Imperial College Healthcare NHS
NHS Trust

Transfusion laboratory management of haematopoietic stem cell transplants (HSCT)

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innovation respect care achievement pride

Overview

- History
- Why is blood transfusion involved?
- What tests are performed in blood transfusion and why?
- What does a protocol look like?
- Quiz time

History

- First published work by Jacobson & colleagues in 1949 regarding animal research
- In 1956 Barnes et al described the treatment of leukaemic mice by lethal irradiation and marrow transplantation
- In 1959 Thomas et al reported an identical twin with terminal leukaemia who was given TBI and IV infusion of marrow from his healthy twin. Recovery and disappearance of leukaemia for 4 months

How does it work?

- How long do you have ??????

Some diseases treated with HSCT

Allogenic

- Acute myeloid leukaemia
- Acute lympoblastic Leukaemia
- Chronic myeloid leukaemia
- Myelodylsplastic syndromes
- Thalassaemia
- Sickle cell anaemia
- Diamond blackfan anaemia

Autologous

- Non-hodgkins lymphoma
- Multiple myeloma

Why are BT services involved ?

- HSCT protocols require transfusion input due to level of complexity of special requirements for patients
- HSCT patients often require intensive blood component support

Pre-treatment tests

- ABO and Rh D group determined
- Antibody screen & identification if required
- DAT performed
- Extended red cell phenotype/genotype determined
- CMV status determined
- HLA Class (I & II) determined

ABO group matches in HSCT

- No incompatibility
- Major ABO incompatibility
- Minor ABO incompatibility
- Major and minor ABO incompatibility

ABO group matches in HSCT

Stem cells do not express ABO antigens

Major ABO Incompatibility

- Recipient has antibodies to donor cells e.g. A marrow into O recipient
- The requires depletion of the red cells from the donor marrow
- Transfusion of red cells of recipient group
- Plasma and platelets of donor group

Major ABO Incompatibility

RECIPIENT	DONOR	RED CELLS	RED CELLS	FFP	PLTS
O	A	O	O	A	A
O	B	O	O	B	B
O	AB	O	O	AB	AB
A	AB	O	A	AB	AB
B	AB	O	B	AB	AB

Minor ABO Incompatibility

- The donor has antibodies to the recipient cells
- Donor derived anti-A and anti-B may react with residual recipient red blood cells
- Haemolysis may occur but it is rarely serious
- Transfusion of red blood cells of donor group
- Plasma and platelets of recipient group

Minor ABO Incompatibility

RECIPIENT	DONOR	RED CELLS	RED CELLS	FFP	PLTS
A	O	O	O	A	A
B	O	O	O	B	B
AB	O	O	O	AB	AB
AB	A	O	A	AB	AB
AB	B	O	B	AB	AB

Major & Minor ABO Incompatibility

- The donor has antibodies to the recipient cells
- Donor derived anti-A and anti-B may react with residual recipient red blood cells. Haemolysis may occur but it is rarely serious

Major & Minor ABO Incompatibility

RECIPIENT	DONOR	RED CELLS	RED CELLS	FFP	PLTS
A	B	O	O	AB	AB
B	A	O	O	AB	AB

Rh D group

- The Rh D antigen is extremely immunogenic
- Rh D negative blood products are always used where either the donor or recipient is Rh D negative

Antibody screen and DAT

- Antibody screen to identify if specific antigen negative blood required
- Genotyping/Phenotyping
- DAT as a baseline test

SaBTO recommendation on CMV and blood components, 2012

- **CMV seronegative red cells and platelets may be replaced with leucodepleted blood components for adults and children post haemopoeitic stem cell transplantation, for all patient groups including seronegative donor/seronegative recipients.**

- **Patients requiring transfusions who may require a transplant in the future may also safely be transfused with leucodepleted products (eg seronegative leukaemia or thalassaemia patients).**

- **CMV PCR monitoring should be considered for all patients (even CMV negative/negative patients) to allow early detection of any possible CMV infection (whether transfusion-transmitted or otherwise acquired).**

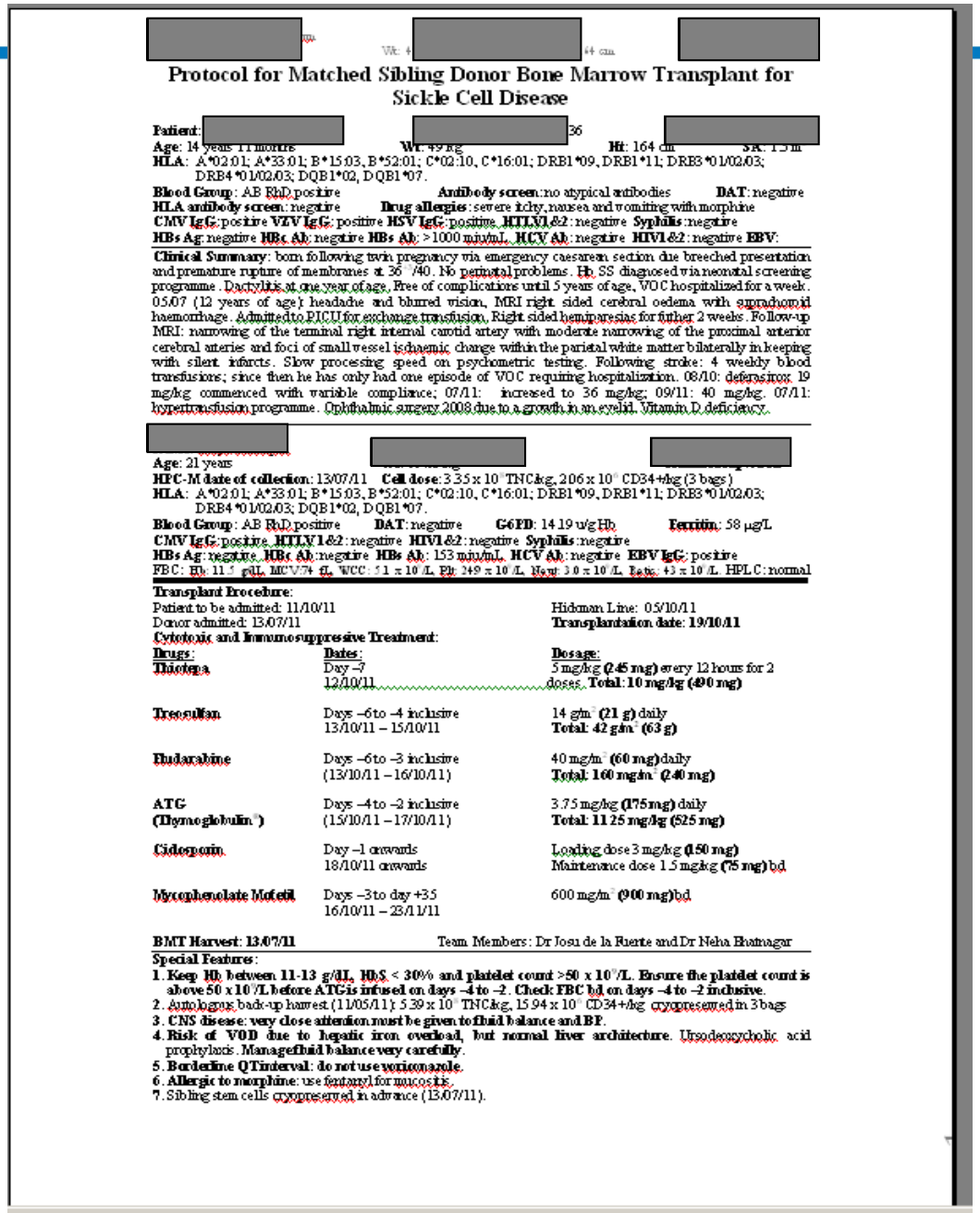
HLA antibodies

- Screen for HLA antibodies to identify problems with the transplant match and also if the screen is positive the patient may require HLA matched platelets

Irradiation of blood components

- What does it do?
  - Prevents proliferation of transfused T lymphocytes
  - BMT patients are severely immuno-suppressed and may develop transfusion associated graft versus host disease. (TA-GvHD) which is invariably fatal.
- What products require irradiation?
  - Cellular components

What does a protocol look like?



Protocol for Matched Sibling Donor Bone Marrow Transplant for Sickle Cell Disease

Patient: [redacted] [redacted] 36
Age: 14 years 11 months **Wt**: 49 kg **Ht**: 164 cm SA: 1.5 m
HLA: A*02:01; A*33:01; B*15:03, B*52:01; C*02:10, C*16:01; DRB1*09, DRB1*11; DRB3*01/02/03; DRB4*01/02/03; DQB1*02, DQB1*07.
Blood Group: AB RhD positive **Antibody screen**: no atypical antibodies **DAT**: negative
HLA antibody screen: negative **Drug allergies**: severe itchy, nausea and vomiting with morphine
CMV IgG: positive **VZV IgG**: positive **HSV IgG**: positive **HTLV1&2**: negative **Syphilis**: negative
HBs Ag: negative **HBc Ab**: negative **HBs Ab**: >1000 miu/mL **HCV Ab**: negative **HIV1&2**: negative **EBV**:

Clinical Summary: born following twin pregnancy via emergency caesarean section due breeched presentation and premature rupture of membranes at 36 /40. No perinatal problems. Hb SS diagnosed via neonatal screening programme. Dactylitis at one year of age. Free of complications until 5 years of age, VOC hospitalized for a week. 05/07 (12 years of age): headache and blurred vision, MRI right sided cerebral oedema with supradural haemorrhage. Admitted to PICU for exchange transfusion. Right sided hemiparesias for further 2 weeks. Follow-up MRI: narrowing of the terminal right internal carotid artery with moderate narrowing of the proximal anterior cerebral arteries and foci of small vessel ischaemic change within the parietal white matter bilaterally in keeping with silent infarcts. Slow processing speed on psychometric testing. Following stroke: 4 weekly blood transfusions; since then he has only had one episode of VOC requiring hospitalization. 08/10: deferasirox 19 mg/kg commenced with variable compliance; 07/11: increased to 36 mg/kg; 09/11: 40 mg/kg. 07/11: hypertransfusion programme. Ophthalmic surgery 2008 due to a growth in an eyelid. Vitamin D deficiency.

[redacted] [redacted] [redacted]
Age: 21 years
HPC-M date of collection: 13/07/11 **Cell dose**: 3.35 x 10^8 TNC/kg, 2.06 x 10^6 CD34+/kg (3 bags)
HLA: A*02:01; A*33:01; B*15:03, B*52:01; C*02:10, C*16:01; DRB1*09, DRB1*11; DRB3*01/02/03; DRB4*01/02/03; DQB1*02, DQB1*07.
Blood Group: AB RhD positive **DAT**: negative **G6PD**: 14.19 u/g Hb **Ferritin**: 58 µg/L
CMV IgG: positive **HTLV1&2**: negative **HIV1&2**: negative **Syphilis**: negative
HBs Ag: negative **HBc Ab**: negative **HBs Ab**: 153 miu/mL **HCV Ab**: negative **EBV IgG**: positive
FBC: Hb: 11.5 g/dL MCV:74 fL WCC: 5.1 x 10^9/L Plt: 249 x 10^9/L Neut: 3.0 x 10^9/L Retic: 43 x 10^9/L HPLC: normal

Transplant Procedure:
Patient to be admitted: 11/10/11
Donor admitted: 13/07/11
Hickman Line: 05/10/11
Transplantation date: 19/10/11

Cytotoxic and Immunosuppressive Treatment:

Drugs:	**Dates**:	**Dosage**:
Thiotepa	Day –7 12/10/11	5 mg/kg **(245 mg)** every 12 hours for 2 doses. **Total: 10 mg/kg (490 mg)**
Treosulfan	Days –6 to –4 inclusive 13/10/11 – 15/10/11	14 g/m^2 **(21 g)** daily **Total: 42 g/m^2 (63 g)**
Fludarabine	Days –6 to –3 inclusive (13/10/11 – 16/10/11)	40 mg/m^2 **(60 mg)** daily **Total: 160 mg/m^2 (240 mg)**
ATG (Thymoglobulin®)	Days –4 to –2 inclusive (15/10/11 – 17/10/11)	3.75 mg/kg **(175 mg)** daily **Total: 11.25 mg/kg (525 mg)**
Ciclosporin	Day –1 onwards 18/10/11 onwards	Loading dose 3 mg/kg **(150 mg)** Maintenance dose 1.5 mg/kg **(75 mg)** bd
Mycophenolate Mofetil	Days –3 to day +35 16/10/11 – 23/11/11	600 mg/m^2 **(900 mg)** bd

BMT Harvest: 13/07/11 Team Members: Dr Josu de la Fuente and Dr Neha Bhatnagar

Special Features:
1. **Keep Hb between 11-13 g/dL, HbS < 30% and platelet count >50 x 10^9/L. Ensure the platelet count is above 50 x 10^9/L before ATG is infused on days –4 to –2. Check FBC bd on days –4 to –2 inclusive.**
2. Autologous back-up harvest (11/05/11): 5.39 x 10^8 TNC/kg, 15.94 x 10^6 CD34+/kg cryopreserved in 3 bags
3. **CNS disease: very close attention must be given to fluid balance and BP.**
4. **Risk of VOD due to hepatic iron overload, but normal liver architecture.** Ursodeoxycholic acid prophylaxis. **Manage fluid balance very carefully.**
5. **Borderline QT interval: do not use voriconazole.**
6. **Allergic to morphine:** use fentanyl for mucositis.
7. Sibling stem cells cryopreserved in advance (13/07/11).

Quiz Time

Q1 The recipient is group A the donor is group O. What type of match is this?

1. ABO compatible
2. Major ABO incompatibility
3. Minor ABO incompatibility
4. Major & minor ABO incompatibility

Q2 The recipient is group A the donor is group O. What group blood would you select?

1. A
2. B
3. O
4. AB

Q3 The recipient is group A the donor is group O. What group FFP & platelets would you select?

1. A
2. B
3. O
4. AB

Q4 The recipient is group A the donor is group B. What type of match is this?

1. ABO compatible
2. Major ABO incompatibility
3. Minor ABO incompatibility

4. Major & minor ABO incompatibility

Q5 The recipient is group A the donor is group B. What group blood would you select?

1. O
2. AB
3. A
4. B

Q6 The recipient is group A the donor is group B. What group FFP & platelets would you select?

1. A
2. B
3. 0
4. AB

A7 The recipient is Rh D negative and the donor is Rh D positive. What Rh D group blood would you select?

1. Doesn't matter
2. Rh D positive
3. Rh D negative

Q8 The recipient is CMV negative and the donor is CMV positive. What CMV status blood would you select?

1. Doesn’t matter
2. CMV negative
3. CMV positive

Q9 Which of the following does **not** require irradiation to prevent TA-G*v*HD?

1. Platelet concentrates
2. Fresh frozen plasma
3. Red cells

SHARED CARE COMMUNICATIONS DOCUMENT FOR IRRADIATED AND SPECIALIST BLOOD COMPONENTS

This section ONLY is to be completed by a member of the clinical team at the Specialist Treatment Hospital and then sent to the Transfusion Laboratory for the remainder of the form to be completed.			
Affix Addressograph here or complete the following details:	Referring hospital:	ABO and RhD Group Details	Specialist Requirements Needed
Patient First and family Name:	Specialist Treatment Hospital:	Donor Group	Irradiated Yes / No
Date Of Birth;	Diagnosis:	Patient Group	CMV Neg Yes / No
NHS / Hospital Number:	Specialist Treatment received:		Patient Informed of Specialist Requirements? Yes / No
Address	Signed:.....Print Name..... Contact number / Bleep.....Date.....		

The following TWO sections are ONLY to be completed by the Transfusion Laboratories.

RBC Antibodies	**Specialist Requirements**	**Additional Requirements**
Historical Antibodies:	HLA / HAP Abs: Yes / No	RBC Phenotype:
Current Antibodies:	Specificity:	Washed RBCs: Yes / No
D.A.T		Washed Platelets: Yes / No
Signed:.....Print Name.....Date.....		

Copy of completed form to be sent by Secure Fax by Specialist Treatment Hospital Laboratory to Referring Hospital Laboratory	**Confirmation of receipt by Referring Hospital Laboratory.** To confirm receipt of this form please sign, print name, and date below and fax back
Date Fax sent.....	Signed:..... Print Name.....
Signed:..... Print Name.....	Specialist requirements input INTO Referring Hospital LIMS computer Yes / No Date.....

A collaborative piece of work between: South East Coast Regional Transfusion Committee, London Regional Transfusion Committee, East of England Regional Transfusion Committee

NHS Blood and Transplant

The Chief Medical Officer's National Blood Transfusion Committee for England and North Wales is working in partnership with the Department of Health to promote safe and effective transfusion practice.

DH Department of Health

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Any Questions?