Cord Blood Stem Cells

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Cord blood (CB) is rich in stem cells. A mean volume of 90ml can be collected from the placenta after birth, either while the placenta is in situ or after being expelled. In this volume there are a mean of $10.2 \times 10^8 \pm 3.7$ nucleated cells and $3.5 \times 10^6 \pm 2.7$ $CD34^+$ cells. The cell content of cord blood is 1 log less than that present in a bone marrow donation.

Cord blood collection and banking requires TGA licensing under the Code of Good Manufacturing Practice for Blood and Tissues. There are three public (not-for-profit) Cord Blood Banks in Australia (Melbourne, Sydney and Brisbane) under the umbrella of AUSCORD, the National Cord Blood Banking Network. Between them there are currently ~7,000 donations stored. A national inventory of 20,000 donations has been set. Because the tissue typing of indigenous groups is different from non-indigenous an additional 2,000 indigenous donations are to be added. Funding has been provided by the State and Federal Governments, with the project to be completed over the next 3 years. The racial distribution in CBB's reflects that of the community in which it is collected. There appear to not be racial barriers to donation. AUSCORD has had 495 searches since 1998. 72 cord blood donations have been sent for transplant, 30% in Australia and 70% overseas to Sth America, Canada, Israel, NZ, France, UK, Malaysia and Hong Kong. This reality reflects the ethnic mix in the inventory. Internationally there are now 116,668 donations stored and available for searching via the internet.

The first related CB transplant (CBT) was performed in Paris in 1988 and the first unrelated in Durham, Nth Carolina in 1993. Since then over 2,000 transplants have been performed world wide and the experience has identified and clarified a range of issues. The majority of CBT's have been performed using mismatched cord blood (less than 10% have been HLA identical). While the frequency of graft-versus-host disease (GVHD) has been lower, engraftment rates and speed of engraftment have been lower and slower respectively compared to bone marrow. There is a significant correlation between degree of matching, nucleated cell dose and outcome. While no controlled trials have been performed, matched paired analyses of sibling transplants show that engraftment, GVHD and survival are lower and treatment related mortality (TRM) is higher after CBT compared to BMT with similar trends after unrelated CBT. However, the majority of unrelated CBT are mismatched compared to unrelated BMT which are either matched or 1 HLA antigen mismatched. When a comparison is undertaken comparing equally matched CB and BM donors GVHD, TRM and survival are better with unrelated CB for the same degree of matching for matched and 1 antigen mismatched donors. A comparison of 2 antigen mismatched donors is not possible as these are not performed using BM.

Adults have also been transplanted using unrelated CB and early results show a slightly lower engraftment rate (83%) and survival (25%) with a higher GVHD and TRM rates.

Advantages of unrelated CB over BM are that CB is immediately available "off-the-shelf", there is a lower risk of GVHD and there is a lower risk of CMV transmission. Fast turn-around time for release of a CB unit is a reality. Disadvantages are the lower cell dose, higher failure to engraft, potential to transmit undiagnosed genetic diseases and CB inventories are not yet big enough to frequently provide fully matched donors.

Areas of exciting future development are the use of multiple cord blood donations for a single patient and expansion of stem cells to increase the transplantable number. Expansion of autologous BM results in faster engraftment and shorter period of neutropenia. This benefit has not yet been realised in CB, where engraftment has not been discernably faster and chronic GVHD may have been more frequent. Further studies are awaited. Dual CBT has been performed in adults where early data suggests engraftment occurs at a speed similar to CBT in children, with no adverse effects (eg no increase in GVHD) seen. Engraftment of both cord blood units has occurred initially in 70% of patients, with one cord blood finally becoming dominant.

Haematopoietic stem cells can, in the right conditions, be transformed into a range of other tissues including heart muscle, bone, brain and liver cells. HSC's have been shown to repair cardiac damage after a heart attack when injected directly or intravenously. The beauty of CB derived stem cells is that they are "young" with long telomere length compared to stem cells taken from adults. Thus, the potential uses of CB derived stem cells in the future are enormous.