Allogeneic Hemopoietic Stem Cell Transplantation: Transfusion issues

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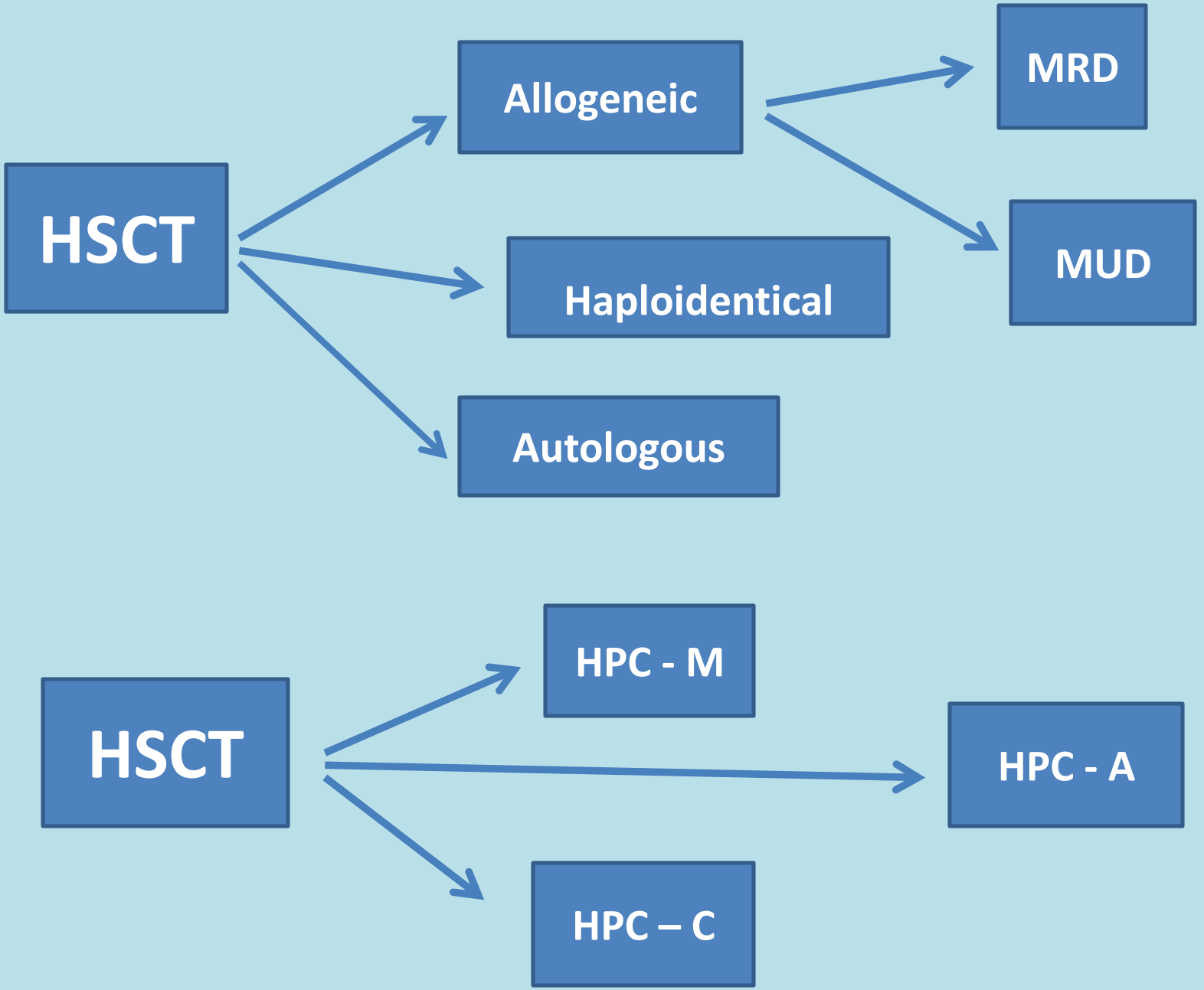

HSCT
Allogeneic
MRD
MUD
Haploidentical
Autologous
HSCT
HPC - M
HPC - A
HPC – C

Red cell antigens, NOT part of the HLA system

Antigen	Chromosome
HLA	6
ABO	9
Rh	1
Kell	7
Kidd	18
Duffy	1
Lewis	19
MNS	4

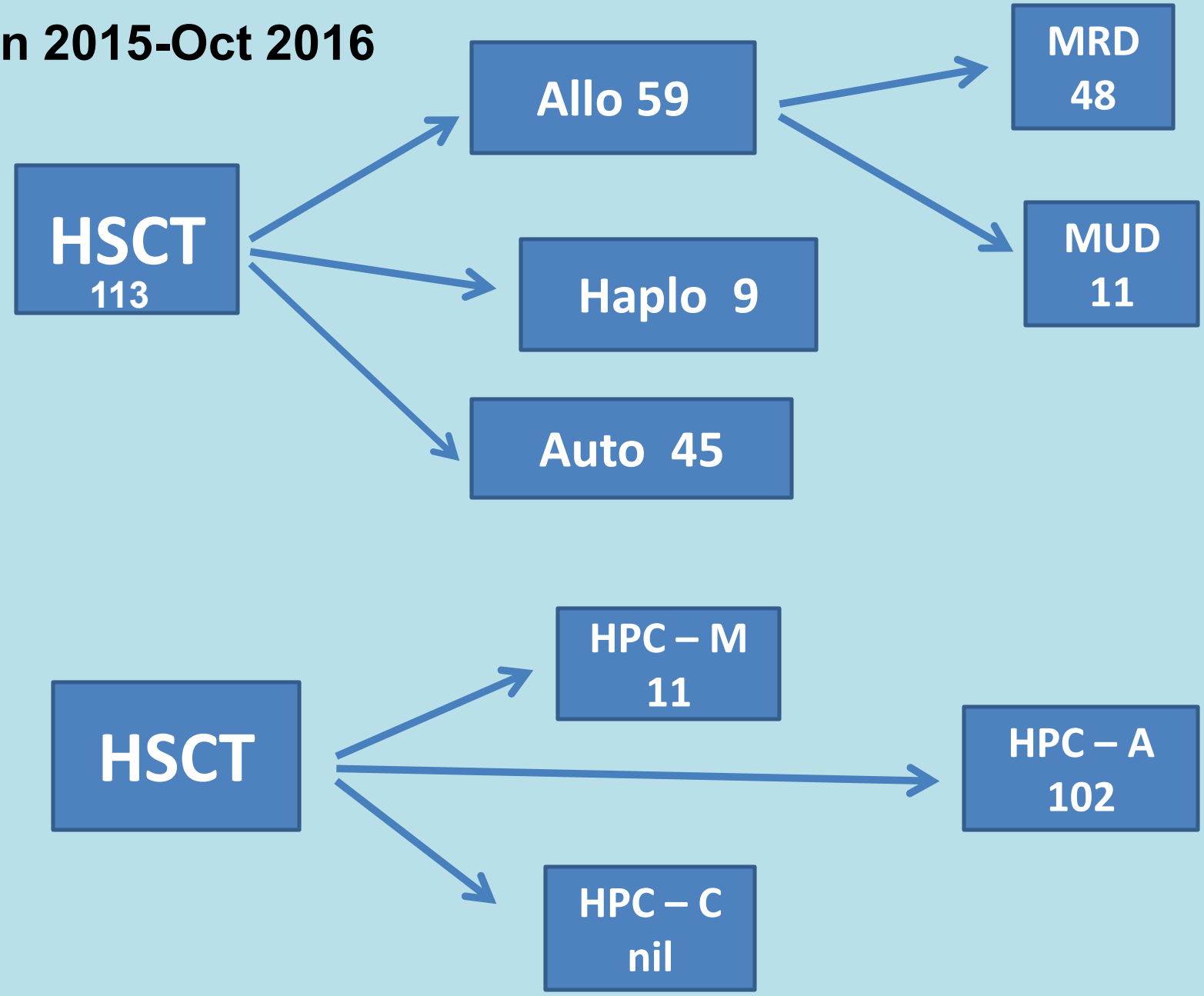
Challenges

Major	Minor	Bidirectional
• Intravascular hemolysis • Continued production of anti-donor iso-agglutinins with delayed engraftment / PRCA	• Intravascular hemolysis • Production of anti A / anti B by donor B lymphocytes • PLS	Both major and minor challenges

Adverse effects of transfusions:

Platelet refractoriness
Allergic reactions
BACON
Red cell alloimmunisation
TRALI
DMSO toxicity

Jan 2015-Oct 2016



Immuno-hematologic evaluation

Pre-HSCT

- ABO & Rh
  Recipient,donor/product
- DAT, Ab screen, auto
  Donor &recipient
- Cross match
  major & minor
- Iso-agglutinin titers

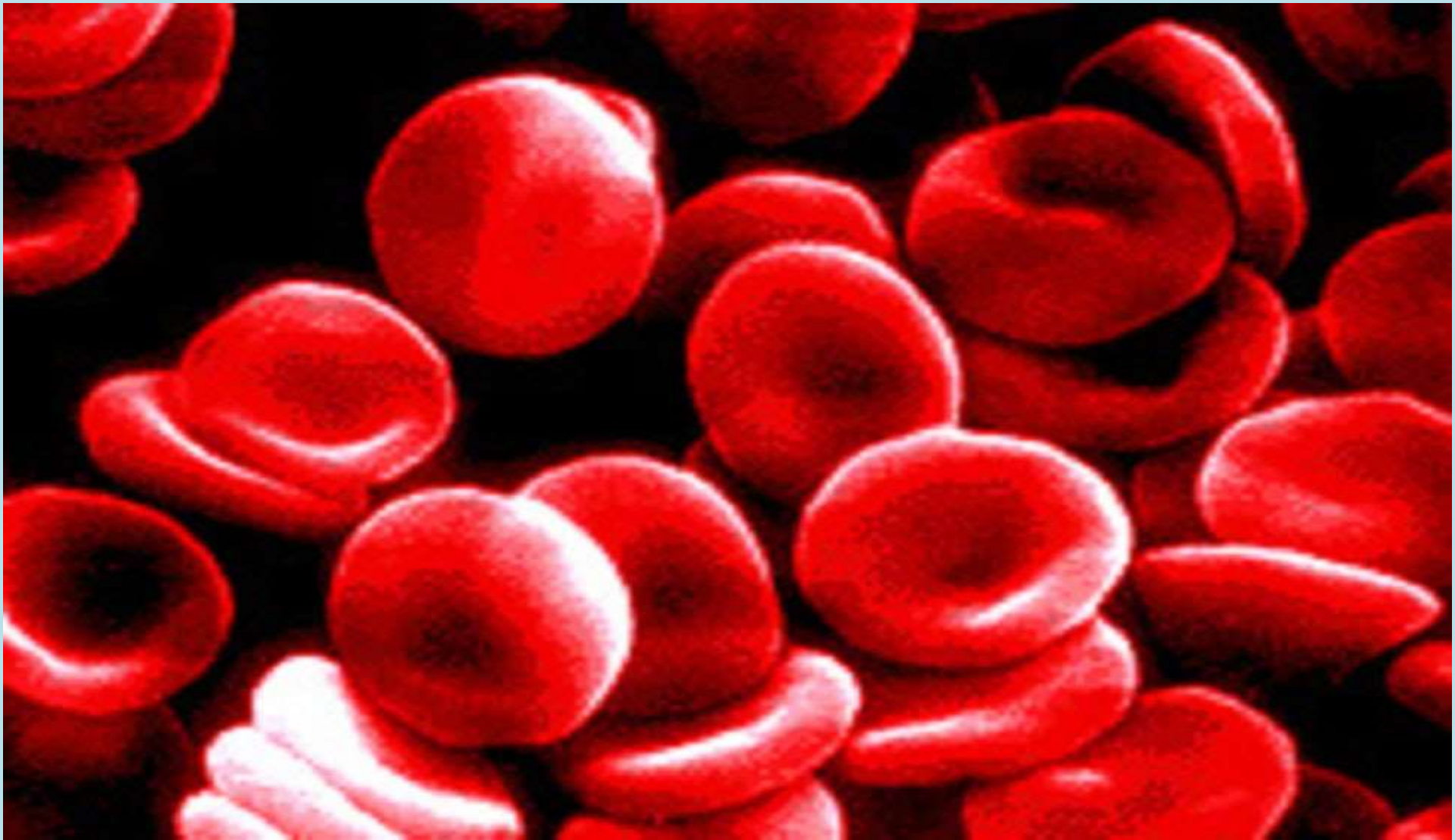
Post-HSCT

- Blood group
  Tube & CAT
- DAT
  antibody screen
- Iso-agglutinin titers

Transfusion policy for ABOi transplants at Tata Medical Center

ABO mismatch	Transfusion policy
Major	**RBC, granulocytes** – O group/recipient type until recipient isoagglutinins disappear **Platelets, FFP** - AB group/donor type until recipient red cells disappear
Minor	**RBC, granulocytes** – O group/donor type until recipient isoagglutinins disappear **Platelets, FFP** - AB group/recipient type until recipient red cells disappear
Bidirectional	Group O RBC until recipient isoagglutinins are undetectable; group AB plasma until recipient red cells disappear, then switch to donor type products

Packed red cells



Packed red cells

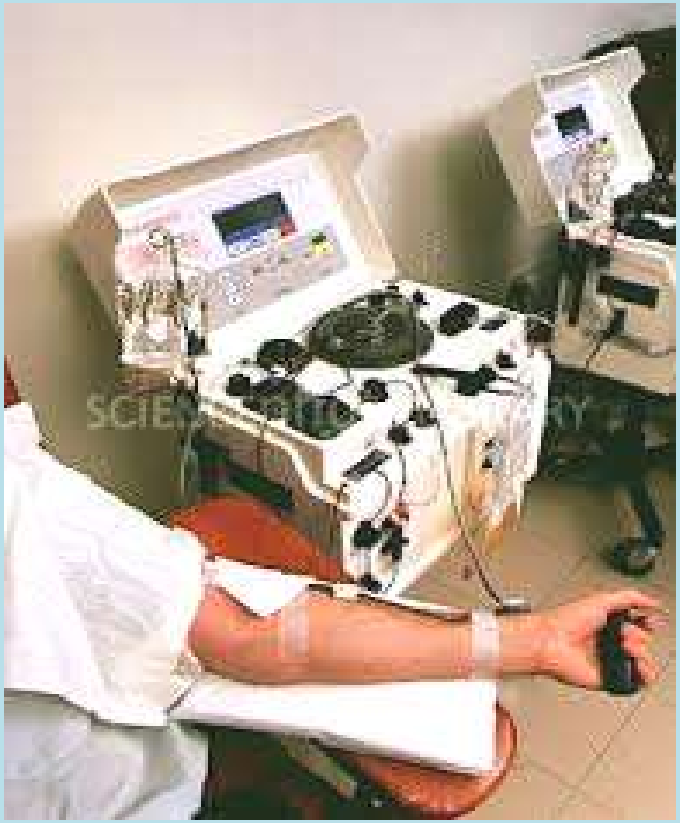
- RBC transfusions for (auto / allo HSCT) donors should be **autologous;** if autologous not possible, allogeneic irradiated RBC given
- Recipient RBC requirements - usually after transplant, until engraftment, more in ABOi, MUD transplants, sometimes pre-transplant (chemotherapy)
- RBC - leuco-depleted, irradiated, compatible with both donor and recipient
- We transfuse at hct < 24% or if symptomatic
- Our red cell alloimmunisation in HSCT is only 1.6%

Red cell alloimmunisation in oncology patients: A study from eastern India

Supriya Dhar and Sabita Basu

Transfusion and Apheresis Science 2015;52: 345-349

Platelets



RDP / SDP – leucoreduced, irradiated

SDP preferred

Platelet transfusions are usually prophylactic, group sp preferred

Trigger: < $10X10^9$/l in absence of bleeding, < $20X10^9$/l with signs of bleeding

Split product into two; interchange donors and products amongst patients

FFP, Cryoprecipitate

- Transfusion requirements for FFP, CP less than that for RBC and platelets
- Increased demand – APML, GVHD, sepsis, bleeding, DIC coagulopathy, liver disease, cyclosporine induced TTP ..... several CPP units issued
- Plasma containing products should be compatible with both donor and recipient, no need for irradiation

Granulocyte transfusions

Indications: Proven infection, refractory to antimicrobials with ANC < 500 /ul

- **Apheresis granulocytes**

  Screened donor- group specific, cross match compatible
  Neupogen 5 ug/kg + 8 mg dexamethasone

- **BC granulocytes**

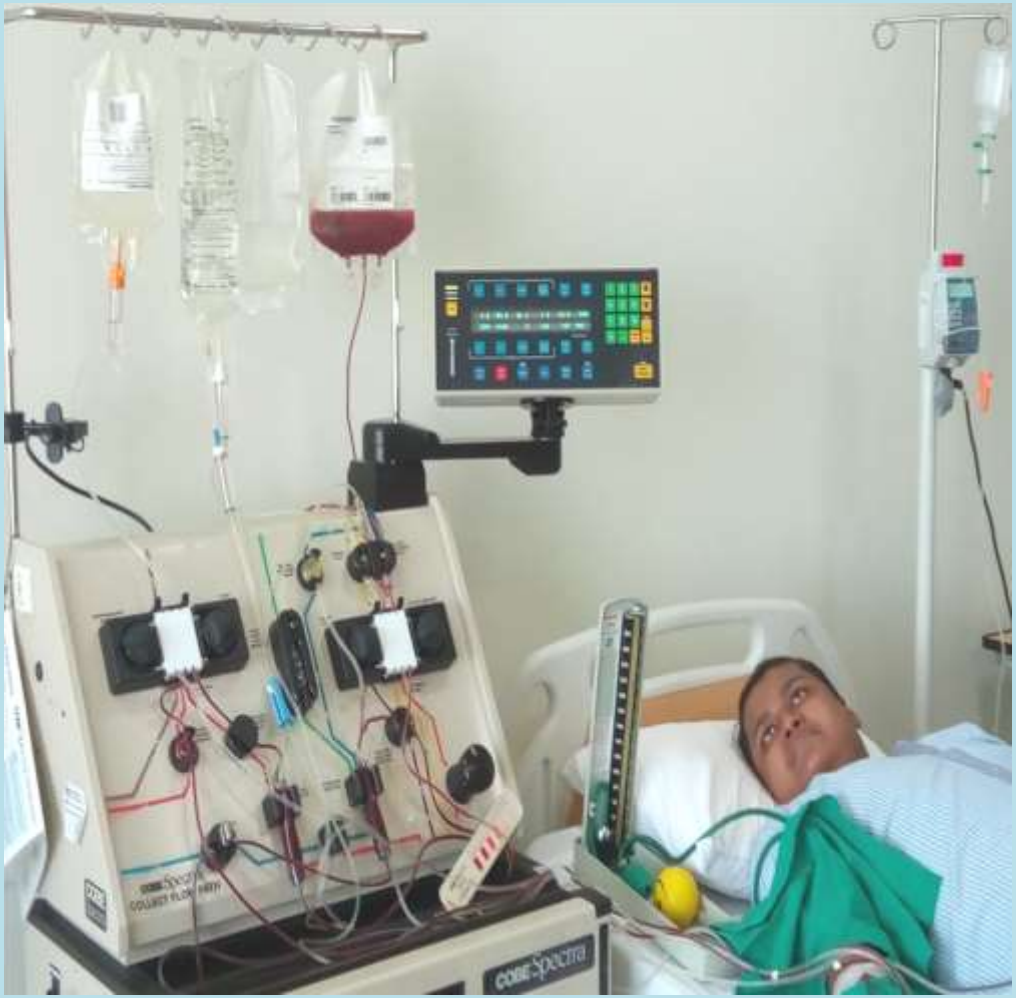
  Group specific BC bags, cross match compatible

  Usually prepared for 3 consecutive days,

  option when apheresis donor is not available / cost constraints

Product cross-matched, irradiated, issued 6-8 hours
Transfused without a filter, allergic reactions

Granulocyte apheresis



Donor lymphocyte infusion

- In relapse after HSCT, an option to avoid another transplant
- Lymphocytes from original stem cell donor are infused to induce remission by a process called the graft-versus-tumor (GVT) effect.
- Whole blood from stem cell donor (specific volume) transfused, without irradiation/ leuco-filter

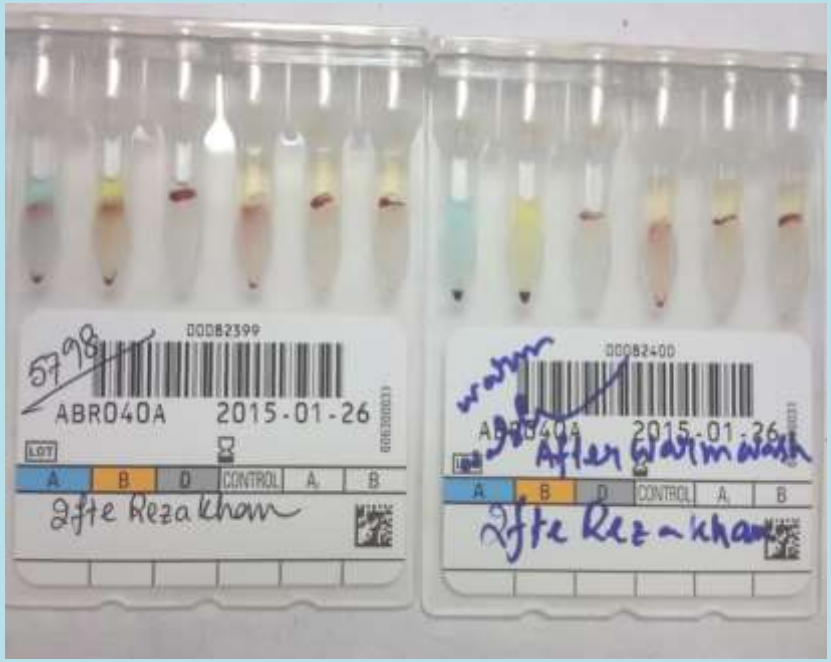
Case 1

- 11 years male child, HSCT for Fanconi anemia from HLA matched, ABO matched sibling donor
- Had complete engraftment by day +28, CMV reactivation since day +40, received valganciclovir
- On day +67, presented in emergency with pallor, deep yellow urine, icterus

Request for 2 RBC received…..

Hb 2.9 g/dl Retic 17.8% LDH 2915 U/l
Bilirubin (unconj) 3.3 mg/dl
Red cell agglutination at room temp

- Type IV blood group discrepancy
- Resolved with warm saline washing
- DAT 4+ IgG and C3
- Autocontrol positive
- Antibody screen: panagglutination



Immune-hemolytic anemia

Alloadsorption done (R1R1,R2R2,rr cells) : no alloantibodies
Thermal amplitude test and DTT treatment revealed mixed type AIHA

Mixed type AIHA due to CMV reactivation

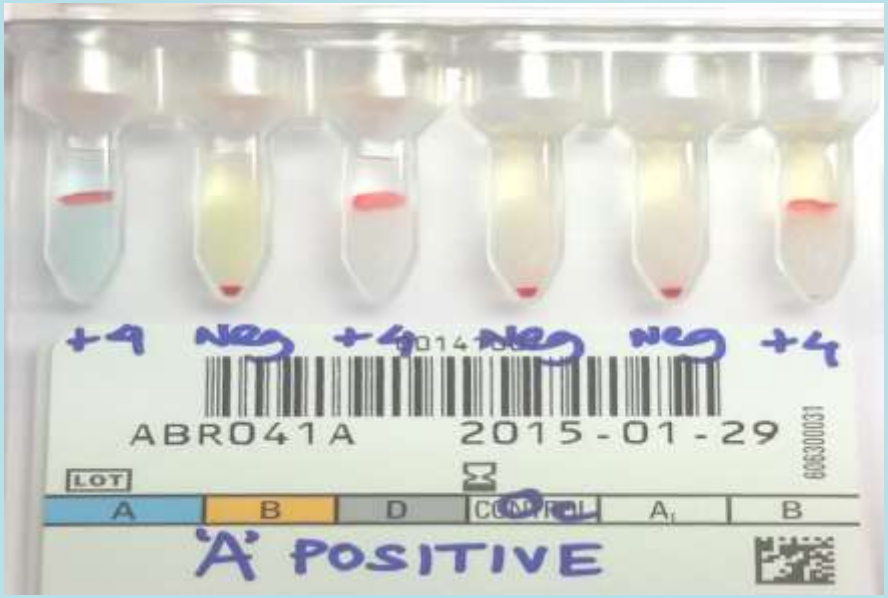
- Phenotype matched RBC (O, DcE/Dce) were transfused, Hb 7.3g/dl post-transfusion
- Rituximab - 4 weeks + steroid

Mixed type AIHA due to CMV reactivation *after HSCT:*

- 3-6 % incidence
- More in young patients, non-malignant disease transplants
- Infections may be an important trigger for autoimmune events after HSCT
- CMV may contribute to the onset of post-transplant complications

Indian J Hematol Bl Transf 2016; 32: 211-13
Datta SS, Reddy M, Basu S, Krishnan S

Case 2



Pre-transplant blood group A positive

B>>A HSCT At 8 weeks

At 16 weeks, anti B titer = 2048

At 16 weeks;

Patient was transfusion dependent,

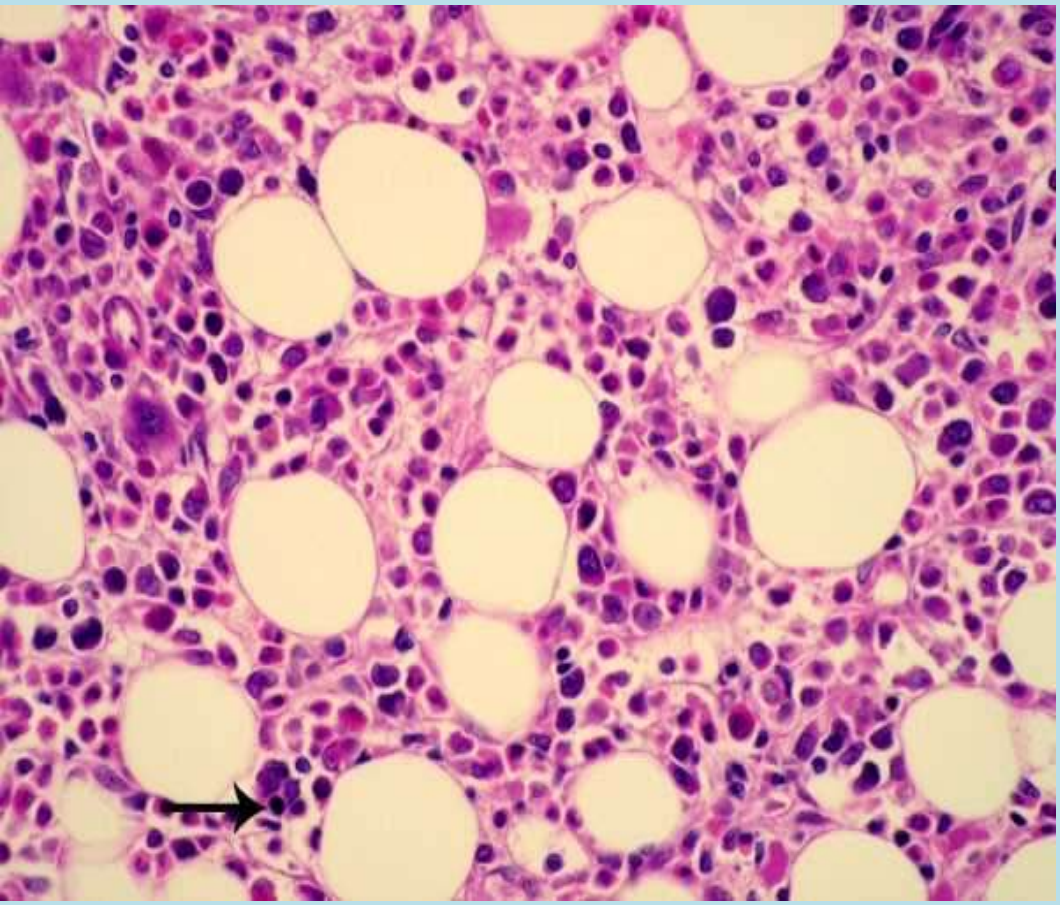
Hb ranged from 5.8-8 g/dl

Reticulocytes 0.05%

ANC > 500/UL

Unsupported platelet count > 20000/cmm

Mixed RBC chimerism



B > > A

Recipient anti B titer = 2048

Time to disappearance of anti B = 22 weeks

Red cell engraftment criteria:

- Independence of RBC transfusion
- Reticulocytes >1%
- 100% donor RBC chimerism
- Coincides with disappearance of recipient anti-donor isoagglutinins

PRCA confirmed on bone marrow biopsy

Risk factors for PRCA :

A > > O transplants, increased time to disappearance of recipient iso-agglutinins, cyclosporine for GVHD prophylaxis

Case 3

- 6 years F child, beta thalassemia major on regular transfusion; every 20-25 days.
- Was receiving phenotype matched RBC, oral iron chelation with S.ferritin monitoring
- Now to undergo allogenic HSCT from her 3 years sister (donor); was complete 6/6 HLA match, both B positive
- Minor cross match was incompatible

Clinically significant, naturally occurring anti M antibody, with both IgG and IgM components in the stem cell donor

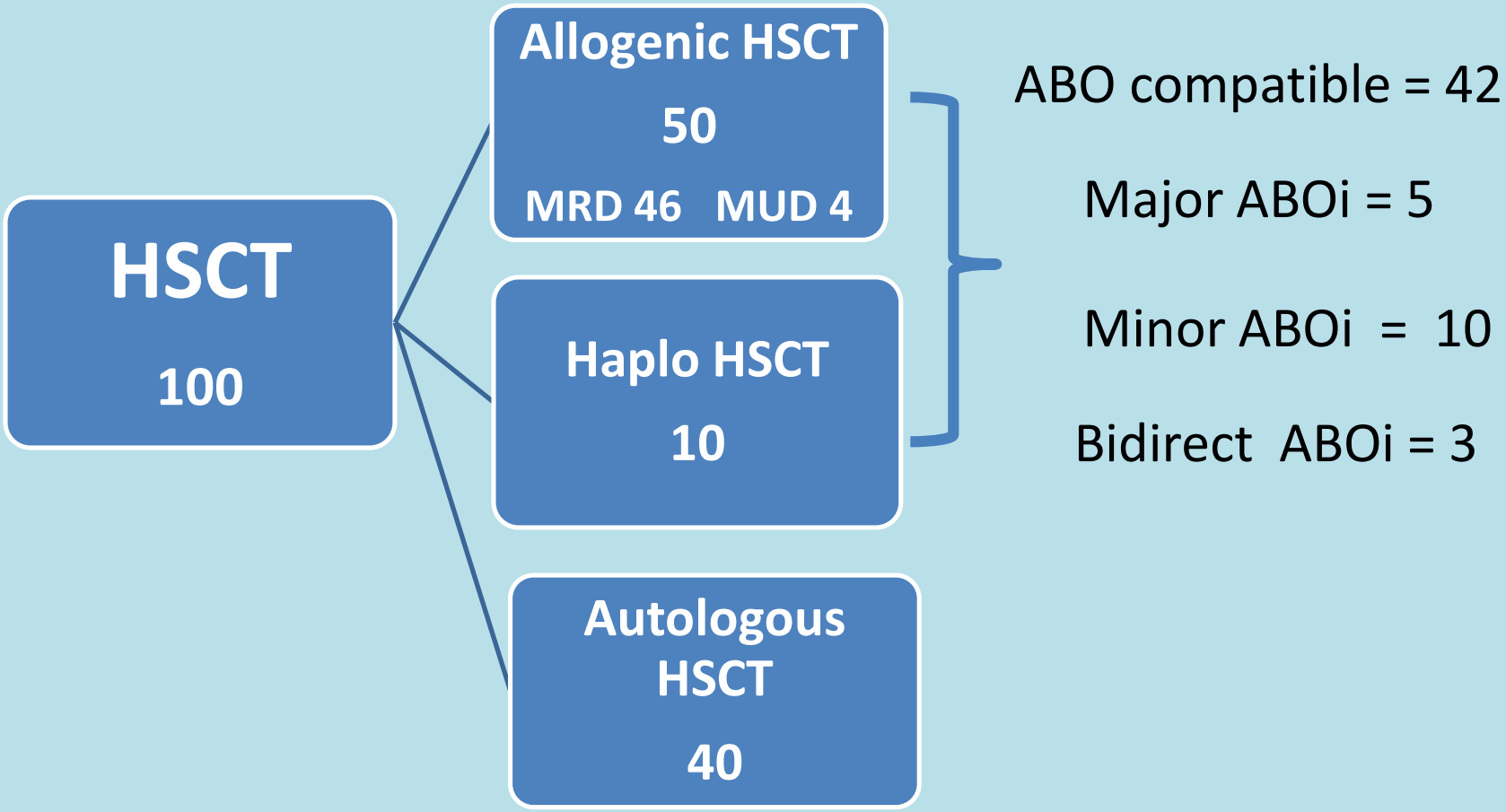
- Recipient was M antigen positive
- Stem cells were harvested from marrow, donor required one RBC transfusion

Group specific, M antigen negative, leucocyte-reduced, irradiated RBC transfused to donor
Harvested product was plasma depleted

Lessons learnt:

- Complete pre-HSCT immuno-hematologic evaluation necessary for donor and recipient
- Stem cell harvest may need modification

Blood product requirement



An analysis of transfusion support in HSCT- report from a centre in India

Datta SS, Basu S and Chandy M

Transfusion and Apheresis science 2015; 53:373-77

First 100 days blood product requirement among different HSCT categories

Blood product	Auto (40)	Allo (50)	Haplo-identical (10)
RBC	1.45 +/- 0.50	6.7 +/- 1.6	7.5 +/- 1.4
RDP	1.85+/- 0.82	8.38 +/- 3.2	15.1 +/- 2.8
SDP	1.87 +/- 0.84	3.26 +/- 1.2	4.3 +/- 1.2
FFP	0.23 +/- 0.10	5.9 +/- 1.8	7.4 +/- 2.2

Mean blood product requirement among the ABO matched groups

Blood product	Major + Bidirectional (08)	Minor + same group (52)	p value
RBC	15.8	5.25	< 0.05
SDP	5.25	3.52	< 0.05
RDP	20.5	6.94	< 0.05
FFP	12.75	3.98	< 0.05

Mean blood product requirement among the allo-HSCT categories (MRD vs MUD)

Blood product	MRD n=46	MUD n=4	p value
RBC	6.43	10	< 0.05
SDP	2.93	7	< 0.05
RDP	6.78	17.5	< 0.05
FFP	4.97	16.5	< 0.05

Factors affecting transfusion requirements

- Type of HSCT
  auto / allo / haplo
- Conditioning regimen (myelo-ablative, reduced intensity)
- Graft source
  HPC-A, HPC-M, HPC-C
- Dose of CD 34 + cells
- Previous chemotherapy
- Time to engraft
- Complications
  GVHD, CMV infection

Message…..

- Transfusion support in allogenic HSCT challenging - immuno-compromised, sepsis, multi-transfused, alloimmunisation, platelet refractoriness
- Immuno-hematologic evaluation to include –red cell phenotype, minor cross match and antibody titers
- Improved HSCT survival rates - organ damage is rising; ESRD occurs due to prior chemotherapy irradiation, sepsis, nephro-toxic drugs; second transplants
- Inappropriate transfusion might compromise transplantation outcome


Thank you
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