Brain Stem Death & Management of the Organ Donor

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Associated clinical guidelines/protocols:
- A Code of Practice for the Diagnosis of Brain Stem Death including guidelines for the identification and management of potential organ and tissue donors. Department of Health.
- Local guidelines / policy for Donation after Circulatory Death (DCD).
- Local guidelines / policy for Donation after Brain stem Death (DBD).

Fundamental Knowledge:
List of topics relevant to PIC that will have been covered in membership examinations.
They will not be repeated here.
- Management of Diabetes Insipidus
- Responsibilities and activities of Specialist Nurses – Organ Donation (SNODs)
- Understand the conditions required for the retrieval of different organs
- Attitude of major religions to brain death and dying

Information for Year 1 ITU Training (Basic)

Year 1 ITU curriculum
- Assessment of brain stem death; preconditions, exclusions and tests for the diagnosis of brain stem death; understand the factors involved in diagnosing brain death in neonates.
- Basics of ITU Management of potential organ donor

Curriculum Notes for Year 1:
Death can be defined as
- The irreversible loss of the capacity for consciousness (cerebral cortex), combined with
- irreversible loss of the capacity to breathe (brain stem).

When the brain stem has been damaged from whatever cause in such a way and to such a degree that its vital functions are irreversibly destroyed, the heart will inevitably stop. The patient is dead, even though respiration and circulation can be artificially maintained.

Performing BSD tests will confirm that death of the brainstem has occurred, and that the patient fulfills the criteria for “legal” death.
Following confirmation of BSD, it is important to consider if it is appropriate to for the patient to donate organs for transplantation, and to enable discussion with the relatives.

The Clinical Lead for Organ Donation (CLOD), and Specialist Nurse for Organ Donation (SNOD) are a useful source of knowledge, education and support and should be involved where appropriate.

**Brain Stem Death (BSD) testing** (1), (2)

The following preconditions must be satisfied before doing BSD tests

1. There should be no doubt that the patient’s clinical condition is due to irremediable brain damage of known aetiology. In patients where the primary pathology is in doubt, then a period of continuing clinical observation and investigation may be necessary.

2. The patient is deeply unconscious, and the coma is not due to depressant drugs hypothermia or potentially reversible circulatory, metabolic and endocrine disturbances.

3. The patient is maintained on mechanical ventilation because spontaneous respiration has been inadequate or ceased altogether. Muscle relaxants, sedatives and opiates have been excluded as a cause of respiratory failure.

4. Relevant drug levels e.g. thiopentone may need to be measured, to ensure they are not responsible for the clinical state (hence the levels need not be zero).

Where organ donation is being considered, BSD tests must be performed by at least two medical Practitioners, registered for >5 years, and are competent in this field. At least one should be a consultant and one should not be primarily involved in the child’s care, (i.e. not members of the same team). They must not be members of the transplant team.

Two sets of BSD tests are performed, and may be carried out by the two practitioners separately or together. The interval between these tests is a matter for clinical judgment.

Although death is not pronounced until completion of the second set of tests, the legal time of death is when the first BSD test is completed indicating brain stem death.

**Criteria – absence of all brain stem reflexes**

- Pupils fixed and unresponsive to light- this assesses cranial nerves II, III
- Absent corneal reflexes – this assesses cranial nerves V, VII
- Absent oculo-vestibular reflexes (Cold calorics. Instil 20mls ice-cold water into each external auditory meatus in turn. Ensure clear access to tympanic membranes – by visualisation of the tympanic membrane prior to this being undertaken) – this assesses cranial nerves III, VI, VIII
- No motor response to painful stimulation in the distribution of the supra-orbital nerve. This removes element of spinal reflex activity. Where there is risk of cervical spine injury, the painful stimulus must be applied below the neck (for example nail bed pressure to elicit a painful stimulus) – this assesses cranial nerves V, VII
- No gag reflex (this must be performed under direct vision) or reflex response to bronchial stimulation to suction catheter – this assesses cranial nerves IX, X
• Apnoea test – No respiratory movement detected even when the arterial PCO$_2$ is >6.65kPa (50 mmHg), against a background of a normal PaO$_2$.

This is best performed last especially as some patients do not tolerate disconnection well and at least you would have finished the other tests. Hypoxia is prevented during disconnection by delivering oxygen through a catheter in the trachea or with a re-breathe circuit connected to deliver oxygen and some CPAP.

It is essential that relatives are kept fully informed and some parents may wish to be present during the tests, as it removes any doubt they may have and helps with grieving. It is important to explain each test and the interpretation. It is important in this situation to explain spinal reflex to the relatives.

**Infants and Children**

*Working party of the British Paediatric Association (1991)* (3) concluded:

- >2 months criteria same as in adults
- 37 weeks gestation - 2 months rarely possible to confidently diagnose BSD
- < 37 weeks gestation criteria cannot be applied
  - Brain stem reflexes development not systematically studied in pre-term infants
  - Many critical functions in the process of or just recently developed
  - Therefore the concept of BSD is inappropriate in this age group. (3,4,6)

At least one of the clinicians performing BSD assessment should be a paediatrician.

As drugs take longer to clear in children, it is prudent to measure drug levels to confirm they play no part in potentiating coma. It has been shown that phenobarbitone levels >25mcg/ml may suppress EEG activity in this age group (7).

Withdrawal of life sustaining therapy is acceptable solely on the basis of the best interests of a devastatingly ill infant (see document from RCPCH on Withholding or withdrawing life sustaining treatment in children (8), and BSD does not need to be confirmed for this to occur.

In the USA a different concept of death is used – whole brain death - so ancillary investigations are required (4), (5) A different age group stratification and a recommended time interval between the two examinations for different ages and different pathologies exists.

Where it may be challenging to undertake a neurological examination, ancillary testing may be helpful. These investigations include:

- EEG, brain stem evoked responses with loss of bio-electric activity in the brain
- CT angiography, 4-vessel angiography, transcranial doppler where absent cerebral blood flow / brain tissue perfusion will be present

Following declaration of brainstem death there are two possible outcomes for the patient:

- Intensive care is withdrawn
- Organ donation is considered

**Organ Donation**

Organ donation is an important part of the process of end-of-life care. Donation can take place following brainstem death (DBD), and circulatory death (DCD).

Use local policy / guidelines when organ donation is being considered and undertaken.
PROCEDURE FOR THE DIAGNOSIS AND MANAGEMENT OF BRAIN STEM DEATH

Identification of Coma

↓ Yes

Clinical evidence of cause of coma
(possibly supported by neuroimaging, neurophysiology, CSF, etc.)

↓ Yes

Exclusion of hypothermia, intoxication, sedative drugs, neuromuscular blocking agents, severe electrolyte, acid base or endocrine abnormalities as causative

↓ Yes

Absent Brain Stem Reflexes
Absent Motor Response
Apnoea PCO₂ ≥ 6.65kPa
These procedures should be clearly explained to relatives

↓ Yes

CLINICAL DIAGNOSIS OF BRAIN STEM DEATH

↓

Eligible for Organ Donation

↓ Yes  ↓ No
Proceed with Enquiries and Testing Prior to Organ Donation Disconnect from Ventilator

18
Donor management
The ICU management, if BSD is not established, will be standard for that physiology. Once BSD has been established and organ donation possible the targets change appropriately away from a neuroprotective ICU to a strategy of optimising organ function in those systems in which donation may be possible.

However if artificial ventilation has not been instituted at the time it is not in the patient’s best interest, and in fact unlawful, to electively ventilate for the sole purpose of preserving organ function (10,11).

Donation after Brain Stem Death (DBD)
Widespread physiologic changes follow BSD and the rapid decline can be stabilised by active donor resuscitation and effective donor management strategies (12,13). The intense sympathetic outflow accompanying BSD leads to a substantial rise in circulating catecholamine levels (sympathetic storm).

- A number of hormonal changes occur and reflect anterior and posterior pituitary failure: 80% of BSD patients develop Diabetes Insipidus (DI)
- Cortisol levels fall and contribute to cardiovascular instability.
- Insulin levels fall leading to hyperglycemia, intracellular energy deficit, anaerobic metabolism and acidosis.
- DIC occurs because of activation of coagulation pathways as the ischaemic brain releases tissue thromboplastin.
- There is upregulation of proinflammatory mediators and activation of endothelial cells, platelets and leucocytes.

Application of a standardised donor management protocol results in significant increases in organs retrieved without any reduction in quality of transplanted organs. There are guidelines available from Canada for the medical management to optimize donor organ potential (13) a UK version is under development.

Cardiovascular support
Aim: Protect heart from ischaemic damage whilst maintaining perfusion to other organs.

- Perform ECG and echo.
- Arrhythmias are common and should be treated.
- Short-acting b-blockers (e.g. Esmolol) useful initially to attenuate sympathetic overactivity, although sympathetic storm is usually short-lived.
- Keep BP within normal age limits: fluid, inotropes or dilators. Aim CVP 6-10 mmHg.
- Invasive CVS monitoring and targeted resuscitation optimise post-transplantation organ function, e.g. initiation of inotropes/vasopressors to preserve organ viability.
- However many conventional treatments for haemodynamic instability may worsen myocardial injury.
- Low dose vasopressin is increasingly being used as first line support, as in addition to treating DI, it also restores vasomotor tone, improves BP and reduces exogenous catecholamine requirements.

Pulmonary support
Aim of mechanical ventilation is to maximize oxygen delivery to transplantable organs.

- Ventilation strategy should change from cerebral protection to lung protection (14).
- Recommended: TV 6-8 ml/kg with PEEP at 5-10 cmH2O and PIP <30cmH2O
- If lungs considered for transplantation: FiO2 and TV should be as low as necessary to achieve a PaO2 > 10kPa and pH 7.35-7.45.
- Routine ETT suction and chest physiotherapy should be continued.
- Fluids should be given cautiously and diurese to normovolemia to prevent pulmonary oedema, but not excessively.

Hormonal support
Diabetes Insipidus is common and should be treated.
Recent guidelines advocate using a standardized hormonal package of methylprednisolone (15 mg/kg bolus), triiodothyronine (4 μg bolus followed by infusion of 3 μg/h) and arginine vasopressin (0.0003-0.0007 U/kg/min).

This is associated with improved organ function and recipient results (15). In addition, insulin may be required to treat hyperglycaemia.

Other support
Correct any coagulopathy and maintain normothermia.

Donation after Circulatory Death (DCD)
In some situations the patient does not fulfil BSD criteria or BSD cannot be determined although it is clear that the patient has a non-survivable injury. In such situations the organs can only be retrieved after somatic death, and a planned withdrawal of life sustaining therapies, which are considered futile, can occur (controlled DCD). The opinion on futility needs to be robust enough to withstand allegations of “conflict of interest”. Occasionally the patient dies before BSD tests can be performed or cardiopulmonary resuscitation after unexpected cardiopulmonary arrest is unsuccessful (uncontrolled DCD). Most of the situations in ICU would fall into category 3 or 5 of the modified Maastricht classification of non-heartbeating donors:

- Category 1: dead on arrival at hospital
- Category 2: unsuccessful resuscitation
- Category 3: awaiting cardiac arrest e.g. after withdrawal of life support
- Category 4: cardiac arrest after confirmation of BSD
- Category 5: unexpected cardiac arrest in a critically ill patient

In view of the improvement in surgical techniques, better postoperative management and range of immunosuppressive drugs, the results with marginal grafts have improved. Solid organs suitable for transplantation following DCD are the kidneys, liver and lungs. It has been shown that organ function is improved with a short period of time from asystole and organ retrieval. Viability is promoted by minimization of the warm and cold ischaemia time and protective measures such as antibiotics, steroids and heparin.

Withdrawal of life sustaining therapies can occur in the ITU (generally if the ITU is next to the Operating Theatre area) or in the anaesthetic room with the surgical team on standby. Infusions of opioids and sedatives can be commenced to ensure the patient is pain free and not distressed.

Death may occur quickly and the family may not have much time with their loved one if organ donation is to be possible. Certification of death should be performed a minimum of five minutes after the cardiorespiratory arrest.

Following withdrawal of life-sustaining therapy, the time period to cardiorespiratory arrest may be prolonged (time) in which case the organs will not be suitable for transplantation because of the prolonged warm ischaemia time, although tissues (heart valves and corneas) can still be used. The correct processes of tissue donation must be followed if this is to be undertaken – and this pathway must be discussed with local SN-ODs.

Measures are taken to improve organ viability after withdrawal of life sustaining therapy. Surgical lines are inserted to initiate cold perfusion before organ retrieval. Aggressive donor management significantly increases the donor pool and the availability of organs for transplantation, but this creates conflict with the primary principle of “best interests” of the patient. However if “best interests” incorporates “the patient’s wishes and beliefs, their general well-being and their spiritual and religious welfare” and it has been ascertained that the patient wished to be a donor, then it is reasonable to assume that they would wish the organs to be donated at maximal viability. These measure can then be accommodated under the term “best interests” and therefore comply with ethical principles. Interesting articles on the ethics of DCD are included below (16,17). The practical difficulties surrounding organ procurement in ‘controlled’ NHBD have been demonstrated recently (18,19,20).

Recent US attempts to provided infants hearts this way remain illegal under UK law (21).
Information for Year 2 ITU Training (advanced)

Year 2 ITU curriculum

- Ancillary neurologic tests and their role: EEG, cerebral perfusion studies, SSEVPs, BSEVPs

Curriculum Notes for Year 2:

Ancillary investigations

In the UK the results of neurophysiological or imaging investigations are not included as part of the criteria. There is at present no evidence that these assist in the determination of BSD. However some of these investigations (EEG, cerebral perfusion scans, 4 vessel angiography) are part of the diagnostic requirement in the USA, Japan and parts of Europe. In a retrospective review of term and preterm infants, EEGs and radionuclide scanning confirmed clinically determined brain death in only one half to two thirds of infants <1 month (7). The morphologic features of evoked potential waves remain basically unchanged by external factors (drug administration, metabolic problems or temperature variations). Hence they have an advantage over the other tests, and can be very useful additional information in suspected brain stem death. Absence of brain stem auditory evoked potentials (BSAEP) and somatosensory evoked potentials (SSEP) can also be seen earlier than electro-cerebral silence on the EEG [18].

Other sources of information:

- GOS / Local Leaflet for parents explaining BSD and tests
- A Code of Practice for the Diagnosis of Brain Stem Death
- Diagnosis of Brain Stem Death in Infants and Children. British Paediatric Association 1991. Unfortunately no longer in print and not archived in the RCPCH website. New working party looking at revision
- Withholding and Withdrawing Life Sustaining Treatment in Children: a framework for Practice. RCPCH May 2004
- Intensive Care Society: Guidelines for adult organ and tissue donation
- Timely Identification and Referral of Potential Organ Donors. NHS Blood and Transplant, September 2012
- Form for the Diagnosis of Death using Neurological Criteria – guidance document circulated by Joe Brierly on behalf of PICS, October 2012 – comments can be sent to dalegardinder@doctors.net.uk

Websites:

http://www.dh.gov.uk/assetRoot/04/03/54/62/04035462.pdf
http://www.dh.gov.uk/assetRoot/04/06/13/82/04061382.pdf
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8. Withholding and Withdrawing Life Sustaining Treatment in Children; a framework for Practice. RCPCH May 2004


