

# The lack of scientific evidence in clinical practice guideline in brain death determination: Implications for organ donation and transplantation

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Human death is universally understood to be a biological phenomenon, that is, the irreversible loss of the body's ability to mitigate entropy. Technological advances in transplantation medicine created the problem of optimally managing the supply of and demand for viable organs. We have previously outlined how irreversible apneic coma was introduced as a criterion of death and was approved by the US President's Commission in 1981.<sup>[1]</sup> The Uniform Determination of Death Act (UDDA) enacted two alternative methods in death determination: (1) Irreversible cessation of circulatory and respiratory functions; or (2) irreversible cessation of all functions of the entire brain, including the brainstem.<sup>[1]</sup> Other countries have adopted the brainstem definition of death. Most jurisdictions have followed the US legislation. Existing laws already disallow the act of procurement to be the proximate cause of the donor's death, reflecting a deontological moral premise that, in the context of organ donation, is referred to as the dead donor rule (DDR). Different cultures and religions do not object to organ donation if and only if vital organs are procured from cadavers and thus, in compliance with the DDR.

The legal and moral legitimacy of procuring organs after determination of death with brain-based criteria, that is, brain death (BD) is centered on its equivalency with biological death. The concept of BD has serious shortcomings in this regard: (1) equivalency with biological death cannot be substantiated by contemporary neuroscience; (2) standard practice

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guideline for BD diagnosis is based only on weak scientific evidence, and (3) the biophilosophical explanation to equate BD and human death lacks logical coherence.

## Neuroscience and brain-based criteria of death

Medical standards based on biological criteria should be empirically valid to ensure uniformity in death determination and to provide assurance that organs are procured from cadavers. Irreversible cessation of the functions of the whole brain, including the brainstem, is the UDDA brain-based criterion of death. Yet, the American Academy of Neurology (AAN) has limited death determination to the clinical triad of: (1) Coma (motor unresponsiveness to noxious stimuli), (2) absent brainstem reflexes, and (3) apnea.<sup>[2]</sup> Nevertheless, in 2008, The President's Council concluded that no pathophysiological evidence exists to equate BD with human death.<sup>[3]</sup> Most of the AAN practice guideline recommendations are assigned the weakest level of scientific evidence.<sup>[2]</sup> It is claimed that no reversible BD cases have been reported with strict adherence to the AAN guideline, that is, a 0% false positive rate (FPR). However, once the clinical triad of BD has been fulfilled, vital

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organs are procured for transplantation or mechanical ventilation is immediately withdrawn.<sup>[2]</sup> Either event has a 100% fatality rate. Therefore, the guideline becomes a self-fulfilling prophesy of irreversibility. Accurate estimate of FPR in death determination is hindered because medical journals are unlikely to publish such cases because of possible medico-legal consequences and negative impact on organ donation. Indeed, the editors of Nature have criticized current failure of BD determination to comply with the UDDA.<sup>[4]</sup> Furthermore, the AAN guideline infers a lack of awareness from absent brainstem reflexes and motor unresponsiveness (except for spinal reflexes) to noxious stimuli.<sup>[2]</sup> Indeed, many neurological functions and somatic integration are retained in BD [Table 1],<sup>[3,5,6]</sup> but are considered irrelevant by proponents of BD. Histopathological findings suggest that, despite compliance with the AAN guideline, almost 60% of donors have no or minimal injury to the brainstem at autopsy.<sup>[1]</sup> A viable brainstem and Reticular Activating System would negate irreversible cessation of consciousness or awareness. Neuroscience has also confirmed that absence of internal and external awareness cannot be inferred from motor unresponsiveness to external stimuli.<sup>[7,8]</sup>

### Biophilosophical rationale for brain-based criteria of death

To continue organ procurement from BD donors, the

**Table 1: Physiological evidence of somatic integration in brain-dead individuals**

Homeostasis of a countless variety of mutually interacting chemicals, macromolecules and physiological parameters, through the functions especially of liver, kidneys, cardiovascular and endocrine systems, but also of other organs and tissues (e.g., intestines, bone and skin in calcium metabolism; cardiac atrial natriuretic factor affecting the renal secretion of renin, which regulates blood pressure by acting on vascular smooth muscle; etc.)
Elimination, detoxification and recycling of cellular wastes throughout the body
Energy balance, involving interactions among liver, endocrine systems, muscle and fat
Maintenance of body temperature (albeit at a lower than normal level and with the help of blankets)
Wound healing, capacity for which is diffuse throughout the body and which involves organism-level, teleological interaction among blood cells, capillary endothelium, soft tissues, bone marrow, vasoactive peptides, clotting and clot lysing factors (maintained by the liver, vascular endothelium and circulating leucocytes in a delicate balance of synthesis and degradation), etc.
Fighting of infections and foreign bodies through interactions among the immune system, lymphatics, bone marrow, and microvasculature
Development of a febrile response to infection
Cardiovascular and hormonal stress responses to unanesthetized incision for organ retrieval
Successful gestation of a fetus in a (brain dead) pregnant woman
Sexual maturation of a (brain dead) child
Proportional growth of a (brain dead) child
Table is reproduced from the white paper "controversies in the determination of death" by the President's Council on Bioethics and source <sup>[3,5]</sup>

President's Council had to redefine human death with a novel biophilosophical rationale. The absence of a living organism's ability to engage "in self-sustaining, need-driven activities critical to and constitutive of its commerce with the surrounding world" is synonymous with death.<sup>[3]</sup> As spontaneous breathing demonstrates "openness to and ability to act upon the world," its absence confirms death.<sup>[3]</sup> Therefore, the President's Council has argued, BD complies with the DDR. This rationale has been challenged and refuted. Conscious patients with brainstem lesions also lack the drive to breathe, but are certainly not considered dead.<sup>[9]</sup> Similarly, fetuses in utero, being without spontaneous respiratory drive, are also not considered dead.

### Implications of erroneous death criteria in organ donation

The lack of scientific and biological validation of death determination with brain-based criteria has profound consequences. First, an incorrect BD diagnosis can deny appropriate medical care to the detriment of those with recoverable neurological injuries. Second, the assumption of absent nociception and/or awareness in BD is likely to harm donors because surgical procurement is performed without general anesthesia. Third, the failure to inform donors and families about controversies regarding brain-based criteria of death is a violation of their right to autonomy. Fourth, current organ procurement practice rests on a utilitarian construct of death that has not been publicly discussed or agreed upon. This construct considers vulnerable persons with catastrophic neurological injuries or apneic coma to be "as good as dead," and ignores pertinent social, historical, and cultural understandings of death and dying.

In conclusion, brain criteria of death are not scientifically validated. BD does not equate with human death so these patients should not be treated as human cadavers. We posit that the language of donation consent or authorization should be revised by replacing "organ donation after death" with "organ donation euthanasia."<sup>10</sup> This would require changing criminal homicide laws and creating new laws that permit organ procurement euthanasia.

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