

BRAIN DEATH

Third Edition

EELCO F.M. WIJDICKS

OXFORD

Brain Death

THIRD EDITION

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ADVANCE PRAISE FOR *BRAIN DEATH,* *THIRD EDITION*

“Dr. Wijidicks’ latest edition of his book on Brain Death is outstandingly authoritative. As the undisputed world authority on the subject, Dr. Wijidicks provides a comprehensive and comparatively unbiased understanding of brain death, from its important conception and legalization to modern approaches, worldwide practice and ethical and legal issues that surround the entity. It is packed with useful tables, as well as helpful video clips that illustrate key findings and educate the reader. In an era where there seems to be increasing controversy about this subject, the book is timely and definitive, and should serve as a strong reference for both clinicians and the lay public alike.”

—**David M. Greer, MD, MA**, Professor of Neurology,
Yale University School of Medicine, New Haven, CT

“One of the multiple requirements for successful organ donation and transplantation is a robust and comprehensive understanding and application of brain death principles. Once again Eelco Wijidicks contributes greatly to the medical community with this definitive resource on this subject.”

—**Susan Gunderson, MHA**, Chief Executive Officer,
LifeSource, Minneapolis, MN

“Dr. Wijidicks is the world’s leading authority on brain death. He continues to advance the knowledge base while honoring the historical context of the brain death concept. This is the definitive resource for all aspects of brain death determination and its intricate relationship to organ donation. If you know very little about brain death, you should read this book. If you think you know a lot about brain death, you should still read this book. The section on clinical problems and common clinical questions is an extremely useful practical guide to managing common complexities of clinical practices in this field.”

—**Sam D. Shemie, MD**, Division of Critical Care Medicine,
Montreal Children’s Hospital,
McGill University Health Centre & Research Institute,
Montreal, Canada

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PREFACE TO THE THIRD EDITION

The clinical diagnosis of brain death requires considerable time and effort and a calibrated approach by capable physicians. The clinical evaluation often comes with a query, an uncertainty, and sometimes even trepidation. A continuously updated and comprehensive work is needed to assist in intensive care unit practices—because the main purpose of establishing the clinical diagnosis of brain death is to bring closure. The declaration of brain death has tremendous implications. The diagnosis of brain death is a legally accepted way of determining the person's death. Once declared, organ transplantation can be considered or care can be withdrawn when there is no consent to preserve organs. The medical profession and its medical organizations consider brain death the death of the individual. I have made my argument regarding brain death determination before and have updated it since the last edition published in 2011.

This book is a practical work, and the core of the text combines the theory and practice of brain death determination. The many perplexities of brain death are examined, therefore the book includes chapters on cultural beliefs, bioethical concerns, and many of the issues associated with organ transplantation.

There are those who would claim that the definition of death cannot be based simply on medical judgment, but should be based on philosophical, religious, and other conceptional categories. Some scholars opine on the basis of theoretical analysis and claim death after catastrophic brain injury is unknowable. Moreover, this new edition arrives at a time when some U.S. courts have recently reconsidered the clinical validity of brain death. None of the challenges have been successful—and certainly not meritorious—but they come up from time to time in the United States and elsewhere.

This new edition introduces considerable new information. It includes discussions on recent court cases and disputations, introduces new research on brain death in the intensive care unit, presents newly unearthed historical data on important differences between UK and US in determining brain death, and provides a thorough discussion of U.S. guidelines and how they

are used in hospital practices and, in a new chapter, a comparison of U.S. guidelines with guidelines elsewhere in the world. It becomes rapidly clear that countries are not on the same page technically but are similar enough in clinical examination. Moreover, in recent years, some of these anticipated problems may have been exacerbated by a lack of training. Organ procurement coordinators consistently report lack of training and lack of adequate conversation to families by involved physicians. There is a sense that education of physicians can be improved, thus teaching brain death determination through complex simulation scenarios is discussed in the book. Several chapters have been revised and refined. I have added more clinical problems and solutions in the final chapter. This edition includes 12 online video clips related to common issues with the interpretation of neurological examination and apnea test.

This book is an outgrowth of the American Academy of Neurology (AAN) practice guideline first published in 1995 and revised in 2010. The AAN guideline is the only comprehensive document in the United States on the determination of brain death; recently the Society of Critical Care Medicine, American College of Chest Physicians, and Association of Organ Procurement, in a consensus statement, recommended that organizations, hospitals, and government entities incorporate these guidelines (*Crit Care Med* 2015;43:1291–1325). Nevertheless, the fruits of decades of clinical research and practice has influenced my approach to this topic and has made this book.

In many instances the diagnosis of brain death concludes with organ and tissue donation and a sense of resolution. This book therefore forays into the practice of procurement. I hope it will give organ procurement officers not only a detailed grounding but also a comprehensive overview of how to resolve conflicts and quandaries. A Checklist pocket card to assist with the documentation of brain death at the bedside is available after emailing the author at Wijde@mayo.edu. I hope this book is useful to neurologists, neurointensivists, neurosurgeons, anesthesiologists, trauma surgeons, pediatric intensivists, and neuroscience and intensive care nursing staff.

EFMW

PREFACE TO THE SECOND EDITION

This book is about a neurologic condition that legally defines death. The clinical criteria of brain death have been well defined and many hospitals, certainly those with a Level 1 Trauma Center designation, have a protocol in place. In a sense therefore its diagnosis is an incontrovertible fact and virtually all practicing physicians would agree. Much has been written about this clinical state and advances have been made in clinical research. Therefore, one of the principle aims of this book is to compress an amazing amount of scholarship, opinions and clinical research into one small volume. Another aim is to present a practical book that can be used at the bedside. This completely rewritten book is a work of primary source research and includes work published in recent publications. I have retained sections and chapters I wrote in the prior edition but greatly expanded and updated them. Mayo Clinic now has detailed data over 300 cases of brain death determinations and many were seen personally.

There are several new features in this book and it includes a discussion of the development of criteria of brain death using new research of documents from the Harvard Committee. The book also expands on the current criteria of countries used throughout the world and highlights the—often inexplicable—differences. There is a comprehensive discussion of the new 2010 American Academy of Neurology guidelines on determining brain death.

I began this book with the proposition that brain death not only means a nonsapient state but death, and this book displays a hard core of common sense in setting it out. Brain death has undeniable fascination and some scholars find the diagnosis of brain death inaccurate. This monograph takes no part in sensationalism and quasi-certainties but brings to the fore a few of the polarities in analysis of the subject matter. Any definition of death progresses through controversy. Most recently a white paper has been published by the President's Council on Bioethics summarizing view points that have been perceived by some as concerning. Without necessarily being a critic of critics, one chapter is devoted to these arguments and, after I read

all that has been said, I approach the topic commonsensical in order to cut through a vast array of philosophical positions.

The complexities of the clinical diagnosis and evaluation of potential pitfalls in brain death remain substantial. As befits such an important topic, I believe the reader would benefit from discussion of common practice problems. I have added 25 commonly asked practice problems when dealing with the neurological examination and management of organ donors. This book will not only help readers to review knowledge on brain death but its main feature is to provide a clinically useful text for practitioners seeing patients with acute catastrophic neurologic disorders evolving to brain death. I hope it will appeal to neurologists, neurointensivists, neurosurgeons, anesthesiologists, trauma surgeons, neuroscience and intensive care nursing staff, transplantation surgeons, and organ procurement organizations.

EFMW

ACKNOWLEDGMENTS

Sources for this book came from many angles. I thank the numerous physicians and healthcare workers who over the years called and e-mailed me with searching questions on the diagnosis of brain death and its potential pitfalls. Many of these questions led to a good deal of thinking, and they are the basis of the clinical problem section deconstructed in this book. I learned much over the years by spending considerable time in our neurosciences intensive care unit, and I appreciate the care of the nursing staff and that they always have to carry this heavy load. I am grateful to them and to our organ transplantation agency, Life Source. Cathy Dudley is intimately involved in the care of organ donors and their families and has been a great help in maintaining an unyielding separation between practice and procurement.

The illustration (representing a brain and its connection with giving) is artfully designed by the incomparable Jim Rownd, who has done many of my book covers. I appreciate the expert video work by Timothy Seelinger, James Jamieson, and Steven Holets. A special thanks to Lea Dacy for doing all the work needed to complete the book and especially for critical editing.

I am again very impressed by the professionalism of everyone associated with Oxford University Press (Amy Whitmer and my long-standing editor, Craig Panner). I greatly value the publisher's continued commitment to produce my books.

On a personal level, I own a great debt of gratitude to my family—my wife, Barbara, and my children, Coen and Marilou—my greatest good fortune.

In modern times, brain death cannot be seen without considering the possibility of organ or tissue donation. I therefore dedicate this book to all families who faced the worst loss but gained by giving life to others.

EFMW

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CHAPTER 1

History of Brain Death

It is seldom remembered that it took many thousands of years to link the brain to the mind. The cardiocentric view prevailed in antiquity, and the unimportance of the brain can be inferred from the practice of the Egyptian embalmers, who commonly removed the brain by trephining the orbit. The brain was discarded, unlike viscera, which were buried with the dead. The Egyptians did not know what the brain was for—as far as they were concerned, intellectual activity took place in the heart.

The physicians who followed Hippocrates can be credited with connecting the brain to the mind. It is difficult to say where this thought started, but Herophilus of Chalcedon (circa 300 BC), after performing human dissections, emphasized that the brain transmitted motor impulses from the soul to the extremities through nerves. There was fierce opposition by Aristotle, who maintained the central position of the heart. The embryo developing within an egg had a beating heart as the first sign of life; thus, Aristotle argued its physiological primacy. He theorized that the naturally cold brain served as a refrigerator to cool the blood's heat and to adjust the organism as a whole. Galen (circa 160 AD) discovered that perception and cognition were affected by brain injury and delineated the cranial nerves. It was only in the 1600s that Thomas Willis further differentiated the cerebral functions and championed neuroanatomy, culminating in his work *Cerebri Anatome*.

The one certain point is that the brain in humans originated from a more primitive but essential brainstem structure with proportionate increases in the volume of the neocortex when species evolve. We learned that consciousness, personality, insights, perception, motion, emotion, memory, learning, language, and things we do every day all originate in the thinking parts of the brain.

Coma (and its clinical neurological evaluation) only gradually emerged in the neurological lexicon.¹² Until the mid-twentieth century, severe brain injury led to respiratory arrest because of the inability to keep an open upper airway and often simultaneous insufficient respiratory drive. Circulatory and cardiac arrest soon followed after collapse of the blood pressure in an apneic, cyanotic patient. After the introduction of the mechanical ventilator and, in particular, endotracheal intubation, comatose patients could be adequately supported. This unprecedented intervention in patients with a massive brain injury resulted in the arrival of a new neurological condition. This neurological state was characterized by coma, irreversibly absent brainstem reflexes and apnea, uncontrolled diuresis, and loss of vascular tone. With the additional absence of electroencephalographic (EEG) tracings and profound brain necrosis at autopsy, this state became known as brain death. With this additional definition of death, however, clinical criteria had to be developed, although good understanding already existed among neurologists about the meaning of this state. Henry Beecher, chairman of the Harvard Ad Hoc Committee to Examine the Definition of Brain Death, said that “we should, first, abandon the ancient sign of death—the cessation of the heartbeat.”¹ This chapter chronicles the development of these neurological criteria in the United States. This chapter mostly focuses on the medical side of it and not the legal wrangling. Development in other countries—as far as is known—is described in Chapter 3. In the United States, the initial attempt to determine death based on neurological criteria is often attributed to the 1968 Harvard criteria,¹ but the first steps toward using loss of cerebral function to define death actually began a decade earlier.²⁶

DEFINING NEUROLOGICAL CRITERIA FOR DEATH

One of the earliest articles to describe brain death was in 1956 by Löfstedt and von Reis, who reported on six mechanically ventilated patients with absent reflexes, apnea, hypotension, hypothermia, and polyuria.¹⁴ Cerebral blood flow, determined by angiography, was absent. However, death was declared following cardiac arrest, which occurred in 2 to 26 days. Cerebral necrosis was present at autopsy in all cases.

The more serious literature on brain death determination started in France and with 2 major articles in 1959. Wertheimer, Jouvét, and Descotes were among the first to propose criteria for these new clinical states (“A propos du diagnostic de la mort système nerveux . . .”)²⁴ (Figure 1.1). Wertheimer and Descotes were both neurosurgeons treating major traumatic brain injury and Jouvét was a neurologist. This article largely focused, like many before it, on the significance of the isoelectric EEG, but it also documented shutting off the ventilator to stimulate the respiratory centers while increasing respiratory acidosis. Absent medulla

**A PROPOS DU DIAGNOSTIC
DE LA MORT DU SYSTÈME NERVEUX**

**Dans les comas avec arrêt respiratoire
traités par respiration artificielle**

PAR MM.

P. WERTHEIMER, M. JOUVET et J. DESCOTES

(Lyon)

L'usage de plus en plus répandu de la respiration artificielle ou de la respiration assistée permet de remédier aux syncopes respiratoires survenant chez des malades porteurs de lésions encéphaliques, tumorales ou traumatiques. L'étiologie de ces apnées prolongées est multiple: elles s'observent chez des traumatisés graves, soit immédiatement, soit au contraire plus tardivement, et, dans ce dernier cas, elles sont souvent le fait d'un changement de position ou d'un accident d'aspiration ou de réanimation. Ces apnées prolongées, en rapport avec l'atteinte des structures nerveuses, peuvent être réversibles dans certains cas heureux et nous avons pu en rapporter deux cas dont un suivi de guérison (thèse de A. Jeunet, Lyon 1957). Parfois, cependant, aucune reprise de respiration spontanée ne s'annonce comme cela fut le cas pour quatre malades dont le tableau clinique semblable mérite d'être rapporté.

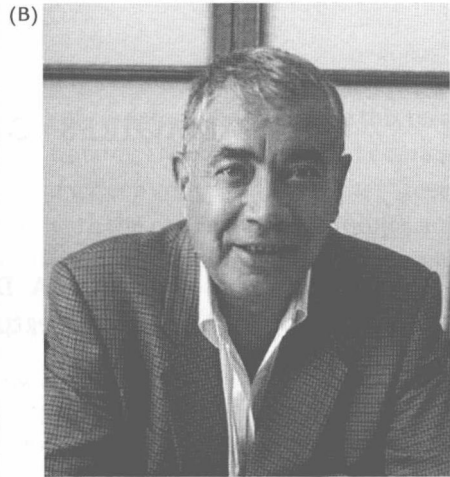
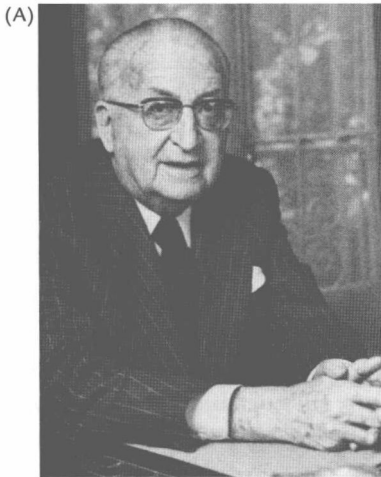


Figure 1.1 Cover page of article on “death of the nervous system” (La mort du système nerveux), main authors Pierre Wertheimer (A) and Michel Jovet (B).

oblongata function was further confirmed with no change in pulse rate with carotid compression, ocular pressure, and intravenous injection of atropine and amphetamine. Wertheimer’s et al. article, although introducing new findings, did not clearly distinguish their clinical state (despite calling it “death of the nervous system”) from other neurological conditions. Several months later, in 1959, neurologists Mollaret and Goulon published an article entitled “Le coma dépassé,” which more comprehensively defined death based on neurological criteria.¹⁷ It was an extension of earlier anecdotal observations of comatose patients with isoelectric EEG recordings, absent intracranial flow, or total or near-complete brain necrosis at autopsy.

Mollaret and Goulon's article is considered a signature piece in the development of clinical criteria of death by neurological standards (Figure 1.2).¹⁷ The authors presented 23 cases from the Claude Bernard Hospital in Paris with a new type of coma they called *coma dépassé*—coma that went well beyond (*dépassé*) the deepest comas so far described. It is best translated as “irretrievable coma” (M. Goulon, personal communication), but currently French physicians translate it as “brain death.” Although both authors (Figure 1.3) used the term in their hospital service for several years before publication, they were dissatisfied with it. In fact, they encouraged readers to propose a better term.¹⁷ The article by Mollaret

REVUE NEUROLOGIQUE

MEMOIRES ORIGINAUX

LE COMA DÉPASSÉ (MEMOIRE PRÉLIMINAIRE)

PAR MM.

P. MOLLARET et M. GOULON

Après quatre années de réflexion, nous croyons venu le moment d'ajouter un chapitre nouveau au domaine traditionnel des comas.

Précisons de suite que ce problème du coma dépassé a été mis, l'année dernière, au programme de la prochaine Journée de Réanimation de l'Hôpital Claude-Bernard du 7 octobre 1959, en vue d'une mise au point intégrale.

La présente communication, qui n'a ainsi qu'une valeur préliminaire, peut être offerte, peut-être, en hommage à la XXIII^e Réunion Neurologique Internationale, qui a accepté de tenir une de ses séances dans le Centre de Réanimation où fut élaboré ce travail. Précisons également que le coma dépassé a déjà conquis droit de cité dans l'important volume qui vient de paraître de H. Fischgold et P. Mathis (*Obnubilations, comas et stupeurs*, Masson édit., Paris, 1959, p. 5 et pp. 51-52) ; nous remercions ces auteurs d'être venus se faire présenter les premiers malades et d'avoir donné place à quelques-uns de nos documents.

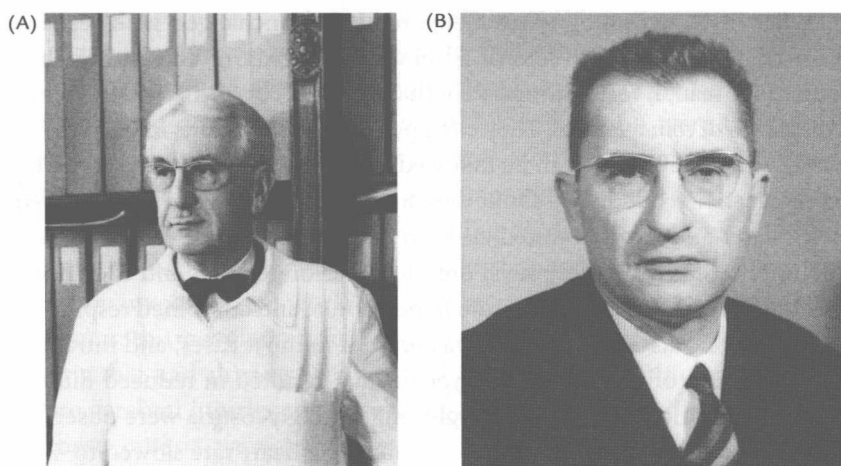


Figure 1.3 Neurologists (A) Pierre Mollaret and (B) Maurice Goulon.

and Goulon is a landmark for a number of reasons. For one thing, it distinguished *coma dépassé* from other types of comatose states. Before this term was introduced, French neurologists, notably Déjérine, classified coma as *coma leger* (“light coma”), *coma profond* (“deep coma”), *coma carus* (“deepest coma,” with reflexes abolished but with the patient still breathing), and *coma vigil* (“vegetative state”). Mollaret and Goulon’s new term, *coma dépassé*, would be another category.

Mollaret and Goulon correctly asked the most critical ethical questions: Do we have the right to stop resuscitation using criteria that attempt to define the boundary of life and death? Does life support have to be maintained as long as the heart beats and perfuses vital organs? How about the religious position? Professor Goulon felt that *coma dépassé* was a disturbing condition for an observer, and it led him to question “where the patient’s soul dwelled” (M. Goulon, personal communication).¹⁰

In addition to their foresight regarding future ethical quandaries, Mollaret and Goulon presented a well-documented description of brain death, although they did not call it that way or even *mort cérébrale*. In retrospect, their article’s details of the neurological examination are striking. *Coma dépassé* was said to be characterized by immobility of the eyeballs in a neutral position, mydriasis, absent light reflex, absent blinking with stimuli, absence of swallowing reflexes, drooping of the jaw, absence of motor responses to any stimuli, muscle hypotonia, tendon areflexia, equivocal plantar reflexes, absence of spontaneous respiration after discontinuation of ventilation, immediate cardiovascular collapse as soon as vasopressors are stopped, and a disturbance of thermoregulation with a core temperature, which depends on the environmental temperature.