

The appropriate use of group O D negative red cells

Summary

This guidance is designed to ensure that hospitals and NHS Blood and Transplant (NHSBT) can work within a consistent framework to ensure equal access for patients to available group O D negative and K negative (K-) red cells based on need. It also aims to prevent significant shortages of O D negative and K- blood. This guidance covers both clinical and laboratory management and is endorsed by the National Blood Transfusion Committee (NBTC).

Method

The recommendations are based on the previous NBTC Guidelines on the Appropriate use of O D negative red cells, national audits for the usage of O D negative red cells,¹ and practical considerations. They are consistent with the BSH guidelines for pre-transfusion compatibility procedures² and management of patients with major haemorrhage.³ For female patients, the age of 50 years is considered the upper limit of childbearing potential.²

Background

Although usage of red cells has reduced by 25% over the last 15 years, demand for O D negative red cells as a percentage of the overall demand continues to rise. Blood services worldwide have encountered shortfalls of O D negative red cells and demand may exceed supply. It is important that NHSBT and hospitals work together to reduce the risk of group O D negative red cell shortages by managing both supply and demand. In the event of blood shortages, the NBTC red cell shortage plan should be activated.⁴ For emergency preparedness and mass casualty situations refer to relevant guidance from the NBTC and NHS England.^{5,6}

Clinical management

O D negative red cells

Group O D negative blood may be used for transfusion of red cells in an emergency.^{3,7} However, over dependence on group O D negative transfusions may have a negative impact on blood stock management. Patients where the use of group O D negative red cells is essential should be prioritised.

1. Indications for usage of Group O red cells

A. Major haemorrhage

Major haemorrhage is associated with a variety of conditions including multiple trauma, childbirth, gastrointestinal bleeding, liver transplantation and complex surgery. All emergencies may require urgent transfusion of red cells. Major

haemorrhage where group O red cells may be required generally involves the following scenarios:

- Patients with unknown blood group.
- Patients with known blood group without a current valid blood group sample.
- Patients with only one ABO group result at the time when blood is required.
- Non group O patients with a current valid blood group and a negative antibody screen where group specific red cells are not readily available.

B. Other clinical conditions

- Patients with a discrepancy between the ABO group on the current blood grouping sample and a historical result in an emergency setting. For routine transfusions, the blood group should be confirmed with a repeated sample.
- Patients with mixed field ABO reactions in the absence of a previously confirmed blood group.
- Patients undergoing ABO incompatible stem cell transplantation (prior to engraftment).
- When ABO compatible blood is not available due to stock shortages (either locally or nationally) or due to complex phenotypic requirements.

2. D selection

The use of D negative red cells should be prioritised based on gender assigned at birth and age for the following clinical reasons:

- D negative patients with immune anti-D must be given D negative red cells to avoid a delayed haemolytic transfusion reaction.
- D negative females (including D variants) and female patients of unknown blood group (in an emergency), with child-bearing potential (≤ 50 yrs old) should be given D negative red cells to prevent D alloimmunisation.
- Children (<18 years old) of unknown blood group in an emergency.^{2,7}
- D negative red cells may be given as an acceptable substitution in the absence of Ro units for patients needing phenotyped red cells e.g. sickle cell patients.

Weak D

- Refer to BSH guidelines for pre-transfusion compatibility procedures for guidance².

3. Minimising unnecessary usage of O D negative red cells

A. Emergency usage:

- In an emergency, hospitals should ensure availability of technologies and validated processes to allow urgent provision of group specific blood (if possible within 15 minutes) to minimise avoidable usage of O D negative red cells.
- Protocols and appropriate training should be in place to ensure pre-

transfusion compatibility sample(s) are obtained prior to administration of the first emergency unit of red cells (to avoid the development of mixed field reactions and the need for ongoing administration of O D negative blood).

B. Major haemorrhage:

- D negative adult males or women >50 years old with no known anti-D antibodies undergoing major haemorrhage may receive O D positive red cells.²
- Hospitals should consider usage of O D positive red cells for unknown adult male patients and women > 50 years. The risk of an adverse outcome is likely to be low in this emergency setting and helps conserve O D negative supply.⁸
 - If D positive red cells are given to a female of childbearing potential (≤ 50 years), consideration should be given to the use of anti-D immunoglobulin (plus exchange transfusion for large scale transfusion) to reduce the risk of alloimmunisation to the D antigen.⁹

C. Mixed field reactions following transfusion of O D negative red cells to non-O D negative patients:

- For patients who received O D negative red cells and developed mixed field reactions, group specific blood can be used where there is a previously documented blood group (on two occasions) or there is a history of previous transfusion and the mixed field results include the patient's previously documented blood group. Appropriate local protocols should be developed and risk assessed.

D. Blood group incompatible transplantation:

- For non-ABO matched stem cell transplantation where either donor or recipient is group O, group O blood should be selected. It is also acceptable to use group O red cells when there is both a major and minor mismatch between donor and recipient (e.g., when donor is group A and recipient is group B). If both donor and recipient are D positive, group O D positive blood should be used.
- When either the recipient or donor is D negative, D negative red cells should be selected until engraftment and establishment of the patient's new blood group.
- For ABO incompatible solid organ transplants, where either donor or recipient is group O, group O blood must be selected. It is not necessary to use D negative red cells for D positive patients receiving grafts (liver, kidneys) from D negative donors. Patient with passenger lymphocyte syndrome post-transplant may require group O D positive or O D negative red cells depending on the antibody involved.

E. Neonatal usage:

- For neonates needing group O blood, O D negative blood is required only for D negative neonates and for D positive neonates with maternal anti D detected.

F. Ro patients and patients with complex phenotype requirements

- For Ro patients needing phenotyped matched blood, e.g. patients with sickle cell disease where Ro units are not available, O D negative red cells should be selected only in the absence of ABO identical D negative units.
- For patients with complex phenotypic requirements, every effort should be made to order blood in advance to increase the chance of identifying blood within the patient's own ABO/ D blood group.
- If specific phenotyped red cells are not available for the patient's blood group, consider:
 - For D positive patients with complex phenotypic requirements matching O D negative red cells should be selected only in the absence of suitable O D positive units.
 - For D negative patients with complex phenotypic requirements O D negative red cells should be selected if there is no other ABO compatible option.
 - For patients with complex red cell phenotype requiring significant number of units (exchange transfusion) if ABO D identical red cells are not available, keep substitutes with O D negative units to the minimum.

4. K negative and K positive red cells:

Nine percent of Caucasians are positive for the K antigen (K+), but the K antigen is rarer in other ethnic groups. Anti-K can cause severe haemolytic transfusion reactions and haemolytic disease of the fetus and newborn (HDFN). It is therefore important that patients of childbearing potential are offered only K- red cells in order to avoid sensitisation, reactions and risk for development of HDFN. However, K+ red cells can be safely transfused in various other settings and appropriate stockholding offers stability to the supply chain.

A. Transfusing K+ red cells

The following patients can safely receive K+ red cells:

- Male patients, not regularly transfused and with no known anti-K, regardless of their K status.
- Female patients >50 years, not regularly transfused and with no known anti-K, regardless of their K status.

B. Transfusing K- red cells

The following patients should be offered K- red cells:

- All patients with detectable or historical anti-K
- All K- and K unknown female patients of childbearing potential (≤ 50 years old)
- Regularly transfused K- patients requiring Rh and K matched red cells
- Bone marrow transplant patients where the donor or the recipient has anti-K, until engraftment. After engraftment red cells matching the patient's post-graft K phenotype should be transfused

5. Stockholding

Appendix 1 contains guidance on stockholding of O D negative red cells. Also refer to the Blood Stocks Management Scheme (BSMS) website for updates. <http://www.bloodstocks.co.uk/>

Summary of recommendations

Mandatory Indications for use of O D Negative Red Cells

- O D negative patients with anti-D
- O D negative females with child-bearing potential (≤ 50 years)
- O D negative patients < 18 years old
- In an emergency to children and females ≤ 50 years old of unknown blood group

Recommended Indications for the use of O D Negative Red Cells

- O D negative patients who will receive repeated transfusions, or are likely to become transfusion-dependent, e.g. haemoglobinopathy, aplastic anaemia, myelodysplasia.

Acceptable Indications for use of O D Negative Red Cells

- If suitable group specific red cells are unavailable use O D negative red cells only for D negative neonates or neonates with known maternal anti-D.
- For patients with ABO incompatible bone marrow transplantation where there is a discrepancy on the D antigen between donor and recipient and till the engraftment.
- For ABO incompatible solid organ transplantation, O D negative red cells may be temporarily required in the event of passenger lymphocyte syndrome with active haemolysis (from D negative graft to D positive recipient).
- For patients with complex phenotypic requirements, every effort should be made to order blood in advance to identify blood within the patient's own ABO/ D blood group. O D negative red cells may be used to help with complex phenotypic matching.

Patients requiring O D negative and K- red cells:

- O D negative patients with detectable or historical anti-K.
- O D negative K- and K unknown female patients of childbearing potential (≤ 50 years old)
- Female patients ≤ 50 years old of unknown blood group receiving blood as an emergency
- Regularly transfused O D negative and K- patients requiring Rh and K matched red cells
- Bone marrow transplant patients (with the appropriate indication to receive O D negative red cells) where the donor or the recipient has anti-K, until engraftment. Post engraftment transfuse red cells matching the patient's K phenotype.

Use of O D negative K+ red cells

- O D negative male patients and female patients > 50 years old with no historical or detectable anti-K.
- Male patients and female patients > 50 years old in an emergency (blood group unknown).

Use of O D Positive Red Cells

- O D negative patients receiving large volume blood replacement (> 8 units) except in children, females of child bearing potential (≤ 50 years) and patients with immune anti-D.
- Adult males and women > 50 years old who are D negative or whose D status is unknown in emergency situations.
- For patients with mixed field reactions after receiving O D negative red cells, group specific blood can be used provided appropriate grouping results are available. Local protocols should be developed and risk assessed.

References

1. Re-Audit of the usage of group O RhD negative red cells, 2010: Re-Audit of the usage of group O RhD negative red cells <https://hospital.blood.co.uk/audits/national-comparative-audit/national-comparative-audit-reports/>
2. Milkins, C., Berryman, J., Cantwell, C., Elliott, C., Haggas, R., J. Jones, J., Rowley, M., Williams, M., Win, N. (2013) Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfusion Medicine* , **23**, 3-35
3. Hunt, B.J., Allard, S., Keeling, D., Norfolk, D., Stanworth, S.J., Pendry, K. (2015) A practical guideline for the haematological management of major haemorrhage. *Br J Haematol.*, **170**, 788-803
4. National Blood Transfusion Committee: A Plan for NHS Blood and Transplant and Hospitals to address Red Cell Shortages Updated Version August 2016 <https://www.transfusionguidelines.org/document-library/documents/nbtc-red-cell-shortage-plan-august-2016>
5. Emergency Preparedness, Resilience and Response guidance for Hospital Transfusion Teams, NBTC 2019: <https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/working-groups#Emergency>
6. Clinical guidelines for use in a trauma major incident or mass casualty event, NHS England 2018: https://www.england.nhs.uk/wp-content/uploads/2018/12/version1_Major_Incident_and_Mass_casualty_guidelines-Nov-2018.pdf
7. New, H.V., Berryman, J., Bolton-Maggs, P.H.B., Cantwell, C., Chalmers, E.A., Davies, T., Gottstein, R., Kelleher, A., Kumar, S., Morley, S.L., Simon J. Stanworth, S.J., on behalf of the British Committee for Standards in Haematology (2016) Guidelines on transfusion for fetuses, neonates and older children. *Br J Haematol.*, **175**, 784-828
8. Selleng, K., Jenichen, G., Denker, K., Selleng, S., Müllejans, B., Greinacher, A.(2017) Emergency transfusion of patients with unknown blood type with blood group O Rhesus D positive red blood cell concentrates: a prospective, single-centre, observational study. *Lancet Haematol.*, **4(5)**, e218-e224
9. Qureshi, H., Massey, E., Kirwan, D., Davies, T., Robinson, S., White, J., Jones, J., Allard, S.(2014) BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. *Transfusion Medicine*, **24**, 8-20

Appendix 1

Guidance on Stock Management

Please also refer to the Blood Stocks Management Scheme (BSMS) website for any updates <http://www.bloodstocks.co.uk/>

Adequate stock management policies should be in place both in hospitals and blood services to minimise wastage and unnecessary usage of O D negative red cells. Hospitals should review regularly, O D negative stocks using the following points as a guidance:

- Aim for O D negative stocks as a percentage of total red cell stock of 12.5% or less.
- Aim for minimal wastage of O D negative red cells of at least less than 4% of total O D negative stock.
- Hospitals should monitor the number of days their stocks are held before being transfused (Issuable Stock Index - ISI) aiming for the ISI for O D negative to between 3-4 days.
- Hospitals should monitor the number of units of O D negative red cells that are transfused to non- O D negative patients in order to avoid time expiry. Appropriate adjustments should be made to stocks to minimise this practice.
- Hospitals should monitor the number of units of O D negative red cells transfused due to unavailability of group specific D negative blood or O D positive red cells.
- Phenotyped red cell units and units meeting other special requirements (for example irradiated) should be ordered as group specific, and provided as such by blood services, wherever possible. This includes orders for Ro patients.
- Hospitals providing blood to the (air) ambulance (pre-hospital care) should audit usage and adjust the number of units carried in boxes accordingly. Keeping multiple boxes with fewer units should be considered to avoid wastage.
- Hospitals should review usage of O D negative blood from satellite fridges and consider reducing the number held. O D negative red cells kept in satellite fridges must be rotated to avoid wastage.
- If remote issue is in use, regular review of the stocks of O D negative red cells in each fridge should be performed. All stock held in remote fridges should be rotated back into stock with enough shelf life remaining to allow the units to be used before time expiry. Adequate number of O D positive units should be kept to avoid unnecessary usage of O D negative as a substitution.
- For emergency use, consider stocking O D negative units for use in women and O D positive/K+ units for males and women ≥ 50 years old. Prioritise usage of O D negative K- units for women < 50 years old. Risk assess usage of O D positive blood for male patients and women ≥ 50 in pre-hospital care.
- Hospitals using low volumes of red cells should consider stock sharing arrangements with appropriate adjustments of requests to NHSBT to minimise wastage or transfusion to non O D negative patients to avoid wastage.
- Aim to keep 10% to 20% of O D negative blood as K+ to support stability of the supply chain for O D negative K- red cells. This does not apply to specialist facilities serving a fixed patient demographic (i.e. Women's and/or children's hospitals).

Disclaimer

While the advice and information in these recommendations is believed to be true and accurate, neither the authors nor the National Blood Transfusion Committee accept any legal responsibility for the content of these recommendations.

GUIDELINE REVIEW AND STATUS

First approved by the Transfusion Medicine Clinical Policies Group in September 1999, and published in Blood Matters, Issue 2, September 1999.

Revised by the Transfusion Medicine Clinical Policies Group in June 2000. Second revision September 2002

Guidelines for the Use of Group O D Negative Red Cells including contingency planning for large scale emergencies INF/MED/CM/024/01 April 2003 D Stainsby and MF Murphy for the NBS Transfusion Medicine Clinical Policies Group and made available to hospital transfusion laboratories in England and North Wales.

Reviewed January 2009 by H Doughty and M Rowley for the Patients Clinical Team following the National Blood Transfusion Committee Audit of the Usage of Group O RhD negative red cells.

Reviewed July 2019 by D Foukaneli, Consultant Haematologist, NHSBT and Cambridge University Hospitals NHS Foundation Trust, on behalf of the NBTC and the NHSBT O D negative working group. Members of the group contributing to the review include M Bend, Blood Stocks Management Scheme, NHSBT ; A Charlton, Consultant Haematologist NHSBT; S Cotton, Blood Stocks Management Scheme, NHSBT; H Doughty, Consultant in Transfusion Medicine, NHSBT; L Green, Consultant Haematologist, NHSBT and Bart's Health NHS Trust; F Regan, Consultant Haematologist, NHSBT & Imperial College Healthcare NHS Trust; Y Scott, Transfusion Laboratory Manager, The Newcastle upon Tyne Hospitals NHS Foundation Trust.

Reviewed September 2024 by the National Transfusion Laboratory Managers Group and Dr Fateha Chowdhury, Consultant Haematologist in Transfusion Medicine NHSBT and Chair NBTC Emergency Planning Working Group.

We are also grateful to NBTC members for additional comments and feedback. The NBTC includes wide representation including from Regional Transfusion Committees together with various Royal Colleges and professional bodies.