

Children as haematopoietic stem cell donors: ethically challenging and legally complex

Clinicians should be aware of the particular physical and psychological risks of haematopoietic stem cell donation in the paediatric setting, and the varying laws between states and territories

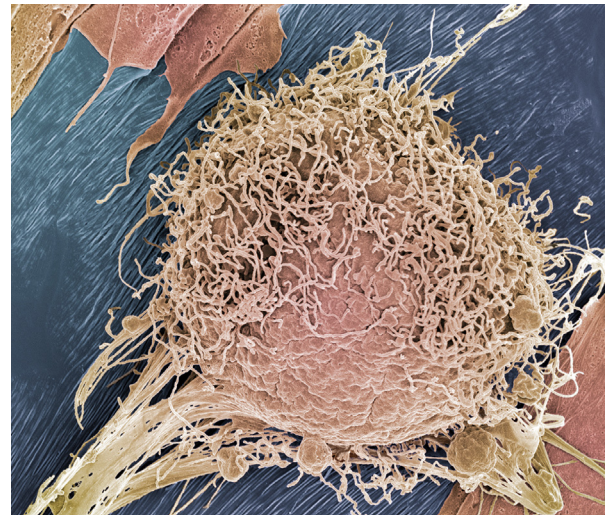
Allogeneic donor blood and bone marrow transplantation can treat a range of malignant and non-malignant diseases. For children with aplastic anaemia, severe combined immunodeficiency, leukaemia, sickle-cell disease, thalassaemia and inborn errors of metabolism, it may provide the only possibility of cure and long term survival. Although associated with considerable recipient mortality (5–12% transplant-related mortality at one year)¹ and morbidity, advances in tissue typing, supportive care, patient selection, conditioning regimens and the prevention and treatment of graft-versus-host disease have dramatically improved outcomes, with up to 80% of recipients becoming long term survivors of bone marrow transplant.²

Children have acted as allogeneic haematopoietic progenitor (stem) cell (HPC) donors for tissue-matched recipients, usually siblings, since 1968.^{3,4} While many children requiring a transplant rely upon matched unrelated donors identified from donor registries and umbilical cord blood banks, in Australia these registries are only searched if the child lacks a sibling or their sibling proves not to be matched. More than a third of children who receive allogeneic transplants — on average 32 annually over the past decade (Australian Bone Marrow Transplant Recipient Registry, unpublished data) — will receive them from child siblings.^{3,5} In recent years, increased attention has been given to the interests of donor children and to the ethical, legal and regulatory issues raised by the donation of HPCs by healthy siblings.^{3,5,6} This article considers whether current regulation of paediatric HPC donation is adequate.

Ethical issues

HPCs are collected from the donor's peripheral blood or bone marrow or, less often, from their umbilical cord blood. Both peripheral blood and bone marrow donation carry small, but significant physical, psychological and social risks. These risks must be carefully considered as donation is non-therapeutic, providing no medical benefit to the donor. Donor children have not always had their needs met, with reports of failure to provide donors with sufficient information or psychological support following bone marrow transplant.⁶

Bone marrow harvest requires general anaesthesia and, although relatively safe (mortality less than 1 per 10 000 donations, with no reported deaths in paediatric donors⁵), is associated with post-operative morbidity including nerve, bone and tissue injury, pain, anaemia, pulmonary emboli, fatigue, headache, nausea, sickle-cell crises and risks associated with transfusion.^{4,5,7} Peripheral blood



stem cell harvest, an option in older child donors, also poses risks including venous injury and anxiety related to insertion of large gauge catheters required for apheresis, thrombocytopenia and adverse effects related to use of sedatives. More significantly, because peripheral blood stem cell donors receive cytokines (granulocyte colony-stimulating factor), most will experience short term adverse effects, including myalgia, arthralgia, headache and fatigue, and risk rare but more serious adverse effects including uveitis and splenic rupture. They may also face uncertain long term risks including possible (but unproven) increased risk of leukaemia.⁸

Families undoubtedly benefit when a beloved child survives. There is also some limited evidence that children may obtain a psychological benefit from donating, including improved sibling relationships, enhanced familial closeness and feelings of pride.^{9,11} However, these small studies also show that donation may cause social and psychological harms, with donors sometimes feeling isolated, abandoned, angry or responsible for poor transplant outcomes, and experiencing increased anxiety, depression, lower self-esteem and behavioural problems.⁹⁻¹¹

As donors are children, and because donation is non-therapeutic and occurring within a family, serious questions arise regarding the degree to which donors can consent, or assent, to donation, and parents' capacity to make decisions in the interests of both their sick and donor children. The ethical problem is that while parents are expected to make decisions that are in their child's best interests and not determined (solely) by others interests

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doi: 10.5694/mja1700758

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(whether siblings, parents or the family unit), this simply may not be possible in the context of sibling donation.

In general, every effort is made to assist parents to make decisions for their children and treat each child fairly and justly, with donors and recipients being assessed, educated and cared for by different medical teams. Consequently, in situations where a tissue-matched child expresses reluctance or voices objections to donating, the donor's clinicians are obliged to focus on that child's best interests and not the interests of the potential recipient.

Australian law

Legislation

State and territory legislation governs when children can act as HPC donors.¹²⁻¹⁹ The law varies throughout Australia and, while often not explicit, the effect of the law is that children are treated differently depending on their capacity to understand the nature of what is being asked of them.

Children who understand (mature children)

Parental consent and child agreement is generally required for a mature child to lawfully donate to their family member. Exceptions exist in South Australia, where consent from an independent committee is required, and the Northern Territory, where children donating tissue are not expressly considered.^{14,16}

A medical practitioner must be satisfied that the child understands the nature and effect of the removal of the tissue and the nature of the transplantation, and agrees with the proposed procedure. In practice, this level of understanding is likely to be similar to determining whether a child is *Gillick* competent for a given decision.

To meet this legal standard of competency a child must be assessed as having "a sufficient understanding and intelligence to enable [the child] to understand fully what is proposed".²⁰

Children who do not understand by reason of age (immature children)

The law regarding immature children varies significantly around Australia. Only in New South Wales, Victoria and Queensland does the legislation expressly allow immature children to donate in some circumstances.^{13,15,18} Box 1 shows how the level of legal protection offered through procedural safeguards differs significantly between these three states. Some uncertainty exists about how a child's demonstrated unwillingness to participate should be treated, with the NSW law providing the clearest indication.

The legislation in the rest of Australia does not expressly consider immature children. However, an offence exists if tissue is removed other than in accordance with the appropriate consent or authority.^{12,14,16,17,19} Where the legislation contains no mechanism to provide such consent or authority, it is an offence for clinicians to remove tissue, unless permitted by court order. This variation in Australian law is undesirable, creates confusion and places clinicians at risk of prosecution. The case study in Box 2 illustrates the need for different legal processes depending on the location of the children.

Children who do not understand due to cognitive disability

Australian legislation does not mention children who are unable to understand due to cognitive disability. Where such a child is a proposed donor, a court (or a tribunal)

1 Legislative conditions for lawful tissue donation in the three Australian states with legislation that specifically provides for an immature child to donate tissue

Legislation	Recipient's relationship to donor	Level of harm to donor	Level of harm to recipient without donation	No. of medical practitioners certifying legal conditions met	Independent medical practitioner involvement	Effect of donor's objection
New South Wales: <i>Human Tissue Act 1983</i> , Pt 2, Div 3–5	Sibling	Risk to child's health (including psychological and emotional health) is "minimal"	"Likely to die or suffer serious and irreversible damage to his or her health"	Two	Required: at least one of the two	If child has "some understanding of the procedures involved" and "repeatedly and consistently expressed an unwillingness" to proceed, then unlawful to remove tissue
Queensland: <i>Transplantation and Anatomy Act 1979</i> , Pt 2, Div 2A–3	Sibling or parent	Risk to child is "minimal"	"Likely to die"	Three	na	Unclear
Victoria: <i>Human Tissue Act 1982</i> , Pt 2, Div 3–4	Sibling	na	"Likely to die"	One	na	Unclear

na = not applicable. ♦

2 Case study

Aisha is diagnosed with acute lymphoblastic leukaemia at 6 years of age. She is treated with chemotherapy and achieves a complete remission. Unfortunately, at routine follow-up 2 years later, she is found to be pancytopenic. Bone marrow biopsy demonstrates relapse. She is referred for consideration of bone marrow transplant, and she and her siblings are tissue-typed. Fortunately, her 8-year-old brother Jalil is found to be a human leucocyte antigen match. While Jalil's parents are delighted that he is able to donate to his sister, they are also worried about the risks that donation may pose to him and the legal processes that they need to go through in order to allow him to donate. ♦

must provide authorisation for a tissue harvest. Without this, clinicians may commit an offence.¹²⁻¹⁹

Court cases

Where legislative conditions cannot be met, or no avenue for authorisation is provided in legislation, a court order can be sought. Three reported cases have come before the Family Court of Australia (Box 3). The court must decide whether allowing a child to donate will be in that child's best interests. Given the lack of physical benefit, the focus has been on the potential psychological benefits to the donor. In applying the best interests test, a number of relevant factors have been considered (Box 4). In making a decision, the court relies on expert evidence from clinicians and psychologists.

Given the small number of reported cases, it is possible that the law is not known or followed in some places, and that unlawful tissue removal is occurring. No known

prosecutions have occurred for offences relating to tissue removal from children.

Professional standards and clinical practice

Outside of the law, international professional guidelines and standards may influence clinical practice.^{4,5} Domestically, the National Health and Medical Research Council provides guidelines applicable to paediatric donors.²¹ For accredited hospitals, the FACT-JACIE international standards have specific requirements for related, including paediatric, donors.²² While variation exists, best practice usually entails:

- an assessment of minimal risk to the donor;
- an intimate ongoing relationship between donor and recipient;
- independent clinicians for donor assessment and care;
- child donor specific processes (eg, use of donor advocates and focusing on the donor's best interests);
- donor involvement (to an age-appropriate extent) in the decision-making process; and
- formalised medical and psychological follow-up for donors.

These are sensible recommendations likely to result in donors' needs being met. Increasingly, in Australia, hospitals are implementing practices with input from multi-disciplinary teams to ensure that these practical safeguards protect donor children's interests. If ethically challenging situations arise, referral to clinical ethics

3 Family Court cases dealing with an application for a child to be a donor in circumstances where state human tissue legislation could not be satisfied

Case	Donor age	Recipient relationship to donor	Outcome
<i>In the marriage of GWW and CMW</i> (1997) 21 Fam LR 612	9 years	Adult aunt	Court authorised the procedure and declared the parents able to consent to the procedure
<i>E v E</i> [1999] FamCA 2403	15 years	Adult uncle	Court authorised the procedure and declared child capable of providing consent
<i>Re Inaya (Special Medical Procedure)</i> (2007) 38 Fam LR 546	13 months	Child cousin	Court authorised the parents to consent to the procedure

4 Factors used by the Family Court in deciding what is in a proposed donor child's best interests

Relevant factor	Explanation
Existing and potential future relationship between the donor and recipient	Where the relationship between donor and recipient is shown to be strong, there is an assumption that prolonging this relationship through providing a cure for the recipient's condition will benefit the donor child
Known physical risks of acting as a donor	The main physical risks identified in the cases (Box 3) are those associated with use of a general anaesthetic; the level of risk is usually identified as low and recovery is noted to be rapid
Expected psychological benefit of acting as a donor	The psychological benefit is likely to be greater where a close relationship exists between the child and the recipient; psychological detriment if the procedure is not authorised has also been considered where a child has expressed a wish to donate
Wishes of the child (where the child is able to express a view)	The older the child, the more likely the court is to consider their expressed views to be a significant factor in deciding what is in that child's best interest; where a child is considered <i>Gillick</i> competent, a court may allow the child to consent themselves to acting as a donor (<i>E v E</i> [1999] FamCA 2403)

services (where these exist) and/or the court is appropriate.

Conclusion

Where safeguards are in place to ensure donors' interests are considered and acted upon, children can ethically act as donors. Donor children are part of a family in which members have intersecting and interdependent needs and interests. The benefits to both the recipient and family unit, including the donor, can be profound. But peripheral blood stem cell and marrow donation is not without risk, and clinicians need to be cognisant of both the ethical complexities involved in children acting as HPC donors and of the current regulatory environment.

Australian law regarding paediatric HPC donation lacks uniformity. While this is true of many areas of health care, and although few cases involving paediatric donors have come before the courts, it remains important that sufficient legal safeguards exist to protect vulnerable children and that physicians have surety that their

practice is consistent with the law and does not leave them liable for offences when their practice is consistent with accepted medical and ethical standards. It is in the interests of both paediatric donors and the clinicians who are committed to the best interests of donor children and their carers that the laws surrounding paediatric donation are consistent and that the confusion and inequities that characterise this area of law are removed. While regulatory reform requires an investment of time and resources, if this is done with close involvement of clinicians through organisations such as the Bone Marrow Transplant Society of Australia and New Zealand then it should be possible to improve the law in the interests of all stakeholders in ways that enable, and do not compromise, the care of donors and recipients and their families.

Competing interests: Shih-Ning Then is currently a member of the NHMRC Organ and Tissue Working Committee. The views expressed in this article are those of the authors and do not represent the views of the Committee.

Provenance: Not commissioned; externally peer reviewed. ■

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