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Aspects of deceased organ donation in paediatrics

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Editor's key points

- Children are more likely to die waiting transplantation than adults because fewer organs are available.
- Infant transplantation is hampered by limitations on the diagnosis of death using neurological criteria.
- This and other barriers to donation must be addressed urgently.

Summary. Organ transplantation offers children in acute or chronic severe organ failure similar opportunities to adults. However, while the number who might benefit is relatively low, significantly fewer cadaveric donors exist for any given child compared with an adult. Incompatible organ size and relatively low donation rates mean that despite living parental donation and innovations to reduce donated organ size, children die before organs become available. The severity of the UK situation is compounded by restrictions on paediatric living donation, uncertainties over the application of brain death criteria, and ethical concerns about the use of donation after circulatory death. The UK Department of Health's Organ Donation Task Force suggested the means by which the adult donor pool might be increased, recommending that outstanding ethical and legal issues be resolved, but made no specific recommendations about children.

Keywords: brain death; death; ethics; intensive care units, neonatal; intensive care units, paediatric; organ transplantation; paediatrics; tissue and organ procurement

In the UK, children form ~2% of the active transplant waiting list compared with around 1.5% in the USA.[1][2] While children have a lower median waiting time for organs than adults, there are significantly fewer cadaveric donor organs available. Increasing the numbers of living donors and surgical reduction of available organs (e.g. dividing livers for transplant) are unlikely to overcome the shortfall.[3] Children are therefore more likely to die or suffer significant morbidity awaiting transplantation, which is unfortunate because both graft and recipient survival tend to be higher for children than adults. Indeed, similar to adults, some children are not even listed for transplantation when their clinicians consider the chance of an organ becoming available to be negligible.

There are significant differences in the incidence, causes, nature, and management of death in children, all of which impact upon the potential pool of paediatric donors. Around 2100 neonates and 3700 older children (aged up to 19) die each year in England.[4] Death in childhood has become less common over the last century, largely as a result of improved sanitation, antibiotics, and immunization. Furthermore, the provision of ever-safer paediatric anaesthesia and paediatric intensive care unit (PICU) and neonatal intensive care unit (NICU) has underpinned surgery for congenital heart disease, survival from sepsis, and perinatal illness. In addition, some cancers such as leukaemia which were previously always fatal are now relatively curable, although with late effects.

A far greater proportion of children that die do so within the intensive care environment in comparison with adults, although the causes of death are somewhat different. In infancy, birth-related issues such as prematurity and congenital malformations predominate, with metabolic disease and malignancy joining these causes in early childhood. Trauma is an increasingly significant cause of death in school-age children.[5] Aggressive intensive interventions such as bone marrow transplant, extracorporeal support, and the use of experimental therapies reduce an already limited organ donor pool, as many children die with significant organ impairment, or have underlying genetic, metabolic, or malignant diseases, which preclude donation. Furthermore, deaths in childhood after traumatic brain injury are decreasing, because of general measures such as cycle helmets, seatbelts, and speed restrictions as well as developments in neurocritical care. For instance, although the overall benefits remain uncertain, decompressive craniectomy has significantly reduced the incidence of brain death in children. Furthermore, subarachnoid haemorrhage is very rare indeed in childhood, while there is almost 100% survival of children presenting with intracerebral haemorrhage in modern PICU.[6]

In contrast, while organ availability is decreasing, improved organ support, especially mechanical cardiac support, is increasingly allowing children in either acute or chronic severe organ failure to be kept alive. Hence, the number of children who could potentially benefit from solid organ transplantation is increasing. Consequently, although organs transplanted into children come from the same overall sources as in adults, there are proportionately more live-related transplants, usually from adult relatives. These include live-related kidney, partial liver, and partial lung transplantation. However, there remain no alternatives to cadaveric cardiac or small bowel transplant.

Furthermore, unlike in the USA, competent children do not donate organs to their siblings or relatives,[7] so children in Europe only donate organs after death. In contrast to adult practice, the most common causes of brain death in children are trauma and hypoxic–ischaemic encephalopathy. Dead donation in PICU shares many similarities to adult practice with most following either traumatic or hypoxic brain injury. The criteria for the neurological cardiorespiratory determination of death in children are identical to those used in adult intensive care,[8] with the caveat that there are specific age-related issues with applicability of brain-stem death criteria, which are explored below.

ICU issues

There are <30 children's ICUs in the country, and an overall annual total of between 40 and 50 deceased organ donors under the age of 18 yr.[1] Clearly, this is much lower than in adults, with even the larger units having at most a handful of organ donors per year, and some units having none. Furthermore, there is currently no deceased paediatric donation from Departments of Emergency Medicine or from NICU in the UK.

Within the PICU, most deaths occur as a result of withholding or withdrawing intensive care support, although this is often after prolonged attempts at organ support, and is often preceded by several days of discussion with the family. While such decisions are not rushed, in the PICU, it is common to discontinue from full intensive care support rather than slowly wean, if it is thought invasive therapies can no longer benefit the child.[9]

Neurological determination of death in children

Although there are only minor differences in how brain death tests are conducted in children when compared with adult practice, there are very significant differences in whether a child can be tested or not. For instance, owing to issues with agents such as propofol which are specific to paediatric practice, drugs such as morphine and midazolam, which have far longer durations of action after an infusion, are commonly used to sedate children. Because of this, it may be days before formal brain-stem testing can be performed in appropriate cases, and children who do not fulfil these criteria rarely progress to fulfil them later. While these issues might be overcome with more clarity with regard to ancillary testing, there are more fundamental issues regarding the neurological determination of death in very young children.

Current UK guidelines regarding neurological diagnosis of death in children state:

> 'Between thirty-seven weeks of gestation and two months of age, it is rarely possible confidently to diagnose death as a result of cessation of brain-stem reflexes and below thirty-seven weeks of gestation the criteria to establish this cannot be applied.'[8] [10]

In contrast, the USA, Australia, Canada, and other European countries all permit confirmation of brain death in infancy by clinicians happy to do so. This enables parents to consider the donation of their brain-dead baby's organs. The current UK code however means that the only source of hearts for the UK infant heart transplant programme are those retrieved from infants certified as brain dead in Europe, as infants dying in the UK cannot donate. A number of groups have been asked to review this bizarre and untenable situation, including the Academy of Medical Royal Colleges Donation Ethics Committee,[11] the Royal College of Paediatrics and Child Health, and the British Association of Perinatal Medicine.

In paediatric practice, specific management of the brain-dead organ donor to improve the number and quality of organs retrieved is far from standard, although recently national protocols have been provided for this, together with other practical pathways in organ donation.[12] Indeed, the ability of individual PICUs to contact the specific senior nurse in organ donation, discuss organ donation, and consent families for donation seems far from uniform.[13]

Anencephalic donation

Anencephaly is the most severe form of neural tube defect and incompatible with long-term survival. Most pregnancies are terminated after antenatal diagnosis, and those that carry to term are often stillborn. However, there are still 10–20 live born anencephalic infants in England and Wales annually.[14] Historically, anencephalic infants have worldwide been an important source of organs for infant transplantation programmes, although the last anencephalic donation in the UK occurred some decades ago. In the USA, the extremely controversial undertaking of the removal of organs for transplantation from anencephalic infants before the confirmation of death was rapidly halted after widespread public and professional outcry.[15] [16] Indeed, all anencephalic donation programmes in the USA ceased after ethical debate, and the Canadian ethical enquiries concurred that there are serious difficulties with brain death certification in anencephalic infants, which preclude donation after brain-stem death (DBD).[17] Currently, no country seems to retrieve organs from anencephalic infants, with the most recent European transplant reported in Italy in 1999.[18] In contrast to contemporary international opinion, current UK guidance (from a 1988 Working Party on Organ Transplantation in Neonates report)[19] permit such donation and was unchanged, and arguably therefore endorsed, in subsequent publications from both the British Paediatric Association document that established UK paediatric brain-stem death,[10] and the more recent Academy of Medical Royal Colleges code of practice on the diagnosis and confirmation of death.[8] The original Working party report suggested:

> '...that the absence of the forebrain in anencephalic infants together with apnoea shall be recognized as death.'[19]

The report went on to advise that:

> '…organs for transplantation may be removed from anencephalic infants when two doctors who are not members of a transplant team agree that spontaneous respiration has ceased.'[19]

It would appear then that current UK guidance endorses organ retrieval from anencephalic infants, at least in theory.

Donation after circulatory death

As in adults, the chronic shortage of organs has led to a resurgence of donation after circulatory death (DCD) within paediatric intensive care in the last decade.[20] While legal[21] and ethical[22] guidance is equally apt for paediatric practice, ethical reservations exist surrounding the timing of confirmation of death after circulatory arrest and the extent to which ante-mortem interventions may be justifiable. There are no age limits to DCD, other than acceptance of organs by retrieval teams, usually linked to organ size. However, as with adults, ethical concerns have hitherto precluded retrieval of hearts from paediatric DCD donors yet paradoxically have not prevented attempts at lung transplantation.

Most DCD from children follows severe hypoxic–ischaemic encephalopathy or traumatic brain injury. These children do not survive for long periods after discontinuation of invasive organ support. In paediatric practice, terminal extubation of the dying child is regarded as acceptable best practice, being consistent with an end-of-life management with best interests as its focus.[9]

The highest quality organs for transplantation are obtained when the process of dying is controlled to facilitate donation because the shorter the interval between circulatory arrest and the declaration of death, the less the warm ischaemic injury to organs. As in adult practice, death is confirmed after 5 min continuous circulatory arrest in accordance with overall AOMRC guidance.[12] Transfer of the dying child to the operating theatre for extubation is commonplace in paediatric DCD, although this remains an overall rare event for most units. The lawfulness of ante-mortem interventions such as the administration of inotropes or heparin, femoral cannulation, or the use of extracorporeal support remain at a similar juncture to in adult practice.[18] While such steps may potentially improve donation, they must be balanced by the fundamental, inviolable, principles that underpin the care of a dying child.

Organizational aspects

The Senior Nurses and Clinical Leads in Organ Donation that cover a children's hospital, or a PICU as part of their hospital, have access to standardized national protocols, local mandatory guidelines, and a designated consultant in every PICU with responsibility for organ donation.[23] However, if advances in terms of neonatal organ donation are to be made, then fundamental organizational change will be necessary as neonatal units have no experience of the donation process, or indeed of neurological certification of death.[24] Whether this would entail transfer of dying infants to larger units for donation, closer liaison with the regional PICU or attendance of retrieval teams to smaller units with expert retrieval anaesthetic support is unclear. Certainly, DCD is *technically* possible from such infants without a change in how death is diagnosed and confirmed. For DBD, adaptation of standard international protocols seems sensible, although this would need to include confirmatory testing in terms of demonstration of absent cerebral blood flow, and a 24 h stand-off time with re-testing before retrieval.

Surgical aspects

As with most paediatric surgical specialities, paediatric transplantation is faced with the challenge of training a future workforce for comparatively rare surgical undertakings. Simulation of organ retrieval from children for trainees remains a distant hope, and the sheer variation in size of the child donor and recipient adds great complexity. The relatively low number of paediatric donors threatens the long-term viability of organ-specific retrieval teams; this represents a pressing organizational challenge for retrieval and transplantation services.

Surgical implications for DCD organs are largely similar to the adults except for one organ—the heart. An American unit from Denver has recently reported a series of three successful infant heart transplants using organs retrieved from infant DCD donors.[22] The report sparked considerable controversy, not least because the duration of asystole used to confirm death was reduced from 120 s in the first of the series to 75 s for the subsequent cases—as the first patient required extracorporeal membrane oxygenation after transplantation. It also raised significant questions about the irreversibility of 'death', the sanctity of the dead donor rule, and a confirmation of death based on cardio-respiratory criteria before transplanting the heart.

The furore generated in the aftermath of the Denver experience has had a chastening effect on the heart transplant community. However, the current status of paediatric heart transplantation is desperate, with 29% of patients on mechanical circulatory assist before heart transplantation and 20% dying on the waiting list awaiting heart transplantation.[25] For this reason, two paediatric heart transplant units in the UK are now actively assessing the feasibility of undertaking heart transplants using grafts from DCD donors, confirming death according to current UK guidance, and overcoming temporary postoperative ventricular failure with mechanical assist devices.[26 27]

Conclusions

Deceased donation in the paediatric population has a number of predictable differences from that in adults. The rarity of death in children and differences in donor size mean that children requiring an organ transplant have less potential donors than adults, although this is perhaps balanced by the fewer numbers of children 'competing' on the transplant list. Certain potential donors in the UK do not donate, whether due to differences in structures, or

medical standards such as national brain death certification rules in infants. One of the fundamental challenges in improving paediatric organ donation is its rarity, with even the biggest UK paediatric intensive care units seeing only a handful of donations per year. Technical advances in critical care and transplantation mean more children may be salvaged by transplantation, yet most children who die cannot donate due to antecedent medical contra-indications, or severe organ impairment. It is increasingly critical therefore to maximize donation where possible, and this should include urgent addressing of the current standards for the neurological determination of death in children, and exploration of cardiac DCD and anencephalic donation.

Declaration of interests

J.B. is a clinical lead for organ donation for his Trust.

References

1 NHS Blood and Transplant. Transplant activity in the UK activity report 2010–11. Available from http://www.organdonation. nhs.uk/ukt/statistics/transplant_activity_report/current_activity_ reports/ukt/activity_report_2010_11.pdf (accessed 1 October 2011)

2 Health Resources and Services Administration/Organ Procurement and Transplantation Network. US national transplant data 2011. Available from http://optn.transplant.hrsa.gov/latestData/ rptData.asp2011 (accessed 1 October 2011)

3 Brierley J. Organ donation. In: Holcroft R, ed. *Treatment Strategies in Paediatrics*. The Cambridge Research Centre, CRC, 2010; 56–9

4 Department of Health. Palliative care statistics for children and young adults. Available from http://www.dh.gov.uk/en/ Publicationsandstatistics/Publications/PublicationsStatistics/DH_ 074701 (accessed 1st October 2011)

5 Pearson GA, Ward-Platt M, Kelly D. How children die: classifying child deaths. *Arch Dis Child* 2011; **96**: 922–6

6 Li AH, Armstrong D, terBrugge KG. Endovascular treatment of vein of Galen aneurysmal malformation: management strategy and 21-year experience in Toronto. *J Neurosurg Pediatr* 2011; **7**: 3–10

7 Brierley J, Larcher V. Organ donation from children: time for legal, ethical and cultural change. *Acta Paediatr* 2011; **100**: 1175–9

8 Academy of Medical Royal Colleges. *A Code of Practice for the Diagnosis and Confirmation of Death*. London, 2008

9 Royal College of Paediatrics and Child Health. *Withholding or Withdrawing Life Saving Treatment in Children: A Framework for Practice*. London, 2004

10 British Paediatric Association. Diagnosis of brain-stem death in infants and children. *Conference of Medical Royal Colleges and Their Faculties in the United Kingdom*. London, 1991

11 Academy of Medical Royal Colleges. UK Donation Ethics Committee annual report. Available from http://www.aomrc.org.uk/ donations-ethics-committee.html (accessed 1 October 2011)

12 Map of Medicine. Clinical pathways for organ donation. Available from http://www.organdonation.nhs.uk/ukt/about_us/professional_ development_programme/pathways.jsp (accessed 1 October 2011)

13 Brierley J. Paediatric organ donation in the UK. *Arch Dis Child* 2010; **95**: 83–8

14 Botting B. Trends in neural tube defects. *Health Stat Q* 2011; **10**: 5–13

15 American Medical Association. Council on Ethical and Judicial Affairs. *The Use of Anencephalic Neonates as Organ Donors*. Chicago, IL: American Medical Association Code of Medical Ethics Report, 1994

16 American Medical Association. Council on Ethical and Judicial Affairs. *The Use of Anencephalic Neonates as Organ Donors— Reconsidered*. Chicago, IL: American Medical Association, 1995

17 Use of anencephalic newborns as organ donors. *Paediatr Child Health* 2005; **10**: 335–7

18 Parisi F, Squitieri C, Carotti A, Di Carlo D, Gagliardi MG. Heart transplantation on the first day of life from an anencephalic donor. *Pediatr Transplant* 1999; **3**: 150–1

19 Department of Health and Social Security. Report of a working party on organ transplantation in neonates. *Proceedings of the Conference of Medical Royal Colleges and Their Faculties in the United Kingdom*. London, 1988

20 Kolovos NS, Webster P, Bratton SL. Donation after cardiac death in pediatric critical care. *Pediatr Crit Care Med* 2007; **8**: 47–9

21 Department of Health. *Legal Issues Relevant to Non-heartbeating Organ Donation*. London, 2009

22 National Health and Medical Research Council (Australia). *Organ and Tissue Donation After Death, for Transplantation Guidelines for Ethical Practice for Health Professionals*. Canberra, 2007

23 The Paediatric Intensive Care Society. Standards for the care of critically ill children. Available from http://www.rcoa.ac.uk/docs/ sccic_2010.pdf (accessed 1 October 2011)

24 Brierley J. Neonatal organ donation: has the time come? *Arch Dis Child Fetal Neonatal Ed* 2011; **96**: F80–3

25 Irving C, Parry G, Cassidy J, Hasan A, Griselli M, Kirk R. Outcomes following infant listing for cardiac transplantation: the impact of strategies introduced to counteract limited donor availability. *Arch Dis Child* 2010; **95**: 883–7

26 Osaki S, Ishino K, Kotani Y, *et al.* Resuscitation of non-beating donor hearts using continuous myocardial perfusion: the importance of controlled initial reperfusion. *Ann Thorac Surg* 2006; **81**: 2167–71

27 Gundry SR, Fukushima N, Eke CC, Hill AC, Zuppan C, Bailey LL. Successful survival of primates receiving transplantation with 'dead,' nonbeating donor hearts. *J Thorac Cardiovasc Surg* 1995; **109**: 1097–102