Diagnosis of brain death in children

Technology and the inadequate lexicon of death

Medicine and society continue to thoughtfully struggle with the definition of death, especially with the progression of sophisticated life-support systems that challenge our concepts. The questions of when a disease is irreversible, when further treatment is ineffective, or when death has occurred are of great consequence. These are independent of and galvanised by the practice of organ donation.

Historically, there was little need for diagnostic or conceptual precision with regard to death. In hospital practice, death occurred after cardiorespiratory arrest upon a doctor’s determination. The criteria used were not articulated and remained untaught, ranging from absence of movement, breathing, heart sounds, pulse, or electrocardiogram activity, generally at the discretion of the attending physician. Observation was not required because the irreversibility of death was not a practical concern. The advent of organ donation, as an immediate consequence of death, increasingly mandates precision in the concept and diagnostic criteria of death.

There are three basic physiological mechanisms of death: primary cardiac arrest; primary respiratory arrest, which via hypoxaemia causes a secondary cardiac arrest; or primary brain arrest, which via interruption of airway control and respiratory drive causes a secondary respiratory arrest and then cardiac arrest. Irrespective of initial disease state, all critical illnesses threaten life in this manner. Interruption of this cascade with various forms of life support is fundamental to critical-care practice. Traditional life-sustaining technologies are deployed with the use of artificial airways, mechanical ventilation, haemodynamic support with inotropes and vasopressors, and renal replacement treatments. Advanced support includes extracorporeal systems such as membrane oxygenation and artificial hearts (ventricular assist devices such as the Berlin heart). The principle behind their application is to sustain vital function to allow time or treatment (medical or surgical) to reverse the underlying life-threatening state.

Medicine has advanced to the point that nearly all vital organs can be supported by technology or replaced by transplantation. Complete and irreversible, terms commonly used when defining death, deserve fresh scrutiny. Complete and irreversible arrest of the heart does not lead to death, as long as oxygenated circulation is mechanically provided. In the early 1990s, the initial use of extracorporeal cardiac support was to replace failing or arrested heart function as a bridge to recovery. If native heart function did not recover over days, the machine was stopped and the patient died.1 This approach is now increasingly used as a bridge to transplantation when heart recovery is not possible.

Survival of the individual organs and the organism is related to adequacy of oxygenated blood flow and this is the principle goal of critical-care support. If recovery after cardiac arrest is possible, it is not judged by the ability to reanimate the heart, but rather the ability to reanimate the brain once spontaneous or mechanical circulation has been re-established. The final event leading to cardiac arrest is loss of coronary blood flow and cardiopulmonary resuscitation (CPR) is aimed at restoring coronary blood flow. However, the loss of cerebral blood flow is the primary issue. Outcome studies after cardiac arrest principally assess the degree of hypoxic–ischaemic brain injury and poor outcomes do not distinguish between death and vegetative survival.2

The brain is the only organ that cannot be supported or replaced by technology. For all forms of severe brain injury, intensive care does not replace any functions of the brain. Mechanical ventilation merely interrupts the way brain failure leads to death and neuroprotective treatments limit secondary brain injury. Brain death was once thought to consistently lead to cardiac arrest because of the associated haemodynamic instability.1 Contrary to existing perceptions, any degree of brain failure, including brain death, can be sustained indefinitely with mechanical ventilation and vigilant care. This finding was shown in a case series of brain death in pregnancy with fetuses brought to term.3

Although visionary in concept, the lexicon of brain death and the varying international definitions are a source of confusion. Does the term “brain death” refer to death of the brain itself or does it refer to death as determined by the loss of neurological function? The answer depends on the concept of brain death accepted and this varies according to jurisdiction. In the USA, a whole brain definition (cerebral hemispheres and brainstem) for brain death is codified based on the irreversible cessation of all functions of the brain, including the brainstem.4 This is distinct from the UK where a brainstem-based definition of death is in place.5

In brain injury associated with mass effect or generalised oedema, loss of whole brain function usually occurs by the sequence of raised intracranial pressure, rostral-caudal brainstem herniation, and cerebrocirculatory arrest. However, complete and irreversible loss of brainstem function can be seen in isolated brainstem injury without the typical herniation sequence (eg, massive brainstem infarction), which may or may not be accompanied by complete loss of cerebral hemispheric function. The mechanism of loss of consciousness in brainstem death is related to interruption of the ascending reticular activating system.

Common to the UK and the USA definition and in general harmony with international practice,7 the determination of brain death is based on the absence of the clinical functions of the brain: loss of consciousness, unresponsive coma, and loss of brainstem reflexes including the capacity to breathe. Variability in regional and international practice are well documented; however, there is reassuring consistency in these fundamental clinical
criteria. That the clinical assessment for loss of neurological function in brain-death examinations detects only the absence of brainstem function must be understood. The clinical examination cannot distinguish the complete loss of whole brain function from the isolated loss of brainstem function. The distinction between whole brain and brainstem death can be made on the basis of cause of brain injury and neuroimaging. This distinction can be confirmed only by the use of an ancillary test that shows the absence of electroencephalographic activity or, preferably, the absence of intracerebral blood flow. As there are no currently adequate tests for the confirmation of brain death in instances of isolated primary brainstem injury, ancillary testing is often used in the USA but only rarely in the UK.

Death is determined after cardiac arrest by the loss of the clinical function of heart activity and is based on the absence of circulation. Similar to cardiac arrest, brain death is better understood as brain arrest, the complete loss of the clinical expression of brain function. There is no further deterioration of clinical neurological function that is possible. The terminology of the Uniform Definition of Death Act stating “irreversible cessation of all function of the entire brain” is problematic. Arguments are made that laboratory evidence of retained hypothalamic-pituitary activity is inconsistent with the whole-brain formulation. These arguments become irrelevant when brain death is equated to brain arrest.

The most concrete functional correlate of brain arrest is the absence of cerebral blood flow, although this is not invariably. Of note, cardiocirculatory arrest effectively leads to brain arrest as cerebral blood flow is also arrested. Existing but limited human studies show that an isoelectric electroencephalographic pattern is manifest within 20 s after circulatory arrest. Although brain-death examinations are not done after circulatory arrest, the permanent absence of cerebral blood invariably leads to brain arrest in a short time frame.

Paradoxically, although there is general comfort with the irreversible nature of brain death, the concept of reversibility is being questioned in regard to cardiocirculatory definitions of death. In advanced hospital practice, cardiac arrest is only reversible if physicians do not apply existing methods to reanimate the circulation. If traditional CPR is not successful, e-CPR (the urgent deployment of extracorporeal heart-lung machines such as extracorporeal membrane oxygenation) may be used. These issues become most relevant in the intensive care unit where withdrawal of life support may result in cardiac arrest and CPR is not indicated or applied. Whether the heart can be resuscitated is less of an issue than if it will be.

Reversibility is only relative to the context in which the cardiac arrest occurs. As suggested by Bernat, the term irreversibility should be reconsidered in the cardiocirculatory determinations of death in favour of permanence.

Although brain-based definitions of death are widely accepted, there remains skepticism about their conceptual basis and lingering concerns that they were created for the utilitarian purpose of transplantation. The evolution of non-heart beating donation, or donation after cardiac death, has further pressured us to reflect on what we mean by the word death. Clinical practice and medical literature does not clearly distinguish the various domains in which death may be defined—eg, medical, legal, religious, spiritual, existential, philosophical. Practitioners remain confused.

In view of the complexities of advanced technologies, the operational concepts of death cannot fulfill all these domains. The use of the single term death is inadequate to describe the many facets of the process. This fact should be acknowledged and addressed. Criteria for death, as defined in the medical and legal domain, once met, should lead to concrete consequences, including no legal requirement to provide ongoing resuscitative or support technologies, loss of personhood and individual rights, possibility for organ donation and autopsy, execution of legal will and estate, life insurance, burial, or cremation proceedings, etc.

There is a need to reformulate the definition of brain death to reflect current clinical realities and our evolving understanding. Although difficult to influence the entrenched lexicon, we advocate abandoning the term brain death in favour of the neurological determination of death. In our Canadian consensus guidelines, we attempt to address this conceptual and practical confusion by defining death determined by neurological criteria as follows: “irreversible loss of capacity for consciousness combined with the irreversible loss of all brainstem function including the capacity to breathe”. This may occur as a consequence of intracranial hypertension or primary brainstem injury, or both.

Brain death is better understood as brain arrest—the complete loss of clinical brain function. If there is a known proximate cause accounting for the brain arrest, and an absence of reversible or confounding conditions, then the neurological determination of death is the corresponding process and procedure to determine this death.

S D Shemie
Division of Pediatric Critical Care, Montreal Children’s Hospital, McGill University Health Centre, Montreal, Quebec, Canada
sam.shemie@muhc.mcgill.ca

I have no conflicts of interest.

Clinical issues of brain death in children
The most important issue generating concerns with regard to brain death in paediatrics involves the essence of childhood—the child’s brain is a developing organ. Development from infancy through childhood converts the potential for higher neurological functioning into actual higher neurocognitive ability. Development of the CNS during infancy and childhood is exceptionally complex and not completely understood. Major developmental changes include glial-cell maturation,
axonal arborisation, increase in synaptic numbers, and continuing dendritic development, and while many researchers believe that anatomic neurodevelopment ends by 2 years of age others believe it continues beyond the first decade of life.16 During this time, there is also changing patterns of vulnerability to injury and different responses to the injury itself.15 This innate potential for improved neurological function adds uncertainty to a diagnosis of brain death, which at its heart involves absolute certainty of irreversibility. The 1981 report of the Medical Consultants on the Diagnosis of Death16 concluded that the irreversible cessation of the entire brain, including the brainstem, was a fundamental definition of death.

There are many poignant examples of the effect of this developmental reality. Most important, The Task Force for the Determination of Brain Death in Children17 could not define brain death in infants younger than 7 days of age and recommended longer observation periods in infants and children than in adults. Almost two decades after this task force, well-accepted guidelines for determining brain death in preterm infants and full-term infants younger than 7 days of age have still not been developed. The recommendations for ancillary testing, especially in children younger than 1 year of age, are also a reflection of the uncertainty secondary to developmental issues.

Around a third of paediatric deaths in intensive care units involve brain death. The criteria for brain death in children remain similar to adults. The physical examination is the central feature, but an irreversible cause must be established. Hypothermia, which is more common in infants and children than in adults, must be excluded along with other correctable factors that affect the physical examination. Apnoea testing is an essential part of the physical examination and recommendations for a PaCO2 greater than 8·0 kPa as a stimulus threshold are still common. However, case reports confirmed by the all too frequent experience of clinicians indicate that the carbon dioxide threshold necessary to determine apnoea with absolute certainty is occasionally higher in children than in adults. Some authors now recommend that PaCO2, greater than 12·0 kPa in infants and children be achieved to conclude that there is apnoea.16,19 Ancillary tests such as electroencephalography may be less conclusive in paediatrics; cases in infancy exist for recovery of electroencephalographic activity following electrocerebral silence. Cerebral-blood-flow studies as ancillary tests are becoming more frequently used in infants and children, although the reliability of techniques to measure cerebral blood flow at the rates seen in infants and children often have not been conclusively studied.

Another important issue present in paediatrics that stems, in part, from the child’s neurocognitive potential is the lack of acceptance of brain death by parents. In fact, many patients diagnosed with brain death do not have irreversible cessation of functions of the entire brain. As argued by Truog and Robinson,20 posterior pituitary function and other brain function is widely accepted to be preserved sometimes in those diagnosed with brain death. If so, then why do we place such value on pupillary responses, but not on the preservation of salt and water homeostasis? In light of the uncertainties generated by the physiology of brain development and the real observation that many patients diagnosed with brain death do not have irreversible cessation of the entire brain, it is understandable that some parents as surrogate decision makers have ethical, religious, and practical questions concerning the legitimacy of the concept of brain death.

When a child becomes brain dead, the decisions regarding withdrawals and limitations of care are taken away from the family. Does this relieve them of the burden of decision making and reduce the potential for long-term guilt or do they continue to want to fulfill their parental responsibilities as decision makers? Is the opportunity to orchestrate the act of withdrawing mechanical ventilation support a valuable time for them? Unfortunately, we know very little about how parents view the quality of death and dying when their child develops brain death.

In view of these issues, it would seem reasonable that physicians would want to use widely accepted guidelines in the diagnosis of brain death. The Guidelines for the Determination of Brain death in Children20 were developed by a diverse and respected group of organisations representing many aspects of society. Yet, physicians frequently violate these guidelines. A multi-institutional study of US paediatric intensive care units found that 25% of patients did not have a documented apnoea test, 22% who did have a documented apnoea test did not fulfill the prerequisite criteria for testing, and 6% did not have repeat examinations.21 Further data document an even more erratic application of the guidelines.22 The Task Force for the Determination of Brain Death in Children published its report almost two decades ago.23 Since that time, new medical and ethical issues have arisen. There are increasing pressures to procure organs, reduce costs, and improve the quality of death and dying. A new national or international effort is needed to reassess the current definition of brain death and the appropriate criteria to determine brain death in infants and children. It is also time to assess the effect of a diagnosis of brain death on the quality of death and dying.

Murray M Pollack
Critical Care Medicine, Children’s National Medical Center, Washington DC, USA
mpollack@cnmc.org

I have no conflicts of interest.
Is it morally acceptable to remove organs from brain-dead children?

In Japan, according to several surveys, around 30% of the population do not accept brain death as death of the human being. The current law on organ transplantation was established on the basis of the idea of pluralism on human death—that is, people can determine beforehand, if they want, whether to choose brain death as their own death or not, and if they have not declared anything, their death is diagnosed by the cessation of heartbeat. Personally, I highly appreciate Japanese pluralism on human death because it shows a deep respect for the diversity of ideas on life and death.

The basic policy of organ transplantation from brain dead donors in Japan is: “From those who wish to donate to those who wish to receive.” This is called the donor’s prior declaration principle. According to this principle, only when a donor has declared his or her consent beforehand in the form of a donor card, can both a legal brain-dead diagnosis and an organ removal become possible on the premise that the family does not refuse it.

However, this principle has created some difficult problems we had never imagined. The most difficult of which is organ removal from a brain-dead child. First, the current guideline stipulates that the legal brain-death diagnosis of a child younger than 15 years of age must not be performed because the statement of a child younger than 15 years of age written in a donor card is not deemed legally valid. This means that organ transplants from brain-dead children younger than this age are forbidden. Second, doctors and nurses continue caring for brain-dead children until their heart naturally stops beating because a brain-dead child is regarded as legally alive under the current law for the above reason, and since most parents wish to continue caring for their brain-dead child, sometimes the heart of a brain-dead child continues beating more than a month in a hospital. A doubt about the idea of infant brain death is beginning to arise among specialists.

How should we think about organ transplantation from brain-dead children? First, as I noted above, there are many people in Japan who think that a brain-dead patient with a warm body should not be considered dead even if he or she has permanently lost consciousness. The 6 year old son of Dr Tateo Sugimoto was hit by a car and became brain dead. Sugimoto was a neurologist; however, he could not accept the view that his brain-dead son was dead. He continued to think that his son was alive until his heart stopped beating. According to Alan Shewmon, brain-dead children are more likely than brain-dead adults to progress to a state of chronic brain death. In 1995, a Japanese baby became brain dead soon after she was born. She grew taller and “lived” until the age of 4 years in the state of brain death. These cases strongly suggest that it should be considered reasonable for the parents to believe that their brain-dead child is alive, especially when the child’s body is warm, the limbs move, or the child grows taller. Pluralism on human death should not be abandoned, especially in the case of children.

Second, concerning the donor’s prior declaration principle, Dr Tateo Sugimoto and I have proposed to revise the current law and allow children between 6 years and 15 years to be able to have donor cards and express their wishes on brain death and organ transplants. A donor card without the signature of a person with parental authority should not be accepted. This approach is the only way to remove organs from brain-dead children, maintaining the donor’s prior declaration principle. In Article 12 of Convention on the Rights of the Child, we can find this expression: “States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child.” This is the basic idea of our proposal.

Then, what about when a brain-dead child does not have a valid donor card, or when the child is younger than 6 years of age? I think in this case the organs should not be removed from a brain-dead child even if the parents wish to do so. The silent child might have been thinking that a brain-dead person is not really dead, or it might be that organ removal was against the child’s inner wish. Organ removal from such a child is equivalent to exploitation of a “living” child. Children have the right not to be exploited by the desire of adults. When a brain-dead child has said nothing about brain death, we have to think that the child has a right to live and die peacefully, fully protected against the interests of others. One might say that this means to discard babies with severe diseases who can’t survive without transplantation. Last year a 1 year old Japanese baby received five organs in the USA, but unfortunately she lived only 5 months and died early this year. By contrast, the brain-dead baby, mentioned above, “lived” 4 years with her parents in a hospital. Every year her birthday was celebrated by the medical staff. No one can decide which life is superior to or more valuable than the other. It is time to reconsider organ transplantation from brain-dead children.

Masahiro Morioka
Osaka Prefecture University, Osaka, Japan
info@lifestudies.org
I have no conflicts of interest.

Personal experiences of brainstem-death testing in children

The death of a child is a tragedy that families must live with for the rest of their lives. When that death occurs due to death of the brainstem, this places an extra burden on relatives—that of being able to understand that death has occurred and that further treatment is therefore futile. As a neurotrauma intensivist I am required to perform brainstem death tests about 20 times per year, fortunately only once or twice is this for a child. The
bravery of families facing such a catastrophe, while remaining focussed on doing the best for their child and all the while being able and willing to discuss issues such as organ donation at such a time, is a source of astonishment and admiration to me.

One cannot change events leading up to such tragic deaths, my only hope is that by acting with care and respect one can somehow ease some of the suffering both at the time and in subsequent grief. I believe that this involves ensuring that the families understand the circumstances leading up to the death, the nature and implications of a diagnosis of brainstem death, and are given the opportunity to consider organ donation.

Brainstem death can be a difficult concept for relatives to understand, despite explanations from medical and nursing staff. The most common causes of brainstem death are head injury and subarachnoid haemorrhage, which often occur unexpectedly in young, previously healthy individuals. There is often no external sign of injury and although the brainstem is dead, the patient is warm and pink due to inotropes and warming devices and the chest rises and falls due to artificial ventilation. Previous questionnaire studies have shown that a third of relatives of patients diagnosed as brainstem dead did not understand that death had occurred. However, for some relatives certain circumstances leading up to the death, the nature and implications of a diagnosis of brainstem death, and are given the opportunity to consider organ donation.

In the same study organ donation was permitted by nine families who all found this a positive experience and three family members who had not allowed this option had subsequently regretted this decision. This finding has confirmed our belief that families do get comfort from allowing donation to proceed and that this option should always be discussed with them, even if it seems extremely intrusive or difficult to facilitate.

I remember the death of a little 5 year old boy whose family would not even speak to me, so entrapped in their grief that they even appeared hostile, on the edge of physical aggression. I hesitated to mention organ donation, but when I did, the idea slowly dawned that something good could come out of this, not only did they agree, but it also seemed to allow them to discuss other aspects of care. The resurgence of interest in non-heart-beating organ donation has also increased the possibility of organ donation for some families of older children. Two cases spring to mind, one a 10 year old girl, certified through brainstem testing, whose family wanted to consider donation but could not do this while she appeared to them alive, warm, and pink. Ventilation was withdrawn and she donated her kidneys after asystole and they had had an opportunity to sit with her. Another tragic case was of a 14 year old boy who presented to the accident and emergency department following a massive spontaneous intracerebral bleed with fixed pupils and brainstem herniation on the CT scan. He was reviewed by the consultant neurosurgeon who informed his family that treatment should be withdrawn because there was no possibility for survival. As this treatment plan had already been decided with the family, he was not
transferred to intensive care for assessment of brainstem function, but he was transferred to a side room on a ward where the family could sit peacefully with him during treatment withdrawal and the possibility of organ donation was raised. They allowed donation to proceed and the family gained great comfort from the transplantation of four organs including the lungs. This family were grateful for time spent with him in a peaceful side room, rather than treatment being withdrawn in a busy emergency room.

Being sensitive to the needs of the family is vital at this time. Many of these needs are not obvious to the family at the time, but they may be grateful for such thoughts in future years, which may constitute their abiding memory of the worst time of their lives. One of the most emotional times in my career was performing the tests on a 2 year old child, much loved by incredibly strong parents who sat and held his hand throughout, talking continuously of family and his pets, and having declined organ donation, we decided together to entube him on his mother’s lap, dressed in his pyjamas so she could cuddle him as if asleep at bedtime, while we all left the room. They thanked us for this consideration. If we cannot change the outcome, it is my desperate hope that the families can at least leave hospital knowing that they have been treated with compassion and respect as if looking after one of our own family members.

Stephen Bonner
The James Cook University Hospital, Middlesbrough TS4 3BW, UK
Steve.bonner@stees.nhs.uk
SB sits on the Joint Medical Royal Academy Committee on the Diagnosis of Death and the Intensive Care Advisory committee to UK Transplant.

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