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UMBILICAL CORD BLOOD BANKING

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Current therapeutic uses of umbilical cord blood stem cells and the promise of these cells for the treatment of degenerative diseases in the future have led to the establishment of cord blood banks in many parts of the world. Although umbilical cord blood banking raises many ethical and legal issues, this article focuses on the controversy created by the coexistence of public and private cord blood banks in many countries. Policy statements adopted by professional associations and advisory groups indicate that, based on the current state of medical evidence, childbearing women with no current or potential familial need of stem cell transplantation should be encouraged to donate cord blood to public banks. Collected cord blood that does not meet standards for transplantation should be made available for research, and options should be provided to parents so that they can make informed decisions regarding which types of research they are willing to support.

The umbilical cord, previously considered as waste and discarded at birth, is a source of haematopoietic stem cells that can currently be used for the treatment of blood malignancies and inherited blood and metabolic disorders.¹

As an alternative to bone marrow transplants, umbilical cord blood presents certain advantages: it can be collected at birth, without pain to either mother or child; the number of potential donors is high; after collection, typing, testing and freezing can be quickly performed, making the stem cells rapidly available for shipping to any recipient.

In addition, transplants of partial HLA² matches are more successful with umbilical cord blood cells than with bone marrow cells. Disadvantages include a longer time to engraftment for cord blood transplants compared to bone marrow, which can leave the recipient vulnerable to infections, the risk of transmission of a hereditary disease through cord blood stem cells (which would be undiagnosed in the donor at birth), and the often comparatively low stem cell count in collected cord blood.³

Since the first report of successful cord blood transplantation in 1988, more than 6000 transplantations have been performed worldwide.⁴ The use of umbilical cord blood cells is well established in children,⁵ but not so

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in adults, because a unit of umbilical cord blood collected at delivery often does not yield enough cells to treat adults. Research has shown that the stem cells found in a unit of cord blood would not suffice to treat adults weighing more than 110 pounds. Certain strategies, such as cell expansion and transplantation of cells from multiple cords, are currently being developed and more successful cord blood transplants are being performed on adults participating in these trials.⁶

In addition to blood precursor cells, umbilical cord blood apparently also contains stem cells that can differentiate into other types, such as cartilage, fat, hepatic, cardiac and neural cells,⁷ prompting speculation as to the potential use of cord blood stem cells for regenerative medicine. Advances in the expansion of cord blood stem cells may then solve the insufficiency problem thereby allowing increased transplantations to treat degenerative conditions in adults.⁸ However, this remains largely speculative at the present time.

Current therapeutic uses of umbilical cord blood stem cells and the promise of these cells for the treatment of degenerative diseases in the future have led to the establishment of cord blood banks in many parts of the world.⁹ Although this practice raises questions of safety and other ethical, legal and social issues, the present discussion will focus on certain aspects of the coexistence of public and private banks.

Public and Private Banks. Public banks make cells available to anyone who might need them on the basis of a good HLA match. To fulfill this function, these banks store large numbers of samples of transplant-suitable cord blood stem cells with the goal of maximizing the chances of finding a donor match for any unrelated recipient. Their aim is to provide equitable access to stored cord blood stem cells, while not limiting participation to families who have the financial means. Public banks in the United States generally charge between \$15,000 and \$35,000 per unit of cord blood provided for transplantation, a cost usually covered by health insurance.¹⁰ By one count, there are 28 public cord blood banks in the United States;¹¹

there are two such banks in Canada. One estimate put the world supply of cord blood units in public banks (in 2004) at between 175,000 and 200,000.¹²

In contrast, private banks will process and store umbilical cord blood for a fee, reserving it for the use of the "donor" child or family rather than making it available to all who may need it. The purpose of these banks is to allow families that can afford the preparation (between \$1000-2000) and annual storage (between \$100-200) fees access to cord blood for eventual use.¹³ Recent reports show that well-known figures, such as football stars and royalty,¹⁴ who have had recourse to these banks have contributed to publicize this practice and highlighted the promises held out to buyers, such as the reported assertion by one football player that these cells would provide insurance against tendon or cartilage problems.¹⁵ One organization has identified 41 private banks in North America, 42 in Europe and 28 in Asia.¹⁶ No reliable statistics are available as to the number of units in private banks.

A recent initiative, the Virgin Health Bank, proposes a "dual" approach to cord blood banking, dividing the collected umbilical cord blood between a public bank (80% of the collected blood), where the cells will be available for anyone's use, and a private bank (20% of the collected sample), where the remaining cells will be available to the "donor" child or family in case of need.¹⁷ Parents choosing this option will pay fees comparable to those of other private banks.¹⁸ It should be noted that currently unavailable cell expansion technology will be required to obtain sufficient numbers of cells for currently known treatment from these privately banked samples, and also for their use in regenerative medicine.

The coexistence of private and public banks in many countries has created a controversy, and is discussed in recent policy statements or opinions issued by professional organizations¹⁹ and other advisory groups.²⁰

Medical Rationale for Banking. These policies and opinions state that, in the current state of medical knowledge, the probability of autologous or familial use of umbilical cord blood stored at birth is very low, except for

particular situations, so that non-directed donations to public registries should be widely encouraged.²¹ The probability of developing a disease that will require an umbilical cord blood transplant is very low in the general population, so that it is currently highly unlikely for a family with no history of blood disease or metabolic disorder to ever need banked cord blood.²² In addition, if a genetic disease is present, cells from the patient's own cord blood cannot be used, as they will contain the disease-causing mutation. In some non-genetic diseases such as leukemia, cells containing malignancy markers were found in the umbilical cord blood of the patient, making their use for treatment questionable. There have been isolated reports of successful treatment of leukemia and aplastic anemia with autologous cord blood transplantation,²³ but current medical opinion still weighs on the side of public banking of cord blood to ensure the availability of transplants to all who need them, rather than favour those who have the means to store blood but may be unable to use it.

Representative Public Banks. HLA types are genetically determined, so that the probability of finding a matching donor is generally greater within one's racial or ethnic group. Thus, it is important for public cord blood banks to collect a sufficiently large number of samples from various racial and ethnic groups to ensure a good match for as many potential recipients as possible. It has been noted that patients from minority groups have difficulty finding a matching graft. As an example, in one bone marrow bank in the United States, African Americans had a 30% chance of finding a match while Caucasians had an 80% chance.²⁴ An American study noted that cord blood banks did not initially achieve better representation of minorities in samples than bone marrow banks,²⁵ although targeted interventions can improve this.²⁶ This gap must be remedied for public banks to reach their full potential, and the importance of recruiting donors from minority groups is underlined in some policies.²⁷ One study found that cord blood from certain ethnic groups may have lower cell count or an increased incidence of infectious disease,²⁸ suggesting a necessity to target these groups more effectively to permit collection of sufficient numbers of transplantation-suitable units.

There is a need to build awareness about cord blood banking among members of such communities and to establish mechanisms to ensure that all populations have a fair opportunity to participate in cord blood banking and use.²⁹ Generally, public banks restrict cord blood collection to a local network of hospitals, thus making it difficult for parents outside their target population to donate. One possible solution to increase the representation of minorities in cord blood banks is to expand the network of hospitals from which they collect donations to include those that serve minority groups, a strategy that has been used successfully in at least one case.³⁰ Additional suggested measures to increase the representation of minorities in public cord banks include education as to the benefits of cord blood transplantation,³¹ increasing the number of minority members hired as employees for the cord blood program, allowing donor recruitment during labour rather than requiring pre-natal recruitment, public service announcements, outreach through local community organizations and the distribution of educational materials in various languages.³²

In addition to increasing minority donor recruitment, most policies recommend that publicly-funded directed storage of cord blood be offered to families at risk of disorders that require transplantation, or which have a rare HLA type, to ensure equality of access to treatment.³³

Research Use of Unsuitable Samples. Collected umbilical cord blood may not be suitable for transplantation; the amount of cells in the cord blood may be insufficient, or the blood may test positive for an infectious or genetic disease. Indeed, about half of the cord blood units collected and intended for banking are not frozen for potential transplant use.³⁴ A strong case exists for using these samples in research, and a recent position statement by a professional organization has been taken to task for largely ignoring this possibility and focusing too closely on current therapeutic uses of cord blood.³⁵ It is interesting to note that the American and Canadian professional organizations surveyed here have also focused on current therapeutic use rather than research. The French CCNE, although approving of research, considered in 2002 that

the then-available sources of cord blood were adequate for research.³⁶

The promise of research should be taken into account when drafting consent forms and communicating with patients. One Quebec public cord bank, Héma-Québec, seeks consent to research use of cord blood unsuitable for transplantation at the same time as it obtains consent to donation. This approach has the merit of streamlining the consent process and potentially increasing the number of samples available for research. However, it requires that information be made available as to the type of research to be carried out with the donated cord blood, since parents may have objections to certain types of research. For instance, one study found that mothers polled six months after cord blood donation expressed concerns about genetic testing and research; with respect to research, there was discomfort about the possibility of use of donated umbilical cord blood being used for genetic manipulation or "cloning".³⁷ Thus, precise information about planned research use should be provided to patients.

Parent Information and Consent. Given the current presence of two main types of players on the cord blood bank scene, it is important to consider whether and how parents obtain information about their options. Studies have shown that women are not well informed on these matters but want access to more and better information, and that pregnant women wish to be informed early enough in their pregnancy to have time to assimilate the information before making their decision.³⁸ Currently available sources of information appear patchy at best: because public banks usually only collect from a small number of hospitals, they may not disseminate information in other settings. Private banks may distribute materials in obstetrical clinics and practitioners' offices, but there is some concern about the objectivity of the information contained in these materials.³⁹ Studies show that women would like health professionals to be available as a source of information.⁴⁰ However, if the clinic or practitioner is affiliated with a commercial bank, information obtained from that source may be suspect, and some policy statements explicitly require that affiliations and conflicts of interest should be clarified for the patient.⁴¹

These studies also show that once informed, most women would consider donation to a public cord blood bank, although they have concerns about certain aspects of the process.⁴²

The lack of adequate information provided by a trusted source, as well as the difficulty of donating cord blood to a public bank when one is not available in the birthing hospital, often results in parents knowingly or unknowingly relinquishing all rights over their child's cord blood and assuming that the hospital staff will dispose of it as it does other types of biological waste. It has been estimated that in 99 percent of all deliveries the cord blood is discarded at the time of birth.⁴³ This suggests that adequate information about cord blood banking options may increase the number of cord blood units collected for public use, providing hope for the recruitment of donors to expand public banks to reach their potential.

Conclusion. Although umbilical cord blood banking raises many ethical and legal issues, the focus of this discussion has been the coexistence of public and private cord blood banks. The policy statements of professionals associations and advisory groups consulted so far all indicate that, based on the current state of medical evidence, childbearing women with no current or potential familial need of stem cell transplantation should be encouraged to donate cord blood to public cord blood banks. However, public registries must meet the goal of providing matches to as many as possible to justify the expense involved in creating and maintaining them. Because public banks require a great diversity of cells with HLA types from different populations so as to provide acceptable donors for as many as possible, it is important to encourage a wider collection base and create an information sharing network among cord blood banks to facilitate searches. Obtaining an increase in cord blood donations for public banks will require that reliable information be provided to childbearing women. In addition, to ensure fair access to healthcare services to all, families at risk of specific diseases treatable by cord blood transplantation should have the opportunity to store their child's cord blood in a public registry for their exclusive use, as recommended by most of the policies surveyed.⁴⁴

Given the emerging promise of cord blood stem cells, collected cord blood that does not meet standards for transplantation should be made available for research, and options should be provided to allow parents to choose the types of research they are willing to support.

Public banks that meet these criteria should bring a common benefit justifying the investment. For this reason, results from a recent American initiative should be followed closely. The *Stem Cell Therapeutic and Research Act of 2005*,⁴⁵ passed in December 2005, aims to increase the inventory of cord blood samples in American public banks by 150 000 units of high-quality cord blood. Approximately 79 million dollars have been allocated to this program through 2010. Cord blood banks participating in the program will have to comply with all federal quality standards and be accredited by an authority to be determined. A central system of match-searching and reservation of units for transplant will be established. Measures will be implemented to favour donations from minority groups, so that members of underrepresented populations have the same probability of finding a match as other members of the population. Collected cord blood that is not appropriate for clinical use will be made available for peer-reviewed research. A pilot project is established to collect and store cord blood units from families where a

first-degree relative has been diagnosed with a condition that will benefit from transplantation, at no cost to the family. This program is thus consistent with many of the recommendations contained in the EGE opinion, and its implementation should be a source of important data.

Although most policy statements discourage private banking given the current state of medical knowledge, they are not usually in favour of prohibiting it.⁴⁶ Some European countries have prohibited private banking on their territory (Italy, France and Spain), but private banking is considered to be increasing overall, and at a faster rate than public banking.⁴⁷ Given this reality, mechanisms by which private banks may contribute to the common interest should be explored.

Suggestions made to date include a contribution by private banks to the funding of public banks, public-private research collaborations or the donating cord to public banks of cord blood units that are no longer required. This last suggestion would be realizable only if all private cord blood units had been collected, tested and stored following standards applicable to public banks and *Current Good Manufacturing Practice* (CGMP) rules.

Should advances in stem cell research provide evidence to support autologous banking of cord blood in the future, governing authorities would, in our opinion, need to consider the feasibility and costs associated with the systematic collection of cord blood from all newborns. This would solve the problem of supply and diversity and ensure fair access by all individuals to compatible cells, if not their own. This perspective is consistent with the opinion of the French CCNE on cord blood banking, which states that should autologous use of cord blood prove to be useful, the principles of justice and equity should predominate and autologous storage should not be a service left to commercial banks but become routine and underwritten by public authorities.⁴⁸ The EGE's opinion concurs, stating that if the use of one's own cord blood cells becomes of value in the future, "storage should not be a service left to commercial banks but should be taken over by the public sector in order to ensure fair access to healthcare services for everybody."⁴⁹

- ¹ Diseases that may be treated with umbilical cord blood stem cell transplantations include leukemias, lymphomas and inherited diseases such as sickle cell anemia, Fanconi anemia, severe combined immunodeficiency, and Hurlers syndrome. See http://www.marlow.org/PATIENT/Understnd_Disease_Treat/Lrn_about_Disease/index.html (last accessed January 23, 2007).
- ² HLA refers to "human leukocyte antigens". These are proteins expressed on the surface of an individual's cells, used by the immune system to distinguish "self" from "non-self" cells, and are largely responsible for transplant rejections. Much variation of these proteins is found in human populations. Six of these proteins have been identified as being most clinically relevant for tissue transplant purposes, and should be an exact match between donor and recipient to decrease the odds of tissue rejection by the recipient. Most tissue transplants therefore aim to exactly match donor and recipient for these six antigens. Cord blood stem cell transplants, however, seem to tolerate more "mismatches", and work with as little as four HLA matches. See Rubinstein P, "Why Cord Blood," (2006) *Human Immunology* 67:398-404.
- ³ See Brunstein C and Wagner J, "Umbilical Cord Blood Transplantation and Banking," (2006) *Annual Reviews in Medicine* 57:403-17, and Gunning J, "Umbilical cord cell banking- Implications for the future," (2005) *Toxicology and Applied Pharmacology* 207(2 Suppl):538-43.
- ⁴ Moise K, "Umbilical Cord Stem Cells" (2005) *Obstetrics and Gynecology* 106:1393-1407.
- ⁵ Brunstein and Wagner, *supra* note 3, and Ballen KK, "New trends in umbilical cord blood transplantation," (2005) *Blood* 105:3783-3792 both contain an overview of recent adult trials.
- ⁶ Brunstein and Wagner, *supra* note 3, summarize some of these trials.
- ⁷ Kögler G, Sensken S, Airey JA, Trapp T, Muschen M, Feldhahn N, et al., "A new human somatic stem cell from placental cord blood with intrinsic pluripotent differentiation potential," (2004) *Journal of Experimental Medicine* 200:1 23-135. See also McGuckin C et al., "Embryonic-like stem cells from umbilical cord and potential for neural modeling," (2006) *Acta Neurobiologiae Experimentalis* 66:321-39.
- ⁸ Sanz MA, "Cord-blood transplantation in patients with leukemia - a real alternative for adults," (2004) 351 *New England Journal of Medicine* 35:2328.
- ⁹ Saginur M, Kharaboyan L, Knoppers BM, "Umbilical Cord Blood Stem Cells: Issues with Private and Public Banks," (2004) 12 *Health Law Journal* 12: 22.
- ¹⁰ Moise, *supra* note 4.
- ¹¹ See http://www.parentsguidecordblood.com/content/usa/banklists/publicbanks_new.shtml?navid=9, (last accessed January 24, 2007).
- ¹² Steinbrook R, "The cord blood controversies," (2004) *New England Journal of Medicine* 351:2255-2257.
- ¹³ "Private cord blood banks," (2004) *The Medical Letter on Drugs and Therapeutics* 46:21-22.
- ¹⁴ Templeton S-K, "Footballers use babies for 'repair kits'," *Sunday Times*, August 27, 2006, available at <http://www.timesonline.co.uk/article/0,,2087-2330444,00.html> (last accessed January 23, 2007); Fuchs D, "Royal baby reignites debate on storing cord blood," *The Guardian*, February 27, 2006, available at <http://www.guardian.co.uk/international/story/0,,1718555,00.html> (last accessed January 23, 2007).
- ¹⁵ See Templeton S-K, *supra* note 14.
- ¹⁶ Numbers for Central and South America are 24, Australia and New Zealand, 4, and Africa, 3, according to www.parentsguidecordblood.com (last accessed January 24, 2007).
- ¹⁷ Personal communication, Virgin Health Bank, February 16, 2007.
- ¹⁸ The Virgin Health Bank website advertises a price of 1 500 pounds, or approximately 2940 US dollars, for this service, which includes storage of the cord blood held in the private bank for 20 years. See <http://www.virginhealthbank.com/TheCost.html> (last accessed February 27, 2007).
- ¹⁹ The following statements from professional associations will be discussed here: American College of Obstetricians and Gynecologists, Committee on Obstetric Practice opinion "Routine storage of umbilical cord for potential future transplantation," (1997) *International Journal of Gynaecology and Obstetrics*, 58: 257-259 [United States]; American Academy of Pediatrics ("APA") - Policy Statement - "Cord Blood Banking for Potential Future Transplantation," (2007) *Pediatrics* 119:165-170 [United States]; Royal College of Obstetricians and Gynaecologists ("RCOG")- Scientific Advisory Committee, *Umbilical Cord Blood Banking. Opinion paper no. 2, 2006* [United Kingdom]; Society of Obstetricians and Gynecologists of Canada ("SOGC"), SOGC Clinical Practice Guidelines - "Umbilical Cord Blood Banking: Implications for Perinatal Care Providers," (2005) *Journal of Obstetrics and Gynecology Canada* 156:263-274 [Canada].
- ²⁰ The following opinions are referred to here: France, National Consultative Bioethics Committee ("CCNE"), *Umbilical cord blood banks for autologous use or for research*. Opinion No. 74, December 2002; European Group on Ethics in Science and New Technologies ("EGE"), *Opinion no. 19 - Umbilical cord blood banking*. Brussels, 2004.
- ²¹ All the policy statements and opinions referred to in notes 19 and 20, *supra*, are of this opinion at present.

- ²² Fisk NM et al., "Can routine commercial cord blood banking be scientifically and ethically justified?" (2005) *Public Library of Science Medicine* 2: e44.
- ²³ Hayani A et al., "First report of autologous cord blood transplantation in the treatment of a child with leukemia," (2007) *Pediatrics* 119:296-300; Frichtman S et al., "The successful treatment of severe aplastic anemia with autologous cord blood transplantation," (2004) *Biology of Blood and Marrow Transplantation* 10:741-742. In 2004, *Medical Letter* (*supra* note 13) reported 7 autologous cord blood transplants worldwide since 1998.
- ²⁴ Laver J et al, "Assessment of Barriers to bone marrow donation by unrelated African-American potential donors," (2001) *Biology of Blood and Marrow Transplantation* 7:45-48.
- ²⁵ Ballen KK et al., "Racial and ethnic composition of volunteer cord blood donors: comparison with volunteer unrelated marrow donors," (2002) *Transfusion* 42:1279-1284.
- ²⁶ Ballen KK et al., "Racial Diversity with High Nucleated Cell Counts and CD34 Counts Achieved In a National Network of Cord Blood Banks," (2004) *Biology of Blood and Marrow Transplantation* 10:269-275.
- ²⁷ APA, *supra* note 19, recommendation 11 to institutions; EGE, *supra* note 20, opinion 2.10.
- ²⁸ The study reported in Ballen et al., *supra* note 25, notes that cord blood units from African-Americans average fewer cells than those of other groups, and that units from populations of Asian origin have a higher incidence of hepatitis infection, for example.
- ²⁹ Kurtzberg J, Drapkin Lyerly A, Sugarman J, "Untying the Gordian knot: policies, practices, and ethical issues related to banking of umbilical cord blood," (2005) 115:10 *The Journal of Clinical Investigation* 2592 at 2595.
- ³⁰ *Supra* note 25.
- ³¹ Grossman B et al., "Barriers and motivations to blood and cord blood donations in young African-American women," (2005) *American Journal of Hematology* 78:198-202.
- ³² Plant M and Knoppers BM, "Umbilical cord blood banking in Canada: socio-ethical and legal issues," (2005) *Health Law Journal* 13:187-212.
- ³³ See RCOG, *supra* note 19, recommendation 5; AAP, *supra* note 19, recommendation 1 to physicians; CCNE, *supra* note 20, pp. 4-5; EEG, *supra* note 20, opinion 2.9.
- ³⁴ Ballen KK, *supra* note 5. To this should be added the evidence from one major American transplant centre, which states that as many as 50% of the samples shipped for transplant presented quality issues.; Brunstein and Wagner, *supra* note 3.
- ³⁵ Chan S, "Cord-blood-banking - what are the real issues?" (2006) *Journal of Medical Ethics* 32:621-22.
- ³⁶ CCNE, *supra* note 20, p. 5.
- ³⁷ Danzer E et al., "Attitudes of Swiss mothers toward unrelated umbilical cord blood banking 6 months after donation," (2003) *Transfusion* 43:604-608.
- ³⁸ Perlow JH, "Patients' Knowledge of Umbilical Cord Blood Banking," (2006) *Journal of Reproductive Medicine* 51:642-648; Sugarman J, Kaplan L, Cogswell B and Olson J, "Pregnant Women's Perspectives on Umbilical Cord Blood Banking," (1998) *Journal of Women's Health* 7:747-757; Fernandez CV, Gordon K, Hof MV, et al., "Knowledge and attitudes of pregnant women with regard to collection, testing and banking of cord blood stem cells," (2003) *Canadian Medical Association Journal* 168:695-698.
- ³⁹ EGE, ACOG, SOGC and CCNE note the necessity to control private banks' advertising claims. See also Moise K, *supra* note 4.
- ⁴⁰ Sugarman et al. and Fernandez et al., *supra* note 38.
- ⁴¹ APA, *supra* note 19, recommendation 9 to institutions; SOCG, *supra* note 19, recommendation 15.
- ⁴² Such as not compromising their safety or that of their child during delivery, the protection of confidential information (such as the results of tests for infectious and genetic diseases), and the possibility that the cord blood might be required for their own family. See Sugarman et al., *supra* note 38.
- ⁴³ International Cord Blood Society webpage "Don't throw it away!" : http://www.cordblood.org/index.php?rm=common_page&id=10 (last accessed January 24, 2007).
- ⁴⁴ *Supra* note 33.
- ⁴⁵ *Stem Cell Therapeutic and Research Act of 2005*, Pub. L. No. 109-129, 119 Stat. 2550.
- ⁴⁶ RCOG, *supra* note 19, recommendation 2; APA, *supra* note 19, recommendations 2, 9, 10 to institutions; CCNE, *supra* note 20 at 7; EGE, *supra* note 20, opinion 2.2.
- ⁴⁷ Nietfeld & Veiter, *Statistics of Autologous Cord blood Storage and Use*, presentation, October 2004.
- ⁴⁸ CCNE, *supra* note 20 at 9.
- ⁴⁹ EGE, *supra* note 200, opinion 2.11.