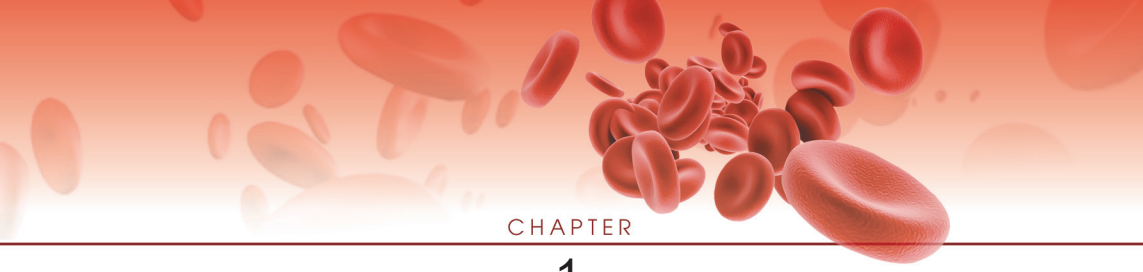

CHAPTER

1

Safe Use of Blood

Before transfusing check the compatibility report, the label attached to the blood bag for the following:

- IP number
- Name of the patient including middle name and surname.
- The name and IP number should tally.
- Blood group.
- Donor registration number.
- Date of collection and date of expiry.

At the bedside confirm the patient's identity which should be checked from:

- The records of the patient.
- The patient himself verbally.
- In unconscious patients identify the patient from wrist band.

Following are the most important points:

1. Do not infuse any other medication along with blood.
2. A doctor should supervise the event.
3. When transfusing blood, watch the patient for first 15 minutes for vitals. Then watch every 30 minutes till transfusion is completed.
4. Rate of transfusion for whole blood/PRBCs should be 1 ml/minute and transfusion should be completed within 4 hours.
5. Avoid transfusion from family members in view of graft versus host disease (GVHD).

Blood transfusion is not without risks. Hence overweigh the benefits for the patient.

The reason for this is:

- Blood cannot be manufactured. It has to come only from **donors**.
- The red cells have antigens on their surface.
- In routine practice, it is necessary to determine the compatibility of certain red cell antigens between the donor and the recipient.
- Blood can be a source of blood transmitted infectious diseases.

There are many blood group systems. Amongst these, the two most important blood groups in blood transfusion are:

- ABO System
- Rh System

ABO and Rh compatible blood is mandatory requirement. Testing for rare blood groups can be sometimes encountered. **Do not transfuse unless clear indication is present. Some of the indications of blood transfusion are given below.**

- Chronic anaemias with Hb less than 6 gm/dl.
- Less than 7 gm/dl when patient is symptomatic and undergoing surgery.
- Less than 8 gm/dl with CVS problems.
- With 6–10 gm/dl only when severe bleeding or complications of inadequate hypoxia are expected.
- Blood loss of 30–40% of circulating blood volume (CBP).
- In anaemia/severe heart or pulmonary disease/when bleeding continues with blood loss of 15–30% of CBP.
- In obstetrics patients Hb less than 7 gm/dl, not amenable to timely therapies antenataly.
- In concealed haemorrhage with abruptio placenta, to replenish the concealed blood loss irrespective of symptoms.

Points to keep in mind for neonates:

- In neonates 10–20 ml/kg body weight blood can be given.
- Blood less than 7 days is preferred for neonatal transfusion.
- In neonates only antigen grouping is done.
- Blood to be given to neonate should be compatible with mother's serum.
- If mother's and baby's group are the same, use Rh negative blood of baby/mother's ABO group. If not the same, use 'O' Rh negative blood.

- In neonates, rate of transfusion should be 10–20 ml/kg to be given over 4 hours.

Points to keep in mind regarding transfusion

- One unit of whole blood will increase Hb by 1 gm/dl and PCV by 3%. 1 unit of packed red cells has 250 mg of iron.
- Iron that can be removed by the body is 1 mg/day.
- One unit of single donor platelets (SDP) will increase platelet count by 30,000–60000 platelets/cmm.
- One unit of random donor platelets (RDP) will increase the platelet count by 4,000–6000 platelets/cmm.
- Preserve the platelets at 22–24 degree C in agitator.
- Transfuse platelets, if platelet count is less than 10,000 cells/cmm. With antibodies to platelets, platelet transfusion may not be of use.
- Platelet increase is observed after 1 hour and again at 20–24 hours of platelet transfusion.
- Preserve the whole blood/PRBCs at 1–6 degree C.
- FFP once collected from the Blood Centre, can be preserved at 1–6 degree C and has to be used within 6 hours.

Observe for transfusion reactions (TR). These can be due to many reasons, e.g. alloantibodies, autoantibodies, complement activation, GVHD, etc. These can be classified as:

Acute transfusion reactions—immunological

- Febrile non-haemolytic transfusion reaction (FNHTR) allergic reactions
- Anaphylactic and anaphylactoid reactions
- Acute haemolytic transfusion reactions (AHTRs)
- Transfusion related acute lung injury (TRALI)

Acute transfusion reactions—non-immunological

- Bacterial contamination
- Transfusion—associated circulatory overload (TACO)
- Physical and chemical haemolysis
- Metabolic derangements

Delayed transfusion reactions—immunological

- Delayed haemolytic transfusion reaction (DHTR)

- Transfusion associated graft-versus-host disease (TA-GvHD)
- Post-transfusion purpura

Delayed transfusion reactions—non-immunological

- Iron overload
- Transfusion transmitted diseases

Immediate adverse effects of transfusion and their management

Category 1: Mild reactions			
Signs	***Symptoms***	***Possible cause***	***Immediate management***
Urticaria/ rash	Pruritis (itching)	Allergic	1. Stop transfusion 2. Assess patient 3. An antihistamine may be required 4. Transfusion may be restarted if no other signs/symptoms are present 5. If signs/symptoms worsen, treat as Category 2.
Category 2: Moderately severe reactions			
Signs	***Symptoms***	***Possible cause***	***Immediate management***
Flushing Urticaria Rigors Fever Restlessness Tachycardia	Anxiety Pruritis Palpitations Mild dyspnea Headache	Allergic (moderately-severe) Febrile non-haemolytic transfusion reaction: Antibodies to white cells or platelets Antibodies to proteins including IgA Possible contamination with pyrogens and/or bacteria	1. Stop transfusion and maintain IV line with normal saline 2. Contact medical officer 3. Patient may require antihistamine medication and/or paracetamol 4. Further investigation and management according to clinical features If investigation required: Complete transfusion reaction form and send blood pack, form and samples to blood bank

(*Contd.*)

Category 3: Life-threatening reactions			
Signs	***Symptoms***	***Possible cause***	***Immediate management***
Rigors Fever Restlessness Hypotension Tachycardia Dark Urine Unexplained bleeding (DIC)	Anxiety Chest pain Pain at infusion site Respiratory distress Loin/back pain Headache Dyspnea	1. Acute intravascular haemolysis (wrong blood) 2. Bacterial contamination and septic shock 3. Fluid overload 4. Anaphylaxis Transfusion related acute lung injury (TRALI)	1. Stop transfusion and maintain IV line with normal saline 2. Contact medical officer on duty 3. Manage immediate needs: a. Fluid for hypotension b. Oxygen c. Adrenaline for anaphylaxis d. Diuretic for fluid overload 4. Further management according to likely cause 5. Bedside clerical checks of all forms, labels and patient identification for correctness of the unit and the intended recipient are required. Reconfirm ABO, Rh and antibody screen and crossmatch tests. 6. Complete transfusion reaction form and the unit and all tubing should be returned to the blood bank, along with post-infusion blood and urine samples (DCT, urine hemoglobinuria, serum bilirubin, hemoglobinaemia, urea, creatinine, electrolytes, urine output, coagulation screen

(*Contd.*)

7. Additional samples sometimes required for (a) Blood cultures, (b) HLA or neutrophil antibodies, (c) Anti-IgA antibodies and (d) HLA typing
8. The reaction should be documented in the patient's chart. Once these initial measures have been implemented, the investigation of the reaction by the transfusion service can proceed

ACUTE HAEMOLYTIC REACTIONS

Causes

- The majority of haemolytic reactions are caused by transfusion of **ABO incompatible** blood, e.g. group A transfused to group B patient or vice versa.
- Antibodies in the patient's plasma will hemolyse the incompatible red cells.

Even a small volume of incompatible blood (5–10 ml) can cause severe reactions and large volumes increase the risk.

Symptoms: Chills, fever, pain (along IV line, back, chest), hypotension, dark urine, uncontrolled bleeding due to DIC.

The common cause of AHTR is transfusion of ABO incompatible blood and this can be due to:

- Errors in blood request form
- Taking wrong sample into prelabeled sample tube
- Incorrect labeling of the sample tube sent to the blood centre
- Inadequate checks of the blood against the identity of the patient while starting a transfusion
- In a conscious patient signs and symptoms appear within minutes of starting the transfusion; sometimes even less than 10 ml have been given.

- In an unconscious or anaesthetized patient, hypotension and uncontrolled bleeding (DIC) may be the only signs.
- Hence monitor the patient at the start of transfusion.

Prevention of Errors

1. Correctly label the blood samples and request forms.
2. Place the patient's blood sample in the sample tube.
3. Always check the blood against the identity of the patient at the bedside before transfusion.
4. Proper identification of the patient from sample collection through to blood administration, proper labeling of samples and products are essential. Prevention of non-immune haemolysis requires adherence to proper handling, storage and administration of blood products.

Management: Immediately stop transfusion. Notify hospital blood centre immediately (another patient may also have been given the wrong blood!). These patients usually require ICU support and therapy includes vigorous treatment of hypotension and maintenance of renal blood flow.

FEBRILE REACTIONS

This is the most common cause of TR.

Cause: Recipient antibodies reacting with white cell antigens or white cell fragments in the blood product or due to cytokines which accumulate in the blood product during storage. Fever occurs more commonly with platelet transfusion than red cell transfusion.

It is important to distinguish from fever due to the patient's underlying disease or infection (check pre-transfusion temperature). Fever may be the initial symptom in a more serious reaction such as bacterial contamination or haemolytic reaction and should be taken seriously.

Management

- If fever is present, give paracetamol.
- Follow the steps of 'immediate management' of an acute transfusion reaction. For isolated fever or chills in some

patients, the treating doctor may choose to restart the transfusion. If the fever is accompanied by significant changes in blood pressure or other signs and symptoms, the transfusion should be ceased and investigated.

- Check for HLA antibodies in patients having repeated febrile reactions.

Prevention: A proportion of patients who have febrile reactions will have similar reactions to subsequent transfusions. Many are prevented by pre-storage leucocyte filtration.

URTICARIAL (ALLERGIC) REACTIONS

Cause: Caused by **foreign plasma proteins**. On rare occasions, this is associated with laryngeal oedema and bronchospasm.

Management

- If urticaria occurs in isolation (without fever and other signs), slow the rate or temporarily stop transfusion.
- If symptoms are mild, administer **anti-histamine medication** before restarting the transfusion. If associated with other symptoms, cease the transfusion and proceed with investigation.

Investigation

In case of mild urticarial reactions with no other signs or symptoms, it is not necessary to submit blood specimens for investigation. It is also usually possible to restart the transfusion. Such a decision should be made after assessment by the treating doctor.

ANAPHYLACTIC/ANAPHYLACTOID REACTIONS

Anaphylactic and anaphylactoid reactions have signs of cardiovascular instability including hypotension, tachycardia, loss of consciousness, cardiac arrhythmia, shock and cardiac arrest. Sometimes respiratory involvement with dyspnea and stridor are prominent.

Cause: In some cases, patients with IgA deficiency, who have anti-IgA antibodies can have these reactions.

Management

- Immediately stop transfusion, supportive care including airway management may be required. Adrenaline may be indicated. Usually given as 1:1000 dilution, 0.01 mg/kg subcutaneously/IM or slow IV.
- **Investigate** for IgA levels and anti-IgA antibodies.

Prevention: Patients with anti-IgA antibodies require special blood products such as washed red blood cells and plasma products prepared from IgA deficient donors.

BACTERIAL CONTAMINATION

Cause: Bacteria may be introduced into the blood pack at the time of blood collection from sources such as donor skin, donor bacteraemia or equipment used during blood collection or processing. Bacteria may multiply during storage. Gram positive and Gram negative organisms have been implicated. **Platelets are more frequently implicated than red cells.**

Some contaminants, particularly **pseudomonas species grow at 2–6 degree C** and **staphylococci** grow at **20–24 degree C.**

Signs and symptoms appear rapidly after starting the infusion, but may be delayed for a few hours.

Symptoms: Common symptoms are very high fever, rigor, profound hypotension, nausea and/or diarrhoea. **A severe reaction may be characterized by sudden onset of high fever, rigors and hypotension.**

Management

- Immediately stop the transfusion and notify the hospital blood centre. After initial supportive care, blood cultures should be taken and high dose broad-spectrum anti-microbials need to be administered.
- Laboratory investigation will include culture of the blood pack.

Prevention

- Inspect blood products prior to transfusion. Some but not all bacterially contaminated products can be recognised (clots, clumps, or abnormal colour).

- Maintaining appropriate cold storage of red cells in a blood centre refrigerator is important.
- Transfusions should not proceed beyond the recommended infusion time (4 hours).

FLUID OVERLOAD

1. Fluid overload can result in heart failure and pulmonary oedema
2. May occur when:
   - Too much fluid is transfused.
   - The transfusion is too rapid.
   - Renal function is impaired.
3. Fluid overload is likely to occur in patients with
   - Chronic severe anaemia
   - Underlying cardiovascular disease

TRANSFUSION-RELATED ACUTE LUNG INJURY

Transfusion related acute lung injury (TRALI) is a clinical diagnosis of exclusion characterised by **acute respiratory distress and bilaterally symmetrical pulmonary oedema with hypoxaemia developing within 2 to 8 hours after a transfusion**. A chest X-ray shows interstitial or alveolar infiltrates when no cardiogenic or other cause of pulmonary oedema exists.

Cause: Pulmonary vascular effects are thought to occur secondary to cytokines in the transfused product or from interaction between patient's white cell antigens and donor antibodies (or vice versa).

Management

- **Symptomatic support for respiratory distress includes oxygen administration** and may require intubation and mechanical ventilation.
- Symptoms generally resolve over 24–48 hours.

HYPOTHERMIA

Cause: Rapid infusion of large volumes of stored blood contributes to hypothermia. Infants are particularly at risk during exchange or massive transfusion.

Prevention and management

- Appropriately maintained blood warmers should be used during massive or exchange transfusion.
- Additional measures include warming of other intravenous fluids and the use of devices to maintain patient body temperature.

HYPERKALEMIA

Cause: Stored red cells leak potassium proportionately throughout their storage life. Irradiation of red cells increases the rate of potassium leakage. Clinically significant hyperkalemia can occur during rapid, large volume transfusion of older red cell units in neonates and children.

Prevention: Red cells are irradiated just prior to issue especially in neonates and children. Blood less than 7 days old is generally used for transfusion in neonates (e.g. cardiac surgery, ECMO, exchange transfusion).

DELAYED HAEMOLYTIC TRANSFUSION REACTION (DHTR)[1]

DHTR commonly occurs after 24 hrs, may occur several days after administration of red cells usually from 2 to 14 days.

Cause: Patients may develop antibodies to red cell antigens. Antibodies can occur naturally, or may arise as a consequence of previous transfusion or pregnancy. A delayed haemolytic reaction occurs when a patient develops an antibody directed against an antigen on transfused red cells. The antibody may cause shortened red cell survival, with clinical features of fever, jaundice and lower than expected haemoglobin following transfusion.

Prevention: An antibody screen is performed as part of pre-transfusion testing. When an antibody is detected, it is identified and appropriate antigen negative blood is provided. Sometimes antibodies fall below detectable limits and may not be detected by pretransfusion testing.

TRANSFUSION ASSOCIATED GRAFT-VERSUS-HOST DISEASE (TA-GvHD)

Cause: TA-GvHD occurs from donor lymphocytes in a susceptible transfusion recipient. These donor lymphocytes proliferate and damage target organs especially bone marrow, skin, liver and gastrointestinal tract. The clinical syndrome comprises fever, skin rash, pancytopenia, abnormal liver function and diarrhoea and is fatal in over 80% of cases. **The usual onset is about 12 days of** post-transfusion period.

Also, can occur in immunocompetent recipients of blood from a biologically related (directed) or HLA identical donors. The disease is also reported in immunologically compromised patients.

Prevention: Gamma irradiation of cellular blood products (whole blood, red blood cells, platelets, granulocytes) for patients of risk group has to be given.

Risk groups

- Recipients of blood from biologically related (directed) or HLA matched donors.
- Patients with congenital immunodeficiency
- Patients receiving granulocyte transfusions
- Patients with Hodgkin's disease
- Allogeneic and autologous peripheral blood stem cell (PBSC) and bone marrow transplant recipients
- Patients with aplastic anaemia receiving immuno-suppression
- Patients treated with purine analogue drugs

Post-transfusion purpura: For details refer to transfusion reactions.

TRANSFUSION RELATED IMMUNE MODULATION (TRIM)

Allogenic blood transfusion may be associated with immuno-suppression, increased risk of infection and cancer recurrence.

Cause: Unknown, possibly mediated by donor white cells or plasma.

IRON ACCUMULATION

Cause: Iron accumulation is a predictable consequence of chronic RBC transfusion. Organ toxicity begins when reticulo-endothelial sites of iron storage become saturated. Liver and endocrine dysfunction creates significant morbidity and the most serious complication is cardiotoxicity which causes arrhythmias, and congestive heart failure. Patients receiving chronic transfusion should monitor their iron status monitored and managed by their physician.

Management and pevention: Iron chelation therapy is usually commenced early in the course of chronic transfusion therapy.

INFECTIOUS DISEASE TRANSMISSION

A variety of infectious agents may be transmitted by transfusion. Hence proper screening is essential.

ALLOIMMUNISATION

In this, the antibodies are formed to the antigens those are not present on the person's blood cells.

Red cell alloimmunization: Patients experiencing alloantibody formation are asymptomatic. The alloantibody is discovered at the time of pre-transfusion testing. Appropriate antigen negative blood should be supplied.

Prevention: Alloimmunisation to the D and K (Kell) antigens is prevented by the provision of Rh(D) negative and Kell negative blood for Rh(D) negative, Kell negative patients respectively. This is important for females with child-bearing potential as these antibodies can cause severe haemolytic disease of the newborn during pregnancy.

Risk groups: Patients with sickle cell disease or major haemo-globinopathy syndromes who are chronically transfused are at greatest risk of alloantibody formation. Prior to commencing transfusion, patients with these conditions should have extended red cell phenotyping performed. Blood matched for the patient's Rhesus and Kell antigens is usually supplied for transfusion

Platelet alloimmunization: When thrombocytopenic patients do not achieve the expected post-transfusion platelet count increment, they are said to be refractory. This usually occurs in patients receiving frequent platelet transfusions.

Causes: There are clinical and immunological causes of platelet refractoriness. Clinical causes include sepsis, DIC, bleeding, fever, some drugs, and enlarged spleen.

Immunological causes include the development of antibodies to human leucocyte antigens (HLA) or human platelet antigens (HPA).

Management: Immunological refractoriness can be managed by the provision of HLA or HPA matched platelets.

Prevention: Leucocyte reduction of blood and blood products to levels less than 10^6/unit reduces the likelihood of alloimmunisation. This can be achieved through the use of pre-storage or bedside leucocyte reduced blood products.