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NATIONAL GUIDELINE ON CLINICAL USE OF BLOOD – 2022,

Ministry of Health, Maldives

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Contents

Foreword

Blood transfusions are needed for a wide range of health conditions including anaemia, complications during pregnancy and childbirth, severe trauma due to accidents, and surgical procedures. They are also regularly used for patients with conditions such as sickle cell disease and thalassaemia. In the Maldives, further demand for blood transfusion results from relatively large population of thalassaemia patients requiring routine blood transfusion, which further highlights the importance of standardization of blood services in the country.

Safe, effective and quality-assured blood and blood components contribute to improving and saving millions of lives worldwide every year, on the other hand, unsafe blood transfusion can worsen the conditions of the patient and may contribute to life threatening complications. In order to ensure proper use of blood, a National Blood Policy was launched on 14 November 2018, in alignment with this policy, the National Guideline on Clinical Use of Blood is an essential guideline for Maldivian Blood Services and clinicians for day-to-day practice.

I greatly appreciate the members of the National Blood Council (NBC) for taking the initiative to complete and finalize this vital guideline. I extend my gratitude to WHO for the assistance and guidance; in particular, we owe an immensurable debt to the WHO consultant, Dr. Zarin Soli Bharucha for the valuable contribution to develop this guideline. I thank all the stakeholders including Maldivian Blood Services, the management of IGMH, Hulhumale Hospital, ADK Hospital, Tree Top Hospital for the constructive contribution.

It is important that over the next few years we develop the National Blood Transfusion Service and a Central Blood Bank and establish a system that donors can donate blood directly to the blood bank instead of directed donation with enhancing public awareness as well as training of health professionals.

I am confident that the National Guideline on Clinical Use of Blood will be widely available to all health Professionals in every health facility where blood transfusion service is provided, to ensure using the right product for the right patient in the right dose at the right time for the right indication throughout the country.

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Chapter 1 – Introduction

Blood is a precious and scarce human resource. Transfusion of blood & blood component are a lifesaving intervention and an essential part of modern healthcare to maintain blood volume in life threatening acute situations, improve oxygen transport in anaemia, correct bleeding & coagulation disorders and as a supportive therapy in chronic haematological disorders.

Although there are tremendous benefits of receiving blood transfusion unfortunately the concern regarding safety and availability of blood is an ongoing challenge for blood transfusion services. Blood transfusion is associated with risk of transfusion transmitted Infections (TTIs), transfusion related complications and immune related problems. The transfusion-associated risks that prevail are:

- Bacterial Contamination of blood/components – introduction of bacteria during blood collection
- Threat of emerging /unknown viruses which may be transmitted but will be detected after many years as has been seen with transmission of HCV in thalassemia patients.
- Early window period donation limits detection of antibodies in the donor serum by current assays.
- Transmission of unknown pathogens for which no assays are available
- Donor Leukocytes in blood may cause adverse immune responses and adverse reactions in the recipient.
- Accidental transfusion of incorrect blood.
- Transfusion of ABO incompatible blood.

Adverse events cause medico legal issues as well as dampen the reputation of the blood centres/hospital. Also, some serious consequences such as transmission of HIV and hepatitis need utmost attention through safe pre transfusion measures.

1.1 Blood for transfusion is considered safe when it is:

- Donated by a healthy donor through a careful selection process.
- Screened and free from any agents that could be harmful to the patient.
- Processed by modern methods of testing, component production, storage and transport of blood.
- Transfusion should be given only when absolutely necessary for the benefit of the patient's health. Unnecessary transfusions should not be given.
- Administered under the supervision of a staff trained in safe transfusion process and able to manage any adverse transfusion reaction appropriately.
- Clinically effective and provides benefit to the patient.

Transfusion decision therefore necessitates one to weigh the benefits against the risks that could lead to severe morbidity and even mortality. Even though the risks are well documented, the clinicians need to be on alert as not to fail in recognizing their occurrence when ordering transfusions.

1.2 Clinical Use of blood

The supply of adequate, safe, effective blood and blood products efficiently can only be achieved if due attention is paid to relevance of clinical use of blood products. Ensuring safety and clinical effectiveness of blood through safe donors, with accurate, reliable quality-controlled testing and processing requires significant human and financial resources. It is a joint responsibility of the blood transfusion service, the prescribers of blood as well as the support and commitment of the administrative authorities to provide adequate resources to substantiate blood supply for its appropriate use.

Blood transfusion therapy depends upon the availability of different blood components. The blood components, used separately or in combinations, can meet the transfusion need of most patients and minimize the risks of blood transfusion. **Clinical use of blood** and blood component ensures using the **right product** for the **right patient** in the **right dose** at the **right time** for the **right indication**.

Blood and blood products should be used in an efficient manner to avoid unnecessary use, which can lead to shortages for patients in real need and unnecessary exposure to risks of transfusion in patients who do not need blood.

1.3 Strategies for safe and appropriate clinical use of blood

- Prevention, early diagnosis, and effective treatment of anaemia that could result in need for transfusion.
- Avoid preoperative transfusion to raise haemoglobin.
- Use good anaesthetic and surgical techniques to reduce blood loss.
- Use pharmacological options and medical devices to reduce blood loss such as aprotonin, tranexemic acid and DDAVP.
- Avoid transfusion for a misconception of early discharge from hospital.
- Evaluate the patient in total and not just depend on Haemoglobin or other laboratory findings.
- Use only the component that is needed, and the amount required.
- Use genetically engineered recombinants such as rFVIII, rFIX, rFVIIa, rEPO.
- Use replacement fluids to maintain normovolemia and avoid unnecessary transfusions.

Safety is a concern for clinicians, patients as well as their families. Blood should always be used appropriately and judiciously only when clinically indicated and at the same time clinicians should be fully aware of prompt management in case of any adverse event. Clinical staff must ensure that patients are properly identified, while taking their samples and starting a transfusion.

Clinicians should discuss the need for a transfusion with the patient regarding benefits and risks and get patients approval for transfusion in the form of informed consent.

Measures to reduce adverse reactions such as febrile transfusion reactions by the use of modified components as leucoreduced packed red cells in patients undergoing repeated transfusion should be taken wherever necessary.

Clinicians should also consider alternative strategies to reduce the use of allogenic blood such as blood conservation techniques in surgery, autologous transfusion, or the use of pharmacological agents for their patients.

It is extremely important to develop an interactive communication between the blood providers and blood prescribers to ensure an effective clinical interface for:

- An adequate supply of safe blood and blood components accessible to all in need.
- Appropriate clinical use of blood and blood components.

The best blood is the one that you have not transfused

Chapter 2 – Blood Supply

The blood supply chain needs to be efficient and effective. Ensuring safe and adequate blood supply through recruitment and retention of safe blood donors is a vital function of the National Blood Transfusion Service. The blood should be accessible to all areas in the country. Currently the blood supply is supported by blood collected from directed and voluntary donations. Majority of the blood transfusions are directed donations, which is not as safe as voluntary non-remunerated donations, as donors may not reveal true information with regards to risky behaviour.

Voluntary non remunerated regular blood donors provide the safest blood for transfusion as they are well informed, and their blood is time tested. The National blood policy recommends phasing out directed donors and achieving 100% voluntary blood donation.

2.1 Types of Blood Donors

- Voluntary non remunerated blood donors
- Replacement/Relative donors
- Professional donors (Remunerated donors)
- Autologous blood donors
- Donors for special procedures (Plateletpheresis / Plasmapheresis / Erythrocytopheresis / Hematopoietic stem cell collection)
- Directed or designated donors

2.2 Voluntary non-remunerated blood donors

The voluntary donors give blood voluntarily without receiving any remuneration in the form of money or for money. Their primary motivation is to help unknown recipients and not to obtain any personal benefit.

They are the safest donors because they are more likely to be free from TTI as they have been educated about the importance of safe blood. Once they become repeat donors, they are screened each time they donate blood thereby reducing the chances of window period donation.

2.3 Replacement/Relative donors

The replacement donors come to the BTS with a request from the physician treating the patient, giving particulars of the patient like name, ward, hospital ID, diagnosis, and an estimate of the blood and blood components likely to be required. Members of the patient's family are under pressure to donate

blood and may conceal potentially important information about their health status, particularly the risk of transmitting an infectious disease.

Relatives who cannot find suitable or willing donors within the family may seek replacement donors who are prepared to give their blood for payment. Donors who are paid by the patient's family are less likely to reveal any reasons why they may be unsuitable as donors.

2.4 Professional donors

They give blood in return for money. Though strictly banned by regulations, they still continue to donate blood under the garb of replacement donors. They do not reveal their unsuitability to donate blood. Paid donors present a major risk to the safety of the blood supply for the following reasons.

- Paid donors undermine the voluntary non remunerated system of blood donation which is the foundation of a safe blood supply.
- The highest incidence and prevalence of transfusion-transmissible infections are generally found among commercial or paid donors.
- They are often under nourished, in poor health and may donate their blood more frequently than it is recommended. This may have harmful effects on their own health as well as present a risk to the recipients.

2.5 Directed Donors

- Directed donations are donations from designated donors for a specific patient.
- There is no scientific evidence that directed donation is safer than volunteer blood.
- A directed donor program creates additional strain on the inventory management.
- Directed blood units from blood relatives should be discouraged as there is a chance of TA-GVHD hence if insisted on the blood should be irradiated to prevent possibility of TA-GVHD.
- Husband's blood should not be used for the wife as there is a likelihood of immunising the wife against the husband's antigens and is likely to develop antibodies which pose a danger of HDN in the future pregnancy.
- With the objective of optimising utilisation of homologous blood supply and reducing or eliminating the risk factors, perioperative blood conservation strategies should be implemented. Use of autologous transfusion is one of the alternatives.

2.6 Autologous Donors

They are donors who donate blood for themselves, to be used at a later date. Recipients who serve as their own donors receive the safest possible blood since the risks of TTI and alloimmunization are completely eliminated but adverse reactions due to bacterial contamination, clerical mistakes and storage related problems can still occur.

It should only be considered in a patient in whom you anticipate that the surgery will result in sufficient blood loss to require homologous transfusion.

2.7 Aphaeresis donors

They are a special category of donors who willingly donate only the specific blood component required for a patient. They need to be screened thoroughly before the procedure on the aphaeresis machine.

2.8 Donor suitability for blood donation

Prospective donors are assessed for suitability to donate blood depending on their general health, well-being, medical history, lifestyle behaviours and any risks pertaining to transfusion transmitted infections.

Donors should be above the age of 18years, weigh 45/55 kg for whole blood/ component donation and have a minimum Hb of 12.5gm% for all donations except autologous/apheresis where the criteria are different as described later under autologous/apheresis blood donations.

2.9 Mandatory Blood Screening tests

All donated blood units undergo mandatory screening for HIV, HCV, HBV, and syphilis markers before issue of blood to the patients.

2.10 Autologous Blood Donation -Various methods

Autologous blood is an excellent option for patients with rare blood groups and alloantibodies.

It is acceptable at times in some forms to Jehovah's Witnesses. It helps supply of blood in remote and isolated areas and on the whole reduces the need for homologous blood.

The principal methods of autologous transfusion are:

1. Preoperative blood donation.
2. Acute normovolemic haemodilution.
3. Blood salvage.

These techniques can be used alone or in combination so that you do not use any homologous unit once autologous transfusion is started.

2.10.1 Pre operative Autologous Donation (PAD)

- This technique involves the collection and storage of the patient's own blood prior to elective surgery.
- This procedure can be done both in adult and paediatric age groups. It is technically difficult in children under 8 years or < 25 kg.
- Minimum haemoglobin of the patient should be 11 gm / dl.
- 1 unit of own blood (10-15% of blood volume) can be collected every 5-7 days.
- First donation collected should not be longer than 35 days prior to surgery.
- Last donation should be 72 hours before surgery.
- Oral iron supplement should be given to patient.
- Autologous blood cannot be put in the homologous pool.
- If found positive for any transfusion transmissible infection, it should not be used.

Criteria for medical exclusion

1. Active bacterial infection
2. Positive serological markers for transfusion transmissible infections
3. Epilepsy
4. Prolonged or frequent angina left main stem disease, aortic stenosis, cyanotic heart disease. Other patients with cardiac diseases can be considered after assessment by a cardiologist
5. Patient on β – blockers or angiotensin converting enzyme (ACE) inhibitor
6. Uncontrolled hypertension
7. Pregnancy especially with impaired placental flow or intrauterine growth retardation

2.10.2 Acute Normovolemic Hemodilution (ANH)

This involves removing a predetermined volume of the patient's own blood immediately prior to the commencement of surgery and its simultaneous replacement with sufficient crystalloid or colloid fluid to maintain the blood volume.

- During surgery, the hemodiluted patient will lose fewer red cells for a given blood loss.

- The autologous blood collected should subsequently be reinfused, during surgical bleeding (within 4 hours at room temperature). However, if plans are made to use after 6 hours, it should be refrigerated (in a blood bank refrigerator) and used within 24 hours.
- A fresh unit of autologous blood contains a full complement of coagulation factors and platelets.
- The basic safeguards should be maintained and the patients who cannot compensate for the reduction in oxygen supply due to haemodilution should be excluded.
- Volume of blood to be removed should be carefully assessed and strictly replaced with crystalloid (at least 3 ml for every 1 ml blood collected) or colloid (1 ml for every 1 ml collected).
- It is vital to monitor the patient and maintain blood volume and oxygen delivery at all times, particularly when surgical blood loss occurs.

2.10.3 Intra Operative Blood Salvage (IOBS)

This involves the collection of shed blood from a wound, body cavity or joint space and its subsequent reinfusion into the same patient. Methods of blood salvage include:

- Simple suction collection systems - blood is collected through very low suction to avoid hemolysis of red cells, into a blood collection bag containing anticoagulant.
- Simple suction collection systems can be used in dire emergencies with strict aseptic precautions. Red cells should be washed before transfusion.
- Automated suction collection systems, the cell-savers are commercially available devices that collect, anticoagulated, wash, filter and resuspend the red cells in crystalloid fluid prior to reinfusion.
- IOBS is contraindicated if blood is contaminated with bowel contents, bacteria, fat, amniotic fluid, urine, malignant cells and other irritants.

2.10.4 Post Operative Blood Salvage (POBS)

- Blood collected only during first 6 hours post operatively should be used
- Blood drained from mediastinal space in cardiac surgery and joint spaces in orthopaedic surgery is collected. Blood may be simply filtered before transfusion or may be washed, concentrated and suspended in isotonic solution.
- Chances of contamination are high, and the actual volume collected may be small, hence it is not much in use.

Chapter 3 – Clinical Transfusion Practices

3.1 Appropriate Use of Blood

Transfusion of blood and its products is an integral part of modern health care. The transfusion services are under constant pressure and concern over safety, cost, and availability of blood. Despite rigorous processes and procedures to ensure safe blood transfusion, the risk of complication still exists. Therefore, there is a need to ensure appropriateness of transfusion. Safe, efficient, and effective blood transfusion is a responsibility of blood transfusion services and the prescribers.

Appropriate blood transfusion is defined as the transfusion of safe blood products to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means. Appropriate use of blood reduces the potential risks of blood transfusion.

3.2 Prerequisite for Appropriate Use of Blood

- Commitment from Ministry of Health
- National Blood Policy
- Availability of alternatives, disposables, and devices
- Guidelines for clinical use of blood and its use
- National Blood Council (NBC)
- Hospital transfusion committees
- Clinician awareness
- Medical audit to assess appropriate use
- Hemovigilance to increase awareness regarding TTI risk

3.3 Clinician's Role

- Clinicians should follow National guidelines of clinical use of blood.
- Decision to transfuse blood should be taken by a clinician who is treating the patient after due considerations of the patient's clinical and laboratory parameters.
- It is essential to record the reason / need for transfusion in the patient's file

3.4 Considerations to be taken by the clinician before prescribing blood

- Can you minimise the patient's need for transfusion?

- Is there any other treatment you could consider before giving blood – such as IV fluids and any drugs that achieve haemostasis?
- Are there specific clinical or laboratory indications for blood transfusion?
- Are you likely to achieve any improvement in the patient's clinical condition?
- What other options are there if blood for transfusion is not available in time?
- Will a trained person monitor this patient during transfusion and respond immediately if any acute transfusion reactions occur?
- Have you recorded the decision and reasons for transfusion on the patient's chart and the blood request form?
- Do the benefits outweigh the risks of this transfusion?
- Will you use blood transfusion for yourself or your dear one in this condition?

3.5 Informed Consent

In order to abide by the principle of autonomy or self-determination, it is obligatory to obtain an informed consent prior to transfusion, from the recipient or his relative.

The requisites of informed consent are:

- Inform the patient about the need for blood, risks involved in transfusion and non-transfusion as well as about the alternatives available.
- His/ her written consent should be taken in the language he / she understands best only after providing information. Make sure the informed consent form is signed by the patient.
- In case of children below the age of 18, in unconscious patients or those incapables of decision-making process, the parent or the next of kin must sign the consent.

3.6 Guidelines for the person obtaining consent:

- Describe the blood product to be transfused. Inform the patient or alternate decision maker of material risks and benefits of the transfusion and any alternatives.
- Give the patient the opportunity to ask questions.
- Document that consent was obtained by completing a transfusion consent form.
- Clearly document the reason for transfusion in the patient's chart.
- Whenever possible, consent for transfusion should be discussed early enough to allow for blood alternatives to be considered

- In case the patient refuses to receive transfusion, it is important to document it with his signature and a witness.
- While respecting the wish of the patient, it is necessary to provide alternative strategies available.

3.7 Instructions regarding Pre transfusion sample Collection and sending blood samples to the blood bank

Pre transfusion testing should be performed in order to prevent transfusion of incompatible donor red cells that might result in an immune-mediated haemolytic transfusion reaction (HTR). Requests should contain sufficient information for accurate recipient identification (ID) to avoid any errors.

3.8 Instructions for Blood Sample to be sent with Requisition Form to the Blood Bank:

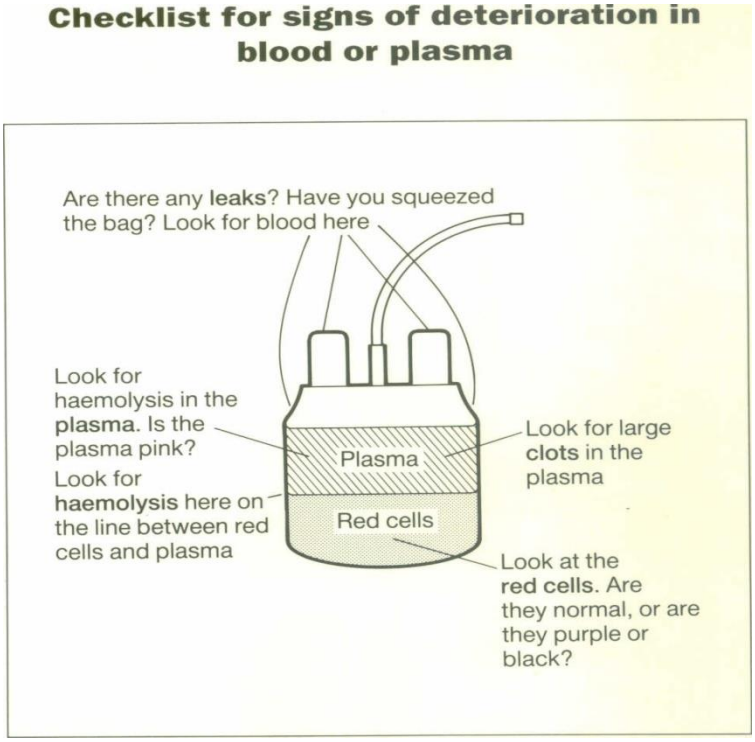
- If one unit of blood is intended, a 3-5 ml sample in EDTA vial should be sent.
- For every additional unit 1 ml more blood in plain vial should be sent.
- From infants (age < 4 months) send EDTA sample of mother and infant. 5cc clotted blood from the mother and 1cc EDTA blood from the baby must be sent. For repeated transfusions only a sample from the mother is enough.
- For double volume exchange transfusion (DVET) send 3 ml mother's sample along with neonatal EDTA sample.
- Blood sample for cross matching should not be collected more than three days before the intended transfusion
- When requesting plasma components or platelet concentrate if blood group has not been checked, blood sample should be sent with the request.
- Telephone request in a real emergency situation should be accepted, but a written request must be followed.
- In the case of investigations of transfusion reaction, post transfusion clotted blood sample and EDTA blood sample should be sent with the remains of the implicated blood unit. A properly filled reaction form must accompany.
- Deliver the sample and requisition form to the blood bank.
- Blood bank laboratory performs antibody screen and compatibility tests. In case of problems in crossmatching, blood bank may require more time to locate a unit of blood that is compatible.

3.9 Receipt of Blood and Blood Component for Transfusion Instructions for Administration of blood

- The unit of blood for transfusion should be collected just prior to starting the transfusion. Use a clean cool box to transport blood bag from blood bank to the ward.
- Never store blood or blood components in unmonitored domestic refrigerators as optimum storage conditions cannot be assured. Platelet bags should not be stored in a refrigerator. Temperature of an air-conditioned room is their optimum storage temperature (22 – 240C). Use them as soon as possible after receipt.
- Always Inspect the blood bag as shown in figure 4.1 for haemolysis, change of colour turbidity and leakage. By the time the bag reaches the ward the distinct separation between the red cells and plasma is not visible, however the red colour with a metallic shine will indicate haemolysis.
- Visually check the blood unit for clots, unusual colour, and any leaks.
- Completely haemolysed packed red blood cell unit can be recognised by change in colour from red to black. In case of any doubt, you can get blood units checked from Dept. of Transfusion Medicine staff before transfusion
- Blood components like cryoprecipitate and FFP should be used immediately on receipt in ward.
- Saline washed red cells prepared by open system should be used within 06 hours.
- Ensure administration of blood within half an hour of issue from the blood bank. If there is a delay return the blood pack to the blood bank within 30 minutes without damaging the blood bag. Non-medical reasons for delay in starting a blood transfusion should be avoided.
- Except in emergency avoid blood transfusion at night.
- For routine transfusion use 18G needles. For paediatric transfusion use 23 G scalp vein set.
- Administer blood or blood components through the disposable transfusion set with a filter.
- Check and record the blood pressure, pulse rate, temperature before, during and after transfusion.
- The rate of infusion depends on the condition of the patient. It is a recommended practice to start the infusion slowly for the first fifteen minutes approximately at the rate of 100 ml / hour or 1-6 ml / minute (24 drops). After the 15 minutes if no adverse reactions occur the rate can be increased. Packed cells may be infused in 2 hours and whole blood transfusion must complete in 4 hours. An exception for rapid transfusion of whole blood is in patient's having congestive heart failure or a patient in danger of fluid overload; use of packed red cells would alleviate this problem.
- Observe the patient for any transfusion reactions; febrile reactions, haematuria, oliguria, hypotention etc.

- In case of any transfusion reactions stop the blood transfusion and inform the physician concerned and blood bank. [Depending on the signs and symptoms, or in mild reactions, the transfusion maybe temporarily stopped, and resumed at a slow rate after assessing the patient]
- Send remaining blood unit or component unit and 5cc of clotted post transfusion blood sample along with the transfusion reaction form to the blood bank for the investigations.
- In the case of uneventful transfusion note the time of finishing the blood transfusion and the exact amount of blood transfused.
- **Please note blood transfusion is a dangerous procedure which can cost a patient's life. It must be done with extreme caution and care by authorised personnel only. All procedures and steps must be strictly followed. Your carelessness can cost a patient's life.**

Figure 1



3.10 Steps at the Time of Transfusion

3.10.1 Before starting transfusion check the following

- Patient's name and identity. Document that checking is done and is correct. Patient's name and admission number on crossmatch report
- Donor unit number on crossmatch report and blood bag
- Blood group of unit and patient's blood group

- Expiry date of blood bag
- Verify all checks and in case of doubt do not start the transfusion

3.10.2 Starting the Transfusion

- Record the name and signature of the nurse who checked the identity of the patient and who started the transfusion.
- Reconfirm patient identification information by a second individual to prevent any human error.
- There is no need for routine premedication of the patient. Only if the patient has had a febrile reaction during previous transfusion, antipyretic may be given. Routine use of antihistaminic is not indicated, as allergic reactions are very rare.
- Wash hands before starting a transfusion.
- Record date and time of beginning and termination of blood transfusion with signature of the transfusionist.
- Check before starting transfusion that there is no air bubble in IV line, the filter is wet and the drip chamber is not more than half full.
- Monitor patient's pulse, blood pressure and temperature prior to initiation and during blood transfusion.
- Observe for the first 30 minutes as risk of catastrophic events like ABO haemolytic reactions and anaphylactic reactions are maximal during this period.
- Record the amount of blood transfused.

3.11 Blood Warming

- There is no need to warm blood in elective transfusion where a unit of blood is transfused over 2-4 hours. Warming of blood is not necessary for routine transfusions.
- Keeping the patient warm is more important than warming infused blood.
- It is a misconception that infusion of blood without warming is responsible for febrile reactions.
- As blood flows drop by drop it attains body temperature.
- Warming of blood results in increased red cell metabolism, reduced 2,3-DPG and increased risk of bacterial growth.

3.11.1 Indications for warming of blood

Warmed blood is most commonly required in:

- Large volume rapid transfusions:

  - Adults: greater than 50 ml/kg/hour
  - Children: greater than 15 ml/kg/hour
- Transfusions to neonates
- Exchange transfusion in infants
- Patients with clinically significant cold agglutinins.

Warming of blood is useful when rapid transfusion of components is required, especially in trauma or surgery settings because infusion of cold blood /components can cause hypothermia and cardiac complications, increasing morbidity and mortality for the patient. Transfusion at rapid rates (100ml/min) for 30 minutes of refrigerated blood can lower the temperature of the sino-atrial node to below 30°C and cause ventricular arrhythmias and cardiac arrest.

3.11.2 Procedure of blood warming in case of need

Blood should only be warmed in a blood warmer. Blood warmers should have a visible thermometer and an audible warning alarm and should be properly maintained.

- Use a monitored electric warmer or temperature monitored water bath. Do not warm blood to over 37°C.
- Blood warmers are commercially available. These warm the blood as it flows through the tubing.
- Blood should not be warmed by placing in a microwave, on a heat source, or in unmonitored hot water or by using other devices not specifically approved for blood warming.

- **Blood should never be warmed in a bowl of hot water as this could lead to haemolysis of the red cells which could be life-threatening.**

3.12 Addition of Drugs and Medications to Blood Bag / Blood Set

- **Except normal saline, addition of drugs to blood bag should never be done.** Use only 0.9% sodium chloride for injection USP to dilute packed red cells for reducing viscosity. Whenever required, saline should be added to the blood bag preferably in the blood bank
- Do not use IV line used for any other intravenous solution except normal saline and 5% albumin for transfusing blood.
- Do not use 5% dextrose or Ringer Lactate for dilution of packed red cells as it causes hemolysis of red cells.

- Simultaneous administration of 5% dextrose results in haemolysis while Ringer Lactate causes clotting of blood in the tubing.
- Addition of drugs may cause changes in the blood pH. A change in the pH and ionic molecular constituent of the administered drug can make it ineffective. Besides it may lead to bacterial contamination.
- In case a reaction occurs, it would be impossible to ascertain the cause responsible for the reaction.

3.13 Blood Transfusion Filters

All blood components must be infused using transfusion sets with inbuilt filters (standard filter – 170μ) as it helps to remove clots, cellular debris and undesirable particles.

3.14 Rate of Transfusion

- For first 15 minutes transfuse at a slow rate - approximately 25-50 ml blood.
- In case of no reaction increase the rate depending on the recipient's hemodynamic status
- All blood transfusions must be completed in 4 hours' time limit. In a hemodynamically stable patient transfusion can be completed within 2 hours. However, for a hemodynamically unstable patient it should take up to 4 hours.
- In case medical condition of recipient demands transfusion over a longer period request the blood bank to divide the unit into aliquots and transfuse each over 4 hours as there is a risk of bacterial contamination of the blood clots collected in the set filter.
- In elderly patients and in patients with congestive cardiac failure adjust the rate and volume to avoid the risk of cardiac overload. Consider the use of diuretics in these cases.
- When rapid transfusion is required, blood pressure cuff is not ideal for providing external pressure on blood bag to increase the rate of infusion, as it can cause barotraumas and haemolysis but if used in emergency the cuff pressure should be 100-150 mm Hg.
- Commercially available in line infusion pump is the method of choice and may be used when available for regulating and monitoring the rate.
- Infuse platelet concentrate at 1- 2 ml per minute or as tolerated by the patient.
- To avoid circulatory overload, the plasma volume of apheresis platelet concentrate can be reduced by the blood bank.

3.15 Measures to increase blood flow rate

In case the blood flow rate is slow, one should take following measures to increase the flow rate

- Elevate blood container
- Check size and patency of needle / catheter
- Examine filter for excess debris
- Examine blood bag for presence of small clots
- Shake the blood bag gently during transfusion as the red cells tend to sediment

Table 1: Blood component administration to adults (doses and transfusion rates are for guidance only and depend on clinical indication)

Blood Components	**Administration of Blood & Blood Components**
Packed Red Blood Cell (PRBC)	Transfusions must be completed within 4 hours of removal from controlled temperature storage.
	Many patients can be safely transfused over 90–120 minutes per unit.
	A dose of 4 mL/kg raises Hb concentration by approximately 10 g/L. Note: The common belief that one red cell pack = 10 g/L increment only applies to patients around 70 kg weight – the risk of transfusion-associated circulatory overload (TACO) is reduced by careful pre-transfusion clinical assessment and use of single-unit transfusions, or prescription in millilitres, for elderly or small, frail adults where appropriate.
	During major haemorrhage, very rapid transfusion (each unit over 5–10 minutes) may be required.
Platelets	One adult therapeutic dose (ATD) (Pool of four units of RDPs or single-donor apheresis unit) typically raises the platelet count by $20–40\times10^9$/L.
	Usually transfused over 30–60 minutes per ATD.
	Platelets should not be transfused through a giving-set already used for other blood components.
	Start transfusion as soon as possible after component arrives in the clinical area.
Fresh Frozen Plasma (FFP)	Dose typically 12–15 mL/kg, determined by clinical indication, pre-transfusion and post-transfusion coagulation tests and clinical response.
	Infusion rate typically 10–20 mL/kg/hour, although more rapid transfusion may be appropriate when treating coagulopathy in major haemorrhage.
	Because of the high volumes required to produce a haemostatic benefit, patients receiving FFP must have careful haemodynamic monitoring to prevent TACO.
	FFP should not be used to reverse warfarin (prothrombin complex is a specific and effective antidote)
Cryoprecipitate	Typical adult dose is two five-donor pools (ten single-donor units).
	Will raise fibrinogen concentration by approximately 1 g/L in average adult.
	Typically administered at 10–20 mL/kg/hour (30–60 min per five-unit pool).

3.16 At the end of blood transfusion

- Transfusionist should identify himself / herself clearly and monitor patient's condition and vital parameters.
- Return transfusion reaction form to the blood bank.
- Observe the patient for one hour
- Monitor for post transfusion effects as per component transfused and patients' clinical condition, along with the post transfusion sample and the transfusion reaction form.
- Dispose of the used blood bag after transfusion along with other bio hazardous waste in ward if there is no reaction.
- In case of transfusion reaction send the bag back to the blood bank along with a sample and the transfusion reaction reporting form.

3.17 Patient Bedside Safety

Table 2: Checklist for Safe Blood Transfusion

BEFORE	**DURING**	**AFTER**
• Check patient identity: name, date of birth, hospital registration / National Identification Number. • Check compatibility report with product identity: blood group, unit no., expiry date • Check Product integrity • Document date and time of starting • Check TPR • Check if correct set is used • Check if specific needs are provided (e.g. warming, irradiation, Leuco depletion filter.) • Check there is no air bubble in the line, filter is wet and drip chamber is not more than half full • Start transfusion • If transfusion is delayed store the product at correct temperature	• Observe closely for first 15-30 minutes • Monitor Temperature, Pulse, Respiratiory rate (TPR) • Monitor rate of flow – maintain slow rate for first 30 minutes • Observe the clinical status of the patient • Check venepuncture site • Change set if required • If any adverse reaction occurs: - Take immediate action - Stop the transfusion - Inform clinician - Record - Inform Blood Bank	• Document time and volume • Check TPR and record • Dispose bag / set / needle • Observe patient for half hour • Look for any delayed reaction • Look for evidence of improved clinical status

3.18 Documentation

Documentation of every step is a legal requirement. All documentation should to be kept confidential. Following information should be recorded to prove appropriate use of blood:

i. Reason for transfusion
ii. Tests done to decide regarding need for transfusion
iii. Screening tests done on blood before use
iv. Number of units transfused and observations during transfusion
v. Patient's health before and after transfusion
vi. Tests done to record post transfusion improvement

3.19 Traceability of blood

The records should be such that it is possible to trace the blood unit to donor as well as recipient and vice versa.

3.20 Don'ts for Blood Transfusion

- Do not use blood without mandatory screening tests
- Do not insist on use of fresh blood
- Do not ask for all blood units which are crossmatched at one time
- Do not delay initiation of blood transfusion once the blood has reached the ward
- Do not warm blood without proper monitoring
- Do not use pre-transfusion medication routinely
- Do not transfuse one unit over more than 4 hours
- Do not use one transfusion set for more than 4 hours or for more than 2 units of blood.
- Do not use the transfusion set used for other infusions for transfusing blood components
- Do not leave patients unmonitored during the blood transfusion. Avoid routine transfusions at night.
- Do not add any medication to blood bags
- Do not forget to return unused blood to the blood bank for safe disposal
- Do not use unmonitored refrigerators for storage.

- Do not store platelets in a refrigerator
- Do not be complacent about checking patient's identity
- Do not use blood from immediate relatives unless irradiated

3.21 Hospital Transfusion Committee (HTC)

For implementation of Good Clinical Practices (GCP) it is necessary to establish Hospital Transfusion Committees in all hospitals.

3.21.1 Members of Hospital Transfusion Committee should include

- Medical Director or medical superintendent as chairman
- Senior consultants of all clinical specialties that prescribe blood
- Staff responsible for supply of intravenous fluids and disposable transfusion equipment
- Matron or senior nurse
- MO I/C blood bank as secretary
- This committee should meet at least twice a year. A copy of the minutes should be forwarded to Director NBTS for information and actions as required.

3.21.2 Responsibilities of the Hospital Transfusion Committee

The Role of HTC should be:

- To monitor safety, adequacy, accessibility and reliability of supply of blood, blood products and intravenous fluids
- To procure blood and components from National Blood Centre as per need
- To ensure use of blood as per guidelines
- To develop MSBOS
- To monitor use of blood and blood products using defined indicators
- To monitor transfusion practices in wards and operation theatres
- To monitor blood bank operations
- To conduct training for staff concerned
- To develop policies, systems and documents for record keeping
- To investigate and report all errors and mishaps. To implement measures of error prevention in future

- To review incidences of adverse reactions or errors associated with transfusion for which corrective and preventive actions are taken
- To plan any future needs regarding expansion of activities, procurement of equipment and reagents
- To review the procedures and introduce new technologies as per need
- To evaluate and resolve problems faced by hospital and blood bank staff
- To forward all reports to NBTS for compiling country reports
- To comply with all recommendations of NBTS
- To avoid coercion of patients and their relatives to replace blood
- To provide measures for safety of staff
- To provide facilities to ensure correct transfusion practices
- To implement non-profit cost recovery system and ensure that all patients receive blood without any discrimination and commercial motives.

3.22 Hemovigilance

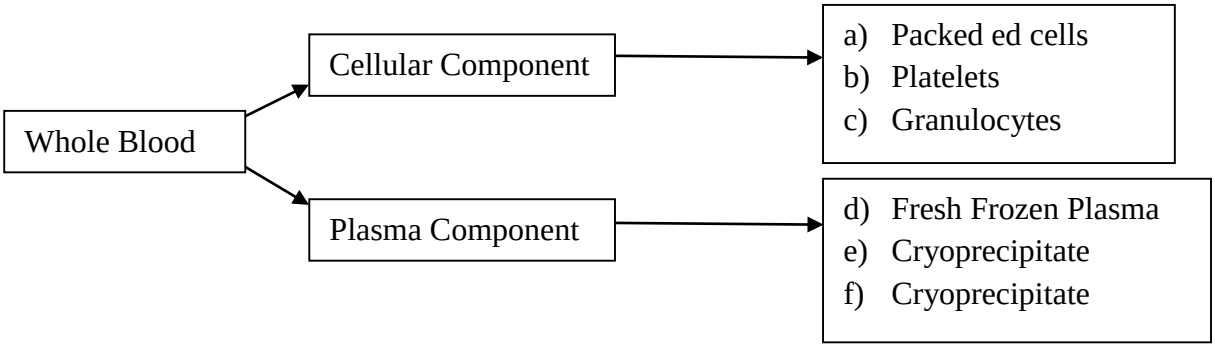
This is set of surveillance procedures, from the collection of blood and its components to the follow up of recipients to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products and to prevent their occurrence or recurrence.

The major aim of the hemovigilance is to track adverse events related to blood transfusions and to help identify trends and recommend best practices and interventions required to improve blood safety in the country.

All the clinical colleagues should report all transfusion reaction related to blood to the Hospital transfusion committee/blood bank

Chapter 4 – Whole Blood and Blood Products

Figure 2: Whole blood is an essential source of therapeutic blood products, having both cellular and plasma components.



Difference in the specific gravity of each cellular component, availability of sterile blood bag systems (single, double, triple, quadruple), equipment's as refrigerated centrifuge and advancement in component preparation techniques makes it possible to separate whole blood from a single blood donor into three or four blood components. These components are individually stored at appropriate temperature to preserve their function to be used as per patient's need. Patient receives only the component required to treat his condition.

4.1 The different types of Blood Components (Cellular and Plasma) and Plasma Derivatives

4.1.1 Red Blood Cells

- Packed Red blood cells (PRBC) in CPDA-1
- Red Blood Cells (Adenine-Saline Added,SAGM)
- Red Blood Cells Leukocytes Reduced (LR-RBC)
- Red Blood Cells Deglycerolized
- Red Blood Cells Irradiated
- Red Blood Cells Washed
- Red Blood Cells Apheresis

4.1.2 Platelets

- Random donor platelets (RDP)
- Pooled Platelets

- Single donor Apheresis Platelets (SDAPs)
- Platelets Leukocytes Reduced (RDP/SDAP)
- Platelets Irradiated

4.1.3 Granulocytes

- Granulocyte Concentrate
- Apheresis Granulocytes

4.1.4 Plasma components

- Fresh frozen plasma
- Single donor plasma
- Cryoprecipitate
- Cryo-poor plasma
- Liquid Plasma

4.1.5 Plasma derivatives

- Albumin 5% & 25%
- Plasma Protein Fractions
- Factor VIII concentrate
- Immunoglobulins
- Fibrinogen
- Other coagulation factor

Paediatric PRBC units can be prepared by dividing adult PRBC unit into three parts using sterile connecting device and using transfer bags attached to the mother bag.

4.2 Advantages of blood components

1. A single donation benefits several different patients.
2. Components such as white cells or plasma proteins which are not necessarily required in certain patients are not to be transfused, thereby preventing transmission of infections as CMV, TTI etc.
3. The storage is optimised by the correct choice of anticoagulant, additive solution, temperature, bag type and other quality parameters to ensure effectiveness of each component for the longest period.

4.3 Whole Blood:

Whole blood is a complex tissue from which clinically appropriate components are processed. If not processed further into components it maintains its properties for a limited period only. It is recommended not to use whole blood in hospitals where blood components are made available by the National blood transfusion service.

Many of the components, particularly platelets and clotting factors, deteriorate in whole blood within hours of donation viz:

- Deterioration of unstable coagulation blood factors like V and VIII.
- Decreased platelet viability and diminution beyond 12 hours of collection, thereby not effective in treatment of patients requiring platelets.
- Stored blood contains no viable platelets.
- Deterioration of Leucocytes with release of proteases.
- Formation of microaggregates.
- Decreased 2, 3 DPG levels – (However it regenerates after transfusion in the circulation of the recipient)
- Increased potassium level in plasma due to release of the intracellular potassium.
- Increased acidity of the plasma.

The clinical indications for using whole blood are limited since RBC concentrates are more appropriate in most situations where O2-carrying capacity needs boosting.

Limited Indications of Whole Blood:

- Exchange transfusion in neonates
- Massive haemorrhage

4.4 Selection of ABO compatible donor red cells for crossmatching

Identical ABO group or ABO compatible blood should be used. Rh negative patients should get Rh negative blood especially women in childbearing age group.

Side effects: -

- Circulatory overload in cases of decompensated anaemia, heart, and renal failure.
- Formation of antibodies in the patient against donor red cell antigens and human leukocyte antigens (HLA) leading to transfusion reactions
- Transfusion transmitted infections (TTIs).

- Citrate intoxication in neonates and in patients with impaired liver function getting massive transfusion.
- Hyperkalemia in massive transfusion.

4.5 Fresh Blood

Blood collected within last 24 hours is usually called "fresh" as it contains all the blood components. It is advisable to the clinicians not to prescribe fresh blood due to following reasons: -

- Providing less than 24 hours old blood is not possible if reliable tests are to be carried out for transfusion transmissible infections.
- Demand for fresh whole blood as a source of coagulation factors, platelets and white blood cells is unjustified as such specific components could be administered.
- **In many countries where blood component therapy is available, fresh blood has become a nonentity in transfusion practice. Particular component of blood that is needed for treatment is transfused**
- There is no added advantage of fresh blood over stored blood if transfusion is prescribed for correcting anaemia
- Many infectious agents like spirochetes, malarial parasites, bacteria do not survive at storage temperatures after few days making stored blood safer.
- Blood less than 5 days old is recommended for exchange transfusions in newborns to prevent hyperkalaemia and to supply red cells with adequate content of 2,3-DPG.
- Blood less than 10 days old can be used for patients with hepato-renal problems as they cannot take care of the metabolites such as K, ammonia and haemolysis developed in blood during storage.
- Multi transfused patients require to be transfused blood < 10 days old to avoid frequent transfusions.
- In all other cases blood up to expiry date can be used for increasing haemoglobin.
- Unjustified use of recently collected blood also increases the wastage of other blood units due to outdating. Hence it is preferable to follow first in first out (FIFO) policy.
- Use of whole blood is not encouraged as this may lead to depletion in the supply of the blood components. The transfusion of components not required poses an increased risk to the patient

4.6 Cellular Components

4.6.1 Red Cell Components

Packed Red Cells components are obtained by removal of plasma either by sedimentation method or centrifugation of whole blood. Depending on the blood bag used for collection and processing of blood, packed red cells are designated as PRBC (CPDA-1) and PRBC (SAGM)

Table 3: Specification for Red Blood Cell component of whole blood

Parameter	Whole Blood (WB)	PRBC (CPDA-1)	PRBC-SAGM
Description	Whole blood collected from blood donor in CPDA-1 Solution	Red blood cell concentrates from which most of plasma has been removed	Red cell concentrate from which major part of the plasma and the buffy coat layer has been removed with subsequent addition of a nutrient Solution (SAGM).
Volume	399 ml (350 + 49 ml CPDA-1); 513 ml (450 + 63 ml CPDA-1)	200 to 300 ml	250 to 350 ml
Haemoglobin	12 g /100ml	20 g/ 100 ml (≥45g /bag)	20 g/ 100 ml ≥45g /bag
Haematocrit	30-40%	65-75%	55-65%
Storage temperature	+2 to +6°C in approved blood bank refrigerator, with fitted temperature chart and alarm		
Shelf Life	35 days	35 days	42 days
Indications	▪ Replacement of red cells in acute blood loss ▪ Exchange transfusion ▪ Patient needing red cell transfusions where PRBCs are not available	▪ Replacement of red cells in anaemic patients ▪ In acute blood loss along with crystalloids and colloids	▪ Replacement of red cells in anaemic patients ▪ Patients who have experienced febrile reactions to previous red cell transfusion.
Administration	• Transfuse using standard blood transfusion set with 170µm filter. • Transfusion should be started within 30 minutes of issue. • Complete transfusion within 4 hours of commencement		

4.6.2 (PRBC-CPDA-1)

Red blood cell concentrates from which most of plasma has been removed.

4.6.3 Red Cells in Additive Solution (PRBC-SAGM)

Red cells suspended in an additive solution containing saline, adenine, glucose, and mannitol (SAGM) extends the shelf life to 42 days. Haematocrit is reduced to 50-55% and the viscosity of blood is also reduced allowing ease of transfusion during surgery.

4.7 Modified Red Cells Products

4.7.1 Leukoreduction

Leukoreduction (LR) is a technical term for the removal of leucocytes (white blood cells) from blood components using special filters. This can be performed during the manufacturing of blood components via pre-storage LR at the time of or soon after collection as well as before transfusion through a special filter through the transfusion set.

The leucocytes present in donated blood have no therapeutic role in transfusion and may be a cause of adverse transfusion reactions. Removal of leucocytes may therefore have a number of potential benefits for transfusion recipients, including:

- Reduced risk of febrile non-haemolytic transfusion reactions (FNHTR)
- Reduced risk of CMV transmission
- Reduction in storage lesion effect
- Reduction in the incidence of bacterial contamination of blood components
- Possible reduced risk of transfusion-associated graft vs host disease (TA-GVHD)
- Possible reduction in transfusion related immunomodulatory (TRIM) effects, including cancer recurrence, mortality, non-transfusion transmitted infection
- Possible reduced risk of transmitting variant Creutzfeldt-Jakob Disease (CJD)

Pre-storage LR means blood is filtered as soon as possible preferably within 48 hrs of donation. it has been shown to reduce FNHTR. Two mechanisms thought to cause FNHTR are:

- Cytokines released into stored components from contaminating white blood cells;
- The reaction of recipient antibodies with 'foreign' donor white blood cell antigens

Therefore, removal of white blood cells from blood components by leukoreduction provides a preventive measure against these two possible underlying causes of FNHTR.

On demand leukoreduction by filtration where usage is low and requested only when required for a particular patient. It is done by using a filter, sterile connecting device and transfer bag in the blood bank. This is cost effective as cost of filters if used for all bags is high.

4.7.2 Buffy coat removed (Leuco-reduced) Red Cells in Additive Solution (RC-BCR in SAGM)

Whilst separating the red cells, when quadruple bags with top bottom system are used, the buffy coat is separated out before preparation of red cells and platelets. After this the additive solution is added to the red cells. The residual leucocyte count is $<5 \times 10^8$. Micro-aggregate formation during storage is greatly reduced in BC removed red cells. This is suitable for use in multi transfused patients to prevent febrile non-haemolytic transfusion reactions.

4.7.3 Washed Red Cells Unit

Washing of red cells with sterile normal saline removes unwanted plasma proteins, including antibodies. Washing of red cells removes up to 90% of the leucocytes. The residual leucocyte count is <5x 108 that prevents febrile transfusion reactions, but not HLA alloimmunization. Plasma removal during washing eliminates antibodies and other plasma constituents that cause adverse effects in recipients. Washed red cells are given to patients who require red cells with a low protein supernatant. There will be some loss of red cells with washing itself. The following groups of patients should receive washed components:

- Reactions to transfused plasma proteins (e.g., IgA deficiency)
- Severe allergic reactions of unknown cause
- Severe reactions despite leucocyte depletion
- Paroxysmal nocturnal haemoglobinuria who experiences reactions despite group-specific leucocyte depleted fresh red cells

Precaution: Since washing of red cells makes it an open system, transfusion is recommended within 6 hours.

4.7.4 Cryopreserved Red Cells

Cryopreservation of red cells extends the shelf life of red cells up to ten years if preserved at -80°C. 40% glycerol is used as Cryo protective and cryopreservation is usually done for rare blood group

types. The red cells need to be thawed at 37°C for 20 minutes before washing with saline prior to its usage.

4.7.5 Irradiated Red cells

Blood components containing viable lymphocytes upon transfusion are known to cause immunomodulation in the recipients. Therefore, these blood components may be irradiated to prevent the proliferation of T-lymphocytes, which is the immediate cause of Transfusion-associated graft-versus-host disease (TA-GVHD).

The minimum dose achieved in the irradiation field should be 25 Gamma with no part receiving greater than 50 Gamma. Red cells may be irradiated at any time up to 14 days after collection, and thereafter stored for a further 14 days from irradiation. Platelets can be irradiated at any stage in their 5-day storage and thereafter can be stored up to their normal shelf life of five days after collection. Granulocytes for all recipients should be irradiated as soon as possible after production. Gamma irradiation of red cells may also increase level of extracellular potassium. The clinical significance of this potassium load depends on both the speed and volume of the transfusion, as well as the age of the blood.

4.8 Transfusion for Packed Red Cells

Group specific red cell concentrate is the best option for assuring blood group compatibility. In case of shortage, use of alternative blood group is possible in consultation with medical officer of blood bank as per table below:

Table 4: Selection of ABO Compatible Donor Red Cells

Recipient ABO group	Donor ABO group			
	1st choice	2nd choice	3rd choice	4th choice
O	O	None	None	None
A	A	O	None	None
B	B	O	None	None
AB	AB	A	B	O
Oh (Bombay Group)	Oh	None	None	None

55% of blood collected is O group in Male.

4.9 Selection of Rh compatible donor red cells:

- Rh positive patients can be transfused with Rh positive and Rh-negative blood.
- Rh negative blood can be used for Rh positive patients without any problem as Rh-negative blood does not have any naturally occurring Rh antibodies.
- Only 4% of blood collected in Male is Rh negative. Hence if a Rh-negative patient does not require this blood when it is in storage it gets wasted due to outdating.
- **Rh negative males or elderly females** with no potential for childbearing can safely receive Rh positive blood in circumstances where Rh negative blood is not available.
- **Rh negative female patient in the childbearing age** must receive Rh negative blood. In circumstances where a surgery is planned or forthcoming childbirth, the blood bank should be informed at the earliest to make Rh negative blood available as Rh-negative blood is always not readily stocked at the blood banks.
- In case of emergency when Rh negative blood is not available, it may be necessary to use Rh D positive blood.
- Following transfusion of >15ml up to 1 unit of blood, it is advisable to give IV anti-D IgG at dose of 50- 75 IU/ml of blood. All efforts should be made to make Rh negative blood available at the earliest once urgency is managed.
- Red cell concentrates can be transported in cool boxes with freeze packs. If freeze pack is not available, ice in a double plastic bag should be used to avoid direct contact of ice with the blood bag.
- It is preferable to transfuse immediately as domestic refrigerators in clinical areas do not achieve optimum temperature of 40C. If blood bank refrigerator is available in clinical area, blood can be stored for a longer period.
- Transfusion of 1 unit of red cell concentrate can increase haemoglobin level by 1 gm / dl in an adult patient.
- Transfusion set with standard 170μ filters should be used for administration.

4.10 Pheno-typed Red Cells (Extended blood grouping)

Apart from ABO and Rh, 28 more known blood groups are there on red cells. Repeated transfusion makes the recipients more prone to develop allo-antibody against various blood groups. Blood group matched (pheno-typed) red cells are transfused in patients prone to receive multiple units

1. Thalassemia

2. Patients on dialysis therapy
3. Hemato-oncology patients

Thalassemia patients should be provided with Rh and Kell blood group matched units to reduce the risk of alloimmunization. Phenotyping (extended blood grouping) can be performed for platelets as well for patients requiring specific antigen-negative components such as platelets in cases of platelet refractiveness due to alloimmunisation.

4.11 Platelet Concentrate

Platelet concentrates are prepared from blood donations collected within 12 minutes of venepuncture and processed within 6-8 hrs of collection of blood stored at 22-24°C. Donor should not have taken asprin 72 hours prior to donation

4.11.1 Random Donor Platelets (RDP)

Platelet concentrate made from a unit of whole blood by centrifugation of whole blood.

Prepared by two methods using: -

1. Platelet rich plasma (PRP)
2. Leuco-reduced Platelets (Buffy coat leucocyte reduced)

1 unit of RDP prepared from 450 ml whole blood should have at least 50 x 10^9 platelets but is less if prepared from 350ml whole blood.

Volume of 1 unit RDP is approximately 50 ml, and one unit of platelet concentrate increases the platelet count by 10,000 to 20,000/ul of blood.

4.11.2 Aphaeresis Platelets / Single Donor Platelets (SDP)

Platelet concentrate obtained from single donor by apheresis using a cell separator machine is called single donor platelet. All other components are returned to the donor. The platelets collected may be leucocyte reduced.

Volume of 1 unit SDP is 200 – 350 ml and one unit of SDP should have 300 x 10^9 platelets equivalent to approximately 6 units RDP. The shelf life is 5 days.

4.11.3 Platelet Concentrates – RDP/SDP

- Platelet concentrates are stored in a platelet incubator at 22°C – 24°C on a platelet agitator or rotor.
- Platelet concentrate should be transported without ice and transfused as soon as possible. Do not store in a refrigerator.

- It is always better to transfuse ABO specific platelets (RDP) except in case of ~~1~~short supply of platelets.
- Blood group specificity is not considered, if random donor platelet concentrate is not contaminated with red cells. ABO compatible platelets can be used.
- SDAPs should be ABO group specific.
- Rh D negative platelet concentrate should be given whenever possible to Rh D negative patients, particularly to women who have not reached the menopause.
- If Rh D positive platelets are transfused to a Rh D negative woman of childbearing potential, it is recommended that anti-D should be given. A dose of 250 IU anti-D I/M. should be sufficient to cover 5 adult therapeutic doses of platelets within a 6-week period. It should be given subcutaneously in thrombocytopenic patients.

Table 5: Specification for Platelet component of whole blood

Parameter	**Platelet Concentrates (PC)**	**Apheresis Platelets (SDAP)**
Description	Platelet concentrates are prepared from either 350 ml or 450 ml whole blood. They are also called Random donor platelets (RDP)	Platelet concentrate derived from blood donor using an apheresis machine and disposable kit. It is also called single donor apheresis platelets (SDAP)
Volume	50 to 90 ml	200-300ml
Platelet Content	3.5 to 4.5 X 10^{10} /unit	3 to 7 X 10^{11} /unit
Dosage	1 unit of platelet concentrate/10 kg body weight: in a 60 or 70 kg adult, 4–6 RDP	One pack of platelet concentrate collected from a single donor by apheresis is usually equivalent to one therapeutic dose
Storage and Shelf Life	3 to 5 days at 20°C to 24°C (with agitation)	5 days at 20°C to 24°C (with agitation)
Indications	a. Thrombocytopenia b. Platelet function defects c. Prevention of bleeding due to thrombocytopenia, such as in bone marrow failure	a. Same as for RDPs b. Patients experiencing frequent febrile reactions with platelet concentrate
Administration	a. Transfuse using standard blood transfusion set with 170µm filter. b. Initiate transfusion slowly for first 15 minutes unless massive blood loss.	a. Same as Random donor platelets, but b. ABO compatibility is more important as plasma volume is large
Do not store at 2°C to 6°C in Refrigerators as it makes them non-functional **Caution:** Platelets are prone to develop bacterial contamination; Transfusion should be started immediately after receiving the units in the ward and should be completed over a period of about 30 minutes.		

4.12 Transfusion of Platelets

Table 6: Suggested ABO Group for platelet (RDP) transfusion

Recipients ABO group	**Component ABO group**			
	1st choice	**1st choice**	**1st choice**	**1st choice**
AB	AB	A	B	O
A	A	AB	B	O
B	B	AB	A	O
O	O	A	B	AB

Swirling test should be performed before transfusion, a visual check to see scattering of light by platelets with normal morphology.

4.13 Granulocyte Concentrate

4.13.1 Buffy Coat Granulocyte Concentrate

1 unit of Buffy Coat should have at least 1 - 2 x 10^9 white cells, and 9.5g of haemoglobin (60% hematocrit) in 50ml if amount of whole blood collected is 450 ml. Granulocyte concentrate made from a unit of whole blood.

4.13.2 Apheresis Granulocyte

Granulocyte concentrates prepared by apheresis contain $1x10^{10}$ granulocytes.

4.13.3 Selection of ABO Compatible Granulocytes

- Granulocyte concentrate or buffy coat should be ABO & Rh group specific.
- For granulocyte transfusions compatibility test is required as the product is heavily contaminated with red cells.

4.13.4 Storage and Administration of Granulocytes

- Granulocyte concentrates are stored at 22-24°C without agitation up to 24 hours. **Do not refrigerate.**
- Granulocyte concentrates should be irradiated to prevent Graft vs Host Disease (GVHD) before use whenever possible.
- Transfusion sets with standard filters (170μ) should be used for administration.

- With availability of sensitive antibiotics and growth factors, use of granulocytes has reduced except in neonatal septicaemia as neonatal macrophages are not capable of phagocytosis.

4.14 Plasma Components

Plasma is the liquid removed from a centrifuged unit of whole blood.

Fresh Frozen Plasma (FFP) is prepared by snap freezing the plasma component of whole blood within 6-8 hrs of collection.

- FFP is stored at -20°C or lower and has a shelf life of one year.
- FFP contains labile as well as stable coagulation factors.

When in frozen form the plastic of the bag is rigid and fragile, requiring care while handling.

- Volume of 1 unit of FFP is 200-220 ml stored at >-30°C
- Compatibility testing is not necessary for FFP.
- Should be thawed in a plasma thawed at 37°C before issue from the blood bank
- Should be transfused immediately on receipt in the ward / operation theatre.
- Once thawed FFP should not be refrozen.

Table 7: Suggested ABO Group Selection for Plasma/FFP transfusion

Recipients ABO group	**Component ABO group**			
	1st choice	**2nd choice**	**3rd choice**	**4th choice**
AB	AB	None	none	None
A	A	AB	none	None
B	B	AB	none	None
O	O	AB	A	B

- Rh group need not be considered in FFP/Plasma transfusions as there is no red cell in the product.

4.15 Cryoprecipitate

4.15.1 Preparation: -

Cryoprecipitate is prepared from FFP by thawing at +4°C and suspending in 10-20 ml plasma. One unit of Cryoprecipitate contains approximately

- 150 mg Fibrinogen
- 80 IU Factor VIII
- von Willebrand factor
- Some Factor XIII activity

4.15.2 Indications: -

- Congenital or acquired fibrinogen deficiency
- For treatment of hemophilia A and von Willebrand disease when factors are not available
- For treatment of DIC in combination with other blood components
- Treatment of bleeding tendency associated with uremia who are non-responsive to dialysis
- As a fibrin sealant in absence of commercially available products

4.15.3 Dose and administration:

- Each unit increases fibrinogen by 5 to 10mg%. In a bleeding patient, a reasonable target for fibrinogen is 100mg%.
- ABO compatible cryoprecipitate is not required.
- No crossmatching is required
- 6 to 8 units are needed normally, and they are pooled and transfused within 4 hours
    - Stored at >-30°C. Thawed at 37°C in the blood bank.
    - Cryoprecipitate once thawed cannot be refrozen and reused.
    - Transfuse immediately on receipt in the ward /operation theatre.

4.15.4 Cryosupernatant / Cryopoor Plasma (CSP/CPP)

- Cryopoor plasma (cryoprecipitate depleted or 'cryosupernatant') is the supernatant plasma removed during the preparation of cryoprecipitate from FFP.
- Cryosupernatant plasma provides stable clotting factors but is depleted in FVIII and fibrinogen.
- Cryosupernatant is deficient in high molecular weight multimers of vWF, but contains vWF metalloproteinase and hence superior to FFP for therapeutic plasma exchange in case of thrombotic thrombocytopenic purpura (TTP).
- ABO group selection for transfusion is same as in plasma/FFP.

4.16 Liquid or stored plasma

- Plasma separated from whole blood anytime during storage period.
- Provides stable coagulation factors.

Table 8: Specification for Plasma component of whole blood

Parameter	Fresh Frozen Plasma (FFP)	Cryoprecipitate
Description	Plasma separated from one whole blood donation within 6 hours of collection and then rapidly frozen to –30°C to -80°C	Prepared from fresh frozen plasma by collecting the precipitate formed during controlled thawing at +4°C.
Volume	150–220 ml	15 to 20 ml
Content	• Contains normal plasma levels of stable clotting factors, albumin and immunoglobulins. • Factor VIII level at least 70% of normal fresh plasma levels.	• Factor VIII: 80–100 IU/ bag; • Fibrinogen: 150–300 mg/bag
Dosage	Initial dose of 15 ml/kg	1 bag / 10 kg body weight
Storage and Shelf Life	At –30°C to -80°C for up to 1 year; Use preferably within 6 hrs after thawing at 37°C	
Indications	Replacement of multiple coagulation factor deficiencies: e.g. • Liver disease • Warfarin (anticoagulant) overdose • Depletion of coagulation factors in patient receiving large volume transfusions • Disseminated intravascular coagulation (DIC) • Thrombotic thrombocytopenic purpura (TTP)	• As an alternative to Factor VIII concentrate in the treatment of inherited deficiencies of: A. von Willebrand Factor (von Willebrand's disease) B. Factor VIII (haemophilia A) C. Factor XIII • As a source of fibrinogen in acquired coagulopathies: e.g., disseminated intravascular coagulation (DIC)
Administration	A. Must normally be ABO compatible to avoid risk of haemolysis in recipient. B. Infuse using a standard blood administration set (with 170µm filter) as soon as possible after thawing. C. Labile coagulation factors rapidly degrade; use within 6 hours of thawing	A. Can be transfused across ABO barrier. ie do not need compatibility testing. B. After thawing, infuse as soon as possible through a standard blood administration set. C. Must be infused within 6 hours of thawing.

4.17 Plasma Derivatives

These are procured commercially as fractionation facility is not available in Maldives.

These derivatives include Albumin 5%, Albumin 20%

Immunoglobulin – IM/IV

FVIII & FIX

The plasma fractionation process requires viral inactivation to minimise the risk of transmitting infections.

Factors VIII & IX and immunoglobulins are also made by recombinant DNA technology and are often favoured because there is no risk of transmitting infections. However, the costs are high.

4.18 Storage of Blood & Blood Components Prior to Transfusion

The 'Blood cold Chain' is the system for storage & transportation of blood & blood components so that they are kept at the correct temperature at all times from collection from donor to administration to the patient. Any break in the blood cold chain increases the dangers for the recipients of blood components.

Clinical staff is responsible for ensuring that blood products issued by the BTS for transfusion are kept at the correct temperature until their infusion into the patient.

4.18.1 Red Cells & Whole blood

Red cells & whole blood must always be stored at a temperature between +2 degree C to +6-degree C. They must never be allowed to freeze. The upper limit of 6 degree C is essential to minimize the growth of any bacterial contamination in the unit of blood.

Below 2 degree C Red cells become haemolysed. Haemolysed cells if transfused cause renal failure & fatal bleeding problems. Whole blood & red cells should be issued from the blood bank in the blood transport box or insulator carrier that will keep the temperature under 10-degree C.

Group specific red cells are issued after proper cross matching. Once issued red blood cells should be transfused within ½ hour of release from BTS. If not required should be sent back to BTS immediately.

4.18.2 Fresh Frozen Plasma (FFP)

Fresh Frozen Plasma is stored in BTS at -40 degree C or colder until it is thawed before transfusion. Most of the clotting factors are stable at refrigerator temperature except for factor V & VIII. Its approximate volume is 150-175 ml/bag. It is thawed at 30 degree C - 37degree C water bath. It takes about 30-45 minutes to thaw the FFP. It is transported in a blood transport box in which the temperature is maintained between +2 to 6-degree C. Once thawed it should be infused within 30 minutes.

If not required for immediate use it can be kept at 2 degree C – 6 degree C & transfused within 24 hours. Once thawed the FFP cannot be refrozen & has to be discarded. So as not to waste blood components, demand only when essential & in the required quantities. Group specific FFP has to be

transfused after proper cross matching. However, AB group plasma being a neutral plasma (no antibodies) can be transfused to any group patient.

4.18.3 Platelets – Platelet Rich Plasma (PRP)/ Platelet Concentrate (PC)

Platelet components are stored at 22 degree C -24 degree C in platelet agitator to maintain platelet function. Volume of platelet concentrate is 30-50 ml & volume of PRP 150-170 ml. One unit of Single donor (Aphaeresis platelet) has a volume 150-300ml. Platelet components are to be transported in a blood transport box that keeps the temperature at about 20 degree C – 24-degree C. **DO NOT REFRIGERATE** the platelet components. Transfuse platelets as soon as possible. Whenever large quantities of platelets are required for special procedures, inform the BTS at least 24 hours in advance. Platelet concentrate of any group can be transfused to any group patient, but PRP has to be group specific.

4.18.4 Cryoprecipitate

It is stored at -40 degree C or lower. The volume of cryoprecipitate is 25-30 ml. It is thawed at 30 degrees to 37 degree C water bath which takes about 15-30 minutes. Once thawed it should be transfused within 30 minutes. If not immediately transfused it is kept at 2 degree C- 4 degree C & can be transfused within 4 hours of thawing. It cannot be refrozen, if not transfused, it has to be discarded.

Table 9: Optimum Storage conditions for blood components

COMPONENT	**Storage Temp.**
Whole Blood	2^0 - 8^0 C
Red Cell Concentrate	2^0 - 8^0 C
Recorrected Red Cell Concentrate with SAGM	2^0 - 8^0 C
Platelet Concentrate (RDP/SDP)	20^0 - 24^0 C with agitation
Granulocyte Concentrate / Buffy Coat	20^0 - 24^0C
Fresh Frozen Plasma Cryo poor plasma/plasma	< -30^0C

Chapter 5 – Guidelines for Use of Blood and Blood Components in Acute Blood Loss

5.1 Blood Transfusion in Acute Blood Loss

Accidents, surgery, childbirth, stomach ulcers, and blood vessel rupture can cause a sudden loss of blood. Although all types of blood loss may cause complications, it is the large and rapid blood losses that occur during surgery and trauma that are most likely to cause severe complications or death. The amount of blood loss that may lead to complications depends on the individual person. It is affected by factors such as body size and the presence of certain health conditions.

The more blood is lost, and the faster it is lost, the more severe the symptoms and complications.

It is important to estimate blood loss and treat the hypovolemic shock which is a medical emergency. Severe blood and fluid loss impedes the heart to pump sufficient blood to the body. As a result, tissues cannot get enough oxygen, leading to tissue and organ damage. If left untreated, this condition can be fatal. Complications can be more serious in people taking blood thinners or those with bleeding disorders.

5.2 Estimation of Blood Loss

- Amounts of blood loss is based on patient's initial presentation and assumed that the patient is a 70 kg male with a blood volume of 70ml/kg.
- The rapidity of the volume lost may be as important as the total volume of haemorrhage.
- Many of the signs and symptoms are non-specific.
- A number of other parameters will affect the patient's vital signs and physical findings.
- It is necessary to assess surgical blood loss throughout the surgical procedure. Many of the autonomic and central nervous system signs of significant hypovolemia can be masked by the effects of general anaesthesia. Monitor the signs of hypovolemia (HR, BP, CVP and urine output)
- The volume of expected surgical blood loss that necessitates fluid replacement and blood transfusion is shown in Table 10

5.3 Acute haemorrhage

It may be classified into different categories as per American college of surgeons on the basis of blood loss and signs and symptoms.

Table 10: Classification of Acute Haemorrhage

American College of Surgeons Classification of Acute Haemorrhage				
Class	I	II	III	IV
Blood loss (ml)	< 750	750- 1500	1500-2000	≥ 2000
% Blood loss	< 15%	15-30%	30-40%	≥ 40%
Pulse rate	< 100	> 100	> 120	≥140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or increased	Decreased	Decreased	Decreased
Capillary refill	Normal	Delayed	Delayed	Delayed
Respiratory rate	14- 20	20- 30	30- 40	< 35
Urine output (ml)	>30	20- 30	5- 15	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Recommended fluid replacement	**0.9 % saline, 3:1***	**0.9 % saline, 3:1***	**0.9% saline + red cells**	**0.9% saline + red cells**

5.4 Management of acute blood loss

- Replacement of blood volume and not red cell mass should be the first priority in managing acute blood loss.
- Losses of red cell mass are better tolerated than losses of blood volume.
- Expansion of blood volume leads to improvement in oxygen delivery to the tissues thereby reducing the need for red cell transfusions
  - **Class I blood loss**: no fluid replacement therapy is needed in an otherwise healthy individual

- **Class II blood loss**: maintain an adequate intravascular volume by fluid replacement therapy which improves the red cell transport and thereby oxygen delivery to the tissues.
- **Class III blood loss**: healthy, non-anaemic patients may even respond well to fluid replacement, but those with pre- existing anaemia or with increased risk of organ ischemia will need red cell transfusion.
- **Class IV blood loss:** urgent fluid replacement therapy and red cell transfusion is indicated since such a patient will be in a state of hemorrhagic shock.

5.5 Role of replacement fluids:

Isotonic crystalloid solutions like normal saline or Ringer's lactate is the first initial choice for volume expansion. Dextrose solutions do not contain sodium and are poor replacement fluids. Hence, they should not be used to treat hypovolemia. The volume of crystalloid fluids needed to restore the intravascular volume is approximately 3 to 4 times the estimated blood loss.

If colloids are used, they are given in a volume equal to the blood volume lost. They provide longer duration of plasma volume expansion than crystalloids but are expensive in comparison to crystalloids.

Table 11 : Non-Plasma Colloid Volume Expanders

Product	Source	Conc. of solution	Average Mol. Wt.	Intravascular persistence	Approximate frequency of severe acute reactions
Modified Fluid Gelatine	Heat degraded Cattle borne gelatine*	3-4%	35,000	50% of infused volume persists for 4-5 hours	1 in 10,000 infusions
Hydroxy ethyl starch	Maize starch, chemically modified	6%	450,000 265,000	similar to or longer than Dextran 70	1 in 20,000 infusions
Dextran 70	Hydrolysed Starch	6%	70,000	50% of infused volume persists for 24 hours	1 in 10,000 infusions
Dextran 40	Hydrolysed starch	10%	40,000	Shorter than Dextran 70	1 in 50,000 infusions

* Beware of nvCJD

Chapter 6 – Guidelines for Blood Transfusion in Anaemia

Although the haemoglobin concentration is an important indication of anaemia, it is necessary to consider patient's clinical condition to judge the need for red cell transfusion. The decision to transfuse red cells in a case of anaemia should be guided by following parameters

- Cause of anaemia
- Severity and chronicity
- Patient's ability to develop compensatory mechanism
- Extent of blood loss
- Tissue hypoxia and its prevention

Table 12: Levels of Anaemia

Mild	> 9 g /dl	Usually, asymptomatic
Moderate	6-9 g /dl	Symptoms on exertion
Severe	< 6g /dl	Symptoms at rest

6.1 Role of Red Cell Transfusion in Anaemia

- The main function of red cells is to increase oxygen carrying capacity and avoid tissue hypoxia. Oxygen delivery depends on oxygen content of the blood and the cardiac output.
- If haemoglobin concentration falls the oxygen delivery is affected. In this case the compensatory mechanism comes into action. There is increase in cardiac output, reduced viscosity of blood and peripheral vasodilatation which support oxygen delivery.

6.2 Guidelines for Red Cell Transfusion in anaemia

- Prevention of anaemia is a vital issue which requires introduction of health education programme, dietary supplementation, and fortification of food products. Control of infections such as hookworm infestation is also important
- It is important to diagnose and treat the cause of anaemia. Transfusion should be kept as last resort as it may suppress erythropoiesis.
- Patient's clinical condition and not the laboratory result should be the determining factor for transfusion needs.
- Chronic, asymptomatic anaemic patients do not require blood transfusion.
- Anaemic patients having coexisting cardiac, pulmonary disease or both or Cerebro-vascular disease may require transfusion at higher haemoglobin levels than an otherwise healthy patient.

- The symptoms/signs of hypoxia to be looked for in a decompensated anaemic patient that needs blood transfusion.

Table 13: Signs/ Symptoms of hypoxia

Easy fatigability	Transient ischemic attacks
Shortness of breath, chest pain -postural hypotension	Angina-tachycardia
Syncope, fainting attacks	Swelling legs
Fainting attacks	Dyspnoea

- Anaemic patients with hypovolemia of some etiology should be corrected by restoring intravascular volume with crystalloids.
- Red cell transfusions should not be advised to increase colloid osmotic pressure, or used as volume expanders, substitutes for iron, B12 supplements, or to improve wound healing or sense of well-being.
- Do not transfuse more than the required amount of blood. The aim of blood transfusion in these patients is to treat life threatening hypoxaemia and not to raise haemoglobin to normal level.

6.3 Acute onset Anaemia

- In acute anaemia red cell transfusion is indicated if haemoglobin concentration is 7g/dl or less.
- Patients over 65 years of age, those with cardiac or respiratory disease may tolerate anaemia poorly and should be transfused when haemoglobin is < 8g/dl.
- In case of acute blood loss during surgery or in patients with acute haemorrhage up to 30% of loss, normovolemia can be maintained with use of replacement fluids. More than 30% blood loss may require replacement of red cells.
- Adequate volume replacement, maintenance of blood pressure and use of inotropic drugs to maintain cardiac output needs to be considered before red cell transfusion.
- Use of red cells corrects prolonged bleeding time in uremic patients. However, in other haemostatic disorders it is important to evaluate need for other blood components.

Table 14: Haemoglobin alone is not the trigger for transfusion

If Hb > 10g /dl	RC Transfusion unlikely to be appropriate
If Hb < 7g /dl	RC Transfusion likely to be appropriate
If Hb 7 - 10g /dl	May be appropriate only on clinical judgment

6.4 Guidelines for Blood Transfusion in Chronic Anaemia

6.4.1 Blood Transfusion in Nutritional Anaemia

Blood transfusion is only occasionally required in anaemia due to nutritional deficiencies. Administrations of appropriate haematinics in adequate doses generally correct symptoms and raise haemoglobin. Blood transfusion (packed red blood cells are preferred) is considered only if the patients have severe and life-threatening decompensation i.e., patients having signs and symptoms of following:

- Congestive heart failure e.g., severe breathlessness
- Cerebrovascular insufficiency e.g., giddiness and syncope
- Coronary insufficiency

In these cases, the cause of anaemia should be established and treated.

- Monitor for development and worsening of cardiac failure, if so, give injection frusemide 20 to 40 mg i.v. bolus or 1-3 ml / kg bodyweight.
- Appropriately treat infections (particularly lung infection).

6.4.2 Guidelines for red cell transfusion in Thalassemia

1. Blood transfusion is occasionally needed in patients with thalassemia intermedia.
2. Thalassemia major patients are transfusion dependent. Regular and periodic blood transfusions are essential from early life in patients with severe thalassemia (homozygous beta thalassemia major)
3. Always take blood samples from the patient for haematological investigations before ordering a blood transfusion. It is preferable to do an extended grouping of the patient before initiating the transfusion process so that if antibodies develop in future, it is easy to identify them.
4. Patients with good cardiopulmonary conditions should be transfused every 3/4 weeks with pack cells at a rate of 2-3 hours per unit.
5. Pre-transfusion haemoglobin level should be maintained at 10 gm/dl. This level of haemoglobin is considered adequate to suppress extramedullary erythropoiesis and excessive absorption of iron from the gut.
6. Post transfusion haemoglobin should not rise above 14g/dl as higher levels will increase blood viscosity and the risk of thrombosis.
7. Patients with cardiac failure or with very low haemoglobin levels (less than 5mg / dl) should receive 5ml /kg body weight of packed red cells at a rate of 2ml /kg / hour.

8. Annual blood consumption should be calculated by dividing the total volume of blood transfused over 12 months by patient's weight in the middle of the year. If the blood consumption is higher than 200ml /kg body weight, splenectomy should be considered.

6.4.3 Guidelines of transfusion in Sickle cell disease

Blood transfusions are not indicated as a routine to raise haemoglobin but should be reserved for specific indications. The aim is to raise the haemoglobin concentration to normal steady state but never raised acutely to > 10g /dl as this is likely to increase blood viscosity.

6.4.3.1 Indications for simple top up transfusion

- Severe anaemia
- During surgery or anaesthesia
- Splenic or hepatic sequestration
- Aplastic crisis / severe vaso-occlusive events
- Prophylactic transfusions to prevent stroke

6.4.3.2 Indications for hyper transfusion

- Patients on regular transfusions to prevent recurrence of stroke
- To delay or prevent deterioration in end organ

This aims at maintaining haemoglobin level between 10-14g/dl and HbS below 25%.

6.4.3.3 Indications for exchange transfusion

- Acute chest syndrome to reduce sickling and increase oxygen carriage without an increase in viscosity
- Conditions such as stroke and priapism
- Exchange transfusion reduces the percentage of HbS in the blood. It may also be used to minimize iron overload in patients on regular transfusions.

6.4.3.4 Indications in surgery

- Top up transfusion aiming for Hb 8 -10g/ dl

- Minor and straightforward procedure (e.g., tonsillectomy, cholecystectomy) can be safely undertaken without transfusion in most patients.
- Transfusion should be performed preoperatively for major procedure e.g., hip or knee replacement, organ transplantation, eye surgery and for major abdominal surgery

6.5 Problems of multiple transfusions in patients with hemoglobinopathies

a) Alloimmunization: antibody detection and compatibility testing can prevent haemolytic transfusion reactions. Always take blood samples from the patient for haematological investigations before starting a blood transfusion.

b) It is preferable to perform extended red cell phenotyping and antibody screening at reference lab at Maldivian Blood Services before commencing regular transfusion therapy. It is also advisable to use indirect antiglobulin crossmatch technique for each unit being transfused.

c) Non haemolytic febrile transfusion reactions can be prevented by use of saline washed or buffy coat removed packed red blood cells and preferably leuco-depleted red cells if available. Pre-medication with paracetamol orally one hour before blood transfusion reduces unpleasant symptoms.

d) Prevention of Transfusion transmitted infections: Hepatitis B, C and HIV
   - Use blood from voluntary non-remunerated blood donors that has undergone all mandatory tests.
   - Give hepatitis B vaccine to all patients who are HBsAg negative and to freshly diagnosed cases before starting a transfusion regimen.

e) Iron overload causes damage to endocrine organs, liver, and heart. Iron chelation therapy should be considered after 10 transfusions and started once ferritin level is more than 1000 **µ**g/l. Administer desferrioxamine 40 mg/kg daily subcutaneously or use appropriate oral iron chelation therapy.

1. Blockage of peripheral veins: Steps to preserve veins should be undertaken from early life.
2. Hyperviscosity: can precipitate vascular occlusion.
   - Maintain circulating fluid volume.
   - Transfuse only to maximum haemoglobin level of 12g/dl
   - Exchange red cell transfusion may be required to achieve a sufficient reduction of HbS red cells without increasing viscosity.

6.6 Guidelines for Transfusion in patient with warm autoimmune haemolytic anaemia (WAIHA)

- Patients with warm reactive autoantibodies range from those with no apparent decreased red cell survival to those with life threatening anaemia.
- The clinical decision to initiate transfusion therapy in WAIHA depend on multiple factors including patients' clinical status, the potential benefit of transfusion, the potential response to other therapeutic modalities, status of serologic evaluation and pretransfusion testing. Severe but stable anaemia at initial presentation is often well tolerated and may respond during the first week of therapy to corticosteroids.
- When autoantibody is active in serum it may be difficult to exclude the presence of alloantibodies which increase the risk of adverse reaction.
- Transfusion may stimulate alloantibody production, complicating subsequent transfusion.
- Transfusion may intensify the autoantibody, increasing haemolysis and making serological testing more difficult.
- Transfusion may depress compensatory erythropoiesis; destruction of transfused cells may increase hemoglobinemia and haemoglobinuria. In patients with active haemolysis, transfused red cells may be destroyed more rapidly than the patient's own red cells. In rare cases this may promote hypercoagulability and DIC. Transfusion reactions if they occur may be difficult to investigate.

6.6.1 Transfusion in Acute WAIHA.

- Transfusion is especially problematic for patients with rapid in vivo haemolysis, who may present with very low haemoglobin level and hypotension.
- Patients with rapidly falling haematocrit may exhibit coronary insufficiency, congestive heart failure, cardiac decomposition, or neurologic impairment.
- Under these circumstances, transfusions are usually required as a life saving measure and need not be withheld solely because of serologic incompatibility.
- The volume transfused should usually be the smallest amount required to maintain adequate oxygen delivery. Transfuse the unit found suitable by blood bank slowly and under strict vigilance for transfusion reactions.
- Use pre- medication with steroids. Use of IV IgG is known to be effective.

6.6.2 Transfusion in chronic WAIHA.

- Most patients with WAIHA have a chronic stable anaemia, often at a relatively low haemoglobin level. Those with haemoglobin levels above 8g /dl, rarely require transfusion, and many patients with levels of 5g /dl can be managed with bed rest without transfusions.
- Transfusion will be required if the anaemia progresses or is accompanied by symptoms such as severe angina, cardiac decompensation, respiratory distress, and cerebral ischemia.

6.7 Guidelines for Transfusion in Cold Hemagglutinin Disease

- Patients suffering from Cold agglutinin Disease can often be managed without transfusion. Acute red cell destruction may be reduced by keeping the patient in a warm room, to prevent complement binding by the cold agglutinin.
- Steroid therapy is not usually successful. In the event that severe anaemia necessitates red cell transfusion, washing red cells to remove residual plasma as a source of additional complement is not required.

6.8 Guidelines for transfusion in G6PD deficiency

- G6PD deficiency is commonly asymptomatic and can cause jaundice and anaemia precipitated by infection, drugs or chemicals.
- Haemolysis will stop once the cells that are most deficient in G6PD have been destroyed. It is important to remove or treat any identified cause.

Transfusion requirement

- Transfusion is not required in most cases of G6PD deficiency.
- Transfusion may be lifesaving in severe haemolysis when the haemoglobin continues to fall rapidly.
- Exchange transfusions are indicated for neonates at risk of kernicterus and who are unresponsive to phototherapy.

6.9 Guidelines for Transfusion in patients with bone marrow failure or suppression due to chemotherapy

- Chemotherapy, irradiation therapy and bone marrow transplant commonly suppress bone marrow further and increase the need for transfusion support with red cells and platelets until remission occurs.
- Anaemia due to the underlying disease and to treatment may become symptomatic and require red cell replacement. A red cell component is preferable to whole blood as the patient is at risk of circulatory overload.

Protocol for Transfusion

1. If repeated transfusions are likely to be needed, use leucocyte reduced red cells and platelets wherever possible, to reduce the risk of reactions and of alloimmunisation.
2. Avoid transfusing blood components from any blood relative to prevent the risk of TA-GVHD.
3. Some immunosuppressed patients are at risk of cytomegalo virus infection transmitted by blood transfusion. This can be avoided or reduced by transfusion blood that is tested and contains no CMV antibodies or by using leuco-depleted blood components.

Chapter 7 – Blood Transfusion in Major Surgery

1. Available evidence does not support the use of single criteria such as preoperative Hb concentration to decide on preoperative blood transfusions.
2. The surgeon has to take a decision on the basis of patient's condition, type of surgery – whether major or minor, duration of surgery, anticipated blood loss, clinical condition of patient and anaesthesia and surgical technique to be used.
3. Blood transfusion practices in elective surgery vary greatly between hospitals and individual surgeons. These differences are due to:
   - Medical condition of patients
   - Surgical and anaesthetic techniques available
   - Guidelines on the use of blood
   - Availability of blood products and its cost
   - Use of alternatives to transfusion.

7.1 Factors to be considered for Initial patient assessment

- Age of the patient
- Preoperative haemoglobin concentration
- Pre-existing medical condition e.g., hypertension, diabetes, chronic renal failure, peripheral vascular disease, bleeding diathesis, chronic obstructive pulmonary disease, cardiac problems
- Medications in use

7.2 Preoperative haemoglobin (Hb) level

A threshold Hb level of approximately 7g/dL in a well-compensated and otherwise healthy patient presenting for surgery is accepted. However, a higher Hb level will be required if the patient has:

- Symptoms/signs of inadequate compensation of anaemia and insufficient O_2 supply to the organs
- Coexisting cardio respiratory disease like ischemic heart disease
- Major surgery is planned, or a significant blood loss is anticipated (> 1000 ml in an adult or > 10 ml / kg in a child)

7.3 Planning for Blood Transfusion in Major Surgery depends on the operation

- Whether blood normally is used for this type of operation.
- Can the need be reduced or eliminated?

- Can the transfusion trigger be lowered?
- Can the patient be treated with haematinics?
- Can the blood loss be avoided?

7.4 Protocol for Major Surgery

1. Keep ready one or two intravenous access, a pressure infusion and warming device for an impending blood loss
2. Use surgical and anaesthetic techniques to reduce operative blood loss
3. Optimise all components of the O_2 delivery system in order to improve the O_2 supply to the tissues considering the following equation:

   Hb x O_2 saturation x cardiac output (CO) = O_2 supply to the tissues

   - Ensure normovolemia, thereby increasing the CO
   - Following general anaesthesia, the effects of hypoxia will be compounded in a patient with an already reduced Hb level or in hypovolemia. Therefore, it is essential to give supplementary O_2 in the postoperative period.
   - The replacement of blood loss with fluids results in haemodilution, which reduces the viscosity of blood, which in turn improves capillary blood flow and CO, thus enhancing the supply of O_2 to the tissues.
   - Increase the inspired O_2 concentration to raise the saturation of Hb.
   - Transfuse if necessary to raise the Hb concentration.
   - Use only the blood component the patient needs and, in the quantity, required.
4. To avoid haemostatic problems
   - Do Coagulation screening for all major surgeries.
   - If a patient is found to have thrombocytopenia or an abnormal coagulation screen (prolonged PT or APTT) the procedure should be postponed while the cause of the abnormality is identified. If a congenital bleeding disorder is found, the patient must be managed accordingly or in conjunction with a haematologist.
   - If the platelet count is below 100 x 10^9/l before surgery, which is likely to cause significant blood loss or bleeding in a critical site e.g., CNS, it must be investigated before starting the procedure.
   - Unless it is contra-indicated to do so, warfarin anticoagulation should be stopped before elective major surgery in time to allow the prothrombin time ratio to approach normal. This should be guided by a local protocol for preoperative anticoagulant management.

- A single dose of aspirin (½ tablet of 150 mg or ½ junior aspirin 75 mg) impairs platelet function for several days. Aspirin should be stopped at least 7 days before planned major surgery, if safe to do so. When an aspirin-induced platelet defect contributes to abnormal bleeding platelet transfusion is likely to be effective. In case aspirin is very essential to the patient, local haemostatic measure e.g., fibrin glue should be considered.

7.5 Blood Ordering Schedule

- A blood schedule is a guide to expected normal blood usage for elective surgical procedures, which lists the number of units of blood to be routinely grouped or crossmatched, screened and held for each procedure preoperatively.
- The development and use of a blood ordering a schedule enables the identification of procedures that can be accommodated by the group and screen procedure. This will lead to:
  - Reduction in unnecessary compatibility testing
  - Reduction in the return of unused blood
  - Reduction in wastage due to outdating
  - More efficient management of blood inventory.

7.6 How to develop a maximum surgical blood ordering schedule (MSBOS)

A blood ordering schedule should be developed by each hospital transfusion committee in accordance with National guidance on the adaptation of a model blood ordering schedule for local use. The hospital transfusion committee (HTC) can evolve a maximum surgical blood ordering schedule (MSBOS) by auditing blood usage in their hospital.

The process of developing a blood-ordering schedule involves the following steps:

- Retrospective analysis of requests for blood over at least a 6- month period
- For each surgical procedure, analysis of:
  - Type of procedure
  - Reason for request of blood
  - Number of units crossmatched
  - Number of units transfused
  - Percentage of units used
- Calculation of the C: T ratio (crossmatch to transfusion ratio). A realistic objective for surgical procedure is a C: T ratio of approximately 2.5 -3 :1

Table 15: MSBOS

Procedure	**Action**	**Procedure**	**Action**
General surgery		**Obstetrics & Gynaecology**	
Cholecystectomy	G & S	Termination of pregnancy	G & S
Laparotomy: planned exploration	G & S	Normal delivery	G & S
Liver biopsy	X-M 2	Caesarean section	G & S
Hiatus hernia	G & S	Placenta praevia/retained placenta	X-M 4
Partial gastrectomy	X-M 2	Antepartum / postpartum	X-M 2
Colectomy	G & S	haemorrhage	
Mastectomy: simple	X-M 2	Dilatation & curettage	G & S
Mastectomy: radical	X-M 2 (+2)	Hysterectomy:abdominal or	G & S
Thyroidectomy: partial/total	G & S	vaginal:simple	
Cardio thoracic		Hysterectomy:abdominal or	X-M 2
Angioplasty	G & S	vaginal:extended	
Open heart surgery	X-M4 (+4)	Myomectomy	X-M 2
Bronchoscopy	G & S	Hydatidiform mole	X-M 2
Open pleural/lung biopsy	G & s	Oophorectomy(radical)	X-M 4
Lobectomy/pneumonectomy	X-M 2	**Orthopaedics**	
Vascular		Disc surgery	G & S
Aortic-iliac endarterectomy	X-M 4	Laminectomy	G & S
Femoral endarterctomy	G & S	Removal hip pin or femoral nail	G & S
Femoro-popliteal bypass	G & S	Total hip replacement	X-M 2(+2)
Ileo-femoral bypass	X-M 2	Ostectomy/bone biopsy (except	G & S
Resection abdominal aortic	X-M 6 (+2)	upper femur)	
aneurysm		Nailing fractured neck of femur	G & S
Neurosurgery		Laminectomy	G & S
Craniotomy,	G & S	Internal fixation of femur	X-M 2
Meningioma	X-M 4	Internal fixation: tibia or ankle	G & S
Head injury, Extradural haematoma	G & S	Arthroplasty: total hip	X-M 3
Vascular surgery (aneurysms, A-V	X-M 3	Spinal fusion(scoliosis)	X-M 2
malformation)		Spinal decompression	X-M 2
		Peripheral nerve surgery	G & S

Urology			
Ureterolithotomy	G & S		
Cystostomy	G & S		
Ureterolithotomy & Cystostomy	G & S		
Crystotomy	X-M 4		
Open nephrolithotomy	X-M 2		
Open prostatectomy (RPP)	X-M 2		
Transurethral reaction	G & S		
Prostatectomy (TURP)	X-M 2		
Renal transplantation			
X-M = Crossmatch G & S = ABO / Rh group and antibody screen (+) Indicates additional units may be required, depending on surgical complications			

- Surgical procedures with a blood usage of less than 30% should be included in the group and screen (G&S) category. In this case the availability of the blood of a specific group is ascertained besides possibility of immediate cross match as no antibodies are present
- Monitoring and evaluation of the blood-ordering schedule by verifying compliance
- Periodic review and, where appropriate, revision of the blood ordering schedule

7.7 Techniques to Reduce Operative Blood Loss

7.7.1 Surgical techniques

- Prompt, meticulous and minimally invasive surgery
- Meticulous attention to surgical techniques and bleeding points
- Use of appropriate diathermy, haemostatics (collagen, felt warm packs)
- Positioning of the patient to encourage free unobstructed venous drainage at the operative site. The level of the operative site should be a little above the level of the heart whenever possible.
- Use of vasoconstrictors – e.g., adrenaline with local anaesthesia
- Use of tourniquets - Inflation pressure should be approximately 100-150 mmHg above the systolic blood pressure. For a bloodless operative field, the limb should be first exsanguinated using bandage or elevation prior to inflation.

7.7.2 Anaesthetic techniques

- Avoid episodes of hypertension/tachycardia due to sympathetic over activity by providing adequate levels of anaesthesia and analgesia.
- Avoid coughing, straining and patient manoeuvres, which increase venous pressure.
- Hypercarbia can cause vasodilatation and reduce blood loss, but due to associated risks it is not recommended.
- Regional anaesthesia (epidural/spinal).
- Hypotensive anaesthesia can reduce blood loss. This is safe in expert hands only.
- Avoid hypothermia

7.7.3 Use of pharmacological agents

- Antifibrinolytic drugs - Aprotonin and tranexamic acid inhibit the fibrinolytic system of blood and encourage clot stability.
- Desmopressin (DDAVP) acts by increasing the release of Factor VIII
- Use of local haemostatic agent e.g., Fibrin glue
- Use of F VIIa to control bleeding

Chapter 8 – Guidelines for Massive Blood Transfusion

Massive transfusion is defined as:

- Replacement of the patient's total blood volume within 24 hours
- A replacement of 50% of circulating blood volume in < than 3 hours
- Transfusion of more than 150ml/minute (provides better idea of blood loss, for a quicker response)

8.1 Massive Transfusion

It is management of a case where rapid infusion of substantial volumes of fluids together with red cell replacement is likely to be required over a few hours as a result of major bleeding. The protocol in such cases should be to:

- Maintain adequate blood volume
- Maintain sufficient oxygen carrying capacity
- Secure haemostasis by
- Estimating blood volume (70 mL / kg in adult; 80 mL / kg in infants).
- Inserting a large IV cannula, obtain blood samples and infuse crystalloid as rapidly as possible until an acceptable systolic blood pressure is restored. Maintain adequate blood oxygen transport capacity.
- Use of Dextran and Hydroxy Ethyl Starch (HES) should be limited to 1.5 litre per 24 hours in an adult (refer to package insert)
- Avoiding saline in patients with severe liver disease in whom sodium overload is a special risk. Also take care with 5% Albumin in these patients for the same reason.
- Inform the blood bank of the urgency, ABO and Rh D compatible blood to be made available rapidly after receipt of the sample.
- If red cell loss is life threatening, un-crossmatched group O Rh-negative red cells can be used, if the patient blood group is unknown.
- Regular haemoglobin or haematocrit assessment to monitor blood and fluid therapy, but restoration of normovolemia is the first priority.
- Coagulation screens should be performed to help detect haemostatic failure (usually due to DIC) and to guide the use of blood components.
- Patients with major haemorrhage require monitoring of pulse rate, blood pressure, CVP, blood gases and acid-base status. A urinary catheter should be inserted, and urine output monitored. Dedicated care by the midwifery, nursing and medical staff is vital. Transfer to ICU should be considered early.

- Laboratory tests of haemostasis help to identify the need for blood components to control micro vascular bleeding. The platelet count, prothrombin time (PT) or activated partial thromboplastin time (APTT) should be monitored during large transfusions to guide replacement therapy.

8.2 Blood component replacement:

- When there is no pre-existing haemostatic problem, replacement of up to 1 blood volume (8-10 units of blood in an adult) with red cells and non-plasma fluids is unlikely to cause haemostatic problems due to dilution.
- In an adult, platelets should be given if there is severe micro vascular bleeding (MVB) with a platelet count below 50 x 109/l (especially if more than one blood volume has been replaced) or if laboratory results suggest there is DIC.
- FFP should be used only where there is micro vascular bleeding (MVB) with laboratory results that show abnormal coagulation. A dose of 15 ml/kg is conventional if the fibrinogen level is below 1 g/l and DIC has been diagnosed with severe bleeding. The fibrinogen level should be raised by giving cryoprecipitate (initially in an adult at least 15 packs containing in total 3-4 gm fibrinogen).
- There is no evidence of giving prophylactic platelets or plasma to patients undergoing large transfusions reduces the risk of MVB. Routine prophylactic use of these products for major surgery is not recommended.

8.3 Complications of massive transfusion

- **Hypocalcemia -** The citrate anticoagulant in some blood components bind ionised calcium. This could lower plasma ionised calcium levels, but usually rapid liver metabolism of citrate prevents this. In neonates and patients who are hypothermic, the combined effects of hypothermia and hypocalcaemia may be cardiotoxic. If there is ECG increases in Q-T interval or clinical evidence of hypocalcaemia, 5 ml of 10% calcium gluconate (for an adult) should be given IV slowly. If necessary, the dose should be repeated till the ECG is normal. Note that red cells in additive solution contain only traces of citrate.
- **Hyperkalemia -** The plasma or additive solution in a unit of red cells or whole blood stored for 4-5 weeks may contain 5-10 mmol of potassium. In the presence of acidaemia and hypothermia this additional potassium can lead to cardiac arrest. This is best prevented by keeping the patient warm.

- **Hypothermia -** Rapid transfusion of blood at 40c can lead to cardiac arrest. The best safeguard is to keep the patient warm. A blood warmer should be used in adults receiving large volumes of blood at rates above 50 ml/kg/hr (in children above 15 ml/kg/hr)
- **Acid base disturbances -** Despite the lactic acid content of transfused blood, (1-2 mmol/unit of red cells, 3-10 mmol / unit of whole blood) fluid resuscitation usually improves acidosis in a shocked patient. In practice, transfused citrate can contribute to metabolic alkalosis when large volumes of blood components are infused at a fast rate e.g., 1 unit every minute in an average 70 kg person. Often factors like hypovolaemia, hypotension, liver disease, hypothermia, hyperkalaemia can aggravate this problem.
- **Adult respiratory distress syndrome -** The risk is minimised if good perfusion and oxygenation are maintained, and over-transfusion is avoided. The use of albumin solutions to maintain the plasma oncotic pressure > 20mmHg is often stated to be important. The uses of micro aggregate filters are advisable when stored blood is transfused. These filters are most useful.
- Dilutional coagulopathy may also result with large volume of store blood. Adequate platelets and FFP need to be transfused.

8.4 Post Operative Care

- Monitor vital signs and surgical sites including drains
- If signs of hypoxia appear give supplementary oxygen
- Ensure normovolemia and continue replacement fluids till adequate oral intake is established
- Give analgesics to relieve pain to avoid hypertension and restlessness that aggravates bleeding
- Transfuse blood in case of signs if inadequate tissue oxygenation in presence of continued bleeding
- Consider surgical re-exploration
- Use haematinics in the later post operative period to restore haemoglobin level
- Do not use unnecessary blood transfusion with an idea of early discharge.

Chapter 9 – Guidelines for Platelet Transfusion

9.1 Platelet Deficiency

Deficiency of Platelets is termed as thrombocytopenia and is either due to quantitative or qualitative functional defects in platelets.

9.2 Quantitative platelet disorders – Thrombocytopenia

9.2.1 Due to reduced production of platelets

- Chemotherapy
- Radiotherapy induced myelosuppression
- Bone marrow transplantation
- Myelodysplastic syndrome
- Aplastic anaemia
- Bone marrow infiltration with neoplasm

9.2.2 Increased destruction of platelets

- Exsanguinating blood loss
- Hypersplenism
- Immune thrombocytopenia
- DIC
- Septicaemia
- Viral infections e.g., dengue

9.3 Qualitative Platelet Disorders- Thrombocytopathy

- Glanzemann's thrombesthenia
- Bernard Soulier's syndrome

9.4 Platelet Transfusion

Platelet transfusions are indicated for the prevention and treatment of haemorrhage in patients with thrombocytopenia or platelet function defects. Potential benefits include reducing morbidity / mortality

resulting from minor and major bleeding. The decision to transfuse platelets depends on the clinical condition of the patient, platelet count and cause of thrombocytopenia

It is important to treat the patient and not just the platelet count. Treatment of the underlying cause of dysfunction (ex. Platelet toxic drugs like aspirin) should be attempted first. In such cases platelet transfusions may be required even with platelet counts within the normal range.

9.5 Indications for Platelet Transfusion

9.5.1 Bone marrow failure (due to disease, cytotoxic therapy or irradiation)

Serious spontaneous haemorrhage due to thrombocytopenia alone is unlikely at platelet count above $10x10^9/l$

- **Acute leukemia (excluding pro myelocytic leukemia**)

  Threshold for platelet transfusion can be lowered from $20x10^9/l$ to $10x10^9/l$. Threshold can be reduced further to $5x10^9/l$ in the absence of fever> 38°C or fresh minor haemorrhage

- **Acute pro myelocytic leukemia**

  The presence of a coagulopathy would be expected to increase the likelihood of haemorrhage at any given platelet count. A minimum platelet count should be kept above $20x10^9/l$ in patients who are haemorrhagic.

- **Hemopoietic stem cell transplantation**

  The risk of mucosal injury is generally higher in bone marrow transplantation (BMT) than with chemotherapy for acute leukemia. Threshold for platelet transfusion can be lowered to $10x10^9/l$. Peripheral blood stem cell transplantation results in a shorter duration thrombocytopenia than BMT.

- **Chronic stable thrombocytopenia**

  Patients with chronic and sustained failure of platelet production, as patients with myelodysplasia or aplastic anaemia, may remain free of serious haemorrhage with platelet counts consistently below $10x10^9/l$ or even below $5x10^9/l$. long term prophylactic platelet transfusions may best be avoided in these patients because of the risk of alloimmunization and platelet refractoriness, and other complications of transfusion.

Therapeutic platelet transfusions should be used to treat overt haemorrhage, and such patients may require prophylactic platelet transfusions to prevent recurrent haemorrhage during unstable periods associated with infection or active treatment.

9.6 Prophylaxis for Surgery

- Bone marrow aspiration and biopsy may be performed in patients with severe thrombocytopenia without platelet support, provided adequate surface pressure is applied.
- For lumbar puncture, epidural anaesthesia, gastroscopy and biopsy, liver biopsy, laparotomy or similar procedures, the platelet count should be raised to at least $50x10^9$/l.
- For operations in critical sites such as the brain or eyes, the platelet count should raise to 100x109/l
- It should not be assumed that the platelet count will rise just because platelet transfusions are given, and the preoperative platelet count should be checked to ensure that the above thresholds have been reached.

9.7 Platelet function disorders

- Patients with platelet function disorders rarely need platelet transfusion. Even patients with severe inherited platelet function disorders such as Glanzmann's thrombasthenia only have sporadic bleeding and may have no bleeding for years although heavy bleeding may occur with the fist menstrual period.
- Negligible or no excessive bleeding can be expected in patients with acquired platelet function disorders as the impairment in platelet functions much less than in Glanzmann's thrombasthenia.
- Acquired causes of platelet dysfunction can exacerbate bleeding in patients who already have impaired hemostasis.
- Withdraw drugs known to have antiplatelet activity.
- Correct any underlying condition known to be associated with platelet dysfunction, if possible
- Correct hematocrit to >30% in patients with liver failure, either with the use of recombinant erythropoietin or red cell transfusion
- Consider the use of DDAVP in patients with inherited dysfunction defects, such as storage pool disease
- Consider the use of DDAVP or cryoprecipitate in patients with uraemia
- Use platelet transfusions where the above methods are not appropriate or are ineffective

9.8 Massive transfusion

- Platelet count should not be allowed to fall below $50x10^9$/l in patients with acute bleeding
- A higher target level of $100x10^9$/l has been recommended for those with multiple trauma or central nervous system injury.

9.9 Disseminated intra vascular coagulation (DIC)

Platelet transfusions are a part of the management of acute DIC, where there is bleeding associated with thrombocytopenia in addition to management of the underlying disorder and coagulation factor replacement.

- Frequent estimation of the platelet count and coagulation-screening test should be carried out.
- Maintain platelet count > $50x10^9$/l, as in massive blood loss.
- In chronic DIC, or in the absence of bleeding, platelet transfusion should not be given merely to correct low platelet count.

9.10 Cardiopulmonary bypass (CPB)

- There is no place for prophylactic transfusion of platelets in patients undergoing CPB. Microvascular bleeding, as indicated by continued bleeding /oozing from surgical incisions and venous cannulation sites is the hallmark of platelet related bleeding.
- This usually occurs as a consequence of either thrombocytopenia with a reduced platelet count (<$50x10^9$/l) or acquired platelet dysfunction. CPB induces a transient reversible platelet dysfunction. Platelet count following CPB gives no indication of functioning platelets.
- The use platelet transfusion should be reserved for those patients who are experiencing excessive post operative bleeding and in whom a surgical cause has been excluded.
- The preoperative assessment of patients attending for cardiac surgery should include thorough review of all medications likely to interfere with platelet function, and in these instances, consideration may be given to delaying surgery, the use of appropriate peri-operative pharmaco-therapy (e.g., aprotinin) or recognition that platelet transfusion may be required.

9.11 Liver transplant surgery

- Massive transfusion and hyperfibrinolysis, which occur on reperfusion of the donor liver, may indicate platelet transfusion.

9.12 Immune thrombocytopenia

9.12.1 Autoimmune thrombocytopenia

- Platelet transfusion should be reserved for patients with life-threatening bleeding from the gastrointestinal or genitourinary tracts into the central nervous system or other sites associated with sever thrombocytopenia
- A large number of platelet concentrates may be required to achieve haemostasis as a result of reduced survival of the transfused platelets.
- Other therapies such as intravenous methylprednisolone and immunoglobulin should be given at the same time to maximize the chances of stopping the haemorrhage and raising the platelet count.

9.12.2 Neonatal alloimmune thrombocytopenia (NAIT)

- The optimal approach to the postnatal management of NAIT is to suspect it on clinical grounds and to transfuse compatible platelets as soon as possible, as delay in the provision of effective treatment may result in an increased risk of severe haemorrhage. It is not necessary to wait for laboratory confirmation of the diagnosis.
- The transfusion of human platelet antigen (HPA) –HPA-1a negative, HPA- 5b negative platelet concentrate will result in least delay in providing treatment and will be effective in around 95% of cases of NAIT. **(However, this facility is not yet available in Maldives)**
- Transfusing platelet concentrate prepared from the mother, which is gamma irradiated and washed, in order to minimize the transfusion of maternal antibodies that may otherwise prolong the neonatal thrombocytopenia is the alternative available.
- The blind transfusion of random donor platelets is unlikely to be effective.

9.12.3 Post transfusion Purpura

- Platelet transfusions are usually ineffective in raising the platelet count. However, they may be used in an attempt to control severe bleeding in the acute phase. High dose IV Ig 2g/kg over 2-5 days is the treatment of choice which raises platelet count.

9.13 Treatment of Dengue Fever/Dengue Haemorrhagic Fever Grade III-IV Profound shock: -
With undetectable pulse and blood pressure, if shock still persists and the haematocrit level continues declining

- Transfuse fresh whole blood 10 ml/kg as a bolus
- Monitor vital signs every 30-60 minutes

9.13.1 In case of severe bleeding

1. Transfuse fresh whole blood 20 ml/kg
2. Transfuse platelet rich plasma transfusion exceptionally when platelet counts are below 5,000–10,000/mm^3
3. After blood transfusion, continue fluid therapy at 10ml/kg/h and reduce it stepwise to bring it down to 3 ml/kg/h and maintain it for 24-48 hrs

Table 16: Transfusion Triggers for Platelet Transfusion

Asymptomatic patient: (prophylactic)	10,000/µl (or even <5000/µl)
Febrile Neutropenia /uncomplicated BMT	20,000/µl
Bleeding other than petechiae and bruises, mucocutaneous bleeds, DIC, BMT with complications like fever/ Uncontrolled hypertension septicaemia/infection/DIC/bleeding/GVHD 50,000/µl	50,000/µl
Elective invasive procedures like central venous line insertion or surgery	> 50 and < 75,000/µl
Major Surgery	50,000/µl
Surgery on vital organs e.g., eye/brain	100,000/µl

9.14 Calculation of Dosage of Platelets

- Volume of platelet concentrates to be transfused depends on baseline platelet count, desired increment, and surface area of recipient. It is calculated as per the formula given below.

- (Plt increment x BV (70ml/kg) divided by correction factor 0.67 (33% of platelets are pooled in the spleen) (Ref: Guidelines for the Use of Platelet transfusions BJH (2003) 122:10-23)
- As a general guideline, an adult requires 6-8 RDP or 1 SDP. This should be repeated every alternate day till the indication for platelet transfusion has resolved. Half-life of platelets is short, especially under conditions associated with rapid consumption. Hence more frequent transfusions will be required if the patient has DIC, septicaemia, hypersplenism, and/or simultaneous administration of Amphotericin B.
- There should be a gap of at least 6-8 hours between platelet transfusions and Amphotericin B infusion to avoid risk of pulmonary infiltrates and ARDS.

9.15 Administration of platelets

- Platelets should be transfused as soon as these are received and should be transfused at a rapid rate using normal transfusion set with filter.

9.16 Response to Platelet Transfusion

- 1 unit RDP raises the platelet count by approximately10,000/μl
- 1 unit SDP raises the platelet count by approximately 40-50,000/μl
- Clinical Response is the most important indication of the effectiveness of the transfusion. e.g., Cessation of bleeding, Resolution of headache (if there is impending intracranial bleeding)
- Laboratory Response to a prophylactic platelet transfusion should be assessed by measuring increase in patient's platelet count.

CCI (corrected count increment) at 1 hour and 24 hours

$$CCI = \frac{\text{(Post platelet count – Pre platelet count) (per μl) x BSA } (m^2)}{\text{Platelet transfused } (10^{11})}$$

Table 17: Response to Platelets Transfusion

Response	**C. C. I.**	
	At 1 hour	**At 24 hours**
Normal response	> 7000	> 4,500
Platelet Refractoriness	< 4000	< 4000
Hyper consumption	> 7000	< 4000

9.17 Contraindications to Platelet Transfusions

1. Thrombotic Thrombocytopenic Purpura (TTP)

- Platelet transfusions are contraindicated unless there is life-threatening haemorrhage, as they have been temporarily associated with exacerbation of TTP.

2. Heparin Induced Thrombocytopenia (HIT)

- Heparin induced thrombocytopenia is a drug induced immune thrombocytopenia, that is frequently associated with severe thrombosis. Platelet transfusion should not be administered as acute arterial thrombosis can result.

3. Idiopathic Thrombocytopenic Purpura (ITP)

- Unless the patient is undergoing splenectomy and the platelet count is extremely low, platelet transfusion is not of use.

4. Post Transfusion Purpura

9.18 Platelet refractoriness

- This is suspected whenever there is a poor response to platelet transfusion (CCI of less than 4000). This is usually due to HLA alloantibodies. Differential diagnosis will also include DIC, fever, hypersplenism, post BMT, simultaneous use of Amphotericin B and improperly stored platelets. It can be prevented by the use of leucodepletion filters.
- Treatment of refractoriness is either use HLA matched platelets or use of SDP under cover of IV immunoglobulin

Chapter 10 – Guidelines for Transfusion of Plasma Components

Fresh Frozen Plasma (FFP) is Prepared from whole blood within 6 hours of collection and frozen immediately in a plasma freezer. It contains both stable and unstable coagulation factors like fibrinogen, factor V and VIII

Liquid plasma is plasma separated from whole blood any time during storage period. It contains only stable coagulation factors.

10.1 Transfusion of Fresh Frozen Plasma

- FFP should only be used to replace single clotting factor deficiency for which no specific factor concentrate is available.
- For multiple coagulation factor deficiencies as in case of DIC, FFP along with platelets are required only in case of bleeding.
- For haemorrhagic disease of newborn, 10-20 ml/kg FFP in the IV with vitamin K is recommended.
- In neonates at risk of bleeding from invasive procedure due to significant coagulopathy, FFP is indicated.
- In Plasma exchange use of FFP is recommended in case of TTP to replace metalloproteinase enzyme which is deficient in TTP leading to accumulation of HMW-VWF causing excess platelet activation and consumption.
- For over anticoagulation from excessive effects of warfarin FFP only has a partial effect and should never be used for reversal of warfarin in absence of severe bleeding.
- Liver disease patients with prolonged PT are unlikely to benefit from FFP. Routine use of FFP in these cases is questionable.
- In Massive transfusion FFP replacement is required. The amount replaced should be guided by the coagulation tests. Requirement of FFP in case of CABG should be guided by thromboelastogram.

10.1.1 Administration of FFP

Once thawed the plasma should be used immediately especially for correction of unstable clotting factors. It cannot be refrozen after thawing. Integrity of the bag should be checked before use Note: Transfusion of FFP or liquid plasma does not require cross matching

10.1.2 Adverse Reactions of FFP

- Acute allergic reactions are common.
- Febrile, non-haemolytic reaction
- Viral transmission
- Bacterial contamination – sepsis

10.1.3 Contra Indications of FFP

- For simple volume replacement in adults or children use of crystalloids is safer and cheaper. In case when colloids or albumin are required but not available, it is preferable to use CSP and not FFP.
- Except for TTP, other cases of plasma exchange should be managed with saline/albumin.
- There is no justification for using FFP to reverse a prolonged INR in the absence of bleeding
- FFP should not be used for nutritional support or immunological deficiency states.

10.2 Transfusion of Cryoprecipitate

A component prepared from FFP by thawing at +4ºC and suspending it in 10 -20 ml plasma.
One unit should contain factor VIII: 80- 100iu/pack and fibrinogen 150-300mg/pack

10.2.1 Indications of Cryoprecipitate

- For raising the fibrinogen level in case of dysfibrinogenemia or hypofibrinogenemia.
- In cases of DIC and massive transfusion cryoprecipitate is recommended, as the fractionated virus inactivated product is yet not available. Replacement is required if fibrinogen level is less than 1 g/l.
- It is also useful when specific coagulation concentrates such as F VIII, V, XI and XIII are not available.
- For mild and moderate Haemophilia, A, in absence of AHF cryoprecipitate is useful.
- Treatment of bleeding tendency associated with uremia who are non-responsive to dialysis
- As a fibrin sealant in absence of commercially available products

10.2.2 Dose and administration:

- Each unit increases fibrinogen by 5 to 10mg%. In a bleeding patient, a reasonable target for

fibrinogen is 100mg%. 6 to 8 units are needed normally, and they are pooled and transfused within 4 hours

- ABO compatibility of cryoprecipitate is not required. No crossmatching is required

10.3 Guidelines for Plasma Fractions

10.3.1 Coagulation Factors

10.3.1.1 Haemophilia A & B (Factor VIII & Factor IX deficiency)

- For acute bleeding administration of the particular coagulation factor is essential.
- Earlier the replacement of coagulation factors the lesser is the dose required.
- Factor replacement is absolutely necessary before invasive procedures, tooth extraction, surgery etc.
- Never aspirate hemarthrosis without adequate factor replacement.

Table 18: Dosage of Factor VIII/ alternatives for treatment of Haemophilia A

Severity of bleed	Expected F VIII level	Required Factor VIII dose	Follow up treatment
1.Hemoarthrosis	50-80%	25-40 U/Kg	For 2-3 days or more
2.Soft tissue/muscle	50-80%	25-40 U/Kg	For 2-3 days or more
3.Epistaxis	50-80%	25-40 U/Kg + Antifibrinolytic therapy for 7-10 days	Occasionally
4.Hematuria	50-80%	25-40 U/Kg + fluids & bed rest	Occasionally
5.CNS system	100%	50 U/Kg	14-21 days
6.Major surgery Soft tissue, Orthopedic, Retro peritoneal	100%	50 U/Kg 50 U/Kg 50 U/Kg	10-14 days 3-9 weeks 10-21 days

Note:

1. Pooled cryoprecipitate containing 240-260 U of Factor VIII, is usually obtained from 3x 250 ml of fresh frozen plasma

2. For 1,2, and 3 above, repeat dose 12 hourly if bleeding persists or swelling is increasing. With more severe bleeds, it is usually necessary to continue treatment with half of total daily dose 12 hourly for 2-3 days or occasionally longer.

3. For 6, start therapy 8 hours before surgery. Continue 12 hourly therapy till 48 hours post-operatively. If no bleeding occurs, scale down gradually over next 3-5 days.

4. As adjunct to factor replacement in mucosal or gastrointestinal bleeding and surgery, give fibrinolytic inhibitor. Tranexamic acid (oral) 500-1000 mg three times a day. Do not use for haematuria.

5. In an emergency, use fresh frozen plasma to treat bleeding in haemophiliacs (give 3 bags initially) if none of the above are available.

6. Careful assessment of the patient's fluid intake is important to avoid fluid overload when using fresh frozen plasma or large doses of cryoprecipitate.

10.3.1.2 Adjustments in dosage of Factor VIII

- 1 IU of Factor VIII raises the level by 2%
- The dose can be calculated on the assumption that Factor VIII is primarily distributed intravascularly.
- Patients should receive a loading as well as a maintenance dose to achieve and maintain the haemostatic level of F VIII.
- The loading dose is calculated as per the formula below.
- Desired F VIII level*– the patient's baseline level* x Body Weight (Kg)/2
- *As percentage of normal
- Assuming the average half-life to be 12 hrs, 50% of the loading dose should be administered every 12 hrs

Table 19: Dosage of Factor IX for treatment of Haemophilia B

Type of haemorrhage	**Expected rise**	**Initial dose**	**Follow up treatment**
Haemoarthrosis	20%	15-20 U/Kg	For 2-3 days or more
Soft tissue /muscle	20%	15-20 U/Kg	For 2-3 days or more
Epistaxis	20%	15-20 U/Kg followed by antifibrinolytic therapy for 7- 10 days	Occasionally. Omit antifibrinolytic therapy if dose repeated
Haematuria	20%	15-20 U/Kg+ fluids & bed rest	Occasionally
C NS system	40%	35-40 U/Kg	14-21 days
Major surgery Soft tissue Orthopaedic	40%	 35 U/Kg 35 U/Kg	 10-14 days 3-9 weeks
Retroperitoneal	40%	35-40 U/Kg	10-21 days

Note:

1) Repeat within 24 hours if bleeding continues.

2) Accurate diagnosis is essential, as Factor VIII concentrate and cryoprecipitate are not useful for haemophilia B.

3) As adjunct to replacement therapy: Tranexamic acid (oral): 500-1000 mg three times a day, as for haemophilia A. (75 mg / Kg / day in divided doses.)

10.3.1.3 Adjustments in dosage of Factor IX

- Recovery of Factor IX is lower than that of Factor VIII as it is distributed to both intravascular and extra vascular spaces.
- 1 IU. of Factor IX raises the level by 1%
- The half-life of Factor IX ranges from 11 – 27 hrs.
- To achieve and maintain haemostatic levels, the patients should receive a loading dose followed by maintenance doses.
- The loading dose Factor IX is calculated as follows.
  (Desired F IX level*– the patient's baseline level* x Body Weight (Kg)
  *As percentage of normal
- Assuming the average half-life to be 24 hrs, 50% of the loading dose should be administered every 24 hrs

10.4 Regular prophylaxis

Regular prophylactic treatment may be given to affected patients. A dose of 15-20 units/Kg is generally employed and given two to three times per week. Prophylaxis is based on the rationale that spontaneous haemorrhage only occurs when the factor VIII:C level is below 1-2% and it is intended that regular infusions will maintain a level above this.

10.5 Development of Inhibitor and therapy

- One of the most problematic complications of haemophilia treatment is the development of inhibitors to FVIII or FIX. Presence of these inhibitors greatly increases the risk of life-threatening bleeds. Inhibitors to FVIII or FIX occur in approximately 20 to 30 % of severe haemophilia A patients and 1.5-3% of severe haemophilia B patients.
- The treatment of inhibitors is predicated primarily on their titre -measured in Bethesda units (BU)
- The treatment of patients with low titre inhibitors (<5 BU) consists of the administration of large enough doses of human FVIII or FIX concentrates to saturate the inhibitor and to provide adequate clotting factor activity levels.

- The treatment of patients with high titre inhibitors (>10BU) several treatment options are available. These include:

10.5.1 Prothrombin Complex Concentrate (PCC) -Contains activated forms of factors VII, IX and X contained in FIX complex.

- These products are effective in 48% to 64% of bleeding episodes, and are considered first- line therapy for uncomplicated bleeding events.
- Their use is limited by the potential for inducing thrombotic complications and the inability to predict haemostatic response on the basis of laboratory testing (e.g., PT, APTT, coagulation factor assay) due to the presence of factors that artificially shorten in vitro clotting assays in a manner that does not correlate to clinical haemostasis.

10.5.2 Recombinant factor VIIa

- Highly effective in the management of spontaneous bleeding episodes which are life or limb threatening.
- Infused as a bolus. Continuous infusion of 50µg/kg/hr is effective in surgery. Antifibrinolytics are administered concurrently.
- The standard adult dose of recombinant factor VIIa is 90µg/kg
- In children the mean half-life is substantially reduced to 1.32 hours and thus higher doses of up to 200- 250µg/kg may be required.

10.5.3 Immune tolerance induction

- Daily administration of factor concentrates is recommended until the inhibitors disappear. It can lead to permanent neutralization of the antibody and thus permit future treatment with usual factors.

10.6 Von Willebrand's Disease

- Fresh frozen plasma may be adequate to control bleeding in mild disease (subject to tolerance of volume).
- Cryoprecipitate for moderate disease. It is the product of choice in type IIB and severe type III von Willebrand's disease. Repeat dose of cryoprecipitate after 24-48 hours.
- Intermediate purity factors VIII concentrate contain virally inactivated von Willebrand's factor.
- Platelet transfusion will be required for platelet type vWD.

- Treatment aims to normalize BT either by increasing endogenous vWF levels by DDAVP or by replacing vWF with an intermediate purity F VIII which contains some vWF, or by cryoprecipitate which also contains vWF.
- DDAVP: 0.3-0.4 mg/kg IV lasts 4-8 hours and obviates the need to use plasma products. The dose can be repeated every 24 hours, but the effect is reduced after some days of treatment. F VIII products are reserved for patients non-responsive to DDAVP.
- In Type IIb with thrombocytopenia do not give platelet transfusion or DDAVP. Give only F VIII.
- In Type III when vWF is deficient, it should be replaced with F VIII which is also deficient

10.7 Other Inherited Coagulation Disorders

Table 20: Replacement Therapy in Other Inherited Coagulation Disorders

Severity of bleed	**Expected F VIII level**	**Required Factor VIII dose**	**Follow up treatment**
1.Hemorosis	50-80%	25-40 U/Kg	For 2-3 days or more
2.Soft tissue/muscle	50-80%	25-40 U/Kg	For 2-3 days or more
3.Epistaxis	50-80%	25-40 U/Kg + Antifibrinolytic therapy for 7-10 days	Occasionally
4.Hematuria	50-80%	25-40 U/Kg + fluids & bed rest	Occasionally
5.Central nervous system	100%	50 U/Kg	14-21 days
6.Major surgery Soft tissue Orthopedic Retro peritoneal	100%	 50 U/Kg 50 U/Kg 50 U/Kg	 10-14 days 3-9 weeks 10-21 days

- The replacement therapy regimens suggested in this table are for major bleeding or surgical prophylaxis. Patients with minor bleeding may require lower dosages of these replacement materials. Confirmation of haemostatic levels of the appropriate coagulation factor being replaced should be done, with dosage adjustments performed as needed.

* Recommended only if purified factor replacement therapy is not available.

++ Plasma after removal of cryoprecipitate is satisfactory

** Prothrombin complex concentrates are thrombogenic and should be used only for major bleeding or major surgery. Antifibrinolytic drugs (EACA, tranexemic acid) should not be used in conjunction with prothrombin complex concentrates.

10.8 Disseminated Intravascular Coagulation

Purpose of transfusion support in DIC is to maintain adequate platelet count and fibrinogen levels until the underlying disease is brought under control. Outcome of DIC depends upon underling disease and presence or absence of complications.

Decision to transfuse blood products depends upon clinical bleeding rather than laboratory reports alone. If there is no bleeding, then products are not indicated.

10.8.1 Transfusion support in DIC

- Cryoprecipitate 1 pack / 6kg in adults (8-10 packs) to maintain plasma fibrinogen level 100 mg/dl
- Alternatively fresh frozen plasma: 1 pack / 15 kg body weight (4.5 packs in adults)
- Platelet concentrate: If platelet count is less than $50x10^9$/l. Generally, 4-5 packs as required in adults
- Packed cells transfusion: to maintain haemoglobin 8 g%

10.9 Transfusion Support in Bleeding due to Liver Disease

- Transfusion of blood products is required if clinical bleeding is associated due to coagulopathy.
- Fresh frozen plasma contains all the coagulation factors and natural inhibitors. However large volume of FFP is required to be transfused (1-1.5 litres)
- Prothrombin complex concentrate (PCC): contains II, VII, IX, and X and is sometimes useful.
- Vitamin K.

10.10 Transfusion support in Disorders of Vitamin K-Dependent Coagulation Factors:

Vitamin K is a fat-soluble vitamin found primarily in green vegetables and liver. It is a co-factor for the synthesis of F II, VII, IX, and X which takes place in the liver.

10.10.1 Common causes of deficiency of Vitamin K-dependent factors

- Coumarin anti-coagulants (Warfarin). Some drugs such as certain antibiotics may cause bleeding by displacing Warfarin bound to plasma proteins.

- Vitamin-K deficiency due to inadequate diet or malabsorption.
- Liver disease, leading to decreased production of F II, VII, IX, and prolonged PT is usually a feature of severe liver disease.

10.10.2 Management of Vitamin K deficiency:

- Remove the underlying cause of Vitamin K deficiency.
- Treat malabsorption or dietary deficiency.
- Stop anticoagulants.
- Replace coagulation factors with FFP, platelet concentrates and fibrinogen as necessary.
- Reverse Warfarin with Vitamin K IV if the patient is bleeding and the PT is prolonged (INR > 4.5). Doses of Vitamin K exceeding 1 mg may make the patient refractory to additional Warfarin for up to 2 weeks.

Chapter 11 – Transfusion in Obstetric cases

11.1 Haematological changes in pregnancy

The following haematological changes occur during pregnancy:

- 40-50% increase in plasma volume, reaching its maximum by week 32 of gestation, with similar increase in cardiac output
- Increase in red cell volume by approximately 18-25%, though more slowly than the increase in plasma volume
- Natural reduction in haemoglobin concentration: normal or elevated haemoglobin may signify pre-eclampsia in which plasma volume is reduced
- Increased iron requirement, particularly in last trimester
- Increases in platelet activation and levels of coagulation factors, particularly fibrinogen, Factor VIII and Factor IX
- Fibrinolytic system is suppressed
- Increased susceptibility to thromboembolism.

11.2 Anaemia in pregnancy

Stage of pregnancy	Anaemic if less than (g/dl)
•First trimester: 0-12 weeks	11.0
•Second trimester: 13-28 weeks	10.5
•Third trimester 29 weeks –term	11.0

- Further investigation is needed if haemoglobin concentration does not return to normal by 8 weeks postpartum.

11.3 Prevention of anaemia in pregnancy

- The need for transfusion can often be avoided by the prevention of anaemia through:
- Education about nutrition, food preparation and breastfeeding
- Adequate maternal and child health care
- Access to family planning information, education and services
- Clean water supplies
- Adequate facilities for the disposal of human waste.

- Prophylactic administration of iron and folic acid is strongly indicated during pregnancy in countries where iron and folate deficiency is common. Examples of the dose regime are:
  - Optimum daily dose to prevent nutritional anaemia in pregnant women:
    - 120 mg elemental iron
    - 1 mg folate.
  - When anaemia is already present, especially if severe, higher daily therapeutic doses may be more effective:
    - 180 mg elemental iron
    - 2 mg folate.

anaemia

11.4 Clinical assessment of anaemia

When anaemia is detected, it is important to determine the cause and assess its severity, including any evidence of clinical decompensation. Assessment should be based on:

- Patient's clinical history
- Physical examination
- Laboratory investigations to determine the specific cause of anaemia: e.g., serum B12, folate or ferritin.

11.5 Transfusion in Obstetric anaemia

- The decision to transfuse blood should not be based on haemoglobin levels alone, but also on the patient's clinical need.
- The following factors must be taken into account:
- Stage of pregnancy
- Evidence of cardiac failure
- Presence of infection: e.g., pneumonia, malaria
- Obstetric history
- Anticipated delivery: Vaginal, Caesarean section
- Haemoglobin level.

11.6 Major obstetric haemorrhage

- Acute blood loss is one of the main causes of maternal mortality. It may be a result of excessive bleeding from the placental site, trauma to the genital tract and adjacent structures, or both.

Increasing parity increases the incidence of obstetric haemorrhage.

- Serious haemorrhage may occur at any time throughout pregnancy and the puerperium.
- Major obstetric haemorrhage can be defined as any blood loss occurring the peripartum period, revealed or concealed, that is likely to endanger life.
- At term, blood flow to the placenta is approximately 700 ml per minute. The patient's entire blood volume can be lost in 5-10 minutes. Unless the myometrium contracts on the placental site appropriately, rapid blood loss will continue, even after the third stage of labour is complete.
- Obstetric bleeding may be unpredictable and massive
- Major obstetric haemorrhage may result in clear signs of hypovolaemic shock but because of the physiological changes induced by pregnancy, there may be few signs of hypovolaemia, despite considerable blood loss.

11.7 Prevention of major obstetric haemorrhage:

Identify the patient at risk of haemorrhage.

11.7.1 Before the onset of labor:

- Proven abruption placentae
- Known placenta Previa.
- Multiple pregnancies.
- Pre-eclampsia/gestational hypertension.
- Previous PPH.

11.7.2 Risk factors apparent during labor/delivery:

- Delivery by emergency cesarean section
- Retained placenta
- Operative vaginal delivery prolonged labor (> 12 hours)
- Big baby (> 4 kg).
- Pyrexia in labor
- Coagulation defects or patients on anticoagulants may intensify all of the above.

- Management of the third stage of labor actively by prophylactic oxytocics
- Syntometrine (Ergometrine 0.5 mg plus Oxytocin 5 IU) or Oxytocin 10 units IV.

- In the rare event of a woman coming to delivery fully anticoagulated on Warfarin, FFP should be given rapidly to return the PT to normal (urgent reversal of Warfarin anticoagulation = 5-8 ml/kg of FFP). On delivery, the infant should be given Vitamin K and FFP and screened for internal haemorrhage.
- In the event of a woman coming to delivery while receiving therapeutic Heparin, the infusion should be stopped. Heparin activity will fall to safe levels within an hour. Protamine sulphate will reverse activity more rapidly, if required.
- Prophylactic platelet transfusion is rarely indicated in surgical situations with thrombocytopenia due to decreased platelet production when the platelet count is > 100 x 109/1 and is indicated when platelet count is < $50x10^9/1$.
- Vaginal delivery or small episiotomy procedures ordinarily associated with insignificant blood loss may be undertaken if the platelet count is < 50 x 109/1. Management of all cases of ante-partum haemorrhage should be in a hospital facility with a blood bank. An ultrasound examination should be performed to determine the placental site, presence of retro placental hematoma, fetal viability and maturity. The fetus should be monitored daily, with a cardiotocogram (CTG) where appropriate.
- Deliver at 37-38 weeks gestation, or earlier if the bleeding endangers the mother or the fetus. Give anti-D Ig for Rh negative women who are bleeding.

11.8 Management of Major Obstetric Haemorrhage

It is an emergency and resuscitative measures include the following measures

11.8.1 Resuscitate

1. Administer high concentrations of oxygen.
2. Head down tilt/raise legs.
3. Establish intravenous access with 2 large-bore cannulae (14 g or 16 g).
4. Infuse crystalloid replacement fluids or colloids as rapidly as possible. Restoration of normovolaemia is a priority.
5. Call extra staff to help:
   - Senior obstetrician
   - Senior anaesthetist
   - Midwives
   - Nurses

6. Alert the haematologist (if one is available)
7. Ensure assistants are available at short notice
8. Inform blood bank of this is emergency.
   - Give group 0 negative antibody-screened blood, and/or un-crossmatched group specific blood until fully crossmatched blood is available.
9. Use a pressure infusion device and warming device, if possible.

11.8.2 Monitor/Investigate

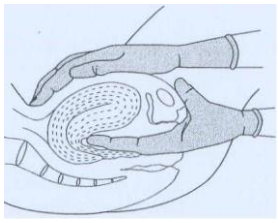
1. Send sample to the blood bank for crossmatching of further blood, but do not wait for crossmatched blood if there is serious haemorrhage.
2. Order full blood count
3. Order coagulation screen
4. Continuously monitor pulse rate and blood pressure
5. Insert urinary catheter and measure hourly output
6. Monitor respiratory rate
7. Monitor conscious level
8. Monitor capillary refill time
9. Insert central venous pressure line, if available, and monitor CVP.
10. Continue to monitor haemoglobin or haematocrit

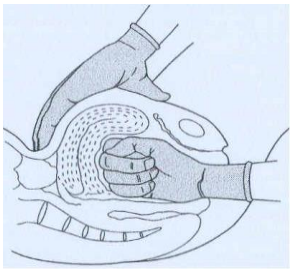
11.8.3 Stop the Bleeding

1. Identify the cause.
2. Examine cervix and vagina for lacerations.
3. If retained products of conception and uncontrolled bleeding, treat as disseminated intravascular coagulation.
4. If uterus hypotonic and atonic:
   - Ensure bladder is empty
   - Give IV oxytocin 20 units
   - Give IV ergometrine 0.5 mg
   - Oxytocin infusion (40 units in 500 ml)
   - 'Rub up' fundus to stimulate a contraction
   - Bi-manual compression of the uterus as shown below)

11.8.4 Bi-manual compression of the uterus

Press the fingers of one hand into the anterior fornix. The whole fist can be inserted if a good pressure is not obtained as the vagina is lax.





- If bleeding continues, Inject deep intramuscular or intramyometrial prostaglandin (e.g., Carboprost 250 mg) directly into uterus (dilute 1 ampoule in 10 ml sterile saline).
- Consider surgery earlier rather than later.
- Consider hysterectomy earlier rather than later.

11.9 Disseminated Intravascular Coagulation

- In disseminated intravascular coagulation (DIC), the coagulation and fibrinolytic systems are both activated leading to deficiencies of the coagulation factors, fibrinogen and platelets.
- In Obstetrics, DIC is a cause of massive haemorrhage. If DIC is suspected, do not delay treatment while waiting for the results of coagulation factors.

11.10 Management of Disseminated Intravascular Coagulation

1. Treat the cause:
   - Deliver fetus and placenta
   - Evacuate uterus, as indicated for retained or necrotic tissue.
2. Give uterine stimulants to promote contraction: e.g., oxytocin, ergometrine and/or prostaglandin.
3. Use blood products to help control haemorrhage. In many cases of acute blood loss, the development of DIC can be prevented if blood volume is restored with a balanced salt solution: e.g., Hartmann's solution or Ringer's lactate.
   If needed for oxygen perfusion, give the fresh whole blood available (or packed red cells).
4. Avoid the use of cryoprecipitate and platelet concentrates unless bleeding is uncontrollable.
5. If bleeding is not controlled and if coagulation tests show very low platelets, fibrinogen, prolonged PT or APTT, replace coagulation factors and platelets with:
   - Cryoprecipitate: at least 15 packs, prepared from single donor units, containing 3-4 gm

fibrinogen in total.

- If cryoprecipitate is not available, give: Fresh frozen plasma (15 ml/kg): 1 unit for every 4-6 units of blood to prevent coagulation defects resulting from use of stored red cell concentrates/suspensions.
- If there is thrombocytopenia, give: Platelet concentrates: rarely necessary to control obstetric haemorrhage with DIC in a woman with previously normal platelet production.
- If these blood components are not available, give the freshest whole blood available (ideally no more than 36 hours old)

6. Give broad spectrum antibiotics, as indicated, to cover aerobic and anaerobic organisms.

Chapter 12 – Guidelines for Use of Blood Components in Neonates and Paediatric Patients

NEONATAL AND PAEDIATRIC TRANSFUSIONS

Children are more likely to receive transfusions than any other age group. 45-60% of all blood transfusions are used in paediatric patients especially in developing countries.

For transfusion purposes in children there are two groups:

1. Neonates and infants < 4 months
2. Infants > 4 months and older children

12.1 Paediatric Transfusions

- Transfusion therapy differs in children as compared to adults.
- Children have better cardio-vascular adaptive mechanism to tolerate anaemia.
- Child's blood volume varies with age and body weight and hence amount to be transfused must be carefully calculated. Full term babies have blood volume of 85 ml/kg. Premature babies have average blood volume of 100 ml/kg.
- Infants and children can tolerate greater expansion of blood volume than adults. Amount to be transfused may be approximately 20 ml/kg of blood or 10 to 15 ml/kg of packed red blood cells.
- If a child has signs and symptoms of impending cardiac failure or congestive cardiac failure, then restrict the amount of packed blood cells to 3-5 ml/kg at a time and give transfusions more frequently. Injection Furasemide may be given in the dose of 1 mg/kg body weight prior to the transfusion.
- If a child is severely anaemic, partial exchange transfusion may be given by removing child's blood and infusing packed RBCs.
- In children 3 ml of packed red blood cell per kg will raise the Hb by approximately 1 g/dl or 10 ml of packed red blood cells per kg increases haematocrit by 10% or Hb by 3 g /dl.
- Samples for detailed investigations should be collected before starting the transfusion.

12.2 Transfusions in Neonates

The neonate is small with immature physiology. Those requiring transfusions are mainly premature, sick and unable to tolerate minimal stress.

Table 21: Haemoglobin Concentration in children

Age	Hb concentration g/dl
Cord blood	+16.5
Day 1	+18.0
1 month	+14.0
3months	+11.0
6months-6years	+12.0
7-13 years	+13.0

- Indication for transfusion in neonates and infants differ according to weight, gestational age and circumstances of delivery and subsequent maturation. Normal Hb and HCT values vary with age and with gestational age in the new-born period.

Table 22: Serial Hb values (gm/dl) in Infants

Birth Wt. in gms.	**Age in Weeks**				
	2	**4**	**6**	**8**	**10**
500-1000	16.0 14.8 – 17.2	10.0 6.8-13.2	8.7 7.0-10.2	8.0 7.1-7.8	8.0 6.9-10.2
1001-1200	16.4 14.1-17.2	12.8 7.8-15.3	10.5 7.2-12.3	9.1 7.8-10.4	8.5 7.0-10.0
1201-1400	16.2 13.6-18.8	13.4 8.8-16.2	10.9 8.5-13.3	9.9 8.0-11.8	9.8 8.4-11.4
1401-1500	15.6 13.4-17.8	11.7 9.7-13.7	10.5 9.1-11.9	9.8 8.4-12.0	9.9 8.4-11.4
1501-2000	15.6 13.5-17.7	11.0 9.6-14.0	9.6 8.8-11.5	9.8 8.4-12.1	10.1 8.6-11.8

According to WHO criteria, infants and children are considered to have anaemia if their Hb concentration falls below the levels shown in Tables 9.3 and 9.4

Table 23: Mean Hb Values (g/dl) in Term and Pre-term Neonates and Their Changes during the First Month of Life

Week	**Term Infants**	**Premature Infants 1200-1500 g**	**Small Premature Infants < 1200 g**
0	17	16.4	16
1	18.8	16	14.8
3&4	15.9	13.5	13.4

Table 24: Normal Blood Indices beyond the Neonatal Period Expressed as Mean ± SD			
Age	**Hb (g/dl)**	**Hct(%)**	**MCV (Femtolitres)**
1 Month	14 ± 4	43 ± 12	104 ± 19
2 Months	11.5 ± 2.5	35 ± 7	96.1 ± 19
3-6 Months	11.5 ± 2	35 ± 6	91 ± 17
1 Year	12 ± 1.5	36 ± 3	76 ± 8
2-6 Years	12.5 ± I	37 ± 3	81 ± 6
6-12 Years	13.5 ± 2	40 ± 5	80 ± 9
12-18 Years	14 ± 2	42 ± 6	89 ± 11

- Physiological anaemia of newborn develops around 2 to 3 months and these full-term neonates do not have any clinical symptoms and do not need any treatment or blood transfusion even though Hb level drops to 9 gm% during this period.
- However, in premature babies the nadir of Hb can be as low as 7 gm% and even lower around 6 to 8 weeks of age and they may become symptomatic with failure to thrive, respiratory distress, apnoea, tachycardia, bradycardia, etc. These children need transfusion at the rate of 10 ml/kg body weight of packed red cells. Injection of Recombinant Human Erythropoietin may be useful in preventing anaemia of pre-maturity reducing the need for transfusion.
- The commonest cause of anaemia in newborn period particularly in premature babies in neonatal intensive care units are iatrogenic due to blood taken for laboratory investigations. Maintain a record of all the blood taken for investigations from these babies and if more than 10% of baby's blood volume is removed over a week, replace by packed cells. Measure haemoglobin on entry to the nursery and at regular intervals at least weekly thereafter.
- Consider normal Hb values and physiological variation at different gestational age and other factors such as weight and cardiorespiratory distress before ordering the blood transfusion.

12.3 Selection of Blood Component

- ABO antigens in the cord red cells are not fully developed.
- Interpretation of blood groups may be difficult if the neonate has received an intrauterine transfusion (IUT)

- Infants do not synthesize demonstrable amount of anti-A and anti-B till 4 months of age. Therefore, crossmatching is performed using mother's serum / blood sample.
- Small volume transfusions can be given repeatedly over first 4 months without serological testing, provided no maternal antibodies are present and DAT in infant's sample is negative. If either of these is positive, full compatibility testing is required.
- In infants and children older than 4 months, an ABO group, Rh type and antibody screen for unexpected antibodies and cross matching must be performed as in case of adults.
- The blood used for infants should be irradiated if there has been an IUT or blood is from first degree relatives.

12.4 Indications for transfusion of whole blood

- Acute blood loss greater than 1 blood volume.
- Exchange transfusion (plasma reduced whole blood – Hb of 15 gm /dl)
- Cardiovascular bypass surgery
- Extra corporeal membrane oxygenation (ECMO)

12.5 Transfusion of packed red cells

- Hb concentration less than 13 g/dl (venous) or Hct < 40% in neonates less than 24 hours old.
- Hb concentration < 13 g/dl or Hct < 40% associated with severe pulmonary or cyanotic heart disease or congestive heart failure.
- Hb concentration < 10 g/dl or Hct < 30% during neonatal period with signs and symptoms of anaemia such as tachycardia, tachypnoea, apnoea, bradycardia, poor weight gain, poor cry and feeding difficulties.
- Hb concentration < 8 gm/dl or Hct 20-25% in infant with asymptomatic anaemia. (Except nutritional anaemia where transfusion may not be necessary and may be treated with haematinics)
- Acute blood loss > 10% of total blood volume.
- To correct iatrogenic blood loss, when > 10% of total blood volume is removed for laboratory testing over 7 days.

12.6 Dose of blood transfusion

Packed Red: 10 ml/kg

Whole blood: 20 ml/kg

Rate of blood transfusion: 3 ml/kg/hr

12.7 Transfusion Practice in Paediatric Patients

- To limit donor exposure, use pedi-packs and if these are not available use aliquots prepared by blood bank.
- Do not reuse the residual blood in the bag after transfusion of some amount from the unit of blood, to avoid contamination especially if prepared by open system.
- All transfusions needed for one neonate should be preferably supplied by one donor or obtained from a single blood unit reserved exclusively for the use of each infant.
- If single bag is used for blood collection, it is preferable to use transfer bags attached using sterile connecting device (SCD) for separating small volumes needed for transfusion. Dedicating aliquots from a single unit of red cells or apheresis platelets using SCD to allow sequential transfusion from the same donor unit in patients requiring regular transfusions reduces the chances of alloimmunisation. When SCD is in use, the unit of blood can be used till its original shelf life,
- The walk-in donor programme is not permissible, as this can lead to potentially life threatening serological and viral transfusion mishaps.

12.8 Paediatric Transfusion in Cardiac Surgery

- Infants undergoing cardiac surgery should receive red cells < 5days of age.
- Older blood up to 35 days shelf life can be used for children over 1 year of age though < 10 days old blood is preferable when used intra operatively and when large volumes are transfused rapidly.
- The blood collected in additive solution is not optimal for infants under 6 months of age due to theoretical concerns of toxicity but in children above 6 months there is no evidence to suggest it is detrimental and can be used.
- The choice of priming fluid for the bypass circuit- whole blood, red cells, colloid or crystalloid depends on size of the patient, volume of extracorporeal circulation and haemoglobin concentration.
- Routine use of FFP has not been found beneficial in cardiac surgery unless there is documented coagulopathy. In fact, neonates may have significantly low coagulation factors before bypass, and these may be further reduced by dilution.
- DDAVP has not been found to reduce blood loss in children.

- High dose of aprotonin helps to reduce blood loss in patients undergoing complex or repeat procedures
- Low dose aprotonin used in priming the pump is ineffective.
- Tranexamic acid reduces blood loss in cyanotic children undergoing surgery
- Vitamin K deficiency should be corrected preoperatively.
- Platelet transfusions are useful for thrombocytopenic bleeding or when platelet function is impaired.
- Use of tropical fibrin glue is effective.
- Infants with congenital cardiac lesions are likely to have Di George's syndrome and hence should be transfused irradiated cellular components.

12.9 Platelet Transfusion in Paediatrics

- Normal range of platelet count in newborn is similar to adults and older children. Platelet count less than $100x10^9$/l in newborn full-term infants as well as the premature infants is considered abnormal.
- In the absence of other coagulopathies - Thrombocytopenic term infant who is in stable clinical condition rarely bleeds unless the platelet count < $20x10^9$/l
- A higher threshold is recommended in small, sick, premature infants or those with other complicating illnesses especially in first few days when the risk of periventricular bleeding is higher and there is coexisting coagulopathy.

12.10 Triggers for platelet transfusion in children

For platelet transfusions in neonates:

- Platelet count < $20x10^9$/l irrespective of weight, gestation, and general condition.
- Platelet count < $30x10^9$/l with bleeding.
- Platelet count < $50x10^9$/l without bleeding in the presence of complications like DIC, sepsis, necrotising enterocolitis.
- Platelet count < 50-$100x10^9$/l for impending surgery or invasive procedure.
- Qualitative platelet defect with either clinical bleeding or preoperatively.

12.11 Dosage of Platelets

- In the absence of platelet consumption 1 unit/5 kg. body weight or10 ml / kg body weight of RDP increases the platelet count at 1 hour by 30-50 $x10^9$/l.
- Platelets do not have Rh antigen on its surface. However, it is ideal to have ABO/Rh group specific platelet concentrate but in practice it is acceptable to give ABO/Rh non- specific platelet transfusion if RDP is not contaminated with red cells. When Rh-negative child receives Rh-positive platelets, Rh IgG should be given.
- In neonatal alloimmune thrombocytopenia (e.g., HPA-A1 negative mother and HPA-A1 positive child) HPA compatible platelets are required in addition to high dose IV Ig. The minimum platelet count of 30x109/l is recommended because HPA antibodies can impair platelet function. If HPA compatible platelets are not available, mother's platelets preferably washed, can be given.

12.12 Transfusion of fresh frozen plasma (FFP) in Paediatric cases

12.12.1 Indications

- Clotting time of normal infant is longer than in adults and of premature infants it may be even longer.
- Use of FFP in neonates is indicated in following cases:
- Haemorrhagic disease of newborn with massive blood loss or in premature babies not responding to vitamin K.
- Reversal of drug effect in a baby born to a mother who has taken coumarin derivatives, phenobarbitone and phenytoin.
- Unspecified coagulation disorder in a bleeding neonate.
- For invasive procedure in a bleeding infant with prolonged PT or APTT 1.5- 2 times normal.
- Thrombotic thrombocytopenic purpura/ Haemolytic uremic syndrome
- Protein S, Protein C and Antithrombin III natural anticoagulant deficiency
- Reconstitution of whole blood for exchange transfusion.
- For DIC and other causes of fibrinogen deficiencies cryoprecipitate should be used.

12.12.2 Contra indications for FFP

1. As a replacement fluid for hypovolemia
2. For management of neonatal hypotension to prevent periventricular haemorrhage

3. For treatment of polycythaemia unless there is coexisting coagulopathy
4. In septic patients to improve immune function. Use of FFP in these patients increases mortality although the reason is not known.

12.12.3 Dosage of FFP

- 10-15 ml/kg. body weight: ABO group compatible
- No cross matching is required. It should be transfused immediately after thawing and should not be refrozen.

12.13 Granulocyte Transfusion in Paediatrics

1. Normal neutrophil levels vary with postnatal age. At birth it is 5-10x10^9/l which falls to 2-6 x10^9/l by the end of first week. Therefore, neutropenia at birth is 2x10^9/l and after one week is 1x10^9/l.
2. Severe neonatal sepsis not responding to antibiotics as in meningitis, septicaemia and necrotising enterocolitis, associated with severe neutropenia.
3. During severe neutropenia < 3 x10^9/l at 1 week age and < 1 x 10^9/l after 1 week age.
4. Alloimmune neonatal neutropenia is analogous to HDN occurring due to maternal neutrophil specific antibodies. The infections in this case are controlled effectively with antibiotics, G-CSF and IV IG. Plasma exchange and maternal granulocytes are rarely indicated.

   Dose: 10-15 ml/kg every 12-24 hrs. (1- 2 x 10^9 granulocytes / kg)

The granulocyte pack should be ABO/Rh compatible, CMV negative and irradiated.

Chapter 13 – Adverse Reactions to Blood Transfusion

Even though all efforts are taken to ensure the safety of transfusion, preventable clerical errors and inappropriate transfusions still account for a significant proportion of reported transfusion-related adverse events.

Serious or life-threatening acute reactions are rare but any unexpected symptoms that appear while the patient is being transfused must not be overlooked, as they may be early warning signs of a serious reaction.

Any adverse reaction that occurs during the administration of blood and blood component must be considered as a haemolytic transfusion reaction unless proved otherwise. The initial presenting symptoms of a serious haemolytic transfusion reaction is similar to febrile non haemolytic transfusion reaction thus any adverse reaction should be treated as potentially life threatening.

Early recognition and initiation of treatment could reduce mortality. If the patient experiences an adverse reaction during or following transfusion of a blood component, clinical staff must report this to the blood bank as soon as possible.

The blood bank should also be notified as soon as possible if it is believed that the patient has received a wrong blood component or fractionated product, received one intended for another patient, that the transfusion did not meet requirements or that the transfusion was inappropriate. It should be noted that the patient may not always experience or show a 'reaction' in these situations.

13.1 Classification of Adverse Reactions

Transfusion reactions may be Acute or chronic in nature. Acute reactions usually occur during or up to 24 hours following the end of a transfusion and may be due to immune or non-immune etiology.

Table 25: Acute transfusion Reactions (<24 hrs)

Immunologic	**Etiology**
• Haemolytic transfusion reaction	• ABO incompatibility
• Febrile non-haemolytic transfusion reaction	• Anti-leucocyte antibodies, cytokines
• Allergic	• Antibodies to plasma proteins
• Anaphylaxis	• Antibodies to IgA
• Transfusion related acute lung injury (TRALI)	• Antibodies to Leucocytes/ complement

Table 26: Acute transfusion Reactions (<24 hrs)

Nonimmunologic	**Etiology**
• Marked fever with shock	• Bacterial contamination
• Atypical reaction with hypotension	• Associated with ACE inhibitors
• Congestive heart failure	• Volume overload
• Air embolism	• Air infusion via IV line
• Hypocalcaemia	• Citrate toxicity
• Hypothermia	• Rapid infusion of cold blood
• Hypokalaemia and hyperkalaemia	• Red cell storage lesions

Delayed reactions usually occur after 24 hours and up to 7 days following the end of a transfusion and may be due to immune or non-immune etiology.

Table 27: Delayed adverse reaction to transfusion (> 24 hrs)

Immunologic	**Etiology**
• Marked Alloimmunization to RBC, WBC, platelets, Plasma protein, HLA	• Exposure to antigens of donor origin
• Haemolytic	• Anamnestic response to donor red cell antigen
• TA-GVHD	• Engraftment of transfused functional lymphocytes
• Post - transfusion purpura	• Anti-platelet antibodies
• Immunomodulation	• Related to leucocytes
• Hypothermia	• Rapid infusion of cold blood

Table 28: Delayed adverse reaction to transfusion (> 24 hrs) -

Non-Immunologic	**Etiology**
• Iron overload	• Repeated transfusions
• Transfusion transmitted diseases	• Infectious agents

13.2 Transfusion Reaction Management and Investigation

a) Stop the transfusion immediately.
b) Maintain IV access for treatment if necessary but do not flush the blood tubing
c) Check vital signs
d) Take necessary resuscitative measures to stabilize the patient.
e) Verify that patient ID matches the compatibility label and compatibility report.

f) Verify that the blood unit number matches the compatibility label and report

g) Notify the physician but remain with the patient.

h) Notify the blood bank of the reaction.

13.3 Protocol to be followed for Evaluation of Transfusion Reaction

Send the following to the blood bank immediately

a) Implicated Blood bag with BT set

b) Post transfusion blood samples in

- 2 ml EDTA sample.
- 3 ml plain vial sample.

c) Completely filled and signed transfusion reaction form indicating signs/symptoms of reactions)

d) In case of suspected bacterial contamination: Send cultures both from the patient as well as blood bag at the bedside immediately.

13.4 Investigation to be done as per symptoms in transfusion reaction.

- Complete hemogram
- Plasma haemoglobin
- Coagulation profile
- Bilirubin (Unconjugated/conjugated)
- Urea; Creatinine
- Serum electrolytes
- Next voided urine for haemoglobin testing:
- Monitor urine output if haemolysis suspected
- Chest X-Ray if patient has new respiratory symptoms
- Blood cultures from the patient:
    - Drawn from a different vein
    - Antibiotics should be started immediately if bacterial sepsis suspected.

13.5 Signs and Symptoms of Acute Transfusion Reaction

Table 29: Type of Transfusion Reaction with Signs and symptoms

Type Of Reaction	Clinical Signs & Symptoms
Haemolytic Transfusion Reaction	• Fever/Chills,Hypotension/Tachycardia, Cola Coloured Urine, Nausea, Vomiting, Pain In Flanks/Back/Abdomen/Chest Etc. • **Unconscious patients** • Oozing from wound or IV site • Hypotension • Haemoglobinuria
Bacterial Contamination	• Fever, Chills, Hypotension, Nausea, Vomiting, Dyspnoea and Diarrhoea.
Transfusion Related Acute Lung Injury (TRALI)	• Dyspnoea Or Cyanosis, Fever, Tachycardia, • Hypotension
Febrile Non-Haemolytic Transfusion Reaction (FNHTR)	• Fever, Chills, Rigors, Cold, Headache, Nausea, Vomiting
Allergic/Anaphylactic Reaction	• Pruritis, Urticaria, Flushing, Angioedema, • Hoarseness, Stridor, Wheezing, Chest Tightness, Dyspnoea, Cyanosis, Anxiety, Nausea, Vomiting, Abdominal Cramps and Diarrhoea

13.6 Acute Haemolytic Transfusion Reaction

1. Transfusion of Incompatible red cells react with the patient's anti-A or anti-B antibodies and cause an acute haemolytic transfusion reaction (AHTR). Such a reaction can activate complement and cause disseminated intravascular coagulation (DIC) and acute renal failure. The reaction is usually most severe if group A red cells are transfused to a group "O" patient.
2. Transfusion of ABO-incompatible blood almost always arises from pretransfusion sample labelling errors or from failure to perform required checks prior to giving the transfusion. If red cells are administered to the wrong patient (i.e., any patient other than the one for whom the red cells were supplied) the chances of ABO incompatibility are about 1 in 3. Rarely, AHTR is due to a non-A, non-B, complement fixing antibody. Such reactions reported most commonly involve the Kell, Duffy and Kidd antigen group systems.
3. Acute haemolysis may also occur following transfusion of plasma-rich blood components such as platelets or FFP from donors with high titres of anti-A or anti-B that react with patient red cells.

4. In a conscious patient even a few millilitres of incompatible blood may cause symptoms within a few minutes of starting the transfusion. The patient may become restless or distressed and experience pain at the infusion site, fever, flushing, breathlessness, or abdominal, flank or substernal chest pain. The severity varies widely as it is dependent on the titre of blood group antibody in the recipient, the quantity of blood transfused and other factors such as age.
5. In an unconscious or anaesthetised patient, hypotension and uncontrollable bleeding due to DIC may be the only signs of an incompatible transfusion. Oliguria is common and is often followed by acute renal failure.
6. If AHTR is suspected, the transfusion must be stopped, the line maintained with intravenous saline and urgent steps taken to confirm or exclude this possibility

Table 30: Lab Evidence

• Direct antiglobulin test positive • Indirect bilirubin increased • No rise/inadequate rise in haemoglobin	• Hemoglobinema • Hemoglobinuria

13.6.1 Management of Acute Haemolytic Transfusion reaction

- Stop blood transfusion immediately find out if the blood is being transfused to any other patient as in case of mix up it may be that blood bags for two patients was exchanged.
- Maintain intravenous access with crystalloid, if necessary, with ionotropic support.
- Maintain blood pressure and pulse.
- Maintain adequate ventilation and oxygenation.
- Administer a diuretic and/or institute fluid diuresis.
  - Mannitol IV
  - Fruesemide IV bolus (dose appropriate for weight).
- Send blood samples (5 ml of plain blood and 2 ml of EDTA blood) to blood bank and for full blood count and blood picture.
- Send urine sample to biochemistry laboratory to check for haemoglobinuria.

13.6.2 If intravascular haemolysis is confirmed

- Monitor renal status (blood urea and creatinine) to consider haemodialysis.

- Monitor coagulation status (prothrombin time, activated partial thromboplastin time, fibrinogen, fibrin degradation products).
- If sepsis is suspected, send samples for appropriate cultures.
- If haemoglobin is markedly reduced, compatible red cell transfusion may be required to combat hypoxemia.

13.6.3 Prevention of Acute Haemolytic Transfusion reaction

- Minimise human error
- Follow up of every step from phlebotomist to medical technologist to the person administering blood
- Person responsible for transfusion has the last opportunity to prevent misidentification and is the first one to identify a transfusion reaction.

13.7 Signs and Symptoms of Delayed Haemolytic Transfusion Reaction

Table 31: Type of Delayed Transfusion Reaction with Signs and Symptoms

Type Of Reaction	**Clinical Signs & Symptoms**
Delayed Haemolytic Transfusion Reaction	1. More common in multiply transfused and multiparous women 2. Occurs 3 – 7 days post transfusion 3. Fever 4. Jaundice 5. Dark coloured urine

13.8 Delayed Haemolytic Transfusion Reaction

- A delayed haemolytic transfusion reaction (DHTR) is one in which evidence of increased red cell destruction develops, usually between 24 hours and 28 days, following a transfusion.
- The symptoms and clinical or laboratory signs are similar to AHTR but are usually less severe, with inadequate rise or unexplained fall in the post-transfusion haemoglobin. Clinically significant DHTR is rare and seldom fatal but can cause additional problems for a patient who is already seriously ill.
- DHTR occurs due to immunization to a red cell antigen from an earlier transfusion or pregnancy. The level of antibody is low to be detected in the pre transfusion sample. After transfusion of red

cells bearing the target antigen, a rapid secondary immune response boosts the antibody level so that, after a few days, transfused red cells bearing the relevant antigen is rapidly destroyed. Antibodies of the Kidd and Rh systems are the most frequent cause of DHTR.

Lab Evidence

- Extra vascular haemolysis
- Absence of anticipated Hb or HCT rise following blood transfusion
- Indirect hyper bilirubinemia
- Rarely haemoglobinuria

Diagnosis

- Presence of alloantibodies in post transfusion sample

13.8.1 Management of Delayed Haemolytic Reaction

- Observe urine output
- For further transfusion use only phenotyped red cells or transfusion of blood that lacks the responsible antigen

13.8.2 Prevention

- Antibody screening of all patient samples using a sensitive technique
- Issue medical alert to these patients
- Maintain record of the offending antibodies

13.9 Febrile Non-Haemolytic Transfusion Reaction (FNHTR)

- Fever or rigors during red cell transfusion affect 1 - 3% of recipients and are usually attributed to the transfusion of white cells present in blood components.
- Febrile non-haemolytic transfusion reactions (FNHTR) generally occur more frequently in patients who have been alloimmunised to leucocyte antigens as a result of pregnancy or recurrent transfusion. The use of leucocyte-depleted blood components has reduced the occurrence of FNHTR.
- Febrile reactions during platelet transfusion have been attributed to leucocyte- and platelet-derived cytokines that accumulate in the product during storage.

13.10 Classical symptoms of FNHTR

- Shivering, usually 30 - 60 minutes after the start of the transfusion, followed by fever. Most reactions can be managed by slowing or stopping the transfusion and giving an antipyretic such as paracetamol.
- FNHTR, although unpleasant, are not life-threatening, however it is important to remember fever or rigors can also be the early symptoms of a severe acute haemolytic transfusion reaction or transfusion of bacterially contaminated blood.

13.11 Management of FNHTR: -

Give antipyretics such as paracetamol for symptomatic rise in temperature.

13.11.1 Prevention: -

Recurrent severe FNHTR in patients who require repeated transfusion of red cells or platelets may be prevented by the use of washed cellular components.

13.11.2 Premedication

Premedication with antipyretics and/or antihistamines prior to transfusion is not advised as it is both unnecessary and may modify important signs of a transfusion reaction. Steroids are not appropriate for the treatment or prevention of FNHTR.

13.12 Allergic & Anaphylactic Reaction

Allergic reactions represent a spectrum of severity from mild, where the patient simply experiences isolated urticaria or a rash, though to fatal anaphylactic shock.

13.12.1 Allergic reaction

- These present as urticaria, rash, allergic dyspnea (stridor, cyanosis, wheezing), localized angioedema or generalized pruritis without hypotension during or within 4 hours of transfusion. These reactions are commonly associated with transfusion of components with large volumes of plasma, for example platelets and FFP.
- Symptoms usually subside if the transfusion is slowed, and parenteral antihistamine is given. The transfusion may be continued if there is no progression of symptoms after 30 minutes.
- A rise of mast cells supports the diagnosis of an allergic reaction.

13.12.2 Anaphylactic reaction

- These are rare but life-threatening complications that occur during or very shortly after transfusion and are differentiated from mild/moderate allergic reactions by its severity where, in addition to mucocutaneous features, there is respiratory distress, bronchospasm, severe hypotension and hypothermia/ hypotonia or syncope).
- Anaphylaxis may occasionally be associated with antibodies against IgA in patients who have extremely low levels of IgA in their plasma or other genetic variants of plasma proteins. If this is the suspected cause the patient should, if possible, not be transfused.

13.12.3 Management of Allergic Transfusion Reaction

- Stop transfusion
- Treat shock
- Start IV crystalloids
- Inj Adrenaline 1:1000 solution - 0.3 to 0.5 ml SC or IM.in mild
  In severe cases use 1: 10,000 IV
- Give IV hydrocortisone 100 mg.
- Give IV chlorpheniramine 50 mg.
- Treatment with an antihistamine or hydrocortisone for generalized allergic reactions is appropriate. Premedication may be appropriate before transfusing a patient who has previously experienced repeated allergic reactions. Routine premedication with antihistamines prior to transfusion is however not advised, as it is both unnecessary and may modify important signs of a transfusion reaction.

13.12.4 Prevention

- Used washed cellular components
- Encourage autologous transfusion
- Use platelets/plasma from IgA deficient donors

13.13 Hypotensive Transfusion Reaction

- Hypotensive transfusion reactions are defined as a drop in systolic blood pressure ≥ 30 mmHg during or within one hour of transfusion together with a systolic blood pressure ≤ 80 mm Hg. Most

reactions occur very rapidly within minutes of starting the transfusion and respond to ceasing the transfusion together with supportive care.

- These may occur more frequently in patients receiving angiotensin converting enzyme (ACE) inhibitor therapy.

13.14 Bacterial Contamination/Sepsis

1. Bacterial sepsis, though rare, is the leading microbial cause of transfusion mortality. Sources of bacteria in blood components include contamination from skin organisms at the phlebotomy site due to ineffective skin disinfection, skin plugs introduced to units during phlebotomy, transient bacteremia in donors and, rarely, contamination during handling and processing of components.
2. Bacterial contamination occurs more likely in components stored at room temperature (20 - 24C) such as platelets, than with red cells (stored at 2 - 6C). Common organisms associated with contamination include Staphylococcus epidermidis, Staphylococcus aureus, Bacillus cereus, Group B streptococci, Escherichia coli, Pseudomonas species and other gram-negative organisms.
3. Platelet-associated sepsis is not normally catastrophic and can occur several hours after post-transfusion in contrast to the sepsis and toxaemia from bacterially contaminated red cells which are often rapid and catastrophic, with reported mortality rates of up to 60%. Septic and toxic reactions may be life threatening.

13.14.1 Situation that increase the risk of bacterial contamination and its consequences

- Inadequate donor screening missing h/o diarrhoea or dental treatment
- Inappropriate storage conditions for blood
- Improper blood warming prior to transfusion
- Keeping blood in unmonitored nursing stations or domestic refrigerators.
- Undue delay in initiating blood transfusions after blood is issued by the blood bank or after blood is taken out of the blood bank refrigerator.
- Components requiring storage at room temperature e.g., platelets.
- Transfusion over a period of more than 4 hours.
- Entry port contamination while thawing or warming blood component
- Addition of any medication to blood bag

13.14.2 Management of Transfusion Reaction due to Bacterial contamination:

- Stop the transfusion immediately and investigate.
- Inspect blood bag for signs of bacterial overgrowth
- Brown- or purple-coloured red cells or plasma
- Presence of clots
- Opaque or muddy plasma
- Peculiar odour
- Haemolysis
- Ask for urgent patient and blood unit culture and Gram stain.
- Culture at 4oC, 20-24o C, 37oC temperature for aerobic, anaerobic
- Initial treatment involves managing the haemodynamic complications of sepsis and administration of intravenous antibiotics covering the usual pathogens associated with transfusion-related sepsis.

13.14.3 Prevention of bacterial contamination

- Predonation identification and deferral of potentially bacteraemic donors
- Enhanced disinfection of the skin at the phlebotomy site
- Diversion of the initial 10 - 40 mL blood collected into a separate container
- Bacterial monitoring of platelet components using an automated bacterial detection system
- Visual inspection of the blood component for abnormal appearance (such as discoloration or haemolysis) should be carried out both prior to release from the Blood Bank and before administration. Blood components must not be transfused beyond their expiry date.

13.15 Post-transfusion Purpura

- Post-transfusion purpura (PTP) is a rare but potentially lethal complication of transfusion of red cells and platelets. It is characterized by the sudden onset of severe thrombocytopenia, typically 5 - 12 days following transfusion, often associated with haemorrhage.
- PTP is most often seen in females (90% of cases) and in particular those with a history of pregnancy.
- Transfusion causes an anamnestic response boosting human platelet-specific antigen (HPA) antibodies previously stimulated by pregnancy or earlier transfusion. The resulting thrombocytopenia is due to alloantibody-mediated destruction of the transfused platelets as well as destruction of the patient’s own platelets.

13.15.1 Management of Post Transfusion Purpura:

- High dose intravenous immunoglobulin, 2 g/kg body weight, administered in divided doses over 2 - 5 consecutive days.
- Plasma exchange and corticosteroids have been used in the past but an increase in platelet count is significantly delayed when compared to intravenous immunoglobulin.
- If platelet transfusion is unavoidable, platelets that are compatible with the patient's antibody should be used although survival of the platelets may be impaired during the acute phase of the syndrome. If future transfusions are planned, red cell or platelet components from donors negative for the implicated HPA antigen(s) should be selected. There is Self-limited recovery in 21 days.

13.16 Transfusion-Associated Circulatory Overload (TACO)

TACO usually occurs within 6 hours of completion of the transfusion. When too much fluid is transfused or the transfusion is too rapid for a patient, fluid overload can lead to systemic and pulmonary venous engorgement. Cardiogenic pulmonary oedema and acute respiratory failure occurs.

13.16.1 Symptoms

Symptoms of transfusion-associated circulatory overload (TACO) include acute respiratory distress, tachycardia, increased blood pressure, evidence of fluid overload, an enlarged cardiac silhouette and new or worsening pulmonary oedema in the chest X-ray. Evidence of fluid overload may include a documented positive fluid balance and/or a clinical response to diuretic therapy.

13.16.2 Diagnosis

Diagnosis is supported by an elevated serum B-type natriuretic peptide (BNP) or the accompanying N-terminal fragment (NT-pro BNP) to more than 1.5 times the pretransfusion value (if available) and/or an increase in mean arterial pressure or increase pulmonary wedge pressure.

13.16.3 Management of TACO

- Stop the transfusion, make the patient sit upright, and administer oxygen and diuretic therapy. Give vasodilator therapy and/or non-invasive ventilatory support with continuous positive airways pressure (CPAP) Venesection can also be considered.

- TACO is most commonly seen in patients with low body weight, the elderly, infants or children, those with a history of cardiac, respiratory or renal insufficiency, and in the setting of red cell transfusion for chronic anaemia. Volume overload is a special risk with albumin solutions. Patients with chronic anaemia are normovolaemic or hypervolaemic have signs of cardiac failure before any fluid is infused. Each unit should be given slowly, and the patient closely observed. Pre-emptive diuretic therapy is helpful.

13.17 Transfusion-Related Acute Lung Injury (TRALI)

- Transfusion-related acute lung injury is a significant transfusion-related event and is one of the most common causes of fatal transfusion reactions.
- TRALI is characterized by acute respiratory distress due to non-cardiogenic pulmonary oedema, developing during or within 4-6 hours of transfusion.
- Plasma components containing antibodies against the patient's white blood cells are implicated. Transfusion is followed by a severe reaction with acute respiratory distress, accompanied by chills and/or fever, Hypoxia, hypotension,
- Chest X-ray shows numerous, mainly perihilar, nodules with Bilateral pulmonary infiltrates (lower lung fields) without cardiac enlargement or raised engorgement of the vessels (Normal CVP)
- Transient leucopenia or neutropenia associated with TRALI.
- Implicated donors are almost always alloimmunised multiparous women.
- Diagnosis of TRALI is therefore a clinical and radiographic diagnosis
- TRALI is a clinical syndrome rather than a disease which occurs due to interaction of human leucocyte antigen (HLA) or neutrophil-specific (HNA) antibodies of donor origin with the recipient's white cells.

13.17.1 Diagnosis

Antibody detection of HLA class I and II, HNA in donor(s) and recipient and further identification by HLA typing to confirm presence of the corresponding antigen(s). A crossmatch between donor serum and recipient white cells is also useful, with a positive result strongly implicating the particular donor(s).

13.17.2 Management of TRALI

Usually involves intensive care respiratory support and High dose steroids methyl prednisolone 1 g IV bolus

TRALI risk reduction strategy is to use FFP manufactured from plasma collected only from male donors.

13.18 Differential diagnosis of TACO and TRALI

- Acute respiratory distress during or shortly following transfusion may be due to TACO, TRALI, a severe allergic reaction or the patient's underlying condition. Unfortunately, many of the early signs and symptoms are not discriminatory and can occur in other types of transfusion reactions. Most FNHTR and allergic reactions can however be readily identified as such.
- It is important to distinguish between TACO and TRALI because of the relatively high mortality for TRALI. Invasive measurements such as central venous and pulmonary wedge pressures are useful (elevated in TACO) but are not consistently diagnostic or readily available, particularly in less severe cases. Measurement of serum B-type natriuretic peptide (BNP) or the accompanying N-terminal fragment (NT-pro BNP) is useful in the differential diagnosis of TACO.
- BNP is secreted from the cardiac ventricles as a result of ventricular pressure overload and volume expansion, such as occurs with TACO. Low levels of BNP can help exclude TACO however, whilst high levels may favour TACO, they do not necessarily exclude TACO.

13.19 Transfusion-Associated Dyspnoea (TAD)

- Only a minority of transfusion reactions are associated with predominantly respiratory features however these are some of the most serious transfusion-related adverse events. Included in this group are TACO, TRALI and allergic reactions, particularly of the more severe type.
- The term transfusion-associated dyspnoea (TAD) is used by haemovigilance programmes to record events with significant respiratory distress, occurring within 24 hours of transfusion, that do not meet the criteria of TRALI, TACO or allergic reaction nor are explained by the patient's underlying condition.

13.20 Transfusion-Associated Graft-Versus-Host Disease (TA-GVHD)

- Transfusion-associated graft-versus-host disease is a rare complication of transfusion caused by engraftment and proliferation of transfused donor T-lymphocytes which destroy recipient cells

carrying "foreign" human leucocyte antigens (HLA). Immunodeficient patients such as allogeneic bone marrow transplant recipients receiving cellular components and fetuses receiving intrauterine transfusions are at special risk for this disease. TA-GVHD has also occurred in immunologically normal patients after transfusion of blood from a relative.

- TA-GVHD is fatal in almost all cases with a Mortality > 90-99%. Acute TA-GVHD begins from 4 - 40 days after transfusion with high fever followed by a diffuse erythematous skin rash progressing to erythroderma and desquamation. Gastrointestinal symptoms occur as 3 to 4 liters of watery diarrhoea over 24 hours along with liver dysfunction -Jaundice and elevated liver enzyme and, unlike GVHD following stem cell transplants, pancytopenia is common.

13.20.1 Patients at risk of GVHD

- All newborn and premature babies
- Leukaemia
- All immunocompromised patients
- Recipient of transfusion of blood from blood relative
- HLA matched blood component
- Donor of the same ethnic background with limited HLA diversity

Table 32: Components Implicated/Non-Implicated in GVHD

Components implicated in TA-GVHD	**Components not implicated in TA-GVHD**
Whole blood	FFP
Packed red cells	Cryoprecipitate
Granulocytes	
Platelets &Platelet rich plasma	

13.20.2 Prevention

Gamma irradiation of cellular blood components (red cells and platelets) to a minimum dose of 25 Gray (Gy) targeted to the central position of the container and 15 Gy to all other parts of the container. The irradiation dose must not exceed 50 Gy.

13.21 Iron Overload / Haemosiderosis

Transfusion-dependent patients receiving red cells over a long period become overloaded with iron. Chelation therapy may be used to minimise or reverse accumulation of iron for these patients.

13.22 Transfusion-Related Immunosuppression

Allogeneic blood transfusion can cause suppression of the recipient's immune system. However, the mechanism behind the effect and the consequences resulting from such transfusion-related immunomodulation (TRIM) remain unclear.

13.23 Transfusion-Transmitted Infection

Blood donors, like anyone else, can occasionally carry an infectious agent, sometimes for a long period, without having any clinical signs or symptoms. Blood collected from such donors can transmit the infection to the recipient. For this reason, donors are interviewed at each, and every visit and laboratory tests are performed on each unit of blood.

13.23.1 Prevention of transfusion transmissible infections

- Enrolment of voluntary non-remunerated regular blood donors
- Information, screening, and counselling of donors
- Testing of all donated blood units in accordance with national standards.
- Barring release of untested blood
- Implementation of more sensitive tests to reduce window period
- Use of recombinant products
- Use of virally inactivated products
- Use of HBV vaccine in patients who are regularly transfused and in patients with low immunity levels

Chapter 14 – Therapeutic Plasma Exchange (TPE)

In therapeutic apheresis, whole blood is removed from the patient into an instrument that separates its components via a centrifugation process. The goal is to selectively remove a substantial proportion of one or more components causing disease while returning the remaining components to the patient, with or without replacement of the removed component. The rationale to use therapeutic apheresis can be based on mechanistic knowledge of the disease pathophysiology or evidence that therapeutic apheresis is clinically beneficial.

14.1 Issues regarding plasma exchange procedures:

a. Need to decide number of plasma volumes to exchange.

b. Calculation to determine approximate volume of replacement fluid needed

- Approximate total blood volume: adult male ~70 mL/kg; adult female ~65 mL/kg.

Term infant: 80-90 mL/kg; children: 75-80 mL/kg.

- Example: 83.6 kg adult male with hematocrit 24%.

Approximate 1.0 plasma volume (PV) = [total blood volume] X (1_hematocrit) = [(83.6 x 70 mL/kg)] X (1-0.24) = 4449 mL.

Table 33: Type of techniques available for TPE and their comparison

Parameter	Centrifugal Type TPE	Membrane Type (Dialysis Machine) TPE
Access	Peripheral dual needle/ CVA	Central venous access (CVA) catheter/fistula
Anticoagulant	Citrate	Heparin
Apheresis procedure versatility	May be used for plasmapheresis and other cytapheresis procedures such as stem cell collection and cell depletion	Cannot be used for cytapheresis
Plasma extraction efficiency rate	~80%	30%-35%
RBC loss	Minimal risk	Possible risk
Hemolysis	Minimal risk	Possible risk

Category definition for the diseases treated by Therapeutic Plasma Exchange (TPE). [Recommendations by American Society for Apheresis (ASFA), 2013]

Table 34: Category Definitions

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.

II	Disorders for which apheresis is accepted as second line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstance

Table 35: Neurological Indication

S.No.	Disease Name	Disease Condition	Category
1	Acute inflammatory demyelinating polyneuropathy (Guillain-Barre Syndrome)		I
2	Chronic inflammatory demyelinating polyradiculoneuropathy		I
3	Hyperviscosity in monoclonal gammopathies	Symptomatic	I
		Prophylaxis for rituximab	I
4	Myasthenia gravis	Moderate-severe	I
		Pre-thymectomy	I
5	PANDAS [paediatric autoimmune neuropsychiatric disorders associated with streptoccal infections]; sydenham's chorea	PANDAS exacerbation	I
		Sydenham's chorea	I
6	Paraproteinemic demyelinating polyneuropathies	IgG/IgA	I
		IgM	I
		Multiple myeloma	III
7	Acute disseminated encephalomyelitis		II
8	Lambert-Eaton myasthenic syndrome		II
9	Multiple Sclerosis	Acute CNS inflammatory demyelinating disease	II

		Chronic progressive	III
10	Myeloma cast nephropathy		II
11	Voltaged gated potassium channel antibodies		II
12	Acute inflammatory demyelinating polyneuropathy (Guillain-Barre Syndrome)	Post IVIG	III

Table 36: Nephrological Indications

S.No.	Disease Name	Disease Condition	Category
1	ANCA- associated rapidly progressive glomerulonephritis (Granulomatosis with polyangiitis; Wegener's Granulomatosis)	Dialysis dependent	I
		DAH [diffuse alveolar haemorrhage]	I
2	Anti-glomerular basement membrane disease (Goodpasture's syndrome)	DAH	I
		Dialysis independent	I
		Dialysis dependent & no DAH	III
3	Cryoglobulinemia	Sever	I
4	Focal segmental glomerulosclerosis	Recurrent in transplanted kidney	I
5	Haemolytic uremic syndrome, atypical	Factor H antibodies	I
		Complement gene mutations	III
		MCP mutations	IV
6	Renal transplantation, ABO compatible	Antibody mediated rejection	I
		Desensitization, living donor, positive crossmatch due to donor specific HLA antibody	I
		Desensitization, high PRA deceased donor	III
7	Renal transplantation, ABO Incompatible	Desensitization, live donor	I
		Humoral rejection	II
		Group A2/A2B into B, deceased donor	IV
8	Haemolytic uremic syndrome,infection-associated	Shiga toxin associated	IV
9	Haemolytic uremic syndrome,infection-associated	S. pneumonae associated	III

10	Immune complex rapidly progressive glomerulonephritis		III

Table 37: Hematological Indications

S.No.	Disease Name	Disease Condition	Category
1	Thrombotic thrombocytopenic purpura		I
2	Thrombotic microangiopathy, drug associated	Ticlopidine	I
		Clopidogrel	III
		Cyclosporine/ Tacrolimus	III
		Gemcitabine	IV
		Quinine	IV
3	HSCT [hematopoietic stem cell transplant] , ABO incompatible	Major HPC, Marrow	II
		Major HPC, Apheresis	II
4	Aplastic anaemia; pure red cell aplasia	Aplastic anaemia	III
		Pure Red Cell Aplasia	III
5	Autoimmunic haemolytic anaemia: WAHA; cold agglutinin disease	Sever WAHA [warm autoimmune haemolytic anaemia]	III
		Sever Cold agglutinin	III
6	Henoch-Schonlein purpura	Crescentric	III
		Severe extrarenal disease	III
7	Heparin induced thrombocytponia	Pre-cardiopulmonary bypass	III
		Thrombosis	III
8	Red cell alloimmunization in pregnancy	Prior to IUT availability	III
9	Thrombotic microangiopathy, HSCT associated	Refractory	III
10	Coagulation factor inhibitors	Autoantibody	III

		Alloantibody	IV
11	Immune thrombocytopenia	Refractory	IV

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