



BLOOD TRANSFUSION IN OBSTETRICS

This is the first edition of this guideline.

1. Purpose and scope

Obstetric conditions associated with the need for blood transfusion may lead to morbidity and mortality if not managed correctly. The increasingly important issues in blood transfusion are adverse events associated with transfusion, including potential infection and potential transmission of prions, rising costs and the possible future problems of availability. Unfortunately, information from randomised controlled trials to inform best practice is largely unavailable in the discipline of blood transfusion.

The aim of this guideline is to offer guidance about the appropriate use of blood products that neither compromises the affected woman nor exposes her to unnecessary risk. Strategies to maximise the haemoglobin (Hb) level at delivery as well as to minimise blood loss are also discussed. It is envisaged that this guideline will be incorporated into a protocol for each unit to disseminate locally.

2. Background

Obstetric haemorrhage remains a major cause of maternal mortality in the UK, with substandard management identified as a contributor in 80% of the cases.¹ It is estimated that there are more than 4000 cases of severe haemorrhage each year in the UK. The majority of these cases will need blood transfusion.

Retrospective analyses of the clinical scenarios often criticise the employment of blood transfusion as 'too little, too late'. Women at high risk of losing greater than 1000 ml should be strongly advised to deliver in a setting where blood transfusion and intensive care facilities are available.^{1,2}

Evidence
level III

Blood transfusion may be a life-saving procedure but it is not without risk. Recipients may rarely develop transfusion-transmitted infection as well as suffer immunological sequelae such as red cell alloimmunisation. The major risk of blood transfusion, however, is of a patient receiving an 'incorrect blood component'.³ Strict adherence to correct sampling, crossmatch and administration procedures is therefore of paramount importance, even in an emergency.

3. Identification and assessment of evidence

This RCOG guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines. The Cochrane Library (including the Cochrane Database of Systematic Reviews, DARE and EMBASE), TRIP, Medline and PubMed electronic databases were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. The search was restricted to articles published between 1966 and

December 2006. The databases were searched using the relevant MeSH terms including all subheadings and this was combined with a keyword search. Search words included 'obstetrics and blood transfusion', 'tranexamic acid', 'factor VIIa', 'cell salvage', 'antifibrinolytics', 'aprotinin', 'haematinics', 'autologous transfusion' and the search limited to humans and English language. The National Library for Health and the National Guidelines Clearing House were also searched for relevant guidelines and reviews. Guidelines and recommendations produced by organisations such as British Committee for Standards in Haematology Transfusion Taskforce and various national bodies were considered. Where possible, recommendations are based on available evidence and the areas where evidence is lacking are annotated as 'good practice points' ✓.

4. How can the chance of transfusion be reduced?

Anaemia should be treated.



If the haemoglobin level is less than 10.5 g/dl in the antenatal period, consider haematinic deficiency once haemoglobinopathies have been excluded. Oral iron should be the preferred first-line treatment for iron deficiency.



Parenteral iron is indicated when oral iron is not tolerated, absorbed or patient compliance is in doubt.



Parenteral therapy offers a shorter duration of treatment and a quicker response than oral therapy.⁴ It is, however, more invasive and expensive to administer. Iron sucrose is given in multiple doses whereas iron dextran may be given as a single total-dose infusion.

Recombinant human erythropoietin (rHuEPO) is mostly used in the anaemia of end-stage renal disease. rHuEPO has been used both antenatally and postpartum in women without end-stage renal disease without any adverse maternal, fetal or neonatal effects.^{5,6}

Use rHuEPO in clinical practice for non-end-stage renal anaemia is still to be established and should only be used in the context of a controlled clinical trial.



Anaemia not due to haematinic deficiency (for example, haemoglobinopathies and bone marrow failure syndromes) should be managed by blood transfusion where appropriate in close conjunction with a haematologist.



Blood loss at delivery should be minimised.



Active management of the third stage of labour is recommended to minimise blood loss.⁷



Women at high risk of haemorrhage should be advised to deliver in hospital.



Optimal management of women on anticoagulants, such as low-molecular-weight heparin, will minimise blood loss.⁸



Clear evidence from randomised trials supports the active management of the third stage of labour as a method of decreasing postpartum blood loss.^{9,10}

5. General principles of blood transfusion

All women should have their blood group and antibodies status checked at booking and at 28 weeks of gestation.^{11,12}



Women should have a group-and-save or crossmatch sample taken according to a locally agreed and regularly monitored maximum surgical blood ordering schedule (MSBOS), depending on the obstetric diagnosis.¹¹

C

If any blood component therapy is contemplated, a sample for group-and-save must be sent to the blood transfusion laboratory.



It should be borne in mind that many hospitals send antenatal serology offsite for economies of scale. It is advised that the results of grouping and antibody screen should be made easily available for the local unit. The National Institute for Health and Clinical Excellence (NICE) suggested that neither a group-and-save nor crossmatch sample should be taken from healthy women with an uncomplicated history who are due to have a caesarean section.¹² This, however, should be interpreted and implemented according to local arrangements for antenatal testing and provision of blood components. This decision should also take into account whether the laboratory provision is offsite and transport times.

Evidence level IV

Patient blood samples used for crossmatching red cells should be no more than 7 days old.

C

Red cell alloimmunisation is most likely to occur in the last trimester, therefore no pretransfusion sample should be more than 7 days old and ideally should be fresh.¹⁴

Evidence level IV

Only Kell-negative blood should be used for transfusion in women of childbearing age, owing to the high risk of alloimmunisation and subsequent haemolytic disease of the newborn (unless a woman is known to be Kell positive).

C

Unlike anti-c, anti-K in pregnancy is more likely to have been induced by previous transfusion; this can be prevented.¹⁵

Evidence level IV

Cytomegalovirus (CMV) seronegative red cells and platelets should be used for CMV seronegative pregnant women.

C

Where the CMV status is unknown, CMV seronegative products should be used to avoid transmission of CMV to the fetus although the UK policy of universal leucocyte depletion substantially reduces if not eliminates the risk of CMV transmission.¹⁵

Evidence level IV

Urgent transfusion should not be delayed if CMV seronegative components are not immediately available.



For women with known placenta praevia, some obstetric centres make 2 units of crossmatched red cells available in the issue fridge. These units should be replaced every week by newly crossmatched units.¹⁴



6. What are the strategies to minimise the use of banked blood?

6.1 Is there a use for pre-autologous blood deposit?

In pregnancy, pre-autologous deposit is not recommended.



Blood can be pre-deposited and kept for up to 5 weeks. This procedure is not recommended. In pregnancy, concerns have been raised regarding placental insufficiency, whether the woman will make up her Hb before delivery and whether the collected units will be sufficient in the event of major obstetric haemorrhage. This procedure does not prevent the most common error in blood transfusion, which is 'incorrect blood component transfused', nor does it alter the risk of bacterial contamination.

Under European Union legislation, only blood establishments are permitted to perform this procedure, which makes it untenable in the majority of obstetric units.¹⁶

6.2 *Is there a use for intraoperative cell salvage?*

Cell salvage is recommended for women in whom an intraoperative blood loss of more than 1500 ml is anticipated.

C

Cell salvage should only be used by healthcare teams who use it regularly and have the necessary expertise and experience. Consent should be obtained and its use in obstetric patients should be subject to audit and monitoring.

C

Intraoperative cell salvage (IOCS) is the process by which blood shed within the surgical field is retrieved by an anticoagulated suction apparatus and collected within a reservoir from where it is centrifuged, washed and pumped into an infusion bag. This salvaged blood can then be returned to the patient. This process is effective in reducing the need for allogenic red cell transfusion and has been widely used in adult orthopaedic and cardiac surgery without complication.¹⁷ The use of IOCS in obstetric practice has been limited, owing to concerns about contamination by amniotic fluid, specifically the risks of amniotic fluid embolism, and by fetal blood cells, particularly the risk of anti-D formation. Common markers of amniotic fluid contamination can be found in the maternal circulation after most deliveries.¹⁸ The IOCS, together with the use of modern leucocyte depletion filters, has been shown to be effective at removing the common markers of amniotic fluid embolism.¹⁹ However, it will not remove fetal blood cells and therefore adequate anti-D immunisation (as determined by Kleihauer test 1 hour after the procedure) will be required to prevent rhesus immunisation in Rh D-negative women.²⁰

Evidence level IIb

The NICE guideline on intraoperative blood cell salvage in obstetrics (IOCS) in obstetrics recommends that, when used, it should be used by healthcare teams who use it regularly and have built up expertise and experience, that patients should be consented for its use, which should be subject to audit and monitoring.²¹

Evidence level IV

The financial cost of cell salvage may be offset by savings accrued from reducing the amount of allogenic blood transfused. In general, IOCS has been recommended for non-obstetric patients in whom an intraoperative blood loss of more than 1500 ml is anticipated.²² IOCS would not, therefore, be required for most caesarean sections if a similar threshold were to be adopted.

IOCS has been used during caesarean section in a number of case series and trials without any reported complications related to receiving salvaged blood.²¹ The total number of obstetric patients who have received salvaged blood in these published studies, however, is in the low hundreds and the possibility of rare catastrophic events has not been ruled out.

Evidence level III

In one study with 68 patients included in the review by NICE, the mean postoperative haemoglobin level was significantly greater in the group which had blood cell salvage than in the control group: 10.4 (SD 1.5) compared with 8.1 (SD 1.4) g/dl⁻¹. Also 2.9% (1/34) patients who received cell salvage required an allogenic blood transfusion compared with 23.5% (8/34) of the control group.²³

IOCS has a role in the management of patients who refuse allogenic blood transfusions and may reduce the need for allogenic blood transfusion for those patients who are at risk of significant intraoperative haemorrhage.

Evidence level IV

This procedure may have a role in obstetric practice in reducing the exposure of obstetric patients to the risks of allogenic blood transfusion. It is recognised, however, that the use of cell salvage in obstetrics remains

controversial and that experience of its use remains limited.

7. How can major haemorrhage be managed?

There should be a clear local protocol on how to manage major obstetric haemorrhage. This should include early involvement of a consultant obstetrician, anaesthetist and haematologist and the blood bank. The protocol should be practised in 'fire-drills' to inform and train relevant personnel.



Massive blood loss may be defined as the loss of 1 blood volume within a 24-hour period. Normal blood volume in the adult is taken as approximately 7% of ideal body weight.²⁴ Other definitions include 50% blood volume loss within 3 hours or a rate of loss of 150 ml/minute.²⁵

7.1 Are there mechanical strategies that can be employed?

Mechanical strategies are discussed in the RCOG Green-top Guideline on Management of Postpartum Haemorrhage (in preparation).

7.2 What blood components can be used for obstetric haemorrhage?

Red cells: when should red cells be used?

Where there is no history of irregular antibodies and none are detected during screening, group-specific compatible blood can be provided within 10 minutes plus transport time. If irregular antibodies are found, or are known to have been present on a previous occasion, then blood must be crossmatched, as obtaining compatible blood may need several units to be crossmatched. Antibodies may delay crossmatch greatly and this should be taken into account when planning care.



In an extreme situation and when the blood group is unknown, O Rh D negative red cells should be given (although these may be incompatible for patients with irregular antibodies).



There are no firm criteria for initiating red cell transfusion.²⁶

The decision to perform blood transfusion should be made on both clinical and haematological grounds. Transfusion is rarely indicated in the stable patient when Hb is greater than 10 g/dl and is almost always indicated when less than 6 g/dl.^{26,27}



In what circumstances should fresh frozen plasma (FFP) and cryoprecipitate be used?

It is essential that regular full blood counts (FBC) and coagulation screens are performed during the bleeding episode. FFP, cryoprecipitate and platelets should not be given on clinical suspicion alone unless there is delay in obtaining blood results.



Infusion of FFP should be considered before 1 blood volume is lost.

In the bleeding woman with disseminated intravascular coagulation (DIC), a combination of FFP, platelets and cryoprecipitate is indicated.



The FFP and cryoprecipitate should ideally be of the same group as the recipient. If unavailable, FFP of a different ABO group is acceptable, provided that it does not have a high titre anti-A or anti-B activity.²⁸



No anti-D prophylaxis is required if an Rh D negative woman receives Rh D positive FFP or cryoprecipitate.²⁸

B

Fibrinogen levels should be maintained above 1.0 g/l by the use of FFP as above or two pools of cryoprecipitate.²⁹

C

There is insufficient evidence to suggest that FFP is useful in major blood loss in the absence of DIC. Its use should be guided by the use of coagulation tests.²⁸

B

Dilution of coagulation factors is the primary cause of coagulopathy in major blood loss following volume replacement with crystalloid or colloid and transfusion of red cell components. During DIC, all coagulation factors, especially fibrinogen, factor V, factor VIII and factor XIII, are depleted. Those at risk are women who have been exposed to prolonged hypoxia, hypovolaemia or hypothermia (for instance, owing to inadequate resuscitation).³⁰ Obstetric conditions predisposing to DIC include amniotic fluid embolism, placental abruption³¹ and pre-eclampsia. A DIC-like syndrome can result from activation of the coagulation cascade secondary to tissue trauma.

DIC should be suspected when there is profuse bleeding from the site of trauma and oozing from the sites of venepuncture and intravenous line insertions.

There are no data to substantiate transfusion triggers for clotting factors but common practice is to administer FFP 12-15 ml/kg to keep the activated partial thromboplastin time (aPTT) and prothrombin time ratios less than 1:5. If DIC is strongly suspected and clotting studies take a long time, transfusion of FFP should be considered before results are available if haemorrhage is otherwise difficult to control.²⁹

Evidence level IV

Clinically significant fibrinogen deficiency develops after a loss of about 150% of blood volume – earlier than any other haemostatic abnormality when packed red cell concentrates are used in replacing major blood loss.³²

Once the FFP has been ordered, it takes at least 30 minutes to thaw and issue. During this time, resuscitation should be continued with volume expanding fluids or red cells as appropriate.

It should be borne in mind that, at present in the UK, most units of FFP (as is the case with red cells, platelets and cryoprecipitate) are not virally inactivated and that transfusion with these products offers a small risk of transfusion transmitted infection.

When should platelets be used?

The platelet count should not be allowed to fall below 50 x 10⁹/l in the acutely bleeding patient.²⁵

C

A platelet transfusion trigger of 75 x 10⁹/l is recommended to provide a margin of safety.²⁹

C

A platelet count of 50 x 10⁹/l may be anticipated when approximately two blood volumes have been replaced by fluid or red cell components.³³

Platelets may not be on-site in many units, so their need should be anticipated and good communication with the transfusion laboratory maintained.

C

Rh D-negative women should receive Rh D-negative platelets. The platelets should ideally also be group compatible.

B

Anti-Rh D immunoglobulin (at a dose of 250 iu) will be needed if the platelets are Rh D positive and the recipient Rh D negative.³⁴ This is not necessary if a caesarean hysterectomy has been performed.

B

Anti-D immunoglobulin at a dose of 250 iu will be sufficient to cover five adult therapeutic doses of platelets given within a 6-week period. Doses may be given subcutaneously to minimise bruising and haematomata in women with thrombocytopenia.³⁴

Platelets may be given via an unused blood-giving set, although a platelet-giving set reduces wastage because it has less dead space. Transfusion of platelets through a giving set previously used for red cells is not recommended.²⁹

7.3 Pharmacological strategies

Is there a use for recombinant factor VIIa (rFVIIa) therapy?

The use of rFVIIa may be considered as a treatment for life-threatening postpartum haemorrhage but should not be considered as a substitute for, nor should it delay the performance of, a life-saving procedure such as embolisation or surgery, nor the transfer to a referral centre.³⁷

C

There is no evidence to support the prophylactic use of rFVIIa to reduce blood loss for caesarean sections.



In the event of intractable obstetric haemorrhage, the administration of rFVIIa may be an option to be discussed with the haematologists.

C

The availability and use of rFVIIa may be limited, owing to its financial cost and therefore it is advisable to consult with the local haematology department to determine its availability and prepare advance local guidance on indications for its use in managing intractable haemorrhage. Consideration should be given to keeping rFVIIa in the blood bank stock in case of any bleeding emergency. Alternatively, a protocol should be available for procuring it urgently.



Factor VIIa has a pivotal role in initiating the process of blood coagulation. The introduction of rFVIIa has stimulated interest in its use in the nonhaemophilic patient, particularly in patients with intractable bleeding despite corrective measures, such as replacement of plasma coagulation factors, fibrinogen, platelets and red cells. There are case reports of the effectiveness of rFVIIa in intractable obstetric haemorrhage but experience of its use in non-haemophilic bleeding remains limited.³⁸

Evidence level III

The incidence of thrombotic complications in non-haemophilic patients following the administration of rFVIIa is unknown.^{39,40} The efficacy and safety of the use of rFVIIa for cases of obstetric haemorrhage remains to be established.

8. How should intrapartum anaemia be managed?

If the Hb is less than 7 g/dl in labour or in the immediate postpartum period, the decision to transfuse should be made according to the individual's medical history, age and symptoms.



9. How should the woman be managed in the postnatal period?

If the Hb is less than 7–8 g/dl in postnatal period, where there is no continuing or threat of bleeding, the decision to transfuse should be made on an informed individual basis. In fit, healthy, asymptomatic patients there little evidence of the benefit of blood transfusion.⁴¹



If unexpected severe bleeding is encountered, investigations should be made postnatally into possible bleeding diatheses. These investigations should be performed on a non-urgent basis at least 3–6 months after delivery.



10. How should women who refuse blood transfusion be managed, including Jehovah's Witnesses?

Hb should be optimised before delivery to prevent avoidable anaemia.



The pharmacological, mechanical and surgical procedures to avert the use of banked blood and blood components should be considered at an early stage.



The treating clinician will need to establish which blood products or blood sparing techniques (if any) are acceptable. An advance directive should be completed and carried in the hand-held notes, although a woman should always be given the opportunity to change her mind about the use of blood products.

The woman may wish to wear a 'no blood' wristband to make it clear to all members of the treating team that blood transfusion is not to be used.

Antenatal planning is essential and haematinics should be given if Hb is less than 10.5 g/dl.

The code of practice for the surgical management of Jehovah's Witness patients by the Royal College of Surgeons (England) and Management of Anaesthesia for Jehovah's Witnesses by the Association of Anaesthetists of Great Britain and Ireland provide useful information.^{42,43}

11. Auditable standards

1. Are there local protocols for management of massive haemorrhage in obstetrics?
2. Is there familiarity with the local protocol with relevant members of staff (clinicians, midwives, biomedical scientists, porters)?
3. Are all major haemorrhages reviewed to ensure that the communication chain worked and that there was no delay in provision of blood products?

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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG.

APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: *Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/clingov1). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels	Grades of recommendations
Ia Evidence obtained from meta-analysis of randomised controlled trials.	A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
Ib Evidence obtained from at least one randomised controlled trial.	B Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
IIa Evidence obtained from at least one well-designed controlled study without randomisation.	C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)
IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.	Good practice point
III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.	<input checked="" type="checkbox"/> Recommended best practice based on the clinical experience of the guideline development group.
IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.	

DISCLAIMER

The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken.

The Guidelines review process will commence in December 2010 unless otherwise indicated