Thermal Integrity of Shipping Containers Used by Private Cord Blood Banks

Introduction

Cord blood (CB) collected after the healthy birth of a baby has been used to treat more than 30 000 patients suffering from more than 70 diseases.[1] Private storage of umbilical CB for family use is becoming a more common practice. More than 780 000 CB units are currently in private CB banks worldwide.[2] These banks operate both nationally and internationally, often receiving CB from distant locales. Therefore, transport times can last many hours, including ground transportation from the hospital to the airport, cargo loading, air transit with connecting flights, potential airport delays, and ground transportation from the airport to the CB processing laboratory.

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While the US Food and Drug Administration (FDA) does not specify the acceptable temperature range of CB during transport, it does state that the liquid storage of CB in the laboratory should be maintained in the range of 15°C to 25°C and that temperature changes should be minimized during transport.[3] Furthermore, studies investigating CB cell recovery and viability have shown that acceptable liquid storage temperatures range anywhere from 4°C to room temperature (RT).[4,5]

Severe temperature exposure for CB during shipment may be caused by many factors, such as geographic temperature variation, seasonal temperature variation, temperatures within ground transport vehicles, temperatures within aircraft cargo holds, and potential delayed cargo loading times that result in extended periods of time on the airport tarmac. Temperatures within ground transport vehicles and delays on the tarmac can be particularly problematic; a parked car in sunlight has been shown to reach internal temperatures as high as 55°C to 78°C when outside temperatures are 27°C to 38°C.[6] Moreover, within the first 10 minutes, the temperature in an enclosed vehicle has been shown to rise to an average of 82% of its eventual 1-hour rise.[7] A study of temperature ranges experienced during shipment of laboratory mice revealed temperatures as extreme as –7.6°C and 65.6°C.[8]

Although it is customary to use thermal data loggers to record temperature variation during the course of specimen transport of publicly donated CB, the author is unaware of any private CB banks currently using thermal data loggers to document thermal integrity during the course of specimen transport. Consequently, there are no real-time data commonly available to gauge the effectiveness of shipping containers to maintain thermal integrity and insulate the contents during transit. Each CB bank must validate its shipping containers to adequately maintain temperature and measure the temperature of CB when it arrives at its processing laboratories. However, if the validation is not thorough enough and no data logger is present, the temperature to which the contents have been exposed in the course of shipment is unknown. Currently, the shipping containers used by most private CB banks consist of cardboard boxes with foam inserts, polystyrene boxes, thin plastic snap-top containers or, in 1 case, a vacuum-insulated shipping container. Some contain a temperature stabilizing pack (TSP).

Given the critical need for thermal protection of the CB specimen in the course of transit, this study was undertaken to assess the impact of a controlled environment on the thermal integrity of the various private CB shipping containers currently in use.

Materials and methods

Sixteen shipping containers were obtained from 16 private CB banks through obstetricians and individuals who were recipients of the containers. The containers' construction and contents were documented. Descriptions of the shipping containers are detailed in **Table 1**. All of the shipping containers were tested under the same conditions. Payloads of 100 mL CB units, including citrate-phosphate-

TABLE 1. Descriptions of cord blood shipping containers

Cord blood bank	External dimensions	Construction	Method of temperature protection	Acceptable temperature range printed on box	Style of box
1	17.25″ x 2.875″ x 12″	Cardboard and urethane foam	Urethane foam and TSP	Maintain at room temperature	Top loading box with removable urethane lid
2	11.75″ x 2.75″ x 8.75″	Cardboard and packaging foam	Packaging foam	Keep at room temperature	Top loading box
3	11.5″ x 2.75″ x 7.875″	Cardboard and packaging foam	Packaging foam	Keep at room temperature	Top loading box
4	13.5″ x 2.75″ x 9.75″	Cardboard and polystyrene foam	Polystyrene foam and TSP	Avoid extreme temperatures—keep 50°F-80°F/10°C-27°C	Top loading box
5	12″ x 2″ x 9″	Cardboard and packaging foam	Packaging foam	Keep at room temperature	Top loading box
6	12.5″ x 2.25″ x 9″	Cardboard	TSP and an insulated sealable foil pouch	Keep at room temperature	Top loading box
7	13.5″ x 3″ x 8.75″	Cardboard	Insulated sealable foil pouch	Store at room temperature	Top loading box
8	13.5″ x 2.75″ x 10″	Cardboard and packaging foam	Packaging foam	Avoid temperature extremes—keep temperature between 39°F-80°F/4°C-27°C	Top loading box
9	13.5″ x 3″ x 9.75″	Cardboard and packaging foam	Packaging foam	Do not freeze; temperature 55°F-85°F	Top loading box
10	14.5″ x 3″ x 10.25″	Cardboard and packaging foam	Packaging foam	Keep at room temperature	Top loading box
11	9″ x 5.5″ x 6.5″	Cardboard and packaging foam	Packaging foam	Keep at room temperature	Cube-like clamshell box
12	13.75″ x 6.25″ x 10.25″	Cardboard and polystyrene foam with packaging foam panels	Polystyrene foam externally with foam packaging internal panels	Please store at room temperature; do not refrigerate	Top loading box
13	12.5″ x 3″ x 9.5″	Cardboard and packaging foam	Packaging foam	None	Top loading box
14	12.5″ x 2.5″ x 8.5″	Cardboard	Insulated foil pouch	Do not expose to extreme heat or cold; store at 4°C-30°C	Top loading box
15	10.25″ x 11″ x 9.75″	Cardboard, vacuum insulated panels and rigid plastic cooler	Vacuum insulated panels surrounding rigid plastic cooler containing phase-change solution	Store at room temperature	Top loading box with removable vacuum insulated top panel and rigid plastic cooler inside
16	14.5″ x 7.75″ x 13″	Cardboard and urethane foam	Urethane foam and 2 TSPs	Must be kept at room temperature	Top loading box with removable urethane lid

TSP, temperature stabilizing pack.

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dextrose, were collected in FDA-approved 510(k) sterile CB collection bags (Pall Corporation, Port Washington, New York) and used to simulate CB shipments. Cord blood payloads were obtained from public CB banking collection sites from units designated for banking or research.

The shipping containers and CB units were sent to Fisher BioServices in Rockville, Maryland for independent testing. The testing report was delivered in June 2011. A target temperature range of 4°C to 27°C was identified, with 27°C representing the upper range of RT. All shipping containers and payloads (one 100 mL CB in each shipping container) were equilibrated to 20°C prior to testing and all were packed according to instructions provided by the individual cord blood banks. An environmental chamber and benchmark thermal validation system (Kaye Validator® 2000, GE Kaye, Billerica, Massachusetts) were used to create the test environments and measure the performance of the shipping containers. Each shipping container had a thermocouple placed at the top, bottom, and side of the CB bag. Two profiles, a "winter stress" and a "summer stress," were used. The maximum temperature stress settings used were –20°C and 47°C, respectively. Although exposure to lower and higher temperatures during actual specimen transport was possible, these were thought to be reasonable temperatures to expect during the course of transit. To simulate a flight delay, a cycle time of 8 hours at a stress setting, followed by 8 hours at 20°C, was used and was repeated until thermal failure was detected. Temperature readings were recorded at 1-minute intervals.

TABLE 2. Results of cord blood shipping container tests, in order from longest to shortest time to failure, for each temperature profile

SUMMER PROFILE 47°C for 8 hours and then 20°C for 8 hours Repeat cycle until failure		WINTER PROFILE –20°C for 8 hours and then 20°C for 8 hours Repeat cycle until failure	
Cord blood bank	Time until outside 4°C-27°C range	Cord blood bank	Time until outside 4°C-27°C range
15	61 hours, 45 minutes	15	84 hours, 21 minutes
16	5 hours, 14 minutes	16	25 hours, 22 minutes
1	1 hour, 19 minutes	1	3 hours, 24 minutes
12	46 minutes	4	2 hours, 35 minutes
4	44 minutes	6	2 hours, 30 minutes
6	41 minutes	12	1 hour, 26 minutes
11	28 minutes	11	57 minutes
10	25 minutes	13	55 minutes
9	24 minutes	3	49 minutes
8	24 minutes	8	42 minutes
13	22 minutes	10	41 minutes
3	21 minutes	9	36 minutes
7	18 minutes	2	30 minutes
2	17 minutes	7	23 minutes
5	16 minutes	14	23 minutes
14	16 minutes	5	19 minutes

Results

The results are summarized in **Table 2**. Failure of the thermal integrity of the containers for the summer profile occurred in as short a time as 16 minutes and as long as 61 hours and 45 minutes. A similar broad range of times to failure of thermal integrity was seen for the winter profile, ranging from 19 minutes to 84 hours and 21 minutes.

Discussion

The FDA recommends that CB be transported in a shipping container designed to minimize temperature changes during transit.[3] By this standard, the performance of 15 of the 16 shipping containers used by private CB banks is of potential concern. The majority of these shipping containers exceeded the target temperature range and failed within minutes. Only 1 shipping container performed well in both profiles and maintained the target temperature range for days.

It can be hypothesized that the poorly performing shipping containers had a less robust construction. Most of these containers were constructed simply of cardboard with packaging foam cutouts for supplies. Most did not use a TSP to insulate the CB while in transit. While some had the acceptable temperature range during shipment printed on the exterior of the shipping container, no shipper can guarantee that this range will not be exceeded. Interestingly, most of these marked containers maintained temperatures within these acceptable ranges for only minutes when subjected to the temperature variations of the study.

In many cases, the insulation was so poor that the temperature within the shipping containers quickly equilibrated to 20°C when the profile cycled back to 20°C. This leads the author to believe that temperature data collected by the CB banks at the time of receipt of the CB shipment may not be relevant; the shipping containers may equilibrate quickly in the air-conditioned ground transport from the airport and in processing laboratories as they wait to be checked in, masking the loss of thermal integrity that occurred during transport. Construction of the highest-performing shipping container was unique in that it consisted of vacuum-insulated panels surrounding an interior thermal cooler, with phase-change solution within the walls and lid of the cooler.

The data demonstrate that more attention and resources are needed by nearly all private CB banks to improve the design of the shipping containers used to transport CB specimens if thermal integrity is to be assured. The private CB banking industry or the FDA should urgently create standards of acceptable thermal range during specimen transport as well as standards for the thermal performance of CB transport containers. In addition, it should become routine to include thermal data loggers within each container to confirm and document thermal integrity during transport. Moreover, standardized thermal performance testing of CB shipping containers by an independent testing laboratory should be performed at regular intervals or with any change in the design of a container. These findings should be published by the CB banking companies for review by the medical profession and the public.

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References

1. National Cord Blood Program. List of diseases treated with NCBP units: diagnosis for transplantation with NYBC CB units. New York Blood Center. 2010 http://www.nationalcordbloodprogram.org/patients/utilization_outcomes.html Accessed July 17, 2011.
2. Butler MG, Menitove JE. Umbilical cord blood banking: an update. *J Assist Reprod Genet*. 2011;28(8):669-676.
3. Food and Drug Administration. Guidance for industry: minimally manipulated unrelated allogeneic placental/umbilical cord blood intended for hematopoietic reconstitution for specified indications. Rockville, MD: CBER Office of Communication, Outreach, and Development; 2009.
4. Hubel A, Carlquist D, Clay M, McCullough J. Short-term liquid storage of umbilical cord blood. *Transfusion*. 2003;43(5):626-632.
5. Campos L, Roubi N, Guyotat D. Definition of optimal conditions for collection and cryopreservation of umbilical cord hematopoietic cells. *Cryobiology*. 1995;32(6):511-515.
6. Centers for Disease Control and Prevention. Fatal car trunk entrapment involving children-United States, 1987-1998. *MMWR Morb Mortal Wkly Rep*. 1998;47(47):1019-1022.
7. Null J. Heatstroke deaths of children in vehicles. San Francisco, CA: Department of Geosciences, San Francisco State University; 2011. http://ggweather.com/heat/ Accessed July 17, 2011.
8. Syversen E, Pineda FJ, Watson J. Temperature variations recorded during interinstitutional air shipments of laboratory mice. *J Am Assoc Lab Anim Sci*. 2008;47(1):31-36.

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