BLOOD COMPONENT SUPPORT OF RhD NEGATIVE INDIVIDUALS

REASON FOR ISSUE: Update reference throughout to females of child bearing potential from <55yrs to <50yrs (refer to CCP829).

1. INTRODUCTION

Transfusion of RhD positive blood components to an RhD negative patient can result in the formation of anti-D.

The risk is greatest when RhD positive red cell components are transfused.

Formation of anti-D following transfusion of RhD positive platelets is also recognised.

Sensitisation following transfusion of RhD positive frozen plasma components is unlikely, as the small amounts of red cell stroma present are less immunogenic than intact red cells [1].

Whenever possible steps should be taken to avoid transfusion of RhD positive red cell or platelet components to RhD negative recipients. Clinical situations will however emerge when this is necessary. This policy aims to provide guidance on this issue.

The recommendations contained within this policy are based on BCSH Guidelines on the use of fresh frozen plasma [1] and platelets [2].

2. SCOPE

This policy applies to all Blood Banks. It provides guidance on the transfusion of RhD positive components to RhD negative recipients and guidance on the use of RhD immunoglobulin following transfusion of RhD positive components to RhD negative recipients.

3. RISK ASSESSMENT

Any clinical intervention aims to ensure that the likely clinical benefit of a procedure exceeds the risks associated with the intervention. The formation of anti-D following transfusion of RhD positive blood components might result in a number of consequences:

An absolute requirement for RhD negative support for future transfusions
Within New Zealand this should be manageable. Problems might however be encountered in other countries.

Haemolytic transfusion reactions when RhD positive red cell components are transfused
Delayed haemolytic reactions might occur in individuals who have been sensitised but in whom anti-D is not easily detectable by current pretransfusion testing approaches. The risk is likely to be higher in patients previously transfused with RhD positive components and women who have had pregnancies.

Haemolytic disease of the newborn
This risk applies to females of child bearing age and female children. Particular care should be undertaken to avoid transfusion of RhD positive components to this group of patients.

Formation of anti-D will not occur when RhD negative components are transfused. Timely administration of RhD immunoglobulin following transfusion of RhD positive components may also prevent primary immunisation to RhD.

4. TRANSFUSION OF RED CELL COMPONENTS

RhD negative red cell components are generally freely available.

Transfusion of RhD Positive red cells to an RhD negative recipient should only be considered in emergency settings when a patient is requiring large numbers of red cells units and this might result in a shortage of RhD negative components for other patients.

The following principles (also summarised in appendix A) therefore apply:

Transfusion of RhD positive red cells to females of less than 50 years (including female children) should only be considered in life threatening situations. This should only take place following discussion with a Transfusion Medicine Specialist or Haematologist.

Transfusion of RhD positive red cells to females 50 years of age and over can be considered in life threatening situations after discussion with a Transfusion Medicine Specialist. In the elective transfusion situation transfusion of RhD positive red cells to females 50 years and over is not encouraged due to the possibility of the presence of undetectable immune anti-D. If transfusion of RhD positive red cells is the only option available this should only take place following discussion with a Transfusion Medicine Specialist.

Transfusion of RhD positive red cells to RhD negative males who do not have pre-existing anti-D may be necessary in clinical emergencies involving significant blood loss. In the event that such circumstances arise then an early decision on a switch to RhD positive red cell units may avoid unnecessary depletion of RhD negative units. This can be managed through local protocols. Advice should be sought from a Transfusion Medicine Specialist or Haematologist in the event of doubt or uncertainty.

Transfusion of RhD positive red cells to RhD negative males undergoing elective surgery should only be considered when supplies of RhD negative red cell components are low. This can be managed through local protocols. Advice should be sought from a Transfusion Medicine Specialist or Haematologist in the event of doubt or uncertainty.

RhD immunoglobulin is unlikely to prevent formation of anti-D when a whole unit of red cells is transfused. In the event that inadvertent administration of RhD positive red cells is given then advice should be sought urgently from a Transfusion Medicine Specialist or Haematologist.

5. TRANSFUSION OF PLATELET CONCENTRATES

Limited supplies of RhD negative platelet concentrates are available. The major NZBS manufacturing sites and blood banks will endeavour to ensure that at least one adult therapeutic dose of group O RhD negative platelets is available at all times.

Two types of platelet concentrate are currently available namely pooled buffy coat derived platelets (manufactured from a pool of four donations) and apheresis platelets. All platelet concentrates are leucodepleted pre-storage.

Red cell contamination levels with these products is less than with previous forms of platelet products. Red cell contamination does however still occur with leucodepleted concentrates and so the risk of sensitisation is reduced but not eliminated.

Recent analysis of NZBS PAS pooled and PAS apheresis platelets indicates red cell contamination levels of 0.078 and 0.012ml respectively. Evidence indicates that as little as 0.03ml of red cells can lead to alloimmunisation to RhD.

The policies described in section 5.1 and 5.2 that follow, apply to RhD negative patients requiring platelet concentrates.

5.1 Patients with Conditions other than Haematological Malignancies

The clinical priorities for using RhD negative platelets are:

RhD negative females of less than 50 years (including female children) who require platelet support for trauma or surgery i.e. where the requirement for support is short lived; and

RhD negative females of less than 50 years (including female children) requiring repeated platelet support for non-malignant conditions where future pregnancies are possible.

Whenever RhD positive platelets are transfused to RhD negative recipient in the above categories then RhD immunoglobulin must be offered. If the requirement for RhD immunoglobulin is in doubt then it should be offered. Section 7 of this document provides advice on the administration and required dose.

In thrombocytopenic patients including neonates or those with severe coagulation disorders an RhD immunoglobulin product suitable for intravenous administration is preferred. When not available a standard Rh D immunoglobulin product can be given by subcutaneous injection.

Other RhD negative patients who require short term platelet support should be given RhD negative platelets if available. Particular efforts should be made to provide RhD negative platelets to young male children (on paediatric wards). If however RhD positive platelets are transfused in this setting then RhD immunoglobulin is not required.

Whenever only RhD positive platelets are available for transfusion to a patient who has formed immune anti-D then it is safe to do so since the red cell content is very small to cause any problems related to haemolysis. Approval by TMS/MO is not necessary for this.

5.2 Patients with Haematological Malignancies and Other Patients Requiring Long Term Platelet Support

The management of RhD negative patients with haematological malignancies and similar diseases is particularly problematic. Repeated platelet support is likely to be required. The risk of sensitisation is however less because of the immunosuppressive effects of treatment and in some cases the underlying primary condition [3, 4]. The following approach will be adopted:

RhD negative children should whenever possible receive RhD negative platelets. RhD immunoglobulin should be considered when RhD positive platelets are given to female children in this group. The final decision on the appropriateness of RhD immunoglobulin lies with the consultant responsible for the care of the patient. In the event that RhD immunoglobulin is required then section 8 (and similarly Appendix B) of this document provides advice on the administration and required dose.

Whenever possible female patients of child bearing age should receive RhD negative platelets. RhD immunoglobulin is not normally required when these patients receive RhD positive platelets. The consultant responsible for care of the patient may make an exception to this for individual patients with good prognosis disease. In this setting the consultant will be responsible for ensuring that the hospital blood bank and ward staff are aware of the requirement to administer RhD immunoglobulin. In the event that RhD immunoglobulin is required then section 8 (and similarly Appendix B) of this document provides advice on the administration and required dose.

For other patients, RhD positive platelets may be used unless there is a specific protocol (agreed by TMS / Haematologist) to the contrary.

Other than where identified above, RhD immunoglobulin treatment is not necessary when RhD positive platelets are administered to this group of patients.

6. TRANSFUSION OF FRESH FROZEN PLASMA AND CRYOPRECIPITATE

Although frozen plasma components may contain small amounts of red cell stroma, sensitisation following transfusion of RhD positive units is most unlikely, as stroma is less immunogenic than intact red cells.

Therefore FFP and cryoprecipitate of any RhD type may be given regardless of the RhD type of the recipient.

No RhD immunoglobulin need be given if RhD negative patients receive RhD positive FFP or cryoprecipitate [1].

7 RhD POSITIVE BONE ALLOGRAFTS

Normal bone marrow cellularity varies with age with the average cellularity being around 50% in a donor population aged between 40yrs and 70yrs. There have been several reports of Rhesus immunization after bone allografting. Typically femoral heads are used which on the average contain 10-15mL of bone marrow with a considerable donor variation in the proportion of red and yellow marrow.There is the possibility that more than one femoral head may be used and the amount of other types of osseous bone bone allografts will vary from case to case. Taking this into consideration a standard dose of 625IU of RhD immunoglobulin is recommended to cover the number of RhD positive red cells in a RhD positive bone graft. This recommendation applies predominantly to RhD negative female recipients of childbearing potential. For femoral heads the dose should be calculated based on 625IU of RhD immunoglobulin per femoral head.

8. DOSAGE AND ADMINISTRATION OF RhD IMMUNOGLOBULIN

Where a requirement for administration of RhD immunoglobulin has been identified then the following approach must be adopted:

RhD immunoglobulin should be administered as soon as possible following transfusion and must be completed within 72 hours of commencement of the transfusion.

The standard dose of 625 IU RhD immunoglobulin will be more than adequate to cover a single transfusion episode. It is acceptable in most situations to use the smaller 250iu dose for single platelet transfusions. In the event that repeated transfusion occurs then further standard doses of RhD immunoglobulin should be administered every 4 weeks.

In thrombocytopenic patients or those with severe coagulation disorders an RhD immunoglobulin product suitable for intravenous administration is preferred. When this is not available an intramuscular RhD immunoglobulin product can be given by subcutaneous injection.

9. REFERENCES

1. BCSH Guidelines for the use of fresh frozen plasma, cryoprecipitate and cryosupernatant BJH 2004, 126, 11-28
2. BCSH Guidelines for the use of platelet transfusions. BJH 2016, 176, 365-394
3. Cid. J., Ortin X., et al. Absence of anti-D alloimmunisation in haematologic patients after D-incompatible platelet transfusions. Transfusion 2002, 42 (2) 173-176
4. Molnar R., Johnson R. et al. Absence of D alloimmunisation in D- paediatric oncology patients receiving D-incompatible single donor platelets. Transfusion 2002, 42 (2) 177-182
5. Knaepler H, Ascherl R, Kretschmer V. [Immunization against blood group antigens after allogeneic bone transplantation]. Chirurg 1990;61:830-2.

Appendix A: Criteria for Use of RhD Positive Blood Components for RhD Negative Recipients

1. Red Cell Components

Use of RhD positive red cell components for RhD negative recipients should only occur in emergency settings requiring large numbers of red cell units which would result in shortage of RhD negative components.

RhD positive red cells should only be considered in recipients who do not have pre-existing (or a history) of anti-D.

Administration of RhD immunoglobulin is usually not required when RhD positive red cell components are transfused to RhD negative recipients in an emergency. If an RhD positive transfusion is inadvertently administered in women of child bearing potential, specialist advice must be sought where a decision to administer of Rh D immunoglobulin will be made which will include appropriate dosage.

Patient Category	Reason for Transfusion	Criteria	Authorisation / Advice
Females <50 years old (including female children)	Clinical emergency with significant blood loss	Life threatening emergency only, when insufficient Rh(D) Neg red cells available	TMS / Haematologist
Females ≥50 years old	Emergency and elective transfusion	When insufficient RhD Neg red cells available	TMS / Haematologist
Males	Clinical emergency with significant blood loss	Make early switch to RhD Pos red cells to conserve RhD Neg red cell stock	Registered Medical Laboratory Scientist Document on Technical Advice Form for regular TMS review
	Elective surgery	Only if supplies of RhD Neg red cells are low	

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2. Platelet Concentrates

(i) Patients with conditions other than haematological malignancies

Patients should receive RhD negative platelets if available, particularly females (<50 years old) and young male children on paediatric wards.

Patient Category	Reason for Transfusion	Criteria	Authorisation / Advice
Females <50 years old (including female children)	Trauma or surgery needing short term support On-going and future pregnancies possible	Clinical priority is to use RhD Neg platelets Use Rh(D) Pos platelets only if absolutely no RhD Neg platelets available Anti-D Ig should be given if RhD Pos platelets used	TMS / Haematologist to use RhD Pos platelets
Young male children (On Paediatric wards)	Short term support	Particular effort must be made to provide RhD Neg platelets. Use RhD Pos platelets only if insufficient RhD Neg platelets available. Anti-D Ig is not required if RhD Pos platelets given	Registered Medical Laboratory Scientist Document on Technical Advice form for regular TMS review
Other patients	Short term support	Decision based on likely availability of RhD Neg platelets Use RhD Pos platelets only if insufficient RhD Neg platelets available Anti-D Ig is not required if RhD Pos platelets given	Registered Medical Laboratory Scientist Document on Technical Advice form for regular TMS review

(ii) Patients with haematological malignancies and other patients requiring long-term platelet support

Patients should be given RhD negative platelets if available. Although repeated platelet support is likely to be required, risk of sensitisation to anti-D is lessened due to immunosuppressive effects of treatment and in some cases the underlying condition.

Patient Category	Reason For Transfusion	Criteria	Authorisation / Advice
Female children	On-going support	Clinical priority for use of RhD Neg platelets; Only use RhD Pos platelets if absolutely no Rh(D) Neg platelets available Anti-D Ig should be considered with decision made by Consultant responsible for care of patient	TMS / Haematologist to use RhD Pos platelets

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Patient Category	Reason For Transfusion	Criteria	Authorisation / Advice
Male children	On-going support	Use RhD Pos platelets only if insufficient RhD Neg platelets available Anti-D Ig is not required if RhD Pos platelets given	Registered Medical Laboratory Scientist Document on Technical Advice form for regular TMS review
Females of childbearing age (<50 years old)	On-going support	RhD Neg platelets should be used whenever possible. Use of RhD Pos platelets at TMS / Haematologist discretion based on likely availability of RhD Neg platelets Anti-D Ig is not normally required - Consultant responsible for patient may make exception if good prognosis expected	TMS / Haematologist to use RhD Pos platelets
Other patients	On-going support	RhD Pos platelets may be used unless RhD Neg platelets specifically requested by TMS / Haematologist (within agreed local protocol) Anti-D Ig not normally required – Consultant responsible for patient may make exception if good prognosis expected	Registered Medical Laboratory Scientist Document on Technical Advice form for regular TMS review TMS / Haematologist – if unable to meet protocol

3. Fresh Frozen Plasma / Cryoprecipitate

Although frozen plasma components may contain small amounts of red cell stroma, sensitisation following transfusion of RhD positive units is most unlikely, as stroma is less immunogenic than intact red cells.

FFP and cryoprecipitate of any RhD type may be given regardless of the recipient's RhD status. No anti-D immunoglobulin need be given if RhD negative recipients receive RhD positive FFP or cryoprecipitate.

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Appendix B: Dosage and Administration of RhD Immunoglobulin

When	Dosage	Route Of Administration	Frequency
ASAP and within 72 hours of commencing transfusion	Standard Dose i.e. 100 IU/ml of RhD Pos red cells transfused*	Subcutaneous	Single transfusion episode - standard dose* of RhD Ig normally adequate Repeated transfusions - RhD Ig should be administered every 4 weeks
		Intravenous – thrombocytopenic patients or those with severe coagulation disorders**	

* CSL RhD Immunoglobulin available as 625 IU single dose vial

** Use product registered for intravenous use