

Brain Death : Its Relevance in the Era of Organ Transplantation

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Abstract :

Physicians and health care workers throughout the world have accepted fully 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 organ transplantation.

Key Words : Brain Death, Organ Transplantation
Introduction :

Death is the great certainty of life - it's the inevitable end.^[1] 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 brain 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.^[2] Though 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. Organ donation is the positive outcome of this grave tragedy.

Definition : Brain death is a state of irreversible cessation of all cerebral functions with preservation of cardiac activity and maintenance of respiratory and somatic functions by artificial means.^[3]

The three essential elements of brain dead are:

1. Widespread cortical destruction.
2. Global brainstem damage.
3. Destruction of medulla

Determination Of Brain Death :

The determination of brain death can be considered to consist of the following steps:

1. The Clinical Evaluation- Prerequisites^[4]

A. Establish Irreversible And Proximate Cause Of Coma : The cause of coma can usually be established by history, examination, neuroimaging, and laboratory tests.

Effect of a CNS-depressant drug must be excluded by history, drug screen, or, if available, drug plasma levels. Prior use of hypothermia (e.g., after cardiopulmonary resuscitation for cardiac arrest) may delay drug metabolism. There should be no severe electrolyte, acid-base, or endocrine disturbance. Normal core temperature must be achieved before diagnosis of brain death can be entertained. In most patients, a warming blanket is needed to raise the body temperature and maintain a normal or near-normal temperature (36°C). There should be no recent administration or continued presence of neuromuscular blocking agents (this can be defined by the presence of a train of four twitches with maximal ulnar nerve stimulation).^[5]

B. Achieve Normal Systolic Blood Pressure : Hypotension from loss of peripheral vascular tone or hypovolemia (diabetes insipidus) is common; vasopressors or vasopressin are required to maintain systolic blood pressure. Neurologic examination is reliable with a systolic blood pressure 100 mm Hg.

C. Neurologic Examination By Two Physicians : Two physicians are required to certify the time of death, when organ donation is planned, both physicians should affirm that the clinical evaluation meets accepted medical standards, and that the data fully supports the determination of brain death. Legally, all physicians are allowed to determine brain death. Neurologists, neurosurgeons, and intensive care specialists may have specialized expertise. As per the Transplantation of Human Organs Act (THOA) of India four doctors are required to certify the brain death. Examination is carried out by two doctors only but the hospital in-charge and case in-charge also have to sign the certificate of brain death (Form 10).(Annexure I)

2.The Clinical Evaluation- Neurologic Assessment :

A. Coma : Patients must lack all evidence of responsiveness. Eye opening or eye movement to noxious stimuli is absent. Central painful stimulation (e.g. supraorbital ridge, temporomandibular joint or nail bed pressure) should not produce a motor response other than spinally mediated reflexes.

Spine mediated reflexes : Certain reflexive and spontaneous movements may be seen in significant proportion of those declared dead by cerebral criteria. These are likely generated by spinal motor generators and do not invalidate an otherwise complete and clear diagnosis of brain death. Common movements include triple flexion of the lower limb (at the ankle, knee and the hip) either spontaneously or in response to stimulus. Deep tendon and abdominal reflexes are often preserved. Fine jerking of the finger or toe may be observed in some cases and rarely more complex movements are seen. The LAZARUS sign with abdominal flexion, adduction and flexion of arms can be seen commonly triggered by neck flexion but has been seen with hypoxic stimulation of cervical neurons during apnea testing or with hypotension. When brain perfusion scans are performed on patients with such movements, they invariably have confirmed lack of cerebral function.^[6,7,8]

B. Absence Of Brainstem Reflexes :

- i. **Absence Of Pupillary Response To Bright Light :** is documented in both eyes. Usually the pupils are fixed in a midsize or dilated position (4–9 mm). Constricted pupils suggest the possibility of drug intoxication.
- ii. **Absence Of oculocephalic Reflex (DOLL'S Eye Reflex) :** In oculocephalic testing, the head is briskly rotated horizontally and vertically. There should be no movement of the eyes relative to head movement.
- iii. **Absent Oculovestibular Reflex (CALORIE Test) :** is tested by irrigating each ear with ice water (caloric testing) after the patency of the external auditory canal is confirmed. The head is elevated to 30 degrees. Each external auditory canal is irrigated (one side at a time) with approximately 30 - 50 mL of ice water. Movement of the eyes should be absent during one minute of observation. Both sides are tested, with an interval of several minutes.
- iv. **Absence Of corneal Reflex :** is demonstrated by touching the cornea with a piece of tissue paper,

a cotton swab or squirt of water. No eyelid movement should be seen.

- v. **Absence Of Facial Muscle Movement to A Noxious Stimulus :** Deep pressure on the condyles at the level of the temporomandibular joints and deep pressure at the supraorbital ridge should produce no grimacing or facial muscle movement.
- vi. **Absence Of The Pharyngeal And Tracheal Reflexes :** The pharyngeal or gag reflex is tested after stimulation of the posterior pharynx with a tongue blade or suction device. The tracheal reflex is most reliably tested by examining the cough response to tracheal suctioning. The catheter should be inserted into the trachea and advanced to the level of the carina followed by 1 or 2 suctioning passes.

C. Apnea Test : conducted to demonstrate the absence of respiratory drive. Absence of a respiratory drive is tested with a Hypercarbia (CO₂) challenge.

The prerequisites of the apnea test are:

1. Normotension
2. Normothermia
3. Euvolemia
4. Eucapnea (PaCO₂ 35–45 mm Hg)
5. Absence of hypoxia
6. No prior evidence of CO₂ retention for example in patients of Chronic Obstructive Pulmonary Disease, severe obesity, neuromuscular paralysis and patients with high cervical spinal cord lesions).

PROCEDURE :

1. Adjust vasopressors to maintain a systolic blood pressure of approximately 100 mm Hg.
2. Pre-oxygenate for at least 10 min with 100% Oxygen to a PaO₂ of 200 mm Hg.
3. Reduce ventilation frequency to 10 breaths per minute to eucapnea.
4. Reduce positive end-expiratory pressure (PEEP) to 5 cm H₂O (oxygen desaturation with decreasing PEEP may suggest difficulty with apnea testing).
5. If oxygen saturation (SaO₂) remains 95% by pulse oximetry, obtain a baseline blood gas analysis (PaO₂, PaCO₂, pH, bicarbonate, base

excess).

6. Disconnect the patient from the ventilator.
7. Preserve oxygenation (e.g., place an insufflations catheter through the endotracheal tube and close to the level of the carina and deliver 100% O₂ at 6 L/min).
8. Look closely for respiratory movements for 8 - 10 minutes. Respiration is defined as abdominal or chest excursions and may include a brief gasp.
9. Abort if systolic blood pressure decreases to <90 mm Hg.
10. Abort if oxygen saturation measured by pulse oximetry is ~85% for ~30 seconds. Retry procedure with T-piece, CPAP 10 cm H₂O, and 100% O₂ 12 l/min.
11. If no respiratory drive is observed, repeat blood gas (PaO₂, PaCO₂, pH, bicarbonate, base excess) after approximately 8 minutes.
12. If respiratory movements are absent and arterial PCO₂ is ≥ 60 mm Hg (or 20 mm Hg increase in arterial PCO₂ over a baseline of normal arterial PCO₂ of 30-35 mm Hg) the apnea test result is positive and supports the clinical diagnosis of brain death.

If the test is inconclusive but the patient is hemodynamically stable during the procedure, it may be repeated for a longer period of time (10–15 minutes) after the patient is again adequately pre-oxygenated.

ANCILLARY TESTS^[9]

Confirmatory tests are optional in most guidelines and are reserved where clinical diagnosis of brain-death including apnea test cannot be completed or is doubtful.^[10] In clinical practice, EEG, cerebral angiography, nuclear scan, TCD, CTA, and MRI/MRA are currently used ancillary tests in adults (see below). Other ancillary tests that may be used to confirm brain death include multimodality evoked potential studies and the atropine test.^[11]

Common Confirmatory Tests In Brain Death :

Cerebral angiography

- Contrast medium under high pressure in both anterior and posterior circulation injections.
- No intracerebral filling at the level of the carotid or vertebral artery entry to the skull
- Patent external carotid circulation
- Possible delayed filling of the superior

longitudinal sinus

- Electroencephalography
- Minimum of eight scalp electrodes.
- Interelectrode dependencies should be between 100 and 10,000.
- Integrity of the entire recording system should be tested.
- Electrode distances should be at least 10 cm. Sensitivity should be increased to at least 2 μ V for 30 minutes with inclusion of appropriate calibrations.
- High-frequency filter setting should be at 30 Hz, and low-frequency setting should not be below 1 Hz.
- There should be no electroencephalographic reactivity to intense somatosensory or audiovisual stimuli.
- Transcranial Doppler ultrasonography
- Bilateral Insonation. The probe is placed at the temporal bone above the zygomatic arch or the vertebra-basilar arteries through the sub-occipital transcranial window.
- The abnormalities should include a lack of diastolic or reverberating flow, small systolic peaks in early systole and a lack of flow found by the investigator who previously demonstrated normal velocities.

Cerebral scintigraphy (technetium Tc 99m Hexametazine) :

Injection of isotope within 30 minutes of reconstitution. Static image of 500,000 counts at several time intervals: immediately between 30 and 60 minutes and at 2 hours. There is no uptake of isotope in brain parenchyma ("hollow skull phenomenon") in brain-death.

Conclusion : Despite the fact that the concept of brain-death was introduced more than forty years ago and has been widely accepted, differences continue with its concept and justification. In the current era, the organ transplantation programs are successful and well established. Increasing number of organs are being successfully transplanted. and the demand for donor keeps increasing by the day. The organ transplantation is the only hope for end stage organ failures patients. The limiting step in any organ transplant program (barring a few like bone marrow, stem cell and kidney where live donors are available) is availability of the

donor organs. There always is acute shortage of availability of the organs for transplantation. The braindead patients are the potential organ donors and therefore the timely diagnosis and declaration of brain dead patients cannot be overemphasized and must be promoted among the health care workers and the members of the society alike.

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