

STEM CELL NETWORK POLICY ON UMBILICAL CORD BLOOD COLLECTION

Preamble:

The objectives of the Stem Cell Network Policy Development Committee are to provide informed input into the development of public policy and to promote ethical conduct in stem cell research. The Committee recognizes that there is a current debate in Canada over whether or not a national initiative on umbilical cord blood (UCB) collection is warranted. In this regard, the Committee hopes that this policy statement will be a beneficial resource for Canadian policy-makers who are charged with making this decision. It is intended to encourage responsible policy and practices through cooperation between the public and private sectors and to foster research on UCB-derived hematopoietic stem cells in an effort to develop efficacious therapies for human disease.

Purpose:

To elucidate the Stem Cell Network's position on the importance of UCB-derived stem cells for transplantation and to delineate the arguments surrounding the creation of a national UCB collection initiative that draws on the existing expertise and resources in both the public and private sectors.

Background:

UCB is increasingly valued as a resource for transplantation – both autologous and allogeneic – and for cellular therapy. Since 1988, hematopoietic stem cells from UCB transplants have been used for the treatment of various malignant and non-malignant disorders including lymphoid and myeloid leukemias, Fanconi's anemia, aplastic anemia, β -thalassemia, sickle cell disease, Hurler's syndrome and others. To date, more than 5000 UCB transplants have been performed worldwide.ⁱ UCB is now clinically recognized as an appropriate alternative to allogeneic sources of hematopoietic cells for transplantation in children with no HLA identical sibling or well-matched, unrelated adult bone marrow donor. Recently, multiple cord blood unit transplants are being proposed as a strategy to accelerate engraftment rates post transplant. These, and other strategies such as blood stem cell expansion may further broaden the use of cord blood-based hematological transplantation.

Importantly, potential uses of UCB cells for the treatment of diseases other than blood disorders (e.g. "cellular therapy" or "cytotherapy") have gained prominence. Although much of this work is preliminary, it has been suggested that UCB cells may be useful in the treatment of a variety of diseases including, among others, degenerative neuromuscular disorders, ischemic heart disease, diabetes, stroke and other vascular disorders.ⁱⁱ The relative potency of UCB stem cells is a topic of emerging interest among basic translational and clinical researchers.

Over the past several years, UCB has become a topic of increasing interest amongst the general public in Canada and abroad. Expectant parents frequently question whether they should bank their infant's UCB for potential future clinical use for that child or a family member. At present, the options for UCB collection in Canada are limited, especially outside of the Greater Toronto Area. There are over a dozen UCB collections in Canada – three public libraries, one each Alberta, Quebec and Ontario, and 11 private cord blood banks. Despite the increasing number of

UCB collections, the vast majority of umbilical cord blood is routinely discarded during the birthing process.ⁱⁱⁱ It is estimated that approximately 1,191 publicly available and searchable UCB samples are banked in Canada.^{iv}

Based on data prepared by the Canadian Blood and Marrow Transplantation Group and the Canadian Hematology Society, we know that approximately 600 allogeneic hematopoietic cell transplants were performed in Canada in 2004; of these, fewer than 25 recipients received UCB and nearly 400 were from sibling donors. Given that only 30-35% of those patients requiring a transplant will have an appropriately matched sibling it is expected that approximately 600 – 700 patients per year in Canada could benefit from transplants based on an alternative cell source such as UCB.^v The likelihood of finding a suitable donor for an individual who requires a transplant will be maximized by ensuring that there exists a robust UCB collection that represents the unique ethnic diversity of the Canadian population.

Though there is clear interest in developing a robust public repository of UCB samples in Canada, there remains no concerted, national effort to establish such a collection (or series of linked collections) that could readily be accessed for clinical and research purposes. A national UCB initiative in Canada is thus imperative to capture this valuable resource.

Existing Professional Guidelines and Policy Statements:

In response to increased interest in UCB collection, several recent policy statements, practice guidelines and advisory documents on UCB collection have been published by influential organizations (see, Table 1).

Table 1: Published Professional Guidelines and Policy Statements on Umbilical Cord Blood Banking.

Society of Obstetricians and Gynaecologists of Canada, Maternal/Fetal Medicine Committee “Umbilical Cord Blood Banking: Implications for Perinatal Care Providers” (March 2005) 27 <i>Journal of Obstetricians and Gynaecologists of Canada</i> 263, online: SOGC < http://sogc.medical.org/guidelines/public/156E-CPG-March2005.pdf >.
The American Academy of Pediatrics, “Cord Blood Banking for Potential Future Transplantation” (2007) 119 <i>Pediatrics</i> 165, online: AAP < http://aappolicy.aappublications.org/cgi/reprint/pediatrics;104/1/116.pdf >.
American Medical Association, <i>Umbilical Cord Blood Transplantation: Current Scientific Understanding</i> , Report 2 of the Council of Scientific Affairs (A-03), June 2003, online: AMA < http://www.ama-assn.org/ama/pub/category/14516.html >.
Institute of Medicine, Committee on Establishing a National Cord Blood Stem Cell Bank Program, <i>Cord Blood: Establishing a National Hematopoietic Stem Cell Bank Program</i> , E.A. Meyer, K. Hanna and K. Gebbie, Eds. (Washington D.C.: National Academy of Sciences, 2005) online: NAP < http://www.nap.edu/catalog/11269.html >.
The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, <i>Umbilical Cord Blood Banking</i> , College Statement, July 2005, online: RANZCOG < http://www.ranzcog.edu.au/publications/statements/C-obs18.pdf >.
Royal College of Obstetricians and Gynaecologists (UK), Scientific Advisory Committee, <i>Umbilical Cord Blood Banking</i> , Opinion Paper 2, June 2006, online: RCOG < http://www.rcog.org.uk/resources/Public/pdf/umbilical_cord_blood_banking_sac2a.pdf >.

Upon review of the above listed documents, several common themes are evident:

- The medical care of the pregnant woman and her infant is paramount. Procedures to collect UCB must not interfere with the provision of appropriate medical care.
- Public UCB collection should be encouraged.
- There is insufficient evidence to recommend UCB collection and storage for later personal or family use in the absence of a defined medical risk (e.g. a sibling or other family member with a genetic or malignant condition that could potentially benefit from UCB transplant).
- All cord blood collections – both public and private – should be required to operate in compliance with agreed upon accreditation standards to ensure safety of blood products for therapeutic use.

Stem Cell Network of Canada Policy Statement:

In light of current knowledge about the current clinical utility of UCB for transplantation purposes and the potential for innovative new therapies to be developed using hematopoietic stem cells derived from UCB, the Stem Cell Network supports the development of a National Cord Blood Collection Initiative that:

1. utilizes and builds on the national and provincial expertise and resources that currently exist in both the public and private sectors in Canada;
2. seeks to increase the ethnic diversity of UCB donors to ensure that the benefits of banking will accrue equitably to all Canadians;
3. is buttressed by regulatory and professional standards that ensure privacy, quality and safety in public and private UCB banks whether the intended use is autologous or allogeneic;
4. depends on a robust informed consent or refusal process and the provision of up-to-date information for donors and for the public;
5. is responsive to the medical needs of pregnant women and their infants, and the desire to promote altruistic donation of valuable biologic materials, otherwise discarded, to a public resource;
6. is respectful and supportive of the health professional-patient relationship and of the role of the health-related and scientific professions in society;
7. promotes and facilitates research efforts examining the potential clinical uses of stem cells obtained from UCB to understand and treat human disease.
8. Incorporates a program to track and monitor clinical outcomes of all patients receiving treatments involving hematopoietic stem cells;
9. is linkable and accessible through existing national and international registries;
10. is executed through a not-for-profit entity with independent ethics review and appropriate scientific oversight; and is supported by the Federal, Provincial and Territorial governments who will commit to long-term funding of the Initiative.^{vi}

ⁱ William Ying Khee Hwang *et al*, “A Meta Analysis of Unrelated Donor Umbilical Cord Blood Transplantation versus Unrelated Donor Bone Marrow Transplantation in Adult and Pediatric Patients” (2007) 13 *Biology of Blood and Marrow Transplantation* 444; Mary Eapen *et al*,

“Outcomes of Transplantation of Unrelated Donor Umbilical Cord Blood and Bone Marrow in Children with Acute Leukaemia: A Comparison Study” (2007) 369 *Lancet* 1947; Vanderson Rocha & Elaine Gluckman, “Outcomes of Transplantation in Children With Acute Leukaemia” (2007) 369 *Lancet* 1906; Vanderson Rocha & Elaine Gluckman, “Clinical Use of Umbilical Cord Blood Hematopoietic Stem Cells” (2006) 12 *Biology of Blood and Marrow Transplantation* 34; William Arcese et al, “The Therapeutic Use of Cord Blood” (2006) 4 *Cell Preserv. Technol.* 161; Karen K. Ballen, “New Trends in Umbilical Cord Blood Transplantation” (2005) 105 *Blood* 3786; P. Rubenstein, “Why Cord Blood” (2006) 67 *Hum. Immunol.* 398. *See also*, Bone Marrow Donors Worldwide (BMDW) Registry at www.bmdw.org. At present BMDW registry lists approximately 264,000 units of UCB available for transplant (as at June 11, 2007).

ⁱⁱ Olle Lindvall & Zaal Kokaia, “Stem Cells for the Treatment of Neurological Disorders” (2006) 441 *Nature* 1094; Nedime Serakinci & W. Nicol Keith, “Therapeutic Potential of Adult Stem Cells” (2006) 42 *Eur. J. Cancer* 1243; Paul R. Sanberg et al, “Umbilical Cord Blood-Derived Stem Cells and Brain Repair” (2005) 1049 *Ann. N.Y. Acad. Sci.* 67; Jill Hows, “Adult Stem Cell Therapy Beyond Haemopoietic Stem Cell Transplantation? An Update” (2005) 14 *Transpl. Immunol.* 221; Augusto Pessina & Laura Gribaldo, “The Key Role of Adult Stem Cells: Therapeutic Perspectives” (2006) 22:11 *Curr. Med. Res. Opin.* 2287; Erika Check, “Cardiologists Take Heart from Stem-Cell Treatment Success” (2004) 428 *Nature* 880; Julio C. Voltarelli *et al*, “Autologous Nonmyeloablative Hematopoietic Stem Cell Transplantation in Newly Diagnosed Type 1 Diabetes Mellitus” (2007) 297 *JAMA* 1568.

ⁱⁱⁱ Inception Biosciences estimates that estimates that cord blood is banked in less than 2% of Canadian births. Personal communication, Laura Grey, VP Research Strategy and Business Development, Inception Biosciences). *See also*, Conrad V. Fernandez, Kevin Gordon, Michiel van den Hof, Shaureen Taweel, Francoise Baylis, “Knowledge and Attitudes of Pregnant Women with Regard to Collection, Testing, and Banking of Cord Blood Stem Cells” (2003) 168 *CMAJ* 695. Approximately 70% of pregnant women surveyed reported poor or very poor knowledge about UCB banking.

^{iv} Canadian Blood Services, “Assuming the Need for a National Canadian Cord Blood Bank, How Do We Establish One that Best Meets the Needs of Canadian Patients?” Discussion document prepared for CBS National Cord Blood Bank Syntegration Workshop, Ottawa, ON, June 1-3, 2007 [unpublished paper] at 11, citing WMDA Stem Cell Registry Annual Report, 2005.

^v Armand Keating & Lothar Huebsch, “Umbilical Cord Blood Transplantation in Canada” Prepared for the Canadian Blood and Marrow Transplantation Group and the Canadian Hematology Society for a Symposium on Establishing an National Cord Blood Bank System for Canada, Toronto, ON, 24 June 2005.

^{vi} This Stem Cell Network Policy Statement expands on the nine points of consensus reached at a multi-stakeholder meeting entitled “The Future of Cord Blood Banking in Canada – Workshop #2” hosted by the Health Law Institute in Edmonton, Alberta Canada, on June 14, 2006. The workshop was the second stakeholder meeting following one held at the Université de Montreal in August, 2005 and hosted by the CRDP. Both workshops funded by Stem Cell Network of Canada Catalyst Grant funding (Bartha Maria Knoppers, Principal Investigator).

Attendees at the June 2006 workshop in Edmonton included the following individuals: Timothy Caulfield, Lori Sheremeta (University of Alberta), Bartha Maria Knoppers, Linda Kharaboyan

(Université de Montreal), John Akabutu (Alberta Cord Blood Bank), Morris Blajchman (Inception Biosciences), Rose Geransar (University of Calgary), Mindy Goldman (Canadian Blood Services), Stuart Irwin (Cells for Life), Kathryn Jervis (Health Canada), Andre Lebrun (Hema Quebec), Locksley McGann (University of Alberta, Canadian Blood Services), Vyta Senikas (Society of Obstetricians and Gynaecologists of Canada), Ernest Stacey (Lifebank), Jane Virro (Victoria Angel Registry of Hope), Phyllis Warkentin (Foundation for the Accreditation of Cellular Therapy), Joan Yates (Inception Biosciences), Peter Zandstra (University of Toronto).

Related works the Catalyst Team include: Lorraine Sheremeta, Margo Plant & Bartha Maria Knoppers, "The Future of Cord Blood Banking in Canada" (2006) 14 Health Law Rev. 41; Lorraine Sheremeta, "Public Meets Private: Challenges for Informed Consent and Umbilical Cord Blood Banking in Canada" (2006) 15:2 Health Law Rev.; Margo Plant and Bartha Maria Knoppers, "Umbilical Cord Blood Banking in Canada: Socio-Ethical and Legal Issues" (2005) 13 Health Law J. 187; Madelaine Saginur, Linda Kharaboyan, Bartha Maria Knoppers, "Umbilical Cord Blood Stem Cells: Issues With Private and Public Banks" (2004) 12 Health Law J. 17.