Getting the Counts
Balancing Donor Safety with Recipient Need

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John Miller, MD             Karen Plewacki, RN
Kimberly Johnson, RN        

Learning Objectives

At the end of this session, you’ll be able to:

• Formulate a clear collection plan using the NMDP Verification Form
• Gain insight into apheresis & collection center best practices for complex / non standard requests & potential troubleshooting options
• Summarize best practices for communication when product requests are not met
For Each Case Study We Will:

1. Present scenario & background info (5 minutes)
2. Discuss scenario in round table groups (10 minutes)
3. A center perspective (10 minutes)
4. General discussion & questions (5 minutes)

Case 1

- 97 kg male recipient with AML
  - PBSC request
  - CD34 cell count of $970 \times 10^6$ $(10 \times 10^6$ CD34 cells/recipient kg)
  - Final product cell concentration $< 200 \times 10^9$/L
- International TC
- Domestic AC
- 58 kg female donor
Important PBSC Details

- NMDP PBSC protocol requires a PBSC product to be at least 200 mL
  - No cell concentration requirement
- NMDP median apheresis procedure efficiency is 36% overall
- NMDP median product cell concentration is $276 \times 10^9/L$ (DPSM Data 2011)
- PBSC data indicates smaller female donors have a higher risk for lower than requested product counts

WMDA & Product Cell Concentration

World Marrow Donor Association (WMDA) guidelines for couriers & the transportation of hematopoietic progenitor cells (marrow, apheresis & therapeutic cells)

“Although this may vary according to local protocols, anticoagulant will be added to apheresis product during collection on the cell separator and as programmed by the apheresis machine. For long distance transportation and/or overnight storage of HPC(A), the final concentration of nucleated cells in the collection is important for viability. To minimize the loss of the viability, the concentration of nucleated cells should be reduced by the addition of autologous plasma in the processing laboratory.”
Plasma Dilution

• Survey of 10 centers (large and small)
• Key points related to TC requested plasma dilution:
  – 100% of ACs can add plasma
  – 70% of AC add a determined amount of plasma / 30% calculate

Discussion Questions

• Is the cell count feasible (970 X 10^6 CD34+ cells)?
• Consider the following factors in this collection:
  – Likely longer transportation time
  – Donor is female & weighs 58 kg
• What key communications need to be given to the TC?
  – Cell count feasibility
  – Product cell concentration
A Center Perspective

Karen Plewacki, RN, HP, MT(ASCP) BB
Kim Johnson RN, HP
Apheresis Associates of Northern Virginia

Verification
Points to Consider

- Small female donor unlikely to collect this cell count
- Recipient is large, however TC has asked for essentially double the usual transplant cell dose
- Verification is signed by us and sent back to the DCC

Points Continued

- We cannot predict the future! There is no way to know ahead of time how well a donor will mobilize.
- TC is told we will do our best to collect their dose while maintaining donor comfort and safety
Other Tools We Use

• We use peripheral CD34 and our collection efficiency (we have calculated to be between 50-65%) to help us gauge mobilization and collection end time and final counts

• We sample the product around 10L, we use the result to extrapolate out what we will have at 24L

• Using the product CD34 at 10L, the WBC count on the product we can estimate a good approximation of what we will end up with at 24L

Ask for Help!

• If we determine we will fall far short of the TC’s goal, we contact Ruth Bakken at NMDP.

• Have as many pieces of information as possible to give her, i.e. donor’s WBC ct, donor’s CD34 counts (if known), platelet count(currently), TC’s order, your guess for what the collection will give at 24L, how the donor is doing.

• Doing a planned protocol deviation (MUST HAVE NMDP APPROVAL TO DO THIS), 30L
Collecting Plasma

• We use a set amount of plasma to be added to the product while on the machine.
• Generally 200 mL, unless the WBC Ct on the product is very high!
• Example: > 400K add 250ml, >500K add 300ml

How to add Plasma on Spectra
Adding Plasma on Spectra

Less Than Adequate Mobilization
Helpful Info

- How do we know if the donor mobilized?
  Obtain the peripheral CD34 cell count (pre-apheresis) & calculate anticipated cell yield

\[
\text{Absolute peripheral CD34 count} \times \text{Planned liters of whole blood to be processed} \times 36 \% \text{ efficiency rate (NMDP overall network median)} = \text{Anticipated total CD34 cell yield}
\]

Less than Requested Cell Counts

- Manage case by case
  - PBSC dose: <1 \( \times 10^6 \) CD34 cells / kg
    - Allow emergency alternative collection as soon as the donor is recovered
  - PBSC dose: 1 – 2 \( \times 10^6 \) CD34 cells / kg
    - Variable depending on clinical scenario
  - PBSC dose: > 2 \( \times 10^6 \) CD34 cells / kg
    - Monitor for potential engraftment in next three weeks prior to allowing an emergency alternative collection
Emergency Product Collection

<table>
<thead>
<tr>
<th>Emergency Product Requests</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (PBSC - BM)</td>
<td>27</td>
</tr>
<tr>
<td>Total number (PBSC - PBSC)</td>
<td>5</td>
</tr>
<tr>
<td>Median time to 2nd Collection (PBSC - BM)</td>
<td>3 days</td>
</tr>
<tr>
<td>Average time to 2nd Collection (PBSC – BM)</td>
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</tr>
<tr>
<td>Median time to 2nd Collection (PBSC – PBSC)</td>
<td>20 days</td>
</tr>
<tr>
<td>Average time to 2nd Collection (PBSC – PBSC)</td>
<td>17.6 days</td>
</tr>
</tbody>
</table>

Criteria for data: any subsequent donation within 21 days of initial donation
Time period: all subsequent donations meeting above criteria recorded in NMDP systems

NMDP Protocol Deviations

Deviations:

Filgrastim administration: Sixth dose on day six
Apheresis procedure: Process greater than 24 liters whole blood

<table>
<thead>
<tr>
<th></th>
<th>Filgrastim on Day 6</th>
<th>Processed &gt; 24 liters whole blood</th>
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</thead>
<tbody>
<tr>
<td>Planned</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>Unplanned</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Data taken from MasterControl From April 16, 2011 to September 24, 2013 (17 months).
Case 2

- 100 kg male recipient with MDS
  - Marrow request
  - $400 \times 10^8$ nucleated cells ($4 \times 10^8$ nucleated cells / recipient kg).
  - ACD ratio of 1:5
- 55 kg female donor
  - Hemoglobin 11.1 g/dL @ pe

Important Details

- NMDP median marrow concentration is $18.3 \times 10^6$ nucleated cells / mL
- NMDP Standards allow 20 ml of marrow / donor kg
- Autologous donation guidelines:
  - $>395 \times 10^8$ nucleated cells = 3 autologous units
Anticipate potential cell yield

Donor Kg
\[ \times \]
Maximum volume of product / kg (20 mL/Kg)
\[ \times \]
NMDP median marrow cell concentration (18.3 \times 10^6 cells/mL)

= Anticipated total nucleated cell yield (may wish to change the decimal place so the answer is in “x 10^8 cells”)

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<table>
<thead>
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<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (BM - PBSC)</td>
<td>7</td>
</tr>
<tr>
<td>Total number (BM – BM)</td>
<td>2</td>
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<tr>
<td><strong>Median time to 2\textsuperscript{nd} Collection (BM – PBSC)</strong></td>
<td>16 days</td>
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<tr>
<td><strong>Average time to 2\textsuperscript{nd} Collection (BM – PBSC)</strong></td>
<td>14.6 days</td>
</tr>
<tr>
<td><strong>Median time to 2\textsuperscript{nd} Collection (BM – BM)</strong></td>
<td>7.5 days</td>
</tr>
<tr>
<td><strong>Average time to 2\textsuperscript{nd} Collection (BM – BM)</strong></td>
<td>7.5 days</td>
</tr>
</tbody>
</table>

Criteria for data: any subsequent donation within 21 days of initial donation

Time period: all subsequent donations meeting above criteria recorded in NMDP systems
Less than Requested Cell Counts

• Manage case by case
  – Marrow dose: \(<1 \times 10^8\) nucleated cells / kg
    • Allow emergency alternative collection as soon as the donor is recovered
  – Marrow dose: \(1 – 2 \times 10^8\) nucleated cells / kg
    • Variable depending on clinical scenario
  – Marrow dose: \(> 2 \times 10^8\) nucleated cells / kg
    • Monitor for potential engraftment in next three weeks prior to allowing an emergency alternative collection

Discussion Questions

• What might we anticipate the final product count to be?
• Is the requested cell count feasible?
• Should we deviate from the request?
• What key communications need to be given to the TC?
  – Anticipated cell yield
  – Anticipated use of anticoagulants
  – Anticipated use of media / additives
Case 2 – limiting factors

- **TNC Request:**
  TNC 400 x 10e8 = 2,186 mL of bone marrow (for median TNC count of 0.183x10e8/mL)

- **Donor/recipient anthropometric discrepancy:**
  Donor is almost half the size of the recipient. Her estimated TBV is 3,500 mL (marrow volume requested represents 62% TBV).

- **Donor has borderline hemoglobin**
  Can she tolerate a 20 mL/kg blood loss? Can she even donate autologous blood?
TNC request -
What marrow volume is safe to donate?

- 20 mL/kg is usually well tolerated in non-anemic and non-obese donors
- On average, a 20mL/kg BMH drops the hemoglobin about 4-5 g/dL
- In donors with borderline hgb it can result in symptomatic anemia.
- For this donor, post-BMH hgb 7.1-6.1 g/dL. Is this an acceptable risk?

(Note on the side)
Donor/recipient antropometric discrepancy

- Petite donor
  the 20 mL/kg rule applies
- Obese donor
  the 20 mL/kg rule does not apply
  We calculate bone marrow volume to be no more than 30% of estimated donor’s TBV

Relationship between blood volume and BMI

How we proceed?

- Usually, the prescription comes before the donor evaluation is available.  
  *(We only know reported weight and height).*

- Never promise more than what we can reasonably obtain based on donor anthropometric measurements.

- Our TNC will be $201 \times 10^8$ (2 x108/kg)

How we proceed?

Donor evaluation results become available

- Donor has borderline hemoglobin- hgb is 11.1 g/dL!

- Sometimes a female weighing 55 Kg comes with a healthy package. Vital signs?

- Evaluate if we can improve her borderline hemoglobin “easy fixes”  
  - Nutritional deficiency (RBC indices, serum iron, blood smear)  
  - Evaluate possibility of organ dysfunction (e.g. hypothyroidism)  
  - Medical history ongoing blood losses that we can stop

- Optimize her status prior to the procedure
Can she donate autologous blood?

- The use of autologous donations (AD) has been considered an established blood conservation measure in major elective surgery, particularly orthopedic surgery.

- Large prospective randomized studies on this population of patients suggested that two variables show significant relationship to net RBC gain after AD and translated in clinical benefit to the patients:
  - the length of the interval between last donation and surgery
  - the hematocrit at baseline.

- Our goal would be to obtain 1 autologous unit at least 3 weeks before the harvest, if hgb/hct can improve with treatment.

Our Plan for this case

- Always with the idea that this may be the only donor for this recipient.
- Communicate early about the TNC that can be provided
- If we can treat H/H - We would propose a delay on the donation (x weeks) to optimize donor’s pre-procedure status.
- For HPC-A we would just treat anemia and find her suitable

TC may want to consider HPC-A – easier preparation, possibility of better counts
Recipient may or may not be able to wait.

Anticoagulants and Additives

- We never collect marrow without heparin
- We add ACD-A when at least we have 500 mL of marrow in the collection bag.

Our standards for HPC-M
- Heparin: 10U/mL of marrow
- ACD-A: 1:10 ratio
- Plamalyte-A : 1:10 ratio

Our ranges for HPC-M:
- Heparin: 5-20 U/mL
- 5U with high ACD-A concentrations
- 20U when no ACD-A and domestic travel
- ACD-A: <1:10 (only for international travel >20 hours)
Concluding Questions / Thoughts

THANK YOU!

- Corina Gonzalez, MD
- Kim Johnson, RN, HP
- Karen Plewacki, RN, MT(ASCP) BB, HP
- NMDP staff
  - Ruth Bakken
  - Kuchen Hale
  - Marie Matlack
  - Katie Newcomb