Table 2. Fluid therapy and blood product transfusion (see sections 5.3.3, 5.3.4 and 5.3.5)

Crystalloid	Up to 2 l isotonic crystalloid.
Colloid	Up to 1.5 I colloid until blood arrives.
Blood	If immediate transfusion is indicated, give emergency group O, rhesus D (RhD)-negative, K-negative red cell units. Switch to group-specific red cells as soon as feasible.
Fresh frozen plasma (FFP)	Administration of FFP should be guided by haemostatic testing and whether haemorrhage is continuing:
	<ul> <li>If prothrombin time (PT) or activated partial thromboplastin time (APTT) are prolonged and haemorrhage is ongoing, administer 12–15 ml/kg of FFP.</li> <li>If haemorrhage continues after 4 units of red blood cells (RBCs) and haemostatic tests are unavailable, administer 4 units of FFP.</li> </ul>
Platelet concentrates	Administer 1 pool of platelets if haemorrhage is ongoing and platelet count less than 75 $\times$ $10^9\mbox{/l}.$
Cryoprecipitate	Administer 2 pools of cryoprecipitate if haemorrhage is ongoing and fibrinogen less than 2 g/l.

A high concentration of oxygen (10–15 l/min) via a facemask should be administered, regardless of maternal oxygen concentration. If the airway is compromised owing to impaired conscious level, anaesthetic assistance should be sought urgently. Usually, level of consciousness and airway control improve rapidly once the circulating volume is restored.

Establish two, 14-gauge intravenous lines; a 20 ml blood sample should be taken and sent for diagnostic tests, including full blood count, coagulation screen, urea and electrolytes, and to cross-match packed red cells (4 units). The urgency and measures undertaken to resuscitate and arrest haemorrhage need to be tailored to the degree of shock (Table 2).

The cornerstones of resuscitation during PPH are restoration of both blood volume and oxygen-carrying capacity. Volume replacement must be undertaken on the basis that blood loss is often underestimated. Compatible blood (supplied in the form of red cell concentrate) to replace red cell loss should be transfused as soon as available, if necessary. The clinical picture should be the main determinant of the need for blood transfusion and time should not be unnecessarily spent awaiting laboratory results. Constitutions should draw on the expertise of their colleagues in anaesthesia, haematology and transfusion medicine in determining the most appropriate combination of intravenous clear fluids, blood and blood products for continuing resuscitation. Guidance from the British Committee for Standards in Haematology summarises the main therapeutic goals of the management of massive blood loss as maintaining:

Evidence level 4

- Hb greater than 80 g/l
- platelet count greater than  $50 \times 10^9/l$
- prothrombin time (PT) less than 1.5 times normal
- activated partial thromboplastin time (APTT) less than 1.5 times normal
- fibrinogen greater than 2 g/l.

### 5.3.3 Fluid replacement

Fluid replacement is a crucial component of PPH treatment, although a dilutional coagulopathy may occur when large volumes of crystalloid, colloid or red cells are used with insufficient transfusion of fresh frozen plasma (FFP) and platelets. Traditionally, a total volume of 3.5 I of clear fluids (up to 2 I of warmed isotonic crystalloid as rapidly as possible, followed by up to a further 1.5 I of warmed colloid if blood is still not Evidence available) comprises the maximum that should be infused while awaiting compatible packed red cells. While there is controversy as to the most appropriate fluids for volume resuscitation, 68-70 the nature of fluid infused is of less importance than rapid administration and warming of the infusion.<sup>71</sup> The woman needs to be kept warm using appropriate measures to prevent hypothermia which in turn could exacerbate acidosis.<sup>72</sup>

There have been no RCTs comparing the use of colloids with other replacement fluids for the resuscitation of women with PPH. Guidelines from the World Health Organization (WHO) $^{73}$ recommend that intravenous fluid replacement for PPH should be with isotonic crystalloids in preference to colloids. A Cochrane review<sup>74</sup> compared colloids with crystalloids for fluid resuscitation in critically ill, nonpregnant patients (patients with burns, trauma or following surgery). This review concluded that resuscitation with colloids was not associated with an improvement in survival and that the use of one particular colloid, hydroxyethyl starch, might increase mortality.

Evidence level I++

#### 5.3.4 Blood transfusion

There are no firm criteria for initiating red cell transfusion. The decision to provide blood transfusion should be based on both clinical and haematological assessment.



The use of blood and blood products in obstetric practice is addressed in the RCOG Green-top Guideline No. 47.13 There are no firm criteria for initiating red cell transfusion 75,76 and the decision to provide blood transfusion should be based on both clinical and haematological assessment. While blood transfusion is almost always required when the Hb is less than 60 g/l and rarely required when the Hb is more than 100 g/l, patients with acute haemorrhage can have normal Hb and clinical evaluation in this situation is, therefore, extremely important. Between 2009 and 2012,3 there were at least three maternal deaths where an acute point of care Hb measurement result is thought to have falsely reassured staff. Furthermore, the Serious Hazards of Transfusion reporting scheme has highlighted the risk of errors in using near patient testing of Hb measurements to guide transfusion.<sup>77</sup> While single Hb/ haematocrit estimations may be misleading and can lead to delays in initiating red cell transfusion, serial measurements may be helpful to monitor ongoing progress. Guidelines from the European Society of Anaesthesiology<sup>78</sup> recommend that repeated measurements of serum lactate and base deficit, together with haematocrit/Hb, are made during haemorrhage and resuscitation to assess tissue perfusion and oxygenation; however, it has not yet been shown whether the outcome of severe bleeding can be improved if volume resuscitation is guided by serum lactate concentration and base deficit.

Evidence level 4

Selection of red cell units for transfusion.

Major obstetric haemorrhage protocols must include the provision of emergency blood with immediate issue of group O, rhesus D (RhD)-negative and K-negative units, with a switch to group-specific blood as soon as feasible.



If clinically significant red cell antibodies are present, close liaison with the transfusion laboratory is essential to avoid delay in transfusion in life-threatening haemorrhage.



All delivery units, especially small units without a blood bank on site, should maintain a supply of group O, RhD-negative blood.



Intraoperative cell salvage should be considered for emergency use in PPH associated with caesarean section and with vaginal delivery.



Pregnant women (and women of childbearing age) who are RhD negative must only receive RhD-negative blood to avoid the risk of D alloimmunisation.<sup>79</sup> Previous blood transfusion is an important cause of alloimmunisation, with antibodies other than anti-D, in particular anti-K, causing severe haemolytic disease of the fetus and newborn.<sup>80</sup> Accordingly, unless a woman is known to be K positive, only K-negative blood should be used for transfusion in women of childbearing age.<sup>79</sup> The aim of antibody screening is to determine the presence of red cell antibodies of likely clinical significance. In addition to the risk of haemolytic disease of the fetus and newborn,<sup>80</sup> these red cell antibodies may have implications for the selection of blood for transfusion in the mother owing to the risk of haemolytic transfusion reactions, and the laboratory should select red cell units negative for the relevant antigen for cross-matching. Close liaison with the transfusion laboratory is essential, with input if needed from the clinical haematology team and specialist advice from the national blood service.

Evidence level 4

All delivery units, especially small units without a blood bank on site, should maintain a supply of group O, RhD-negative blood, as this might offer the only means of restoring oxygen-carrying capacity within an acceptable timescale. The minimum number of units of group O, RhD-negative, K-negative blood to be maintained on site should be agreed within local protocols and should reflect the likely period of delay in the arrival of further supplies should an emergency arise; small delivery units remote from the nearest blood bank will require a larger minimum supply than those a short distance from a blood bank.

### Cross-matching versus electronic issue of blood

The principles of blood grouping, antibody testing and selection of blood in pregnancy are addressed in the RCOG Green-top Guideline No. 47. 13

The majority of laboratories in the UK now use automated testing for blood grouping and antibody testing with advanced information technology systems for documentation and reporting of results. The hospital transfusion laboratory can readily provide red cells that are ABO and RhD compatible using electronic issue with no cross-matching needed, provided that the patient does not have any antibodies and there are robust automated systems in place for antibody testing and identification of the patient. In this setting, since blood can be readily issued, there is no need to reserve units for individual cases. Where electronic issue is not available, a locally agreed maximum surgical blood ordering schedule should be used to decide how many red cell units should be reserved and available for particular cases, based on the obstetric diagnosis. In unforeseen haemorrhage, group O, RhD-negative and K-negative units must be immediately available for emergency use, with a switch to group-specific blood as soon as feasible.

Evidence level 4

# Cytomegalovirus (CMV) status

In elective transfusion in the antenatal period, CMV-seronegative products should be used to avoid transmission of CMV to the fetus, although, the UK policy of universal leucocyte depletion substantially reduces the risk of CMV transmission.<sup>81,82</sup> In an emergency, such as PPH, standard leucocyte-depleted components should be given to avoid delay, and CMV-negative blood or platelets are not needed for transfusion during delivery or in the postpartum period.<sup>82</sup>

Evidence level 4

## Intraoperative cell salvage

Intraoperative cell salvage (the process whereby blood shed during an operation is collected, filtered and washed to produce autologous red blood cells [RBCs] for transfusion to the patient) is commonly being used in cardiac, orthopaedic and vascular surgery with a relative reduction of blood transfusion of 38% and an absolute risk reduction of 21%. Cell salvage does not appear to impact adversely on clinical outcomes. Salvage should be considered for emergency use the Centre for Maternal and Child Enquiries (CMACE) and the Association of Anaesthetists of Great Britain and Ireland. It has been proposed that cell salvage should be considered for emergency use in PPH associated with both caesarean section and vaginal delivery. Although large prospective trials of cell salvage with autotransfusion in obstetrics are lacking to date, no single serious complication leading to poor maternal outcome has been directly attributed to its use. A large RCT is currently in progress comparing intraoperative cell salvage with donor blood transfusions (standard care) during caesarean section in women at risk of haemorrhage (SALVO study, UKCRN ID14032).

Evidence level 4

## 5.3.5 Blood components

There are limited data to inform best clinical practice for the management of haemostatic impairment during PPH, but the principle of management is to prevent and treat haemostatic abnormalities during bleeding, but not to correct abnormalities in nonbleeding women. It is not known whether haemostasis should be corrected to normality for pregnant or nonpregnant women.

Methods to assess haemostatic impairment during PPH include clinical observation, laboratory-based tests (PT, APTT, Clauss fibrinogen and platelet count) and point of care testing.<sup>89</sup> Studies in patients following surgery show that laboratory or point of care testing leads to appropriate use of blood components<sup>90</sup> and both may be used simultaneously. Coagulopathies may evolve rapidly and repeated testing (such as every 30 minutes) during continued bleeding and observation of trends are more useful than single measurements.

Evidence level 3

Routine coagulation tests are widely available and have well-regulated quality control. <sup>89,91</sup> They include PT, APTT, Clauss fibrinogen assay and platelet count. However, turnaround times are often too slow to be clinically useful in acute and rapidly evolving bleeds, and inevitably reflect the past haemostatic status of the woman. Clauss fibrinogen should always be measured as part of the routine coagulation screen because it falls early and may be reduced to a clinically significant level despite a normal PT/APTT. <sup>89,91,92</sup> Platelet number should be measured as part of the full blood count.

Point of care testing using viscoelastometry, such as thromboelastography (TEG<sup>®</sup>, Haemonetics, Braintree, Massachusetts, USA) and rotational thromboelastometry (ROTEM<sup>®</sup>, Tem, Munich, Germany), combined with an agreed treatment algorithm, has been associated with decreased blood loss and blood product use, both outside and within the obstetric setting.<sup>89,93,94</sup> The main advantage is that results are known sooner than for laboratory tests. Point of care testing using TEG<sup>®</sup> and ROTEM<sup>®</sup> has been recommended by the Obstetric Anaesthetists' Association/Association of Anaesthetists of Great Britain and Ireland.<sup>95</sup> However, NICE has concluded that there is insufficient evidence to recommend the routine adoption of viscoelastometric point of care testing in the management of PPH.<sup>96</sup> If used, a quality control protocol should be agreed with the haematology laboratory.

Evidence level 4

## Transfusion of FFP

If no haemostatic results are available and bleeding is continuing, then, after 4 units of RBCs, FFP should be infused at a dose of 12–15 ml/kg until haemostatic test results are known.



If no haemostatic tests are available, early FFP should be considered for conditions with a suspected coagulopathy, such as placental abruption or amniotic fluid embolism, or where detection of PPH has been delayed.



If PT/APTT is more than 1.5 times normal and haemorrhage is ongoing, volumes of FFP in excess of 15 ml/kg are likely to be needed to correct coagulopathy.



Clinicians should be aware that these blood components must be ordered as soon as a need for them is anticipated, as there will always be a short delay in supply because of the need for thawing.



Formulaic protocols, such as I:I or 6:4 RBC:FFP, based on data derived from traumatic bleeding, have been advocated for the management of major haemorrhage.<sup>69,71</sup> However, there is no evidence that this improves outcomes in PPH. The drawbacks of early FFP are that the majority of women with PPH will have normal coagulation at the time of administration,<sup>97–99</sup> and that it is associated with an increased risk of transfusion-associated circulatory overload (TACO)<sup>100</sup> and transfusion-related acute lung injury.<sup>101</sup> FFP results in relatively small increments in fibrinogen level, and to increase the level rapidly, cryoprecipitate or fibrinogen concentrate are required.<sup>102</sup>

There are limited data on the utility of laboratory and point of care coagulation tests to guide FFP replacement during PPH. Abnormal PT/APTT suggests progression towards significant haemostatic impairment, while PT/APTT greater than 1.5 times normal demonstrate that severe and established haemostatic impairment has occurred. 67,68,103

Evidence level 4

If the PPH has stopped, no FFP is required. If haemorrhage is ongoing and the last PT/APTT results are available and are prolonged, 12–15 ml/kg of FFP should be requested and infused with the aim of maintaining the PT/APTT at less than 1.5 times normal. <sup>68</sup> If the PT/APTT is greater than 1.5 times normal, a larger volume of FFP is likely to be required to correct these parameters, <sup>104</sup> and this may be associated with an increased risk of TACO. If the PT/APTT are normal, then no FFP is required, although repeated testing should be performed if bleeding persists.