

Brainstem death

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Summary

The practice of diagnosing death varies between countries. It is particularly important when futility of treatment is discussed or when patients are considered for organ donation. The clinical features and diagnosis of brainstem death are described.

INTRODUCTION

This article describes the practice behind the diagnosis of brainstem death in the UK. Set definitions and criteria allow this concept to be applied for the purposes of withdrawal of critical care, when it is deemed to be futile. It also allows the harvest of organs in a heart-beating patient, where there is no chance of recovery of neurological function.

However, this practice is not international and has taken time to develop. Neurological death has long been, and still is, a difficult concept to define. There are other contexts for death which are easier to rationalise. The concept of a 'somatic death', where death is undeniable as a result of body decomposition or catastrophic injury such as decapitation is straightforward. A 'cardiovascular' death, in which there is a clear absence of any form of cardiac output or circulation, is also indisputable. But neurological death is more of a problem. This problem initially arose in the late 1950s when advances in critical care left physicians to be faced with patients who were severely brain injured, with no prospect of recovery, but were seemingly kept alive by mechanical ventilation.

Western culture agrees that the death of the brain equates to the death of an individual and should involve an irreversible inability to breathe and an irreversible lack of capacity for consciousness.

However, brain death can be taken to mean death applying to either the whole of the brain, or just the brainstem. Practice in the USA and in many European countries follows the principle of 'whole brain death'. Unlike in the UK, where the concept of brainstem death is used, those countries require confirmation of the loss of all forms of brain function.

Although the actual clinical tests used are the same, it is the role of other, confirmatory, investigations that differ. While a patient with brainstem death can be confirmed dead in the UK, the presence of cortical electrical activity on EEG or intracranial blood flow, as seen on cerebral angiography, would preclude this diagnosis in the USA. Needless to say, many controversies relating to these concepts still persist.

This article concentrates on practice in the United

Kingdom, following criteria proposed by the Conference of Royal Colleges in 1976.

ANATOMY

The brain is made up of three main embryological segments:

1. Forebrain (prosencephalon) - the cerebral hemispheres, thalamus and hypothalamus,
2. Midbrain (mesencephalon),
3. Hindbrain (rhombencephalon) - the pons, medulla oblongata and cerebellar hemispheres.

The brainstem is the physical link between the cerebral cortex and the spinal cord and it consists of the midbrain, the pons and the medulla. Most of the cranial nerve nuclei are contained here. In addition, and of particular relevance to this topic, the pons contains the reticular activating system that is vital for cortical arousal and conscious awareness, whilst the medulla contains centres that control cardiorespiratory function.

PHYSIOLOGY AND PATHOLOGY OF BRAIN INJURY

The brain is particularly susceptible to injury. It has a high metabolic requirement, comprising 20% of the body's oxygen consumption and receiving 15% of the total cardiac output.

Swelling occurs in the injured brain, with the effects of swelling exacerbated by the brain's location in the fixed volume skull. The consequent rise in intracranial pressure opposes cerebral perfusion pressure and limits cerebral oxygen delivery. This in turn contributes towards the secondary brain injury that neurocritical care aims to limit.

Intracranial pressure (ICP) that is raised to a sufficient level, for a sufficient duration, causes brainstem ischaemia and death. This may be associated by coning - a grossly elevated ICP that forces the brainstem downwards through the foramen magnum.

Neuronal tissue has no capability for repair and regeneration, so treatment options are aimed at prevention of brain injuries - both primary and secondary.

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CLINICAL FEATURES OF BRAINSTEM DEATH

In addition to profound reduction in conscious level, there are specific clinical features of brainstem death.

Damage to cranial nerve nuclei within the brain stem may cause specific neurological signs (termed *localising signs*). False localising signs describe palsies of the 3rd (or 6th, which has a long intracranial course) cranial nerve lesions that result from stretching of the nerve as it passes forwards towards the eye. The oculomotor nerve is prone to damage by herniation of the uncus of the temporal lobe or another expanding lesion, as it crosses the free edge of tentorium cerebelli. The defect of ocular gaze is therefore a manifestation of a secondary pressure effect, rather than a direct effect of the brainstem injury (hence the term *false*).

As the brainstem is compressed, pressure and ischaemia cause more systemic changes. Initially, ischaemia of the vasomotor areas within the brainstem causes systemic hypertension in an attempt to restore cerebral perfusion. This, coupled with hypertensive stimulation of the baroreceptor reflex, causes bradycardia (Cushing's sign). This may then be followed by a variety of arrhythmias and ECG abnormalities, mediated by abnormal sympathetic outflow from the brain stem, and hypotension due to systemic vasodilatation.

Hypothalamic and pituitary failure causes a reduction in thyroid hormone synthesis and secretion, which contributes to the cardiovascular changes, whilst a lack of antidiuretic hormone causes craniogenic diabetes insipidus. There may also be loss of thermoregulation usually causing hypothermia.

DIAGNOSIS OF BRAINSTEM DEATH

There is no statutory definition of death in the UK. After *brain death criteria* were proposed by the Conference of Royal Colleges in 1976, courts in England and Northern Ireland adopted them for the diagnosis of death. A Department of Health (UK) guideline defines death as the '*irreversible loss of capacity for consciousness, combined with irreversible loss of the capacity to breathe*'. This essentially defines brainstem death and is equivalent to the death of an individual.

PRECONDITIONS FOR BRAINSTEM DEATH TESTING

1. There must be an identifiable pathology causing irremediable brain damage. This may be intra- or extracranial.
2. The patient must be deeply unconscious.
 - a. Hypothermia must be excluded as the cause of unconsciousness and the patient's core temperature should be over 34°C.
 - b. There should be no evidence that the patient's state is due to depressant drugs. This refers to narcotics, hypnotics and tranquillisers, as well as neuromuscular blocking drugs. A careful drug history is required, whilst drug levels and antagonists may need to be used.
 - c. Potentially reversible circulatory, metabolic and endocrine disturbances must have been excluded as the cause of the continuing unconsciousness. Some of these disturbances may occur as a result of the condition, rather than the cause, and these do not preclude the diagnosis of brainstem death.

3. The patient must be apnoeic, needing mechanical ventilation. This condition must not be secondary to the effect of sedative drugs or neuromuscular blockade. This may require testing with a nerve stimulator to show intact neuromuscular transmission. Alternatively, demonstration of tendon reflexes can also demonstrate intact transmission.

BRAINSTEM DEATH TESTING

In the UK, the tests must be carried out by two doctors who have held full registration with the General Medical Council for more than five years, one of whom should be a consultant. Both should have adequate experience of interpreting the results and neither should be a member of the transplant team.

Two sets of tests should be performed to remove the risk of observer error. The two doctors may perform the tests together or separately and, although no defined time interval has to elapse between the tests, it should be of sufficient duration to reassure the patient's next-of-kin.

The time of death is recorded when the *first test* indicates brain death.

The rules apply to children over the age of two months and cannot be applied to those below 37 weeks gestation. It is rarely possible to apply the criteria to children between these ages.

Once brainstem death has been diagnosed, cessation of the heart beat follows within a short period. This has been confirmed and validated in published series.

THE TESTS

1. **Pupils must be fixed** in diameter and not responsive to incident light. (Cranial nerves II, III).
2. There must be **no corneal reflex** (avoid damaging the cornea). (Cranial nerves V, VII).
3. **Vestibulo-ocular reflexes are absent**. No eye movements occur following the slow injection of at least 50ml ice cold water over one minute, into each external auditory meatus. Note that the normal reflex is deviation of the eyes away from the side of the stimulus. Access to the tympanic membrane should be confirmed by otoscopy. Injury or pathology may prevent this test being performed on both sides – this does not invalidate the test. (Cranial nerves VIII, III).
4. **No motor responses** in the cranial nerve distribution should occur as a result of stimulation of any somatic area. No limb movement should occur in response to supra-orbital pressure. (Cranial nerves V, VII).
5. **No gag reflex** should occur in response to posterior pharyngeal wall stimulation with a spatula. (Cranial nerve IX).
6. **No cough** or other reflex should occur in response to bronchial stimulation by a suction catheter being passed down the endotracheal tube. (Cranial nerve X).
7. **No respiratory movements** should occur in response to disconnection from the ventilator ('apnoea test'). Hypoxia should be prevented by preoxygenation and insufflation of oxygen through a tracheal catheter. This tests the stimulation of respiration by

arterial carbon dioxide tension which should be allowed to rise to 6.65kPa – confirmed by arterial blood gases.

MANAGEMENT OF BRAINSTEM DEAD PATIENT

Relatives, partners and carers need to be kept informed of the patient's condition in a sympathetic and appropriate manner, that is tailored to the individuals concerned. Standard medical care must be continued in those in whom brain stem death has not been conclusively established and may be continued after this, in order to maintain the condition of organs for donation. This may include maintaining fluid and electrolyte balance or haemodynamic parameters.

Initiating mechanical ventilation in those patients thought to have irremediable brain damage, who stop breathing before brain stem death testing can occur, is only justified if it is of benefit to the patient. It is unlawful for this to occur in order to preserve organ function.

ORGAN DONATION

A local transplant coordinator should be contacted early once the potential for organ donation is recognised. Once brainstem death has been established, the priority becomes preserving and optimising the potential transplantable organs.

Respiratory support should be continued, maintaining normal blood gas parameters, but minimising the harmful effects of positive pressure ventilation (e.g. avoidance of excessive positive end-expiratory pressure and excessive FiO_2).

Hypotension is common following brain stem death and can compromise the perfusion of transplantable organs. It may occur as a result of decreased sympathetic tone, diabetes insipidus, cold diuresis

or cardiac dysfunction. It should be treated with fluids, vasopressors or inotropes as appropriate.

Normothermia should be maintained as per standard critical care management, as it may contribute to coagulopathy, acidaemia, cardiac arrhythmias and diuresis. Endocrine support may also be required to reduce the need for inotropes and delay cardiac arrest. Vasopressin, insulin, tri-iodothyronine and methylprednisolone may all be used.

CONTRAINDICATIONS TO ORGAN DONATION

- Positive HIV, Hepatitis B or C, HTLV, syphilis or malaria tests
- Evidence of Creutzfeldt-Jakob disease
- Progressive neurological disease of unknown cause (e.g. Alzheimer's, Parkinson's, motor neurone disease)
- Untreated systemic sepsis
- Uncontrolled hypertension or end-organ damage from hypertension or diabetes mellitus
- Malignancy
- A previous transplant recipient who has received immunosuppressive treatment.

FURTHER READING

Statement by the Honorary Secretary of the Conference of Medical Royal Colleges and their Faculties in the UK on 11 Oct 1976; Diagnosis of Brain Death. *British Medical Journal* 1976; **2**:1187-1188

Department of Health; A Code of Practice for the Diagnosis of Brain Stem Death. HMSO, London 1998.