

# Provision of Red Cell Transfusion Support for Transfusion Dependent Patients

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## 1.0 Definition

Transfusion dependent patients are those who require frequent and long-term transfusion support to sustain life. Most such patients have been diagnosed with one of the following conditions:

- thalassemia syndromes
- severe aplastic anaemia (SAA)
- sickle cell disease (SCD)
- myelodysplastic syndromes (MDS)
- other congenital or acquired chronic anaemias

## 2.0 General

In addition to the potential complications of red blood cell (RBC) transfusions common to all recipients, there are special problems that are unique in transfusion dependent patients who are on chronic transfusion support.

In this document, policies for red cell transfusion support and the principles on which they are based are discussed. The purpose of this document is to establish uniform policies for the benefit of medical and scientific staff who may be involved in giving advice on serological problems and on the optimal use of red cells. Clinical management of complications such as iron overload, hyperhaemolysis in SCD etc are not dealt with herein, nor does the document include the selection of blood for patients who may require frequent transfusions for a limited period but are not expected to require lifelong red cell replacement. Hence this policy does not apply to those unlikely to require lifelong transfusions, e.g. leukaemia patients undergoing chemotherapy.

The aim of good transfusion practice in transfusion dependent patients is to:

- minimise the risk of alloimmunization to RBC antigens
- ensure maximum survival of transfused red cells
- ensure the presence of optimal number of RBCs per unit transfused

## 3.0 Special problems

### 3.1 Alloimmunization to red cell antigens.

Due to the diversity of RBC antigens among different individuals, multi-transfused patients are likely to be exposed to many allogeneic RBC antigens. Exposure to foreign RBC antigens is more likely when there are racial differences between the blood donor population and the recipients<sup>1</sup>, such as in SCD patients receiving blood from Caucasian donors.

## Provision of Red Cell Transfusion Support for Transfusion Dependent Patients

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Up to about 30% of transfusion dependent patients are reported to develop RBC antibodies,<sup>1-3</sup> most of which are within the Rh and Kell systems.<sup>4,5</sup> There is a significant reduction in alloimmunisation rate (dropped from 3% to 0.5% per unit) by providing blood matched for Kell and Rh (CDE) antigens.<sup>6</sup> These antigen matching protocols have been associated with reduced alloimmunisation rate and decreased incidence of haemolytic transfusion reactions in patients with SCD.<sup>7</sup> Similar recommendation (providing Rh and K matched units) was made in patients with Thalassemia.<sup>8</sup>

Since 1997 blood banks in the UK adopted the policy of providing blood matched for Rh (C, c, D, E, e) and Kell antigens, in addition to ABO matching for patients with sickle cell disease and thalassemia.

### 3.2 Difficulty in assigning antibody specificity

Some patients, especially those with multiple RBC alloantibodies, show reactions in serological tests for which antibody specificity cannot be assigned. Selecting suitable blood for these patients is extremely difficult. In such situations, the only option is to select units that match the patient's phenotype / genotype, as clinically relevant. This is possible only if the full phenotype of the patient has been determined before initiating the transfusion programme. Serological typing is simple, quick and could be undertaken by NHSBT Red Cell Immunohaematology (RCI) laboratories. If however, the patient has already been transfused, phenotypes for most blood group antigens can be predicted by molecular methods in the RCI laboratory.

### 3.3 Variation of the volume of RBC in each unit transfused.

Since the introduction of universal leucodepletion in the UK, there is a small but significant decrease in the red cell volume in all RBC units. This is due to the loss of 10-30ml of RBC in the filtration procedure. In units where the buffy-coat has been removed to prepare platelet concentrates, there is an additional loss of 30-50ml of RBC resulting in a total reduction by 40-80ml RBC. Transfusion of these low volume units may not achieve the desired Hb level resulting in the patient requiring a higher number of units for each transfusion episode. To minimise donor exposure, units with the greatest volume of red cells should be selected.

## Provision of Red Cell Transfusion Support for Transfusion Dependent Patients

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### 3.4 Donations from individuals with sickle cell trait (HbAS genotype).

The main goals of transfusion in SCD patients are to reduce the HbS level and/or to elevate the Hb. The former would not be achieved effectively if the unit transfused was from an HbAS donor. Therefore, only RBC units that are screened and found to be negative for HbS should be used for transfusion to SCD patients.

## 4.0 Recommendations

### 4.1 Extended RBC phenotyping

Perform extended RBC phenotyping serologically prior to initiating the transfusion regime. Patients should be tested for the following RBC antigens: C, c, D, E, e, M, N, S, s, Lu<sup>a</sup>, Lu<sup>b</sup>, K, k, Kp<sup>a</sup>, Kp<sup>b</sup>, Fy<sup>a</sup>, Fy<sup>b</sup>, Jk<sup>a</sup> and Jk<sup>b</sup>. All Afro-Caribbean patients should also be typed for Js<sup>b</sup>.

Patients who are S-, s- should have their U antigen status determined. In already transfused patients with either strong free autoantibody or multiple alloantibodies, send 5 ml EDTA blood sample to the local NHSBT RCI laboratory to be forwarded to the International Blood Group Reference Laboratory (IBGRL) in Filton for molecular typing.

### 4.2 RBC antigen matching

Select ABO and K compatible red cell units that are also matched for D, C, E, c, e, for example when the patient is:

- R<sub>0</sub> – select preferably R<sub>0</sub>. rr only if R<sub>0</sub> unavailable
- R<sub>1</sub>r – select E neg
- R<sub>1</sub>R<sub>1</sub> – select R<sub>1</sub>R<sub>1</sub>
- R<sub>2</sub>R<sub>2</sub> – select R<sub>2</sub>R<sub>2</sub>
- R<sub>2</sub>r – select C neg

If clinically significant RBC antibodies are present, select antigen negative units and issue blood compatible in the crossmatch by IAT according to national guidelines.<sup>9</sup>

**NB** In addition to selecting Rh/K matched units, matching for Fy(a-b-) or U- is not required unless Duffy antibodies or anti-U are present. Nevertheless, some centres have “extended matching” protocols aiming to match Duffy, Kidd, MNS and Lewis antigens for SCD patients whenever possible.<sup>10</sup>

## Provision of Red Cell Transfusion Support for Transfusion Dependent Patients

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### 4.3 Selection of RBC units.

To minimise excessive donor exposure and to get maximum benefit, select units with the largest volume available, preferably units with approximately 300 ml or more.

For patients with SCD, all units selected must be negative for HbS. Units tested for HbS and found negative are marked '**HbS Neg**' on the pack label. If the only suitable donations are not tested previously, the NHSBT Donation Testing laboratory should undertake HbS testing and, if necessary, will release the index units under concession.

### 4.4 Age of the RBC units.

#### 4.4.1 For all patients

Ideally, the red cell units selected for transfusion dependent patients who require frequent transfusions should be less than 2 weeks old to ensure maximum possible survival in the patient's circulation. On some occasions, this may not be possible. In such situations, freshest available suitable units may be transfused.

#### 4.4.2 For patients with SCD

Where possible, red cell survival post-transfusion should be maximised by selection of 'fresh' red cells. Red cells should be ideally less than 14 days for top-up transfusions and less than 7-days old for exchange transfusion,<sup>11</sup> but this may not be possible where the patient has multiple red cell alloantibodies. In such situations freshest available suitable units may be transfused.

- 5.0** Paroxysmal nocturnal haemoglobinuria: these patients have an increased sensitivity to complement mediated lysis. In the past washed cells were provided but there is evidence that leucodepleted red cells in SAG-M are suitable and have been shown not to increase haemolysis.<sup>12</sup> Therefore washed cells are not required.

## Provision of Red Cell Transfusion Support for Transfusion Dependent Patients

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### References

1. Yazdanbakhsh K, Ware R, Noizat-Pirenne F. Red blood cell alloimmunization in sickle cell disease: pathophysiology, risk factors, and transfusion management. *Blood* 2012, **120**: 528-537.
2. Rosse WF, Gallagher D, Kinney TR, Castro O, Dosik H, Moohr J, Wang W, Levy PS. Transfusion and alloimmunization in sickle cell disease. The Cooperative Study of Sickle Cell Disease. *Blood*, 1990 Oct 1; **76**(7): 1431-1437.
3. Vichinsky E, Neumayr L., Trimble S, Giardina PJ, et al. Transfusion complications in thalassemia patients: a report from the Centers for Disease Control and Prevention. *Transfusion* 2014, **54**: 972-981.
4. Mijovic A, Perera G J, Thein S L. Red blood cell alloimmunization in sickle cell disease – prevalence and trends: A single centre cross-sectional study from United Kingdom. *Transfusion* 2013, **53**: 3279-80.
5. Redman M, Regan F, Contreras M. A prospective study of the incidence of red cell alloimmunisation following transfusion. *Vox Sang* 1996; **71**(4): 216-220.
6. Vichinsky EP, Luban NLC, Wright E, Olivieri N, et al. Prospective RBC phenotype matching in a stroke-prevention trial in sickle cell anemia: a multicenter transfusion trial. *Transfusion* 2001; **41**:1086-1092.
7. Trembl A, King K E. Red Blood cell alloimmunization: lessons from sickle cell disease. *Transfusion* 2013; **53**: 692-695.
8. Spanos T, Karageorga M, Ladis V, Peristeri J, et al. Red cell alloantibodies in patients with thalassemia. *Vox Sang* 1990; **58**(1): 50-55.
9. British Committee for Standards in Haematology (BCSH) Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfusion Medicine* 2013; **23**: 3-35.
10. La Salle-Williams M, Nuss R, Le T et al. Extended red blood cell antigen matching for transfusions in sickle cell disease: a review of 14-year experience from a single centre. *Transfusion* 2011; **51**: 1732-1739.
11. United Kingdom Blood Services Handbook of Transfusion Medicine 5<sup>th</sup> edition. Editor: D Norfolk. TSO 2013.
12. Sherman SP, Taswell HF. The need for transfusion of saline-washed red blood cells to patients with paroxysmal nocturnal hemoglobinuria: a myth (abstract). *Transfusion* 1977; **17**: 683.