



Brain Death: Diagnosis and Clinical Application

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Abstract

Brain death has a story of nearly one full century. In most cases brain death occurs as a sequelae to increased intracranial pressure. Nearly every neurosurgeon has experienced it. In addition, neurologist, emergency care physicians and intensivists may also experienced brain death state. However it is unlikely that all clinicians will encounter this condition. The fact is that there are a large number of medical professional lacking on criteria of drain death. A particular aim of this article is to give every neurosurgeon and intensivist sufficient theoretical knowledge to feel confident in diagnosing brain death.

Key words : Brain death. diagnosis. clinical application.

INTRODUCTION

Recent advances in resuscitative and life support technology have stimulated a refinement of the traditional concepts that are used to determine

death of the individual. Even when all brain function has completely ceased, cardiovascular, pulmonary and other functional systems may be

maintained by artificial means or may still be viable. Irreversible loss of all brain function is called brain death. It is an increasingly important clinical diagnosis in the ICU because patients with brain death are often considered as donor candidates for organ transplantation. Clinically, the most relevant definition of brain death is the irreversible loss of all integrated neuronal functions. In this situation there is widespread devastating brain damage. The term integrated is essential because recovery of some metabolic and electric activity occurring in certain brain regions after prolonged total ischemia has been reported, even with irreversible loss of the functional integrity of the brain.¹

Philosophically, to view brain death as the brain death of the individual is appropriate because (1) the brain is the essential site where human personality exists as well as the origin of integrated function of the organism as a whole; (2) brain death inevitably leads to cessation of vital functions, usually within 2 weeks of the cardiac arrest, unless extraordinary means have been taken; and (3) virtually all vital organs can be artificially maintained and/or replaced in man, except for the brain. These considerations have led to the belief that death of the brain is equivalent to the death of the individual.¹

Definition of brain death

Brain death is defined as irreversible cessation of all functions of the entire brain, including the brainstem. Using this definition the term brain

obviously includes both the cerebral hemispheres (cortex and deep structure) as well as the cerebellum and brainstem. It seems generally accepted that brain function represents the presence of life whereas persistent cardiopulmonary function with no brain function does not. The traditional definition of death also implies brain death, because the cessation of cardiopulmonary function inevitably leads to brain death within minutes. Thus there are not two different concepts of deaths; death and brain death are equivalent. Rather, there are two different sets of criteria that may be used to diagnose brain death. Today society accepts that death of the brain is equivalent to death of the person and the death of the brain is equivalent to death of the individual^{1,2,3}.

Representative Brain Death Criteria

*Harvard Criteria (1968)*¹

The Harvard criteria were the first and therefore remain the most important published criteria for brain death. The Harvard criteria defined irreversible coma as follows :

1. Unreceptivity and unresponsivity
2. No movement or breathing
3. No reflexes
4. Isoelectric EEG

All above tests shall be repeated at least 24 hours later with no change.

*Minnesota Criteria (1971)*¹

The Minnesota criteria are unique in that the emphasis is more upon clinical judgment. It was Mohandas and Chou, who formulated this criteria.

Minnesota criteria as follows :

1. No spontaneous movement
2. No spontaneous respiration
3. Absence of brainstem reflexes
4. All of the findings above remain unchanged for at least 12 hours
5. Brain death can be pronounced only if the pathological processes responsible for status 1-4 above are deemed irreparable with presently available means.

*United Kingdom Criteria (1976)*¹

The United Kingdom brain death criteria are based on the concept of brainstem death as judged by clinical examination, with emphasis on the prerequisites; that is, absence of brainstem reflexes and apnea, not requiring the EEG.

Brain death should be considered under the following conditions:

1. The patient is deeply comatose
2. The patient is being maintained on a ventilator because spontaneous respiration is inadequate or has ceased all together
3. No doubt that the patient's condition is due to irreversible structural brain damage
4. Brainstem reflexes are absent

5. Criteria include : repetition of testing (24 hours interval), integrity of spinal reflexes, not necessary to perform EEG or cerebral angiography, body temperature more than 35°C, decision made by two doctors in charge

*The Collaborative Study (National Institutes of Health, 1977)*¹

Criteria (to be present for 30 minutes at least 6 hours after the onset of coma and apnea) are as follows:

1. Coma with cerebral unresponsiveness
2. Apnea
3. Absent cephalic reflexes and dilatated pupils
4. Electrocerebral silence
5. The diagnosis should be validated by the demonstration of absence of CBF

*The President's commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (1981)*¹

The criteria are as follows:

1. An individual with irreversible cessation of circulatory and respiratory function is dead.
2. An individual with irreversible cessation of all function of the entire brain including brainstem is dead. Cessation is recognized when cerebral and brainstem function are absent. Irreversibility is recognized when

the cause of the coma is established, the possibility for recovery is excluded and the cessation of brain functions persists for an appropriate period of observation.

3. EEG and blood flow studies may also be required, depending on the circumstances.

Swedish Criteria (The Swedish Ministry of Health and Social Affairs, 1984)¹

These Swedish criteria are influenced by the implication of cerebral death as total cerebral infarction as described by Ingvar and Widen, and hence emphasize cerebral angiography.

1. The cause of the condition is known. Intoxication and hypothermia are excluded.
2. Clinical neurologic examination, carried out on at least two occasions with an interval of two hours shows : unconsciousness, unreactive pupils, loss of corneal reflexes, absence of spontaneous movement, absent cardiac cerebral reflexes and complete cessation of spontaneous respiration.
3. Supplementary EEG show a complete cessation of electrical activity
4. Cerebral angiography show lack of circulation of the brain.

Japanese Criteria (Brain Death Study Group, Ministry of Health and Welfare, 1987)¹

1. Prerequisite : a known irreparable organic lesion, detected by computerized

tomography. Exclusion : children under 6 years, hypothermia, drug intoxication or metabolic disorders.

2. Deep coma : 300 Japan Coma Scale and 3 Glasgow Coma Scale
3. Apnea confirmed by apnea test
4. Absence of brainstem reflexes
5. Isoelectric EEG
6. The preceding criteria must be present for a 6-hour period or longer if necessary

Indonesian Criteria (Indonesian Medical Association, 1988)⁵

Indonesian Medical Association (IDI) stating that an individual who has sustained (1) irreversible cessation of circulatory and respiratory functions and (2) irreversible cessation of all functions of entire brain, including brainstem, is dead.

Brain Death Criteria are as follows :

1. Prerequisites : A known irreversible structural brain damage, coma, and in apneic condition. Drug intoxication, hypothermia and metabolic disorders are excluded.
2. Absence of brainstem reflexes
3. Apnea confirmed by apnea test
4. All above tests shall be repeated at least 25 minutes until 24 hours later with no change, or depend on the institution protocol.

Reasons to Declare Brain Death

There are compelling ethical and practical reasons for physicians to know the criteria of brain death and apply them. The determination of brain death has assumed importance for three reasons^{2,4}:

1. Transplant programmes require the donation of healthy peripheral organs for success. The early diagnosis of brain death before the systemic circulation fails allows the salvage of such organs. However, ethical and legal considerations demand that if one is to declare the brain dead, the criteria must be clear and unassailable.
2. Even if there were no transplant programme, the ability of modern medicine to keep brainless bodies going for extended periods with antibiotics, mechanical respirators, and vasoconstrictor drugs often leads to prolonged, expensive and futile exercises accompanied by great emotional strains on family and medical staff. Conversely the recuperative powers of the brain sometimes can seem astounding to the uninitiated and individual patients who uninformed physicians might give up for hopeless brain damage or dead sometimes make unexpectedly good recoveries. It is even more important to know when to fight for life than to be willing to diagnose death.

3. Critical care facilities are limited and expensive and inevitably plays a drain on other medical resources. Their best use demands that one identify and select patients who are most likely to benefit from intensive techniques, so that these units are not overloaded with individuals who can never recover cerebral function.

Cardiac activity can be supported for many days in those whose brains have irreversibly ceased all function. Physiological derangements, namely, cardiovascular instability, thermovariability and anterior and posterior pituitary insufficiency and altered nutritional needs can be corrected. It is possible to maintain a brain dead patient for prolonged periods, with the record now being 107 days. However, except in rare circumstances for example, in an attempt to salvage a viable fetus, such treatment is inappropriate, since it ignores the reality of the situation, keeps the family and friends in a limbo of uncertainty and false hope, violates the trust placed in the physician by the family and society to recognize death, requires health care workers to treat an essentially dead body, expends resources without benefit, and might be perceived as an indignity to and abuse of the body.^{2,4}

Advances in transplantation provide the possibility of using the organs of a brain-dead person to improve or even to save the lives of others and even save considerably sums because of diminished medical costs and increased

productivity. The advances being made are reflected in the rising numbers of transplant and rising rates of organ and donor survival.⁴

Nowadays, many physicians still do not fully understand brain death or support organ retrieval because they do not realize the desperate need for organs and do not appreciate the consolation the family can gain from organ donation. To facilitate organ donation, most states have passed “*required request*” laws, but these have not had much effect. In addition, organs are lost when patients were not vigorously resuscitated or supported. The result is that there are longer and longer lists of potential recipients, many of whom will die waiting for organs and the problem is worsening.⁴

There have been many proposals including improvement in donor identification and care, more effective contact with donor families, and universal checking for donor cards. Other solutions suggested include mandated decision making, presumed consent and rewarded gifting. The code of Medical Ethics of the American Medical Association (1992) declares, “The voluntary donation of organs in appropriate circumstances is to be encouraged”, and organized neurosurgery has supported this approach.⁴

Prepequisites

Before the declaration of brain death is considered, there are essential prerequisites. First, the cause of coma should be clarified. Without knowing the cause, the diagnosis of brain death

should never be made. There should be no doubt that the patient’s condition is due to irremediable structural brain damage. In this regard, conditions under which the diagnosis of brain death should be considered are well described in the report by the conference of Royal Colleges and Faculties of the United Kingdom. All the other published criteria stress prerequisites similar to those of the British criteria. In essence, the patient must be in an unresponsive coma, and dependent on a ventilator because spontaneous respiration is inadequate or absent. All criteria require normothermia and the absence of both sedative drug intoxication and cardiovascular shock. When the brainstem and hypothalamic centers are damaged, thermal regulation and vasomotor control may be impaired.¹

After reviewing these criteria, it is clear that brain death is a clinical concept that can be diagnosed with clinical findings and appropriate ancillary test, if necessary.¹

Table 1. Confounding Agents/Condition that must be Absent before Brain Death Testing

Shock/hypotension	
Hypothermia < 32 C	
Drugs :	Anesthetics
	Paralytic
	Methaqualone
	Barbiturate
	Diazepam
	High-dosebretylium
	Mecloqualone

Amitriptyline
 Meprobamate
 Trichloroethylene
 Alcohols
 Brain stem encephalitis
 Guillan-barre syndrome
 Metabolic encephalopathy
 Severe hypophosphatemia

(Source : Adapted from Powner DJ, et al: Controversies in brain death certification. In Ayres SM Ed.: Textbook of Critical Care 3th ed. Boston, WB Saunders Company, 1995, chap. 173, p 1580.)

Absence of brainstem reflex

Brainstem reflexes reflect brainstem function, involving pathways from the midbrain to the lower medulla. Total absence of brainstem reflexes indicates marked dysfunction of the cranial central nervous system. Although respiration is one of the most important brainstem reflexes, determination of irreversible loss of spontaneous respiration deserves separate discussion. Brain death is clearly different from vegetative state, because the former requires the absence of all brainstem reflexes. In the vegetative state and the apallic syndrome, brainstem reflexes are often present and their presence exclude the diagnosis of brain death.¹

The single most important brainstem reflex is pupillary. Other reflexes is importance include the

oculocephalic, oculovestibular and cough reflex. As previously mentioned, the concept of brainstem death emphasizes the absence of brainstem reflexes. Although the rest for brainstem reflexes enable to be determined, there are several conditions under which brainstem reflexes have to be carefully evaluated. Anticholinergic drugs and ganglion blocking agents may dilate and fix the pupils. Oculovestibular reflexes can be modified by the presence of ototoxic agents such as antibiotics, antidepressants and anticonvulsant.¹

Table 2. Brain Stem Reflexes.

Pupillary reflex : in a semidark room, a strong source of light should be shone into each eye sequentially while carefully observing for change in pupil size in both eyes.

Extraocular movement : These may be tested initially by turning the patient's head from side to side with the head elevated 30° (oculocephalic or doll's eye reflex). Since this movement does not provide a maximum stimulus, if this examination shows no doll's eyes response, the ear canals should be irrigated with ice water (oculovestibular reflex, calorics). For this test, the ears must be free of significant wax and the drums should not be perforated. The head is elevated 30° and each ear drum in turn is irrigated with 50ml of ice water using a syringe and small cannula. Any movement of the eyes demonstrates that some brain stem pathways are functioning.

Corneal reflex : A steril piece of cotton or other tissue is lightly touched to the cornea (not the conjunctiva). Any eyelid movement during this maneuver suggests some brain stem function.

Gag reflex : A tongue depressor or other object is touched against the back of the pharynx or the endotracheal tube is moved. Movement of the uvula or retching constitutes a positive response and excludes the diagnosis of brain death.

Cough reflex : A cannula is passed through the endotracheal tube into the tracheobronchial tree or the endotracheal tube is irrigated. Any movement or coughing excludes the diagnosis of brain death.

(Source : Adapted from Kauffman HM. Brain death following head injury In : Narayan RK, Wilberger JE, Povlishock JT. Eds. Neurotrauma. McGrawhill Company; 1998; chap. 56, p.824.)

Absence of Spontaneous Respiration

Confirmation of apnea is the most essential test in diagnosing brain death, and anesthesiologists must fully understand the apnea test. Apnea is an early indication of impending brain death, usually being present before signs of circulatory impairment appear. In this situation respiration becomes entirely dependent on mechanical ventilation. The apnea test should be performed, without subjecting the patient to an anoxic risk, after all other criteria have been met. The principle of apneic oxygenation have been known in anesthetic practice since the 1950s. However, this

technique has become popular only recently in the apnea test. The goal of the apnea tests to increase the PaCO₂ sufficiently to stimulate the medullary respiratory center, while maintaining PaO₂ at safe level. The level of PaCO₂ sufficient for inducing respiratory effort is at 55-60mmHg. During the apnea test repeated blood gas analysis is strongly recommended; usually the PaCO₂ increases approximately 2,5-4,3 mmHg/min¹.

Today the apnea test must be rigorous because of its importance in meeting the brain death criteria. The time necessary for the apnea test depends in part on the previous state of oxygenation and the body temperature. Ropper reported movements of the arm, shoulder and thorax during apneic testing, that resembled respiratory movements in five brain-dead patients. These movements were believed to be elicited at the level of the spinal cord and may still be consistent with the diagnosis of brain death.¹

Table 3. Apnea Test

1. Preoxygenate for at least 10 minutes with 100% O₂ and at the same time adjust the respirator so that PCO₂ is about 40mmHg
2. Disconnect the respirator and give O₂ at 8 to 12 L/min. by tracheal cannula.
3. If hypotension and/or arrhythmias develop at any time, stop the test and place the patient immediately back on the respirator. If this happens, EEG or cerebral blood flow tests or consultation should be obtained

4. During disconnection from a respirator, the patient should be observed continuously for spontaneous respirations. If there are none in 10 minutes, draw blood gases and place the patient back on the respirator. The PCO₂ must be greater than 60 mmHg to be sure of stimulating the medullary respiratory centers maximally. If the PCO₂ is greater than 60 mmHg and there is no respiratory effort, the patient is apneic.
5. Obviously, if there is any respiratory effort, the patient is not apneic and not brain dead.

(Source : Adapted from Kauffman HM. Brain death following head injury In : Narayan RK, Wilberger JE, Povlishock JT. Eds. Neurotrauma. McGrawhill Company; 1998; chap. 56, p.824.)

Observation Periods

The cessation of all brain function must persist for an appropriate period of observation and/or trial of therapy, and it's depend on the age of the patient and the confirmatory test utilized. The absence of cerebral blood flow as measured by radiologic techniques is the only measure of cerebral function that does not require additional clinical observation and laboratory evaluation to confirm the diagnosis of brain death. These are recommended observation periods during which patient (adult and children older than 5 years) fulfills criteria of clinical brain death before the patient may be pronounced dead²;

1. In situation where overwhelming brain damage from an irreversible condition is well established (e.g. massive intracerebral hemorrhage), some experts will pronounce death following a single valid brain death exam in conjunction with a clinical confirmatory test.
2. If an irreversible condition is well established, and clinical confirmatory tests are used, it is advisable to wait until 6 hours.
3. If an irreversible condition is well established and no clinical confirmatory tests are used, it is advisable to wait until 12 hours before make a final declaration.
4. If diagnosis is uncertain and no clinical confirmatory tests, wait 12-24 hours after the patient first meets the clinical criteria of brain death to make the final declaration.
5. If anoxic injury is the cause of brain death, it is advisable to wait until 24 hours, or may be shortened if cessation of cerebral blood flow is demonstrated.

Confirmatory Test in Brain Death

Among the many confirmatory test, the EEG and cerebral angiography are the most commonly used. Non-filing angiography was stressed by European investigators. It must be noted that any confirmatory tests should be used in conjunction with appropriate clinical criteria and should be based on clinical judgment. No single test for the diagnosis of brain death is available at present or

will likely ever emerge. Use of certain confirmatory tests makes it possible to shorten periods of observation¹.

Electroencephalogram

As mentioned before, some of the published criteria clearly indicated that EEG is unnecessary for the diagnosis of brain death. However, the EEG is perhaps the most commonly used ancillary procedure in the diagnosis of brain death. It has been reported that 17 percent of brain dead patient will have activity on their EEGs, if the Minnesota criteria are followed. Iso-electric or electric silence can be defined when the EEG shows the following condition : there is no evidence of electric activity over 2 uV when it is recorded from scalp electrode pairs 10 or more cm apart, with interelectrode impedance between 100 and 10,000 ohms. In addition, for the diagnosis of brain death, it may be necessary to sustain this for a period of 30 minutes. Electrocerebral silence may indicate irreversible dysfunction of the cerebrum if the cause of coma is not intoxication or metabolic disturbances that may be reversible. If the absence of both cortical and brainstem function is required for the diagnosing of brain death an isoelectric EEG is an important adjunct. However, whether or not the EEG is necessary remains controversial¹.

Some believe that serial cerebral angiography is the definitive method for diagnosing brain death. Particularly in Scandinavia, confirmation of arrested circulation in cerebrum brainstem and

posterior fossa was considered to be essential for the diagnosis of brain death, based on the concept of total brain infarction. There is little doubt that the complete cessation of brain blood flow over 20 minutes inevitably leads to neuronal death in the adult human at normothermia. Carotid angiography alone does not visualize the circulation of the entire brain. The blood flow in the carotid and basilar system may cease concurrently, but usually the vertebrobasilar circulation is seen for several hours after the cessation of carotid flow. Four-vessel angiography seems to have special value in cases of suspected drug intoxication and hypothermia. In these patients clinical findings and the EEG maybe misleading¹.

Radioisotope angiography with intravenous injection of technetium-labeled albumin and subsequent cranial scanning has also been used to demonstrate absent cerebral blood flow. This procedure can be done at the bedside if portable imaging equipment is available. A limitation of this technique is that the vertebral system is not visualized. Variations in isotope flow patterns have also been reported¹.

Digital subtraction angiography has also been recommended as a method that can directly assess intracranial circulation with fewer cardiopulmonary side effects than conventional contrast angiography¹.

CT may visualize indirectly the presence of intracranial blood flow, allowing evaluation of the

appearance of intravenous contrast material on rapidly sequence scans. This methods appears to be increasingly more available and hence may become useful in diagnosing brain death¹.

Table 4. Confirmatory Test for Brain Death

Evaluate neuronal function

Electroencephalogram or cerebral function monitor

Evoked potentials

Biochemical tests of cerebrospinal fluid or jugular venous blood

Evaluated intracranial blood flow

Contrast angiography, MR or CT imaging

Radionuclide perfusion studies

Xenon-enhanced computed tomography

Digital subtraction angiography/venography

Ophthalmic artery blood flow

Transcranial Doppler study

Miscellaneous (optional)

ICP higher than systolic blood pressure

Sustained cerebral perfusion pressure , 5 mmHg

Brain biopsy

(Source : Adapted from Powner DJ, et al: Controversies in brain death certification. In Ayres SM Ed.: Textbook of Critical Care 3th ed. Boston, WB Saunders Company, 1995, chap. 173, p 1580. And Gireesh K, Arunkumar R. Brain Death. Chennai :South India Publishing House; 1998)

Brain Death in Children

Brain death in neonates and premature has always been subject for debate due to the fact that children can sustain a longer time of hypoxia than adults before irreversible brain damage arises. Also the time interval between the initial onset of brain death and cardiac arrest might be quite prolonged.²

The criteria described earlier generally are restricted to adults and children older than 5 years old. Specific criteria considered useful in infants and young children have been published by the Task Force for the Determination of Brain Death in Children. Nevertheless, there is not yet broad professional consensus on the criteria for the diagnosis of brain death in the pediatric population. A knowledgeable specialist using any of the currently employed criteria can probably be accurate, but use of the criteria requires experience and judgment. Thus, consultation with such an individual should be obtained for the diagnosis of brain death in children 5 years of age or less^{3,4}.

Table 5. Guidelines after Task Force on Brain Death in Children

- I. Prerequisite to evaluation :
 - History of cause of coma and eliminates reversible condition
- II. Physical Examination Criteria :
 - Coma
 - Apnea using standardized testing

Absent brainstem function

Midposition or fully dilated pupils unresponsive to light

Absent spontaneous eye movement, oculocephalic and oculovestibular reflex

Absent movement of bulbar musculature

Absent corneal, gag, cough, sucking, and rooting reflex

Flaccid tone and absent spontaneous or induced movements

Findings on examination should be consistent with brain death during entire observation

III. Age-specific observation

7 d - 2 mo – two examinations and EEG separated by 48 hours

2 mo – 1 y – two examinations and EEG separated by at least 24 hour or initial examinations with no cerebral blood flow in confirmatory test

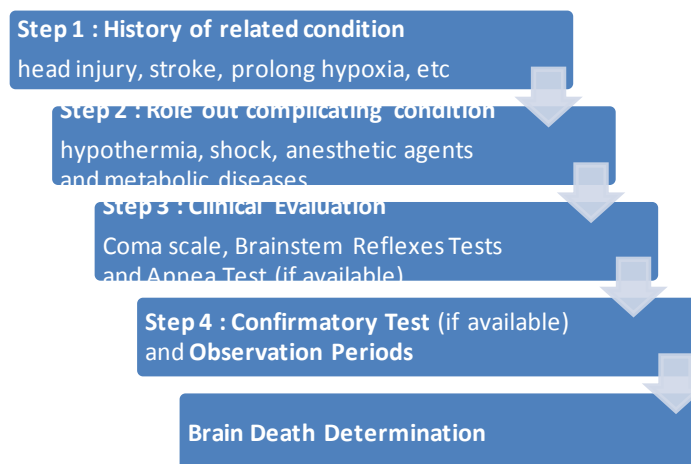
Older than 1 y – two examinations at least 12 hours apart with EEG and cerebral radionuclide studies opti

Certification Process

Brain death certification should be performed according to an individual institution's policy. This should include a protocol detailing clinical and confirmatory tests, their frequency and interval between tests. Two or more appropriately licensed physicians with experiences in brain death certification should perform the examination. The protocol should be adhered to rigidity, in order to minimize the possibility of death certification when brain function exists. Transplant physicians are generally not involved in brain death certification of a potential organ donor to avoid conflicts of interest. Brain death certification is equivalent to the pronouncement of death, and the time documented for this certification is considered the time of death medically and legally. Certification of death is the physicians's duty. Seeking consent is inappropriate but the family must be informed of the certification process. In cases which lie within a corner's jurisdiction, permission is not required for death certification or termination of medical therapy, but consent of the coroner and the next of kin must be obtained for the removal of organs for transplantation⁶.

(Source : Adpted from Powner DJ, et al: Controversies in brain death certification. In Ayres SM Ed.: Textbook of Critical Care 3th ed. Boston, WB Saunders Company, 1995, chap. 173, p 1580.)

Figure 1. A simple Model Algorithm for Determining Brain Death



The figure above is a simple algorithm that recommended by the author to use at the institution with lack of facilities and equipment, like many health institution in Indonesia.

Some criteria (and state laws) suggest that two physicians must agree on the diagnosis of brain death, particularly when organ retrieval is being considered. If an EEG is done, the electroencephalographer may be the second physician. However, if the diagnosis is straight forward and clear, and if the physician involved is well trained and experienced, it would seem reasonable for a single physician to certify brain death⁴. Once a patient is declared brain dead, life support can legally be terminated. Some believe that the physician has the authority and responsibility to stop the respirator and other life-sustaining treatment when a patient is dead and that the option to continue care should not be given to the family. Others feel they should ask

families for permission to stop care and turn off the respirator⁴.

The Pitfalls in the diagnosis of brain death

Potential pitfalls accompany the diagnosis of brain death, particularly when coma occurs in hospitalized patients or those who have been chronically ill. Almost none of these will lead to serious error in diagnosis if the examining physician is aware of them and attends to them when examining individual patients who are considered brain dead. Some of these pitfalls are in the following table².

Table 6. Pitfalls in the Diagnosis of Brain Death

Findings	Possible Cause
1. Pupils fixed	Anticholinergic drugs
	Neuromuscular blockers
	Preexisting disease
2. No oculo-vestibular reflexes	Ototoxic agents
	Vestibular suppressants
	Preexisting disease
3. No respiration	Posthyperventilation apnea

References:

- Neuromuscular blockers
4. No motor activity
- Neuromuscular blockers
- “locked-in” state
- Sedative drugs
5. Isoelectric EEG
- Sedative drugs
- Anoxia
- Hypothermia
- Encephalitis
- Trauma

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(Source: Adapted from Gireesh K, Arunkumar R. Brain Death. South India Publishing House; p.78.)

Conclusion

In summary, it would seem today that much greater attention must be given to understanding the public and professional perception of brain death, to educating both groups, to assisting in the development of improved and appropriate medical criteria and in the enactment of laws by all the states still lacking adequate statutory provision of brain death, perhaps to assuring legal and ethical exemption for those who by reason of conscience cannot accept the concept of brain death.