the entire brain." But persistence of a single noncritical brain function does not indicate that the function of the brain-as-a-whole has irreversibly ceased.

Despite being widely accepted for decades, the brain-as-a-whole concept remains vague and challenging to defend.[43,44] Conceptions of the brain's role as a control center or "somatic integrator" have been criticized because many vital body functions operate independently or in parallel with the brain.[45,46] Other authors, including us, have emphasized that critical functions, such as cardiorespiratory circulation or consciousness, define the-brain-as-a-whole.[43] The President's Council on Bioethics' 2008 report suggests that "the work of self-preservation" performed by the brain should be regarded as central.[45]

Yet none of these brain-as-a-whole refinements seem to adequately rebut important criticisms or clarify responses to key clinical and ethical questions: Which specific functions are essential for life? Why are critical functions found in the spinal cord or elsewhere regarded as less important?[14,44] Why should autonomic and hormonal

functions not be regarded as key parts of "the work of self-preservation"[45]? Proposed brain-as-a-whole definitions seem superficially reasonable but, to date, no necessary and sufficient criteria have been formulated to define life or death of an organism as a whole.

Reconciliation

Although the UDDA requires "irreversible cessation of all functions of the entire brain" to diagnose BD,[1,2] as just discussed, accepted medical standards are only achievable through physicians' use of currently available diagnostic tests, which do not assess function loss irreversibility or brain functions other than motor responses and respiration. This mismatch between legal criteria and what's achievable via currently available tests for diagnosing BD means that false-positive diagnoses of BD are possible in cases of low but not absent brain perfusion or brain stem destruction. How should this mismatch be reconciled?

We propose 3 options: improving testing, amending the UDDA, or accepting the inevitability of mismatch.[47]

Improving testing. To preserve the UDDA, testing standards must be tightened. Mandating repeat examinations after a minimal-interval waiting period might help.[48] Many experts recommend this strategy in certain cases (eg, primary brain stem injuries),[23] and this strategy would apply when hypoperfusion mimics function loss irreversibility. One limitation of this strategy is that the duration of an interval that would sufficiently ensure brain function cessation irreversibility remains unknown. Prolonged waiting is not feasible or desirable for many reasons, including fewer patients qualifying as organ donors.[49]

Another strategy for improving tests would be to mandate ancillary testing to assess whole-brain function more comprehensively. A drawback of this strategy, however, is that ancillary tests are expensive, not always available, and can generate false positives and false negatives.[23] Another method—universal perfusion scanning—also might not eliminate the mismatch between accepted standards for diagnosing BD and the whole-brain criterion of death, because viable brain tissue might survive below commonly accepted neuroimaging detection thresholds.[7,8,16] Even future technological advances that expand our understanding of consciousness or render today's ancillary tests obsolete might not help clearly distinguish live patients from dead ones. Thus, it seems reasonable to conclude that testing for whole-brain function will evolve and that establishing enduring standards that render tolerance for ambiguity unnecessary will be challenging, if not impossible.

Amend the UDDA. A second strategy is to amend the UDDA to align it more closely with clinical practice. Since death is difficult to define[14] and since transitions from living, to dying, to death resemble a continuum more than they resemble the binary concept currently enshrined in law,[50] amendment would be reasonable. One option would be to define BD in terms of cessation of function of the brain-as-a-whole, although a lack of tests for measuring functioning of the brain-as-a-whole[7,38] remains. Another option would be to define BD in terms of *brain stem death*, as in the UK.[51] This definition would address the mismatch, but practical and philosophical problems would remain for patients who retain consciousness or a quiescent, potentially revivable brain, despite absence of evidence of brain stem function.[8]

Accept mismatch. A third strategy involves preserving BD as defined in the UDDA, while accepting that tests for BD offer only approximations of BD. Death is irreversible by definition, but physicians have always relied on permanent cessation of circulation and respiration to determine death without needing to prove function loss irreversibility.[15] Death can be viewed as a process on a continuum that has important clinical and ethical dimensions, but legally BD is a discrete event.[13,14,50]

Since it might be impossible to conclusively demonstrate irreversibility and loss of all brain functions, acknowledging the limitations of accepted standards is more intellectually honest and might help overcome public misperceptions and mistrust.[11,50] A risk is that accepting the mismatch means accepting that some patients' BD diagnoses will probably be wrong.[10,14,15,52,53] However, it comports with current declarations of CD, which is routinely diagnosed based on permanent cessation of function (ie, resuscitation attempts either are not attempted or have failed and been aborted), not on biologic irreversibility.[15]

A Fourth Strategy?

Revising both legal criteria for BD and diagnostic capacity to assess BD might be the best way to address the mismatch between the two. Doing so might help respond to current public skepticism and lack of understanding of BD[54,55,56,57] and acknowledge lay tendencies to care more about prognosis than abstractions.[54,57,58,59] Such a change could obfuscate determinations of a time of death and require a refinement of the dead donor rule,[60] which expresses general clinical and ethical consensus that a person must be dead before their organs can be retrieved. When one acknowledges that current testing can only imperfectly approximate BD, the question of whether to abandon the dead donor rule will also need to be carefully considered.[60,61,62,63]

References

1. National Conference of Commissioners on Uniform State Laws. Uniform Determination of Death Act. https://www.uniformlaws.org/HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=341343fa-1efe-706c-043a-9290fdcfd909. Approved 1980. Accessed July 29, 2020.
2. Guidelines for the determination of death. Report of the medical consultants on the diagnosis of death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *JAMA*. 1981;246(19):2184-2186.
3. Burkle CM, Pope TM. Brain death: legal obligations and the courts. *Semin Neurol*. 2015;35(2):174-179.
4. Quality Standards Subcommittee of the American Academy of Neurology. Practice parameters for determining brain death in adults (summary statement). *Neurology*. 1995;45(5):1012-1014.
5. Wijdicks EFM, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2010;74(23):1911-1918.
6. Nakagawa TA, Ashwal S, Mather M, Mysore M. Clinical report—guidelines for the determination of brain death in infants and children: an update of the 1987 task force recommendations. *Pediatrics*. 2011;128(3):e720-e740.
7. Dalle Ave AL, Bernat JL. Inconsistencies between the criterion and tests for brain death. *J Intensive Care Med*. 2020;35(8):772-780.

8. Shewmon DA. Truly reconciling the case of Jahi McMath. *Neurocrit Care*. 2018;29(2):165-170.
9. Shewmon DA. Chronic "brain death": meta-analysis and conceptual consequences. *Neurology*. 1998;51(6):1538-1545.
10. Bernat JL. Controversies in defining and determining death in critical care. *Nat Rev Neurol*. 2013;9(3):164-173.
11. Lewis A, Bernat JL, Blosser S, et al. An interdisciplinary response to contemporary concerns about brain death determination. *Neurology*. 2018;90(9):423-426.
12. Bogel-Burroughs N. A prisoner who briefly died argues that he's served his life sentence. *New York Times*. November 8, 2019. https://www.nytimes.com/2019/11/08/us/prisoner-dies-life-sentence.html. Accessed December 19, 2019.
13. Bernat JL. On irreversibility as a prerequisite for brain death determination. *Adv Exp Med Biol*. 2004;550:161-167.
14. Chiong W. Brain death without definitions. *Hastings Cent Rep*. 2005;35(6):20-30.
15. Bernat JL. On noncongruence between the concept and determination of death. *Hastings Cent Rep*. 2013;43(6):25-33.
16. Astrup J, Siesjö BK, Symon L. Thresholds in cerebral ischemia—the ischemic penumbra. *Stroke*. 1981;12(6):723-725.
17. Shewmon DA. The case of Jahi McMath: a neurologist's view. *Hastings Cent Rep*. 2018;48(suppl 4):S74-S76.
18. Coimbra CG. Implications of ischemic penumbra for the diagnosis of brain death. *Braz J Med Biol Res*. 1999;32(12):1479-1487.
19. Vrselja Z, Daniele SG, Silbereis J, et al. Restoration of brain circulation and cellular functions hours post-mortem. *Nature*. 2019;568(7752):336-343.
20. Russell JA, Epstein LG, Greer DM, Kirschen M, Rubin MA, Lewis A; Brain Death Working Group. Brain death, the determination of brain death, and member guidance for brain death accommodation requests: AAN position statement [published online ahead of print January 2, 2019]. *Neurology*.
21. Lewis A. Reconciling the case of Jahi McMath. *Neurocrit Care*. 2018;29(1):20-22.
22. Robbins NM, Bernat JL. Practice current: when do you order ancillary tests to determine brain death? *Neurol Clin Pract*. 2018;8(3):266-274.
23. Wijdicks EF. Determining brain death. *Continuum*. 2015;21(5):1411-1424.
24. Robbins NM. Reader response: Brain death, the determination of brain death, and member guidance for brain death accommodation requests: AAN position statement. *Neurology*. 2019;93(21):947.
25. Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD. Detecting awareness in the vegetative state. *Science*. 2006;313(5792):1402.
26. Cruse D, Chennu S, Chatelle C, et al. Bedside detection of awareness in the vegetative state: a cohort study. *Lancet*. 2011;378(9809):2088-2094.
27. Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. *N Engl J Med*. 2010;362(7):579-589.
28. Bernat JL. The definition, criterion, and statute of death. *Semin Neurol*. 1984;4(1):45-51.
29. Machado C. Consciousness as a definition of death: its appeal and complexity. *Clin Electroencephalogr*. 1999;30(4):156-164.
30. Laureys S. Science and society: death, unconsciousness and the brain. *Nat Rev Neurosci*. 2005;6(11):899-909.

31. Nair-Collins M, Northrup J, Olcese J. Hypothalamic-pituitary function in brain death: a review. *J Intensive Care Med*. 2016;31(1):41-50.
32. Truog RD. Is it time to abandon brain death? *Hastings Cent Rep*. 1997;27(1):29-37.
33. Machado C, Defina P, Estévez M, et al. A reason for care in the clinical evaluation of function on the spectrum of consciousness. *Funct Neurol Rehabil Ergon*. 2018;7(4):89-99.
34. Walter U, Fernández-Torre JL, Kirschstein T, Laureys S. When is "brainstem death" brain death? The case for ancillary testing in primary infratentorial brain lesion. *Clin Neurophysiol*. 2018;129(11):2451-2465.
35. Grigg MM, Kelly MA, Celesia GG, Ghobrial MW, Ross ER. Electroencephalographic activity after brain death. *Arch Neurol*. 1987;44(9):948-954.
36. Kleen JK, Scott RC, Holmes GL, et al. Hippocampal interictal epileptiform activity disrupts cognition in humans. *Neurology*. 2013;81(1):18-24.
37. Ung H, Cazares C, Nanivadekar A, et al. Interictal epileptiform activity outside the seizure onset zone impacts cognition. *Brain*. 2017;140(8):2157-2168.
38. Bernat JL, Culver CM, Gert B. On the definition and criterion of death. *Ann Intern Med*. 1981;94(3):389-394.
39. Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death. A definition of irreversible coma. *JAMA*. 1968;205(6):337-340.
40. Wijdicks EF, Pfeifer EA. Neuropathology of brain death in the modern transplant era. *Neurology*. 2008;70(15):1234-1237.
41. Walker AE, Diamond EL, Moseley J. The neuropathological findings in irreversible coma. A critique of the "respirator." *J Neuropathol Exp Neurol*. 1975;34(4):295-323.
42. Hernández-Hernández M. *Persistence of Cerebral Electrical Activity After the Clinical Diagnosis of Brain Death: Incidence, Outcome and Comparative Analysis of the Electroencephalogram Versus Computed Tomography Angiograph* [doctoral thesis]. Santander, Cantabria, Spain: Universidad de Cantabria; 2017.
43. Bernat JL. Refinements in the organism as a whole rationale for brain death. *Linacre Q*. 2019;86(4):347-358.
44. Shewmon DA. The "critical organ" for the organism as a whole: lessons from the lowly spinal cord. *Adv Exp Med Biol*. 2004;550:23-41.
45. President's Council on Bioethics. *Controversies in the Determination of Death: A White Paper by the President's Council on Bioethics*. https://repository.library.georgetown.edu/bitstream/handle/10822/559343/Controversies%20in%20the%20Determination%20of%20Death%20for%20the%20Web.pdf?sequence=1&isAllowed=y. Published December 2008. Accessed December 1, 2019.
46. Shewmon DA. The brain and somatic integration: insights into the standard biological rationale for equating "brain death" with death. *J Med Philos*. 2001;26(5):457-478.
47. Bernat JL, Dalle Ave AL. Aligning the criterion and tests for brain death. *Cambridge Q Healthc Ethics*. 2019;28(4):635-641.
48. Hernández-Hernández MÁ, Marco de Lucas E, Muñoz-Esteban C, Hernández JL, Fernández-Torre JL. The observation period after clinical brain death diagnosis according to ancillary tests: differences between supratentorial and infratentorial brain injury. *J Neurol*. 2019;266(8):1859-1868.
49. Lustbader D, O'Hara D, Wijdicks EF, et al. Second brain death examination may negatively affect organ donation. *Neurology*. 2011;76(2):119-124.

50. Truog RD. Defining death-making sense of the case of Jahi McMath. *JAMA*. 2018;319(18):1859-1860.
51. Pallis C. ABC of brain stem death. From brain death to brain stem death. *Br Med J (Clin Res Ed)*. 1982;285(6353):1487-1490.
52. Miller FG, Truog RD. The incoherence of determining death by neurological criteria: a commentary on *Controversies in the Determination of Death: A White Paper by the President's Council on Bioethics*. *Kennedy Inst Ethics J*. 2009;19(2):185-193.
53. Bernat JL. Conceptual issues in DCDD donor death determination. *Hastings Cent Rep*. 2018;48(suppl 4):S26-S28.
54. Siminoff LA, Burant C, Youngner SJ. Death and organ procurement: public beliefs and attitudes. *Soc Sci Med*. 2004;59(11):2325-2334.
55. Shah SK, Kasper K, Miller FG. A narrative review of the empirical evidence on public attitudes on brain death and vital organ transplantation: the need for better data to inform policy. *J Med Ethics*. 2015;41(4):291-296.
56. Siminoff LA, Mercer MB, Arnold R. Families' understanding of brain death. *Prog Transplant*. 2003;13(3):218-224.
57. Kilcullen JK. "As good as dead" and is that good enough? Public attitudes toward brain death. *J Crit Care*. 2014;29(5):872-874.
58. Crowley-Matoka M, Arnold RM. The dead donor rule: how much does the public care … and how much should we care? *Kennedy Inst Ethics J*. 2004;14(3):319-332.
59. Nair-Collins M, Green SR, Sutin AR. Abandoning the dead donor rule? A national survey of public views on death and organ donation. *J Med Ethics*. 2015;41(4):297-302.
60. Miller FG, Truog RD, Brock DW. The dead donor rule: can it withstand critical scrutiny? *J Med Philos*. 2010;35(3):299-312.
61. Truog RD, Robinson WM. Role of brain death and the dead-donor rule in the ethics of organ transplantation. *Crit Care Med*. 2003;31(9):2391-2396.
62. Veatch RM. Killing by organ procurement: brain-based death and legal fictions. *J Med Philos*. 2015;40(3):289-311.
63. Bernat JL. Life or death for the dead-donor rule? *N Engl J Med*. 2013;369(14):1289-1291.

Nathaniel M. Robbins, MD is an assistant professor of neurology at the Dartmouth College Geisel School of Medicine in Hanover, New Hampshire. He specializes in clinical neurophysiology, neuromuscular disorders, and international neurology.

James L. Bernat, MD is a professor emeritus of neurology and medicine at the Dartmouth College Geisel School of Medicine in Hanover, New Hampshire, where, until 2018, he was also the Louis and Ruth Frank Professor of Neuroscience. His scholarly interests are ethical and philosophical issues in neurology. He is the author of *Ethical Issues in Neurology*, 3rd ed, (Lippincott Williams & Wilkins, 2008).

Citation
AMA J Ethics. 2020;22(12):E1038-1046.

DOI
10.1001/amajethics.2020.1038.

Acknowledgements
Dr Robbins receives research funding from the Dartmouth Clinical and Translational Science Institute under award number UL1TR001086 from the National Center for Advancing Translational Sciences of the National Institutes of Health and from Vertex Pharmaceutical, the Dartmouth Diamond Foundation, the Reeves Foundation, and the Mary Hitchcock Foundation.

Conflict of Interest Disclosure
The author(s) had no conflicts of interest to disclose.

This article is the sole the responsibility of the author(s) and does not necessarily represent the views of the National Institutes of Health. The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.

ISSN 2376-6980