

# Blood component support in HSCT

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Time: 4:40 PM to 4:55 PM

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# Content

- Objective
- Preparedness
- Support in blood group incompatible settings
- Granulocyte transfusion
- Refractory thrombocytopenia
- Newer techniques

# Objective and Planning

- Provide safe and effective blood products throughout the pre-, intra-, and post-transplantation periods
- Critical for optimizing overall survival and outcomes
- Anticipate the requirement
  - Conditioning: minimal transfusion
  - Aplasia phase (Day 0–20): maximum dependence
  - Engraftment: platelet reqt may continue post neutrophil engraftment
  - Chronic GVHD: possible intermittent support
- Restrictive transfusions vs Liberal transfusions : Similar outcomes

# Factors influencing the extent of support

- **Primary disease**
- **HSCT donor type**
  - Auto HSCT < AlloMSD < AlloMUD < Haplo
- **Type of regimen**
  - RIC/nonmyeloablative regimens < myeloablative regimens
- **Phase of transplant**
- **Complications**
  - Scenarios: Cytopenia, sepsis, mucositis, procedures
  - PRCA, GvHD, PLS, AIHA, TMA, SOS
- **Blood group incompatibility**

# What is mandatory ?

- Leucoreduction except for granulocytes
- Irradiation for all products except stem cells
- **Appropriate blood product based on phase of HSCT**
- BMT unit's policy for thresholds

# Leucoreduction

- Red blood cell products contain about  $2 \times 10^9$  leucocytes
- Platelet product contains  $2 \times 10^6$  leucocytes
- Options:
  - Pre-storage leucoreduced products
  - Leucocyte reduction filter during transfusion
- Aim: Less than  $1 \times 10^6$  leucocytes in the product
- Benefits: Reduces....
  - FNHTR (esp Pre-storage leucoreduction)
  - CMV transmission
  - HTLV-1, HTLV-2, Herpesvirus, EBV, Trypanosoma cruzi
  - Alloimmunization by reducing HLA sensitisation



# Irradiation

Gamma irradiation Caesium-137, 25Gy

- Induces chemical cross links in the DNA of irradiated donor lymphocytes preventing their proliferation
- Prevents **Transfusion-Associated Graft-vs-Host Disease (TA-GVHD)**

## BSH guidelines:

- Allo HSCT: (all 4 criteria)

1. >6 months have elapsed since the transplant date
2. The lymphocyte count is  $>1.0 \times 10^9/L$
3. The patient is free of active cGVHD
4. The patient is off all immunosuppression

- Auto HSCT:

- 7 days prior to and during harvest
  - to prevent the collection of viable allogeneic T lymphocytes, which can potentially withstand cryopreservation
- until 3 months post transplant

- *Some patients may require indefinite irradiation based on their conditioning regimen, disease, or previous therapy (e.g., Hodgkin lymphoma or prior purine analog treatment)*



# Clinical scenarios and desired cut offs

Scenario	Component	Threshold / Target
General Hb cutoff	RBC	< 7g/dL
Aplastic phase (day 0–20)	Platelets	<10k prophylaxis
Aplastic with fever/mucositis	Platelets	<20–30k
Peri-engraftment bleeding	Platelets	maintain $\geq$ 50k
CNS bleed	Platelets	maintain $\geq$ 100k
Symptomatic anemia	RBC	Hb <8 g/dL
Cardiac disease	RBC	Hb < 9-10 g/dL
Coagulopathy with bleeding	FFP	INR >1.5
Low fibrinogen	Cryo	<150–200 mg/dL

# Selecting appropriate blood groups for recipients of ABO mismatched stem cell transplants

	Donor	Recipient	Phase I: All components	Phase II and Phase III				
				Red cells	Platelets		FFP	
					First choice	Second choices**	First choice	Second choices
<b>Major ABO incompatibility</b>	A	O	Recipient	O	A	AB*, B, O	A	AB
	B	O	Recipient	O	B	AB*, A, O	B	AB
	AB	O	Recipient	O	AB*	A, B, O	AB	-
	AB	A	Recipient	A, O	AB*	A, B, O	AB	-
	AB	B	Recipient	B, O	AB*	B, A, O	AB	-
<b>Minor ABO incompatibility</b>	O	A	Recipient	O	A	AB*, B, O	A	AB
	O	B	Recipient	O	B	AB*, A, O	B	AB
	O	AB	Recipient	O	A	A, B, O	AB	-
	A	AB	Recipient	A, O	A	A, B, O	AB	-
	B	AB	Recipient	B, O	B	B, A, O	AB	-
<b>Bi-directional ABO incompatibility</b>	A	B	Recipient	O	B	B, A, O	AB	-
	B	A	Recipient	O	A	A, B, O	AB	-

# Phases of HSCT

- **Phase I:** Pre-transplant  
(period from diagnosis to transplant)
- **Phase II:** Post-transplant immediate phase  
(period from transplant to RBC engraftment)
- **Phase III:** Post-transplant after engraftment

# Major ABO incompatibility

- Presence of anti-A, anti-B or anti-A, B **antibodies in the recipient's plasma** incompatible with donor red cells
  - e.g., group O recipient and donor group A, B or AB
  - group A, B recipient and donor group AB
- Risk depends on the volume of red cells infused and the titre of Ab present
- Acceptable volume: 10-20 ml of RBCs in stem cell product
- Issues:
  - Acute hemolysis at time of stem cell infusion
  - Delayed hemolysis due to production of antibodies by residual host lymphocytes
  - PRCA (8-26%): Rx with PE, Rituximab, Daratumumab
  - Delayed engraftment
- Pretransplant measures:
  - Iso-agglutinins can be removed from recipients if the titer  $\geq 1:128$  via plasmapheresis or extracorporeal immunoadsorption

# Minor ABO incompatibility

- Presence of anti-A, anti-B or anti-A, B **antibodies in the donor's plasma** incompatible with the recipient's red cells
  - e.g.- donor group O and recipient group A, B or AB
  - donor group A or B and recipient AB
- Issues:
  - **Acute hemolysis** of recipient RBCs at time of **marrow infusion** caused by anti-A or anti-B in the plasma of the donor product
  - **Delayed hemolysis** of recipient RBCs due to **passenger lymphocyte syndrome** (1-3 weeks after infusion with positive DAT, self limiting)
    - donor plasma cells contained within the transplanted graft will elaborate increasing levels of iso hemagglutinins directed at recipient RBCs
  - Late engraftment of leucocytes has been noted for minor incompatibility compared to major and bidirectional incompatibility

# Major plus minor (“bidirectional”) ABO incompatibility

- When both the donor and recipient’s plasma have anti A, anti-B or anti-B, anti-A antibodies reactive with recipient and donor cells respectively
  - e.g., donor group A and recipient group B or vice versa
- Issues: as for major and minor mismatches

# Compatible HSCT or Major / minor / bidirectional incompatible HSCT

	Haemopoietic stem cell donor				
	Blood group	O	A	B	AB
Haemopoietic stem cell recipient	O	Compatible	Major	Major	Major
	A	Minor	Compatible	Bidirectional	Major
	B	Minor	Bidirectional	Compatible	Major
	AB	Minor	Minor	Minor	Compatible

# Transfusion strategy for peri-transplantation

ABO incompatibility	Recipient	Donor	Phase I		Phase II			Phase III
			All product	RBC	PLT 1st	PLT 2nd	Plasma	All product
Major	O	A	Recipient	O	A	AB, B, O	A	Donor
	O	B	Recipient	O	B	AB, A, O	B	Donor
	O	AB	Recipient	O	AB	A, B, O	AB	Donor
	A	AB	Recipient	A	AB	A, B, O	AB	Donor
	B	AB	Recipient	B	AB	B, A, O	AB	Donor
Minor	A	O	Recipient	O	A	AB, B, O	A	Donor
	B	O	Recipient	O	B	AB, A, O	B	Donor
	AB	O	Recipient	O	AB	A, B, O	AB	Donor
	AB	A	Recipient	A	AB	A, B, O	AB	Donor
	AB	B	Recipient	B	AB	B, A, O	AB	Donor
Bidirectional	A	B	Recipient	O	AB	B, A, O	AB	Donor
	B	A	Recipient	O	AB	A, B, O	AB	Donor

# Donor and recipient relationship associated with Rh D

Donor antigen	Recipient antigen		
	D negative with anti-D	D negative without anti-D	D positive
D negative with anti-D	Identical	Identical	Minor incompatibility
D negative without anti-D	Identical	Identical	Minor mismatch
D positive	Major incompatibility	Major mismatch	Identical

Jekarl DW, Kim JK, Han JH, Lee H, Yoo J, Lim J, Kim Y. **Transfusion support in hematopoietic stem cell transplantation.** BR 2023;58:S1-S7.

# Transfusion strategy in Rh incompatibility

- Pre-transplant: recipient-type red cells and platelets
- Post-transplant:
  - HSCT recipients should receive D-negative red cells and platelets except when both the HSC donor and recipient are D-positive
  - Major Rh D incompatibility: D-negative blood components to be given until D-positive red cells are detected. Thereafter can receive D-positive components
  - Minor Rh D incompatibility: D-negative blood components should be given indefinitely

## Minor Rh incompatibility

- Delayed hemolysis can occur due to donor lymphocyte-derived anti-D
- Risk is higher if donor has been previously sensitized to D Ag

# Rare scenarios

- **Second HSCT in a patient with an incompatible ABO blood group from the first donor**
  - Give RBCs of the O blood group
  - Give platelets or plasma of the AB blood group
- **For patients with diseases that predispose to alloimmunization**

e.g., myelodysplastic syndrome -may consider RBC Ag typing and providing RBCs accordingly( matched for RhD, RhC, RhE, and K (Kell) antigen), to prevent alloantibody formation

Feasibility/policy ?
- **Cord blood transplants:** Two different source with different ABO blood group
- **Prior monoclonal Ab treatment interfering with cross matching**

e. g., anti CD38 (Daratumumab), anti-CD 47

# Granulocyte Transfusion: $1 \times 10^{10}$ granulocytes

- Indications:
  - Proven or probable bacterial or fungal infection with fever for 24–48 hours with persistent morbidity
  - No response to antimicrobials in life threatening infections
  - Absolute neutropenia ( $<0.5 \times 10^9/L$ )  $<0.2$  ??
  - Expected recovery of bone marrow function
- GT can be a therapeutic option as a bridging therapy until the recovery of white blood cells

# Challenges of granulocyte transfusion

- Has to be ABO compatible with recipient plasma **cos the product contains donor RBCs**
- CMV matching
- Infused within 24 hrs
- Timely recruitment of designated donors:
  - at least 3 days are required for the donor pre-transfusion test, mobilization and collection
- Mobilization of granulocytes using G-CSF and dexamethasone could raise ethical problems and **donor** safety issues
- Adverse effects in **recipient**: fever, alloimmunization, and TRALI

# Refractory thrombocytopenia

- Check Corrected Count Increment (CCI)
- Causes:
  - Alloimmunization
    - antibodies directed against HLA class I antigens or human platelet antigens (HPAs)
  - Sepsis
  - Splenomegaly
- Options:
  - Platelets lacking the HLA antigens against which they have developed antibodies
  - Epitope matching
  - Serologically crossmatched platelets
- Avoid random donor platelets if heavily alloimmunized

# Refractory thrombocytopenia

- Concern: Donor-specific HLA antibodies can lead to poor engraftment and increased incidence of graft failure
- Desensitization with immunosuppression or plasma exchange
- Post HSCT platelet refractoriness: Daratumumab (B cell depletion therapy)
- Prevention:
  - Leukoreduction reduces HLA sensitization from blood transfusion
  - ABO matched platelet transfusion decreases HLA-antibody formation

# CMV requirements for blood components in HSCT recipients

- CMV-negative components are not required irrespective of serological status of donor and recipient for HSCT **except for granulocytes**
- Granulocytes for CMV-negative HSCT recipients should be CMV-negative

# Other component and their indications

- FFP for deranged INR/PT only with bleeding
- Cryoppt if fibrinogen <150–200 mg/dL
- Pre-procedure fibrinogen target 250 mg/dL

## Points to remember:

- Hepatic dysfunction
  - Synthesis of both natural pro- and anti-coagulants is altered
- Inflammatory state
  - Increased production of procoagulant factors (e.g., factor VIII and von Willebrand factor), in conjunction with disease- and transplant-related factors (e.g., GVHD), may predispose to thrombosis.

# Newer safe products:

## Pathogen reduced platelets and cryoprecipitate

- Pathogen reduction technology(PRT)
  - US FDA approved method
    - addition of a psoralen compound during manufacturing + exposure to UV light >>> nucleic acid damage >>> inactivating of microorganisms
  - Other regions of the world
    - Utilize riboflavin and UV light
    - UV light alone
- Advantage:
  - reduce the risk of CMV transmission
  - Considered irradiation-equivalent
- Disadvantage:
  - Increased cost
  - Lower corrected count increments (CCIs)
  - Debated increase in HLA alloimmunization

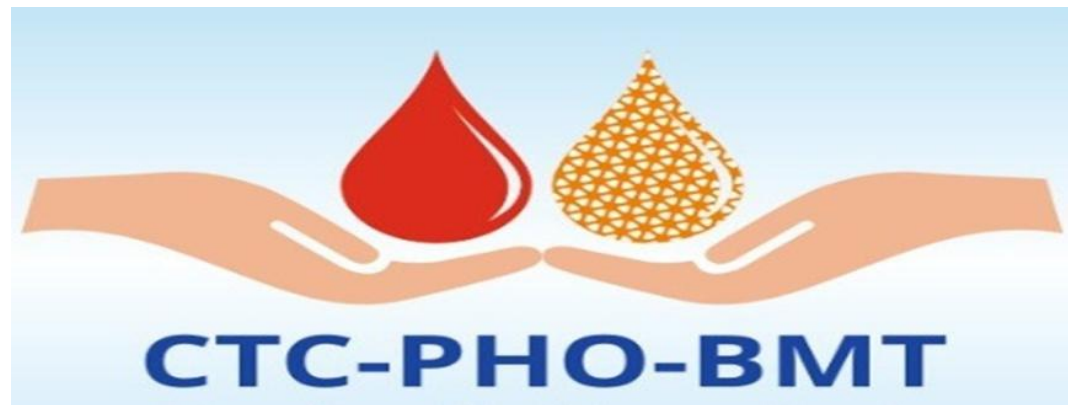
# Conclusions

- Transfusion support for HSCT is an essential part of supportive care
- Needs collaboration in advance between BMT team and transfusion medicine team
- Integral part of pre-transplant counselling  
(Recipient and donor blood group combination)
  - Impact on outcomes
  - Complications
  - Need of timely donors esp for granulocytes

# References

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Thank You



# Question: 1

- Dose of irradiation required for blood component in HSCT ?

Options:

1. 5 Gy
2. 10 Gy
3. 25 Gy
4. 75 Gy

## Question: 2

- Shelf life of granulocyte product is :

Options:

1. 5 days
2. 2 days
3. 12 hours
4. 24 hours