



## History of brain death as death: 1968 to the present



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### ABSTRACT

The concept of brain death was formulated in 1968 in the landmark report A Definition of Irreversible Coma. While brain death has been widely accepted as a determination of death throughout the world, many of the controversies that surround it have not been settled. Some may be rooted in a misconception about the history of brain death. The concept evolved as a result of the convergence of several parallel developments in the second half of the 20th century including advances in resuscitation and critical care, research into the underlying physiology of consciousness, and growing concerns about technology, medical futility, and the ethics of end of life care. Organ transplantation also developed in parallel, and though it clearly benefited from a new definition of death, it was not a principal driving force in its creation. Since 1968, the concept of brain death has been extensively analyzed, debated, and reworked. Still there remains much misunderstanding and confusion, especially in the general public. In this comprehensive review, I will trace the evolution of the definition of brain death as death from 1968 to the present, providing background, history and context.

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“The boundaries which divide Life from Death are, at best shadowy and vague. Who shall say where the one ends and where the other begins.”

[Edgar Allen Poe, *The Premature Burial*, 1844]

### 1. Introduction

It has been more than 40 years since the concept of brain death was introduced; and although it is widely accepted, many of the controversies that surround it have not been settled. Much of the public, and some in the medical profession, still consider brain dead patients to be “for all practical purposes dead” but not *really* dead. This reflects uncertainties about the boundaries that divide life and death and the relationship between death of the cells and tissues and death of the human being. It may also reflect a misconception of history.

### 2. The transition from heart to brain

At the end of the last century, a new definition of *death* was introduced. In the past, the irreversible loss of heart and lung functions had signaled death. The new definition was based on the irreversible loss of brain functions. The transition from heart to brain grew out of several parallel developments that converged in 1968 (Fig. 1). It began in 1947 when Claude Beck performed the first successful defibrillation of a human heart [1]. Suddenly, death was “reversible.” In 1950, Bower and

Bennett developed positive pressure ventilation [2]. The first mass-produced ventilator, the Bird Mark 7, was introduced in 1955 [3]. This created unique diagnostic, prognostic, and ethical dilemmas for comatose patients with brain injuries. Some would recover; others would survive but be devastated or, worse, remain in a vegetative state or in coma. Accurate prognostication was difficult but imperative. Withholding life-saving technology was considered unethical and potentially illegal [4]; but perhaps “extraordinary” measures were not required in all cases, especially for those in severe coma, the “hopelessly unconscious.” Were they not essentially dead already?

In 1954, Robert Schwab, a neurologist at Massachusetts General Hospital, was one of the first to recognize this when evaluating a comatose patient with a massive brain hemorrhage on a respirator. “The question was, ‘Is this patient alive or dead?’ Without reflexes, without breathing, and with total absence of evidence of an electroencephalogram, we considered the patient was dead in spite of the presence of an active heart maintaining circulation. The respirator was therefore turned off and the patient pronounced dead.” [5]. Five years later, French neurologists Wertheimer and Jouvett [6,7] came to the same conclusion. This kind of severe coma was different. It represented “death of the nervous system.” Mollaret and Goulon [8] were not so sure. Although all these patients died of cardiac arrest within days, they were hesitant in calling this condition *death*. “Do we have the right,” they asked, “to stop treatment using criteria that pretend to know the boundary between life and death?” They preferred the term *coma dépassé* or “beyond coma” [8]. This was a *prognosis* of death but not *equal* to death. Schwab [9] disagreed and felt that standardized clinical and electroencephalographic (EEG) criteria could provide the necessary reassurance of “death of the

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Fig. 1. Parallel developments that converged in the formulation of the concept of brain death.

Resuscitation and Critical Care	Coma and Consciousness	Ethics and End-of-Life Care	Organ Transplantation
<p><b>1947</b> - Beck performs first successful cardiac defibrillation [1]</p> <p><b>1947</b> - Moersch develops piston ventilator for use in OR [60]</p> <p><b>1950</b> - Bower and Bennett develop positive pressure ventilation [2]</p> <p><b>1952</b> - Ibsen advances respiratory support and establishes first ICU [61]</p> <p><b>1954</b> - Engstrom introduces volume-cycled ventilator [62]</p> <p><b>1955</b> - Bird develops pressure-cycled ventilator [3]</p> <p><b>1956</b> - Zoll develops external defibrillator (AC) [63]</p> <p><b>1958</b> - Safar develops mouth-to-mouth respiration [64]</p> <p><b>1959</b> - First modern ICUs established (University of Pittsburgh, Peter Safar, UCLA, Max Weil) [65]</p> <p><b>1960</b> - Kouwenhoven develops closed chest massage [66]</p> <p><b>1962</b> - Lown develops portable external defibrillator (DC) [67]</p> <p><b>1966</b> - First cardiopulmonary resuscitation guidelines developed [68]</p>	<p><b>1938</b> - Sugar demonstrates carotid occlusion results in isoelectric EEG [69]</p> <p><b>1949</b> - Moruzzi and Magoun describe ascending reticular activating system [29]</p> <p><b>1953</b> - Rishede reports absent cerebral blood flow in patients with herniation and apnea [70]</p> <p><b>1954</b> - Fessard publishes <i>Mechanisms of Nervous Integration and Consciousness</i> [31]</p> <p><b>1958</b> - Magoun publishes <i>The Waking Brain</i> [30]</p> <p><b>1959</b> - Fischgold describes four stages of coma. Stage IV (coma carus) has absence of reflexes, breathing and isoelectric EEG and 100% mortality [71]</p> <p><b>1959</b> - Werthemier and Jouviet describe "death of the nervous system" [6]</p> <p><b>1959</b> - Mollaret and Gollon describe "coma depasse" [72]</p> <p><b>1963</b> - Schwab establishes triad of criteria for establishing death [9]</p> <p><b>1966</b> - Plum and Posner publish <i>The Diagnosis of Stupor and Coma</i> [73]</p>	<p><b>1954</b> - Fletcher, Harvard Theologist, publishes <i>Morals and Medicine</i>, [74] argues for euthanasia based on patient autonomy</p> <p><b>1957</b> - Pope Pius XII issues <i>The Prolongation of Life</i>, [75] physicians not obligated to offer "extraordinary" measures</p> <p><b>1962</b> - Ayd publishes <i>The Hopeless Case: Medical and Moral Considerations</i> [16] argues for withdrawal of care</p> <p><b>1965</b> - AMA organizes First National Congress on Medical Ethics and Professionalism</p> <p><b>1966</b> - Williamson publishes <i>Life or Death - Whose Decision?</i> [76]</p> <p><b>1966</b> - Beecher publishes <i>Ethics and Clinical Research</i> [27]</p> <p><b>1967</b> - Fletcher publishes <i>Moral Responsibility: Situation Ethics at Work</i>, [77] argues that euthanasia would "harmonize civil law with medical morals."</p> <p><b>1968</b> - Beecher publishes <i>Ethical Problems Created by the Hopelessly Unconscious Patient</i> [32]</p>	<p><b>1954</b> - Murray performs first organ transplant [18]</p> <p><b>1960</b> - First organ transplant managed with immunosuppression [78]</p> <p><b>1962</b> - Murray performs first cadaveric organ transplant [19]</p> <p><b>1963</b> - Starzl performs first liver transplant [20]</p> <p><b>1963</b> - Hardy performs first lung transplant [21]</p> <p><b>1963</b> - Reversal of rejection shown possible using prednisone and azothiaprime [79]</p> <p><b>1966</b> - Kelly performs first pancreas transplant [80]</p> <p><b>1966</b> - CIBA Symposium and Alexandre criteria for declaring death [23]</p> <p><b>1967</b> - Barnard performs first heart transplant [25]</p> <p><b>1968</b> - Cooley performs heart-lung transplantation [81]</p>
<p><b>1968 - Concept of Brain Death</b>  <i>A Definition of Irreversible Coma: Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death published in JAMA</i></p>			

nervous system." In 1963, he proposed a triad of criteria: (1) fixed and dilated pupils, no elicitable reflexes, and no spontaneous movements; (2) apnea; and (3) isoelectric EEG. Those who met the criteria could be considered dead "in spite of cardiac action" [9]. In 1968, he reported on 90 such patients. None survived; and at autopsy, all had extensive necrosis of brain tissue [10], a finding that was consistent with other studies [11–13].

At the same time, there were growing concerns about technology, medical futility, and the ethics of end-of-life care [14,15]. Responding to these concerns, Pope Pius XII, in 1957, decreed that physicians were not obligated to provide "extraordinary" treatment in cases that were deemed "hopeless." In 1962, Frank Ayd, a psychiatrist, published *The Hopeless Case: Medical and Moral Considerations* [16], in which he argued that there was a duty to withdraw care when death appeared inevitable. In 1964, Hamlin [17], a colleague of Schwab's, made the case for defining death by EEG by emphasizing futility: "If complete EEG silence could gain acceptance as proper grounds for withholding fruitless attempts at resuscitation, some of the nobility in death would be preserved...." And in 1965, the American Medical Association held its First National Congress on Medical Ethics and Professionalism to formulate guidelines for end-of-life care.

In parallel with the beginning of the transition from heart to brain for determining death, the field of organ transplantation was also beginning. In 1954, Joseph Murray, from the Peter Bent Brigham Hospital, reported the first successful kidney transplant from one identical twin into another [18]. In 1962, Murray performed the first successful cadaveric kidney transplant [19]. The following year, Starzl et al [20] achieved the first liver transplant; and Hardy et al [21], the first lung transplant. Usually, cadavers were used and many recipients died soon after transplantation. Most believed that "live donors" would improve the odds of success. Surgeons were uneasy though

about removing organs from live ventilated patients, even if they had catastrophic brain injuries [22].

In November 1966, at the CIBA Symposium on Transplantation in London, Guy Alexandre, a Belgian surgeon and one of Murray's former fellows, described 5 criteria he had used to declare death and harvest organs for transplantation. Alexandre's 5 criteria were similar to Schwab's triad: "1) complete bilateral mydriasis; 2) complete absence of reflexes ... 3) complete absence of spontaneous respiration ... 4) falling blood pressure, necessitating increasing amounts of vasopressive drugs ... 5) a flat EEG" [23]. Although some applauded Alexandre for his boldness and innovation, others deemed it ethically suspect [24]. The biggest milestone in transplantation occurred in South Africa on December 3, 1967, when Christiaan Barnard carried out the world's first successful human heart transplant [25].

### 3. 1968 – The Harvard Ad Hoc Committee and the new definition

Three months earlier, in September 1967, Henry Beecher, Chair of Anesthesiology at Massachusetts General Hospital, wrote to Robert Ebert, Dean of Harvard Medical School, to call a meeting of the Standing Committee on Human Studies. The reason was to discuss the "ethical problems created by the hopelessly unconscious patient." Beecher explained,

As I am sure you are aware the developments in resuscitative and supportive therapy have led to many desperate efforts to save the dying patient. Sometimes all that is rescued is a decerebrated individual. These individuals are increasing in numbers over the land and there are a number of problems which should be faced up to [26].

This is something that Beecher had spent much of his career thinking about, specifically the need to protect patients from harm. In 1966, he had outlined his concerns in an article called “Ethics and Clinical Research” [27]. And in a lecture given on December 6, 1967, titled *The Right to be Let Alone: The Right to Die—Problems Created by the Hopelessly Unconscious Patient*, he articulated his belief that futile treatment intruded on the rights of the individual and was akin to experimentation. With the allure of advancing technology, we needed to set limits; and Schwab’s triad was a good place to start [28]. Given 3 days after the first heart transplant, Beecher urged caution. Transplantation was experimental and as such needed to be done “within the framework of a clinical trial” [5]. Thus, there was even more of a reason to establish clear guidelines.

Joseph Murray attended the meeting and offered his support. Beecher thanked him for coming: “I cannot tell you how strongly I agree with you that it would be most desirable ... to come to some subtle conclusion as to a new definition of death.” [26]. In January 1968, Ebert sent out the letters of invitation to form an Ad Hoc Committee at Harvard that could formulate the new definition of death. In addition to Beecher and Murray, the Committee would consist of 3 neurologists (Schwab, Raymond Adams, and Derek Denny Brown), a neurosurgeon, and a nephrologist along with an attorney, a neuroscientist, a physiologist, a professor of public health, an historian, and an ethicist.

The starting point of determining what criteria to use naturally would be Schwab’s triad. Adams, however, promoted the idea of “unreceptivity and unresponsivity” as the central feature of *irreversible coma*, a term used to convey the flavor of “coma dépassé.” To that, the committee lumped “no movements or breathing” as the second criterion. Absent reflexes was the third. Finally, isoelectric EEG was the fourth criterion despite arguments that it probably was not necessary given the growing recognition of the central role of the brainstem in consciousness [29–31]. Nevertheless, the EEG was seen as a window into the underlying brain destruction almost always found at autopsy and could serve as a marker not just of irreversible coma but also of nonsurvivability. Its role was downplayed though (“when available it should be utilized”). When patients met the criteria, they would be considered *essentially* dead; but regardless, the condition was not survivable and would inevitably lead to cardiac arrest.

The Committee struggled with this point, brain death as death, going back and forth. In a discussion surrounding an earlier draft, Beecher, based on futility, believed that the definition of irreversible coma permitted withdrawal of treatment with “death to follow.” But then he also thought the “moment of death” could “coincide with brain death while the heart continues to beat” [28]. Schwab, however, now seemed reluctant to make that leap. At a presentation a few months earlier, he said, “At the moment we have to define death as cessation of the heartbeat ... Out of the [Harvard Ad Hoc Committee], there may come a new definition—but that would have to be accepted by lawyers, medical examiners as well as the lay public...” [10]. In a letter to Beecher, Schwab, perhaps thinking the task was too daunting, pressed him to narrow the focus of the group: “Do not attempt to redefine death. Concentrate on agreement as to what constitutes irreversible coma.” [28]. He seemed to be now aligning more with Mollaret and Goulon’s position: “irreversible coma” was *prognostic* of death but not really *equal* to death. Murray did not agree. He marked up his copy of the draft by crossing out the term *irreversible coma* and writing in the word *death*. Beecher had the last word though and seemed to step back from defining brain death as death, writing “It seems clear that any ‘updating’ of the moment of death, in view of the differences among the experts ... would be a *legal* impossibility at present (emphasis in the original).... This is not to argue against ‘updating’; it is to suggest propriety of caution.” [32].

In the end, caution prevailed and the Committee left this fundamental, and conceptually crucial, point vague. In fact, the final title of the article was “A Definition of Irreversible Coma” but the

subtitle was the “Definition of Brain Death” [33]. Even the language of the new definition hedged: “Any organ, brain or other, that no longer functions and has the no possibility of functioning is *for all practical purposes* dead.” (emphasis mine). Thus, the Harvard report did not really provide a fully worked out and conceptually coherent notion of what brain death was. While it hinted at brain death as death, more than anything else, it provided pragmatic guidance for what was ethically permissible for patients with irreversible coma.

There has been much written about the possible role organ transplantation may have played in the work of the Committee. Criticism has been harsh with the charge that the Committee was philosophically naive or that its main objective was to promote transplantation [34–36]. This is historically reductive. However, the way the final paper was framed didn’t help. The only rationale offered for why there was even a need for a reformulation of death was a utilitarian one: it would free up beds (“The burden is great on patients who suffer permanent loss of intellect, on their families, on the hospitals, and those in need of hospital beds already occupied by those comatose patients”), and it would facilitate transplantation (“Obsolete criteria for the definition of death can lead to controversy in obtaining organs for transplantation.”) [33]. To his credit, Murray went out of his way to separate the need for a new definition of *death* from transplantation. In a letter to Beecher, he wrote, “First is the dying patient, and the second, distinct and unrelated, is the need for organ for transplantation.... When to declare death is a problem to be solved whether or not organ transplantation follows.” [26]. Beecher was of the same opinion. However, in the next paragraph, Murray brought them back together in language that reflected generally accepted views of the time.

Can society afford to lose organs that are now being buried?... Patients are stacked up in every hospital in Boston and all over the world waiting for suitable donor kidneys. At the same time patients are being brought in dead to emergency wards and potentially useful kidneys are being discarded. Nevertheless, the concept of brain death was not created to benefit transplantation. Schwab and others had begun formulating the concept in the early 1950s as part of ongoing research into the physiology of consciousness and in the context of end-of-life care. And Beecher viewed transplantation as experimental. However, it is also clear that brain death and organ transplantation became intertwined, which concerned some in the medical community at the time [37].

“A Definition of Irreversible Coma” was published in JAMA on August 5, 1968. That same day, the 22nd World Medical Association met in Sydney, Australia, and announced the Declaration of Sydney [38]. “A couple of years ago, long before the present heart transplant furor,” they explained, “the WMA [World Medical Association] became concerned about the definition of *death* and the establishment of the point of death in this era of resuscitatory arrogance....” Their Declaration stated that:

Death is a gradual process at the cellular level with tissues varying in their ability to withstand deprivation of oxygen. But clinical interest lies not in the state of preservation of isolated cells but in the fate of a person ... the point of death of the different cells and organs is not so important as the certainty that the process has become irreversible... Though overshadowed by the Harvard report, by distinguishing death of the cell from death of the person, the Declaration of Sydney went further in attempting to conceptualize death.

#### 4. 1970s—the aftermath

At the dawn of the new decade, there was growing acceptance of the Harvard definition but also confusion and reticence. In a survey of

more than 400 neurologists, 15% were skeptical and insisted on a traditional cardiopulmonary definition for the declaration of death [39]. Others shared this skepticism. “We do not know with certainty the borderline between life and death, and a definition cannot substitute for knowledge,” argued the philosopher Hans Jonas, “In this state of marginal ignorance and doubt the only course to take is to lean over backward toward the side of possible life” [40]. Nevertheless, throughout the 1970s, various state legislatures and courts began legally recognizing the new standard for determining death, although there was little uniformity in the criteria being used. For example, in 1971, Mohandas and Chou published their “Minnesota Criteria” based on autopsy findings that localized brain death to the brainstem. Thus, the EEG was eliminated altogether [41]. In 1976, a Conference of the Medical Royal Colleges and their faculties in the United Kingdom also emphasized brainstem death [42]. Because both consciousness and respiratory control originated in the brainstem, the argument went, loss of brainstem function equaled death [43]. However, this meant that patients with preserved cortical electrical activity by EEG could be considered dead in the United Kingdom but alive in the United States [44]. The following year, the National Institutes of Health attempted to validate the most commonly used criteria in the United States: coma, apnea, and a flat EEG in a multicenter study [45]. Of 187 patients with all three, 185 “died” from cardiac arrest. The 2 survivors (both with reactive pupils) had drug intoxication. Still, questions about the philosophical and conceptual basis for brain death continued to rumble in the background [46,47].

### 5. 1980s—the President’s Commission

In 1979, the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research was organized to bring clarity to brain death and other ethical issues that had emerged in the 1950s but were crystallized in the case of Karen Ann Quinlan, a young woman in a persistent vegetative state. Recognizing the need for broader guidelines regarding end-of-life care, Congress passed legislation for the landmark President’s Commission. One overarching goal was for Congress to issue a statute “as a means of achieving uniform law on [brain death] throughout the Nation.” In order to do that, however, the Commission first needed to articulate a more convincing and conceptually coherent notion of death. Their report, released in 1981, was titled “Defining Death: Medical, Legal and Ethical Issues in the Determination of Death” [48].

Based in part on an influential paper by Bernat and colleagues [49], the Commission articulated the “Whole Brain” formulation of brain death in which the brain functioned as the great integrator and regulator: “One characteristic of living things which is absent in the dead is the body’s capacity to organize and regulate itself.” Death occurred when the “body’s physiological system ceases to constitute an integrated whole” and that integration was dependent on the integrity of the brain. The resulting statute, the Uniform Determination of Death Act, proposed that death could be determined by (1) “irreversible cessation of circulatory and respiratory functions” or (2) “irreversible cessation of all functions of the entire brain, including the brainstem.” The Uniform Determination of Death Act gave equivalence to death determined by cardiovascular and neurological criteria but did not standardize the neurological criteria that should be used.

### 6. 1990s—American Academy of Neurology Practice Parameters and criticisms

In 1994, the American Academy of Neurology undertook the mission to finally standardize the neurological criteria. Elco Wijdicks, a neurointensivist, led the mission. Practice Parameters were published the following year [50]. The 3 cardinal findings in brain death were to be “coma or unresponsiveness, absence of brainstem reflexes, and apnea.” A protocol for completing the apnea test was

spelled out, and the role of “confirmatory tests” was also clarified: “A confirmatory test is not mandatory but is desirable in patients in whom specific components of clinical testing cannot be reliably performed or evaluated.” Wijdicks would later come out against confirmatory tests because they gave the false sense of an underlying neuropathological correlate, an impression created by the autopsy studies in the 1960s [51]. In 2010, Wijdicks updated the Practice Parameters to allow greater uniformity [52].

Throughout the 1990s, however, criticisms about the report from the President’s Commission persisted. First, although it promoted a “Whole Brain” formulation, meaning loss of *all* brain functions, still some functions, such as hypothalamic-pituitary responses, were inexplicably allowed. Defenders argued that persistence of isolated activity of the neuroendocrine axis was irrelevant and, in any case, could be explained by its extracranial blood supply [44]. Second, the Commission’s main argument was that whole brain death equaled death because, afterwards, the body ceased to be an “integrated organism” and rapidly became a disintegrating collection of organs. However, by then, it was clear that brain-dead patients can show several levels of somatic integration; they did not necessarily “dis-integrate” as promised [53,54].

And then there was the problem of language. *Brain death* has always been problematic. This was recognized from the beginning. “Death is what we are talking about,” Joseph Murray argued, “and adding the adjective ‘brain’ implies some restriction on the term as if it were an incomplete type of death.” [26]. The term also implies death of “the brain,” that is, death of the cells and tissues constituting the brain rather than death of the human being. Some argued that even the single word *death* was inadequate [55].

### 7. 2000s—back to the drawing board

In November 2007, another President’s Council on Bioethics was created to address some of these lingering concerns. Their white paper was appropriately called “Controversies in the Determination of Death” [56]. First, it discarded the ambiguous term *brain death*, replacing it with the philosophically neutral term *total brain failure*. Second, it challenged the various conceptual arguments for brain death advanced over the years and admitted the limitations of the integrative unity position. It then put forward a novel argument that equated death with the “cessation of the fundamental vital work of a living organism—the work of self-preservation.” There is an inner drive for life, the Council posited, that is “achieved through the organism’s need-driven commerce with the surrounding world.” For human beings, this “commerce” is manifested by the drive to breathe combined with consciousness. Total brain failure equals death because the “organism can no longer engage in the essential work that defines living things.” Although seen as a thoughtful and reasoned analysis, not everyone was convinced [57,58].

### 8. The present

That the boundary remains shadowy and vague, at least in the public’s mind, was made painfully obvious last year. On December 12, 2013, physicians at Children’s Hospital in Oakland, CA, pronounced 13-year old Jahi McMath brain dead following complications from a tonsillectomy. Her parents refused to accept it and obtained a restraining order to prevent the hospital from disconnecting her from a ventilator. A court-appointed neurologist confirmed brain death according to the neurological criteria defined in the American Academy of Neurology Practice Parameters. Nevertheless, the court mediated an agreement to transfer Jahi to a facility to continue supportive care.

The concept of death evolved as a result of several parallel developments, transitioning from the traditional cardiopulmonary definition to a brain-based definition of death. And our understanding of that brain-based definition has also evolved since 1968. Still, brain

death continues to be a difficult concept to understand especially for a layperson; the conceptual and philosophical arguments about the nature of death are too far removed from a parent's experience sitting at the bedside of a comatose child. Even most of the experts, in a recent survey of board-certified neurologists, did not have a consistent rationale for accepting brain death as death [59]. As we move forward with advances in resuscitation and critical care, a thorough knowledge of the background, history, and context of the development of brain death is necessary for fully understanding the current meaning of brain death.

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