Overview of Blood and Marrow Transplantation

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Overview

- History of BMT
- Theory behind therapy
- BMT Process
- Long Term Survival

Definitions*

- Allogeneic BMT
- Autologous BMT
- Blood and Marrow Transplant (BMT)
- Conditioning Therapy
- Engraftment
- Graft vs. Host Disease (GVHD)
- Graft vs. Tumor Effect (GVT)
- Haploidentical

*R Refer to definitions handout

- Hematopoietic Progenitor Cell (HPC)
- Hematopoietic (Stem) Cell Transplant (HCT)
- Human Leukocyte Antigen (HLA)
- Mobilization Therapy
- Mixed Chimerism BMT (NonMyeloablative, Reduced Intensity, Mini)
- Sinusoidal Obstructive Syndrome (SOS or VOD)
- Syngeneic

Pluripotent Stem Cell

- Progenitor of all blood cells, "uncommitted"
- Asynchronous division
- Self renewing
- Location
  - Marrow
  - Peripheral Blood
  - Umbilical Cord Blood
- Migratory/homing properties
  - Cord Blood takes longer to "home"
Indications for BMT

- Malignant diseases:
  - Acute and Chronic Leukemia
  - Hodgkin’s Lymphoma and Non-Hodgkin’s Lymphoma
  - Myelodysplastic Syndromes
  - Multiple Myeloma
  - Amyloidosis
  - Selected solid tumors
    - Breast (rare)
    - Renal cell
    - Germ cell
    - Primary CNS
    - Neuroblastoma

- Non-malignant diseases:
  - Hematologic Disorders
    - Aplastic Anemia
    - Fanconi’s Anemia
    - Sickle Cell
    - Thalassemia
  - Congenital Immunodeficiencies
    - SCID
    - Wiskott Aldrich Syndrome
  - Inborn Errors of Metabolism
    - Hurler’s Syndrome
    - Guacher Disease
  - Autoimmune Diseases
    - Systemic Sclerosis
    - Multiple Sclerosis

Stem Cell Sources

<table>
<thead>
<tr>
<th></th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>Bone Marrow</td>
<td>Abundance of stem cells in BMR</td>
<td>Anaesthesia risk for donor</td>
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<td></td>
<td>Lower rate of infections; days; +100 to +365</td>
<td>Post-operative pain for donor</td>
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<tr>
<td>Peripheral Blood</td>
<td>Faster neutrophil and platelet recovery</td>
<td>Bone pain for donor</td>
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<tr>
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<td>Faster immune reconstitution</td>
<td>Slightly higher risk of GvHD</td>
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<td>Reduced treatment-related mortality</td>
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<tr>
<td></td>
<td>Lower rate of infections to day +100</td>
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<tr>
<td></td>
<td>More GvHD effect than BMT or UCMB</td>
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<tr>
<td></td>
<td>Easier collection</td>
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<tr>
<td>Umbilical Cord Blood</td>
<td>More quickly available</td>
<td>Slowest engraftment</td>
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<tr>
<td></td>
<td>Lack of donor risks</td>
<td>Smaller “dose” of stem cells</td>
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<tr>
<td></td>
<td>Less risk of GvHD</td>
<td>Slightly higher rate of early mortality</td>
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<td>More “matches”</td>
<td>Cannot obtain more cells from donor</td>
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Theory behind Therapy: Autologous

- Autologous/Syngeneic:
  - Lethal doses of chemotherapy/radiation therapy if patient not supported
  - Patient’s own stem cells “rescue” the ablated marrow
  - Cure is chemotherapy/radiation, stem cells are supportive care
  - Patient does not require immunosuppression as Graft vs Host disease should not occur

Autologous Process

- Mobilization chemotherapy to collect cells
  - Standard chemotherapy + high dose filgrastim
- “Conditioning” chemotherapy at least 1 month later
- Infusion of stem cells
- Monitor for infection and “engraftment”
- Discharge to primary provider about Day +30
Theory behind Therapy: Allogeneic

Myeloablative:
• Lethal doses of chemotherapy/radiation if patient not supported
• Donor stem cells “rescue” the ablated marrow and provide a new immune system for a graft versus tumor effect
• Cure is both chemotherapy/radiation and stem cells and graft vs tumor effect

Nonmyeloablative:
• Lower doses of chemotherapy/radiation
• Cure is the stem cells and graft vs tumor effect, chemotherapy eliminates microscopic disease
• Also called Mixed Chimerism, Mini, Reduced Intensity

Immunosuppression
• Cyclosporine, tacrolimus, Mycophenolate mofeteil
• Required to prevent Graft vs. Host Disease
• NonMyeloablative and Haploidentical BMT will receive dual immunosuppression
  • NonMyeloablative: Cyclosporine/Tacrolimus and MMF
  • Haplo: Cyclosporine/Tacrolimus, MMF and Cyclophosphamide post transplant
• Immunosuppression taper begins about Day +80 depending on BMT type and is stopped if GVHD symptoms occur

Timeline for Autologous HSCT

Allogeneic Process

• Identify donor
• “Conditioning” chemotherapy for patient
• Filgrastim “mobilization” for donor
• Infusion of HPC
• Monitor for infection, symptoms of GVHD
• Discharge to primary provider about Day +100-120 depending on BMT type
Conditioning Therapy

- Preparing the body for Hematopoietic Cell Infusion
- Chemotherapy
  - Dosed based on body weight, not body surface area
  - Side effects intensified due to much higher doses
- Radiation Therapy
  - Total Body Irradiation (TBI)
  - Radiation-tagged monoclonal antibodies (I-131, Y-90)
- Starts 3-9 days prior to BMT infusion

Infusion of Stem Cells (HPC)

- Infusion can occur inpatient or outpatient
- Infused like a blood product
- Side effects similar to blood products
  - Exception: Cryopreserved cells (autologous or cord blood)
    - Hypersensitivity to DMSO preservative
    - Red cell lysis
Acute Complications

- Pancytopenia
- Infection
- Mucositis
- Acute Graft vs Host disease (allogeneic recipients only)

Infection Prevention

- Avoid ill people and crowds
- Avoid people who have received live vaccines
- No flowers in vases, no planting, no decorative moss in plants
- No vacuuming or dusting
- Immunocompromised, not neutropenic, diet
  - Fresh fruits/vegetables okay
  - No
    - Deli lunch meats
    - Moldy cheeses, pepper jack cheese, mexican soft cheeses
    - Uncooked tofu, meat or seafood
    - Chili peppers
    - Miso
  - Unpasteurized juices

Acute Graft vs Host disease: Allogeneic

- An immunologic reaction to the transplanted HPCs classically occurring in the first 100 days post BMT involving the skin, liver, and gut.
- GVHD is one of the most frequent complications after allogeneic BMT
  - Incidence 30-70% in matched transplants
  - Major cause of morbidity and mortality after BMT
  - Mortality (direct or indirect) can reach 50%

aGVHD

Three-step process
**Long Term Complications:**

**Infection**
- Prolonged neutropenia and immunosuppression greatest risk
- Bacterial
- Fungal
- HSV
- VZV (shingles)
- Cytomegalovirus (CMV): may require weekly monitoring for CMV titers depending on BMT source or type
- Includes viruses previously vaccinated against: revaccine patient 1 year after BMT or after off all immunosuppression

**Long Term Complications: Auto and Allo**
- Neurologic
  - Learning disabilities
  - Cognitive dysfunction
- Endocrine
  - Diabetes
  - Thyroid
- Sexual
  - Decreased libido
  - Delayed puberty
- Fertility
- Emotional
- Renal/Urinary
- Dental
  - Decreased salivary production
  - Gingivitis, Caries
- Relapse
- New malignancy
- Pulmonary
  - Pulmonary fibrosis
  - Bronchiolitis Obliterans
- Cardiac
  - Hypercholesteremia
  - CHF
- Cataracts

**Long-Term Complications: Allo**
- Chronic GVHD
  - Skin
  - Liver
  - Gut
  - Oral
  - Ocular
  - Genital
  - Lung
  - Joints/Fascia
- Requires long term immunosuppression
- Skeletal (due to cGVHD)
  - Osteoporosis and osteopenia
  - Avascular necrosis

**Resources**
- American Cancer Society [www.cancer.org](http://www.cancer.org), select “Treatment & Support > Treatment Types > Other Procedures and Techniques
- National Marrow Donor Program [www.bethematch.org](http://www.bethematch.org), select Physicians