J. Perinat. Med. 35 (2007) 314–321 • Copyright © by Walter de Gruyter • Berlin • New York. DOI 10.1515/JPM.2007.084

Umbilical cord blood collection: do patients really understand?

Nathan S. Fox[1,*], Cladd Stevens[2], Rodica Ciubotariu[2], Pablo Rubinstein[2], Laurence B. McCullough[3] and Frank A. Chervenak[1]

[1] Department of Obstetrics and Gynecology, Weill Medical College of Cornell University, New York, USA
[2] Department of Obstetrics and Gynecology, The New York Blood Center, New York, USA
[3] Department of Obstetrics and Gynecology, The Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, TX, USA

Abstract

Background: Pregnant patients have the option of storing their infant's cord blood with a private/commercial company for possible future use by the child or other family members. Some patients also have the option to donate the cord blood to a public bank for anyone to use. We evaluated patient understanding about cord blood banking in a cohort of patients with access to both options.

Methods: Anonymous questionnaires were collected from 325 pregnant patients seen in our Antepartum Testing Unit.

Results: Compared to those donating to a public bank, women planning on storing with a private/commercial company were less likely to believe that a suitable donor could be found from a public cord blood bank. Women had a strikingly poor understanding regarding the current uses for cord blood therapy. When asked whether cord blood has been used successfully to treat Alzheimer's disease, Parkinson's disease, and spinal cord injury only 28%, 24%, and 24%, respectively, correctly knew that it had not.

Conclusions: Obstetricians should assume that pregnant women are poorly informed about cord blood banking. The decision making process should be conducted with the goal of ensuring every pregnant woman the opportunity to make a well informed decision about cord blood banking.

Keywords: Blood bank; cord blood; placental blood.

*Corresponding author:
Nathan S. Fox
525 East 68th Street,
Box 122
New York, NY 10021
Tel.: +1-212-746-3186
Fax: +1-212-746-0449
E-mail: naf9015@med.cornell.edu

Introduction

Hematopoietic stem cells contained in blood taken from the placenta and umbilical cord (cord blood) after an infant is born can reconstitute bone marrow in recipients undergoing treatment for life-threatening diseases of the blood and immune system and certain inherited metabolic diseases [11, 12, 17, 18, 21, 24, 27, 29]. Since 1993, the New York Blood Center has collected cord blood donated to its National Cord Blood Program for use by anyone who might need it in the future [16, 22, 23]. The Program opened its fourth collection site at New York Weill Cornell Medical Center in September 2001 where patients who have not already decided to store their cord blood with a private/commercial company are given the option to donate their cord blood to this program, free of charge. Patients are approached for consent to donate after delivery, if the cord blood collected had an adequate content of total nucleated cells (TNC) for possible clinical transplantation. Alternatively, some patients arrange during their pregnancy to have their infant's cord blood stored with a private/commercial collection company for a fee, including annual maintenance fees. In these cases, the cord blood is stored for possible future use by the child, a sibling, or other family member. The private/commercial companies market directly to the patients and their obstetricians, requiring a contract signed by the mother in advance of the infant's delivery.

It is recommended that prior to cord blood collection, informed consent should be obtained from the patient [2, 10, 25, 26]. We sought to determine how informed our patients were regarding cord blood storage and whether their beliefs and knowledge influenced their decision making. Our hypothesis was that women are poorly informed about cord blood, and their beliefs about the supposed incremental benefit to private cord blood storage influence their decision. We hypothesized that women choosing to donate their cord blood to a public bank would be more knowledgeable about the uses of cord blood than women choosing to store cord blood with a private/commercial collection company.

Methods

Data collection

Pregnant women seen in our Antepartum Testing Unit (APTU) for routine ultrasound or non-stress testing were eligible for inclu-

sion and were offered an anonymous questionnaire to complete. We believe this is a representative sample of women delivering at our hospital, as all patients who deliver at our institution are typically seen at least once in the APTU, even if only for a second trimester ultrasound. We excluded women who were not yet pregnant or after birth. In addition to demographic questions, the questionnaire included multiple choice questions regarding the sources of information about cord blood, whether they planned on having their cord blood collected and stored, whether they planned to donate to a public bank or store with a private/commercial company, the reasoning behind these decisions, the beliefs about the potential uses for cord blood collected and their knowledge about current therapeutic uses. Patients were allowed to complete only one questionnaire during their pregnancy. The study was approved by the Cornell University Institutional Review Board.

Sample size calculation

In calculating a sample size, we had to make assumptions about the patients' level of understanding about cord blood collection, as we could not find any published data pertinent to our questionnaire. As a primary outcome, we used the mean correct score (out of 10) on a series of questions asking about the current uses for cord blood therapy. We calculated that 80 patients would be needed in each group (donating to a public bank vs. storing with a private/commercial company) to have 80% power to show a 25% difference in the mean score out of 10 with an alpha error of 0.05. We assumed that at the time of completing the questionnaire, approximately 50% of subjects would have already made a decision regarding cord blood storage. We also assumed that, of patients who had already decided, approximately 50% planned on donating to a public bank and 50% would store privately. The study design, therefore, called for an initial survey of 325 patients in order to have data from at least 80 in each decision group.

Statistical analysis

Chi square analysis was used for categorical and ordinal variables. Student's *t*-test was used for analysis of continuous variables (SPSS 12.0 for Windows, 2003, Chicago). A $P \leq 0.05$ was considered significant.

Results

A total of 724 questionnaires were distributed over a six-month period from April to September 2006 and 325 (44.9%) questionnaires were completed. For privacy reasons, we were not able to obtain demographic data from those who did not complete the questionnaire. A total of 176 patients (54%) had already decided to have their cord blood collected after delivery: 95 of these patients (29%) had chosen to store their cord blood with a private/commercial company and 81 (25%) planned to donate to a public bank. The demographics of the entire population, as well as for those planning to donate to a public bank or store with a private/commercial company are listed in Table 1. Overall, our population was well educated, with 94% completing undergraduate university and 58% completing a postgraduate degree. The population was evenly distributed across gestational ages.

Compared to patients planning to donate to the public bank, those who planned on private storage were more likely to be Jewish, less likely to be Hispanic, and more likely to be self-paying for their prenatal care rather than using medical insurance. However, the patients who were self-paying were also more likely to be Jewish (44% vs. 24%, $P = 0.003$) and less likely to be Hispanic (0% vs. 8%, $P = 0.01$). Therefore, self-payment was a likely confounder for the demographic differences between the public donation and private storage groups, as self-paying may reflect greater financial resources to cover private storage costs. The sample size was not sufficient to support a multivariable analysis to address this issue.

Patients who chose to store cord blood privately were asked to choose their primary reason. Whereas 83% responded "as a safeguard for the future ('just in case')", very few reported having a "family history of a certain illness" (5%) or "another child with an illness" (2%).

Table 2 lists responses to questions about patients' sources of information about cord blood. Most patients had seen literature from private/commercial cord blood companies, while few had seen literature from the public cord blood bank ($P < 0.001$). This difference persisted among the 148 (45.5%) subjects who were >24 weeks gestation (92% vs. 35%, respectively, $P < 0.001$).

Table 3 lists responses to questions regarding patients' beliefs about cord blood collection. Some patients, especially those planning to donate to a public bank, felt that their decision about cord blood collection would be influenced by the knowledge that their obstetrician would be paid a fee to collect the cord blood for a private/commercial company. Compared to women who planned to donate to a public bank, women who chose to store their cord blood with a private/commercial company were more likely to believe that their baby or a sibling of this baby would develop a condition that could benefit from cord blood. These women also were more likely to believe that the child's own cord blood could be used if the baby developed a condition that could benefit from cord blood and were less likely to believe that a potential donor could be found in a public bank.

Table 4 lists the responses to questions regarding the patients' knowledge about cord blood collection at New York Weill Cornell Medical Center and the current uses for cord blood-based therapy. Overall, only one-third of patients knew about the New York Blood Center's National Cord Blood Program, although the proportion increased with increasing gestational age (47% of patients >24 weeks). Our patients also had a poor understanding of the current uses for cord blood. The mean correct score (out of 10) was higher for those donating to a public bank compared to those collecting with a private/commercial company (5 vs. 3.9, $P = 0.012$).

Table 1 Demographic characteristics of study participants.

		Overall % (n=325)	Donating to private bank % (n=95)	Donating to public bank % (n=81)
Age	<20	0	0	0
	20–29	12.9	9.5	8.6
	30–39	72.3	71.6	80.2
	≥40	12	14.7	9.9
	NA	2.8	4.2	1.2
Gestational age	<24 weeks	51.4	44.2	49.4
	24–35 weeks	21.8	21.1	21
	≥36 weeks	23.7	30.5	28.4
	NA	3.1	4.2	1.2
Number of children	0	55.4	57.9	51.9
	1	30.8	27.4	33.3
	2	8.9	8.4	9.9
	>2	2.2	2.1	3.7
	NA	2.8	4.2	1.2
Marital status	Married	91.7	89.5	96.3
	Single	5.5	6.3	2.5
	NA	2.8	4.2	1.2
Race	American Indian/Alaskan native	0.3	0	0
	Asian/Pacific Islander	9.2	6.3	3.7
	Black	5.5	2.1	2.5
	Hispanic	6.2	0	8.6*
	White	71.4	83.2	79
	Other	2.2	2.1	2.5
	NA	5.2	6.3	3.7
Religion	Buddhist	0.9	0	0
	Christian	46.8	38.9	49.4
	Hindu	3.1	2.1	1.2
	Jewish	27.4	42.1	23.5**
	Muslim	0.6	1.1	0
	No religion	12	5.3	18.5***
	Other	4.6	5.3	2.5
	NA	4.6	5.3	4.9
Highest level of education completed	1st–8th grade	0	0	0
	9th–12th grade	3.1	1.1	1.2
	Undergraduate college/ University degree	36	32.6	37
	Postgraduate degree	58.2	62.1	60.5
	NA	2.8	4.2	1.2
Method of payment for prenatal care	Self-pay	19.7	27.4	14.8****
	Insurance	77.2	68.4	84
	NA	3.1	4.2	1.2

*P=0.004 comparing public to private donation.
**P=0.009 comparing public to private donation.
***P=0.008 comparing public to private donation.
****P=0.042 comparing public to private donation.

Gestational age did not correlate with correct score (mean correct score for >24 weeks and <24 weeks was 3.8 vs. 3.8, respectively, P=0.9), even when we excluded patients who did not plan to collect.

Discussion

Our study reports on the beliefs and knowledge of a large sample of patients regarding cord blood collection.

Table 2 Patients' sources of knowledge about cord blood donation.

	Overall % (n=325)	Donating to private bank % (n=95)	Donating to public bank % (n=81)
Discussed cord blood collection with obstetrician	36.9	56.8	43.2*
If did not discuss with obstetrician, plan on discussing cord blood collection with obstetrician	153/202 75.7	33/40 82.5	33/45 73.3
Seen/read literature distributed by private/commercial cord blood collection companies regarding cord blood storage	86.5	91.6	96.3
Seen/read ads in magazines/commercials regarding cord blood storage	84.6	86.3	92.6
Seen/read literature distributed by a public cord blood bank regarding cord blood donation	29.2	27.4	37

*P=0.048 comparing private to public donation.

Table 3 Patients' beliefs about cord blood collection, storage and use.

		Overall % (n=325)	Donating to private bank % (n=95)	Donating to public bank % (n=81)	P*
Would it make a difference in a decision to store cord blood with a private/ commercial cord blood bank if you knew that your obstetrician would be paid a fee to collect the cord blood	Yes	25.8	17.9	33.3	0.004
	No	65.2	82.1	53.1	
	NA	8.9	0	13.6	
The chance that my baby would have a condition (at birth or in the future) that could benefit from cord blood during his/her first 10 years of life is about	1 in 100	2.5	2.1	0	0.001
	1 in 1000	15.4	20	3.7	
	1 in 10,000	38.8	31.6	35.8	
	<1 in 10,000	34.2	38.9	56.8	
	NA	9.2	7.4	3.7	
The chance that a sibling who is now healthy would develop a condition that could benefit from this cord blood is about	1 in 100	2.8	4.2	0	0.001
	1 in 1000	18.2	18.9	3.7	
	1 in 10,000	28.6	22.1	29.6	
	<1 in 10,000	40	47.4	63	
	NA	10.5	7.4	3.7	
For most conditions requiring cord blood therapy, could a child use cord blood from his/her own placenta?	Always	23.1	26.3	24.7	0.006
	Usually	31.7	36.8	21	
	Sometimes	21.2	23.2	19.8	
	Rarely	14.8	10.5	25.9	
	Never	2.2	0	6.2	
	NA	7.1	3.2	2.5	
For most conditions requiring cord blood therapy, could a child use cord blood from a sibling's placenta?	Always	2.5	3.2	4.9	0.526
	Usually	34.5	35.8	38.3	
	Sometimes	49.5	54.7	53.1	
	Rarely	5.2	3.2	2.5	
	Never	0.9	0	0	
	NA	7.4	3.2	1.2	
If your child did need cord blood therapy and you did not have cord blood stored from him/her or a sibling, what is the chance cord blood from a public storage bank could be used?	Always	0.9	0	2.5	<0.001
	Usually	14.5	9.5	27.2	
	Sometimes	53.8	60	59.3	
	Rarely	0.9	26.3	7.4	
	Never	2.2	0	2.5	
	NA	7.7	4.2	1.2	

*P-values comparing private vs. public donation.

Table 4 Patients' knowledge about current indications for cord blood transplantation.

		Overall % (n=325)	Donating to private bank % (n=95)	Donating to public bank % (n=81)	P*
Does New York hospital have a system in place whereby you could donate the cord blood to a public cord blood bank?	Yes	35.7	38.9	71.6	
	No	0.3	0	0	
	Don't know	62.2	61.1	27.2	
	NA	1.8	0	1.2	
	Correct answer (Yes)	35.7	38.9	71.6	<0.001
For the following conditions, please indicate whether cord blood has been successfully used as a therapy					
Alzheimer's disease	Yes	8.6	8.4	7.4	
	No	28.3	33.7	43.2	
	Don't know	62.8	57.9	49.4	
	NA	0.3	0	0	
	Correct answer (No)	28.3	33.7	43.2	0.215
Asthma	Yes	1.8	3.2	1.2	
	No	36.6	37.9	53.1	
	Don't know	61.2	58.9	45.7	
	NA	0.3	0	0	
	Correct answer (No)	36.6	37.9	53.1	0.049
Blood cancer (such as leukemia or lymphoma)	Yes	70.8	78.9	87.7	
	No	1.2	1.1	1.2	
	Don't know	17.7	18.9	11.1	
	NA	0.3	1.1	0	
	Correct answer (Yes)	70.8	78.9	87.7	0.221
Certain genetic diseases of the immune system (such as "Bubble Boy" disease)	Yes	35.4	33.7	45.7	
	No	3.4	4.2	4.9	
	Don't know	60.3	60	48.1	
	NA	0.9	2.1	1.2	
	Correct answer (Yes)	35.4	33.7	45.7	0.122
Certain inherited diseases of metabolism (like "Lorenzo's Oil" disease)	Yes	18.2	14.7	24.7	
	No	6.8	7.4	9.9	
	Don't know	74.2	74.7	65.4	
	NA	0.9	3.2	0	
	Correct answer (Yes)	18.2	14.7	24.7	0.129
Diabetes	Yes	7.4	8.4	6.2	
	No	32.9	32.6	46.9	
	Don't know	59.7	58.9	46.9	
	NA	0	0	0	
	Correct answer (No)	32.9	32.6	46.9	0.064
Failure of the bone marrow	Yes	63.7	65.3	76.5	
	No	0.9	1.1	2.5	
	Don't know	35.4	33.7	21	
	NA	0	0	0	
	Correct answer (Yes)	63.7	65.3	76.5	0.135
Parkinson's disease	Yes	14	14.7	17.3	
	No	23.7	24.2	38.3	
	Don't know	60.9	61.1	44	
	NA	0.6	0	0	
	Correct answer (No)	23.7	24.2	38.3	0.05
Red blood cell or hemoglobin disorders (such as sickle cell disease)	Yes	44.6	47.4	50.6	
	No	5.8	7.4	8.6	
	Don't know	48.9	45.3	39.5	
	NA	0.6	0	1.2	
	Correct answer (Yes)	44.6	47.4	50.6	0.651

(Table 4 continued)

		Overall % (n=325)	Donating to private bank % (n=95)	Donating to public bank % (n=81)	P*
Spinal cord injury	Yes	20.3	18.9	21	
	No	24	23.2	34.6	
	Don't know	55.4	56.8	44.4	
	NA	0.3	1.1	0	
	Correct answer (No)	24	23.2	34.6	0.131
Mean correct score (out of 10), SD		3.8±2.9	3.9±2.6	5±3.1	0.012

*P-values comparing correct answer for private vs. public donation.

Among our patients who planned to store cord blood with a private/commercial company, the vast majority said that they were doing so as a safeguard for the future. The American College of Obstetrics and Gynecology (ACOG) Committee Opinion regarding private cord blood collection states, however: "Commercial cord blood banks should not represent the service they sell as 'doing everything possible' to ensure the health of their children" [3]. A recent Policy Statement from the American Academy of Pediatrics (AAP) also states that private storage of cord blood should be discouraged [8]. However, the website from one private/commercial cord blood company marketing to parents states: "Public banks can help ensure an adequate sample for transplant but not the best or most preferable sample. When the issue is survival, this is significant. The families who bank cord blood stem cells want to help ensure the best chance of survival if the cells are needed, not just a chance" [7]. This statement is misleading, does not represent current experience with cord blood donation, and is in direct opposition to the ACOG Committee Opinion and AAP Policy Statement. Such private bank statements are probably a significant source of misconceptions revealed in our study.

Despite their high educational level and having access to multiple sources of information, our population still had a very poor understanding of the current uses for cord blood. Our patients greatly underestimated the ability of a public bank to find a suitable match. Only 15% of patients overall, and 10% of patients storing cord blood privately, believed that a cord blood unit suitable for transplantation could always or usually be found. In contrast, a July 2005 statement from the National Marrow Donor Program indicates that "nearly all (>95%) patients are able to find at least one potential four of six HLA matched cord blood unit on the NMDP Registry, the largest in the United States, and the majority will find a potential five of six match" [20]. With an inventory of 25,000 cord blood units, the New York Blood Center could find a four of six match for 99% of patients seeking a transplant, 65% found a five of six match, and 11% found a six of six match (based on intermediate level of typing for the class I HLA antigens (A and B) and high resolution HLA typing for class II (DRB1*). Whereas a better match correlates with a more favorable transplant outcome, most cord blood transplants to date have been with grafts providing a four out six HLA match [13, 16–18, 21–24, 27, 28].

Our results also indicate that the patients having their cord blood stored privately were more likely to believe that their child would develop a condition that could benefit from cord blood therapy and more likely to believe that, if a condition did develop, the child's own cord blood could be used (autologous transplantation). However, one report estimated that 0.04% (1 in 2700) of cord blood units stored privately would be used for autologous transplantation [15], probably an overstatement (which, the author also acknowledges). In our own experience (over 36,000 units of cord blood donated and stored for a mean of 4.6 years or 169,000 person-years), for example, only one unit of cord blood was sought for autologous use. This unit could not be used however, because the child required transplantation for a genetic disease. Moreover, one private company that advertises 13 years experience with units stored from approximately 108,000 clients [6], reports only six autologous transplants, three of which, were for brain injury (not a currently indicated condition for transplantation) [9]. The other three autologous transplants were for patients with severe aplastic anemia. Importantly, aplastic anemia represents only about 3% of expected marrow transplants among children. None of the autologous transplants were for leukemia or genetic diseases, the diseases representing more than 90% of childhood marrow transplants. The absence of these diseases is not surprising since autologous cord blood transplants cannot be used for genetic disease and is not recommended for childhood leukemia [1, 8]. In fact, there has been only one case report of autologous cord blood transplantation in the treatment of a child with leukemia [4].

We believe that there is little to justify a recommendation for private cord blood storage for possible future autologous transplantation. The chance that the child would contract a disease is small, the chance that child's own cord blood would be used is even smaller, and there is a high probability a match could be found from a public

bank. Additionally, if the cord blood was donated to a public bank, it most likely would still be available for use by that child, if needed and appropriate for a transplant. With our Program, for example, 90% of units stored are still available (80% after 10 or more years of storage). While a given unit has a higher likelihood of being used by someone else as more time passes, so too does the likelihood of finding a suitable match from another donor rise as time passes and more units are donated to public cord blood banks.

Since it is easier to find an HLA match from a closely related donor, and outcomes from related bone marrow donors are generally more favorable than from unrelated donors, private cord blood banks point out that stored cord blood may be useful in case a sibling or other family member develops a condition requiring transplantation. If, at the time of delivery, there is already an affected sibling or other close family member, there is a compelling reason to collect cord blood (directed donation) on the chance (about 25% for a sibling) that it would be suitable for a future transplant, providing a possible stem cell source for the patient with no risk to the donor. Only 2.1% of our patients, however, reported this as a reason for having their cord blood stored with a private/commercial company and the validity of the presumed indication was not verified. Private storage on pure speculation that a family member would become ill in the future with no family history of a risk is substantially less compelling because the likelihood of needing such a unit and that it would be a suitable match and cell dose is rare. Such speculative storage, therefore, is not supported by either Obstetric or Pediatric professional societies [1, 3, 5, 8]. To illustrate this, one of the largest private/commercial companies, for example, reports only 35 transplants for a relative (34 sibling, 1 mother) over a 13-year period and, in essentially all of these cases, the patient was already identified at the time of collection (median time from collection to transplantation was six months) [9]. Few, if any, transplants were done when there was no affected family member at the time of cord blood storage. Similarly, over the past 13 years and an inventory of cord blood units that grew to more than 36,000, we have not been called upon to provide a unit of cord blood for any sibling transplants.

There are data suggesting that delayed cord clamping may reduce the risk of neonatal anemia [14, 19]. In our institution, cord blood is collected after delivery of the placenta. However, in institutions where cord blood is collected before the placenta is delivered, if the collection of cord blood would prompt the provider to clamp the umbilical cord earlier than usual, this could possibly increase the risk of neonatal anemia.

Our data indicate that many patients had an incorrect understanding of cord blood storage and its uses, especially those planning to store privately. Thus, before agreeing to assist in a private/commercial collection, even when there is no opportunity to donate to a public bank, the Obstetrician should discuss the following with the patient:

- Obstetricians who collect blood for private/commercial storage should disclose to the patient any financial compensation or benefit he or she receives from the company.
- The extremely remote possibility that a child will develop a condition that can benefit from cord blood.
- Even if a child develops a condition that could benefit from cord blood transplantation, most such conditions could not utilize the child's own cord blood (autologous stem cell transplantation).
- The current chance of finding an acceptable match (four out of six antigens matching) from a public cord blood bank is approximately 99% and 50–70% for a more favorable match (five out of six). This chance will improve over time as more women donate to public cord blood banks.
- The only conditions currently being treated with cord blood are blood cancers, diseases of the immune system, certain inherited metabolic diseases, bone marrow failure syndromes and red cell or hemoglobin disorders. Patients should be wary of claims of "potential" future use that are purely speculative and not yet proven scientifically.

Only 45% of distributed questionnaires were completed and returned. This could have resulted in bias. However, as our respondents had a very poor overall understanding of cord blood banking, we have no reason to assume that those who did not respond constituted a group with a better understanding of cord blood banking. This survey was conducted relatively early in pregnancy. It is likely that more women would have made a decision regarding cord blood storage if they had been surveyed later in pregnancy. Moreover, at our institution women would still have an opportunity to decide on donation to a public bank when approached after delivery if enough cord blood had been collected to provide a suitable stem cell source. Despite the high proportion of women in our survey who were undecided, in our experience thus far, 95% of patients approached after delivery agreed to donate their cord blood. Future research should focus on strategies to educate women earlier in pregnancy so that they are prepared to make a truly informed decision at the appropriate time.

References

[1] AAP (American Academy of Pediatrics). Cord blood banking for potential future transplantation: Subject review. Work group on cord blood banking. Pediatrics. 1999;104: 116–8.

[2] American Association of Blood Banks. Standards for hematopoietic progenitor cell services. 2nd ed. Behtesda (MD): American Association of Blood Banks; 2000.
[3] American College of Obstetricians and Gynecologists. Routine storage of umbilical cord blood for potential future transplantation. ACOG Committee Opinion 183. Washington, DC: ACOG; 1997.
[4] Ammar H, Lampeter E, Viswanatha D, Morgan D, Salvi S. First report of autologous cord blood transplantation in the treatment of a child with leukemia. Pediatrics. 2007;119: e296–e300.
[5] Armson BA. Maternal/Fetal medicine committee, society of obstetricians and gynaecologists of Canada. Umbilical cord blood banking: implications for perinatal care providers. J Obstet Gynaecol Can. 2005;27:263–90.
[6] Cbr – An Investment in Your Family's Health. The value of saving your newborn's stem cells with Cord Blood registry: Parent Packet. Available at http:// www.cordblood. net/ pdf/CBRParentPacket_Forms_e.pdf. Retrieved October 11, 2006.
[7] Cbr – Common Misconceptions about Cord Blood Banking. Available at http:// www.cordblood.com/cord_blood_ banking_with_cbr/common_misconceptions/index.asp. Retrieved October 11, 2006.
[8] Cord Blood Banking for Potential Future Transplantation. Section on Hematology/ Oncology and Section on Allergy/ Immunology. Pediatrics. 2007;119:165–70.
[9] Cord Blood Registry Stem Cell Therapy Data. Available at http://www.cordblood. com/pdf/transplant_summary.pdf. Retrieved October 11, 2006.
[10] Foundation for the Accreditation of Hematopoietic Cell Therapy. Standards for hematopoietic progenitor cell collection, processing and transplantation. Omaha (NE): FACHT Accreditation Office, University of Nebraska Medical Center; 1996.
[11] Gluckman E, Broxmeyer HE, Auerbach AD, et al. Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical-cord blood from an HLA-identical sibling. N Engl J Med. 1989;321:1174–8.
[12] Gluckman E, Rocha V, Boyer-Chammard A, et al. Outcome of cord-blood transplantation from related and unrelated donors. N Engl J Med. 1997;337:373–81.
[13] Grewal SS, Barker JN, Davies SM, Wagner JE. Unrelated donor hematopoietic cell transplantation: marrow or umbilical cord blood? Blood. 2003;101:4233–44.
[14] Hutton EK, Hassan ES. Late vs. early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. J Am Med Assoc. 2007; 297:1241–52.
[15] Johnson FL. Placental blood transplantation and autologous banking: caveat emptor. J Pediatr Hematol Oncol. 1997:19:183–6.
[16] Kurtzberg J, Graham M, Casey J, Olson J, Stevens CE, Rubinstein P. The use of umbilical cord blood in mismatched related and unrelated hemopoietic stem cell transplantation. Blood Cells. 1994;20:275–83.
[17] Kurtzberg J, Laughlin M, Graham ML, et al. Placental blood as a source of hematopoietic stem cells for transplantation into unrelated recipients. N Engl J Med. 1996; 335:157–66.
[18] Laughlin MJ, Eapen M, Rubinstein P, et al. Outcomes after transplantation of cord blood or bone marrow from unrelated donors in adults with Leukemia. N Engl J Med. 2004; 351:2265–75.
[19] Levy T, Blickstein I. Timing of cord clamping revisited. J Perinat Med. 2006;34:293–7.
[20] National Marrow Donor Program – Likelihood of Finding an Unrelated Donor or Cod Blood Unit. Available at http: //www.marrow.org/ PHYSICIAN/URD_ Search_and_Tx/ Likelihood_of_Finding_an_URD_o/index.html. Retrieved August 23, 2006.
[21] Rocha V, Labopin M, Sanz G, et al. Transplants of umbilical-cord blood or bone marrow from unrelated donors in adults with acute Leukemia. N Engl J Med. 2004;351: 2276–85.
[22] Rubinstein P. Placental blood-derived hematopoietic stem cells for unrelated bone marrow reconstitution. J Hematother. 1993;2:207–10.
[23] Rubinstein P, Rosenfield RE, Adamson JW, Stevens CE. Stored placental blood for unrelated bone marrow reconstitution. Blood. 1993;81:1679–90.
[24] Rubinstein P, Carrier C, Scaradavou A, et al. Outcomes among 562 recipients of placental-blood transplants from unrelated donors. N Engl J Med. 1998;339:1565–77.
[25] Sugarman J, Reisner EG, Kurtzberg J. Ethical aspects of banking placental blood for transplantation. J Am Med Assoc. 1995;274:1783–5.
[26] Sugarman J, Kaalund V, Kodish E, Marshall MF, Reisner EG, Wilfond BS, et al. Ethical issues in umbilical cord blood banking. J Am Med Assoc. 1997;278:938–43.
[27] Wagner JE, Kernan NA, Steinbuch M, Broxmeyer HE, Gluckman E. Allogeneic sibling umbilical-cord-blood transplantation in children with malignant and non-malignant disease. Lancet. 1995;346:214–9.
[28] Wagner JE, Barker JN, DeFor T, et al. Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and nonmalignant diseases: influence of CD34 cell dose and HLA disparity on treatment-related mortality and survival. Blood. 2002;100:1611–8.
[29] Wagner JE, Rosenthal J, Sweetman R, et al. Successful transplantation of HLA-matched and HLA-mismatched umbilical cord blood from unrelated donors: analysis of engraftment and acute graft-versus-host disease. Blood. 1996;88:795–802.

Received February 27, 2007. Revised March 28, 2007. Accepted April 26, 2007. Published online on May 21, 2007.

Current Commentary

Ethical Considerations in Umbilical Cord Blood Banking

Nathan S. Fox, MD, Frank A. Chervenak, MD, and Laurence B. McCullough, PhD

Pregnant patients have the option at delivery of having their cord blood collected and stored for future use. At many hospitals, they have the option of donating their cord blood to the public banking system for future use by anyone who is an appropriate match (public banking). Patients also have the option of having their cord blood stored for a fee with a commercial/private company for future use within their family (private banking). Currently, private banking is not recommended by major obstetric and pediatric professional organizations. We applied current evidence of the risks and benefits of private and public cord blood banking and accepted ethical principles to answer the following two related questions: 1) Do obstetricians have an ethical obligation to comply with a request for private banking? and 2) Do obstetricians have an ethical obligation to routinely offer private banking to women who do not request it? The only situation where there is a known benefit to private banking is when public banking is not available and the patient currently has an affected family member who may benefit from cord blood therapy. We conclude that when presented with a request for private banking, obstetricians have an ethical obligation to explain the lack of proven benefit of this procedure. If the patient still requests private banking, it would be appropriate to comply, because there is minimal or no risk to the procedure. However, obstetricians are not ethically obligated to offer private banking, even when public banking is not available, except in the limited circumstance when the patient currently has an affected family member who may benefit from cord blood therapy.

(Obstet Gynecol 2008;111:178–82)

Hematopoietic stem cells contained in blood taken from the placenta and umbilical cord (cord blood) after an infant is born can reconstitute bone marrow in recipients undergoing treatment for life-threatening diseases of the blood and immune system and certain inherited metabolic diseases.[1–6] Because of this, banking of cord blood at the time of delivery has become an option for pregnant patients. At many hospitals, patients have the option of donating their cord blood free of charge to the public banking system for future use by anyone who is an appropriate match (public banking). The National Cord Blood Program oversees the cord blood stored and provides a searchable database for physicians who care for patients with diseases amenable to cord blood therapy. More information on this program can be found at http://www.nationalcordbloodprogram.org. Alternatively, some patients arrange during their pregnancy to have their infant's cord blood stored with a private or commercial collection company for an initial processing fee followed by annual maintenance fees (private banking). In these cases, the cord blood is stored for possible future use by the child, a sibling, or other family member. Private companies market directly to the patients and their obstetric providers and require a contract signed by the mother in advance of the infant's delivery. Currently, private banking is not endorsed by major obstetric and pediatric professional organizations.[7–9] Despite these recommendations, many patients still choose to have their cord blood collected for private banking.

There are a number of editorials and publications stating that private banking should be discouraged and public banking should be encouraged.[10–12] However, there has been no ethical consideration of two related questions. Do obstetricians have an ethical obligation to comply with a request from a pregnant woman for private banking? Do obstetricians have an ethical obligation to offer private banking routinely to pregnant women who do not request it? The purpose of this article is to provide obstetricians with ethical guidance about private and public cord blood banking by addressing these two questions in relation to applicable ethical principles.

From the Department of Obstetrics and Gynecology, Weill Cornell Medical College, New York, New York; and the Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, Texas.

Corresponding author: Nathan S. Fox, 525 East 68th Street, Box 122, New York, NY 10021; e-mail: naf9015@med.cornell.edu.

Financial Disclosure

The authors have no potential conflicts of interest to disclose.

ISSN: 0029-7844/07

THE RISKS AND BENEFITS OF CORD BLOOD BANKING

Clinical Risks to Mother and Newborn

Umbilical cord blood collection, whether for public or private banking, has few, if any known risks to the mother or her newborn. The cord blood is collected after the baby is delivered and is not needed by the mother or newborn. There are data suggesting that delayed cord clamping may reduce the risk of neonatal anemia.[13,14] In our institution, cord blood for public banking is collected after delivery of the placenta. However, in situations in which cord blood is collected before the placenta is delivered, such as with most collections for private banking, if the collection of cord blood would prompt the obstetrician to clamp the umbilical cord earlier than usual, this could possibly increase the risk of neonatal anemia. It is uncertain whether there are any long-term risks to the newborn associated with early cord blood clamping.

Personal and Social Risks

Additionally, although not a medical risk, there is a significant monetary cost to the patient for private banking. There is no social risk from either private or public banking, provided that both have rigorous and effective policies and procedures for maintaining confidentiality.

Benefits

The benefits of cord blood banking are well known. In many cases of life-threatening illness, cord blood can be used as an alternative to bone marrow donation. This can reduce the need for bone marrow retrievals and this procedure has associated risks to the donor and certainly involves significant discomfort. The controversy regarding the benefits of cord blood banking lies in the supposed incremental benefit of private banking over public banking or, in cases where public banking is not available, discarding the blood and relying on the public banking system for possible future needs. The incremental benefits are thought to be two. Should the need arise for cord blood transplantation in this child or a sibling, there may not be a suitable or optimal match found from a public bank. Secondly, further research may uncover additional uses for cord blood and donating the blood to a public bank or discarding the blood may cause the newborn to miss a "once in a lifetime" opportunity to store this cord blood for future use.

These two potential benefits of private banking seem logical. Unfortunately, they are not supported by current evidence. First, the chance that a particular child will develop a condition requiring cord blood transplantation is very small. It has been estimated that 0.04% (1/2,700) of cord blood units stored would ever be used for autologous transplantation (a patient receiving his or her own cord blood), and this is probably an understatement, which the author acknowledges.[15] This is because the incidence of diseases currently treated with cord blood is low, and most of these patients would not be eligible for autologous cord blood, including those with leukemia and genetic conditions. To illustrate this, one private company that advertises 14 years experience with units stored from approximately 175,000 clients,[16] reports only 13 autologous transplants, 8 of which were for brain injury, cerebral palsy, or diabetes (not currently indicated conditions for transplantation).[17] Additionally, even if the need were to arise, if the cord blood was donated to a public bank, it would likely still be available for that child. In the New York Blood Center, approximately 80% of cord blood units are still available for use after 10 years of storage.[18]

Obstetricians are ethically obligated to recommend public banking when feasible.

Regarding allogenic transplantation (receiving someone else's cord blood) for a sibling, since it is easier to find an HLA match from a closely related donor and outcomes from related bone marrow donors may be more favorable than from unrelated donors, stored cord blood may be useful in case a sibling or other family member develops a condition requiring transplantation. If, at the time of delivery, there is already an affected sibling or other close family member, there is a compelling reason to collect cord blood (directed donation) on the chance (about 25% for a sibling) that it would be suitable for a future transplant, providing a possible stem cell source for the patient, with no risk to the donor. However, private banking on pure speculation that a sibling may develop a condition is less compelling for the same argument that it is very unlikely it will ever be needed. To illustrate this, the same private company with 175,000 clients[16] reports only 38 transplants for a relative (37 sibling, 1 mother) over a 14-year period, and in essentially all of these cases, the affected relative was already identified at the time of collection (median time from collection to transplantation was 9.5 months).[17] Few, if any, transplants were done when there was no affected family member at the time of cord blood banking.

Regarding the possibility of finding a suitable match from the public banking system, a July 2005 statement from the National Marrow Donor Program indicates that

"nearly all (more than 95%) patients are able to find at least one potential 4 of 6 HLA matched cord blood unit on the NMDP Registry, the largest in the United States, and the majority will find a potential 5 of 6 match."[19] The New York Blood Center, the first established public cord blood bank, could find a 4 of 6 match for 99% of patients seeking a transplant, 65% found a 5 of 6 match, and 11% found a 6 of 6 match.[18] Most cord blood transplants to date have been with a 4 of 6 match.[2,4–6] Additionally, recent evidence suggests that outcomes may be similar with related and nonrelated donors.[20–23]

It is impossible to substantiate or refute a claim that cord blood will have many other therapeutic uses in the future. However, this claim is often used by private banking companies with financial interest as a marketing tool to expecting parents. Such claims are strongly discouraged by professional societies.[7–9]

ETHICAL ANALYSIS

The first of our two questions concerns how the obstetrician should respond to a request from a pregnant woman for private banking. The response of the obstetrician should be disclosure of the information that any pregnant woman needs to make an informed decision. To meet this obligation the obstetrician should provide the information about the risks and benefits of cord blood banking that we have just described. In doing so, the obstetrician would be wise to assume, as recent data suggest, that pregnant women do not have a reliable understanding of cord blood banking, whether private or public.[18] The obstetrician therefore should be especially attentive to possible misunderstanding or even misinformation that the patient may bring with her to her request. The obstetrician should objectively point out that claims about the potential advantages of private banking do not withstand close scrutiny, with the exception of the advantages for an already affected family member, as explained above. When this exception applies, there is known benefit and minimal risk, and the obstetrician should recommend cord blood banking. If public banking is not available, the physician should recommend private banking. When the exception does not apply and there is no affected sibling (ie, in the vast majority of cases), the obstetrician should recommend public banking of cord blood if it is available, or no banking at all if public banking is not available, because private banking confers no additional clinical benefit. If the patient makes an informed decision for private banking, it is ethically justifiable to comply, because there is minimal or no risk to the patient. Because there is minimal or no risk, it would seem inappropriate to refuse to assist in a collection for private banking, but it would be ethically justified for the physician to charge an appropriate collection fee for private banking, because this is an elective procedure. However, if the physician is under contract with a private banking company whereby the physician is reimbursed by the company for each collection, this conflict of interest should be disclosed to the patient.

That it is ethically permissible to respond to an appropriately informed request for private banking does not by itself mean there is an ethical obligation to offer private banking to all pregnant women who do not request it. Ethical analysis of requests for private banking is primarily autonomy-based, whereas the main ethical issue in offering private banking is whether doing so is medically reasonable, which is a beneficence-based concept. There must be a reasonable expectation of net clinical benefit from private banking to justify routinely offering it. This is why the question of whether there is an ethical obligation to do so is a separate question from the ethics of responding to spontaneous requests.

Answering this second question requires consideration of possible clinical benefits and risks, because this information is crucial for a beneficence-based judgment of medical reasonableness. Based on the above analysis of benefits and risks, when there is an affected sibling whose medical care may be facilitated by cord blood banking, then out of a beneficence-based obligation to that affected sibling, the obstetrician should not only offer but also recommend cord blood banking. Currently, the public banking system allows for directed donations to treat an affected sibling; therefore, there is no advantage to the affected sibling of private over public banking and this should be made clear to the pregnant woman. However, if there is an affected family member and public banking is not available, private banking should be recommended. As stated above, it would be ethically justified for the physician to charge an appropriate collection fee for private banking; however, if the physician is under contract with a private cord blood collection company, this conflict of interest should be disclosed to the patient. Because cord blood collection is virtually risk-free and can provide a possible life-saving transplantation for an affected sibling, it would follow that obstetricians should routinely inquire about conditions amenable to cord blood therapy as a part of the family history.

In cases in which there is no affected family member (ie, the vast majority of cases), the above analysis of risks and benefits indicates that the pregnant woman should not elect private banking on the basis of a belief that it is neces-

sary to do so to protect the health-related interests of her future child. This is because public banking is currently able to meet virtually all need for transplantable stem cells. A belief on the woman's part that private banking somehow confers an advantage to her future child that public banking does not should be, respectfully but effectively, dispelled. Even though there is minimal risk, because there is no proven benefit to private banking, the physician is not obligated to offer it. This is similar to other birth-related opportunities for patients with minimal or no risk, yet no known medical benefit, such as a professional labor coach or private-duty nurse during the postpartum period. It is acceptable to comply to these well-informed requests, but there is no obligation to offer them.

The main justification for cord blood banking is to ensure an adequate supply of transplantable stem cells that will be of benefit to the patient population generally. As citizens, all of us have a justice-based obligation to come to the rescue of others when we are in a position to do, when our efforts are likely to be successful, and when the self-sacrifice required is reasonable. A pregnant woman is in a position to benefit others by donating cord blood, doing so will be effective in meeting the healthcare needs of the patient population, and no sacrifice of her or her child's health-related interests is required. It follows that recommending public banking, when feasible, is medically reasonable.

Literature distributed to patients, or displayed in physicians' offices, should be consistent with current evidence and the recommendations of the major professional societies.[7–9] Physicians should be very cautious of literature produced by private banking companies, because they have a significant conflict of interest. This literature may be misleading, because these companies are not bound by the same ethical principles as physicians and are not required to ensure the patient makes an informed decision. Providers can find evidence-based material for patients on the following Web sites: http://www.nationalcordbloodprogram.org and http://www.marrow.org.

REFERENCES

1. Gluckman E, Broxmeyer HE Auerbach AD, Friedman HS, Douglas GW, Devergie A, et al. Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical-cord blood from an HLA-identical sibling. N Engl J Med 1989;321:1174–8.
2. Kurtzberg J, Laughlin M, Graham ML, Smith C, Olson JF, Halperin EC, et al. Placental blood as a source of hematopoietic stem cells for transplantation into unrelated recipients. N Engl J Med 1996;335:157–66.
3. Gluckman E, Rocha V, Boyer-Chammard A, Locatelli F, Arcese W, Pasquini R, et al. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. N Engl J Med 1997;337:373–81.
4. Rubinstein P, Carrier C, Scaradavou A, Kurtzberg J, Adamson J, Migliaccio AR, et al. Outcomes among 562 recipients of placental-blood transplants from unrelated donors. N Engl J Med 1998;339:1565–77.
5. Laughlin MJ, Eapen M, Rubinstein P, Wagner JE, Zhang MJ, Champlin RE, et al. Outcomes after transplantation of cord blood or bone marrow from unrelated donors in adults with leukemia. N Engl J Med 2004;351:2265–75.
6. Rocha V, Labopin M, Sanz G, Arcese W, Schwerdtfeger R, Bosi A, et al. Transplants of umbilical-cord blood or bone marrow from unrelated donors in adults with acute leukemia. N Engl J Med 2004;351:2276–85.
7. American College of Obstetricians and Gynecologists. Routine storage of umbilical cord blood for potential future transplantation. ACOG Committee Opinion 183. Washington (DC): ACOG; 1997.
8. Armson BA; Maternal/Fetal Medicine Committee, Society of Obstetricians and Gynaecologists of Canada. Umbilical cord blood banking: implications for perinatal care providers [published erratum appears in J Obstet Gynaecol Can 2005;27:673]. J Obstet Gynaecol Can 2005;27:263–90.
9. American Academy of Pediatrics Section on Hematology/Oncology, American Academy of Pediatrics Section on Allergy/Immunology, Lubin BH, Shearer WT. Cord blood banking for potential future transplantation. Pediatrics 2007; 119:165–70.
10. Edozien LC. NHS maternity units should not encourage commercial banking of umbilical cord blood. BMJ 2006; 333:801–4.
11. Fisk NM, Roberts IA, Markwald R, Mironov V. Can routine commercial cord blood banking be scientifically and ethically justified? PLoS Med 2005;2:e44.
12. Ecker JL, Greene MF. The case against private umbilical cord blood banking. Obstet Gynecol 2005;105:1282–4.
13. Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. JAMA 2007;297:1241–52.
14. Levy T, Blickstein I. Timing of cord clamping revisited. J Perinat Med 2006; 34:293–7.
15. Johnson FL. Placental blood transplantation and autologous banking–caveat emptor. J Pediatr Hematol Oncol 1997; 19:183–6.
16. Cord Blood Registry. Company Overview. Available at: http://www.cordblood.com/aboutus_cord_blood_registry/company_overview.asp. Retrieved July 14, 2007.
17. Cord Blood Registry. Stem Cell Therapy Data. Available at: http://cordblood.net/pdf/transplant_summary.pdf. Retrieved July 14, 2007.
18. Fox NS, Stevens C, Ciubotariu R, Rubinstein P, McCullough LB, Chervenak FA. Umbilical cord blood collection: do patients really understand? J Perinat Med 2007;35:314–21.
19. National Marrow Donor Program. Likelihood of finding an unrelated donor or cord blood unit. Available at: http://www.marrow.org/PHYSICIAN/URD_Search_and_Tx/Likelihood_of_Finding_an_URD_o/index.html. Retrieved July 14, 2007.
20. Davies SM, DeFor TE, McGlave PB, Miller JS, Verfaillie CM, Wagner JE, et al. Equivalent outcomes in patients with chronic myelogenous leukemia after early transplantation of phenotypically matched bone marrow from related or unrelated donors. Am J Med 2001;110: 339–46.
21. Weisdorf DJ, Anasetti C, Antin JH, Kernan NA, Kollman C, Snyder D, et al. Allogeneic bone marrow transplantation for chronic myelogenous leukemia: comparative analysis of unrelated

versus matched sibling donor transplantation. Blood 2002;99:1971–7.

22. Kiehl MG, Kraut L, Schwerdtfeger R, Hertenstein B, Remberger M, Kroeger N, et al. Outcome of allogeneic hematopoietic stem-cell transplantation in adult patients with acute lymphoblastic leukemia: no difference in related compared with unrelated transplant in first complete remission. J Clin Oncol 2004;22:2816–25.
23. Eapen M, Rubinstein P, Zhang MJ, Camitta BM, Stevens C, Cairo MS, et al. Comparable long-term survival after unrelated and HLA-matched sibling donor hematopoietic stem cell transplantations for acute leukemia in children younger than 18 months. J Clin Oncol 2006;24:145–51.