Collecting Umbilical Cord Blood

Dr. Michael T. Medchill, MD
Consent

• **Verify** patient has been consented and meets general eligibility requirements
  ➢ 18+ years old
  ➢ Single gestation (no multiples)
  ➢ 36+ weeks
  ➢ Good health history
  ➢ May verbally consent the patient

(Specific eligibility questions should be directed to coordinator or blood bank.)
Preparing for Collection

- Collection Supplies:
  - Collection Bag
  - 2 Blue Clamps
  - Needle Guard
  - Sterile Adapter (C/S only)

Organize your supplies on the delivery table so they are easily accessible.

The sterile adapter is the only piece that should be placed in a “sterile field”.

[Image of collection supplies]
How Umbilical Cord Blood is Collected

- Baby is not touched
- The mom and baby are not harmed
Deliver the Baby / Clamp the Cord

Following the birth of the baby and prior to delivery of placenta:
Place two surgical clamps or cord clamps on the cord as close as possible to the baby and cut between them.
Cleaning the Umbilical Cord

- Select a cord venipuncture site at the lowest possible point.
- Wipe the cord with gauze or sterile towel to remove excess fluids.
- Clean with Chloraprep swab
Cannulation

Cannulate the umbilical vein (bevel down) with the needle attached to the cord blood bag.
In a Cesarean Section the physician cannulates with the needle on a sterile adapter and CB personnel or other OR assistants can connect the blood bag needle into the sterile adaptor.

Then...the **waiting** game begins
- Stabilize the cord
- Allow sufficient time for **gravity** to empty
- Ensure blood bag is lower
- Gently rock the bag to mix with anticoagulant
- Wait until blood flow ceases and cord appears blanched
IMPORTANT – Collect as much cord blood as possible.

Insufficient volume will render the cord blood unit unusable for stem cell transplant. Larger volume collections mean a larger volume of stem cells collected. Units containing a high volume of cells are optimal for transplantation.
What’s My Big Secret?
Other Blood Samples

If the hospital protocol requires collecting a neonatal sample for ABO typing or cord gas pH testing:

• Take the smallest sample necessary for gas pH testing
• ABO sample can be obtained after CB collected
• Less than 3ml blood volume necessary
Not every umbilical cord has an optimal amount of blood, **BUT** most often there is a lot of blood left behind.
"If you're LUCKY enough to get a second chance at something, don't waste it."

~UNKNOWN
Maximizing the Collection

- Once the blood flow has seemed to stop then re-clamp the cord just above your insertion site.
- Remove the needle and carefully readjust.
- Milk the cord in an upward motion and re-clamp higher.
Maximizing the Collection

• Once the placenta separates and begins to come through the vaginal canal there is another gush of blood that is pushed into the cord.

• Repeat the process of cleaning the cord (with new gauze and Chloraprep) and re-cannulate just above your clamp when you see the cord fill again.
Finishing the Collection

Wait until blood flow into bag ceases and carefully remove needle from cord.

Once blood has drained into bag, immediately cover the needle with the provided needle guard, strip and clamp the tubing, tie off the tubing above the clamps and cut off and dispose of remaining tubing with needle attached according to hospital’s safe needle disposal procedures.
Finishing the Collection

The consenters take over and finish the packing and shipping.
Cord Blood Donation--
It’s the chance to
GIVE LIFE TWICE!
Questions?
2016 Saving Lives

The Clinical /Research Regulatory Experience in Cord Blood Banking: Collection to Infusion

AZ CB Collected = 5669
AZ CB Transplanted = 31

Sharon Miller
UCCBB Director of Regulatory Affairs
FDA and the Public Consent and Collection Team

Guidance for Industry

Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance, contact the Division of Human Tissues, Office of Cellular, Tissue and Gene Therapies at 301-827-2002.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
August 2007
Public Banking to Anonymous Unrelated Recipients (Allogeneic) or Private Banking for Autologous use?

- Risk Based FDA Regulation...less regulation for autologous/ self (and first degree relative) banking
Off-label Use: Injecting a Licensed Cord blood for purposes other than “For use in unrelated donor hematopoietic progenitor cell transplantation procedures in conjunction with an appropriate preparative regimen for hematopoietic and immunologic reconstitution in patients with disorders affecting the hematopoietic system that are inherited, acquired, or result from myeloablative treatment.”

IND Research Use: required for injection of an unlicensed minimally manipulated cord blood (NMDP) or more than minimally manipulated CB.
### Historic 1998 - 2012 UCCBB Indications for Use - Diagnosis of Recipients Infused (Prior to licensure)

<table>
<thead>
<tr>
<th>Indications / Diagnosis</th>
<th># Recipients</th>
<th>% of total infused</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Myelocytic Leukemia (AML) (JML, JMML)</td>
<td>161</td>
<td>30%</td>
</tr>
<tr>
<td>Acute Lymphocytic Leukemia (ALL)</td>
<td>130</td>
<td>24%</td>
</tr>
<tr>
<td>Mucopolysaccharoidosis (MPS)</td>
<td>30</td>
<td>6%</td>
</tr>
<tr>
<td>Hodgkins Lymphoma (HLH) Lymphoma</td>
<td>27</td>
<td>6%</td>
</tr>
<tr>
<td>Chronic Lymphocytic Leukemia (CLL)</td>
<td>15</td>
<td>3%</td>
</tr>
<tr>
<td>Fanconi Anemia</td>
<td>15</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkins Lymphoma (NHL)</td>
<td>14</td>
<td>3%</td>
</tr>
<tr>
<td>Aplastic Anemia (AA)</td>
<td>11</td>
<td>2%</td>
</tr>
<tr>
<td>Chronic Myelogenous Leukemia (CML, JCML)</td>
<td>14</td>
<td>3%</td>
</tr>
<tr>
<td>Severe Combined Immuno Deficiency (SCID, Immunodeficiency)</td>
<td>14</td>
<td>3%</td>
</tr>
<tr>
<td>Myelodysplastic Syndrome (MDS)</td>
<td>8</td>
<td>2%</td>
</tr>
<tr>
<td>Hemophagocytic Lymphohistiocytosis</td>
<td>8</td>
<td>2%</td>
</tr>
<tr>
<td>Wiscott Aldrich Syndrome (WAS)</td>
<td>5</td>
<td>1%</td>
</tr>
<tr>
<td>Biphenotypic Leukemia</td>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>Hurler’s Syndrome</td>
<td>6</td>
<td>1%</td>
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<tr>
<td>Unknown</td>
<td>10</td>
<td>2%</td>
</tr>
<tr>
<td>Multiple Myeloma (MM)</td>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>3</td>
<td>1%</td>
</tr>
<tr>
<td>Osteopetosis</td>
<td>4</td>
<td>1%</td>
</tr>
<tr>
<td>APL, ADL, AMT, B-Thal, Burkits, CGD, FEL, LAD, LPD, Neiman-Pick, Omens, PNH, Renal cell</td>
<td>2 each</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Brain tumor, Breast C, CID, Krabbe, LAL, LCL, mantle cell, MZL, Monosomy 7, MML, PSD, RCMD, Ref Anem, sickle cell, XLP</td>
<td>1 each</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
### FDA REGISTRATION: Annual Autologous and Allogeneic FDA Recovery Site HPC/Tissue Registration

<table>
<thead>
<tr>
<th>PART I - ESTABLISHMENT INFORMATION</th>
<th>PART II - PRODUCT INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. OTHER FDA REGISTRATIONS a. BLOOD FDA 2830 NO.</td>
<td>16. ESTABLISHMENT FUNCTIONS AND TYPES OF HCT/Ps</td>
</tr>
<tr>
<td>b. DEVICES FDA 2851 NO.</td>
<td>Types of HCT/Ps</td>
</tr>
<tr>
<td>c. ORG FDA 2856 NO.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Establishment Functions</th>
<th>Types of HCT/Ps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recover</td>
<td>Season</td>
</tr>
<tr>
<td>Package</td>
<td>Process</td>
</tr>
</tbody>
</table>

| e. Embryo | f. Fetal | g. Heart Valve | h. Ligament |
| i. Oocyte | j. Pericardium | k. Peripheral Blood Stem Cells | l. Sarcoma |
| m. Semen | n. Skin | o. Sexual Cell Therapy Products | p. Tendon |
| q. Umbilical Cord Blood Stem Cells | r. Vascular Graft | |

| a. Parathyroid | b. | c. | d. |

### Address

Clinimmune Labs
Attn: Brian M. Reed, Ph.D.
12635 E. Montview Boulevard
Suite 100
Aurora, Colorado 80045

### Phone Numbers

- Phone: 303-724-0535
- Fax: 303-724-0635

### Date

Date: 12/1/16

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**Image Note:** The image shows a section of a form related to FDA registration for cellular and tissue-based products. The form includes detailed information such as establishment functions, types of HCT/Ps, and address details. The form is part of the FDA's regulatory requirements for the production and distribution of these medical products.
PUBLIC Bank is the second in the world to obtain: FDA Biologic License # 1855 issued May 24, 2012

- How does licensure affect public collection sites and the teams that consent, collect, evaluate and assess donor risk?
FDA Laws and Regulations: Donor risk/eligibility, Consenting and Shipment

- The FDA has moved from the collection and processing of HPC, Cord Blood to the “Storage, Processing and Distribution”.
- FDA: Fresh cord blood must be stored at 15-25 °C (59-77°F)-any deviation will not be licensed.
Public Consent and Collection Team

- Since 2012 FDA biologic licensure for public banking, there is no longer a requirement to obtain IRB research review and approval for the recovery of HPC, Cord Blood waste products banked for clinical use or used as de-identified waste products for research.
- Although cord banking accrediting agencies (AABB, FACT) maintain review of collection hospitals, the FDA does not inspect recovery sites (Labor and Delivery decks). AABB accreditation does require a collection site inspection.
- Informed Donor consenting continues and option to refuse research is offered as an option. Review may still be requested for approval by the hospital IRB.
- The UCCBB goal is to keep it simple!
Maternal Donor Testing for Communicable Diseases

- 21 CFR 1271.80 (b) Maternal Test sample must be collected at, or up to 7 days before or after product cord blood collection.
- Inf D Test sample dilution? >2000 ml colloids up to one hour before collection.
- 21 CFR 1271.80(c) Infectious Disease Test Kits used must be licensed!
HPC Donor Risk Assessment Screen for Communicable Diseases:
History for BOTH Donor and Family
Questionnaires and Hospital History and Physicals
(For HPC, Cord Blood – Both maternal and baby)
Collection Hospital FDA Regulated Donor Risk: H & P Screening Issues: It’s not just infectious disease testing and it’s not just the baby

- Maternal Donor Purified protein derivative (PPD) test for TB +.....Immunized (BCG) or exposure.
- Abnormal PAP test on Maternal Donor....ASCUS is OK.

<table>
<thead>
<tr>
<th>Historic Abnormal PAP Grade</th>
<th>Collection?</th>
<th>Collection-if abnormal before delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCUS</td>
<td>Yes</td>
<td>yes</td>
</tr>
<tr>
<td>AGUS</td>
<td>Yes if normal test before delivery</td>
<td>no-unless donor is stable and can be reached after six week PP result</td>
</tr>
<tr>
<td>LGSIL</td>
<td>Yes if normal test before delivery</td>
<td>no-unless donor is stable and can be reached after six week PP result</td>
</tr>
<tr>
<td>HGSIL</td>
<td>Yes if normal test before delivery</td>
<td>no-unless donor is stable and can be reached after six week PP result</td>
</tr>
</tbody>
</table>

- Chorioamnionitis....antibiotic treatment and maternal/baby blood cultures.
- Family History of Genetic Disease: BMS, BGP, BS, BF
Public Genetic Screening Issues

- Autoimmune disorders: Graves/Hashimotos vs. Hyper and Hypothyroidism? DM I?

<table>
<thead>
<tr>
<th>Autoimmune disorder</th>
<th>M</th>
<th>F</th>
<th>S</th>
<th>GP</th>
<th>A/U</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac Disease</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Crohn's disease or *ulcerative colitis</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Diabetes- insulin dependent- Type I</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Goodpasture's syndrome</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Grave's disease</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
<tr>
<td>Lupus (Systemic)</td>
<td>R</td>
<td>AT</td>
<td>R</td>
<td>AT</td>
<td>AT</td>
</tr>
</tbody>
</table>

- Blood disorders: ITP? Low platelets?
- Gallbladder removed before 30?
- Sickle Cell or Thalassemia Hemoglobin for trait(homozygous) vs disease (disease). SCIDs.

<table>
<thead>
<tr>
<th>Result</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td>F + A + 17.5 % Bart's Carrier per UH Clin Chem</td>
<td>Asian or Pacific Isl</td>
</tr>
<tr>
<td>A+F+S 15.3% sickle cell carrier state</td>
<td>Hispanic</td>
</tr>
<tr>
<td>F+A+D bands present D-Punjab Trait</td>
<td>Hispanic</td>
</tr>
<tr>
<td>F + A + Bart's Trait bands present</td>
<td>Black or African Ame</td>
</tr>
</tbody>
</table>
Quality Sterility Prep for Cleaning the Umbilical Cord for In-Utero Collection method

- Prior to birth of the placenta, select a cord venipuncture site.
- Wipe cord with the gauze to remove excess fluid.
- Clean area with Chloroprep swab provided in kit. *Swipe up with one side of the swab and down with the other.*
- Wait 30 seconds for the Chloroprep to dry before venipuncture.

Please...

* Do **not** allow maternal blood to contaminate venipuncture site.

* Do **not** apply excessive traction to the cord.

* Do **not** manually remove the placenta.
Public Cord Blood: Collection Volume

Blood Volume (mL) = White (CD34+) and nucleated RBC
Avg 150 ml collected CB = Avg 1.7 x 10⁹ TNC = Avg 8.0 x 10⁶ CD34

IMPORTANT - Collect as much cord blood volume as possible to obtain a critical cell dose for clinical use

Insufficient Volume/Cell count = Fresh HPC Research Use CBU

- Inadequate Volume < 100 mL
- Inadequate Clinical Volume > 100 mL
- Clinical Use Volume > 150 mL
MEDIPost:
CARTISTEM is a drug for the treatment of knee cartilage defects caused by degeneration or repeated trauma in the osteoarthritis. It is composed of mesenchymal stem cells isolated and expanded from umbilical cord blood. CARTISTEM does not require donor-recipient matching, nor does it present any immune rejection problem. It is available to any patient and effective even for those above the ages of 50. It is undergoing Phase I/IIa clinical trials.

PNEUMOSTEM aims to treat pulmonary disorders such as bronchopulmonary dysplasia (BPD). BPD is a lung disorder affecting prematurely born infants, causing severe degree of inflammation and fibrosis (tissue-scarring) in the lungs. Pre-clinical study using animal models.

NEUROSTEM aims to treat patients suffering from neuro-degenerative disorders such as Alzheimer’s disease (AD), Amyotrophic Lateral Sclerosis (ALS) and stroke via recovery of functionality and tissues of the central nervous system.
CB Potency: Collected Volume, Total Nucleated Cell (TNC)
Minimal CB Manipulation
Closed Processing System
GMP Clean Room Processing Required

Twenty two separate equipment, clean room, and process validations performed and submitted to FDA after August 2015 Facility move.

FDA Prior Approval Supplement (PAS) to obtain approval to process licensed CBU. IND CBU production allowed for clinical use, until PAS approval.
Licensed products require a package insert from the manufacturer which lists all components of the product, dose instructions and possible adverse events associated with infusion.
To date:
There have been a total of 784 UCCBB CBU shipped for infusion.

31 of those shipped were collected in our partner state of Arizona.

Average TNC of AZCBU Shipped: $2.4 \times 10^9$
### 1999-2012 UCCBB Recipient Demographics

- Review recipient Age, Gender and Diagnosis

<table>
<thead>
<tr>
<th>Recipient Age (yrs) at Infusion</th>
<th>Number of UCCBB Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 yr</td>
<td>72</td>
</tr>
<tr>
<td>2-5 yr</td>
<td>91</td>
</tr>
<tr>
<td>6-11 yr</td>
<td>91</td>
</tr>
<tr>
<td>12-17 yr</td>
<td>57</td>
</tr>
<tr>
<td>18-55 yr</td>
<td>152</td>
</tr>
<tr>
<td>&gt;55 yr</td>
<td>39</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recipient Sex</th>
<th>Number of Male</th>
<th>Number of Female</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient Sex</td>
<td>310/539 (58%)</td>
<td>229/539 (42%)</td>
<td>4</td>
</tr>
</tbody>
</table>
Utilization of UCCBB Minority Cord Blood Units

n = 640

Cumulative Utilization

<table>
<thead>
<tr>
<th>Hispanic</th>
<th>Caucasian</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.135</td>
<td>0.050</td>
<td>0.050</td>
</tr>
</tbody>
</table>

p < 0.0001

B Freed
In 2007, CBU required $1.2 \times 10^9$ TNC to process, in 2012 that number was increased to Collected $2.0 \times 10^9$ (1.8 banked) to focus on banking units that can be used clinically.

\[ y = 877938x + 1E+09 \]

\[ R^2 = 0.05 \]

CBU Released Over Time and TNC

CBU Released from 1998 to 2012

UCCBB CBU Released from 1998 to 2012
First TCH HPC, Cord Blood Transplant
Birth: January 17, 1996
Diagnosis of very high risk Acute Lymphoblastic Leukemia (ALL), t(4;11), April 1996
HSCT: July 24, 1996

1 year after HSCT

4 years after HSCT

R. Quinones
There are over 310 patients alive today because of the You!

14 yo boy (DOB 5/85) Diagnosis: Acute Myelogenous Leukemia (AML) March 1997 Relapse

Proposed rx: Allogeneic BMT

No Matched sibling or other relatives
Matched unrelated marrow: Available in 3-4 months
Matched unrelated cord blood: 5/6 match available immediately

Unrelated cord blood HSCT June 1999

Outcome: Complete Remission In College

R. Quinones
Learning Objectives:

**CBB History and Use-including Research:** AZ CBU are banked as licensed drugs regulated by the FDA. Donors have the option to opt out of “Research Use” of CBU. Hospital IRB are given the option of oversight for CB banked clinically and others as de-identified waste products used for research.

**Challenges and Improvement options:** AZ CBU were being banked with collected TNC $\geq 1.5 \times 10^{9}$. This results in a banked/frozen TNC of about 80% recovery ($\geq 1.2 \times 10^{9}$) that is too small to be considered clinically useful. Raising the collected TNC to $2.0 \times 10^{9}$ will and education on volume and sterility tips for quality CBU banking is helpful.

**Reach Diverse Populations:** AZ CBU banked are primarily Hispanic and most of the units released for transplant are of Hispanic race, thus serving a diverse population of recipients.

**Clinical Applications:** AZ fresh collected CBU that are not banked for clinical use and are not “Opted out” for research by the donor, are released to researchers in AZ. Clinical research is regulated by the FDA and may be utilized under the NMDP IND if minimally manipulated and not qualified as licensed CBU. UCCBB CBU transplants have saved the lives of many recipients with over 20 different diagnosis.
FDA Licensed Banking Costs per Unit
(1,500 units per year @ 25% of collections)

- Collections $694
- Processing $412
- Post processing $415
- Testing $432
- Space, equipment, maintenance $490
- Regulatory and informatics $202
- Indirect costs $185

Total $2,829

HRSA funding $1,282

Net -$1,547
Correlation between EGA and volume collected (total cords)

- Avg. Vol./TNC Col. EGA 35 = 84.0 mL/0.593
- Avg. Vol./TNC Col. EGA 36 = 90.8 mL/0.715
- Avg. Vol./TNC Col. EGA 37 = 90.2 mL/0.756
- Avg. Vol./TNC Col. EGA 38 = 89.9 mL/0.830
- Avg. Vol./TNC Col. EGA 39 = 95.5 mL/0.950
- Avg. Vol./TNC Col. EGA 40 = 94.9 mL/1.019
- Avg. Vol./TNC Col. EGA 41 = 98.4 mL/1.089
- Avg. Vol./TNC Col. EGA 42 = 96.8 mL/1.049

R² = 0.0065
Delayed Cord Clamping Review N=78

Mean
39.6 weeks EGA
118 seconds delayed,
80 mL CB
TNC of $0.76 \times 10^9$

$y = -0.0468x + 86.231$

$R^2 = 0.078$
Percent of TNC that are Stem Cells (CD 34)

Post-Process TNC $\times 10^{9}$ vs. Percent CD34 in Cord Blood

- Mean Percent CD34 = 0.41%
- Expected End Point 0.16% - 0.66% CD34
Complaint Files and Reports of Adverse Infusion Experiences

**Most Common AIE**

- **HTN**: 5
- **Nausea**: 2
- **fever chills**: 1
- **bradycardia**: 0

**Legend**:
- **ANC Engrafted**
- **DOC**
- **DNE**
Access to Transplant

Karen Dodson
Chief Operations Officer
Overview

- Need for Transplant
- Potential Barriers to Transplant and Solutions
- Economic Pressures and Solutions for Cord Blood Banks
The Reason Be The Match Exists

• Our Mission
  *We save lives through cellular therapy*

• Our Moonshot
  *Serve all who need cellular therapy*

• The Need
  20,700 related and unrelated transplants per year
    • 4,600/year for ages 0-19
    • 16,100/year for ages 20-74
Transplants Facilitated by Be the Match

FY 2016 is Forecast
Unmet Need U.S. Market Areas (2011-2013) - Pediatrics Ages 0-19

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Potential Barriers to Unrelated Transplant

Availability: Cord Blood Increases Access for People of Color

CBU

- 69% Caucasian
- 41% People of Color

Adult Donor

- 87% Caucasian
- 13% People of Color

FYTD 2016

Operated by the National Marrow Donor Program®.
Economic: More People Have Insurance

Percentage Uninsured in the U.S., by Quarter

Do you have health insurance coverage?
Among adults aged 18 and older

<table>
<thead>
<tr>
<th>% Uninsured</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>16.1</td>
</tr>
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<td>16.3</td>
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<tr>
<td>15.6</td>
</tr>
<tr>
<td>12.9</td>
</tr>
<tr>
<td>11.9</td>
</tr>
</tbody>
</table>

Quarter 1 2008-Quarter 1 2015
Gallup-Healthways Well-Being Index

GALLUP®
Economic: Changes in Payer Mix

Adult Transplant Programs, NMDP data (collected at Tandem Meeting 2015)
Economic: What happens when a barrier is removed?

HCT in US for MDS over age 65 and CMS coverage

- Estimated

Related
Unrelated

Operated by the National Marrow Donor Program®.
Prospective Study for Sickle Cell Disease, Multiple Myeloma and Myelofibrosis

**Principal Objective:** test whether allogeneic HCT improves health outcomes of affected beneficiaries (no pathogenesis or toxicity studies)

- Compare *survival* with non-allogeneic HCT therapy
- Adequately control for *selection bias* and potential confounding by *specific prognostic factors*
- Address *GVHD* and *transplant-related adverse events*
Patient Assistance Program

FY '15 activity by grant program

- Related Search Assistance*: 138 patients, $61,800 funds paid
- Search Assistance Fund: 568 patients, $1,355,229 funds paid
- Transplant Support Assistance: 1,411 patients, $2,048,020 funds paid

Operated by the National Marrow Donor Program®.
Health Care System: Transplant Center Capacity

• Workforce
  – Education for emerging providers
  – Research focused on the multidisciplinary team

• Space
  – Transplant unit and clinic capacity
  – Patient housing challenges and potential interventions

• Funding
  – Market maps and market potential
Providers: Late or Missing Referrals for TX

Referring physicians may:
• Believe that transplant outcomes have not improved
• Lack understanding of which patients to refer and timing
• Worry about managing post-transplant care

Transplant physicians may:
• Desire further access to expertise about cord blood unit selection and transplant
Providers: Increasing Patient Referrals

Clinical guidelines

Clinical toolkit: referral timing & post-transplant

Mobile app/online clinical & patient guides

Patient toolkit: post-transplant

Operated by the National Marrow Donor Program®.
Providers:
Leveraging Cord Blood Transplant Expertise

CBU Selection

“How I Treat” Publications

Physician Consultants

Treatment Consultation
Social: Be The Match® Patient and Health Professional Services

- Confidential one-to-one support and navigation
- Tailored educational materials
- Financial resources
- Fundraising information
- Insurance appeals
- Peer-to-peer connection
- Caregiver support

Jill, MSW, LICSW, Lead Patient Services Coordinator
• Medical practice has changed since funding began
• Increasing utilization of higher TNC units
• Higher costs to obtain quality, high TNC unit
Decline in Multiple Cord Blood Unit Transplants

FYTD 2015 FYTD 2016

- Declining use of multiple cord blood units for transplant
- Efficiencies realized by high TNC products
- Increase in haploidentical transplants for older patients
Cord Blood Bank Network

Strategically provide funding to support:

- Collection of units in diverse markets
- Collection of high quality, high total nucleated cell count units
- New indications for Cord Blood Transplant
- Transplant outcomes research
Access to Transplant Summary

• The cord blood bank network provides increased access to transplant
• Access has improved across all ages and ethnicities
• An unmet patient need still exists, especially for people of color
• Haploidentical transplants are increasing rapidly; long term outcomes are unknown
• Maintaining a robust network of cord blood banks is critical
Legal Restrictions in Distributing Cord Blood for Research

Kristen Rosati
Coppersmith Brockelman PLC
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Today’s Topics

• Potentially competing policies: advancement of research vs. individual control of tissue and data
• Compliance with the Common Rule
• Compliance with HIPAA
• Compliance with state laws
Potentially Competing Policies

- Advancement of research
  - 21st Century Cures Act
  - Precision Medicine Initiative
  - The Cancer Moonshot
  - Increased funding for NIH
  - The “Learning Healthcare System” (Institute of Medicine)

- Increasing individual control of tissue and data
  - Consent
  - Transparency
The Immortal Life of Henrietta Lacks

Doctors took her cells without asking.
Those cells never died.
They launched a medical revolution
and a multimillion-dollar industry.
More than twenty years later, her children found out.
Their lives would never be the same.

Rebecca Skloot
Apply to “human subjects research” if:

- Research is conducted or supported by a federal department or agency that has adopted the Common Rule (such as HHS)
- Where the institution engaged in the research has agreed to apply the federal regulations under the institution’s Federal wide Assurance (“FWA”) to all human subjects research regardless of the funding source
Common Rule Compliance

- It is only “human subjects” research if the activity: (1) obtains data through intervention or interaction with an individual; or (2) involves identifiable private information

- Key points:
  - Common Rule doesn’t presently apply to non-identifiable biospecimens
  - Common Rule doesn’t presently apply to de-identified data
What changes are proposed?

- Notice of Proposed Rule Making, 80 Federal Register 53933 (September 8, 2015)
- Sweeping changes proposed to the Common Rule:
  - Expands jurisdiction: would apply to all non-FDA regulated, non-exempt and non-excluded human subjects research conducted at a US institution that receives federal support for human subjects research, regardless of funding source for particular research
What changes are proposed?

- Changes the definition of “human subjects” to include non-identifiable biospecimens
  - Will apply prospectively only, three years after the final rule is published

- Requires “broad” consent for biospecimen collection and use for research
  - Will exclude research that generates information already known about an individual for validation testing and development of diagnostic tests

- Requires notification if non-identifiable information could be used for future research without additional consent
What changes are proposed?

- Other proposed changes to informed consent:
  - Changes to the organization of informed consent documents
  - Informed consent for federally funded research must be posted on a federal website within 60 days after the trial closes to recruitment
  - New informed consent waiver criteria
What changes are proposed?

- Under new data privacy and security standards, institutions and investigators will have the option of:
  - Applying the OHRP-specific measures that would function as a safe harbor (not yet published)
  - Apply the requirements of the HIPAA Security Rule
HIPAA Compliance

- HIPAA applies to “covered entities” and “business associates”
- HIPAA applies to “protected health information” (PHI)
  - Demographic information that includes any listed “identifier”
  - Biospecimens without identifiers are not treated as PHI
HIPAA Identifiers

- Data elements about individuals and their family members, household members, or employers:
  - Name;
  - Street address, city, county, precinct, or zip code (unless only the first three digits of the zip code are used and the area has more than 20,000 residents);
  - The month and day of dates directly related to an individual, such as birth date, admission date, discharge date, dates of service, or date of death;
  - Age if over 89 (unless aggregated into a single category of age 90 and older);
  - Certain numbers related to an individual (telephone numbers; fax numbers; social security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers, serial numbers, and license plate numbers; device identifiers and serial numbers);
  - Email addresses, Web Universal Resource Locators (URLs) and Internet Protocol (IP) addresses;
  - Biometric identifiers, such as fingerprints;
  - Full-face photographs and any comparable images; or
  - Any other unique identifying number, characteristic, or code.
De-identification of PHI

  - “Safe Harbor” method
    - Removal of all HIPAA “identifiers”
  - “Expert Determination” method
    - Determination that there is a “very small” risk that the anticipated recipient will be able to identify an individual

- De-identification through coding: HIPAA-compliant code may not be derived from individual identifiers (i.e. no initials, scrambled SSN or medical record number, etc.)
HIPAA Privacy Rule Compliance

1. The research involves only de-identified data

2. The research uses or discloses a “Limited Data Set” (mostly de-identified data) and the covered entity has a “Data Use Agreement” in place with the recipient of the Limited Data Set

3. The research subject or the subject’s authorized representative has signed a written HIPAA authorization
   • If PHI will be used or disclosed in future research, must describe with enough detail so that a person will understand this

4. An IRB has waived the requirement for authorization

5. The activities are just to prepare for research and required representations are obtained from the researchers
6. The use or disclosure is for patient recruitment purposes;

7. The research involves only the information of decedents and required representations are obtained from the researchers;

8. The disclosure of the PHI is required by law; or

9. The research is “grandfathered”
State Laws to Watch

- State health information confidentiality laws that regulate “sensitive” information, such as genetic information or HIV status
- State genetic testing laws, some of which apply to genetic testing conducted in research
- State laws governing the ownership of biospecimens or genetic material
- State laws governing the use or sale of human tissue
- State laws related to research participant rights
Questions?

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Program Overview

Jennifer Botsford, ABRC
April 7, 2016
Arizona Biomedical Research Commission

1984 - Established by Statute
2011 - Moved under ADHS

to identify and support innovative biomedical research
to improve the health of all Arizonans
9 Commissioners

3 Public Members
- Brandy Wells
- Vacant
- Vacant

3 Medical Community Members
- Peter Kelly, MD
- Mitchell Shub, MD
- Hugo Vargas, MD

3 Scientific Community Members
- John Ragan
- Vacant
- Vacant
4 Core Programs

- Research Grants
- Biospecimen Locator
- Research Education
- Public Cord Blood
Public Cord Blood
Arizona is a leader in the field of public cord blood collection

Statute § 32-3212

- 2007
- OB providers required to educate expectant parents about saving cord blood
  - Public donation
  - Private banking
- Distribute ADHS brochure
Established by ABRC in 2011

Funded through Lottery Revenue
  • Disease Control Research Fund

Reimbursement from transplanted cords
Why Donate Cord Blood?

- out of 10 patients lack a family bone marrow match
- Free to Donate
- Diseases can be treated or cured using cord blood
- Non-transplantable units made available for research, with consent
Why Collect in Arizona?

▲ diverse registry = ▲ chance of a match

✓ Unique gene pool
✓ 86% of cord blood units collected in Arizona are from minority donors
✓ 77% of AZ cord blood units used in transplants are for minority patients
Arizona Ethnicity Summary Data for Total Units Collected

- Hispanic, 76%
- Caucasian, 14%
- African American, 5%
- Asian & Other, 4%
- Native American, 1%
Race/Ethnicity
Cord Blood Units Used in Transplants

- Hispanic, 75%
- White, non-Hispanic, 16%
- Native American, 3%
- African American, 3%
- Asian, 3%
Benefits to Arizona

- **Advocate** for and address the needs of underserved citizens
- Increase **awareness** of public cord blood banking
- **Resource** for AZ researchers
- **Attract** cellular, biomedical, and technology **businesses** and organizations to strengthen the **local economy**
What do we do?

Collect and store cord blood

List cord blood units on national and international registries

Educate:

- Expectant parents
- Health professionals
- Public
- Next generation
Process

- Obtain patient’s written consent
- Between birth and delivery of placenta, OB provider collects into bag
- Send to cord blood bank
- Process, test, validate
- Cryopreserve (freeze) within 48 hours
Cord blood is some patients’ best or only hope.

Arizona cord blood units used for transplants around the world.

Arizona cord blood units banked and registered with the National Cord Blood Inventory.
Why is APCBP Successful?

- Partner hospitals
  - Nurse coordinators
  - Consenters
- Local non-profit
- Accredited cord blood bank
Nurse coordinators

- Train consenters in partner hospitals
- Coordinate education, outreach, and overall collection management

Central Arizona
(St. Joseph’s Hospital and Medical Center)

Southern Arizona
(Tucson Medical Center)
• Partners with the nurse coordinators
• Educates and outreaches
  • OB providers
  • Next Generation
  • Community Leaders
  • General public
Consenters

- Placed in partner hospitals
- Answer questions one-on-one and consent moms-to-be
- Present in the delivery room to answer questions and guide new collectors
Cord Blood Bank

- ClinImmune, University of Colorado
  - Accredited by AABB, FACT
  - Test, process, and validate cord blood units
  - Store cord blood units
  - Coordinate with donor hospitals, national and international registries, and recipient hospitals
  - Train AZ hospitals
Abrazo Central Campus reaches out to families and nursing school students

- Families learn
  - Stem cells
  - Arizona Public Cord Blood Program
- Consenter educates local nursing school students

- Joined APCBP in 2011
- 1st cord blood collected by the program was collected at Abrazo Central Campus
Maricopa Integrated Health Systems
building strategy to reach minority mothers through pre-natal classes

- New marketing strategy
  - Include APCBP information in pre-natal classes
  - More time to consider donating
  - Ability to consider before they are in labor

- Joined APCBP in 2011
- 2 cords in 2015 were used in transplants to save lives
EXTRA! EXTRA!

St. Joseph’s Hospital and Medical Center

collects the most transplanted cord blood

- St. Joe’s consistently collects high volume cord blood units
  - more likely to be banked
  - more likely to be transplanted

- Joined APCBP in 2011
- 2000+ collections
- 20+ CBUs sent for transplant
Baby delivered at **Tucson Medical Center** helps save Colorado Patient’s life

- Joined APCBP in 2014
- 2 consenters and 1 nurse coordinator
- 1st cord for transplant was sent this year

“I was so excited to learn that one of our cord blood units was used for transplant! It is so encouraging to know that the selfless generosity of this donor family combined with our efforts has made all the difference in the world to a leukemia patient and their family. The positive ripple effect our program creates is truly immeasurable, and I’m looking forward to more matches in 2016.”

- TMC consenter Ali Baker
Save the Cord Foundation speaks with National Association of Hispanic Nurses at the 2nd Annual Conference, Phoenix Chapter

- Joined APCBP in 2013
- **Thousands** of OB professionals educated
- **Thousands** of students educated
- Educated new & experienced nurses
- Received enthusiastic feedback
- Facilitated new contacts
- Increase minority donations
ClinImmune, University of Colorado sends 32nd Arizona cord blood unit for transplant

- Moves to new upgraded state-of-the-art facility
- Banked over 600 Arizona cord blood units

- AABB certified
- FACT certified
- Partnering with AZ since 2011
Key Messages

Blood left in the umbilical cord after a baby is born is a unique source of life-saving stem cells.

The baby and the mother are not harmed.

Historically, considered medical waste.

Today, collected and stored around the world, both privately and publicly.
Stem cells

I don’t know how to multiply!

It’s easy, silly, just divide!
Questions?

Thank you!
Cord Blood Education, STEM Careers & the Next Generation

Charis Ober
Executive Director
Save the Cord Foundation
Partners in Advancing Public Cord Blood Donation and Education
“Education is the most powerful weapon which you can use to change the world.”

–Nelson Mandela
STEP ONE: **Awareness** and **Education**.

*Without awareness and education nothing happens.*
Who

• Expectant Parents
• Health Professionals
• The Public
• The Next Generation
Parents Amy Vasquez and Chris Colbert with their daughter, who was the 1000th cord blood donor in Arizona at TMC

In a 2014 study of 600+ recent and expectant parents conducted by BioInformant Worldwide LLC, 92% of respondents who elected to publicly donate cord blood stated that they learned about the option through a personal relationship (family, friend, neighbor), while only 3% of those who publicly donated cord blood learned about the option via their Obstetrician.
Lack of Awareness: A Major Problem for Cord Blood Preservation

In a recent study of 600+ recent and expectant parents by BioInformant Worldwide LLC, a research firm specializing in stem cell data, 77% of respondents who did not store cord blood (publicly or privately) stated that it was because they did not know it existed as an option [6].

Respondents Who Did Not Store Cord Blood

- Unaware: 77%
- Aware: 23%
Important Statistics

• U.S. parents privately store cord blood for approximately 2.6% of births
(102,000 / 3,945,000 births = 2.6%).

• If publicly donated cord blood is included too, then approximately 3% of U.S. parents store cord blood at birth
(There are about 5 cord blood units privately stored for every cord blood unit that is publicly donated)
Education Outreach to **Health Professionals**
Physicians, Midwives, Nurses, & Researchers

Left: Arizona Perinatal Trust promotes public cord blood donation & the AZ PCBP

Right: CAPPAC birth professionals learning about cord blood & AZ PCBP

Above: Jennifer Botsford at the University of Arizona Collaborator Fair
Hispanic and Minority Outreach

National Association of Hispanic Nurses Learns about Cord Blood & the Arizona Public Cord Blood Program
The General Public

- July: Cord Blood Awareness Month in Arizona
- Cord Blood Conference on April 7th
- Public information and education via media partnerships
- AZPCBP brochures and posters for expectant parents, OB providers, midwives and the public
Our Education Partners

1. Southern Arizona Arts & Cultural Alliance
2. Teachers in Industry
3. Arizona Science Teachers Association
4. Arizona Public Cord Blood Program
5. Arizona Department of Health Services
6. Arizona Biomedical Research Commission
   - Grants
   - Biospecimen Locator
   - Education
   - Public Cord Blood
NEXT GENERATION: Student Education Outreach

• Elementary, Middle, and High School Programs
• Next Generation Cord Blood Education Program developed with teaching faculty
• Inspiring the next generation of scientists, engineers, and problem solvers!
• STCF Intern program at key Arizona universities
Autism and Brain Disorders

Dr. Joanne Kurtzberg (MD)
Dr. Geraldine Dawson (PhD)

- Developing cell-based therapies to restore damaged areas of the brain
- Cord blood stem cells to treat autism, cerebral palsy, and stroke

Autism and Cord Blood Stem Cells: FDA Gives Green Light for Groundbreaking Clinical Trial

SACRAMENTO, CA – Sutter Neuroscience Institute, a recognized Center of Excellence; and CBR (Cord Blood Registry), the world’s largest stem cell bank, are launching the first FDA-approved clinical trial to assess the use of a child’s own cord blood stem cells to treat select patients with autism. This first-in-its-kind placebo controlled study will evaluate the ability of an infusion of cord blood stem cells to help improve language and behavior. The study is in conjunction with the Sutter Institute for Medical Research.

UCB stem cells rebuild the blood and immune systems

“We have evidence to suggest that certain children with autism have dysfunctional immune systems that may be damaging or delaying the development of the nervous system”

— Dr. Chez

Hearing Loss

Cord Blood Stem Cell Infusion for Children with Acquired Hearing Loss

- Investigating whether cord blood stem cells repair hearing loss
- Hearing ability affects your language development
- Can lead to poor academic and social development

Diabetes

- Isla Robinson: 1st child given her own cord blood to prevent type 1 diabetes
- Researchers hope the immune cells in her umbilical cord blood will reboot her immune system and prevent the damage of insulin producing cells
STCF Internship Program and The Next Generation

- Student outreach by STCF Interns at the University of Arizona, ASU and NAU
- Cord blood Education in the classroom, on campus and with other organizations
- Creating STEM careers

Raising cord blood awareness & research at the U of A
Educating young scientists at AZ Stem Adventure
Tanque Verde Elementary School students learn about cord blood
NEXT GENERATION: Cord Blood
NEXT GENERATION: Cord Blood

VIDEO LINK (optional)
The Big Picture for Our State

• Expand **cord blood donation** across our state

• Make **cord blood education a standard** in our classrooms

• Fund and encourage important **stem cell research** at AZ universities

• Continue important legislative **funding** so the Arizona Public Cord Blood program will become a legacy health initiative to serve the underserved of our state

• **Attract cellular, Bio and Pharma businesses** that provide a scientific business platform for science-based careers
The 6th C’s of Arizona

It’s Cells....Stem cells are the medicine of the future and good business for our state!

Cattle

Cotton

Climate

Citrus

Copper
“The future depends on what we do in the present.”
–Mahatma Gandhi

Education is the key!
Cord blood treatment from the physician’s perspective

Dr Niketa C Shah MD
Bone Marrow Transplant Physician
Center for Cancer and Blood Disorder
Phoenix Children’s Hospital

Assistant Professor of Pediatrics
Department of Child Health
University of Arizona
Introduction

- What is a bone marrow or cord transplant?
  - Healthy bone marrow and blood cells are required to live.
  - Many diseases affect bone marrow so that it cannot function properly.
    - Congenital
    - Acquired
  - A marrow or cord blood transplant could be the best treatment option.
  - For some patients, it may be the only potential cure.
Introduction

Donors for stem cell transplant

- Matched siblings or matched related
- Parents or siblings for haplo-identical
- Matched or Mismatched unrelated

A; living adult volunteers (BM or PBSC)
B; umbilical cord blood units.
Dynamics of Bone Marrow or Cord Transplant

Conditioning therapy to remove abnormal marrow

Day-7

Mucositis
Infections

GI
Renal
Liver
Toxicities

Day 0

Acute GVHD
Idiopathic pneumonia
Infection

Day 14

New BM or Cord Cells Starts Working

Day 100

Late Effects

Chronic GVHD

Immunosuppressive medicines to prevent GVHD

G-CSF
### Difference Between Unrelated BM/PBSC graft Vs Unrelated Cord Vs Haplo identical

<table>
<thead>
<tr>
<th></th>
<th>Unrelated BM/PBSC</th>
<th>Cord</th>
<th>Haplo-identical</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Availability</strong></td>
<td>2-3 months</td>
<td>No wait time 1-10 days</td>
<td>No wait time 1-10 days</td>
</tr>
<tr>
<td><strong>Viability</strong></td>
<td>BM –Hours PBSC-Months</td>
<td>Cryopreserved for years</td>
<td>BM –Hours PBSC - Months</td>
</tr>
<tr>
<td><strong>Donor Discomfort</strong></td>
<td>Yes Anesthesia, Surgery, G-CSF</td>
<td>No</td>
<td>Yes Anesthesia, Surgery, G-CSF</td>
</tr>
<tr>
<td><strong>HLA Matching</strong></td>
<td>Near match or fully match 8-10/10</td>
<td>Mismatch possible 4-6/6</td>
<td>Half match</td>
</tr>
<tr>
<td><strong>Risk of Transplanting Genetic Disease</strong></td>
<td>None</td>
<td>Small possibility</td>
<td>None</td>
</tr>
<tr>
<td><strong>Stem cell Boost</strong></td>
<td>Available for second donation later</td>
<td>None</td>
<td>Available for second donation later</td>
</tr>
<tr>
<td><strong>Extra Cost</strong></td>
<td>Can be costly harvest</td>
<td>Cost of the cord</td>
<td>Can be costly for T cell depletion</td>
</tr>
</tbody>
</table>
## Difference Between Unrelated BM/PBSC graft Vs Unrelated Cord Vs Haplo identical

<table>
<thead>
<tr>
<th></th>
<th>Unrelated BM/PBSC</th>
<th>Cord</th>
<th>Haplo identical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil Engraftment</td>
<td>Rapid 10-21 days</td>
<td>Slower 3-4 weeks (Except double cord)</td>
<td>Rapid 10-21 days</td>
</tr>
<tr>
<td>Immune Reconstitution</td>
<td>Faster</td>
<td>Slower</td>
<td>Slower</td>
</tr>
<tr>
<td>Risk of infection post transplant</td>
<td>++</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Graft Versus Host Disease (GVHD)</td>
<td>Increase with HLA mismatch</td>
<td>Less frequent Less severe</td>
<td>Increase risk</td>
</tr>
<tr>
<td>Hospital Stay</td>
<td>GVHD</td>
<td>Slow engraftment Infection</td>
<td>GVHD</td>
</tr>
<tr>
<td>Experience</td>
<td>More</td>
<td>More</td>
<td>Less</td>
</tr>
</tbody>
</table>
Role of Cord Blood in Transplants by Patient Race

- **Black/African American**: 38% Cord Blood, 62% Bone Marrow or Peripheral Blood
- **American Indian/Alaska Native**: 24% Cord Blood, 76% Bone Marrow or Peripheral Blood
- **Native Hawaiian/Other Pacific Islander**: 71% Cord Blood, 29% Bone Marrow or Peripheral Blood
- **Asian**: 24% Cord Blood, 76% Bone Marrow or Peripheral Blood
- **White**: 12% Cord Blood, 88% Bone Marrow or Peripheral Blood

Source: National Marrow Donor Program/Be The Match FY 2016
Transplant Outcomes based on graft source for Children with High-Risk Acute Lymphoblastic Leukemia- CIBMTR study

Biol Blood Marrow Transplant 18:1204-1210, 2012
Choosing an ideal donor when perfect match does not exist

- Most SCT patients do not have matched sibling or matched unrelated donor.
- Mismatch unrelated donor/cord blood/ haplo identical donor are alternative graft sources.
- No randomized trials comparing the outcome of 3 alternative graft source.
- Effective lymphohematopoetic reconstitution.
- Alternative graft varies
  - time to engraftment, graft failure rate
  - GVHD, Transplant related mortality and relapse risk.

Better understanding of these factors help us to select alternative donor.
Thank you