Cell Processing Labs, Your Best Friends

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Welcome

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VP and Sr. Medical Director, Medical, Quality & Regulatory

NMDP/Be The Match

Disclosures

The following faculty and planning committee staff have no financial disclosures:

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Amy McGarrity	NMDP/Be The Match
John Miller, MD, PhD	NMDP/Be The Match

Learning Objectives

At the conclusion of this session, attendees will be able to:

- Examine TNC optimization processes.
- Provide examples of processing techniques to enhance the quality of products.
- Evaluate best practices in cellular therapy processing.

Cell Processing Labs: Your Best Friends!

Kathryn Bushnell-Crowley, BS, MLS(ASCP)
Cellular Therapy Center
Dartmouth Hitchcock Medical Center

Dartmouth-Hitchcock

Cell Processing Labs: Your Best Friends!

Brief description of our center

Total Nucleated Counts

Neutrophils

Hematocrit

What your best friends can do for you

What you can do for your best friends

Dartmouth-Hitchcock

Dartmouth-Hitchcock Medical Center

- Apheresis Center (Blood Donor Program)
- Collection Center (Blood and Marrow Transplant)
- Processing Lab (Cellular Therapy Center)
- Transplant Center (Blood and Marrow Transplant)
- Patient (Hematology Special Care Unit)

Dartmouth-Hitchcock

AC / CC to TC

NMDP AC

NMDP CC

Cellular Therapy Center (Processing Lab)

Patient

BMT Hematology Special Care Unit

Dartmouth-Hitchcock

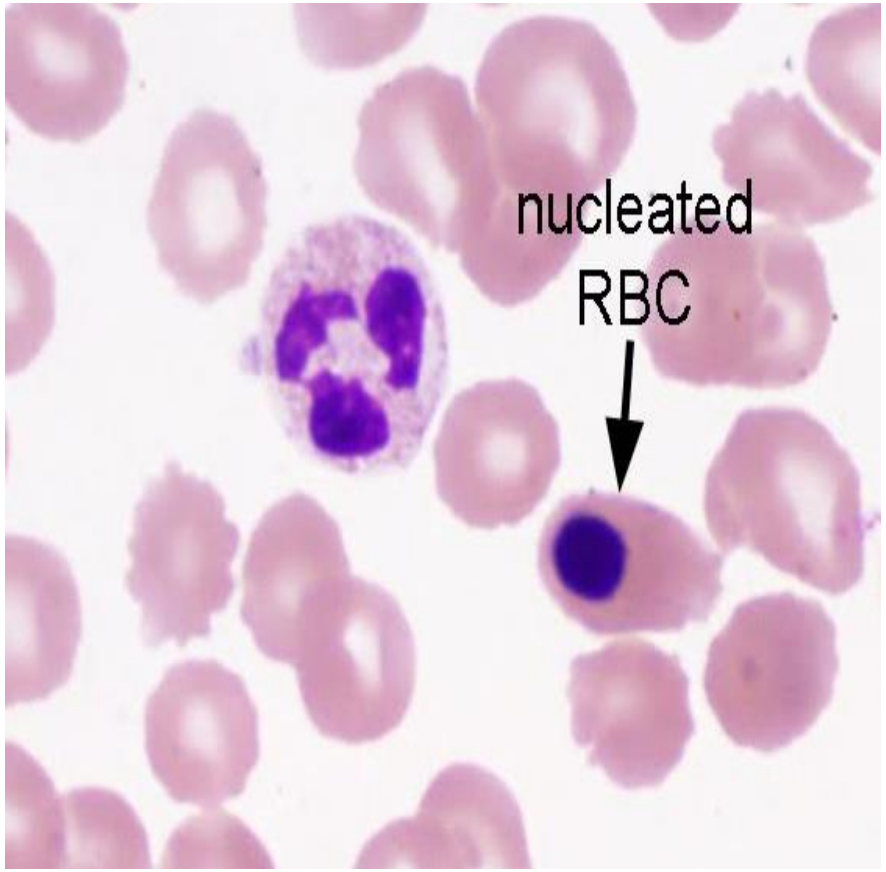
Product Analysis: Total Nucleated Count

Total Nucleated Count is the measurement of the number of nucleated cells and includes white blood cells (WBC) and nucleated red blood cells (NRBCs)

Methodology

Automated analyzer. Can change mode to discount NRBCs. Examples include Sysmex, Coulter, Advia

Manual WBC count – WBCs are counted on a hemocytometer under a microscope



Why is the TNC important?

TNC x volume yields the total number of nucleated cells in the product. When the % of CD34 positive cells is known, that is used to calculate the total number of stem cells in the product.

A high TNC can be diluted prior to shipment to insure better viability. Several studies have found that hematopoietic stem cell (HSC) products can be stored 48 hours or more without significant loss of viability of CD34+ cells if the products are stored at 4˚C and cell concentrations are not too high.

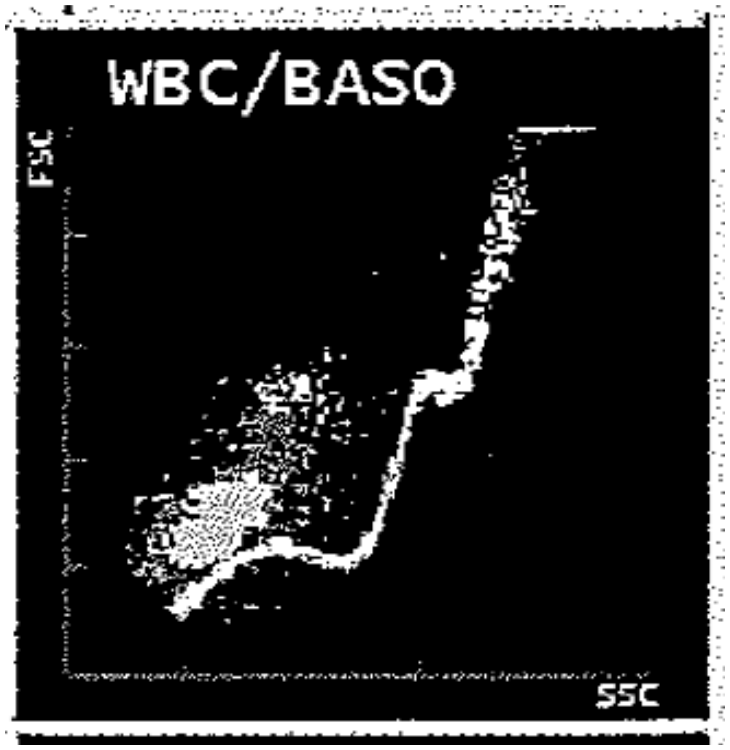
Hematopoietic Progenitor Cells, Marrow HPC(M)

- Hematopoietic Progenitor Cells
  - The good stuff
- RBCs
  - Hematocrit is very high, not the best choice for ABORh Incompatible transplants
- NRBCs
  - Lots. Automated cell counts can ID these, but product analysis doesn't differentiate
- FAT
  - Shows up as a streak on hemogram

HPC(M) TNC

Accurate marrow total nucleated cell (TNC) counts are essential for effective monitoring of bone marrow collection and processing. Aspirated marrow is variably contaminated by fat particles, resulting in overestimation of marrow TNC by automated analyzers.

Picture of Hemogram showing fat streak



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HPC(M) TNC – What to do?

The TNC during marrow harvest is often higher than the post TNC performed by the CTC.

We compared WBC counts by automated analyzer and Flow Cytometry. Flow counts were lower because prep included washing to remove fat and the antibodies used did not count NRBCs

Verify what methods your center uses and use it consistently - All manual counts? NRBCs included? Samples washed?

What else effects HPC(M) TNC?

The cell density of a bone marrow harvest positively correlates with donor body weight and peripheral white blood cell count $P = 0.0475$, $P < 0.0001$, but negatively correlated with the total volume of bone marrow harvest $P < 0.0001$

Product Analysis: Differential

The differential totals the number of each type of WBC. Can be performed manually or automated.

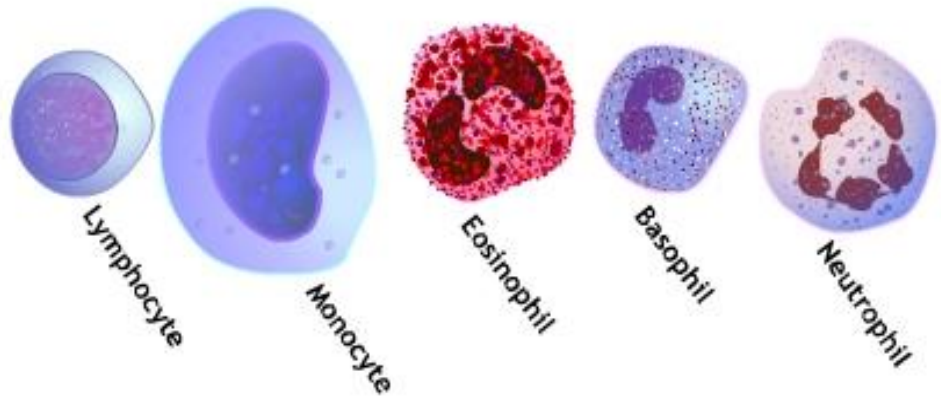
Lymphocytes

Monocytes

Eosinophils

Basophils

Neutrophils



Why is the Differential Important?

Neutrophils both viable and dead cells, and cellular debris (membranes, granule contents, and cytokines) play a direct causal role in the pathobiology of infusion-related toxicities.

Investigators have suggested a variety of ways to address the issue of toxicity because of high granulocyte content of the cryopreserved PBSC product. At the time of collection, obtaining high-quality apheresis products with minimal contamination by mature myeloid cells is desirable.

Product Analysis: Hematocrit

The Hematocrit is the proportion, by volume, of the product that consists of red blood cells.

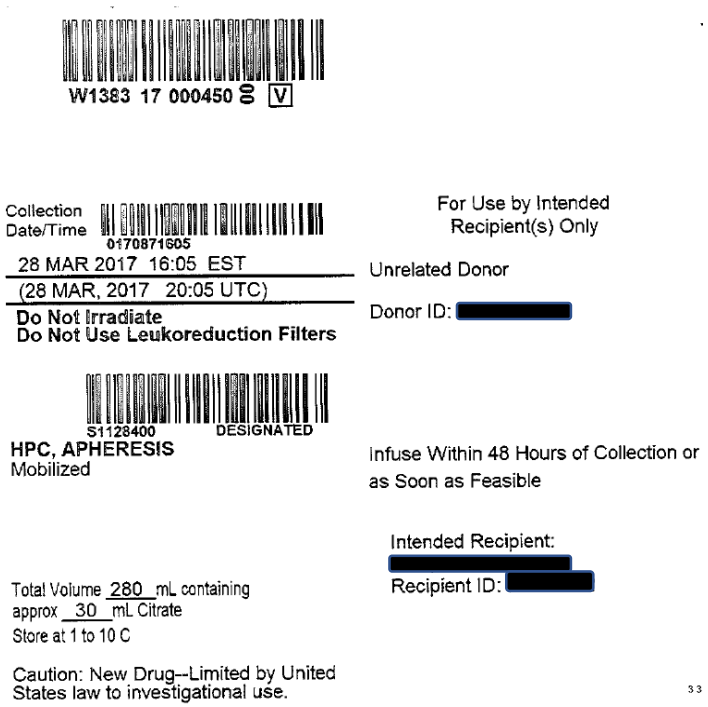
Why is the Hematocrit important?

ABO Incompatible transplants. Processing of Major and Bidirectional incompatible transplants can lead to loss of stem cells. The lower the hematocrit, the less likely the need to remove RBCs.

Your best friends help by

Making ISBT 128 Collection labels for the AC and CC

Re-labeling Products for Shipment



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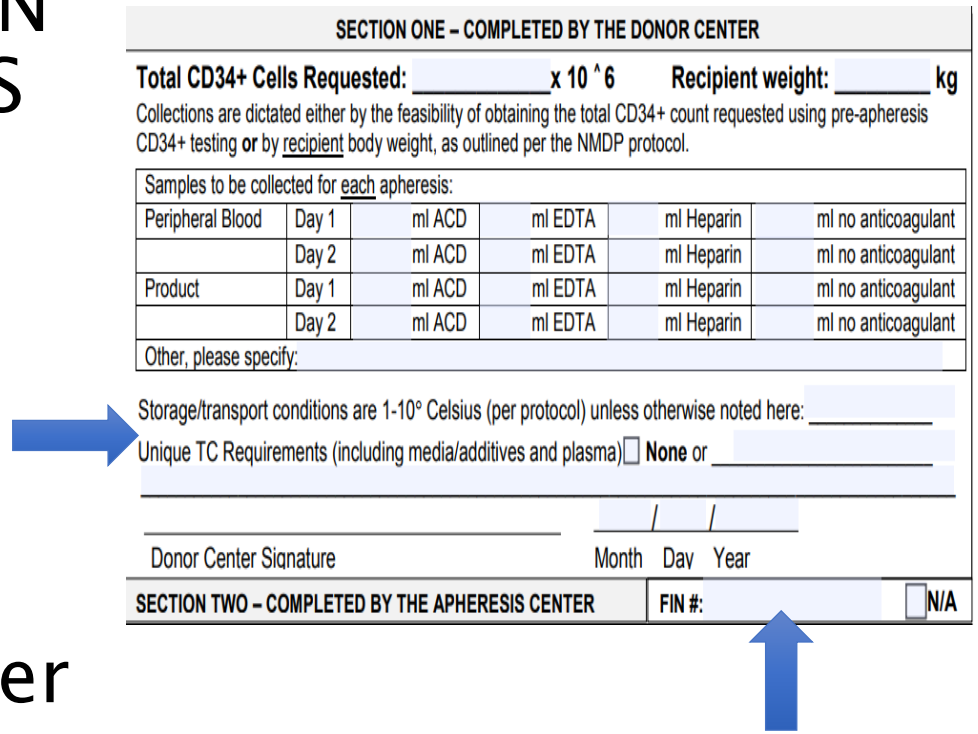
You can help your best friends

NMDP VERIFICATION OF HPC, APHERESIS REQUEST

Verify special instructions

Complete FIN number



SECTION ONE – COMPLETED BY THE DONOR CENTER

Total CD34+ Cells Requested: _____ **x 10 ^ 6** **Recipient weight:** _____ **kg**

Collections are dictated either by the feasibility of obtaining the total CD34+ count requested using pre-apheresis CD34+ testing **or** by recipient body weight, as outlined per the NMDP protocol.

Samples to be collected for each apheresis:								
Peripheral Blood	Day 1		ml ACD		ml EDTA		ml Heparin		ml no anticoagulant
	Day 2		ml ACD		ml EDTA		ml Heparin		ml no anticoagulant
Product	Day 1		ml ACD		ml EDTA		ml Heparin		ml no anticoagulant
	Day 2		ml ACD		ml EDTA		ml Heparin		ml no anticoagulant
Other, please specify:									

Storage/transport conditions are 1-10° Celsius (per protocol) unless otherwise noted here: _____

Unique TC Requirements (including media/additives and plasma) ☐ **None** or _____

_____ ___/___/___

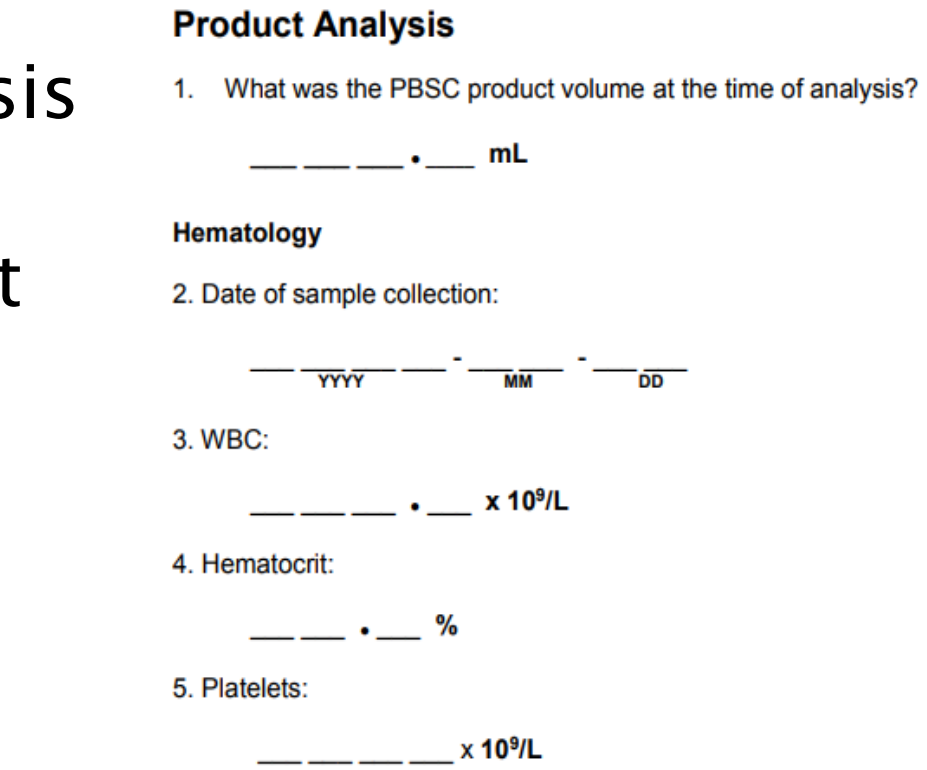
Donor Center Signature Month Day Year

SECTION TWO – COMPLETED BY THE APHERESIS CENTER **FIN #:** ☐ **N/A**

Dartmouth-Hitchcock

Your best friends help by

- Completing Product Analysis Forms
- Faxing forms to Transplant Center and Donor Center ASAP
- CIBMTR 2006 Forms



Product Analysis

1. What was the PBSC product volume at the time of analysis?

___ ___ ___ • ___ **mL**

Hematology

2. Date of sample collection:

___ ____ ___ - ___ - ___
YYYY MM DD

3. WBC:

___ ___ ___ • ___ **x 10^9/L**

4. Hematocrit:

___ ___ • ___ **%**

5. Platelets:

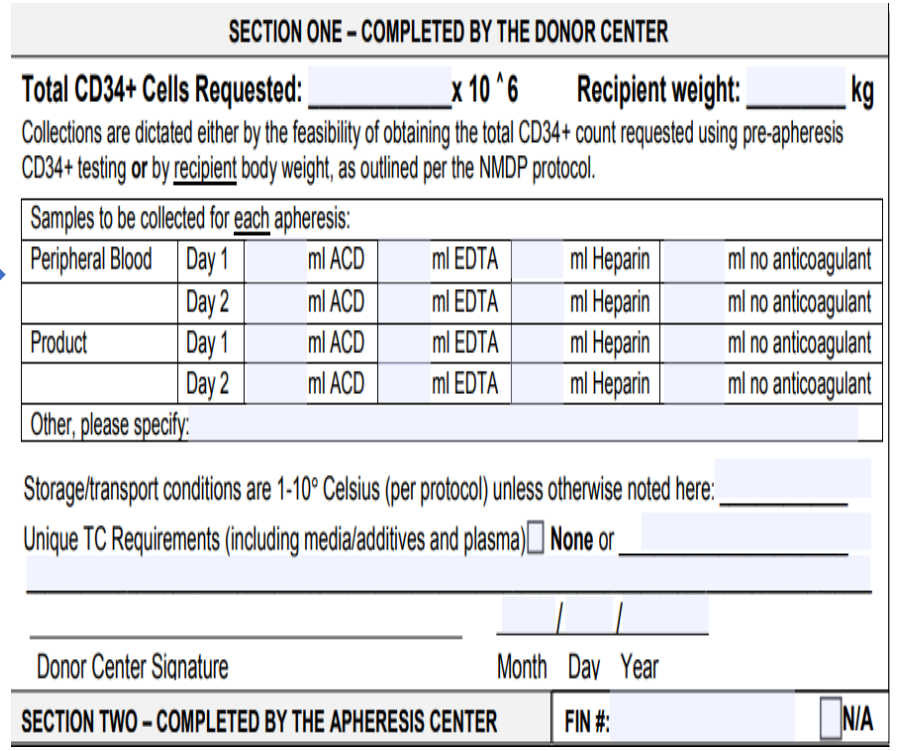
___ ___ ___ ___ **x 10^9/L**

Dartmouth-Hitchcock

You can help your best friends

NMDP VERIFICATION OF HPC, APHERESIS REQUEST

Verify Product samples – Most labs do not want a product sample. If they need they can pull directly from bag.



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Other, please specify:					

Storage/transport conditions are 1-10° Celsius (per protocol) unless otherwise noted here: _____

Unique TC Requirements (including media/additives and plasma) ☐ **None** or _____

_____

_____ ___/___/___

Donor Center Signature Month Day Year

SECTION TWO – COMPLETED BY THE APHERESIS CENTER **FIN #:** ☐ **N/A**

Dartmouth-Hitchcock

Your best friends help by

Contacting TC about strange requests
- Do you really want 10 mL of product in a purple top?

Consulting with Coordinators
- Regarding special handling instructions
- Regarding T Cell requests

You can help your best friends

DONOR WORKUP REQUEST

Verify fax number is present for CD34 results

6. Day of Collection Samples

A minimum of 10 mls of donor peripheral blood must accompany each product collected (used for ABO and Rh confirmation).

Indicate the type of tube(s) required by the transplant center:

	Peripheral Blood		Product	
	Day 1 (marrow and PBSC)	**Day 2** (PBSC only)	**Day 1** (marrow and PBSC)	**Day 2** (PBSC only)
Red Top (No Anticoagulant)	ml	ml	Ml	ml
Yellow Top (ACD)	ml	ml	Ml	ml
Green Top (Sodium Heparin)	ml	ml	Ml	ml
Purple Top (EDTA)	ml	ml	Ml	ml

6.1. **Apheresis Center: Fax CD34+ results to the following number**_____

Product Delivery Information:

Attn/Name: _____

NMDP Transplant Center Name: _____

Address: _____

City, State, Country _____

Telephone number: _____

Dartmouth-Hitchcock

Tips to optimize product @

Collection

Minimize RBC Content

Minimize Neutrophils

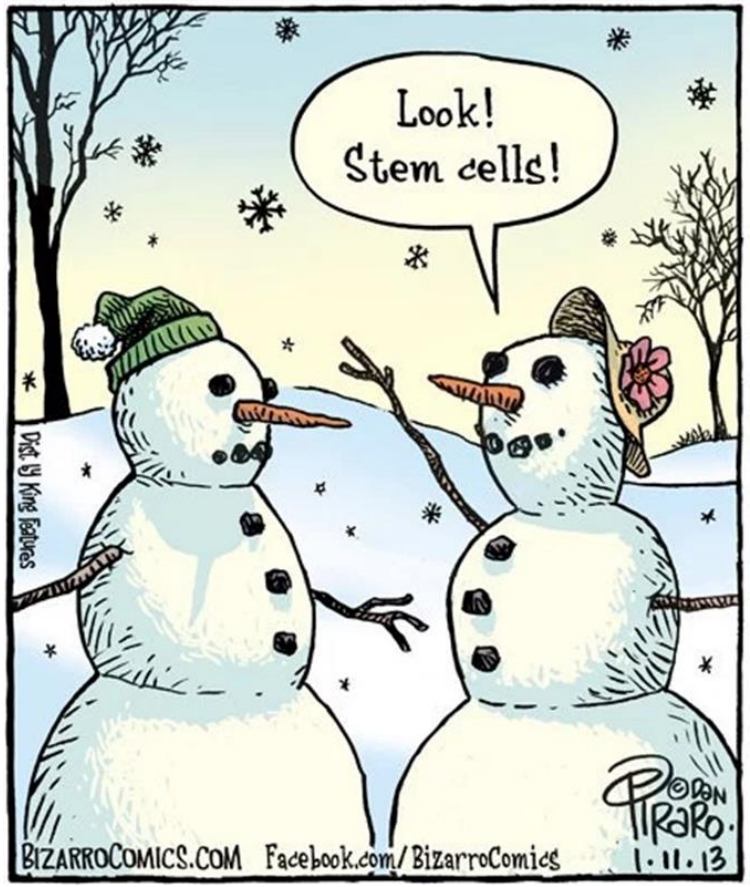
Shipping

Ship cold

Dilute with Concurrent Plasma, Apheresis

Documentation

Fax info to DC and TC ASAP



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Resources

Analysis of the Recovery of Cryopreserved and Thawed CD34+ and CD3+ Cells Collected for Hematopoietic Transplantation
Virginia Fisher, Hanh Khuu, Virginia David-OCampo, Karen Byrne, Steven Pavletic, Michael Bishop, Daniel H. Fowler, A. John Barrett, and David F. Stroncek

Limiting the Daily Total Nucleated Cell Dose of Cryopreserved Peripheral Blood Stem Cell Products for Autologous Transplantation Improves Infusion-Related Safety with No Adverse Impact on Hematopoietic Engraftment
Nandita Khera, Jack Jinneman, Barry E. Storer, Shelly Heimfeld, Megan M.O'Meara, Thomas R. Chauncey, Stephanie J. Lee, Michael Linenberger

Correction of Bone Marrow Nucleated Cell Counts for the Presence of Fat Particles
Stuart A. Bentley, Michael A. Taylor, Donna E. Killian, Susan B. Schoultz, Laura McLannan, Connie A. Bishop, Thomas C. Shea, Mark E. Brecher

Correlation between characteristics of unrelated bone marrow donor and cell density of total nucleated cell in bone marrow harvest.
Kao RH, Li CC, Shaw CK, Wang TF, Chu SC, Chen SH, Yao CY, Huang KP, Wu YF.

Thank you and…

Please reach out if you have questions

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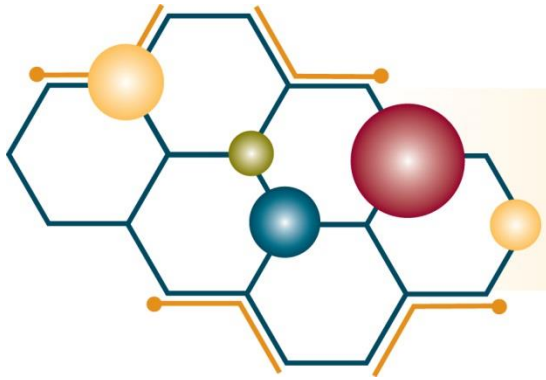


MOLECULAR & CELLULAR THERAPEUTICS

HPCs: Collection, Shipment/Storage, and Processing

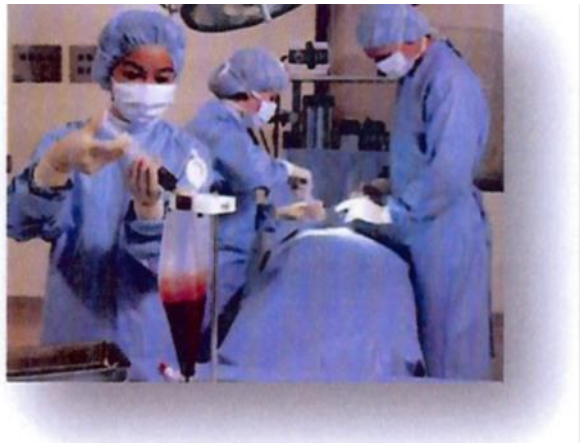
Cell Processing Labs, Your Best Friends
NMDP Council Meeting
November 11, 2017

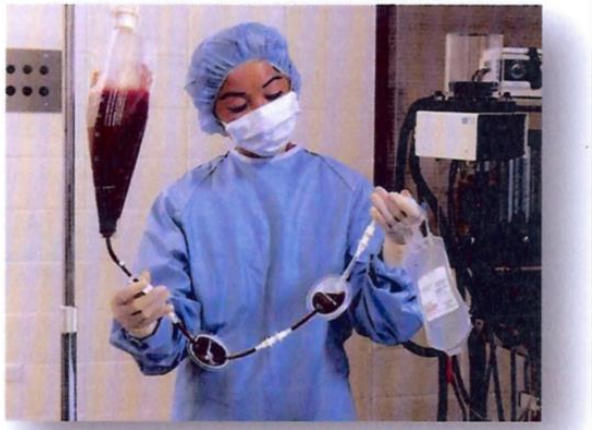
David H. McKenna, M.D.

MOLECULAR & CELLULAR THERAPEUTICS
UNIVERSITY OF MINNESOTA
Driven to Discover℠

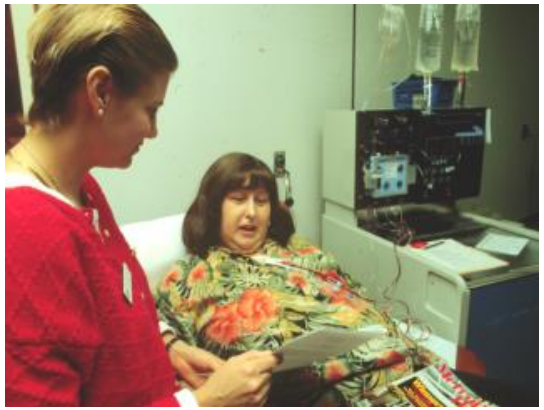
HPC Graft Sources

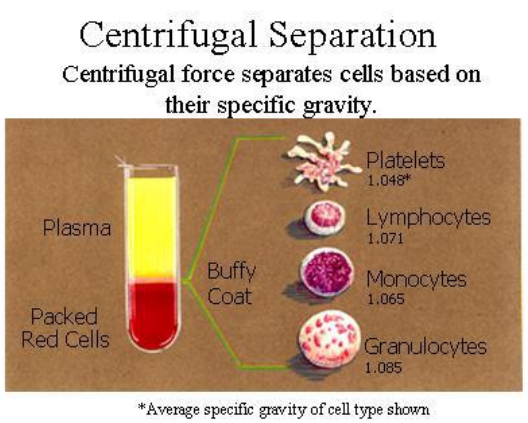
Bone Marrow



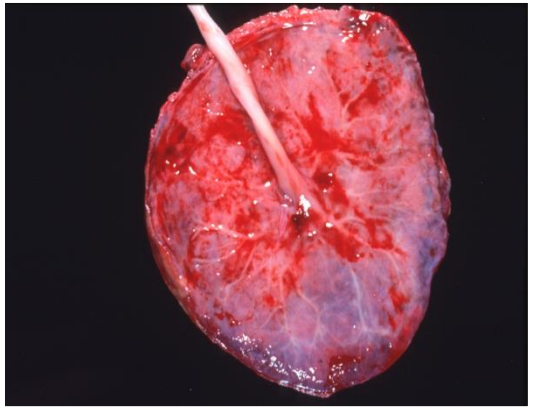


Peripheral Blood





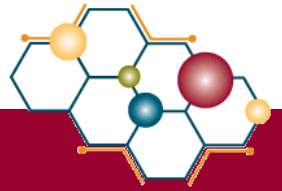
Umbilical Cord Blood



Photos from www.fenwalinc.com

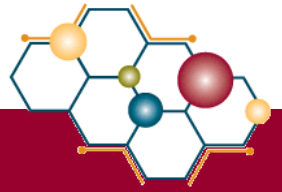
Bone Marrow: General

- Original source of HPCs (~1% in marrow)
- OR harvest under general anesthesia
- 10-15 mL/kg recipient weight (target dose 2-4 x 10^8 NCs/kg) = roughly 1L with adult
- Advantages:
  - 1 procedure
  - Lower T cell content
  - Less chronic GVHD than PB



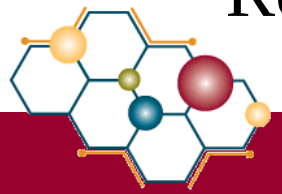
Peripheral Blood: General

- More commonly used than BM (auto/allo)
- Requires mobilization (e.g., G-CSF) and apheresis
- Target dose 5 x 10^6 CD34+ cells/kg
- Advantages:
  - No anesthesia/hospitalization
  - More rapid engraftment
  - Possibly less tumor cell contamination (auto)



Umbilical Cord Blood: General

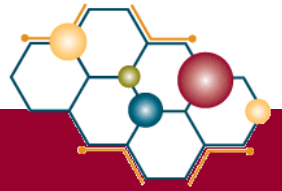
- Collected from placenta
  - OB staff vs. dedicated staff
  - In utero vs. ex utero
- Banked (public vs. private)
- Minimum dose: 1.7-2.0 x 10^5 CD34+ cells/kg
- Advantages:
  - No risk to donor
  - Decreased search time
  - Decreased severity of GVHD
  - Reduced HLA match requirements



The characteristics of the HPCs…

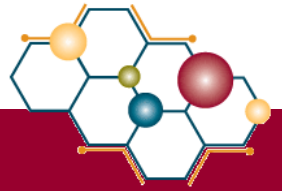
- Volume
- NC count/[NC]
- RBC type and content
- Platelet content
- Plasma…

determine the approach to downstream handling…



Bone Marrow: Characteristics

- 1 L total volume
- 2 x 10^{10} TNC
- 20 x 10^{6} NC/mL
- Hematocrit ~ 40% = 400 mL of RBCs
- Plasma volume ~ 600 mL
- Platelets, fat

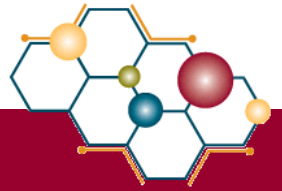


Peripheral Blood: Characteristics

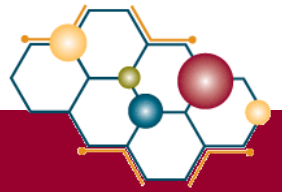
- 200-300 mL total volume
- $\geq 4 \times 10^{10}$ TNC
- $>200 \times 10^{6}$/mL
- <10 mL RBCs

Umbilical Cord Blood: Characteristics

- 25 mL total volume
- 1-2 x 10^9 TNC
- 60 x 10^6 NC /mL
- <5 mL of RBCs
- 10% DMSO



Shipment/Storage



BEST Transportation Survey

- 194 respondents, 90% shipped or received CT products
- 82% specified the conditions for temperature in transit
- 57% monitored temperature in transit
  - 74% of these used a data logger
- Temperature range most commonly specified was 18-24 °C
- Survey respondents indicated a wide range of shipping temperatures and most indicated ‘no adjustment required’ of cell concentration for Therapeutic Cells (e.g., DLI)

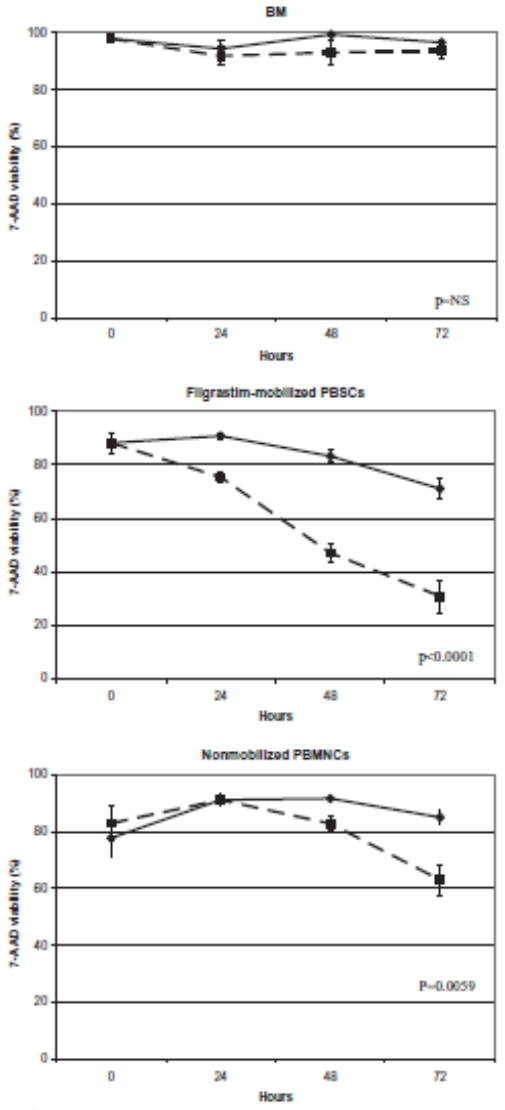
Pamphilon DH, Selogie E & Szczepiorkowski ZM. Transportation of cellular therapy products: report of a survey by the cellular therapies team of the Biomedical Excellence for Safer Transfusion (BEST) collaborative. Vox Sanguinis (2010); 99: 168–173.

Validation of short-term handling and storage conditions for marrow and peripheral blood stem cell products

Grace S. Kao, Haesook T. Kim, Heather Daley, Jerome Ritz, Scott R. Burger, Linda Kelley, Cynthia Vierra-Green, Sue Flesch, Stephen Spellman, John Miller, and Dennis Confer

BACKGROUND: Allogeneic hematopoietic stem cell transplants from unrelated donors are routinely used in the treatment of patients with hematologic malignancies. These cellular products are often collected off-site and require transport from the collection site to transplantation centers. However, the effects of transport conditions and media on stem cell graft composition during short-term storage have not been well described.
STUDY DESIGN AND METHODS: Five bone marrow (BM), four filgrastim-mobilized peripheral blood stem cell (PBSC), and four nonmobilized peripheral blood mononuclear cell (PBMNC) products were collected from healthy volunteer donors and stored at 4 or 20°C for up to 72 hours in 10% PlasmaLyte A plus anticoagulants such as 10% acid citrate dextran-A (ACD-A) and/or 10 IU/mL heparin. Products were evaluated at 0, 24, 48, and 72 hours for cellular content, viability, and metabolic activities.
RESULTS: BM products maintained equivalent cell viability when stored at either 4 or 20°C over 72 hours, but cell viability was better maintained for PBSC products stored at 4°C. The mean viable CD34+ cell recovery for PBSC and BM products stored over 72 hours at 4°C was higher than 75%. Significantly lower CD34+ cell and colony-forming unit recoveries were seen in PBSC products but not BM products stored at room temperature. Faster lactic acid accumulation was observed in PBMNC and PBSC products stored without ACD-A.
CONCLUSIONS: Seventy-two-hour storage of BM, PBSC, and PBMNC products at refrigerated temperature maintains optimal cell viability and recovery. Anticoagulation with ACD-A is preferred over heparin to reduce lactic acid accumulation in the product media.

Transfusion (2011); 51: 137–147.



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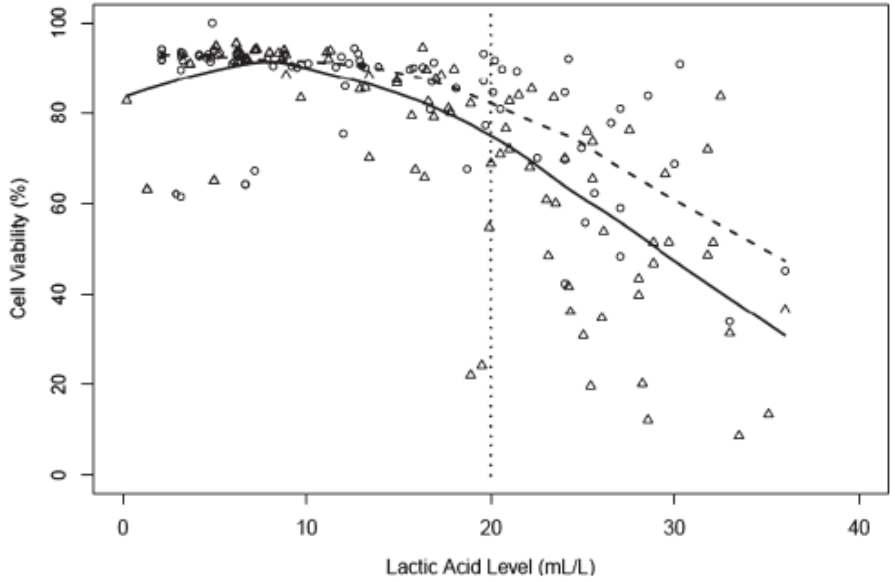


Transfusion (2011); 51: 137–147.

UCB Storage/Shipment

Storage characteristics of cord blood progenitor cells: report of a multicenter study by the cellular therapies team of the Biomedical Excellence for Safer Transfusion (BEST) Collaborative

Derwood Pamphilon, Elinor Curnow, Helen Belfield, Jo-Anna Reems, John McMannis, Lucilla Lecchi, Zbigniew Szczepiorkowski, and David McKenna

- Collections maintained at 4°C retained higher TNC counts, MNC counts and CD45+ cell viability over a 72-96 hr storage period

- Recommend cool storage and processing in <48 hours (ASAP)

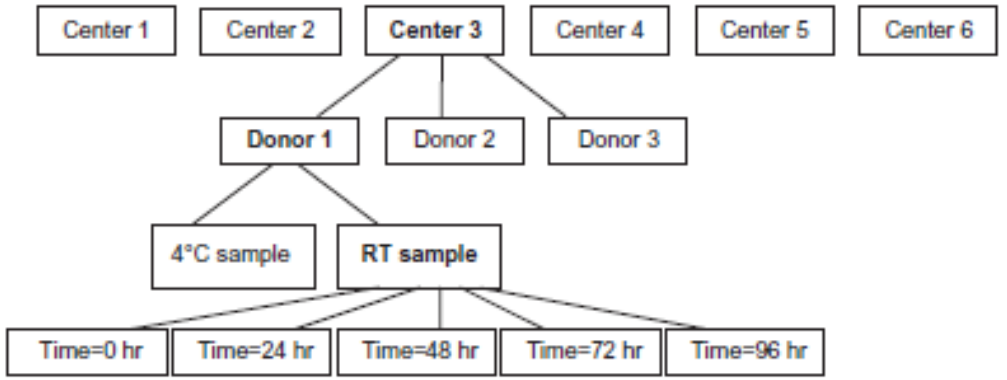
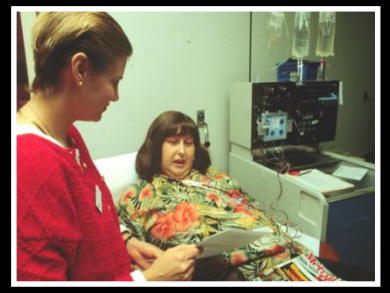


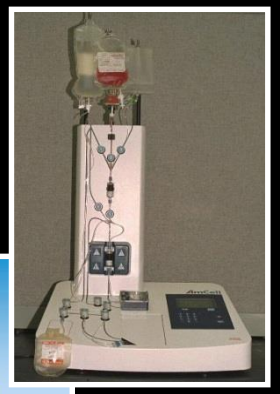
Fig. 1. Schematic of data model. Hierarchical ANOVA was performed, with center treated as a between-donor effect and temperature and time as within-donor effects.

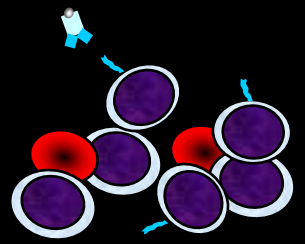
Transfusion. 2011; 51 (6): 1284-1290.

Non-Mobilized Apheresis MNC

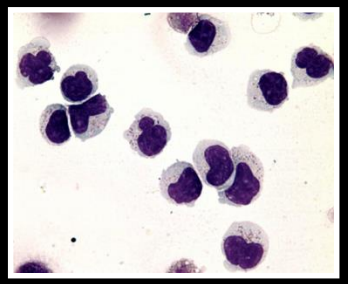
raw material for…



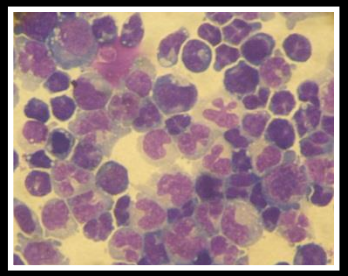


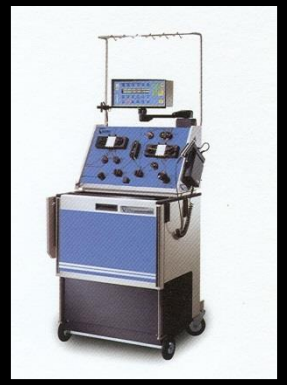


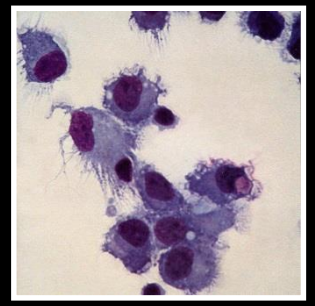
NK cells



Treg cells





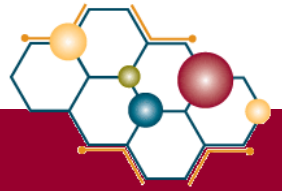


- Donor lymphocyte infusion
- CAR-T cells
- Viral-specific T cells
- Etc…

Dendritic cell photo credit: Celluzzi C and Welbon C. Transfusion (2003); 43 (4).

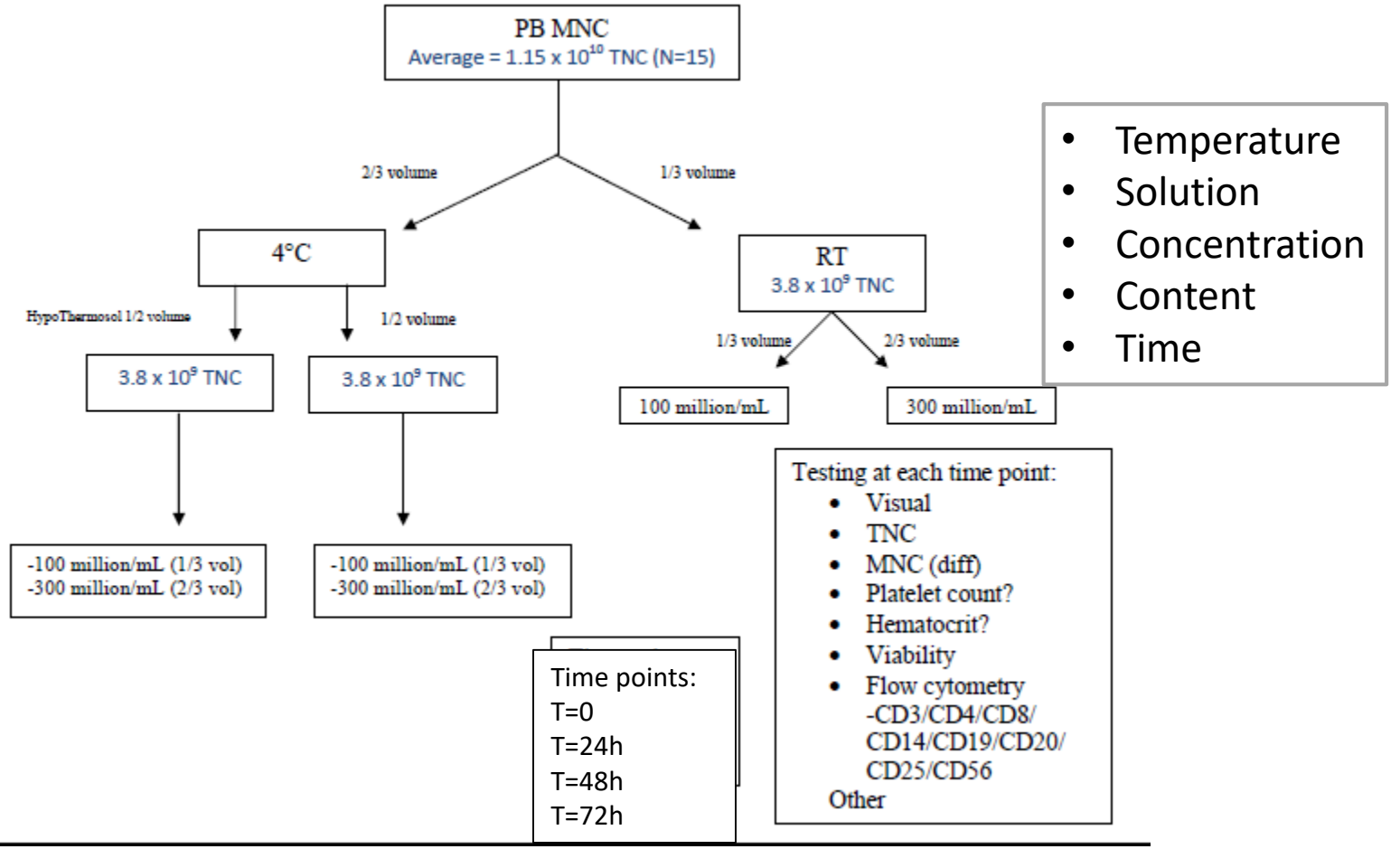
Previous Studies of Non-mobilized MNC Apheresis Collections

- Single center studies
- Small ‘n’
  - typically more focused on mobilized apheresis
- Cell concentration
  - often not modified
- Storage solutions
  - typically just anticoagulant
- Type of bag
  - Transfer bag (non-breathable) vs apheresis bag (breathable)



Optimization of Storage Conditions for Apheresis Research (OSCAR)

- 4 centers; n = 15



TJ Gniadek, HSP Garritsen, D Stroncek, ZM Szczepiorkowski, DH McKenna. Optimal Storage Conditions for Apheresis Research (OSCAR): A Biomedical Excellence for Safer Transfusion (BEST) Collaborative Study. Accepted for publication in Transfusion.

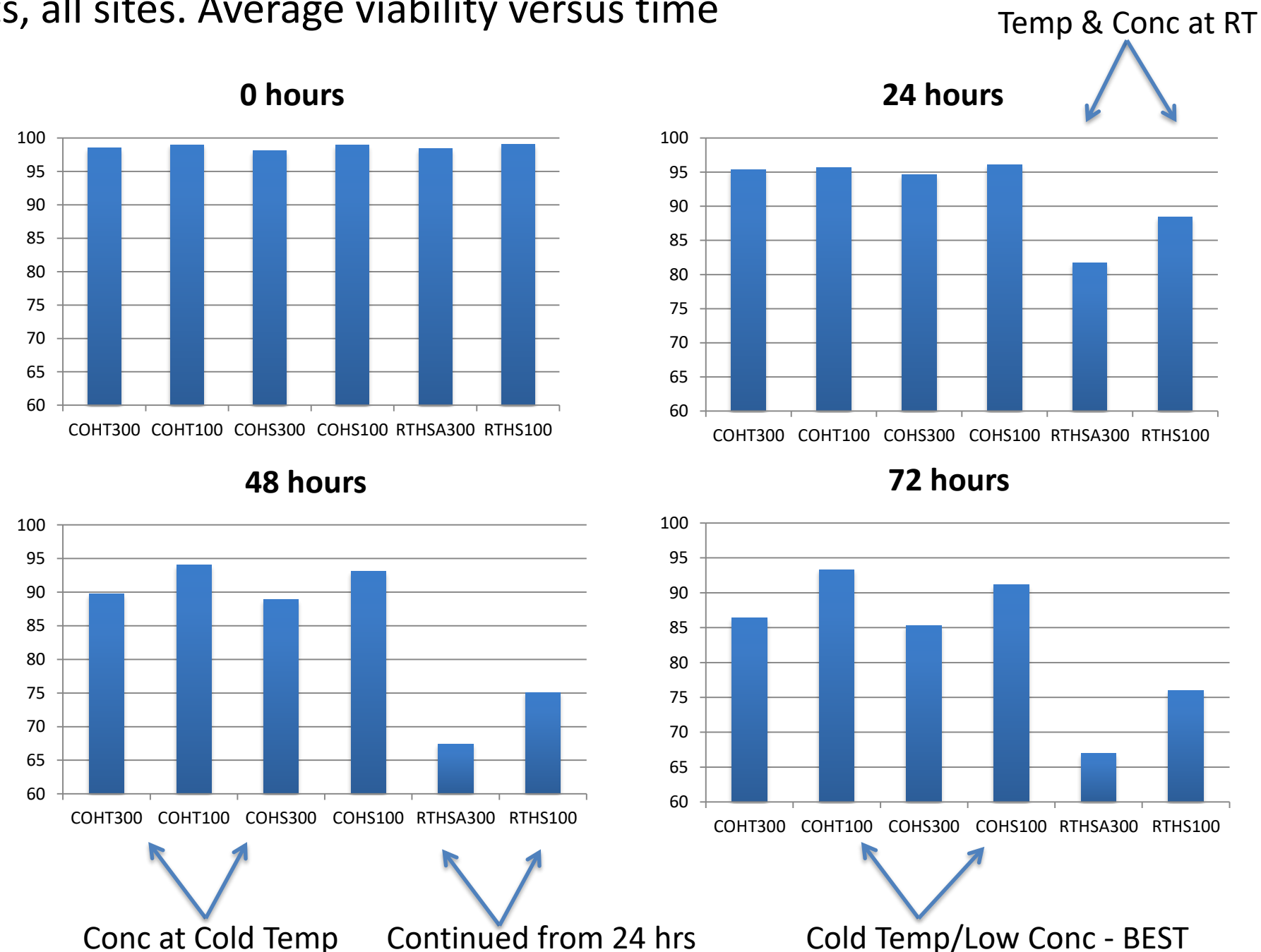
Participating Centers

- National Institutes of Health, Bethesda, MD
  (D. Stroncek)
- Dartmouth-Hitchcock Medical Center, Lebanon, NH
  (Z. Szczepiorkowski)
- Institut für Klinische Transfusionsmedizin,
  Braunschweig, Germany
  (H. Garritsen)
- University of Minnesota, Mpls/Saint Paul, MN
  (D. McKenna)

Results

- Visual –
  - Cold (HT and HSA) – OK
  - RT (HSA) –
    - 300M/mL small aggregates at 72h (NIH1)
    - 300M/mL clots at 48h and 72h (MN3)
    - 300M/mL “clumpy” at 72h (Dart1)
    - 300M/mL “funky!” at 48h (Dart3)
    - 100M/mL clots at 48h and 72h (MN3)

All products, all sites. Average viability versus time

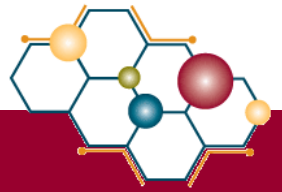


TJ Gniadek, HSP Garritsen, D Stroncek, ZM Szczepiorkowski, DH McKenna. Optimal Storage Conditions for Apheresis Research (OSCAR): A Biomedical Excellence for Safer Transfusion (BEST) Collaborative Study. Accepted for publication in Transfusion.

Summary

- Aggregates/clumping most noted at RT and higher cell concentration (300 M/mL) in HSA
- Cold temperature storage is best for non-mob MNC
  - Evident by 24 hrs
- Cell concentration becomes a factor by 24 hrs at room temperature and 48 hrs at cold temperature

Cell Processing



Why manipulate an HPC graft?

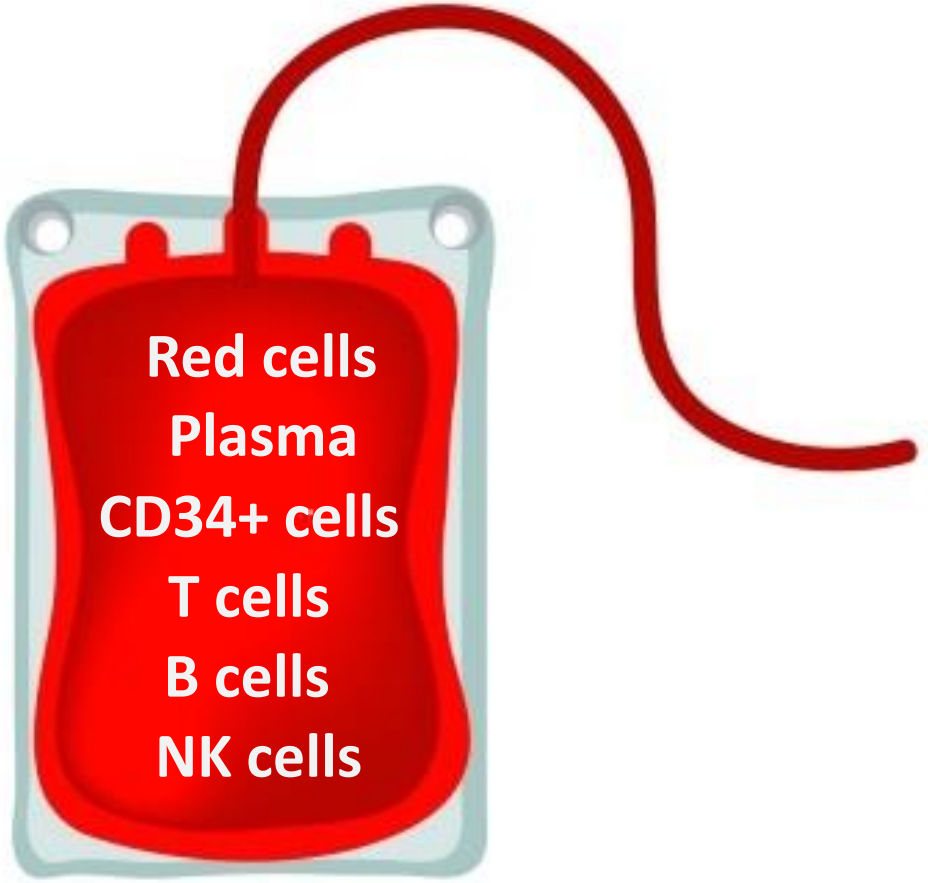
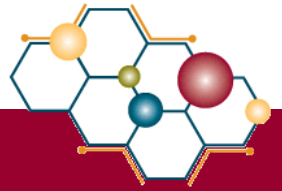


Image courtesy of kjnnt at www.FreeDigitalPhotos.net

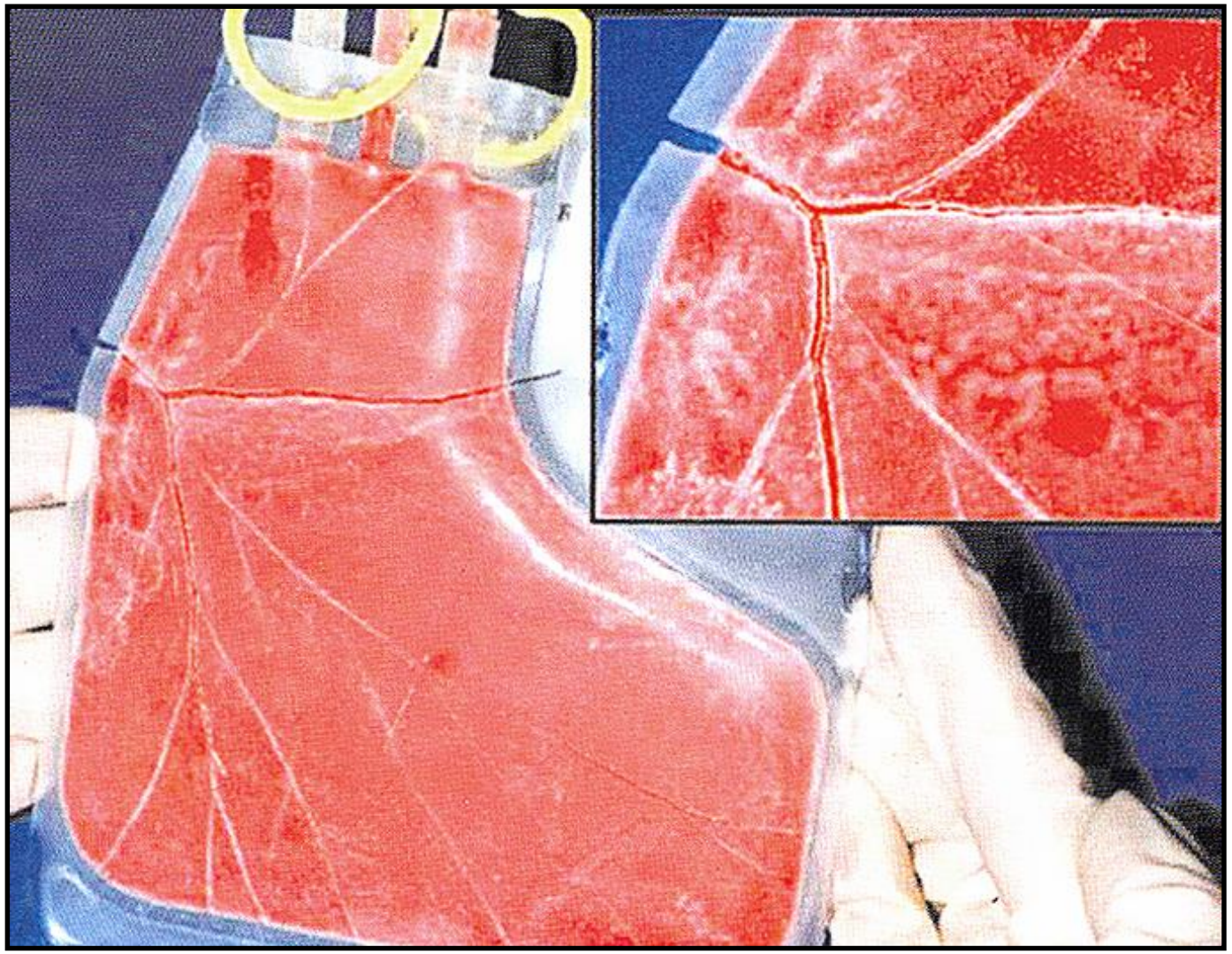
Routine Cell Processing Methods

Procedure	Application
Volume reduction (plasma depletion)	Reduction of incompatible plasma (minor ABO mismatch); Prevention of volume overload in recipient; Concentration of cells for cryopreservation
Red blood cell depletion	Reduction of incompatible red cell (major ABO or other antigen mismatch); Maximization of storage space; Limitation of infusion of lysed red cells and free hemoglobin (cryopreserved products)
Buffy coat preparation	Maximization of storage space; Debulking of red cells prior to further manipulation
Thawing, washing, and filtration	Preparation of HSC products prior to infusion



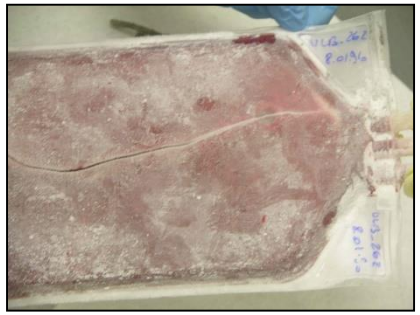
The lab is integral in guiding patient care…

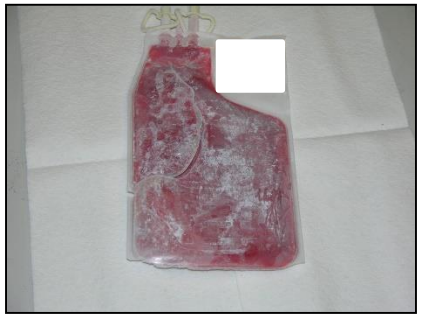
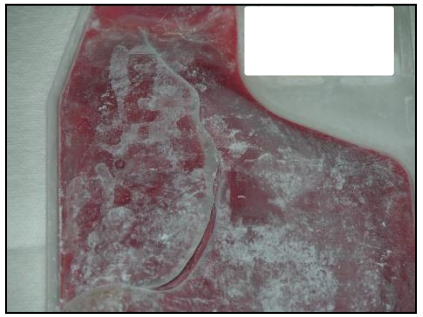
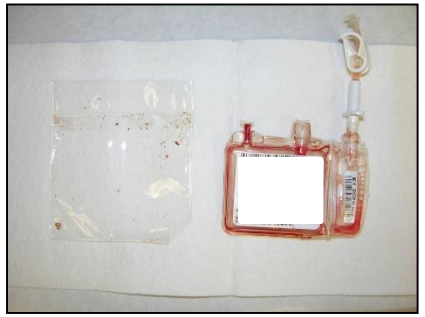
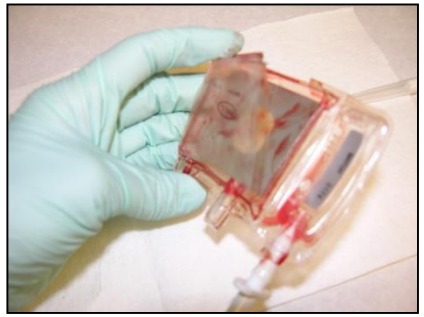
~ *Patient Safety*
~ *Quality Improvement*
~ *Process Improvement*

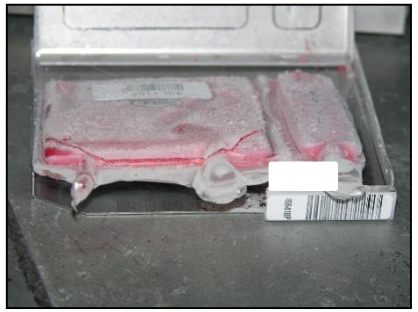


Khuu HM, Cowley H, David-Ocampo V, et al. Catastrophic failures of freezing bags for cellular therapy products: description, cause, and consequences. *Cytotherapy* 2002; 4(6): 539-549.

Personal experience…





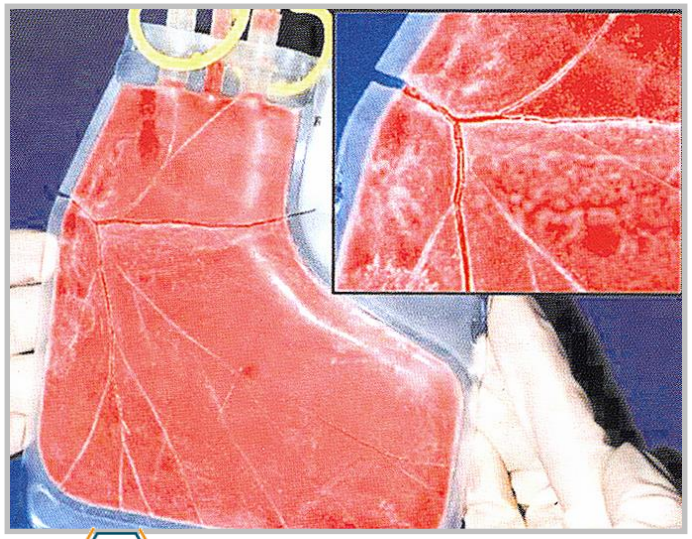
Assessment of UCB Bag Breaks

TRANSPLANTATION AND CELLULAR ENGINEERING

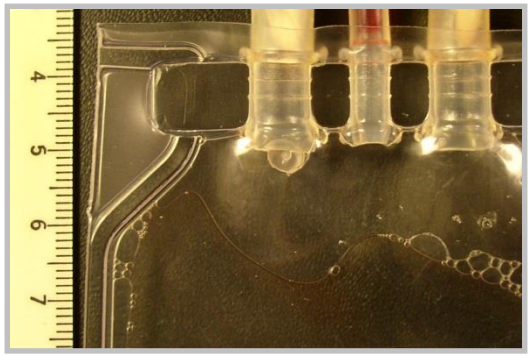
Loss of integrity of umbilical cord blood unit freezing bags: description and consequences

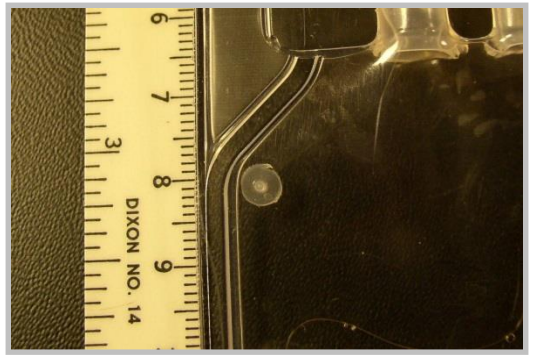
Bharat Thyagarajan, Michael Berger, Darin Sumstad, and David H. McKenna, Jr

Transfusion 2008; 48(6): 1138-1142.



Khuu HM, et al. *Cytotherapy* 2002; 4(6): 539-549.





Impact of Filtration (SBF) on UCB

LETTER TO THE EDITOR

Postthaw filtration of umbilical cord blood does not affect product quality or likelihood of engraftment

Grace Totoe, ••
Division of Transfusion Medicine
Bruce Lindgren, ••
Masonic Cancer Center
Eileen Emrick, BS
Molecular & Cellular Therapeutics
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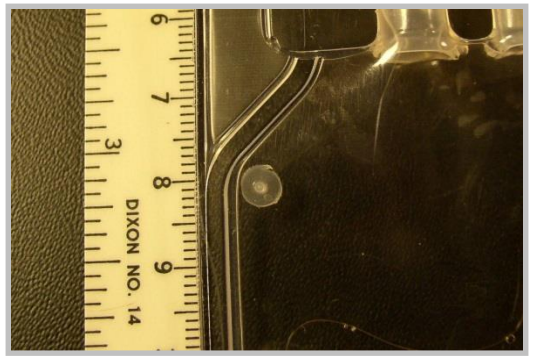
e-mail: mcken020@umn.edu
Division of Transfusion Medicine
Masonic Cancer Center
Molecular & Cellular Therapeutics
University of Minnesota
Minneapolis/Saint Paul, MN

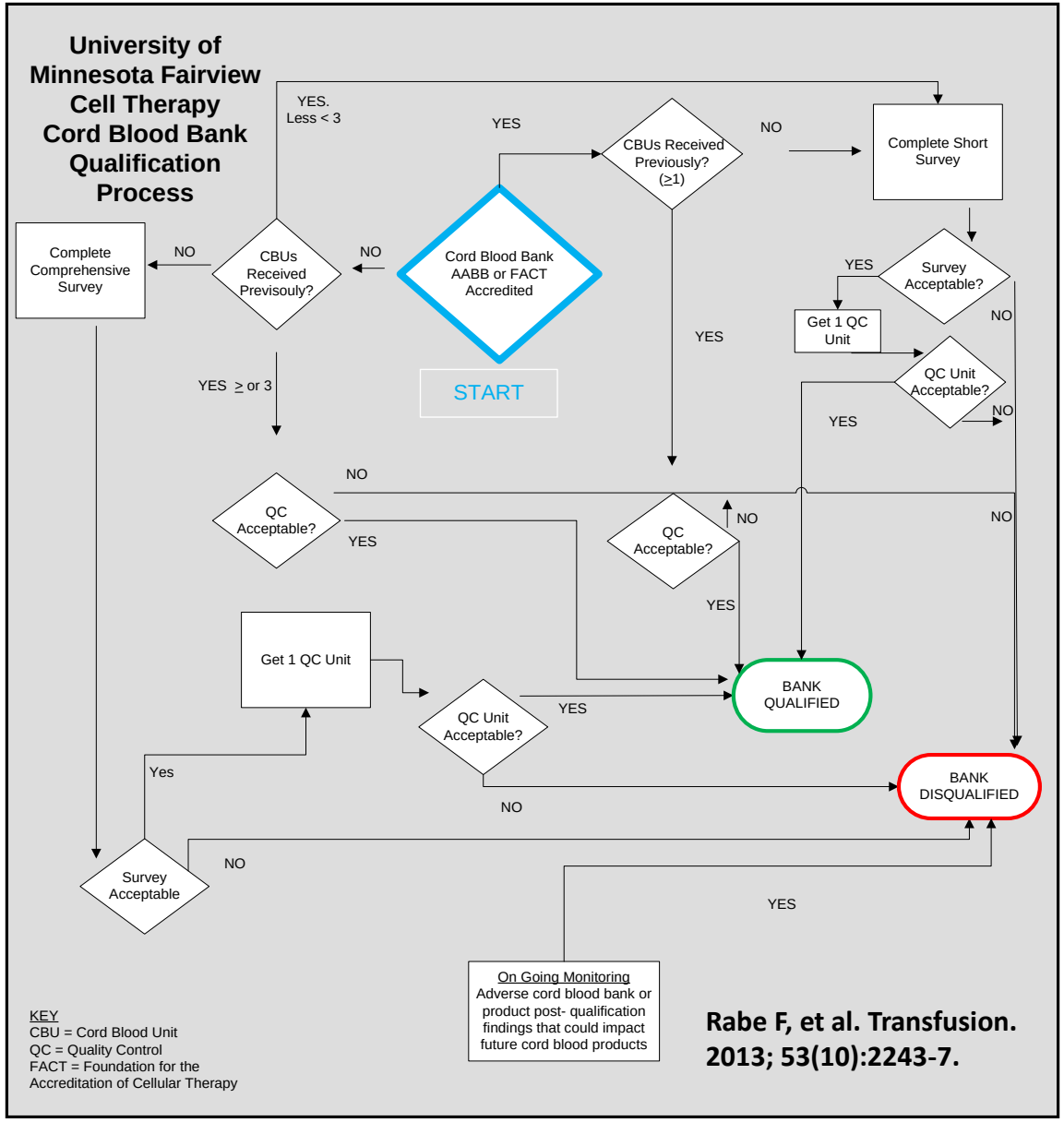
TABLE 1. Summary of change in product QC testing after filtration (postfilter value minus prefilter value)

QC testing	Mean (SD)	Median (range)	Paired t test p value
TNC dose ($\times 10^8$/kg)	−0.005 (0.012)	0.00 (−0.04 to 0.01)	0.095
CD34 dose ($\times 10^6$/kg)	−0.033 (0.090)	0.00 (−0.30 to 0.13)	0.130
CFU (colonies per million cells plated)	50.7 (280.1)	−12.0 (−406.0to881.0)	0.440
Viability (%)	−2.2% (4.7%)	−2.0% (−9.0% to 8.0%)	0.057

Transfusion. 2011 Oct;51(10):2257-8.



Umbilical Cord Blood Bank Qualification



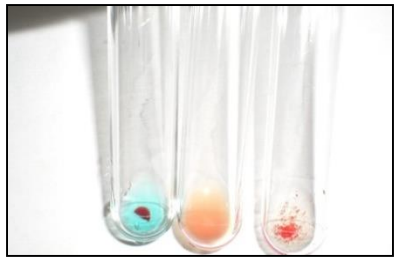
Detection of Mislabeled UCB Units

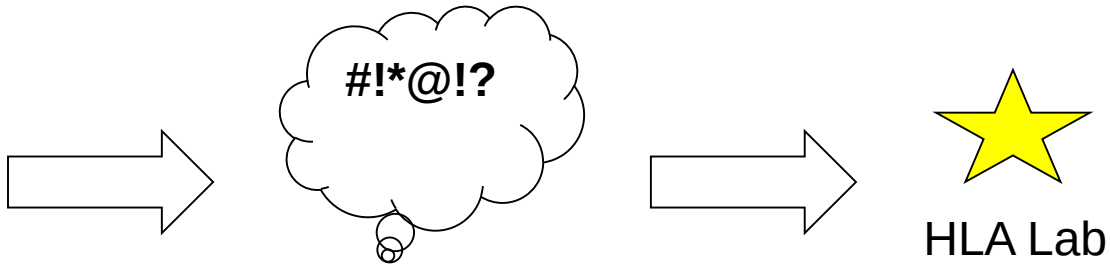
Mislabeled units of umbilical cord blood detected by a quality assurance program at the transplantation center

Jeffrey McCullough,[1,2] David McKenna,[1] Diane Kadidlo,[3] David Maurer,[1] Harriett J. Noreen,[4] Kathy French,[5] Claudio Brunstein,[6] and John E. Wagner[7]

[1]Department of Laboratory Medicine and Pathology, [2]Institute for Engineering in Medicine, and [3]Academic Health Center, [4]University of Minnesota Medical Center, Fairview; and [5]Blood and Marrow Transplant Program and Departments of [6]Medicine and [7]Pediatrics, University of Minnesota, Minneapolis

We instituted procedures to check the identity of cord blood unit provided for transplantation by carrying out ABO and human leukocyte antigen (HLA) typing of the thawed units before transplantation. ABO typing is done using standard techniques. Rapid HLA class I serology is with monoclonal antibody trays (One Lambda Inc) using standard incubations. One mislabeled umbilical cord blood (UCB) unit was detected on the day of intended transplantation by repeat ABO typing of the thawed unit at our transplantation center. Because ABO typing will not detect all labeling errors, the rapid serologic class I HLA typing procedure was done on thawed units just before transplantation for all units without an attached segment. This procedure identified a second mislabeled unit. In a 6-year period, 2 of 871 (0.2%) cord blood units sent to us for transplantation were mislabeled and potentially would have been transplanted incorrectly. This error rate of 1 per 249 (0.4%) patients could have potentially devastating consequences. (Blood. 2009; 114:1684-1688)





Guiding Patient Care…

Development and operation of a quality assurance system for deviations from standard operating procedures in a clinical cell therapy laboratory

D McKenna, Jr[1], D Kadidlo[2], D Sumstad[2] and J McCullough[1,2]

[1]Department of Laboratory Medicine and Pathology, Division of Transfusion Medicine, University of Minnesota Medical School, Minneapolis, MN, USA

[2]Cell Therapy Clinical Laboratory, Fairview-University of Minnesota Medical Center, Saint Paul, MN, USA

CYTOTHERAPY 2003:5(4):314-322.

TRANSPLANTATION AND CELLULAR ENGINEERING

Cell loss and recovery in umbilical cord blood processing: a comparison of postthaw and postwash samples

Vincent Laroche, David H. McKenna, Gary Moroff, Therese Schierman, Diane Kadidlo, and Jeffrey McCullough

TRANSFUSION 2005;45:1909-1916.

TRANSPLANTATION AND CELLULAR ENGINEERING

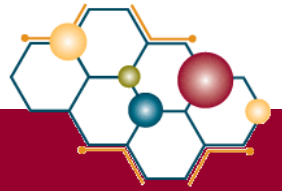
Issues in the quality of umbilical cord blood stem cells for transplantation

Jeffrey McCullough, David McKenna, Diane Kadidlo, Therese Schierman, and John Wagner

TRANSFUSION 2005:45:832-841.

Collection*

*if time permits



Rate/Impact of Contamination

Klein, et al (BBMT 2006):

- Retrospective analysis of 2,935 HSCs (1990-2004)
- 36/2,935 (**1.2%)** contaminated
  - See table (next slide) for breakdown
- Coag-neg Staph (19)
- **One death day +7 post tx (Pseudomonas cepacia)**
- **No additional adverse sequelae**

Klein M, et al. Microbial contamination of hematopoietic stem cell products: incidence and clinical sequela. Biol Blood Marrow Transplant. 2006 Nov;12(11):1142-9.

Rate/Impact of Contamination

Table 1. *Microbially Contaminated Stem Cell Products*

HSC Product	Preprocessing*	Postprocessing*	At Thaw*	Total	Total HSC Products†	Incidence of Contamination (%)
BM	13	9	1	22	1666	1.3
Allogeneic	10	5	0	15	1257	1.2
Autologous	3	4	1	8	409	2.0
PBSC	4	2	0	6	919	0.7
Allogeneic	1	0	0	1	296	0.3
Autologous	3	2	0	5	623	0.8
UCB	3	4	0	7	350	2.0
Related	3	2	0	5	18	27.8 *
Unrelated	0	2	0	2	332	0.6
Total	20	15	1	36	2935	1.2

HSC indicates hematopoietic stem cell; BM, bone marrow; PBSC, peripheral blood stem cell; UCB, umbilical cord blood.
*Phase in processing when contamination occurred.
†Total number of the type of product infused at our center during study period.

Klein M, et al. Microbial contamination of hematopoietic stem cell products: incidence and clinical sequela. Biol Blood Marrow Transplant. 2006 Nov;12(11):1142-9.

Rate/Impact of Contamination

- Padley D, et al (Transfusion 2007):
  - Retrospective analysis of 7,233 HSCs (1998-2006)
  - 119/7,233 (**1.6%**) contaminated
    - See table (next slide) for breakdown
  - Coag-neg Staph (73)
  - **No adverse sequelae**

Padley D, et al. Sterility testing of hematopoietic progenitor cell products: a single-institution series of culture-positive rates and successful infusion of culture-positive products. Transfusion. 2007;47(4):636-43.

Rate/Impact of Contamination

Padley D, et al (Transfusion 2007)

TABLE 1. Product culture-positive rate*

Product	Contamination rate	Excluding culture-positive donors†
Apheresis PBPCs or DLI	111/6975 (1.6)	80/6944 (1.2)
Marrow	8/258 (3.1)	7/257 (2.7)
Total	119/7233 (1.6)	87/7201 (1.2)

* Data are reported as number (%).

† Excluding products collected from donors that had documented positive cultures at the time of collection.

Padley D, et al. Sterility testing of hematopoietic progenitor cell products: a single-institution series of culture-positive rates and successful infusion of culture-positive products. Transfusion. 2007;47(4):636-43.

Rate/Impact of Contamination

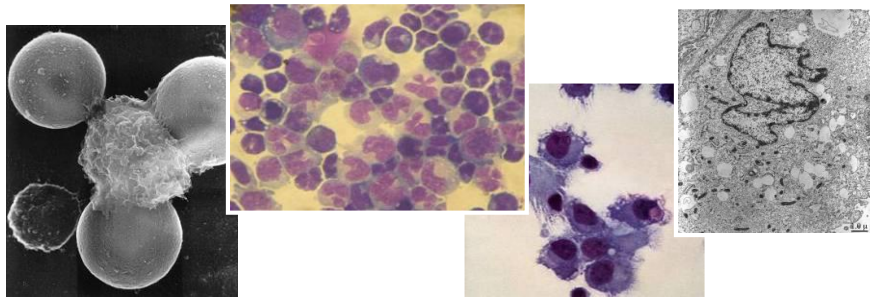
Padley D, et al (Transfusion 2007)

TABLE 2. Organisms isolated from HPC products

Organisms	Isolates	Infused		
		Total	Autologous	Allogeneic
Coagulase negative staphylococci	73	57	49	8
Staphylococcus aureus	8	5	1	4
Corynebacterium sp.	7	5	4	1
Enterococcus faecalis	6	6	6	0
Acinetobacter sp.	3	1	1	0
Moraxella sp.	2	0	0	0
Micrococcus sp.	3	2	1	1
Gram-negative bacillus	3	3	3	0
Stenotrophomonas maltophilia	3	0	0	0
Pseudomonas aeruginosa	2	2	2	0
Acid-fast bacilli	1	1	1	0
Escherichia coli	1	1	0	1
Enterobacter cloacae	1	1	1	0
Filamentous fungus	1	1	1	0
Propionibacterium sp.	1	1	1	0
Ralstonia pickettii	1	1	1	0
Staphylococcus hemolyticus	1	1	1	0
Staphylococcus lugdunensis	1	1	1	0
Streptococcus viridans	1	1	1	0
Chaetomium sp.	1	0	0	0
Chryseobacterium sp.	1	0	0	0
Clostridium perfringens	1	0	0	0
Methylobacterium sp.	1	0	0	0
Pseudomonas fluorescens/putida	1	0	0	0
Group A streptococcus	1	0	0	0

Padley D, et al. Sterility testing of hematopoietic progenitor cell products: a single-institution series of culture-positive rates and successful infusion of culture-positive products. Transfusion. 2007;47(4):636-43.

Thank you!



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&
Materials Management/ Administrative & Support Staff

PACT
Production Assistance for Cellular Therapies
National Heart Lung and Blood Program

BEST

MEDICAL SCHOOL
University of Minnesota

Product Analysis Forms and Formsnet3

- Importance of faxing or transmitting results ASAP
- Enter directly in Formsnet3
  - Standard method of reporting in near future
    - Save on time by not having to fill out paper form
    - Reduce errors by ensuring legibility

For more info reach out to the AC/CC Team

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Evaluation Reminder

Please complete the Council Meeting 2017 evaluation in order to receive continuing education credits and to provide suggestions for future topics.

We appreciate your feedback!