

BRAIN DEATH

Definition

Brain death is a state when the function of the brain as a whole, including the brain stem is irreversibly lost. A person certified to be brain dead is dead.

Diagnosis of brain death (All to be fulfilled)

Preconditions:

- patient is in deep coma, apnoeic and on ventilator
- cause of coma fully established and sufficient to explain the status of patient
- there is irremediable structural brain damage

Exclusions:

- coma due to metabolic or endocrine disturbance, drug intoxication and primary hypothermia (defined as a core temperature of 32 °C or lower).
- certain neurological disorders namely Guillain Barre Syndrome, Miller Fisher syndrome and Locked-in Syndrome
- coma of undetermined cause
- preterm neonates

Diagnostic Criteria (All to be fulfilled)

- deep coma, unresponsive and unresponsive, Glasgow scale 3 / 15
- apnoeic, confirmed by apnoea test
- absent brain stem reflexes confirmed by the following tests:-
 1. Pupillary light reflex.
 2. Oculocephalic reflex.
 3. Motor response in cranial nerve distribution
 4. Corneal reflex
 5. Vestibulo-ocular reflex (caloric test)
 6. Oro-pharyngeal reflex
 7. Tracheo-bronchial reflex

Test

(All conditions and exclusions fulfilled before proceeding to examine and test for brain death)

1. *Pupillary light reflex.*
No response to bright light in both eyes.
2. *Oculocephalic reflex. (Doll's eye response)*
Testing is done only when no fracture or instability of the cervical spine is apparent. The oculocephalic response is elicited by fast, vigorous turning of the head from middle position to 90° on both sides.
3. *Corneal reflex.*
No blinking response seen when tested with a cotton swab.
4. *Motor response in cranial nerve distribution.*
No grimacing seen when pressure stimulus applied to the supraorbital nerve, deep pressure on both condyles at level of the temporo-mandibular joint or on nail bed
5. *Vestibulo-ocular reflex (Caloric test).*
The test *should not* be performed if there is a perforated tympanic membrane. The head is elevated to 30° during irrigation of the tympanum on each side with 50 ml of ice water. Allow 1 minute after injection and at least 5 minutes between testing on each side. Tonic deviation of the eyes in the direction of cold stimulus is absent.

6. Oropharyngeal reflex.

Absent gag response when the posterior pharynx is stimulated.

7. Tracheo-bronchial reflex.

A suction catheter is passed down through the endotracheal tube to the level of the carina or beyond. Lack of cough response to bronchial suctioning should be demonstrated.

8. Apnoea test.

- prerequisites: the patient must be in stable cardiovascular and respiratory state.
- adjust ventilator to maintain PaCO₂ at or around 40 mmHg
- pre-oxygenate with 100% O₂ for 10 minutes
- disconnect from ventilator
- deliver 100% O₂ via tracheal catheter at 6 L/min
- monitor O₂ saturation with pulse oximetry
- measure PaCO₂ after 5 minutes and again after around 8 minutes if PaCO₂ has not exceeded 60 mm Hg
- re-connect to ventilator after the test
- the disconnection of the ventilator shall not exceed 10 minutes at any one time
- the apnoea test is **positive** when there is no respiratory effort with a PaCO₂ of ≥ 60 mmHg
- if during apnoea testing, there is significant hypotension, marked desaturation or cardiac arrhythmias immediately draw an arterial blood sample, re-connect to ventilator and analyse ABG. Should the PaCO₂ < 60 mmHg, the result is indeterminate. It is left to the discretion of the paediatrician to decide whether to repeat the test or to depend on an ancillary test to finalise the clinical diagnosis of brain death.

Note: For patients with chronic lung disease, the baseline PaCO₂ may already be above 40 mmHg. The apnoea test is then considered positive if there is no respiratory effort at a PaCO₂ of 20 mmHg above the baseline PaCO₂

Additional criteria for children

It is generally assumed that the young child's brain may be more resilient to certain forms of injury, although this issue is controversial. The *newborn* is difficult to evaluate after perinatal insults. This relates to many factors including difficulties of clinical examination, determination of the cause of coma, and certainty of the validity of laboratory tests. Hence *no recommendation can be made for preterm infants and newborn less than 7 days old*. Beyond this period, the brain death criteria apply but the interval between two examinations is lengthened depending on the age of the child, and an ancillary test (EEG) is recommended for those less than one year old.

Table 1. Time criteria and ancillary testing in children

Age	Interval between assessments	Recommended no. of EEGs
7 days – 2 mths	48 hours	2
2 mths – 1 year	24 hours	2
> 1 year ¹	12 hours	Not needed

Footnote: 1. If hypoxic ischaemic encephalopathy is present, observation for at least 24 hours is recommended. This interval may be reduced if an EEG shows electrocerebral silence.

Assessment and Certification

- Two specialists who are competent (at least 3 years of postgraduate clinical experience and trained in brain death assessment) in diagnosing brain death are qualified to certify brain death. They should preferably be paediatricians, anaesthesiologists, neurologists and neurosurgeons. Doctors involved in organ transplantation are not allowed to certify brain death.
- A repeat assessment and certification must be carried out after the first (with interval between the 2 examinations depending on the age of the child), not necessarily by the same pair of specialists.
- The 'Brain Death Certification' form is filled up by the first set of doctors (Doctor A and B) and completed by the 2nd set of doctors (Doctor C and D) or Doctor A and B if the same doctors are performing the repeat test. The time of death will then be declared by the doctors performing the repeat test.
- The time of death is at the time of the 2nd testing. Should the patient's heart stop before the repeat test, that will be taken as the time of death.
- Brain death certification must only be done in areas of the hospital with full facilities for intensive cardiopulmonary care of the comatose patients.

Pitfalls in diagnosis

- may occur in patients with
 - severe facial trauma
 - pre-existing pupillary abnormalities
 - sleep apnoea or severe pulmonary disease resulting in chronic retention of CO₂
 - toxic levels of any sedative drugs, aminoglycosides, tricyclic antidepressants, anticonvulsants, chemotherapeutic drugs, neuromuscular blocking agents.
- drug levels are useful if they can be quantified. If the drug level is below the therapeutic range, brain death can be declared.
- when the drug or poison cannot be quantified, observe the patients for at least 4 times the elimination half-life, provided the elimination of the drug or toxin is not interfered with, by other drugs or organ dysfunction.
- when the drug unknown but suspicion of its presence is high, observe the patients for 48 hours for a change in brainstem reflexes and motor response; if none are observed, perform an ancillary test (EEG) for brain death.
- determination of brain death should be deferred in the presence of severe acidosis or alkalosis as this may point to certain intoxication and potentially reversible medical illness or endocrine crisis.
- spontaneous and reflex movements have been observed in patients with brain death. The most common are finger jerks, toe flexion sign and persistent Babinski response. These movements are spinal in origin and do not occur spontaneously. They do not preclude the diagnosis of brain death.

Table 2. Common CNS depressants and pharmacodynamics

Drugs	Elimination T _{1/2}	Therapeutic Range
Midazolam	2 – 5 hours	50 – 150 ng/ml
Diazepam	40 hours	0.2 – 0.8 ug/ml
Carbamazepine	10 – 60 hours	2 – 10 ug/ml
Phenobarbitone	100 hours	20 – 40 ug/ml
Pentobarbitone	10 hours	1 – 5 ug/ml
Thiopentone	10 hours	6 – 35 ug/ml
Morphine	2 – 3 hours	70-450 ng/ml
Amitriptyline	10 - 24 hours	75 – 200 ng/ml