

Clinical Issues in Transfusion for Haemoglobinopathy

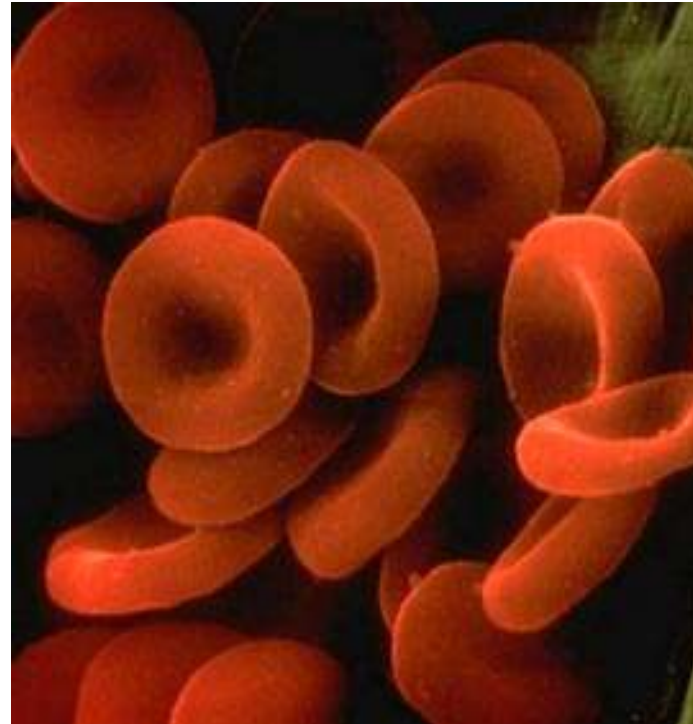
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Haemoglobinopathy

- **Genetic Disorder**
 - Production of normal amount of abnormal Hb e.g HbS
 - Production of reduced amount of normal Hb e.g α or β -Thalassaemia



Rationale for BT



- **Sickle cell Disease**
 - Reduce the production of Hb
- **Significant Thalassaemia**
 - Improve Hb
 - ↓ Erythropoietin
 - ↓ Ineffective erythropoiesis
 - ↓ Hypermetabolism

Transfusion for SCD

- **Acute**

- ↓ Hb
- Life threatening event

- **Chronic**

- CNS events
 - Abnormal TCDs
 - Stroke
 - Silent Infarct
- Recurrent Chest crisis
- Frequent pain events

- **Acute**

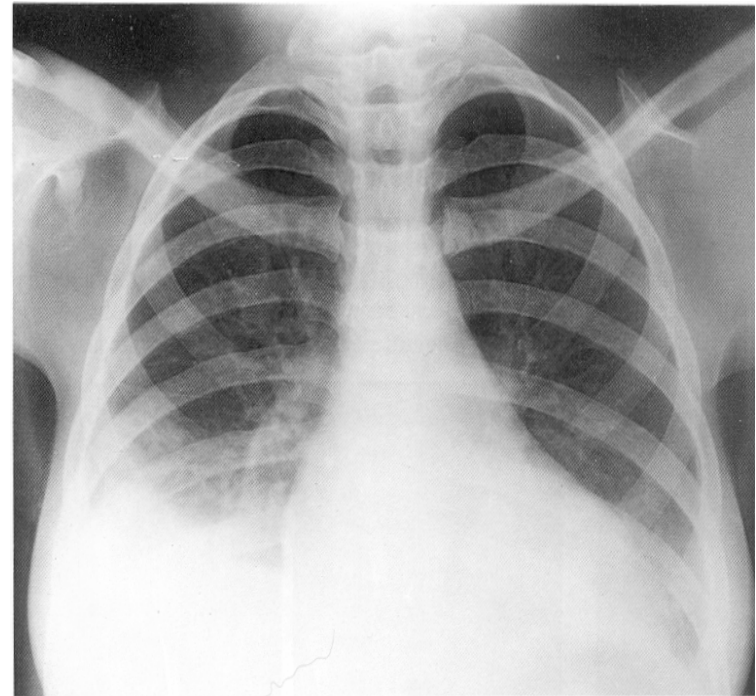
- Simple top up
- Exchange

- **Chronic**

- Simple regular top-up
- Erythrocytapheresis

Problems associated with Blood Transfusion

- Acute
 - Pulmonary oedema
 - Stroke
 - Allergic reaction
 - Haemolytic reaction
- Chronic
 - Infection
 - Antibody formation
 - Iron overload



Iron Overload

Iron overload

- 1ml RCC = 1mg iron
- 1mg = normal adult male daily requirement
- Measurement of iron overload problematic
- Ferritin is not a good measurement



Prevention of Iron overload

- **Avoid transfusion**
 - Hydroxyurea
 - BMT
- **Iron chelation**
- **Administration of Transfusion**
 - Erythrocytapheresis
- **Other types of Oxygen carriage**



Erythrocytapheresis

Advantages

- Controlled
 - Volume
 - HCT
 - HbS level
- Reduces Iron overload

Disadvantages

- IV access
- Trained staff
- Increased red cell requirement (20%)

Irish experience of erythrocyapheresis

Patients and methods

2003-2011; 75 patients

Currently 48 patients with SCD

22 started erythrocyapheresis

(Age 12mo-18 yr; Wt 11.5-63kg)

7 continue;

1 stopped Parent decision

8 changed HU

7 failed (1mo-13mo) –IV access

1 BMT

Ferritin levels –300-1000(mean 600)

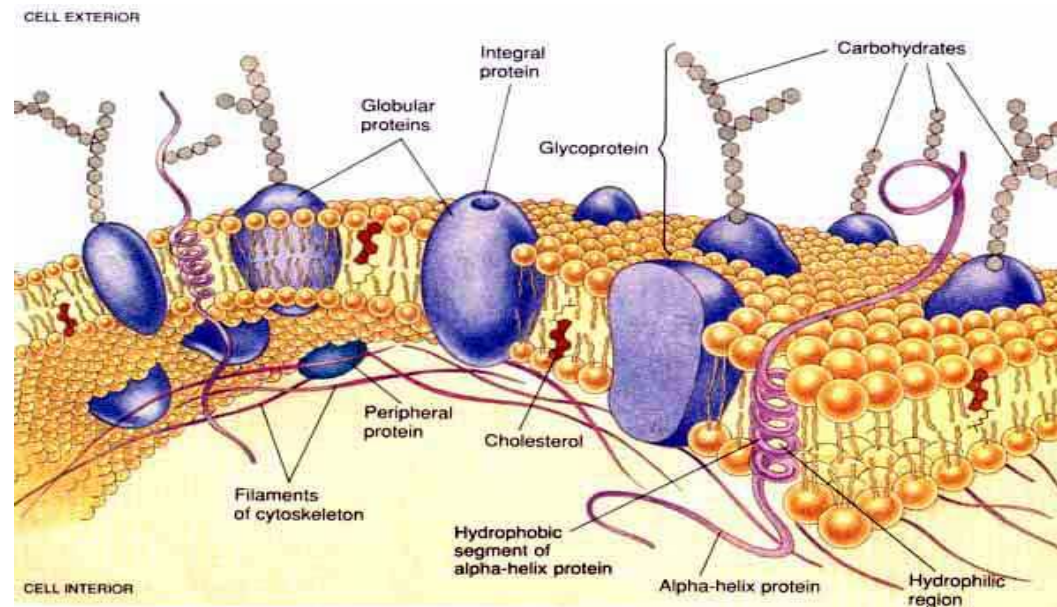
Iron chelation – 1 (Exjade 5mg/kg)

HbS levels 5-18% (mean 9%)

Problems and solutions

- IV access
 - Portacath
 - Permcath
- Increased RC requirement
 - No increase in Ab formation
- Staff
 - Flexability
 - Planning

RC Antibody Formation



ABO phenotype and prevalence

Phenotype	Caucasians	African-Americans
A	40%	27%
B	11%	20%
AB	4%	4%
O	45%	49%

Other Red Cell Antigen Systems

Antigen	System	Tx Reaction	Caucasians (%)	African-American
D	Rhesus	Mild-severe	85	92
C	Rh	Mild-severe	68	27
E	Rh	Mild-mod	29	22
c	Rh	Mild-severe	80	96
e	Rh	Mild-mod	98	98
K	Kell	Mild-severe	9	2
k	Kell	Mild-mod	99.8	>99
Kp ^a	Kell	Mild-mod	2	<1
Fy ^a	Duffy	Mild-severe	66	10
Fy ^b	Duffy	Mild-severe	83	23
Jk ^a	Kidd	None-severe	77	92
Jk ^b	Kidd	None-severe	74	49
U	MNS	Mild-severe	100	>99

How Significant is this?

107 SCD + transfusion vs 51 SCD – BT vs
19 non-SCD + BT ;

**30% SCD+BT & 5% non SCD developed
alloantibodies (K,E,C,Jk^a)**

Vichinsky et al NEngl J Med 1990

STOP trial RC phenotyping; 61 patients
received 1830 units – 8% developed
clinically significant Ab.

**Alloimmunisation ↓ 3% to 0.5% per unit.
Haemolytic transfusion Rx ↓ 90%**

Vinchinsky et al Transfusion 2001



Theoretical and practical implications of Phenotyped RBC transfusion

- 351 patients received 8939 units RBC (ABO & D) – 137 alloimmunised
- If RBCs Rh and K matched as well alloimmunisation ↓ by 53%
- If Rh, K, S, Jk^b & Fy^a ↓ Ab by 70.8%

But

- 13.6% random white donors match Rh and K
- 0.6% would match extended phenotype

Castro et al Transfusion 2002

Other problems with antigens

- D antigen – partial expression
 - Can make an anti-D
- C antigen
 - Can make anti-C
- K subtypes

Solutions

- Patients should be phenotyped prior to first transfusion
- All should receive minimum of ABO, Rh, K matched RCC
- ?Patients should be genotyped and if partial D or C antigen give D and C neg RCC
- Increase ethnic minority donor representation
- ? Transfusion early in life - ↑ immune tolerance

Conclusions

- BT is the cornerstone of treatment of Hbopathy
but
- There are significant side effects

Therefore

- Define benefits vs risks
- Need to consider other treatments
- Need to encourage donors from people of African ethnicity



Acknowledgements

- Colleagues in Blood transfusion
 - Hospital team
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- Surgeons
- ANP/CNS Haemoglobinopathy
- Children and parents with Hbopathy