Brain Death

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Jeffrey M. Singh and Mark Bernstein

10.1 Introduction

Brain death is the determination of death by neurological criteria, in contrast to the traditional determination of death by assessing a lack of circulation and respiration. Brain death is only relevant in patients who have suffered severe brain injuries, many of which are due to neurosurgical conditions, and who are receiving modern critical care, such that they have complete and irreversible loss of all brain function, but their other vital organs are supported and continue to function. Many jurisdictions have equated brain death with death determined by cardiopulmonary arrest, as brain death reflects the notion of irreversibly lost personhood due to the irreversible loss of brain function.

Brain death is important because the concept of brain death exposes a diversity of beliefs in society, and frequently becomes the flashpoint for ethical dilemmas for healthcare teams, or conflicts between healthcare teams and families (Lazar et al. 2001). These conflicts can be a source of anxiety and stress to surgeons and can undermine trust between physicians and families. It is important that all practicing neurosurgeons have a strong understanding of the clinical and ethical framework for the determination of brain death, as well as the specific legal statutes and legal framework supporting brain death in their practice jurisdiction. It is a core issue in the practice of value-based medicine.

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Pearl
Skillful communication surrounding brain death may allow families to start the grieving and closure process earlier, and help them navigate this emotionally and culturally charged issue.

10.2 Illustrative Case (Family's Refusal of Withdrawal of Care After Brain Death Declared)

A 30-year-old woman is brought to the emergency department after a witnessed collapse following which she was found to have a cardiac arrest. Following EMS response and 30 min of resuscitative efforts, she has return of spontaneous circulation and is brought to the emergency department, where she is found on computed tomography to have a large subarachnoid haemorrhage secondary to a ruptured basilar aneurysm. Despite insertion of a ventricular drain, she never recovers motor responses or brainstem reflexes. On the third day in the neurosurgical intensive care unit, she has no response to pain, no brainstem reflexes, and has no respiratory efforts on apnea testing. There are no metabolic or pharmacologic confounders, and she has never received sedatives or paralytic agents. In accordance with local medical guidelines and law, she is declared brain dead.

When the family is informed that she has been declared brain dead, they refuse to accept this determination and are adamant in their belief that she is alive. They refuse to allow discontinuation of the mechanical ventilator, stating that in their eyes she is still alive while her heart is still beating and she is warm. They demand ongoing interventions and care including tracheostomy, enteral nutrition, and mechanical ventilation.

10.3 Approach to the Case

Death is a universal life event which is deeply founded in cultural, religious, and spiritual beliefs. The impact of pronouncing someone dead has immense personal, legal, and social implications. Indeed, death is simultaneously a medical, social, and legal event.

Until the twentieth century, death was determined by medical practitioners by the irreversible interruption of one of the three vital functions: respiration, circulation, and brain function. When an individual had cessation of any of respiration, circulation, or brain function, the termination of the remaining functions quickly followed. This determination was relatively simple and highly valid given the inability of practitioners to intervene and support vital functions. The development of modern life support, specifically positive pressure mechanical ventilation and haemodynamic support, has complicated the determination of death by allowing temporary uncoupling of these three vital functions. Indeed, the circulatory and respiratory systems can be supported for some time despite the irreversible

destruction of the entire brain and brainstem. This requires a novel method for determination of death in these patients, thus the inception of brain death.

In this case, the approach is simply to talk to the family, have others talk to them like their spiritual leader and/or the ethics consultation team, and hope things get resolved favourably. In the uncommon situation of an absolute impasse happening, the healthcare team generally honours the family's wishes as opposed to taking the issue to the legal system. In extreme situations cases have gone to the courts, and in these cases the family is generally ruled against (Life support for pregnant woman ordered removed by Texas judge 2014).

Pearl
When an impasse occurs between a family and the healthcare team over brain death, a number of simple strategies may help: (1) talk at length to the family in simple but informative terms, (2) engage help from ethics teams and/or spiritual leaders, (3) invite the family to witness a brain death test on their loved one, and (4) be as patient and compassionate as possible.

10.4 Discussion

10.4.1 History of Brain Death

As outlined above, the evolution of critical care and life-sustaining therapies required the development of a novel method for determining death in patients with severe and irreversible injuries to the entire brain. Critics of brain death determination have often used the tight temporal association of the development of formal brain death criteria and the advent of organ donation as proof that the concept of brain death was developed to serve a utilitarian purpose of organ donation (Parker and Shemie 2002; Truog and Robinson 2003). This is not entirely correct, as the concept of brain death was already evolving within the medical community prior to the first successful organ transplants.

Medicine had recognized by the mid-twentieth century that brain function was necessary for life, and the irreversible cessation of brain function was sufficient in and of itself for death. There were initially multiple publications of observations that patients who had severe brain injury, persistent unresponsive coma, and apnea had absence of intracranial blood flow on angiography (Riishede and Ethelberg 1953; Wertheimer et al. 1960). Further reports confirmed that such patients also had absence of electroencephalographic activity and uniformly had cardiac arrest upon withdrawal of mechanical ventilation or haemodynamic support. Finally, the term 'coma dépassé' was coined; this later became the foundation for the modern conceptual framework of brain death (Mollaret and Goulon 1959).

Following this seminal paper the concept that patients on respiratory and haemodynamic support could be determined dead by neurological criteria evolved slowly. In the United States, the advent of organ donation precipitated the creation of the Ad Hoc Committee of the Harvard Medical School in 1968 that published the first criteria for the determination of brain death (A definition of irreversible coma 1968). Since then medical associations in countries around the globe have produced guidelines for the diagnosis of brain death (Diagnosis of brain death 1976).

10.4.2 Clinical Determination of Brain Death

The requirement that brain function is necessary for life is justified by the fact that the brain conducts the critical functions of the body as a whole and coordinates the various vital organs to maintain homeostasis. Most medical societies and countries have adopted either the whole-brain (Shemie et al. 2006; American Academy of Neurology 1995) or brainstem formulations of brain death (Diagnosis of brain death 1976).

The majority of jurisdictions require demonstration of whole-brain death, meaning all functions of the brain, including the brainstem, diencephalon, and both cerebral hemispheres, have irreversibly ceased. The pathophysiology of whole-brain death usually involves the progression of severe brain injury to elevated intracranial pressure, critical reduction of cerebral perfusion, and infarction of all brain structures. Consequently, the determination of death under this formulation requires the demonstration of the irreversible cessation of all brain functions. Some jurisdictions, notably the United Kingdom, have adopted a formulation of brain death requiring only irreversible and complete injury to the brainstem (brainstem death), on the rationale that the brainstem is required for arousal and maintenance of respiration and circulation. Consequently, this formulation does not require the irreversible loss of all brain functions but only those required for the integrated functioning of the organism as a whole.

The clinical process of brain death declaration usually includes several components: (1) determination of a mechanism of injury compatible with brain death, e.g. imaging evidence of cerebral herniation; (2) the ruling out of any metabolic or pharmacologic confounders; (3) evaluation of brainstem functions including apnea testing; and (4) confirmatory testing if required (e.g. electroencephalography or transcranial Doppler assessment of blood flow). Some jurisdictions also allow for ancillary testing, which replaces the clinical examination in situations where confounders preclude reliable clinical examination (e.g. barbiturate coma) or when clinical examination is impossible. These are usually imaging examinations which evaluate the presence of intracranial blood flow, with death being confirmed when no cerebral blood flow is evident. It should be noted that brain death declaration should be conducted with the purpose of proving death, with the base assumption that the individual is not dead. Consequently, one of the core principles in the clinical determination of brain death is that the well-being of the patient should not be jeopardized during the determination itself. For example, apnea testing should be

aborted if cardiorespiratory instability develops, and caloric testing should be deferred if there is significant ear or tympanic membrane trauma and irrigation is contraindicated.

Critics have voiced the obvious concern that the two formulations of brain death (whole-brain death and brainstem death) allow for inherent inconsistencies. For example, the whole-brain formulation would require loss of all brain functions, even though neuroendocrine function is observed to persist in some patients (e.g. not all brain-dead patients develop diabetes insipidus from a lack of antidiuretic hormone), and not all patients become poikilothermic (Truog and Miller 2012). This apparent contradiction is sidestepped, however, with the brainstem death formulation. The application of confirmatory or ancillary tests is also problematic, as the whole-brain death formulation would require complete infarction and intracranial circulatory arrest, while this would not be necessarily required in the brainstem formulation. These inconsistencies have led to a call for a global consensus and definition of death to ensure consistent determination across jurisdictions (Smith 2012).

It is important to recognize that the criteria for declaring brain death in neonates and children may be slightly different than that for adults, and especially paediatric neurosurgeons need to be clear on this issue (Nakagawa et al. 2012).

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10.4.3 Prognostic Implications of Brain Death

A key tenet of brain death is the irreversibility of the neurological injury. One retrospective review included over one thousand patients, reported in the literature, who were ventilated until asystole after meeting clinical criteria for brain death and found no survivors (Pallis 1983). A systematic review that was part of an update to the 1995 American Academy of Neurology statement found no reports of neurological recovery after brain death using modern brain death criteria (Wijdicks et al. 2010). Case reports of improvement following determination of brain death are often refuted based on failure to adhere to standard procedures and guidelines, resulting in misdiagnosis of brain death (Gardiner et al. 2012).

For decades, it had been recognized that brain death heralds inevitable cardiovascular collapse. With modern critical care there are now increasing reports of

prolonged somatic or physiological support of individuals following determination of brain death, usually involving the physiological support of pregnant women who were declared brain dead until the baby could be delivered. There is one reported case of a child supported for many years, although the diagnosis of brain death was made in retrospect and was never strictly confirmed according to modern criteria (Repertinger et al. 2006). One retrospective case series found 175 cases of brain death in which the patient was maintained on physiological support for greater than 1 week and found seven patients survived to 6 months. Unfortunately, the rigour of the brain death declarations could not be ascertained retrospectively, and the study included cases of diagnostic controversy (Shewmon 1998). Finally, it should be noted that in these cases of prolonged physiological support, there was no improvement in neurological function, despite the prolonged period of observation, supporting the belief that both the neurological injuries were irreversible and permanent (Gardiner et al. 2012).

10.4.4 Adoption of Brain Death Across Jurisdictions and Cultures

There is broad acceptance of the concept of brain death across medical communities, jurisdictions, religions, and countries. Medical societies in several countries have published consensus statements and guidelines both defining and outlining the clinical determination of brain death (American Academy of Neurology 1995; Australian and New Zealand Intensive Care Society 1993; Shemie et al. 2006). In the United States the concept of brain death was also validated by a Presidential Commission in 1981 that published *A Report on the Medical, Legal and Ethical Issues in the Determination of Death*. This report embraced the concept that the irreversible loss of whole-brain function was death and gave it equivalent footing to death determined by cardiopulmonary criteria. These statements were affirmed in 2008 after the US President's Council on Bioethics performed a detailed review on all of the ethical and philosophical arguments that defined brain death as death and concluded that the definition was still valid (Controversies in the determination of death 2008).

Many jurisdictions do not have a definition of death codified into law. Although death has significant legal implications, there are no legal statutes to support or refute determination of death by cardiopulmonary, neurological, or other criteria. From a legal point of view, a person is considered dead when a qualified person pronounces that no further medical care is appropriate and that a patient should be considered dead under the law. The specific criteria by which a patient is declared dead may vary somewhat across jurisdictions, but it is important for healthcare providers to note that statutory law in most countries does not specifically outline the explicit clinical criteria with which a person is declared dead – the practice and clinical standards of declaring death are usually deferred to the medical profession.

There are several jurisdictions in which brain death has been codified into statutory law. In the United States, the Uniform Determination of Death Act gave

statutory recognition to brain death as a concept and equated it with the more widely recognized concept of death determined by cardiorespiratory arrest (e.g. brain death is death in the eyes of the law) (National Conference of Commissioners on Uniform State Laws 1980). Similar legislation has been passed in Australia and the United Kingdom and supported by the Canadian provincial case law.

Pearl
Brain death has been accepted broadly in ethics, medicine, and law, but some surgeons and societies still have not embraced and adopted it. Furthermore, some individuals do not accept brain death, even though they live within jurisdictions that accept brain death as a group.

10.4.5 Criticism of Brain Death and Accommodation

Despite this widespread acceptance, there remain some populations in which there are strong criticisms of brain death and occasionally rejection of the concept as a whole. For example, in Japan (Lock 1999) and Germany (Schöne-Seifert 1999), there has been gradual acceptance of brain death by the medical and legal communities, but the concept still faces criticism from a significant proportion of the public. Strong religious opposition also exists within certain segments of the Muslim, Buddhist, Native American, and Orthodox Jewish communities globally. Rejection of brain death and insistence on the traditional cardiopulmonary determination of death have been based on ethical or religious arguments (Truog and Robinson 2003).

Accommodation of religious and moral dissent to the concept of brain death varies across jurisdictions. This ranges from non-acceptance and reliance on the traditional cardiopulmonary determination of death in some countries, to conditional acceptance, to accommodation on an individual basis. In Japan, where the traditional Buddhist and Shinto concepts of death require cessation of heartbeat and respiration, brain death is still recognized but is only acknowledged as human death when a transplant is to be performed.

Perhaps the most confusing and variable example of such variability is in the United States, where such legislation falls not under federal law, but to the individual states. New York and New Jersey have enacted legislation to require healthcare providers and hospitals to either accommodate the refusal of the determination of brain death by families or prevent the determination of brain death itself based on the objection of the family. This may lead to the confusing scenario where an individual is dead in one state but not in another or may be conditionally dead depending on their religious or expressed beliefs.

Even within countries in which there is strong support for the concept of brain death within the medical and legal communities, healthcare providers may meet significant objection or disagreement with the determination of death due to misunderstanding, misinterpretation, of other experiences with coma, or personal, cultural, or religious beliefs about death.

When families disagree with the determination of brain death, there have been legal disputes in which families had sought to prevent the withdrawal of nontherapeutic mechanical ventilation from these patients. Very few of these cases have reached resolution in the courts because either the patients progress to cardiorespiratory arrest or the parties find an out-of-court settlement, such as discharging the patient home with nontherapeutic mechanical ventilation.

10.4.6 Ethical Considerations in Conflicts Regarding Acceptance of Brain Death

With the complete and irreversible loss of all cognition in brain death, autonomy (which is fundamentally grounded in cognition) is also permanently lost. An individual, once dead, ceases to be a patient, no further healthcare can be provided, and their physical body is a corpse. This distinction is reflected legally in many jurisdictions by the distinction between a power of attorney for personal care (who is the substitute decision-maker for healthcare decisions) and the estate executor (who carries out the instruction of a will and manages the remaining estate after death). Although physicians may choose to continue providing care to brain-dead patients after the determination, it is an important distinction that this is done out of a sense of caring to the family, rather than a duty of care to, or a fiduciary relationship with the now deceased individual.

Even in considering the scenario that the capable wishes of the patient were to continue nontherapeutic mechanical ventilation and haemodynamic support following brain death, it has been suggested given the societal, legal, and medical implications of brain death that this is one of the few scenarios in which the autonomy of the individual patient or substitute decision-maker should be trumped by that of the physician or by societal consensus (Sprung et al. 1995).

With respect to non-maleficence, a brain-dead patient lacks any cognition or interpretation of the external environment and is insensate. The discontinuation of mechanical ventilation will not be felt by the patient, because in effect it is the discontinuation of medical treatments on a corpse. It is for this reason that anaesthesia is not required for organ procurement. Non-maleficence is a consideration in the provision of nontherapeutic physiological support to brain-dead individuals and includes the indignity of invasive care in an intensive care unit with no benefit to the patient, providing false hope to families, and prolonging the grieving process, including delayed burial or cremation and psychological closure.

Finally, although accommodation of an individual's or group's rejection of brain death respects autonomy, these accommodations must be just and must not infringe on the rights of others. Consequently, the determination of brain death must be consistent across individuals in a jurisdiction, and the provision of nontherapeutic critical care to a brain-dead patient must not deny scarce resources from others.

10.4.7 Brain Death and Organ Donation

Although the concept that the irreversible loss of brain function represents death of the person had been evolving for some time, it was the need for a method to determine death by neurological criteria to allow organ donation to occur that drove the widespread development of consensus definitions. The requirement is driven by the dead donor rule which is an ethical principle of organ donation and transplantation which has at its core two tenets: (1) vital organs should be taken only from dead patients; and (2) living patients should not be killed for or by organ procurement. Consequently, organ procurement can only occur if the patient is declared dead by neurological criteria prior to organ procurement.

If one accepts that brain death is death and as such represents the irreversible loss of personhood and consciousness, the patient (i.e. corpse) is neither harmed nor wronged when vital organs are procured. A dilemma arises, however, if one rejects the construct of brain death itself, in which case the dead donor rule would traditionally preclude organ donation in the absence of brain death, and vital organs would be seen to be procured from a living patient. This conundrum coupled with the modern realities of organ donation from living donors has led several leaders to question the requirement for the dead donor rule, suggesting that it should be replaced by an ethical foundation based on autonomy, consent, and non-maleficence (Truog et al. 2013). In this framework the overriding principles would be autonomy (that the patient consents to organ donation) and non-maleficence (that the patient is neither harmed nor wronged with the organ procurement and dies from the withdrawal of life support and not from the procurement of organs).

Pearl
Brain death is important in the procurement of organs, so other patients can benefit and be saved from death. However the first priority is always the patient who is critically ill, and no treatment should conflict with the duty of care to the patient. This is why nontherapeutic ventilation is very controversial, and it exemplifies a conflict between utilitarian and deontological ethics.

10.4.8 Approach to Conflict Resolution

Conflicts involving brain death and requests for physiological support in brain-dead patients can be extremely distressing for both families and healthcare teams. The sudden and unexpected death of a love one is a traumatic event for families, and the acceptance of death may be made even more challenging by the complexities of brain death as a concept, difficulties in communication, and assimilating these concepts with personal, spiritual, and religious views. Physicians may help avoid these

stressful conflicts by carefully ensuring impeccable practice in the determination of brain death, communication and knowledge of their specific legal rights, and responsibilities in their local jurisdiction.

It is essential that the declaration of brain death is performed with strict adherence to local standards and guidelines. Repeated determinations by independent physicians are advised and in fact required in some jurisdictions. One recent survey demonstrated a disturbing lack of consistency in determination of brain death despite guidelines being disseminated for over a decade (Greer et al. 2008). Family presence during brain death determination may also be helpful at improving family acceptance of brain death, as witnessing the apnea test and the prolonged lack of respiratory efforts over 8–10 min has considerable face validity for individuals whose understanding of death is rooted in the traditional cardiopulmonary criteria (Kompanje et al. 2012). One study found that witnessing brain death determination did help families understand that their family member was dead, but increased emotional distress for the family (Ormrod et al. 2005).

The language conventionally used in communications with families may also contribute to misunderstandings (Molinari 1982). It has been suggested that the term brain death not be used as it implies a distinction from traditional death and replaced by terms such as 'neurological determination of death' (Shemie et al. 2006). Irrespective of language, physicians must be consistent in their communication that the individual is medically (and legally if appropriate) dead. In discussions regarding requests for and discontinuation of physiological support, the use of the term 'life support' is inappropriate and confusing to families and should be avoided. Many families may infer that the discontinuation of these therapies in the brain-dead patient is in fact the proximal cause of death. It is important that physicians patiently and consistently explain (1) the determination of death, (2) the inappropriateness of providing ongoing physiological support in the dead patient, and (3) the timeline for discontinuation of such therapies.

Finally, it is also important that physicians understand their legal rights and responsibilities in their local practice jurisdiction. Where brain death is codified into law, physicians may not have a legal duty to continue to provide treatment to a dead person. However, in jurisdictions in which there is legislation allowing conscientious accommodation, the situation is more complicated: the physician may not be able to proceed with determination without consent of the family or be tasked with providing nontherapeutic ventilation or support to a patient declared brain dead. Many physicians might continue to provide mechanical ventilation and existing therapies but not escalate treatments or treat new conditions while they provide more time for discussion and education of families.

10.5 Illustrative Case Revisited

The family of the 30-year-old woman continues to refuse that their loved one is dead, despite two independent determinations at different time points. They accepted the opportunity to witness the second brain death determination and

were tearful at its conclusion. The physicians know that the local law supports brain death as death and that they are not compelled to the family's request for nontherapeutic ventilation. Nevertheless, they continue with physiological support for an additional 48 h while they continue to have conversations with the family and explain the situation. After the witnessed apnea test and further discussions with the primary team, their church leader, and the hospital bioethicist, the family accepts the diagnosis and assents to discontinuation of physiological support. After this they are approached by the local organ procurement organization they consent to organ donation, leaving a lasting legacy for the memory of their loved one.

Conclusion

Brain death is the neurological determination of death and is widely accepted and equated with death by traditional cardiovascular criteria. Rejection of the concept of brain death on religious or personal beliefs, however, can lead to stressful conflicts between surgeons and families and ethical dilemmas for healthcare providers. Strict adherence to clinical practice guidelines, superlative and patient communication, and thorough knowledge of the specific legal rights and responsibilities of physicians are all important in diffusing conflicts and finding mutually agreeable resolutions to these stressful and tragic scenarios.

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