Peripheral Blood Stem Cell Collection

Laura S Connelly-Smith

University of Washington Medical Center / Seattle Cancer Care Alliance

DOI: 10.15428/CCTC.2017.281675
Peripheral Blood Stem Cell (PBSC) Collection

Hematopoietic stem cells are pluripotent stem cells that are responsible for the formation of blood cells, and, are collected for transplantation. Hematopoietic stem cell transplantation is often referred to as bone marrow transplantation and more aptly as hematopoietic progenitor cell (HPC) transplantation.

Objectives:

• Why we perform PBSC collections?
• How we perform PBSC collections?
• When we perform PBSC collections?
Indications for Hematopoietic Progenitor Cell Transplantation (HPCT)

HPCT is a widely accepted treatment strategy for most hematological malignancies, certain non-hematological malignancies and for several non-malignant conditions.

HPCT includes Allogeneic and Autologous HPCT

- Multiple Myeloma / Plasma Cell Dyscrasia
- Non Hodgkin's Lymphoma
- Acute myeloid leukemia (AML)
- Hodgkin disease
- Acute lymphocytic leukemia (ALL)
- Myelodysplastic syndrome (MDS) / Myeloproliferative disorders (MPD)
- Chronic lymphocytic leukemia (CLL)
- Chronic myeloid leukemia (CML)
- Aplastic Anemia
- Solid tumors e.g. Germ Cell, Ewing's sarcoma, neuroblastoma
- Hemoglobinopathies
- Immune deficiency syndromes
- Some autoimmune and Immune dysregulation disorders
Autologous vs. Allogeneic HPCT

**Autologous HPCT**

- To allow for bone marrow recovery after provision of high-dose chemotherapy
- Regimens do not include immunosuppression
- Patients undergo HPC collection

**Allogeneic HPCT**

- To replace diseased marrow with normal bone marrow from a healthy donor – For graft versus tumor effect via T-lymphocytes
- Regimens contain immunosuppression
- Healthy related or unrelated donors undergo HPC collection
Human Progenitor Cells

CD34 serves as a marker for HPC

CD34+ Cells - Predictor of Stable Engraftment

American Society for Blood and Marrow Transplantation (ASBMT) consensus guidelines (2014):

• 2x10^6 CD34+ cells/kg accepted as minimum threshold however 5x10^6 CD34+ cells/kg recipient weight optimal for Auto HPCT

• 2x10^6 CD34+ cells/kg accepted as minimum threshold however 4-5x10^6 CD34+ cells/kg recipient weight probably ideal for Allo HPCT
Stem Cell Procurement

Peripheral Blood Progenitor Cell Collection

Bone Marrow Harvest

Umbilical Cord Blood Collection
PB vs BM HPC collection

Peripheral Blood
- Larger numbers of CD34+ and CD3+ cells
- Shorter duration of cytopenias
- Enhanced immune reconstitution
- Reduced morbidity

However
- Increased chronic GVHD
- May require central venous access
- Side effects growth factors, chemotherapy, anticoagulant

Bone Marrow
- Surgical procedure $\overset{\text{GA}}{\to}$ spinal
- Pain during recovery
- Less chronic GVHD

<table>
<thead>
<tr>
<th></th>
<th>Bone Marrow</th>
<th>Peripheral Blood</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total nucleated cells</td>
<td>2.3</td>
<td>11.6</td>
<td>0.001</td>
</tr>
<tr>
<td>(TNC) x 10^8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD34 x 10^6</td>
<td>2.4</td>
<td>7.3</td>
<td>0.001</td>
</tr>
<tr>
<td>CD x 10^3</td>
<td>23.8</td>
<td>279</td>
<td>0.001</td>
</tr>
<tr>
<td>Volume ml</td>
<td>12.2</td>
<td>4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Bensinger et al NEJM, 2001 344;175
Peripheral Blood Progenitor Cell collection

Center for International Blood and Marrow Transplant Research Transplant Activity Report Covering 2010-2014

HPC Recovery from Peripheral Blood

HPC collection from peripheral blood results from the combination of:

- Effective mobilization procedures
- Efficient apheresis techniques
Mobilization Regimens

- Chemotherapy +/- G-CSF
- Cytokines:
  Granulocyte Colony Stimulating Factor (G-CSF)
  - filgrastim / lenograstim
  GM-CSF
  - sargramostim
- Novel agents:
  Plerixafor (Mozobil®) +/- G-CSF
Cytokines (G-CSF) $\rightarrow$ MMPs (4 days)

Plerixafor, reversible CXCR4 blocker

Blood

Cytokines
Cytotoxic drugs
Integrin antagonists

Endothelial cell

ICAM-1

LFA-1

Hyaluronic acid

CD44

SDF-1

CXCR4

CD34$^+$ blood stem cell

CD34$^+$ blood stem cell

VCAM-1

VLA-4

Fibronectin

Stromal cell

Marrow

PBSC Mobilization and Apheresis

G-CSF

10-16ug/kg/day

Apheresis

Day
-4
-3
-2
-1
0
+1

Pleriaxafor

240ug/kg/day
Side effects of GCSF

**Common**
Musculoskeletal Pain, “Flu-like”, Arthralgia, Headache
Nausea
Malaise, fatigue
Splenomegaly
Mild thrombocytopenia
Increase LDH, Increase Alk Phos

**Uncommon:**
Fever, Rash, Arthritis

**Rare:**
Severe Thrombocytopenia,
Splenic Rupture/ Bleed
Thrombosis
CD34+ collection in randomized trials of GCSF vs GCSF and Plerixafor (Mozobil®)

- Adverse events with Plerixafor include GI disorders and injection site reactions.
- Earlier randomized studies demonstrated a higher % of myeloma patients reaching $6 \times 10^6$ CD34+ cells/kg with Plerixafor and G-CSF compared to G-CSF mobilized patients alone. Median number of days to reach $\geq 6 \times 10^6$ CD34+ cells/kg was one day vs four days for GCSF alone.
- Additional randomized study in NHL demonstrated a higher % of patients reaching $5 \times 10^6$ CD34+ cells/kg using Plerixafor and G-CSF vs G-CSF alone.
- Cost is a limiting factor for the use of Plerixafor.
Commonly used Apheresis Blood Cell Separators

COBE Spectra  
Spectra Optia  
Amicus

Separation by density centrifugation

Courtesy of Sergio Torloni, MD
Side effects of Venous Access and Apheresis

NMDP prospective trial n=2408

51% Hypocalcemia / Citrate toxicity
20% Nausea
22% Venous Access issues (IV lines infiltrated, multiple attempts, hematomas, poor flow)
1-6% Other – pain, chills, hyper/hypotension

Grading of Side Effects

- Grade 0 5%
- Grade I 57%
- Grade II 32%
- Grade III 6%
- Grade IV <1%
Circulating CD34+ cell numbers are predictive of collected CD34+ cell numbers

Yu J et al, Transfusion, 1999

**Collection Efficiency (CE)** = \[
\frac{\text{Cells in the collection bag}}{\text{Cells through the apheresis device}}
\]

Maximizing collection based on instrument efficiency and donor peripheral CD34+ cell counts can be performed using Predictive Algorithms
Predictive Algorithms

CD34+ cells to be collected per liter (L) = \(\text{peripheral blood CD34+ cells/L} \times \text{CE} \times \text{Body weight in kilograms (kg)}\)

Rationale For CD34-based Collections

- Worldwide Industry Standard Practice
- Ability to project expected cell yield
- Ability to reduce apheresis time
- Process less total blood volume (TBV) to collect the same CD34+ dose

\[\text{TBV to process (L)} = \text{Target number of CD34 cells to be collected} \times \text{recipient weight (kg)} \times \text{Peripheral blood CD34+ cells} \times 0.3^* \text{ (CE)}\]
References

Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- **Employment or Leadership**: No disclosures
- **Consultant or Advisory Role**: No disclosures
- **Stock Ownership**: No disclosures
- **Honoraria**: No disclosures
- **Research Funding**: No disclosures
- **Expert Testimony**: No disclosures
- **Patents**: No disclosures
Thank you for participating in this Clinical Chemistry Trainee Council Pearl of Laboratory Medicine.

Find our upcoming Pearls and other Trainee Council information at www.traineeCouncil.org

Download the free Clinical Chemistry app on iTunes today for additional content!

Follow us: