Brain death worldwide: Accepted fact but no global consensus in diagnostic criteria

Eelco F.M. Wijdicks
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Eelco F.M. Wijdicks, MD

Abstract—*Objective*: To survey brain death criteria throughout the world. *Background*: The clinical diagnosis of brain death allows organ donation or withdrawal of support. Declaration of brain death follows a certain set of examinations. The code of practice throughout the world has not been systematically investigated. *Methods*: Brain death guidelines in adults in 80 countries were obtained through review of literature and legal standards and personal contacts with physicians. *Results*: Legal standards on organ transplantation were present in 55 of 80 countries (69%). Practice guidelines for brain death for adults were present in 70 of 80 countries (88%). More than one physician was required to declare brain death in half of the practice guidelines. Countries with guidelines all specifically specified exclusion of confounders, irreversible coma, absent motor response, and absent brainstem reflexes. Apnea testing, using a PCO_2 target, was recommended in 59% of the surveyed countries. Differences were also found in time of observation and required expertise of examining physicians. Additional provisions existed when brain death was due to anoxia. Confirmatory laboratory testing was mandatory in 28 of 70 practice guidelines (40%). *Conclusions*: There is uniform agreement on the neurologic examination with exception of the apnea test. However, this survey found other major differences in the procedures for diagnosing brain death in adults. Standardization should be considered.

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"Brain death" is the vernacular expression for irreversible loss of brain function. Brain death is declared when brainstem reflexes, motor responses, and respiratory drive are absent in a normothermic, nondrugged comatose patient with a known irreversible massive brain lesion and no contributing metabolic derangements. The determination of brain death in adults has become an integral part of neurologic and neurosurgical practice but may include physicians of any specialty. Institutional policies and legal provisions are in place in the United States and elsewhere.[1,2]

Many major publications have discussed the guidelines in several nations of the world.[2,3] Moreover, one study surveyed 28 countries outside the United States specifically for legal rulings and type of confirmatory test.[4] Recently a survey in Europe involving 12 countries addressed differences in criteria,[5] and the authors proposed to develop a clear set of criteria in the European Union.

The code of practice throughout the world is not widely known. Here the results of a survey of brain death guidelines throughout the world are provided and relevant differences are considered, noting countries without formal guidelines.

Methods. The National Library of Medicine's search service (PUBMED) was used to identify published articles addressing brain death criteria from 1968 to 2000. The criteria from official documents were tabulated and summarized. In addition, the directory of the American Academy of Neurology was used to ask international members through a personal letter to submit published guidelines. The Congress of Neurologic Surgeons Directory was used to contact international members to complete several missing countries throughout the world. Personal letters were sent to physicians in 107 countries. In addition, foreign physicians at the Mayo Clinic were contacted by e-mail to provide contacts with neurologists from their homeland. Simple questions were asked. Is there a legal provision of organ transplantation and brain death in your country? What are the specific guidelines, mandatory qualifications of the physicians, number of physicians needed to declare brain death, time of observation, and need for confirmatory laboratory tests? Some documents were reviewed with the Legal Department at the Mayo Medical Center.

Results. The United Nations lists 189 member states. Data on adult brain death criteria in 80 countries (42%) were obtained and are shown in the table. European, South American, and Asiatic countries are well represented. The United Kingdom criteria for brainstem death

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From the Department of Neurology, Neurological and Neurosurgical Intensive Care Unit, Mayo Medical Center, Rochester, MN.

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Address correspondence and reprint requests to Dr. Eelco F.M. Wijdicks, Department of Neurology (W8B), Mayo Clinic, 201 First Street SW, Rochester, MN 55905; e-mail: wijde@mayo.edu

permeate in the previously colonized countries, and Central and South American countries generally follow the United States position on whole brain death.

Countries with brain death guidelines typically specify exclusion of confounders, irreversible coma, absent motor response to pain stimulus, and the absence of all brainstem reflexes. Official legal standards on organ donation were present in 55 of 80 countries (69%). Brain death guidelines or codes of practice were present in 70 of 80 surveyed countries (88%). To make a definitive diagnosis, one physician was required in 31 guidelines (44%), two physicians in 24 guidelines (34%), and more than two physicians (as many as four) in 11 guidelines (16%). The number of physicians was not specified in four guidelines (6%; see the table). All the recommended guidelines required strict definition of brainstem reflexes, but the presence of apnea using a PCO_2 target value was recommended in only 41 guidelines (59%). Preoxygenation with 100% oxygen followed by 10 minutes of disconnection, with clinical examination for apnea required in 20 of 71 guidelines (29%; see the table). Confirmatory laboratory tests were often mandatory in Europe and Asia. In addition, confirmatory laboratory tests were commonly used to shorten the recommended observation time. Confirmatory tests were not required in many developing countries. (This is probably because these technologic devices were not available on a timely basis.) The observation period for a brain-dead body before final diagnosis was established varied markedly (see the table). The most striking differences in guidelines for the determination of brain death are summarized here per continent.

Criteria in the United States and Canada. The Uniform Determination of Death Act in the United States mandates irreversible cessation of all functions of the entire brain and brainstem. It has been accepted by 44 states and the District of Columbia.[6] The US states have comparable statutes but differences are notable. Virginia specifically calls for a specialist in the neurosciences.[7] Florida mandates two physicians; one must be the treating physician and the other must be board-eligible or board-certified neurologist, neurosurgeon, internist, pediatrician, surgeon, or anesthesiologist.[8] In addition, New York and New Jersey have changed their statutes to accommodate religious objections.[9,10] These amendments require physicians to honor these requests and to continue medical care despite evidence of loss of brain function. One physician determination is sufficient in most states, but statutes in California, Alabama, Iowa, Louisiana, Florida, Virginia, Kentucky, and Connecticut require independent confirmation by another physician. In Alaska and Georgia, a registered nurse is delegated authority to declare death according to the statutory criteria, but with subsequent certification by a physician within 24 hours. In Virginia, there is limited authority given to a registered nurse.[11]

The American Academy of Neurology published practice parameters in 1995.[12] Irreversible loss of whole brain function, as determined by any physician, has been legally justified in Canada,[13] and in 2000 the Canadian Neurocritical Care Group published Guidelines for the Diagnosis of Brain Death that closely mirror the American Academy of Neurology guidelines.[14]

Criteria in Central and South America. Official guidelines have been established in many Central and South American countries. However, there is generally a lack of clear description of the apnea test. Confirmatory tests are optional in the majority of surveyed countries.[15-19]

Criteria in Europe. There is fairly uniform agreement in Europe regarding the criteria for the clinical evaluation of brain death, although there is considerable variation in the use of additional physiologic tests. Eleven of 25 guidelines require a confirmatory test for the diagnosis, and in the remaining countries it "facilitates" the diagnosis. Half of the countries surveyed require that more than one physician be involved in the clinical determination. In Ireland, two sets of tests should be performed by a consultant and a physician with >5 years' appointment engaged in patient care at the acute hospital level. Several countries have longer observation periods when "anoxia" has been the cause of brain death. For example, in Hungary "secondary brain damage" extends observation time to 72 hours.[5,20-35]

Many European countries require apnea tests with provisions of disconnection of ventilator using stimulation of the respiratory centers with acute hypercarbia. The UK criteria require a 20-mm Hg increase from normal PCO_2 baseline or PCO_2 target of 50 mm Hg.[35]

In Turkey, an organ harvesting law has been established and demands a cardiologist, a neurosurgeon, a neurologist, and an anesthesiologist to examine the patient followed by confirmatory testing, often requiring a combination of laboratory tests.[36]

In Georgia, 5-year practice in the neurosciences is required to be eligible as a physician to determine brain death, but this is not specified in Russia.[37]

Criteria in Africa. Virtually all African countries were without legal provisions for organ transplantation, and brain death criteria were difficult to obtain. Notably, Tunisia and South Africa had developed guidelines,[38,39] but a very small sample of east and west African countries did not reveal presence of any practice guidelines.

Criteria in the Middle East. Guidelines for brain death in the Middle East were approved by the Pan-Islamic Council on Jurisprudence in Jordan in 1986 and in Mecca in 1988.[40,41] Official guidelines for brain death determination have not been drafted in many countries. In Israel the director general of the Ministry of Health published criteria for brain death in 1991 that were revised in 1996.[42] A team of two physicians should exclude the treating physician.

Criteria in Asia, Australia, and New Zealand. Major differences are found in Asia, Australia, and New Zealand.[43-50] In India, the Rajya Sabha passed the Transplantation of Human Organs Bill in 1993.[44] Brain death determination follows the British criteria for brainstem death but involves a panel consisting of the doctor in charge of the patient, the doctor in charge of the hospital where the patient was treated, an independent specialist with unspecified specialty, and a neurologist or neurosurgeon. The burden of proof rests with the specialist in the neurosciences, with the other member confirming the diagnosis.

In Bangladesh one of the three observers must be at least an associate professor in academic rank.[43]

The most notable observation time is in Iran, which requires in their guidelines a 12-, 24-, 36-hour observation and three physicians.

Mainland China has no legal criteria for the determina-

Table *Brain death survey in 80 nations*

Continent/country	Law	Guideline	Apnea test	No. of physicians	Observation time, h	Confirmatory test	Reference no.
North America							
United States	P	P	PCO_2	2*	6	Optional	6, 12
Canada	P	P	PCO_2	1	6	Optional	13
Caribbean							
Barbados	A	A	A	A	A	Optional	
Cuba	A	P	PCO_2	2	6 (24)†	Optional	
Jamaica	A	P	A	2	12	Mandatory	
Trinidad and Tobago	A	P	PCO_2	2	A	Optional	
Central and South America							
Argentina	P	P	DVO	1	6	Mandatory	15
Brazil	P	P	DVO	1	6	Optional	
Chile	P	P	DVO	2	A	Mandatory	16
Columbia	P	P	A	2 (N)	A	Optional	17
Costa Rica	P	P	PCO_2	1	24	Optional	
Ecuador	A	A	A	A	A	Optional	
El Salvador	A	P	A	1	6 (24)†	Mandatory	
Guatemala	A	A	A	A	A	Not known	
Honduras	A	A	A	A	A	Not known	
Mexico	P	P	A	A	24	Mandatory	18
Paraguay	A	P	PCO_2	1	24	Optional	
Uruguay	P	P	PCO_2	1	A	Optional	
Venezuela	P	P	PCO_2	2 (N)	12	Optional	19
Europe							
Austria	P	P	DVO	1	12	Optional	5
Belgium	P	P	DVO	3	A	Optional	5
Cyprus	P	P	DVO	2	A	Optional	
Czech Republic	A	P	PCO_2	2	A	Mandatory	20
Denmark	P	P	DVO	2	2 (24)†	Optional	5
Estonia	P	P	PCO_2	1	12	Optional	
Finland	P	P	DVO	1	A	Optional	21
France	P	P	PCO_2	2	A	Mandatory	22
Germany	P	P	PCO_2	2	12	Optional	23
Greece	P	P	DVO	3	6	Optional	24
Hungary	P	P	PCO_2	1	12 (72)†	Mandatory	25
Ireland	P	P	PCO_2	2	A	Optional	26
Italy	P	P	PCO_2	1	6 (24)†	Mandatory	27
Luxembourg	P	P	PCO_2	1	A	Mandatory	5
Malta	P	P	PCO_2	1	6	Optional	
Netherlands	P	P	PCO_2	1	A	Mandatory	28
Norway	P	P	DVO	A	24	Mandatory	29
Poland	P	P	DVO	1	3	Optional	5
Portugal	P	P	PCO_2	1	2–24	Optional	30
Romania	P	P	PCO_2	2	6	Mandatory	
Russia	P	P	PCO_2	2	6 (24)†	Optional	37

* Eight US states only; time within parentheses indicates observation time required in conditions due to anoxia.
† Observation time can be shortened or eliminated if one confirmatory test is positive for brain death.
‡ China resumed control of Hong Kong in 1997.

PCO_2 = target PCO_2 defined (50 or 60 mmHg); A = absent criterion or guideline; DV = disconnection from ventilator only; N = neurologist; MD = medical doctor; P = present; A = absent; LAW = legal standard of organ donation.

tion of brain death. Hong Kong, now under Chinese control, has well-defined criteria that, as expected, closely reflect the UK criteria.

The criteria in Japan have unique features.[45,46] They are as follows: CT scan should detect "irreparable lesions"; the cause of cardiac arrest should be known when it has caused brain death; the ciliospinal reflex should be performed; the apnea test should be performed after loss of seven specified brainstem reflexes and after isoelectric EEG; brain death determination is allowed only if intact tympanic membranes exist[46]; and children <6 years old are excluded.

Although no official national regulatory statute is present in Indonesia, three medical doctors and in some regions a lawyer should be present as an observer to determine brain death.

The Australian and New Zealand Intensive Care Society Statement and Guidelines on brain death were published in July 1993 and are under revision.[50,51] The first formal examination is performed by two physicians after at

Continent/country	Law	Guideline	Apnea test	No. of physicians	Observation time, h	Confirmatory test	Reference no.
Europe (cont'd)							
Slovak Republic	P	P	A	3	A	Mandatory	31
Spain	P	P	PCO_2	1	6(24)†	Optional	32
Sweden	P	P	PCO_2	1	A	Mandatory	33
Switzerland	P	P	PCO_2	2	6(48)†	Optional	34
Turkey	P	P	PCO_2	4	A	Mandatory	
Ukraine	A	P	DVO	A	A	Optional	
United Kingdom	P	P	PCO_2	2	6	Optional	35
Yugoslavia	A	P	DVO	3	A	Mandatory	
Africa							
Egypt	A	A	A	A	A	Not known	
Ghana	A	A	A	A	A	Not known	
South Africa	P	P	PCO_2	2	A	Optional	39
Tanzania	A	P	A	1	A	Mandatory	
Tunisia	P	P	DVO	1	A	Optional	38
Middle East							
Iran	A	P	A	3	12, 24, 36	Mandatory	
Israel	P	P	PCO_2	1	6 (24)†	Mandatory	42
Jordan	A	P	A	1	A	Mandatory	40
Lebanon	P	P	A	2	6	Mandatory	
Oman	P	P	PCO_2	1	6	Optional	40
Qatar	P	P	PCO_2	1	A	Mandatory	40
Saudi Arabia	P	P	PCO_2	2	24†	Mandatory	40
Syria	A	A	A	A	A	Not known	
United Arab Emirates	P	P	PCO_2	1	3	Optional	40
Asia							
Armenia	A	A	A	A	A	Optional	
Bangladesh	P	P	DVO	3	A	Optional	43
China	A	A	A	A	A	Optional	
Georgia	P	P	DVO	3	24	Mandatory	
Hong Kong‡	P	P	PCO_2	1	A	Optional	
India	P	P	DVO	4	A	Mandatory	44
Indonesia	A	P	PCO_2	3	24	Optional	
Japan	P	P	PCO_2	1	A	Mandatory	45, 46
Korea (South)	P	P	PCO_2	1	6	Optional	
Malaysia	P	P	PCO_2	2	12	Mandatory	47
Pakistan	A	A	A	A	A	Not known	
Philippines	A	P	DVO	1	24	Optional	
Singapore	P	P	PCO_2	2	A	Optional	48
Taiwan	A	P	PCO_2	1	6	Optional	49
Thailand	P	P	DVO	3	6	Optional	
Vietnam	A	A	DVO	A	A	Optional	
Oceania							
Australia	P	P	PCO_2	2	2	Optional	50
New Zealand	A	P	PCO_2	2	2	Optional	51

least 4 hours have elapsed; the second examination is performed 2 hours after the first examination, except following primary hypoxic brain injury, in which case the first examination should not be performed until after 12 hours.

Comments and suggestions. The landmark Harvard criteria published in 1968 have held ground tenaciously over the years.[52] However, a major diversity in clinical criteria has evolved worldwide.

In this comprehensive survey, the first of its kind, brain death criteria in some countries are left to the discretion of the physician; in others the criteria have been substantially expanded. Unlike the US statutes, legal standards on organ donation and brain death may specify the methods of clinical determination. There are major differences in number of required physicians, in level of experience and academic rank of physicians, in specialty preferences, and in recommendations for confirmatory tests. Observation time after declaration of brain death varies greatly or is not specified. The "anoxia"

provision of 24-hour observation is prevalent. It can be traced to the President Commission recommendations,[3] and this amendment may have been prompted by additional presence in some patients of cardiogenic shock and thus uncertainty about irreversibility. In addition, brain edema develops later and confirmatory tests may more often show residual brain function when performed soon after clinical assessment. Many nations in the world and several US states require confirmation by a second physician, but there are no data that would give credence to go beyond two. Finally, the apnea test is not consistently performed using PCO_2 monitoring. If the premise of documenting apnea using acute hypercarbia to maximally stimulate the respiratory centers is accepted, it can be concluded that in half of the countries, the apnea test is not performed adequately. Disconnection alone may not be sufficient to document apnea due to posthyperventilation apnea.

The differences between US state laws are noteworthy. The New Jersey religious exemption remains contentious and arguments against it have been published.[53] Other differences involve the specific mention of exclusion of physicians involved in recovery of vital organs; a few states require two physicians and board-eligible or board-certified physicians. It is surprising that two states allow registered nurses, after physician certification, to make the diagnosis of brain death, but it can be assumed this practice is uncommon.

How these striking differences—likely a result of collective decisions by task forces—have evolved is not known. At a philosophical level, it can be argued that these differences could have resulted from dissatisfaction with the original concept of brain death and could reflect cultural attitudes. This argument could certainly apply to countries with extended observation times. However, comparison of the protocols reveals differences in procedural matters, expertise and experience of physicians, method of apnea testing, and preferences for certain confirmatory tests. In many countries, the guidelines seem unnecessarily complicated.

Despite an aggressive effort to obtain data, this survey of brain death throughout the world is not complete. However, to disarm criticism, it includes a large number of densely populated countries. In some countries, transplantation programs never existed or faltered due to economic decline, thus eliminating the need to establish brain death criteria for donation. It is also conceivable that even further modifications of the official guidelines have been introduced in hospital policy manuals, but this could not be investigated with the current data set. Another potential caveat is that despite national guidelines, doubts and misconceptions about the concept of brain death may still prevail with the public. The principle of brain death may conflict with staunch personal beliefs of practicing physicians and may even potentially undermine the initiation of the transplant procedure.

So where do we stand? What can we learn from this survey? The results of this study could suggest further standardization of the determination of brain death. An international task force could specifically address the most important inconsistencies in guidelines and develop criteria for the apnea test. (For example, the apnea test only requires serial measurement of arterial PCO_2, which currently can be measured at the bedside.) This survey shows the need to critically assess the requirements of confirmatory tests and the long periods of observation, and perhaps the anoxia clause may be revisited. Maybe we could do away with confirmatory testing altogether. However, such a task force may be forced to venture into complicated cultural and religious territory and it may be difficult to persuade countries to accept a uniform agreement. Alternatively, representatives from each country may take a second look at their code of practice and recommend a revision. It remains to be seen whether it is possible to scale back the requirements. In some countries, apprehension about errors and physician qualifications could have impacted the development of diagnostic criteria, and these concerns cannot be airily dismissed. In other countries, cultural rejection of the concept of brain death and absence of transplantation programs may have deferred development of clinical guidelines. However, this survey shows that major differences are not so much in the acceptance of the concept of brain death, but in the procedures physicians use to make the final diagnosis.

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