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# Using the brain criterion in organ donation after the circulatory determination of death☆,☆☆,★,★★

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ABSTRACT

The UK, France, and Switzerland determine death using the brain criterion even in organ donation after the circulatory determination of death (DCDD), in which the United States and Canada use the circulatory-respiratory criterion. In our analysis of the scientific validity of the brain criterion in DCDD, we concluded that although it may be attractive in theory because it conceptualizes death as a unitary phenomenon, its use in practice is invalid. The preconditions (ie, the absence of reversible causes, such as toxic or metabolic disorders) for determining brain death cannot be met in DCDD. Thus, although brain death tests prove the cessation of tested brain functions, they do not prove that their cessation is irreversible. A stand-off period of 5 to 10 minutes is insufficient to achieve the irreversibility requirement of brain death. Because circulatory cessation inevitably leads to cessation of brain functions, first permanently and then irreversibly, the use of brain criterion is unnecessary to determine death in DCDD. Expanding brain death to permit it to be satisfied by permanent cessation of brain functions is controversial but has been considered as a possible means to declare death in uncontrolled DCDD.

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## 1. International DCDD Death Determination Practices

Prior to the development of tracheal positive-pressure ventilators in the 1940s and 1950s [1], physicians determined death by showing the prolonged absence of respiratory and cardiocirculatory functions because the functions of the brain and all other organs also ceased at this time [2]. However, once mechanical ventilation could sustain respiratory (and thereby cardiocirculatory) functions, it became possible for a patient with a completely destroyed brain to have respiration and ventilation supported mechanically.

To recognize the essential role of brain function in human life, to allow lawful withdrawal of life-sustaining therapy in cases of profound brain damage, and to address the growing needs of organ transplantation, a new test for death determination was proposed based on the cessation of brain function. In 1968, the Ad Hoc Committee of the Harvard Medical School defined “irreversible coma” or “brain death” as a “new criterion for death” and proposed tests to determine it [3]. In 1981, the medical consultants on the diagnosis of death to the US President's Commission added specificity and consensus to the tests for brain death [4]. In the United States, the most widely accepted brain death test battery for adults is that published in the Report of the Quality Standards Subcommittee of the American Academy of Neurology [5]. The brain criterion of death is now widely accepted around the world [6]. The US President's Commission [4] also discussed the circulatory-respiratory determination of death, which, for simplicity, we shorten to “circulatory death determination.” However, this issue did not become controversial until programs of organ donation after the circulatory determination of death (DCDD) in the 1980s forced physicians to pay greater attention to the exact moment of death [7] because of the time pressures of organ donation [8].

In the United States and many other countries, physicians determine death using 1 of 2 criteria: (1) the irreversible cessation of circulatory and respiratory functions or (2) the irreversible cessation of all functions of the entire brain, including the brain stem [9]. There remains a debate over whether the 2 criteria are independent or whether the circulatory criterion is valid because once satisfied, the brain criterion

*Abbreviations:* DCDD, donation after the circulatory determination of death; DBDD, donation after the brain determination of death; SAMS, the Swiss Academy of Medical Science; EEG, electroencephalogram; CPR, cardiopulmonary resuscitation.

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inevitably becomes satisfied because the brain is destroyed by ischemia from absent circulation.

In Canada, the diagnosis of death is based on the single brain criterion (brain death): "a person is dead when an irreversible cessation of all that person's brain functions has occurred" and is determined either by (1) "the prolonged absence of spontaneous circulatory and respiratory functions" or (2) "when the determination of the prolonged absence of spontaneous circulatory and respiratory functions is made impossible by the use of artificial means of support, the irreversible cessation of brain functions can be determined by any means recognized by the ordinary standards of current medical practice" [10].

In France, the law on Public Health also bases the diagnosis of death on the single brain criterion. Article R 1231-2 refers specifically to cessation of brain functions, while cardiorespiratory functions are artificially sustained [11]. Article R 1231-1 refers to the cessation of brain functions, secondary to the persistent cessation of respiratory and cardiac functions, and states that death can be determined only if 3 criteria are simultaneously met: absence of consciousness and spontaneous motor activity, absence of brain stem reflexes, absence of spontaneous ventilation [11].

In the United Kingdom, there is no legal definition of death and "professional guidance provides the legal standard" [12]. The "Code of practice for the diagnosis and confirmation of death," enacted by the Academy of Medical Royal Colleges, defined death based on the single brain criterion, stating that "the definition of death should be regarded as the irreversible loss of the capacity for consciousness, combined with the irreversible loss of the capacity to breathe" [13]. In the context of the cessation of cardiorespiratory function, this code of practice recommends to confirm death by identifying the following: (1) "the simultaneous and irreversible onset of apnea and unconsciousness in the absence of the circulation," (2) mechanical asystole for at least 5 minutes, and (3) "the absence of pupillary responses to light, of the corneal reflexes, and of any motor response to supra-orbital pressure" [13]. The British Transplantation Society stated that "death is in essence a neurological event and occurs when there is a permanent loss of the capacity of consciousness and all brain stem function," where death is confirmed by the absence of consciousness, respiration, and other brain stem functions, whereas asystole is identified by a flat arterial line or echocardiography [14].

In Switzerland, the diagnosis of death is also based on the single brain criterion. The Swiss Federal Act on Transplantation of Organs, Tissues and Cells, active since 2007, states that "a person is dead when all cerebral functions, including the brain stem, have irreversibly ceased" [15]. In the context of DCDD, the diagnosis of death relies on the determination of the irreversible cessation of cerebral functions, if the absence of cardiac activity has been observed for at least 10 minutes by means of echocardiography, and if the following clinical signs, determined by the Swiss Academy of Medical Sciences (SAMS), have been identified [16]: (1) coma; (2) bilaterally dilated pupils, unresponsive to light; (3) absent oculocephalic and vestibulo-ocular reflexes; (4) absent corneal reflexes; (5) no cerebral response to painful stimuli; (6) absent cough and gag reflexes; and (7) absent spontaneous respiration.

Thus, in some countries, death determination, even in a DCDD donor, is based on the brain criterion rather than on the circulatory criterion. In this article, we analyze the scientific validity and implications of the use of the brain criterion for the determination of death in DCDD.

## 2. Should there be 1 or 2 criteria to determine death?

Determining death based on the single brain criterion is attractive, because it conceptualizes death as a unified phenomenon as one of us stated: the event that separates "the biological processes of dying and bodily disintegration" [17,18]. Death has been defined as "the cessation of functioning of the organism as a whole," whose critical functions include consciousness, control of circulation, respiration and temperature, and control of homeostasis (fluid, electrolytes, neuroendocrine) [17,19].

In practice, physicians determine death in 2 general clinical situations. The first is in the presence of profound global brain damage in which respiratory and circulatory functions are maintained by life-sustaining therapy, particularly mechanical ventilation, and tests for death show the irreversible absence of the clinical functions of the brain. "Brain death" tests have been developed and validated to determine death in this small minority of patients dying in intensive care units [5,20]. The whole-brain criterion is the irreversible cessation of all clinical brain functions, including those of the brain stem. In the UK, the irreversible cessation of brain stem functions is deemed sufficient for death determination. In practice, brain stem death tests are usually equivalent to whole brain death tests.

In the much more common second clinical situation, respiration and circulation have ceased in the absence of cardiopulmonary resuscitation (CPR) or after failed CPR. Physicians diagnose death using the circulatory-respiratory criterion. Using the brain criterion of death in such cases—as practiced in Switzerland and in the UK—is conceptually sound because in the absence of resuscitative efforts, cessation of systemic circulation inevitably produces an irreversible cessation of brain functions. But are brain death tests applicable, feasible, and necessary in the context of DCDD?

## 3. Brain death tests in donation after the brain determination of death

Brain death tests are used to diagnose death in a patient with irreversible loss of all brain clinical functions whose respiratory and circulatory functions are maintained by life-sustaining therapy including mechanical ventilation with endotracheal intubation. Prior to testing for brain death, clinicians must assure 2 essential preconditions that prove irreversibility: (1) the presence of a structural brain lesion that is sufficient to produce the clinical findings (eg, anoxia, major brain trauma, and cerebral hemorrhage) by history, examination, and neuroimaging, and (2) the exclusion of potentially reversible metabolic or toxic effects (eg, electrolyte, temperature, hemodynamic, or endocrine disorders) that might provoke a global but potentially reversible central nervous system depression mimicking brain death [5].

Once these preconditions have been met, brain death tests must show 3 principal findings: unresponsiveness, brain stem areflexia, and apnea. The tests document utter unresponsiveness to noxious stimuli, absence of pupillary response to light and dark, absence of eye movements to vestibuloocular reflex testing, absence of corneal reflexes, absence of facial muscle movement to noxious stimuli, absence of pharyngeal and tracheal reflexes, and true apnea [5]. The apnea test is usually performed last and must show no respiratory effort in the face of hypercapnia maximally stimulating the medullary respiratory centers. The apnea test has similar prerequisites: normotension, normothermia, euvolemia, eucapnia, absence of hypoxemia, and no prior evidence of carbon dioxide retention [5].

Ancillary tests may be performed to confirm the cessation of brain electrical output (electroencephalogram [EEG] and evoked potentials) or to prove the absence of intracranial circulation (cerebral angiography, radionuclide angiography, or transcranial Doppler ultrasound) [5]. Emerging confirmatory tests using computed tomography angiography, magnetic resonance angiography, magnetic resonance perfusion, and single-photon emission computed tomography are promising but not have been sufficiently validated.

## 4. Brain death tests in DCDD

### *4.1. Are brain death tests applicable in DCDD?*

Brain death tests can be applied only if preconditions have been met that identify a structural cause and exclude potentially reversible metabolic or toxic factors. In DCDD, the first condition is met, because complete circulatory cessation inevitably progresses to brain death but the second condition cannot be met. Circulatory arrest violates the precondition excluding hemodynamic disorders. Circulatory arrest causes an

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