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PEARLS OF LABORATORY MEDICINE

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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

	Bone Marrow	Peripheral Blood	Umbilical Cord Blood
Source	Posterior iliac crest primarily; less commonly anterior iliac crest or sternum	Collected after mobilization with recombinant hematopoietic growth factor and/or chemotherapy	Collected at time of delivery
Dose	2-5 x 10^8 stem cells/kg	2 x10^6 stem cells/kg	1.5 – 3.5 x10^7 stem cells/kg
Engraftment	Faster than cord but less than peripheral blood	Fastest	Slowest
T cell Content	Low	Highest (high risk of GVHD)	Low and immature
Other	Commonly used in pediatric patients	Commonly used in adults and autologous	Mainly for allogeneic; rising use in pediatric and adult

Allogeneic Transplants: Types of Conditioning Regimens

	Description	Pros	Cons
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:** ≥ 20,000/uL for 3 consecutive days without transfusion
- **Neutrophils:** Absolute neutrophil count (ANC) of >500/uL 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:
    - 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

    and
  - Bacterial sepsis unresponsive to antibiotic therapy

    or
  - Disseminated fungal or yeast infection

- Minimum dose of granulocytes: 1×10^{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

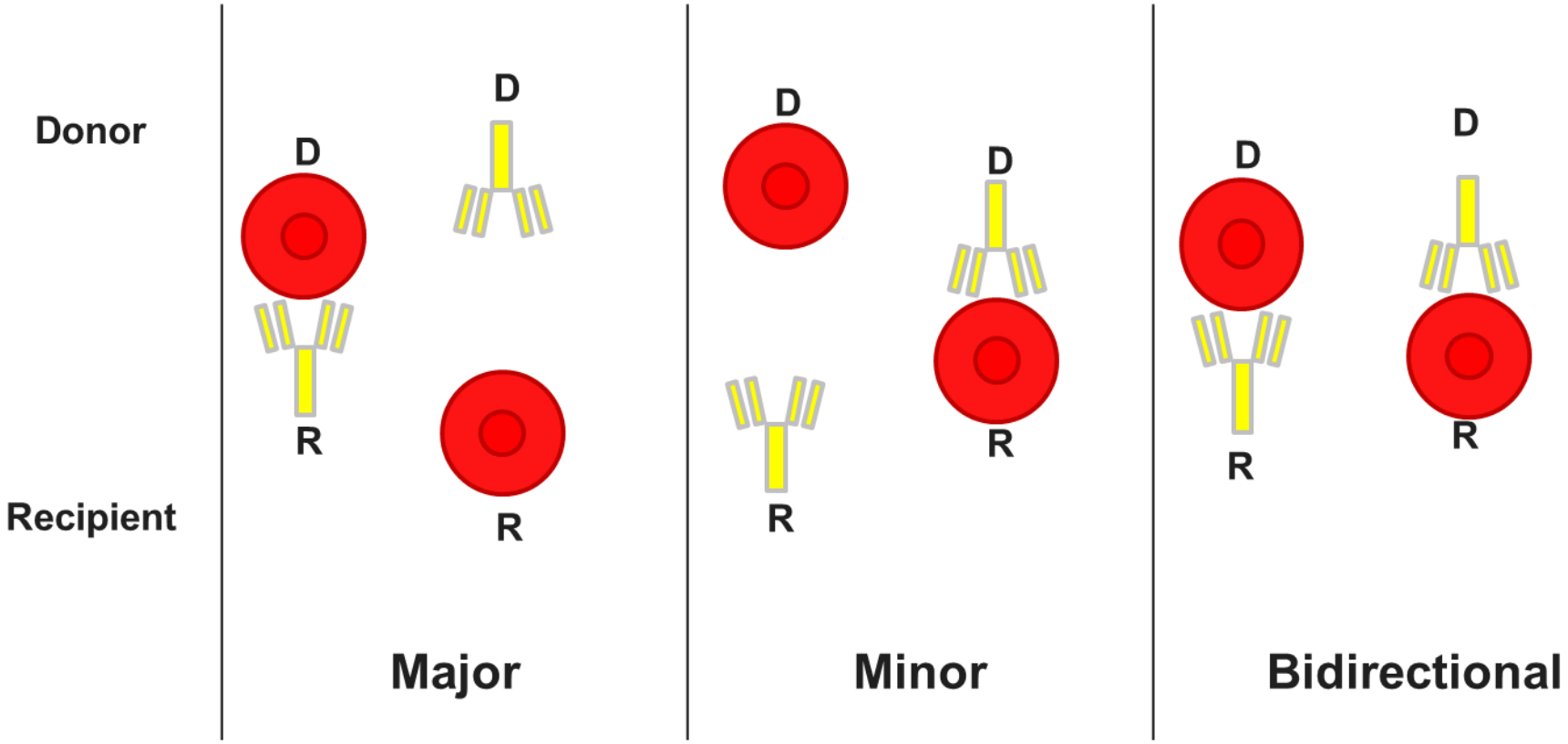

Figure 1: Schematic representation of major, minor, and bidirectional ABO incompatibility between donor and recipient in allogeneic HSCT. D represents the HSCT donor and R represents the HSCT recipient.

Potential ABO Combinations Potentially Existing Between Donors and Recipients for HSCT

		Donor			
		O	A	B	AB
Recipient	O	Compatible	Major	Major	Major
	A	Minor	Compatible	Bidirectional	Major
	B	Minor	Bidirectional	Compatible	Major
	AB	Minor	Minor	Minor	Compatible

ABO Compatibility in HSCT

Mismatch Type	Potential clinical manifestations	Potential interventions
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 isohemagglutinins • Delayed hemolysis caused by either donor's and/or recipient's isohemagglutinins	• Combination of practices used in minor and major ABO incompatibility

Transfusion Support in HSCT

		Pre-Transplant Phase	Transplant Phase		Post-Engraftment Phase
Recipient	Donor	All Components	Red Blood Cells	Plasma & First Choice Platelets	All Components
O	A	Recipient	O	A	Donor
O	B	Recipient	O	B	Donor
O	AB	Recipient	O	AB	Donor
A	O	Recipient	O	A	Donor
A	B	Recipient	O	AB	Donor
A	AB	Recipient	A	AB	Donor
B	O	Recipient	O	B	Donor
B	A	Recipient	O	AB	Donor
B	AB	Recipient	B	AB	Donor
AB	O	Recipient	O	AB	Donor
AB	A	Recipient	A	AB	Donor
AB	B	Recipient	B	AB	Donor

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

1. Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, Fung MK, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. Ann Intern Med 2012;157(1):49-58.
2. Kaufman RM, Djulbegovic B, Gernsheimer T, Kleinman S, Tinmouth AT, Capocelli KE, et al. Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern Med 2015;162(3):205-13.
3. Fung MK, Grossman BJ, Hillyer CD, Westhoff CM, editors. Technical manual. 18th ed. Bethesda (MD): American Association of Blood Banks Press; 2013.
4. Cohn, CS. Transfusion support issues in hematopoietic stem cell transplantation. Cancer Control 2015;22(1):52-59.
5. Price TH, Boeckh M, Harrison RW, McCullough J, Ness PM, Strauss RG. Efficacy of transfusion with granulocytes from G-CSF/dexamethasone-treated donors in neutropenic patients with infection. Blood. 2015 Oct 29;126(18):2153-61. doi: 10.1182/blood-2015-05-645986. Epub 2015.
6. Rowley SD, Donato ML, Bhattacharyya P. Red blood cell-incompatible allogeneic hematopoietic progenitor cell transplantation. Bone Marrow Transplant 2011;46(9):1167-1185.
7. Blin N, Traineau R, Houssin S, Peffault de Latour R, Petropoulou A, Robin M, et al. Impact of donor-recipient major ABO mismatch on allogeneic transplantation outcome according to stem cell source. Biol Blood Marrow Transplant 2010;16(9):1315-1323.
8. Booth GS, Gehrie EA, Bolan CD, Savani BN. Clinical guide to ABO-incompatible allogeneic stem cell transplantation. Biol Blood Marrow Transplant 2013; 19(8):1152-1158.
9. Daniel-Johnson J, Schwartz J. How do I approach ABO-incompatible hematopoietic progenitor cell transplantation? Transfusion 2011;51(6):1143-1149.
10. Fontaine MJ, Mills AM, Weiss S, Hong W-J, Viele M, Goodnough LT. How we treat: risk mitigation for ABO-incompatible plasma in plateletpheresis products. Transfusion 2012; 52(10): 2081-2085.

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