

Guidelines for the rational use of blood and blood products



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Ministry of Health
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Foreword



KETUA PENGARAH KESIHATAN MALAYSIA *DIRECTOR GENERAL OF HEALTH MALAYSIA*

Blood transfusion therapy is a complex process with a number of variables to be taken into consideration. The success of this therapy depends on the doctor who assesses the patient and orders the transfusion, the medical laboratory technician who processes the request and performs the appropriate tests, the transport personnel, the nurse or other clinical personnel who sets up the transfusion and monitors the patient and also the managers and policy makers who provide the resources to make blood transfusion safe.

Transfusing blood and its products has become an integral part of modern health care. Appropriately used, it can improve the quality of life and prevent morbidity and mortality. It remains the most commonly performed tissue transplant. However over the years it is constantly under pressure by concern over safety, cost and availability. Despite rigorous process and procedures in place to ensure safe blood transfusion, the risk of complication still remains. Therefore there is a need to ensure appropriateness of transfusion.

These guidelines are intended to provide a quick reference to practicing clinicians in the use of blood or blood components. Sound clinical judgement and care are still paramount in the process of blood transfusion.

Blood Transfusion Depends on Everyone

A handwritten signature in black ink, appearing to read 'Ismail Merican'.

Tan Sri Datuk Dr Hj. Mohd Ismail Merican
Director General of Health
Ministry of Health Malaysia

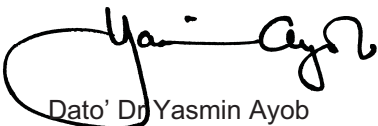
Preface

The Guidelines for the Rational Use of Blood has been prepared by a team of doctors from Pusat Darah Negara with reviewers from various disciplines and institutions. It is intended for doctors involved in prescribing and administering blood and blood products.

In preparing these guidelines we discovered that information on benefits and appropriateness of transfusion is difficult to obtain. Most doctors transfuse based on their clinical experience and many aspects of blood transfusion have not been proven by good clinical trials. Therefore it is not possible to give completely evidenced based facts. Where good evidence is not available we have used current expert opinions on good clinical practice which is accepted worldwide.

Recognising the fact that the decision to transfuse rests solely on the attending doctor, we hope these guidelines can assist doctors decide wisely after careful assessment of risks and benefit. It is not meant to be prescriptive but with the input coming from various disciplines these guideline will benefit doctors in deciding whether transfusion is really necessary, which blood component or product to transfuse and other options if available and more appropriate.

Safe Blood Saves Lives



Dato' Dr Yasmin Ayob
Director
National Blood Centre

GUIDELINES FOR THE RATIONAL USE OF BLOOD AND BLOOD PRODUCTS

INTRODUCTION

The need to ensure the appropriateness of blood transfusion has long been recognized. The approaches used to achieve this are many. Although the nation's blood supply is much safer than it has ever been, the risk still exists. Safety is still a concern for clinicians, patients and their families, and for that reason, clinicians need to ensure that any attending risk can be justified by the potential benefits. Alternative strategies to reduce the use of allogeneic blood should be considered such as blood conservation techniques in surgery, autologous transfusion, or the use of pharmacological agents.

Modification of routine practices can minimize the need to transfuse red cells, such as checking and correcting anaemia before planned surgery, use of erythropoietin to improve haemoglobinization and aprotinin to reduce surgical bleeding. These recommendations outline clinical circumstances in which blood transfusion may be the appropriate therapy. They are not intended as an indication for the use of blood or blood products.

The decision to transfuse varies from patient to patient and should be based on sound clinical judgement.

1. Clinical Decision on Transfusion

Clinical judgement about the balance of risks and benefits should be central to any decision to transfuse. There may be significant variation in the situations in which the use of red cells is appropriate.

- Patients should be informed that transfusion of red cells, plasma or platelets are part of the planned medical or surgical intervention, and information about the risks, benefits and available alternatives are discussed. The patient's consent should be obtained for the planned transfusion and recorded in the patient's medical chart.
- Red cell transfusion should be administered primarily to prevent or alleviate the signs and symptoms of morbidity due to inadequate tissue oxygen delivery.
- There is no single value of haemoglobin concentration that justifies the need for transfusion and the requirements of each patient should be based on their clinical status.
- Red cell products should not be transfused for volume expansion only or to enhance wound healing.
- The decision to transfuse is complex and depends on many factors e.g. the cause of anaemia, its severity, chronicity, the patient's ability to compensate for the anaemia, the likelihood for further blood loss and the need to provide some reserve before the onset of tissue hypoxia.
- For some patients in some clinical situations, it is preferable to use the patient's own blood that has been collected in advance for planned surgery (autologous blood).

2. Surgery and Anaesthesia

Transfusion in surgery and anaesthesia is usually indicated in cases of anaemia, blood loss and coagulopathy.

Among the problems encountered in the peri-operative period are:

- Increased oxygen demand e.g. increased catecholamines, shivering, pain
- Reduced oxygen supply e.g. hypovolaemia and hypoxia

To ensure adequate oxygenation, several important steps can be taken:

- Ensuring optimal volume status
- Adequate analgesia
- Providing supplemental oxygen
- Maintaining normothermia

Transfusing patients with allogeneic blood exposes them to risks such as:

- infection
- adverse immunological and cardiorespiratory morbid events
- theoretical risk of vCJD (variant Creutzfeld Jacob Disease)

Several strategies to reduce exposure to allogeneic transfusion include autologous transfusion, surgical, anaesthetic and pharmacological approaches to reduce blood loss.

Strategies for management of transfusion requirements in elective surgical patients can be divided into three phases:

- **Pre-operative**
- **Intra-operative**
- **Post-operative**

2.1 Pre-operative Management

2.1.1 Surgical Transfusion Checklist

- A surgical transfusion checklist is helpful in deciding the need for transfusion and avoiding red cell transfusion. (See Chart 1)
- The anaesthetist must play a lead role in ensuring good pre-operative assessment and preparation.

CHART 1 : PLANNED SURGICAL TRANSFUSION CHECKLIST

PATIENT IDENTITY		Hospital Number :	
Name :			
I/C Number :		Date of Birth :	
Diagnosis :			
Procedure :	Explained :	Yes / No	
Component Required :	Info Leaflet :	Yes / No	
RELEVANT MEDICAL DETAILS			
Hb			
If anaemic – Diagnosis?	Yes / No	Action to Remedy:	
Anticoagulants/ Antiplatelets agent	Yes / No	Action to Remedy:	
Procoagulants	Yes / No	Action to Remedy:	
Respiratory Status			
Cardiac Status			
AUTOLOGOUS TRANSFUSION			
Discussed :		Yes / No	
Info Leaflet :		Yes / No	
Date Procedure :		Plan Collection :	
OUTCOME			
Components Used :		Discharge :	
COMMENT :			

2.1.2 Treatment of Pre-existing Anaemia

- Assessment of iron status (including non-anaemic patients on long-term aspirin and NSAIDs) is important. If iron deficiency is confirmed, patients should be treated with haematinics for 3 months. (*Refer Page 53*)
- Iron deficiency delays erythropoiesis in the post-operative period, therefore increasing the likelihood of transfusion.
- Asymptomatic normovolaemic anaemia **should not be transfused** pre-operatively.
- Erythropoietin can be used in non-iron deficient adult patients (<70 years old) who are moderately anaemic (Hb 10-13 g/dl). (*Erythropoietin Dose, refer Page 62*)

2.1.3 Predeposit Autologous Donation

- Involves the collection and storage of the patient's own blood prior to elective surgery.
(*Refer Autologous Blood Transfusion, Page 90*)

2.1.4 Avoidance of Drugs that Increase Surgical Blood Loss

- Aspirin, NSAIDs and ticlopidine and clopidogrel should be discontinued at least 7 days prior to surgery.
(*Refer Chart II : Peri-operative Management for Patients on anticoagulation e.g. warfarin and heparin*)

CHART II
PREPARATION OF ANTICOAGULATED PATIENT FOR SURGERY

PATIENTS FULLY ANTICOAGULATED WITH WARFARIN

ELECTIVE SURGERY

- Stop warfarin 3 days pre-operatively and monitor INR daily
- Give heparin by infusion or subcutaneously, if required.
- Stop heparin 6 hours pre-operatively.
- Check INR and APTT ratio immediately prior to surgery.
- Commence surgery if INR and APTT ratio are < 2.0 .
- Restart warfarin as soon as possible post-operatively.
- Restart heparin at the same time and continue until INR is in the therapeutic range.

EMERGENCY SURGERY

- Give vitamin K, 0.5-2.0 mg by slow IV infusion.
- Give fresh frozen plasma, 15 ml/kg. This dose may need to be repeated to bring coagulation factors to an acceptable range.
- Check INR immediately prior to surgery.

Commence surgery if INR and APTT ratio are < 2.0 .

PATIENTS FULLY ANTICOAGULATED WITH HEPARIN

ELECTIVE SURGERY

- Stop heparin 6 hours pre-operatively.
- Commence surgery if INR and APTT ratio are < 2.0 .
- Check APTT ratio immediately prior to surgery.
- Restart heparin as soon as appropriate post-operatively.

EMERGENCY SURGERY

Consider reversal with IV protamine sulphate. 1 mg of protamine neutralizes 100 iu heparin.

PATIENTS RECEIVING LOW-DOSE HEPARIN

It is rarely necessary to stop low-dose heparin injections, used in the prevention of deep vein thrombosis and pulmonary embolism, prior to surgery.

2.1.5 Surgical Blood Ordering Schedule

- This schedule is a reference used to guide clinicians in ordering blood before surgery. (*Refer Chart III below*)

CHART III GUIDELINES ON ESTABLISHING MAXIMUM BLOOD ORDERING SCHEDULE FOR KKM HOSPITALS

The Maximum Surgical Blood Order Schedule (**MSBOS**) is a table of elective surgical procedures which lists the number of units of blood routinely requested, and cross-matched for them pre-operatively. The schedule is based on retrospective analysis of actual blood usage associated with the individual surgical procedure. An important factor that can be considered in the establishment of an MSBOS is the identification of those procedures that can be accommodated performed. Where blood by the group, antibody screen and hold (**GSH**) procedure. For cases where blood is likely to be transfused, a group screen and hold is likely to be transfused, a full cross-match is done. However when antibody screen is positive, compatible blood must be made available in all cases before surgery.

Developing MSBOS

Data on blood request for all procedures for 6 months is analysed. For each procedure, indicate the number of units cross-matched and the number of units transfused.

Calculate the percentage of blood usage:

$$\frac{\text{Total No. of Units transfused}}{\text{Total No. of Units cross-matched}} \times 100 = \quad \%$$

In procedures where blood usage is less than 30%, GSH are performed. Other procedures are allotted a tariff based on the average number of blood transfused.

Example: Table: 1 Calculation of C:T Ratio

Procedure	No. of Operations	Units of Blood Crossmatched	Units of Blood Transfused	% of Units Transfused	C:T Ratio
Caesarian Section	60	120	8	6.6 %	15
Total Hip Replacemen	20	60	40	66 %	1.5

C:T = Crossmatch : Transfusion

In the above example for Caesarian section, GSH is performed, while in Total Hip Replacement, a full cross-match is performed. The number of units cross-matched is based on the average number of units transfused.

In drawing up the schedule, local factors such as expertise available in the hospital and the speed of provision of compatible blood have to be taken into account.

Implementation

MSBOS should be explained to all doctors in the hospitals and the best way is through the Transfusion Committee. Once the draft schedule has been constructed, it should be circulated and discussed. Flexibility should be allowed for individual cases e.g. placenta praevia. When all heads of department have agreed on a schedule, it should be circulated and implemented. Regular monitoring is necessary to detect any problems and for 'fine tuning' of the schedule if necessary.

Confidence in the operation of MSBOS and compliance by users depend on the laboratory being able to provide compatible blood whenever it is required, including urgent requests. This is dependent on the following 5 factors:

- i. Pre-operative blood samples must be obtained from all patients: whether GSH or cross-matching categories. Laboratories will set their time limits on the latest time the samples should be submitted before the date of surgery. This is to ensure ample time is allocated for the grouping, screening and cross-matching of blood. If an irregular antibody is detected, this may delay the provision of compatible blood and the consultant must be informed.

- ii. Serum saved for cross-matching must be accurately labelled and readily accessible.
- ii. Procedures must be clearly defined to enable blood transfusion staff to provide compatible blood safely should an emergency occur during a GSH operation.
- v. Communication between the operating theatre and the blood transfusion laboratory must be clearly defined.
- v. Transporting blood between the laboratory and the operating theatre must have an established priority.

Serological Techniques

- Blood samples from all patients must have a full ABO and RhD grouping and antibody screening done.
- For GSH category, the serum is kept for 48 hours.
- Where antibody screen is positive, antibody identification must be performed and compatible blood cross-matched before surgery is performed.
- If blood is required urgently, blood of the same ABO and RhD can be given after an appropriate 'quick blood has method'. After been issued, the laboratory would continue to do a full cross-match. If any incompatibility is detected, the patient's doctor must be informed immediately.

MAXIMUM SURGICAL BLOOD ORDER SCHEDULE (MSBOS)

GENERAL SURGERY

Abdominal-perineal resection	4
Cholecystectomy	GSH
Gastrectomy	2
Hemicolectomy, Small bowel resection	GSH
Hiatus hernia repair:	
Abdominal	GSH
Transthoracic	2
Inguinal hernia repair	GSH
Laparotomy	GSH
Perforated viscus	2
Mastectomy	GSH
Oesophagectomy	4
Pancreatectomy	4
Portocaval shunt	4

Splenectomy	2
Thyroidectomy, Parathyroidectomy	GSH
Varicose veins	GSH
Vagotomy	GSH
Whipple's procedure	4
GYNAECOLOGY	
Hysterectomy:	
Abdominal, Vaginal	GSH
Wertheim	2
Myomectomy	GSH
Ovarian Cystectomy	GSH
Termination, D & C	GSH
Vaginal Repair	GSH
Manual removal placenta	GSH
Caesarian section	GSH
Evacuation under anaesthesia	GSH
UROLOGY	
Cystectomy	4
Nephrectomy	GSH
Percutaneous nephrolithotomy	GSH
Pyelolithotomy:	
Simple	GSH
Complicated, large Calculus	2
Renal transplant	GSH
Retropubic prostatectomy	2
TUR prostate	GSH
Ureterolithotomy	GSH
ORTHOPAEDICS	
Femoral osteotomy	2
Fractured humerus	GSH
Fractures, neck of femur	GSH
Laminectomy, spinal fusion	2
Harrington rods	4
Putti-Platt shoulder repair	GSH
Total hip replacement	3
Total knee replacement	2
Total shoulder replacement	GSH
MISCELLANEOUS	
Cardiac catheterisation	GSH
Coronary angiogram	GSH
Liver, renal biopsy	GSH
Pacemaker insertion	GSH

- For RhD negative patients, blood bank must be informed at least a week prior to the procedure so as to ensure blood is available before surgery. (**Refer Chart IV below**)

CHART IV

GUIDELINES ON THE TRANSFUSION OF BLOOD AND BLOOD COMPONENTS IN RhD NEGATIVE PATIENTS

Introduction

The Rh blood group system is extremely complex and certain aspects are not fully understood. After the A and B antigens of the ABO system, the D antigen of the Rh system has the most significant implications for transfusion practice. The Rh antigens are well developed at birth and they have not been demonstrated in secretions or in any other tissue other than red cells.

In Malaysia, the frequency of the RhD negative phenotypes based on ethnic groups is as follows: Indians 15%, Malay 2-3% and Chinese < 1%. In general, less than 2% of the population in Malaysia is of RhD negative phenotype.

Clinical Significance

The clinical importance of the Rh blood group system stems from the fact that the D antigen has greater immunogenicity than virtually all other red cell antigens. About 90% of D negative individuals will make anti-D antibodies after the transfusion of large volume of D positive cells, and 70% will respond to repeated small volumes. This anti-D antibody can cause haemolytic transfusion reaction that can lead to disseminated intravascular coagulation and renal failure. Moreover, since they are of IgG subclass, anti-D antibodies can cross the placenta and cause severe haemolytic disease of the newborn. The Rh system is also involved in the specificity of some of the warm autoantibodies of autoimmune haemolytic anaemia.

Recommendation

- It is current practice in KKM blood banking that all blood banks are routinely screened for D antigen prior to transfusion in donor and recipients. As far as possible, all Rh D negative patients must receive D negative whole blood or packed red cells except in certain situations as stated in the recommendation below.
- All blood banks should have a few RhD negative units in their stock based on their requirement. It is also recommended that the blood bank keep a list of their RhD negative donors who can be contacted in an emergency.
- Clinicians in charge of known RhD negative patients must alert the blood bank of their patient's blood need at least a week prior to the requirement date, eg: planned surgeries or expected date of delivery. This is to provide ample time for the blood bank to recruit the appropriate number of donors.
- In the event of life-threatening bleeding / when D negative blood is not available, efforts should be made to try and find D negative blood. In the event that blood may not be made available in time, the treating clinicians may decide to allow RhD positive blood to be given instead. This is safe provided the patient does not have preformed anti-D antibodies.
- **RhD immunoprophylaxis (Anti-D prophylaxis)**
In any D negative women of childbearing age who are not already immunised to RhD, the inadvertent transfusion of D positive blood should be treated by giving a suitable dose of anti-D immunoglobulin. However, in D negative postmenopausal women or in men who have been transfused with D positive blood, consideration of immunoprophylaxis should be given although the consequences to the subject of becoming immunised are not likely to be serious because treatment with large amounts of anti-D immunoglobulins is wasteful and can produce unpleasant effects.
Anti-D immunoglobulin is prepared from plasma collected from donors who have high levels of anti-D antibodies.

In Malaysia, the intramuscular preparation is available, and if given at a dose of 20-25 g (100-125 iu) within 72 hours of a sensitising event, is capable of suppressing primary immunisation by 1 ml RhD positive red cells.

When more than 2 units of RhD positive blood have been transfused, an exchange transfusion with RhD negative blood (once available) should be considered to reduce the load of RhD positive RBCs in circulation; thus reducing the dose of anti-D immunoglobulin required to suppress primary immunisation.

Following exchange transfusion, the residual volume of RhD positive RBCs should be estimated using flow cytometry or resetting. Follow-up tests for RhD positive RBCs should be undertaken every 48 hours and further anti-D immunoglobulin is given until all RhD positive RBCs have been cleared from the circulation.

- As D negative platelet concentrate and plasma are not available, D negative patients who require them can be safely given D positive blood components. However, the blood bank supplying the components should select the product with the least red cell contamination. It is also advisable to give the patient anti-D immunoglobulins to suppress primary RhD immunisation in women of childbearing age. 50 g (250 iu) anti-D immunoglobulin should be given following every three adult doses of platelets.
- **Side effects of Anti-D Immunoglobulin**
Skin: Local erythema, swelling and tenderness at the injection site.
General: Transient rise in temperature, chills, general malaise. Rarely, it can cause shock, hypotension, tachycardia and dyspnoea. In large doses, anti-D immunoglobulins can also cause rapid red cell destruction / haemolysis with haemoglobinuria.

2.1.6 Patients with Pre-existing Coagulopathy

- Pre-existing coagulopathy should be investigated and managed appropriately. (Refer Pages 32, 50, 51 & 62)

2.2 Intra-operative Management

2.2.1 Management of Blood Loss

- Attention to surgical techniques can reduce frequency of allogeneic transfusion.
- Normothermia must be maintained as hypothermia contributes to the development of coagulopathies that will increase pre-operative blood loss. Appropriate action: fluid warmers, thermal drapes, heated humidifiers, forced air warming blankets.
- In major blood loss, where there is evidence of microvascular bleeding, disseminated intravascular dissemination (DIC) must be suspected. Coagulation studies (DIC screen) and platelet count should be performed. Appropriate component therapy can be given based on clinical and baseline investigations.
- Assessment of blood loss, with serial haemoglobin (Hb) estimation and haemodynamic parameters, helps to guide volume and transfusion therapy.
(*Refer Chart V and VI Pages 22 & 23*)

2.2.2 Management of Volume Replacement

- Maintain normovolaemia in the presence of anaemia.
- Pre-operative deficits should be considered for volume replacement e.g. prolonged fasting, nausea, vomiting, diarrhoea.
- Intra-operative losses vary according to surface area exposed, third space interstitial loss and blood loss.
- Initial volume replacement is usually with crystalloid, and later, a combination of crystalloid and colloid.

CHART V - MANAGEMENT OF ACUTE BLOOD LOSS

Need for transfusion is based on estimation of lost circulating volume.

Table I: Calculating Blood Volume

Age Group	Blood Volume
Neonates	85-90 ml/kg
Children	80 ml/kg
Adults	70 ml/kg

Table II: Classification of Hypovolaemic Shock according to Blood Loss (adult)¹⁴

	Class I	Class II	Class III	Class IV
Blood loss: Percentage Volume (ml)	<15 750	15-30 800-1500	30-40 1500-2000	>40 >2000
Blood Pressure Systolic Diastolic	↔	N ↓	↓ ↓	↓↓ ↓↓
Pulse	slight tachycardia	100-120	120 (thready)	>120 (thready)
Capillary Refill	N	slow >2s	slow >2s	undetectable
Respiratory Rate	N	N	tachypnoea >20/min	tachypnoea >20/min
Urinary Flow Rate (ml/hr)	>30	20-30	10-20	0-10
Extremities	N	pale	pale	pale & cold
Complexion	N	pale	pale	ashen
Mental state	alert	anxious	anxious, aggressive or drowsy	drowsy, confused or unconscious
Management	No need for transfusion (Transfuse if: pre-existing anaemia or severe cardioresp disease)	Crystalloid/ colloid (Transfuse if: pre-existing anaemia or reduced cardioresp reserve)	Rapid volume replacement with crystalloid/ colloid Red cell transfusion probably required	Rapid volume replacement with crystalloid/ colloid & red cell transfusion

CHART VI - MANAGEMENT OF HYPOVOLAEMIA IN PAEDIATRIC PATIENTS

Table III : Classification of Hypovolaemia in Children

	Class I	Class II	Class III	Class IV
Blood Volume	<15%	15-25%	25-40%	>40%
Pulse Rate (beats/min)	↑	>150	>150	↑or ↓
Pulse Pressure	N	↓	↓↓	absent
Systolic Blood Pressure	N	↓	↓↓	unrecordable
Respiratory Rate (breaths/min)	N	↑	↑	slow sighing respiration
Capillary Refill Time	N	prolonged	very prolonged	absent
Mental State	N	irritable	lethargic	comatose
Urine Output	<1 ml/kg/hr	< 1ml/kg/hr	<1 ml/kg/hr	< 1ml/kg/hr

- Recognition of hypovolaemia is more difficult than in adults
- Signs of hypovolaemia may only be apparent after 25% of blood volume is lost due to increased physiological reserve.
- Therefore 20 ml/kg of crystalloid fluid should be given should patients show signs of hypovolaemia Class II or greater. These may need to be repeated three times depending on the response.
- If transient or no response to initial fluid challenge → transfuse either 20 ml/kg of whole blood or 10 ml/kg packed red cells.
- Heat loss occurs rapidly in children due to high surface-to-mass ratio. Hypothermic children may be refractory to treatment; thus it is vital to keep warm.

Adequate analgesia must be maintained after initial fluid resuscitation.

2.2.3 Reduction of Oxygen Demand

- Anaemia is better tolerated if oxygen demand is minimized.
- Adequate depth of anaesthesia and adequate analgesia is required to reduce oxygen demand of myocardium and brain tissue.

2.2.4 Intra-operative Blood Salvage (IBS)

- Intra-operative blood salvage (IBS) is the process where blood is collected, washed, concentrated and re-infused at the time of surgery. Useful in cardiac, orthopaedic and vascular surgery, organ transplantation and trauma, and has shown to reduce requirements of allogeneic transfusion.
- For effective and safe use, active management by the lead clinician and adherence to standard operating procedure is required. (**Refer: Autologous Blood Transfusion, Pg 90**)

2.2.5 Antifibrinolytic Agents

- Effective and safe in reducing blood usage, in particular, redo cardiopulmonary bypass surgery, redo valve grafts and liver transplantation.
- Aprotinin and tranexamic acid act by inhibiting fibrinolysis & encouraging clot stability.

2.3 Post-Operative Management

2.3.1 Post-operative Blood Salvage (PBS)

- Post-operative blood salvage (PBS) is the process where blood is collected in the drains and is returned to the patient. It is well-described in cardiac and orthopaedic surgery, in particular, total knee arthroplasty. (*Refer: Autologous Blood Transfusion, Pg 90*)

2.3.2 Management of Volume Replacement & On-going Blood Loss

- Post-operative patients in ICU/HDU require close monitoring of haemodynamic status, oxygenation, pain relief, biochemical and haematological indices and on going blood loss.

2.3.3 Red Cell Transfusion

Table I: Transfusion Trigger for Red Cell Transfusion

Clinical Indication	Trigger Level of Hb for Red Cell Transfusion
Critically-ill patient (Canadian Critical care Trial Group) ⁹	≤ 7 g/dl
Acute blood loss >500 ml in patient with underlying cardiovascular disease ¹⁰	< 7 g/dl
Hip fracture surgery ⁸	< 8 g/dl
Coronary artery bypass grafting ¹¹	< 8 g/dl
Underlying cardiovascular or respiratory disease; elderly	< 8 g/dl

2.4 Transfusion of Blood

2.4.2

General Rule of Thumb

- 10 g/dl is no longer used as transfusion trigger unless the patient has low cardiorespiratory reserve.
- Most haemodynamically stable adult patients will not require transfusion if Hb > 9/dl.
- Transfusion almost always required if **Hb < 6g/dl (particularly in acute anaemia)**.
- Transfusion of allogeneic blood can increase post-operative infections due to immunosuppressive effect.
- Symptomatic anaemia patients should be transfused regardless of the haemoglobin level.
- Each patient should be considered on an **individual basis**, based on:
 - i) clinical signs & symptoms (especially with haemodynamic instability)
 - ii) comorbidity
 - iii) further risk of blood loss

2.4.3 Platelet Transfusion

- The use of platelet transfusion should be reserved for those patients who are experiencing excessive post-operative bleeding and in whom a surgical cause has been excluded.
- Pre-operative cessation of any antiplatelet therapy will minimize the use of platelet transfusion.
- Transfusion is indicated only if the defect cannot be otherwise corrected e.g. congenital platelet abnormality.
(Refer Chart VII next page)

CHART VII : GUIDE FOR THE USE OF PLATELET TRANSFUSION

Table 2: :Indication for Platelet Transfusion	
CLINICAL INDICATIONS	CUT-OFF VALUES OF PLATELET COUNT
HAEMATOLOGICAL MALIGNANCIES	> 20 X 10 ⁹ is the safe limit unless: fever, bleeding, on antibiotics or coagulopathy
PROCEDURES:	
1. BONE MARROW ASPIRATION & TREPINE	> 20 X 10 ⁹ providing adequate surface pressure is applied
2. LUMBAR PUNCTURE, EPIDURAL, OGDS & BIOPSY, INDWELLING LINES, TRANSBRONCHIAL BIOPSY, LIVER BIOPSY, LAPARATOMY	Platelet count should be raised to at least 50 X 10 ⁹
3. FOR OPERATION AT CRITICAL SITES: EYE & BRAIN	Platelet count should be raised up to at least 100 X 10 ⁹
MASSIVE TRANSFUSIONS:	
1. ACUTE BLEEDING	Platelet count should be raised up to at least 50 X 10 ⁹
2. MULTIPLE TRAUMA / CNS INJURY	Higher target level of 100 X 10 ⁹
DISSEMINATED INTRAVASCULAR COAGULATION:	
1. ACUTE DISSEMINATED INTRAVASCULAR COAGULOPATHY (DIC)	Frequent estimation of platelet count & coagulation screen should be done Aim to maintain platelet count at >50 X 10 ⁹
2. CHRONIC DIC / ABSENCE OF BLEEDING	Platelet transfusion should not be given
CABG/ RUPTURED ABDOMINAL AORTIC ANEURYSM:	
PRE-OPERATIVE ASSESSMENT OF MEDICATIONS KIV DELAY SURGERY @ PRE-OPERATIVE TRANSFUSION	Should be reserved for those with post-operative bleeding & surgical cause has been excluded

IMMUNE THROMBOCYTOPAENIA:	
1. AUTOIMMUNE THROMBOCYTOPAENIA	Only for life-threatening bleeding from GIT/GUT/CNS and other conditions with severe thrombocytopenia ($<10 \times 10^9$)
2. NEONATAL AUTOIMMUNE THROMBOCYTOPAENIA (NAITP)	Transfuse compatible platelet ASAP, ideally HPA-1a neg, HPA-5b neg. Platelet prepared from mother should be irradiated and washed.
3. POST TRANSFUSION PURPURA	Platelet transfusion usually ineffective M/B used in acute phase e.g. operation
PLATELET FUNCTION DISORDERS:	
PLATELET TRANSFUSION ONLY INDICATED IF OTHER MEASURES FAIL TO CONTROL THE BLEEDING	
Table 2: CALCULATION OF DOSE:	
RANDOM PLATELET	$>60 \times 10^9$ / UNIT (VOLUME = 50 ml) 1 UNIT RANDOM INCREASES UP TO $5-10 \times 10^9$
1 UNIT APHERESIS	$>200 \times 10^9$ / UNIT (VOLUME = 200-300 ml) EQUALS TO 4-6 UNITS RANDOM PLATELETS
<20 kg CHILD	10 – 15 MI / kg
ADULT	$\frac{\text{PLATELET INCREMENT TARGET} \times \text{BLOOD VOLUME}}{\text{CORRECTION FACTOR (0.67)}}$
**PLATELET TRANSFUSION IS CONTRAINDICATED IN: Thrombotic Thrombocytopenic Purpura (TTP), Heparin-induced Thrombocytopenia (HIT) & Kasabach Meritt Syndrome	

2.4.4 Cryoprecipitate Transfusion

- Transfusion of cryoprecipitate is rarely given except in circumstances where there is evidence of low fibrinogen level or cases of hypo / afibrinogenaemia.
(Refer Chart VIII below)

CHART VIII GUIDE FOR THE USE OF CRYOPRECIPITATE

1. The use of cryoprecipitate may be considered appropriate in patients with fibrinogen deficiency where there is clinical bleeding, an invasive procedure or disseminated intravascular coagulation.
2. The use of cryoprecipitate is not generally considered appropriate in the treatment of haemophilia, von Willebrand disease, or deficiencies of Factor XIII or fibronectin unless alternative therapies are unavailable, such as :
 - von Willebrand's disease, type II or type III, with bleeding, or pre-operatively, when viral-inactivated factor concentrate containing von Willebrand factor activity is not available
 - hypofibrinogenaemia or dysfibrinogenaemia, with bleeding, or pre-operatively
 - replacement therapy in factor XIII deficiency.
 - VWD type I or type II if appropriate factor concentrate containing VWF is not available.

2.4.5 Fresh Frozen Plasma

The use of fresh frozen plasma (FFP) for surgical or traumatic bleeding should be guided by coagulation profiles.
Refer Chart IX.

CHART IX - GUIDE FOR THE USE OF FRESH FROZEN PLASMA (FFP) TRANSFUSION

Indications for FFP:

1. For replacement of single factor deficiencies where specific or combined factor concentrate is not available.
2. For immediate reversal of warfarin effect in the presence of potentially life-threatening bleeding when used in addition to vitamin K.
3. For treatment of multiple coagulation deficiencies associated with acute disseminated intravascular coagulation.
4. For the treatment of thrombotic thrombocytopenic purpura.
5. For the treatment of inherited deficiencies of coagulation inhibitors in patients undergoing high risk procedures where specific factor concentrate is unavailable.
6. In the presence of bleeding and abnormal coagulation parameters following massive transfusion or cardiac bypass surgery or in patients with liver disease.

The use of FFP is generally not considered appropriate in cases of hypovolaemia, plasma exchange procedures or treatment of immunodeficiency state.

3. Trauma and Massive Transfusion

Massive transfusion is defined as transfusion of a volume equal to the patient's total blood volume in less than 24 hours.

High risk patients:

- Prolonged hypotension and shock predispose patients to disseminated intravascular coagulation (DIC) and adult respiratory distress syndrome (ARDS).
- Extensive tissue damage, particularly head injuries, is associated with coagulation abnormalities.
- Hepatic and renal failure patients have abnormalities of haemostasis or plasma proteins and impaired metabolic response to citrate, potassium or glucose infused with stored blood.

3.1 Problems associated with Massive Transfusion

3.1.1 Thrombocytopenia

- Stored blood is devoid of functioning platelets.
- Dilutional thrombocytopenia must be anticipated during massive blood replacement (at least 1.5 blood volume transfused e.g. 7 to 8 litres in adults).
- Platelet count should be maintained at $> 50 \times 10^9/L$.
- In cardiac bypass surgery, bleeding may occur at higher platelet levels due to acquired functional defect.

3.1.2 Coagulation Factor Depletion

- Only mild reductions in total coagulation factors are caused by dilutional effect in massive transfusion.
- Disordered haemostasis is more likely to be due to disseminated intravascular coagulation (DIC):
 - Platelet count $<50 \times 10^9/L$
 - Prolonged PT and APTT ($>1.5 \times$ control)
 - Hypofibrinogenaemia $<150 \text{ mg/dl}$
 - Elevated fibrinogen degradation products
 - Clinically widespread microvascular bleeding
- DIC is more likely if resuscitation is delayed or inadequate.

3.1.3 Oxygen Affinity Changes

- The level of 2,3 diphosphoglycerate (2,3 DPG) falls in stored RBC, and this decrease has been suggested as a potential cause of tissue hypoxia after massive transfusion. Low 2,3-DPG levels have not been shown to be detrimental to massively transfused patients, although for infants undergoing exchange transfusion, blood with near-normal 2,3-DPG levels is frequently requested.
- Transfusion of fresh RBC is recommended in cases of arteriosclerotic vascular disease or poorly vascularised tissue anastomoses.

3.1.4 Hypocalcaemia

- Citrate in anticoagulant binds ionized calcium and lowers plasma calcium level.
- Neonates and hypothermic patients are more vulnerable to citrate toxicity.
- Lowered calcium level has synergistic effect with high potassium level in patients with disturbed cardiac function.

- In patients with evidence of hypocalcaemia (clinically and with ECG changes), IV calcium gluconate (10%) at a dose of 5 ml should be given in 5 minute intervals until ECG has normalized.

3.1.5 Hyperkalaemia

- Plasma potassium content increases during storage of blood.
- Hyperkalaemia and hypocalcaemia impair myocardial function, eventually causing cardiac arrest.
- Avoidance of hypothermia is the best measure to prevent hyperkalaemia and hypocalcaemia.

3.1.6 Acid Base Disturbance

- Lactic acid (end product in red cell glycolysis in blood pack) theoretically contributes to overall acidosis of hypoxic shocked patients.
- Arterial pH should be monitored.
- Sodium bicarbonate should be added to IV fluids when pH < 7.2.
- Citrate metabolism generates bicarbonate, thus metabolic alkalosis is a usual consequence of massive transfusion.

3.1.7 Hypothermia

- Unwanted cooling of the body may result from rapid infusion of blood.
- Blood warmers should be used for rates of infusion exceeding 1 unit per 10 min in adults (50ml /kg /hr) and proportionately less in children (15ml /kg /hr).

- Hypothermia slows down citrate metabolism, potentiates harmful cardiac effects of hyperkalaemia and hypocalcaemia and reduces oxygen release from haemoglobin

3.1.8 Adult Respiratory Distress Syndrome (ARDS)

- Under or over-transfusion should be avoided.
- Plasma oncotic pressure should not fall below 20 mmHg.
- Hypoproteinaemia occurs when excessive amounts of crystalloids are given.

3.2 Management Strategy for Trauma and Massive Transfusion

3.2.1 Sequence of Components

- Treat profound hypotension speedily in preferential order: crystalloids, synthetic colloids/5% albumin. (A recent controlled trial of saline vs albumin infusion in adult ICU patients showed that albumin is considered safe but without demonstrating clear advantage over saline).
- If transfusion is required, initial transfusion with packed red cell is advisable but if bleeding continues, it is sensible to give whole blood. (**Refer Chart V, Page 22 for Calculation of Blood Loss and Fluid Management**)

3.2.2 Laboratory Sample

- Blood sample should be collected for blood grouping, cross-matching, coagulation test and biochemical profile prior to blood transfusion.

3.2.3 Blood Bank Arrangements

- Degree of urgency for transfusion should be accurately conveyed to blood bank.

- Routine procedures for blood grouping, antibody screening and compatibility testing should be followed as far as practicable.
- In an emergency situation:
Group O Rh positive should be supplied first, followed as soon as possible by ABO RhD group specific blood (as the prevalence of RhD negative phenotypes in Malaysia is generally less than 2 % of the population).
- In the event of massive life-threatening bleeding and RhD negative blood is not available, RhD positive blood can be given provided the patient does not have preformed anti-D.
(Refer Chart IV, Page 18)

HAEMATOLOGICAL MONITORING IN MASSIVE TRANSFUSION

Investigation	Target Value
Haemoglobin; Haematocrit	10 g/dl; 0.30
Platelet Count	> 50 x 10 ⁹ /L
Prothrombin Time (PT)	< 1.5 x control
Partial Thromboplastin Time (PTT)	< 1.5 x control
Fibrinogen	> 150 mg/dL

3.3 Choice of Transfusion Material in the Management of Trauma and Massive Transfusion

3.3.1 Crystalloids and Colloids

- Valuable during the initial stage of resuscitation.
- The fluid of choice are isotonic saline and Ringer lactate; synthetic colloids (gelatin, hydroxylethyl starch) or human albumin (5%) solution are the principal alternatives.
- When 2-3 litres of crystalloids have been given, human albumin (5%) can be given to avoid reduction of osmotic pressure. (***For other uses of Human Albumin, refer Chart X below***)

CHART X - USES OF ALBUMIN

USAGE OF HUMAN ALBUMIN

Albumin is a very soluble, globular protein (MW 66,500) accounting for 70-80% of the colloid osmotic pressure of plasma which is the predominant reason for its clinical use.

INDICATIONS AND USAGE

General Principles

The two main indications for the use of human albumin are:

- * plasma or blood volume deficit
- * oncotic deficit resulting from hypoproteinaemia

Volume Deficit

Since the oncotic pressure of human albumin solution is about five times that of normal human serum, it will expand the plasma volume if interstitial water is available for an inflow through the capillary walls.

Oncotic Deficit

The common causes of hypoproteinaemia are protein-calorie malnutrition, defective absorption in gastrointestinal disorders, faulty albumin synthesis (eg: in chronic hepatic failure), increased protein catabolism after operation or in sepsis, and abnormal renal losses of albumin in chronic kidney disease. In these situations, the circulating plasma volume is usually maintained by the renal retention of sodium and water, but this is associated with tissue oedema and an oncotic deficit. Although relief of the underlying pathology is the definitive therapy for the restoration of the plasma protein level, this process takes time to become effective and the rapid correction of an oncotic deficit by the administration of Albumin (Human) 25%, possibly in conjunction with a diuretic, may be indicated.

It is emphasized that although Albumin (Human) may be necessary to prevent or treat the aforementioned acute complication of hypoproteinaemia, it is NOT indicated for treatment of the chronic condition itself.

SPECIFIC INDICATIONS

Justified Usage of Human Albumin

Shock

The definitive treatment for major haemorrhage is the transfusion of red blood cells restoring the normal oxygen transport capacity of the blood. However, the life-threatening event in major haemorrhage is the loss of blood volume and not the erythrocyte deficit. Therefore, the blood volume should, as an emergency measure, be supported by human albumin or another rapidly acting plasma substitute if blood is not immediately available. This will restore cardiac output and abolish circulatory failure with tissue anoxia.

Burns

An optimal regimen for the use of Albumin (Human), electrolytes, and water in the treatment of burns has not been established. Therapy during the first 24 hours after a severe burn is usually directed at the administration of crystalloid solutions in order to maintain an adequate plasma volume. For continuation of therapy beyond 24 hours, larger amounts of Albumin (Human) and lesser amounts of crystalloid are generally used.

Adult Respiratory Distress Syndrome (ARDS)

Several factors are usually involved in the development of the state now commonly called adult respiratory distress syndrome (ARDS), one of these being a hypoproteinaemic fluid overload. In its initial phase, this may be corrected by the use of human albumin, a diuretic, along with careful haemodynamic and respiratory monitoring of the patient. It must be recognized, however, that the beneficial effects of Albumin (Human) in this condition depend on the integrity of the pulmonary microvasculature. Increased permeability to albumin can negate these beneficial effects, and in such circumstances Albumin (Human) could actually contribute to the respiratory distress.

Cardiopulmonary Bypass

An adequate blood volume during cardiopulmonary bypass can be maintained with crystalloids or colloids (albumin). A commonly employed program is an Albumin (Human) and crystalloid pump prime adjusted so as to achieve a haematocrit of 20% and a plasma albumin level of 2.5 g/100 ml in the patient, but the level to which either may be lowered safely has not yet been defined.

Haemolytic Disease of the Newborn

Albumin (Human) may be indicated in order to bind and thus detoxify free serum bilirubin in severely haemolytic infants pending an exchange transfusion. Caution is recommended in hypervolaemic infants.

Acute Nephrosis

Patients with acute nephrosis may prove refractory to cyclophosphamide or steroid therapy and their oedema may even be aggravated initially by steroids. In such cases, a response may be elicited by combining Albumin (Human) 25% with an appropriate diuretic, after which the patient may react satisfactorily to drug therapy.

Unjustified Usage of Human Albumin

Post-operative Hypoproteinaemia

Intra-operative damage of capillary walls, e.g. by blunt dissection, leads to substantial losses of circulating albumin over and above those due to bleeding.

However, this redistribution of albumin in the body rarely causes clinically significant hypovolaemia, and treatment of the resultant plasma oncotic defect with Albumin (Human) is not usually indicated.

Red Cell Resuspension Media

As a rule, the use of Albumin (Human) for resuspending red cells can be dispensed with. However, in exceptional circumstances such as certain types of exchange transfusions and the use of very large volumes of erythrocyte concentrates and frozen or washed red cells, the addition of Albumin (Human) to the resuspension medium may be indicated in order to provide sufficient volume and/or avoid excessive hypoproteinaemia during the subsequent transfusion. If necessary, 20-25 g or more of albumin/liter of red cells should be added as a concentrated solution to the isotonic electrolyte suspension of erythrocytes immediately before transfusion.

Renal Dialysis

Patients undergoing long-term haemodialysis may need Albumin (Human) for the treatment of a volume or an oncotic deficit. The patients should be carefully observed for signs of a circulatory overload to which they are particularly sensitive.

Acute Liver Failure

In acute liver failure, Albumin (Human) may serve the triple purpose of stabilizing the circulation, correcting an oncotic deficit and binding excessive serum bilirubin. The therapeutic approach is guided by the individual circumstances.

Ascites

The use of Albumin (Human) for blood volume support may be indicated if circulatory instability follows the withdrawal of large amounts (>1500 ml) of ascitic fluid.

Third Space Problems of Infectious Origin

The sequestrations of protein-rich fluid during acute peritonitis, pancreatitis, mediastinitis or extensive cellulitis are very rarely of sufficient magnitude to require the treatment of a volume or an oncotic deficit with Albumin (Human).

3.3.2 Red Cells

- Packed red cells transfusion may be adequate during initial resuscitation.
- When bleeding continues, whole blood may be given for further management in restoring blood volume and for oxygen-carrying capacity. (*Refer Chart V Page 22 and Chart VI Page 23*)

3.3.3 Platelet Concentrate

- It is indicated when platelet count $< 50 \times 10^9/L$ and with continuous bleeding.
- Platelet transfusion should be considered early in bleeding patients especially in cardiac bypass patients (platelet functional abnormalities due to aspirin) even at platelet counts between 50 to $100 \times 10^9/L$. (*Refer Alt as indicated in Chart VII Page 27*)

3.3.4 Fresh Frozen Plasma and Cryoprecipitate

- These blood products are used for the correction of coagulation abnormalities.
- Indicated in cases of continuous bleeding with disturbed coagulation tests (PT and APTT $> 1.5 \times$ control).
- In the event of disseminated intravascular coagulation (DIC), it may be necessary to perform the transfusion of platelet concentrate, FFP and cryoprecipitate.
(*Refer Chart VIII and Chart IX, Pages 29 & 30*)

3.3.5 Use of Recombinant FVIIa (rFVIIa) Concentrate

- rFVIIa has been used in patients with overt bleeding who fail to respond to standard therapy.
- Local protocol should be in place and decisions should be made at the consultant level.

3.4 Disseminated Intravascular Coagulation (DIC)

DIC is always secondary to a primary disease state such as septicaemia, postpartum haemorrhage, massive transfusion, trauma, retained dead foetus etc. These result in abnormal and excessive stimulation of the coagulation system, where coagulation factors and antithrombin are deficient and need replacement. Clinical features include excessive uncontrolled bleeding, bruising and oozing from puncture sites.

Management of disseminated intravascular coagulation (DIC)

- The **primary cause** of the DIC should be treated **first**.
- Maintain circulatory volume as in massive transfusion.
- Correct acidosis.
- Component therapy as required.

The clinical picture ranges from major haemorrhage, with or without thrombotic complication, to a clinically stable state that can be detected only by laboratory testing.

LABORATORY TEST

1. Platelet Count
2. Prothrombin Time (PT)
3. Activated Partial Thromboplastin Time (APTT)
4. Thrombin Time (TT): particularly helpful in establishing presence or absence of DIC
5. Fibrinogen: normal concentration at term should be 4.0-6.0 g/L
6. Fibrin degradation products (FDPs/D-Dimer)

If laboratory tests are available, they will show:

- Reduced coagulation factors (so all coagulation tests are prolonged)
- Low fibrinogen level
- Fibrin degradation products; D-dimer, FDP present.
- Low platelet count: $<50 \times 10^9 /L$
- Fragmented red cells on the blood film

If these tests are not available, the following simple test for DIC can be used:

1. Transfer 2-3 ml of venous blood into a clean plain glass tube (10 x 75 mm)
2. Hold the tube in your hand to keep it warm (ie body temperature).
3. After 4 minutes, tip the tube slowly to see if a clot is forming. Then tip it again every minute until the blood clots and the tube can be turned upside down.

The clot will normally form between 4 to 11 minutes but in DIC, the blood will remain fluid well beyond 15 to 20 minutes.

3.4.1 Management includes:

3.4.1.1 Platelet Transfusion

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

Recommendations:

- Aim to maintain the platelet count $> 50 \times 10^9 /L$ in the case of massive blood loss.
- In chronic DIC, or in the absence of bleeding, platelet transfusion should not be given merely to correct a low platelet count. (**Refer Chart VI, Page 23**)

3.4.1.2 Fresh Frozen Plasma (FFP) Transfusion

- FFP is not indicated in DIC with no evidence of bleeding. There is no evidence that prophylactic replacement regimens prevent DIC or reduce transfusion requirement.
- When used for surgical or traumatic bleeding, FFP usage should be guided by coagulation profiles.
- Should not be used as a simple volume replacement/expansion. **(Refer Chart IX below)**

CHART IX - GUIDE FOR THE USE OF FRESH FROZEN PLASMA(FFP) TRANSFUSION

Indications for FFP:

1. For replacement of single factor deficiencies where specific or combined factor concentrate is not available
2. For immediate reversal of warfarin effect in the presence of potentially life-threatening bleeding when used in addition to Vitamin K
3. For treatment of multiple coagulation deficiencies associated with acute disseminated intravascular coagulation
4. For the treatment of thrombotic thrombocytopenic purpura
5. For the treatment of inherited deficiencies of coagulation inhibitors in patients undergoing high risk procedures where specific factor concentrate is unavailable
6. In the presence of bleeding an abnormal coagulation parameters following massive transfusion of cardiac bypass surgery or in patients with liver disease

The use of FFP is generally not considered appropriate in cases of hypovolaemia, plasma exchange procedures or treatment of immunodeficiency state.

3.4.1.3 Cryoprecipitate Transfusion

- Cryoprecipitate may be indicated if the plasma fibrinogen is < 1 g/L, although there is no clear threshold for clinically significant hypofibrinogenaemia **(Refer Chart VIII, Page 29)**

4. Obsterics

4.1 Anaemia in Pregnancy

4.1.1 Anaemia in pregnancy, as defined by WHO, is a haemoglobin concentration of less than 11.0 g/dL in the first and third trimesters.

4.1.2 Amongst the causes of anaemia in pregnancy are:

- Iron deficiency, with or without folate deficiency
- Short birth interval
- Vitamin B12 deficiency
- HIV infection
- Malaria
- Sickle cell disease

4.1.3 However, anaemia alone does not necessitate transfusion unless the health of the mother and / or the foetus is compromised. In the second trimester, a fall of 0.5 g/dL due to increased plasma volume is allowed.

Stage of Pregnancy	Anaemia if Hb is 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

Prevention and management of nutritional anaemia with adequate antenatal care can reduce the prevalence of anaemia and the need for transfusion during pregnancy.

4.2.1 Prophylactic Administration of Haematinics

4.2.1.1 In treating iron and folate deficiency, optimum daily doses needed are:

- 120 mg elemental iron
(eg: 200 mg tablets of ferrous sulphate)
- 500 µg of folate

4.2.1.2 In severe anaemia, higher daily doses of iron should be given to build up iron stores to 200-300 mg:

- 180 mg elemental iron
- 2 mg folate

4.2.2 Red Cell Transfusion

The decision to transfuse red cells is based on:

- clinical symptoms
- stage of pregnancy
- haemoglobin level

Transfusion does not treat the cause of anaemia and does not correct the non- haematological effect of iron deficiency

4.2.2.1 Pregnancy < 36 weeks

- Haemoglobin 5 g/dL or below, even without clinical signs of cardiac failure or hypoxia

4.2.2.2 Pregnancy > 36 weeks

- Haemoglobin 6.0 g/dL or below

4.3 Elective Caesarean Section

When elective caesarean section is planned for patients with a history of ante partum haemorrhage, postpartum haemorrhage and previous history of caesarian section, GSH (Group,Screen and Hold) is recommended.

4.3.1 Prepartum (just before delivery):

- Haemoglobin level between 8.0 and 10.0 g/dL: establish/confirm blood group and save the serum for cross-matching
- Haemoglobin level < 8.0 g/dL: two units of blood should be cross-matched and available

Values given are meant as a guide; and clinical evaluation overrides the need to transfuse.

4.3.2 Blood Loss During and After Delivery

- Approximately 500 ml of blood (250 mg iron) is lost during normal vaginal delivery of a single foetus and up to 1000 ml during caesarean section.
- This blood loss rarely necessitates transfusion provided that the maternal haemoglobin level is 10.0 g/dL before delivery.
- Intravenous or rectal misoprostol and intravenous or intramuscular syntocinon, ergometrine or synthetic oxytocin octapeptide (carbetacin) appears to be safe and effective in an attempt to prevent excessive blood loss during caesarean section under regional anaesthesia.

4.4 Massive Blood Loss

Acute blood loss is one of the main causes of maternal morbidity and mortality. This may occur at any time throughout pregnancy and the puerperium, and the bleeding may be unpredictable and massive.

Table IV: Causes of Acute Blood Loss in Obstetric Patients

Causes :	
i)	Foetal loss in pregnancy which may result in: <ul style="list-style-type: none">• incomplete abortion• septic abortion
ii)	Ruptured ectopic pregnancy <ul style="list-style-type: none">• tubal• abdominal
iii)	Antepartum haemorrhage, which may be caused by: <ul style="list-style-type: none">• placenta praevia• abruptio placentae• ruptured uterus• vasa praevia• incidental haemorrhage from cervix or vagina e.g. polyps
iv)	Traumatic lesions, including: <ul style="list-style-type: none">• episiotomy• laceration of perineum or vagina• laceration of cervix• ruptured uterus
v)	Primary Postpartum Haemorrhage: Any haemorrhage in excess of 500 ml from the genital tract, occurring within 24 hours of delivery

Causes include:

- uterine atony
- retained products of conception
- traumatic lesions abnormally adherent placenta
e.g. placenta accrete clotting defects acute uterine inversion

vi) Secondary Postpartum Haemorrhage :
Any haemorrhage from uterus, after 24 hours and within 6 weeks of delivery.

Causes include :

- puerperal sepsis
- retained products of conception (membrane or placental tissue)
- tissue damage following obstructed labour (which may involve cervix, vagina, bladder or rectum)
- breakdown of uterine wound after caesarian section

vii) Disseminated Intravascular Coagulation (DIC) induced by:

- intrauterine death
- amniotic fluid embolism
- sepsis
- pre-eclampsia
- abruptio placentae
- retained products of conception
- induced abortion
- excessive bleeding
- acute fatty liver

Prompt recognition and correct management of obstetric haemorrhages reduce the number of maternal deaths in pregnancy.

Haemoglobin between 8.0 and 10.0 g/dL: establish/confirm blood group and save the freshly taken serum (GSH) and reserve it for cross-matching.

Haemoglobin < 8.0 g/dL: 2 units of blood should be cross-matched and made available.

4.4.1 Emergency Management of Major Obstetric Haemorrhage

4.4.1.1 Resuscitate

- Administer high concentrations of oxygen.
- Head down, tilt/raise legs.
- Establish venous access with 2 large bore cannulae (14g or 16g).
- Infuse crystalloid replacement fluids or colloids as rapidly as possible. Restoration of normovolaemia is a priority.
- Inform blood bank that this is an emergency.
- Use a pressure infusion device and warming device if possible.
- Call extra staff to help:
 - Senior obstetrician
 - Senior anaesthetist
 - Midwives
 - Nurse
 - Alert the haematologist
 - Ensure assistants are available at short notice

4.4.1.2 Stop the bleeding / definitive treatment procedure

- Identify the cause.
- Examine cervix and vagina for lacerations.
- If retained products of conception and uncontrolled bleeding, treat as DIC.
- If uterus is hypotonic or/and atonic:
 - Ensure bladder is empty
 - Give IV Oxytocin 20 units
 - Give IV Ergometrine 0.5mg
 - Oxytocin infusion (40 units in 500ml)
 - "Rub Up" fundus to stimulate a contraction
 - Bimanual compression of uterus
 - If bleeding continues, 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

4.4.1.3 Monitoring / Investigation

- Send sample to blood bank for matching of further blood, but do not wait for cross-matched blood if there is serious haemorrhage.
- Order full blood count.
- Order coagulation screening.
- Continuously monitor pulse rate and blood pressure.
- Insert urinary catheter and measure hourly output.
- Monitor respiratory rate.
- Monitor conscious level.
- Monitor capillary refill time.
- Insert central venous pressure line if available, and monitor CVP.
- Continue to monitor haemoglobin or haematocrit.

4.5 Disseminated Intravascular Coagulation (DIC)

Disseminated intravascular coagulation (DIC) is a cause of massive obstetric haemorrhage. It may be triggered by abruptio placentae, intrauterine death, eclampsia, amniotic fluid embolism and many other causes.

The clinical picture ranges from major haemorrhage, with or without thrombotic complications, to a clinically stable state that can be detected only by laboratory testing.

(Refer Table on Page 41 for Laboratory tests for DIC)

DIC is always secondary to an underlying process. Main management is to treat the underlying cause. Replacement with blood products is indicated when there is bleeding with acute DIC. The goal is to control bleeding.

4.5.1 Guidelines for the Management of DIC

MANAGEMENT OF DISSEMINATED INTRAVASCULAR COAGULATION (adapted from WHO)

1. Treat the cause
 - Deliver foetus 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 control the haemorrhage and restore blood volume with a balanced salt solution: e.g. Hartmann's solution or Ringer's lactate.
4. If needed for oxygen perfusion, give fresh blood (less than 1 week old).
5. Avoid the use of cryoprecipitate and platelet concentrates unless bleeding is uncontrollable. If bleeding is not controlled and coagulation tests show very low platelets, fibrinogen, prolonged PT or APTT, replace coagulation factors and platelets with:
 - Cryoprecipitate: at least 10 units.
 - If cryoprecipitate is not available, give:
 - fresh frozen plasma (15ml/kg): 1 unit for every 4-6 units of blood to prevent coagulation defects resulting from the use of stored red cell concentrates/suspensions.

4.6 Thrombotic Thrombocytopenic Purpura (TTP)

Diagnosis of TTP in pregnancy is sometimes difficult, especially in pregnant women with systemic lupus erythematosus (SLE), because TTP, pregnancy-associated microangiopathies such as HELLP (Haemolysis, Elevated Liver Enzyme, Low Platelet) and lupus-associated microangiopathy share similar clinical features.

Option of treatment will include the following:

- corticosteroids
- antiplatelet agents
- danazol
- cyclophosphamide
- vincristine sulphate, and
- intravenous IgG

However, the most effective treatment is **plasma exchange** with cryosupernatant.

Summary

Key points to be noted

- Anaemia in pregnancy is a haemoglobin concentration of less than 11.0 g/dL in the first and third trimesters and 10.5 g/dL in the second trimester.
- The diagnosis and effective treatment of chronic anaemia in pregnancy is an important way of reducing the need for future transfusions. The decision to transfuse blood should not be based on haemoglobin levels alone, but also on the patient's clinical need.
- Blood loss during normal vaginal delivery or caesarean section does not normally necessitate transfusion provided that the maternal haemoglobin is above 10.0 – 11.0 g/dl before delivery. The haemoglobin concentration should return to normal by 2 weeks postpartum. If it does not occur, further investigation is required.
- Obstetric bleeding may be unpredictable and massive. Every obstetric unit should have a current protocol for major obstetric haemorrhage and all staff should be trained to follow it.
- If disseminated intravascular coagulation (DIC) is suspected, do not delay treatment while waiting for the results of coagulation tests.

5. General Medicine

5.1 Nutritional Deficiencies

The most common causes are iron deficiency, folate and vitamin B12 deficiency. The principles of management are:
Identify the primary cause or underlying disorders and treat eg: menorrhagia, gastritis, malabsorption syndrome.

5.1.1 Iron Deficiency

Replenish iron stores:

- Recommended doses of Iron therapy:
Ferrous sulphate 200 mg 3x/day for minimum of 4-6 weeks
Increase in haemoglobin level at the rate 0.5-1.0g/dL/week

For monitoring of response:

- Reticulocytes response can be seen on Day 3-5 and peaks between Day 8-10
- If this is ineffective or not tolerated, parenteral iron may be considered.

5.1.2 Folate Deficiency

Recommended dose of folic acid:

- 5 mg daily for 3-6 months

5.1.3 Vitamin B12 Deficiency

Recommended dose of vitamin B12:

- IM 1 mg weekly for 3 weeks then
- IM 1 mg every 3 months for life

Transfusion is **rarely** indicated although it may be considered for patients with signs and symptoms of symptomatic anaemia. Transfusion will correct the anaemia but will not correct the deficiency state.

5.2 Anaemia of Chronic Disease

This is the second most prevalent cause of anaemia and occurs in patients with systemic diseases. The causes are a combination of:

- impaired marrow utilization of iron
- lower than expected rise in erythropoietin
- blunted marrow response to erythropoietin
- erythroid activity suppressed by cytokines.

Transfusion is rarely needed for chronic anaemia.

5.2.1 The Principles of managing patients with Anaemia of Chronic Disease are:

- Exclude the possibility of a haemoglobinopathy
- Identify and correct vitamin deficiencies
- Correct any identifiable cause of blood loss:
 - Treat helminthic or other infections
 - Deal with any local bleeding sources
 - Stop anticoagulant treatment if any
 - Stop drugs that are gastric mucosal irritants eg aspirin, NSAIDs
 - Stop antiplatelet drugs e.g. aspirin, NSAIDs, Flavix, Ticlid

5.2.2 Transfusion is rarely needed for patients with chronic anaemia, except in decompensate situation such as:

- Increased demand for oxygen:
 - infection
 - pain
 - fever
- Reduction in oxygen supply
 - acute blood loss / haemolysis

- pneumonia

- Signs of acute decompensation are:
 - change in mental status
 - diminished peripheral pulses
 - congestive cardiac failure
 - hepatomegaly
 - poor peripheral perfusion (capillary refill > 2 seconds)

5.2.3 Management of Decompensated Anaemia

- Treat infection aggressively

- Give oxygen support

- Correct fluid balance without overloading the patient.

- Decide whether red cell transfusion is needed. Use packed red cells rather than whole blood.

Do not transfuse more than necessary. If one unit of red cells is enough to correct symptoms, do not give 2 units.

- Transfusion of 1 Unit of Packed Cells should not exceed 4 hours.

- Diuretic (IV Frusemide 40 mg) should be considered in patients who are at risk of fluid overload.

Give enough to relieve clinical condition but not to restore the haemoglobin to normal level

5.3 Haemolytic Anaemia

Haemolytic anemias are due to abnormalities affecting:

- Red cell haemoglobin e.g. haemoglobinopathies such as thalassemias, sickle cell disease and enzymopathies such as G6PD deficiency.
- Red cell membrane e.g. spherocytosis, elliptocytosis, immune haemolysis
- Factors extrinsic to red cells e.g. disseminated intravascular coagulation (DIC), hypersplenism, malaria and other infections, drugs and other toxins

5.3.1 Thalassaemia

Patients with thalassaemia have a failure to synthesize haemoglobin normally. Transfusion is important in managing some of these conditions and there are special problems associated with them.

- The goals of transfusion in β thalassaemia major include suppression of erythropoiesis and inhibition of increased gastrointestinal iron absorption as well as correction of anaemia.
- Regular transfusion therapy to maintain haemoglobin levels of at least 10 g/dL. Allows improved growth and development, reduces hepatosplenomegaly due to extramedullary haematopoiesis as well as bone deformities.

5.3.1.1 Approach in Management of Thalassaemia major

- **Transfusion**
 - Regular transfusion to maintain haemoglobin level 10-12g/dl
 - Patient red cells should be phenotyped for Rh, Kidd, Duffy and MNSs blood group before the first transfusion.

- Use of leucodepleted/leucoreduced red cells is recommended to minimize the risk of Febrile Non-Haemolytic Transfusion Reaction (FNHTR), transmission of CMV and alloimmunization.
- **Chelation therapy** : to remove excess iron eg: Desferroxamine, deferiprone.
- **Vaccination against Hepatitis B for all transfusion dependent patients.**

GENETIC DEFECTS AND CLINICAL FEATURES THALASSEMIA

Condition	Genetic Defect	Clinical Features
Homozygous β thalassaemia (β thal. major)	β chain suppression or deletion	Severe anaemia: Hb < 7 g/dL. Dependent on transfusion
Heterozygous β thalassaemia (β thal minor trait)	β chain deletion	Asymptomatic. Mild anaemia: Hb > 10 g/dL.
Thalassaemia intermedia	β chain suppression or deletion	Ranges from asymptomatic to resembling β thalassaemia major: Hb 7-10 g/dL
Homozygous α thalassaemia	All 4 α globin chains deleted	Foetus does not survive (hydrops foetalis)
α thalassaemia minor	Loss of 2 or 3 α genes	Usually mild or moderate
α thalassaemia trait	Loss of 1 or 2 α genes	Symptomless: mild microcytic, hypochromic anaemia

5.3.2 G6PD Deficiency

G6PD deficiency is commonly asymptomatic but jaundice and anaemia are precipitated by infection, drugs and chemicals.
(Refer Chart XIV Page 108)

- Haemolysis in G6PD deficiency is self-limiting and will stop once the cells deficient in G6PD have been destroyed.
- It is important to remove or treat any identifiable cause.
- Transfusion is not required in most cases, but may be life-saving in **severe haemolysis** when the haemoglobin level continues to fall rapidly.

5.3.3 Auto Immune Haemolytic Anaemia (AIHA)

AIHA is an uncommonly occurring haematologic disorder that may arise *de novo* as an idiopathic condition or in conjunction with another illness such as lymphoproliferative disorder or connective tissue disease.

- AIHA can be classified into two major types; those associated with warm antibodies reacting at 37°C and with cold antibodies reacting at 0-5°C.
- Patients with AIHA frequently have anaemia of sufficient severity as to require transfusion.
- However, it is almost impossible to find compatible blood when, as is frequently the case, the autoantibody in the patient's serum reacts with all normal red blood cells.
- The autoantibody may mask the presence of a red cell alloantibody capable of causing a haemolytic transfusion reaction.

5.3.3.1 Management of Autoimmune Haemolytic Anaemia

MANAGEMENT OF AIHA

Warm AIHA	Cold Agglutinin Syndrome	Paroxysmal Cold Haemoglobinuria
<ul style="list-style-type: none"> • corticosteroids • splenectomy • immunosuppression • danazol • IV Ig • High dose cyclophosphamide 	<ul style="list-style-type: none"> • avoidance of cold • cytotoxic drugs • rituximab • plasma exchange 	<ul style="list-style-type: none"> • supportive care

- Transfusion therapy in AIHA is complicated by the difficulty in finding compatible blood.
- The decision to transfuse does not depend on the compatibility results but on an evaluation of the patient's need for transfusion.
- The patient's red cells should be phenotyped for Rh, Kidd, Duffy and MNSs blood groups. These can be used to guide the exclusion of alloantibodies by indicating which antigen specificities the patient is at risk of developing.
- If the patient is clinically stable and responsive to therapy, transfusion may not be required
- Reticulocytopenia indicates a high likelihood of early need for transfusion support.
- The least compatible blood may invariably be transfused in extremely urgent settings such as severe bleeding and symptomatic patients.

5.4 Bone Marrow Failure

Bone marrow failure occurs when the bone marrow is unable to produce adequate cells and usually manifests as pancytopenia.

5.4.1 Main Causes of Marrow Failure or Suppression

- chemotherapy
- radiation treatment of malignant diseases
- marrow infiltration
- aplastic anaemia
- infection
- toxic effects of drugs or chemicals

5.4.2 Management of Bone Marrow Failure

- Treat and remove the underlying disease
- Treat any superimposed infection
- Maintain fluid balance
- Supportive treatment e.g. nutrition, pain control
- Transfusion support:
 - Red cell transfusion**
 - Matched ABO and RhD type
 - Leucoreduced and irradiated packed red cell is preferred
 - Maintain haemoglobin at not less than 8 g/dL (PCV not less than 25%)
 - Platelet Transfusion**
 - ABO and RhD compatible whenever possible (ABO incompatibility can cause reduced expected increment by 10-30%)
 - Leucodepleted and irradiated platelets are preferred

- Maintain platelet level as stated below:
 For **stable afebrile** patients, maintain platelet count above **10X10⁹/L**
 For **febrile** patients or sepsis, maintain platelet count above **20X10⁹/L**
 Failure to respond to platelet transfusion may be due to:
 - infection
 - splenomegaly
 - antibodies against HLA or platelet specific antigen
 - failure to control primary condition
 - some antibiotics or antifungals
 - DIC

5.5 Anaemia in Cancer

5.5.1 Anaemia is common in malignancy. It is due to:

- treatment related to marrow suppression
- bone marrow infiltration
- blood loss
- anaemia associated with chronic disease
- vitamin deficiency
- general malnutrition

5.5.2 Management

- Haematinics supplementation
- Erythropoietin (Epo) may benefit patients receiving myelosuppressive chemotherapy or radiotherapy especially if the anaemia is poorly tolerated.
- Regular Red Cell Transfusion (***Refer Transfusion Trigger Page 67***)

Red cell transfusion is the mainstay of therapy in malignant conditions predominantly with marrow failure set myelodysplasia, myelofibrosis and aplastic anaemia or extensive marrow infiltration such as chronic lymphocytic leukaemia.

5.6 Renal Disease

Anaemia affects 60-70% of patients with chronic renal failure (CRF). This is mainly due to erythropoietin deficiency and reduced red cell survival. Other contributing factors which can cause anaemia usually arise through blood loss exacerbated by haemodialysis, folate deficiency, uraemia and hyperparathyroidism. Many CRF patients also have significant ischaemic heart disease, so peri-operative anaemia should be avoided. A haemoglobin level of 10g/dL is commonly taken as a peri-operative transfusion threshold for this group of patients.

5.6.1 Management

Erythropoietin (EPO)

- Erythropoietin therapy can fully correct anaemia in renal failure.
- It can be administered intravenously, subcutaneously and intraperitoneally. The subcutaneous route is effective at lower doses, and usually commences at 30 -100 units/kg/week given in 2-3 divided doses.
- Anaemia is corrected up to 10-12 g/dL in adults and 9.5 -11 g/dL in children, at a rate of 1g/dL per month.
- Subclinical iron deficiency and impaired mobilization of storage iron are often present, so concomitant iron therapy is usually required.
- Impaired response to rEPO should prompt a suspicion of iron, cobalamin or folate deficiency, haemolysis, infection, occult malignancy, aluminium toxicity and hyperthyroidism.
- Hypertension occurs in one third of EPO treated patients and is dose-dependent.

5.7 Vitamin K Deficiency

Bleeding manifestation in patients with liver pathology is due to underproduction of Vitamin K dependent factors i.e. Factor II, VII, IX, X and abnormalities due to fibrinolysis.

5.7.1 **Deficiency of Vitamin K dependent coagulation factors may be present in the following conditions:**

- haemolytic disease of the newborn (HDN).
- ingestion of coumarin anticoagulants (warfarin).
- Vitamin K deficiency due to malabsorption or inadequate diet.
- liver disease.

5.7.2 **Management:**

- Remove underlying cause of Vitamin K deficiency:
- Stop anticoagulants (Warfarin). See management of reversal of warfarin.
- Treat malabsorption or dietary deficiency.
- Prothrombin Complex Concentrate (PCC) if necessary according to protocol.
- Management of HDN. (**Refer Page 71**)
- Vitamin K is helpful in obstructive jaundice and all cases of deficient of vitamin K. In chronic parenchymal disease of the liver e.g. liver cirrhosis, vitamin K is not helpful.

Adult Dose:

- IV Vit K 10mg slow infusion over 10-15 minutes daily for 3 days.
- IM Vit K 10mg daily for 3 days.

Paediatric Dose:

- IV Vit K 0.2-0.5 mg/kg/day, slow infusion over 10-15 minutes for 3 days.
- IM Vit K 0.2-0.5 mg/kg/day for 3 days.
- Desmopressin or DDAVP has been shown to correct bleeding time in liver cirrhosis.

5.8 Dengue

Dengue virus infections cause a spectrum of illness ranging from asymptomatic, mild, undifferentiated fever to classical dengue fever (DF), dengue fever with haemorrhagic manifestations or dengue haemorrhagic fever (DHF) and dengue shock syndrome (DHSS). Blood and blood component may be indicated in DHF and DHSS. Derangements in the haemostatic system in dengue are not clearly defined.

This may be due to:

5.8.1 Vasculopathy

- The haematocrit in DHF is usually $> 40\%$ but may be as high as 55-60%.
- This haemocentration is due to plasma leakage which starts at the end of the febrile stage and continues up to 24-48 hours of the defervescence phase of the infection.
- Increased capillary permeability leading to plasma leakage is by far the most common cause of shock in DHF.
- Plasma leakage is suspected when there are:
 - rising haematocrit
 - haematocrit $\geq 20\%$ of baseline
 - pleural effusion, ascites
 - males with haematocrit $> 47\%$
 - females with haematocrit $> 40\%$
 - children with haematocrit $> 40\%$

Positive Tourniquet Test

A positive tourniquet test is seen in dengue infection even before the platelets start to fall and this indicates capillary fragility.

5.8.2 Platelet Abnormalities

- **Thrombocytopenia**

The platelet count begins to fall in the febrile stage and is lowest in the shock stage. It can reach a nadir of less than $10 \times 10^9/L$. It then starts to rise by the second afebrile day and normalizes by 7 days.

- **Platelet Dysfunction**

Platelet functions, in particular ADP-induced platelet aggregation and ADP-releasing ability, are impaired.

5.8.3 Coagulation Defects

- In most cases of DHF, there is prolongation of APTT and PT with variable degrees of reduction of coagulation factors II, V, VII, VIII, IX and X. Fibrinogen is constantly decreased and the degree of reduction is relative to clinical severity.
- There is usually a mild form of consumptive coagulopathy which reverts with appropriate intravenous fluid therapy and may not need specific blood components.
- Overt disseminated intravascular coagulation (DIC) with significant bleeding occurs in association with prolonged uncorrected hypovolaemic shock due to plasma leakage.

5.8.4 Management

(Refer: CPG Management of Dengue Fever in Children and CPG Management of Dengue in Adults.)

5.8.4.1 Haemoconcentration

- It is important that fluid therapy is managed carefully.

- Excessive fluid may result in accumulation leading to pleural effusion and ascites. Inadequate fluid replacement will result in hypovolaemia and shock.
- If there is no bleeding manifestation:
 - Encourage to increase oral fluids intake
 - Infuse 0.9% saline/1/5 dextrose saline at 10-20 ml/kg and adjust accordingly.
 - Colloids are indicated in patients with massive plasma leakage and in whom large volume of crystalloids has been given.
- In cases with bleeding manifestation, sudden drop in haematocrit/haemoglobin may indicate occult bleeding. Transfusion of whole blood or packed red cell may be considered.

5.8.4.2 Thrombocytopenia

Platelet transfusion is generally avoided unless:

- there is significant bleeding and platelet counts $< 50 \times 10^9/L$
- platelet counts $< 20 \times 10^9/L$ with impending or established CNS bleed or continuous bleeding from pre-existing peptic ulcer which needs a procedure such as gastroscopy.
- In the absence of bleeding, prophylactic platelet transfusion may be considered when platelet counts are less than $10 \times 10^9/L$.

5.8.4.3 Shock and DIC

- In the presence of DIC, infusions of fresh frozen plasma, cryoprecipitate and platelet concentrates are required. (**Refer Management of DIC Pages 41 and 51**)

5.8.4.4 Use of Recombinant FVIIa (rFVIIa) Concentrates

- rFVIIa has been used in patients with overt bleeding and low platelet counts and those who fail to respond to standard therapy.

Note: Refer: CPG Dengue Infection in Adults and CPG on the Management of dengue infection in the paediatric population.

TRANSFUSION TRIGGERS

Hb Level	Transfusion
< 7g/dL	Lower thresholds may be acceptable in patients without symptoms.
7-10 g/dL	Likely to be appropriate during surgery associated with major blood loss or if there are signs or symptoms of impaired oxygen transport.
> 8 g/dL	May be appropriate to control anaemia-related symptoms on a chronic transfusion regimen or during marrow suppressive therapy.
> 10 g/dL	Not likely to be appropriate unless there are specific indications.

6. Paediatrics & Neonatology

Infants require repeated transfusions more frequently than do older children and adults. The increased need for transfusion is usually due to:

- large volume phlebotomy for blood tests relative to the limited available blood volume
- postnatal physiologic anaemia frequently encountered in conditions involving cardiopulmonary compromise
- limited or delayed responsiveness of infant bone marrow to a variety of haematologic stresses

Transfusion of blood and blood components presents potential risks which may have a more significant outcome for ill, high-risk infants than for older recipients. The potential risks are:

- transfusion-transmitted diseases
- immunosuppressive effects of transfusion
- alloimmunization to red cell, white cell and platelet antigens
- graft-versus-host disease with significant long-term comorbidity

Transfusion in infants must be individualized, based on each infant's clinical status. Special clinical circumstances not covered by the guidelines may be appropriate for transfusion therapy and indications included in the guidelines may not necessarily be clinically beneficial for a given patient.

6.1 Pretransfusion Testing in Infants

An initial pretransfusion specimen from the infant must be tested for ABO/Rh red cell antigens and screened for unexpected antibodies:

- When available, mother's serum or plasma are sent together with the babies' sample

- If no antibodies are detected initially, the red blood cell (RBC) transfusion is ABO-compatible with the infant and the mother, and the unit is either Rh-negative or the same Rh group as the infant
- For infants with ABO haemolytic disease of the newborn, only group O RBCs should be transfused
- For plasma and platelet transfusions, infants should receive ABO-specific components whenever possible to avoid transfusing plasma antibody which is incompatible with the infant's red cell antigens

6.2 Red Blood Cell Transfusions

- Phlebotomy or pre-operative blood loss should be replaced:
 - When > 5% of estimated blood volume (EBV)* is lost, if respiratory support is required and continued blood loss is anticipated
 - When 10% of EBV* is lost, in an otherwise stable infant
 - (*EBV = 80 to 85 ml/kg. For preterm infants, EBV = 85 to 90 ml/kg, but the haematocrit is also lower, depending on gestational age)
- Symptomatic congenital heart disease or congestive heart failure: transfuse cautiously to maintain haemoglobin >13 g/dL (haematocrit>40%)
- Severe respiratory distress: transfuse to maintain haemoglobin >13 g/dL (haematocrit >40%)
- Symptomatic anaemia (tachycardia and/or tachypnoea): transfuse to maintain haemoglobin >10g/dL (haematocrit >30%)

The usefulness of transfusion for infants with symptoms including apnoeic spells, lethargy and failure to gain weight is not clear. Asymptomatic anaemia of prematurity is not an indication for transfusion.

(Refer Management of Hypovolaemia in Paediatric patients Chart VI Page 23 & Transfusion Threshold for Neonates Chart XI Page 70)

CHART XI : SUGGESTED TRANSFUSION THRESHOLDS FOR NEONATES

Transfusion	Transfusion Threshold
<p>Transfusion of Red Cells</p> <p>Anaemia in the first 24 hours</p> <p>Neonate receiving mechanical ventilation</p> <p>Acute blood loss</p> <p>Oxygen dependency (not ventilated)</p> <p>Late anaemia, stable patient (off oxygen)</p>	<p>Hb <12 g/dl</p> <p>Hb <12 g/dl</p> <p>>10% blood volume loss</p> <p>Hb < 8-11g/dl (depending on clinical situation)</p> <p>Hb < 7 g/dl</p>
<p>Transfusion of Platelets</p> <p>Consider in all neonates</p> <p>Consider if increased bleeding risk for e.g.</p> <ul style="list-style-type: none"> ➤ <1000g and <1 week of age ➤ Clinically unstable (e.g. labile blood pressure) ➤ Previous major bleeding (eg: grade 3-4 intraventricular haemorrhage) ➤ Current minor bleeding e.g. petechiae) ➤ Coagulopathy ➤ Planned surgery or exchange transfusion ➤ Major bleeding 	<p><30 x 10⁹/l</p> <p><50 x 10⁹/l</p> <p><100 x 10⁹/l</p>

6.3 Exchange Transfusions (ET)

The main indication for ET is to prevent neurological complication (kernicterus) caused by rapidly rising unconjugated bilirubin concentration. The underlying cause is usually haemolysis (HDN) due to antibodies against the baby's red cells.

- If transfusion is needed, a group O blood unit should be used that does not carry the antigen against which the maternal antibody is directed:
 - For HDN due to anti-D: use group O Rh negative.
 - For HDN due to anti-Rh c: use group O Rh D positive that does not have the c antigen (R₁R₁,CDe/CDe)

- Blood for neonates:
 - fresh blood less than 7 days old.
 - leucoreduced WB/CPDA packed cell reconstituted with fresh frozen plasma.
 - Refer: Guidelines for Neonatal Exchange Transfusion (**Chart XII Page 72**)

CHART XII : GUIDELINES FOR NEONATAL EXCHANGE TRANSFUSION

CALCULATIONS FOR NEONATAL EXCHANGE TRANSFUSION

Partial Exchange Transfusion for Treatment of Symptomatic Polycythaemia

Replace removed blood volume with normal saline or 5% albumin

Volume to be exchanged (ml):

$$\text{Estimated blood volume} \times \frac{(\text{patient's Hct} - \text{desired Hct})}{\text{patient's Hct}}$$

Two-volume Red Cell Exchange Transfusion for Treatment of Neonatal Hyperbilirubinaemia

Replace calculated blood volume with whole blood or red cells suspended in 5 % human albumin

Volume to be exchanged (ml):

$$\text{Estimated blood volume} \times \frac{(\text{patients haematocrit [5\%]} \times 2)}{\text{haematocrit of transfused unit [\%]}^*}$$

*haematocrit

Whole blood	35-45%
Red cell concentrate	55-75%
Red cell suspension	50-70%

TRANSFUSION PROCEDURE

1. Give nothing by mouth to the infant for at least 4 hours after the exchange transfusion. Empty stomach if the infant was fed within 4 hours of the procedure.
2. Closely monitor vital signs, blood sugar and temperature. Have resuscitation equipment ready.
3. For a newborn, umbilical and venous catheters inserted by sterile technique may be used (blood is drawn out of the catheter and infused through the venous catheter). Alternatively two peripheral lines may be used.
4. Use of pre-warmed blood only if a quality-controlled blood warmer is available. Do not improvise by using a water bath.
5. Exchange 15 ml increments in fullterm infants and smaller volume for smaller, less stable infants. Do not allow the cells in donor unit to form a sediment.
6. Withdraw and infuse blood 2-3 ml/kg/min to avoid mechanical trauma to the patient and donor cells.
7. Give 1-2 ml of calcium gluconate solution I/V slowly for ECG evidence of hypocalcaemia (prolonged Q-T interval). Flush tubing with normal saline before and after calcium infusion.
8. To complete two-volume exchange, transfuse 170ml/kg for a fullterm infant and 170-200ml/kg for a preterm infant.
9. Send the last aliquot drawn to the laboratory for determination of haemoglobin or haematocrit, blood smear, glucose, bilirubin, potassium, calcium and group and match.
10. Prevent hypoglycaemia after exchange transfusion by continuous infusion of glucose-containing crystalloid.

6.4 Platelet Transfusions

In thrombocytopaenic patients, platelet transfusion is indicated when the patient is bleeding or bleeding is anticipated. In the presence of intracranial or other life-threatening haemorrhage which occurs especially when the platelet count is less than 10,000, platelet transfusion may be required while other therapy is being instituted.

6.4.1 Non-immune Thrombocytopaenia

Indications:

- platelet count $<20,000/\mu\text{L}$ ($20 \times 10^9/\text{L}$)
- platelet count $<50,000/\mu\text{L}$ ($50 \times 10^9/\text{L}$) with bleeding, or prior to invasive procedures or minor surgery
- platelet count $<100,000/\mu\text{L}$ ($100 \times 10^9/\text{L}$) prior to cardiovascular or neurologic surgery, or other major surgery
- platelet count $<100,000/\mu\text{L}$ ($100 \times 10^9/\text{L}$) with a recent (within one to two weeks) intracranial haemorrhage;
- qualitative platelet defect with bleeding, or prior to invasive procedures or surgery.

6.4.2 Immune Thrombocytopaenia

Neonatal immune thrombocytopaenia is caused by maternal antiplatelet antibodies, either auto- or allo (iso)- immune antiplatelet antibodies, which cross the placenta and interact with foetal platelets. In general, treatment should be definitely instituted for a platelet count $<20,000/\mu\text{L}$; possibly instituted for platelet count $<50,000/\mu\text{L}$; and is not indicated for platelet count $>50,000/\mu\text{L}$.

6.4.2.1 Neonatal Alloimmune (Isoimmune) Thrombocytopaenia

- The treatment of choice is matched antigen-negative platelets, usually washed or resuspended and irradiated maternal platelets. If these are not immediately available, treatment should be initiated as for thrombocytopaenia due to autoantibodies.

6.4.2.2 Thrombocytopaenia due to Maternal Autoantibodies

- Intravenous gammaglobulin (IV IgG), with or without glucocorticoids, is generally useful to increase the platelet count and to prolong platelet survival in this self-limiting disorder. Platelet transfusions are not indicated in the absence of life-threatening bleeding. (*Refer Guide to Platelet Transfusion in Chart VII Page 27*)

6.5 Cryoprecipitate Transfusions

Indications:

- Von Willebrand's disease (VWD), type II or type III, with bleeding; or pre-operatively when viral-inactivated factor concentrate containing Von Willebrand factor activity is not available
- hypofibrinogenaemia or dysfibrinogenaemia with bleeding, or pre-operatively
- replacement therapy in factor XIII deficiency
- VWD type I or type II if appropriate factor concentrate containing VWF is not available

Note:

DDAVP therapy should be considered for patients with mild haemophilia A or Von Willebrand's Disease type I (dose: 0.3 mcg/kg; monitor haemostatic response and urine output). Refer Guide to Cryoprecipitate Transfusion Chart VIII Page 29

6.6 Special Considerations

6.6.1 Cytomegalovirus (CMV)

Blood components from CMV-seropositive donors may contain residual leucocytes which are potentially infectious to seronegative infants. **CMV-seronegative or leucoreduced cellular components** (RBCs, platelets, granulocytes) should be provided for infants who

weigh <1,200 g at birth or who are immunocompromised, and whose mothers are either seronegative or whose serostatus is unknown.

6.6.2 Irradiated Blood Components

Graft-versus-host disease (GVHD) has occurred in infants transfused with cellular blood components and in HLA homozygous adults transfused with blood components from donors with one identical HLA haplotype and one different haplotype. The risks of GVHD to preterm infants who have received a small volume transfusion with red cells or platelets are unknown, although occurrences have been documented. Irradiation of cellular blood components with a minimum of 2,500 rad (25 Gy) is recommended for the following:

- infants < 1500 g birthweight
- infants with known or suspected congenital immunodeficiency syndromes involving T-cells, eg: DiGeorge syndrome
- infants receiving granulocyte transfusions
- infants receiving directed donor blood components from blood relatives
- infants undergoing immunosuppressive therapy or chemotherapy
- infants receiving exchange transfusions

7. Transfusion in Transplantation

Transfusion may influence the outcome of a transplant. Transfusions given pretransplantation may:

- sensitise potential transplant recipient or downregulate immune responses and promote graft acceptance
- cause acquisition of viruses such as hepatitis or CMV
- promote development of alloimmunization to histocompatibility antigens, posing an increased risk of subsequent graft rejection

ABO antigens are important in transplantation practice because they constitute very strong histocompatibility antigens that are expressed in vascular endothelium. Major ABO mismatching can cause rapid graft rejection due to endothelial damage by ABO antibodies and subsequent widespread thrombosis within the graft. Minor ABO incompatibility can be associated with significant haemolytic anaemia caused by ABO antibody production by passenger graft lymphocytes.

7.1 Renal Transplant

rEPO (Recombinant Erythropoietin) is used to correct anaemia in patients with renal failure and thus transfusion of red cells are not routinely practised prior to transplantation unless Hb < 9g/dL.

7.2 Orthotopic Liver Transplantation (OLT)

It is important in OLT to ensure that there is ABO compatibility between donors and recipients:

- Mismatching of ABO results in increase in hyperacute rejection, vascular thrombosis and biliary injury. Massive blood loss and hypocoagulability due to pre-existing liver disease and to the anhepatic interval during the procedure create complex problems

- This results in haemodilution, platelet consumption, disordered thrombin regulation and fibrinolysis, which derange the haemostatic process and is especially severe during the anhepatic and early perfusion stage
- Intra-operative blood salvage is important when there is major blood loss
- The use of pharmacological agents such as aprotinin and tranexamic acid have been shown to reduce intra-operative blood loss. rFVIIa have been used in patients with intractable bleeding. Intra-operative blood recovery (Blood Salvage) is also important in reducing transfusion of allogeneic blood
- Post-operatively, risk of hepatic artery thrombosis may be reduced by avoiding overtransfusion with red cells and platelets

7.3 Haemopoietic Progenitor Cell (Stem Cells) Transplantation

Allogeneic or autologous stem cells may be derived from iliac crest marrow, peripheral stem cells or umbilical cord blood. Development of alloimmunization to histocompatibility antigens poses an increased risk of subsequent graft rejection. Therefore use of blood products should be minimized. Prior to transplantation, transfusion support should include leucocyte-reduced products.

- After transplantation, if ABO differences between donor and recipient exist (major or minor mismatch), the recipient is at risk of severe intravascular haemolysis, delayed red cell engraftment and delayed haemolysis (40-60 days post-transplant). Engrafted donor lymphocytes may produce antibodies against recipient red cell antigens which can induce delayed haemolytic reaction
- All transplanted patients are profoundly immunosuppressed, and thus at risk of fatal TA-GVHD (transfusion associated graft versus host disease) after transfusion of cellular products. Thus all such transfusion units must be irradiated prior to use

BLOOD COMPONENT REGIME POST-TRANSPLANTATION

a) Major Mismatch

	Early	Middle	Late
Red Blood Cells	Recipient	Donor	Donor
Platelets	Donor	Donor	Donor
Fresh Frozen Plasma	Donor	Donor	Donor

b) Minor Mismatch

	Early	Middle	Late
Red Blood Cells	Donor	Donor	Donor
Platelets	Recipient	Recipient	Donor

c) Both major and minor mismatch

	Early	Middle	Late
Red Blood Cells	O	Donor	Donor
Platelets	Recipient	Recipient	Donor
Fresh Frozen Plasma	AB	AB	Donor

8. Anticoagulants and Antithrombotic Agents

A bleeding state may arise either because patients develop a spontaneous pathological anticoagulant, or, from therapy with an anticoagulant or antithrombotic drug.

8.1 Five Major Classes of Antithrombotic Agents in Clinical Use:

- Agents inhibiting platelet function (aspirin, thienopyridines, Gp IIb/IIIa inhibitors).
- Heparins (unfractionated heparin, LMWH, pentasaccharide)
- Coumarin derivatives (warfarin, acenocoumarol)
- Direct thrombin inhibitors (agatroban, bivalirudin, liperudin, ximelagatran)
- Thrombolytic agents (streptokinase, urokinase, tPA)

8.2 Bleeding associated with Antithrombotic Agents

May be major, and defined as:

- A decline in haemoglobin of > 2g/dL
- The need for transfusion of 2 or more units of blood.
- Intracranial, retroperitoneal or fatal bleeding.

8.3 Minor bleeding

Minor bleeding includes all other bleedings such as skin bruising, wound haematoma, epistaxis and haematuria.

8.4 Treatment of Bleeding due to:

8.4.1 Platelet Inhibiting Agents

- Withdrawal of the drugs
- Treatment with proton pump inhibitors
- IV desmopressin (DDAVP) 0.3µg/kg will help to control bleeding from various sites such as nose, gastrointestinal and genitourinary tracts
- Bleeding due to longer acting agents such as thienopyridines (ticlopidine and clopidogrel) may require platelet transfusion
- Major or life-threatening bleeding associated with GpIIb/IIIa (Abciximab, eptifibatide and tirofiban), platelet transfusion or rFVIIa may be effective

8.4.2 Heparin

- Immediate discontinuation of the drugs.
- If bleeding is brisk or life-threatening, IV protamine sulphate at a dose of 1 mg for each 100 units. Large doses of protamine may produce hypotension, bleeding and severe allergic reactions. It is not effective with fondaparinux(anti-Xa)
- For patients with life-threatening bleeds on fondaparinux, consider using rFVIIa
- Heparin-induced thrombocytopenia (HIT) occurs in up to 3% of patients treated with heparin. Platelet transfusion is contraindicated

8.4.3 Coumarin Derivatives: Warfarin

GUIDELINES FOR THE MANAGEMENT OF AN ELEVATED INTERNATIONAL NORMALISED RATIO (INR) IN ADULT PATIENTS WITH OR WITHOUT BLEEDING	
Clinical Setting	Action
INR > therapeutic range but <5.0; bleeding absent	<ul style="list-style-type: none"> • Lower the dose or omit the next dose of warfarin. Resume therapy at lower dose when the INR approaches therapeutic range. • If the INR is only minimally above therapeutic range (up to 10%), dose reduction may not be necessary.
INR 5.0-9.0; *bleeding absent	<ul style="list-style-type: none"> • Stop warfarin therapy: consider reasons for elevated INR and patient-specific factors. • If bleeding risk is high, give vit K₁ (1.0-2.0 mg orally or 0.5-1.0 mg intravenously) • Measure INR within 24 hours,[†] resume warfarin at a reduced dose once in therapeutic range.
INR > 9.0; bleeding absent	<ul style="list-style-type: none"> • Where there is low risk of bleeding, stop warfarin therapy, give 2.5-5.0 mg vitamin K₁ orally or 1.0 mg intravenously. Measure INR in 6-12 hours, resume warfarin therapy at a reduced dose once INR <5.0. • Where there is a high risk of bleeding,[†] stop warfarin therapy, give 1.0 mg vitamin K₁ intravenously. Consider Prothrombinex-HT (25-50 IU/kg) and fresh frozen plasma (150-300 ml), measure INR in 6-12 hours; resume warfarin at a reduced dose once INR is < 5.0.
Any clinically-significant bleeding where warfarin-induced coagulopathy is considered a contributing factor.	<ul style="list-style-type: none"> • Stop warfarin therapy; give 5.0-10.0 mg vitamin K₁ intravenously as well as Prothrombinex-HT (25-50 IU/kg) and fresh frozen plasma (150-300 ml); assess patient continuously until INR <5.0; and bleeding stops.[§] OR • If fresh frozen plasma is unavailable, stop warfarin therapy, give 5.0-10.0 mg vitamin K₁ intravenously; and Prothrombinex-HT (25-50 IU/kg); assess patient continuously until INR <5.0; and bleeding stops.[§] OR • If Prothrombinex-HT is unavailable, stop warfarin therapy; give 5.0-10.0 mg vitamin K₁ intravenously and fresh frozen plasma (150-300 ml); assess patient continuously until INR <5.0, and bleeding stops.[§]

Minor Bleeding: haematuria, epistaxis

Major bleeding: intracranial or major gastrointestinal bleeding

8.4.4 Direct Thrombin Inhibitors

- No specific treatment due to its short half-life of 25-50 minutes.
- If necessary, for renal failure patients, haemodialysis may help to clear the agents since it is metabolised by the kidney.

8.4.5 Thrombolytic Agents

- Immediate discontinuation of the drugs with full blood count and coagulation profile performed.
- Usually the agents will disappear from the circulation within minutes and often nothing needs to be done.
- If there is profuse bleeding or bleeding in vulnerable areas, antifibrinolytic may be infused intravenously:
 - tranexamic acid 0.5-1.0 g every 8 hours or
 - EACA 5g given slowly over 20 minutes followed by continuous infusion 1g/hr
- In thrombocytopenia or reduced fibrinogen, platelet concentrate and fresh frozen plasma may be helpful.

9. General Transfusion Practices

9.1 Filter for Blood Components

All red cell, platelet and plasma transfusions, to infants as well as to adults, must be administered through standard blood-giving set with integral filter.

9.1.1 **Two types of filters used are a 170 µm or a leucocyte-depletion filter.**

- The 170 µm is a clot screen filter that removes gross clots from any blood product and is used in routine blood administration sets
- Leucocyte-depletion filters are designed to remove viable white blood cells from red blood cell and platelet products

9.2 Leucoreduction:

- The small volume of infant blood transfusions renders bedside in-line leucofiltration unfeasible. Leucoreduction by filtration is usually performed in the blood bank or blood centre prior to release of the component
- When leucoreduced components are stored, a standard blood filter should be used prior to administration. This filter can be used to prevent febrile non-haemolytic transfusion reactions, to prevent or delay the development of HLA antibodies, and to reduce the risk of transfusion of CMV

Note: *The usefulness of a leucoreduction filtration device in preventing leucocyte alloimmunization and febrile transfusion reactions, already established in adults receiving transfusions, has yet to be demonstrated in the infant population.*

9.3 Infusion Chambers

Since administration of blood components to infants is generally volume specific, it should be performed using a calibrated chamber device. The chamber may be in the form of a syringe or closed infusion set such as a volumetric buretrol. If a syringe is used, the volume of blood component to be administered may be aspirated through a blood filter administration set attached to the component unit. Blood infusion should be limited to less than four hours.

9.3.1 Infusion Pumps

- Several available mechanical monitoring syringe pump devices allow constant infusion from a syringe with accurate rate- and volume-controlled delivery. Syringe pumps are suitable for volumes between 10 and 50 ml. Smaller volume transfusions, typically under 10 ml per episode, are usually given manually utilizing a syringe containing a prefiltered blood component
- Volumes larger than 50 ml are usually contained within a blood bag or transfer pack and transfused either with a calibrated infusion pump or through an infusion set with a calibrated infusate chamber reservoir, such as a buretrol
- The advantages of electronic infusion devices include such features as flow monitoring, an alarm for high-pressure inflow status, and accurate infusion rates. Many electric infusion pumps are also battery-powered, allowing for patient portability. Infusion pumps require periodic monitoring for flow rate accuracy and possible haemolysis

9.4 Warming Blood Components and Blood-Warming Devices:

All blood components to be transfused to infants should be as close as possible to room temperature, especially when infused through a central venous line. The small volume of blood usually transfused to infants generally makes impractical the use of mechanical blood warmers which require large volumes to pass through the warming coils. For most small volume infant transfusions, blood components may be warmed passively by placing in a temperature-controlled isolette, or at room temperature, for approximately 30 minutes prior to

the transfusion. Blood components should never be warmed directly, as in hot water, although warmed saline can be added using an FDA-approved system.

Note : Microwave devices designed for thawing frozen components should not be used for warming cellular components.

9.4.1 Blood Warmers

Large volume transfusion of infants, such as exchange transfusions or transfusions during surgery, should be performed with a blood warmer to avoid hypothermia in the infant. Prewarmed syringe aliquots may also be taken from the exit port of a standard blood warming device.

9.5 Transfusion Flow Rates

The rate of transfusion depends upon the component, the total volume to be infused, venous access characteristics and the intravascular fluid tolerance of the infant. As a general rule, small transfusions less than 10 ml do not require a pump and are pushed in via a syringe by intermittent small bolus, taking into consideration the volume tolerance of the infant.

- Larger volume transfusions, such as those given for anaemia, should be administered by an infusion device and usually transfused within 2-4 hours
- If the transfusion interval exceeds 4 hours, the blood component should be subdivided and the second portion of the component stored in the blood bank until needed

The following infusion rates are commonly used:

RBC: 3-5 ml/kg/hour

FFP: Within 30 minutes, if the volume does not exceed 5-10 ml/kg

Platelets: 10-15 ml/kg and completed within 30 minutes

9.6 Monitoring Transfusions for Complications and Reactions

Transfusions are usually administered in a special care nursery where monitoring is routine. Blood glucose should be monitored hourly if glucose infusion was interrupted during transfusion, since hypoglycaemia may occur suddenly.

9.6.1 Infusion should be slowed or stopped if any of the following develops during the transfusion:

- apnoea or tachypnoea
- tachycardia, bradycardia or arrhythmia
- cyanosis
- significant change in systolic blood pressure
- significant change in temperature
- haemoglobinuria

Whenever a haemolytic transfusion reaction is suspected, post-transfusion specimens of blood and urine should undergo a transfusion reaction evaluation in the blood bank.

9.7 Special Considerations in Paediatrics

9.7.1 Vascular Access in Infants

- Vascular access can present difficulties in small infants. Typically, venous access is gained by using small standard intravenous catheters or "butterfly" type needles. These devices, generally ranging in size from 21-27 gauge, have been shown to be effective and not to be associated with significant haemolysis. However, use of small caliber devices limits the rate of infusion and the amount of infusion pressure that can be applied, particularly with electronic infusion pumps
- The umbilical vein and other central veins should not be used for routine transfusion except for exchange transfusions, as the possibility of infection and thrombosis exists. However, in neonatal intensive care units, the umbilical vein is commonly catheterized in very sick infants within 48 hours of birth. On rare occasions, venous "cut-downs" may be employed in order to attain vascular access, particularly for longterm care infants

9.7.2 Volume Reduction

Small infants often cannot tolerate a large transfusion volume because of limited circulatory capacity. Therefore, the volume of the transfusate may need to be reduced.

- Volume reduction of cellular components can be achieved by centrifugation and expression of the supernatant prior to transfusion. However, use of volume reduction techniques for platelet components may result in platelet loss and is seldom necessary because the usual dose of 5-10 ml/kg can be tolerated
- Concentrated platelet components should be permitted to rest at room temperature for one hour without agitation prior to resuspension to maximize function. Such superconcentrated platelets must not be stored for more than 2-4 hours

9.7.3 Minimizing Donor Exposure in Infants

Infant exposure to allogeneic blood may be minimized by limiting transfusions to strictly appropriate indications so that the benefits outweigh the risks. If a transfusion is required, a blood aliquot technique should be used whenever possible.

9.7.3.1 Blood Aliquot Techniques

- Using a quadruple pack (quad set), a unit of packed red cells can be aliquotted into satellite bags within a closed system, thereby preserving the expiration date of the original component
- Each of the satellite packs may be utilized as needed either for a single infant requiring multiple transfusions or for more than one infant
- Other systems employ small (20-60 ml) satellite transfer packs which can be filled with blood from a particular blood unit utilizing a sterile docking device. The sterile docking device allows aseptic thermal welding of two segments of blood or infusion tubing, thereby maintaining the sterility and original outdate of the blood component
- The "freshness" of blood is a lesser concern than the risks of additional donor exposure, and aliquots from the same unit may be used for 7-10 days or longer
- Individual syringe aliquots may also be obtained from blood units, either through the use of an injection port placed in the blood component unit or by connecting to the outflow end of a blood infusion set with an in-line filter
- Once a blood component unit is entered, the syringe aliquot and the remaining component will expire in 24 hours. Until dispensed, red cell aliquots should be stored at 1-6° C in a temperature-monitored refrigerator
- Individual syringe aliquots of platelets may be obtained from a platelet unit immediately prior to transfusion.

9.7.3.2 Blood Relatives as Donors

While transfusion of maternal blood carries less inherent transmissible disease risk to the infant, use of blood from the father and other relatives holds no advantage.

- Directed donation from all blood relatives, including the mother, carries an added risk of immune complications, such as alloimmunization to HLA antigens and graft-versus-host disease
- It is important to irradiate components from all blood relatives to avoid the latter complication

9.7.3.3 Small Aliquot Donors

Some centres have utilized blood from individuals having a blood group compatible with the recipient infant's. Small units or half units may be donated by a single donor at repeated intervals over an 8-week period provided the total volume collected does not exceed 550 ml. Collection of blood in volumes under 300 ml requires proportional adjustment of the anticoagulant in the collection bag. In this manner, single-donor whole blood may be made available to particular infants on an as-needed basis.

10. Alternatives to Blood Transfusion

10.1 Autologous Blood Transfusion

Is the collection and subsequent transfusion of the patient's own blood. It prevents transmission of diseases like hepatitis, HIV and syphilis and avoids immunological complications like alloimmunization and transfusion reactions. It is the safest component as it provides the safest blood for those who have alloantibodies. It is most useful in elective and planned surgical procedures.

10.1.1 Types of Autologous Transfusions

- **Predeposit Autologous Blood**

Blood is collected from patients for elective surgery. The blood is stored in the Blood Bank until required

- **Pre-operative Haemodilution**

Blood is collected from the patient shortly before or after induction of anaesthesia. Depending on the patient's initial haematocrit, body weight and the desired haematocrit, up to 2 litres of blood can be withdrawn

- **Intra-operative Blood Salvage**

Blood lost during surgery is collected, processed and returned to the patient

- **Post-operative Blood Salvage**

Blood recovered from drainage tubes is processed and returned to the patient

10.1.2 Predeposit Autologous Blood Transfusion

This can provide an alternative to blood from volunteer donors during surgery. However, it is only appropriate for a minority of patients requiring transfusion. Selection of patients is vital not only on medical grounds but also on reliable dates of surgery, good venous access and patient's commitment to come to the blood bank for autologous blood collection.

Responsibility for the counselling and request of the autologous transfusion lies with the surgeon or anaesthetist managing the patient. A letter of referral has to be made to the blood bank. The availability of the autologous blood should be written in the case notes and request form so that homologous blood is not crossmatched.

The optimal units of blood that can be collected are 2-4 units.

10.1.2.1 Selection of Patients

- Should only be used for procedures where there is a high possibility that the blood will be transfused
- The patient should be negative for the infective markers such as HBV, HCV and HIV
- The patient has no active bacterial infection
- Haemoglobin is >11 g/dL in both men and women
- In adult patients under 50 kg, care must be taken that no more than 12% of the blood volume be withdrawn.
- Patients with cardiorespiratory diseases need to be assessed by the appropriate physician. Patients with significant aortic stenosis, prolonged and/or frequent angina, significant narrowing of the left main coronary artery and cyanotic heart disease should not be offered this procedure
- The patient has no history of epilepsy
- Pregnant patients should be counselled thoroughly before offering this procedure. The risk of hypotension with secondary placental insufficiency could place adverse effects and foetal distress to the unborn child which must be explained to the mother (who is the donor). It is contraindicated in pregnancies complicated by any condition associated with impaired placental blood flow or intrauterine growth retardation including hypertension, pre-eclampsia, diabetes mellitus and any severe medical conditions

10.1.2.2 Collection

- Clinicians should determine the number of units required and refer to the Blood Bank after explaining to the patient and signing consent forms 1 & 2.
- Hb should be monitored before each donation to ensure that it is >11 g/dl. Iron and folate supplements should be given.
- All clinically fit patients going for elective surgery can be bled at the Blood Bank

- **at least 28 days** It is recommended that donations should be 7 days apart but may be as frequent as every 3 days. Four units can be collected as the blood can be kept for. The last phlebotomy should be done, at the latest, 4 days before surgery
- If surgery is postponed, then the oldest autologous blood can be retransfused to the donor and fresh blood collected (“leap-frog” technique)

10.1.2.3 Storage

- A dedicated fridge is allocated for autologous blood collected. Blood is monitored, and once it reaches the expiry date, it is then discarded. Blood collected in CPDA-1 bag can be stored for 35 days. Red cell suspended in optimal additive solution has an extended shelf life of 42 days.
- The autologous collection should be clearly labelled with special **green** labels and the patient’s name must be clearly stated.
- If transfusion becomes necessary, the freshest unit is transfused first.
- All unused blood should be discarded when it expires or is not used. This must be explained to the patient during counseling and consent.

10.1.2.4 Laboratory Tests

- **Serological Tests**
ABO and RhD grouping is done on each bag and results are indicated on the bag. Antibody screening is done on the first donation.
- **Virology Screening**
HBsAg, anti-HIV, anti-HCV and syphilis screening tests are done on the first and last donation. If any is found to be positive, the patients are excluded and the donated blood is discarded.
- **Compatibility Testing**
Upon admission to hospital for surgery, patients with stored autologous blood should have a fresh venous blood sample taken. Test should be done for ABO, Rh group and compatibility testing.

10.1.3 Acute Normovolaemic Haemodilution

This is the removal of the patient's own blood immediately prior to commencement of surgery and simultaneous replacement with sufficient crystalloid / colloid fluids to maintain circulatory blood volume. This procedure ensures that fresh blood is immediately available for blood transfusion for treating the patient's Hb and replenish the coagulation factors and platelets without the need for homologous blood transfusion.

This is recommended when only 1 or 2 units are required. A maximum of 3 units can be taken through this method and it is the most popular method of autologous blood transfusion. It should be considered when potential blood loss is likely to be greater than 20% of blood volume. This procedure is done by the anaesthetist.

10.1.3.1 Benefits of Acute Normovolaemic Haemodilution

- reduction in red cell loss during operation (secondary to reduced haematocrit)
- improved oxygen delivery (secondary to reduction in whole blood viscosity)

10.1.3.2 Procedure

- Check Hb and PCV of the patient. (No need for virology screening of infective markers). However, if the patient is known to be positive upon this screening, exclude this form of autologous transfusion.
- Pre-operative Hb should be >11 g/dL.
- Venesection is done immediately prior before starting surgery.
- Blood is collected into standard blood bag containing CPD. These procedures take 10-20 minutes. The patient's name, date and time collected and order of collection should be stated and labelled on the bag. If blood is to be transfused after more than 6 hours, it must be stored in a blood fridge at +4°C; otherwise store at OT temperature.
- Simultaneously, replace via a 2nd venous line with crystalloid or colloid. (Crystalloid - 3 ml for every 1 ml of blood collected; Colloid - 1 ml for every 1 ml of blood collected)

- Hb can fall to 9 g/dL (PCV 27 %). **Circulatory volume should be maintained at all times.**

$$V = EBV \times \frac{(H_o - H_f)}{H_{av}}$$

V	= volume to be removed
EBV	= estimated blood volume
H _o	= initial Hct
H _f	= desired Hct
H _{av}	= average Hct (mean of H _o + H _f)

- Pre-infusion checks of identity are mandatory.
- Records of collection and re-infusion should be entered into the patient's anaesthetic and/or case notes.
- Any unused autologous blood should be disposed of as hazardous waste, preferably in OT.

10.1.4 Intra-Operative Blood Salvage

Intra-operative blood salvage is the collection of blood from a bleeding source or body cavity during surgery and its subsequent re-infusion into the same patient.

Cell saver blood salvage is used – centrifugation cell-washing devices using disposable components and a centrifuge washing device to collect and wash red blood cells prior to the re-infusion. These devices are useful in large volume blood loss surgery e.g. cardiothoracic surgery and are expensive.

This procedure is usually done by the anaesthetist at the time of surgery.

Contraindications:

- Contamination e.g. gut
- Cancers
- Chronic Obstructive Airway Disease (COAD)
- Sickle cell disease or sickle cell trait

10.1.5 Post-Operative Blood Salvage

This should be considered whenever the post-operation blood loss is sufficient to cause anaemia requiring blood transfusion. Blood may be salvaged from the body cavity and joint spaces and re-infused with or without cell washing.

This is done by the anaesthetist. It is most useful after cardiac surgery and can be used for selected orthopaedic procedures.

Automated blood salvage using the cell saver equipment or manual methods may be used to aspirate, anticoagulate and filter blood to remove debris. The automated machine washes the red cells before re-infusion.

11. Adverse Effects of Transfusion

Blood transfusion can be associated with various adverse effects. Some of these reactions are acute and arise during transfusion or shortly after transfusion, but the clinical effects of others are delayed, sometimes by months or years.

All transfusion reactions must be investigated. Blood transfusion can be associated with various adverse effects. Some of these reactions are acute and arise during transfusion or shortly after transfusion, All personnel involved in ordering and administering transfusions must be able to recognize the signs and symptoms of transfusion reactions and to manage them.

The causes of transfusion reactions include acute and delayed haemolytic transfusion reactions, bacterial contamination, febrile non-haemolytic transfusion reactions, urticaria and anaphylaxis, transfusion-related acute lung injury, post-transfusion purpura and transfusion-associated graft-versus-host disease.

(Chart XIV lists the various types of Transfusion Reactions and their Management refer Page 109)

11.1 Signs and Symptoms

Signs and symptoms that may occur with impending or established transfusion reaction include:

- (a) feeling of apprehension / restlessness
- (b) fever
- (c) chills
- (d) rigors
- (e) pain, at infusion site, or in chest, abdomen or flanks
- (f) changes in blood pressure, either hypotension or hypertension
- (g) respiratory distress
- (h) urticaria, rashes
- (i) nausea
- (j) vomiting

- (k) acute onset of sepsis
- (l) anaphylaxis
- (m) renal shutdown
- (n) abnormal bleeding

11.2 Management of Transfusion Reaction

If an adverse transfusion reaction is suspected,

- i. the transfusion should be **stopped immediately**
- ii. the doctor in charge of the patient must be informed urgently to assess the patient
- iii. further management depends on the type and severity of the reaction
- iv. administer antihistamine intramuscular or intravenous (e.g. chlorpheniramine 0.1mg/kg)
- v. administer antipyretics orally
- vi. monitor patient, if no clinical improvement within 30 mins or if sign and symptoms worsen. Further management depends on the type and severity of the reaction. **(Refer Chart XIV Page 109)**
- vii. The following steps have to be taken to allow investigation for the reaction:
 - (a) An 'immediate' venous blood sample (at least 8-10 ml) should be taken in a plain tube for antibody identification.
 - (b) Another 2-5 ml venous sample should be taken for full blood picture (FBP).
 - (c) A urine sample should be collected and inspected as soon as possible before being sent to the laboratory. This specimen may contain haemoglobin and albumin and often contains red cells as well.
 - (d) The remaining blood bag, containing the partially transfused blood, and all the blood bags cross-matched for the same patient at the same time of the request should be examined for the presence of free haemoglobin or discolouration before being sent to the laboratory.

- (e) 24 hours after the detection of the adverse reaction:
- another venous blood sample should be taken (again at least 8-10 ml in a plain bottle) for further tests

 - another blood sample in EDTA bottle for full blood picture; and
 - another urine specimen for haemoglobinuria
- (f) The “Report of Reaction to Blood or Plasma Transfusion” form (**Chart XIII Page 99**) must be completed.
- (g) Once the investigation of the transfusion adverse event is complete, fill up the transfusion adverse event form in duplicate and send to the blood bank. Send also a copy of this form to the National Blood Centre. (**Refer Chart XV Page 101**)

CHART XIII

LAPORAN REAKSI KEPADA DARAH ATAU PLASMA REPORT OF REACTION TO BLOOD OR PLASMA

Hospital: Ward/Clinic: Patient's Name:

Reg. Number: Age: Sex: Race:

Diagnosis:

1. Date and Time transfusion started:

2. Date and Time of onset of reaction:

3. Blood/Plasma Serial No:

4. Volume Blood/Plasma transfused:

5. Temperature: Before transfusion: After transfusion:

6. **Nature of Reaction:** Tick (✓) positive symptoms/signs:

Chills & rigors Shock Jaundice

Dyspnoea Hypertension Haematuria

Urticaria Hypotension Haemoglobinuria

Pain & Location: Elevated: Date noticed:

7. Solution used for starting drip: N. Saline / 5% Dextrose / Other.....

8. History of previous transfusion: Yes / No Date of last transfusion

9. History of previous reaction:

10. Additional Information:

1. In the case of females:

History of pregnancy Yes / No..... No.of pregnancies:

History of abortion Yes / No No. of abortions:

Tandatangan:

Tarikh:

Nama:

1. When a patient has a reaction to blood plasma, inform Doctor i/c IMMEDIATELY.
2. Report all reactions. Use the following directions for febrile or suspected haemolytic reaction.
3. Preserve the blood bag and giving set with all attached labels, CLOSING IT SECURELY so that cultures can be taken. SEND IMMEDIATELY TO THE BLOOD BANK.
4. Send 10ml of blood to the Blood Bank for investigation.
5. Send the next urine specimen 20 ml to the Pathology Laboratory to be examined for haemoglobinuria.
6. Send at least 10 ml of clotted blood to the Blood Bank 24 hours after the reaction labelled 'Post-transfusion 2'. These will be used for further compatibility tests and for bilirubin determinations. An additional 2.5 ml for Full Blood Picture is also advisable. Similarly, a urine specimen should be sent to the Pathology Laboratory.

RETURN THIS REPORT AT ONCE TO THE BLOOD BANK

Patient's name: _____ Reg. No: _____ Ward: _____

No. of returned blood packs: _____

Date reaction was noted: _____ Date blood was returned: _____

I. RECHECK OF BLOOD GROUPING	ANTI SERA				CELL			ANTI SERA	GROUP	RH
	A	B	AB	AC	A	B	O	D		
Patient:										
1. Pre-Transfusion Sample										
2. Post-Transfusion Sample I										
3. Post-Transfusion Sample II										
Donor:										
1. Blood from Segment										
II. CHECK FOR SENSITISATION AND ATYPICAL ANTIBODY	DIRECT COOMBS TEST ON CELLS	ANTIBODY SCREENING USING SCREENING CELLS								
		RT			37°C / LISS / ALBUMIN			AHG		
		I	II	III	I	II	III	I	II	III
Patient:										
1. Pre- Transfusion Sample										
2. Post- Transfusion Sample I										
3. Post- Transfusion Sample II										
Donor										
III. RECHECK OF CROSS-MATCHINGS:	RT			37°C / LISS / ALBUMIN			AHG			
	I	II	III	I	II	III	I	II	III	
1. Pre-Transfusion Sample with Donor Blood										
2. Post-Transfusion Sample I with Donor Blood										
3. Post-Transfusion Sample II with Donor Blood										
IV. URINE:	HAEMOGLOBIN									
1. Post-Transfusion Sample I										
2. Post-Transfusion Sample II										
V. BLOOD CULTURE	DATE SENT	BACTERIOLOGICAL REPORT								
	1. From Blood Bag									

CONCLUSION

Tandatangan: _____

Nama: _____

Tarikh: _____ PPDK.23.

CHART XV

Reporting format for

ADVERSE TRANSFUSION EVENT

Report ALL adverse events related to transfusion of blood or blood products using this form. Completed forms should be sent to your blood bank for compilation. Where appropriate, treatment of reactions and investigations of events should be carried out using existing protocol.

Patient's Particulars:

Name: I/C no:

Age: Race:

Gender:

Ward:

Hospital:

Products implicated in the Adverse Event: (please tick)

Whole Blood Packed Red Cells Plasma

Platelets Cryoprecipitate Others:

Date of transfusion: Time:

Onset of incident:

- Pre-transfusion
- Immediate (within 24 hours of transfusion)
- Delayed (after 24 hours of transfusion)

Reactions seen / experienced:

- | | | |
|---|---|---------------------------------------|
| <input type="checkbox"/> Fever | <input type="checkbox"/> Nausea | <input type="checkbox"/> Hypertension |
| <input type="checkbox"/> Chill & rigors | <input type="checkbox"/> Vomiting | <input type="checkbox"/> Hypotension |
| <input type="checkbox"/> Rash | <input type="checkbox"/> Headache | <input type="checkbox"/> Diarrhea |
| <input type="checkbox"/> Itchiness | <input type="checkbox"/> Dyspnoea | <input type="checkbox"/> Chest pain |
| <input type="checkbox"/> Flushing | <input type="checkbox"/> Bronchospasm | <input type="checkbox"/> Others |
| <input type="checkbox"/> Urticaria | <input type="checkbox"/> Pulmonary Oedema | |

Other Clinical / Laboratory Findings

Raised bilirubin / jaundice Deranged liver enzymes
Haemoglobinuria Reduced urine input
Unexplained fall in haemoglobin None
Thrombocytopenia (5-12 days post-
Transfusion)
Incorrect transfusion of blood product
Acute transfusion reaction
Haemolytic Non-haemolytic / anaphylaxis
Delayed haemolytic transfusion reaction
Bacterial contamination
Suspected organism
Post-transfusion viral infection
Suspected virus
Post-transfusion purpura
Transfusion-associated graft-versus-host disease (TAGVHD)
Transfusion-related Acute Lung Injury (TRALI)
Near misses*
Specify
Others (e.g. Circulatory overload)

Type of Adverse Event:

*Near misses / pre-transfusion incident – errors detected before transfusion took place e.g. wrong sample, wrong label, wrong blood issued, clerical errors.

Type of Adverse Event:

*Near misses / pre-transfusion incident – errors detected before transfusion took place e.g. wrong sample, wrong label, wrong blood issued, clerical errors.

Reported by:

Name: Designation:

Hospital: Tel no:

Date:

PLEASE SEND REPORT TO:

National Coordinator on Surveillance of Adverse Events in Transfusion, National Blood Centre, Jalan Tun Razak, 50400 Kuala Lumpur
Telephone No: 03-2695 5555 / 2695 5554 Confidential Fax No: 2692 5826

Main Clinical Features of Adverse Events:

	Adverse Events	Common Clinical Features
1	Incorrect blood or component transfused a) ABO compatible b) ABO incompatible	Maybe none or as in acute haemolytic transfusion reaction if patient has antibodies against transfused red cells. Maybe none or major collapse as in acute haemolytic transfusion reaction
2	Acute Transfusion Reaction a) Haemolytic b) Non-haemolytic c) Anaphylaxis	Fever, chills, dyspnoea, chest pain, hypotension, oliguria, DIC Chills, itchiness, rash, urticaria, flushing Urticaria, dyspnoea, hypotension, bronchospasm
3	Delayed haemolytic transfusion reaction	Unexplained fall in Hb, jaundice, dark-coloured urine
4	Bacterial contamination	Fever, rapid onset of shock
5	Post-transfusion viral infection	May take weeks or months to manifest, depending on virus Jaundice, malaise, rash, fever
6	Post-transfusion purpura	Purpura, bleeding, thrombocytopenia 5 - 12 days post-transfusion
7	Transfusion-associated graft-versus-host disease (TAGVHD)	Fever, rash, raised liver enzymes, diarrhea, nausea, vomiting, pancytopenia (1 - 6 weeks post-transfusion)
8	Transfusion-related Acute Lung Injury (TRALI)	Acute respiratory distress (non-cardiogenic), chill, fever, cyanosis, hypoxia, hypotension, bilateral pulmonary infiltrate

FOR BLOOD BANK USE

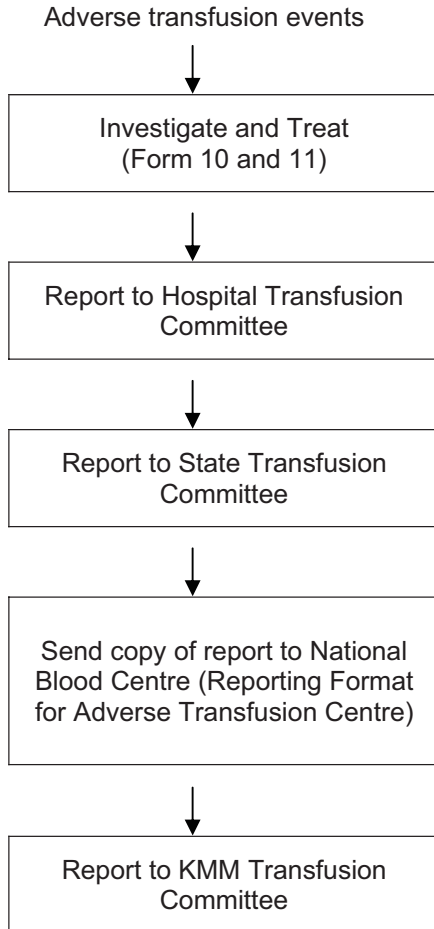
Report No:

Date received:

Date sent to PDN:

Date received by PDN:

Flowchart for Reporting of Adverse Transfusion Events



Note:

1. Every case of adverse reaction must be reported.
2. If the case of adverse reaction involves a seropositive donor, a look-back and recall procedure must be carried out.
3. Identity card number (I/C) and donation date must be submitted to Surveillance Unit, National Blood Centre

12. Consent for Blood Transfusion

Blood transfusion is meant to benefit the patient. Nevertheless, it carries with it various risks to the health of the patient including infectious disease agents (e.g. HIV, hepatitis, syphilis), transfusion reactions and even risk of transfusing wrong blood, which can be fatal. Thus coupled with the decision to transfuse, the medical personnel in charge of the patient also bears the responsibility to explain the benefits, risks and alternatives to transfusion therapy and to ensure that the patient understands the material discussed. Other than in an emergency situation, the patient should be given an opportunity to ask questions, and his/her informed decision should be documented. If the patient is unable to give consent, a responsible family member might be asked to do so. If no family member is available or if in an emergency the need for transfusion leaves no time for consent, it is prudent to note this in the patient's medical notes. (*Refer Chart XVII*)

It is essential that you provide this information in a timely manner that is understood by the patient, and that you ensure this information is understood.

12.1 Frequently Asked Questions: (See *Chart XVIII*)

12.1.1 Why is blood transfusion needed?

Most people cope well with losing a moderate amount of blood (< 20 – 30%) and this can be replaced by crystalloids or colloids. Over the next few weeks the body will make new red cells to replace it. Medication such as iron may help to compensate for the blood loss but if a large amount is lost, then blood transfusion is the best way to replace it rapidly.

- Blood transfusions are given to replace blood lost during operation or after an accident.
- Blood transfusions are used to treat anaemia.
- Some medical treatments or surgery cannot be safely carried out without using blood.

12.1.2 What can be done to reduce the need for blood?

- Eat a well-balanced diet in the weeks before surgery.
- Increase your haemoglobin levels by taking iron and folate.

PRESCRIBING BLOOD: A CHECKLIST FOR CLINICIANS

Always ask yourself the following questions before prescribing blood or blood products for a patient

1. What improvement in the patient's clinical condition am I aiming to achieve?
2. Can I minimize blood loss to reduce this patient's need for transfusion?
 1. Are there any other treatments I should give before making the decision to transfuse, such as intravenous replacement fluids or oxygen?
 2. What are the specific clinical or laboratory indications for transfusion for this patient?
 3. What are the risks of transmitting HIV, Hepatitis, Syphilis or other infectious agents through the blood products that are available for this patient?
 4. Do the benefits of transfusion outweigh the risks for this particular patient?
 5. What other options are there if no blood is available in time?
 6. Will a trained person monitor this patient and respond immediately if any acute transfusion reactions occur?
 7. Have I recorded my decision and reasons for transfusion on the patient's chart and the blood request form?
 8. have I taken the sample from the right patient and labeled it correctly?
 9. Have I taken all the necessary steps to ensure that the blood is transfused to the intended patient?

**Finally, if in doubt, ask yourself the following question.
If this blood was for myself or my child, would I accept the transfusion in these circumstances?**

CHART XIII : LIST OF DRUGS AND CHEMICALS TO BE AVOIDED IN G6PD DEFICIENCY

Drugs given below in bold print should be avoided by people with all forms of G6PD deficiency.

Drugs in normal print should be avoided, in addition, by G6PD-deficient persons of Mediterranean, Middle Eastern, or Asian origin. Items in normal print and within square brackets apply only to people with the African A (⁻) variant.

<p><i>Antimalarials:</i></p> <p>Primaquine [people with the African A (⁻) variant may take it at reduced dosage, 15 mg daily or 45 mg twice weekly under surveillance]</p> <p>Pamaquine Chloroquine (may be used under surveillance when required for prophylaxis or treatment of malaria)</p> <p><i>Sulfonamides and Sulfones:</i> Sulfanilamide Sulfapyridine Sulfadimidine Sulfacetamide (Albucid) Sulfafurazole (Gantrisin) Sallylazosulfapyridine (Salazopyrin) Dapsone* Sulfoxone* Glucosulfone sodium (Promin) Septin</p> <p><i>Other Antibacterial Compounds:</i> Nitrofurans - Nitrofurantoin - Furazolidone - Nitrofurazone</p> <p>[Nalidixic acid] Chloramphenicol <i>p</i>-aminosalicylic acid</p>	<p><i>Analgesics:</i> Acetylsalicylic acid (Aspirin): moderate doses can be used Acetophenetidin (Phenacetin) Safe alternative: paracetamol</p> <p><i>Anthelmintics:</i> β-Naphthol Stibophen Niridazole</p> <p><i>Miscellaneous:</i> Vitamin K Naphthalene* (moth balls) Probenecid Dimercaprol (BAL) Methylene blue Arsine* Phenylhydrazine* Acetylphenylhydrazine* Toluidine blue Mepacrine Doxorubicin Niridazole Phenazopyridine</p>
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CHART XIV : TRANSFUSION REACTIONS AND THEIR MANAGEMENT

1. IMMUNE HAEMOLYTIC TRANSFUSION REACTION

This is defined as the destruction of red cells in the recipient of a transfusion caused by immune alloantibodies of red cells.

Acute Haemolytic Transfusion Reaction

Immediate intravascular haemolysis occurs with ABO-incompatibility while immediate extravascular haemolysis occurs with anti-Rh, Kell or S antibodies. In a conscious patient, even a few ml of ABO incompatible blood may cause symptoms within 1 or 2 minutes.

The symptoms include feelings of doom, agitation, flushing, restlessness, dyspnoea, pain in the abdomen, flank or chest, vomiting and diarrhoea. The signs are fever, hypotension, unexpected bleeding, dark-coloured urine and renal shutdown. In an unconscious/ anaesthetised patient, only the signs will be evident.

Delayed Haemolytic Transfusion Reaction (DHTR)

This is due to extravascular destruction of red cells caused by alloantibodies not detectable at the time of compatibility testing. However, the patient experiences haemolysis of the transfused red cells after an interval of 24 hours up to one week during which an anamnestic response occurs.

The findings are: fall in haemoglobin level after transfusion, jaundice, progressive anaemia, fever, arthralgia, myalgia and serum-sickness-like illness.

The Management of Haemolytic Transfusion Reaction

Investigation

- a) The compatibility label of the blood unit should be checked again to ensure that it corresponds with the patient's name, registration number/IC, request form and case notes.
- b) If a mistake is found, the blood bank should be informed immediately since the unit of blood intended for that patient could be transfused to another patient.
- c) Blood should be taken for the following:
 - 10 ml of clotted blood to the Blood Bank and labelled as post-transfusion sample 1 for
 - repeat ABO and Rhesus grouping
 - repeat compatibility testing
 - antibody screening and Direct Coomb's Test
 - Send another sample 24 hours later and label as post-transfusion sample 2
 - Send FBC in EDTA tube.
 - Send blood sample to biochemistry laboratory for:
 - Serum electrolytes and renal profile
 - Serum bilirubin
 - Send blood for DIVC screening.
- d) All blood bags including unused bags and giving set should be returned to the blood bank for microbiological study.
- e) Urine output should be monitored and presence of haemoglobinuria noted.
- f) An ECG should be done to check for evidence of hyperkalaemia.
- g) Urine should be sent to confirm the presence of haemoglobinuria.

Treatment

- a) The transfusion must be stopped immediately and the doctor in charge of the patient must be informed for further management.
- b) The blood administration set should be changed and venous access maintained using normal saline, initially 20 – 30 ml/kg to maintain systolic blood pressure.
- c) The patient's vital signs should be monitored and urine output should be maintained at >1.5 ml/kg/hr. Monitor with input/output chart.
- d) Maintain airway, give high flow oxygen mask if required.
- e) Give adrenaline 0.01 mg/kg by slow infusion.
- f) Give IV hydrocortisone
- g) If urine output <1.5 ml/kg/hr, fluid challenges should be given with CVP monitoring.
- h) If urine output is still <1.5ml/kg/hr and CVP adequate, then IV frusemide 1 mg/kg should be given, and to be repeated when necessary.
- i) If no diuresis follows frusemide, then 100 ml of 20% mannitol should be given intravenously.
- j) If the urine output, 2 hours after 20% mannitol and frusemide, is < 1.5ml/kg/hr, obtain expert advice as acute renal failure is likely. The patient may need dialysis.
- k) If hypotensive give inotrope (dopamine: IV 1 µg/kg/min)
- l) If bacterial contamination is suspected, treatment with broad-spectrum intravenous antibiotics should be instituted immediately.
- m) If disseminated intravascular coagulation (DIC) develops, replacement of blood components should be guided by clinical state and coagulation screen results.
- n) If the patient needs further transfusion, use rematched blood. There is no increased risk of a second haemolytic reaction.

2. FEBRILE NON-HAEMOLYTIC TRANSFUSION REACTIONS (FNHTR)

FNHTR is defined as a temperature increase of more or equal to 1^o C associated with transfusion and without any other explanation. It is due to anti-leucocyte antibodies in those previously immunised by pregnancy or previous transfusion. The temperature rise may begin early during the transfusion or be delayed in onset for up to several hours after completion. In severe cases, the symptoms include shivering, flushing, palpitations and tachycardia, followed by headache and rigors. The diagnosis of FNHTR is by exclusion of other causes of transfusion reaction as the fever could be due to an acute haemolytic transfusion reaction or by bacterially contaminated blood.

Recommendation:

- a) If FNHTR occurs during transfusion, it can be managed by giving an antipyretic e.g. paracetamol and by slowing the transfusion rate.
- b) If the patient has experienced two or more FNHTR, try
 - paracetamol 1g orally 1 hour before transfusion
 - slow transfusion and keep the patient warm
 - leucocyte-depleted blood components

3. BACTERIAL CONTAMINATION

Contamination of blood at the source, (during collection) or due to faulty storage, can lead to the development of septicaemic shock with high mortality rate in the recipient. Bacteria associated with red cell transfusion are usually cold-growing strains such as *Pseudomonas* or *Yersinia*. Skin contaminants such as staphylococci may proliferate in platelet concentrates stored at 20-22°C.

The signs and symptoms include high fever, shock, haemoglobinuria and renal failure. Gram stain and culture should be requested for diagnosis and vigorous treatment of septic shock and hypotension should be instituted immediately.

4. URTICARIA

The typical urticarial reaction consists of circumscribed areas of cutaneous oedema and itching. It usually occurs within minutes of transfusion without fever or other adverse findings. It is caused by the degranulation of the mast cells in the skin and subsequent release of histamine.

Recommendation:

- a) The transfusion may be temporarily interrupted while an antihistamine (Chlorpheniramine 10 mg by slow intravenous injection) is administered. If urticaria is the only symptom noted, the transfusion may then be resumed.
- b) In a patient who has developed extensive urticaria or a confluent total body rash during transfusion, it would be prudent to discontinue the transfusion even if symptoms have responded to treatment.
- c) For recipients who have had a severe or frequent minor urticaria following transfusion, administering oral antihistamine (Chlorpheniramine 8 mg) 30 minutes before transfusion may be helpful.

5. ANAPHYLACTIC REACTION

An anaphylactic reaction is defined as an immediate generalized hypersensitivity reaction due to activity of IgE antibodies or the presence of anti-IgA in patients with congenital deficiency of IgA. It is a rare but life-threatening complication.

The clinical manifestations include generalized flushing, urticaria, cough, broncho-spasm, dyspnoea, respiratory distress, vomiting, diarrhoea, abdominal pain, arrhythmia, hypotension, syncope and can progress to loss of consciousness, shock and in rare cases, death.

Recommendation:

- a) Treatment of Anaphylaxis
 - Stop the transfusion immediately.
 - Maintain venous access with 0.9% saline.
 - Maintain airway and give oxygen; Salbutamol nebuliser can also be given.
 - Give Adrenaline 0.5-1.0 mg IM, and repeat every 10 minutes according to blood pressure and pulse until improvement occurs.
 - Give Chlorpheniramine 10-20 mg by slow intravenous injection.
 -
- b) In an IgA-deficient recipient requiring transfusion, do not transfuse until after expert advice by the Transfusion Medicine Department.

6. TRANSFUSION-RELATED ACUTE LUNG INJURY (TRALI)

A very severe type of transfusion reaction is the acute, sometimes fatal, pulmonary reaction termed as TRALI. This condition should be suspected in a patient with fever, non-productive cough, hypotension, tachypnoea, dyspnoea and non-cardiogenic pulmonary oedema within 4 hours of initiating the transfusion. Chest x-ray reveals diffuse pulmonary infiltrates. The pathophysiology is due to the transfusion of leucocyte antibodies in the donor that react with the recipient's white blood cells.

Recommendation:

- a) Patients suspected to have TRALI should be managed in an ICU setting in which oxygen therapy and assisted ventilation are often required. Intravenous steroids may be helpful.
- b) The blood bank must be informed so that the implicated donor can be deferred.

7. POST-TRANSFUSION PURPURA (PTP)

PTP is a rare but potentially lethal complication of transfusion, most often seen in multiparous women with platelet-specific alloantibody due to immune-mediated thrombocytopenia. PTP should be suspected in a patient who develops a precipitous fall in platelet count and generalised purpura, occurring 5-9 days after transfusion of red cells or platelets.

Recommendation:

- a) Get expert advice from the Transfusion Medicine Department.
- b) Treatment is with high dose corticosteroids combined with high dose intravenous immunoglobulin.
- c) If platelet transfusion is unavoidable, platelets that are compatible with the patient's antibody is needed in managing PTP.

8. TRANSFUSION-ASSOCIATED GRAFT-VS-HOST DISEASE (TA-GVHD)

TA-GVHD is a rare complication of transfusion and may be acute or chronic. It results from viable lymphocytes from cellular blood component engrafting in an immuno-incompetent patient or in immunologically normal patients after transfusion of a relative's blood. This condition should be suspected in a patient who develops fever, skin rash, diarrhoea, elevated liver enzymes and pancytopenia 1-6 weeks following transfusion. Diagnosis of TA-GVHD could be made by skin biopsy or cytogenetic / HLA analysis to establish the presence of third party lymphocytes.

Recommendation:

- a) Directed donation from a relative to a recipient should be avoided in view of the possibility of shared HLA haplotype.

- b) TA-GVHD is prevented in immuno-incompetent recipient by gamma irradiation of cellular blood components at the recommended dose of 25-30 Gy.

9. OTHER TRANSFUSION REACTIONS

Other adverse transfusion reactions include:

- fluid overload
- metabolic disturbances e.g. hyperkalaemia and hypocalcaemia.
- hypothermia
- embolism
- iron overload
- alloimmunisation to red cell, white cell or platelet antigen.
- immunosuppression and immunomodulation
- transmission of viral infection

These should be managed accordingly.

Chart XVII

CONSENT FORM FOR BLOOD OR BLOOD COMPONENT TRANSFUSION

Date :

Patient's Name : Age :

Identity Card No. : Sex : Male/Female*

Address :

Attending Medical Practitioner : Dr

Identity Card No. :

I, the above named parent/guardian/spouse/next-of-kin of the above-named*, have been informed of the need for a blood transfusion for the patient. The attending medical practitioner has explained to me the risks and benefits involved in the transfusion as well as answering all my inquiries satisfactorily. I understand that despite testing and screening on the blood/blood components for HIV, hepatitis B, hepatitis C and syphilis, there are still risks of developing the disease. I also understand that unavoidable complications of transfusion may also occur.

I fully understand the above and hereby agree to the blood / blood component transfusion.

.....

.....

Signature of the patient/
parent/guardian/spouse/next-of-kin*

Signature of Attending
Medical Practitioner

Name of parent/guardian/spouse/next-of-kin** :

Identity Card No. of the above :

I was present while the above matter was explained to the patient / parent / guardian / spouse / next-of-kin* whose signature appears above. In my opinion, the person referred to has understood the contents of this form and agreed to the transfusion willingly.

.....

Signature of Witness

Name of Witness :

Identity Card No. :

* delete appropriately

** if necessary

BORANG PERSETUJUAN PEMINDAHAN DARAH ATAU KOMPONEN DARAH

Tarikh:

Nama Pesakit : Umur:

No. Kad Pengenalan : Jantina: Lelaki/ Perempuan*

Alamat :

.....

Pengamal Perubatan Yang Merawat : Dr
No. Kad Pengenalan :

Saya, seperti nama tersebut di atas, ibu-bapa / penjaga / suami / isteri / saudara kepada pesakit seperti nama di atas*, telah dimaklumkan bahawa pesakit memerlukan pemindahan darah atau komponen darah. Pengamal Perubatan yang merawat telah memberi penjelasan kepada saya tentang risiko dan kebaikan pemindahan darah dan saya berpuashati dengan semua jawapan yang diberikan kepada soalan-soalan yang saya kemukakan. Saya faham dan sedar, meskipun darah atau komponen darah itu telah menjalani ujian saringan untuk HIV, hepatitis B, hepatitis C dan sifilis, namun risiko jangkitan penyakit menerusi pemindahan darah masih boleh berlaku. Saya juga faham dan sedar bahawa komplikasi pemindahan darah yang lain yang tidak dapat dielakkan juga mungkin berlaku.

Saya benar-benar faham kenyataan di atas dan saya bersetuju untuk menerima pemindahan darah atau komponen darah.

.....
Tandatangan pesakit/ibu-bapa/penjaga/
suami/isteri/saudara terdekat.*

.....
Tandatangan Pengamal Perubatan
yang merawat

Nama ibu-bapa/penjaga/suami/ :
isteri/saudara terdekat**

No. Kad Pengenalan :

Saya memperakui maklumat di atas telah diterangkan kepada pesakit / ibu-bapa / penjaga / suami / isteri / saudara terdekat yang tandatangannya tertera di atas.

Pada hemah saya penama yang dirujuk telah memahami kandungan borang ini dan telah bersetuju untuk menerima pemindahan darah atau komponen darah secara sukarela.

.....
Tandatangan Saksi
Nama Saksi:

No. Kad Pengenalan saksi:

* potong yang tidak berkaitan

** jika perlu

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