

## THE CLINICAL CRITERIA OF BRAIN DEATH THROUGHOUT THE WORLD\*

EELCO F.M. WIJDICKS

The use of neurological criteria of death rather than cardiorespiratory criteria of death is a fascinating chapter in the history of medicine and neurology [1]. This paradigm change came when patients with an acute brain injury could be resuscitated in emergency departments and intensive care units and survived. Apnea would not lead to asystole and the brain lesion could go on to further cause catastrophic damage while the rest of the body was artificially supported. In most cases this resulted in development of brain edema, shift, and eventually massive increase in intracranial pressure that would stop the blood flow at the entrance of the skull base. This would then result in total necrosis of the brain. In other situations, brain and brainstem would become destroyed directly (e.g., encephalitis, intoxications).

Pathologists noted a necrotic brain never seen before ('respirator brain') but there was no good clinical correlate, only fragmentary observations. Most likely, an isoelectric EEG was the first clinical observation that the brain has lost its function – 'Isoelectric EEG with a Heartbeat' [2]. The recognition of loss of all brainstem reflexes including apnea was first described in a comprehensive manuscript by Mollaret and Goulon [3]. This paper was hardly noticed at the time, but should now be considered a landmark paper. It was followed almost 10 years later by 'the Harvard Criteria' written by an Ad Hoc committee in 1968, consisting of representatives of several Harvard schools. Symposia were organized in Sweden, the United Kingdom, and Australia that tried to formulate brain death on the basis of neurologic criteria. Brain death examination became a prerequisite to allow organ donation and its concept has been fully accepted. However, until recently, it was largely unknown how brain death criteria had been codified in different parts of the world. In this paper, I will discuss the results of a recent survey [4].

\* The views expressed with absolute freedom in this paper should be understood as representing the views of the author and not necessarily those of the Pontifical Academy of Sciences. The views expressed in the discussion are those of the participants and not necessarily those of the Academy.

*The Gold Standard*

The Harvard Committee, appointed by the Dean of the Harvard Medical School and chaired by anesthesiologist Henry Beecher included multiple specialties including a transplant surgeon and transplant immunologist [5]. Their presence has been criticized by some and conflict of interest has been suggested. The guideline was written mostly by the neurologists Schwab and Adams, who in only a few drafts within four months completed an important document that included neurologic evaluation of the patient with no brain function. There was a desire to produce a brief but succinct document but also to work swiftly because of a pressing need in the community to provide guidelines. The transplant physicians commented on this document but left the final say to the neurologists. The document was also important because for the first time it clearly mentioned the confounding effect of CNS depressants and hypothermia. The Harvard criteria remain an example of simplicity.

The criteria were as follows.

1. Unreceptivity and unresponsivity.
2. No movements or breathing.
3. No brainstem reflexes.
4. Flat electroencephalogram.
5. With all of tests repeated at least 24 hours with no change and exclusion of hyperthermia (below 90° degrees F or 32.2°C) or central nervous system depressants.

There have been modifications to the clinical examination of the brain dead patient. Undoubtedly, the influential paper by the Harvard Ad Hoc Committee has been the basis of many hospital policies throughout the United States of America.

A few years later, the conference of Medical Royal College in the United Kingdom further defined criteria by describing further details on brainstem examination and determined a target for PaCO<sub>2</sub> to assess breathing drive. This influential document also determined that the brainstem is the main part of the brain to be tested and lead to the term 'brainstem death'. It is noticeable that the somewhat subtle differences between the UK and the US criteria permeate throughout the world, particularly in those countries that were prior colonies of the UK (eg. India)[4]. Much of the work on brain stem death in the United Kingdom should be credited to Pallis [6].

*Brain Death Criteria throughout the World*

I had the opportunity to survey the brain death throughout the world. Through helpful neurologists and neurosurgeons and other physicians, I was able to obtain the original brain death documents of 80 countries throughout the world, representing all major continents (Table 1). There is global acceptance of the concept of brain death. There are no concerns with the validity of the concept and physicians all over the world recognize – without a scintilla of doubt – that when the clinical criteria of brain death are met, the patient has died. However there were major differences in the technical procedures used to arrive at the clinical diagnosis. No major differences were noted when the methods of examination of brainstem reflexes were compared with each other; but there were marked differences in how the apnea test was performed. The presence of apnea using a PaCO<sub>2</sub> target value was used in only 59% of all guidelines. In others, preoxygenation with 100% oxygen followed by 10 minutes disconnection was deemed sufficient. There was no evidence that the insufficient apnea testing was a result of failure to obtain timely arterial blood gasses or a general reluctance to do the test. In Central and South America countries, a large proportion of patients were either examined with disconnection from the ventilator only, or criteria or guidelines for the apnea test were not present. This is potentially concerning because apnea can only be determined after

TABLE 1.

<i>Surveyed Countries (No. of countries)</i>	
United States of America	
Canada	
Caribbean	(4)
Central and South America	(13)
Europe	(29)
Africa	(5)
Middle East	(9)
Asia	(16)
Oceania	(2)

introducing acute hypocarbia resulting in CSF acidosis that in turn maximally stimulates the respiratory centers. Ten minutes disconnection in a patient with a baseline hypocarbia (not uncommon after induced hyperventilation for increased ICP) could potentially show apnea with a PaCO<sub>2</sub> not reaching a target value.

The number of physicians required to diagnose brain death varied significantly throughout the world. In 44%, one physician was required (including Canada); 34%, 2 physicians; and 16%, more than two physicians. In 6%, the number of physicians was not specified. Confirmatory tests were required in 40% of the 80 nations of the world. The complexity of criteria did not seem to be influenced by cultural differences. There was no difference between Eastern and Western civilizations, and the differences were largely already apparent in one single continent. In some countries, an academic grade was needed to perform the test (associate professor level).

The type of confirmatory tests and the need for confirmatory tests has been different throughout many countries. The choice of confirmatory tests seems to be very arbitrary, with Sweden as a notable exception. In this country, a cerebral angiogram has to be performed twice with an adequate period of observation in between documenting an absent of flow to the brain [4]. Surprisingly, in many countries stricter criteria (confirmatory test) were present when organ donation was considered. This is a common qualifier in guidelines throughout the world.

### *Remaining Concerns*

In at least half of the surveyed nations in the world and in several US States, confirmation of brain death requires examination by a second physician. This remains very reasonable, but there is no data to suggest criteria should go beyond two physicians. However having two physicians available in order to determine brain death may lead to logistic problems, but, in most modern neurological intensive care units, this could be done by a designated neurologist or neurointensivist, a neurosurgeon, or anesthesiologist. The documentation of absence of respiratory drive remains essential in the diagnosis of brain death. Although the outcome is likely similar, the apnea testing should not be deferred. Documentation of destroyed respiratory centers is the most important test of medulla oblongata destruction; however, it almost always coincides with marked hypotension. Loss of medulla oblongata function results in loss of vascular tone

that only temporarily can be supported with high and incremental doses of vasopressors and vasopressin.

It should be emphasized that in many civilized countries the cultural attitudes and religious attitudes are very supportive towards brain death and organ donation. There is no evidence to suggest that cultural values play a major role in further complicating the determination of brain death such as multiple observations, multiple confirmatory tests, with multiple physicians. It may simply be a consequence of collective decisions of task forces. Variability among hospital policies may also be present and was recently documented by Posner [7]. We can easily assume that similar differences can be found throughout the world when different hospital policies would have been surveyed. There also is a lingering concern on the accuracy brain death documentation. A study by Wang [8] from the University of California examined patients declared brain dead at Los Angeles County General Hospital and found there were major problems with chart documentation. Cornea reflex was not documented in 43% of the cases, and motor examination was not documented in 34% of the patients. It remains unclear whether this is truly a problem of documentation or a lapse in performing a clinical examination of brain death. The organ donation procurement organizations may play an important role in fact checking these examinations. The accuracy of documentation of brain death in countries outside the US is not known.

When reviewing the complex guidelines of brain death determination and preparation for organ donation, one can only conclude that consensus is needed. This would require a task force that reviews the data and provide evidentiary tables. Acceptance of uniform criteria of brain death would then lead to a more uniform policy for brain death determination. Many countries have come to their own judgment in how to solidify these criteria. Usually special committees have been formed but the members of the committee may not always have been most qualified, active practitioners or major specialties have been missing. Complicating the diagnosis with additional laboratory tests must have been driven by a concern that inaccurate assessment of these fatally injured patients may occur. However, more physicians and more confirmatory tests cannot solve that. What remains needed is appropriate education of staff, introduction of checklists in intensive care units, and brain death examination by designated neurologists who have documented proficiency in brain death examination. A qualifying examination should be considered.

### *Conclusions*

There is broad medical and legal acceptance of the concept of brain death throughout the world. The acceptance of brain death and organ donation permeates throughout countries with different religious values. All major religions have embraced this concept and it allows organ donation (the ultimate gift of life). There are procedural differences that could delay declaration of death and a consensus should be desirable.

### REFERENCES

1. Wijdicks E.F.M, *Brain Death*, Philadelphia: Lippincott Williams & Wilkins, 2001.
2. Wijdicks E.F.M., The neurologist and Harvard criteria for brain death, *Neurology* 2003;61:970-976.
3. Mollaret P., Goulon M., Coma Depasse, *Rev Neurol (Paris)* 1959;101:3-15.
4. Wijdicks E.F.M., Brain death worldwide: accepted fact but no global consensus in diagnostic criteria, *Neurology* 2002;58:20-25.
5. A definition of irreversible coma, Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death, *Jama* 1968;205:337-340.
6. Pallis C., ABC of brain stem death. The position in the USA and elsewhere, *Br Med J (Clin Res Ed)* 1983;286:209-210.
7. Powner D.J., Hernandez M., Rives T.E., Variability among hospital policies for determining brain death in adults, *Crit Care Med* 2004;32:1284-1288.
8. Wang M.Y., Wallace P., Gruen J.P., Brain death documentation: analysis and issues, *Neurosurgery* 2002; 51:731-735; discussion 735-736.