Management of the Pediatric Organ Donor

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Objectives
1. Discuss the Pathophysiology of brain death
2. Discuss the management of the complications of brain death
3. Discuss the techniques of aggressive donor resuscitation and maintenance
4. Review the Consensus Conference Guidelines, and the UNOS Critical Care Pathway for Donor Resuscitation

Introduction
There is a critical shortage of organ donors which is vastly outstripped by the number of patients on transplant lists. In 2003 there were over 86,800 patients on the waiting list (in the USA) for various organs and only 13,200 transplants were performed [1]. This huge discrepancy is unlikely to change in the foreseeable future. The waiting lists continue to grow at an exponential rate with increasing numbers of patients dying waiting for a transplant. There is also an increasing number of older and “expanded” donors: From 1995-2000, donors over 50 years of age increased by 43%, while those less than 50 years increased only 1.6%. This implies that more donors will have co-morbidities and the donor organs may be suboptimal due to the effects of ageing. A significant proportion of donor organs are considered unsuitable for transplantation for various reasons, the most common being “poor organ function”. In the 2003 Annual Report of the Organ Procurement and Transplantation Network it was stated that: “The decision to abandon the recovery of consented organs, as by OPO (Organ Procurement Organization) and transplant personnel, can be subjective and variable. Additional effort needs to be directed towards improving the ability of all organizations to accurately assess organs’ suitability of individual organs for transplantation and to develop national standards for this decision-making process” [2]. It may be possible to optimize these donors by aggressive resuscitative efforts and recover many of those organs that may have been wasted. Donor resuscitation and management is widely acknowledged to be a neglected area of transplant medicine, as evidence now clearly shows that aggressive donor management can significantly improve the numbers and outcomes from transplantation. In order to understand donor management strategies it is helpful to discuss the pathophysiology of brain death.

Pathophysiology of Brain Death
Brain death represents not an event but a process which has profound adverse effects on virtually all organ systems, the most important being cardiovascular and endocrine. Aggressive interventions can stabilize and improve organ donor function and increase the chance of successful transplantation. This review will focus on four areas of particular importance:
1. Cardiopulmonary
2. Endocrine/Metabolic
3. Hematologic
4. Thermoregulatory

Cardiopulmonary
Brain death results in profound hemodynamic instability. The initial reaction (Cushing’s response) to rising intracranial pressure (ICP) is hypertension with reflex bradycardia, and altered breathing. Brainstem herniation is accompanied by a “sympathetic storm” characterized by severe hypertension, tachycardia, arrhythmias, and asystole. This phase is associated by massive levels of serum catecholamines which can cause myocardial ischemia and necrosis, ventricular dysfunction, and pulmonary edema. This short-lived phase is rapidly followed by a prolonged period of spinal shock and
resulting hypotension as the sympathetic outflow is completely disrupted. Hemodynamic instability may be exacerbated by accompanying lung dysfunction as a result of retained secretions, aspiration, pneumonia and atelectasis.

**Endocrine/ Metabolic**
Brain death results in global mitochondrial dysfunction leading to a switch to anaerobic metabolism. Loss of pituitary secretion of ADH causes diabetes insipidus leading to hypovolemia and hypernatremia. Thyroid dysfunction produces what is termed the “sick euthyroid syndrome” with reduced conversion of T4 to T3. Hyperglycemia as a result of peripheral insulin resistance and pancreatic dysfunction may worsen hypovolemia by inducing an osmotic diuresis.

**Hematologic**
Release of brain thromboplastin into the circulation can produce disseminated intravascular coagulation (DIC) and a resulting coagulopathy. Anemia as a result of blood loss from trauma and the coagulopathy will reduce global oxygen delivery.

**Thermoregulatory**
Although hyperthermia is common in the early phase of the sympathetic storm the patient rapidly becomes hypothermic as a result of the loss of central temperature control and profound vasodilation. The patient essentially becomes “poikilothermic” as the body temperature will be dictated by the environmental temperature. Hypothermia produces many undesirable consequences: Myocardial depression and arrhythmias; coagulopathy; diuresis and hypovolemia; and a left-ward shift of the hemoglobin dissociation curve resulting in reduced oxygen delivery.

**Critical Care of Organ Donors**
The main goal is to maintain oxygen delivery and prevent deterioration of the vital organs. The foundations for this are the general intensive care principles for managing all intensive care patients: Hemodynamic stabilization; optimizing mechanical ventilation and oxygenation; preventing infection.

**Hemodynamic Management**
Hypotension, which can be severe and intractable, is the most common problem and can seriously compromise organ perfusion. This is usually due to (i) Hypovolemia from the use of diuretics and fluid restriction during brain resuscitation; inadequate volume replacement following trauma; diuresis from diabetes insipidus and hyperglycemia; (ii) neurogenic shock; (iii) myocardial dysfunction.

Hemodynamic management should begin with aggressive fluid resuscitation using crystalloids, colloids or PRBCs (Hgb>10). This should be guided by a CVP or preferably a PA catheter aiming to keep filling pressures less than 12mmHg. Inotropes should be started after adequate volume loading. Dopamine is the initial drug of choice. If the dose exceeds 10mc/kg/min the epinephrine can be added. Vasopressin (a potent vasoconstrictor) should be added if the patient is still unstable. This drug acts synergistically with epinephrine and may allow a useful reduction in the dose of inotropes which is considered beneficial for the myocardium as it helps to reduce oxygen demand. Echocardiography can be very helpful in distinguishing between ventricular dysfunction and hypovolemia. Serial echoes are useful to monitor response to interventions.
Specific Guidelines for Cardiothoracic Donors
These are based on the UNOS Critical Pathway [3]:

1. Perform echocardiography early. Insert PA catheter especially if the EF<45% or the patient requires high dose inotropes.

2. Correct electrolyte imbalances: Na<150, K>4.0. Treat acidosis.

3. Ventilate using tidal volumes 10-15 ml/kg, PIPs <30cmH2O.

4. Hormonal resuscitation consisting of:
   T3: preferably a bolus followed by infusion
   Vasopressin: Titrated to SVR
   Methylprednisolone 15 mg/kg, Q24h
   Insulin infusion to maintain blood glucose 120-180 mg/dl

5. Volume resuscitation: Albumin if PT, PTT normal; FFP if PT, PTT >1.5Xnormal; PRBCs to keep hemoglobin > 10. Maintain PCWP/CVP 8-12 mmHg.

The recommended endpoints are: MAP>60; CVP/PCWP <12; SVR 800-1200; CI >2.5; LVSWI >15; Dopamine dose < 12 mc/kg/min.

Pulmonary System
The goals are to maintain arterial saturation above 90% and a PaO2>60mmHg using the lowest inspired oxygen, low PIPs, low levels of PEEP and tidal volumes of 12-15 ml/kg. If the patient is a potential lung donor then “lung protective strategies” using tidal volumes of 8-8 ml/kg may help minimize barotrauma. There is evidence to show that the quality of donor lungs can be improved by relatively simple measures such as: Judicious endotracheal suctioning, bronchodilators, chest physiotherapy, bronchoscopy and lavage, small volume resuscitation, and steroids.

Endocrine Dysfunction
Diabetes insipidus due to central ADH deficiency occurs in 70-80% of brain dead patients and leads to hypovolemia and hypernatremia, as well as loss of potassium, calcium, magnesium, and phosphate. Treatment is with Desmopressin (loading dose 8ng/kg, then 4ng/kg/h). If hypotension is present also then vasopressin can be used.

Many critical illnesses including brain death (and cardiopulmonary bypass) are associated with thyroid dysfunction. This is characterized by low T3 but normal TSH and T4 levels. It is often termed “euthyroid sick syndrome”. Thyroid hormones are responsible for optimal growth, development, function and maintenance of body tissues. T3 (the biologically active form of thyroid hormones) binds to receptors in the plasma membrane, mitochondria and nucleus. It increases protein synthesis and energy metabolism. It increases oxygen utilization, heat production, glucose and amino acid uptake. It increases mitochondrial number, size and activity. Brain death is associated with a global mitochondrial dysfunction with a change to anaerobic metabolism and lactic acidosis. It leads to depletion of myocardial high energy phosphates and cellular dysfunction. Myocardial injury is further worsened by the obligatory ischemia and the adverse effects of CPB. This may be a factor in early graft failure. Experimental and clinical evidence has shown beneficial effects of T3 in improving donor heart function [4,5,6]. Hence, T3 has become part of the recommended protocol for cardiac donors.

Does Aggressive Donor Management Improve Outcomes?
In a landmark paper published in 1995, the Papworth Hospital group in Cambridge, UK showed that by using invasive hemodynamic monitoring and a standard donor management protocol (steroids, insulin, vasopressin and T3) they “transformed” a significant proportion of initially “unacceptable” donors (which fell outside their minimal accepted criteria) into acceptable donors. 84% of these were alive and well 4 years after transplant [7]. This led to a wider acceptance of this aggressive approach of donor resuscitation and maintenance.
The UNOS Critical Pathway and Hormonal Resuscitation have been endorsed by the American Society of Transplantation and the American Society of Transplant Surgeons. A recent Consensus Conference made specific recommendations for management of cardiac donors [8]. Two large retrospective analyses have shown that aggressive pharmacological management and hormonal resuscitation resulted in significantly more organs being utilizes and also improved function [9,10].

Conclusions
Donor shortage is the critical limiting factor for transplantation. Donor management should be the responsibility of all individuals involved in the procurement and transplantation process. Wider acceptance and implementation of aggressive donor management and hormonal resuscitation may increase organs available for transplant.

References
3. [www.UNOS.org](http://www.UNOS.org) UNOS Critical Care Pathway.