

# Umbilical cord blood banking: public good or private benefit?

Gabrielle N Samuel, Ian H Kerridge and Tracey A O'Brien

**A**llogeneic haematopoietic stem cell transplantation (HSCT) (see glossary of terms in Box 1) is a curative therapy for many malignant and non-malignant conditions, including leukaemia, bone marrow failure syndromes, immunodeficiencies and inborn errors of metabolism. Unfortunately, only 30% of patients in need of HSCT will find a suitable human leukocyte antigen (HLA)-matched, related donor. The only option for other patients is to search for an unrelated volunteer donor.

However, many patients cannot find a suitably matched donor in bone marrow donor registries. Further, because the probability of finding a donor is higher within the same ethnic group as the recipient, and because most volunteers on the United States, European and Australian registries are of northern Caucasian descent, there is a powerful ethnic bias that makes transplantation a much less likely option for many patients from non-Caucasian and indigenous populations.<sup>1</sup> This is a particular issue in Australia, which has a large Indigenous population as well as many people who have immigrated from Asia, the Middle East, India and South America, or who are of mixed ethnic backgrounds.

Over the past decade, these difficulties have led to umbilical cord blood (UCB) being increasingly used as an alternative source of stem cells for HSCT in patients who do not have a matched bone marrow or peripheral blood donor. Over 7000 UCB transplants have now been performed worldwide, with more than 150 paediatric UCB transplants performed in Australia.<sup>2</sup> Successful UCB transplant programs have led to the establishment of two types of UCB banks: public banks and for-profit private banks.

Here, we argue that there is adequate social and medical justification for public UCB banks; however, based on current knowledge of the therapeutic uses of UCB stem cells, private UCB banking is not similarly justified.

## UCB as a stem cell source

UCB transplantation offers a number of advantages as a stem cell source for HSCT, compared with other stem cell sources (Box 2). UCB is widely available; UCB collection is non-invasive, safe and painless; and UCB contains stem cells that can be successfully transplanted with a higher degree of mismatch compared with bone marrow from unrelated donors,<sup>4</sup> without being associated with a higher likelihood of graft-versus-host disease.<sup>5,6</sup> In addition, UCB is cryopreserved and so provides a readily accessible source of stem cells.

The main disadvantages of UCB have historically been the inferior speed of haematopoietic stem cell recovery and higher graft failure rates compared with peripheral blood and bone marrow, which relates directly to the smaller stem cell "dose" in UCB units. Until recently, this was thought to preclude UCB transplantation in older children and adults. However, improved outcomes with single UCB unit transplants in adults<sup>7</sup> and the use of "double cord" transplants, where two partially matched UCB units are transplanted,<sup>3</sup> have led to increasing use of UCB transplantation in adults.

## UCB banking in Australia

There are two types of UCB banks in Australia: government or community-funded public banks and for-profit private banks.

## ABSTRACT

- Haematopoietic stem cell transplantation (HSCT) is an accepted curative therapy for many malignant and non-malignant conditions affecting children and adults.
- Where possible, stem cells for HSCT are provided by human leukocyte antigen (HLA)-matched, related donors. Only 30% of patients have a suitable matched donor; for other patients, donors are sought from bone marrow registries or public umbilical cord blood (UCB) banks.
- While public UCB banks have been established to support transplant programs in Australia and internationally, parents also have the option of storing their child's UCB in a private commercial UCB bank for personal or family use.
- In contrast with public UCB banks, there is little social or medical justification for private UCB banking, as it provides no benefit to the community and little benefit to parents (other than reassurance and amelioration of regret), due to the very low likelihood of requiring autologous UCB later in life.
- Should UCB prove to be beneficial for tissue repair or replacement in the management of degenerative disorders, such as diabetes and Parkinson's disease, then a stronger case may be made in support of commercial banking of UCB for personal use. This may have a major impact on public UCB programs.

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## 1 Transplantation terminology

**Haematopoietic stem cells:** These have the capacity to proliferate and differentiate to produce all types of blood cells.

**HLA matching:** Human leukocyte antigens (HLAs) determine the immunological identity of a cell and are encoded by genes within the major histocompatibility complex (MHC). Antigens are inherited from parents as a unit (or haplotype), and genes that encode HLAs are highly variable. Conventional matching between donor and recipient requires matching of both antigens at class I (A, B and C) and the class II (DRB1) antigen, resulting in a 6/6 match. Immune complications after transplant are often the result of differences in HLAs between donor and recipient.

**Engraftment:** The point at which it can be stated that the donor stem cells are successfully producing blood cells in the recipient. This is assessed by the neutrophil and platelet count (neutrophils,  $> 0.5 \times 10^9/L$  and platelets,  $> 20\text{--}50 \times 10^9/L$  for 3 consecutive days).

**Graft-versus-host disease:** A post-transplant complication in which the donor immune cells recognise the host cells as foreign and attack organs, including skin, liver and gut; it can be lethal.

**Haematopoietic stem cell recovery:** The time taken for the donor haematopoietic cells to engraft and generate adequate numbers of white cells and platelets. ♦

## 2 Advantages and disadvantages of using umbilical cord blood (UCB) as a stem cell source for HSCT, compared with other stem cell sources

Advantages	Disadvantages*
<ul style="list-style-type: none"> <li>• Collection is non-invasive, safe and painless</li> <li>• Widely available</li> <li>• Rapid availability</li> <li>• Can be transplanted with a higher degree of HLA mismatch</li> <li>• Reduced graft-versus-host disease</li> </ul>	<ul style="list-style-type: none"> <li>• Limited cell dose</li> <li>• Higher graft failure rates</li> <li>• Inferior speed of haematopoietic stem cell recovery</li> <li>• Higher rates of infection</li> </ul>

HSCT = haematopoietic stem cell transplantation. HLA = human leukocyte antigen. \*Recent evidence suggests that these disadvantages will be ameliorated by the co-transplantation of two UCB units from different donors (ie, a "double cord" transplant).<sup>3</sup> ♦

These differ in both their scientific rationale and their medical utility. Public UCB banks are altruistic, store donated UCB for public access, and are analogous to volunteer bone marrow donor registries. In contrast, private UCB banks will, for a fee, store a child's UCB for personal or family use. It should be noted that transplant centres themselves also store "directed" family UCB donations if a family member is known to have (or potentially has) a disease that can be treated with transplantation.

Australia has three public UCB banks (including 11 collection centres), located in Sydney, Melbourne and Brisbane. All are affiliated with the Australian Bone Marrow Donor Registry and are nationally coordinated by AusCord, the National Cord Blood Collection Network of Australia. The Sydney Cord Blood Bank also collects UCB at Royal Darwin Hospital, specifically targeting the Indigenous population. At the end of 2006, 17239 UCB units were available for searching by Australian transplant centres. Four private UCB banks also operate in Australia — Biocell, StemLife, Cell Sense and Cryosite. These banks offer to store UCB for 18 years at a cost of around \$250 per year.<sup>8</sup>

UCB banking and donation raises a series of important epistemic, social, ethical and legal concerns, including those regarding ownership of UCB (which was initially considered a waste product but is now deemed to be owned by the child);<sup>9</sup> the processes for obtaining consent for collection and storage of UCB; issues relating to confidentiality; and social justice issues relating to equity of access and care.

### Redressing inequity: donor recruitment and storage of UCB

Public UCB banks have, for the most part, been very successful in making HSCT a real option for Australian patients who require a transplant. These banks attract considerable public support and donation from a broad range of Australians and are significantly more ethnically diverse than existing bone marrow registries.

However, there are a number of political and structural challenges facing public UCB banking in Australia. Collecting and storing UCB is expensive and requires considerable and continuous government support. There are only a limited number of collection centres and these tend not to be located in regional or culturally diverse areas, resulting in continued low donation and recruitment rates from ethnic minority and Indigenous groups.<sup>10</sup>

Although Australian public UCB banks show significantly more ethnic diversity than their bone marrow registry counterparts,<sup>11</sup> public UCB banks are still characterised by under-representation of many ethnic groups, particularly Aboriginal Australians and Pacific Islanders.<sup>11</sup>

Given the increase in UCB transplantation and the persistent under-representation of Indigenous Australians and ethnic minorities in UCB banks, recruitment strategies that best meet the needs of potential transplant recipients need to be developed. This will not be a simple task, as such policies must take account of cost-benefit, specific population need, community support, and equity concerns.

### Consent and coercion in UCB banking and donation

In contrast to public UCB banking, questions have been raised about the assumptions upon which private UCB banking is based. These assumptions include:

- that UCB will provide a valuable and appropriate resource for use in transplantation and regenerative medicine;
- that stem cells present in UCB could not (easily) be collected from other sources (eg, from peripheral blood or bone marrow) at the time that they are needed; and
- that the likelihood of needing UCB stem cells is sufficiently great to justify the expense of long-term storage of UCB.

Each of these assumptions is questionable — the promise of regenerative medicine is yet to be shown in clinical trials; the conditions for which HSCT is performed often require stem cells from allogeneic sources rather than from the patient, and stem cells can generally be obtained from alternative sources when required for HSCT; and the vast majority of people will never develop a haematological malignancy or any other indication for HSCT, so will never require the use of their own haematopoietic stem cells (estimates of the likelihood of requiring one's own stem cells for autologous transplantation later in life vary between 1 in 20000 and 1 in 200000<sup>12,13</sup>).

A number of professional groups have raised concerns about the marketing campaigns used by private UCB banks, arguing that these banks frequently use powerful advertising designed to sell possible, rather than real, applications of UCB, to capitalise on parental anxiety about their child's future and on hopes that stem cells will soon deliver therapeutic applications.<sup>14</sup> Indeed, it has been noted that marketing campaigns for private UCB banking often fail to reveal, or overestimate, the true likelihood of needing stored UCB, which some national and international bodies claim is a critical misrepresentation of data.<sup>15,16</sup>

Concerns regarding the legitimacy of storing UCB for personal or family use and the marketing strategies used by private banks have led many international groups<sup>13,15-17</sup> to recommend that:

... appropriate information should be given to the consumers willing to use their [commercial UCB banks'] services, including the fact that the likelihood that the sample may be used to treat one's child is currently negligible, that the future therapeutic possibilities are of a very hypothetical nature and that up until now there is no indication that the present research will lead to specific therapeutic applications of one's own cord blood cells.<sup>17</sup>

This advice remains true. However, these recommendations are based on current knowledge of the therapeutic uses of UCB stem cells, and, although the potential therapeutic utility of UCB for personal use may have been overstated to serve commercial ends,

this field of research is extraordinarily vibrant and there is some (increasing) evidence to support the idea that UCB may have use beyond autologous HSCT. If evidence emerges that UCB does have value in the treatment of a wider range of disorders, then the grounds upon which parents make decisions about UCB donation and storage are also likely to change.

### Exploring further applications for UCB in stem cell therapy

In recent years, great attention has been devoted to establishing whether UCB stem cells may have a role in tissue repair (regenerative medicine). This interest in UCB stem cells has arisen for two reasons. First, recent research has established that UCB stem cells can demonstrate plasticity (ie, the ability under the correct conditions to differentiate into a variety of cells other than blood cells, such as neural cells, cardiac cells and osteoblasts),<sup>18-21</sup> suggesting a role for them in the treatment of diseases such as diabetes, cerebral vascular disease and Parkinson's disease.<sup>22</sup> Second, as the collection and use of UCB cells does not involve the destruction of an embryo, their use in research and therapy avoids many of the moral concerns raised by embryonic stem cell research.

While much of the excitement surrounding UCB research is based on hope, rather than evidence, should UCB stem cells prove to have wider therapeutic application, another set of different but equally serious questions will probably arise regarding the maintenance of social equity in health care, when only a small proportion of the population are able to afford UCB storage for personal or family use.<sup>23</sup> While state-provided storage of all UCB for personal use may, although extremely costly, satisfy social justice concerns,<sup>17</sup> such a "solution" may also threaten the real and symbolic value attached to altruistic donation of tissues and, perhaps in the end, the very existence of public UCB banks.

### Competing interests

None identified.

### Author details

Gabrielle N Samuel, PhD, Research Associate<sup>1</sup>

Ian H Kerridge, MPhil, FRACP, FRCPA, Associate Professor and Director,<sup>1</sup> and Haematologist/Bone Marrow Transplant Physician<sup>2</sup>

Tracey A O'Brien, FRACP, BMed, MHL, Paediatric and Adolescent Haematologist/Oncologist and Head, Cord and Marrow Transplant Program<sup>3</sup>

1 Centre for Values, Ethics and the Law in Medicine, University of Sydney, Sydney, NSW.

2 Haematology Department, Westmead Hospital, Sydney, NSW.

3 Centre for Children's Cancer and Blood Disorders, Sydney Children's Hospital, Sydney, NSW.

Correspondence: gsamuel@med.usyd.edu.au

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