Transfusion support and Impact of ABO Mismatch on Allogeneic Stem cell Transplant

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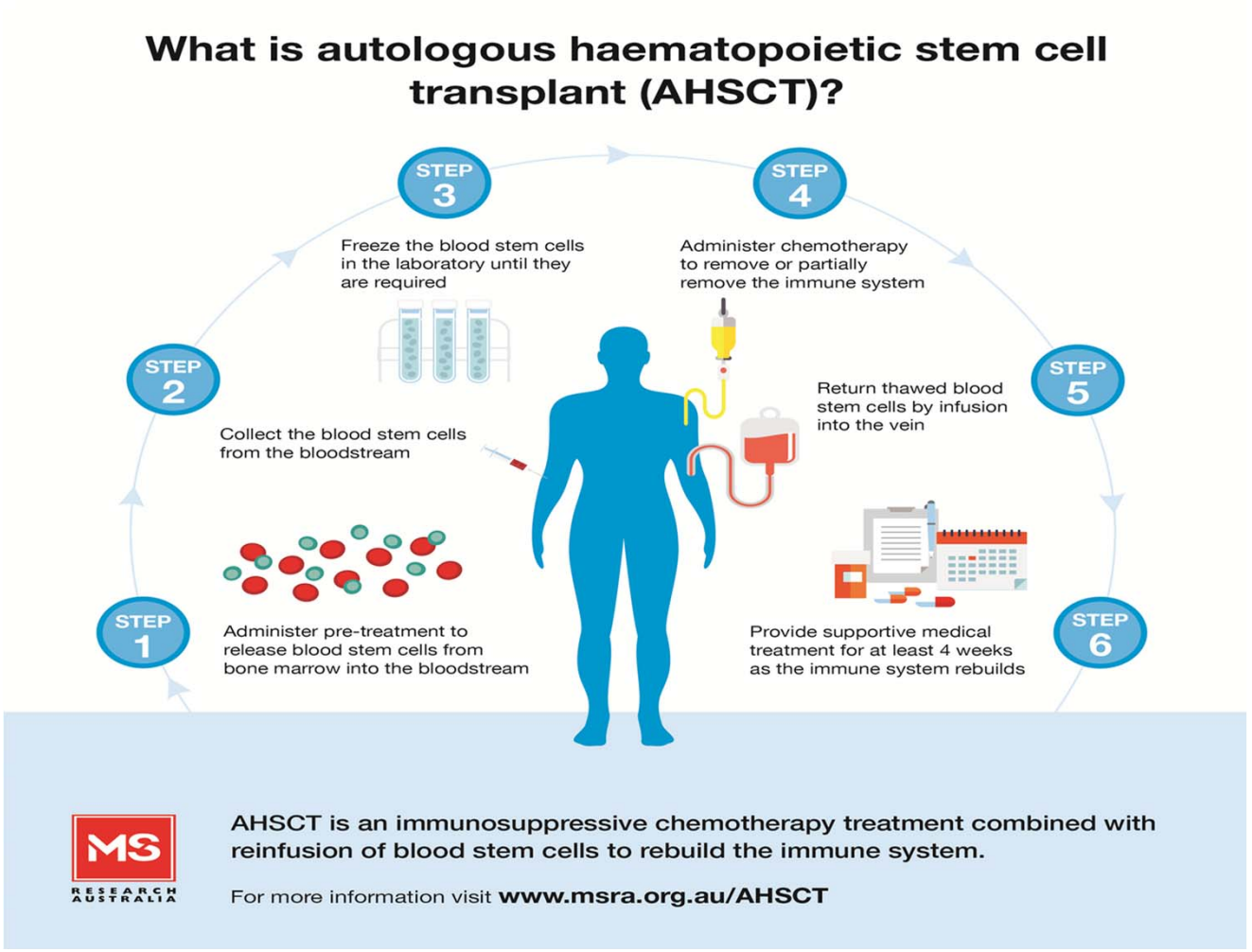
Types of Stem cell transplant

Autologous HSCT



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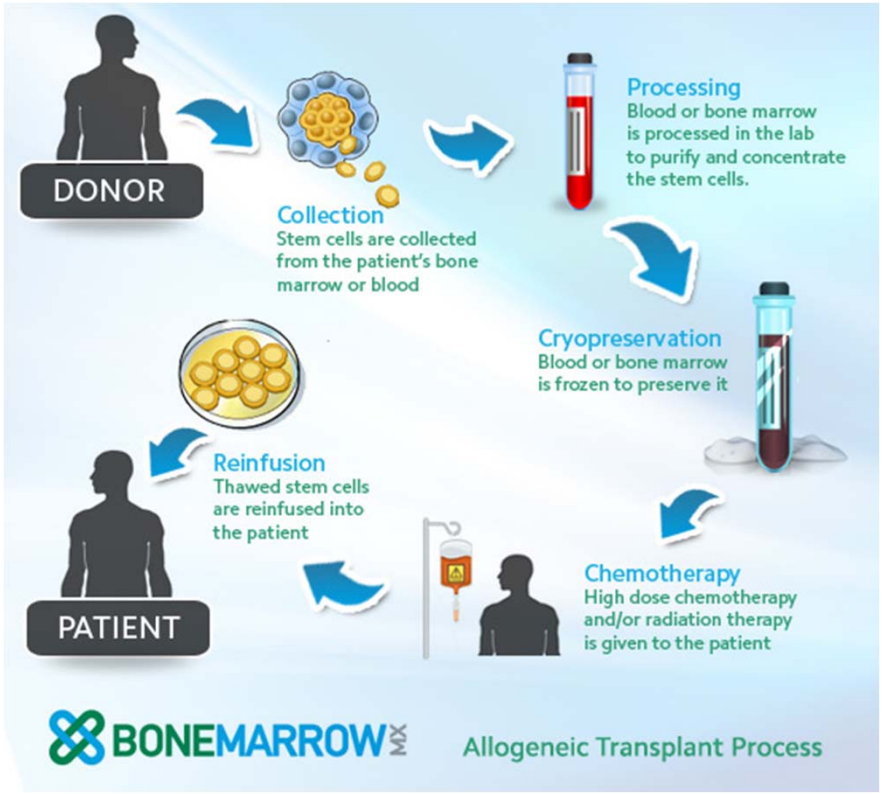
Allogeneic HSCT

Donor could be

- HLA- matched relative
- HLA- matched unrelated donor
- HLA mismatched family member
- Unrelated umbilical cord blood



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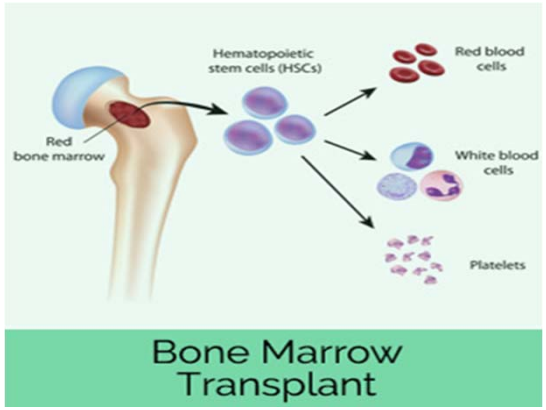
Source of Allogeneic stem cell transplant

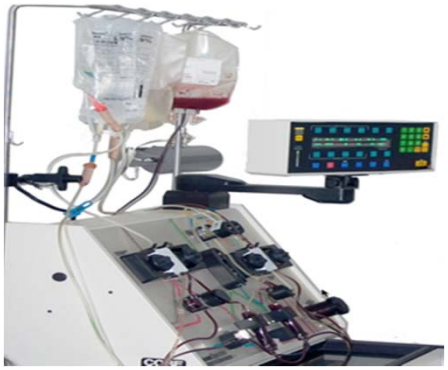
1 Bone Marrow Transplant

- Stem cells directly collected from bone marrow
- Using invasive procedure in the operating room
- Are able to collect all the cells you need



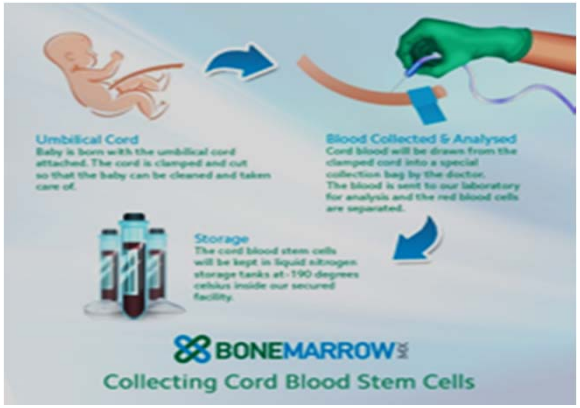
2 PBSC (Apheresis)

- Very often can obtain needed cell dose



3 Cord Blood

- Limiting factor is small cell dose



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Pre transplant Work up

- Blood group/ Ab screen
- Extended Red cell phenotype
- IHA titre in case of ABO incompatibility between donor and recipient
- DAT
- Haemolytic assessment

Pre-transplant support

- CMV status
- Irradiated
- Leukoreduced components

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Peri transplant phase

From time of immunosuppression to engraftment

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HLA and ABO Ags

- HLA Ags are expressed on chr 6p21 and devided into 3 regions
- The genomic region is very critical to engraftment, prediction of clinical outcomes and the potential harm from GVHD and the benifit from GVL
- ABO Ags are expressed on chr 9q34 and are inherited independently of HLA Ag
- HLA matched allogeneic HPC donor demonstrate some degree of ABO incompatibility
- 25-50% HLA matched allogeneic transplants are ABO incompatible

Any Allogeneic HSCT will be one of these

- ABO compatible

- Major ABO incompatible :
  - Recipient has isoagglutinins directed against the corresponding A or B antigens on donor RBCs e.g. from type **A, B, AB donor to O recipient**

- Minor ABO incompatible :
  - Donor has isoagglutinins directed against the corresponding A or B antigens on the recipient's RBCs e.g. from type **O donor to A, B, AB recipient**

- Bidirectional :
  - Both Recipient and Donor possess isoagglutinins against each other

    From type **A donor to B recipient**, vice versa

ABO Incompatibility

HPC Donor

HPC Recipient

Blood Group	O	A	B	AB
O	Compatible	Major	Major	Major
A	Minor	Compatible	Both	Major
B	Minor	Both	Compatible	Major
AB	Minor	Minor	Minor	Compatible

Issues with Major ABO Incompatible HSCT

- Recipient lymphocytes continue to produce IHA's (against donor red cell Ag) for up to 3-4 months
  - Haemolysis of red cells at time of graft infusion
    - Antibodies stay around for many weeks post-transplant
    - Destroy red cell precursors

- May delay RBC engraftment,
  - However may not impact Platelet / Neutrophil lines

- RBC chimerism may exist for weeks to months
  - Potential for delayed haemolysis

- Risk of Pure Red Cell Aplasia

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Issues with Minor ABO Incompatible HSCT

- Haemolysis of recipient red cells
  - -7-14 days post Tx
  - - Production of isohemagglutinins in donor graft
    - - Attempt to reduce volume of plasma in stem cell infusion

- Clinical sign of haemolysis 10-15%

- Chance of delayed hemolysis due to “passenger lymphocytes”
  Passenger Lymphocyte Syndrome
  – 5-15 days post transplant, rare after 6-8 weeks
  – Measure antibodies against recipient RBC Ag

- May have life time ABO discrepancy

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Total Allogeneic HSCT at Austin Health (Oct 2015 - Oct 2016)

No of transplants	Recipient's blood group	Donor's blood group	Donor Source	Match type
1	A POS	AB POS	Sibling	Major
2	O NEG	O POS	MUD	Identical
3	A POS	APOS	MUD	Identical
4	A POS	A POS	Sibling	Identical
5	O POS	O POS	MUD	Identical
6	O POS	A POS	Sibling	Major
7	O POS	O NEG	MUD	Identical
8	O POS	A POS	MUD	Major
9	B POS	AB POS	Sibling	Major
10	O POS	A POS	Sibling	Major
11	A POS	A NEG	MUD	Identical
12	O POS	O POS	MUD	Identical
13	A POS	B NEG	MUD	Bidirectional
14	O POS	O POS	Sibling	Identical
15	A NEG	A NEG	MUD	Identical
16	O NEG	O POS	MUD	Identical

Identical = 10

Major ABO Incompatible = 5

Minor ABO Incompatible = 0

Bidirectional = 1

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Patient 13

- 23 year old Male
- AML
- Transplant conditioning: Busulfan and Cyclophosphamide (Bu/Cy)
- Recipient Blood Group: A Positive
- Donor Blood Group : B Negative

Bidirectional ABO and Rh Incompatibility

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Patient 13 ABO Testing
Recipient: A Pos Donor: B Neg

Day	Anti-A	Anti-B	Anti-D	A1 Cell	B Cell
0	4+	0	4+	0	3+
3	4+	0	3+	0	2+
10	4+	0	3+	0	1+
15	3+ MF	0	3+ MF	0	0
28	3+ MF	3+ MF	3+ MF	0	0
56	2+ MF	4+ MF	2+ MF	0	0
88	1+ MF	4+	1+ MF	0	0
92	1+ MF	4+	0 MF	0	0

ABO Type Post-Transplant

- Over weeks to months, recipient develops donor hematopoiesis and immune function
- Grafts may contain some anti-A/B or RBCs from donor
  -Amount increase with engraftment
- Recipient red cell type at first
  -Slowly transitions to donor type
  -Will have mixed field in the transition
  -Is often weak due to chemotherapy
  -Slow transition to donor back type
  -Often is weak, incomplete, or not present
- Transfused products can obscure transition

Post-transplant monitoring

- Hb, retic
- Anti-A and anti-B isohaemagglutinins
  - IgG and IgM titres weekly from D+4
  -If titre >1:128 pre-transplant, monitor 2x/wk until <1:16, then weekly until disappearance
  -Followed until it is undetectable for 2 consecutive weeks except in patients with persistent RBC transfusion

Recommended Transfusion Strategy

Transfusion Support Recommendations for ABO-Incompatible HPC Transplantation

	Recipient	Donor	Phase I*	Phase II†				
			All Products	RBCs	Platelets		Plasma	
					First Choice	Second Choices	First Choice	Second Choices
Major	O	A	Recipient	O	A	AB, B, O	A	AB
	O	B	Recipient	O	B	AB, A, O	B	AB
	O	AB	Recipient	O	AB	A, B, O	AB	NA
	A	AB	Recipient	A	AB	A, B, O	AB	NA
	B	AB	Recipient	B	AB	B, A, O	AB	NA
Minor	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	NA
	AB	A	Recipient	A	AB	A, B, O	AB	NA
	AB	B	Recipient	B	AB	B, A, O	AB	NA
Bidirectional	A	B	Recipient	O	AB	B, A, O	AB	NA
	B	A	Recipient	O	AB	O, A, B	AB	NA

NA indicates not applicable.

* Time period from diagnosis to transplantation.

† Time period from transplantation to RBC engraftment.

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Transfusion Strategy at Austin

Transfusion Support Recommendations for ABO-Incompatible HPC Transplantation

Recipient	Donor	Phase I*	Phase II†				
		All Products	RBCs	Platelets		Plasma	
				First Choice	Second Choices	First Choice	Second Choices
O	A	Recipient	O	A	AB, B, O	A	AB
O	B	Recipient	O	B	AB, A, O	B	AB
O	AB	Recipient	O	O	A, B, O	AB	NA
A	AB	Recipient	A	A	A, B, O	AB	NA
B	AB	Recipient	B	B	B, A, O	AB	NA
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	NA
AB	A	Recipient	A	O	A, B, O	AB	NA
AB	B	Recipient	B	A	B, A, O	AB	NA
A	B	Recipient	O	B	B, A, O	AB	NA
B	A	Recipient	O	O	O, A, B	AB	NA

NA indicates not applicable.

* Time period from diagnosis to transplantation.

† Time period from transplantation to RBC engraftment.

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Suggested Protocol to Switch to Donor-type Blood

- Only donor-type red cells present (Without mixed field population)
- No transfusion for 90-120 days (Varies with organisations)
- No incompatible isohemagglutinins against the new RBC phenotype can be detected in 2 consecutive blood samples
- 100% donor type by molecular studies
- Negative DAT at the time of switch (Varies with organisations)

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Post engraftment

Recipient	Donor	Phase III‡				
		RBCs	Platelets		Plasma	
			First Choice	Second Choices	First Choice	Second Choices
O	A	Donor	A	AB, B, O	A	AB
O	B	Donor	B	AB, A, O	B	AB
O	AB	Donor	AB	A, B, O	AB	NA
A	AB	Donor	AB	A, B, O	AB	NA
B	AB	Donor	AB	B, A, O	AB	NA
A	O	Donor	A	AB, B, O	A	AB
B	O	Donor	B	AB, A, O	B	AB
AB	O	Donor	AB	A, B, O	AB	NA
AB	A	Donor	AB	A, B, O	AB	NA
AB	B	Donor	AB	B, A, O	AB	NA
A	B	Donor	AB	B, A, O	AB	NA
B	A	Donor	AB	A, B, O	AB	NA

Does ABO Incompatibility impact HSCT outcomes?

- HLA system is inherited independently from ABO blood group system
- ABO incompatibility does not appear to affect graft failure or rejection (HPC do not express ABO antigens)
- Does not affect survival, although may be related to prolonged RBC aplasia or delayed hemolysis
- Many other variables impact patient outcomes with this complex therapy
  - Baseline disease/stage/risk
  - conditioning, co- morbidities
  - HSCT dose
  - HSCT source
  - GVHD prophylaxis
  - Supportive care regimens
  - Transfusion support regimens

Summary

- ABOi HSCT poses a unique challenge to the clinical transplantation unit, the HPC processing lab and the transfusion medicine service
- There are potentially significant consequences of ABO mismatched. transplant
- ABO matching is not required for a successful HSCT
- Transfusion support of ABOi HSCT recipients is not standardized
- The decision to switch a patient's blood type is highly variable across institutions.
- ABO is a single detail in the scope of all other issues in hematologic malignancy and HSCT

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JUST OUTSIDE THE BOX

Blood transfusion, the Russian way

Any Questions ?

Thank You

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