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Clinical Science

BRAIN DEATH : GUIDELINES & ISSUES

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ABSTRACT

Brain death is a clinical diagnosis with a irreversible absence of cerebral and brain stem functions. In all cases the confirmatory tests are not mandatory but a repeat evaluation is generally recommended. The diagnosis and confirmation largely remains a complex clinical, ethical and social issue for physicians, family members and society at a large. The concept of the "dead-donar rule" closely linked to the increasing need for organ transplantation has created conflicts of interests between the demand for organs and the need for a scientifically and philosophically valid definition of human death. Finally, physicians are entrusted to apply accepted standards and practices while making the diagnosis and confirmation of brain death and should exhibit patience and provide emotional support to the family.

INTRODUCTION

In present era of critical care, 'the care of a severely brain injured patient' is one of the toughest challenges for a critical care physician. Initial therapy provided for patients with severe brain injury or insult, is directed towards preservation and restoration of neuronal function. When this primary treatment is unsuccessful and the patient's condition evolves to brain death, the critical care physician has the responsibility to diagnose brain death with certainty and to offer the patient's family the opportunity to donate organs and /or tissues.

Physicians, health care workers and even the laypeople throughout the world have well accepted that a person is dead when his or her brain is dead. Although the widespread use of mechanical ventilators and other advanced critical care services have transformed the course of terminal neurologic disorders. Vital functions can now be maintained artificially for a long period of time after the brain has ceased to function. There is a need to diagnose brain death with utmost accuracy and urgency because of an increased awareness amongst the masses for an early diagnosis of brain death and the requirements of organ retrieval for transplantation. Physicians need not be, or consult with, a neurologist or neurosurgeon in order to determine brain death.

Concept Of Brain Death

Brain death is a clinical diagnosis in which there are absences of cerebral and brain stem functions and irreversibility of the state. Confirmatory tests are not mandatory in all cases, but a repeat evaluation is generally recommended. Physicians are entrusted to apply accepted standards and practices when making the diagnosis or brain death, and should exhibit patience and provide emotional support of the family. The concept of brain death emerged during the 1950s when, as a consequence of developments in critical care, clinicians were faced for the first time with the prospect of an apparently alive' patient sustained by mechanical ventilation long after brain function had ceased. The development of organ transplantation and the associated need to determine death before organ retrieval led to the publication of the first widely accepted standard for the confirmation of brain death by an ad hoc Committee of the Harvard Medical School in 1968. Although this early link with organ donation might give the impression that brain death was a construct designed only to facilitate donation, this is incorrect. Most importantly, the

confirmation of brain death allows the withdrawal of therapies that can no longer conceivably benefit an individual who has died.

In 1981, the report of the medical consultants on the diagnosis of death to the US President's Commission recommended that the criteria for diagnosis of brain death should be seen as synonymous with the definition of death of the organism as a whole. Brain death is declared when brain stem reflexes, motor responses and respiratory drive are absent in a normothermic, non-drugged comatose patient with a known irreversible massive brain lesion and no contributing metabolic derangements.

The absence of brain stem function is judged by lack of spontaneous eye movements, mid-position of the pupils of the eyes and lack of response to oculocephalic and caloric tests; paralysis of bulbar musculature, gag movement and cough and corneal function; and absence of decelerate response to noxious stimuli. Occasionally, extensor or flexor posturing can be seen as a transitional phenomenon just after brain death becomes evident. Spinal reflexes may persist in some cases, and the toes often flex slowly in response to plantar stimulation; a well-developed Babinski's sign is unusual.^[1-2]

Definition

Brain death is defined as the irreversible loss of all functions of the brain, including the brainstem. The three essential findings in brain death are coma, absence of brainstem reflexes, and apnoea. An evaluation for brain death should be considered in patients who have suffered a massive, irreversible brain injury of identifiable cause. The common clinical condition that produces irreversible loss of brain stem functions includes severe head injury, hypertensive intracerebral hemorrhage, aneurysmal subarachnoid hemorrhage, severe hypoxic ischemic brain insults and fulminant hepatic failure. The evaluation of a potentially reversible, should include clinical and neuro-imaging evidence of an acute CNS catastrophe that is compatible with the clinical diagnosis of brain death. A patient determined to be brain dead is legally and clinically dead.

The Confounders Of Brain Death

Before making a diagnosis of brain death it is mandatory to exclude any condition that might confound the subsequent examination of cortical or brain stem function. The condition

that may confound the clinical diagnosis of brain death are :

- a. Shock/hypotension
- b. Hypothermia (temperature < 32°C)
- c. Drugs known to alter neurologic, neuromuscular function and electroencephalographic testing like anesthetic agents, neuromuscular blocking agents, barbiturates, benzodiazepines, high dose bretylium, amitriptyline, meprobamate, trichloroethylene, alcohols.
- d. Brain stem encephalitis.
- e. Guillain-Barre' syndrome.
- f. Encephalopathy associated with hepatic failure, uremia and hyperosmolar coma.
- g. Severe hypophosphatemia.

Persistent vegetative state (PVS) : A separate condition, refers to a vegetative state lasting longer than 1 month. In contrast to brain death, patients with PVS have preservation of brain stem and hypothalamic functions and may exhibit arousal or wakefulness.

In the United States, the Uniform Determination of Death Act mandates irreversible cessation of all functions of the entire brain and brain stem.

Diagnosis Of Brain Death

The American Academy of Neurology published practice parameters to standardize the criteria for the diagnosis of brain death in adults. The guidelines for children have some unique features, dealing specifically with the age group from full-term newborn to 5 years old. These features are mainly focused on the changing periods of recommended observations relative to the patient's age.

In general, confirmatory tests for the diagnosis of brain death are not required in adults and children over 1 year of age, but are recommended in children <1 year of age or in situations where the neurologic examination cannot be adequately performed.^[2-3]

Confirmatory Tests Of Brain Death

1. The assessment of electrical activity by EEG or somatosensory evoked potentials (SSEP).
2. Assessment of cerebral blood flow by radionuclide studies, transcranial Doppler ultrasound or angiography.

It should be emphasized that any or the suggested confirmatory tests many produce similar results in patients with catastrophic brain damage, who do not as yet fulfill the clinical criteria of brain death, the EEG provides confirmation of brain death. Most institutions prefer this corroboration of the clinical features, by the demonstration of electrocerebral silence when there is no electrical potential of more than 2 V, during atleast a 30-minute recording that adheres to the minimal technical criteria adopted by the American Electroencephalographic Society. Cerebral unresponsiveness and a flat (isoelectric) EEG do not always signify brain death, and both findings may occur in some reversible conditions - e.g., profound hypothermia or intoxication with sedative or hypnotic drugs, and immediately following cardiac arrest. Although in the United States a flat EEG test is not required to certify death, it is considered to have confirmatory value. In the UK it is not considered to be of value because any continuing activity it might reveal in parts of the brain above the brain stem is held to be irrelevant to the diagnosis of death on the Code of Practice criteria.

The diagnosis of brain death needs to be rigorous, in order to be certain that the condition is irreversible. Legal criteria vary, but in general they require neurological examinations by two independent physicians. The exams must show complete and irreversible absence of brain function (brain stem function in UK), and may include two isoelectric (flat-line) EEGs 24 hours apart (less in other countries where it is accepted that if the cause of the dysfunction is a clear physical

trauma there is no need to wait that long to establish irreversibility). The patient should have a normal temperature and be free of drugs that can suppress brain activity if the diagnosis is to be made on EEG criteria.

In addition, the brain death significance of isoelectric EEG in children (especially infants) has not been validated, and there have been a number of case reports showing the recovery of brain function and EEG activity following a period of isoelectric EEG.

During SSEP measurements, the bilateral absence of N20- P22 response with median nerve stimulation is supportive of the diagnosis. Some centers have utilized radionuclide scan, cerebral angiography or transcranial Doppler ultrasound, although there are technical pitfalls in these methods.

A radionuclide cerebral blood flow scan that shows complete absence of intracranial blood flow must be considered with other exams – temporary swelling of the brain, particularly within the first 72 hours, can lead to a false positive test on a patient that may recover with more time.

CT angiography is neither required nor sufficient test to make the diagnosis.

Guidelines for determining Brain Death in children

The brain of infants and young children have increased resistance to damage and may recover substantial functions even after exhibiting unresponsiveness on neurological examination for longer periods as compared to adults. When applying neurological criteria to determine death in children younger than one year, longer observation periods are required. The guidelines to determine brain death in children include :

- Concurrent coma and apnoea
- Absence of brain stem function
- Pupils unreactive to light (mid-position or dilated)
- Absence of spontaneous eye movement, or no response to oculocephalic and oculovestibular tests
- Absence of movement of bulbar musculature, including facial and oropharyngeal muscles (corneal, gag cough, sucking and rooting reflexes)
- Absent respiratory movements with patient off the ventilator.
- Apnoea test using "standardized methods"
- Absence of hypotension (for age) or hypothermia
- Flaccid muscle tone, absence of spontaneous movements (excluding spinal reflexes)
- Examination consistent with brain death throughout the period of testing and observation
- Observation and testing according to age :
- Reliable criteria have not been established of brain death in children less than 7 days old.
- 7 days to 2 months : Two examinations and EEGs separated by 48 hours
- 2 months to 1 year : Two examinations and EEGs separated by 24 hours
- Older than 1 year : With an irreversible cause, laboratory tests not required and an observation period of atleast 12 hours recommended; atleast 24 hours of observation recommended if it is difficult to assess the extent and reversibility of brain damage (e.g., following a hypoxic ischemic event). The observation period may be reduced if EEG demonstrates electrocerebral silence or the cerebral radionuclide and angiographic study does not visualize cerebral arteries.

Guideline for determining Brain Death in adults

Brain death is the absence of clinical brain function when the proximate cause is known and demonstrably irreversible.

Pre-requisites

- Clinical or neuroimaging evidence of an acute CNS

catastrophe that is compatible with clinical diagnosis

- No drug intoxication or poisoning
- Core temperature 32°C

The three cardinal findings in brain death are coma or unresponsiveness, absence of brain stem reflexes and apnoea.^[3-4]

(A) Coma or unresponsiveness

- No cerebral or motor response to pain in all extremities (nailbed pressure and supraorbital pressure)

(B) Absence of brain stem reflexes

Pupils (Cranial nerve II & III)

- Absent Pupillary Reflex
No response to direct and consensual bright light
Size :Mid-position (4 mm) to dilated (9 mm)

Ocular movement (Cranial nerve III, IV & VI)

- Absent oculoccephalic reflex (testing only when no fracture or instability of the cervical spine or skull base is apparent)
- Absent oculovestibular reflex so no deviation of the eyes to irrigation in each ear with intact tympanic membrane with 50 ml of cold water (allow 1 minute after injection and atleast 5 minutes between tests on each side)
- Facial Sensation and Facial Motor Response (Cranial Nerve V, VII & IX)
- No facial sensation and facial motor response
- Absent corneal reflex to touch with a throat swab
- Absent jaw reflex
- No grimacing to deep pressure on nail bed, supraorbital ridge or temporo-mandibular joint
- Pharyngeal and tracheal reflexes (Cranial Nerve IX & X)
- Absent Gag reflex so no response to stimulation of the posterior pharynx with tongue blade
- Absent cough reflex so no cough response to tracheo-bronchial suctioning

C Apnoea Test (Absent respiratory efforts in presence of hypercarbia)

Generally the apnoea is performed after the second examination of brain stem reflexes. The apnoea test need only to be performed once when its results are conclusive.^[5] Before performing the apnoea test, the physician must determine that the patient meets the following conditions :

- Core temperature $\geq 36.5^{\circ}\text{C}$ or 97.7°F
- Systolic blood pressure 90 mmHg
- Euvolemia (option: positive fluid balance in previous 6 hrs)
- Normal PCO_2 (option: Arterial $\text{PCO}_2 \geq 40$ mmHg)
- Normal PO_2 (option: Preoxygenation to obtain arterial $\text{PO}_2 \geq 200$ mmHg)

Procedure to perform Apnoea Test

- Connect a pulse oximeter and disconnect the ventilator.
- Deliver 100% oxygen (O_2), 6 l/min, into the trachea (option: Place a cannula at the level of the carina)
- Look closely for respiratory movements (abdominal or chest excursions that produces adequate tidal volume)
- Measure arterial PO_2 and PCO_2 , and pH, after approximately 8 minutes and reconnect the ventilator
- If respiratory movements are absent and arterial PCO_2 is ≥ 60 mmHg (option: 20 mmHg increase in PCO_2 over a base line normal PCO_2), the apnea test is positive i.e. it supports the diagnosis of brain death
- If respiratory movements are observed, the apnea test is negative i.e. it does not supports the diagnosis of brain death and the test should be repeated
- Connect the ventilator if, during testing, the systolic blood pressure becomes 90 mmHg or the pulse oximeter indicates significant oxygen desaturation and cardiac

- arrhythmias are present; immediately draw an arterial blood sample and analyze arterial blood gas.
- If PCO_2 is 60 mmHg or PCO_2 increase is 20 mmHg over baseline normal PCO_2 , the apnea test is positive.
- If PCO_2 is <60 mmHg or PCO_2 increase is <20 mmHg over baseline normal PCO_2 , the test result is indeterminate, and an additional confirmatory test can be considered.^[6-8]

Certification Of Brain Death

The diagnosis of brain death is primarily clinical. No other tests are required if the full clinical examination, including each of two assessments of brain stem reflexes and a single apnoea test, are conclusively performed.

Brain death can be certified by a single physician privileged to make brain death determinations. However, before a patient can become an organ donor, in USA the New York State law requires that the time of brain death must be certified by the physician who attends the donor at his death and one other physician, neither of whom shall participate in the process of transplantation. This requirement ensures that all evaluations meet accepted medical standards, and that all participants can have confidence that brain death determination has not been influenced by extraneous factors, including the needs of potential organ recipients.

When two physicians are required to certify the time of death, i.e., when organ donation is planned, both physicians should affirm that the clinical evaluation meets accepted medical standards, and that the data fully support the determination of brain death. Generally, both physicians should observe the patient, review the medical record, and note whether any additional information is required to make a definitive determination. Neither physician should certify brain death unless all aspects of the determination have been completed. Clinical observations compatible with the diagnosis of Brain Death.

The following manifestations are occasionally seen and should not be misinterpreted as evidence for brainstem function :

- (I) spontaneous movements of limbs other than pathologic flexion or extension response (It is very important for family members and health care professionals to be aware of natural movements also known as Lazarus sign or Lazarus reflex that can occur on a brain-dead person whose organs have been kept functioning by life support. The living cells that can cause these movements are not living cells from the brain or brain stem, these cells come from the spinal cord. Sometimes these body movements can cause false hope for the family members.)
 - (ii) respiratory-like movements (shoulder elevation and adduction, back arching, intercostal expansion without significant tidal volumes)
 - (iii) sweating, flushing, tachycardia
 - (iv) normal blood pressure without pharmacologic support or sudden increases in blood pressure
 - (v) absence of diabetes insipidus
 - (vi) deep tendon reflexes; superficial abdominal reflexes; triple flexion response
 - (vii) Babinski reflex
- Responsibility of Physician Determining Brain Death & Medical record documentation

All phases of the determination of brain death should be clearly documented in the medical record; The medical record must indicate :

- Etiology and irreversibility of coma / unresponsiveness
- absence of motor response to pain
- absence of brainstem reflexes during two separate examinations separated by at least 6 hours
- absence of respiration with $\text{pCO}_2 > 60$ mm hg
- justification for, and result of confirmatory tests if used
- Withdrawl of cardiorespiratory support & the Dead-donor

rule of organ donation

When a patient is certified as brain dead and the ventilator is to be disconnected, the family should be treated with sensitivity and respect. If family members wish, they may be offered the opportunity to attend while the ventilator is disconnected. However, family members should be prepared for the possibly disturbing clinical activity that they may witness when organ donation is contemplated, ventilatory support will conclude in the operating room and family attendance is not appropriate.

The major difficulties that arise in relation to brain death are those involving the sensitive relationship with the patient's family and other medical professionals. The task of dealing with these matters often falls to the neurologist. In addition to imparting bad news to the family, the major impetus for medical, community and legal acceptance of brain death is the need for organ donation from "beating-heart" donors.

The "dead-donor rule" requires patients to be declared dead before the removal of life-sustaining organs for transplantation. Therefore, brain death is essential to current practices of organs retrieval, because it legitimizes organ removal from bodies that continue to have circulation and respiration, thereby avoiding ischemic injuries to the organs. The physicians involved in the patient's care should be in close communication with the family during the process of determining brain death. The interpretation of clinical examination as well as findings should be clearly explained. The issue of organs transplantation should be raised after adequate time has passed for them to absorb the shock of the circumstances (and the physicians should be aware of whether family members perceive "brain death" as tantamount to death). It is important to clarify that the diagnosis of brain death is not required in patients with overwhelming brain injuries, for medical supports to be withdrawn.

CONCLUSION

Brain death is the complete and irreversible loss of cerebral and brain stem function. In most countries and in most situations, brain death is considered to be equivalent to cardiopulmonary death. The diagnosis of brain death is usually made by neurological examination, provided certain prerequisites are met; the underlying cause is understood; the etiology is capable of producing neuronal death and confounding from drug intoxication or poisoning, metabolic derangements, and hypothermia have been ruled out. The neurological examination must demonstrate coma, no brain-generated response to external stimuli and absent brain stem reflexes. The potential for organ donation offers comfort to the bereaved and should be offered to the families, but it should not be the impetus for the diagnosis of brain death.

REFERENCES

1. Guidelines for the determination of death : Report of the medical consultants on the diagnosis of death to the President's commission for the study of ethical problems in medicine and biomedical and behavioural research. JAMA. 1981;246:2184-6.
2. Guidelines for the determination of brain death in children. Pediatrics 1987; 80:298-300.
3. Practice parameters for determining brain death in adults. Neurology 1995; 45:1012-1014.
4. Wijdicks EF. Determining brain death in adults. Neurology 1995; 45:1003-1011.
5. Willatts SM, Drummond C. Brain death and ventilator trigger settings. Anesthesia 2000; 55:676-7.
6. Ruiz-Garcia M, Gonzalez-Astiazaran A, Collado-Corona MA et al. brain death in children : Clinical neurophysiology and radioisotopic angiographic findings in 125 patients. Child Syst. 2000; 16:40-45.
7. Banasiak KJ and Lister G. Brain death children Cuur. Opin. Pediatr. 2003; 15:288-293.
8. Sapsosnik G, Rizzo G, Vega A, Sabbatiello R, Deluca JL. Problems associated with the apnea test in the diagnosis of brain death. Neuro India 2004; 52:352-5.