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PERSPECTIVES

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Brain Death Criteria: Medical Dogma and Outliers

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The diagnosis of brain death (BD†) is legally and medically accepted. Recently, several high-profile cases have led to discussions regarding the integrity of current criteria, and many physiologic problems have been identified to support the necessity for their reevaluation. These include a global variability of the criteria, the suggestion of a clinical "hierarchy," and the resultant approximation of BD. Further ambiguity has been exposed through case reports of reversible BD, and an inconsistent understanding from physicians who are viewed as experts in this domain. Meeting BD criteria clearly does not equate to a physiologic "death" of the brain, and a greater community perspective should be considered as the dialogue moves forward.

INTRODUCTION

Brain death (BD) is the accepted legal and medical standard in the US. [1]. Its determination is based on updated guidelines for both children [2] and adults [3] that delineate a regimented series of clinical criteria conducted largely at the bedside. When the criteria have been fulfilled, the patient is declared dead and organ support continues only if organ donation is planned.

For years, few families in America legally challenged BD [4]. However, recently, a number of high profile cases [4,5] have disputed current BD criteria by questioning in part, accepted medical standards. The lawsuits have not been frivolous [4], and in response, legal revisions have ensued [6] with physicians' power to declare BD being threatened [5].

Challenging accepted medical standards is a lonely proposition because the voice is commonly viewed as unsavory or extreme. Opposition to current BD criteria has unfortunately become analogous to poor understanding [7], sensationalism, and fundamental religious beliefs or fanaticism [8]; even physicians' objections are generally viewed as outliers. However, what if the medical dogma had obvious contradictions and the "outliers" were actually able to articulate a physiologic rationale on why current BD guidelines are problematic?

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†Abbreviations: BD, brain death; UDDA, Uniform Determination of Death Act.

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CURRENT BRAIN DEATH GUIDELINES

Current pediatric and adult BD guidelines are based on a 1981 definition provided by the President's Commission Uniform Determination of Death Act (UDDA) [2,3]. It states that BD is a clinical diagnosis of absent brain function that is both irreversible and involves the entire brain [2,3]. Irreversibility is established by determining the proximate cause of coma, potential for recovery, and serial neurologic evaluations [2]. To confirm absence of brain function, protocolized bedside neurologic examinations are performed that evaluate for complete loss of responsiveness, spontaneous or induced movements, and brainstem reflexes [3]. Potential confounding factors are considered prior to conducting BD evaluations, as certain medications are discontinued and factors including hypothermia, hypotension, and metabolic derangements are corrected [2,3]. Apnea testing objectively measures brainstem function with the absence of respiratory drive supporting a BD diagnosis [3]. Finally, ancillary tests may be considered under unique situations to assess for brain function (electroencephalogram) or cerebral blood flow (radionucleotide imaging, angiography).

PROBLEM 1: GLOBAL DIFFERENCES IN BRAIN DEATH CRITERIA

Surprisingly, notable differences throughout the world exist in the criteria for diagnosing BD [9,10]. These include the brainstem reflexes that need to be absent for the criteria to be fulfilled [11]. For example, British and Australian requirements do not include spontaneous eye movement, the oculocephalic reflex and an absent motor response to pain in the somatic distribution [10]. Apnea test standards also differ among countries [12], in both their duration (5 to 15 minutes) [10] and interpretation of objective arterial blood gases (no pH guidelines to <7.4) [10,11]. Other worldwide variations include the number of physicians required to make a BD diagnosis (one to three; nurse practitioner to specified specialists) [10] and whether confirmatory lab tests are mandatory in making the BD diagnosis [9].

The global variability in BD criteria reflects the lack of certainty and precision in making the diagnosis of BD [13]. Calls for an international consensus have been made because patients declared dead in one district could be considered alive in the neighboring jurisdiction [14]. This however, would not be a simple task, as many different cultures, religions, and laws continue to struggle with the concept of BD [15].

PROBLEM 2: WHAT BRAINSTEM REFLEXES?

Current American BD criteria focus largely on the brainstem, a primitive yet absolutely vital region that connects the cerebrum to the spinal cord. Currently accepted bedside evaluations for brainstem reflexes may include the absence of: i) pupillary response to light; ii) ocular movements (using oculovestibular and oculocephalic testing), corneal reflex; iii) facial muscle movement to noxious stimuli; and iv) pharyngeal and tracheal reflexes. Their utility is largely derived from recommendations provided by a sentinel report published in 1968 [16]. However, the evidence for selecting and utilizing these specific brainstem reflexes and/or function is lacking. What if a patient met BD criteria but exhibited other brainstem reflexes that were not part of the criteria?

A 9-month-old boy was found unresponsive after co-sleeping with a parent in bed [17]. Three days after an aggressive resuscitation, his first BD examination was consistent with cessation of brain function. Sixteen hours later, while supraorbital pressure was applied, some pressure was inadvertently applied to his eyelid. His heart rate rapidly dropped, only to quickly recover once the pressure was relieved: a manifestation of the oculocardiac reflex. Although the oculocardiac reflex traverses along two major components of the brainstem, it is not part of the current BD criteria. What did this mean?

The case should raise a Spockian eyebrow. How should physicians interpret the obvious presence of brainstem reflexes that are not consistent with current BD criteria? Was this patient really BD? Ethically, an intentional evaluation of the oculocardiac reflex would be problematic, as it could induce a cardiac arrest in patients that have yet to be declared BD. However, a strong argument for potentially endangering patients has been made against the apnea test, which could dramatically increase cerebral blood flow and intracranial pressures to a very tenuous yet "alive" brain [18]. In this case, the BD examination was adjourned, mechanical ventilation was withdrawn, and the boy was pronounced dead shortly thereafter.

PROBLEM 3: "REVERSIBLE" BRAIN DEATH?

In medicine, death is inevitable, irreversible, permanent, and final. To be consistent, the criteria must ensure these tenants are fulfilled once BD has been established. The concept of reversible "brain death" is an ostensible self-contradiction: death cannot be reversed. Shockingly, case reports have documented patients who met BD criteria but would later recover partial neurologic functioning.

One such case described a 3-month-old girl that was confirmed BD following profound hypoglycemia [19]. Three days after hospital admission, BD was documented. The second exam for BD was completed two days

later and confirmed the initial assessment. Life sustaining support was not withdrawn, and 38 days later the infant regained spontaneous respiration. Similarly, we offer the case of a 55-year-old male that was confirmed BD secondary to respiratory failure [20]. Three days after presenting to hospital, his first and second examination satisfied BD criteria. Twenty-four hours later, upon arrival to the operating room for organ procurement, the patient regained brainstem reflexes and spontaneous respirations.

Without hyperbolizing these examples to offer farfetched conclusions, the magnitude of these patients' neurological devastation and extremely dire prognosis cannot be overstated. While the documented reversibility does not infer a favorable patient recovery or physician negligence, it does demonstrate ambiguity to the central tenant of "irreversibility" and violates the medical concept of death [21]. "Surviving" BD suggests that current clinical criteria need to be re-evaluated.

PROBLEM 4: WHOLE BRAIN DEATH?

The American BD criteria first acknowledge the UDDA statement of "irreversible cessation of *all* functions of the entire brain" [22]. Paradoxically, the criteria follow with a limited evaluation of incomplete brainstem reflexes and function, by consequently offering the clinician with merely an approximation of BD. With the obvious violation of UDDA's second central tenant, compelling defenses became absolutely necessary.

One argument suggested that medical experts have the ability to determine the "critical clinical functions of the brain" [23,24] and to establish a hierarchal order for BD [25]. In other words, some functions of the brain are far more important than others; their superior or critical functions define the whole brain. An absence of critical functioning makes the other "lesser" brain functioning irrelevant.

Another position was to look at different definitions of BD – including brainstem death – that requires confirmation of irreversible loss of consciousness and capacity to breath [26]. However, regardless of how these arguments are spun, patients that have been declared BD can have intact hormonal regulation (ADH), EEG activity, brainstem evoked potentials, cerebral blood flow and the ability to maintain a prolonged pregnancy to the birth of a healthy child [27]. These obvious brain functions are not seen as "critical" and can coincide with irreversible loss of consciousness. Does their presence suggest BD?

PROBLEM 5: PHYSICIANS' MISUNDERSTANDINGS

Neurosurgeons, intensivists, and neurologists direct care for the neurologically devastated patients in the hospital. The American Academy of Neurology concedes that neurologists possess a special expertise in BD declaration [28]. Furthermore, academic manuscripts on BD use wide brush strokes to comment on its widespread acceptance, understanding, and factuality, and the ignorance of public perceptions. But behind the bravado, do physicians uniformly have a thorough understanding of BD?

A survey to Canadian pediatric intensivists questioned their conceptual reasoning of BD and clinical findings that exclude a BD diagnosis [29]. It revealed illogical statements and significant confusion about BD concepts and brain functions. A similar survey was addressed by over two hundred American neurologists and demonstrated an unclear understanding of BD diagnostic testing and an inconsistent "rationale for accepting BD as death" [30].

In actuality, neurology and neurosurgery residents may have limited opportunities and exposures to BD evaluations during their training [31]. Likewise, resident physicians also demonstrated a poor awareness towards identifying BD [32]. Not surprisingly, when combined with an identified lack of training, a significant variability was seen in how physicians conduct their BD exam [33].

PUBLIC CONSULTATION

One cannot discuss brain death without talking about organ donation, which is exactly why organ donation should be left out. It confuses the issue with strong emotions, obvious medical needs, and its tremendous benefits. It can also evoke a strong and rational desire around utilitarianism. However, if we are able to park organ donation to the side, then the discussion is really around two facts.

First, current brain death criteria should be understood as inconsistent and medically indefensible. This is based on the global differences of BD criteria, incomplete assessment of the brain, problems of irreversibility, and sound evidence to suggest that brain may still be active. Laywers and bioethicists are amused about the ignorance of the medical community. Shah argues that BD is legal fiction – "a legal fiction arises when a law treats something as true, though it is known to be false or not known to be true, for a particular legal purpose" [34].

Should families' then feel distressed or distrust if BD criteria are indefensible and/or legal fiction? The second fact, as summarized by a headline in The Atlantic – "Nobody Declared Brain Dead Ever Wakes Up Feeling Pretty Good" [35] – could provide much needed relief. It provides a key perspective that regardless of what criteria or definition of BD a patient may fulfill, an extremely dire outcome should be expected.

If BD criteria are, at the very least, sensitive in detecting neurologically devastated patients with extremely

poor outcomes, then it may be time for the discussion to leave the academic boardroom. How should these patients be managed? Should these patients have the right to very costly life sustaining support for an indeterminate period of time? Should these patients be eligible for organ donation? The questions have now come full circle [16] and challenging BD dogma leads to uneasy discussions. In accordance to the dead donor rule, organ donation cannot occur, leaving withdrawal of life sustaining support versus prolongation of "life" as the only two options. Prioritizing public consultation would facilitate a more inclusive approach to balance the institutional dogma leading these discussions. This is not unprecedented, as federally sponsored, funded, and directed initiatives around controversial medical topics (*i.e.* xenotransplantation) have resulted into community engagement, public workshops, and advisory groups, and concluding reports that have directed policy [36].

CONCLUSION

Advanced technology and medical practice continue to present societies with similar issues that prompted the sentinel BD dialogue in 1968 [16]: how should we ethically and humanely navigate the realities of patients with little to no discernible brain function. The current BD guidelines are the result of several ambitious and independent processes that sought to address these challenges. They are however, flawed, self-contradictory, and are now beginning to be challenged. The language in current guidelines should reflect these flaws by eliminating all references to whole brain death and adequately addressing their limitations. Recognizing these limitations and opening up a public dialogue should improve trust to our institutions, rather than hiding behind medical dogma.

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