



**14**

**TRANSFUSION REACTIONS**

**14.1 INTRODUCTION**

Transfusion of blood and blood products are reported to cause reactions during or after procedure specially in patients who receive multiple transfusions. These are referred to as **transfusion reactions (TR)** and may vary in severity from mild to life threatening and fatal reactions. The transfusion centre must maintain a record of all reported transfusion reactions.



**OBJECTIVES**

After reading this lesson, you will be able to:

- describe the types of transfusion reactions
- explain the investigations of these reactions

**14.2 TRANSFUSION REACTION**

Transfusion reactions are **classified** into immunological and non-immunological, each of which being further subclassified as acute (occur within 24 hours) and delayed (occur in days-months) (Table 14.1).

**Table 14.1 Classification of transfusion reactions**

Type	Immediate	Delayed
Immunological reactions	Hemolytic Febrile non haemolytic	Hemolytic Alloimmunization to red cell, platelet, leucocyte antigens

## MODULE

Hematology and Blood  
Bank Technique



Notes

## Transfusion Reactions

Non immunological	Anaphylactic Allergic Transfusion related acute lung injury Septicemia  Circulatory overload Hyperkalemia  Hypocalcemia	Post transfusion purpura GVHD Immunomodulation  Transfusion transmitted infections Transfusion hemosiderosis Pulmonary microembolisation
-------------------	--	--

### Immunological reactions: Immediate

#### 1. Acute Hemolytic transfusion reaction (AHTR)

Hemolytic transfusion reactions are of two types:

- A. Intravascular (acute hemolytic) transfusion reaction
- B. Extravascular (delayed hemolytic) transfusion reaction

Intravascular transfusion reactions occur soon after transfusion of blood and are caused by red cell antibodies in the recipient which destroy the donor red cells. Usually associated with transfusion of ABO incompatible blood, this type of reaction (also known as acute hemolytic TR) is very severe and life threatening. It occurs as a result of activation of the complement system which mediates IgM induced red cell destruction within the circulation.

#### Causes of hemolytic transfusion reaction

Acute hemolytic reactions can result from clerical errors or technical errors.

##### I. Clerical errors

These include the following

1. Incorrect identification of patient at the time of sample collection.
2. Incorrect labeling of recipient sample.
3. Incorrect labeling of blood bag.
4. Confusion in the identity of patient at the time of transfusion.
5. Issue of a wrong unit of blood.

##### II. Technical errors

These may result from

1. Error in blood grouping

## Transfusion Reactions

2. Error in cross matching due to which incompatibility is not detected
3. Presence of weak antibodies which are not detected by routine tests.
4. Incorrect interpretation of test results.

The following investigations are done in patients with AHTR:

- (a) Pre-transfusion and post-transfusion plasma of the patient is examined for evidence of free hemoglobin or bilirubin
- (b) Measuring plasma haptoglobin and free hemoglobin levels in patient's urine
- (c) Direct antiglobulin test is performed on pre-transfusion and post-transfusion sample
- (d) Repeating the compatibility test of the patient's serum (Pre-transfusion and post-transfusion) against donor red cells from the bag
- (e) Using indirect Coombs test checking the donor plasma against patient's red cells



### INTEXT QUESTION 14.1

1. Reactions to blood transfusion during or after is referred as .....
2. Transfusion reactions are classified as ..... & .....
3. Commonest causes of hemolytic transfusion reaction is .....
4. Acute hemolytic reactions can result from ..... or ..... errors

### 2. Febrile non hemolytic transfusion reaction (FNHTR)

This is defined as an increase in temperature of 1°C or more above the baseline temperature of the patient during or within 24 hours of transfusion which cannot be ascribed to any other causes. It is associated with transfusion of cellular components and is more common in patients receiving multiple transfusions and in multiparous women.

FNHTR result from **Alloimmunization to antigens on leucocytes and platelets**. The antibodies (HLA antibodies and platelet specific antibodies) in the recipient react with the antigens on donor leucocytes and platelets with activation of complement and release of cytokines which release pyrogens.

The **symptoms** are **mild** and include **fever** with or without chills and rigor.

The reaction can be **prevented** by Leucoreduction of blood products and use of apheresis platelets

## MODULE

Hematology and Blood  
Bank Technique



Notes



Notes

**3. Allergic reactions**

These reactions are mild and result from the reaction of IgE attached to mast cells/basophils of recipient with proteins or other soluble substances in donor plasma. There is release of histamine which causes itching and urticaria. The reactions are more frequent after transfusion of whole blood and plasma. The patient complains of redness, pruritis, skin rash and urticaria. The reactions can be **prevented** by transfusion of washed red cells, reducing the amount of plasma in the transfused blood by centrifugation and washing the cellular components to remove residual plasma.

**4. Anaphylactic reactions**

This is a immediate hypersensitivity reaction which may begin after infusion of only a few ml of plasma or plasma containing product. While some of these reactions are immediate others occur after as long as one hour after transfusion. The reaction is seen in patients who are IgA deficient and develop IgA antibodies after blood transfusion/pregnancy.

**5. Transfusion Related Acute Lung Injury (TRALI)**

This refers to the occurrence of acute lung injury within 6 hours of transfusion. It results from granulocyte specific and anti-HLA antibodies in the donor, which reacts with recipient leucocytes in the pulmonary microvasculature resulting in agglutination of granulocytes in the capillaries of the lung. There is activation of complement in the pulmonary vascular bed which leads to capillary endothelial damage and accumulation of fluid in the alveoli. Donors of plasma which causes TRALI should be examined for the presence of granulocyte specific antibodies and anti-HLA antibodies. The reaction can be **prevented** by use of leucocyte depleted blood components.



**INTEXT QUESTIONS 14.2**

1. Febrile nonhemolytic transfusion reactions occurs ..... or ..... hours of transfusion
2. Febrile hemolytic transfusion reactions results from ..... to antigen on ..... & .....
3. Febrile hemolytic transfusion reaction can be prevented by ..... of blood products & use of ..... platelets
4. Allergic reactions results from reaction of ..... attached to .....

## Transfusion Reactions

5. In allergic reactions itching & urticaria is caused by release of .....
6. Anaphylactic reactions are seen in patients who are ..... deficient
7. Transfusion related acute lung injury results from ..... specific & ..... antibodies
8. Transfusion related acute lung injury can be prevented by use of ..... depleted blood component

## 14.3 NON IMMUNOLOGICAL REACTIONS: IMMEDIATE

### 1. Septicemia

This is an important cause of fatality associated with blood transfusion. The organisms implicated are *Yersinia*, *Pseudomonas*, *Enterobacter*, and *Serratia*. These enter and contaminate blood through blood bags, from a donor with asymptomatic bacteremia, unclean skin and skin core which enters from the collection needle. This type of transfusion reaction is uncommon as blood itself has bactericidal activity and storage of collected blood bags at low temperatures inhibits the growth of the microorganisms.

### 2. Circulatory overload

This results from transfusion of whole blood in excessive volume or high speed. Transfusion of blood to severely anemic patients with congestive heart failure and elderly patients with limited cardiac reserve may result in pulmonary edema.

To prevent these reactions, slow blood transfusion is given and the patient is closely monitored. Infusion of red cell concentrate in place of whole blood and volume reducing apheresis platelets can also be helpful in preventing these reactions.

## Immunological reactions: Delayed

### 1. Delayed Hemolytic Transfusion Reaction (DHTR)

In DHTR there is destruction of the transfused red cells 2-10 days after blood transfusion. It results from an anamnestic antibody response to antigens of the Rh, Kidd, Kell and Duffy blood groups. These patients are immunized by a previous transfusion or pregnancy following which a primary antibody response occurs. This is delayed in onset, the peak is reached slowly and the antibody level gradually declines. The antibody is hence not detected during antibody screening and compatibility testing. On re-exposure to the immunogenic red cell antigen, a brisk immune response occurs and high IgG titers occur within few days. The donor red cells are coated with the antibody and they are removed by

## MODULE

Hematology and Blood  
Bank Technique



Notes

## MODULE

Hematology and Blood  
Bank Technique



Notes

## Transfusion Reactions

macrophages of the reticuloendothelial system (mainly liver and spleen). The red cell destruction is hence also known as extravascular transfusion reaction. The patient may be asymptomatic. If symptoms are present they are mild and include fever, fall in hemoglobin and jaundice 5-7 days after transfusion. Investigations include screening for red cell antibodies. The direct antibody test is often positive. The antibody should be eluted from the red cells and identified.

### 2. Post transfusion thrombocytopenia

Severe thrombocytopenia can develop 7-10 days after platelet transfusion due to platelet specific antibodies. This is seen in patients who have been immunized earlier by platelet transfusion and in multiparous women. The patient complains of fever with chills and generalized purpura a week after the transfusion. The thrombocytopenia is self limiting.

### 3. Graft versus host disease (GVHD)

Cellular concentrates of red cells, platelets and granulocytes contain immunocompetent T lymphocytes. When transfused into immunodeficient recipients, these donor T lymphocytes recognize the host HLA antigens as foreign and mount an immune response thus causing GVHD. Irradiation of blood products containing lymphocytes prior to transfusion to patients at risk helps prevent GVHD.

### Non immunological complications: Delayed

#### 1. Iron overload

Each unit of red cells contains 0.25g of iron. Patients who receive repeated blood transfusion such as thalassemia major, other hemolytic anemias progressively accumulate iron. The iron gets deposited initially in the reticuloendothelial system and then in the parenchymal cells of various organs causing growth retardation, sexual dysfunction, hepatic and cardiac dysfunction and other features. The accumulated iron is removed by the administration of iron chelators.

#### 2. Transfusion transmitted infections

Various infections can be transmitted by transfusion of blood. These are HIV, Hepatitis B, Hepatitis C, syphilis and malaria. It is thus mandatory to screen all collected units of blood for all these infections. The organisms, their component screened and the method of screening are given in Table 14.2.

**Table 14.2** Infectious agents transmitted through blood and their screening method

Agent	Component screened	Method
Hepatitis B	HBsAg	ELISA
Hepatitis C	Anti-HCV	ELISA
HIV	Anti-HIV1,2	ELISA, particle agglutination assays and spot test
Syphilis	Treponemal antigen	VDRL, TPHA
Malaria	Malaria antigen	Malaria antigen assay



Notes



**INTEXT QUESTIONS 14.3**

- Each unit of blood is screened for the following infections except
  - HIV
  - HBsAg
  - Hepatitis A
  - Malaria
- Hemolytic transfusion reaction is most often due to
  - Rh incompatibility
  - ABO incompatibility
  - Minor blood groups
  - Any of the above
- The test preferably done for HIV screening is
  - ELISA
  - Rapid test
  - Both
  - Neither



**WHAT HAVE YOU LEANT**

- Reactions to blood transfusion during or after transfusion of blood and blood components are referred as transfusion reactions
- Transfusion reaction may be classified as Immunological & Non-immunological reactions
- Acute reactions occurs within 24 hours and delayed reactions occurs in days to months
- Immediate immune reactions are hemolytic transfusion reaction, febrile nonhemolytic transfusion reaction, allergic reactions, anaphylactic reactions, transfusion related acute lung injury

## MODULE

Hematology and Blood  
Bank Technique



### Notes

## Transfusion Reactions

- Hemolytic transfusion reaction occurs commonly because of ABO incompatibility and result from clerical or technical errors
- Febrile nonhemolytic transfusion reaction result from Alloimmunization to antigens on leucocytes and platelets
- Febrile hemolytic transfusion reaction can be prevented by leucoreduction of blood products and use of apheresis platelets
- Allergic reactions are caused by IgE attached to mast cells/basophils
- Anaphylactic reactions is seen in patient with IgA deficiency
- Transfusion related Acute lung injury results from granulocyte specific and anti HLA antibodies and can be prevented by use of leucocyte depleted blood components
- Immediate nonimmunological reactions are bacterial contamination, circulatory overload
- Circulatory overload can be prevented by slow blood transfusion
- Delayed immunological reactions are Delayed hemolytic transfusion reaction, post transfusion thrombocytopenia, Graft versus host disease
- Delayed non-immunological reactions are Iron overload, transfusion transmitted infections



## TERMINAL QUESTIONS

1. Classify transfusion reactions
2. Explain how you will investigate transfusion reactions
3. Describe immediate immunological reactions
4. Explain hemolytic transfusion reaction



## ANSWERS TO INTEXT QUESTIONS

### 14.1

1. Transfusion reaction
2. Immune & Non-Immune
3. ABO incompatibility
4. Clerical, technical



**14.2**

1. During, within 24 hours
2. Alloimmunization, Leucocytes and Platelets
3. Leucoreduction, apheresis
4. IgE, mast cells/Basophils
5. Histamine
6. IgA
7. Granulocytes, Anti HLA
8. Leucocyte

**14.3**

1. Hepatitis A
2. ABO incompatibility
3. ELISA

**MODULE**

Hematology and Blood  
Bank Technique



**Notes**