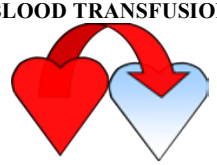
REPUBLIC OF RWANDA
MINISTRY OF HEALTH

P.O.BOX 84 KIGALI

National Directives on Rational Use of Blood and Blood Components in Rwanda

RWANDA BIOMEDICAL CENTER
A Healthy People. A Wealthy Nation

NATIONAL CENTER FOR BLOOD TRANSFUSION



OCTOBER 2018, Version 03

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FOREWORD

Blood Transfusion is the science of using human blood and its components wisely. Without Transfusion Medicine, many deaths would be registered in the Maternities because of obstetrical hemorrhages, in Pediatrics because of anemia from malaria and other parasites and in Surgery because of bleeding. In developed countries, progress in cardiac surgery and chemotherapy for cancer would be very limited without the large quantities of blood they require.

While Blood Transfusion is essential, it also carries risk. Transfusion complications including immunological accidents and Transfusion Transmitted Diseases put the patient's life in danger.

In Rwanda, at least more than 83 000 units of blood components are transfused to patients each year, and many of those transfused are children and parturient. The most important indications for transfusion are hemorrhagic obstetrical complications, malaria, surgery and chronic diseases.

In order to meet all transfusion needs, more than 68 000 blood units are necessary to be collected every year and the quantity may increase due to constant improving of the quality and accessibility of health care services in Rwanda. In fact, at 5.7 collections/1000 population we are now still behind the WHO recommendation of 10/1000.Therefore, the National Centre for Blood Transfusion is dedicated to collecting enough blood for transfusion. Blood must be of the best quality: contamination risks should be minimized and attention should be paid to prevent complications.

To reach optimal blood safety, strategies are defined and implemented in order to recruit blood donors from infectious low risk groups, to make blood donors regular donors, to organize blood collection, to preserve, screen and process blood, to distribute it and to use it rationally and appropriately. To ensure that each precious gift of donation is used wisely, it is also necessary to have usage Guidelines.

Activities linked to blood transfusion are carried out by the National Centre for Blood Transfusion division/Centre National de Transfusion Sanguine (NCBT/CNTS), a division of Rwanda Biomedical Center (RBC), to which enough resources (human, financial and material) must be provided to achieve its mission and create a long term sustainability.

In May 2010, the RBC/National Center for Blood Transfusion, in collaboration with different health professionals mostly involved in blood transfusion, had developed the Rwanda national guidelines for rational use of blood and blood components in Rwanda to help health professionals to transfuse blood and blood products rationally and safely to all patients in need.

However, since February 2010 up to now, there have been some changes in production of blood components in Rwanda such as introduction of cryoprecipitate AHF production, aphaeresis technique in blood components collection and automation of blood components preparation. Hence, those Guidelines needed to be revised to incorporate crucial updates and some specific blood transfusion protocols such as massive transfusion.

These revised guidelines will help health professionals to transfuse blood safely to all patients in need. Health Care Professionals are

encouraged to follow and respect faithfully all the instructions of these guidelines. At the hospital level, the staff are requested to respect the Guidelines related to rational use of blood, based on the principle that blood is used only when nothing else can be done to save a life.

Hospital transfusion committees are being set up to manage blood use in hospitals and help in reporting to the National Center for Blood Transfusion all incidents and reactions related to blood transfusion.

I am convinced that if blood transfusion guidelines are correctly applied, the results will include better transfusion outcomes, fewer complications and reduced overall costs.

Then, I urge all the concerned persons to use appropriately these revised Guidelines so that blood therapy is put to its rational use.

Dr Diane GASHUMBA

Minister of Health / Rwanda

Acknowledgement

The Rwanda Biomedical Center through the National Center for Blood Transfusion, would like to express its sincere gratitude to all organizations and persons, especially medical specialists who have contributed to the revision and finalization of the National Directives for the Rational use of blood and blood components.

These guidelines would have not been completed without the contribution of many organizations and people.

Our deepest appreciation goes to:

- Government of Rwanda
- The World Health Organization (WHO), Rwanda Office and Afro Region;
- The Centers for Disease Control and Prevention(CDC-RWANDA);
- To all Physicians, Researchers and Consultants as well as others who have actively contributed in the revision of these guidelines.

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List of abbreviations

AABB : American Association of Blood Banks
AHF : Anti Hemophilic Factor
AHTR : Acute hemolytic transfusion reaction
AIDS : Acquired Immunodeficiency Syndrome
BP : Blood Pressure
CDC : Centers for Disease Control and Prevention
CHUB : Centre Hospitalier Universitaire de Butare
CHUK : Centre Hospitalier Universitaire de Kigali
CXR : Chest X-Ray
CVP : Central Venous Pressure
DDAVP : Desmopressin
DIC : Disseminated Intravascular Coagulopathy
dL : Deciliter
ED : Emergency Department
FBC : Full Blood Count
FFP : Fresh Frozen Plasma
GI : Gastro-Intestinal
Gr : Gram
GVHD : Graft-Versus-Host Disease
JVP : Jugular Venous Pressure
LFTs : Liver Function Tests
HBV : Hepatitis B Virus
Hct : Hematocrit
HCV : Hepatitis C Virus
HELLP : Hemolytic anemia, Elevated Liver enzymes and Low Platelet count
Hgb : Hemoglobin
HIV : Human Immunodeficiency Virus
HLA : Human Leucocytes Antigens
HUS : Hemolytic Uremic Syndrome

ICU : Intensive Care Unit
INR : International Normalized Ratio
KFH : King Faysal Hospital
KG : Kilogram
LDH : Lactate dehydrogenase
µL : Microliter
MBTP : Massive Blood Transfusion Protocol
MCH : Maternal and Child health
mL : Milliliter
NCBT : National Center for Blood Transfusion
NCDs : Non Communicable Diseases
NUR : National University of Rwanda
Plt : Platelet
PT : Prothrombin Time
PTT : Partial Thromboplastin Time
RBC : Rwanda Biomedical Center
RBCs : Red Blood Cells
RFTs : Renal Function Tests
RMH : Rwanda Military Hospital
SAGM : Salt Adenine Guanine Mannitol
TACO : Transfusion Associated Circulatory Overload
TBV : Total Blood Volume
TMS : Transfusion Medicine Specialist
TPR : Temperature, Pulse, Respiration
TRALI : Transfusion Related Acute Lung Injury
TTP : Thrombotic Thrombocytopenic Purpura
USA : United States of America
WB : Whole blood
WBC : White Blood Cells
WHO : World Health Organization

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INTRODUCTION

These revised Directives provide guidance to clinicians as well as other health professionals involved in blood transfusion on how to use rationally blood & Blood Components in Rwanda; which means safe blood components should be transfused only to treat a condition leading to significant morbidity or mortality that cannot be prevented or managed effectively by other means.

The risks associated with blood transfusion relate to the blood product itself and the donor, in particular, the transmission risk of infectious diseases, such as hepatitis B and C, syphilis and HIV/ AIDS. Blood Transfusion is also associated with immunological risks which may be acute or delayed.

The National Center for Blood Transfusion minimizes the infectious risk transmission in the following ways:

- Recruitment of donors from low risk groups,
- Administration of a donor history questionnaire to potential donors before donation,
- The pre-donation medical examination to identify and exclude subjects at risk for infection,
- Screening all blood donations for Transfusion Transmissible Infections (HIV, hepatitis B and C, syphilis),
- And finally by implementation of a well-established quality management system and quality control.

Even though these measures are respected, the transfusion risk is never reduced to zero because of the following obstacles:

- The sensitivity of the biological tests which, although very high, is not absolute.
- The "window period" which defines the period between the infection and the appearance of detectable serologic markers; these can take from few weeks to several months.

Given these known and hypothetical risks of transfusion, as well as the cost, liability and workload involved with this therapy, directives on the rational use of blood & Blood Components in Rwanda are paramount.

1. BLOOD COMPONENT THERAPY

1.1. Red blood cells

Description

Red cells are obtained by the centrifugation of whole blood followed by aseptic removal of the plasma supernatant. After this separation, a storage solution (e.g. SAGM) is generally added to red blood cells, allowing a storage period of 42 days at +2 to +6 °C.

Each unit contains about 200ml of packed red cells. Pediatric doses may be prepared by aseptically dividing a RBC unit into several smaller units. One donation can result in the production of several units which can be used by the same patient. This preparation is available from the NCBT by request.

Indications for RBC in Adults

- Hb < 6g/dl in the setting of:
  - Normal or high plasma volume and with heart failure,
  - Severe chronic anemia with fatigue, intolerance, etc
  - Anemia in Late pregnancy, with fatigue, tachypnea when non responsive to iron and folic acid
- Hb<7gr/dl for ICU patients with unstable hemodynamics
- Hb<8gr/dl in orthopaedic patients in perioperative period, active GI bleeding.
  Hb≤8gr/ dl Cardiac patients scheduled for cardiac and none cardiac surgery

Acute bleeding greater than or equal to **25%** blood volume (trauma, massive bleeding during surgery) sufficient to produce signs of

hypovolemia unresponsive to crystalloid or colloid infusions regardless of hemoglobin level. (Note: **Blood volume (mL) = weight (kg) x 70 mL/kg.)**

Indications for RBC in neonates and children

Neonatal

- **Hb< 12 g/dl** and severe respiratory distress including intubation, high O2 demand
- **Hb <10 g/dl** with low O_2 requirements
- **Hb <8 g/dl** in normal newborn nursery

Children

- Hb<6gr/dl with or without cardiopulmonary decompensation
- Hg between 6 and 10g/dl depending on the clinical situations, on specific diseases, please refer to other existing specific guidelines.

- **Hb<6gr/dl in the setting of:**
- Malaria
- Severe malnutrition and unresponsive to oral supplementation
- Acute severe bleeding-analogous to adult]
- **Patients on chemotherapy:**

➢ **Hb≤7gr/dl or Hb<9gr with symptoms**

Dosing

A dose of 1 unit of compatible Red Blood Cells will increase the hemoglobin level in an average sized adult who is not bleeding or hemolyzing by approximately **1 g/dL or Hct by 3 %.**

In neonates, a dose of 10-15 mL/kg is generally given. This dose using CPD-SAGM packed red cells with hematocrit of approximately 60 % will increase the hemoglobin by about **3 g/dL**.

Administration

It is done intravenously using an adequate catheter and transfusion set to prevent mechanical damage and haemolysis of RBCs.

Depending on clinical circumstances of the patient, the normal duration of the infusion for an adult is between 30 minutes at a rate of 120 drops per minute and 4 hours at a rate of 20 drops per minute. For pediatric patients, the transfusion rate varies between 2 and 5 ml/kg/hour. The transfusion rate may be increased for individuals in hypovolaemic shock.

1.2. Fresh Frozen Plasma (FFP)

Description

FFP 8 hours

- FFP (Fresh Frozen plasma) 8 hours is obtained by aseptically separating plasma from RBCs after centrifugation within 8 hours of collection, frozen and stored at ≤ - 30 °C.

FP 24 hours

- FP (Frozen plasma) 24 is obtained by aseptically separating plasma from RBCs after centrifugation within 24 hours of collection, frozen and stored at ≤ - 30 °C.

Storage

The maximum duration of storage is 12 months at ≤ - 30°C; the duration period can be increased depending on the temperature.

Indications for FFP/FP in adults

Considering first using other volume replacement - crystalloids which can substitute blood products as both can restore blood pressure to the patient in shock after acute blood loss and these products are free of any viral transmission risk.

- Clinical Disseminated Intravascular Coagulopathy (DIC),
- Acute hemorrhages secondary to coagulation factor deficiency (INR greater than 1.5 and elevated PT), including bleeding on Coumadin/Warfarin therapy
- As part of treatment of severe hemorrhages with liver failure,
- Massive transfusion (with coagulopathic bleeding),
- Thrombotic Thrombocytopenic Purpura (TTP) or Hemolytic Uremic Syndrome (HUS) with active bleeding.

Indications for FFP in pediatrics

- The indications for FFP are generally the same as in adult,
  - However simple prolongation of INR<2.0 in a newborn is not an indication as all infants are born with a deficiency of vitamin K dependent factors.
- Burns and bleeding with severe hypoproteinemia.

Dose

- **Adult and children**: 10-15 mL/kg body weight. Do not transfuse unless the pretransfusion PT is 1.5 times greater than the normal mean value or the INR is greater than 1.5.

- **Expected result**: **Adult**: In a 70 kg adult, each 250-300 mL unit will increase the activity of plasma clotting factors by about 4-5%, and fibrinogen by about 10 mg/dL.
- **Children**: Expect significant shortening of the pretransfusion PT if it is greater than 1.5 times the normal mean value and if the INR is greater than 1.5.

Administration

The FFP must be thawed quickly in an appropriate plasma thawer at 37 °C and transfused with a blood component administration set with a standard filter at a flow rate of 5-10 mL/min. After thawing, the FFP must be used within 24 hours if stored at 4°C. Refreezing is prohibited.

1.3. Platelet Concentrates

Platelets can be obtained using different methods:
Pheresis platelets ("plateletpheresis"); a platelet concentrate (250-400 mL) obtained by plateletpheresis (thrombapheresis or thrombocytapheresis) of a single donor who is connected to a blood processor for 1½ hours, collecting enough platelets for an effective transfusion adult dose.

Whole blood-derived platelet concentrates; a platelet concentrate (45-65 mL) separated from a whole blood donation by centrifugation. **4 to 6** units are needed to make an effective transfusion adult dose. Both techniques are used in Rwanda.

Each random donor platelet concentrate (derived from whole blood donation) contains greater than $5x10^{10}$ platelets. A dose of six contains approximately 3 $x10^{11}$ platelets while one unit from plateletpheresis

also contains approximately 3 x10^{11} platelets. One adult therapeutic dose typically increases the platelet count by at least 30-60 x 10^{9}/liter (30 000 - 60 000 platelets/µL).

Storage:

At the blood bank: 5 days' maximum if stored at 20-24°C with slow continuous agitation.

It should be immediately used after delivery to the requesting department.

Without agitation, platelets can remain intact within 24 hours, but it is always necessary to respect the temperature of storage (ambient temperature).

Indications for platelets in adults

- Platelet count ≤ 10,000 plts/µL to all patients who are chronically thrombocytopenic due to failure of production.
- Platelet count ≤20,000plts/ µL in case of elective central venous catheter insertion
- Thrombocytopenia with Platelet count < 50,000/µL in patient with
  - active bleeding
  - impending major surgery,
  - Lumbar puncture
- Thrombocytopenia with platelets count <70,000/ µL in patients undergo neurosurgery, retino-surgery, Spinal surgery
- Platelet dysfunction with normal platelets count.
  - Due to anti platelets drugs: Aspirin, Plavix
  - Due to congenital disorder of platelet function (Bernard Soulier, Glantzman's thrombasthenia, etc)

Indications for platelets in neonates and pediatrics

Neonatal

- A prophylactic transfusion trigger of < 50,000/µL for a <32 week Premature at risk for intraventricular hemorrhage
- Platelet count < 20,000/µL in regular newborn nursery

Other pediatric

- Platelet count < 10,000/µL
- Platelet count < 20,000/µL in patient with severe mycositis, DIC, coagulopathy, splenomegaly, anticoagulant therapy, lumbar puncture, or higher likelihood of bleeding
- Platelet < 50,000/µL impending surgery,
- Platelet count < 50,000/µL in patient with active bleeding
- Platelet dysfunction with normal platelets count.
  - Due to anti platelets drugs: Aspirin, Plavix
  - Due to congenital disorder of platelet function (Bernard Soulier, Glantzman's etc)

Dosing

- 4 to 6 random donor platelet concentrates are commonly used in adults.
- For small adults and older children, one platelet concentrate unit per 10 kg body weight.
- For Aphaeresis units: 1 unit of 240-300ml for an adult
- For neonates and infants, 5-10 mL per kg body weight is commonly used in any preparation of platelets.
- One platelet concentrate increases the platelet count by about 10,000/µL
- One unit of apheresis platelets increase the platelets count up to 50,000/ µL

NB: Platelets refractoriness will be defined as inadequate rise in platelets counts as measured within 6hours of platelets transfusion.

Causes may include: Immune and none immune mediated

Administration

Platelet concentrates are transfused through a blood component administration set using standard filter (pore size: 170-260 μ) with a flow rate of 5-10 ml/min.
Like red cell components, administration of the platelets must follow the rule of the compatibility of ABO and Rhesus systems between the donor and the recipient.

1.4. Cryoprecipitate AHF (Cryoprecipitate)

Description

Cryoprecipitate antihemophilic factor (AHF), also known as cryoprecipitate (Cryo) are produced by thawing fresh frozen plasma slowly in refrigerated conditions (1-6 C) until all but a small precipitate is thawed. The cold thawed product is centrifuged in the cold leaving the precipitated fibrinogen and factor VIII at the bottom of the bag.

The supernatant is removed leaving the cold-precipitated protein plus 10-15 mL plasma to be refrozen and stored frozen at -18 °C or colder for 12 months. Cryoprecipitates contain Factor VIII, fibrinogen, von Willebrand Factor and Factor XIII.

Content

One unit contains 150-250 mg of fibrinogen, 40-70% von Willebrand Factor, 80-120 units Factor VIII and 20-30% Factor XIII.

Volume

Approximately 5-20 mL per unit.

Storage

Cryoprecipitated AHF is stored at –18 °C or colder for up to 1 year. A unit of thawed Cryo can be stored up to 6 hours at room temperature. After multiple units are pooled prior to transfusion they must be used within 4 hours at room temperature storage.

Dose

- **Adult:** One unit (5-20 mL) of cryoprecipitate per 10 kg body weight increases the fibrinogen level in the recipient by approximately 40-50 mg/dL
- **Children**: 1 to 2 units/10 kg.
- **Expected result**: **Adult:** One unit will increase Factor VIII activity by approximately 4% and fibrinogen by approximately 7-10 mg/dL in a 70 kg adult.
- **Children**: 1 to 2 units/10 kg will raise fibrinogen level by approximately 60 to 100 mg/dL.

Indications for Cryoprecipitate

Adults and Children

- Active bleeding associated with Fibrinogen deficiencies (<100mg/dl) and factor XIII deficiency.

- Patients with hemophilia or von Willebrand's disease who are bleeding and when bleeding is unresponsive to desmopressin (DDAVP) or prophylactically prior to surgery.
- Targeted fibrinogen level must be above 100mg/dl

Table 1: Summary on indications, dosing & storage for blood components

Typical indications in which BLOOD COMPONENTS should be ordered :		**Dosing , Dose response and storage conditions:**			
Blood component	**Indications**	**Dose & Transfusion duration**	**Dose response**	**Storage**	**Expiration**
RBCs (HCT 50-70%) (200ml/ bag)	-Hgb < 6g/dL in case of anemia with intolerance signs -Bleeding exceeding 25% of total blood volume	5-10mL/ kg **(in ≤ 4h)**	↑ Hgb by 1-2g/dL (adult)	2-6 Celsius	42 days
Platelets: Whole blood derived (5.5x1010PLT/ 1 unit), (50ml/bag) OR Apheresis	Thrombocytopenia when: -PLT count < 10,000/mm³ -PLT count < 50,000/mm³ with bleeding or scheduled for major surgery -Treatment with prolonged bleeding time	5 mL/kg (or 1 whole blood-derived unit/10kg) (4 to 6 WB derived units or 1 apheresis	↑Platelets by 30,000 - 50,000/µL	20-24 C with continuous gentle agitation	5 days

platelets ($3.3x10^{11}$ PLT/1 unit) 250 ml / bag	-Documented platelet dysfunction	unit for an adult) **(in 20-30mn)**			
FFP (thawed plasma at 37 C) (300 ml / bag)	-Replacement of isolated or multiple clotting factor deficiencies (Factors II, V, X, XI), PT & PTT > 1.5 normal -End-stage liver disease -DIC, Massive blood transfusion -Treatment of TTP or HUS causing active bleeding -Anticoagulant overdose (coumadin), prolonged INR	10-15 mL/kg (**(in 20-30 mn)**	↑Fibrinogen by about 10mg/dL ↑ Plasma clotting factors by about 4-5%	≤ –18 C	1 year
Cryoprecipitate AHF (5-20 ml/ bag)	-Hypofibrinogenemia (≤ 100mg/dL) -Dysfibrinogenemia -Hemophilia A or Von Willebrand disease - Massive haemorrhage	1 unit / 7-10 kg **(in 30-60 mn)**	↑ Fibrinogen level by about 40-50 mg/dL	≤ –18 C	1 year

Note: When writing a transfusion indication, refer to the predefined indications onto Hemovigilance system. If a physician finds that the transfusion indication of the patient was not pre-defined, he/she writes clearly a new transfusion indication.

2. MASSIVE BLOOD TRANSFUSION PROTOCOL (MBTP)

2.1. Introduction

In order to streamline the management of blood transfusion requirements in major bleeding episodes occurring in adult patients within transfusing facilities in Rwanda and assist the interactions of the hospital team treating the patient and the blood products supplying service, a massive transfusion protocol has been established. It should be noted that any instance of massive blood transfusion may have unique clinical features and the Protocol may need to be tailored to the individual patient circumstances.

It applies to all transfusing facilities. It also applies to the management of massively bleeding patients requiring massive blood transfusion. The MBTP can be initiated by any physician. The MBTP is a complex set of concurrent processes which require effective leadership within a functioning multidisciplinary team.

2.2. Definition

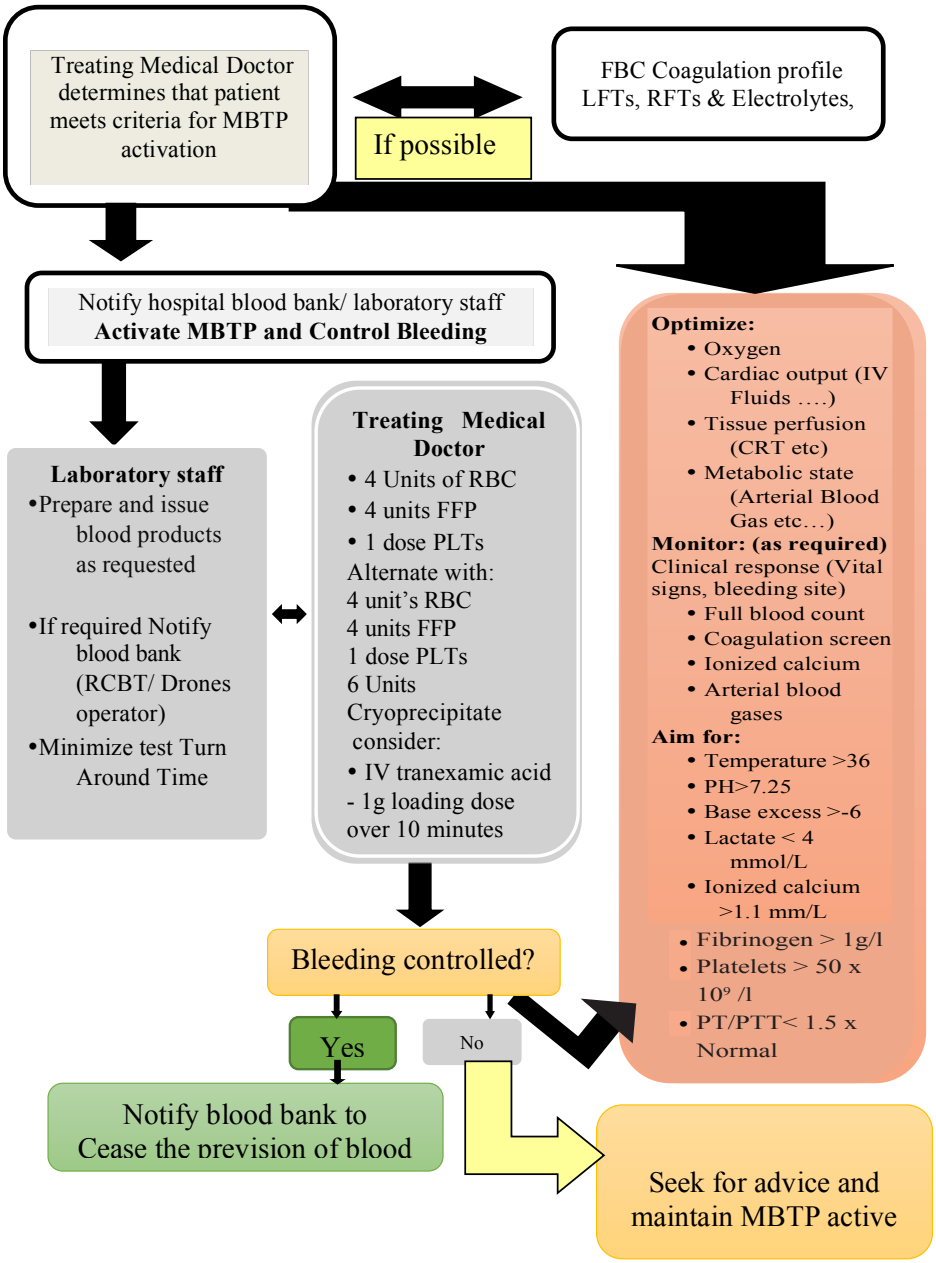
Massive blood transfusion is considered in the following situations:

- Blood loss rate of 150 ml / min
- Half of TBV (Total Blood Volume) replaced over 3 hours
- 1 TBV replaced over 24 hours
- 10 RBCs transfused over 24 hours or from time of ED admission to ICU transfer
- 20 RBCs transfused in the course of a hospital admission

2.3. Rationale for Massive Blood Transfusion Protocol

In case of massive bleeding, transfusing fresh whole blood would seem ideal but the time required to conduct safety tests on blood is long enough to cause significant depletion of coagulation factors and platelets considering that each type of blood component requires their optimal storage conditions. Therefore, administering RBCs, coagulation factors and platelets together maintains the physiological constitution of blood and prevents deficit of one or more constituents. Massive Blood Transfusion Protocol well implemented leads to safe and judicious use of blood components.

Figure 1: Flowchart of Massive Blood Transfusion Protocol (MBTP)



3. ADVERSE TRANSFUSION REACTIONS

The most common complications of transfusion are febrile nonhemolytic and chill-rigor reactions. The most serious complications are acute hemolytic reaction due to ABO incompatible transfusion and transfusion-related acute lung injury, which have very high mortality rates.

Early recognition of symptoms suggestive of a transfusion reaction and prompt reporting to the blood bank are essential. The most common symptoms are chills, rigors, fever, dyspnea, light-headedness, urticaria, itching, and flank pain. If any of these symptoms (other than localized urticaria and itching) occur, the transfusion should be stopped immediately and the IV line kept open with normal saline. Transfusion reactions are classified either based on time elapsed between the start of transfusion and occurrence of a reaction (acute or delayed) or based on the cause of a reaction (immunological and non-immunological).

Table 2: Types, Symptoms & Signs, Prevention and Management

Type/Cause	Signs/Symptoms	Prevention	Treatment
Febrile (non haemolytic) Transfusion Reaction (FNHTR) Onset during or within 4 hours following transfusion	unexplained fever ≥38°C and a temperature rise of at least 1°C but <1.5°C from pre-transfusion baseline, chills, rigors May be present: tachycardia, headache, nausea, flushing, anxiety, hypertension or occasionally hypotension, back pain, and/or angina	If previous transfusion reactions. Consider pre-transfusion antipyretic Paracetamol 1g po	- Stop the Transfusion -Check label and recipient identity -Send Haemovigilance notification to Blood Bank -Antipyretic Paracetamol 1g po and monitor closely -Steroids are not appropriate treatment for minor reactions

Allergic Reaction -More common with Plasma and Platelet Components -Onset: from commencement to 4 hrs	Erythematous rash with itching, urticaria (hives), Angioedema, Periorbital itch, erythema and oedema,Conjunctival oedema, Minor oedema of lips, tongue and uvula, May be present: Cough,Hypotension and tachycardia, Dyspnoea, Chills and rigors, Loin pain and angina, Severe anxiety	For recurrent mild reactions, prophylaxis with antihistamine to alleviate symptoms, eg Loratadine 10mg or Cetirizine 10mg po Routine prophylaxis for all recipients before transfusion is not indicated	-Stop transfusion -Check label and recipient identity - Replace IV set and give saline to keep vein open and/or maintain BP -Antihistamine, eg Loratadine 10mg or Cetirizine 10mg po, Promethazine 25-50 mg IV (max rate 25 mg/min) if moderate -Increased monitoring, eg BP,15 – 30min -Send Haemovigilance notification to BB -Hydrocortisone may be considered
Anaphylactic /Anaphylactoid Allergic Reaction (severe) -Rapid onset May be due to an antibody	Life-threatening reaction: Cough, respiratory distress, Chills and rigors, Loin	Discuss with BB Physician before requesting: IgA deficient blood/blood products	-Stop transfusion -Check label and recipient identity -Adrenalin 1:1000 IM and repeat at 5-10 min intervals if required: - Adult: 0.5mg / 0.5 mL

in the recipient reacting with a plasma protein in a blood component -IgA -Haptoglobin -Other plasma protein	pain and angina, Severe anxiety, Severe hypotension, shock and tachycardia, Widespread urticaria with skin flushing and itching, Wheezing, stridor, change in voice Note: Respiratory symptoms may dominate in anaesthetised recipients	may be appropriate if recipient is known to have absolute IgA deficiency or to have anti-IgA -Washed cellular components may be indicated where the cause of the reaction is not identified	- Children 0.01mg/kg IM; min dose 0.1mL, max dose 0.5mL - Replace IV set and give rapid IV colloid or saline, eg adults 2 L, children 20 mL/kg, until SBP>90 mmHg -Consider Hydrocortisone 4mg/kg (200-400 mg IV) -Consider H1-antihistamine, eg Loratadine or Cetirizine 10 mg po for itch or angioedema. -H2-antihistamine, eg Ranitidine may be added for severe reactions. -Note: Sedating antihistamines, eg Promethazine contraindicated -ICU liaison - Send Haemovigilance notification to Blood Bank

Hypotensive Reaction	Hypotension – fall in systolic BP >30 mm Hg during or within 1 h of completing transfusion and systolic BP ≤ 80 mm Hg		-Stop transfusion -Replace the IV infusion set and infusesaline to manage BP -Symptomatic management until resolved -Send Haemovigilance notification to Blood Bank
Acute Haemolytic Reaction -Onset within 24 hours, usually immediate -ABO or other incompatible RBC transfusion reaction - Improper handling and storage of blood	Some or all of – Unexplained fever >1°C, Chills, rigors, Pain up arm, Chest, abdominal or low back pain, Dyspnoea, Tachycardia, Hypotension, shock, Haemoglobinaemia, and haemoglobinuria, Oliguria with dark urine or	-Check well recipient's ID (2 persons) and labeling of pre-transfusion blood sample at recipient's side -Careful monitoring of recipient for first 15 min of each unit transfused -Store and handle	-Stop transfusion -Check label and recipient identify -Replace IV set and start normal saline -Treat shock and maintain blood pressure with IV saline infusion - Investigate possible DIC and treat if clinically significant bleeding - Diuretic, eg Furosemide 1-2 mg/kg IV and/or Mannitol, may help maintain urine flow -Hydrocortisone may be considered -Samples to assess renal and liver function, DIC and haemolysis, eg full

	anuria,Nausea, vomiting, Diarrhoea, Pallor, jaundice, Bleeding (due to DIC)	blood components within specifications	blood count, unconjugated bilirubin, LDH and haptoglobin -Send Haemovigilance notification to Blood Bank
Delayed Haemolytic Reaction Onset usually 1-7 days' post transfusion but may be up to 28 days - Recipient has previously been immunised to a blood group antigen, usually by transfusion or pregnancy.	• Worsening anaemia and jaundice from destruction of red cells • Often asymptomatic but rarely splenomegaly, haemoglobinaemia and haemoglobinuria • Renal impairment	Blood group antibodies should be recorded on the Blood Service national database so that compatible red cell components can be provided for future transfusions Note. Delay may	Investigate haemolysis: • Full blood count with film comment • Direct antiglobulin test (may be negative when most red cells cleared) • Blood group antibody screen (may be negative until red cells cleared) • Liver function tests • Haptoglobin concentration falls while haemolysis is occurring

	may occur in severe cases • Blood screen shows unexpected anaemia and spherocytes may be present on film	occur when providing compatible red cells for transfusion	• LDH • Send Haemovigilance notification to Blood Bank if reaction is suspected
Bacterial Sepsis **Frequency:** Platelet components: <1:10,000 Red cell components: <1:250,000 - Rapid onset ➢ Blood component contains bacteria that have grown to a high concentration ➢ Most commonly affects	• Rigor, chills, fever • Shock, usually within minutes of starting transfusion • Respiratory distress, wheezing and oxygen desaturation • Pain up arm • Chest and back / loin pain • Nausea, vomiting	• Collect, store and handle blood components within specifications • Inspect products for any visual abnormality or defect in unit container before transfusing:	• Stop transfusion • Replace IV set; give saline to maintain BP and/or keep vein open • Send Haemovigilance notification to Blood Bank • Notify Blood Bank by phone and contact TMS urgently • Obtain blood cultures from recipient if sepsis suspected • Give antibiotics: a broad-spectrum penicillin or cephalosporin and

platelet components; rarely affects red cells	• Explosive diarrhoea may occur with *Yersinia enterocolitica* sepsis • Most common infecting agents: staphylococcal species (platelet components), gram negative species (red cell components)	o a visibly clumped platelet component o an unusually dark red cell component o punctured or leaking bag	gentamicin 5mg/kg Note: Blood Bank will arrange urgent Gram stain and cultures on blood component and report any positive findings
TACO: Transfusion Associated Circulatory Overload Rapid onset after infusion of a volume of fluid that is clinically significant for the affected recipient.	Increased blood pressure Rapid bounding pulse Respiratory distress with raised resp. rate, dyspnoea, cough, pink frothy sputum,	Restrictive transfusion practice Monitor fluid balance esp. in elderly and children, and recipients with cardiovascular or	Stop transfusion Seek urgent medical assessment Sit recipient upright with legs over side of bed, administer oxygen, diuretic (Frusemide 1-2 mg/kg IV), CPAP ventilation

-Main risk factors: Elderly recipient with impaired cardiovascular state or renal impairment Infusion too rapid for recipient o Volume infused too great, especially if normovolaemic	crepitations and oxygen desaturation consistent with pulmonary oedema Raised JVP and CVP Nausea Acute or worsening pulmonary oedema on CXR Restlessness, anxiety	renal disease Transfuse at a rate appropriate for recipient Give a diuretic immediately **prior** to a transfusion if cardiovascular reserve is impaired or a large transfusion is required Avoid elective transfusions at night Always prescribe paediatric transfusion dose in mL, **not** in Units.	Phlebotomy may be necessary Demonstration of raised BNP may help to distinguish from TRALI Send Haemovigilance notification to Blood Bank

Post Transfusion Purpura **Frequency:** <1:100,000 (mostly occurs in women who have been pregnant) - Onset about 5-12 days after transfusion of cellular blood components Recipient has produced an antibody to an HPA (human platelet-specific antigen). The antibody forms immune complexes with transfused platelet antigens resulting in clearance of most circulating platelets	Severe thrombocytopenia often with purpura and possibly other bleeding Thrombocytopenia will persist for 1-2 weeks	• Restrictive transfusion practice • Notify Blood Bank and TMS promptly so that relevant investigations can be initiated. Further transfusions will require selected components. Note: Delay may occur for supply of cellular blood products.	• Consult Transfusion Medicine Specialist or Haematologist if a recipient of cellular blood components develop an unexpected severe thrombocytopenia in the following 1-2 weeks • Test for HPA antibodies • If not bleeding – monitor • If clinically significant bleeding – intravenous immunoglobulin and/or plasma exchange are recognized treatments • Avoid random-donor platelet transfusion • If life-threatening bleeding – platelet components lacking the relevant HPA antigen are desirable

TRALI: Transfusion Associated Lung Injury **Frequency:** <1:5,000 Onset within 6 hours following transfusion of plasma or plasma containing cellular components ➢ One recognized mechanism involves a donor antibody reacting with recipient neutrophil- or HLA-antigens causing cell activation that results in acute severe microvascular lung injury ➢ Other contributing factors may exist	• Onset of severe dyspnoea and cyanosis proceeding to respiratory failure with bilateral infiltrates on CXR within 6 hours of transfusion • If the reaction occurs during anaesthesia the lungs become very stiff from rapidly developing pulmonary exudate • Absence of left atrial hypertension (circulatory overload)	• Restrictive transfusion practice o Transfuse with Male-only FFP o HLA-antibody testing of apheresis platelet donors - Notify Blood Bank so that donor(s) can be assessed for relevant antibodies and implicated donor(s) withdrawn from the active donor panel	• Intensive care management for respiratory failure • Diuretics are not usually helpful • Send Haemovigilance notification to Blood Bank • Notify Blood Bank by phone and contact a transfusion medicine Specialist urgently • Tissue typing samples will be required

Transfusion associated Graft versus Host Disease (TA-GVHD) **Frequency:** Rare but fatal - A risk for TA-GVHD exists with: o Congenital cellular immune deficiency o Intrauterine transfusion and neonatal exchange transfusion o Hodgkin lymphoma o Some chemotherapy agents, eg purine analogues o Transfusion of cellular components from near genetic relative	- Clinical syndrome with fever, rash, liver dysfunction, diarrhoea and pancytopenia occurring 1-6 weeks following transfusion with no other apparent cause	• Irradiate cellular blood components to inactivate residual lymphocytes	• Consult with a Haematologist and Transfusion Medicine Specialist to investigate and establish diagnosis • Send Haemovigilance notification to Blood Bank

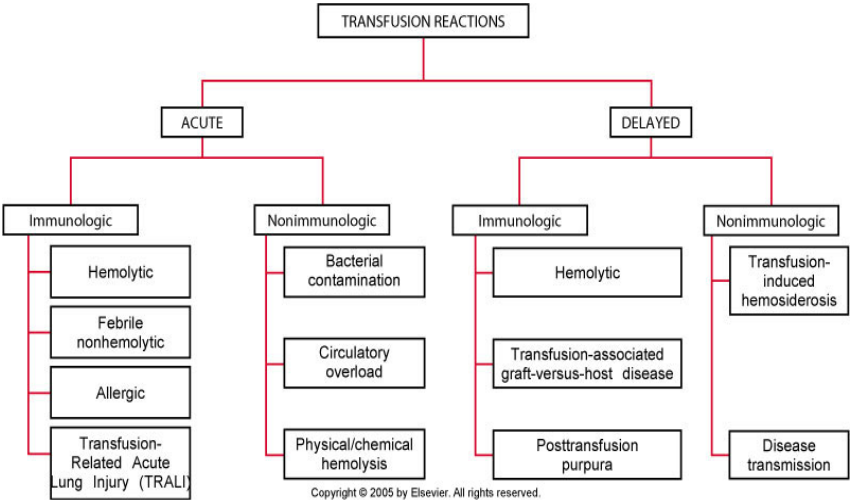
○ HLA-matched apheresis platelets ○ Severe immunodepression			
Cooling - Progressive onset during rapid infusion of large volumes of cold fluids, including blood products (more than 50 mL/kg/h in adults or 15 mL/kg/h in children)	• Reduced temperature • May be associated with cardiac rhythm irregularity and a negative inotropic effect • Impaired platelet function and	• Give large fluid infusions through a warmer designed for rapid infusion of blood components and follow the manufacturer's instructions	• Limit heat loss from the recipient and monitor BP/TPR • If further blood components required, infuse through a warmer • Note: Reliable determination of temperature requires core temperature measurement

	coagulation	• Equipment must be properly maintained and validated to ensure the correct temperature is achieved as excessive temperature will produce hemolysis	

NOTE: Adverse Events Reporting

When an adverse event is discovered on a blood transfusion recipient, the patient physician must report it on the Transfusion reaction report form. The form must be transmitted to the hospital laboratory and the latter record it onto the Hemovigilance system.

Figure 2: Classification of Transfusion Reactions



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4. ALTERNATIVES TO BLOOD TRANSFUSION

4.1. Introduction

There are multiple therapeutic resources to reduce or avoid allogenic blood transfusion (other person's blood). These options involve clinical strategies with medicine and/or specific equipment to treat the patient with anaemia and/or blood coagulation disorder (for instance, low platelet). On the other hand, there are also surgical strategies with evidences to reduce blood loss by the patient during surgery. One can also save the use of blood components, already short in the blood banks, by specific measures to treat the patient to be more tolerant to the anaemic situation.

4.2. Description

Bloodless medicine encompasses many situations beyond patients who refuse transfusion. Examples include situations in which blood is simply not available, a previously transfused patient with multiple alloantibodies or an incompatible crossmatch for other reasons, and surgical procedures performed in areas of limited (or highly infectious) blood supply.

Over the past decade, "bloodless medicine" has evolved into "patient blood management". This uses a three-pronged interdisciplinary approach, leaving transfusion as the last resort. The following are emphasized:

- Optimizing haematopoiesis,
- Minimizing bleeding and blood loss (blood conservation), and
- Harnessing and optimizing physiological tolerance of anaemia (through application of all available therapeutic resources)

Approaches: Various approaches include breathing 100 percent oxygen, hyperbaric oxygen therapy, transfusion of the patient's own red cells either collected in advance or recycled during surgery, erythropoietin, and intravenous iron.

Meticulous haemostasis is necessary in patients undergoing surgery or bleeding from other causes. The clinical team and patient must realize that, in a patient who refuses transfusion, if the bleeding cannot be stopped the patient will die.

All of these issues require close and continuing consultation among haematologists, intensivists, surgeons, anaesthesiologists, and transfusion medicine specialists, as well as the patient care team and the patient and/or patient decision maker(s).

Reducing blood loss — Blood conservation approaches are especially applicable in the intensive care unit and the operating room. Multiple studies have found mean daily phlebotomy losses in medical-surgical ICUs of approximately 41 mL/day. Conservation practices have been recommended, including decreased testing, small volume sampling, closed sampling circuits, and point-of-care micro-testing.

Other general practices include close attention to the degree of anticoagulation (if used), minimizing use of agents with antiplatelet activity (e.g. aspirin, nonsteroidal anti-inflammatory agents, clopidogrel), and meticulous attention to haemostasis and technical blood losses during surgery (e.g. use of haemostatic surgical devices, fibrin glue and tissue adhesives; controlled hypotension; elevating the surgical field above the rest of the body).

In bleeding patients, anti-fibrinolytic drugs (e.g. aminocaproic acid, tranexamic acid) may decrease the need for transfusion. Recombinant factor VIIa has been effectively used to reduce haemorrhage and the need for transfusion in some Witness patients with gastrointestinal bleeding, surgical bleeding, or combat trauma.

Many clinicians believe that as long as the fibrinogen concentration is >100 mg/dL (1 g/L), everything is fine with their patient's haemostasis. However, in a bleeding patient who will not accept red cell transfusion but will accept fibrinogen, it should be supplemented until at least in the normal range. In a patient facing acute life threatening bleeding, supplementation of fibrinogen to at least the high end of the normal range may be advantageous.

Reversal of anticoagulation — A patient who is anticoagulated, haemorrhaging, and refusing blood products is in special peril. Interventions depend on the anticoagulant:

1. Warfarin - Prothrombin complex concentrates (PCCs) have proven to be as good as or better than FFP at reversing warfarin anticoagulation; four-factor PCCs are preferred over three-factor PCCs. High dose (5-10 mg) of IV Vitamin K can fully reverse Warfarin induced anti-coagulation. However, because its effect is delayed other more rapidly acting agents are typically co-administered.

2. Direct oral anticoagulants - For direct thrombin inhibitors such as dabigatran and direct factor Xa inhibitors such as apixaban, edoxaban, and rivaroxaban, reversal agents are available or under development.

3. Erythropoiesis-stimulating agents (ESAs) and intravenous iron
The use of recombinant human erythropoietin(rhEPO) and iron is acceptable. Recombinant human erythropoietin has been shown to be useful, both preoperatively and in critical situations where bleeding has been stopped but the hemoglobin (Hgb) is very low. The onset of action of rhEPO is four to six days, provided that the patient has sufficient vitamin B12, folate and iron stores.

In pregnant women, the prevention of iron deficiency anaemia can be ensured by adequate monitoring with at least three antenatal visits in the perinatal period, iron and folic acid supplementation and / or prophylaxis or treatment of malaria and intestinal parasites. This can reduce the frequency and the severity of anaemia.

NOTE: In other non-obstetric patients, Iron supplement is only recommended for iron deficiency anaemia patients after clinical evaluation and laboratory investigations.
Prevention or treatment of malaria, systematic deworming and a varied and balanced diet allow to reduce the frequency and the severity of anaemia.

APPENDICES

1. Blood order form
2. Emergency Release of Blood form
3. Blood Transfusion posters

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