Better Blood Transfusion
Level 2

BLOOD COMPONENT USE

Self-Directed Learning Pack

Effective Use of Blood Group
Scottish National Blood Transfusion Service
2005

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Contents

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Introduction

Better Blood Transfusion is a self-directed learning programme developed by the Effective Use of Blood (EUB) Group of the Scottish National Blood Transfusion Service (SNBTS). The EUB Group aims to improve transfusion practice and minimise the risk to patients and practitioners involved in the transfusion process. The EUB specialist clinicians, nurses and information technologists promote the effective and efficient use of the donor gift by working in partnership with hospitals in order to develop a clinical effectiveness programme in transfusion.

The Better Blood Transfusion continuing education programme has been designed to assist practitioners involved in the transfusion process to provide high standards of care to patients. The programme has been developed at three levels, with some aspects of the programme being designed particularly for those with limited access to conventional training courses.

Level 1: Safe Transfusion Practice
Safe Transfusion Practice, the first unit in the series, has been designed for all staff groups involved in the administration of blood components, including medical and nursing staff, operating department practitioners and clinical support workers. The self-directed learning pack, *Safe Transfusion Practice*, complements the face-to-face teaching materials produced as part of the unit. It covers the following area of practice:

- Blood group serology
- Ordering blood
- Collecting and storing blood components
- Administering blood components
- Monitoring the transfused patient

The Level 1 materials are being used throughout the NHS in Scotland and are available on www.learnbloodtransfusion.org.uk

Level 2: Blood Component Use
Blood Component Use focuses on the constituents of blood components and plasma derivatives and summarises the indications for use, therapeutic risks and benefits, and management of adverse events. It has been designed for practitioners for who regularly use blood and blood components in their day-to-day practice. As with Level 1, this unit id available face-to-face teaching practice, which is a useful resource for trainers already involved in the delivery of training to health care workers using the Level 1: Safe Transfusion Practice materials.

> **Section 1: Safe and Appropriate Transfusion Practice** describes good practice in the use of blood components and the importance of gaining consent when transfusing patients.
>
> **Section 2: Blood Group Serology** explains the importance of the ABO and Rh blood groups in pre-transfusion testing and compatibility in blood transfusion practice.
>
> **Section 3: Red Blood Cells** outlines the nature of available red cell components and examines factors that influence their use.

Section 4: Platelets focuses on the normal function of platelets and the uses of platelet transfusions.

Section 5: Plasma Components outlines the manufacture and use of fresh frozen plasma and cryoprecipitate.

Section 6: Plasma Derivatives looks at the different plasma derivatives produced, their appropriate use and problems that may be associated with them.

Section 7: Massive Transfusion outlines the unique problems and management of patients requiring large volume transfusions.

Section 8: Management of Transfusion Reactions describes the signs and symptoms of acute and delayed transfusion reactions and their management.

Level 3: Appropriate Transfusion Practice
Appropriate Transfusion Practice will deal with issues such as the use of transfusion guidelines and triggers, and alternatives to allogeneic transfusion.

Using the programme

Before commencing the Level 2 programme, you should have attended a Level 1: Safe Transfusion Practice session or have completed the Level 1 self-directed learning pack.

GOOD TRANSFUSION PRACTICE

The Level 1 pack, *Safe Transfusion Practice*, emphasised the following points.

1 **The majority of transfusion errors involve the administration of a unit of blood intended for another patient.**

2 **The transfusion of an incompatible blood component is the commonest cause of acute transfusion reactions. These may be fatal.**

3 **The blood sample tube for compatibility testing should be labelled at the patient's bedside after the sample has been taken. It should never be pre-labelled.**

4 **The major cause of the transfusion of an incorrect blood component is a failure in the procedure for checking the patient's identification details, the documentation and the component when it is collected from the hospital transfusion laboratory or removed from the blood refrigerator.**

5 **A failure to perform a formal check of the component with the patient at the bedside is the single most important contributor to the transfusion of the incorrect blood component, which is potentially fatal.**

6 **Inadequate monitoring of the patient may result in the life-threatening delays in the recognition and management of a severe transfusion reaction.**

7 **If a severe transfusion reaction is suspected, the transfusion should be stopped and urgent medical advice sought.**

8 **Parents or guardians must be involved in the decision to transfuse their child.**

The Level 2 self-directed learning pack has been developed by subject specialists to assist clinicians in ensuring the effectiveness of their clinical transfusion practice. Throughout, the text, key points are highlighted in 'Good Transfusion Practice'.

Identifying your learning priorities

At the beginning of each section, there is a list of learning outcomes, which outline what you should be able to do when you have completed that section. These learning outcomes are included on pp. 9-10 to provide a framework for you to access your current knowledge, skills and experience in relation to transfusion practice and to identify areas on which you particularly need to focus.

For each learning outcome, tick the box on the scale that most closely corresponds to the point you feel you are at now, using a scale of 1 to 4 where 1 represents a high level of knowledge, skills and experience and 4 equals none at all.

Make a note of any sections that you consider to be a particularly high priority for you. This should help you to plan your study time and identify any areas where you would particularly like help.

The length of time needed to complete this pack will vary with each individual. As there may be some material that is new to you, take as much time as you need to work through each section.

Validation of the Better Blood Transfusion Programme is currently being sought.

	1	2	3	4
Section 1				
1 List the main risks from blood transfusion in the UK	☐	☐	☐	☐
2 Discuss with the patient the anticipated benefits of receiving blood	☐	☐	☐	☐
3 Outline recent national guidelines that are attempting to improve transfusion practice	☐	☐	☐	☐
4 Obtain appropriate consent for transfusion	☐	☐	☐	☐
Section 2				
1 Order blood so that adequate time is available for the laboratory to perform the required test	☐	☐	☐	☐
2 Explain the reasons for different considerations in relation to the compatibility of red cells, platelets and plasma	☐	☐	☐	☐
3 Clearly communicate your requirements for blood to the hospital transfusion laboratory	☐	☐	☐	☐
4 Determine when a further blood sample is needed in a recently transfused patient	☐	☐	☐	☐
Section 3				
1 Explain the main characteristics of the available red cell components and why they are selected in particular clinical circumstances	☐	☐	☐	☐
2 Make an informed decision on whether or not a red cell transfusion is indicated in a particular clinical situation	☐	☐	☐	☐
3 Use your local Maximum Surgical Blood Ordering Schedule appropriately to reduce unnecessary cross-matching of blood	☐	☐	☐	☐
Section 4				
1 Explain how platelet concentrates are produced and the impact this has on their supply and potential risks to the patient	☐	☐	☐	☐
2 Make an informed decision on whether or not platelet transfusion is indicated in a particular clinical situation	☐	☐	☐	☐

Section 5

1 Explain how fresh frozen plasma and cryoprecipitate are produced and the impact this has on their supply and potential risks to the patient

2 Make an informed decision on whether or not fresh frozen plasma or cryoprecipitate transfusion is indicated in a particular clinical situation

Section 6

1 Explain how plasma derivatives are produced and the steps taken to minimise any risks of viral transmission

2 Understand the nature of the more commonly used plasma derivatives and outline how these are administered

3 Know when and how to administer albumin and intravenous and intramuscular immunoglobulins

Section 7

1 Anticipate the problems that may arise during a massive transfusion

2 Manage the transfusion support of a massive haemorrhage effectively

Section 8

1 Recognise acute and delayed transfusion reactions

2 Manage an acute transfusion reaction and know when to ask for advice and assistance

3 Identify the initial manifestations of transfusion reactions and know when to seek advice over the investigation of more complex problems

4 Use your knowledge of transfusion risks in making decisions regarding transfusion therapy for your patients

1

Safe and Appropriate Transfusion Practice

The UK transfusion services have invested enormous resources to provide blood that is amongst the safest in the world. However, no blood component can be considered to be completely free of risk. It is therefore the responsibility of each practitioner who prescribes blood and blood components to ensure the safe and appropriate transfusion practice – the prescribing and administration of the correct blood component, which has been stored under optimal conditions, only when there is a clear clinical indication for transfusion.

A number of studies of transfusion have demonstrated wide variations in the frequency of red cell transfusion and the administration of other blood components. The main factor determining how much blood is administered to a particular patient group is the individual clinician, reflecting widely differing beliefs in the potential risks and benefits of transfusion.

The purpose of this section is to help you to understand good practice in relation to blood transfusion and recognise the importance of providing information, including the risks and alternatives, in simple and comprehensible language to patients who may require a transfusion.

Learning Outcomes

When you have completed this section you should be able to:

1. **List the main risks from blood transfusion in the UK.**
2. **Discuss with the patient the anticipated benefits of receiving blood.**
3. **Outline recent national guidelines aimed at improving transfusion practice.**
4. **Obtain appropriate consent for transfusion.**

Level 1 links

The basic principles of safe and effective transfusion practice are covered in depth in the Level 1 self-directed learning materials: Better Blood Transfusion.

More details about the Serious Hazards of Transfusion (SHOT) scheme can be found in Sections 1.2-1.8.

NHS hospitals must have the means to ensure that, when a patient requires treatment with a blood product, it is given:

- To the right patient
- In the right dose
- At the right time
- Using the right method and equipment
- For the right reason

Introduction
The potential risks associated with transfusion have been highlighted by the Serious Hazards of Transfusion (SHOT) Scheme, which was launched in November 1996. It is a voluntary, anonymous reporting scheme covering both NHS and private hospitals in the United Kingdom and Ireland. Its aim is to collect data on the serious sequelae of the transfusion of blood and blood components in order to:

- Inform policy within transfusion services
- Improve standards of hospital transfusion practice
- Aid production of clinical guidelines for the use of blood components
- Educate users on transfusion hazards and their prevention

SHOT data indicate that, overall, the risks associated with transfusion in the UK are comparatively low at approximately 1:11,000 transfusions. Serious cases of morbidity, such as renal failure or admission to intensive care occurs at a rate of approximately 1:75,000 transfusions while mortality occurs at a rate of 1:375,000 transfusions (SHOT, 2004). In 2003, the first possible transmission of variant Creutzfeldt-Jakob Disease (vCJD) by blood transfusion was described. The transfusion occurred in 1996, the blood donor at the time was well, but went on to develop symptoms of vCJD in 1999 and died the following year. The recipient was diagnosed with vCJD in 2003. To minimise any risks that patients may be exposed to vCJD through transfusion, the UK Blood Services will not accept blood donations from people who believe they have had a transfusion since 1980. This may have an impact on the supplies of blood available in the future. Adverse transfusion events are covered in more detail in Section 8.

Given the potential risks associated with transfusion, every blood transfusion you prescribe or administer must therefore have a defined and justifiable indication.

1.1 Good practice in the use of blood components

The appropriate use of blood components is an important public health and clinical governance issue. It is crucial that good transfusion practice becomes a basic part of patient care. By using blood only when no other alternative therapy is available, you will improve the safety of the transfusion process and avoid the unnecessary use of donor blood.

The correct prescribing of blood components is vital. Treatment with blood components can:

- Save the life of a patient who loses a large volume of blood
- Enable patients to have surgery that involves loss of a large volume of blood
- Enable patients to receive treatment for leukaemia or cancer
- Maintain or improve the health of patients with some chronic conditions.

However, blood components – like other treatments, including those specifically intended as alternatives to blood components – are not free of risk. As practitioners, you should prescribe blood components only when you judge, using the best evidence available, that the treatment is likely to offer a worthwhile benefit to your patient.

GOOD TRANSFUSION PRACTICE

You should prescribe blood only when no suitable alternative is available.

Good clinical practice will always dictate that you should take a cautious approach to the prescription and administration of blood components. You should take all reasonable steps to inform individual patients/ guardians of the potential benefits and risks of receiving blood components.

Everyone involved in the transfusion process, including all personnel working within the UK transfusion services and NHS Trusts, shares a responsibility to work together to:

- Ensure that current practice is consistent with the principles outlined above
- Improve public understanding of the outcomes of treatment with blood components with the aim of promoting realistic expectations of the levels of effectiveness and safety.

A number of guidelines and guidance documents provide a rational and practical framework on which to improve your transfusion practice:

- The Scottish Intercollegiate Guidelines Network (SIGN) guideline *Perioperative Blood Transfusion for Elective Surgery* (2001) aims to maximise patient safety by helping you as a clinician to decide when transfusion is appropriate. The guideline provides evidence- based guidance on how to predict the need for transfusion and on haemoglobin transfusion thresholds as well as information on alternatives to transfusion, including cell salvage.
- The British Committee for Standards in Haematology (BCSH) *Guidelines for the Clinical Use if Red Cell Transfusions* (2001) presents evidence intended to guide transfusion practice for adults. Guidance is given on the general principles of transfusion, indications for red cell transfusion, managing acute blood loss, haemoglobin concentrations and abnormal haemostasis. BCSH has also published guidelines on the use of fresh frozen plasma and platelets, irradiated blood components and the transfusion of infants, which are referred to throughout this learning pack.
- The Association of Anaesthetists of Great Britain and Ireland *Blood Transfusion and the Anaesthetist: Red Cell Transfusion* London: Association of Anaesthetists of Great Britain and Ireland, (2001) provides guidance on the appropriate use of red cell transfusion highlighting the importance of pre-operative assessment of the patient. Information on alternatives to transfusion is addressed.
- The Health Services Circular 'Better Blood Transfusion: Appropriate Use of Blood' (2002) provides guidance on making blood transfusion safer, avoiding the unnecessary use of donor blood and providing better information to patients and the public about transfusion. The circular includes an annex providing detailed information on the functions and responsibilities of the hospital transfusion committee (HTC) and how to develop an effective clinical strategy in order to promote good transfusion practice in Trusts.
- The *Handbook of Transfusion Medicine* (McClelland, 3rd ed 2001) (4th edition *in press*) is a pocket guide designed to help you ensure that, when a transfusion is required, the right product is given to the right patient at the right time and for the right reason. The guide covers all aspects of transfusion from the production of blood products to their clinical use.

The website addresses from these resources are available on p. 69.

The guidance below is included in the *Handbook of Transfusion Medicine* as an example of the type of core standards that can be adopted to ensure safe transfusion practice:

Core Standards for Safe Transfusion

- Every patient who may require transfusion during an impatient stay or day patient episode should wear an identity band on which is recorded legibly then patient's correct minimum identification data. This should be worn during the period in which transfusion may be needed.
- For each transfusion episode there should be a note in the patient's case file signed by the responsible clinician that records the reason for the transfusion.

- When the patient's condition before transfusion permits communication, there should be a record in the patient's case notes to show what information was given to the patient about the risks and benefits of the planned transfusion. Where appropriate it should record that the relevant alternatives to transfusion have been explained and offered to the patient.
- There should be effective arrangements to ensure that the clinician, the hospital transfusion laboratory and where relevant the patient have access to the information required to ensure that the correct blood product can be selected.
- Where the transfusion of donor blood may safely and effectively be avoided by the use of appropriate alternative therapy, the alternative should be available and the patient should be informed accordingly.
- Clinicians, hospital blood bank and the hospital transfusion committee should demonstrate that effective steps are in place to minimise the wastage of donated blood products.
- Hospitals should maintain records of the final fate of each blood component pack, i.e. whether it is transfused, discarded or returned to Blood Services.
- Hospitals should participate in national quality improvement programmes for transfusion practice and should submit reports of adverse events and near-miss incidents to the Serious Hazards of Transfusion scheme.

GOOD TRANSFUSION PRACTICE

Check that a copy of the local protocol on transfusion, based on national guidelines, is available in your clinical area. Ensure you are fully familiar with it.

1.2 The role of the hospital transfusion committee (HTC)

The hospital transfusion committee performs a central role in improving transfusion practice including:

- Promoting best practice through the development of local protocols based on national guidelines
- Promoting the education and training of staff involved in the blood transfusion process
- Leading multi-professional audit on blood transfusion
- Providing feedback on audit of transfusion practice and the use of blood within the Trust

GOOD TRANSFUSION PRACTICE

Your hospital should have a hospital transfusion committee, which includes a representative of your clinical speciality.

Both the Departments of Health in the UK (2002) and SHOT (2004) recommend that each hospital should employ a transfusion practitioner, such as a specialist nurse or biomedical scientist, to assist in the implementation of the HTC's objectives. The hospital transfusion practitioner, in conjunction with a lead consultant in blood transfusion and the hospital transfusion laboratory (HTL) manager, can support clinical teams in the safe and effective use of blood as well as actively promoting good transfusion practice. The hospital transfusion practitioner also has a pivotal role in providing or facilitating training and education for all hospital staff involved in the transfusion process.

1.3 Consent for transfusion

Why consent is essential

At present, there is no legal requirement in the UK to gain specific consent from the patient for the transfusion of blood components. It is, however, usually sought as part of general consent. As stated in the Department of Health's *Good practice in Consent: Implementation Guideline* (DOH, 2001), 'Patients have a fundamental legal and ethical right to determine what happens to their own bodies'.

Involving the patient in the consent process is therefore not only a common courtesy, but respects the right of the patient to be included in decisions about his or her treatment. This process will ultimately promote trust between you as the health care professional and your patient. Consent to transfusion may be given implicitly, orally or in writing and must be bestowed voluntarily and not under any form of duress or undue influence. For the consent process to be valid, the patient must be competent and have received sufficient information to make an informed decision.

GOOD TRANSFUSION PRACTICE

You should inform patients requiring transfusion of the benefits, risks and expected outcomes of transfusion and give them the opportunity to discuss and agree to their proposed treatment.

Gaining consent

Your patients must be provided with adequate information before they consent to any form of treatment. It is imperative that you discuss the proposed treatment with them in language that they understand and that encourages them to enter into a dialogue about their forthcoming, should they wish to do so. In any discussion you have with patients about their transfusion, you must include information about the risks and benefits of their proposed treatment as well as informing them about alternative treatments, where appropriate. A useful summary of the risks of transfusion is given in the British Committee for Standards in Haematology *Guidelines for the Clinical Use of Red Cell Transfusions* (BCSH, 2001).

Gaining consent is not about acquiring a signature on the consent from; there is no legal requirement to seek written consent for transfusion in the UK. However, it is essential that you clearly document the patient's verbal consent to the intervention and the discussion, which led to the agreement.

Patient information leaflets are a useful aide to promoting discussion but should never be used as a substitute for providing specific guidance or advice

on transfusion therapy to your patient.

GOOD TRANSFUSION PRACTICE

A number of tools are available to help your patients' access relevant information on the transfusion of blood components, including the following websites:

- **National Blood Service**
  http://www.blood.co.uk
- **Scottish National Blood Transfusion Service**
  http://www.scotblood.co.uk
- **British Blood Transfusion Society**
  http://www.bbts.org.uk
- **Handbook of Transfusion Medicine (McClelland, *3rd ed 2001)* (4th edn, 2005: *in press*)**
  http://www.transfusionguidelines@org.uk

Providing information

When providing information on transfusion to your patients, it is important that you do so in a timely manner. The most appropriate timing will obviously depend on patients' individual circumstances; patients undergoing elective surgical procedures, for example, should be given the relevant information in the outpatient or pre-admission clinic. If any patients decide they wish to receive an alternative therapy, such as autologous donation or cell salvage, this will allow you sufficient time to refer them to the appropriate facility. Patients who require a transfusion as part of their medical treatment should be given the opportunity to discuss the proposed transfusion and/or any available alternatives prior to the pre-transfusion blood sample being taken.

If the patient cannot communicate because, for instance, a paediatric patient or incompetent at the time, it is essential that you explain the proposed transfusion treatment to the patient's relative or carer. It must be stressed however, that consent issues should not delay necessary transfusion in an emergency situation (DOH, 2000). Gaining consent for transfusion is one of a number of initiatives that have been promoted in recent years to improve transfusion practice. Other initiatives include the education of health care professionals in the use of blood and blood components, better definition of clinically significant risk and the support of audit of transfusion practices as a means of improving practice. These initiatives will be discussed in Better Blood Transfusion, Level 3: *Appropriate Transfusion Practice*.

2

Ensuring Donation and Patient Compatibility

As noted in the Introduction, the SHOT scheme has shown that red cell incompatibility has caused severe morbidity and mortality. Over the period 1996-2003, errors resulted in 219 patients receiving red cell units, which were ABO (or other red cell group) incompatible. Of these, 15 patients died and 77 patients suffered sever morbidity, including renal failure and intensive care unit admission.

The basic immunohaematology of ABO groups has already been covered in Section 2 of Level 1: *Safe Transfusion Practice* and you should refer back to this section for further information. The purpose of this section is to help you understand the importance of ABO and RhD groups in relation to the transfusion of red cells, platelets and plasma. It also describes pre-transfusion testing. An understanding of these issues will enable you to perform an informed pre-transfusion check of the blood component against the patient's details and make better use of your hospital transfusion laboratory.

Learning outcomes

When you have completed this section you should be able to:

1 Order blood tests so that adequate time is available for the laboratory to perform the required tests.

2 Explain the reasons for different considerations in relation to the compatibility of red cells, platelets and plasma.

3 Clearly communicate your requirements for blood to the hospital transfusion laboratory.

4 Determine when a further blood sample is needed in a recently transfused patient.

Level 1 links

Blood component compatibility is covered more fully in Level 1: Section 2.

Remember: the transfusion of incompatible blood components is the commonest cause of acute transfusion reactions. These may be fatal.

2.1 Red cell compatibility

Red cells have a large number of blood group antigens on their surface. The most important of these for transfusion purposes are the antigens, which produce the ABO and the RhD groups.

If red cells carrying A or B antigens are transfused to an individual who has antibodies to these antigens, a severe immune reaction can occur because the donor cells are not compatible with the recipient. To be compatible, the donor red cells must not carry the antigens, which correspond to the antibodies in the patient's plasma. A transfusion of incompatible cells can lead to:

- Massive haemolysis
- Disseminated intravascular coagulation (DIC)
- Renal failure
- Shock

Individuals may die from circulatory collapse, severe bleeding or renal failure:

Table 1: Red cell compatibility

Patient blood Group	Antigens on cell surface	Antibodies in plasma	Compatible red cells
O	None	Anti-A, Anti-B	O
A	A	Anti-B	A, O
B	B	Anti-A	B, O
AB	A,B	None	AB, A, B, O
Unknown	Unknown	Unknown	O

It is unusual to give RhD negative patients RhD negative blood cells, where possible, as RhD positive blood can stimulate the production of anti-D if transfused into an RhD negative patient. This infrequently causes an acute problem as the antibody takes several days or weeks to appear and will not lead to rapid cell destruction. As RhD negative blood is often in short supply, it may be necessary to use RhD positive blood for transfusion into RhD negative patients in some circumstances.

It is, however, particularly important to use RhD negative red cells when transfusing females of childbearing potential to prevent the possibility of haemolytic disease of the newborn in any future pregnancy. Likewise, those patients who already have anti-D in their blood must receive RhD negative blood.

Table 2: RhD compatibility

Patient's Rh group	Compatible red cells
RhD positive	RhD positive or RhD negative
RhD negative	RhD negative

2.2 Pre-transfusion testing

When blood is required for transfusion, the patient's blood sample is tested for the presence of these antigens and antibodies through a group and screen or cross-match.

Group	ABO and RhD group (antigens)
Screen	Presence of antibodies in the serum
Cross-match	Blood is selected for the patient and tested for compatibility with the patient's serum
Save	Serum is saved for up to 7 days

GOOD TRANSFUSION PRACTICE

You are responsible for ensuring that the patient's blood sample is correctly labelled. Incorrect labelling can result in an incompatible transfusion, which may cause a fatal reaction.

A cross-match is requested for all patients who require, or are likely to require red blood cells. That is they have a greater that 1 in 3 chance of transfusion, otherwise a group and screen adequate. This enables the hospital transfusion laboratory to screen the blood for unexpected antibodies and provide blood rapidly if it required. Patients found to have antibodies will automatically have blood cross-matched to prevent fatal delays in finding suitable blood in an emergency.

A full cross-match will take at least 30-40 minutes to perform and may take much longer if the patient has unexpected antibodies. If blood is required more urgently 'group compatible' cells can be requested from the laboratory; these are the same ABO and RhD group as the patient, but no antibody screen or formal cross-match has been completed. In a life-threatening extreme emergency, group O negative red cells, may be used. Ultimately, this decision is the clinician's responsibility, but it is important to discuss this with the hospital transfusion laboratory (HBT) as soon as possible. When requesting blood from the laboratory, don't forget the time it takes to transport the sample to the laboratory and the blood components from the laboratory to the patient.

You must ensure that you communicate your patient's requirements to the HTL in a timely manner, stating clearly the urgency of the request. Never use the term "ASAP" as this can lead to confusion. Send samples to the laboratory as soon as you can after the potential need for blood becomes apparent. This will allow more time for laboratory staff to work on the sample and thus minimise any risk of incompatibility.

Platelets, fresh frozen plasma and cryoprecipitate are issued on the basis of the patient's blood group (see below); they are not cross-matched against the patient as they do not have the large number of RBC antigens. A group and save sample is required for the first transfusion episode; thereafter, these components can be released on the basis of the historic blood group.

2.3 Pre-transfusion testing in the recently transfused patient

After any transfusion or pregnancy when the patient is exposed to foreign antigens, there is a risk that the patient may develop antibodies to other red cell antigens. In order to ensure that these are detached prior to the next transfusion, it is important to consider the timing of the cross-match sample. The current BCSH guidelines on pre-transfusion testing recommend the timings shown in Table 3.

Table 3: Timing of sampling (adapted from the *Guidelines for Compatibility Procedures in Blood Transfusion Laboratories*, BCSH, 2004)

Patient previously transfused within	Sample to be taken not more than
3-14 days	24 hours before transfusion
15-28 days	72 hours before transfusion
29 days-3 months	1 week before transfusion

Patients who are frequent transfusions (e.g. daily) require a new blood sample at least every 72 hours to screen for the development of irregular antibodies.

GOOD TRANSFUSION PRACTICE

The performance of the blood grouping and antibody screen tests is the most important step in the provision of compatible blood and blood components

If a recently transfused patient requires a further transfusion, a further blood sample may need to be sent to the hospital transfusion laboratory

Your hospital's laboratory handbook or blood request form should clearly identify the time required for the testing of blood samples and provision of blood components

Your hospital's blood request form should enable you to state your requirements clearly and easily, including the degree of urgency of your request

Your local hospital transfusion committee is an appropriate body to receive feedback on these issues.

2.4 Platelet compatibility

Platelets are suspended in large volumes of plasma (200-300mL), so it is important to consider plasma compatibility when administering them. Since a small quantity of red cells is also present in platelet packs, RhD negative platelets should be given to RhD negative females of childbearing potential. An alternative, but less ideal, strategy is to give RhD positive platelets followed by an injection of anti-D to clear the red cells from the circulation.

Currently, in the UK, only group O and group A platelets are produced routinely. In order to prevent cases of severe haemolysis, all group O platelet donations are tested for the level of anti-A and anti-B. It is usual to give group A or low titre group O platelets to patients who are group B or group AB.

2.5 Plasma compatibility

Plasma compatibility is important when administering fresh frozen plasma (FFP), cryoprecipitate and platelets (which are suspended in a large volume of donor plasma) as antibodies in the donor plasma (anti-A or anti-B) could react with the antigens present on the recipient's red cells. Group AB plasma contains no anti-A or anti-B and can therefore be safely given to any patient as it is compatible with all blood groups.

Table 4: Plasma compatibility

Patient blood group	Compatible plasma
O	O, A, B, AB
A	A, B
B	B, AB
AB	AB
Unknown	AB

In an emergency, when the patient's blood group is unknown, group AB plasma can be used safely. Conversely, group O plasma contains both anti-A and anti-B and can therefore be given safely only to group O patients.

If small amounts of incompatible plasma are transfused to an adult patient, this usually does not cause major clinical problems as the antibodies are diluted in the patient's blood volume and only a very small amount of antibody is available to bind to each red cell. As such, the massive immune reaction seen when incompatible red cells are transfused is not generated. However, some donors have very high levels of anti-A and/or anti-B in their plasma, which cause severe haemolysis. High levels of anti-A are most often found in group O donors, so the most dangerous combination is to give group O plasma to group A patients. A number of cases of this are seen in the UK every year because staff have mistakenly assumed that group O plasma or platelets can be given to all patients.

Although FFP may contain small amounts of red cell stroma, sensitisation following administration of RhD positive FFP to RhD negative patients is most unlikely as stroma is less immunogenic than intact red cells. The current BCSH guidelines on FFP use recommend that, FFP of any Rh type may be given regardless of the Rh status of the recipient. If an RhD negative patient receives RhD positive FFP, they will no longer require an anti-D prophylaxis (BSCH, 2004).

Cryoprecipitate contains only about 20 mL of plasma from a single donor. It is common to mix donations form a number of different ABO groups together in order to obtain sufficient for an adult dose. This avoids the administration of a clinically significant volume of incompatible plasma.

GOOD TRANSFUSION PRACTICE

Different considerations apply to the ABO compatibility of red cells and of platelets and plasma.

3

Red blood cells

Red blood cells are the most frequently used blood component in the UK. In 2002-3, 2,678,098 units of red blood cells were issued. There is increasing interest in the appropriate use of red cells and alternatives to red cell transfusion. Both the Scottish Intercollegiate Guideline Network (2001) and the British Committee for Standards in Haematology (2001) have published guidelines to the use of red cells.

The purpose of this section is to outline the nature of available red cell components and explain how these can be modified to create safer components for particular patient groups. It also addresses the factors that need to be considered when determining whether or not a red cell transfusion is indicated.

Learning outcomes

When you have completed this section you should be able to:

1 Explain the main characteristics of the available red cell components and why they are selected in particular clinical circumstances.

2 Make an informed decision on whether or not a red cell transfusion is indicated in a particular clinical situation.

3 Use your local Maximum Surgical Blood Ordering Schedule appropriately to reduce the unnecessary cross-matching of blood.

Level 1 links

The ordering, collection, checking and administering of red cells are covered in more detail in Level 1: Sections 3, 4 and 5.

Remember:

- Check the patient's key identifiers
- Red cells are stored at +2ºC to +6ºC
- Transfusion must be completed within four hours of puncturing the pack
- Monitor the patient appropriately in accordance with hospital guidelines

3.1 Red cells for transfusion

All available red cell components in the UK are prepared from whole blood donations from voluntary, non-remunerated UK donors. During the manufacturing process, the white cells are removed by passing the blood through a filter (a process called leucodepletion). This reduces the total red white cell count in a unit to less than 5×10^6.

Storage
Red cells have a shelf life of up to 35 days and must be stored in a validated blood refrigerator within a temperature range of 4ºC ± 2ºC. It is vital to keep red cells in the refrigerator at all times other than when they are actually being checked or transfused. Red cells that have been out of the refrigerator for over 30 minutes and that are not in the process of being transfused should be returned to the hospital transfusion laboratory for discard due to the risk of possible bacterial contamination. Red cells should be administered within four hours of spiking the pack to reduce the risk of adverse reactions due to possible bacterial contamination.

GOOD TRANSFUSION PRACTICE

Red cells should be transfused within four hours of spiking the pack.

The checking and administration of red cells are covered in Section 5 of Level 1: *Safe Transfusion Practice*.

3.2 Red cells in optimal additive solution

Optimal additive solution contains saline, adenine, glucose and mannitol (SAGM). This helps to maintain red cell function and viability and reduces the haematocrit to produce flow characteristics similar to those of whole blood. Plasma is removed from whole blood and replaced with SAGM solution. Red cells in optimal additive solution are now the most commonly used red cells. A suspension of red cells in optimal additive solution has an approximate total volume of 300mL with a haematocrit of 0.55-0.65. Since the packs contain little plasma, it is possible to use this preparation of red cells in patients with

ABO compatible or identical blood groups. For example, group O cells can be transfused to nearly all patients safely in a life-threatening emergency.

GOOD TRANSFUSION PRACTICE

Red cells in optimal additive solution are the appropriate component for most red cell transfusions.

3.3 Paedipacks

A paedipack system is commonly used for sequential top-up transfusions in neonates. A unit of red cells in optimal additive solution is divided into 4-5 aliquots of 50-60mL at the time of production. This enables the neonate to be transfused on a number of occasions with red blood cells from the same donor, thus reducing the risk of the transmission of infection. The unit is safe to use up to its expiry date.

Paedipacks should not be used for large volume transfusions or exchange transfusions in neonates because of the potential toxicity of large volumes of additive solution in these infants. Further information on paediatric transfusion is available in section 7 of the Level 1 *Safe Transfusion Practice* material. The BCSH has published guidelines on the transfusion of neonates and older children (BCSH, 2003).

3.4 Whole blood

Whole blood is the original blood donation in anticoagulant solution from which no components have been moved, apart from the white cells. One unit contains approximately 470mL blood mixed with 63mL anticoagulant. The haematocrit is 0.35-0.45. As the unit contains plasma and red cells, whole blood of the same ABO group as the recipient should be used.

Whole blood is now rarely indicated. It is however, in exchange transfusions and large volume transfusions in children under the age of 6 months and to prime extracorporeal circuits in low bodyweight, e.g. in extracorporeal membrane oxygenation (ECMO), apheresis, haemodialysis and cardio pulmonary bypass.

3.5 Standard red cell concentrate

Standard red cell concentrate is a suspension of red cells with a haematocrit of 0.65-0.75. Standard concentrates are rarely used today.

3.6 Special requirements

Groups of patients with specific risks from transfusion have additional special requirements when receiving red blood cells. It is the responsibility of the prescribing doctor to identify these requirements and clearly state them on the blood request form. If you work in a unit treating haematology or immunodeficient patients, you should be aware of local protocols for requesting cytomegalovirus (CMV) negative and/ or irradiated blood components. BCSH guidelines (1996) are available on the use of irradiated

blood components.

CMV negative components
CMV negative components are produced from donations that have been specifically screened for cytomegalovirus by serological techniques and have been found to be negative. CMV negative components are currently indicated for:

- CMV negative patients undergoing bone marrow or solid organ transplantation
- Premature neonates weighing less than 1500g with CMV negative mothers
- All intrauterine transfusions

As CMV is found in the white cells in blood, leucodepletion is thought to make blood 'CMV safe'. Many clinicians consider that leucodepleted blood can safely be used in most situations where CMV negative blood would be indicated. One exception to this is in profoundly immunosuppressed patients, such as those undergoing bone marrow transplantation, where clinicians may feel the risks of CMV infection are so high that CMV negative blood is preferable.

Irradiated components
Irradiation is used to destroy any T lymphocytes remaining in the blood donation, which may cause graft-versus-host disease in vulnerable patients. If an immunocompromised patient receives red cell that are not irradiated, the donor's T cells can cause tissue and organ damage leading to death. This particularly important in patients with:

- Congenital immunodeficiency states
- Hodgkin's disease
- Patients undergoing bone marrow or peripheral blood stem cell transplantation
- Patients receiving mobilisation chemotherapy for peripheral blood stem cell harvesting. In this instance donor T cells may be harvested and cyropreserved, causing a risk to the patient when they are re-infused at transplantation.

Washed red cells
Washed red cells are rarely used and are indicated only for patients with:

- Paroxysmal nocturnal haemaglobinuria
- Severe recurrent transfusion reactions

GOOD TRANSFUSION PRACTICE

Your local protocol should identify patients who require CMV-negative and/ or irradiated blood components.

3.7 Indications for red cells

There is no consensus on the precise indications for red cell transfusions and marked variation in clinical practice has been demonstrated (Sirchia et al, 1994). Many doctors still prescribe blood components for reasons that are not supported by clinical evidence or widely accepted clinical guidelines. Many of the errors reported to the SHOT scheme in the period 1996- 2001 have resulted from unnecessary transfusions. Each transfusion must have a document valid, defined and justifiable reason.

The prime reason for the transfusion of red cells is to treat or avoid inadequate delivery of oxygen to the tissues. It is unclear when tissue hypoxia is corrected after transfusion and there is no easy way to measure this at present.

The following factors may influence the decision to transfuse.

1 **Cause of the anaemia**
Anaemia secondary to iron, B12 or folate deficiency will respond well to appropriate haematinic replacement.

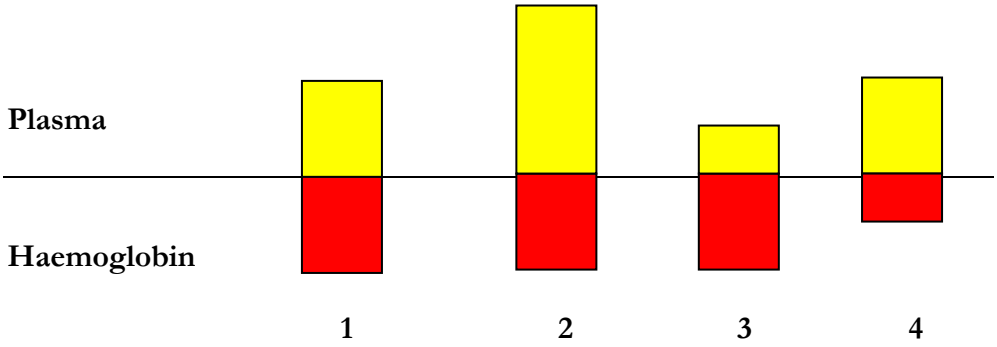
2 **Haemoglobin level**
This should be interpreted in relation to the patient's fluid status (see Figure 1).

3 **Patients' symptoms and their ability to compensate for the anaemia**
Patients with signs of inadequate oxygen delivery, or compensatory changes that may be detrimental, will require transfusion. These may include acidosis, tachycardia or tachypnoea. Patients should be assessed to determine the presence of any other morbidity, which may affect oxygen delivery. Cardiopulmonary disease may impair the ability to compensate for low haemoglobin levels while other causes of a high metabolic rate may increase the patient's demand for oxygen.

4 **Likelihood of further blood loss**
Patients with ongoing blood loss or a high probability of further blood loss are likely to require transfusion.

5 **Chronicity of the anaemia**
Patients with chronic anaemia will adapt to lower haemoglobin levels. Transfusion to normal levels may offer no symptomatic benefit.

Figure 1: Haemaglobin level and fluid status



Laboratory results	Normal Hb	Reduced Hb	Increased Hb	Normal Hb
Clinical condition	Normal	Increased plasma volume	Dehydration	Acute blood loss

Case 1: Normal patient

Case 2: A low haemoglobin is reported from the laboratory because the plasma volume is increased, so the overall haematocrit is reduced. However, the patient would not need a transfusion as he or she has adequate overall amounts of red cells. This may commonly be seen in patients with severe cardiac failure who are fluid overloaded, as the patient is treated with diuretics, the plasma volume falls and the haemoglobin appears to rise. This may also be seen in the peri and post operative situation due to administration of large volumes of crystalloid.

Case 3: Conversely, in this case, the reduction in plasma volume causes a raised haematocrit and the haemoglobin is reported to be higher than expected (spurious polycythaemia).

Case 4: Equal reductions in both plasma volume and red cell volume leave the haematocrit unchanged. Once the patient is resuscitated with clear fluids or colloids, the haemoglobin concentration will fall and the patient is therefore more likely to need transfusion than the results initially suggest.

In summary, the decision to transfuse a patient should be taken on an individual basis, taking many medical and physiological factors into account. The decision process must consider the risks of transfusion versus non-transfusion for the individual patient: this may include risks of myocardial ischaemia in a patient with pre-existing ischaemic heart disease who is not transfused or the risks of alloimmunisation in a female of childbearing potential. Published guidelines e.g. SIGN (2001) BCSH (2001) offer some help in making these decisions, but ultimately it is your responsibility as the prescribing doctor to decide what is most appropriate for the individual patient.

GOOD TRANFUSION PRACTICE

- **Before making the decision to transfuse, consider whether any other treatments, such as oral iron therapy, are more appropriate**
- **You should also consider whether the benefits of transfusion outweigh the potential risks for this patient**
- **Record your decision, the reasons for the transfusion and the outcome in the patient's notes.**
-

3.8 Guidelines for red cell transfusion

All clinical areas should have guidelines for the transfusion of red cells. A number of consensus statements and guidelines have been published nationally and internationally. In 2001, the Scottish Intercollegiate Guideline Network produced a national clinical guideline on the management of perioperative use of red cell transfusion.

Following a systematic review of the literature, the BCSH (2001) made the following recommendations for the management of patients requiring transfusion in the perioperative period:

- Transfusion is likely to be required at haemoglobin >70g/L
- Transfusion is unjustified at haemoglobin >100g/L
- Patients with cardiovascular disease or those likely to have cardiovascular (e.g. elderly patients) are likely to benefit from transfusion when their haemoglobin level falls below 80g/L.

Again, individual patient assessment is very important. Table 5 summarises indications for red cell transfusion.

It has been shown that patients who are anaemic preoperatively are more likely to require transfusion; a full blood count 4-6 weeks preoperatively will allow anaemia to be detected and iron replacement therapy to take effect (Handbook of Transfusion Medicine, p42, 2001:).

GOOD TRANSFUSION PRACTICE

Your decision to transfuse should be based on clinical guidelines, but you must assess each patient on an individual basis.

Table 5: Indications for red cell transfusion (BCSH, 2001)

Red cell transfusion is indicated in the following clinical situations
1 Acute blood loss ♦ Red cells are likely to be required once blood losses are >30% blood volume, or when Hb <70g/L
2 Anaemia in critical care ♦ Clinical trials have suggested that outcomes are no worse using a restrictive transfusion strategy (Hb <70g/L) than a liberal strategy (trigger Hb<100g/L) and may be better in the less critically ill group
3 Perioperative transfusion ♦ Aim to manage the patient so transfusion so transfusion is necessary
4 Chronic anaemia ♦ Transfusions should raise Hb just above the lowest concentration that is associated with symptoms ♦ Consider the use of erythropoietin
Red cells are not indicated
♦ When Hb >100g/L ♦ In situations where alternatives to transfusion exist: e.g. iron deficiency anaemia
GOOD TRANSFUSION PRACTICE **The efficacy of red cell transfusion should be monitored using clinical and laboratory parameters**

3.9 Maximum Surgical Blood Ordering Schedule (MSBOS)

A Maximum Surgical Blood Ordering Schedule (MSBOS) is a local blood ordering tariff for common surgical procedures, which has been agreed between the surgeons, anaesthetists and hospital transfusion laboratory staff in order to reduce blood wastage (BCSH 1992). Many operations do not require transfusion so there is no need to cross-match blood routinely; in these cases, a group and screen would be adequate.

If the likelihood of transfusion being required is less than 1 in 3 for a given operation, the MSBOS would indicate that a group and screen only is required.

For an operation for which transfusion is often required, the MSBOS should reflect actual blood use for patients having that specific operation in that particular unit.

Where an MSBOS exists, it is important to state the procedure on the blood request form and to add any information that may alter the requirement for blood, such as the presence of a coagulation disorder.

Every hospital should have its own MSBOS. Every MSBOS will be different as it will reflect local conditions, such as the time taken to deliver cross-matched red cells.

GOOD TRANSFUSION PRACTICE

When ordering blood for a surgical procedure, consult your local MSBOS in order to reduce blood wastage and unnecessary cross-matching.

4

Platelets

Platelet components for transfusion became available in 1959. Within 3 years, the mortality rate due to haemorrhage in patients with acute leukaemia fell from 67% to 37%. Following an initial steep rise in the demand for platelets, this increase has now slowed. In 2002-2003 251,741 platelet components were issued in the UK.

The purpose of this section is to help you understand the normal function of platelets and when platelet transfusions should be used.

Learning outcomes

When you have completed this section, you should be able to:

1 Explain how platelet concentrates are produced and the impact this impact has on their supply and the potential risks to the patient.

2 Make an informed decision on whether or not platelet transfusion is indicated in a particular clinical situation

Level 1 links

The ordering, collection, checking and administration of platelets are covered in Level1: Sections 3, 4 and 5.

Remember:

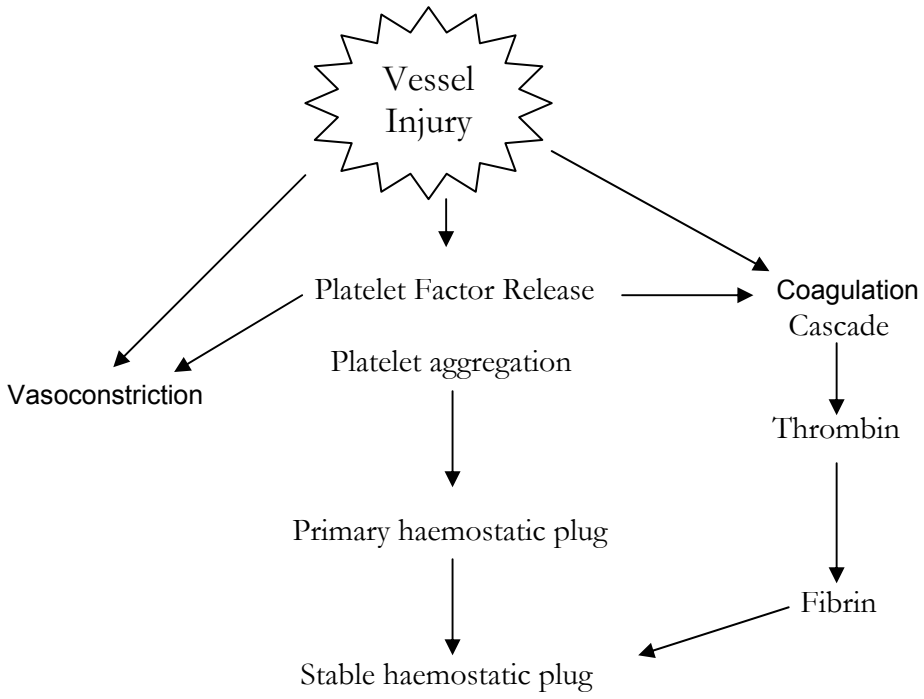
- Check the patient's key identifiers
- Platelets are stored at monitored room temperature
- Transfusion must be completed within 4 hours of spiking the pack
- Monitor the patient appropriately in accordance with Trust guidelines

4.1 Platelet structure and function

Platelets are one of the cellular components found in blood. They are derived from megakaryocytes in the bone marrow. Platelets play a primary role in the maintenance of haemostasis: i.e. the prevention of bleeding. This may fail because:

- Platelets are present in insufficient numbers (thrombocytopenia)
- An inherited or acquired functional defect: e.g. aspirin therapy.

Figure 2: Role of platelets in haemostasis



4.2 Provision of platelets for transfusion

Platelets can be obtained from whole blood donations or by aphaeresis. All platelets for transfusion are leucodepleted. A single adult dose of platelets should contain >240 x 10^9 platelets.

Platelets from whole blood donations (pooled platelets)
If anticoagulated blood is left to stand for long enough, the cellular components settle into discrete layers according to their density. The combined layers of white cells and platelets are referred to as the 'buffy coat'. Buffy coats from four or five whole blood donations are pooled together with plasma from one donor to form one platelet pool (a standard adult dose). The pool is centrifuged again and filtered to separate the white cells from the platelets.

Apheresis platelets
'Apheresis' means to 'selectively remove'. The apheresis machines currently in routine use in the UK use centrifugation to separate platelets from anticoagulated whole blood drawn from volunteer donors. Platelet-rich plasma is collected, while the remaining blood constituents are returned to the donor. By apheresis, it is possible to collect the equivalent of five donations' worth of platelets from a single donor during a procedure, which takes 35-90 minutes.

Apheresis units have the advantage of reducing the number of donors to which the recipient is exposed during transfusion (i.e. one donor instead of four or five if pooled platelets are used). This reduces the risk of transfusion-transmitted infections and the immune complications of transfusion. Apheresis does, however, present additional risks to the donor, which is fully explained when the donor gives consent for the procedure.

GOOD TRANSFUSION PRACTICE

One platelet transfusion may involve exposure to four or five donors with a corresponding increased risk of transfusion-transmitted infection.

Storage
Platelets are stored at a monitored temperature of 22ºC ± 2 and are gently agitated throughout storage period to encourage gas transfer through the semi-permeable storage bag. They should never be refrigerated.

Platelets currently have a shelf-life of five days, which means they expire just before midnight on the fifth day after collection from the donor, the day of collection being day 0. This short shelf-life is a challenge to providing adequate supplies of this component.

The component at most risk of bacterial contamination highlighted by Health Protection Agency Communicable Diseases Surveillance Centre (HPACDSC) and SHOT (2002) is platelets. Between 1997 and 2000 out of 21 bacterial cases reported, 17 were platelet units. Please refer to section 8 page 60 for more information.

4.3 Platelet prescription, selection and issue

The decision to transfuse platelets to a patient must be take by a doctor. In most hospitals, only experienced haematology and blood transfusion medical staff have authorisation to request the laboratory personnel to issue platelets for a particular patient. Standard doses of platelets are:

- Adult: 1 unit
- Child: 10-15m/L kg body weight

Unlike red cell transfusions, there is no formal cross-match procedure for matching platelet donations to recipients. However, the recipient's ABO group and RhD type must be taken into consideration when selecting appropriate platelets. If the issuing laboratory has not determined this already, a blood sample must be submitted. Platelet compatibility is covered in Section 2.4. Refer back to this now.

The storage, checking and administration of platelets are covered in Level 1.

4.4 Indications for platelet transfusion

The normal range for the platelet count in peripheral blood at all ages is 15-400 x 10^9/L. A platelet count below this level (thrombocytopenia) is not, in itself, justification of a platelet transfusion. Isolated thrombocytopenia, in the absence of any other abnormality, is likely to be complicated by serious spontaneous haemorrhage if the count remains above 20 x 10^9/L. However, minor haemorrhage, such as bleeding from the nose (epistaxis) or purpura (a red pin-prick rash arising from pinpoint bleeding into the skin) may occur at a platelet count less than 50 x 10^9/L.

In deciding whether or not platelet transfusion is warranted for as given level of thrombocytopenia, you must also consider:

- The underlining cause of the thrombocytopenia
- Any other clinical factors that may predispose to bleeding

The BCSH has published national guidelines (2003) on the use of platelet transfusions, which are summarised in Table 6.

Table 6: Summary of indications for platelet transfusion

Platelets are indicated in the following clinical situations
1 Bone marrow failure ♦ Patients who are bleeding ♦ Prophylactic platelet transfusions
2 Platelet function disorders if other methods, such as drug withdrawal, are unsuccessful
3 Massive transfusion once >1.5 blood volumes replaced or microvascular bleeding
4 Cardiopulmonary bypass surgery in the presence of bleeding
5 Disseminated intravascular coagulation
Platelets are not indicated in the following conditions
♦ Thrombocytopenic purpura ♦ Immune thrombocytopenia ♦ Post-transfusion purpura

GOOD TRANSFUSION PRACTICE

- **In some cases of thrombocytopenia, platelet transfusion may not be indicated; ensure that the platelet count is accurate before acting on it**
- **If thrombocytopenia is an unexpected finding in a particular patient, the test should be repeated on a fresh sample and a blood film examined.**

In some patients, the platelet count may be within the normal range, but the platelets are dysfunctional, resulting a bleeding tendency. Platelet dysfunction may be inherited or acquired.

Prophylactic platelet transfusion

Most of the platelet transfusions that are currently administered are given to prevent bleeding in patients with bone marrow failure. Such patients have usually received chemotherapy or radiotherapy, which has resulted in significant thrombocytopenia. Although there may be no current bleeding, the risk of serious haemorrhage into, for example, the gut or brain, is perceived to be so high that platelet transfusion is warranted.

There has been much debate over the level of thrombocytopenia, which justifies prophylactic platelet transfusion. Spontaneous bleeding is minimal until the platelet count is less than 5×10^9/L. Currently 10×10^9/L is widely accepted as the limit below which prophylactic platelet transfusion is justified in an otherwise stable patient. This approach should, of course, be modified in the presence of other complicating factors such as fever, recent surgery or in patients at increased risk of bleeding. Patients undergoing surgery will require a higher platelet count to prevent excessive bleeding:

- Minor procedures: e.g. lumbar puncture, epidural, biopsy – aim to raise the platelet count $>50 \times 10^9$/L
- Critical sites: e.g. eye, brain – aim to raise the platelet count to $>100 \times 10^9$/L

As the rise in platelet count can be unpredictable always check the platelet count again before sending the patient to theatre.

GOOD TRANSFUSION PRACTICE

- **Platelets play a primary role in the maintenance of clotting**
- **Most platelets are given to prevent rather than treat haemorrhage**
- **Platelets should be transfused in accordance with clinical guidelines, but also with reference to the individual patient's clinical status**

Platelet transfusion in the presence of excessive consumption
Consider a patient who has been brought into accident and emergency (A&E) following a road traffic accident. Blunt injury to the abdomen may have resulted in lacerations to the liver and spleen. Significant blood loss into the abdominal is ongoing. The patient is shocked. A&E staff, in anticipation of significant blood loss, are administering units of red cells and fluids.

It could be predicted that this patient's platelet count will be reduced because of the combined effects of dilution, consumption at the sites of bleeding and DIC. Previously, various formulae were used to guide the requirement for platelet transfusion during massive transfusion. However, as discussed in Section 7, the platelet count may be remarkably well preserved in such situations. In the face of surgical bleeding (i.e. bleeding from major vessels, as opposed to generalised ooze from the surface of disrupted tissue), platelet transfusion is therefore, unhelpful if the count remains above 50 x 10^9/L.

Platelet transfusion in this situation should be guided by laboratory results. In reality, in the early stages of such an incident when the situation is changing rapidly, blood counts on which to base such decisions are not available quickly enough. A pragmatic review often has to be adopted. However, once surgical intervention is complete, every effort should be made to maintain the platelet count above 100 x 10^9/L. Massive transfusion is covered in more detail in Section 7.

Platelet transfusion for platelet function disorders
Patients with platelet functional disorders rarely require platelet transfusion to prevent haemorrhage. However, these patients are likely to require platelet support or alternative measures if they undergo surgery or have a bleeding problem.

In patients with acquired platelet dysfunction, it may be possible to correct the defect and avoid platelet transfusion; for example, it may be possible to withdraw medication, such as aspirin, which has anti-platelet activity.

The management of patients with inherited platelet functional disorders is complex and should be discussed with the haematologist responsible for their care. Some of these patients may require platelets, but others will benefit from alternatives such as desmopressin or recombinant Factor VIIa.

GOOD TRANSFUSION PRACTICE

- **Platelet therapy is a specialised treatment; you should consult your local haematologist for guidance**
- **Platelets are in short supply. Don't waste them.**
- **Record your decision, the reasons for transfusion and the outcome in the patient's notes**
- **The efficacy of platelet transfusion should be monitored using clinical laboratory parameters.**

4.5 Platelet refractoriness

Platelet refractoriness is defined as the repeated failure to achieve a satisfactory increment after platelet transfusion. Possible reasons for platelet refractoriness include the following.

1 Splenomegaly/ hypersplenism: an increased proportion of transfused platelets are pooled in the spleen and are therefore not available to contribute to haemostasis.

2 Disseminated intravascular coagulation: platelets are consumed by indiscriminate activation of the coagulation mechanism.

3 Drugs: some drugs may sensitise platelets, which results in their accelerated destruction.

4 Bone marrow transplantation (graft-vs.-host disease; cytomegalovirus infection, microangiopathic syndromes: e.g. veno-occlusive disease).

5 Presence of platelet autoantibodies: e.g. immune thrombocytopenia.

6 Presence of platelet alloantibodies: e.g. HLA or HPA antibodies.

4.6 Special cases where platelet transfusion is NOT indicated

Platelet transfusion is not indicated in a few situations where the thrombocytopenia results from an immune mediated problem. Of these conditions, the most commonly encountered is the autoimmune disease immune thrombocytopenia purpura (ITP).

In these circumstances, alternative therapies, such as intravenous immunoglobulin, are indicated. At best, platelet transfusion will be effective due to rapid platelet destruction. At worst, the underlying condition can deteriorate.

Immune thrombocytopenia purpura (ITP)
Immune thrombocytopenia arises when the patient, for reasons, which are unclear, develops a platelet antibody: i.e. an antibody directed against the patient's own platelets. Platelets are destroyed prematurely, mainly in the spleen. For a given platelet count, the risk of haemorrhage in ITP is significantly less than it is for bone marrow failure because, in ITP, young active platelets are continually being released from the bone marrow.

If platelets are transfused, they will be destroyed as quickly as native platelets, so there is usually no point in administering platelets to patients with ITP.

If there is a requirement to raise the platelet count (for example, to cover a surgical procedure), use intravenous immunoglobulin or steroids. Platelets may be transfused if the disease is resistant to this treatment and a surgical procedure is unavoidable, but very large doses may be required to prevent haemorrhage.

5

Plasma components

The method of separating blood into its components was pioneered during the Second World War. Since then, the use of plasma components has continued to rise and studies have demonstrated that they are often misused. In 2002-2003, 377,381 units of fresh frozen plasma and 95,768 units of cryoprecipitate were issued in the UK.

The purpose of this section is to help you understand the correct indications for the use of FFP and cryoprecipitate. You should also refer to section 2.5 for advice on selecting the appropriate blood group.

Learning outcomes

When you have completed this section you should be able to:

1 Explain how fresh frozen plasma and cryoprecipitate are produced and the impact this has on the supply and potential risks to the patient.

2 Make an informed decision on whether or not fresh frozen plasma or cryoprecipitate transfusion is indicated in a particular clinical situation.

Level 1 links

The ordering, collection, checking and administration of fresh frozen plasma and cryoprecipitate are covered in Level 1: Sections 3, 4 and 5.

Remember:

- Check the patient's key identifiers
- Allow 15-30 minutes for frozen plasma and cryoprecipitate to be thawed in the hospital transfusion laboratory before issue
- Transfusion must be completed within 4 hours of spiking the pack
- Monitor the patient appropriately in accordance with hospital guidelines

5.1 Manufacture and storage of plasma components

Fresh frozen plasma (FFP)

Fresh frozen plasma is plasma obtained from leucodepleted whole blood from a single donor. It is prepared by separating and freezing the plasma to −30ºC within 6-8 hours of blood collection (i.e. FFP is "frozen when fresh"). The pack volume varies between 200mL and 300mL and the UK Transfusion Services also supply 50mL packs of FFP for paediatric use.

FFP contains both the labile and stable components of the coagulation, fibrinolytic and complement systems, the proteins that maintain oncotic pressure and modulate immunity, and other proteins that have diverse activities. Great care is taken during freezing and thawing to preserve all the coagulation factors and their activity.

FFP is stored in a frozen state at -30ºC for up to 2 years and must be thawed rapidly when required for use. Allow 15-30 minutes for this procedure. Each unit of FFP should be thawed only in the hospital transfusion laboratory using either a thermostatically controlled waterbath (35ºC-37ºC) or a specially modified microwave oven. It should be issued with a prescription form in the same manner as for red cells.

Once thawed, FFP cannot be refrozen. Unused packs of FFP should be returned to the hospital transfusion laboratory for appropriate destruction, as they are unsuitable for reissue to another patient.

Cryoprecipitate

Cryoprecipitate is prepared from fresh frozen plasma by slow thawing at +4ºC to +6ºC; the resulting precipitate is separated from the supernatant and stored frozen at -30ºC for up to one year. Cryoprecipitate contains fibrinogen, Factor VIII and von Willebrand Factor in higher concentrations than plasma. Most of the components are now available as individual concentrates. Cryoprecipitate should be thawed at 35ºC-37ºC in the hospital transfusion laboratory prior to issue.

5.2 Hazards of fresh frozen plasma

In order to reduce the risk of viral transmission, FFP can be subject to pathogen inactivation. Currently these methods are effective in destroying lipid-enveloped viruses (such as hepatitis B, hepatitis C, HIV-1 and HIV-2), but not hepatitis A or parvovirus B19. In the UK, two types of pathogen inactivated plasma are available: methylene blue treated (UK Transfusion Services) or solvent detergent processed (i.e. Octoplas). Availability of these components may be restricted to selected patient groups, you should check your local policy. Pathogen inactivation can also lead to some loss of coagulation factors in FFP, for example, reduced levels of fibrinogen and FV111 in Methylene Blue treated FFP.

In the UK, FFP for neonates and children born after 1 January 1996 is now obtained from non-UK blood donors and is virus inactivated.

Other risks of FFP include:

- Transmission of disease
- Anaphylactoid reactions
- Alloimmunisation
- Excessive intravascular volume
- Transfusion-related acute lung-injury (TRALI)

These risks will be covered in detail in Section 8. It is important that you are aware that the SHOT reporting scheme has identified that, in relation to the number of units of red blood cells given, acute reactions to FFP and platelets were more frequent (FFP 5 times; platelets 6.5 times).

Table 7: Total issues of blood components from the UK transfusion services 2002-2003 (SHOT, 2002)

Red cells	2,678,098
Fresh frozen plasma	377,381
Platelets	251,741
Cryoprecipitate	92,768
Total	3,399,988

Table 8: Acute transfusion reactions: components implicated (233 reports, SHOT 2004)

Red cells	95
Fresh frozen plasma	71
Platelets	63
Combination of components	4

All patients receiving plasma components should be monitored (e.g. temperature, pulse and BP change) as an early and appropriate initial response will minimise any possible adverse consequences and may be life saving.

5.3 Indications for the use of fresh frozen plasma

Despite its widespread use studies have demonstrated that fresh frozen plasma is often misused (Eagleton et al, 2001). The studies have shown that clinicians have insufficient knowledge of the situations in which its use is appropriate.

There is a paucity of well documented indications for the use of FFP. Only a small number of patients require transfusion of whole plasma; most patients require a single protein, such as albumin or Factor VII. There is no justification for the use of FFP as a volume expander or a nutritional source; safer alternatives exist. FFP should be used only when there is 'abnormal bleeding' with laboratory results that show abnormal coagulation. 'Abnormal bleeding', means microvascular bleeding (e.g. spontaneous oozing from mucosa or venepuncture sites) rather than bleeding from incisions. FFP will not stop bleeding in the heparinised patient. In fact, it may increase the effect of heparin, which works by interacting with antithrombonin III (ATIII). Since FFP is a good source of ATIII, it can increase the heparin effect particularly in patients who have used up most of their own ATIII. In a heparinised patient who has started to bleed, the heparin should be reversed, coagulation reassessed and only then should FFP be given if it is still indicated.

The current recommended clinical indications for the use of FFP are (BCSH 2004):

1 Replacement of a single inherited coagulation factor deficiency when specific or combined factor concentrates are unavailable.

2 Replacement of multiple coagulation factor deficiencies due to severe Bleeding and/ or disseminated intravascular coagulation (DIC); treatment must be directed at removing the underlying cause of DIC. If there is no bleeding, do not give blood components in an attempt to normalise laboratory results. There is no evidence that prophylactic replacement regimens prevent DIC or reduce transfusion requirements.

3 Thrombotic thrombocytopenic purpura (TTP): FFP is currently the treatment of choice, usually in conjunction with daily (initially) plasma exchange.

4 Reversal of warfarin effect: never use FFP for the routine reversal of vitamin K deficiency. Vitamin K should be administered when there is no evidence of severe bleeding. When patients are actively bleeding or require emergency surgery, prothrombin complex concentrates (PCCs) is the product of choice because they are virus inactivated. Alternatively, FFP can be used to achieve immediate haemostasis.

5 Severe liver disease: FFP may be used to provide haemostatic support in the presence of haemorrhage and for short-term prophylaxis to cover invasive procedures.

6 Surgical bleeding and massive transfusion: whether and how much FFP should be used, should be guided by timely tests of coagulation, including near patient testing.

GOOD TRANSFUSION PRACTICE

- **FFP is often misused and should be used only in accordance with clinical guidelines and with reference to the individual patient's clinical status**
- **FFP carries a significant risk of viral transmission and acute transfusion reactions; consider whether the benefits of transfusion outweigh the possible risks for this patient**
- **FFP should not be used for the management of hypovolaemia; crystalloids and colloids are safer, cheaper and more easily available**
- **Record your decision, the reasons for transfusion and the outcome in the patient's notes.**

5.4 Administration of fresh frozen plasma

The dosage of FFP depends upon the clinical situation and underlying disorder; the recommended starting dose for both adults and children is generally 10-15mL/kg, although this may be exceeded in massive bleeding. It is important to monitor the response, both clinically and with measurement of prothrombin time (PTR) and partial prothrombin time (PPT) or with specific factor assays.

The appropriate adult dose is 2-4 packs and the typical pack volume is between 200-300mL per pack (50mL packs are available for children). A fibrinogen result of <1g/L suggests the need for cryoprecipitate.

The benefit of the administration of FFP can be demonstrated by assessing the outcomes such as:

- Cessation of bleeding
- Clinical improvement
- Rise in plasma levels of fibrinogen and other coagulation factors
- Correction of coagulation tests: i.e. prothrombin time and activated partial thromboplastin time

GOOD TRANSFUSION PRACTICE

Assess the efficacy of FFP against clinical and laboratory parameters.

5.5 Indications for the use of cryoprecipitate

The most common request for cryoprecipitate is to improve fibrinogen levels in dysfibrinogenaemia and acquired hypofibrinogenaemia seen in massive transfusion and DIC.

Cryoprecipitate is also the treatment of choice for patients with renal failure who develop uraemic bleeding. In these patients, coagulation tests are normal, but platelet dysfunction is present due to interaction with Willebrand Factor. This is resolved by supplying large volumes of normal von Willebrand Factor.

GOOD TRANSFUSION PRACTICE

- **Cryoprecipitate is used almost exclusively as a treatment for low fibrinogen levels: e.g. in DIC**
- **Cryoprecipitate is often misused and should be used only in accordance with clinical guidelines and with reference to the individual patient's clinical status**
- **Cryoprecipitate carries a significant risk of viral transmission and acute transfusion reactions; consider whether the benefits of transfusion outweigh the potential risks for this patient**
- **Record your decision, the reasons for transfusion and the outcome in the patient's notes.**

5.6 Administration of cryoprecipitate

The final volume of each donor unit is about 20mL. The standard dose for an adult is 8-10 donor units, which is equivalent to 160-200mL. This will result in an adequate clinical response, although this may not be apparent until some hours after the infusion.

For children, 5-10mL per kilogram is the standard dose.

Once thawed, cryoprecipitate is ready for immediate use and should be given as soon as possible to preserve the maximum activity. Cryoprecipitate is usually transfused over a period of 30-45 minutes using a standard blood component transfusion set.

GOOD TRANSFUSION PRACTICE

The efficacy of plasma transfusion should be monitored against clinical and laboratory parameters.

6

Massive transfusion

Massive transfusion is defined as the transfusion of one or more blood volumes in less than 24 hours. The commonest causes of massive transfusion in the UK are:

- Gastrointestinal haemorrhage (50-150/100,000 population per year)
- Trauma
- Ruptured aortic aneurysms
- Major obstetric bleeds

Patients receive large volumes of red cells in optimal additive solution in addition to crystalloid and colloid solutions. Inadequate resuscitation with prolonged hypotension and shock predisposes the patient to disseminated intravascular coagulation. Extensive tissue damage, particularly in head injuries, can also be associated with coagulation disturbances.

The purpose of this section is to help you understand the problems associated with massive transfusion and how to manage the patient requiring massive transfusion.

Learning outcomes

When you have completed this section you should be able to:

1 Anticipate the problems that may arise during a massive transfusion.

2 Manage the transfusion support of a massive haemorrhage effectively.

Level 1 links

It is essential that the urgency of the request for blood components is accurately communicated to the hospital transfusion laboratory. It may be appropriate to use group O RhD negative blood in the initial management of patients requiring massive transfusion.

See Level 1: Section 3.4

6.1 Definition of Massive Transfusion

Massive transfusion is the replacement of a patient's total blood volume with allogeniec or salvaged blood in less than 24 hours. For an adult, this is typically greater than 8-10 units of blood in addition to large volumes of crystalloid and colloid. Patients receiving large volumes of red cells in optimal additive solution usually have numerous other medical problems, such as hypotension, renal or hepatic failure, which compound the difficulties in their management.

6.2 Management of massive transfusion

GOOD TRANSFUSION PRACTICE

The main priority is to control the source of major bleeding. Remember no amount of blood components will stop blood loss through large wounds.

General management

1 Insert large IV cannulae and obtain blood samples
2 Infuse crystalloid rapidly until an acceptable systolic blood pressure is achieved.
3 Manage other aspects of the patient's condition. Remember the ABC principle:
   Airway, breathing, circulation
   Temperature
   Analgesia
4 Request a coagulation screen.
5 Transfuse red cells to maintain adequate blood oxygen transport capacity.
6 Achieve surgical control of bleeding
7 Warm IV fluids if large volumes are being given.
8 Regularly monitor:
   Pulse
   Systolic blood pressure
   Pulse pressure
   Urine output

Management of transfusion issues
Red cell transfusion is indicated once blood volume losses exceed 20%. Crystalloid and colloid solutions can be used to support blood volume satisfactorily until this point. However, in the presence of large ongoing blood losses, do not delay red cell transfusion (see Appendix 1).

GOOD TRANSFUSION PRACTICE

Your hospital should have a protocol for the management of major haemorrhage
Early losses are effectively managed using crystalloids or colloids
Find out where your hospital holds stocks of group RhD O negative blood for use in an emergency.

Fresh frozen plasma is likely to be required once losses exceed one blood volume. FFP will be required if there is:

- Evidence of microvascular bleeding: e.g. bleeding from line sites, venepuncture sites, gum bleeding
- Documented coagulopathy (prolonged APTT or PT) in the presence of ongoing bleeding.

Platelets are likely to be required once losses are greater than 1.5 blood volumes, or sooner, if there is evidence of microvascular bleeding.

Table 9: Transfusion management of blood loss

Blood loss	Transfusion
<20%: up to 1 litre (adult)	Crystalloid
>20%: more than 1 litre	Red cells + crystalloid and/or colloid
1 blood volume or more	Red cells + crystalloid and/or colloid ± blood components

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GOOD TRANSFUSION PRACTICE

- **Coagulopathy and thrombocytopenia are not expected until losses are greater than one blood volume unless the patient has an underlying problem i.e. liver disease**
- **Microvascular bleeding at any point indicates coagulopathy, which requires treatment**
- **Coagulation support may be needed much sooner in patients with rapid consumption of coagulation factors: e.g. DIC, shock.**

Cryoprecipitate is used for the management of hypofibrinogenaemia and is indicated if the fibrinogen is less than 0.8g/L. It is rarely required immediately and may delay the issue of other more urgently required products if requested at this point. In a few circumstances where the risk of DIC is very high (e.g. massive obstetric haemorrhage or significant head injuries) it may be prudent to request cryoprecipitate in the first phase of management.

Request a coagulation screen as soon as possible during a massive transfusion.

The results will help to guide treatment, but this should not be delayed while waiting for the results.

A summary of the management of massive transfusion is shown in Appendix 1.

6.3 Problems associated with massive transfusion

GOOD TRANSFUSION PRACTICE

Inadequate early resuscitation predisposes to disseminated intravascular coagulopathy (DIC).

The following problems may be specifically associated with massive transfusion:

Thrombocytopenia
Platelet count will halve for every 1 x total blood volume replaced, and depending on the starting count will usually fall to 5-100 x 10^9/L after 2 x blood volume replacement, or transfusion of more than15 units of red cells. However, DIC or a pre-existing thrombocytopenia may exacerbate this.

Coagulopathy
In general, where plasma reduced and optimal additive red cells are used, a PTR of >1.5 (clotting factors approximately 50% of normal) will be reached after replacement of 1-1.5 x blood volume or transfusion of 8-12 units of red cells. Abnormal bleeding is unlikely to be a problem above this level. A PTR of >1.8 (clotting factors approximately 30% of normal) will be reached after replacement of 2 x blood volume. The development of DIC may lead to a significant coagulopathy at an earlier point. Fibrinogen concentration halves with every 0.75 x blood volume replaced and is likely to fall to <1g/L after replacement of 12 units of red cells or 1.5 x blood volume (depending on baseline levels).

Hypothermia
The rapid infusion of red cells, which are stored at 4ºC, can cause hypothermia, which may worsen any coagulopathy. Blood warmers should be used when red cells are transfused at rates greater than 50mL/kg/hour in adults.

The following conditions may all be associated with massive transfusion:

- Hypocalcaemia (secondary to the citrate in some optimal additive solutions)
- Hyperkalaemia (secondary to increasing cell release of potassium during storage)
- Changes in oxygen affinity (due to decreased 2,3 DPG in stored blood). These very rarely cause clinical problems in adult patients.

7

Plasma derivatives

Plasma derivatives are partially purified preparations of human plasma proteins, such as albumin or immunoglobulins. They are manufactured from thousands of plasma donations, which are pooled together. As plasma from any single donor could introduce infectious agents into the batch, scrupulous attention is paid to testing for transmissible viruses and steps are taken to inactivate viruses during processing. However, no blood product can be guaranteed to be 'risk free'.

The purpose of this section is to examine the different plasma derivatives and help you to understand the appropriate use of plasma derivatives and problems associated with their use.

Learning outcomes

When you have completed this section you should be able to:

1 Explain how plasma derivatives are produced and the steps taken to minimise any risks of viral transmission.

2 Understand the nature of the more commonly used plasma derivatives and outline how they are administered.

3 Know when and how to administer albumin and intravenous and intramuscular immunoglobulins.

7.1 Manufacture of plasma derivatives

All plasma used in the manufacture of UK plasma derivatives are tested for standard markers of infectivity:

- Anti-HIV
- Anti-HCV
- HBsAg
- HTLV-1

In addition, all plasma pools undergo nucleic acid testing for HAV, HBV, HCV and HIV. Pools of plasma for between 5000 to 20,000 individual donations are processed using the technique of fractionation. Temperature, pH, ethanol and changes in ionic strength are used to separate the plasma into fractions. Further purification steps are then performed. Plasma derivatives undergo virus inactivation to further reduce the risk of the transmission of viruses that have not been detected by the donor screening and testing regimes in place. Some of these inactivation steps are effective mainly against lipid enveloped viruses, including HIV and hepatitis B and C viruses, whilst others are effective against both enveloped and non-enveloped viruses, such as hepatitis A.

Since October 1999, plasma derivatives made in the UK are manufactured from plasma that is obtained from a non-UK source. Research studies have shown that there are steps during the manufacturing process that remove prions, however it is uncertain that these processes reflect the way in which the natural infective agent behaves. The risk of transmission of vCJD, from a plasma derivative, although extremely low, cannot be assumed to be zero. (JPAC Position Statement 2003)

The final products are all solutions or freeze dried powders. Unlike other blood products, plasma derivatives have a long shelf life. Since they do not contain red cell antigens or significant red cell antibodies, compatibility is not an issue. These products will not be labelled for a specific patient, but remember that all plasma derivatives are blood products and their administration, including all batch numbers and expiry dates; should be carefully documented.

GOOD TRANSFUSION PRACTICE

- **Plasma derivatives are made from large pools of non-UK derived plasma from appropriately screened and tested donors; virus-inactivation steps are applied, but cannot guarantee complete absence of the risk of viral transmission**
- **Plasma derivatives should be used only in accordance with clinical guidelines and with reference to the individual patient's clinical status**
- **Consider whether the benefits of transfusion outweigh the potential risks for the patient**
- **Record your decision, the reasons for transfusion and the outcome in the patient's notes.**

7.2 Albumin

Human albumin solutions are used in a range of medical and surgical problems. Albumin is used for:

- Emergency treatment of shock and other conditions where the restoration of blood volume is urgent
- Burns
- Hypoproteinaemia

Human albumin solution contains albumin, small amounts of other plasma proteins, sodium and stabilisers. It is available as a solution of 4.5% or 20%. Human albumin solutions are more expensive than other colloids and crystalloids and allergic responses are well documented. They should not be used for the management of hypo-albuminaemia secondary to nutritional deficiency where enteric feeding is more appropriate.

GOOD TRANSFUSION PRACTICE

Albumin is available in two different concentrations with very different indications for use. Many uses lack an evidence base.

Human albumin 4.5%

4.5% human albumin is iso-oncotic with human plasma. It is usually supplied in a 400mL bottle, which is stored at room temperature. The dosage should reflect circulating blood volume, rather than measures of albumin levels, and will vary according to patient size and the severity of the illness or fluid/protein losses. It is usually administered through a standard infusion set at rates of 5-15mL per minute, although this varies according to clinical need.

The indications for 4.5% albumin are controversial. It is licensed for the restoration and maintenance of circulation blood volume where the use of a colloid is felt to be appropriate. However, a systematic review (Roberts et al, 1998) that examined randomised controlled trials of the use of albumin versus crystalloids or nothing, in the resuscitation of critically ill patients, did not show any benefit from the use of albumin. Until now, the necessary trials have not been performed to clarify its role. The Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (CTG) conducted the "Saline versus Albumin Fluid Evaluation" (SAFE study) – a randomised control trial comparing albumin and saline for intravascular volume resuscitation in 7000 patients treated in intensive care. This study showed equivalent effectiveness between 5% albumin and saline for resuscitation. There is no firm evidence that the use of colloid solution is superior to another or that colloid solutions are associated with better outcomes than crystalloid in patients with trauma, burns or following surgery (SAFE 2004).

GOOD TRANSFUSION PRACTICE

Simply raising a patient's albumin level does not improve outcome and other fluids may be effective for raising blood pressure: e.g. crystalloids or synthetic colloids.

Human albumin 20%
20% albumin has an oncotic pressure approximately 3-4 times higher than that of normal human plasma and infusion will therefore expand plasma volume by drawing in extravascular fluid. It is supplied in 100mL bottles and again is infused through a standard infusion set at rates of 1-2mL per minute.

20% albumin solutions are used in the management of:

- Hypoproteinaemic oedema associated with nephritic syndrome (diuretic resistant oedema)
- Ascites in liver disease

Careful monitoring of fluid and electrolyte balance is essential when using this product.

GOOD TRANSFUSION PRACTICE

20% albumin expands the infused volume 3-4 times by drawing in extravascular fluid, which may lead to cardiac failure.

7.3 Immunoglobulin products

Immunoglobulins are the antibodies produced by B-lymphocytes in response to infection. Immunoglobulins are therefore important for the correct functioning of the immune system, fighting bacterial infections, neutralising viruses and activating the complement systems.

Immunoglobulins are being used to treat an increasingly wide range of conditions. Intravenous immunoglobulin can cause severe adverse reactions, is costly and in short supply. It should only be prescribed when there is good evidence of its effectiveness. Immunoglobulins are given when the patient fails to make adequate antibodies or as protection against particular infections. In other instances they are used to modify the way in which the patient's immune system is working, usually by 'blocking' the action of other harmful antibodies.
Immunoglobulins may be administered:

- Intravenously
- Intramuscularly
- Subcutaneously

Different preparations are used for each route and are <u>not</u> interchangeable.

Intravenous immunoglobulin (IV IgG)
Intravenous immunoglobulin has been available for clinical use since the 1980s and has now largely replaced the use of intramuscular immunoglobulin, with the exception of specific preparations (e.g. hepatitis B immunoglobulin). The most common uses (see Table 10) are:

- Low doses: replacement therapy in primary and secondary hypogamma-globulinaemias
- High doses: treatment for idiopathic thrombocytopenic purpura and a wide range of neurological conditions

Table 10: Licensed indications of intravenous immunoglobulins

Intravenous IgG
♦ Primary hypogammaglobulinaemia
♦ Secondary hypogammaglobulinaemia
♦ HIV infected children with recurrent infection
♦ Kawasaki's disease
♦ Idiopathic thrombocytopenic purpura (ITP)
♦ Bone marrow transplant
♦ Guillain Barre syndrome

However, in clinical practice, requests are often made for a much wider range of clinical indications, e.g. decisions should be evidence-based and clinician's should refer to their local protocol.

- Neonatal septicaemia
- Post-transfusion purpura (PTP)
- Chronic idiopathic demyelinating polyneuropathy (CIDP)

Intravenous immunoglobulin permits large doses of immunoglobulin to be infused into the patient. The doses used vary according to the indication, but is essential that a maximum dose of 2g/kg is not exceeded in any one treatment episode. There is a risk of acute renal failure when these doses are exceeded, particularly with IV IgG products stabilised with sucrose. In the elderly, who are particularly at risk, a dose of 0.4g/kg in 24 hours may be more appropriate.

Risk factors include:

- Pre-existing renal insufficiency
- Diabetes mellitus
- Age over 65
- Hypovolaemia
- Overweight
- Concomitant nephrotoxic medicinal products.

Infusion rates are given in the product data sheets and it is important that these are not exceeded. The infusion is started slowly and gradually increased to a maximum infusion rate in the absence of any reactions. For a 60kg adult the start rate for IV IgG produced by SNBTS would be 18mL/hour, with a maximum rate of 144mL/hour. Other immunoglobulin products will have different infusion rates and you should check the relevant data sheet. Standard blood administration observations should be performed during the infusion.

Adverse reactions are uncommon, but are more frequently seen at rapid infusion rates. Adverse reactions that are well recognised include:

- Allergy
- Anaphylaxis
- Fever and muscle pain
- Acute renal failure

GOOD TRANSFUSION PRACTICE

Safe administration of immunoglobulins requires strict adherence to recommended infusion rates and doses.

Further information is available in the SNBTS Compendium of Product and Component Information (2002) (http://www.snbts-compendium.org.uk).

Intramuscular immunoglobulin (IM IgG)
Today, intramuscular immunoglobulins are primarily specific immunoglobulins used for the prevention of hepatitis A, hepatitis B, tetanus and varicella zoster infection and anti-D immunoglobulin for the prevention of Rh immunisation in pregnancy (specific immunoglobulins).

Subcutaneous immunoglobulin (SC IgG)
Products that are licensed for intramuscular administration are being used subcutaneously for some patients. However, a licensed product has recently been introduced in the UK.

Table 11: Licensed indications for intramuscular and subcutaneous immunoglobulins

Intramuscular IgG
♦ Primary hypogammaglobulinaemia
♦ Secondary hypogammaglobulinaemia
♦ Prevention of specific infections: e.g. hepatitis B, varicella zoster
♦ Prevention of haemolytic disease of the newborn: e.g. anti-D Ig

Subcutaneous IgG
♦ Primary hypogammaglobulinaemia

Although intramuscular IgG is licensed for primary and secondary hypogammaglobulnaemia, current practice in the UK is to promote immunoglobulin home therapy. Patients and their carers are taught to administer intravenous or subcutaneous immunoglobulins, allowing a more holistic approach to caring for these patient groups.

7.4 Other plasma derivatives

Many other plasma derivatives are available for patient use, such as Factor VIII and IX concentrates and prothrombin complex concentrates. On the whole, their use is very specialised and out with the remit of this learning pack. Generally, their use should be guided by haemophilia directors or other consultant haematologists.

8

Management of transfusion reactions

Blood transfusion, like any treatment, can harm as well as benefit the patient. In the seven-year period 1996-2003, the SHOT scheme reported 90 deaths and 249 cases of major morbidity related to transfusion. Whilst the incidents reported in the 'incorrect blood component transfused' category were without exception preventable, the immunological complications of transfusion are unpredictable and difficult, if not impossible, to prevent.

The purpose of this section is to make you aware of the types of adverse event that can occur in relation to transfusion and enable you to manage the immediate event in order to minimise the degree of morbidity experienced by your patients.

Learning outcomes

When you have completed this section you should be able to:

1 Recognise acute and delayed transfusion reactions.

2 Manage an acute transfusion reaction and know when to ask for advice and assistance.

3 Investigate the initial manifestations of transfusion reactions and know when to seek advice over the investigation of more complex problems.

4 Use your knowledge of transfusion risks in making decisions regarding transfusion therapy for your patients.

Level 1 links

More details about the SHOT scheme can be found in Level 1: Sections 1.2 to 1.8.

ABO incompatibility is covered in Section2.2.

Initial management of an adverse event is covered in Section 6.3.

8.1 Acute transfusion reactions

Serious or life-threatening acute reactions are extremely rare. They include:

- Acute intravascular haemolysis
- Septic shock
- Anaphylaxis
- Transfusion-related acute lung injury (TRALI).

GOOD TRANSFUSION PRACTICE

Many acute transfusion reactions have very similar initial presentations and rapid, appropriate management can have a major impact on the outcome.

Acute transfusion reactions occur within 24 hours of transfusion, but signs and symptoms of an acute haemolytic transfusion reaction may appear within minutes of commencing the transfusion.

The most common type of reaction you are likely to observe is fluid overload in patients where the transfusion is administered too rapidly or if an excessive volume is given. Signs and symptoms include:

1. Acute dyspnoea
2. Tachypnoea
3. Non-productive cough
4. Raised jugular venous pressure (JVP)
5. Basal lung crackles
6. Hypertension
7. Tachycardia

Management

1. Stop the transfusion and sit the patient up.
2. Administer high concentrations of oxygen (at least 60%)
3. Administer a diuretic: e.g. frusemide 20-40mg by slow IV injection (maximum injection rate 4mg/minute)
4. Continue to observe the patient closely. Seek expert help if the patient's condition fails to improve.

In a patient with significant cardiac disease, restricting the transfusion to 1 unit of red cells in each 12-hour period should reduce the risk of left ventricular failure. Volume overload is a special risk with 20% albumin solutions.

Other common reactions include:

- Fevers
- Rigors (non-haemolytic febrile reaction)
- Allergic reactions (urticaria or pruritis)

These are the most common acute reactions affecting 1-2% of recipients of red cell components and are more commonly seen in recipients of platelets or FFP.

The majority of febrile reactions can be managed by stopping the transfusion and administering an antipyretic, such as paracetamol. Once the patient has been assessed and any treatment given, the transfusion can be started at a slower rate. Allergic reactions to an antihistamine such as chlorpheniramine. If the patient has repeated febrile or allergic reactions as a result of receiving a transfusion, these drugs can be prescribed prophylactically.

Appendix 2 summarises the signs and symptoms, possible causes and management of acute transfusion reactions.

GOOD TRANSFUSION PRACTICE

- **Never ignore a mild transfusion reaction; it may be the beginning of a severe reaction**
- **Correct initial management of an acute transfusion reaction may be life saving**
- **An acute transfusion reaction may be an indication that the wrong unit of blood has been given to the patient. Always check the patient's identity, the pack and the documentation before administration and in the event of an adverse reaction.**

Intravascular haemolytic transfusion reactions

Intravascular haemolytic transfusion reactions are caused by incompatible red cells reacting with the patient's anti-A or anti-B antibodies (see Level 1: Section 2.2). If an ABO incompatible blood component is transfused to the patient, the red cells are destroyed in the circulation. This can lead to disseminated intravascular coagulation (DIC) and renal failure. Even a few millilitres of incompatible blood can cause an acute transfusion reaction within minutes of the transfusion commencing.

Management

If you suspect a severe reaction:

1 Stop the transfusion immediately and replace the giving set, keeping the line open with normal saline to maintain the systolic blood pressure.
2 Recheck the identity of:
  Patient
  Blood unit
  Documentation
3 Commence appropriate resuscitation treatment, including maintaining the patient's airway and administering high flow oxygen therapy.
4 Seek expert medical advice: e.g. from the haematologist and/or the intensivist.
5 Inform the hospital transfusion laboratory of any acute transfusion reaction and return the blood unit (as well as any unused and used bags) with the giving set and the appropriate samples.

Septic transfusion reactions
Septic transfusion reactions are more commonly seen during platelet transfusions, but can also occur with red cell transfusions. As large amounts of endotoxins may be present in the bag, the reaction can be overwhelming, with hypertension, hypoxia and circulatory failure. The patient may not be pyrexial initially. Inspection of the bag may reveal clumps of platelets or discoloration/ haemolysis in a red cell pack.

Management
The initial management is the same as for intravascular haemolytic transfusion reactions. Stop the transfusion immediately and commence the appropriate treatment.

Septic transfusion reactions are frequently fatal. Rapid administration of broad-spectrum antibiotics with appropriate circulatory and respiratory support is therefore indicated whenever there is a suspicion that the reaction may be septic in nature.

Severe allergic or anaphylactic type reactions
Severe allergic or anaphylactic type reactions are rare, but can be life-threatening. Complications usually occur early in the transfusion. These types of reaction are most commonly seen with the administration of plasma-containing components: e.g. platelets and fresh frozen plasma.

Signs and symptoms include:

- Dyspnoea
- Bronchospasm
- Nausea and vomiting
- Hypotension
- Chest pain

Management
The initial management is the same for intravascular haemolytic transfusion reactions. Stop the transfusion immediately and commence the appropriate treatment.

GOOD TRANSFUSION PRACTICE

Acute intravascular haemolysis (usually due to the administration of the 'wrong blood'), anaphylaxis and septic reactions may all present in similar ways. Empirical therapy may be necessary while awaiting the outcome of investigations.

Transfusion-related lung injury (TRALI)
TRALI is an under-diagnosed life threatening complication of transfusion, which in many cases is missed or misdiagnosed as volume overload or respiratory distress syndrome. The SHOT scheme has shown that TRALI is the second most common cause of transfusion-related morbidity or mortality, second only to ABO incompatible transfusions (SHOT, 2004). TRALI has been reported to occur after transfusion of all blood components however, plasma-containing components such as FFP and platelets are more frequently implicated.

There are two proposed pathophysiologic mechanisms for TRALI. The antigen-antibody theory and the neutrophil priming theory, both leading to increased pulmonary capillary permeability, resulting in pulmonary oedema (Kleinman et 2004).

TRALI usually occurs within 6 hours of completion the transfusion. Signs and symptoms include:

- Acute onset of respiratory distress
- Hypoxia
- Bilateral infiltrates on frontal chest x-ray
- No evidence of circulatory overload or other likely cause

Management
There is no specific treatment for TRALI. Treatment is largely supportive to allow time for the lung injury to subside. If you suspect TRALI:

1 Stop the transfusion immediately and administer high concentration oxygen.
2 For more severe cases IV fluid and mechanical ventilation may be required.

Any suspected cases should be referred initially to the local Blood Centre by the hospital transfusion department staff or clinician for full investigation. The referring clinician will be encouraged to report the incident to SHOT.

The blood services in the UK are looking at a number of measures to reduce the risk of TRALI. Strategies include manufacturing FFP using male only donors. The aim being to minimise the risk of the plasma containing leucocyte antibodies being transfused to the recipient (leucocyte antibodies are produced mainly as a result of pregnancy). Other strategies include decreasing the amount of plasma in red cell components and resuspension of platelets in platelet additive solution or using male plasma to suspend platelet pools.

GOOD TRANSFUSION PRACTICE

Report any suspected case of TRALI to the hospital transfusion laboratory so that it can inform the blood transfusion that supplied the unit. It may be necessary to prevent the donor from giving further donations in case they cause reactions in subsequent patients.

Investigations of acute transfusion reactions

1 Immediately report all acute transfusion reactions, with the exception of mild hypersensitivity, to the hospital transfusion laboratory.

   If you suspect the patient is having a severe life-threatening reaction, seek help immediately from the duty anaesthetist, emergency team or whoever is available and skilled to assist.

2 Record the following information on the patient's notes:
   Type of transfusion reaction
   Length of time after the start of transfusion that the reaction occurred
   Volume, type and pack numbers of the blood products transfused

3 Take the following samples and send them to the hospital transfusion

laboratory for investigations:
Immediate post-transfusion blood samples (1 clotted and 1 anti-coagulated: EDTA/Sequestrene) from the vein opposite the infusion site for:

- Full blood count
- Coagulation screen
- Direct antiglobulin test
- Urea, Creatinine, Electrolytes

Blood culture in a special blood culture bottle
Blood unit and giving-set containing red cell and plasma residues from the transfused donor blood
First specimen of the patient's urine following the reaction.

4 Complete a transfusion reaction report form

5 After the initial investigation of the reaction, send the following to the hospital transfusion laboratory for investigations:
Blood samples (1 clotted and 1 anticoagulated: EDTA/Sequestrene) taken from the vein opposite the infusion site 12 hours and 24 hours after the start of the reaction
Patient's 24-hour urine sample.

6 Record the results of the investigations in the patient's records for future follow-up, if required.

8.2 Delayed transfusion reactions

Delayed transfusion reactions can occur within days, months or even years following transfusion and essentially fall into two categories, shown in Table 125.

Table 12: Delayed transfusion reactions

Transfusion-transmitted infections
♦ HIV (1 & 2)
♦ Hepatitis A
♦ Hepatitis B
♦ Hepatitis C
♦ Cytomegalovirus (CMV)
♦ Chagas disease
♦ Malaria
♦ Syphilis
♦ HTLV-1 & 2

GOOD TRANSFUSION PRACTICE

Non-infectious delayed reactions are generally less serious, although occasionally they can be life threatening.

Transfusion-transmitted infections
Recognised infections that can be transmitted by blood transfusion are outlined in Table 12 above.

Effective donor selection and laboratory testing procedures have been developed and introduced to prevent transmission of most of these infections. As a result, the incidence of these infections is very low in the UK (see Table 13).

Table 13: Cases of transfusion-transmitted infections reported to National Blood Service/ Health Protection Agency Communicable Surveillance Centre (NBS/HPACDSC) 1995-2003 (SHOT, 2004)

Infection	Number	(recipients)	Deaths
Hepatitis A	2	(2)	0
Hepatitis B	10	(11)	0
Hepatitis C	2	(2)	0
HIV	2	(4)	0
Bacteria	29	(29)	7
Malaria	2	(2)	1
HTLV-l	2	(2)	0
Possible vCJD	1	(1)	1
Total	**50**	**(53)**	**9**

Bacterial contamination of a blood component, although an extremely rare event, is the commonest cause, often fatal, reported transfusion-transmitted infection. Between 1997-2003, 29 cases were reported to the NBS/HPACDSC (SHOT, 2004).

Twenty-five cases were due to bacterial contamination of platelet units (16 of which had been stored for more than three days) and four cases were due to contaminated red cell units. This resulted in seven deaths.

You should be aware of the risk of bacterial contamination, especially when administering a platelet transfusion, and that the patient may die as a result. New methods of reducing the risk have been developed, including the introduction of national donor arm cleansing policies and diverting the initial few millimetres of a donation into a disposable pouch, thus discarding skin bacteria that may have entered the needle at venepuncture.

GOOD TRANSFUSION PRACTICE

Check each unit for visible signs of deterioration. Adhere to the correct time limits for administration.

In 2003, the first possible transmission of variant Creutzfeldt-Jakob Disease (vCJD) by blood transfusion was described in the UK (see Introduction p. 12). Precautions are in place in the UK to try to reduce the risk of vCJD transmission from blood transfusion, including, increased donor selection restrictions, leucodepletion of all blood components, and the use of virally inactivated FFP for children born after 1996. Further precautionary measures in the UK, e.g. prion filtration are being considered.

Delayed haemolytic transfusion reactions
Delayed haemolytic transfusion reactions are a rare type of transfusion reaction usually seen in patients who have developed red cell antibodies in the past from a previous transfusion or pregnancy. The antibodies that cause delayed haemolytic transfusion reactions are usually undetectable when the patient's blood is screened in the hospital transfusion laboratory, but another red blood cell transfusion can quickly boost the antibody response.

Common signs and symptoms experienced by the patient include:

- Fever
- Falling haemoglobin or a smaller rise in Hb than expected
- Jaundice
- Haemoglobinuria

GOOD TRANSFUSION PRACTICE

If a patient shows signs of any of these features occurring within 2 weeks of the transfusion, you should consider a delayed haemolytic reaction and order appropriate investigations.

Investigations should include:

- Haemoglobin concentration
- Direct antiglobulin test
- Urea and electrolytes
- Bilirubin or haptoglobin
- Urinalysis

The hospital transfusion laboratory should investigate a fresh sample for the presence of new antibodies. Specific treatment is rarely needed, although further transfusion may be required.

Other rare adverse events
A number of other immunologically mediated transfusion reactions are occasionally seen, but these so rare that they will not be discussed in detail here. However, you should consult with your haematologist if you detect any otherwise unexplained event arising within days of 3-4 weeks of a transfusion, including:

- Thrombocytopenia (possible post-transfusion purpura)
- Skin rash with fever and gut or liver dysfunction (possible transfusion-associated graft-versus-host disease).

In addition, you should be aware that frequent transfusions over a prolonged period will deliver a significant iron load to the patient which may lead to manifestations of iron overload (haemosiderosis), including:

- Liver and endocrine dysfunction
- Grey skin
- Cardiac problems

If you have a patient who is likely to need ongoing transfusions (>every 3-4 weeks) for a period of >4-6 months, ask the haematologist if they should be considered for iron chelation therapy (or possible venesection once the need for regular transfusions has passed).

8.3 Reporting transfusion incidents

You should record all suspected transfusion reactions in the patient's case notes. All serious adverse events should be documented in the patient's case notes and reported to the consultant haematologist. They should also be reported, usually by the consultant haematologist, to the SHOT scheme.

GOOD TRANSFUSION PRACTICE

- **Document all suspected transfusion reactions in the patient's case notes**
- **Report all severe transfusion reactions to the consultant haematologist**
- **All severe transfusion reactions are reportable to the Serious Hazards of Transfusion scheme.**

Glossary of terms

Anti-HCV	Anti-hepatitis C virus
Autologous donation isovolaemic haemodilution	Preoperative blood donation; perioperative
Blood administration set	Infusion set incorporating a 170-200 mm mesh filter, for infusion of blood component
Blood components	Whole blood, red cells, plasma, platelets, cryoprecipitate prepared by the Regional Transfusion Centre
Blood group identical	Same ABO and RhD group
Blood request form	Standard form bearing details of patient, test/ component/ product required which accompanies blood sample to the laboratory
Cell salvage	Salvage from operation site (intraoperative); salvage from operation site (postoperative)
Compatible	Not possessing an antigen or antibody that may induce a haemolytic reaction in the recipient (may not be blood group identical)
Cross-match	Selection and compatibility assessment of red cell units
Cryoprecipitate	Fibrinogen rich component formed by collecting the precipitate which forms in fresh frozen plasma on thawing at 4ºC
Fresh frozen plasma	Plasma removed from whole blood donation and frozen (FFP) within 8 hours of donation
Group and screen	Test to determine ABO and RhD group and screen for atypical red cell antibodies
HbsAg	Hepatitis B surface antigen
HIV	Human immunodeficiency virus
HTLV	Human T-cell leukaemia virus
Leucodepletion	Filtering at the time of production to reduce white cell count contamination
Patient compatibility	Adhesive label bearing patient's details and unique number label of component, which is applied to the blood pack by the hospital transfusion laboratory prior to issue

Platelets: apheresis	Platelets prepared by apheresis (continuous flow separation) from one donor and sufficient for one adult dose
Platelets: pooled	Platelets collected from four or more blood donations and pooled in one bag to give an adequate adult dose
Prescription form/ sheet	Form issued by the hospital transfusion laboratory bearing patient details, test results and details of component and with section for documenting details of prescriber, checker and infusion rate
Red blood cells (RBCs)	Any blood component whose principal constituent is red cells
Red cells in Additive Solution/ Red cells in Optimal Additive Solution (RCCs in OAS)	Citrated blood donation with almost all the plasma removed and 100mL added nutrient solution
Standard red cell concentrate (RCC)	Citrated blood donation with most of the plasma removed
Whole blood	Original blood donation with citrate anticoagulation (no component removed)

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Resources

Association of Anaesthetists: Blood Transfusion and the Anaesthetist: Red cell transfusion (2001)
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British Blood Transfusion Society
http://www.bbts.org.uk

British Committee for Standards in Haematology (BCSH) Guidelines
http://www.bcshguidelines.com

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http://www.transfusionguidelines@org.uk

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http://www.snbts-compendium.org.uk

Serious Hazards of Transfusion (SHOT) Annual Report (2002)
http://www.shot.edmon.co.uk

Appendix 1

Management of Massive Transfusion: adapted from *Handbook of Transfusion Medicine* (McClelland, 4th edn, 2004)

• Arrest bleeding	• Early surgical or obstetric intervention • Upper G/I tract procedures • Interventional radiology	
• Contact key personnel	• Most appropriate surgical team • Duty anaesthetist • Blood bank	
• Restore circulating volume N.B. In patients with major vessel or cardiac injury, it may be appropriate to restrict volume replacement after discussion with surgical team	• Insert wide bore peripheral cannulae • Give adequate volumes of crystalloid/blood • Aim to maintain normal BP and urine output >30mL/hr in adults (or 0.5mL/kg/hour)	• Blood loss is often underestimated • Refer to local guidelines for the resuscitation of trauma patients and for red cell transfusion • Monitor CVP if haemodynamically unstable
• Request laboratory investigations	• FBC, PT, APTT, Fibrinogen; blood bank sample, biochemical profile, blood gases • Ensure correct sample identity and use of red label for transfusion samples • Repeat FBC,PT,APTT, Fibrinogen every 4 hrs, or after 1/3 blood volume replacement, or after infusion of FFP	• Take samples at earliest opportunity as results may be affected by colloid infusion • Misidentification is commonest transfusion risk • May need to give FFP & platelets before the FBC and coagulation results available
• Request suitable red cells N.B. All red cells are now leucocyte-depleted. The volume is provided on each pack, and is in the range of 220-420mL.	• *Blood needed immediately* - use 'Emergency stock' group O RhD neg • *Blood needed in 15-60 minutes* - uncrossmatched ABO group specific will be provided when blood group known (15-60 minutes from receipt of sample in laboratory) • *Blood needed in 60 minutes or longer* - fully crossmatched blood will be provided	• Contact Blood Transfusion laboratory or oncall MLSO and provide relevant details • Collect sample for group and crossmatch before using emergency stock • Emergency use of RhD pos blood is acceptable if patient is male or postmenopausal female • Blood warmer indicated if large volumes are transfused rapidly • Consider use of cell salvage
• Consider the use of platelets	• Anticipate platelet count <50 x 10^9 /L after 1.5-2 x blood volume replacement • Dose – 10mL/kg body weight for a neonate or small child, otherwise one 'adult therapeutic dose' (one pack)	• Target platelet count:- >100 x 10^9 /L for multiple/CNS trauma >50 x 10^9 /L for other situations • May need to use platelets before laboratory results available - take FBC sample before platelets transfused
• Consider the use of FFP	• Anticipate coagulation factor deficiency after blood loss of 1-1.5 x blood volume • Aim for PT & APTT < 1.5 x mean control and fibrinogen >1.0g/L • Allow for 30 mins thawing time • Dose - 12-15 mL/kg body wt=1 litre or 4 units for an adult	• PT/APTT >1.5 x mean control correlates with increased surgical bleeding • May need to use FFP before laboratory results available - take sample for PT, APTT, fibrinogen before FFP transfused
• Consider the use of cryoprecipitate	• To replace fibrinogen & FVIII • Aim for fibrinogen > 1.0g/L • Allow for 30 mins thawing time • Dose - 1pack/10kg body wt	• Fibrinogen <0.5 strongly associated with microvascular bleeding
• Suspect DIC	• Treat underlying cause if possible	• Shock, hypothermia, acidosis - risk of DIC • Mortality of DIC is high

Appendix 2

Management of Acute Transfusion Reaction