



# KINGDOM OF CAMBODIA

## National guidelines for transfusion practice

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MINISTRY OF HEALTH



NATIONAL BLOOD TRANSFUSION  
CENTRE in Cambodia



PEPFAR: U.S. President's Emergency  
Plan for AIDS Relief



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# Chapter 1

## **BLOOD TRANSFUSION SAFETY**

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### **PRACTICE POINTS**

There are three pillars of transfusion safety:

- Donor selection – voluntary non-remunerated donors, screened by questionnaire and interview for behaviour and medical risk factors.
- Donation testing – serology and future nucleic acid testing for known transmissible diseases.
- Patient identification and monitoring – the greatest risk of severe morbidity or mortality is due to ABO incompatible blood due to incorrect patient or sample identification.

There are three pillars of patient blood management:

- Optimise patient haemoglobin and red cell mass.
- Minimise blood loss and gain haemostasis.
- Optimise patient tolerance to anaemia.



# Chapter 1

## BLOOD TRANSFUSION SAFETY

### 1.1 PATIENT BLOOD MANAGEMENT

Patient blood management (PBM) is the timely application of evidence-based medical and surgical concepts designed to maintain haemoglobin concentration, optimise haemostasis and minimise blood loss in an effort to improve patient outcomes. A patient focus in all aspects of health care is important and is equally relevant to transfusion practice. Defining the patient needs helps define the safety, decision making and administration standards for the use of blood and blood products in Cambodia.

### 1.2 BLOOD TRANSFUSION SAFETY

Blood transfusion is an essential part of modern health care. Used correctly, it can save life and improve health. However blood is expensive, and as with any therapeutic intervention, may result in acute or delayed complications. Transfusion carries a risk of transmission of infectious agents, such as HIV, hepatitis viruses, syphilis and Chagas disease.

Donor selection is the first step in transfusion safety. WHO/BCT/BTS has developed guidelines and recommendations based on World Health Assembly Resolution 28.72 of 1975, which urges Member States to develop national blood transfusion services based on voluntary non-remunerated blood donation.

The risks associated with transfusion can only be avoided by close collaboration between the National Blood Transfusion Centre (NBTC) and clinicians in managing the components of the transfusion process for which they are each responsible:

- An adequate supply of safe blood and blood products.
- The effective clinical use of blood and blood products.

Safe and adequate supplies of blood are dependent on the implementation of an integrated strategy for blood safety:

1. The establishment of a well organized, nationally-coordinated blood transfusion service, with quality systems in all areas.

2. The collection of blood only from voluntary non-remunerated donors from low-risk populations.
3. The screening of all donated blood and blood products for transfusion transmissible infections (TTIs), including the human immunodeficiency virus (HIV), hepatitis viruses, syphilis and other infectious agents, and good laboratory practice in all aspects of blood grouping, compatibility testing, component preparation and the storage and transportation of blood products.
4. A reduction in unnecessary transfusions through the appropriate clinical use of blood and blood products, and the use of alternatives to transfusion, wherever possible.

### 1.3 BLOOD AND BLOOD PRODUCT SAFETY

A prerequisite for the effective clinical use of blood is a well-organized blood transfusion service (BTS) that is able to provide blood and blood products that are safe, accessible at reasonable cost and adequate to meet national needs.

Only blood which has been obtained from appropriately selected low-risk voluntary non-remunerated donors and has been screened for transfusion-transmissible infectious agents, in accordance with national requirements, should be issued for transfusion.

Prior to each donation the potential donor is selected according to national / international suitability guidelines. This means that the potential donor completes a questionnaire that is focused on risk behaviour. Further the donor's health is checked to minimize the risk for the donor as well as the recipients. Potential donors with increased risk of infectious diseases, like hepatitis or AIDS are requested not to donate blood anymore.

Each unit of donor blood (donation) needs to be tested for:

- hepatitis B surface antigen (HBsAg),
- antibodies against *Treponema pallidum* (TP),
- antibodies against hepatitis C virus (HCV), and

- antibodies against human immune deficiency virus type 1 and 2 (HIV-1/2).

The following tests should be performed where feasible:

- antibodies against human T-cell lymphotropic virus type I and II (HTLV-I and II),
- other viral and parasite antibody testing where appropriate e.g. Malaria, Chagas disease, and
- bacterial testing of platelets.

Nucleic acid amplification tests (NAT) are designed to narrow the infection window phase however they are not currently available in Cambodia:

- HCV RNA (HCV NAT)
- HBV DNA (HBV NAT)
- HIV DNA (HIV NAT)

Only units that are negative to required tests are released for distribution. In rare cases of medical urgency it might be considered appropriate to release products based on the results of the previous (historic) tests. In these rare occasions a medical statement from the clinician, including patient consent when possible, is mandatory.

Currently not available in Cambodia are specific pathogen reduction technologies and timed quarantine methods. Further increase of the safety by application of specific virus inactivation methods is at the moment not yet possible for erythrocytes and platelets. The restricted expiry time makes the application of a quarantine method to increase the safety, impossible. The safety of plasma for transfusion purposes is increased by application of a quarantine policy or a virus inactivation method.

The pillars of safety to minimize pathogen transmission are:

- a reliable, stable voluntary non-remunerated and regular, donor system,
- appropriate suitability testing (donor selection),
- proper documentation, and
- standardized laboratory testing.

Together these minimize the risk of infection with blood transmissible infectious agents.

### 1.3.1 Whole blood donation

Male donors may give blood 4 times per year, female donors 3 times per year.

The standard in Cambodia is 350 mL blood, collected in 49 mL sodium citrate, phosphate-dextrose-adenine (CPDA-1) anticoagulant /

preservation solution. Currently most blood is stored as whole blood in CPDA-1. Whole blood, stored at 20–24° C, can also be further processed within 24 hours into blood components. Blood components produced from whole blood are erythrocytes, platelets and plasma. The plasma is frozen and stored below –30°C as Fresh Frozen Plasma. Pooled plasma can be manufactured into products such as albumin and immunoglobulins.

Platelets are usually isolated from platelet rich plasma after centrifugation of whole blood.

### 1.3.2 Apheresis

Blood donation by apheresis is not yet available in Cambodia. The apheresis process allows the collection of single components e.g. plasma or platelets, with the return of non-collected components to the donor. In this way a relatively large amount of one component can be harvested from one donor.

## 1.4 PRODUCT LABEL

Each blood product (in-process, intermediate and finished product) must be labelled with a product label containing at least the following information:

- unit identification number (donation number),
- product identification,
- producer identification (blood establishment),
- collection date,
- expiry date / time,
- ABO blood group and RhD type,
- test information (tested and found negative),
- possible other typing (e.g. c, E and K), and
- possible modifications (e.g. irradiation/ leucocyte depletion/washing).

Units used for autologous or directed (specific for a special patient) transfusion are provided with a label on which this is specifically indicated.

## 1.5 PATIENT IDENTIFICATION

There must be a robust mechanism for positive patient identification (ID). This is very important for transfusion practice but is also important for pharmaceuticals, surgery and other aspects of health care.

All patients should be identified on admission and by their full name and at least 2 other identifiers.

These could include:

- full name,

- age or date of birth,
- full address,
- hospital identification number, and
- government issued ID (preferably photo ID).

Prior to any medical intervention (e.g. sample collection, transfusion) the patient should be identified by their full name and at least one other identifier, usually age, date of birth or hospital identification number (if wristbands are used).

If a patient is unconscious or cannot provide verbal confirmation of identity, a family member may be used to confirm identification. If no family member is available, each hospital needs to have a policy and procedure in order to provide a temporary identification to a patient. This temporary identification must be used for all patient identification, sample collection and transfusion.

## 1.6 TRANSFUSION SAFETY

The recipient of a transfusion may experience adverse events unrelated to transmissible disease risk. All adverse events require specific clinical management.

Immune based transfusion adverse events may be immediate or delayed:

### Immediate

- **Haemolytic transfusion reaction** - most commonly due to ABO mismatch caused by

patient identification or clerical mistakes. In many countries this is the most common fatal transfusion reaction.

- **Allergy** - mild urticaria is relatively common and life-threatening anaphylaxis is rare.
- **Febrile non-haemolytic transfusion reactions** are due to residual leucocytes and cytokines in the blood components.
- **Transfusion related acute lung injury (TRALI)** is the leading cause of transfusion mortality in some countries. It is characterized by acute respiratory failure and radiological changes within 6 hours of a transfusion.

### Delayed

- **Haemolysis** due to antibodies to transfused antigens.
- **Post-transfusion purpura** is characterized by thrombocytopenia within 2 weeks of a transfusion due to anti-platelet antibodies.
- **Transfusion associated graft versus host disease** is rare and due to engraftment of donor lymphocytes into a patient.

Non-immune adverse events include bacterial sepsis, circulatory overload and iron overload.



## Chapter 2

# QUALITY SYSTEMS FOR CLINICAL TRANSFUSION

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### PRACTICE POINTS

- Safe patient care relies on a safe hospital system.
- It is important that the entire transfusion ('vein to vein') chain is traceable. This means that the blood establishment and the hospital blood bank should have a clear documentation and archive of all critical steps.
- Haemovigilance systems provide valuable data on the occurrence of transfusion-related adverse events and as a result drives initiatives to enhance the safety of the transfusion process.



## Chapter 2

# QUALITY SYSTEMS FOR CLINICAL TRANSFUSION

### 2.1 ESTABLISHING A QUALITY SYSTEM

Blood transfusion may be a life-saving treatment for patients but is not without risk. Safe transfusion is dependent on having a safe and reliable blood supply, and also a safe clinical transfusion process. All healthcare institutions that transfuse blood should have policies and procedures in place for every step of the clinical transfusion process. Appropriate and correct systems aid in the safety of patients.

Management commitment and support are essential in ensuring that a hospital quality system for clinical practice is developed and supported, and that all staff understand the importance of quality and the consequences for patients of failure in the quality system.

#### 2.1.1 Establishing a system and procedures to support the implementation of the guidelines

Guidelines are a supportive set of indicators and motivators to implement rational practice on an evidence base. They are an integral part of a larger system to manage the quality of operations in daily practice, allowing proper standardization, consistency of implementation of processes and procedures, and monitoring and evaluation to be able to continuously improve.

To be able to demonstrate good clinical practice, documentation of what is to be done and what has been done is paramount. The hospital quality system on the clinical use of blood should include standard operating procedures for the following stages in the clinical transfusion process and, ideally, standard outcome documentation such as a transfusion reaction report form.

It is important to transfuse blood based on evidence. All hospitals require a blood transfusion policy based on the national guidelines for effective and rational use of blood products. The policy is determined by the Hospital Transfusion Committee (HTC) and endorsed by the hospital executive or board.

### 2.1.2 Key elements for hospital transfusion policy

#### Managerial

- A hospital transfusion policy in compliance with the National Guidelines for Transfusion Practice.
- Strategies to implement the policy and achieve the goals set based on a National Quality (QS) and Quality Management System (QMS) e.g. standards and guidelines, annual quality plan.

#### Operational

- Operational system based on written instructions, e.g. standard operating procedures (working instructions) and equipment operating procedures.
- Key elements of a management and quality system are standard procedures for all stages of the clinical transfusion process:
  - a. Ordering blood and blood products in routine and emergency situations.
  - b. The selection and compatibility procedure.
  - c. Issue of blood and blood products.
  - d. Storage and transportation of blood and blood products.
  - e. Administration of blood and blood products.
  - f. Recording all transfusions in patient records including indication and consent.
  - g. Monitoring the patient before, during and after transfusion.
  - h. Management, investigation and recording of transfusion reactions.
- Efficient system for transportation and storage of blood and blood products in the clinical setting (cold chain).
- Practical outcome documents to allow appropriate communication, monitoring and evaluation, for example:
  - a. Availability of standard blood request form.



- b. Availability of blood ordering schedule.
- c. Availability of transfusion reaction report form.
- d. A standard consent form which includes transfusion consent.
- e. A standard compatibility test form.
- f. Clinical indications for transfusion.
- g. A standard checklist for monitoring the patient.

Annexes 4 and 5 include guidance on the monitoring of the transfused patient, and investigating and recording acute transfusion reactions.

The decision to transfuse blood or blood components must be based on a careful assessment of clinical and laboratory findings which indicate that a transfusion is necessary to save life or prevent significant morbidity.

Responsibility for the decision to transfuse rests with individual prescribers of blood, although this may be made in consultation with the National Blood Transfusion Service.

## 2.2 TRACEABILITY

Traceability is an essential element of haemovigilance. The blood component manufacturer, the hospital blood bank and hospital wards must keep records to trace from which donor or donors a specific patient has received a blood product, and when this took place. The documents of this administration must be kept for at least 10 years depending on national regulations.

The purpose of this documentation is that after a post transfusion infection a contaminated donor can be traced. Also recipients of products from recognised contaminated donors must be able to be traced to any recipient.

## 2.3 HAEMOVIGILANCE

Haemovigilance is the observing, recording, analysing and reporting of transfusions when something goes wrong; and using the lessons learned to take action to avoid it going wrong again.

It is important that the entire transfusion ('vein to vein') chain is traceable. This means that the blood establishment and the hospital blood bank should have a clear documentation and archive of all critical steps.

NBTS has responsibility for documentation of donor identification and any donor adverse events.

The hospitals have responsibility for the documentation of clinical decision making, compatibility testing and patient outcomes including adverse events. Investigation of adverse events is a joint responsibility.

Haemovigilance is the assurance and registration / documentation of this entire process. In the hospital it is preferably guided by the haemovigilance coordinator. This person collects all data and provides them to the provincial or regional blood establishment coordinator after processing of these data. The data collected from the associated hospitals are provided to the national coordinator in a compiled form.

## 2.4 MAXIMUM BLOOD ORDERING SCHEDULE

A Group & Screen or cross-match should be performed for all surgical patients at predictable risk of bleeding and in those patients where uncommon and unexpected bleeding may be catastrophic. The hospital transfusion laboratory must give special consideration to patients with a positive antibody screen.

A Maximum Blood Order Schedule (MBOS) can be used to gauge expected blood use for patients undergoing a specific procedure and assists in ordering blood. Institutional factors affect the format of an MBOS and include:

- The presence of an onsite laboratory and whether it is staffed 24 hours a day or not,
- The availability of blood and blood products and distance from Transfusion Service,
- The availability of O erythrocyte units, and
- Clinical demand, clinical specialties and local surgical practice.

## 2.5 HOSPITAL TRANSFUSION COMMITTEE

The Hospital Transfusion Committee (HTC) has a role in ensuring clinical governance and risk management, appropriate use of precious blood products and to improve patient care and safety.

All major hospitals should have or establish a HTC (or equivalent) for oversight and governance of transfusion practice. The HTC should:

- monitor and improve transfusion practice,
- promote appropriate use of blood,
- report and investigate adverse events and transfusion reactions,
- monitor blood utilisation, stock availability and wastage.

- provide an active forum to facilitate communication between those involved with transfusion,
- ensure implementation of the Kingdom of Cambodia National Transfusion Guidelines,
- review on an annual basis MBOS, and
- promote transfusion training and education activities.

The HTC should meet on a regular basis and at least quarterly.

The membership of the HTC should include a range of health professionals involved in transfusion, including physicians, nurses, transfusion staff, hospital administration, and other personnel as needed. The chair of the committee should report to the hospital executive so that practice changes can be endorsed and authorized.

Both clinical and laboratory perspectives are critical in obtaining the safest and most practical policies for transfusion activities. The members of the HTC can help provide this input on behalf of, and preferably in collaboration with, members of their own departments.

The HTC has a role in reviewing blood stock supply and demand data. This may include the management of blood shortages and the use of a MBOS. The HTC also has a role in reviewing the cold chain management for storage, handling and transportation of blood components.

*See Annex 1. Hospital Transfusion Committee Terms of Reference*

*See Annex 2. Indicators for monitoring and evaluation of the Hospital transfusion chain.*



## Chapter 3

# MAKING THE DECISION TO TRANSFUSE

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### PRACTICE POINTS

- Determine the best treatment for the patient which may include transfusion. Treat the cause of cytopenia (anaemia or thrombocytopenia) or plasma protein deficiency in preference to transfusion.
- Transfusion usually only gives temporary relief.
- Always balance risk and benefit of transfusion for the individual patient.
- Gain consent prior to transfusion.
- IV fluids are first line therapy for hypovolaemia and blood loss.
- Crystalloids are the preferred IV fluid for initial resuscitation.



## Chapter 3

# MAKING THE DECISION TO TRANSFUSE

### 3.1 BALANCE OF RISK AND BENEFIT

The decision to use blood transfusion as part of clinical management is dependent upon:

- the balance of benefits and risks to the individual patient, and
- alternative or complementary therapies.

#### 3.1.1 Aims of transfusion

Erythrocyte transfusion aims to increase oxygen carrying capacity to improve tissue oxygenation.

Plasma infusion aims to replace reduced plasma protein levels and will assist to increase oncotic pressure.

Platelet transfusion aims to reduce bleeding risk due to thrombocytopenia or functional platelet defects.

Whole blood transfusion aims to provide red cells. Platelets become non-functional with fridge (2-6°C) storage. Many plasma proteins, especially Factors V and VIII, are severely reduced with room temperature or fridge storage.

#### 3.1.2 Risk and Benefits

Blood transfusion carries a component safety risk, such as transmissible disease and immune modulation. The administration of the component carries risk associated with consent, fluid balance and incorrect patient identification.

The decision to transfuse blood or blood products should always be based on a careful assessment of clinical and laboratory indications that transfusion is necessary to save life or prevent significant morbidity. Before any transfusion, the clinician should ask the following questions:

- Is blood transfusion really needed?
- If YES, what does the patient really need?

Volume replacement; improved tissue oxygenation; haemostatic control; plasma protein replacement or improved immune function?

- Which component(s) are being considered?
- Are there alternatives?
- How much is needed, how often and how long?

- What is the optimal way and time of administration of the transfusion?
- What indicators should be used to measure outcomes?

### 3.2 DECISION TO TRANSFUSE

The following principles apply:

1. Transfusion is only one element of the patient's management.
2. Patients should be clearly identified.
3. Prescribing decisions should be based on the national guidelines on the clinical use of blood, taking individual patient needs into account.
4. Blood loss should be minimized to reduce the patient's need for transfusion.
5. The patient with acute blood loss should receive effective resuscitation (intravenous replacement fluids, oxygen, etc.) while the need for transfusion is being assessed.
6. The patient's haemoglobin value, although important, should not be the sole deciding factor in starting transfusion. The decision to transfuse should be supported by the need to relieve clinical signs and symptoms and prevent significant morbidity and mortality (multiple organ failure).
7. The clinician should be aware of the risks of transfusion-transmissible infection in the blood and blood products that are available for the individual patient.
8. Transfusion should be prescribed only when the benefits to the patient are likely to outweigh the risks.
9. The clinician should record the reason for transfusion clearly.
10. Patients should give consent for transfusion which should be documented in the patient case record.
11. A trained person should monitor the transfused patient and respond immediately if any adverse effects occur.

The decision to transfuse a patient is governed by many clinical factors, examples of which are listed in table 3.1 (see below).

Prescribing decisions should be based on individual patient needs and national guidelines. Decisions should also be based on knowledge of local patterns of illness, the resources available for managing patients and the safety and availability of blood and intravenous replacement fluids.

Responsibility for the decision to transfuse ultimately rests with individual clinicians.

### 3.3 ALTERNATIVES TO TRANSFUSION

All decision making around transfusion should include assessment of possible alternatives. Placing the patient’s needs in the centre of decision making is very important and is now called “Patient Blood Management”. A patient with low blood volume typically needs volume expansion and may not require transfusion. A patient with anaemia primarily due to iron deficiency rarely needs a transfusion and iron therapy is more appropriate.

#### 3.3.1 Intravenous replacement therapy

The administration of intravenous replacement fluids restores the circulating blood volume and so maintains tissue perfusion. In severe haemorrhage, initial treatment (resuscitation) with intravenous replacement fluids may be life-saving and provide time to control the bleeding and order blood for transfusion, if necessary.

- Replacement fluids are used to replace abnormal losses of blood, plasma or other extracellular fluids by increasing the volume of the vascular compartment. Principally in:
  - treatment of patients with established hypovolaemia: e.g. haemorrhagic shock, and
  - maintenance of normovolaemia in patients with ongoing fluid losses: e.g. surgical blood loss.
- Intravenous replacement fluids are the first-line treatment for hypovolaemia. Initial treatment with these fluids may be life-saving and provide some time to control bleeding and obtain blood for transfusion, if it becomes necessary.

Table 3.1 Clinical factors which determine the need for erythrocyte transfusion

1. Reduction in Red Cell or Hb	
<b>External bleeding</b>	Trauma Planned surgery
<b>Internal Bleeding</b>	Non-traumatic e.g. peptic ulcer; varices; ectopic pregnancy; antepartum haemorrhage; ruptured uterus
	Traumatic e.g. chest; spleen; pelvis; femur
<b>Haemolysis</b>	DIC Sepsis Malaria; Dengue Haemorrhagic Fever
2. Patient’s ability to tolerate anaemia	
<b>Perform clinical assessment</b>	Age Co-morbidities e.g. pre-eclampsia; renal failure; cardiorespiratory disease; chronic lung disease; acute infection; diabetes
	Current cardiorespiratory and oxygenation status Check: pulse rate; BP; signs of cardiac failure; urine output and fluid balance; angina; respiratory rate and/or distress; conscious state
<b>Perform laboratory assessment</b>	Current laboratory values Check: Hb; MCV; Platelet count; coagulation profile (aPTT, INR, Fibrinogen)

- Crystalloid solutions with a similar concentration of sodium to plasma (e.g. normal saline or balanced salt solutions) are effective as replacement fluids. Dextrose (glucose) solutions do not contain sodium and are poor replacement fluids.
- Crystalloid replacement fluids have a short half life and may be needed in slightly greater volume (one and a half times) than the volume lost in order to correct hypovolaemia.
- All colloid solutions (albumin, dextrans, gelatins and hydroxyethyl starch solutions) can be used in volume replacement but have not been shown to be superior to crystalloids for resuscitation. Dextrans may interfere with ABO blood group determination.
- Colloid solutions should be infused in a volume equal to the blood volume deficit.
- Plasma can correct hypovolaemia but it should not be used as a replacement fluid.
- Plain water should never be infused intravenously. It will cause haemolysis and will probably be fatal.
- In addition to the intravenous route, the intra-osseous, oral, rectal or subcutaneous routes can be used for the administration of fluids.

Volume need shall be met with alternatives (IV fluids) –

### Crystalloids (e.g. normal saline)

Advantages:

- Readily available.
- Easy to store.
- Easy to use.
- Not immunogenic and not toxic.
- No infection risk.
- Low cost.
- Equal to colloids for fluid resuscitation.

Disadvantages:

- No oncotic (colloid osmotic) pressure.

### Colloids (e.g. albumin and starch solutions)

Advantages:

- Readily available.
- Easy to store.
- Easy to use.
- Not toxic.
- No infection risk.

- Provide oncotic (colloid osmotic) pressure.
- Low cost.

Disadvantages:

- Short survival.
- Sometimes immunogenic.
- Sometimes effect on coagulation (platelets).
- Sometimes interferes with blood group determination and cross-match.
- Possible delay in albumin synthesis.

### 3.3.2 Drugs

Consideration should be given to medications as alternatives to transfusion. Improvement of haemoglobin with iron, folate and vitamin B12 may be appropriate for many patients. Erythropoiesis can be stimulated by erythropoietin and related drugs.

Avoidance of anti-platelet drugs (e.g. clopidogrel and aspirin) and anti-coagulants (e.g. warfarin) may reduce bleeding and the need for platelet, plasma and erythrocyte transfusions.

Some medications (e.g. steroids) improve platelet counts in patients with immune thrombocytopenia as platelet transfusions are not beneficial in these patients. Vasoconstrictors and ionotropes are important medications in resuscitation but seldom change the need for transfusion.

#### 3.3.2.1 Iron

Iron deficiency is common and replacement may be achieved by oral therapy in most cases. Transfusion is rarely indicated for isolated iron deficiency. See chapter 4 for additional information.

#### 3.3.2.2 Tranexamic Acid

An anti-fibrinolytic useful in reducing bleeding and the need for erythrocyte transfusion in surgical and trauma settings. A large study of blood use in trauma indicates a 30% reduction in the use of blood products when given within 3 hours of trauma. Tranexamic acid should be considered for all trauma and surgical patients who are expected to need large volume transfusions.

A standard adult dose of tranexamic acid for trauma is 1g IV within 3 hours of trauma followed by 1g IV over 8 hours. The same dose protocol can be used for planned surgery.

Some studies also suggest a role in bleeding secondary to thrombocytopenia. Tranexamic acid may be useful in patients with bleeding and thrombocytopenia when there are no platelets

available for transfusion. May also be considered when bleeding is poorly controlled after platelet transfusion.

Tranexamic acid is available in both IV and oral.

### **3.4 INFORMED CONSENT**

Medical intervention should only occur with the consent of a patient or their legal guardian. A physician should seek consent from the patient prior to the transfusion and after having informed the patient about possible risks and appropriate alternatives. The indication for transfusion, the patient's consent and the outcome of the transfusion should be documented in the patient's file for traceability purposes and consistent with sound patient record keeping. Refusal of transfusion also needs to be documented. Refusal of consent for religious or personal reasons must be documented in the patient's medical record. Where a patient refuses consent to specific blood products both those not to be administered and acceptable alternatives should be clearly documented. Where a parent or guardian refuses to consent to administer blood or blood products to a child in an emergency situation local state or national legislation or guidelines should apply.

### **3.5 ORDERING THE TRANSFUSION**

Before administering blood products, it is important to clearly write the reason for transfusion in the patient file. If the patient later has a problem that could be related to the transfusion, the records should show who ordered the products and why. This information is also useful for conducting an audit of transfusion practice. The record you make in the patient file is your best protection if there is any medico-legal challenge later on.

### **3.6 THE PRESCRIPTION**

The order for the blood product should contain:

- the patient name and UR number or date of birth,
- the type of blood component required,
- the time over which it is to be administered, and
- any related medication such as premedication or diuretics that may be required.

*See Annex 3. Example of a model blood request form as advocated by WHO.*







## Chapter 4

# INDICATIONS FOR BLOOD COMPONENTS, IRON & HAEMOSTATIC DRUGS

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### PRACTICE POINTS

- Specific indications, including Hb and platelet count triggers, can help clinical decision making.
  - Hb < 7 g/dL – often appropriate to transfuse erythrocytes.
  - Hb > 10 g/dL – rarely appropriate to transfuse erythrocytes.
  - Oral iron therapy is preferable to transfusion in iron deficient patients.
  - Plasma is used to treat plasma protein deficiencies.
  - Platelets are appropriate when there is bleeding and thrombocytopenia; thrombocytopenia ( $< 10 \times 10^9/L$ ) due to marrow suppression; neonates with thrombocytopenia or patients undergoing neurosurgery with platelet counts  $< 50-100 \times 10^9$ .
- Tranexamic acid and DDAVP may play a role in haemostasis, even during thrombocytopenia.
- Tranexamic acid reduces transfusion requirement in massive transfusion.
- Iron should be given in preference to transfusion in patients with iron deficiency.



## Chapter 4

# INDICATIONS FOR BLOOD COMPONENTS, IRON & HAEMOSTATIC DRUGS

### 4.1 ERYTHROCYTES

Erythrocytes are only administered dependent upon the patient's symptoms, age and cardiovascular status. The most important questions to consider in the decision making for transfusion are:

- Could the patient compensate for the existing anaemia (cardiovascular status)?
- How intense and how much is the patient bleeding?
- Is there an increased use of O<sub>2</sub> (temperature, cold shiver, sepsis)?
- Are there signs of atherosclerosis (brain, heart, vessels, kidney)?
- What is the state of tissue perfusion (release of O<sub>2</sub>)?

#### 4.1.1 Haemoglobin Thresholds

The decision to transfuse erythrocytes should never be based on an Hb or Hct value only. Primary diagnosis, modifying clinical circumstances, functional capacity, ability to tolerate anaemia and availability of blood components are all relevant factors in the decision to transfuse.

##### **Hb ≤ 6 g/dL (Hct 20%):**

Consider a transfusion if the Hb ≤ 6 g/dL (Hct 20%) in case of:

- Chronic asymptomatic anaemia.
- Acute blood loss in healthy person; < 60 years, ASA I1, normovolaemic, blood loss from 1 location.

NOTE: Most patients do cope well with a low Hb (down to 6-7g/dL). For these patients, normalisation of the Hb is not needed. Functional impairment, e.g. organ failure, may develop at lower Hb values and transfusion may be justified.

##### **Hb ≤ 7 g/dL (Hct 24%):**

Consider a transfusion at a Hb ≤ 7 g/dL (Hct 24%) in case of:

- Acute blood loss in healthy person; > 60 years, ASA I, normovolemic, blood loss from 1 location.

- Acute blood loss in healthy person < 60 years, normovolemic and blood loss at more locations (poly-trauma).
- As pre-operative minimum; < 60 years, expected blood loss > 500 mL.
- Patient has sepsis.
- In the post-operative phase (uncomplicated) after open heart surgery.
- ASA II an III patient; uncomplicated.

##### **Hb ≤ 8 g/dL (Hct 27%):**

Consider transfusion when the Hb ≤ 8 g/dL (Hct 27%) in case of:

- ASA IV patient.
- Patient is not capable to increase the cardiac output.
- Patient with serious cardiopulmonary disease.
- Patient with cerebrovascular symptomatology (ischaemia).

##### **Hb ≥ 10 g/dL (Hct 33%):**

- Hb of 10g/dL is well tolerated and transfusion above this value is not required.

#### 4.1.2 Special Considerations

##### **Newborn and Children**

Erythrocyte transfusion is indicated in the following circumstances:

- During the first 24 hours post partum, a capillary haemoglobin level < 10 g/dL and clinical symptoms of anaemia (organ failure).
- During ECMO and a Hb level < 10 g/dL.
- During oxygen application and a Hb level < 9 g/dL.
- Stable premature, younger than 4 weeks and a Hb level < 8 g/dL.
- Stable premature, older than 4 weeks and a Hb level < 6.5 g/dL .
- A child (not neonate) will generally tolerate a lower Hb than an adult.

## Critical Bleeding and Massive Transfusion

Critical Bleeding has many definitions:

- loss of one blood volume over 24 hours or
- the need to use 10 units of red cells or
- half the blood volume in 4 hours or
- bleeding at > 150 mL per minute.

Critical bleeding should be managed by a critical bleeding protocol which includes clinical assessment and laboratory results such as Hb, coagulation and acid-base measurements.

### Major Bleeding:

For any blood loss of 20–25% of the blood volume, volume should be replaced by colloid or crystalloid solutions. Depending on the clinical situation (e.g. presence of organ failure) and the Hb level, in addition to volume supplementation, erythrocytes may be given (see chapter 13).

### 4.1.3 The Role of Iron

Many causes of anaemia are complicated by iron deficiency due to chronic blood loss, inadequate intake or co-morbidities. Low ferritin (less than 20–30 µg/L or determined by local laboratory reference ranges) is diagnostic of iron deficiency; however in patients with inflammatory conditions or chronic illness, the ferritin may be within normal range (up to 60 in children and 100 in adults) despite iron deficiency. Microcytosis (low MCV) may be due to iron deficiency however there are several other common causes (e.g. thalassaemia) and it cannot be relied on for diagnosis. Provided the patient has a functional bone marrow, a trial of full dose oral iron replacement therapy will cause an increased reticulocyte count within 1–2 weeks and may be diagnostic.

Oral iron therapy is preferable to transfusion in patients with iron deficiency.

### 4.1.4 Indications for whole blood

#### Indications for whole blood:

- Red cell replacement in acute blood loss with hypovolaemia, when replacement fluids are not available
- Exchange transfusion
- Patients needing red cell transfusions where red cell concentrates or suspensions are not available

Generally, erythrocytes are the product of choice for anaemia correction and improving oxygen carrying

capacity.

### Contraindications

- Risk of volume overload in patients with:
  - Chronic anaemia.
  - Incipient cardiac failure.
- Whole blood which has been stored at 2–6°C, or stored at room temperature for > 24 hours does not contain useful platelets or adequate labile clotting factors (e.g. FVIII). Whole blood should not be relied upon when trying to replace these blood components.

### 4.1.5 Hb AND Hct CONVERSION

Approximate conversion values for normocytic patients without significant haemolysis:

Hb (g/L)	Hb (g/dL)	Hb (mmol/L)	Hct (%)
40	4	2.5	14
50	5	3.1	17
60	6	3.7	20
70	7	4.3	24
80	8	5.0	27
90	9	5.6	30
100	10	6.2	33
110	11	6.8	36

Alternatively use these formulae:

$$Hb (g/dL) = Hct (\%) \times 3$$

The constant depends upon the method of measurement and varies between 2.7 – 3.4.

$$Hb (mmol/L) = 0.621 \times Hb (g/dL)$$

## 4.2 PLASMA

### Indications:

- Bleeding or risk of major blood loss with demonstrated combined coagulation factor deficiency (massive blood loss, L-asparaginase therapy, severe liver disease, disseminated intravascular coagulation).
- Plasmapheresis in thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (HUS).
  - Albumin may be a suitable substitute in TTP and HUS.
- Coagulopathy caused by envenomation from snake bites. Some snake venoms contain coagulation factors which often disrupt normal coagulation leading to mucocutaneous bleeding

and sometimes thrombosis. Antivenom is the most potent therapy, which replacement of plasma clotting factors is important supportive care. Measurement of coagulation parameters may guide therapy.

- Isolated Factor deficiency when no suitable concentrate exists e.g. Factor V deficiency, F XIII deficiency.

#### **Contraindications:**

- Hypovolaemia by itself.
- Routine in (major) surgical operations.
- Immunodeficiency.
- Sepsis in newborns.
- Diet support / recuperation / parenteral nutrition.

### **4.3 PLATELETS**

#### **Indications:**

##### *To treat bleeding:*

- Thrombocytopenia as a consequence of bone marrow insufficiency or abnormal platelet function with active moderate or severe bleeding.
- Massive blood loss and a platelet count  $< 50 \times 10^9/L$ .

##### *Prophylaxis:*

- Prophylactic platelet transfusion is often appropriate for patients with thrombocytopenia as a consequence of bone marrow insufficiency (e.g. chemotherapy) and a platelet count of  $< 10 \times 10^9/L$ .
- Higher thresholds may be relevant in certain clinical situations e.g.: Patients with platelet defects and risk of bleeding  $< 20-50 \times 10^9/L$  and patients undergoing neurosurgical procedures  $< 50-100 \times 10^9/L$ .
- Neonates often require higher platelet count:
  - Well premature baby  $20 \times 10^9/L$ .
  - Birth weight  $< 1500$  g and ill  $50 \times 10^9/L$ .

- Overt bleeding/surgery  $50 \times 10^9/L$ .
- Prior to exchange transfusion  $< 100 \times 10^9/L$  (during or after exchange transfusion).

#### **Contraindications**

Platelets should not be given to patients with platelet destruction such as:

- immune thrombocytopenic purpura (ITP);
- thrombotic thrombocytopenic purpura (TTP) and
- heparin-induced thrombocytopenia (HIT)

unless there is life-threatening haemorrhage, in which case high dose steroids (or alternative) should be given in combination with platelets.

#### **4.3.1 Haemostasis medications**

There is no substitute for platelet transfusion for a patient with bleeding due to thrombocytopenia.

When platelets are not available, haemostasis may be supported by:

- tranexamic acid or,
- intravenous desmopressin (DDAVP).

**Tranexamic acid** is anti-fibrinolytic. It may reduce bleeding in both patients with and without thrombocytopenia and is now part of standard therapy in early critical bleeding. It carries a thrombosis risk and should be used with caution in patients at risk of thrombotic complications. Tranexamic acid can be administered before or after platelet transfusions if required.

**DDAVP** causes platelets and endothelium to release endogenous factor VIII (FVIII). This may assist haemostasis independent of platelets, particularly in patients with FVIII or vWF deficiencies. DDAVP has not been shown to reduce bleeding in patients without haemophilia or von Willebrand's disease. Flushing and plasma sodium changes are the most common adverse events. Thrombosis is a risk for any medication which increases haemostatic potential.



## Chapter 5

# BLOOD COMPONENT INFORMATION

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### PRACTICE POINTS

#### Erythrocytes:

- Must be ABO compatible.
- Erythrocytes for neonates must be cross-matched against maternal samples.
- Must be RhD compatible for females of child bearing capacity.
- Best component for improving oxygen carrying capacity.

#### Whole Blood:

- Must be ABO compatible.
- The plasma will be deficient in FV and FVIII and possibly other coagulation factors.
- Does not contain viable platelets.
- Used as a substitute for erythrocytes when erythrocytes are not available.

#### Plasma:

- Fresh Frozen Plasma (FFP) contains coagulation proteins and albumin.
- Needs to be ABO compatible.

#### Platelets:

- One dose is 4-6 whole blood derived units.
- Are indicated for bleeding due to severe thrombocytopenia or platelet dysfunction.
- May be indicated for prevention of bleeding in some patients.
- Patients who develop refractoriness to platelets usually have an HPA or HLA antibody and may benefit from HPA or HLA matched platelets.
- Should be ABO compatible.



# Chapter 5

## BLOOD COMPONENT INFORMATION

### 5.1 ERYTHROCYTES

Erythrocytes (also known as Red Cell suspension or Red Cells) is the standard product for the treatment of anaemia if transfusion is appropriate.

Erythrocytes can be split into paediatric units called paedi-packs. These units are used for neonates and children who require a transfusion of a volume less than one unit of erythrocytes.

#### 5.1.2 Indications and contraindications

See chapter 4.

Erythrocyte transfusions are given to increase oxygen carrying capacity by treating anaemia.

#### 5.1.3 Storage conditions erythrocytes

##### Storage time and temperature:

Unless labelled differently: 35 days at 2–6° C

##### Storage time after spiking/opening the bag:

20–24° C      max 4 hours

#### 5.1.4 Compatibility testing

Selection of ABO and RhD:

Erythrocytes must always be ABO and RhD compatible, though not necessarily identical with the recipient (see Table 5.1). To reduce the risk of sensitisation, all RhD negative females of child bearing potential should receive RhD negative blood. Only women who are known to be RhD positive should receive RhD positive blood.

For children younger than 3 months the selection of ABO, RhD blood groups and typing for allo-antibodies should be compatible with the mother (see Table 5.2). ABO choice is indicated in the table. If there is any doubt, Group O erythrocytes will always be compatible with any ABO groups of mother and child.

On request, paediatric units (paedi-packs) with a volume of 70–100 mL prepared from one single donation may be kept for the same patient. This practice will reduce donor exposure to the neonate.

Table 5.1 ABO compatibility of erythrocytes, whole blood or platelets.

Patient	Compatible ABO donor group	Preference when more than one group is compatible*			
		O	A	B	AB
Unknown	O	1			
O	O only	1			
A	A or O	2	1		
B	B or O	2		1	
AB	AB or A or B or O	4	2	3	1

\*A preference of "1" implies this is the best ABO blood group to choose for that patient, "2" second best and so on. If there is no number, that ABO blood group is not compatible for the patient and should not be used.

Table 5.2: Choice of ABO blood group donor erythrocytes in the first 3 months:

Child	Mother	Donor erythrocytes for child
O	O, A, B or AB	O
A	A or AB	O or A
A	O or B	O
B	B or AB	O or B
B	O or A	O
AB	AB	O, AB, A or B
AB	A	O, A or AB
AB	B	O, B or AB

### 5.1.5 Recommendation prevention of immunization by c, E and Kell

Determination of blood group types, other than ABO and RhD (phenotyping) on erythrocytes is currently not available in Cambodia.

Provision of Kell negative blood for all females of child bearing potential (girls and women of child bearing age) is recommended. Provision of c and E compatible blood for females of child bearing should be considered.

Provision of c, E and K compatible blood is recommended for patients with an inherited disease who need transfusion during their entire life (e.g. Thalassaemia). If at all possible, full phenotype specific blood, to minimize the risk of immunization, should be provided for patients on chronic transfusion programs.

Phenotyped erythrocytes are important when finding compatible blood for patients with alloimmune antibodies, including haemolytic disease of the newborn.

### 5.1.6 Citrate side effects

Whole blood and erythrocyte concentrates are stored in solutions containing approximately 1.2g citrate. A healthy adult liver can metabolise 3g citrate every 5 minutes. Transfusion rates higher than 1 unit per 5 minutes or transfusion in patients with severe liver impairment may develop hypocalcaemia due to citrate toxicity. Routine administration of calcium after a transfusion is not required.

### 5.1.7 Characteristics of Erythrocytes

From 350 mL whole blood, collected in 51 mL sodium citrate solution (CPD-A), plasma is separated. About 54–60 mL of plasma is left on the erythrocytes.

Cross-match is based on the red cell antigens. The volume of plasma (containing ABO antibodies) is low and not clinically relevant.

Target value	
Volume	210–230 mL (for paediatric use 70–100 mL)
Hct	65–75 %

This is the standard erythrocyte product for transfusion (see chapter 4) and should be used preferentially to Whole Blood whenever possible or available.

### 5.1.8 Characteristics of Whole Blood

Whole blood (350 mL in 49 mL CPDA-1 solution), unprocessed, is used when Erythrocytes are not available. Whole blood is composed of plasma in which the cells (red cells, platelets and white cells) are suspended. The oxygen carrying and release capacity per volume is half of that of a red cell concentrate.

Platelets are non-functional and some plasma proteins are at low concentrations.

Target value	
Volume	380–410 mL (for paediatric use 70–100 mL)
Hct	35–45 %

#### 5.1.8.1 Indications and Contraindications

See chapter 4. Whole blood is given to correct anaemia or improve oxygen carrying capacity when no erythrocytes are available.

The plasma component of whole blood has reduced labile factors e.g. Factor VIII. The platelet component of whole blood is not functional due to storage – platelets are not viable when stored at 2–6°C.

#### 5.1.8.2 Choice of blood group when using Whole Blood

Whole blood contains red cells which are coated in ABO antigens and plasma containing ABO antibodies. Red cell ABO antigen mis-match may lead to life-threatening ABO transfusion reactions. Mis-matched plasma antibodies may lead to haemolysis. Group identical cross-match is ideal for whole blood

as the red cell antigen and plasma antibodies are both matched. If group identical is not available, red cell antigen group compatibility is more important than plasma compatibility.

Some donors have low titre anti-A and anti-B and these donors pose a lower risk of haemolysis.

For example, a group A patient (red cell antigen A present and anti-B in the plasma) should be transfused group A whole blood. Second choice should be group O whole blood with low titre anti-A. If transfusion is essential and neither choice is available, always choose blood compatible with the patient's red cell antigen as third choice, in this example, group O blood.

Table 5.3: Whole blood ABO compatibility preferences

Patient	Whole Blood Product choice		
	1st	2nd	3rd
O	O		
A	A	O low titre anti-A, anti-B	O
B	B	O low titre anti-A, anti-B	O
AB	AB	A	O low titre anti-A, anti-B

### 5.1.8.3 Storage conditions

Between +2°C and +6°C in an approved blood bank refrigerator, fitted with a temperature chart and alarm. During storage at +2°C and +6°C, changes in composition occur resulting from red cell metabolism (pH, K<sup>+</sup>).

Transfusion should be started within 30 minutes of removal from refrigerator and completed within 4 hours.

### 5.1.8.4 Citrate side effects

See note about citrate and calcium in section 5.1.6

Whole blood may cause volume overload and fast transfusion of larger numbers of units may cause hypothermia.

## 5.2 PLASMA

Fresh Frozen Plasma (FFP) contains all clotting factors and albumin in approximately the same concentrations as circulating plasma.

Plasma from a unit of whole blood or plasma

obtained by apheresis is snap frozen as soon as possible after collection (within 8 hours) and thawed at 37° C shortly before use.

### 5.2.1 Indications

See chapter 4 for indications and contra-indications.

### 5.2.2 Storage conditions

Storage time / temperature: 12 months at -25° C or lower; 24 months at -30° C or lower.

### 5.2.3 Compatibility

Fresh Plasma should be transfused ABO compatible. If FFP is screened for antibodies then cross-match is not necessary.

Table 5.4: ABO compatibility of FFP and Cryoprecipitate

Patient	Plasma group (donor)
O	O, A, B or ab
A	A or AB
B	B or AB
AB	AB

Note: AB plasma is the "universal" plasma donor – it is compatible for any patient.

### 5.2.4 Side effects

See chapter 13 on Adverse events.

### 5.2.5 Characteristics of Plasma products

#### 5.2.5.1 Fresh Plasma, frozen and thawed

A whole blood collection has the plasma separated by centrifugation and frozen rapidly to reach a temperature below -30°C within 1 hour. The plasma is stored at -25°C and when needed for transfusion, the unit is thawed in an aseptic water bath at 30-37°C. Thawing is performed by putting the frozen bag of plasma in an overwrap to avoid contamination from the water bath.

	Target value
Volume	230 mL
Factor VIII	at least 0.7 IU/mL
Stable clotting factors	80–100%
Albumin	4g/dL

For children usually smaller amounts can be used (paediatric units: 75-100 mL).



Plasma should be administered within 4 hours after thawing and should not be frozen again.

#### 5.2.5.2 Solvent / Detergent treated plasma

Solvent/detergent treated pooled plasma is not available in Cambodia. SD Plasma is prepared by the addition of Tri-(n-butyl)-phosphate [TNBP and detergent (Triton X-100)] to a pool of fresh plasma. This results in a chemical inactivation of specially enveloped viruses. The plasma pools consist of at least 500 individual donations.

### 5.3 CRYOPRECIPITATE AND CRYODEPLETED PLASMA

Fresh Frozen Plasma is slow thawed at 4°C until a precipitate forms. This precipitate is collected and frozen as cryoprecipitate. Cryoprecipitate is a concentrate of fibrinogen, Factor VIII, von Willebrand factor and Factor XIII. Cryoprecipitate is thawed at 37° C shortly before use. A standard adult dose is 5–10 units of cryoprecipitate.

The residual plasma can be frozen and used for clinical purposes. It is called Cryodepleted plasma and can be used to treat patients with Thrombotic Thrombocytopenic Purpura (TTP).

Neither cryoprecipitate nor cryodepleted plasma are available in Cambodia.

#### 5.3.1 Indications

When fibrinogen concentrate is not available, cryoprecipitate is indicated for fibrinogen replacement in patients who are bleeding, or at risk of bleeding, due to low fibrinogen levels e.g. patients with DIC, massive blood loss and congenital fibrinogen deficiencies.

When specific protein concentrates are not available, cryoprecipitate can be used to treat or prevent bleeding in patients with congenital or acquired deficiencies of Factor VIII (Haemophilia A) or von Willebrand disease (VWD).

Cryoprecipitate can be used for congenital deficiency of Factor XIII.

#### 5.3.2 Storage conditions

Storage time / temperature: 12 months at –25° C or lower; 24 months at –30° C or lower.

#### 5.3.3 Compatibility

Ideally cryoprecipitate and cryodepleted plasma should be transfused ABO compatible (See table 5.4). If the collected plasma is screened for antibodies then cross-match is not necessary. If the

plasma has not been screened, then cross-match against patient red cells is required.

#### 5.3.4 Side effects

*See chapter on Adverse events*

### 5.4 PLATELETS

Platelets are the standard product for the treatment of thrombocytopenia or congenital or acquired platelet function defect (thrombocytopathy) if transfusion is appropriate.

Platelets are derived from whole blood, one unit contains about 50 mL and  $50 \times 10^9$  platelets. A standard adult dose, to elevate the patient platelet count by  $20\text{--}40 \times 10^9/L$ , is 4–5 units.

Platelet transfusion should always be based on the clinical situation supported by information on the platelet count.

#### 5.4.1 Indications

See chapter 4 for indications and contra-indications

#### 5.4.2 Storage conditions

Storage time: 5–7 days, with continuous gentle agitation

Storage temperature: 20–24° C (platelet cabinet)

As soon as the product leaves the climatized cabinet it should be transfused within 4 hours.

#### 5.4.3 Compatibility

ABO blood groups are present on platelets. Provision of ABO compatible platelets is desirable however crossing groups is possible. Choice of ABO group is the same as choice of erythrocytes (table 5.1). If the collected plasma is screened for antibodies then cross-match is not necessary. If the plasma has not been screened, then cross-match against patient red cells is required.

Erythrocytes may be present in a platelets product. Therefore transfusion of platelets from a RhD positive donor to a RhD negative patient may cause antibody formation against RhD antigen. If the prevention of anti-D antibodies is indicated (females of child bearing potential) at least 375 IU anti-D immunoglobulin should be administered intramuscular (or subcutaneous in case of thrombocytopenia).

#### 5.4.4 Evaluation

The most important indicator of effectiveness is control of bleeding. A platelet count within 30min

– 4 hours following a platelet transfusion is a good guide to improvement of platelet count.

If there is concern of poor response on clinical grounds, a corrected count increment (CCI) can be calculated and may provide additional information to the post-platelet transfusion count. The CCI gives some guidance around the possible cause of poor platelet transfusion response.

CCI calculation: Determine the platelet count in the peripheral blood before, 1 hour after and/or 16–24 hours after transfusion (1 hour/16–24 hours post counts).

$$\text{CCI} = \frac{\text{post transfusion - pretransfusion platelet count (x10}^{11}\text{)}}{\text{number of platelets transfused (x10}^{11}\text{)}} \times \text{body surface (m}^2\text{)}$$

An insufficient 1-hour post count (CCI < 8) indicates an allo-immunization or drug depending antibodies, but is also seen in sepsis, severe GvHD, use of amfotericin-B, venous occlusive disease, splenomegaly and overt bleedings. A sufficient 1-hour post count, but a poor 16-hours post count (CCI < 4.5) generally excludes alloimmunisation as the cause of low response. Other causes such as infection, disseminated intravascular coagulation, and GvHD should be considered.

### 5.4.5 Patients refractory to platelet transfusion

Some patients develop refractoriness to platelet transfusions due to alloimmunisation to HLA or HPA antigens. This is indicated by poor clinical response and rapid clearing of transfused platelets according to post-transfusion platelet count or CCI.

HLA-compatible platelets should be considered if a platelet transfusion of ABO compatible random donors at least twice resulted in an insufficient CCI-value, HLA antibodies have been demonstrated and clinical factors associated with increased platelet consumption are excluded. If not all above mentioned requirements are fulfilled, a test transfusion may be considered.

Timely communication between the clinician, the head of the blood transfusion laboratory in the hospital (hospital blood bank) and the responsible physician (clinical consulting service) of the blood establishment, should take place because of the logistics of HLA compatible platelets, donor selection and mobilization, and the necessary tests for infectious disease markers.

HLA antibody testing and provision of HLA

compatible platelets are not yet available in Cambodia.

### 5.4.6 Side Effects

See chapter on Adverse Events

### 5.4.7 Characteristics of Platelet product

#### 5.4.7.1 Platelets, single unit

From one unit of whole blood (PRP) the platelets are isolated and re-suspended in plasma or platelet additive solution.

	Target value
Volume	50-70 mL
Platelets	mean > 55 x 10 <sup>9</sup>
Leukocytes	< 50 x 10 <sup>6</sup>
Erythrocytes	< 5 x 10 <sup>9</sup>

#### Indication

Standard product for the treatment of thrombocytopenia and/or thrombocytopathy in children < 10 kg body weight.

#### 5.4.7.2 Platelets, pooled

Currently platelet concentrates are not yet pooled, but are to be developed soon from 4-6 ABO identical whole blood units (PRP) the platelets are isolated and pooled in plasma or platelet additive solution.

	Target value
Volume	230 mL (180–250 mL)
Platelets	300 x 10 <sup>9</sup> (max. conc. 1.6 x 10 <sup>9</sup> / mL)
Leukocytes	< 0.1 x 10 <sup>6</sup>
Erythrocytes	< 5 x 10 <sup>9</sup>

#### Indication

Standard for adults (5 units) for the treatment of thrombocytopenia / thrombocytopathy.

For transfusion to children less (2–4) donor units are pooled.

## 5.5 MODIFICATIONS

The following modifications are not yet available in Cambodia.

### 5.5.1 Washed erythrocytes

Erythrocytes are washed in saline three times and resuspended in a red cell additive solution. This process removes many proteins from the erythrocyte component.

Washed erythrocytes can be given to patients with IgA deficiency who have anti-IgA antibodies and patients with recurrent and severe allergic reactions.

### 5.5.2 CMV seronegative

Blood donations in Cambodia are not currently screened for CMV. When CMV testing is available, the provision of CMV seronegative components may be an appropriate option in the following clinical indications :

- Intra-uterine transfusions and neonates.
- All pregnant women regardless of CMV status having antenatal transfusion with ongoing pregnancy.
- CMV seronegative recipients of allogeneic or autologous stem cell, bone marrow or solid organ transplants.
- CMV seronegative recipients of highly immunosuppressive chemotherapy.

There is small risk of new CMV disease in immunosuppressed CMV seropositive patients who receive CMV seropositive blood components.

Leucodepletion within 24 hours of blood collection

is regarded by some international blood services to be equivalent to CMV seronegative components.

### 5.5.3 Irradiation of blood components

Irradiation of blood components removes lymphocytes within the blood component. This reduces the risk of transfusion associated graft-versus-host disease (TA-GVHD).

The following groups of patients should get irradiated components:

- recipients of intrauterine transfusion,
- neonates who have previously received intrauterine transfusions,
- patients with congenital immune deficiencies or Hodgkin lymphoma,
- patients receiving nucleoside analogues or alemtuzumab,
- recipients of stem cell or bone marrow transplants,
- recipients of directed donations from family members, and
- recipients of HLA-compatible single donor platelets and granulocyte transfusions.





## Chapter 6

# BLOOD REQUEST & SAMPLE INFORMATION

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### PRACTICE POINTS

- All requests need to have full patient identification, date, reason for transfusion, number of units of each component required and signature of prescribing physician.
- All blood samples for pre-transfusion testing must be accompanied by a request form specifying patient details, test required, blood component required, reason for transfusion and location of patient.
- Autologous blood has limited use when donor blood is available.
- Directed donations should be discouraged. Voluntary donation is safer, cost effective and more practical.



## Chapter 6

# BLOOD REQUEST & SAMPLE INFORMATION

### 6.1 REQUEST FOR BLOOD PRODUCTS – IN THE HOSPITAL

The request for blood products should be in writing at the hospital blood bank or transfusion laboratory using a special request form. The following data should be on this form:

- Patient identification (full name, age or birth date and hospital identification number).
- Diagnosis and indication for transfusion.
- Requested product(s) and number of units.
- Date and time of request and desired delivery.
- Name, signature and phone/pager number of the prescribing physician.

If known the following information must be mentioned:

- ABO blood group and RhD.
- Did the patient receive transfusion earlier? If YES when was the last?
- Has the patient been pregnant?
- Are previous transfusion reactions known?
- Have red cell antibodies ever been detected?

### 6.2 REQUEST OF BLOOD PRODUCTS – AT THE BLOOD ESTABLISHMENT

The hospital blood bank or transfusion laboratory orders all needed blood products from the regional or national blood establishment.

#### 6.2.1 Ordering and delivery of blood products

Any order from hospital blood bank or transfusion laboratory to the regional or national blood establishment by phone must always be confirmed by a special form that is faxed to the blood establishment. Electronic ordering is also possible. Consultation about the blood transfusion policy should always be possible with the Clinical Consulting Service calling directly or indirectly via the issuing department.

Ordering is based on the decision to transfuse and comprises several steps:

- Completion of the request form.

- Collection and labelling of the samples with patient identification.
- Documentation in the patient file.
- Transportation to the laboratory.

The hospital blood bank should be supplied with a stock of regular blood components, sufficient to cover a week's consumption including emergencies.

Stock control is a responsibility of the hospital blood bank.

The blood establishment delivers the products and confirms the agreement (written) with the hospital blood bank or transfusion laboratory.

#### 6.2.2 Emergency requests

In unforeseen (emergency) cases blood products may be delivered outside the regular hours. The ordering procedure does not deviate from the normal procedure except that there is usually contact with the Clinical Consulting Services. Therefore the blood establishment is contactable 24 hours per day.

In case the public telephone is not working, and if applicable, the national emergency telephone network to which all hospitals and blood establishments are connected may be used.

#### 6.2.3 Directed blood products

Directed donations are not recommended as irradiation of blood products is not currently available in Cambodia.

Directed donations increase the risk of transfusion associated Graft versus Host Disease (GVHD). The recipient's immune system is unable to recognise the transfused homozygous HLA lymphocytes as foreign, whereas the transfused lymphocytes recognise the host cells as foreign and mount an immunological attack.

Transfusion associated Graft Versus Host Disease leads to profound marrow aplasia with a mortality rate > 90%. Survival is rare with death typically occurring within 1–3 weeks of first symptoms.

NB: In Cambodia relatives are recruited to donate

instantaneously on some occasions. This type of blood donation is not in compliance with WHO and IRC recommendations and increases the risk of transfusion transmissible infection and transfusion-associated Graft versus Host Disease.

#### 6.2.4 Autologous blood donation

Autologous blood donated preoperatively increases the risk of receiving any transfusion. Preoperative autologous blood should only be used in exceptional circumstances, such as a patient with a rare blood group or multiple red cell antibodies whose transfusion requirements cannot be met with allogeneic blood.

Preoperative autologous blood collection is only recommended where there is a reasonable expectation that blood will be required for the condition or procedure. Checking the local Maximum Blood Order Schedule (MBOS) for estimated blood usage requirements during surgery will assist in decision making.

The indications for transfusion of autologous blood should be the same as for allogeneic blood.

Patient suitability for autologous collections is based on the ability to tolerate several venesections taken over a short period of time, age, adequate venous access, and reliable dates for elective surgery.

Autologous blood collections are subject to the same testing criteria as allogeneic collections within the Blood Service. Autologous blood should be tested for hepatitis B, hepatitis C, HIV 1/2 and syphilis

Should a test on a collection fail initial screening, the patient and referring doctor will be notified and further collections suspended pending the results of further testing. Collections confirmed as positive for a transfusion-transmissible infection are discarded and no further collections undertaken.

In order to protect the safety of the allogeneic system, autologous blood which is not transfused to the patient cannot be used for any other patient.

Autologous blood collection is subject to the same collection, storage and processing requirements as allogeneic blood collection.

### 6.3 TAKING BLOOD SAMPLES FOR COMPATIBILITY TESTING

Taking blood samples for compatibility testing is one of the critical elements of the clinical transfusion chain. One of the most frequent errors is 'wrong blood in tube', where erroneously two patients

have been mixed up during the sample collection procedure – a human error with sometimes dramatic consequences.

#### 6.3.1 The sample collection procedure

1. Only collect samples from one patient at a time.
  2. Complete collection and labelling before performing any other task.
  3. If the patient is conscious at the time of taking the sample, ask him or her to identify themselves by given name, family name, age/ date of birth and any other appropriate information.
  4. Ask the patient to spell his/her given and family name if able.
  5. Check the patient's name against:
    - patient's identity wristband or label,
    - patient's medical notes, and
    - completed blood request form.
  6. If the patient is unconscious, ask a relative or a second member of staff to verify the patient's identity.
  7. Take the blood sample into the type of sample tube required by the blood bank. For adults, this is usually 4 mL, with no anticoagulant. Sample volume and anticoagulant may vary according to local protocols. Paediatric samples are often 1 mL or less.
- Label the sample tube clearly and accurately with the following information at the patient's bedside at the time the blood sample is being taken:
- patient's given name and family name,
  - patient's age and or date of birth,
  - patient's hospital identification number,
  - patient's ward,
  - date, and
  - identification of person taking the sample.
- Ensure that the patient's name is spelt correctly. Do not label the sample tube before obtaining the specimen because of the risk of putting the patient's blood into the wrong tube.
8. If the patient needs further red cell transfusion, send a new blood sample for compatibility testing.

This is particularly important if the patient has had a recent red cell transfusion that was completed more than 24 hours earlier. Antibodies to red cells may appear very rapidly as a result of the immunological

stimulus given by the transfused donor red cells.

A fresh blood sample is essential to ensure that the patient does not receive blood which is now incompatible.

When a patient has been transfused in the preceding 3 months, a sample can only be held for 72 hours while awaiting a decision to transfuse. Otherwise the sample can be held for up to 7 days (according to local protocols).

It is vital that all the details on the blood sample tube label match those on the blood request form and are uniquely identifiable with the patient.

Any failure to follow correct procedures can lead to incompatible transfusions.

Blood bank laboratory staff are acting correctly if they refuse to accept a request for compatibility testing when either the blood request form or the patient's blood sample are inadequately identified or the details do not match. If there is any discrepancy, they should request a new sample and request form.

#### **6.4 TRANSPORT OF BLOOD SAMPLES**

Blood samples for compatibility testing should be transported closed (capped) and in a rack, placed in a proper (clean and disinfected) container.

Do not transport samples in syringes with or without attached needles.





## Chapter 7

# PRE-TRANSFUSION LABORATORY TESTING

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### PRACTICE POINTS

- The laboratory will only accept appropriately labelled forms and samples.
- Blood Group: The lab will determine ABO group by forward and reverse group with comparison to historic records or repeat sample, and perform RhD group.
- Group and Screen: The lab will determine ABO and RhD group and test the patient serum or plasma against red cells of known phenotype (“screen”).
- Cross-match when screen cells are negative, is an “immediate spin” to confirm ABO compatibility.
- Cross-match when screen cells are positive by antibody determination, selection of suitable antigen negative erythrocytes and cross match by antiglobulin testing.
- Finding a compatible unit of blood in a patient with antibodies can result in delay to transfusion.
- Group O erythrocytes are the universal ABO donor cells.
- Group AB plasma is the universal plasma donor.



## Chapter 7

# PRE-TRANSFUSION LABORATORY TESTING

### 7.1 LABORATORY SAMPLE LOG AND RECORD KEEPING

The transfusion laboratory will only accept samples which have been appropriately labelled and have an accompanying request (order) form.

All transfusion request forms and samples must have at least two patient identifiers e.g. full name (first and surname) and age or date of birth. If the hospital operates a unique patient identification number system, this number must also be present. The ward or clinic, along with requesting doctor must be identified.

The staff member performing the patient identification and labelling of the sample must sign a declaration (as part of the request form) verifying the sample.

Failure to correctly complete the request forms and label the sample may lead to rejection of the sample.

All blood request forms and accompanying blood samples must be registered in the Laboratory information system or log book. Mandatory information to be recorded in the laboratory is:

- date and time of reception,
- patient first name and surname,
- patient date of birth or age,
- patient specific identification number if available,
- department and ward, and
- name of person who delivered the request.

Request form and blood sample have to be inspected for completeness and integrity before starting the work up.

To avoid any clerical or procedural error –

- If the blood request form is not complete, the ward needs to be contacted to supply the missing information.
- If the blood sample label is not complete and/or the blood sample does not meet the basic requirements of quality and integrity, the ward needs to be contacted to supply a new sample.

- Severe acute haemolytic transfusion reactions are invariably caused by transfusing red cells that are incompatible with the patient's ABO type. These reactions can be fatal. They most often result from:
  - Errors in labelling the patient's blood sample.
  - Errors when collecting the unit of blood for transfusion.
  - Failure to carry out the final identity check of the patient and the blood pack before infusing the unit of blood.

### 7.2 BACKGROUND INFORMATION ON BLOOD GROUPS AND COMPATIBILITY

It is essential that all blood is tested before transfusion in order to:

- ensure that transfused red cells are compatible with antibodies in the recipient's plasma, and
- avoid stimulating the production of new red cell antibodies in the recipient, particularly anti-D.

All pre-transfusion test procedures should provide the following information about both the units of blood and the patient:

- ABO group,
- RhD type, and
- presence of red cell antibodies that could cause haemolysis in the recipient.

#### 7.2.1 ABO blood group antigens and antibodies

The ABO blood groups are the most important in clinical transfusion practice. There are four red cell types: O, A, B and AB.

All healthy normal adults of group A, group B and group O have antibodies in their plasma against the red cell types (antigens) that they have not inherited:

- Group A individuals have antibody to group B.
- Group B individuals have antibody to group A.
- Group O individuals have antibody to group A and group B.
- Group AB individuals do not have antibody to group A or B.

These antibodies are usually of IgM and may also be IgG class. These are said to be “naturally occurring” as they appear within the first months of life and are present in all people life-long.

### 7.2.2 ABO incompatibility: haemolytic reactions

Anti-A or anti-B recipient antibodies are almost always capable of causing rapid destruction (haemolysis) of incompatible transfused red cells. Blood which has not been compatibility tested or blood given to the wrong patient may cause life-threatening haemolysis.

Typically, at least one third of unmatched transfusions will be ABO incompatible and may lead to severe or fatal reactions.

## 7.3 COMPATIBILITY AND BLOOD COMPONENTS

### 7.3.1 Red Cell Components

In red cell transfusion, there must be ABO and RhD compatibility between the donor’s red cells and the recipient’s plasma.

- Group O individuals can receive blood from group O donors only.
- Group A individuals can receive blood from group A and O donors.
- Group B individuals can receive blood from group B and O donors.
- Group AB individuals can receive blood from AB donors, and also from group A, B and O donors.

Note: Group O erythrocytes can be given to patients with any blood group.

#### 7.3.1.1 RhD red cell antigens and antibodies

Red cells express many antigens. In contrast to the ABO system, individuals rarely make antibodies against these other antigens. Exposure to red cell antigens can occur with previous transfusion or during pregnancy and childbirth. These events can immunise an individual, causing that person to make an antibody.

The most important is RhD. A woman with anti-D due to previous sensitisation and antibody product is at risk of:

- haemolytic disease of the newborn in a subsequent pregnancy, and
- rapid destruction of a later transfusion of RhD positive red cells.

Other important antigens include:

- Rh system: C, c, E, e,
- Kidd,
- Kell,
- Duffy, and
- Lewis.

These antibodies can also cause severe acute or delayed reactions to transfusion.

### 7.3.2 Plasma and Components Containing Plasma

In plasma transfusion, group AB plasma can be given to a patient of any ABO group because it contains neither anti-A nor anti-B antibody.

- Group AB plasma (no antibodies - can be given to any ABO group patients.
- Group A plasma (anti-B) - can be given to group O and A patients.
- Group B plasma (anti-A) - can be given to group O and B patients.
- Group O plasma (anti-A + anti-B) - can be given to group O patients only.

Safe blood transfusion depends on avoiding incompatibility between the donor red cells and antibodies in the patient plasma.

NOTE: In some disease states, anti-A and anti-B may be difficult to detect in laboratory tests.

## 7.4 RED CELL TESTS

Laboratory quality systems need to be in place to ensure accurate and reproducible test results. The following tests should be available in a transfusion laboratory however several are not available throughout Cambodia yet.

### 7.4.1 ABO and RhD group

Ideally all samples are tested for ABO group by forward and reverse group. RhD type should be determined on all samples. Comparison to historical records or testing a second sample improve accuracy of testing and reveal any labelling or clerical mistakes. Appropriate controls (positive and negative) are required for all pre-transfusion tests.

Forward group: Testing a dilute sample of patient red cells against standardised anti-A and anti-B (and anti-AB if desired) reagents.

Reverse group: Testing of patient plasma or serum against known A1 and B red cells. This is not required for babies < 4 months age.

RhD group must be determined by direct agglutination using an anti-D reagent.

## 7.4.2 Screen cells

Testing the patient plasma or serum against 2 or 3 cell suspensions of known antigen phenotype by Indirect Antiglobulin Test (IAT) will detect the presence of any red cell allo-antibodies in the patient. In general, particularly in previously transfused or pregnant patients, a screen cell result is valid for 72 hours before repeat testing is required.

## 7.4.3 Allo-antibody determination

A positive result with either screen cell indicates the presence of an antibody. Testing patient plasma or serum against a panel of known phenotype red cells may allow determination of antibody specificity. Additional testing, beyond the scope of this document, may be required.

## 7.4.4 Cross-match

When the screen cells are negative, group compatible erythrocytes are chosen. Patient plasma or serum is tested against a segment of red cells from the unit. Immediate spin will confirm ABO compatibility. Performing an IAT will confirm compatibility with other antigen/antibody systems.

## 7.5 PRE-TRANSFUSION TESTING

A doctor may request the following combinations of tests:

- Blood group.
- Group and Screen.
- Cross-match.

### 7.5.1 Blood Group

The laboratory will perform:

- ABO group – forward and reverse group with comparison to historic records or repeat sample.
- RhD group.

These tests will only determine ABO and RhD groups. The serum or plasma will be stored in the refrigerator or freezer for 7 days in case a screen or cross-match is required.

### 7.5.2 Group and Screen

The laboratory will perform:

- ABO group – forward and reverse group with comparison to historic records or repeat sample.
- RhD group.
- Screen cells – test the patient serum or plasma against red cells of known phenotype.

- Antibody determination if screen cells are positive.

If antibody cannot be determined, the patient serum or plasma will be cross-matched by IAT method to red cells from segments of several units of blood.

### 7.5.3 Cross-match

The laboratory will perform:

- ABO group – forward and reverse group with comparison to historic records or repeat sample.
- RhD group.
- Screen cells – test the patient serum or plasma against rec cells of known phenotype.
- If screen cells are negative, cross-match (patient serum or plasma against red cells from the segment of chosen ABO/RhD compatible unit) by immediate spin method shall confirm ABO compatibility. Cross-matched erythrocyte or whole blood component may be released.
- If screen cells are positive, antibody determination should occur. Antibody determination and selection of suitable units may take some time leading to potential delay in transfusion. In some cases surgery may need to be delayed.

If the antibody(ies) cannot be determined, the patient serum or plasma will be cross-matched by IAT method to red cells from segments of several units of blood until one unit is found to be compatible.

A patient with a warm auto-immune haemolytic anaemia will have a positive Direct Antiglobulin Test (DAT). These autoantibodies react at 37°C and may prevent a compatible unit being found. If the patient needs a transfusion, ABO/RhD compatible blood which has the lowest reactivity on cross-match testing should be chosen.

### 7.5.4 Cross-match in laboratories without Screen Cells

All transfusion laboratories must be able to perform ABO and RhD typing; and immediate spin cross-match. These tests will ensure ABO compatibility.

It is preferable that all transfusion laboratories be able to screen for antibodies by screen cells. If that is not possible, ABO/RhD compatible blood needs to be cross-matched using IAT methods with the patient's serum or plasma.

### 7.5.5 Urgent blood for transfusion

Pre-transfusion testing, selection of unit(s) and

cross-match may take an hour or more. Urgent clinical need for blood can be provided:

- Immediate requirement – provide O RhD negative erythrocytes or whole blood for women of child bearing potential. Males may receive O RhD positive erythrocytes or whole blood.
- Urgent (< 15 minutes) – ABO/RhD group should be determined and ABO compatible erythrocytes or whole blood can be supplied.
- Urgent (< 45 minutes) – ABO/RhD and screen cells should be known. Either ABO compatible or cross-matched erythrocytes or whole blood can be supplied.

#### 7.5.6 An IAT cross-match is always necessary in case of:

- Newborn (until the age of 4 months); always cross-match with serum of the mother.
- Patients with congenital or acquired abnormality in the erythropoiesis for which frequent erythrocytes have to be given [e.g. thalassaemia major and (congenital) hypoplastic anaemia].
- Patients in whom previously erythrocyte allo-antibodies have been detected.

### 7.6 SELECTION OF BLOOD COMPONENTS

All erythrocyte and whole blood transfusions require ABO/RhD typing, antibody screen and cross-match performed.

The specific unit of erythrocytes or whole blood should be selected according to age of the units. Generally, good inventory management is to use the oldest units first. The main exceptions to this rule are intra-uterine, neonatal and young children transfusions. These patients should receive youngest blood to reduce the risk of storage lesion

problems e.g. high potassium.

All plasma products and platelets should be released oldest units first.

A compatibility label should be attached firmly to each unit of blood by the laboratory, showing the information seen in Table 7.1 (below). The label should be attached in such a manner that the compatibility label and the blood product cannot become separated.

### 7.7 BLOOD COMPONENT STORAGE AND DELIVERY IN THE HOSPITAL

Refrigerators and freezers in which blood products are stored, should fulfill the requirements of Good Manufacturing Practice (GMP). This means that they must be provided with a temperature registration and an acoustic alarm. The course of the temperature must be documented. Refrigerators and freezers should be periodically validated (test on high and low alarm) and regularly defrosted and cleaned.

Transportation should always follow the principles of “cold chain” and “direct routing”. If blood needs to travel significant distance or may not be transfused within 4 hours, then the blood should be transported and stored short term in a validated insulated container called a “shipper”.

Tubes containing blood, reagents, food, etc shall not be stored in a blood storage cabinet. So called domestic refrigerators and freezers are not suitable to store blood products for transfusion.

#### 7.7.1 Erythrocytes and Whole Blood

To keep the quality and to prevent bacterial growth they shall be stored at a temperature of 2–6° C (see Table 7.2). Erythrocytes warmed up to > 10° C

Table 7.1 The information necessary for a compatibility label.

THIS BLOOD IS COMPATIBLE WITH:	UNIT NR:
Patient's name:	
Patient's hospital reference number or date of birth:	
Patient's ward:	
Patient's ABO and RhD group:	
Expiry date:	
Date of compatibility test:	
Blood group of blood unit:	

may not be restored and shall be transfused within 24 hours. Erythrocytes shall not be stored for more than half an hour outside the refrigerator for transport to the ward or performing a compatibility test etc.

### 7.7.2 Platelets

These shall be transfused as soon as possible after reception in the hospital blood bank or ultimately within 6 hours after delivery by the blood bank

They must be stored until transfusion at room temperature (20–24°C) (not in the refrigerator!) and must be gently rocked or agitated while stored. In a conditioned platelet storage cabinet platelets have a

shelf life of maximal 5–7 days (see Table 7.2).

### 7.7.3 Fresh Plasma and Cryoprecipitate

To preserve the activity of the coagulation factors, FFP must be stored at a temperature of –25°C (1 year) or < –30°C (2 years) (see Table 7.2).

Thawing may take place in a water bath at 30-37°C (refresh, clean/disinfect daily) packed in an extra plastic bag or by means of any other validated method (e.g. specially developed microwave).

After thawing the product (fresh plasma) must be transfused as soon as possible to preserve the coagulation factors.

Table 7.2 Storage conditions of blood products.

Product	Storage temperature	Shelf life
Erythrocytes (EC) in additive solution	2–6°C	35 days
Platelet concentrate (PC)	20–24°C	5–7 days
Frozen Fresh Plasma (FFP)	< 25°C	1 year



## Chapter 8

# ADMINISTRATION OF BLOOD COMPONENTS

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### PRACTICE POINTS

Give the right blood product to the right patient at the right time. Failure to correctly check the patient or the pack can be fatal.

At the bedside:

- correctly identify the patient and the blood components to be transfused, and
- observe the patient throughout the transfusion.

All transfusions should be completed within 4 hours.

A typical erythrocyte transfusion is 2 hours.

Medications and IV fluids (apart from normal saline) should not be given through the same cannula during a transfusion.

Routine administration of calcium after a transfusion is not required.



## Chapter 8

# ADMINISTRATION OF BLOOD COMPONENTS

### 8.1 TRANSPORTING THE BLOOD PRODUCT TO THE WARD

#### 8.1.1 Collecting the pack from the Transfusion Laboratory

Written documentation should be taken to collect the blood from transfusion service that includes patient's first name, surname, and hospital reference number /date of birth or age.

Collect the pack only when you are ready to start the transfusion.

If blood needs to travel significant distance or may not be transfused within 4 hours, then the blood should be transported and stored short term in a validated insulated container called a "shipper".

#### 8.1.2 Delivery to the ward

When the selected and compatibility tested unit(s) of blood arrive at the ward, Operating Room or Intensive Care Unit, the label and the bag must be inspected for:

- Integrity and any signs of deterioration, clots, leaks or discoloration.
- Cross-match information and compatibility label information.
- Patient identification details matches the patient for whom the blood was requested.

If any checks fail, contact or return the pack to the hospital transfusion service.

Blood transfusion should be started within 30 minutes of leaving the transfusion service unless it is stored in a validated shipper.

Return blood not being used promptly to the hospital transfusion laboratory.

### 8.2 PREPARATION FOR THE TRANSFUSION

#### 8.2.1 Equipment for blood administration

Cannulas for infusing blood products:

- Must be sterile and never be reused.
- Use flexible plastic cannulas, if possible, as they are safer and preserve the patient's veins.

- A doubling of the diameter of the cannula increases the flow rate of most fluids by a factor of 16.

Administration sets for whole blood, erythrocyte, plasma, platelets and cryoprecipitate transfusions must be:

- new and sterile for each patient with an integral 170–200 micron filter and a preferably a Y-set connection port,
- changed at least 12-hourly (or more frequently in very warm climates) during blood component transfusion or earlier if the filter is blocked or flow rate is slowed, and
- discarded after use according to standard hospital protective precaution policy.

A new IV line should ideally be used for each blood product. In cases where limited IV administration lines are available platelets and plasma should be administered before erythrocytes and whole blood (Yellow blood products before Red products). If platelets are administered after erythrocytes or whole blood they will become trapped by the debris accumulated in the blood filter.

Paediatric patients should have a special paediatric IV set if possible. These allow the blood or other infusion fluid to flow into a graduated container built into the infusion set. This permits the volume given, and the rate of infusion, to be controlled simply and accurately and reduces the risk of over transfusion.

#### 8.2.2 Pre-medication

Routine administration of pre-medication is not required.

- Recurrent febrile reactions: Consider pre-medication with paracetamol. Prestorage leucodepletion, within 24 hours of collection, is more effective in reducing recurrent febrile reactions.
- Recurrent allergic reactions: Consider pre-medication with an antihistamine and/or corticosteroid.

If a pre-medication is ordered ensure it is given with sufficient time to have effect.



### 8.2.3 Pre-transfusion checks

The blood should be checked at the patient's side by two staff members at the same time. The staff should be registered nurses or doctors.

See Annex 4 "Transfusion Administration Checklist" for additional information. The staff should check the details:

- Blood product type is the same as the prescription.
- Blood pack label, compatibility paperwork and the patient details are identical and correct.
- Ask the patient to say their name and confirm the patient identification band details are identical and correct.
- Expiry date of blood pack.
- Integrity and any signs of deterioration, clots, leaks or discoloration.

If any checks fail contact or return the pack to the hospital transfusion service.

## 8.3 COMMENCING THE TRANSFUSION

One of the staff members who checked the blood product must then spike or start the transfusion.

The patient should be in a setting where he or she can be directly observed and resuscitation equipment is available.

Ideally only transfuse during business hours when the largest number of senior staff are available. Transfusion after hours should take place if the patient is unstable and there is sufficient staff to monitor the patient. Transfuse one blood component at a time. Any reaction can then be attributed to a certain product.

Each unit of blood or blood component should be completed within four hours of the bag being punctured or less in high ambient temperatures. Typically a unit of erythrocytes is infused in 1–2 hours while platelets and plasma are infused over 20–30 minutes. In emergency situations all blood components can be administered faster. If a unit is not completed within four hours, discontinue its use and dispose of the remainder through the clinical waste system.

## 8.4 DURING THE TRANSFUSION

### 8.4.1 Observations

Monitoring and evaluating the transfused patient is an important part of the bedside transfusion process. This will allow any adverse event or

alteration in the patient's state to be detected as early as possible. This will ensure that potentially lifesaving action can be taken quickly. It will also determine if any action needs to be taken before the blood transfusion starts.

Severe reactions often present during the first 15–30 minutes of a transfusion. All patients, in particular unconscious patients, should be monitored during this period and for the first 15–30 minutes of each subsequent unit. For each unit of blood transfused, monitor the patient:

- before starting the transfusion,
- as soon as the transfusion is started,
- 15–30 minutes after starting the transfusion,
- at least every hour during transfusion, and
- on completion of the transfusion.

At each of these stages, record the following information on the patient's chart:

- patient's general appearance,
- vital signs: temperature, pulse, blood pressure, respiratory rate, and
- fluid balance:
  - oral and IV fluid intake, and
  - urinary output.

The patient should be educated to notify a nurse or doctor immediately if he or she becomes aware of any reactions such as shivering, flushing, pain or shortness of breath or begins to feel anxious.

### 8.4.2 Recording the transfusion

The following information should be recorded in the patient file:

- Whether the patient and/or relatives have been informed about the proposed transfusion treatment and consent should be documented.
- The reason for transfusion.
- Signature of the prescribing clinician.
- Pre-transfusion checks:
  - patient's identity,
  - blood pack,
  - compatibility label, and
  - signatures of the staff performing the pre-transfusion identity check.
- The transfusion:
  - type and volume of each product transfused,
  - unique donation number of each unit transfused,
  - blood group of each unit transfused,

- time at which the transfusion of each unit commenced,
- signature of the person administering the blood component, and
- monitoring of the patient before, during and after the transfusion.
- date and time the transfusion is completed,
- volume and type of all products transfused,
- unique donation numbers of all products transfused, and
- any adverse effects.

### 8.4.3 Medication during a transfusion

Do not add any medicines or any infusion solutions other than 0.9% sodium chloride to any blood component.

Never add calcium or calcium containing fluids to a transfusion. Never add dextrose solutions as these may cause haemolysis.

If an intermittent medication has to be given either insert another IV cannula or:

1. stop the transfusion,
2. flush the IV line with 0.9% sodium chloride through the IV access port closest to the patient to clear the blood component from the line and cannula,
3. administer the medication as required,
4. flush the line with similar volume required to clear the line initially and then
5. recommence the transfusion and complete within required timeframe.

Use a separate IV line if an intravenous fluid other than 0.9% sodium chloride has to be given at the same time as blood components or in major blood loss to rapidly infuse replacement fluids (volume).

### 8.4.4 Medication after a transfusion

Routine use of IV or PO calcium after a transfusion is not required. Consider when the patient is symptomatic or a large volume has been transfused in a short time such as a massive transfusion.

- Whole Blood and erythrocyte concentrates are stored in solutions that contain approximately 1.2 g of citrate. A healthy liver can metabolise 3 g citrate every 5 minutes. Transfusion rates higher than 1 unit per 5 minutes or transfusion in patients with severe liver impairment may develop hypocalcaemia due to citrate toxicity.

### 8.4.5 Warming of blood

Keeping the patient warm is more important than warming the infused blood.

There is no evidence that warming blood is beneficial to the patient when the infusion is slow. A 70 kg patient with a temperature of 37° C will tolerate a 400 g blood pack at 15°C and the patient's temperature will readjust quickly.

At infusion rates greater than 100 mL/minute, cold blood may be a contributing factor in cardiac arrest for adults.

Warmed blood is most commonly required in:

- large volume rapid transfusions e.g. greater than 50 mL/kg/hour for adults,
- exchange transfusion in neonates, and
- patients with clinically significant cold agglutinins.

Blood should be warmed in a dedicated blood warmer. Blood warmers should have a visible thermometer and an audible warning alarm and should be properly maintained. Red cells must not be warmed above the set point temperature of the approved device, commonly 41°C. Older types of blood warmer may slow the infusion rate of fluids.

Dry heat blood warming equipment is preferable due to the risk of contamination from infected water bath warmers. If a water bath warmer is used it must be emptied and cleaned, as per hospital equipment cleaning policy, after use and stored dry.

Body heat can be used to warm a blood pack if required and a blood warmer is unavailable. The pack should be wrapped to avoid cross infection and the ports protected.

Blood should never be warmed in a bowl of hot water or on a radiator as this could lead to haemolysis of the red cells which could harm the patient and be life-threatening.

### 8.4.6 External Pressure Devices

These devices make it possible to administer whole blood or erythrocytes within a few minutes and should only be used in an emergency situation and with a large gauge venous access needle.

The external pressure device should:

- exert pressure evenly over the entire bag,
- have a gauge to measure the pressure,
- never exceed 300mm Hg of pressure, and
- be monitored at all times when in use.

### 8.4.7 Equipment used in transfusion

Any equipment used to administer blood products needs to:

- be validated by the manufacturer to not damage blood cells by the action of the equipment,
- have clear instructions for staff to use the equipment,
- be used as specified by the manufacturer, and
- have a regular maintenance program.

## 8.5 TIME LIMITS FOR TRANSFUSION OF BLOOD COMPONENTS

There is a risk of bacterial proliferation or loss of function in blood products once they have been removed from the correct storage conditions. This is particularly true in warm climates. All blood components must be infused within 4 hours of start of transfusion. See table 8.1.

Table 8.1 Time limits for infusion

	Start Infusion	Complete Infusion
Whole Blood Erythrocytes	Within 30 minutes of removing unit from refrigerator	Within 4 hours. Typically within 1–2 hours.
Platelets	Immediately	Within 4 hours. Typically within 20–30 minutes.
FFP Cyroprecipitate	Immediately after thawing	Within 4 hours. Typically within 20–30 minutes.

Table 8.2 Administration set as 15 drops per mL administration times

Volume	1 hour	2 hours	3 hours	4 hours
400 mL	100 drops per minute	50 drops per minute	35 drops per minute	25 drops per minute

Table 8.3 Administration set as 20 drops per mL administration times

Volume	1 hour	2 hours	3 hours	4 hours
400 mL	135 drops per minute	66 drops per minute	45 drops per minute	33 drops per minute

### 8.5.1 Calculation Guide for Administration of Whole Blood in drops per minute

Whole blood contains 350 mL blood plus 49 mL of additive solution. Administration sets can either provide 15 or 20 drops per mL blood. The following tables (8.2 and 8.3) provide the number of drops per minute to complete a 400 mL transfusion in a given time.

## 8.6 AFTER THE TRANSFUSION

To ensure the patient receives all of the blood product administer IV 0.9% Sodium Chloride, in a volume approximating the “line prime” volume, in order to clear the blood component from the line. This additional fluid should only be given if the patient is at low risk of fluid overload.





## Chapter 9

# MASSIVE TRANSFUSION

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### PRACTICE POINTS

- Massive transfusion is required when there is either an expected blood loss of:
  - > one blood volume (70 mL/kg) in 24 hours, or
  - > half a blood volume in 4 hours.
- Major blood loss should be managed by an experienced team using a protocol.
- Massive transfusion protocols can be directed by laboratory results or formula based.
- For every 2-4 units of erythrocytes, one unit of FFP should be given. Cryoprecipitate and platelets should be considered after 4-8 units of erythrocytes.
- Tranexamic acid, 1g over 10 minutes followed by 1g over 8 hours IV, should be given within 3 hours of trauma leading to major blood loss.



## Chapter 9

# MASSIVE TRANSFUSION

### 9.1 CRITICAL BLEEDING AND MASSIVE TRANSFUSION

Critical bleeding is bleeding requiring massive transfusion. This is defined as:

- Loss of one blood volume (adult: 70 mL/kg) in 24 hours,
- Need for 10 units of red cells in 24 hours,
- Need to replace half blood volume in 4 hours, or
- Blood loss of > 150 mL per minute.

All definitions are relevant. The most useful definitions in practice are a loss of one blood volume in 24 hours or half a blood volume in 4 hours.

### 9.2 PHYSIOLOGICAL EFFECTS OF MAJOR BLOOD LOSS

Risk factors for mortality with major blood loss and massive transfusion are:

- hypothermia,
- thrombocytopenia,
- increased INR and aPTT,
- low fibrinogen, and
- low pH and low bicarbonate levels.

The aetiology of these changes are:

- hypovolaemia,
- anaemia and hypoxia (organ failure),
- consumption of coagulation and other plasma proteins,
- consumption of platelets, and
- metabolic derangements, hypothermia and acidosis.

### 9.3 MASSIVE TRANSFUSION PROTOCOL

Massive transfusion cannot occur in isolation. Surgery and interventional radiology play large roles in stopping bleeding. Tranexamic acid has a significant role in the reduction of erythrocyte and platelet needs in massive transfusion (CRASH2 study).

A standard adult dose of tranexamic acid for trauma

is 1g IV within 3 hours of trauma followed by 1g IV over 8 hours.

Massive transfusion should follow a protocol endorsed by the local transfusion committee or clinical practice and quality committee. An overview of Massive Transfusion Protocol (MTP) is presented:

#### Step 1 Recognition and Activation

The senior clinician recognizes the patient meets criteria for massive transfusion:

- either expected blood loss of > one blood volume (70 mL/kg) in 24 hours, or
- expected blood loss of > half a blood volume in 4 hours.

This may occur in:

- severe trauma e.g. thoracic, pelvic, abdominal, and
- major obstetric, gastrointestinal or surgical bleeding.

The senior clinician activates the massive transfusion protocol.

#### Step 2 Patient Management

Bleeding control:

- Control bleeding with compression, tourniquet and specific surgical or radiological intervention.
- Consider cell salvage.
- Resuscitation.
- Use crystalloid (e.g. 0.9% sodium chloride) first at approximately 1.5-2 times estimated blood loss, and consider the addition of colloid later.
- Avoid hypothermia – use active warming techniques.
- Permit mild hypotension (systolic 80–100mm Hg).
- Keep the patient warm (aim for > 35°C).

Medication:

- If trauma is < 3 hours ago, give 1g Tranexamic Acid over 10 minutes followed by 1 g over 8 hours.
- Recombinant FVIIa should not be routinely used.

- DDAVP has no role.

Laboratory testing:

- Obtain baseline full blood count (Hb and platelet count); coagulation (aPTT, INR, Fibrinogen), biochemistry (especially calcium) and arterial blood gases (pH, base excess, lactate).
- While there is active large volume blood loss, repeat blood tests every 30–60 minutes may be required.

Blood Products:

- Based on the availability of testing, the patient should either receive blood components:
  - based on results, or
  - according to a formula.
- Results based blood products:

Test result	Blood component
Hb < 70 g/dL	1–2 units erythrocytes
Platelets < 50x10 <sup>9</sup> /L	4–5 units of WB derived platelets
INR > 1.5	FFP 15 mL/kg
Fibrinogen < 1.0 g/L	3–4 g fibrinogen which equates to 8–10 units cryoprecipitate

- Based on a formula:
  - Start with a pre-defined Massive Transfusion Pack (MTP) which consists of:
    - 4 units erythrocytes, and
    - 2 units FFP.
  - If bleeding is not controlled, give a second MTP (4 units erythrocytes and 2 units FFP) and add:
    - 5 units platelets (1 standard adult dose)

- 8–10 units cryoprecipitate (1 standard adult dose)

- Continue with additional MTP, with cryoprecipitate and platelets with each second MTP, until bleeding is controlled.

### Step 3 Stand-down

It is important to inform the laboratory and transfusion service that the massive transfusion protocol is finished.

The Hospital Transfusion Committee or Clinical Governance Committee should review all cases of massive transfusion.

## 9.4 NOTES ON AVAILABILITY OF BLOOD COMPONENTS

In most regions of Cambodia, FFP, Platelets and cryoprecipitate is not available.

In some regions erythrocytes are not available and only whole blood is available.

Whole Blood can be used as a substitute for erythrocytes however the volume is about double that of an erythrocyte.

Whole Blood, once > 24 hours old and refrigerated, does NOT contain any viable platelets and the labile coagulation factors are severely reduced. Stored whole blood is not a substitute for FFP or platelets or cryoprecipitate.

Unrefrigerated whole blood < 24 hours old does contain adequate platelets and coagulation factors. Unrefrigerated whole blood should only be used if full transmissible disease screening can occur. Some regions internationally use “emergency donor panels (EDP)”, however blood derived from emergency donors carries an increased risk. The hospital, government regulators and clinicians need to approve the use of an EDP in advance and the patient (or legal delegate) is required to consent.







## Chapter 10

# PAEDIATRICS & NEONATOLOGY

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### PRACTICE POINTS

- The most common causes of anaemia in children are nutritional and infectious. Treatment of the underlying cause is the primary consideration.
- If hypoxia occurs despite the normal compensatory responses to anaemia, immediate supportive care is required. If the child continues to be clinically unstable, a transfusion may be indicated.
- The decision to transfuse should not be based on the haemoglobin level alone, but also on a careful assessment of the child's clinical condition.
- Hb < 4g/dL is an indication for transfusion.
- Hb 4-6g/dL is an indication for transfusion if the patient is hypoxic, acidotic, impaired consciousness or has high parasitaemia.
- In some conditions, such as haemoglobinopathies (sickle cell disease and thalassaemia) repeated red cell transfusions may be indicated.

Refer to the national paediatric guidelines.



# Chapter 10

## PAEDIATRICS & NEONATOLOGY

### 10.1 INTRODUCTION

Neonates and children are not just small adults, they are different in their metabolic and physiologic behaviour. Therefore pathophysiology in paediatrics and neonatology is different from what can be observed in adolescents and adults.

A number of key principles that apply:

- The prevention and early treatment of anaemia is a vital part of the strategy to reduce the need for paediatric transfusion.
- If hypoxia occurs despite the normal compensatory responses to anaemia, immediate supportive care is required. If the child continues to be clinically unstable, a transfusion may be indicated.
- The decision to transfuse should not be based on the haemoglobin level alone, but also on a careful assessment of the child's clinical condition.
- In patients at risk of circulatory overload, transfusion of red cells is preferable to whole blood. Paediatric blood packs (70–100 mL) should be used, if available, to decrease exposure to multiple donors.
- In some conditions, such as haemoglobinopathies (sickle cell disease and thalassaemia) repeated red cell transfusions may be indicated.
- There are very few indications for transfusing fresh frozen plasma.
- Inappropriate and ineffective use can pose both transmissible (e.g. HIV and hepatitis) and non-transmissible risk and should be avoided.

### 10.2 CAUSES OF PAEDIATRIC ANAEMIA

#### 10.2.1 Decreased production of normal red blood cells

- Nutritional deficiencies due to insufficient intake or absorption (iron, B12, folate).
- HIV infection.
- Chronic disease or inflammation.
- Lead poisoning.

- Chronic renal disease.
- Neoplastic diseases (leukaemia, neoplasms invading bone marrow).
- Congenital or acquired aplasia or hypoplasia.

#### 10.2.2 Increased destruction of red blood cells

- Malaria.
- Haemoglobinopathies (sickle cell disease, thalassaemia).
- G6PD deficiency.
- RhD or ABO incompatibility in the newborn.
- Autoimmune disorders.
- Spherocytosis.

#### 10.2.3 Loss of red blood cells

- Hookworm infection.
- Acute trauma.
- Surgery.
- Repeated diagnostic blood sampling.

### 10.3 INDICATIONS FOR TRANSFUSION

- Haemoglobin concentration of  $< 4$  g/dL, irrespective of the clinical condition of the patient, is an absolute indication for erythrocyte transfusion.
- Haemoglobin concentration of 4–6 g/dL, is an absolute indication for erythrocyte transfusion if any the following clinical features are present:
  - Clinical features of hypoxia:
  - Acidosis (usually causes dyspnoea).
  - Impaired consciousness.
  - Hyperparasitaemia ( $> 20\%$ ).
- Haemoglobin  $> 6$  g/dL is the same as adult indications.

### 10.4 SPECIAL EQUIPMENT FOR PAEDIATRIC AND NEONATAL TRANSFUSION

Never re-use an adult unit of blood for a second paediatric patient because of the risk of bacteria entering the pack during the first transfusion and proliferating while the blood is out of the refrigerator.

Where possible, use paediatric blood packs which

have been produced in a closed sterile system. These allow repeat transfusions to the same patient from a single donation unit.

Infants and children require small volumes of fluid and can easily suffer circulatory overload if the infusion is not well controlled. If possible, use an infusion device that makes it easy to control the rate and volume of infusion.

## 10.5 TRANSFUSION PROCEDURE

If transfusion is needed, give sufficient blood to make the child clinically stable.

5 mL/kg erythrocytes or 10 mL/kg whole blood are usually sufficient to relieve acute shortage of oxygen-carrying capacity. This will increase haemoglobin concentration by approximately 2–3 g/dL unless there is continued bleeding or haemolysis.

An erythrocyte transfusion is preferable to whole blood for a patient at risk of circulatory overload, which may precipitate or worsen cardiac failure. 5 mL/kg of red cells gives the same oxygen-carrying capacity as 10 mL/kg of whole blood and contains less fluid volume to overload the circulation.

Where possible, use a paediatric blood pack and a device to control the rate and volume of transfusion and although rapid fluid infusion increases the risk of volume overload and cardiac failure, give the first 5 mL/kg to relieve the acute signs of tissue hypoxia. Subsequent transfusion may be given slower e.g. 5 mL/kg of red cells over 1–2 hours. Aim to give all transfusion over < 2 hours. Any transfusion needs to be completed in < 4 hours. The clinical state of the patient will determine the maximum tolerated rate.

A syringe driver can be used to administer a small volume to a neonate or infant. IV lines and syringes used for transfusing blood components should:

- incorporate an in-line filter [170-200 micron];
- be single use only and discarded appropriately;

- have Leur-lock connections;
- have a label attached showing date and time of preparation and expiry date and time; and
- identical donor and patient information as the original pack from which the component was drawn.

Give frusemide 1 mg/kg by mouth or 0.5 mg/kg by slow IV injection to a maximum dose of 20 mg if patient is likely to develop cardiac failure or pulmonary oedema. Do not inject it into the blood pack.

Monitor during transfusion for signs of an adverse event in the same manner as adult patients.

Re-evaluate the patient's clinical condition after transfusion. A repeat haemoglobin or haematocrit may also be beneficial. If the patient is still anaemic with clinical signs of hypoxia or a critically low haemoglobin level, give a second transfusion of 5–10 mL/kg of red cells or 10–20 mL/kg of whole blood. Continue treatment of anaemia to help haematological recovery.

## 10.6 NEONATAL TRANSFUSION

### 10.6.1 Selection of components

See table 10.1.

### 10.6.2 Specific clinical situations (neonatal)

#### 10.6.2.1 Exchange transfusion

The main indication for neonatal exchange transfusion is to prevent neurological complications (kernicterus) caused by a rapidly-rising unconjugated bilirubin concentration. This occurs because the immature liver cannot metabolise the breakdown products of haemoglobin. The underlying cause is usually haemolysis (red cell destruction) due to antibodies to the baby's red blood cells and is called Haemolytic Disease of the Newborn (HDN).

Table 10.1 Selection of components

Product	Indication	Special requirements
Whole blood	Exchange transfusions for HDN	Freshest blood available (less than 5 days after collection), free of relevant allo-antibodies
Erythrocytes	"Top up" transfusion to raise Hb in symptomatic chronic anaemia. This is most commonly due to frequent blood sampling in premature infants	Small dose unit (paediatric pack from a single donation) to minimise exposure to different donors

If exchange transfusion is needed:

- Use a group O blood unit that does not carry the antigen against which the maternal antibody is directed:
  - For HDN due to anti-D: use group O RhD negative.
  - For HDN due to anti-Rh c: use group O RhD positive that does not have the c antigen (e.g. R1R1, CDe/CDe).
- An exchange transfusion of about two times the neonate's blood volume (about 170 mL/kg) is most effective to reduce bilirubin and restore the haemoglobin level; this can usually be carried out with one unit of whole blood.
- A unit of whole donor blood will normally have a haematocrit of 37–45%, which is adequate for neonatal needs. There is no need to adjust the haematocrit of the unit, raising the unit Hct to 50–60% may risk polycythaemia.

#### 10.6.2.2 Sampling in critically ill neonates

Record the volume of each blood sample taken. If 10% of the blood volume is removed over 24–48 hours, check patient's Hb level as a transfusion may be indicated.

#### 10.6.2.3 Convalescent and low birth weight babies

- Measure the haemoglobin at weekly intervals. The haemoglobin level will drop 1 g/dL per week on average.
- Do not transfuse on the basis of the haemoglobin level alone. Haemoglobin levels of 7 g/dL or less require investigation, but transfusion may not be required.
- A reticulocyte count will assist in determining the need for transfusion.
- Iron, folate and vitamin E may minimise the need for transfusion.

- Consider transfusing an infant if anaemia is thought to be the cause of:
  - Poor weight gain.
  - Fatigue while feeding.
  - Tachypnoea and tachycardia.
  - Other signs of decompensation.

#### 10.6.3 Minimising the risks and increasing the effective use of neonatal transfusion

The following practical measures reduce the risks of neonatal transfusion and increase its effectiveness:

- For an infant who is likely to need several 'top-up' transfusions over a period of days or weeks, use red cells in additive solution prepared in paediatric packs from a single unit of blood.
- Reduce blood loss from diagnostic sampling:
  - avoid unnecessary repeat compatibility testing,
  - avoid non-essential laboratory tests, and
  - where possible, the laboratory should use micro-methods and should select suitable small sample tubes.
- Avoid transfusing blood donated by blood relatives as the risk of graft versus host disease is increased.

#### 10.6.4 Fresh frozen plasma

Fresh frozen plasma should only be used for specific clinical indications for which it is proved to be effective:

- The correction of clinically important bleeding tendencies due to deficiency of plasma clotting factors.
- For infusion or exchange transfusion treatment of the rare conditions of thrombotic thrombocytopenic purpura (TTP) or haemolytic uraemic syndrome (HUS).



## Chapter 11

# OBSTETRICS

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### PRACTICE POINTS

- Anaemia is common in pregnancy due to increased plasma volume, co-morbidities and nutrition.
- Prophylactic iron and folate during pregnancy is indicated.
- The decision to transfuse blood should not be based on haemoglobin levels alone, but also on the patient's clinical need.
- Obstetric bleeding may be unpredictable and massive. Every obstetric unit should have a current protocol for major obstetric haemorrhage.
- If disseminated intravascular coagulation is suspected, do not delay treatment while waiting for the results of coagulation tests.
- The administration of Anti-D immunoglobulin to all RhD negative mothers within 72 hours of delivery or any sensitising event during pregnancy (e.g. miscarriage, antenatal haemorrhage, invasive procedure) is the preferred approach to the prevention of Rh disease of the newborn.

Refer to the national obstetric guidelines.



# Chapter 11

## OBSTETRICS

### 11.1 INTRODUCTION

During pregnancy the physiology and metabolism of the female changes to accommodate the fetus and placenta. A number of key aspects are of importance:

- Anaemia in pregnancy is a haemoglobin concentration of less than 11 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.
  - 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 is suspected, do not delay treatment while waiting for the results of coagulation tests.
  - The administration of anti-RhD immunoglobulin to all RhD negative mothers within 72 hours of delivery or any sensitising event during pregnancy (e.g. miscarriage, antenatal haemorrhage, invasive procedure) is the preferred approach to the prevention of Rh disease of the newborn.
- Increase in red cell volume is modest, 0–25%, though more slowly than the increase in plasma volume.
  - Normal or elevated haemoglobin may signify pre-eclampsia in which plasma volume is reduced.
  - Increased iron requirement, particularly in last trimester.
  - Increases in platelet activation and levels of coagulation factors, particularly fibrinogen, Factor VIII and Factor IX.
  - Fibrinolytic system is suppressed.
  - Increased susceptibility to thromboembolism.

#### 11.2.1 Blood loss during delivery (normal)

- About 500 mL of blood during normal vaginal delivery.
- Over 500 mL during caesarean section.

This blood loss rarely necessitates transfusion provided that the maternal haemoglobin is above 10.0–11.0 g/dL before delivery. Further investigation is needed if haemoglobin concentration does not return to normal by 8 weeks postpartum

#### 11.2.2 Prevention of anaemia in pregnancy

The need for transfusion can often be avoided by the prevention of anaemia through:

- education about nutrition, food preparation and breastfeeding,
- adequate maternal and child health care,
- access to family planning information, education and services,
- clean water supplies, and
- adequate facilities for the disposal of human waste.

Prophylactic administration of iron and folic acid is strongly indicated during pregnancy in countries where iron and folate deficiency is common.

### 11.2 HAEMATOLOGICAL CHANGES IN PREGNANCY

The following haematological changes occur during pregnancy:

- 40–50% increase in plasma volume, reaching its maximum by week 32 of gestation, with similar increase in cardiac output.

Examples of the dose regime are:

- Optimum daily doses to prevent nutritional anaemia in pregnant women:
  - 120 mg elemental iron, and
  - 1 mg folate.
- When anaemia is already present, especially if severe, higher daily therapeutic doses may be more effective:
  - 180 mg elemental iron, and
  - 2 mg folate.

### 11.3 TRANSFUSION

The decision to transfuse blood should not be based on haemoglobin levels alone, but also on the patient's clinical need. The following factors must be taken into account:

- stage of pregnancy,
- evidence of cardiac failure,
- presence of infection: e.g. pneumonia, malaria,
- obstetric history,
- anticipated delivery, vaginal or caesarean section, and
- haemoglobin level.

#### 11.3.1 Major obstetric haemorrhage

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

Serious haemorrhage may occur at any time throughout pregnancy and the puerperium.

Major obstetric haemorrhage can be defined as any blood loss occurring in the peripartum period, revealed or concealed, that is likely to endanger life.

At term, blood flow to the placenta is approximately 700 mL per minute.

The patient's entire blood volume can be lost in 5–10 minutes. Unless the myometrium contracts on the placental site appropriately, rapid blood loss will continue, even after the third stage of labour is complete.

- Obstetric bleeding may be unpredictable and massive.
- Major obstetric haemorrhage may result in clear signs of hypovolaemic shock but because of the physiological changes induced by pregnancy, there may be few signs of hypovolaemia, despite considerable blood loss.

Signs of hypovolaemia include:

- Tachypnoea,
- thirst,
- Hypotension,
- Tachycardia,
- increased capillary refill time,
- reduced urine output, and
- decreased conscious level.

It is therefore essential to monitor and investigate a patient with an obstetric haemorrhage, even in the absence of signs of hypovolaemic shock. Be ready and prepared to resuscitate, if necessary.

### 11.4 RhD NEGATIVE PREGNANCY

A person has the RhD negative phenotype when the RHD gene is absent. Homozygosity or heterozygosity for RHD will lead to a RhD positive phenotype. The majority of the Cambodian population is RhD positive.

An RhD negative pregnant woman is at risk of developing anti-D if her fetus is RhD positive. Generally the first pregnancy sensitises the woman and subsequent exposure will cause anti-D production. Circulating anti-D can cross the placenta and cause significant in-utero anaemia and hyperbilirubinaemia called Haemolytic Disease of the Newborn (HDN).

HDN can be prevented by the prevention of anti-D antibody formation in women with child-bearing potential (pre-adolescent or menstruating females):

- Only transfuse RhD negative erythrocytes to RhD negative females of child-bearing potential.
- If a female of child-bearing potential is exposed to RhD (e.g. RhD positive platelet transfusion), offer adequate Anti-D within 72 hours to haemolyse any transfused red cells.
- Offer prophylactic Anti-D injections to all pregnant RhD negative women and Anti-D for any pregnancy event which may be complicated by fetomaternal haemorrhage.

Note: Once a patient has developed anti-D, administration of prophylactic Anti-D is not effective.

Anti-D is an intramuscular preparation (IM) and is used for prophylaxis against sensitising events and for routine prophylaxis. Intravenous Anti-D is available and should be considered when larger doses are required.

### 11.4.1 Routine Anti-D prophylaxis

Prophylaxis is indicated for RhD negative women who have not already made anti-D. Either:

- at least 500 IU given IM at 28 and 34 weeks, or
- at least 1250 IU given IM at 28 weeks.

These doses should be given irrespective of previous doses of Anti-D.

### 11.4.2 Anti-D event prophylaxis

Prophylaxis is indicated for the following potentially sensitising events in RhD negative women who have not already made anti-D:

Before 12 weeks (First trimester):

- Uncomplicated spontaneous miscarriage without pain has a low risk of sensitising the woman and Anti-D is not required.
- Any other event involving pain, bleeding, instrumentation (including amniocentesis), ectopic pregnancy or termination of pregnancy requires a dose of at least 250 IU given IM.

After 12 weeks:

- For any event which may involve fetomaternal haemorrhage, administer at least 500 IU Anti-D given IM.

Potentially sensitising events are:

- abdominal trauma,
- antepartum haemorrhage, both revealed and concealed,
- external cephalic version,
- miscarriage or termination of pregnancy,
- intrauterine death,
- ectopic pregnancy,
- intervention with a sampling device e.g. chorionic villus sampling, and
- delivery.

A standard dose of at least 500 IU given IM is required. If Kleihauer testing is available, estimate the size of the fetomaternal haemorrhage and the dose of Anti-D can be increased. Approximately 100–125 IU Anti-D is required for every 1 mL fetal red cells (0.5 mL fetal whole blood) involved in the fetomaternal haemorrhage.

All Anti-D is administered IM. Some preparations can be administered IV and this can be useful if very large doses are required.





## Chapter 12

# MALARIA & DENGUE

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### PRACTICE POINTS

- Malaria causes haemolysis which may be life-threatening, especially in young children and pregnant women.
- For adults, consider transfusion if haemoglobin < 7 g/dL.
- For children, always transfuse if haemoglobin < 4 g/dL.
- Consider transfusion if haemoglobin 4–6 g/dL and clinical features of hypoxia; acidosis; impaired consciousness or hyperparasitaemia (> 20%).
- Dengue Haemorrhagic Fever requires good medical supportive care. Clinical indications for red cell, platelet and plasma transfusion are the same as for other medical and surgical indications.



## Chapter 12

# MALARIA & DENGUE

Annual outbreaks of these mosquito borne diseases can affect both children and adults. Malaria may cause severe haemolysis. The Dengue virus can cause severe diffuse haemorrhage and anaemia as part of Dengue Haemorrhagic Fever. Prevention and early diagnosis may reduce the need for transfusion.

This chapter does not deal with all aspects of diagnosis and management of these infectious illnesses, rather the transfusion requirements as part of patient management.

### 12.1 MALARIA

The diagnosis and treatment of malaria and any associated complications are a matter of urgency as death can occur within 48 hours in non-immune individuals. Malaria presents as a non-specific acute febrile illness and cannot be reliably distinguished from other causes of fever on clinical grounds.

The differential diagnosis is therefore broad.

- The clinical manifestations may be modified by partial immunity acquired by previous infection or sub-curative doses of antimalarial drugs.
- Since fever is often irregular or intermittent, history of fever over the last 48 hours is important.
- Malaria in pregnancy is more severe and is dangerous for mother and fetus; partially immune pregnant women, especially prima gravidae, are also susceptible to severe anaemia due to malaria.
- Young children who have not yet developed some immunity to the parasite are at particular risk.

#### 12.1.1 Management

Promptly treat infection and any associated complications, following local treatment protocols. Urgent treatment on basis of clinical assessment may be required if delays in laboratory investigations are likely. Correct dehydration and hypoglycaemia and avoid precipitating pulmonary oedema with fluid overload.

Specific treatments for serious complications:

- Transfusion to correct life-threatening anaemia.
- Haemofiltration or dialysis for renal failure.
- Anticonvulsants for seizures.

In endemic malarial areas, there is a high risk of transmitting malaria by transfusion. Give the transfused patient malaria chemoprophylaxis.

#### 12.1.2 Transfusion

Erythrocyte transfusion is preferable to whole blood in order to maximise oxygen-carrying capacity without extra volume.

Adults, including pregnant women:

- Consider transfusion if haemoglobin < 7 g/dL.

Children:

- Always transfuse if haemoglobin < 4 g/dL.
- Transfuse if haemoglobin 4–6 g/dL and clinical features of hypoxia; acidosis; impaired consciousness or hyperparasitaemia (> 20%).

### 12.2 DENGUE FEVER AND DENGUE HAEMORRHAGIC FEVER

Dengue is transmitted by a mosquito (*Aedes aegypti*) and caused by any of the Dengue flaviviruses (DEN-1, DEN-2, DEN-3 and DEN-4). The Dengue virus can cause Dengue Fever (DF), or the more severe disease, Dengue Haemorrhagic Fever (DHF).

DHF clinical manifestations are:

- sudden onset of fever, severe headache, myalgias and arthralgias, leukopenia, thrombocytopenia and mucocutaneous hemorrhagic manifestations,
- complicated by shock and life-threatening haemorrhage.

#### 12.2.1 Incidence

- Variable, depending on epidemic activity.
- Globally, there are an estimated 50 to 100 million cases of DF and several hundred thousand cases of DHF per year.
- Average case fatality rate of DHF is about 5%.
- With good medical management, mortality due

to DHF can be less than 1%.

### 12.2.2 Risk groups

- Residents of or visitors to tropical urban areas.
- Increased severe and fatal disease in children under 15 years.
- No cross-immunity from each serotype, therefore a person can theoretically experience four Dengue infections.

### 12.2.3 Prevention

The emphasis for Dengue prevention is on sustainable, community-based, integrated mosquito control with limited reliance on insecticides (chemical larvicides and adulticides).

Preventing epidemic disease:

- requires a coordinated community effort to increase awareness about dengue/DHF,
- how to recognise it, and
- how to control the mosquito that transmits it.

Residents are responsible for keeping their yards and patios free of sites where mosquitoes can be

produced.

### 12.2.4 Treatment

There is no specific medication for treatment of a Dengue infection and the focus is on symptomatic relief and maintenance of oral fluids. Analgesia (pain control) is usually needed and acetaminophen (paracetamol) is preferable to aspirin or non-steroidal anti-inflammatories due to their anti-platelet effects. Hospitalisation for DHF is often required.

### 12.2.5 Transfusion

When the haemorrhagic fever becomes life threatening due to blood loss and thrombocytopenia, transfusion with red cells and/or platelet concentrate is indicated. Haemoglobin and platelet triggers (chapter 5) are appropriate. Fresh frozen plasma may have a role in haemostasis and its use should be guided by coagulation testing.





## Chapter 13

# ADVERSE TRANSFUSION EVENTS

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### PRACTICE POINTS

- The most common severe reaction is ABO incompatibility caused by mis-identification or mis-labelling of the blood component, patient or pre-transfusion sample.
- Patients receiving a transfusion should be observed prior to, within 15 minutes of commencing, at the conclusion and within 1 hour after a transfusion.
- If in doubt, stop the transfusion and give IV fluids.
- Always perform blood culture and culture of the residual blood component after a high fever.



# Chapter 13

## ADVERSE TRANSFUSION EVENTS

### 13.1 CLINICAL PRESENTATION AND DIAGNOSIS

Adverse transfusion reactions that may develop during or following transfusion of a blood component are divided into acute and delayed. See Annex 5 for tables of symptoms, diagnoses and management.

Acute adverse events occur during a transfusion or within 6-12 hours of a transfusion. Symptoms and signs include:

- fever and/or chills,
- rash,
- dyspnoea,
- anxiety,
- urticaria,
- changes in blood pressure,
- tachycardia, and
- haemolysis (dark urine, pallor).

Delayed reactions may be asymptomatic, such as

development of an allo-antibody and early stages of a transfusion transmitted infection. Haemolysis, neutropenia and bleeding problems are uncommon features of other delayed reactions (see Table 13.1).

If an acute transfusion reaction occurs, first stop the transfusion then check the blood pack labels and the patient’s identity. If there is any discrepancy, do not restart the transfusion and consult the blood bank.

In order to rule out any possible identification errors in the clinical area or blood bank, stop all transfusions in the same ward or operating room until they have been carefully checked. In addition, request the blood bank to stop issuing any blood for transfusion until the cause of the reaction has been fully investigated and to check whether any other patient is receiving transfusion, especially in the same ward or operating room, or at the same time.

For the signs and symptoms, possible causes and management of the three broad categories of acute transfusion reaction to aid in immediate management see below.

Table 13.1 Adverse Event by symptom:

Symptom	Possible Adverse Event
Fever	Bacterial contamination of product and patient infection Acute haemolytic transfusion reaction Febrile non-haemolytic transfusion reaction (FNHTR)
Dyspnoea	Transfusion related acute lung injury (TRALI) Transfusion related circulatory overload (TACO)
Urticaria	Minor allergy First signs of severe allergy or anaphylaxis
Anaphylaxis	Anaphylaxis
Hypotension	Bradykinin mediated hypotension
Haemolysis	Acute haemolytic transfusion reaction Delayed haemolytic reaction
Cytopenias	Transfusion associated graft versus host disease (TA-GVHD) Post transfusion purpura (PTP) Transfusion associated alloimmune thrombocytopenia or neutropenia
Viruses, parasites and prions	Various potential transmissible diseases

## 13.2 Management, investigation and recording acute transfusion reactions

1. Stop the transfusion and keep the IV line open with 0.9% sodium chloride while making an initial assessment of the acute transfusion reaction and seeking advice.
2. Treat symptoms on the basis of presumed diagnosis.
  - a. Adrenaline, corticosteroids and anti-histamines for anaphylactic and allergic reactions.
  - b. Acetaminophen (paracetamol) for fever.
  - c. Antibiotics after blood culture has been taken for suspected bacterial infection.
  - d. IV fluid resuscitation, respiratory support including oxygen and possibly dialysis for acute haemolysis.
  - e. IV fluids for hypotensive reactions.
  - f. Oxygen for respiratory distress.
3. Immediately report all acute transfusion reactions, with the exception of mild urticarial reactions, to a medical officer and to the blood bank that supplied the blood.
4. Record the following information on the patient's notes:
  - type of transfusion reaction,
  - length of time after the start of transfusion that the reaction occurred,
  - volume and type of blood products transfused, and
  - unique donation numbers of all products transfused.
5. Immediately when the reaction occurs, take the following samples and send with a request form to the blood bank for laboratory investigations:
  - immediate post-transfusion blood samples (1 clotted and 1 anticoagulated: EDTA) from the vein opposite the infusion site,
  - blood culture in a special blood culture bottle, if septic shock due to a contaminated blood unit is suspected, and
  - the blood unit and giving set containing red cell and plasma residues from the transfused donor blood the first specimen of the patient's urine following the reaction.

6. Complete a transfusion reaction report form.
7. After the initial investigation of the transfusion reaction, send the following to the blood bank for laboratory investigations:
  - blood samples (1 clotted and 1 anti-coagulated: EDTA) taken from the vein opposite the infusion site 12 hours and 24 hours after the start of the reaction, and
  - a patient's urine sample within at least 24 hours after the start of the reaction.

## 13.3 SPECIFIC ADVERSE TRANSFUSION EVENTS

### 13.3.1 FEBRILE NON-HAEMOLYTIC TRANSFUSION REACTION (FNHTR)

Fever of  $> 1^{\circ}\text{C}$  from pre-transfusion temperature is most commonly due to FNHTR.

Bacterial contamination and acute haemolytic transfusion reactions need to be excluded.

The fever may be accompanied by chills (cold shivers), nausea and vomiting.

#### 13.3.1.1 Cause

This reaction is non-haemolytic and is usually caused by the presence of leucocytes or cytokines in the transfused blood. Recipient antibodies to donor leucocytes can also cause FNHTR. Such adverse reactions are unpleasant but transient.

Fever during or shortly after transfusion is less commonly caused by transfusion of incompatible blood or bacterial contamination of the blood product. See bacterial contamination.

#### 13.3.1.2 Action

- Stop transfusion.
- Give symptomatic relief e.g. acetaminophen (paracetamol) for fever and pethidine (meperidine) for rigors.
- Maintain IV access with 0.9% NaCl (normal saline).
- If there is any doubt about the diagnosis, investigate and manage according to the bacterial contamination or acute haemolysis protocols.

#### 13.3.1.3 Future policy

Some patients experience recurrent FNHTR. Leucocyte depletion of erythrocyte and platelet products within 24 hours of collection reduces FNHTR and is the most effective prophylaxis. Bedside leucodepletion (bedside filtration) is less effective

but still very useful.

Pre-medication with acetaminophen (paracetamol) has not been shown to be effective. Antihistamines have no role in treatment or prevention.

### **13.3.2 ALLERGY: ITCHING, URTICARIA, GLOTTIS OEDEMA, ANAPHYLACTIC SHOCK**

#### **13.3.2.1 Cause**

The majority of allergic reactions are unexplained. These reactions may be caused by antibodies in the patient against plasma proteins of the donor, most commonly in a recipient who is IgA deficient and has developed an anti-IgA antibody. Other causes include the presence of allergens or cytokines in the blood product.

#### **13.3.2.2 Action**

##### **Itching and/or urticaria**

In general the transfusion should be stopped as urticaria may precede a more severe allergic reaction. Administer antihistamines

##### **Glottis oedema and/or anaphylactic shock:**

Stop transfusion immediately. Do not restart. Administration of antihistamines, corticosteroids, adrenaline, vasopressors and supportive care as required.

- Investigation: IgA and anti-IgA in the patient.

#### **13.3.2.3 Future policy**

In case of anti-IgA: washed erythrocytes and platelets or use of donations from known IgA deficient donors. Consultation with the blood provider is essential. In case of repeated anaphylactic shock, consider use of washed erythrocytes or platelets.

Antihistamines and/or corticosteroids prior to transfusion may be useful for repeated moderate - severe allergic reactions.

### **13.3.3 ACUTE HAEMOLYTIC TRANSFUSION REACTIONS (AHTR)**

#### **13.3.3.1 Cause**

Acute haemolytic reactions are predominantly due to ABO incompatibility. These are predominantly caused by administrative errors leading to "wrong blood in tube" and errors of patient identification. International studies confirm that AHTR due to ABO incompatibility is the most common cause of fatal transfusion reaction.

AHTR may also be caused by recipient alloantibodies to transfused red cell antigens.

In case of ABO incompatibility haemolysis signs and symptoms may appear within minutes of infusing only 5–10 mL of blood. Close observation at the start of the infusion of each unit is essential. The reaction will last for several hours and may be fatal.

In case of allo-antibodies against erythrocytes the reaction may start some hours later and may last several days.

In an unconscious or anaesthetised patient, hypotension and uncontrolled bleeding may be the only signs of an incompatible transfusion.

Symptoms: warm feeling at infusion site and in the face, cold shiver, restlessness, anxiety, high fever, chest pain, pain in the limbs, dyspnoea, nausea, tachycardia, hypotension, bleeding tendency caused by disseminated intravascular coagulation (DIC), jaundice, dark urine, and impaired kidney function with oliguria/anuria.

#### **13.3.3.2 Action**

Urgent treatment is required.

- Stop transfusion immediately, leave needle in situ and commence normal saline (0.9% NaCl).
- Check pulse rate, blood pressure and temperature.
- Hypotension must be treated with fluids and vasopressors and perfusion of the kidney must be guaranteed.
- Fluid supply if necessary supplemented with mannitol 20% and/or furosimide IV to obtain a minimal urine production of 1–2 mL/kg/hour.
- Alkalinisation of the urine using Na-bicarbonate is indicated. Urgent haemodialysis may be required.
- Treatment of coagulation defects and hyperpyrexia as required.

Investigations:

- Check the entire administrative procedure. Specific investigations to find the root causes may indicate system changes in order to prevent future AHTR.
- Residual blood component needs repeat ABO and RhD blood group testing.
- Patient blood should be investigated for, ABO and Rh blood groups, and screening for allo-antibodies which needs to be compared to pre-transfusion results. Repeat testing of stored



pre-transfusion sample is also essential.

- Bacteriologic cultures should be done from both patient and donor blood.
- Other laboratory investigations: Haemoglobin, LDH, bilirubin, haptoglobin, platelet count, coagulation profile, fibrinogen, fibrin degradation products (FDP), creatinin, free haemoglobin in serum and urine.

#### 13.3.3.3 Future policy

- Prevention of administrative (human) errors.
- Compatible erythrocytes.

### 13.3.4 DELAYED HAEMOLYTIC TRANSFUSION REACTION

This reaction is the consequence of recipient allo-antibodies against erythrocytes which are below the level of detection at the time of antibody screening. Between 2 and 10 days after transfusion the haemoglobin decreases with jaundice, fever, spherocytosis, high LDH, positive antibody screen and sometimes haemoglobinuria.

#### 13.3.4.1 Cause

The patient is immunised during a previous pregnancy or transfusion however the antibody titre is below the level of detection. The transfusion functions like a booster with a secondary immune response and the production of high titre antibodies after some days, resulting in haemolysis of donor erythrocytes.

#### 13.3.4.2 Action

- Check of administrative procedure of last transfusion (Identification of patient and donor, transfusion history, type & screen report and/or cross-match etc).
- Investigation of patient's blood for antibodies against erythrocytes before and after transfusion (direct antiglobulin test, screening against panel test erythrocytes).
- Other laboratory investigation: LDH, bilirubin, haptoglobin, free haemoglobin in serum and urine.

#### 13.3.4.3 Future policy

Typed compatible erythrocytes. The information linked to patient data on the presence of antibodies against erythrocytes must be recorded in the blood transfusion laboratory (hospital blood bank) for the life time of the patient as well as on the blood group card and/or SOS badge.

### 13.3.5 TRANSFUSION TRANSMISSIBLE INFECTION (TTI) - BACTERIA

A blood component with bacterial contamination may cause bacteraemia or sepsis and require immediate intervention. Bacterial contamination is a significant risk with platelets due to their storage at room temperature.

#### 13.3.5.1 Action

- Stop transfusion.
- Disconnect blood product as soon as possible, keep needle in situ, connect clean giving set primed with physiologic saline (0.9% NaCl).
- Check whether indeed the right blood products are transfused.
- Collect blood from the patient for repeat compatibility testing (if erythrocytes are transfused) and blood culture.
- Send all blood bags used before or during the adverse transfusion reaction to the hospital blood bank for repeat compatibility testing (if erythrocytes are transfused) and to microbiology for blood culture. Compatibility testing of erythrocyte products that are not yet used, should also be repeated.

#### 13.3.5.2 Future policy

Bacterial testing of platelet components during manufacture.

### 13.3.6 TRANSFUSION TRANSMISSIBLE INFECTION (TTI) - VIRUSES, PARASITES and PRIONS

Unfortunately there is still a substantial residual risk of transmissible disease in Cambodia because:

- the prevalence of TTI markers in the community is high,
- over 80% of donors are family replacement donors, a practice which carries a statistically higher risk of TTI,
- many donors are single time donors (e.g. family replacement donors). Repeat donors have lower risk of carrying a transmissible disease due to their frequency of testing,
- there may be a substantial number of donors in a window period (infectious) due to the current reliance on serological testing rather than NAT,
- ordering of blood is largely ad hoc,
- test performance is not fully consistent and standardised, and
- confirmatory testing is not yet fully developed.

Notes: Cytomegalovirus (CMV) transmission risk is high. Over 50% of the population is seropositive (anti-CMV IgG positive) for CMV. The virus is latent in leucocytes and therefore a seropositive donor, or transfusion of non-leucodepleted blood carries a significant risk of transmission of CMV. Patients who are sero-negative for CMV, and have a compromised immune system should receive CMV safe blood products (anti-CMV negative or filtered).

Other blood transmissible diseases like malaria, toxoplasmosis, babesiosis, and Chagas disease can occur. The most common is malaria and recipients of blood components from endemic or epidemic areas should receive chemoprophylaxis.

Prions, e.g. the cause of variant Creutzfeldt-Jakob disease, can be transmissible by blood but Cambodia does not have documented human or bovine cases.

### 13.3.7 TRANSFUSION ASSOCIATED GRAFT VERSUS HOST DISEASE (TA-GVHD)

This is a rare and often fatal complication. Residual leucocytes in the transfusion establish a graft versus host reaction in the recipient. This is more common in immunocompromised patients, however immunocompetent patients are also at risk. The practice of transfusing HLA haploidentical blood (e.g. from a related family donor) increases the risk of TA-GVHD. Irradiation kills residual immune cells in the blood component. Irradiated blood components should be used for some patient categories (see table).

Patients requiring irradiated whole blood, erythrocytes or platelets:

- Patients with congenital immunodeficiency states.
- Intrauterine transfusions.
- Neonatal exchange transfusions.
- Patients with lymphoproliferative diseases.
- Patients undergoing bone marrow or stem cell transplants.
- Recipients of directed transfusions from family members.
- Recipients of HLA-matched platelets.
- Patients treated with purine analogs (e.g. fludarabine), purine antagonists (e.g. bendamustine), alemtuzumab and anti-thymocyte globulin.

TA-GVHD could be prevented by:

1. The use of voluntary allogeneic donor blood rather than family donors.

2. Irradiation of cellular products (on request) with at least 25 Gy (2500 rad).

### 13.3.8 TRANSFUSION RELATED ACUTE LUNG INJURY (TRALI)

Transfusion related acute lung injury (TRALI) may occur as commonly as 1 in 2500 transfusions and in some countries has become the leading cause of transfusion related mortality. It is defined as acute lung injury, without another cause, occurring during or within 6 hours of transfusion. Acute lung injury is characterised by increasing oxygen requirement, decreasing blood oxygenation and new changes on chest X-ray. The key differential diagnosis is fluid overload, however TRALI does not respond to diuretic therapy. This condition is probably caused by leucocyte agglutinins in donor plasma against leucocytes of the recipient.

TRALI is treated with supportive care and patients often require ventilation. Diuretics and steroids are not useful.

#### 13.3.8.1 Future policy: Prevention

The lead theory of pathogenesis relates to the presence of anti-HLA antibodies in the transfusion against HLA in the recipient. Women, particularly after pregnancy, have a higher incidence of anti-HLA antibody. Many blood providers internationally only supply plasma collected from males in order to reduce the risk of anti-HLA antibody transmission and thereby reduce the risk of TRALI. Cambodia is not in a position to consider this strategy yet.

### 13.3.9 TRANSFUSION ASSOCIATED CARDIAC OVERLOAD (TACO)

Fluid overload, Transfusion Associated Cardiac Overload (TACO), may occur easily due to the oncotic nature of blood products. Patients with cardiorespiratory compromise should be closely monitored and the erythrocyte transfusion may need to run over 4 hours rather than the usual 1–2 hours. Oxygen and diuretic therapy as needed.

### 13.3.10 POST-TRANSFUSION PURPURA (PTP)

PTP is caused by the transfusion of platelet antigen positive blood into a recipient who does not express that antigen and has previously developed antibodies to that antigen. The most common antigens involved are the platelet specific antigens, in particular the transfusion of HLA-1a positive blood to a HLA-1b homozygous patient. Thrombocytopenia occurs 1–24 days after transfusion.

Treatment with IVIg and prevention is by transfusion of antigen negative platelets.

Alloimmunisation can occur to other platelet or neutrophil antigens in a similar manner to red cell alloimmunisation. The clinical significance of these alloimmunisations is variable.

### 13.3.11 COMPLICATIONS OF MASSIVE TRANSFUSION

Complications include:

- Dilutional coagulopathy. This can be mitigated by inclusion of plasma and fibrinogen (or cryoprecipitate) into the massive transfusion.
- Hypothermia. Rapid transfusion of large volumes of cold blood can cause cardiac arrhythmia and worsen core temperature fall.
- Hypotension, worsened coagulopathy and platelet dysfunction are all consequences of hypothermia.
- Citrate toxicity and hypocalcaemia. Citrate is usually metabolised rapidly in the liver, however during massive transfusion and hypothermia, this capacity may be overwhelmed. Treat tetany (muscle spasms), paraesthesias and other signs of hypocalcaemia (e.g. arrhythmias and hypotension) with 1 g calcium chloride IV (max rate 100 mg/minute). Routine use of calcium after transfusion is not required.
- Hyperkalaemia is more common in neonates with massive transfusion but can complicate adult massive transfusion.



# ANNEX

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# ANNEX 1

## TEMPLATE HOSPITAL TRANSFUSION COMMITTEE TERMS OF REFERENCE

### Role

- To promote the safe and effective use of blood.
- To provide consultative and support services with relation to transfusion practices and activities.
- To review supply and demand of blood products, maximum blood order schedules and pre-transfusion laboratory test data.
- To ensure the dissemination of national guidelines to staff involved in transfusion practice.
- To write and review policies, protocols or procedures for safe and effective transfusion practice within the hospital.
- To ensure the provision of suitable education around transfusion practice.
- To promote the reporting of adverse events and near miss events; review these events and recommend and implement changes to prevent future adverse events.
- To commission audits of compliance with transfusion guidelines, policies and procedures.
- To develop key performance indicators (KPI) regarding transfusion and develop action plans.
- To communicate with internal and external bodies regarding transfusion quality matters as required.

### Membership

The committee membership shall include physicians, nurses, transfusion staff, hospital administration, and other personnel as needed.

It should include:

- Medical administrator representative who will be chair.
- Representatives of major specialty users of blood.
- Consultant haematologist for blood transfusion.
- Senior nursing officer.
- NBTC Blood Bank representative.

### Chairing of meeting and secretariat services

The chair is elected by general director of the hospital and will report to them on behalf of the committee.

Secretary is elected by the transfusion committee and will provide the minutes of the meeting and be responsible for arranging meetings.

### Reporting

The transfusion committee will report to general director of the hospital.

### Frequency

It shall meet at least quarterly.

### Agenda

1. To implement Cambodian transfusion guidelines and standards.
2. To review Blood use, stock availability and non-use of blood, and liaise with NBTC to evaluate ordering practices, and recommend corrective measures, if needed.
3. To implement and/or review arrangements for staff training regarding transfusion policies.
4. To ensure that events involving near misses and adverse outcomes are reviewed and corrective action taken where appropriate.
5. Any other matters related to Blood transfusion practice within the hospital.

# ANNEX 2

## INDICATORS FOR MONITORING AND EVALUATION OF THE HOSPITAL TRANSFUSION CHAIN

### Indicators for monitoring and evaluation

#### 1. Adequacy and reliability of supply of safe blood and blood products

- Number of units requested.
- Number of units cross-matched.
- Number of unfilled requests for blood.
- Number of elective surgeries cancelled because of blood shortages.
- Number of units issued for transfusion.
- Number of units issued and returned unused.
- Number of units discarded.
- Number of units issued without screening for infectious disease.
- Markers (HIV, hepatitis, syphilis and other nationally-required tests).
- Number of units issued without compatibility testing.

#### 2. Adequacy and reliability of supply of:

Intravenous replacement fluids:

- Crystalloid solutions, including normal saline (0.9% sodium chloride).
- Colloid solutions.

Drugs used in:

- Anaemia.
- Malaria.
- Labour and delivery.
- Shock.
- Child-spacing (to reduce pregnancy-associated anaemias).
- Haemolytic disease of the newborn (immunoglobulin Anti-D).

Medical devices for:

- Blood salvage.
- Maximisation of intravascular volume (pressure cuffs).

Sterile disposable equipment:

- Needles.
- Syringe.
- Blood sample tubes.
- Blood giving sets, including cannulae/needles.

#### 3. Proportion of blood and blood products used by each clinical speciality:

- Requests for blood and blood products by patient category.
- Transfusion of blood and blood products by patient category.

## ANNEX 2 CONTINUED

### INDICATORS FOR MONITORING AND EVALUATION OF THE HOSPITAL TRANSFUSION CHAIN

#### 4. Use of national guidelines on the clinical use of blood

- Percentage of clinicians trained in the use of the guidelines.
- Percentage of clinicians using the guidelines as a basis for clinical decisions for transfusion.

#### 5. Establishment of a system and procedures to support the implementation of the guidelines

- Availability of blood request form.
- Availability of blood ordering schedule.
- Efficient system for transportation and storage of blood and blood products in the clinical setting.
- Availability of transfusion reaction report form.
- Availability of standard operating procedures for:
  - Ordering blood and blood products in routine and emergency situations.
  - Issue of blood and blood products.
  - Storage and transportation of blood and blood products.
  - Administration of blood and blood products.
  - Recording all transfusions in patient records.
  - Monitoring the patient before, during and after transfusion.
  - Management, investigation and recording of transfusion reactions.

#### 6. Compliance with national guidelines on the clinical use of blood

Number of transfusions given in accordance with national guidelines.

Number of transfusions not given in accordance with national guidelines.

Outcome of transfusions:

- Acute complications of transfusion.
- Delayed complications of transfusion.
- Mortality.



# ANNEX 3

## EXAMPLE OF A MODEL BLOOD REQUEST FORM AS ADVOCATED BY WHO

**EXAMPLE OF BLOOD REQUEST FORM  
(WHO Department of Blood Safety, Geneva, CH)**

Hospital/: \_\_\_\_\_ Date of request: \_\_\_\_\_

**PATIENT DETAILS**

Family name: \_\_\_\_\_ Date of birth: \_\_\_\_\_ Gender: \_\_\_\_\_  
 Given name: \_\_\_\_\_ Ward: \_\_\_\_\_

Hospital reference No.: \_\_\_\_\_ Blood group (if known):

ABO	_____
RhD	_____

**HISTORY**

Diagnosis: \_\_\_\_\_ Antibodies Yes / No \_\_\_\_\_  
 Reason for transfusion: \_\_\_\_\_ Previous transfusion Yes / No \_\_\_\_\_  
 Haemoglobin: \_\_\_\_\_ Any reactions Yes / No \_\_\_\_\_

Relevant medical history: \_\_\_\_\_ Previous pregnancies/stillbirths/abortions Yes / No \_\_\_\_\_

**REQUEST**

Group, screen and hold patient's serum  Red cells  units  
 Provide product  Plasma  units  
 Date required: \_\_\_\_\_ Whole Blood  units  
 Time required: \_\_\_\_\_ Other  units  
 Deliver to: \_\_\_\_\_

**NAME OF DOCTOR (print):** \_\_\_\_\_ **SIGNATURE:** \_\_\_\_\_

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

**LABORATORY USE ONLY**

Donation pack No.	Donor typing		Compatibility testing				Patient ABO	Time of issue
	ABO	Rh	AHG	Room temp saline	Date of match	Time of match	Rh D	

Signature of tester: \_\_\_\_\_

# ANNEX 4

## TRANSFUSION ADMINISTRATION CHECKLIST

### Give the right blood product to the right patient at the right time.

#### Before blood product is collected:

- Medical prescription for product written and complete.
- Check for pre-medications and any instructions for after or during transfusion.
- Transfuse stable patients in daylight hours so they are able to be observed. Transfuse overnight in emergencies. Check urgency with doctor, if there is doubt, do not delay transfusion.
- Blood product ordered and available.
- Informed consent obtained and documented by doctor (where circumstances allow), and the procedure explained to the patient.
- IV access patent and sufficient to allow adequate flow rates.
- IV Blood Administration Set incorporating 170–200 micron filter used and change at least every 12 hours or with new type of IV fluid.
- Baseline observations (T, P, R, BP) taken and documented.

#### Blood Product Collection - Always take written patient details

- Blood collection / request form completed with Full Name, Age or Date of Birth or Unit Record Number of the right patient.
- Complete documentation required by transfusion service provider.

#### After blood product is delivered/collected

- Follow standard precautions.
- Start red cells within 30 minutes of issue and complete within 4 hours.
- Checking: a final patient identity check must be undertaken at the bedside by two appropriate staff, one of whom must then connect and spike the pack.
- Check:


- - Blood pack label, compatibility paperwork and the patient details are identical and correct.
  - Ask the patient to say their name and confirm the patient identification band details are identical and correct.
  - Expiry date of blood pack.
  - Visually inspect the blood pack before use it is intact - no leaks, clots or unusual colouring or haemolysis.
- If any checks fail contact/ return the pack to the hospitals transfusion service

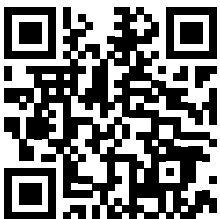
#### Observations

- Ensure the patient is observed closely during the first 15- 30 minutes.
- Temperature, Pulse and Respirations hourly during the transfusion.
- Temperature, Pulse and Respirations and Blood Pressure and on completion.
- If the patient deteriorates contact the doctor.
- Ensure documentation is complete:
  - Fluid balance chart.
  - Transfusion observations including those taken at end of transfusion.
  - Administration times (start and finish).
  - Checking signatures and printed name.
  - Pack/donation number documented in the patient's medical record.
  - Outcome of transfusion documented in patient's medical record.
  - Discard IV lines appropriately.

# ANNEX 5

## TABLES OF ADVERSE EVENT RECOGNITION AND MANAGEMENT

Adverse Events			
Suspected Signs & Symptoms	Possible Etiology	Action	Investigation
Fever ( $\geq 38^{\circ}\text{C}$ ) and/or chills and rigors	<p>38°C to &lt;39°C and no other symptoms</p> <hr/> <p>&lt;39°C and other symptoms (hypotension, tachycardia)</p> <hr/> <p><math>\geq 39^{\circ}\text{C}</math></p>	<p>-STOP transfusion, exclude serious adverse events</p> <p>-Anti-pyretics</p> <hr/> <p>-STOP transfusion</p> <p>-Check patient identity against identity on component label</p> <p>-IV antibiotics if sepsis possible</p> <p>-Maintain good urine output</p>	<p>-Reaction form to Transfusion Laboratory</p> <hr/> <p>-Blood cultures on patient and suspected blood product</p> <p>-Reaction form and EDTA for G&amp;S</p> <p>-If plasma haemolysis suspected send request for FBE, Bilirubin, LDH, Coags, electrolytes, haptoglobin, urinalysis</p>
Rash or Urticaria (hives)	<p>&lt;<math>\frac{2}{3}</math> body and no other symptoms</p> <hr/> <p>&gt;<math>\frac{2}{3}</math> body and no other symptoms</p> <hr/> <p>With Dyspnoea, airway obstruction, hypotension</p>	<p>-STOP transfusion</p> <p>-Antihistamine</p> <hr/> <p>-STOP transfusion</p> <p>-Antihistamine with/without corticosteroid</p> <hr/> <p>-STOP transfusion</p> <p>-Seek urgent medical advice</p> <p>-Adrenaline and oxygen support</p>	<p>-None</p> <hr/> <p>-Reaction form and EDTA for G&amp;S</p> <hr/> <p>-Reaction form and EDTA for G&amp;S</p> <p>-Perform haptoglobin &amp; IgA testing</p> <p>- IgA deficient and/or washed components</p>
Dyspnoea SOB, $\downarrow$ O <sub>2</sub> saturation	<p>Transfusion associated circulatory overload</p> <hr/> <p>TRALI (Transfusion related acute lung injury)</p> <p>(<i>May become a medical emergency</i>)</p> <hr/> <p>Bacterial contamination or AHTR (acute haemolytic transfusion reaction)</p> <p>(<i>May become a medical emergency</i>)</p>	<p>-STOP transfusion</p> <p>-Diuretics</p> <p>-Oxygen</p> <p>-Sit patient upright</p> <hr/> <p>-STOP transfusion</p> <p>-Assess chest xray for infiltrates</p> <p>-Oxygen, possible intubation, ventilation</p> <p>-Notify the Blood Service</p> <hr/> <p>-STOP transfusion</p> <p>-Check patient identity against identity on component label</p> <p>- IV antibiotics if sepsis possible</p> <p>-Maintain good urine output</p>	<p>-Reaction form and EDTA for G&amp;S</p> <hr/> <p>-Reaction form and EDTA for G&amp;S</p> <p>-Perform chest xray</p> <hr/> <p>- Blood cultures on patient and suspected blood product</p> <p>-Reaction form and EDTA for G&amp;S</p> <p>-If plasma haemolysis suspected send request for FBE, Bilirubin, LDH, Coags, electrolytes, haptoglobin, urinalysis</p>



Visit our website at **[cambodiablood.com](http://cambodiablood.com)** to review and download the National Transfusion Guidelines.

Alternatively use your smart phone to download a QR code reader, and scan the code to visit our website.