Jennifer Shamai MS, RN, AOCNS, BMTCN
Professional Practice Leader
Department of Clinical Practice And Professional Education

How the Experts Treat Hematologic Malignancies
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DISCLOSURES

No Disclosures
Objectives

• Discuss recipient and donor eligibility, evaluation, and management
• Review recipient, caregiver, and donor education
• Discuss the process of collecting and storing stem cells

Note: the primary reference source for this course is Ezzone, S. (2013) Hematopoietic stem cell transplantation: a manual for nursing practice. Oncology Nursing Society, Pittsburgh, PA
Recipient Eligibility

• General considerations
  – Extent of underlying disease
  – Chemotherapy-sensitive disease
  – Remission status
  – Adequate organ function and performance status
  – No life-threatening viral exposures or comorbidities
  – Age

• Variations among transplant centers
Recipient Evaluation and Management

- Health history
- Physical examination
  - Laboratory evaluation
    - CBC, chem profile, electrolytes, LFTs, BUN, PTT, INR, GFR, ABO/Rh, pregnancy test
    - Infectious disease testing: Hep B, Hep C, HIV, CMV, HSV
    - Histocompatibility testing (HLA)
  - Organ function testing: echocardiogram, pulmonary function tests, dental exam
  - Disease evaluation
    - Bone marrow aspirates and biopsies
    - Lumbar puncture
Recipient Evaluation and Management

• Psychosocial assessment
  – Financial issues
  – Psychological well-being
  – Family concerns
• Comprehension of procedure, risks, side effects, and complications
• Ability to comply with therapy
• Informed consent
  – Pediatric considerations
Recipient Education

• HSCT is an intense and complicated process
  – Based on complex concepts
  – High levels of distress prior to HSCT
• Pre-transplant education topics
  – Conditioning regimen
  – Cell infusion
  – Supportive medications
• Best practices
  – Individualized and ongoing education with comprehension evaluation
  – Utilize multimodal methods
    • Teach-back http://www.teachbacktraining.org/
Caregiver Education

• Physical and psychosocial elements of process
• Role of the caregiver
  • Demands of care
• Changing roles within the family
• Identification of key support people for activity delegation
• Group participation and support networks
• Discharge planning – recipient and caregiver/family
• Pediatric considerations
  – Child life specialists
Recipient and Caregiver Education

• **Resources**
  – Blood and Marrow Transplant Information Network
    • Books, monthly newsletters, and on-line support network
    • [http://www.bmtinfonet.org/](http://www.bmtinfonet.org/)
  – National Marrow Donor Program/Be The Match Registry
    • Resources for patients and families
    • [https://bethematch.org/For-Patients-and-Families/](https://bethematch.org/For-Patients-and-Families/)
  – BMT Support Online
    • Peer support, education, and awareness
    • [http://bmtsupport.org/](http://bmtsupport.org/)
Donor Selection and Care

• Thorough clinical evaluation
  – Complete medical history, physical examination, blood tests
  – Psychosocial assessment

• Donor education
  – Collection process
  – Outcomes of collection and recipient
  – Anonymity of donors for unrelated transplants

• Voluntary process with informed consent

• Other considerations
  – Legal aspects – pediatric donation, joint-custody
  – Ethical aspects – psychological effects, motive for donation, pressure to donate, discovery of unknown medical conditions
Unrelated Donors

- Majority of patients do not have HLA-compatible related donor (~70%)
- National and international registries provide unrelated donor options
- Process
  1) Obtain the patient’s HLA
  2) Perform a preliminary search
  3) Formal search is initiated
  4) Donor work-up
National Marrow Donor Program

- Largest database of marrow, cord blood and stem cell donors
- Facilitate transport of unrelated products to the transplant center
Collection Process

1) Donor/recipient evaluated for collection
2) Transplant physician writes a collection and processing order
   • Recipient and donor information
   • Treatment plan
   • Collection protocol – mobilization, target dose
   • Processing and cryopreservation method
3) Product is collected
4) Lab determines the number of cells collected – CD34+ cells
5) Additional collections performed if necessary
Stem Cell Mobilization

- Stimulation of stem cells that originate in the bone marrow to move into the peripheral blood
  - Number of circulating stem cells in the blood is lower than in the bone marrow
- Results in fewer apheresis collections and faster hematopoietic recovery after transplant
- Methods
  - Chemotherapy
  - Hematopoietic growth factors
  - Chemokine antagonists
Stem Cell Mobilization

• Chemotherapy: cyclophosphamide, ICE, R-ICE
  – Transient increase in circulating stem cells following standard chemotherapy
  – Disadvantages: neutropenia, sepsis, failure to mobilize

• Colony stimulating factors: G-CSF, GM-CSF
  – Reduce cytopenia and increase number of circulating progenitor cells
  – Side effects: bone pain, arthralgia/myalgia, fever, malaise

• Chemokine antagonists: plerixafor (Mozobil®)
  – Schedule: G-CSF up to 8 days, plerixafor on day 4
  – Side effects: GI symptoms, injection-site reactions, headache, fatigue, arthralgias, dizziness
Stem Cell Collection – Bone Marrow Harvest

- HPCs harvested from the posterior iliac crests via multiple large-bore needle aspirations
- Collection procedure:
  - Scheduled in the OR
  - Multiple needle aspirations of bone marrow
  - Side effects: post-procedural pain and anesthesia complications
  - Harvested product is filtered and processed
- Assess: bleeding, drainage, hematoma development
Bone Marrow Harvest
Stem Cell Collection – PBSC Apheresis

• Donors are connected to an apheresis machine via central or peripheral vascular access
• Blood is removed from the patient and passes through a cell separator
  – Centrifuge separates blood components by cell density
  – Stem cell layer is isolated, and remaining blood returned
PBSC Apheresis

• Procedure
  • Outpatient
  • 12-15 liters of blood
  • 2-4 hours
  • May need multiple collections

• Requires vascular access

• Advantages
  – Outpatient procedure
  – Option for those with a tumor in the marrow or had pelvic irradiation that caused marrow fibrosis
PBSC Apheresis

• Side effects and complications
  – Hypocalcemia from citrate toxicity
  – Hypovolemia
  – Chilling
  – Peripheral and central catheter complications
  – Decreased platelets and/or hemoglobin

• Pediatric considerations
  – Volume of blood processed must be based on the child’s size (200-250 ml/kg)
  – Pre-prime with irradiated RBCs if more than 10-15% of the child’s total blood volume is needed for priming
  – Typically not performed in children under 13 years of age
Stem Cell Collection – Umbilical Cord Blood

- Stem cells collected at the time of childbirth from the umbilical cord and placenta
- Scheduled prior to delivery
- Cord blood center must have the ability to collect and arrange for storage of the product
- Frozen and stored after collection
  - Donated to public cord blood bank
  - Stored in private cord banks
- Ethical issues
Umbilical Cord Blood Collection

- **Procedure**
  - Placenta and umbilical cord is removed from delivery room
  - Cleanse and puncture the umbilical vein with a 16 or 17 gauge needle
  - Blood is drained by gravity into a blood bag

- **Products are counted, tested for infectious diseases, HLA-typed**

1. Baby is born with umbilical cord and placenta attached.
2. After the cord is tied and cut, some blood is left in the blood vessels of the placenta and cord.
3. This cord blood is extracted from the umbilical cord using a special collection bag.

Parts of the umbilical cord used in extraction of cord-blood stem cells

Source: New York Blood Center

The Wall Street Journal
Cord Blood Collection

Photographs courtesy of A. Scaradavou, NYBC
Stem Cell Processing

• Blood and HLA typing
• Sterility and infectious disease testing
• Volume reduction
• Autologous stem cell purging
  – Negative cell selection: removing tumor cells
  – Positive cell selection: removing stem cells from the product
• Allogeneic processing
  – ABO incompatibilities – red cell or plasma-depletion
  – T-cell depletion: remove enough T lymphocytes to minimize graft versus host disease (GVHD)
Cryopreservation

- Preserve stem cells and prevent cell damage during freezing or thawing
- Cryoprotectant dimethyl sulfoxide (DMSO) followed by controlled-rate freezing
- Storage in liquid nitrogen freezers
- Preparation, storage, and thawing performed by specialized technologists
- Adverse effects: infusion reactions