CHAPTER 4

CLINICAL TRANSFUSION PROCEDURES

Key points

1. Providing the right blood component to the right patient at the right time is a team effort involving many members of the health care staff.

2. Clear communication strategies, established policies, written standardized procedures and staff training are key to safe transfusion practice.

3. Details of the following are outlined:
   - pretransfusion laboratory testing requirements;
   - blood storage and transportation requirements; and
   - blood administration procedures.

4. The indications and processes for blood component modification are discussed.

Learning outcomes

After studying this chapter, the reader will be able to describe:

- principles of safe clinical transfusion practice, including patient identification, component selection and monitoring during transfusion

- principles of laboratory compatibility testing

- principles of blood component selection, including requirements for modified components.

4.1 Introduction: getting the right blood to the right patient at the right time

Once the decision to transfuse has been made, everyone involved in the transfusion process shares the responsibility to ensure the right blood gets to the right patient at the right time. Box. 4.1 summarizes the main steps in this process and outlines the tasks performed by the various health professionals involved in transfusion.

National guidelines on the clinical use of blood should always be followed in all hospitals where transfusions take place. A local transfusion committee should monitor clinical blood use and review transfusion reactions. It should also ensure that national guidelines are followed and oversee appropriate training.

Initial training and ongoing competency assessment for all staff involved in transfusion and covering the entirety of the transfusion process is a quality systems requirement. Audit of all processes according to a regular audit schedule also contributes to quality improvement by highlighting necessary changes to procedures or training.

In addition, clinical audit to ensure that blood utilization policies are followed is an important quality improvement tool. Guidelines with audit templates are available.

Each hospital should ensure that the following are in place:

- a blood request form;
- a maximum blood ordering schedule (MSBOS) for common surgical procedures;
- guidelines on clinical and laboratory indications for the use of blood, components and alternatives to transfusion;
- defined responsibilities for medical, blood bank and nursing staff and midwives, as well as assistants and students;
- standard operating procedures (SOPs) for each stage in the clinical transfusion process;
- clinical and laboratory audit with feedback of results contributing to ongoing practice changes.

All staff involved in the transfusion process should be trained and should follow SOPs. Development of SOPs requires local input by the transfusion service or blood bank and ideally they are prepared in collaboration with medical and nursing staff. These are often based on national or international standards and adapted for local use. The written procedures should be available to all staff involved in the transfusion process.(*1*,*2*,*3*,*4*)

Responsibility for keeping SOPs up to date and available for training staff to use them should be defined by hospital management, along with the programme for training of clinical staff in administering blood and monitoring patients during and following transfusion.

Box 4.1. Steps in the clinical transfusion process

Getting the right blood to the right patient at the right time

1. Assess the patient's clinical need for blood and when it is required. (*clinical/physician*) 4.1
2. Inform the patient or guardian about the proposed transfusion treatment and document consent and indication for transfusion. (*clinical/physician*) 4.2.1
3. Determine the urgency of transfusion. (*clinical/physician*) 4.2.2
4. If blood is needed urgently, contact the blood bank by telephone or use the approved method for urgent requests. (*clinical*) 4.2.3
5. Select the blood component and quantity required. Use a blood ordering schedule as a guide to transfusion requirements for common surgical procedures. (*clinical/physician*) 4.2.4
6. Complete the blood request form accurately and legibly. (*clinical*) 4.2.6
7. Verify the patient's identity at the bedside. (*clinical/laboratory*) 4.2.5
8. Obtain and correctly label a blood sample for compatibility testing. (*clinical/laboratory*) 4.2.7
9. Send the blood request form and blood sample to the blood bank. (*laboratory/clinical*) 4.3
10. Perform pretransfusion tests and select compatible units. (*laboratory*) 4.3
11. Deliver blood components by designated staff (maintaining approved transport conditions). (*laboratory/clinical*) 4.4
12. Store blood components in correct storage conditions if not immediately required for transfusion. (*laboratory/clinical*) 4.4.2
13. Check: (*clinical*) 4.6
    - identity of patient
    - identity of blood product
    - patient's blood request documentation.
14. Check required pre-medications. (*clinical*) 4.7
15. Record baseline vital signs (blood pressure, respiratory rate, temperature and pulse). (*clinical*) 4.7.1
16. Administer blood component. (*clinical*) 4.7.2
17. Document in the patient's notes: (*clinical*) 4.7.4
    - type and volume of each component transfused
    - unique donation number of each unit transfused
    - blood group of each unit transfused
    - time at which the transfusion of each unit started and ended
    - identity of the person administering the blood.
18. Monitor the patient before, during and after transfusion. (*clinical*) 4.7.3
19. Identify and respond immediately to any adverse effect. (*clinical*) 4.7.4
20. Record any transfusion reactions in the patient's notes and report according to hospital policy and procedure. (*clinical/laboratory*) 4.7.4

4.2 Ordering blood components

4.2.1 Obtaining an informed transfusion consent

Once transfusion is deemed necessary, it is important that the treating physician explains the proposed transfusion to the patient (or guardian), as part of informed consent. The consent discussion should be recorded in the patient's notes or on a specific informed consent form that the patient signs once explanations have been given.

The transfusion consent discussion includes:

- information about the anticipated benefits of the transfusion and the reason it is required;
- the potential non-infectious and infectious hazards of transfusion;
- the potential risks of not receiving the transfusion;
- outlining available alternatives appropriate to the medical condition;
- the opportunity for the patient to ask questions;
- documentation that consent was obtained and the indication for transfusion;
- written documentation for the patient indicating the component(s) transfused.

A transfusion consent might be waived during an emergency. The consent form may also serve to document refusal of transfusion. Patients of the Jehovah's Witness faith and some other faith- based or cultural groups may choose not to receive any or all blood components. In some cases, plasma fractions and autologous or non-cellular blood components may be acceptable, and these options should be discussed.

In many countries the law defines it as an assault to transfuse a patient who has refused, even if refusal is life-threatening. The Jehovah's Witnesses may have a liaison worker trained to assist patients, relatives and hospital staff in these difficult instances.

As patients may have no recollection of the consent discussion, a written record that the patient has been given the information and that questions have been answered is valuable in a medico- legal setting. It is important to be familiar with local rules.

4.2.2 Defining the urgency of transfusion

When there are clinical and laboratory indications that transfusion is required, the procedure for ordering will depend on the urgency of the requirement as defined below:

- emergency need for immediate use (within 10–15 minutes, if blood products are not maintained in the emergency room or intensive care units themselves);
- urgent need (within 1 hour);

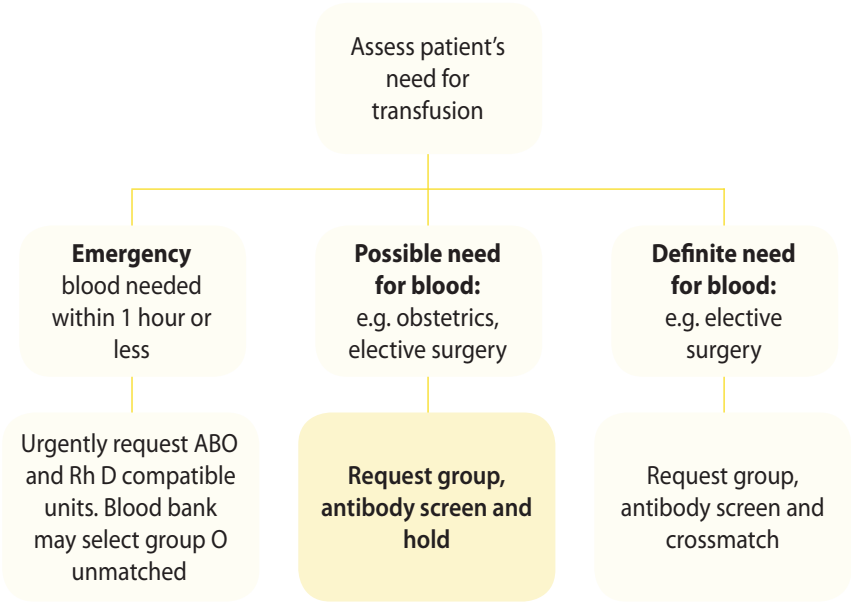
- routine but definite need for blood (within 3–4 hours);
- routine, possible need for blood.

Urgent blood requirements may be termed "emergency" or "stat" with release of group specific or group O unmatched red cells as soon as possible. It is important to ensure agreement regarding the specific language used by clinical and blood bank staff to avoid misinterpretation of urgency. Categories of urgency with specific language denoting expected time to blood delivery may be defined.

Routine blood requirements are ordered as a crossmatch and lead to patient and donor blood group testing, patient antibody screening and a method for compatibility testing.

A *possible* need for blood may be ordered as a group and screen. This request leads to a patient blood group and antibody screen with no donor or compatibility testing until or unless units of red cells are requested (Fig. 4.1).

Figure 4.1. Blood ordering policy



4.2.3 Ordering blood in an emergency

In the accident and emergency/casualty department, operating room or labour ward, it is often necessary to order blood urgently. There may be several massively bleeding patients who need blood quickly. In these situations, mistakes in identifying patients and labelling blood samples can easily occur. It is essential that procedures for ordering blood in an emergency are clear and simple and that everyone knows and follows them (Box 4.2).

Box 4.2. Ordering blood in an emergency

1. Insert intravenous (IV) cannula, collect a blood sample for compatibility testing.
2. For each patient, label the blood sample tube and the blood request form with the patient's name, date of birth and unique hospital number at the bedside. If the patient is unknown, use an emergency reference number according to hospital SOP.
3. Communicate the transfusion request by telephone and transport samples to the blood bank; ensure that the blood bank is informed of the patient's location and any transfers to other clinical areas.
4. Use consistent patient identifiers on all subsequent requests for the same patient.
5. Identify a single staff member to order blood and communicate with the blood bank. This is especially important if several injured patients are being treated at the same time.
6. Communicate the urgency of the transfusion request.
7. Ensure that both physicians and the blood bank know:
   - who is transporting testing samples and blood components to and from the blood bank; and
   - where the patient will be.

Notes

1. The blood bank will send group O un-crossmatched blood if there is no time for the completion of pre-transfusion testing.
2. Un-crossmatched emergency blood (O RhD-positive or O RhD-negative) may be available from an emergency fridge after hours and/or routinely in certain locations in the hospital.
3. Completed documentation concerning the units used, including the unit number, should be returned to the blood bank as soon as possible after the units are transfused.

4.2.4 Ordering blood for elective surgery

Sufficient time between the blood order and the time of surgery allows for completion of compatibility testing and helps ensure availability of compatible blood. Requests for blood for elective surgery should be guided by a local blood ordering schedule.

Many elective operations rarely require blood transfusion. Therefore, it is unnecessary for a compatibility test (crossmatch) to be performed for every surgical procedure.

Time and money can be saved by avoiding unnecessary crossmatching while still ensuring blood is readily available for all patients who need it. Identifying those surgical patients who should have a "group and screen" (see section 4.3.4), and those who require a crossmatch can be determined through development of a maximal surgical blood ordering schedule (MSBOS).

The MSBOS is a table of expected blood use for each elective surgical procedure. It lists the number of units of blood routinely crossmatched for each surgery type. It should reflect the expected blood use for common procedures and depends on the complexity of surgery and the expected blood loss. The MSBOS should also inform the use of a group and screen for patients undergoing procedures for which transfusion is rarely required.

An MSBOS should always be developed locally by the hospital transfusion committee together with clinicians responsible for prescribing blood and the blood bank. It may be prepared in accordance with national guidance or adapted from a model MSBOS for local use. See Chapter 8 for details on the process of developing an MSBOS.

The MSBOS is a guide to optimize blood use and compatibility testing and should never overrule actual patient need as determined by clinical assessment. In facilities where inexperienced staff manage preoperative blood ordering, standardized ordering practices may be particularly beneficial.

The MSBOS should be regularly reviewed and adjusted to ensure that it remains effective.

4.2.5 Patient identification

Prior to blood sampling for pretransfusion testing each patient should be clearly identified using a unique identity wristband or other attached marker with:

- a unique hospital reference number;
- full name; and
- date of birth.

Without clear identification and a policy for identifying the patient, group-specific blood cannot be safely administered. The patient's unique identifiers should be used on the blood sample tube, blood request form and all testing documentation.

When a patient cannot be reliably identified at the time of admission, the hospital reference number should always be used to identify the patient until full and correct details are available and communicated to the hospital blood bank. For subsequent testing and transfusion, the unique hospital ID number should be formally associated with the patient's name and date of birth.

4.2.6 The blood request form

When blood is required for a transfusion, the prescribing clinician must complete a standard blood request. All the details requested must be filled in accurately and legibly.

An example of a blood request form is given in Fig. 4.2. This sometimes includes a compatibility test record, which should be completed in the laboratory before the blood is issued.

The essential information for the blood sample and request form includes:

- unique patient identifiers (see section 4.2.5);
- the quantity and type of blood components required; and
- the time and place at which they are needed.

Blood bank staff are correct to refuse a sample for testing when either the blood request form or the patient blood sample are inadequately identified, or the details do not match, as these samples frequently contain the wrong patient's blood in the tube (known as a WBIT error).

Figure 4.2. Example of a blood request form

HOSPITAL: _____ Date of request: _____

PATIENT DETAILS

Family name: _____ Date of birth: _____ Gender: _____

Given name: _____ Ward: _____

Hospital reference no.: _____ Blood group (if known): ABO ☐

Address: _____ Rh D ☐

_____

HISTORY

Diagnosis: _____ Antibodies: Yes/No _____

Reason for transfusion: _____ Previous transfusions: Yes/No _____

Haemoglobin: _____ Any reactions: Yes/No _____

Relevant medical history: _____ Previous pregnancies: Yes/No _____

REQUEST

☐ Group, screen and hold patient's serum

☐ Provide product

Date required: _____

Time required: _____

Deliver to: _____

Whole blood ☐ units

Red cells ☐ units

Plasma ☐ units

Platelet concentrate ☐ units

NAME OF DOCTOR (print): _____ **SIGNATURE:** _____

IMPORTANT: *This blood request form will not be accepted if it is not signed or any section is left blank* .

LABORATORY USE ONLY

Patient ABO ☐

Rh D ☐

	Donor typing		Compatibility testing						
Donation pack no.	ABO	Rh	Antibody screen	AHG XM	RT Saline XM	Date of match	Time of match	Date of issue	Time of issue

Signature of tester: _____

4.2.7 Blood samples for blood group and compatibility testing

Box 4.3 outlines the steps involved in taking a blood sample for compatibility testing.

All staff responsible for taking blood samples should be specifically trained for this task. National rules or standards should be followed if available. Where these are not available, procedures and training materials may be adapted from international publications.

The blood bank should not accept requests for blood unless all the patient's details on the blood sample match those on the blood request form. When details do not match, a new sample and request form are required and use of unmatched group O red cells may be considered if there is a need for urgent transfusion before testing is complete.

Box 4.3. Procedure for taking blood samples for compatibility testing

1. If the patient is able to answer, ask him or her to identify themselves by given name, family name, and date of birth. If the patient is unable to answer, ask a relative or staff member to verify the patient's identity.

2. Check the patient's name against:
   - patient's identity wristband or label;
   - patient's medical notes; and
   - completed blood request form.

3. Take the blood sample into the appropriate sample tube.

4. Label the sample tube clearly and accurately at the patient's bedside immediately after the blood sample is taken. Never label samples away from the patient. The label should include:
   - given name and family name
   - date of birth
   - hospital reference number
   - location
   - date
   - signature/documentation of person taking the sample.

   Never sign for a sample collected by a colleague.

   Ensure that the patient's name is spelled correctly.

   Do not label tubes before obtaining the specimen because of the risk of putting the intended patient's blood into the wrong tube.

5. A medical record entry indicating the time and date and tests collected may be required.

6. Transport the blood sample and request form to the blood bank.

4.3 Blood groups and pretransfusion testing

The International Society of Blood Transfusion (ISBT) Working Party Committee on Red Cell Immunogenetics and Blood Group Terminology recognizes and defines blood group systems.(*5*)

ABO, Rh, Kell, Kidd, Duffy, MNS, P, Lewis and Lutheran are the nine major blood group systems. For several of these blood groups, antibodies to their associated antigens are clinically significant because they can cause acute haemolytic transfusion reactions, delayed haemolytic transfusion reactions and/or haemolytic disease of the fetus and newborn. (*6,7,8,9,10*)

The main goals of pre-transfusion testing are to:

- ensure compatibility of transfused red cells with antibodies in patient plasma; and
- avoid stimulating the production of new red cell antibodies in the recipient, particularly anti-RhD.

Pretransfusion test procedures include patient testing for:

- ABO group
- RhD type
- antibody screen
- antibody identification, if screen positive.

Pretransfusion test procedures confirm donor:

- ABO group
- RhD type
- antigen type (phenotype) for antigens corresponding to patient antibodies, if present.

The next pretransfusion step involves compatibility testing.

In addition to the blood group testing, the blood bank is responsible for:

- ensuring that only units of blood that have been tested and found negative for transfusion- transmissible infections are tested for compatibility;
- ensuring clear and correct labelling of donor red cell units with ABO and RhD typing;
- checking that a blood request form has been fully completed and that identifiers match those on the patient's blood sample;

- selecting blood components: potential alternatives should be discussed with the ordering physician as required;
- performing compatibility testing (crossmatch) and ensuring that red blood cell (RBC) units with a safe ABO and RhD type are supplied for the patient;
- labelling compatible RBC units specifically for the patient and issuing them as required: the blood bank may reserve these units for a limited time according to local policies;
- appropriate identification of un-crossmatched group O red cells issued in an emergency.

4.3.1 ABO antigens and antibodies

ABO blood groups are the most important in red cell transfusion. Red cells are classified as: O, A, B and AB. Individuals who lack A or B antigens have antibodies in plasma corresponding to the antigen missing from red cells or other tissues (see Table 4.1). Red cell antigen typing for ABO is sometimes referred to as the "forward" group while detection of corresponding antibodies in plasma (or serum) is the "reverse" group (Table 4.1).

ABO antigen and antibody testing are important for patient and donor testing. Anti-A and anti-B antibodies occur "naturally" without prior sensitization to the corresponding antigen through transfusion. Therefore, these antibodies are present in almost all individuals.

Table 4.1. Expected forward and reverse reactions for ABO blood groups

	Forward (antigen testing)		Reverse (antibody testing)	
Blood group	**Anti-A antisera**	**Anti-B antisera**	**Group A red cells**	**Group B red cells**
	Patient/donor red cells		**Patient/donor plasma**	
A	+	–	–	+
B	–	+	+	–
O	–	–	+	+
AB	+	+	–	–

+ agglutination / – no agglutination.

4.3.2 ABO incompatibility: the risk for haemolytic reactions

Safe blood transfusion depends on avoiding incompatibility between the donor's red cells and the patient's antibodies. Severe acute haemolytic transfusion reactions are nearly always caused by transfusing red cells that are ABO incompatible with the patient. These reactions can be fatal. They most often result from errors made in identifying the patient when blood samples are being taken for pretransfusion testing or when red cells are transfused.

Anti-A or anti-B recipient antibodies can cause destruction (haemolysis) of incompatible transfused red cells as soon as they enter the circulation. Since group O red cells lack A and B antigens, they may be given to individuals of any ABO blood group and should be used if un- crossmatched transfusion is required.

In some circumstances, such as plasma and whole blood transfusion, it is also important that the donor antibodies are compatible with the patient's red cells or that they are present at a low titre.

It is not always essential, however, to give blood of the identical ABO group. Compatible blood groups can be selected (see Table 4.2).

Because of the importance of ABO compatibility for safe transfusion, ABO testing on both patient and donor samples should ideally be confirmed on more than one sample to ensure the test results match. A current sample may be compared to a historical typing result or the group may be confirmed on a second sample collected at a different time than the first. Similarly, donor ABO testing should be performed at the time of donor blood collection and labelling, and again at the transfusion facility.

Careful records of ABO blood groups of donors and recipients should be maintained and routinely reviewed at the time of blood group testing as part of ABO confirmation.

Table 4.2. Red cell, platelet and plasma compatibility in the ABO system

Blood group of recipient	A/B antigen on recipient red blood cells	A/B antibodies in recipient plasma	Compatible plasma from donor group	Compatible red cells from donor group	May receive platelets from group
A	A	Anti-B	A, AB	A, O	A, AB, B, O
B	B	Anti-A	B, AB	B, O	B, AB, A, O
AB	A, B	None	AB	A, B, AB, O	AB, A, B, O
O	None	Anti-A, anti-B	A, B, AB, O	O	O, AB, A, B

Source: adapted from Gupta A, Bigham M. Blood components. In: Clarke G, Chargé S, editors. *Clinical guide to transfusion* [Online]. Ottawa: Canadian Blood Services; 2021 (https://professionaleducation.blood.ca/en/transfusion/clinical-guide/blood-components, accessed 1 February 2021).

4.3.3 RhD antigens and antibodies and other blood group antigens

Red cells have many non-ABO antigens. In contrast to the ABO system, antibodies in these blood group systems are "acquired antibodies". Individuals rarely make antibodies against these antigens unless they have been exposed to them by previous transfusion or during pregnancy and childbirth.

The most important and most antigenic of the non-ABO antigens is the RhD antigen. Anti-D antibody develops after an antigen-negative individual is sensitized by RhD-positive red cells. For example, an RhD-negative woman may develop anti-D following pregnancy with an RhD-positive baby or following transfusion of RhD-positive red cells. Even a single transfusion of RhD-positive red cells to a RhD-negative person may provoke anti-D alloimmunization.

Anti-D antibodies are "clinically significant antibodies". This indicates that they can cause:

- haemolytic transfusion reaction by rapid destruction of RhD-positive red cells in a sensitized recipient with anti-D antibodies;
- haemolytic disease of the newborn in a subsequent pregnancy of a RhD-negative woman with a previous RhD sensitization.

Because RhD exposure will frequently result in alloimmunization of an RhD-negative individual, efforts should be made to transfuse such individuals with RhD-negative blood to prevent the formation of anti-D. This is especially important in women with childbearing potential.

There are many other antigens on the human red cell. Examples include:

- Rhesus: C, c, E, e
- Kell: K, k
- Duffy: Fy^a, Fy^b
- Kidd: Jk^a, Jk^b

Like anti-D, antibodies in these blood group systems are mainly acquired antibodies following exposure to the corresponding antigen through transfusion or during pregnancy and childbirth. These antibodies may be clinically significant.

In the presence of clinically significant antibody/antibodies in the recipient plasma, red cells selected for transfusion should be negative for the corresponding antigen and/or crossmatch compatible.

Prophylactic phenotype matching of red cells for these antigens (in the absence of antibodies in the recipient plasma) is not routine practice. That said, there are groups of patients who benefit from "antigen matched" red cells, such as those who are chronically transfused.

Prophylactic antigen matching is particularly important in patients with sickle cell disease or thalassaemia. If possible, Rh (CcDEe) and Kell matched red cells should be provided to these patients. This strategy can prevent the formation of antibodies against these red cell antigens, and the associated complications.

4.3.4 Group and screen

The "group and screen" procedure is also known as a type and screen.

The patient's ABO and RhD type are determined and an antibody screening test is performed. If the screen is negative, the plasma (or serum) is stored (refrigerated or frozen) in the laboratory for several days. The validity of the group and screen is typically 72 hours (3 days) for patients who have been transfused or are pregnant, and up to 45 days for non-transfused, non-pregnant patients being evaluated for elective surgery.

If the patient has a valid group and screen, the blood bank will usually need only 15–30 minutes to have crossmatched blood ready for issue for that patient.

If the initial sample has a positive antibody screen, the antibody is identified and donor blood that is negative for the antigen is found through antigen typing and then a crossmatch. These units can then be kept on hand for the patient for a predefined period.

This approach optimizes the blood bank's RBC inventory by avoiding holding multiple crossmatched units of red cells for patients when they are unlikely to need them, while ensuring that red cells can be provided quickly if required.

4.3.5 Serological compatibility testing

A serological crossmatch refers to compatibility testing of patient and donor samples by mixing patient plasma and donor red cells, with evaluation for agglutination and haemolysis. If no agglutination or haemolysis is present, the donor and recipient are compatible.

A full serological crossmatch involves several steps starting with assessment for agglutination or haemolysis immediately after mixing and centrifugation of cells and serum. This step is called the **immediate spin (IS) crossmatch**.

The next step involves incubation of cells and serum at 37 °C followed by washing, centrifugation and review for agglutination. This phase will detect uncommon immunoglobulin M (IgM) antibodies that directly cross-link the cells and are reactive at 37 °C. After washing, anti-human globulin (AHG) is added and the cells are again incubated, centrifuged and the tubes reviewed for agglutination. This is termed the **AHG crossmatch.** This phase of reactivity detects immunoglobulin G (IgG) antibodies from patient plasma that are bound to the donor red cells.

This full serological crossmatch procedure will detect IgG antibodies and IgM anti-A and anti-B and is the most sensitive compatibility test. It may be enhanced through addition of potentiators such as polyethylene glycol (PEG) or low ionic-strength saline (LISS) which shorten the incubation time and increase the sensitivity for antibody detection.

The crossmatch may be abbreviated at the IS step in a patient with a negative antibody screen and no history of clinically significant red cell allo-antibodies. Here, the IS crossmatch ensures donor and recipient ABO compatibility. The IS crossmatch can be completed in approximately 5 minutes and is useful when transfusion is urgent.

Following red cell transfusion, a recipient may occasionally develop an antibody to donor red cell antigens over several days to weeks.

In a recipient previously exposed to red cells with prior antibody development, repeat red cell transfusion can result in an anamnestic antibody response with a rapid rise in antibody levels over a few days.

To detect new antibodies, pretransfusion antibody screening and compatibility testing within 3 days (72 hours) before planned transfusion is widely recommended. With ongoing transfusion, repeat testing at 3-day intervals is usually required. Permanent records of blood groups and detectable antibodies are required.

Records must be reviewed with each transfusion request to ensure ABO and Rh are consistent with historical records, and that previously detected antibodies are taken into account.

Neonatal transfusion represents a special testing circumstance, since most neonates do not have anti-A or anti-B in their plasma. When performing blood group testing on a neonate, it is permissible to test the forward blood group only. Crossmatch of neonatal samples may involve testing maternal plasma with ABO-compatible donor red cells, as antibodies in neonates are those passively acquired from the mother. Repeat compatibility testing is not generally required after an initial crossmatch for the first 4 months of life, as neonates are not expected to make new antibodies. Local policies may vary.

4.3.6 Other systems for ensuring red cell compatibility

In some countries, a "bedside" test is used to determine the ABO group of the patient and of the blood units supplied. This is performed using a grouping card pretreated with blood typing reagents, which is supplied with detailed instructions.

Another method is called a **computer crossmatch** and depends on a validated system to confirm testing results on patient samples and donor red cells. This system requires that donor units have two ABO tests and that patient samples have two ABO tests and a negative antibody screen and no historical record of antibodies. The computer confirms ABO compatibility based on the test results for patients with a negative antibody screen and a negative antibody history.

4.3.7 Compatibility problems

If antibody screening or a positive crossmatch indicate an antibody, further tests are needed. Once the antibody has been identified, red cell units negative for the corresponding antigen may be provided.

Compatible donor red cells for patients with red cell antibodies are necessary to avoid a haemolytic transfusion reaction. Depending on the antibody/antibodies, the search for antigen-negative red cells, and compatibility testing, can cause considerable delay.

When urgent transfusion is required, and compatible red cells are not immediately available the risk of delay in transfusion must be weighed against the risk of a haemolytic transfusion reaction. Non-ABO antibodies are most likely to cause a delayed reaction, which may pose less risk to the patient than a delay in transfusion.

When a patient has a pan-reactive auto-antibody, it is sometimes necessary to transfuse red cell units that are not compatible. Again, the risk of withholding transfusion in this situation must be weighed against the risk of a haemolytic reaction. Ideally, in this situation, donor red cells that are as closely matched to the recipient's red cell phenotype as possible should be transfused. For example, C/c E/e and Kell tested red cells that match the recipient's red cell phenotype could be provided to the recipient if possible.

4.4 Collecting blood components prior to transfusion

One cause of transfusion reactions is the transfusion of a unit of red cells that was intended for a different patient. This may be due to mistakes made when collecting blood from the blood bank. Therefore, it is essential that an SOP for the collection of blood from the blood bank is in place. Staff should be appropriately trained, and the procedure followed.

An example is given in Box 4.4.

Box 4.4. Procedure for collecting blood from the blood bank

1. Bring written documentation with patient identifiers.

2. Ensure that the details on the attached compatibility label exactly match the details on the patient documentation:
   - patient's family name and given name
   - patient's hospital reference number
   - patient's ward, operating room or clinic
   - patient's ABO and RhD group
   - donor unit ABO and RhD group.

3. Enter the required information in the blood collection register. Include:
   - time of issue
   - ABO group issued (may be ABO-compatible or ABO-identical).

4.4.1 Storing and transporting blood components

Consult the circular of information for blood and blood components provided by the blood supplier for details of storage temperature and duration of storage.

4.4.2 Storage and transport requirements

The proper storage of blood components depends on:

- regularly monitored storage equipment including blood bank refrigerators, freezers and platelet agitators, and satellite blood refrigerators;

- controlled temperature during transportation of blood and blood components.

Two rules govern the storage and transportation of blood components:

- **4-hour rule: Transfusion should be completed within 4 hours of initiation.** Transfusion must be initiated within 30 minutes of removal of blood or blood components from controlled-temperature storage.

- **30-minute rule: Components left out of controlled-temperature storage for more than 30 minutes without initiating transfusion should be discarded.**

Note that in some countries this rule is evolving and additional information is available in published blood administration guidelines.

- Equipment used for blood storage should be regularly maintained and connected to emergency power which is checked at defined intervals to ensure an immediate switch to emergency power if needed.

- Storage equipment should have alarms with audible signals. Alarm activation points should be set at temperatures that allow time for corrective action to be taken before blood components reach unacceptable temperatures. Equipment should be monitored at least twice per day and records must be kept.

- Thermometers used in storage equipment should be checked against certified calibrated thermometers at least annually and the checks documented.

- Procedures outlining alternative storage arrangements when equipment for storing components is malfunctioning should be developed.

- Once components have left the designated storage equipment, the transfusion should begin within 30 minutes of removal. If the transfusion is delayed, storage in a temperature- monitored satellite blood refrigerator or validated transport box is acceptable.

- Typically, transport boxes are validated for specific numbers and types of components for specified intervals.

- Clinical staff are responsible for ensuring that blood components issued by the blood bank are kept at the correct temperature until transfused.

- All clinical staff who retrieve blood components should be trained to comply with procedures for blood refrigeration.
  - When stored in a refrigerator with reagents or blood samples, components should be segregated to avoid possible contamination.
  - The door should be opened only when necessary to remove or replace blood.
  - Arrange the blood to allow air circulation. Store blood containers upright (e.g. in baskets) or laid flat on shelves.
  - The time of removal of blood from controlled storage should be documented.

4.5 Visual inspection

Blood components must be inspected for signs of deterioration and the visual inspection documented.(*11*)

Discoloration or signs of leakage may be a warning that blood is bacterially contaminated and could cause transfusion-transmitted sepsis with serious or fatal consequences for the recipient. Other visual signs may indicate donor or manufacturing problems leading to compromise of components.

When blood components fail visual inspection, the hospital's procedure for action and reporting should be followed. The unit should be quarantined to prevent use, and should have clearly labelled tags affixed as well as being physically separated from the routine inventory.

4.5.1 When to perform visual inspection

Inspection for signs of deterioration should be performed:

- before shipping to another facility;

- upon receipt from the supplier or another facility;

- during component manufacturing;

- at the time of compatibility testing;
- before issue from the blood bank;
- on arrival in the ward or operating theatre;
- upon return to inventory; and
- when a transfusion reaction is reported.

4.5.2 How to perform visual inspection of the blood components (Fig. 4.3)

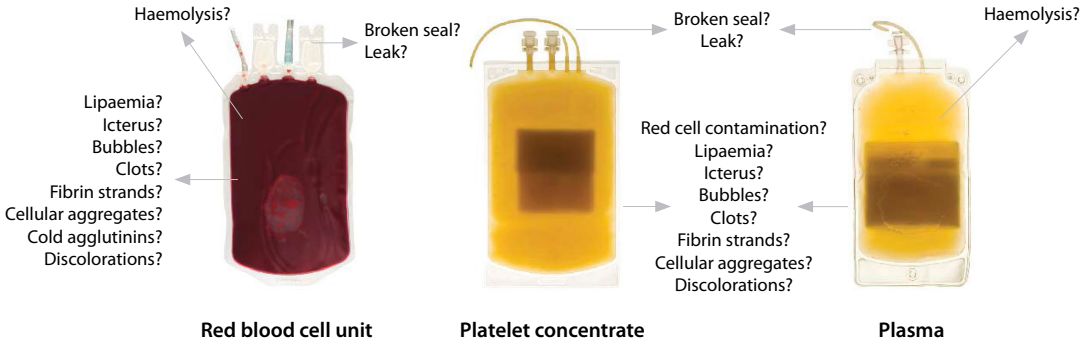
- Inspection of the blood product should take place in a well-lit area.
- Segments should not be used to assess a red cell component as they may not reflect the content of the unit.
- Mix red cells and allow them to settle until the colour of the plasma layer is visible.
- Note that normal cryoprecipitate appears as a thick, opaque, whitish concentrated precipitate at the bottom of the bag. Upon thawing it appears as an even, thick whitish liquid.
- Evaluate for haemolysis (light pink to dark red) in the supernatant of red cells and in platelets or plasma.
- Check red cells for dark purple to black discoloration indicating possible bacterial contamination.
- Inspect for large or unusual air bubbles, clots, fibrin strands, grey discoloration and opacity in any component, which may also indicate bacterial contamination.
- Note any clots or fibrin strands (small to large dark red or purple masses and/or white masses or thread-like strands that do not disperse with manipulation).
- Assess for lipaemia (opaque or milky white colour).
- Assess for icterus (bright yellow to brown appearance).
- Note cellular aggregates (white or opaque masses that do not disperse with manipulation).
- Look for cold agglutinins (large RBC masses that do not disperse with manipulation).
- Check for any signs of damage or leakage of the container.

4.5.3 Actions in response to affected components

If there are signs of haemolysis; discoloration or features that lead to a suspicion of bacterial contamination; damage or leakage in the unit; large clots; fibrin strands; cellular aggregates or cold agglutinins, the unit should not be transfused. The blood bank must be informed, and the unit discarded or quarantined for further evaluation.

Blood components with lipaemia or icterus are generally acceptable for transfusion unless the features interfere with testing.

Figure 4.3. Signs of deterioration in red cells, platelets and plasma



Source: Reproduced with permission from Visual Assessment Guide. Ottawa: Canadian Blood Services; 2009. (https://profedu.blood.ca/en/transfusion/best-practices/visual-assessment-guide.)

4.6 Pretransfusion steps

Before obtaining a blood component for transfusion, the patient record should be checked for the transfusion order and consent records. The blood component should be obtained and transported from the hospital blood bank or satellite blood refrigerator according to local procedures.

Prior to transfusion, it is vital to confirm the patient's identification and to perform component verification in the presence of the recipient. This is especially important in an emergency setting, where emergency identifiers should be checked.

The identity check confirming that the blood component is the correct one for the identified patient is the crucial final opportunity to detect an identification error and prevent a potentially incompatible transfusion.

4.6.1 Transfusion instructions and requesting the blood components

- The transfusion request and blood administration instructions are prescribed by a physician or authorized practitioner.
- Recent laboratory values and patient condition determine the necessity for the transfusion and guide the appropriate dose and rate of infusion.
- The blood tests listed in Table 4.3 may be used to monitor the need for and/or effectiveness of the transfusion.

Table 4.3. Tests used to monitor the need for and/or effectiveness of the transfusion

Blood component/product	Laboratory blood test
Red blood cells	Haemoglobin
Platelet	Platelet count
Frozen plasma	International Normalized Ratio (INR)
Cryoprecipitate	Fibrinogen

- Instructions for transfusion must include:
  - patient's first and last name and a unique identifier
  - location
  - diagnosis/indication
  - type of blood components required
  - number of units required or volume (for paediatric patients)
  - patient's weight (for paediatric patients)
  - urgency of the transfusion
  - any special requirements (for example, irradiation or washed components)
  - rate of infusion
  - pre-medications or diuretics if required
  - prescriber's name.

4.6.2 Equipment required for blood administration

Cannulae for infusing blood products:

- should be flexible plastic for preserving venous integrity;
- must be sterile, disposable and never reused; and
- of the recommended IV access size (Table 4.4).

Table 4.4. Sizing of cannulae for infusing blood products

Blood component	IV access size
Red blood cells – routine transfusion in adults	20–22 G (gauge)
Red blood cells – rapid transfusion in adults	16–18 G
Other blood components	Any size
Children	22–25 G
All components – adults and children	Central venous access device (CVAD)
Note: Rapid transfusion under pressure through a small IV cannula can cause haemolysis.	

- Leukoreduced red cells and platelets, frozen plasma and cryoprecipitate should be infused through a standard blood administration set containing an integral 170–260-micron filter to remove fibrin strands or clots.

- Flush the blood tubing, completely wetting the filter. For small paediatric patients, the blood tubing may be primed with the blood component instead of normal saline to avoid volume overload.

- Transfuse platelets through a fresh administration set. Red cells may follow platelets through the same blood administration set, but should not precede platelets.

- Frequency of changing the blood administration set and number of products that can be transfused through an infusion set depends on the type of infusion set used. The manufacturer's recommendations should be followed. Twelve hours is usually considered the maximum time of use because of the risk of bacterial proliferation.

- Paediatric transfusion sets should be used for paediatric patients. When blood components are being administered by syringe, the blood must be drawn into the syringe by an aseptic technique through an approved blood filter.

- When transfusing through a central venous access device with multiple lumens, medications and/or solutions can be infused through other lumens without damaging the blood components if the device is approved for this purpose.

- Pumps/rapid infusion devices:
  - are used in patients with major haemorrhage: infusion rates from 6 to 30 L/hour are possible;
  - often incorporate a blood warmer;
  - require a large-gauge venous access catheter.

- Blood warming is indicated for rapid transfusions. Cold blood can cause venous spasm.

- Blood warmers are most commonly used for:
  - rapid transfusion rates (adults: >50 ml/min, children: >15 ml/kg per hour);
  - exchange transfusion in infants and neonates;
  - trauma situations where core-rewarming measures are indicated;
  - patient rewarming during cardiopulmonary bypass procedures;
  - transfusion for patients with clinically significant cold agglutinins.

- Blood should only be warmed in a specifically designed, maintained and approved blood warmer set at 37 °C. Blood warmers should have a visible thermometer and an audible warning alarm for temperatures exceeding 42 °C. The operating temperatures should be documented on the patient infusion record.

- Red cells must not be warmed above the set point temperature. Overheating may cause haemolysis.

- Blood should never be warmed by placing it under the patient, near a radiator, heater or a stove, or by placing it in a bowl of hot water as this could lead to the haemolysis of the red cells and liberation of potassium ions (K^+) which could be life-threatening. Standard microwave ovens should not be used as they cause focal overheating and red cell haemolysis.

- Blood warmer, administration and pump sets must incorporate an approved blood filter (170–200 microns).

4.6.3 Collecting the blood component

Before picking up the blood component from the blood bank, ensure that the patient is ready for the transfusion:

- Connect the primed IV tubing to the patient's IV site to ensure patency.
- Properly identify the patient being transfused.
- Administer any premedication that may be ordered.
- Arrange for component pickup from the blood bank using appropriate documentation.

4.6.4 Component and patient verification

Checking blood immediately prior to the transfusion is critical as this is the last opportunity to identify any errors in identification of the recipient.

When issuing the blood from the blood bank, the blood bank should provide identification documentation and a compatibility label with the issued blood units, including all the information shown in Fig. 4.4. The compatibility information should be attached to each component.

Figure 4.4. Example of a compatibility label

Patient's given name	Patient's surname/family name
Patient's date of birth	Patient's hospital number (identity number)
Patient's location	Patient's ABO and RhD blood group
Donation number of blood unit	Type of component
Expiry date	Donor unit blood group
Special requirements	
Interpretation of compatibility test: ❑ Compatible ❑ Least incompatible ❑ Uncrossmatched, issued for emergency transfusion	
Technologist:	Date:

Upon arrival of the issued blood component at the clinical area, the information on the accompanying document should be checked against the transfusion order and the compatibility label of the unit. This includes verifying:

- that the unique component identifiers on the component label match those on the accompanying compatibility label;
- that the unique patient identifiers on the component match those of the intended recipient;
- the ABO and RhD compatibility of the component and the recipient; and

- that the blood component has passed the visual assessment.

The final identity check should be made at the patient's bedside immediately **before** beginning the transfusion. It should be performed by two clinical team members, at least one of whom should be a registered nurse or physician (Box 4.5).

If any discrepancies are detected during the checking process, **do not proceed**. Contact the blood bank.

One of the two staff involved in the checking process **must** hang the blood immediately after checking and commence the transfusion. If there is a delay, the checking process **must** be repeated.

Blood transfusion must be started as soon as possible after the blood has been received from the blood bank and transfusion completed within 4 hours of initiation.

Box 4.5. Blood component check and confirmation of patient's identification at the patient's bedside

1. Obtain the following to perform the patient identity check:
   - the blood unit;
   - the compatibility label; and
   - the transfusion order.

2. Blood component checks:
   - Check the transfusion order for component type and volume required.
   - Verify consent.
   - Visually inspect the component.
   - Check donation number on the bag and compare it to the compatibility label.
   - Check the ABO and RhD blood group on the unit label and compare to the patient blood group on the compatibility label.
   - Check the expiration date on the blood component label.
   - Check any special requirements in the transfusion order and confirm on the unit label and/or compatibility label (e.g. irradiation).

3. Confirmation of patient identification:
   - Check the patient's identity wristband is securely attached.
   - Ask the patient or a staff member to identify the recipient.
   - Follow the hospital guidelines for identification of patients with unconfirmed identity.
   - Ensure that the stated full name and date of birth are identical to those on the wrist band, blood component compatibility label and the transfusion order.
   - Ensure that the hospital number on the compatibility label is identical to the blood order, medical record and identity wrist band.

4. Do not proceed if any discrepancies are found or if there are any concerns regarding the integrity of the component. Contact the blood bank.

5. The compatibility label must remain attached to the blood unit throughout the transfusion.

4.7 Administration of blood components (*12,13,14,15*)

4.7.1 Initiating the transfusion

In non-urgent situations, transfusions should take place during the daytime hours if possible, as more staff are usually available to assist if an adverse event occurs than are available at night.

No medicines or infusion solutions other than normal saline (0.9% sodium chloride, NaCl) should be added to any blood component.

- Additives such as calcium can cause citrated blood to clot.
- Dextrose solution (5%) can lyse red cells.

If an intravenous fluid other than normal saline or a colloid solution must be given at the same time as blood components, it should be given through a separate IV line to avoid any risk.

Patients must be appropriately monitored to detect transfusion reactions as quickly as possible.

The following are general steps for preparing and initiating a blood transfusion:

- Explain the transfusion procedure to the patient.
- Instruct the patient or caregiver regarding signs or symptoms of transfusion reaction.
- Ensure pre-medications are given if ordered.
- Obtain baseline vital signs including:
  - temperature;
  - blood pressure;
  - pulse;
  - respiration rate;
  - oxygen saturation (if available);
  - auscultation for patients at risk for volume overload.
- Confirm that the blood component matches the transfusion order.
- Confirm the blood component expiry date and time.
- Complete the component and patient verification process at the bedside in the presence of the patient (Box 4.5).
- Obtain the required equipment (see section 4.6.2).
- Prime the administration line and filter.
- Initiate the transfusion. Start with a slow rate unless transfusion is extremely urgent.

- When transfusion is complete, disconnect the blood tubing and follow local SOPs for retention of blood bags and tubing (for example keep in a fridge for 24 hours). Dispose of the used blood tubing and blood bags in the biohazard container after the required storage interval.

4.7.2 Dosage, time limit, rate of administration and expected outcome

Transfusion should be commenced and completed within a specified time.

- Time limits have been determined where temperatures in hospital buildings are between 22 °C and 25 °C. If the ambient temperature is very high, shorter "out-of-refrigerator" times should be used.

- If a unit is not completed within the allowed time limit, discontinue its use and dispose of the remainder according to hospital policies.

Appropriate transfusion rates vary significantly between patients according to their individual clinical circumstances. (*16,17,18*) Some patients are at a greater risk for circulatory overload and require slower transfusion. For very slow infusion rates that exceed the allowable time limit, and where sterile facilities for dividing units are available, consider dividing the component to allow transfusion of smaller volumes within the allowable time. Alternatively, once the maximum allowable time is reached, if further transfusion is still required, an additional unit should be requested.

For neonates and children, the exact volume and time for transfusion should be prescribed.(*19,20*) Dose or transfusion volume for paediatric patients should be calculated and prescribed in millilitres with a specified transfusion rate (see Table 4.5).

Table 4.5. Dosage, time limit, rate of administration and expected outcome of transfused components

		Adults	Paediatric patients
RED BLOOD CELLS	**Dose**	• Based on the haemoglobin (Hb) level • Transfuse one unit at a time then reassess	• 10–15 ml/kg or use transfusion formula: **[desired Hb (g/L)–actual Hb (g/L)] × weight (kg) × 0.5** • Transfuse one dose at a time then reassess • Transfusion volume should generally be calculated to take the post-transfusion Hb to no more than 20 g/L above the transfusion threshold, usually a maximum of one unit
	Time to start	Within 30 minutes of their removal from controlled temperature storage	
	Rate of administration and infusion time	• Start slowly (50 ml/hour) for the first 15 minutes • Rate may be increased if transfusion is well-tolerated with no adverse reaction • One unit is usually transfused over 2 hours • Consider slower rates for patients at risk of circulatory overload • During major haemorrhage, very rapid transfusion (each unit over 5–10 min) may be required	• Start slowly (1 ml/kg per hour) for the first 15 minutes • Usual administration rate : 5 ml/kg per hour • Maximum administration rate: 150 ml/hour
	Maximum infusion time	4 hours from the time of their removal from controlled- temperature storage	
	Expected increment/ dose	• Each dose is expected to raise the Hb level by about 1 g/dL	

		Adults	Paediatric patients
PLATELET CONCENTRATES	**Dose**	• 4–5 units random donor platelets (or one pool) • 1 apheresis unit	• Neonates and children < 40 kg: 1 whole blood platelet unit per 10 kg • Children ≥ 40 kg: a single apheresis unit or equivalent
	Time to start	Immediately upon arrival in the clinical area	
	Rate of administration and infusion time	• Start slowly (50 ml/hour) for the first 15 minutes • Recommended transfusion time per dose is >60 minutes, preferably slower to avoid administering large cytokine bolus quickly	• 10–20 ml/kg per hour
	Maximum infusion time	4 hours from time of their removal from controlled-temperature storage	
	Expected increment/ dose	• Each dose should raise the platelet count by at least $15–25 \times 10^9$/L and up to 40×10^9/L. • If increments in platelet count are not adequate, investigation for platelet refractoriness should be commenced.	
FROZEN PLASMA	**Dose**	Based on the coagulation status of the patient as measured by laboratory tests, and/or clinical indication e.g. plasma exchange.	
	Time to start	As soon as possible after thawing to avoid loss of labile clotting factors	
	Rate of administration and infusion time	• Start slowly (50 ml/hour) for the first 15 minutes • Infusion rate is typically 10–20 ml/kg per hour, although more rapid transfusion may be appropriate when treating coagulopathy in major haemorrhage • Recommended infusion time is 60–120 minutes/unit	• 10–20 ml/kg per hour • Start at no more than 5 ml/minute
	Maximum infusion time	4 hours from time of their removal from controlled temperature storage	
	Expected increment	Not applicable	
CRYOPRECIPITATE	**Dose**	• 5–10 units of whole blood- derived cryoprecipitate or 5 units of apheresis cryoprecipitate	• 5–10 ml/kg to maximum of 10 units
	Time to start	As soon as possible after thawing	
	Rate of administration	• Infusion rate is typically 10–20 ml/kg per hour (30– 60 min per five-unit pool)	• 10–20 ml/kg per hour (i.e over 30– 60 minutes) • Start at no more than 5 ml/minute
	Maximum infusion time	4 hours from time of their removal from controlled temperature storage	
	Expected increment	Each dose will increase the fibrinogen by 0.5 g/dl	

4.7.3 Monitoring the transfused patient

Ensuring patient safety is the most important aspect of caring for a patient during transfusion. Baseline observations and monitoring during and after the transfusion will help to detect any signs and symptoms of a transfusion reaction. Early detection ensures that action can be taken quickly and efficiently. The steps are outlined in Box 4.6.

Box 4.6. Monitoring the transfused patient

1. For each component transfused, monitor the patient:
   - pre-transfusion (within 30 minutes)
   - after the first 15 minutes
   - at prescribed intervals according to hospital policy and depending on clinical condition and specific transfusion orders
   - on completion of the transfusion
   - during any transfusion reaction.

   Repeat with each subsequent unit.

2. Repeat vital signs more often for patients:
   - at greater risk for circulatory overload (elderly patients, paediatric patients, patients with cardiovascular disease)
   - who have experienced previous transfusion reactions
   - who are clinically unstable.

3. At each stage, document in the medical record:
   - general appearance
   - temperature
   - pulse rate
   - blood pressure
   - respiratory rate (O_2 saturation if available)
   - chest auscultation for patients at risk for volume overload
   - fluid balance (if indicated).

4. Monitor the patient closely for the first 15 minutes of the transfusion to detect early signs and symptoms of transfusion reaction.

5. Continue to monitor the patient after the end of the transfusion to identify any signs and symptoms of delayed transfusion reactions.

6. Provide discharge instructions concerning possible signs and symptoms to the recipient or to a responsible caregiver if direct medical observation or monitoring will not be available post-transfusion.

If a transfusion reaction is suspected, immediately stop the transfusion and maintain vascular access. The blood administration IV tubing should be disconnected. Return the component and tubing to the blood bank together with a report of the reaction.

4.7.4 Documenting the transfusion

The following information should be recorded in the patient's notes

1. **Pretransfusion documentation** (see section 4.2)

2. **During transfusion:**
   - pretransfusion checks of patient's identity, blood unit and compatibility label;
   - record of vital signs made before, during and after transfusion;
   - the transfusion details,
     - date of transfusion
     - type and volume of each component transfused
     - unique donation number of each unit transfused
     - blood group of each unit transfused
     - time at which the transfusion started and ended
     - any equipment used (for example, pumps and blood-warming devices)

  - any transfusion-related adverse event
  - any follow-up testing done,
- name and signature of the staff initiating the transfusion.

3. **Post-transfusion**
   - Record the management and outcome of any transfusion reactions or other adverse events.
   - Record whether the transfusion achieved the desired outcome (for example, an improvement in symptoms).

4.8 Component manipulations

Many post-collection manipulations of donor blood may be undertaken to provide optimal transfusions to specific patient groups.

4.8.1 Leukoreduction

Leukoreduction is the removal of donor white blood cells (WBC) from the blood component, aiming for residual < 5 × 10^6 WBC/unit. This may be accomplished in several ways:

- Apheresis donations may be optimized to exclude WBC from the collected donor blood.
- Whole blood donations, red cells and platelets may be filtered to remove WBC using specific leukoreduction filters.

These methods provide pre-storage leukoreduction removing donor WBC prior to storage of components.

Bedside leukoreduction includes a leukoreduction filter in the IV set used to transfuse the red cells or platelets to the patient. This method can be used if facilities are not available for pre-storage leukoreduction. In this setting the leukoreduction occurs after the blood has been stored for some time post-donation and WBC fragments or cytokines released from WBC into the stored blood component may be transfused.

Effective pre-storage leukoreduction limits febrile transfusion reactions and human leukocyte antigen (HLA) alloimmunization in recipients. Pre-storage leukoreduction also decreases the potential for transmission of bloodborne pathogens that are leukocyte-associated. This includes cytomegalovirus (CMV) and human T-lymphotropic viruses (HTLV). Leukoreduction may contribute to decreased risk of transmission of prions.

Plasma components do not require leukoreduction as leukocytes are present in limited numbers following plasma separation and do not typically survive freezing and thawing.

In the absence of universal leukoreduction, leukoreduced components could be reserved for patients with frequent febrile transfusion reactions, those who may be harmed by HLA alloimmunization (such as future organ or stem cell transplant recipients, or those who require frequent platelet transfusion) and those most at risk from transmission of CMV by transfusion (see section 4.8.4).

4.8.2 Irradiation (*21,22,23,24*)

Irradiation refers to the use of gamma or X-ray treatment of cellular blood components to inactivate lymphocytes present in the blood donation. This is important as a means of preventing transfusion- associated graft-versus-host-disease (TA-GVHD). TA-GVHD is a rare, serious complication occurring in transfusion recipients where the donor is a first- or second-degree relative, recipients of HLA-matched platelets and very occasionally among transfusion recipients with profound cell- mediated immunodeficiency.

Prevention depends on successful inactivation of viable lymphocytes in the donated blood. This process is not replaceable by having the component leukoreduced. Leukoreduction does not remove enough leukocytes to substitute for irradiation in preventing TA-GVHD in at-risk recipients. It is likely to be beneficial in reducing risk, however, and might be considered as a helpful measure if irradiation is not available. In addition, a comprehensive review(*23*) has shown that TA-GVHD has never been reported with red cell units transfused more than 14 days following collection. This suggests that longer storage time may favourably impact the risk of TA-GVHD. Where irradiated and leukoreduced units for an at-risk recipient are not available, pre-storage leukoreduced red cells > 14 days post collection may provide a measure of safety although such a unit should still be considered to have a high risk of causing TA-GVHD and is not ideal for transfusion.

Ideally, irradiation of the red cell occurs immediately prior to transfusion, without prolonged post- irradiation storage. Irradiation damages RBC membranes as well as the targeted leukocytes. Consequently, irradiated red cell components have increased supernatant haemolysis, potassium and other changes. Irradiated red cell components have a decreased shelf-life and there is a limit on the age of a unit of red cells that is eligible for irradiation. As the shelf-life of platelets is short, no further reduction in shelf-life is required post-irradiation.

Frozen plasma components (such as fresh frozen plasma and cryoprecipitate) do not require irradiation. However, plasma that is never frozen may contain viable leukocytes and should be irradiated prior to transfusion to at-risk recipients.

The dose of radiation is at least 15 cGy delivered to all portions of the component. Commercially available stickers provide confirmation of irradiation through a colour change with radiation exposure.

Examples of guidelines for irradiation of blood products and on the patients for whom irradiation is indicated can be found on several websites (see references).

4.8.3 Washed red cells and platelets

Washing of red cells and platelets refers to the sequential mixing of the blood component with saline, followed by centrifugation and supernatant removal, repeated one or more times. This process gradually decreases the plasma and plasma proteins present in the supernatant of the cellular blood components. This technique usually applies to red cells but can be utilized for platelets.

Methods for washing include manual addition and removal of saline, or automated cell washing. The latter allows for a closed system without risk of bacterial contamination and with limited reduction in component shelf-life. Because of the open system required for washing of blood components with the manual methods, the shelf-life of the washed product is often decreased to 24 hours post-wash. With automated closed system washing, a 7–14-day post-wash expiry of manipulated components may be allowable depending on local standards and policies.

Washing blood components is most commonly indicated for patients with a history of severe allergic or anaphylactic reactions. Occasionally these reactions reflect IgA deficiency with anti- IgA antibodies or an-haptoglobinaemia with anti-haptoglobin antibodies. In either case, or in the more common idiosyncratic allergic/anaphylactic events, washing serves to remove plasma proteins (including IgA and haptoglobin) from an RBC component and may prevent such reactions.

Some advocate the use of washed red cells for prevention of mild allergic reactions but there is little evidence supporting this practice. With no evidence of benefit and potentially increased risk of component contamination, washing to prevent minor allergic reactions is not generally recommended.

In patients with the rare transfusion-associated complication called post-transfusion purpura, washed red cells may also be provided.

4.8.4 CMV testing

A large number of healthy individuals are cytomegalovirus (CMV) seropositive. Most are asymptomatic. These individuals carry CMV within their leukocytes in a latent form and, if they are blood donors, they may pass CMV to a transfusion recipient. Serological testing of blood donors for anti-CMV antibodies is one way of preventing transfusion-associated CMV transmission. The other is effective pre-storage leukoreduction. Since CMV is cell-associated, effective leukoreduction removes CMV-containing leukocytes and markedly reduces the risk of CMV transmission to transfusion recipients.

Both CMV antibody testing and pre-storage leukoreduction are acknowledged as effective means of dramatically reducing the risk of transfusion-transmitted CMV. Whether the combination of antibody testing and leukoreduction confers additional benefit remains controversial.

Many blood suppliers have ceased CMV testing where leukoreduced blood components are routinely available. Some jurisdictions continue to use CMV antibody testing as a means of identifying donors whose blood components should not be used in patients most at risk of transfusion-transmitted CMV.

Patient populations deemed at highest risk from CMV infection include the fetus receiving intrauterine transfusion and recipients of allogeneic bone marrow or stem cell transplantation who are CMV seronegative and who have received a donation from a CMV-seroposivite bone marrow or stem cell donor. CMV seronegative pregnant women may also be considered high risk owing to the significant adverse effects of prenatal maternal CMV infection on the fetus.

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Suggested reading

Immunohaematology laboratory practice

Transfusion Science Standing Committee Australian & New Zealand Society of Blood Transfusion. Guidelines for transfusion and immunohaematology laboratory practice; Revised 1st Edition January 2020. https://anzsbt.org.au/wp-content/uploads/2021/01/FINAL-Guideline_- for_Transfusion_and_Immunohaematology_Laboratory_Practice_Published_20210125.pdf

Pre-transfusion testing

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Blood administration

Robinson, A. Harris, S. Atkinson, C. et al. The administration of blood components: a British Society for Haematology Guideline. Transfusion Medicine, 2018, 28, 3–21 (with audit templates) https://b-s-h.org.uk/guidelines/guidelines/administration-of-blood-components/