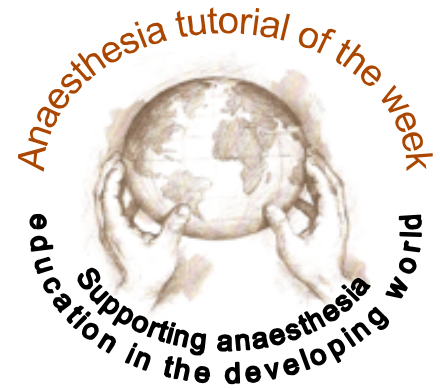


BRAINSTEM DEATH
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Questions:

1. The following can be associated with brainstem death:
 - a. Hypothermia
 - b. Diabetes mellitus
 - c. Cushing's reflex
 - d. Cardiac arrhythmias

2. The following are required for brainstem death testing:
 - a. Two doctors with at least 3 years of medical registration
 - b. Four vessel cerebral angiography
 - c. Core temperature of above 34°C
 - d. An iso-electric EEG

3. The following are contra-indications to organ donation:
 - a. Major trauma
 - b. Intravenous drug abuse
 - c. Syphilis infection
 - d. Diabetes mellitus

4. Brain stem death testing must include:
 - a. Testing for apnoea with an arterial CO₂ of greater than 7.0 kPa
 - b. The absence of a corneal reflex
 - c. Two sets of tests separated by 24 hours
 - d. Absent vestibulo-ocular reflexes bilaterally

Brainstem Death

INTRODUCTION

As intensive care practices and facilities improved and became more widely available, it became a more common occurrence for severely brain damaged patients to be supported with mechanical ventilation. There has never been an actual statutory definition of death in the United Kingdom, unlike in the United States of America, and this was one factor that led to the development of brainstem death criteria. These would allow futile treatments to be withdrawn and organs to be donated if appropriate, safe in the knowledge that there would be no chance of a recovery.

This article describes the basic science behind brainstem death, the methods of testing for brainstem death and discusses the management of these patients.

ANATOMY:

The brain is made up of three main embryological segments.

1. Fore-brain (prosencephalon). Cerebral hemispheres, thalamus and hypothalamus
2. Mid-brain (mesencephalon).
3. Hind-brain (rhombencephalon). Pons, medulla oblongata, 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 article – the pons contains the reticular activating system that is vital for cortical arousal and conscious awareness, whilst the medulla contains centres that control cardio-respiratory 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 may occur in the injured brain and the effects of this in a fixed-volume container such as the skull are well known. The consequent rise in intra-cranial pressure opposes cerebral perfusion pressure and limits cerebral oxygen delivery. This in turn contributes towards the secondary brain injury that neuro-critical care aims to limit.

Ultimately, a significantly raised intra-cranial pressure will cause brainstem death by causing coning – the brainstem is forced through the foramen magnum.

Neuronal tissue is one of the few with no capability for repair and regeneration so treatment options are really aimed at prevention of brain injuries – both primary and secondary.

CLINICAL FEATURES OF BRAINSTEM DEATH:

There will obviously be a profoundly reduced level of consciousness but there are specific clinical features that may also be present.

Localising signs such as cranial nerve lesions may be seen, depending upon the site of any lesion or injury. False localising signs such as 3rd and 6th cranial nerve lesions can also occur. The former is as a result of stretching of the oculomotor nerve over the tentorium cerebelli, usually by herniation of the uncus or

another expanding lesion. The latter may occur as the abducens nerve, with its long intracranial course, is stretched by swelling.

As the brainstem is compressed, pressure and ischaemia cause more systemic changes. Initially, Cushing's reflex occurs, with hypertension and a subsequent bradycardia (mediated by the baroreceptor reflex) attempting to restore cerebral perfusion. This may then be followed by a variety of arrhythmias 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 anti-diuretic hormone causes diabetes insipidus. There will also be a loss of thermoregulation with hypothermia being the usual finding.

DIAGNOSIS OF BRAINSTEM DEATH:

There is no statutory definition of death in the UK. After the "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 guideline defines death as the "irreversible loss of capacity for consciousness, combined with irreversible loss of the capacity to breathe". This essentially defines brain stem 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 extra-cranial.
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 brain stem 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:

The actual 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 50mls of 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. Hypoxia should be prevented by pre-oxygenation 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 6.65 kPa – confirmed by arterial blood gases.

MANAGEMENT OF BRAINSTEM DEAD PATIENT:

It goes without saying that relatives, partners and carers need to be kept informed of the patient's condition in a sympathetic and appropriate manner. This obviously needs to be 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 co-ordinator 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 FiO₂).

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.

CONTRA-INDICATIONS 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.

ANSWERS TO QUESTIONS:

1. Hypothermia and cardiac arrhythmias may occur in response to pituitary failure and brainstem ischaemia / compression respectively. Diabetes insipidus also occurs as a result of pituitary failure, whilst Cushing's reflex is a haemodynamic response to raised intra-cranial pressure.

2. The two doctors who perform brainstem death testing must each have at least five years of GMC registration. There is no requirement for EEG or radiological investigations in the United Kingdom. Hypothermia must be treated before brain stem death can be established.

3. See list above.

4. There is no mandatory interval between the two sets of brain stem death tests.

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.