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Title: Transfusion Support in Hematopoietic Stem Cell Transplant

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Transfusion Support for Hematopoietic Stem Cell Transplant (HSCT)

• Overview of HSCT
  • Types
  • Conditioning Regimens
  • Engraftment

• Overview of Transfusion Support in HSCT
  • Blood Products
  • Transfusion Indications

• ABO-Incompatible HSCT
  • Transfusion Considerations
  • Complications
Two Types of Hematopoietic Stem Cell Transplant (HSCT)

1. **Allogeneic**
   - Pros: Graft versus tumor (GVT) effect; patient does not require adequate marrow; can use less intensive pre-transplant conditioning
   - Cons: Graft versus host disease (GVHD; slower recovery of immune system)

2. **Autologous**
   - Pros: No GVHD
   - Cons: No GVT; stem cells may have been previously damaged by prior treatment regimens
# Overview of HSCT Sources

<table>
<thead>
<tr>
<th></th>
<th>Bone Marrow</th>
<th>Peripheral Blood</th>
<th>Umbilical Cord Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Source</strong></td>
<td>Posterior iliac crest primarily; less commonly anterior iliac crest or sternum</td>
<td>Collected after mobilization with recombinant hematopoietic growth factor and/or chemotherapy</td>
<td>Collected at time of delivery</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>2-5 x 10^8 stem cells/kg</td>
<td>2 x 10^6 stem cells/kg</td>
<td>1.5 – 3.5 x 10^7 stem cells/kg</td>
</tr>
<tr>
<td><strong>Engraftment</strong></td>
<td>Faster than cord but less than peripheral blood</td>
<td>Fastest</td>
<td>Slowest</td>
</tr>
<tr>
<td><strong>T cell Content</strong></td>
<td>Low</td>
<td>Highest (high risk of GVHD)</td>
<td>Low and immature</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Commonly used in pediatric patients</td>
<td>Commonly used in adults and autologous</td>
<td>Mainly for allogeneic; rising use in pediatric and adult</td>
</tr>
</tbody>
</table>
# Allogeneic Transplants: Types of Conditioning Regimens

<table>
<thead>
<tr>
<th>Description</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
</table>
| **Myeloablative** | High dose chemotherapy and/or total body irradiation (TBI) | • Kills underlying tumor  
• Suppress host immunity (allogeneic transplant) | • Very immunosuppressive  
• Toxic to elderly and very young  
• Longer transfusion requirements – delayed engraftment |
| **Nonmyeloablative or Reduced-Intensity Conditioning (RIC)** | Less intensive chemotherapeutic or TBI conditioning regimens | • Induce enough immunosuppression to allow engraftment and prevent rejection  
• Relies on allogeneic GVT  
• Less transfusion requirements | • Less tumor control |
Engraftment: Definitions

- **RBC**: 1% reticulocytes in peripheral blood or on day of last transfusion with no transfusions for 30 days

- **Platelets**: $\geq 20,000/\mu$L for 3 consecutive days without transfusion

- **Neutrophils**: Absolute neutrophil count (ANC) of $>500/\mu$L for 3 consecutive days
Peri/Post-Transplant Transfusion Thresholds

- RBC transfusion support until engraftment (~6 weeks)
  - Stable patient threshold: 7-8 g/dL
  - Cardiac patient threshold: > 8g/dL
- Autologous HSCT: maintain adequate erythropoietin levels and require less RBC support
- Factors affecting length of support:
  - Stem cell dose in graft
  - ABO incompatible grafts
  - Myelosuppressive regimens
  - Incidence of GVHD
Peri/Post-Transplant Transfusion Thresholds

• Platelet transfusion support:
  • Threshold 10,000/uL for nonbleeding patient
  • Threshold > 20,000/uL with:
    o Heparin therapy, GVHD, Viral Infection
  • Threshold >50,000/uL for active bleeding

• Factors affecting length of support:
  • Allogeneic HSCT issues: unrelated donor delays engraftment as does use of bone marrow as source
  • Presence of acute GVHD, VOD, or CMV infection
  • Stem cell dose in graft
  • Methotrexate prophylaxis used for GVHD
Granulocyte Transfusions

- HSCT patients have periods of severe neutropenia
- Indications for granulocyte transfusions:
  - Absolute neutrophil count <500/uL
  - Bacterial sepsis unresponsive to antibiotic therapy
  - Disseminated fungal or yeast infection

- Minimum dose of granulocytes: $1 \times 10^{10}$/infusion
  - Transfuse daily until infection resolves or neutrophil counts recover
The RING study: A Randomized Controlled Trial of GCSF-Stimulated Granulocytes in Granulocytopenic Patients

• Randomized controlled trial to evaluate efficacy of granulocyte transfusions

• Subjects eligible for the study:
  • Neutropenia (ANC<500)
  • Proven/probable/presumed bacterial or fungal infection

• Subjects randomized to receive either:
  • Standard antimicrobial therapy
  • Standard antimicrobial therapy plus daily granulocyte transfusions from normal donors stimulated with G-CSF and dexamethasone

• Primary endpoint: survival plus a microbial response

• **Outcome**: differences in primary endpoint success rates for both arms were not statistically significantly different
  • Trial had low accrual so power to detect clinical effect was low
ABO-Incompatible HSCT

4 Types of Compatibility Between Donor and Recipient:

1. Compatible
2. Major Incompatibility
3. Minor Incompatibility
4. Bidirectional Incompatibility
Types of ABO - Incompatible HSCT

Figure 1: Schematic representation of major, minor, and bidirectional ABO incompatibility between donor and recipient in allogeneic HSCT. D represents the HSCT donor and R represents the HSCT recipient.
## Potential ABO Combinations Potentially Existing Between Donors and Recipients for HSCT

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Donor</th>
<th>O</th>
<th>A</th>
<th>B</th>
<th>AB</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>Compatible</td>
<td>Major</td>
<td>Major</td>
<td>Major</td>
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<tr>
<td>A</td>
<td>Minor</td>
<td>Compatible</td>
<td>Bidirectional</td>
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<td>Minor</td>
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# ABO Compatibility in HSCT

<table>
<thead>
<tr>
<th>Mismatch Type</th>
<th>Potential clinical manifestations</th>
<th>Potential interventions</th>
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</thead>
</table>
| **Major**     | • Acute hemolysis during stem cell infusion  
                • Delayed RBC engraftment  
                • Pure red cell aplasia | • Red cell depletion of stem cell component especially bone marrow  
                                • Isohemagglutinin reduction in recipient by therapeutic plasma exchange  
                                • Erythropoiesis-stimulating agents |
| **Minor**     | • Acute hemolysis during stem cell infusion  
                • Delayed hemolysis from donor passenger lymphocytes | • Plasma reduction of stem cell component  
                                • Serial monitoring of blood counts, DAT, hemolysis panel Day 5-15 post HSCT |
| **Bidirectional** | • Immediate hemolysis caused by donor’s and/or recipient’s isoheagglutinins  
                            • Delayed hemolysis caused by either donor’s and/or recipient’s isoheagglutinins | • Combination of practices used in minor and major ABO incompatibility |
## Transfusion Support in HSCT

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Donor</th>
<th>Pre-Transplant Phase</th>
<th>Transplant Phase</th>
<th>Post-Engraftment Phase</th>
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<tbody>
<tr>
<td>O</td>
<td>A</td>
<td>Recipient</td>
<td>O</td>
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<td>Recipient</td>
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Conclusions

- HSCT is used in the treatment of many different hematological and non-hematological diseases

- Transfusion support is varied depending on source of stem cell graft and conditioning regimen

- The ABO blood group system is not a barrier to successful allogeneic HSCT transplantation

- There must be a clear understanding of potential adverse events for ABO-incompatible HSCT

- Clear communication between the transplant program, HSC processing laboratory, and blood bank is required
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**: None Declared
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- **Expert Testimony**: None Declared
- **Patents**: None Declared
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