Brain stem death

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Abstract

The concept of brain and brain stem death developed from the observation of patients in apnoeic coma. Specific pre-conditions must be met before the diagnosis can be made through the clinical testing of brain stem function. Although the exact definition of brain death and some of the details for testing vary across the globe, the majority of tests carried out are similar. We define brain stem death and the clinical tests used to confirm it. The use of ancillary testing can have a role in patients where clinical tests are not possible.

Keywords apnoeic coma; brain death; brain stem death; brain stem death testing

Royal College of Anaesthetists CPD matrix: 1AO1, 2CO1, 2CO6

Learning objectives

After reading this article, you should be able to:

- describe the anatomy of the brain stem and the physiological changes associated with brain stem death
- identify the pre-conditions required and the clinical tests used for brain stem death assessment

Anatomy

The brain stem is the posterior part of the brain, adjoining and structurally continuous with the spinal cord. It is divided in to three distinct areas; the medulla, the pons and the midbrain (Figure 1). The pons contains the reticular activating system that is vital for cortical arousal and conscious awareness, whilst the medulla contains the centres that control cardio-respiratory function.

Diagnosis of death

Prior to the advent of intensive care, the diagnosis of death was relatively simple. Death occurred at the cessation of respiration which inevitably led to the cessation of circulation. The advent of long-term ventilation techniques in the 1950s meant inadequate ventilation no longer immediately led to circulatory death. With the advent of these techniques, case series of patients with profound irreversible apnoeic coma began to be described.

These patients had no angiographic evidence of blood flow to the brain, although no obstruction to flow was demonstrated at autopsy. They had no spontaneous respiration, an absence of all electroencephalogram (EEG) activity, areflexia, polyuria and vasopressor dependent hypotension. These patients proceeded to circulatory death if artificial ventilation or vasopressors were discontinued. These finding were characteristically described in 1958 as 'coma dépassé' (i.e. 'beyond coma'.)

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The formalisation of criteria to diagnose brain death occurred in 1968 when the Harvard Committee and the World Medical Assembly produced statements that became the first widely accepted standards for the confirmation of brain death. The development of standards for diagnosis of brain stem death allowed for appropriate treatment limitations to be put in place for these patients. Although the concept of brain death evolved relatively contemporaneously with the first allogenic organ transplants, it developed independently.

The statements have been refined over time and different countries have produced their own guidelines. The current UK definition of death is that described by The Academy of Medical Royal Colleges (UK) description of death:

> *'Death entails the irreversible loss of those essential characteristics which are necessary to the existence of a living human person and, thus, the definition of death should be regarded as the irreversible loss of the capacity for consciousness, combined with irreversible loss of the capacity to breathe.'*

Brain stem death

There remain global differences in nomenclature regarding brain stem death. In some countries (e.g. Australia, New Zealand, USA), demonstration of whole brain death is required to determine death. In the majority of cases of brain stem death, acute whole brain injury is evident radiologically. However, in cases of isolated brain stem injury, whole brain injury is not evident and blood flow to the rest of the brain remains. Such patients could therefore not be defined as brain dead in some countries.

Confirming brain stem death is the basis of determining death in patients in apnoeic coma in the UK. The cessation of brain stem function does not necessarily entail cessation of neurological activity in the whole brain. Any potentially remaining function in brain other than the brain stem is not seen to constitute the essential characteristics necessary for a living human existence and so these patients can be defined as dead in the UK.

Physiological changes associated with brain-stem death

Cardiovascular – initially there is a massive sympathetic discharge, resulting in tachycardia and hypertension. With further swelling Cushing's reflex occurs in one third of patients (hypertension with bradycardia), in an attempt to maintain cerebral perfusion. The sympathetic surge subsequently dissipates and is followed by vasodilatation induced hypotension in the

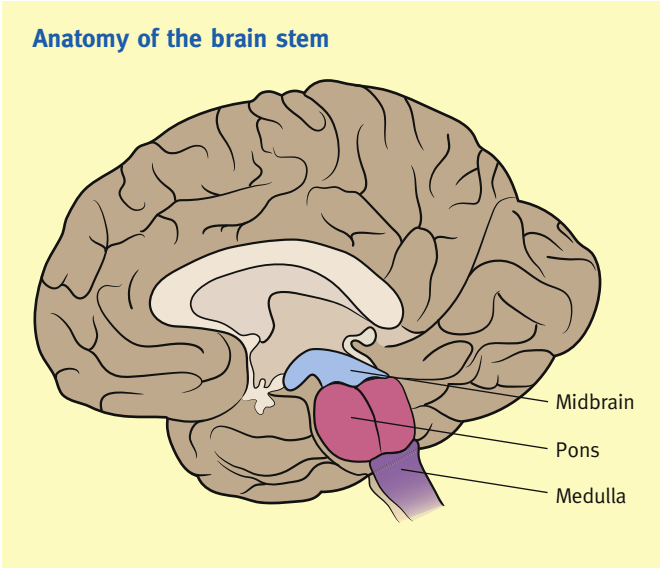

Figure 1

majority of patients. Arrhythmias can also occur. Any hypotension may be worsened by concomitant hypovolaemia.

Endocrine – pituitary failure causes a reduction in anti-diuretic hormone (ADH) production. This results in an inappropriate diuresis (neurogenic diabetes insipidus) with resulting hypovolaemia and hypernatraemia. There is reduced thyroid hormone synthesis and secretion as well as reduced cortisol production. These hormonal changes can also adversely affect the cardiovascular state. Hypothalamic failure leads to loss of thermoregulation. The patient may need active control of body temperature.

Diagnosis

Clinical assessment of brain stem function alone can determine brain stem death in the UK. However, clinical testing can only be undertaken when specific preconditions are met.

UK tests must be carried out twice by two doctors (at least one a consultant) registered for >5 years. They should be competent to conduct and interpret the tests and have no clinical conflict of interest. There is no set time limit to repeat tests but both physicians take part in both sets. If both sets confirm brain stem death, the time of death is the time of first set completion.

The UK testing process for children is the same as the adult process. Diagnosis of brain death in premature newborns and full term infants <2 months old is not possible.

Preconditions

1) Evidence of a defined aetiology of irreversible brain damage.
2) The exclusion of potentially reversible causes of coma:
    a. depressant drugs
    b. primary hypothermia
    c. significant circulatory, metabolic or endocrine disturbance.
3) The exclusion of potentially reversible causes of apnoea.

In most cases of apnoeic coma the cause of brain damage is known. The most common causes are trauma, sub-arachnoid haemorrhage, intracranial haemorrhage and hypoxic brain injury. Occasionally the cause of coma cannot be established. Without a recognized cause, patients cannot be determined brain dead and testing cannot be performed.

Actions of sedative or depressant medication should be excluded. This will depend on the drugs in question, co-existing renal or hepatic failure and the patient's pharmacokinetics. Specific drug levels can be tested (e.g. thiopentone or midazolam). Antagonists may be useful if opioid or benzodiazepines may be contributing to the coma. Neuromuscular blocking drugs can be excluded as the cause of apnoea by the use of a peripheral nerve stimulator.

Patients should be warmed to a core temperature of >34 °C to exclude primary hypothermia as a cause of coma. If therapeutic hypothermia post cardiac arrest has been instituted, the patient must be allowed to rewarm before brain function is formally assessed. UK recommendations are that brain stem death testing is deferred for at least 24 hours once normothermia is achieved, to allow any residual sedative drugs to be metabolised (sedative drug clearance possibly being reduced by therapeutic hypothermia).

Potentially reversible circulatory, metabolic and endocrine causes should be excluded (Table 1). Many of these changes may occur during the brain stem death process. The majority of patients will need vasopressor support to maintain a blood pressure sufficient to allow testing to proceed. Electrolyte correction may be difficult and rapid correction purely for the purposes of brain death testing may be detrimental – too rapid correction of hyponatraemia may itself result in the development of central pontine myelinolysis and coma. Although rare, severe hypothyroidism and Addisonian crisis may result in coma and should be excluded by hormonal assays if any clinical suspicion is raised.

Co-existing high cervical spinal injuries may limit clinical testing and ancillary tests may be required.

Clinical assessment

Brain stem reflexes are tested by clinical examination and the respiratory response to hypercarbia (apnoea test) is assessed.

Conditions precluding brain stem death testing (UK)

Temperature	**< 34 °C**
Circulatory	Inability to maintain MAP consistently > 60 mmHg
Metabolic	Na <115 or >160 mmol/L
	K < 2 mmol/L
	Mg <0.5 or >3 mmol/L
	Phosphate <0.5 or >3 mmol/L
	Glucose <3.0 or >20 mmol/L
	$PaCO_2$ > 6.0 KPa
	pH <7.35 or >7.45
	PaO_2 < 10 KPa
Endocrine	Clinical suspicion of significant endocrine abnormality

Table 1