1 Background information

Quick info:

Donation after Brain-stem Death, Adult Pathway

Scope:

• Donation after Brain-stem Death (DBD), also known as Heartbeating Donation (HBD), refers to the retrieval of organs and eye tissue for the purposes of transplantation after death that is confirmed using neurological criteria (brain-stem death).

• In the UK, DBD programmes currently support the retrieval and transplantation of the following solid organs:
  • Heart
  • Lung
  • Kidney
  • Liver
  • Pancreas
  • Small bowel (stomach, ileum, jejunum, colon, abdominal wall, spleen)
  • Facial tissue (in some parts of England)

• Tissue donation from potential DBD donor, including when solid organ donation does not progress

• Donation from all care settings, most commonly but not exclusively ICUs and Emergency Medicine Departments

Out of scope:

• Donation from paediatric patients
• Tissue donation from tissue only donors
• However information is provided on tissue only donation for patients who start on the clinical pathway

Incidence and prevalence:

• The incidence of diagnosed brainstem death on ICUs in the UK has declined considerably over recent years, with the Potential Donor Audit recording 1147 cases in 2008/9 compared to 1339 in 2004/5. There has been a corresponding fall in the number of heartbeating brain-stem donors, from 664 to 611 respectively. DBD donors donate an average of 4 organs per donation.


2 Information resources for patients / families

Quick info:

An information leaflet for families is available here: Organ and Tissue Donation Information for Families

3 Updates to this pathway

Quick info:

This is the first version of this pathway.

4 Management of brain-stem dead donor

Quick info:

Pathophysiology of heart-beating brain-stem dead donor

The deranged pathophysiology of the heartbeating brainstem dead donor is multi-factorial, and is to a greater or lesser extent a consequence of 1. the primary pathology suffered by the patient, 2. the complications of critical care treatments and, specifically, therapies that are directed towards resuscitation of the acutely injured brain, 3. the altered physiology associated with brainstem death, and 4. a systemic inflammatory response that is centred upon the pulmonary microcirculation.

Overview of management of brain-stem dead donor

Physiological changes occurring during the development of brain death may lead, if untreated, to rapid deterioration and cardiac arrest even if ventilation is continued. There may be variations in timing and rapidity of change, but there are generally predictable derangements which can be moderated, or even reversed to some extent.
The aim is to restore stability, and maintain or improve organ function to enhance the likelihood of successful transplantation. Intensive monitoring and therapy will be necessary. This is best delivered in a Critical Care environment such as an Intensive Care Unit (ICU), and by those who have experience of specialist intensive care. General ICUs may not manage these situations on a regular basis. Although many of the therapies are similar to those delivered to other ICU patients, there are specific recommendations for monitoring and drugs which may not be regularly used, and therefore the use of guidelines, and collaboration with transplant units and Specialist Nurses Organ Donation may be helpful.

In the UK currently, an average of four organs are retrieved from each heartbeating donor, with kidney and liver retrieval in approximately 90% of cases. Retrieval of thoracic organs is much less common (25% and 18% of heartbeating donors respectively for heart and lungs), and represents a significant obstacle to heart and lung transplantation. Packages or ‘bundles’ of donor management techniques are associated with increased numbers of donors, organs per donor, and function of subsequently transplanted organs.

Optimal management of the brain-dead heartbeating organ donor can maximise the potential for organ donation by reducing loss of donors prior to retrieval, and improving chances of organs being transplantable.

5 General care

Quick info:
It is important to present clear, unambiguous information to relatives, who are often present at the bedside. Regular agreed communication with relatives and care in use of language are essential. This should be consistent from all multidisciplinary team members.

The change in focus to donor management from ICU care will not in most cases reduce the level of nursing required—indeed it may increase. Use of evidence-based guidelines together with advice from Specialist Nurses Organ Donation or units will aid bedside management.

As soon as possible, action should be taken to give methylprednisolone 15mg/Kg intravenously.

Existing brain directed cardiovascular targets and therapies should be reviewed and should be replaced with donor organ goals, which are usually easier to attain. Cardiovascular support if in progress should continue as directed by these new goals, and can usually be reduced if hypovolaemia is corrected. (see Cardiovascular Management).

Reduced metabolic rate, loss of hypothalamic control and vasodilation result in heat loss and hypothermia. Monitor temperature and commence or continue active warming treatments.

Initiate or continue enteral feeding until otherwise instructed by the retrieval team.

Maintain tight glycaemic control with insulin if necessary.

Continue antibiotics and other medications as indicated.

Lung protective ventilation should continue as before, with suction as indicated, positioning and ventilator settings to limit atelectasis, recruitment manoeuvres (particularly following suction or apnoea testing) if required. Avoidance of excessive fluid administration is associated with more likely lung donation.

Initial donor management may vary little from previous care, particularly if haemodynamic stabilisation has been achieved prior to the confirmation of brain-stem death, but an early intensive review is required with donation as the prime focus. In particular early consideration should be given to determining whether further invasive monitoring is necessary.

References:

6 Cardiovascular management

Quick info:
Around the time of brain-stem death, there can be a ‘Cushing response’ of dramatic cardiovascular changes with hypertension, bradycardia, and central diversion of blood volume. Associated myocardial ischaemic changes and arrhythmias are common. This period is not always present, may be transient or masked by ongoing therapy.

Following this there can be a variable intensity and duration of ‘sympathetic storm’ with tachycardia, vasoconstriction and blood pressure instability, usually involving episodes of hypertension. Treatment of these rapid changes can be difficult, and short-acting agents should be used. There may well be vasoactive infusions already in progress which can be reduced.
Following this, a more consistent syndrome with marked vasodilation and relative hypovolaemia develops. Fluid losses from all sources may worsen this, for example the development of diabetes insipidus is common.

Failure to achieve cardiovascular stability will lead to rapid deterioration in organ function, and cardiac arrest. Active donor management can prevent this.

Rapid restoration of circulating volume without overload is essential. Restoring vascular tone with drugs such as vasopressin is helpful.

Suitable donor cardiovascular goals may be less difficult to achieve than previous therapeutic targets. Flow monitoring facilitates rapid titration of therapies, and should be strongly considered at an early stage.

When goals are achieved without high dose catecholamine infusions, the chance of donor hearts being transplantable increases.

References:


Murugan et al. 'Preload responsiveness is associated with increased interleukin-6 and lower organ yield from brain-dead donors.' Critical care medicine (2009) vol. 37 (8) pp. 2387-93

Venkateswaran et al. 'The haemodynamic effects of adjunctive hormone therapy in potential heart donors: a prospective randomized double-blind factorially designed controlled trial.' European Heart Journal (2009) 30, 1771-1780

Venkateswaran et al. 'Echocardiography in the Potential Heart Donor.' Transplantation. 89(7):894-901, April 15, 2010


7 Respiratory management

Quick info:

Donors will usually have been ventilated for some time in a critical care area. Modern critical care where possible uses a 'lung protective' type of ventilation, with tidal volumes in the region of 6-8 ml per Kg ideal body weight, and inspiratory pressures limited to <30 cm H₂O. Positive End-Expiratory Pressure (PEEP) is applied to maintain open airways and lung units. 'Recruitment manoeuvres' with sustained, but safe, levels of inspiratory pressure can dramatically improve oxygenation and reduce inspired oxygen requirements.

Inspired oxygen concentrations are generally adjusted to maintain peripheral oxygen saturations above 90% or a PAO₂ of >8.0 kPa. Minute ventilation can often be reduced significantly.

Donors may have lung pathology which affects respiratory management, for example-cardiac failure, Acute Respiratory Distress Syndrome (ARDS), aspiration or nosocomial pneumonia. In addition, at the time of brain death, marked central diversion of blood volume and elevated pulmonary artery pressures may lead to severe neurogenic pulmonary oedema.

The apnoea test during testing for brain-stem death frequently results in significant lung collapse and worsening blood gases. It is vitally important to ensure that formal re-recruitment of lung is performed after apnoea testing.

In the UK Lungs are only retrieved from a minority of donors, but active donor management protocols can increase the numbers of transplantable lungs. Methylprednisolone use is associated with reduced lung water and more lungs suitable for transplant. Lung protective ventilation and avoidance of fluid overload are also key strategies.

References:


8 Renal and electrolyte management

Quick info:

Donors have commonly undergone very active management with fluids and vasoactive drugs. Blood and fluid losses may have been significant, or are ongoing. Therapies such as mannitol, diuretics and hypertonic saline may have been given. Overall fluid and electrolyte balance may well be markedly deranged.

In addition, diabetes insipidus commonly develops in brainstem dead donors. The resulting polyuria will result in further electrolyte and water losses and hypovolaemia. Attempts to treat associated hypernatraemia with dextrose solutions may have led to hyperglycaemia and osmotic diuresis.
Early assessment of overall fluid status is essential. Physical examination and cardiovascular assessment should allow estimation of intravascular effective volume, and degree of peripheral oedema. Review of input/output charts and recent blood and urine electrolytes will help direct corrective treatment if required. Electrolyte disturbance may be associated with cardiac irritability and arrhythmias. Correction of abnormalities is beneficial to recipients. Hypernatraemia in the donor is associated with poor liver graft function. Lung transplantation is more likely to occur if a negative fluid balance is attained. The overall goal will be to maintain urine output, aim for normal plasma electrolytes, avoid fluid overload, and if possible achieve a negative fluid balance.

References:
Dictus and Vienenketter 'Critical care management of potential organ donors: our current standard.' Clinical Transplantation (2009) 23 (Suppl. 21) 2-9

9 Hormonal management

Quick info:
Brain death results in variable hormonal changes in the donor. Posterior pituitary function is commonly lost, with development of diabetes insipidus. If inadequately treated, this may result in hypernatraemia, hypovolaemia and hypotension. Anterior pituitary function may be relatively unaffected, with normal levels of Adrenocorticotropic hormone (ACTH), thyroid stimulating hormone (TSH) and growth hormone. There may be a decline in Triiodothyronine (T3) in some cases, with normal or low TSH values. T3 supplementation as part of a programme of intensive donor management has been associated with increased numbers of organs retrieved, and better function in implanted organs. It is a component of many donor management protocols. More recent studies suggest that T3 supplementation may add little to an intensive donor management protocol which includes vasopressin and methylprednisolone, and suggest its use only if cardiac performance is unresponsive to volume loading and restoration of vascular tone. Insulin infusion may provide benefits of anti-inflammation and reduced cytokines in addition to the benefits of good glycaemic control.

References:
Rosendale et al. 'Aggressive pharmacologic donor management results in more transplanted organs.' Transplantation (2003) vol. 75 (4) pp. 482-7
Venkateswaran et al. 'The haemodynamic effects of adjunctive hormone therapy in potential heart donors: a prospective randomized double-blind factorially designed controlled trial.' European Heart Journal (2009) 30, 1771-1780

10 Blood and coagulation management

Quick info:
Donors may have sustained multiple trauma, surgical procedures, or massive blood loss. Evidence of associated coagulopathies or low haemoglobin may be present. These will have been treated using local protocols, policies and transfusion triggers. Continued active bleeding which is not surgically controllable will require ongoing transfusion and coagulation correction. Release of coagulation activators from necrotic brain tissue may lead to disseminated intravascular coagulation (DIC) and consumptive coagulopathy. Hypothermia and elevated catecholamines can contribute to poor platelet function.

References:
Dictus and Vienenkoetter. 'Critical care management of potential organ donors: our current standard.' Clinical Transplantation (2009) 23 (Suppl. 21) 2-9

11 Cardiovascular monitoring

Quick info:
Continuous ECG monitoring should be in progress. A 12-lead ECG should be performed, and repeated if there are subsequent changes in monitored complexes.

A recent chest X-ray examination is required.

Transthoracic echocardiography if available should be performed, and may reveal significant structural abnormalities, but even poor initial function may well improve with active management. Repeat or transoesophageal examination can be helpful.

Intra-arterial and central venous pressure should be continuously monitored and displayed.

Cardiac output monitoring will considerably assist effective donor management and should be strongly considered at an early stage. Choice of technique will be dictated by local expertise and equipment. Users should be aware of the limitations of the technique chosen. Pulmonary artery catheters are frequently used by cardiothoracic donor management teams.

Routine ICU clinical review (e.g. good urine output, lack of hyperlactaeemia or metabolic acidosis, normal central or mixed venous oxygen saturations) suggests effective resuscitation.

12 Respiratory monitoring

Quick info:
A recent chest X-ray should be available, or a new one obtained and reviewed.

Routine ventilator parameters are measured and recorded including peak and plateau airway pressures.

Continuous peripheral oxygen saturations and intermittent blood gas analysis. Cardiothoracic transplant units may request blood gas analysis on higher concentrations of inspired oxygen to allow calculation of oxygenation indices.

Secretions (if present) should be sent for microscopy and culture. Antibiotic therapy may be indicated if purulent. Bronchoscopy for diagnosis or therapy should be performed if indicated clinically.

13 Renal and electrolyte monitoring

Quick info:
Review of charts and clinical examination with particular attention to estimating effective intravascular volume and overall fluid status is the first priority. Attention is paid to hourly urine output, particularly looking for any suggestion of the onset of diabetes insipidus.

Urinary electrolytes may be useful in estimating losses, but may well be affected by the overall clinical condition, or therapies such as mannitol and diuretics.

Plasma electrolytes should be measured. The most frequent derangements are hypernatraemia, hypokalaemia, hypomagnesaemia and hypophosphataemia.

14 Hormonal monitoring

Quick info:
Formal hormonal monitoring does not seem necessary for effective donor management.

Blood results similar to the ‘sick euthyroid syndrome’ may be present if measured.

Clinical signs and laboratory values (polyuria, hypernatraemia) suggesting diabetes insipidus should prompt treatment with vasopressin or desmopressin.

Close attention should be given to glycaemic control with insulin infusion, and this may be made more difficult because of the administration of methylprednisolone and /or 5% dextrose. A minimum of 1 unit / hour of insulin is advised.

Good glycaemic control with insulin infusion. Insulin infusion at 1 unit/hour minimum may be beneficial.

15 Blood and coagulation monitoring

Quick info:
Routine full blood counts as clinically indicated will allow consideration of the need for transfusion of red blood cells. The relevant transfusion trigger should allow for any potential for ongoing losses or operative losses at the retrieval operation.

Coagulation screening or thromboelastography will allow targeted therapy if there is active bleeding.

16 Set cardiovascular goals

Quick info:
Adequate organ perfusion without excessive volume loading and ideally no vasopressor support. Early use of advanced monitoring and restoration of vascular tone may allow limitation of excessive volume.

**Suggested initial goals** - these are guidelines only, and may be altered by individual clinical circumstances and responses to treatment. Experienced senior review and/or discussion with Specialist Nurses Organ Donation or transplant units may be necessary.

- Sinus rhythm 60-100 beats per minute
- Central Venous Pressure <12 mm Hg
- Pulmonary arterial pressure <12 mm Hg
- Mean arterial pressure 60-80 mm Hg
- Cardiac Index >2.4 L/min/m²
- Mixed venous oxygen saturation >60% (if measured)

If advanced monitoring is being used, a haemodynamic profile may be generated which will guide further therapy.

### 17 Set respiratory goals

Quick info:
- Routine ‘protective’ ICU ventilation should be continued to maintain adequate oxygenation on the lowest possible inspired oxygen concentration.
- Routine methods to prevent aspiration, retention of secretions and atelectasis should be maintained.
- Peripheral oxygen saturation of 92-95% or pO₂ of >8kPa are acceptable if cardiac output, haemoglobin concentration and oxygen delivery are well maintained.
- Positive End Expiratory Pressure and lung recruitment manoeuvres should be utilised when lung collapse and atelectasis are likely.

### 18 Set renal and electrolyte goals

Quick info:
- Adequate effective circulating volume should be maintained (see Cardiovascular management)
- A normal urine output of 1-2 ml/kg/hour is usually attainable. Marked rise in urine output (>4 ml/Kg/hour) may well be due to the development of diabetes insipidus, and should be treated early.
- Electrolyte disturbances should be treated aiming for target of normal values.
- Overall goal is haemodynamic stability with a negative overall fluid balance if possible.

### 19 Set hormonal goals

Quick info:
- Treat diabetes insipidus if present. If vasopressin is being given for cardiovascular management, this may be effective treatment for diabetes insipidus (DI) also.
- Insulin 1 unit/hour minimum and as indicated. Avoid hyperglycaemia and hypoglycaemia.
- Consider liothyronine (tri-iodothyronine, T₃) administration (4 microgram bolus, 3 microgram/hour infusion), particularly if cardiac performance is suboptimal. Discuss with cardiothoracic retrieval team if considering its use.

### 20 Set blood and coagulation goals

Quick info:
- Haemoglobin level will be dictated by local protocols and guidelines if the donor has been a stable ICU patient with no ongoing losses. If losses are continuing, a higher trigger will be chosen. A value of 10 grams/decilitre is often quoted.
- Coagulation derangement on screening should only be treated if there is significant ongoing bleeding, but preparation for a donor operation should include availability of targeted blood products if required.
- For some units Group and Save will be adequate. If, however, the donor is some distance from a blood bank, consider having 2 units of blood immediately available for the donor operation, with a recent cross-match sample and arrangements for further units if required. Blood transfusion remains rare and O negative blood can be used.
- If blood is to be rapidly transfused adequate venous access and fluid warming equipment is required.
21 Cardiovascular therapy

Quick info:
At the time of brain-stem testing, many potential donors will have been undergoing treatment which may include osmotic therapy and vasoactive drugs. Change of cardiovascular goals after brain-stem death can allow rapid reduction in dosage of drugs, particularly if judicious fluid loading is performed. Reduction or removal of high dose catecholamine infusions is often possible. Bradycardia will be unresponsive to atropine, and a short-acting beta-agonist may be used if necessary such as isoprenaline or dobutamine. Tachycardia will usually be related to systemic inflammation or hypovolaemia. If associated with marked hypertension, short acting beta-blockade with esmolol could be used. Arrhythmias may respond to electrolyte replenishment (see renal and fluid management)

The first priority is to restore an effective circulating volume. If intravascular volume is estimated as being necessary, 3-5 ml/Kg of a balanced crystalloid or colloid should be given as a rapid bolus, and repeated if necessary. Assessment of effectiveness is based on available data such as arterial pressure variation. Knowledge of change in cardiac output is invaluable if responses are not rapid and failure to promptly respond to appropriate fluid administration should mandate more advanced cardiovascular monitoring.

Fluid administration should always be titrated against measurable effect, and excessive volume administration should be avoided. When resuscitation has been effective, further fluid administration should be, if possible, limited and aim for a ‘negative’ balance.

If Cardiac Index is in the target range (>2.4 L/min/m²) but hypotension and marked vasodilation is present, the most effective first intervention may in fact be restoration of vascular tone with vasopressin (1 unit slow bolus, repeated if ineffective, followed by infusion of up to 4 units/hour). If higher doses of vasopressin prove necessary, it is important to re-evaluate fluid status to ensure unrecognized hypovolaemia has not developed.

If cardiac index is unresponsive to volume loading and restoration of vascular tone, inotropic support is required. Tri-iodothyronine (T3) has been used effectively as part of a package of donor care by many (4 microgram bolus and infusion of 3 microgram/hour for an adult donor) and may be recommended by recipient cardiothoracic units as standard first line or ‘rescue’ therapy. Catecholamine infusion may be indicated if there is no improvement. Although many donor management programmes use these infusions liberally, there is general agreement that high doses (particularly of norepinephrine) are associated with fewer hearts being retrieved and concerns with poor graft function and survival. Choice of drug(s) will be dictated by clinical findings and results of invasive monitoring.

In some cases, if response to catecholamine infusion is inadequate, a trial of hydrocortisone 50-100 mg intravenously may improve cardiovascular parameters.

22 Respiratory therapy

Quick info:
Head-up positioning and regular turning should be continued, with suction as clinically indicated, but being aware of the potential for derecruitment. Recruitment manoeuvres should be performed after suctioning, after apnoea testing, or if saturations are deteriorating. Tidal volumes 6-8 ml/Kg are suitable initial settings, and probably similar to prior settings. Peak inspiratory pressures should be limited to 30 cm H₂O if possible. Respiratory frequency may be able to be reduced, particularly if mild permissive hypercapnia is tolerated.

Positive End Expiratory Pressure may be applied as necessary, but usually a minimum of 5 cm H₂O.
Cardiovascular changes such as arterial pressure variation during recruitment manoeuvres and ventilation should be noted, and may prompt changes in fluid loading or vasoactive support.

Inspired oxygen should be as low as possible while maintaining peripheral saturations of the order of 92-95%, or pO₂ of >8kPa. If oxygen concentrations are raised for blood gases to determine oxygenation indices, they should be reduced immediately after gas analysis.

23 Renal and electrolyte therapy

Quick info:
If increased intravascular volume is required, boluses of balanced crystalloid or colloid are appropriate (see Cardiovascular management) until haemodynamic goals are achieved. Donor management protocols involving use of crystalloids and colloids are well described, with similar outcomes and there is no evidence to suggest one approach is better than the other.
Diabetes insipidus should be treated at an early stage. If there is a dramatic unexplained rise in urine output treatment should be commenced even before confirmation by urinary and plasma electrolytes. Vasopressin infusion as used for cardiovascular management will often effectively treat diabetes insipidus, or DDAVP 1-2 micrograms intravenously bolus.

If hyponatraemia is a problem, Ringer lactate solution or dextrose-containing solutions may be chosen. Dextrose solutions may lead to hyperglycaemia and osmotic diuresis, so insulin infusion may need to be increased.

Electrolyte disturbance with low potassium, magnesium, calcium or phosphate should be treated using appropriate local protocols. Maintenance intravenous fluids should be limited if ongoing losses are not excessive.

The enteral route not be neglected for fluid input, and continued enteral feeding is appropriate if in progress.

24 Hormonal therapy

Quick info:
Vasopressin given for cardiovascular management (1 unit bolus, 0-4 units/hour infusion) may provide adequate treatment of diabetes insipidus, or add DDAVP (Desmopressin) 1-2 micrograms intermittently intravenously if required.

Insulin 1 unit/hour minimum. Aim for plasma glucose 4-9 mmol. l-1
T₃ 4 microgram bolus plus microgram/hour infusion if indicated. (Discuss with cardiothoracic unit).

25 Blood and coagulation therapy

Quick info:
Blood and blood products are transfused as indicated clinically. The relevant transfusion trigger should allow for any potential for ongoing losses or operative losses at the retrieval operation.
Coagulation testing should be performed, and coagulopathy should be expected, but treatment may not be necessary unless there is active bleeding. Results of testing will assist with targeted therapy if required.
For some units Group and Save will be adequate. If, however, the donor is some distance from a blood bank, consider having 2 units of blood immediately available for the donor operation, with a recent cross-match sample and arrangements for further units if required. Blood transfusion remains rare and O negative blood can be used.
Thromboelastography may assist targeted therapy during a donor operation.
Adequate venous access and fluid warming is required for the donor operation.

26 Goals optimised

Quick info:
Donor management is an on-going and intense process. Physiological variables should be continually reassessed against target values and prioritised as appropriate. Active management of one system may impact on others, and frequent re-evaluation is necessary. This may be particularly so for fluid status.
By this stage, often some agreement will have been reached on likely organs to be retrieved. This may allow modification of priorities- for example if thoracic organs are not being retrieved, fluid administration may be more liberal to ensure good urine output.
The Specialist Nurse in Organ Donation will probably be able to estimate a time for starting the retrieval operation. This should be communicated to the operating theatre and anaesthesia teams to ensure that appropriate priority is given to ensuring staffing.
The anaesthesia team should be familiar with the procedure, or discuss with the retrieval team the sequence and likely pitfalls. Ensure crossmatch and recent blood values are available.

27 Arrival of retrieval team(s)

Quick info:
Surgical teams for abdominal and thoracic organs may arrive separately. Some cardiothoracic teams will have trained donor management staff who may organise more invasive monitoring or change current therapies, although they will usually have been in prior contact with the donor ICU.
Current teams are self-sufficient for scrub and perfusion staff, but need local anaesthesia support for transfer to theatre and in-theatre management.

28 Transfer to operating theatre for donation procedure
Quick info:
Transfer to theatre is as for any ICU patient, and appropriately experienced medical and nursing staff are involved. A formal checklist and handover should be in place, usually a modification of routine theatre procedures.

- 2 name bands on patient correctly completed with name and date of birth
- Brain-stem death test sheet correctly completed
- Copy of completed consent/authorisation form
- Blood group - hard copy of form

Relatives may wish to accompany the donor to the theatre reception area, and should receive appropriate support.
Management of brain-stem dead donor
Medicine > Organ donation > Donation after Brain-stem Death, Adult

Key Dates

Due for review: 02-Sep-2012
Locally reviewed: 05-Sep-2010, by England & Wales
Updated: 05-Sep-2010