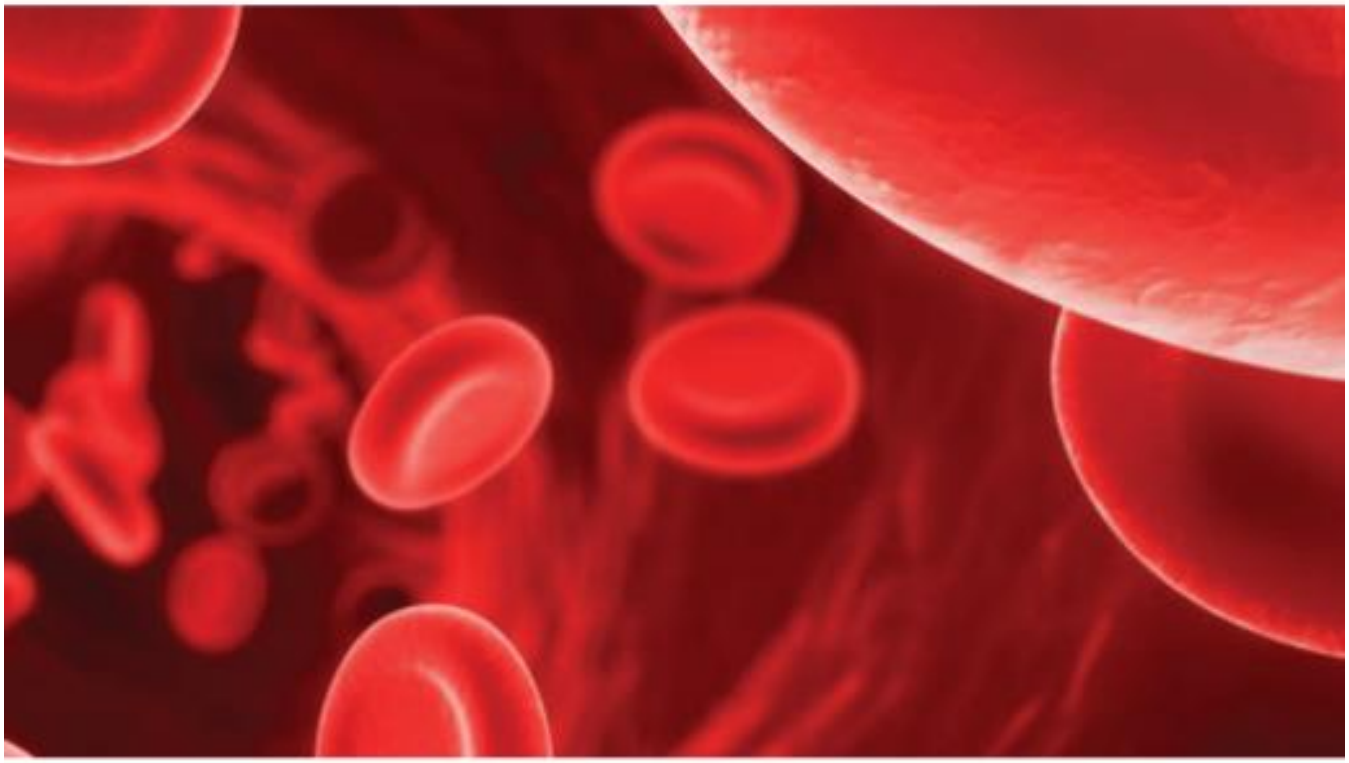


Handbook on Clinical Use of Blood

3rd edition 2020

National Blood Centre
Ministry of Health, Malaysia

in collaboration with

Malaysian Blood Transfusion Society

HANDBOOK ON CLINICAL USE OF BLOOD

3rd edition
2020

Ministry of Health, Malaysia
Jalan Tun Razak
50400 Kuala Lumpur, Malaysia
Tel: 03-2613 2688 | Fax: 03-2698 0362
Web: http://www.pdn.gov.my

FOREWORD

DIRECTOR-GENERAL OF HEALTH

"Primum non nocere" which translates to "first, do no harm" is the fundamental principle of the Hippocratic Oath in the art of practising medicine. 13 years ago, the National Blood Centre published the Guidelines for the Rational Use of Blood and Blood Products to assist healthcare workers in making sound clinical judgement weighing between the benefits and risks of blood transfusion therapy, with the ultimate purpose of doing no harm, ensuring patient safety and optimizing patient care.

For the past years, profound efforts are continuously carried out by the blood transfusion service to achieve this aim, encompassing recruitment of voluntary low risk blood donors along with thorough screening methods for the nation's blood safety. Blood and blood products is then stored adhering to international quality requirement standards. These efforts are then continued by transfusion medicine specialist and multidisciplinary healthcare professionals assessing the patient's condition to subsequently make a timely decision for blood transfusion as indicated. Blood transfusion must be prescribed judiciously only if the benefits outweigh the risks.

The handbook provides a perspective on evidence-based strategies in making that decision for various clinical scenarios, including Patient Blood Management, Massive Transfusion Protocol for critically bleeding patients and early intervention methods for planned procedures. In the current era, evolving technology has been integrated into the medical field, providing more developed treatments for certain diseases and a large potential capacity for digitalized healthcare. This promotes a transparency in the healthcare practice, allowing a national haemovigilance monitoring and utilization of available resources whenever possible to prevent unnecessary blood transfusion.

I am delighted with the publication of this revised handbook that will provide a standardized approach to blood transfusion to enhance quality of care for patients. The blood transfusion service and all clinical healthcare personnel should constantly work hand in hand in the mutual effort of providing the best outcome for our patients.

Datuk Dr. Noor Hisham Abdullah
Director-General of Health
Ministry of Health Malaysia

FOREWORD

DEPUTY DIRECTOR-GENERAL OF HEALTH (MEDICAL)

Blood transfusion is one of the most common procedures carried out in almost all Ministry of Health hospitals for planned treatments as well as lifesaving urgent interventions. It depends on many factors that requires justification based on the needs of individual patients. The Malaysian healthcare system is reinforced by a nationally coordinated blood transfusion service that functions to ensure safe and sufficient blood supply for patients requiring blood transfusion. Despite recent technology and advancement offering alternatives to blood transfusion, blood from voluntary non-remunerated donors still remains as a crucial resource for patient treatment.

This Handbook on Clinical Use of Blood provides valuable information regarding transfusion process and usage of blood in different clinical settings. A major portion of this publication emphasize on the concept of Patient Blood Management, which is an initiative to optimize care for patients who may require blood transfusion with an evidence-based approach. It provides clinical recommendations of principles on managing various multidisciplinary scenarios. This is part of a good transfusion practice effort to ensure appropriate usage of blood with the aim of enhancing patient outcomes and reducing transfusion-related risks.

A multidisciplinary speciality is required with wide range of working knowledge on blood transfusion as a therapy and I would like to thank and congratulate the working group for their achievement and continuous effort to update this handbook and consolidate data based on available scientific literature to ensure patients receive the best complete treatment possible. I hope that the transfusion process will be administered in a standardised manner throughout Malaysia. Evidently, this publication would assist and guide all healthcare professionals in the clinical management and treatment of all patients.

Datuk Dr. Hj Rohaizat bin Hj Yon
Deputy Director-General of Health (Medical)
Ministry of Health Malaysia

PREFACE

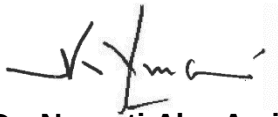
DIRECTOR OF NATIONAL BLOOD CENTRE

Blood, its labile components and plasma derived medicinal products are therapeutic products of human origin and play critical role in health care. The availability and equitable access of safe and quality blood are important in achieving universal health coverage. In Malaysia, blood contributes to treatment of thousands of lives each year. Blood is required for child and maternal health; management of patients with acquired conditions such as cancer and inherited blood disorders as well as being a critical treatment option in the management of life-threatening conditions such a trauma and support complex medical and surgical procedures.

The National Blood Centre had released the “Guidelines for the Rational Use of Blood and Blood Products” in 2007 to assist doctors involved in prescribing and administering blood and blood products to patients. This publication has since gone through an extensive process of review and updating and is renamed as ‘Handbook on Clinical Use of Blood’.

This handbook is designed to provide recommendations, references and practical information on the judicious and safe use of blood and blood products for patient management based on current evidence and international best practices. All the chapters in the handbook ranging from ordering blood to the administration of blood to the patient at the bedside have been revised together with the chapters on the use of blood in specific medical- and surgical-based discipline. Several new topics have been added including Patient Blood Management, massive transfusion protocol, autologous blood transfusion and therapeutic apheresis.

I would like to acknowledge all the editors, writers, external reviewers, publication coordinators and other contributors for their effort and valuable time in revising this edition. It is hoped that the availability of the Handbook will improve transfusion practices and translate into better patient outcome and quality of care for all patients receiving blood and blood products.



Dr. Noryati Abu Amin
Senior Consultant Transfusion Medicine
Director, National Blood Centre Kuala Lumpur
(National Head of Service for Transfusion Medicine)

EDITORIAL GROUP

WRITING GROUP

Dato' Dr. Yasmin Ayob
Senior Consultant Haematopathologist
National Heart Institute

Dato' Dr. Roshida Hassan
Senior Consultant Haematopathologist
National Heart Institute

Dr. Afifah Haji Hassan
Senior Consultant Haematopathologist
Head of Pathology Department
Hospital Sungai Buloh

Dr. Tun Maizura Bt Mohd Fathullah
Senior Consultant Haematopathologist
Deputy Director I
National Blood Centre

Dr Zanariah Kassim
Consultant Haematopathologist
Hospital Sultanah Aminah, Johor Bahru

Dr. Nor Nazahah Mahmud
Transfusion Medicine Specialist
Deputy Director II
National Blood Centre

Dr. Norasrina Ishak
Transfusion Medicine Specialist
National Blood Centre

Dr Shahnaz Irwani Sabri
Transfusion Medicine Specialist
Hospital Queen Elizabeth II, Sabah

Dr. Zalina Mahmood
Transfusion Medicine Specialist
Hospital Raja Perempuan Zainab II

Dr. Ailin Mazuita Mazlan
Transfusion Medicine Specialist
National Blood Centre

Dr. Intan Iliana bt Iliassa
Transfusion Medicine Specialist
Hospital Serdang

Dr. Mohammad Masrin Md. Zahrin
Transfusion Medicine Specialist
Hospital Umum Sarawak

Dr. Norhaza Abd Rahim
Transfusion Medicine Specialist
Hospital Pulau Pinang

Dr. Rosyidi Rejab
Transfusion Medicine Specialist
Hospital Sultanah Bahiyah, Kedah

Dr. Idaleswati Nor Mohamed
Transfusion Medicine Specialist
National Blood Centre

Dr. Norazlina Hamzah
Transfusion Medicine Specialist
Hospital Melaka

Dr. Noor Azlina Kamis
Transfusion Medicine Specialist
Hospital Sultan Abdul Halim, Sg Petani

Dr. Nor Amiza Mat Amin
Transfusion Medicine Specialist
Hospital Melaka

Dr. Sabariah Md. Noor
Transfusion Medicine Specialist
Hospital Raja Permaisuri Bainun, Ipoh

Dr. Mohd Muhaimin Kambali
Transfusion Medicine Specialist
Hospital Sultanah Nur Zahirah

Dr Nor Hafidza Haron
Transfusion Medicine Specialist
Hospital Tengku Ampuan Rahimah, Klang

Dr. Rahimah bt Abdul Wahab
Transfusion Medicine Specialist
Hospital Taiping

Dr. Rohaida binti Abdul Rahman
Transfusion Medicine Specialist
Hospital Sultan Ismail

Dr. Ong Chiew Ping
Transfusion Medicine Specialist
Hospital Tuanku Jaafar, Seremban

Dr. Azmanira binti Aziz
Transfusion Medicine Specialist
National Blood Centre

Dr. Sabeha Sahabudin
Medical Officer
National Blood Centre

**And all MMED Transfusion Medicine 2008 – 2013*

EXTERNAL REVIEWERS

Dr. Anuwar Ariff Mohamed Omar
Consultant Anaesthetist
Hospital Melaka

Dr. Carol Lim Kar Koong
Consultant Obstetrician
Hospital Ampang

Mr. Hafizan Mohd Tajri
Consultant Surgeon
Hospital Kuala Lumpur

Datuk Dr. Harjit Singh S/O Pritam Singh
Senior Consultant Hepatobiliary Surgeon
Prince Court Medical Centre

Dr. Liu Wen Jun
Consultant Physician
Hospital Sultanah Aminah, Johor Bahru

Dr. Mahfuzah Mohamed
Consultant Paediatrician
Hospital Shah Alam

Dr. Mawar Ayub
Emergency Physician
Hospital Kuala Lumpur

Dato' Dr. Mohd Nazeri Nordin
Senior Consultant Cardiothoracic Surgeon
National Heart Institute

Dr. Muniswaran A/L Ganesham @ Ganeshan
Consultant Obstetrician
Hospital Kuala Lumpur

Dr. Nirmala Devi A/P Baskaran
Consultant Obstetrician
Hospital Gleneagles, Kuala Lumpur

Dr. Nurul Zaynah Nordin
Nephrologist
Hospital Kuala Lumpur

Dr. Sharifah Shahnaz Syed Abd Kadir
Consultant Haematologist
Hospital Ampang

Dr. Vijayan A/L Padmanathan
Consultant Obstetrician
Hospital Gleneagles

Ms. Suryati Mokhtar
Consultant Hepatobiliary Surgeon
Hospital Selayang

PUBLICATION

Madam Lam Tsuey Peng, Sally
Madam Wan Nor Azma Wan Salleh

ACKNOWLEDGEMENT

Medical Development Division, Ministry of Health Malaysia

TABLE OF CONTENTS

LIST OF APPENDIX

LIST OF APPENDIX

ABBREVIATIONS

ABBREVIATION	DEFINITION
AHG	Anti-Human Globulin
ALI	Acute Lung Injury
ANH	Acute Normovolemic Haemodilution
APTT	Activated Partial Thromboplastin Time
AS	Additive Solution
CABG	Coronary Artery Bypass Grafting
CAIHA	Cold Autoimmune Haemolytic Anaemia
CCI	Corrected Count Increment
CKD	Chronic Kidney Disease
CMV	Cytomegalovirus
CPB	Cardiopulmonary Bypass
CPD	Citrate Phosphate Dextrose
CPDA-1	Citrate Phosphate Dextrose Adenine
CRP	C-reactive Protein
CTR	Crossmatch:Transfusion Ratio
CVP	Central Venous Pressure
DAT	Direct Anti-globulin Test
DHTR	Delayed Haemolytic Transfusion Reaction
DIC	Disseminated Intravascular Coagulation
ECG	Electrocardiogram
ECP	Extracorporeal Photopheresis
EDTA	Ethylenediamine Tetraacetic Acid
EPV	Estimated Plasma Volume
FAST	Focused Assessment with Sonography for Trauma
FBS	Foetal Blood Sampling
FFP	Fresh Frozen Plasma
FMH	Foetomaternal Haemorrhage
FNHTR	Febrile Non-Haemolytic Transfusion Reaction
FSE	Foetal Scalp Electrode
GSH	Group, Screen and Hold

ABBREVIATIONS

ABBREVIATION	DEFINITION
GTP	Gestational Thrombocytopenia
GXM	Group and Crossmatch
Hb	Haemoglobin
HCT	Haematocrit
HIT	Heparin-induced Thrombocytopenia
HIV	Human Immunodeficiency Virus
HLA	Human Leucocyte Antigen
HPA	Human Platelet Antigen
HSCT	Haematopoeitic Stem Cell Transplantation
HTC	Hospital Transfusion Committee
HTN	Hypertension
HUS	Haemolytic Uraemic Syndrome
IA	Immunoadsorption
IBCT	Incorrect Blood Component Transfusion
IC	Identity Card
IL	Interleukin
IMV	Intermittent Mandatory Ventilation
ITP	Immune Thrombocytopenic Purpura
IV	Intravenous
LCP	Leucocytapheresis
LDH	Lactate Dehydrogenase
MAHA	Microangiopathic Haemolytic Anaemia
MAP	Mean Airway Pressure
MgSO4	Magnesium Sulphate
MSBOS	Maximum Surgical Blood Ordering Schedule
N/A	Not Available
NaCl	Sodium Chloride
NHCC	National Haemovigilance Coordinating Centre
NS	Normal Saline
NYHA	New York Heart Association Functional Classification
OLT	Orthotopic Liver Transplantation

ABBREVIATIONS

ABBREVIATION	DEFINITION
PAD	Predeposit Autologous Donation
PAIg	Platelet-associated Immunoglobulin
PBM	Patient Blood Management
PCR	Polymerase Chain Reaction
PID	Primary Immunodeficiency
PO	Per Os (orally)
POCT	Point of Care Testing
pT	Prothrombin Time
RBC	Red Blood Cell
RCV	Red Cell Volume
rEPO	Recombinant Erythropoeitin
ROTEM	Rotational Elastometry
SC	Subcutaneous
STC	State Transfusion Committee
SVO_2	Mixed Venous Oxygen Saturation
TA	Therapeutic Apheresis
TBV	Total Blood Volume
TEG	Thromboelastography
TI	Transfusion Index
TNF	Tumour Necrosis Factor
TPE	Therapeutic Plasma Exchange
TSAT	Transferrin Saturation
TTI	Transfusion-transmitted Infection
TTP	Thrombotic Thrombocytopenic Purpura
WAIHA	Warm Autoimmune Haemolytic Anaemia

IMPORTANT POINTS TO REMEMBER

1. Is the transfusion really necessary?
2. Does the benefit outweigh the risk?
3. Is there any appropriate alternative?
4. Not all anaemic patients require transfusion.
5. There is no universal transfusion trigger, each patient should be evaluated individually.
6. Decision making:
    a. Transfusion should not be based on laboratory result alone
    b. Transfusion should be based on clinical assessment and evidence-based guidelines
7. Discuss the risks, benefits and alternatives with the patient and/or family members of the patient before informed consent is obtained.
8. Documentation:
    a. Reason for transfusion
    b. Benefits of transfusion
    c. Any adverse events associated with transfusion
    d. Report all adverse events
9. Ensure right blood for right patient by checking patient's identity before blood sampling and transfusion. Do not transfuse if there is any discrepancy.
10. Timely provision of blood saves lives.
11. Monitor patient's vital signs during and after transfusion.

1.0 GENERAL INFORMATION

1.1 INTRODUCTION

The Handbook on Clinical Use of Blood is written for all health practitioners involved in treating a patient who requires blood transfusion therapy, particularly doctors, nurses and medical assistants working in the hospital setting. The handbook is divided into four main components:

(1) The first three chapters provide general information. Chapter 1 focuses on pre-transfusion testing and standardized step-by-step transfusion process. Chapter 2 introduces the concept of Patient Blood Management, elaborating the three fundamental pillars to optimize care of patients who may require blood transfusion. Chapter 3 provides an outlook on clinical indication and administration of blood, blood components and plasma-derived products.

(2) The ensuing parts are written more specifically to cater to distinct clinical scenarios and have been divided based on disciplines, such as medical, surgical and anaesthesia, obstetric and gynaecology as well as paediatric. It contains summarized information meant as a reference for clinicians in their respective field. The handbook has also been updated with more specialized topics such as cardiothoracic, massive haemorrhage, therapeutic apheresis, solid organ transplant and haemopoetic stem cell transplant.

(3) Chapter 16 describes the adverse effect of blood transfusion and provides a general approach to manage a patient under those circumstances. Chapter 17 expands on the nationwide haemovigilance programme monitoring all adverse events.

(4) Last but not least, the appendices and “blood components indications and administration” insert are consolidated quick reference guides for all clinical practices.

1.2 ORDERING BLOOD AND BLOOD COMPONENTS FOR TRANSFUSION

The decision to transfuse shall be made based on clinical judgement. The benefits and risks shall be assessed and alternative therapy considered. Among the risks of blood transfusion are the transmission of infectious disease agents and transfusion reactions.

The clinician managing the patient shall be responsible for prescribing blood for that patient. The decision should be discussed between the clinician and doctor in-charge of the hospital blood bank if necessary.

1.2.1 Processes, procedures, methods and records

Each hospital shall establish adequate documentation of processes, procedures and methods pertaining to the ordering of blood and blood components for transfusion. Records shall be kept according to the stipulated time.

1.2.2 Consent for transfusion

a) The patient must give written informed consent prior to blood transfusion.

b) The clinician in charge of the patient shall explain to the patient the benefits, risks and alternatives to transfusion therapy, and ensure that the patient understands the issues discussed. The patient should be given time to think and an opportunity to ask questions. The decision of the patient regarding which therapy to take shall be clearly documented and consent shall be taken by the clinician in-charge or a fully registered medical practitioner. *Refer to **APPENDIX I** for a sample of a consent form for blood or blood component transfusion.*

c) If for any reason, the patient is unable to personally give consent, a family member of the patient shall be asked to do so. If no such family member is available, or in emergencies when the need for transfusion leaves no time for consent, the decision shall be made by two fully registered medical practitioners. This decision shall be clearly documented.

d) Each hospital shall develop its own policy for obtaining consent from patients receiving long term transfusion support, example annual consent for thalassemia cases.

1.2.3 Positive patient identification

a) Positive patient identification is a process to accurately identify patients thus avoiding medical error.

b) The phlebotomist shall ensure that the patient is correctly identified by:

   i. Asking the patient to state his/her full name and identity card (IC) number (use at least 2 identifiers) in open ended questions such as “Can you tell me your full name and IC number?”
   ii. Checking the answers given against the information stated on the patient’s identification wristband and/or case notes.

c) If it is not possible to identify the patient in the above manner (*e.g.* in the case of an unconscious patient, paediatric patients or in cases of emergencies), the phlebotomist shall identify the patient by asking the relative or carer to name the patient and then check the answer given against the information stated on the patient’s identification wristband and case notes.

1.2.4 Taking and labelling patient’s blood sample

a) The process of taking and labelling of blood samples is critical to ensure that the right blood sample is collected from the right patient.

b) The above procedure shall be carried out as **one process** by **one personnel at the bedside.**

c) Only **one patient** shall be attended to at any **one time** until completion.

d) The phlebotomist shall clearly and accurately label the blood sample at the patient’s bedside immediately after blood taking.

e) Use of pre-printed labels are not encouraged. If this cannot be avoided the hospital shall be responsible to establish and implement a procedure to ensure that patient is correctly identified using the pre-printed labels.

f) Information on the label shall include, at the minimum, the patient's full name, hospital registration number (or IC number), the date and time of collection and the initial of the phlebotomist.

1.2.5 Blood samples for red cell transfusion

a) Collect the required amount of blood into the appropriate sample tube as follows:

Table 1.1: Amount of blood samples required for first time red cell transfusion

Infant up to 4 months old	Older than 4 months old
Infant: 1.5 – 2 mL blood sample in EDTA tube. Mother: 3 – 5 mL blood sample in EDTA tube.	3 – 5 mL of blood sample in EDTA tube.

b) Repeated red cell transfusion

Table 1.2: Amount of blood sample required for repeat red cell transfusion

Infant up to 4 months old	Older than 4 months old
No further sample required for repeated transfusion for the same admission provided there are no unexpected maternal red cell antibodies in the maternal/infant serum, and the infant's Direct Anti-globulin Test (DAT) is negative when first tested. If either the antibody screen or the DAT (or both) are positive, further sample will be necessary for serological investigation or full compatibility testing.	If a patient requires repeated red cell transfusion during the same admission, each request for red cells shall be accompanied by a new blood sample of 3 – 5 mL of blood in EDTA tube.

c) Elective cases

For elective cases, samples should be sent to the hospital blood bank during office hours at least 24 hours before the blood is required except for rare blood groups and/or RhD negative where the hospital blood bank should be informed at least 5 working days in advance. Appropriate arrangement is necessary to ensure that the blood units are available in a timely manner.

1.2.6 Blood samples for blood components (other than red cells) transfusion

a) A new request for blood component other than red cells shall be accompanied by a blood sample.

b) For a patient who has at least two previous blood grouping records at the hospital blood bank, a new blood sample need NOT accompany the request for blood component. However, a copy of the previous request form clearly stating the blood grouping results shall be attached to the new request form.

c) For ABO mismatched haematopoietic stem cell transplantation, this is not applicable. A new sample must accompany all requests in the immediate post-transplant period until the patient's blood group has changed to that of the donor.

d) If previous request form is not available, a fresh blood sample shall be sent to the hospital blood bank to determine the patient's blood group.

1.2.7 Request forms

a) The clinician shall ensure that each request form is duly completed. *Refer **APPENDIX II** for an example of a blood transfusion request form.*

b) The clinician shall ensure that the quantity of red cells requested for elective surgical patients follows the Maximum Surgical Blood Ordering Schedule (MSBOS) of each hospital. *Refer **Section 5.5: Maximum Surgical Blood Ordering Schedule (MSBOS).***

c) The clinician shall sign and clearly state his/her name in block letters on the request form.

1.2.8 Type of request

a) Group, screen and hold (GSH)

b) Group and crossmatch (GXM)

Table 1.3: Difference between Group, Screen and Hold (GSH) with Group and Crossmatch (GXM)

Group, Screen and Hold (GSH)	Group and Crossmatch (GXM)
i) Determination of the ABO and RhD grouping and screening for unexpected red cell antibodies. In the event of positive antibody screening for operations or procedures, every effort shall be made to provide blood that is antigen negative (with respect to the identified antibody).	i) Hospital blood bank shall perform crossmatching of units of blood identified for issue to a patient, if using tube method: • at room temperature • at 37°C • at AHG phase If the laboratory uses other standard methods (*e.g.* column agglutination technology), manufacturer's recommendations shall be followed.
ii) Patient's serum or plasma is subsequently retained for 48 hours in the hospital blood bank so that it is available for use in the event that crossmatched blood is required within that period.	ii) When a clinically significant red cell antibody is identified, every effort shall be made to provide blood that is antigen negative (with respect to the identified antibody). This is to avoid risks of haemolytic transfusion reaction or anamnestic response.
iii) Recommended for cases in which the likelihood of transfusion is less than 30% and should be used in conjunction with a locally established Maximum Surgical Blood Ordering Schedule (MSBOS).	iii) Where fully compatible blood is not available, and the patient needs urgent transfusion, the hospital blood bank shall discuss with the clinician in charge of the patient for the issue of the most compatible blood. The decision to use the most compatible blood shall be made after taking into consideration:- • the potential risks of adverse reactions • the potential risks of harm to the patient owing to delay in transfusion arising from the search for fully compatible blood.

Group, Screen and Hold (GSH)	Group and Crossmatch (GXM)
	iv) Crossmatched samples, after testing, shall be retained securely and under appropriate storage conditions, for a minimum of 7 days for the purpose of any investigation, if required. Local policies pertaining to the period of retaining the samples shall be established.
	v) The ward personnel shall be responsible to ensure that blood that is no longer required for transfusion is returned to the hospital blood bank as soon as possible.
	vi) Crossmatched blood in the hospital blood bank that has not been issued shall be released into stock after 48 hours.

1.2.9 Receiving requests

The hospital blood bank personnel shall ensure that the request form is duly completed and the corresponding samples are correctly labelled. Information on the request form and the label of the sample shall match.

1.2.10 Rejection of requests

a) Rejection of requests shall comply with local policies and procedures.

b) However in **LIFE THREATENING SITUATIONS,** the hospital blood bank shall immediately facilitate the resolution of any discrepancies that cause the rejection of the request by discussing the case with the requesting clinician. Any resolution including that made through a telephone conversation shall be fully documented.

1.3 PRE-TRANSFUSION TESTING

Pre-transfusion testing in the laboratory includes at least ABO and RhD grouping, antibody screening and crossmatching. Other relevant tests such as antibody identification or subgroup identification are carried out when necessary. The rationale is to ensure that the right blood type is given to the patient.

1.3.1 Registration of request for transfusion

The hospital blood bank shall register all requests for transfusion.

1.3.2 Determination of ABO and RhD Group

a) Blood grouping shall be carried out twice.

b) All unanticipated findings noted when determining the ABO and RhD grouping tests shall be fully investigated and documented.

Refer to ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.***

1.3.3 Antibody screening

Antibody screening is mandatory for all requests for blood transfusion.

Refer to ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.***

1.3.4 Record of previous transfusions

a) Record of previous transfusions shall be traced prior to new blood transfusion.

b) Any discrepancy between the current and previous blood group shall be fully investigated and documented.

1.3.5 Antibody identification

a) Antibody identification shall be carried out whenever the antibody screening test is positive, and/or incompatible crossmatch is detected. There may be possibilities of delay in blood supply depending on the type of antibody or antibodies present.

b) In situations where the results of antibody identification are inconclusive, or in difficult cases, the hospital blood bank shall consult a reference laboratory.

c) In the event where the above consultation is unable to provide resolution, the hospital blood bank should refer the case to the reference laboratory for further investigation. The hospital blood bank shall:

   i. Send a sample of 10 mL of whole blood in EDTA tube and 10 mL of whole blood in plain tube accompanied by a duly completed request form.
   ii. Provide the reference laboratory with initial laboratory findings.
   iii. Notify the reference laboratory before sending the samples.

Table 1.4: Guide for the selection of suitable red cell units for transfusion in the presence of antibodies

Specificity	Clinical significance	Selection of units
Rh antibodies	Yes	Antigen negative
Kidd antibodies	Yes	Antigen negative
Duffy antibodies	Yes	Antigen negative
Kell antibodies	Yes	Antigen negative
Anti-S, -s	Yes	Antigen negative
Anti- A1, -P1, -N	Rarely	Red cells compatible by AHG at 37°C
Anti-M, Anti-Mia	Rarely	Red cells compatible by AHG at 37°C
Anti-M reactive at 37°C	Yes	Antigen negative
Anti-Le ^{a}, - Le $^{a+b}$, Anti-Le ^{b}	Rarely	Red cells compatible by AHG at 37°C
Anti-Le ^{a}, - Le $^{a+b}$, Anti-Le ^{b} reactive at 37°C	Yes	Antigen negative
High titre low-avidity antibodies	Unlikely	Seek advice from Reference Laboratory
Antibodies against low/high frequency antigens	Depends on specificity	Seek advice from Reference Laboratory

1.3.6 Selection of non-red cell components

a) Plasma and platelet selected for transfusion shall be compatible and preferably of the same ABO group. Table 1.5 below provides recommendation for selection of plasma and platelet transfusion.

b) If platelets of the recommended groups are not available, platelets of other groups may be given. Platelet in order of preference should be:

   i. ABO antigen compatible (not plasma incompatible).
   ii. ABO antigen incompatible.

Table 1.5: Guide for selection of plasma and platelet

ABO blood group of patient	ABO group of plasma to be issued in order of preference	ABO group of platelet to be issued*
Unknown (request sample for baseline grouping)	Issue AB if urgent	Issue O if urgent
O	O, AB	O
A	A, AB	A
B	B, AB	B
AB	AB (A or B if AB not available)	A or B

1.3.7 Transfusion Records

All transfusion records, in the form of hard or soft copies or both, shall be archived for not less than 20 years.

Refer to ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.***

1.4 TRANSFUSION PROCESS

Correct patient identification before commencing administration of blood or blood components is critical to ensure that the right blood is transfused to the right patient.

1.4.1 Identification check prior to transfusion

a) Each hospital shall establish a procedure for carrying out bedside identification checks by two person to prevent any error occurring at this stage. The checks shall include the blood bag label, blood compatibility label, request form and the patient's identity.

b) Each unit of blood supplied by the hospital blood bank shall be appropriately labelled and accompanied by a blood bag label **(Figure 1.1)**.

c) The blood compatibility label **(Figure 1.2)** shall be duly completed by the hospital blood bank and shall carry at least the following information:

   i. Full name of patient.
   ii. Identity card or passport number of patient.
   iii. Hospital registration number of patient.
   iv. ABO and RhD blood group of patient.
   v. Unique pack number (donation barcode number) of the blood product.
   vi. Date of issue.
   vii. Type of component.

d) The hospital blood bank may choose to use the PPDK 1 card for this purpose.

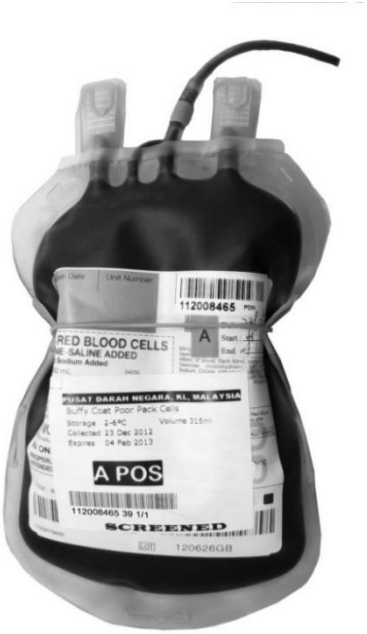


Figure 1.1: Example of a blood bag label

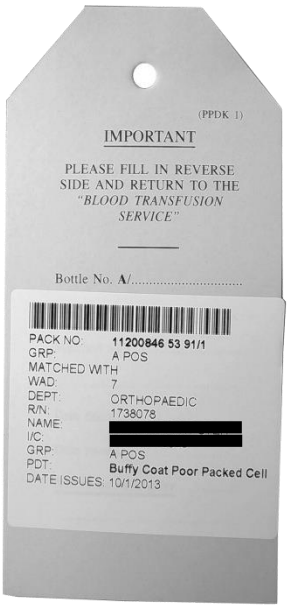
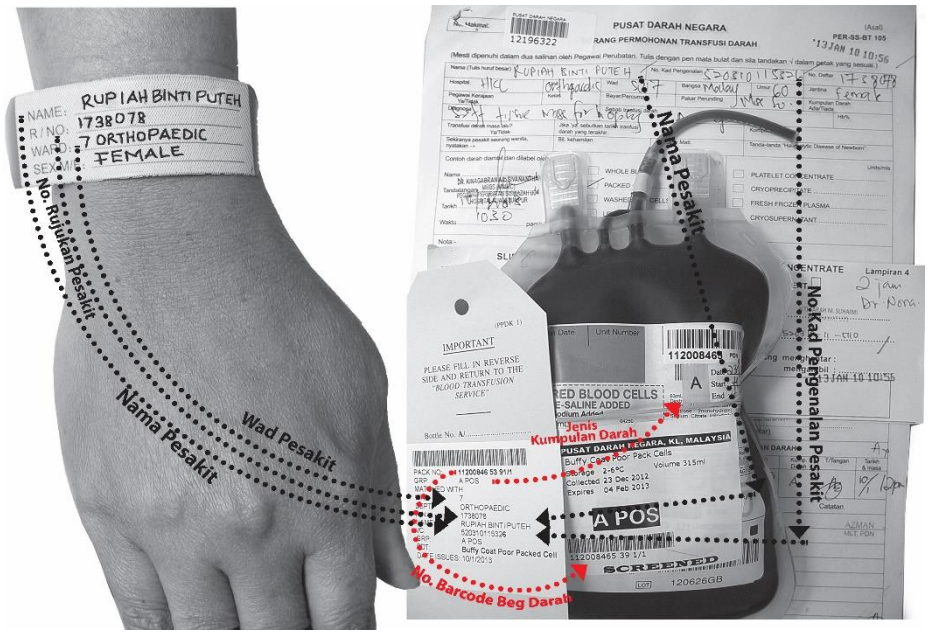


Figure 1.2: Example of a blood compatibility label (PPDK 1)

e) A check shall be conducted to ensure that the patient's information (listed in 1.4.1c above) on the blood compatibility label match those on the:

i. Blood bag label.
ii. Patient's wristband.
iii. Patient's blood request form.
iv. Case notes.

Figure 1.3: Cross-checking of patient's wristband, blood request form, PPDK 1 card and blood bag label



f) The blood or blood component shall also be visually checked for:

i. Discolouration.
ii. Presence of clots/clumps.
iii. Presence of foamy appearance.
iv. Any leakage.
v. Expiry date and time.

g) A competent personnel (doctor or paramedic) shall perform all the steps in 1.4.1b to 1.4.1f above and a second person (doctor or paramedic) shall counter-check that the steps mentioned have been carried out correctly. These shall be carried out just **BEFORE** the transfusion. The checking and the counter-checking shall be documented in a transfusion checklist form. *Refer **APPENDIX III** for example of blood/blood product transfusion checklist.*

h) In the event of any discrepancy in the identity check of intended recipient, blood compatibility label, request form and blood component, the blood bank shall be informed immediately. The implicated blood shall be returned immediately to the blood bank for appropriate measures to be taken. The chain of custody shall be documented.

i) **DO NOT** transfuse if there is any non-compliance to any of the requirements stated in 1.4.1b to 1.4.1g above.

All the steps performed above are intended to minimize the risk of a patient receiving wrong blood. Failure to adhere to these steps may lead to wrong blood transfusion resulting in harm or even death of the patient.

1.4.2 Monitoring of patient during transfusion

a) The patient shall be closely observed and monitored during blood transfusion.

b) Parameters to be monitored shall include:

i. Blood pressure.
ii. Pulse rate.
iii. Temperature.
iv. Signs and symptoms of acute transfusion reactions.

c) The vital signs shall be monitored and recorded:

i. Before starting transfusion.
ii. During the transfusion (close observation and monitoring for the first 5 to 10 minutes, and subsequently half hourly and then hourly. Perform vital sign monitoring every 15 minutes for unconscious patients receiving transfusion).
iii. After completion of transfusion.

The first 50 mL of red cells should be transfused slowly as it serves as an *in vivo* compatibility testing.

Refer ***Section 16.0: Adverse Effect of Transfusion.***

1.4.3 Record keeping

a) The following information for each transfusion shall be recorded into the patient's case note:

   i. Type of product transfused.
   ii. Identification of product transfused (donation barcode number).
   iii. Time transfusion starts and ends.
   iv. Date of transfusion.
   v. Adverse transfusion reaction, if any.

b) A copy of the blood request form (with clear compatibility test results from the blood bank) shall be kept with the patient's case notes.

1.4.4 Duration for transfusion of blood and blood components

a) Red cells:

   i. Red cells should be transfused within 30 minutes of removal from the blood refrigerator. The transfusion of each unit of red cells shall not exceed 4 hours from removal from the blood refrigerator.
   ii. There is significant risk of bacterial contamination if a unit of red cells is kept at room temperature for too long.

b) Platelet:

   i. Platelets should be transfused once received from the hospital blood bank.
   ii. The transfusion of each pack of pool platelet concentrate (4 – 6) or a plateletpheresis should be completed within one hour.
   iii. If transfusion cannot be started promptly, the platelets should be returned to Blood Bank within 1 hour of issue, for proper and safe storage.

Do not refrigerate platelets. Keep platelets at room temperature (20 – 24°C).

c) Fresh frozen plasma:

i. Once thawed, standard FFP or methylene blue treated FFP may be stored at 4 ± 2°C in an approved temperature-controlled blood refrigerator before administration to a patient as long as the infusion is completed within 24 hours of thawing.
ii. The transfusion of FFP should be completed within 4 hours of issue out of controlled temperature environment.
iii. Pre-thawed plasma can also be stored at 4 ± 2°C for up to 120 hours for use only in patients who develop unexpected major bleeding (*e.g.*: following major trauma).
iv. This extended storage of pre-thawed FFP for patients with unexpected haemorrhage was recommended to enable rapid provision of FFP for these patients where delay would be detrimental while also limiting FFP wastage.
v. All clotting factors except protein C decrease between 24 and 120 hours after thawing.
vi. Most factor VIII loss occurs within the first 24 hours following thawing after which the rate of loss decreases.
vii. For other clotting factors, the loss of activities is more linear once thawed.
viii. However, with the exception of FVIII, mean levels remain above 70% at 120 hours.
ix. To minimize the risk of bacterial growth during extended storage of thawed plasma (>24 hours), thawing methods that do not directly expose primary plasma packs to water must be used, and time out of controlled storage must be kept to a minimum.
x. Pre-thawed FFP that is out of a controlled temperature environment must be returned to blood bank immediately within 30 minutes if not used.

d) Cryoprecipitate

i. Once thawed, cryoprecipitate must not be refrozen and should be used immediately.
ii. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

e) Granulocytes (pooled or apheresis)

i. Pooled granulocytes must be transfused as soon as possible after collection and the very latest should be commence by midnight on the day following the donation (day 1).
ii. Granulocytes are issued on a named patient basis only, are kept at room temperature (20 – 24°C) without agitation.
iii. If returned, units can be reissued (to that named patient only) within the lifespan of that unit.

1.4.5 Blood administration sets

a) **ALL** blood and blood components shall be transfused through a blood administration set containing special IV tubing with an integrated filter (170 – 260 μm) to remove blood clots and particles.

b) The tubing of the administration set shall ONLY be primed with 0.9% NaCl or with the blood component itself.

c) If an administration set has previously been used for the transfusion of red cells, it shall **NOT** be used for transfusing platelets. A fresh transfusion set shall be used.

d) One blood administration sets may be used for transfusing 4 – 6 units of blood and blood components within 4 hours.

e) A mechanism may exist in the IV setup to allow the administration of 0.9% NaCl in the event of transfusion reaction *e.g.* a “Y” port.

1.4.6 Microaggregate filters

a) Microaggregate filters retain degenerating platelets, fibrin strands and red cell clumps of 20 – 40 μm. These are formed in all blood stored beyond 5 – 10 days after preparation.

b) Microaggregate filters are not used for routine blood administration. These filters are recommended to be used in:

i. Cardio-pulmonary bypass.
ii. Patients with pre-existing lung disease receiving large volume transfusion.

Microaggregate filters shall not be used for granulocyte and platelet transfusions.

1.4.7 Leucocyte filters

a) The reduction of the numbers of leucocytes in red cells can be achieved by using leucocyte filters designated for this purpose.

b) Leucocyte filters may be used for the following purposes:

i. To decrease the incidence of febrile non-haemolytic transfusion reactions.
ii. To reduce the rate of HLA alloimmunization.
iii. To reduce the rate of platelet alloimmunization.
iv. To decrease the incidence of CMV transmission.

Leucocyte filters shall not be used for granulocyte transfusions.

1.4.8 Blood warmers

a) Blood warmers are rarely needed during routine transfusion as there is no evidence that warming blood is beneficial to patients when the transfusion is slow (1 unit over 2 hours). Warmed blood minimizes the incidence of hypothermia, cardiac arrest and arrhythmia associated with massive transfusion of cold blood components.

b) Indications for use:

i. Massive or rapid transfusion.
    a. >15 mL/kg/hour in children.
    b. >50 mL/kg/hour in adult.

ii. Transfusion in neonates, *e.g.* exchange transfusion.
iii. Cold agglutinin syndrome.

c) When using blood warmers, ensure that:

i. Blood warmers shall be validated before use and maintained regularly.
ii. Each blood warmer shall have a visible thermometer and an audible warning device to detect malfunctions and to prevent haemolysis.
iii. **NEVER** warm blood by placing in hot water, microwave, on a radiator, under running water or near any uncontrolled heat source.
iv. **NEVER** refrigerate blood which has been warmed.
v. Recheck the blood unit against the intended recipient before commencing the transfusion if the blood has been placed in a common blood warmer.

1.4.9 Sodium Chloride (0.9% NaCl) / Normal saline

a) 0.9% NaCl is iso-osmotic with red blood cells. Red cells may be diluted with 0.9% NaCl to improve the flow rate.

b) Medications or solutions, other than 0.9% NaCl, **SHALL NOT** be administered through the same tubing used for blood transfusion.

The reasons for this are:

- Other solutions may affect the properties of the blood components *e.g.* Ringer's lactate solution which contains calcium additive can cause citrated blood to clot, and 5% dextrose solution can cause haemolysis.
- It may be difficult to determine the cause of an adverse transfusion reaction (whether it is due to the blood or blood component, the medication or to an interaction of the above).

c) If administration of medication is required and there is no other venous access available to allow separate administration of medication:

i. Stop the transfusion and flush the IV tubing with 0.9% NaCl before administrating medication.
ii. Flush the medication with 0.9% NaCl before resuming transfusion.

1.4.10 Discontinued transfusion

a) Any blood remaining from a discontinued transfusion **SHALL NOT** be used.

b) Remnants of blood shall be clearly labelled as “USED BLOOD” and returned to the hospital blood bank immediately.

c) Details and reasons for discontinuing the transfusion shall be clearly documented in the patient’s case notes.

1.4.11 Return of used blood bags

a) The ward shall be responsible for the return of used blood bags and the completely filled compatibility card (PPDK card/label) to the hospital blood bank within 24 hours. Used blood bag should not be mixed with compatibility card in the yellow plastic bag. Compatibility card should be returned separately for the purpose of documenting traceability of the blood or blood component bag.

b) The ward shall correctly and completely fill up a compatibility card. The compatibility card shall contain at least the following information:

i. Name of hospital.
ii. Ward.
iii. Full name of recipient.
iv. Identity card/passport number of recipient/hospital registration number of recipient.
v. Recipient’s blood group (ABO and RhD), age and gender.
vi. Date of transfusion.
vii. Time transfusion starts and ends.
viii. Volume transfused.
ix. Adverse transfusion reaction, if any.
x. Name and signature of staff starting transfusion.
xi. Name and signature of staff filling up card or form.

c) The hospital blood bank shall keep the used blood and blood component bags in a duly marked and designated refrigerator for 7 days after transfusion.

1.4.12 Return of untransfused blood

a) The ward shall return all untransfused blood immediately to the hospital blood bank. *Refer **APPENDIX IV** for instructions on proper handling of blood and blood components in the ward.*

b) Untransfused blood and blood components that are returned to the blood bank must be kept in an appropriate condition and temperature.

c) The ward shall inform the hospital blood bank if any of the unused blood returned to the blood bank has not complied with the storage or transportation temperature.

References

1. MMC Guideline: Consent for treatment of patients by registered medical practitioners. 2013.

2. Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.

3. Guide of the preparation, use and quality assurance of Blood Components, European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS), EDQM, 19th Edition, 2017.

4. Green L, Bolton-Maggs P, Beattie C *et al*. British Society of Haematology Guidelines on the spectrum of Fresh Frozen Plasma and Cryoprecipitate products: Their handling and use in various patients groups in the absent of major bleeding, BJH Guidelines, 2018. 181:59 – 60.

2.0 PATIENT BLOOD MANAGEMENT (PBM)

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 outcome *(SABM, 2015)*. It can also be defined as the appropriate provision and use of blood, its components and derivatives, and strategies to reduce or avoid the need for blood transfusion, with the ultimate goal of improved patient outcome *(AABB, 2014)*.

Patient blood management is a multidisciplinary, evidence-based approach to optimizing the care of patients who might require blood transfusion. PBM puts the patient at the centre of the decision-making process in regard to blood transfusion to ensure they receive the best treatment and to reduce unnecessary and inappropriate use of blood and blood products. The PBM approach has been used widely in many countries and had shown overwhelmingly positive outcomes.

The primary concepts of PBM are: (1) optimizing red cell mass, (2) minimizing blood loss and (3) maximising patients' tolerance of anaemia *(Isbister, James P. 2013)*. Peri-operative morbidity and mortality are markedly reduced for patients who come to surgery without anaemia and who have evidence-based transfusion policies utilized. Implementation of PBM will lead to good clinical transfusion practice, and will serve as a tool for clinical governance.

The three main pillars in patient blood management are:

a) To optimise erythropoiesis.

b) To minimise blood loss.

c) To harness and optimise physiological reserve of anaemia.

Each pillar of patient blood management can be further divided into pre-operative, intra-operative and post-operative.

1st Pillar: To optimise erythropoiesis	
Pre-operative	Detect anaemia Restrictive transfusion practice Single unit transfusion policy Identify underlying disorder causing the anaemia Manage the disorders Refer case if further evaluation is needed Treat suboptimal iron stores/iron deficiency
Intra-operative	Timing surgery with optimization of erythropoiesis and red blood cell mass
Post-operative	Manage anaemia and iron deficiency Single unit transfusion policy Restrictive transfusion practice Manage medication and possible drug interaction

2nd Pillar: To minimise blood loss	
Pre-operative	Identify and manage bleeding risk Minimise iatrogenic blood loss & phlebotomy Pre-operative autologous blood donation (in selected cases)
Intra-operative	Meticulous haemostasis and surgical technique Blood-sparing surgical technique Anaesthetic blood conserving strategies Autologous blood options (ANH & cell saver) Pharmacological/haemostatic agents
Post-operative	Vigilant monitoring and management of post-operative bleeding Keep patient warm Treat infection promptly Avoid secondary bleeding/haemorrhage Minimise iatrogenic blood loss & phlebotomy Haemostasis/anticoagulation management

3rd Pillar: To harness and optimise physiological reserve of anaemia	
Pre-operative	Formulate patient-specific management plan • Appropriate blood conservation modalities to minimise blood loss, optimise red cell mass and manage anaemia • Assess/optimise patient's physiological reserve and risk factors • Compare estimated blood loss with patient-specific tolerable blood loss • Restrictive transfusion strategies • Optimise cardiopulmonary function
Intra-operative	Optimise cardiac output Optimise ventilation and oxygenation Restrictive transfusion strategies
Post-operative	Optimise anaemia reserve Maximise oxygen delivery Minimise oxygen consumption Avoid/treat infections promptly Restrictive transfusion strategies

PBM does not necessarily apply only to patients undergoing surgery. It can be incorporated into wider clinical practices in other groups of patients such as in:

a) Critical bleeding or massively transfused patient.

b) Perioperative care.

c) Medical.

d) Critical care.

e) Obstetric & gynaecology.

f) Neonatal and paediatric.

References

1. National Blood Authority, Australia PBM modules.

2. JPAC – Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee.

3. AABB – American Association of Blood Banks.

4. Isbister, James P. The three-pillar matrix of patient blood management – An overview, Best Practice & Research Clinical Anaesthesiology, Volume 27, Issue 1, 69 – 84.

3.0 CLINICAL ADMINISTRATION OF BLOOD COMPONENTS

3.1 RED CELL TRANSFUSION

There may be a significant variation in conditions for which the use of red cells is considered appropriate. The general rules are:

a) The decision to transfuse is complex and depends on many factors *e.g.*: the cause of anaemia, its severity, chronicity, the patient's ability to compensate for the anaemia, the likelihood for further blood loss and the need to provide some reserve before the onset of tissue hypoxia.

b) Red cell transfusion should be administered primarily to prevent or alleviate the signs and symptoms of morbidity due to inadequate tissue oxygen delivery.

c) There is no single value of haemoglobin concentration that justifies the need for transfusion and the requirements of each patient should be based on their clinical status. It is generally accepted that a haemoglobin of 7.0 g/dL and above is tolerable for a healthy adult with no medical condition.

d) Red cell products should not be transfused solely for volume expansion or to enhance wound healing.

e) In certain clinical situations, it is preferable to use the patient's own blood that has been collected in advance for planned surgery (autologous blood). *Refer **Section 4.0: Autologous Blood Transfusion**.*

3.1.1 WHOLE BLOOD (WB)

Component description:

a) Blood taken from a suitable donor and collected into a pyrogen-free anti-coagulant bag without further processing. One unit of WB contains approximately 350 mL – 450 mL of blood and 49 mL – 63 mL of anti-coagulant/preservative.

b) The shelf life is dependent on the anti-coagulant/preservative used (28 to 35 days).

Indication:

a) In neonates where whole blood is used for exchange transfusion to prevent hyperkalaemia (preferably less than 5 days old).

b) If whole blood is available, can be given to patients with active bleeding of greater than 25% of total blood volume loss. If not available, red cell is used.

Contraindication and precaution:

a) Should not be given to patients with chronic anaemia who are normovolaemic and require only an increase in red cell mass.

b) WB must be transfused with extreme caution in patients with expanded plasma volume, heart failure or with hyperviscosity states.

c) Like any other cellular blood product, WB should be irradiated before transfusion for patients with profound cellular immune-deficiency or those receiving transfusion from genetically-related donors.

d) Rapid transfusion of large volume of WB may lead to hypothermia or hyperkalaemia.

Dosage and administration:

a) Dosage depends on the clinical needs of the patient and it must be adjusted accordingly.

b) One unit of WB will increase the haemoglobin by about 1 g/dL or the haematocrit by 3 – 4% in adults. In paediatric patients, 8 mL/kg will result in an increase of haemoglobin of approximately 1 g/dL.

c) Each unit of WB should complete transfusion within 4 hours of commencement.

d) Exchange transfusion is indicated in neonates born with clinically significant anaemia with or without hyperbilirubinemia due to haemolytic disease of the newborn or other causes. Preferably, WB units that are irradiated and less than 5 days old should be used for this purpose.

e) WB to be transfused must be tested to ensure compatibility with patient's serum except in life-threatening emergencies. For neonatal exchange transfusions, it should be compatible with maternal serum.

f) WB must be transfused intravenously through a blood administration set with an integrated 170 – 200 micron filter.

Storage:

a) Store at +2°C to +6°C in a validated blood refrigerator.

3.1.2 RED CELLS

Component description:

a) A component obtained by removing most of the plasma from whole blood.

Indication:

a) To increase the oxygen-carrying capacity of blood due to red cell loss or reduced erythropoiesis.

Contraindication and precaution:

a) Red cell must be transfused with extreme caution in patients with expanded plasma volume, heart failure or with hyperviscosity states.

b) Like any other cellular blood product, red cell should be irradiated before transfusion for patients with profound cellular immune-deficiency or those receiving transfusion from genetically-related donors.

c) Rapid transfusion of large volume of red cell may lead to hypothermia or hyperkalaemia.

Dosage and administration:

a) Dosage depends on the clinical needs of the patient and it must be adjusted accordingly.

b) One unit of red cell will increase the haemoglobin by about 1 g/dL or the haematocrit by 3 – 4% in adults. In paediatric patients, 8 mL/kg will result in an increase of haemoglobin of approximately 1g/dL.

c) Each unit of red cell should complete transfusion within 4 hours of commencement.

d) Red cell to be transfused must be tested to ensure compatibility with patient's serum except in life-threatening emergencies. For neonatal transfusions, it should be compatible with maternal serum.

e) Red cell must be transfused intravenously through a blood administration set with an integrated 170 – 200 micron filter.

Storage:

a) Store at +2°C to +6°C in a validated blood refrigerator.

3.1.3 RED CELLS, LEUCOCYTE-DEPLETED

Component description:

a) A component obtained from red cells by removing the leucocytes via filtration to a residual leucocyte content of $< 1x10^6$ per unit.

b) Leucocyte depletion is divided into pre-storage filtration and post-storage filtration. Pre-storage filtration will be carried out on the blood within 48 hours of collection. Bedside filtration does not ensure reduction of leucocytes, nor of the released cytokines.

Indication:

a) For patients who have had repeated febrile non-haemolytic transfusion reactions. To reduce the frequency and severity of febrile reactions.

b) Prevention of platelet refractoriness against HLA immunization and HPA immunization in transfusion-dependent patients.

c) Prophylaxis against HLA alloimmunization in patients who require intensive or long term haemotherapy such as in thalassemia patients.

d) To decrease the incidence of CMV transmission.

Contraindication and precaution:

a) Same as contraindication and precaution for red cells.

Dosage and administration:

a) Same as contraindication and precaution for red cells.

Storage:

a) Same as storage of red cells.

3.1.4 RED CELLS, CRYO-PRESERVED/DEGLYCEROLIZED

Component description:

a) A component derived from thawing frozen red cells, where most of the cryoprotectant (glycerol) is removed. Freezing (glycerolization) of red cells is carried out within 7 days of donation and deglycerolized red cells are obtained by removing the cryoprotectant.

Indication:

a) This is used for long-term preservation of red cells with rare phenotypes.

Contraindication and precaution:

a) Same as contraindication and precaution for red cells.

Dosage and administration:

a) Same as dosage and administration of red cells.

Storage:

a) Red cell, cryopreserved: less than – 65°C.

b) Deglycerolized red cells: 4 ± 2°C, Maximum shelf life of 14 days (subject to local validation).

3.1.5 RED CELLS, IRRADIATED

Component description:

a) Red cells that are irradiated with gamma rays (25 Gy) or X-rays at any time up to 14 days after collection to inactivate T-cell lymphocytes to prevent transfusion-associated graft versus host disease (TA-GVHD).

Indication:

a) To prevent transfusion-associated graft versus host disease:

i. All severe T lymphocyte immunodeficiency syndromes.
ii. Aplastic anaemia patients receiving immunosuppressive therapy with anti-thymocyte globulin (ATG).
iii. Patients receiving the biological immunosuppressive agent alemtuzumab (anti-CD52).
iv. Blood donors from first- or second-degree relatives.
v. All blood for intrauterine transfusion (IUT).
vi. All recipients of allogeneic/autologous haemopoietic stem cell transplantation.
vii. All adults and children with Hodgkin lymphoma at any stage of the disease.
viii. Patients treated with purine analogue drugs.

Refer ***Section 16.0: Adverse Effect of Transfusion***.

Contraindication and precaution:

a) Same as contraindication and precaution for red cells.

Dosage and administration:

a) Same as dosage and administration for red cells.

Storage:

a) 4 ± 2°C.

b) Red cells may be irradiated at any time up to 14 days after collection, and thereafter stored for a further 14 days from date of irradiation or up to the expiry date of the blood, whichever is earlier.

3.1.6 RED CELLS, WASHED

Component description:

a) A component derived from red cells or whole blood through sequential washing in an isotonic solution, followed by re-suspension of the red cells in an additive or saline solution. Prepared according to in-house validated protocol (manual or automated). Red cells or whole blood is suspended in the isotonic solution and the supernatant containing protein is removed. The total protein of the final supernatant shall be less than 0.5 g per unit.

Indication:

a) For patients who have had anaphylaxis with previous blood transfusions

b) For IgA deficiency patients.

Contraindication and precaution:

a) Same as contraindication and precaution for red cells.

Dosage and administration:

a) Same as dosage and administration for red cells.

Storage:

a) 4 ± 2°C.

b) Shelf life for open system (manual) must never exceed 24 hours.

c) The shelf life for closed system (automation) is 7 – 14 days (subjected to local validation).

3.2 PLATELET TRANSFUSION

3.2.1 PLATELET CONCENTRATE, RANDOM

Component description:

a) A component derived from whole blood containing majority of the original platelet content, suspended in plasma. The whole blood used for preparation of platelet concentrate shall meet the following criteria: Contains >5.5 x 10^{10} platelets in 60 – 70 mL of plasma.

Indication:

a) To provide platelet replacement for quantitative or qualitative (functionally abnormal) deficiency of platelet or due to a significant haemostatic problem.

b) Platelet count should be maintained at or above 50 x 10^9/L in trauma patients.

c) In patients who are undergoing surgery or invasive procedures who have platelet counts <50 x 10^9/L.

d) In patients with platelet count <100 x 10^9/L who have intracerebral, pulmonary, or ophthalmic haemorrhages.

e) Prophylactic transfusion for patients who have platelet count <10 x 10^9/L with active bleeding.

f) Prophylactic platelet transfusion in interventional radiology procedure:

   i. The decision to transfuse platelets to an individual patient should take into account the relative risks and benefits.
   ii. In the absence of acute bleeding, the administration of platelets may be considered appropriate at a platelet count of <20 x 10^9/L.
   iii. No improvement in bleeding complications or clinical outcomes when pre-procedural platelet transfusions were provided for platelet counts exceeding 50 × 10^9/L.
   iv. Pre-procedural platelet transfusions may be best reserved for those with active bleeding or more critical levels of thrombocytopenia.

Refer to respective clinical transfusion sections & ***APPENDIX V****.*

Contraindication and precaution:

a) Platelet concentrate is contraindicated in rapid platelet destruction/consumption:

   i. Autoimmune thrombocytopenic purpura (ITP) as platelets in the non-bleeding patient are rapidly cleared by the circulating antibodies*.
   ii. Thrombotic thrombocytopenic purpura (TTP) as transfused platelets may worsen the situation as they are consumed by the thrombi at critical sites*.
   iii. Heparin-induced thrombocytopenia (HIT) in order to avoid limb and life-threatening thrombosis*.

   **only transfuse platelet to treat life-threatening bleeding*

b) Platelet transfusion is of little clinical value in renal disease patient with (creatinine >3 mg/dL) as the transfused platelets may succumb to the same metabolic derangement causing platelet dysfunction. Instead these patients would benefit from cryoprecipitate transfusion.

c) Patients may have chills, fever and allergic reactions with platelet transfusion. DO NOT treat fever with aspirin as this will inhibit platelet function.

d) Repeated transfusions may lead to alloimmunization, resulting in refractoriness.

e) ABO compatible platelets should be used whenever possible as:

   i. Plasma in incompatible units of platelets may cause a positive direct anti-globulin test (DAT) but rarely caused haemolysis in the recipient.
   ii. The presence of ABH antigens on platelets could be targeted by the recipient's isoagglutinins.

f) Platelet concentrate contains a few red cells and when prepared from RhD positive donors may result in the production of anti-RhD antibodies in RhD negative patients. Where the product is labelled as RhD positive and given to an RhD negative female of reproductive years or younger, consideration should be given to prophylaxis with anti-D.

g) Recipients with severe cellular immune-deficiency and those receiving transfusion from related donors should be transfused with irradiated platelet concentrate to prevent TA-GVHD.

Dosage and administration:

a) 1 unit of platelet concentrate per 10 – 15 kg (typically 4 – 6 units in adults). One unit of platelet typically increases the platelet count by 5 – 10 x 10^9/L in a 70 kg adult.

b) 1 adult therapeutic dose is equivalent to 4 – 6 units.

c) Platelet concentrate must be transfused intravenously through an infusion set with an integrated 170 – 200 micron filter.

d) Platelet concentrate should be transfused once received from the hospital blood bank.

Storage:

a) Store at 20 – 24°C with agitation preferably in a platelet agitator.

b) Platelet concentrate must not be refrigerated.

c) Platelet should not be taken out of its storage condition unless for immediate transfusion. Transfusion of platelet concentrates should be completed within 1 hour of issue.

d) If transfusion cannot be started promptly, the platelet concentrates should be returned to blood bank within 1 hour of issue for proper and safe storage.

3.2.2 PLATELETPHERESIS

Component description:

a) A component containing platelets collected from an individual donor using an automated cell separation procedure and contains more than 2 x 10^{11} platelets. This is equal to 6 – 8 units of random platelet concentrates. The

volume of plasma in the product varies from 250 – 300 mL. Shelf life is 5 days from collection.

Indication:

a) Same as indication for random platelet concentrate.

b) Useful in situations where there is a need to limit exposure to multiple donors.

Contraindication and precaution:

a) Same as contraindication and precaution for random platelet concentrate.

Dosage and administration:

a) One unit apheresis will increase the platelet count of a 70 kg adult by 20 – 40 x 10^9/L.

Storage:

a) Same as storage for random platelet concentrate.

3.2.3 PLATELET, IRRADIATED

Component description:

a) Platelet component irradiated with gamma (25 Gy) or X-ray.

b) Platelet function is maintained and the shelf life is 5 days from collection.

Indication:

a) To prevent transfusion-associated graft versus host disease.

Contraindication and precaution:

a) Same as contraindication and precaution for random platelet concentrate.

Dosage and administration:

a) Same as dosage and administration for random platelet concentrate.

Storage:

a) Same as storage for random platelet concentrate.

3.2.4 PLATELET, WASHED

Component description:

a) Platelet prepared by sequential washing in an isotonic solution (0.9% NaCl solution) to remove plasma protein before resuspension into saline. Platelet shall be used immediately after preparation.

Indication:

a) For patients who have had anaphylaxis with previous blood transfusions of product containing plasma.

b) For IgA deficiency patients.

Contraindication and precaution:

a) Same as contraindication and precaution for random platelet concentrate.

Dosage and administration:

a) Same as dosage and administration for random platelet concentrate.

Storage:

a) Same as storage for random platelet concentrate.

b) When an open system has been used for the preparation of washed platelets, shelf life must not exceed 6 hours.

3.3 PLASMA TRANSFUSION

3.3.1 FRESH FROZEN PLASMA (FFP)

Component description:

a) Plasma is obtained from whole blood donation within 24 hours of collection (preferably within 12 hours) or from apheresis donation. It contains proteins such as all clotting factors, immunoglobulin and albumin.

Indication:

a) Bleeding patients with multiple coagulation factor deficiencies (*e.g.* liver disease, disseminated intravascular coagulation, dilutional coagulopathy due to massive blood loss/volume replacement).

b) Congenital factor deficiency for which there is no coagulation factor concentrate available.

c) For treatment of TTP, infusion of ≥2 litres may be necessary and is often combined with plasma exchange. It is preferable to use cryosupernatant in plasma exchange for TTP.

d) Immediate reversal of warfarin effect in the presence of potentially life-threatening bleeding when used in addition of Vitamin K where 3 or 4-factor prothrombin complex concentrate (PCC) is not available.

e) Prophylactic FFP transfusion in interventional radiology procedure:

   i. Prophylactic plasma transfusion is commonly performed before interventional radiology procedures. It is associated with deleterious effects and high costs of blood product utilization. The most common cited reason is for correction of abnormal coagulation test prior to invasive procedure.
   ii. Inappropriate FFP transfusion is usually based on three assumptions:
      - Prolonged INR/PT correlate with risks of bleeding.
      - FFP transfusion can correct abnormal PT/INR and reduce risks of bleeding.
      - Prophylactic FFP transfusion results in less bleeding. (*Segal and Dzik, 2005*)

iii. Prior studies failed to show a correlation between mild-to-moderate coagulation abnormalities (i.e. INR ≤ 2) and bleeding complications in patients undergoing invasive percutaneous procedures. (Segal, Dzik 2005)
iv. FFP has minor effect on mild to moderate prolongation of pre transfusion PT/INR and there is no relationship between mild prolongation and estimation of blood loss. (Abdel Wahab et al, 2006)
v. Recommendations:
    - Abnormal standard coagulation tests (PT/APTT) and INR are poor predictors of bleeding risk in non-bleeding patients prior to an invasive procedure.
    - FFP does not reliably normalize mild-to-moderate elevations in INR. In the absence of active bleeding FFP is not recommended for the correction of a mild coagulopathy. Therefore decreasing an elevated INR for the prevention of bleeding complications remains theoretical at best.
    - A detailed personal and family bleeding history, drug history and the bleeding risk associated with the planned procedure must be assessed as a matter of routine for all patients undergoing a planned procedure.
    - Standard coagulation tests should be considered in patients undergoing procedures with a moderate or high bleeding risk, any patients on anticoagulants, or those who have a personal/family bleeding history.
    - Patients with a positive personal/family bleeding history should be discussed with haematology as standard clotting test results may be normal in the presence of a significant bleeding tendency.
    - Impact of commonly used dose of FFP to correct clotting results or to reduce bleeding risk is very limited particularly when PT or INR are between 1.5 – 1.9.

Contraindication and precaution:

a) Should not be used:

i. For volume expansion.
ii. As a source of protein in nutritionally-deficient patients.

Dosage and administration:

a) Typically the volume of FFP from whole blood donation is 150 – 250 mL.

b) 1 mL FFP contains approximately 1 unit coagulation factor activity.

c) The dose of FFP will depend on clinical circumstances. In most cases 10 – 20 mL/kg will provide adequate amount of clotting factors and is expected to increase the level by 20 – 30%. Laboratory testing can be used as a guide in diagnosis and monitoring effectiveness of FFP transfusion.

d) FFP is thawed at 37°C for immediate use.

e) Transfusion of FFP should be completed within 4 hours of issue from controlled temperature environment.

f) The ABO group of plasma component selected for transfusion should be group compatible with the recipient. Refer to **Table 1.5**.

Storage:

a) The shelf life of FFP depends on the storage temperature. If stored at -18°C to -25°C, the shelf life is 3 months and if stored below -25°C, it can last for 36 months.

b) Once thawed, FFP must not be refrozen.

c) Once thawed, FFP may be stored at 4 ± 2°C in an approved temperature-controlled blood refrigerator before administration to a patient as long as the infusion is completed within 24 hours of thawing.

3.3.2 CRYOPRECIPITATE TRANSFUSION

Component description:

a) Concentrated source of certain plasma protein prepared from FFP which contain cryoglobulin fraction such as concentrated Factor VIII, Factor XIII, von Willebrand factor, fibrinogen and fibronectin. The volume of 1 unit is 30 – 40 mL.

Indication:

a) Generally indicated if plasma fibrinogen < 1 g/L.

b) In massive bleeding and DIC with bleeding.

c) To correct the haemostatic defects in congenital/acquired fibrinogen deficiency.

d) Factor XIII deficiency (where Factor XIII concentrate is not available).

e) May be of clinical value for treating uraemic patients with bleeding.

f) Prophylactic fibrinogen/cryoprecipitate transfusion in interventional radiology procedure:

   i. The routine use of cryoprecipitate and fibrinogen concentrate in patients with coagulopathy is not advised. The underlying cause of coagulopathy should be identified.
   ii. The decision to transfuse cryoprecipitate or fibrinogen to an individual patient should take into account the relative risks and benefits.

Dosage and administration:

a) Generally 1 unit/5 – 10 kg of patient will increase fibrinogen level by 5 mg/dL. The actual dose should be determined from the recipient's measured fibrinogen level, the nature of bleeding and other relevant clinical finding.

b) The recommended adult therapeutic dose is 2 pools of 5 units (10 units) which will raise plasma fibrinogen by 1 g/L.

Storage:

a) Once thawed, cryoprecipitate must not be refrozen and should be used immediately.

b) If delay is unavoidable, the component should be stored at ambient room temperature and used within 4 hours.

3.3.3 CRYOSUPERNATANT TRANSFUSION

Component description:

a) Cryosupernatant is the supernatant remaining after cryoprecipitate has been removed from FFP. It is essentially plasma component that has been depleted of Factor VIII, fibrinogen, fibronectin and factor XIII. The volume of 1 unit is 200 mL.

Indication:

a) Plasma component used for plasma exchange in thrombotic thrombocytopenic purpura or haemolytic-uraemic syndrome.

Dosage and administration:

a) Standard dosing is 10 – 15 mL/kg body weight.

b) For plasma exchange dosage, refer to section on plasma exchange. *Refer* ***Section 14.0: Therapeutic Apheresis.***

Storage:

a) Similar to storage of FFP.

3.4 GRANULOCYTE TRANSFUSION

Component description:

a) Granulocytes, pooled is a component that contains granulocytes obtained by pooling of up to 12 buffy coats, suspended in either plasma or a mixture of platelet additive solution and plasma. Granulocytes, pooled contains on average 11.0 × 10^9 granulocytes per unit.

b) Granulocytes, pooled has a significant content of red blood cells, lymphocytes and platelets. Thus, granulocytes components should undergo the same compatibility testing as red cells.

c) Granulocytes, pooled must be irradiated.

Indication:

a) Severe neutropenia, defined as ANC <0.5 x 10^9/L due to congenital or acquired bone marrow failure syndromes.

   i. Receiving active treatment in an attempt to achieve disease remission.
   ii. Proven or highly probable fungal or bacterial infection that is unresponsive to appropriate antimicrobial therapy as demonstrated by visible spreading lesions on skin, mucosa or radiological examination.
   iii. In whom neutrophil recovery is expected (ANC >0.5 x 10^9/L) in the near future and/or in whom definitive therapy of curative potential is planned.

Dosage and administration:

a) The recommended dose for an adult is 1 – 2 units daily and for a child 0.3 x 10^9 granulocytes/kg.

Storage:

a) Granulocytes are issued on a named patient basis only, are kept at room temperature (20 – 24°C) without agitation.

b) If returned, units can be reissued (to that named patient only) within the lifespan of that unit.

c) Granulocytes, pooled are not suitable for storage and must be transfused as soon as possible after collection.

d) If unavoidable, storage must be limited to the shortest possible period. At the very latest, transfusion should commence by midnight on the day following donation (day 1).

3.5 PLASMA-DERIVATIVE PRODUCTS

These are products that are supplied from the transfusion service (National Blood Centre).

3.5.1 Human albumin

Component description:

a) **Albumex® 20** - Human Albumin 20% (200 g/L) – contains Human Albumin 200 g/L, Sodium 48 – 100 mmol/L, octanoate 32 mmol/L.

Indication:

a) Hypoproteinaemia in the acutely ill patient: can be given when there are existing or anticipated clinical problems or complications from reduced oncotic pressure, and/or as an adjunct to diuretic therapy.

b) Shock: May be used for the resuscitation of patients in shock due to acute loss of blood or plasma, but 4 – 5% human albumin is preferred when available.

c) Burns: Extensive burns are followed by sequential shifts in the distribution of body water, salt and proteins, resulting in hypovolaemic shock and circulatory failure. Initially (during the first 24 hours), there is an increased vascular permeability leading to loss of water and proteins into the extravascular compartment and haemoconcentration. Large volumes of crystalloid solutions should be infused to restore the constricted intravascular fluid space and smaller amounts of albumin solution are required to maintain adequate plasma volume and colloid osmotic pressure.

d) Adult respiratory distress syndrome: The clinical syndrome is characterised by inadequate oxygenation secondary to pulmonary interstitial oedema, complication of shock and post-operative state resulting in a decreased central

venous pressure, decreased plasma albumin concentration, rising blood pressure, reduced cardiac output, lowered pulse rate and a reducing renal output. The acute condition can be controlled by diuretics and human albumin solution in amounts sufficient to maintain vital signs. In patients who have undergone abdominal surgery, the intravenous administration of albumin solution (20%) immediately after the operation has been shown to improve lung compliance and gaseous exchange.

e) Haemodialysis: can be used to assist with the rapid removal of excess extravascular fluid and to maintain perfusion pressure.

f) Plasma exchange: The choice of replacement fluid and its concentration are determined by the particular clinical situation and the frequency of the procedure.

g) Iso-oncotic albumin solution is the preferred replacement solution. If the patient's serum albumin level is not maintained, concentrated albumin (20%) may be indicated. If exchange occurs less frequently than once a week, less concentrated colloids may be appropriate.

Contraindication and precaution:

a) Must not be used if there is a history of allergy to this product.

b) Patients with cardiac failure, pulmonary oedema or severe anaemia.

c) Not justified in hypoproteinaemic states associated with chronic cirrhosis, malabsorption, protein-losing enteropathies, pancreatic insufficiency or undernutrition.

d) In chronic nephrosis, infused albumin solution (20%) is promptly excreted by the kidneys with no relief of the chronic oedema.

3.5.2 Intravenous Immunoglobulin (IVIg)

Component description:

a) **Intragam® P –** contains on average 61% IgG_1, 36% IgG_2, 3% IgG_3 and 1% IgG_4, contains only trace amounts of IgA (nominally <0.025 mg/mL). Has 6 g human protein and 10 g of maltose in each 100 mL bottle.

Indication:

a) Replacement IgG therapy in:

   i. Primary immunodeficiency (PID).
   ii. Myeloma and chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections.
   iii. Congenital or acquired immune deficiency syndrome with recurrent infections.

b) Immunomodulatory therapy in:

   i. Immune Thrombocytopenic Purpura (ITP), in adults or children at high risk of bleeding or prior to surgery to correct the platelet count.
   ii. Allogeneic bone marrow transplantation.
   iii. Kawasaki disease.
   iv. Guillain-Barré Syndrome (GBS).

Contraindication:

a) Patients who have had a true anaphylactic reaction to a human immunoglobulin preparation.

3.5.3 Prothrombinex complex concentrate (PCC)

Component description:

a) Human prothrombinex complex concentrate containing purified human coagulation factors II, IX and X and low levels of factor V and VII.

Indication:

a) Acquired deficiency of the prothrombin complex coagulation factors caused by treatment with vitamin K antagonists, or in case of overdose of vitamin K antagonists when rapid correction of the deficiency is needed (*e.g.*: warfarin reversal). *Refer* ***Section 13.0: Transfusion in Medicine and Haematology.***

b) Congenital deficiencies that need perioperative bleeding prophylaxis, in any vitamin K dependent coagulation factors (if purified specific coagulation factor product is not available).

c) Prevention or treatment of bleeding in Haemophilia B (when pure factor IX concentrate is not available), Factor II and Factor X deficiency.

Contraindication:

a) Evidence of active thrombosis or disseminated intravascular coagulation.

b) Known hypersensitivity to the active substances (including those who have known allergy to heparin or history of heparin-induced thrombocytopenia).

3.5.4 Plasma-derived factor VIII concentrate (Biostate)

Component description:

a) Contains factor VIII and von Willebrand factor.

Indication:

a) Prevention and treatment of bleeding in Haemophilia A.

b) Prevention and treatment of bleeding in von Willebrand disease.

c) Immune tolerization in Haemophilia A with inhibitor.

Contraindication and precaution:

a) Known patient with hypersensitivity to the active substances.

References

1. British Society of Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding.

2. Guide of the preparation, use and quality assurance of Blood Components, European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS), EDQM, 19th Edition, 2017.

3. Shaz, B. H., Hillyer, C. D., Roshal, M., & Abrams, C. S. (Eds.). (2013). *Transfusion medicine and hemostasis: clinical and laboratory aspects*. Newnes.

4. Product Information Albumex® 20

5. Product Information Intragam® P

6. Product Information : Prothrombinex®-VF

4.0 AUTOLOGOUS BLOOD TRANSFUSION

Autologous blood transfusion is the collection and subsequent transfusion of the patient's own blood. It prevents transmission of diseases like hepatitis, HIV and syphilis and avoids immunological complications like alloimmunization, immunosuppression (immunomodulation) and some transfusion reactions. It is the safest component as it provides the safest blood for those who have alloantibodies or rare blood. It is indicated for patients having elective surgical procedures for which blood transfusion is very likely required and patient is at risk for significant blood loss.

Local policy and standard operating protocol shall be established in each hospital.

4.1 TYPES OF AUTOLOGOUS TRANSFUSION

4.1.1 Predeposit Autologous Blood (PAB)

Predeposit autologous blood donation is not recommended unless in certain circumstances such as a patient with rare blood group or multiple red cells alloantibodies. In this situation, planning and evaluation of the patient is crucial before PAB is attempted. In PAB, patient's blood is drawn a unit at a time, usually from three to five weeks before an elective surgical procedures or earlier if freezing is required and stored in the blood bank before transfusion at the time of surgery.

Indication of PAB: Patients with rare blood group or multiple red cells alloantibodies with significant expected blood loss resulting from elective surgery.

4.1.2 Acute Normovolaemic Haemodilution (ANH)

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

Indication of ANH: Recommended when only 1 – 2 units of blood is required. It should be considered when potential blood loss is likely greater than 20% of blood volume.

4.1.3 Intra-operative Blood Salvage (IBS)

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

4.2 SELECTION OF PATIENT

4.2.1 Inclusion criteria

a) The level of haemoglobin depends on the procedure.

4.2.2 Exclusion criteria

a) Unwillingness of patient to undergo procedure.

b) Positive for Syphilis, Hepatitis B, Hepatitis C, HIV or other relevant infection.

c) Evidence of acute infection.

d) Severe haemodynamic problems, active systemic infections or a history of serious reactions to donation (such as seizure).

e) Significant aortic stenosis, prolonged and/or frequent angina, significant narrowing of the left main coronary artery, cyanotic heart disease and malignancy.

f) History of epilepsy.

g) Patients with diarrhoeal illnesses in the days or weeks before donation should not donate as their donated blood may be at increased risk of bacterial contamination.

h) Haematological disease (*e.g.* sickle cell disease, cold agglutinin disease).

i) Renal failure.

j) *Pregnant.

*Autologous collection in an uncomplicated pregnancy should not be performed, unless circumstances exist that increases the risk of transfusion. However, both the ordering clinician and the blood bank specialist need to carefully consider the risks of the collection procedure against any perceived benefit.

Patients with rare blood groups may opt for PAB where blood can be frozen until required.

4.3 PREDEPOSIT AUTOLOGOUS BLOOD TRANSFUSION

a) Selection of patient will be done by the treating surgeon or anaesthetist.

b) The patient should be able to tolerate repeated loss of the predetermined volume collected which is normally no more than 10% of their estimated blood volume.

c) A letter of referral shall be made to the blood bank and the blood bank specialist/doctor have to assess the patient before admitting into the autologous programme.

d) Blood collection begins three to five weeks before the elective surgery, depending on the number of units required and the last collection should not be less than 3 days (72 hours) prior to surgery.

e) It is recommended that donations should be 7 days apart but may be as frequent as every 3 days. Six units can be collected as the blood can be kept in an optimal additive solution for up to 42 days.

f) The availability of the autologous blood should be written in the case notes and request form so that allogenic blood is not crossmatched.

g) Haemoglobin should be >11 g/dL in both men and women.

4.3.1 Collection

a) Clinicians should determine the number of units required and inform the doctor or specialist in-charge of the blood bank in the referral letter. ***(APPENDIX VI)***

b) Written consent is obtained after adequate explanation is given to the patient. ***(APPENDIX VII)***

c) Haemoglobin level should be monitored before each donation to ensure that it is >11 g/dL.

d) Iron supplements (preferably intravenous route) should be prescribed before the first donation until surgery.

e) Erythropoietin may be considered.

f) The last donation should take place 3 days before surgery to allow for the re-equilibration of the blood volume.

g) If the surgery is postponed, then the oldest autologous blood can be reinfused and fresh blood collected ("leap-frog" technique).

4.3.2 Storage

a) Preferably, a dedicated refrigerator should be allocated to store the autologous blood collected. Blood collected in CPDA-1 bag can be stored for 35 days. Red cell suspended in optimal additive solution has an extended shelf life of 42 days.

b) The autologous collection should be clearly labelled with special labels. The patient's name and an indication 'autologous use only' must be clearly stated.

c) If transfusion becomes necessary, the freshest unit is transfused first.

d) All unused blood should be discarded when they expire. This must be explained to the patient during counselling and consent.

4.3.3 Laboratory Tests

a) Serological tests

   i. ABO and RhD grouping is performed on each bag and results are indicated on the bag. Antibody screening is performed ONLY on the first donation.

b) Microbiological screening

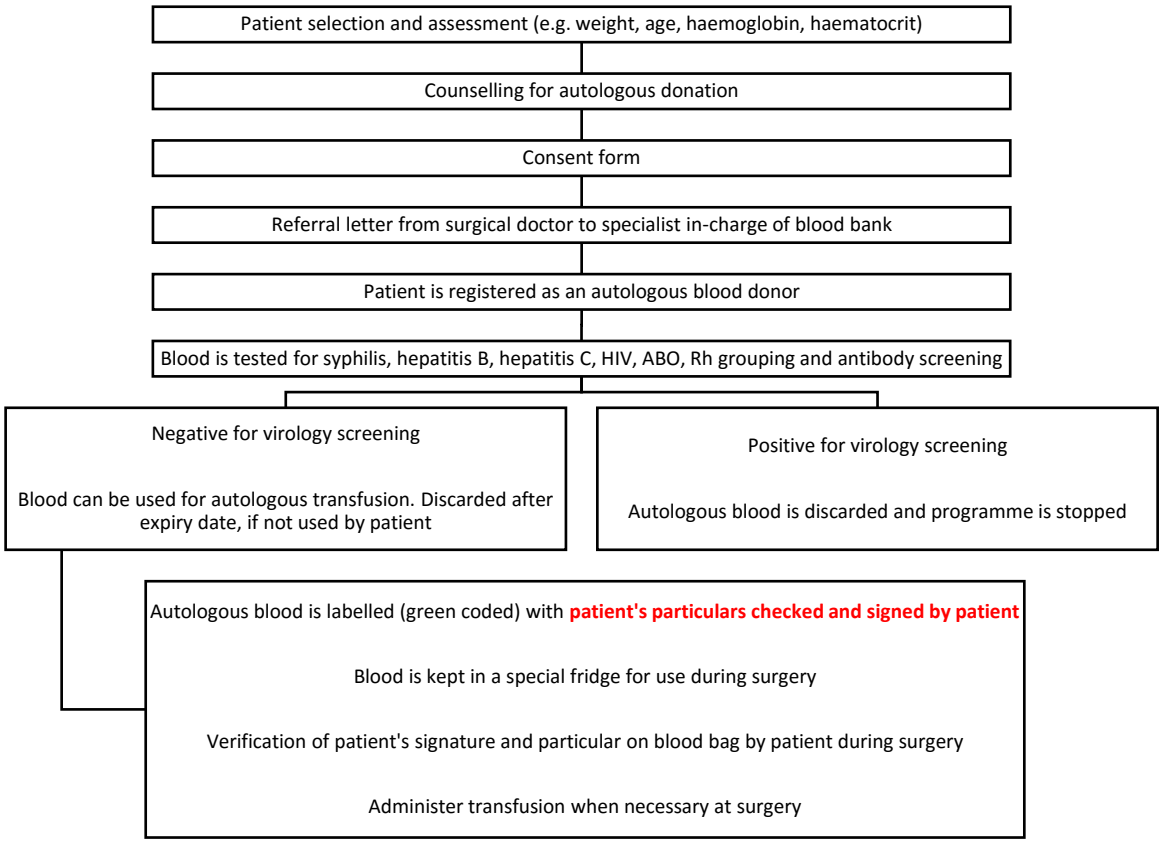
   i. HBs-Ag, anti-HIV 1/2, anti-HCV and syphilis screening tests are done on the first and last donations. If any test is found to be positive, the patients are excluded and the donated blood is discarded. Nucleic acid testing (NAT) is not mandatory.

c) Compatibility testing

   i. Upon admission to hospital for surgery, patients with stored autologous blood should have a fresh venous blood sample taken. Test should be done for ABO, RhD group, antibody screening and crossmatching with the autologous blood stored.

The summary of activities for predeposit autologous blood is shown in Figure 4.1.

Figure 4.1: Summary of activities for predeposit autologous blood transfusion



4.4 ACUTE NORMOVOLAEMIC HAEMODILUTION (ANH)

In ANH, the patient's own blood is collected immediately prior to commencement of surgery along with simultaneous replacement using sufficient crystalloids and colloids. It is recommended that 3 mL crystalloid or 1 mL of colloid is infused for replacement for each 1 mL of blood withdrawn to maintain circulatory blood volume.

ANH is recommended when only 1 or 2 units of blood are required. It should be considered when potential blood loss is likely to be greater than 20% of blood volume. Pre-operative haemoglobin level must be more than 12 g/dL. Blood bag containing CPDA-1 is used as CPDA-1 is easily and quickly metabolized in the absence of liver disease and does not induce a clinical coagulopathy when re-infused slowly. It can be provided by the blood bank, preferably using a single bag instead of a triple bag which is usually used in blood donation drive. This procedure should only be performed by the anaesthetist.

4.4.1 Benefits of acute normovolaemic haemodilution

a) Reduction in red cell loss during operation secondary to reduced haematocrit.

b) Improved oxygen delivery secondary to reduction in whole blood viscosity.

c) Blood is stored at room temperature for a short time, thus deterioration of clotting factors and cells are minimal.

4.4.2 Procedure

a) Full explanation should be given to the patient regarding the nature of the procedure.

b) Patient's haemoglobin and haematocrit level should be checked.

c) Screening of infective viral markers is not required. However, if the patient is known to be positive for these markers, he/she is excluded from ANH.

d) Venesection is done immediately prior to surgery.

e) The blood volume to be removed can be calculated using the following formula:

$$V = EBV\ x\ \frac{(Hi - H_f)}{H_{av}}$$

$V - volume\ to\ be\ removed$

$EBV - estimated\ blood\ volume$

$H_i - initial\ hematocrit$

$H_f - desired\ hematocrit$

$H_{av} - average\ hematocrit\ (mean\ of\ H_i\ and\ H_f)$

f) Blood is collected in standard blood bags containing CPDA-1. This procedure takes 10 – 20 minutes (2 units). The patient's name, date of collection, time of collection and order of collection should be stated and labelled on the bag.

g) Simultaneously, blood is replaced via a second venous line using crystalloids or colloids.

h) The haemoglobin can fall to 9 g/dL (haematocrit 27%). Circulatory volume should be maintained at all times.

i) The blood is stored at room temperature and re-infuse during surgery after major blood loss has ceased, or sooner if indicated. When stored at room temperature (up to 8 hours), the platelet functions and coagulation factors are still preserved. If the blood is not re-infuse after 8 hours of collection, it can be stored in a monitored refrigerator (2 – 4ºC) for up to 24 hours.

j) Pre-infusion checks of patient's identity and the blood units are mandatory.

k) Blood units are re-infused in the reverse order of collection. The first unit collected will be the last unit transfused. It would have the highest haematocrit and concentration of coagulation factors and platelets.

l) Records of collection and re-infusion should be entered into the patient's anaesthetic and/or case notes.

m) Any unused autologous blood should be disposed as hazardous waste.

4.5 INTRA-OPERATIVE BLOOD SALVAGE

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

b) For effective and safe use, active management by the lead clinician and adherence to standard operating procedure is required.

c) Records of the procedure should be documented.

d) This procedure is mostly used in cardiac surgery, trauma surgery and liver transplant. It is carried out by the anaesthetist at the time of surgery.

e) It is contraindicated in malignancies, chronic obstructive airway disease, sickle cell disease, sickle cell trait and surgeries with high risk of contamination such as gastrointestinal surgery.

4.5.1 PROCEDURE

a) Shed blood is aspirated from the operative field into a specially designed centrifuge to concentrate the salvaged red cells.

b) Citrate or heparin anti-coagulant is added and the contents are filtered to remove clots and debris.

c) The salvaged red cells are then re-suspended in normal saline with a resultant haematocrit of 50 – 80%.

d) The salvaged red cells may be transfused immediately or within 48 hours of processing kept at room temperature (18 – 22°C). If the product is refrigerated at 2 – 6°C within 4 hours of processing, reinfusion can occur within 24 hours.

e) The red cells are transfused through 170 µm – 200 µm screen filter, as in a standard blood administration set.

f) Any unused autologous blood should be disposed as hazardous waste.

4.6 AUTOLOGOUS PLASMA FOR EYE DROPS

Eye drops made from autologous plasma are used in ocular surface disorders. Plasma can accelerate and enhance healing, reduce inflammation and improve haemostasis. Patient selection is similar to predeposit autologous blood transfusion and the responsibility of counselling and requesting for the autologous transfusion lies on the ophthalmologist managing the patient. After processing at the blood bank, the autologous plasma eye drop aliquots will be issued to the treating ophthalmologist. The autologous plasma must be stored at -20ºC for maximum up to 6 months. Once thawed, it should be used immediately or can be stored in 4 degree for daily usage up to 16 hours. Autologous eye drops should not be used by anyone else.

References

1. Rossi's Principles of Transfusion Medicine, 4th edition, 2009.

2. Clinical Review Autologous Transfusion, BMJ 2002;324, 772-5

3. Guidelines on Autologous Blood Transfusion, Pusat Perkhidmatan Darah Hospital Kuala Lumpur dan Bahagian Perkembangan Perubatan Kementerian Kesihatan Malaysia.

4. Guidelines for policies on alternatives to allogeneic blood transfusion. Predeposit autologous blood donation and transfusion, 2007

5. Cell salvage as part of a blood conservation strategy in anaesthesia, Ashworth. A. and Klein. A. A., British Journal of Anaesthesia 105 (4): 401–16 (2010)

6. AABB Technical Manual, 2015, 17th edition

7. Handbook of Transfusion Medicine, Norfolk D. 5th edition (2013)

8. G Geerling, G, S MacLennan, D Hartwig. Autologous serum eye drops for ocular surface disorders. The British Journal of Opththalmology. 2004;88(11):1467-1474. Doi:10.1136/bjo.2004.044347.

5.0 TRANSFUSION IN SURGERY AND ANAESTHESIA

Transfusion in surgery and anaesthesia is usually indicated in cases of anaemia, blood loss and coagulopathy. Several strategies to reduce exposure to allogeneic transfusion include autologous transfusion, surgical, anaesthetic and pharmacological approaches to reduce blood loss.

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

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

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

- Pre-operative.
- Intra-operative.
- Post-operative.

Table 5.1: Patient Blood Management In Surgical Patients

	Optimise the Patient's Red Cell Mass	**Minimise Blood Loss**	**Improve Patient Tolerance of Anaemia and Rationalise Blood Product Usage**
Preoperative	• Detect anaemia • Identify the cause • Treat the cause • Manage iron deficiency • Treat other haematinic deficiencies • Stimulate erythropoiesis • Recommend specialist consultation, if necessary	• Identify and treat haemostatic abnormalities • Minimise iatrogenic blood loss • Plan and re-assess procedures • Use autologous blood donation for selected cases	• Assess the patient's physiological reserve • Optimise cardiac output through maintenance of normovolaemia and rational use of vasoactive substances • Compare estimated blood loss with the patient's tolerable blood loss • Plan blood conservation modalities • Use restrictive transfusion protocols

	Optimise the Patient's Red Cell Mass	Minimise Blood Loss	Improve Patient Tolerance of Anaemia and Rationalise Blood Product Usage
Intraoperative	• Timed surgery with haematological optimization	• Use meticulous haemostasis • Use blood-sparing surgical techniques • Use induced hypotension in selected cases • Keep low venous pressure • Use intraoperative blood salvage • Use haemostatic drugs (tranexamic acid) • Use point of care haemostasis tests	• Optimise cardiac output • Optimise ventilation and oxygenation • Use restrictive transfusion protocols • Use acute normovolaemic haemodilution in selected cases
Postoperative	• Assess anaemia • Manage iron deficiency • Stimulate erythropoiesis • Awareness of drug interactions which can aggravate anaemia	• Monitor closely haemostasis and bleeding • Avoid secondary haemorrhage • Assess antithrombotic prophylaxis and treatment management • Reduce iatrogenic blood loss • Maintain normothermia • Plan autologous blood conservation modalities in selected cases • Use prophylaxis of upper gastrointestinal bleeding	• Optimise the patient's physiological reserve • Maximise oxygen delivery • Minimise oxygen consumption • Use restrictive transfusion protocols • Avoid/Treat infections promptly

Adapted from Filipescu et al. Perioperative Patient Blood Management Programme. Multidisciplinary recommendations from the Patient Blood Management Initiative Group (2017).

5.1 PRE-OPERATIVE MANAGEMENT

a) The anaesthetist and surgeon must play a lead role in ensuring good pre-operative assessment and preparation.

b) Pre-operative anaemia should be identified, evaluated and managed:

   i. Assessment of iron stores and institution of iron therapy.
   ii. Procedure is planned to allow optimization of haemoglobin.

c) Anaemia screening for patients undergoing elective surgery must be done in a timely manner to allow enough time for diagnosis and management of anaemia and the underlying cause.

d) Prior to the surgery, the estimated blood loss that can be tolerated by the patient and the lowest acceptable haemoglobin level should be estimated.

e) Use of anti-coagulant and anti-platelet agents should be reassessed pre- and post-operatively.

5.1.1 Treatment of pre-existing anaemia

a) Anaemia is a global health problem, affecting approximately 30% of the population. 30 – 50% of the cases are caused by iron deficiency.

b) Peri-operatively, patients with anaemia need more blood transfusion and their outcome is less favourable.

c) Therefore, anaemic patients must be identified and treated before surgery.

d) Please refer to ***APPENDIX VIII:*** *Algorithm for patient red cell mass optimization.*

5.1.2 Treatment of thrombocytopenia

For most surgical procedures, the safe threshold for platelet count is more than 50 x 10^9/L while surgery in critical areas may require a higher threshold as shown in the table below.

Table 5.2: Safe threshold for platelet count in surgery and invasive procedure

Indication	Safe threshold for platelet count	
Most invasive surgery (including post-cardiopulmonary bypass)	100 x 10^9/L	
Neurosurgery or posterior eye surgery	100 x 10^9/L	
Prevention of bleeding associated with invasive procedures	Lumbar puncture	50 x 10^9/L
	Central-line insertion	50 x 10^9/L
	Liver, renal* or transbronchial biopsy	50 x 10^9/L
	Gastrointestinal endoscopy with biopsy	50 x 10^9/L
Spinal anaesthesia	100 x 10^9/L	
Epidural anaesthesia	100 x 10^9/L	

**** Prior to renal biopsy, ensure potential risk of bleeding are corrected: anaemia (iron and erythropoietin), uraemia (dialysis). If renal biopsy is urgent, consider desmopressin (DDAVP) pre-procedure or estrogen if time allow.***

5.1.3 Predeposit Autologous Donation (PAD)

PAD is a procedure in which patient's blood is withdrawn before surgery to be stored and re-infused if required during the surgery or immediate post-operative period. *Refer **Section 4.0: Autologous Blood Transfusion**.*

5.1.4 Avoidance of drugs that increase surgical blood loss

a) In the setting of emergency surgery, the decision depends on how soon the surgery needs to be performed.

   i. For surgery that can be delayed for 6 to 12 hours and requires reversal of warfarin, the INR can be corrected by giving intravenous vitamin K (2 – 5 mg).

ii. For surgery that cannot be delayed and requires reversal of warfarin, the INR can be corrected with PCC (30 IU/kg) and intravenous vitamin K.

b) The decision on bridging therapy depends on the bleeding risk of surgery versus the thromboembolic risk of a patient. Discussion with the physician / haematologist is required as management of each patient should be individualised based on patient factors.

c) Many patients awaiting planned surgery receive warfarin or other drugs (aspirin, NSAIDS, ticlopidine and clopidogrel) that affect blood coagulation or platelet function. Where it is safe to do so, it is generally advised that such drugs be stopped prior to major surgery, giving sufficient time for their effect on coagulation to decline. ***(APPENDIX IX)***

d) Refer peri-operative management for patients on anticoagulation. ***(APPENDIX IX, APPENDIX X and APPENDIX XI)***

Table 5.3A: Periprocedure management of warfarin and requirement for bridging heparin therapy

Assess thrombotic risk	
Low risk	Primary low-risk thromboprophylaxis (*e.g* Fontan surgery, stable).
Medium risk	Vascular thromboembolism >3 months from onset. Primary thromboprophylaxis for dilated cardiomyopathy, rheumatic valvular heart disease and mechanical heart valves.
High risk	Vascular thromboembolism ≤3 months from onset. Pulmonary embolism. Recurrent thromboembolism. Primary thromboprophylaxis for primary pulmonary hypertension. Past history of prosthetic valve thrombosis. Homozygous protein C deficiency.
Assess risk of periprocedure bleeding. Patients undergoing procedures with low risk of bleeding do not require interruption of warfarin therapy. These procedures include: • Tooth extractions and endodontic (root canal) procedures. • Small skin excisions (*e.g.* skin biopsy). Stop warfarin 5 days prior to the scheduled operative procedure. Determine strategy for periprocedure bridging therapy based on estimated risk for thrombosis.	

Adapted from Clinical Practice Guidelines: Prevention and Treatment of Venous Thromboembolism, Ministry of Health Malaysia, August 2013.

Table 5.3B: Periprocedure management of warfarin and requirement for bridging heparin therapy

Risk	Preprocedure bridging	Postprocedure bridging*	Restart of warfarin*
Low	No.	No.	Usual maintenance dose on night of procedure.
Intermediate	Enoxaparin 1 mg/kg BD when PT-INR <2; continue until AM of day prior to procedure (PM dose on day before and AM dose on day of procedure omitted).	Enoxaparin 1 mg/kg BD, beginning PM of day of procedure (if no bleeding concerns); else begin on AM of day after procedure.	Restart warfarin at usual maintenance dose on PM of the day after the procedure provided no contraindications. Check PT-INR 3 days later and titrate dose. Continue enoxaparin until PT-INR >2.
High	Enoxaparin 1mg/kg BD when PT-INR <2; continue until AM of day prior to procedure. Commence unfractionated heparin (starting at 20 unit/kg/hour) 4 hours after last dose of enoxaparin and continue until 1 hour prior to procedure.	Restart unfractionated heparin (UFH) 1 hour postprocedure (if no bleeding concerns) and adjust using APTT (target 60 – 80 seconds). Maintain on UFH as long as higher bleeding risk. Restart enoxaparin 1mg/kg BD as soon as bleeding risk low (start at same time of stopping UFH).	Restart warfarin at usual maintenance dose at day 5 postprocedure provided no contraindications. Check PT-INR 3 days later and titrate dose. Continue enoxaparin until PT-INR >2 (aim for anti-Xa activity of 0.5 – 1.0 unit/mL).
* Timing of postprocedure anticoagulation depends on assessment of risk of postprocedure bleeding. Close consultation advised with surgeon/physician performing the procedure.			

Adapted from Clinical Practice Guidelines: Prevention and Treatment of Venous Thromboembolism, Ministry of Health Malaysia, August 2013.

5.1.5 Patients with pre-existing coagulopathy

a) Pre-existing coagulopathy should be investigated and managed appropriately.

b) Incidental finding of prolonged PT and APTT should be verified and investigated.

c) Generally it is safe to proceed with surgery in cases where prolongation of PT and APTT is not more than 1.5 times of normal value.

5.2 INTRA-OPERATIVE MANAGEMENT

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

a) Ensuring optimal volume status.

b) Adequate analgesia.

c) Providing supplemental oxygen.

d) Maintaining normothermia.

5.2.1 Management of blood loss

a) A meticulous surgical technique in all surgical procedures can significantly reduce the transfusion requirement.

b) Bleeding during surgery may be due to surgical causes or disorders of haemostasis. Management should be aimed at treating the underlying cause. Blood components should be considered in disorders of haemostasis.

c) For massive haemorrhage management, refer to ***Section 10.1: Massive Haemorrhage.***

d) Anti-fibrinolytic agents are effective and safe in reducing blood usage, in particular, cardiopulmonary bypass surgery, valve grafts and liver transplantation.

e) Tranexamic acid acts by inhibiting fibrinolysis and encouraging clot stability. ***(APPENDIX XII)***

5.2.2 Management of volume replacement

a) Every effort should be made to maintain normovolaemia and heart rate within the normal range, with proper administration of appropriate fluids.

5.2.3 Reduction of oxygen demand

a) Anaemia is better tolerated if oxygen demand is minimised.

b) Adequate depth of anaesthesia and adequate analgesia is required to reduce the oxygen demand of myocardium and brain tissue.

5.2.4 Intra-operative Blood Salvage (IBS)

a) Intra-operative blood salvage (IBS) is the process where blood is collected from the patient, washed, concentrated and re-infused at the time of surgery. Useful in cardiac, orthopaedic and vascular surgery, organ transplantation and trauma, and has shown to reduce requirements of allogeneic transfusion.

5.3 POST-OPERATIVE MANAGEMENT

5.3.1 Management of volume replacement & ongoing blood loss

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

b) The source of bleeding should be identified early and appropriate action should be taken immediately, including endoscopic or surgical control of bleeding.

c) Adequate oxygenation, restricted phlebotomies, haemostatic pharmacologic therapy, adequate analgesia, maintenance of normovolaemia and normal body temperature and careful re-evaluation of anti-coagulant and anti-platelet drugs are simple and effective blood conservation strategies in the post-operative period.

5.4 TRANSFUSION OF BLOOD AND BLOOD COMPONENTS IN SURGERY

General Rule of Thumb

a) Transfusion may be considered when haemoglobin is less than 8 g/dL and is almost always required if haemoglobin **< 7 g/dL, particularly in acute anaemia or haemodynamically compromised**.

b) Haemoglobin 10 g/dL is no longer used as transfusion threshold unless the patient has low cardiorespiratory reserve.

c) Transfusion of allogeneic blood can increase post-operative infections due to immunosuppressive effect and increase risk of VTE.

d) Each transfusion should be considered based on **individual patient clinical condition**:

   i. Clinical signs & symptoms, especially haemodynamic instability.
   ii. Co-morbidities.
   iii. Further risk of blood loss.

*Refer **Section 3.0: Clinical Administration of Blood Components.***

Before ordering blood in preparation for planned surgery, ask yourself:

Can I reduce this patient's need for transfusion by correcting anaemia, stopping warfarin or checking for a coagulation disorder?

Patient blood management targets and interventions for elective surgery

- Optimise the haemoglobin concentration before planned surgery.
    - Detect anaemia, identify cause and treat.
    - Haematinics.
- Optimise iron stores before surgery, even if patient is not anaemic.
- Optimise haemostasis before planned surgery.
    - Identify congenital coagulation disorders.
    - Withdraw drugs that impair haemostasis (if safe to do so).
- Improve haemostasis during surgery.
    - Anaesthetic techniques.
    - Surgical techniques.
    - Positioning.
    - Anti-fibrinolytic drugs.
    - Avoid hypothermia.
    - Collect and re-infuse blood lost during surgery.
    - Intra-operative blood salvage.

5.5 MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE (MSBOS)

MSBOS is a reference used to guide clinicians in ordering blood before elective surgery. MSBOS is important to reduce unnecessary pre-operative blood order and allows more efficient management of blood. It is recommended that a hospital transfusion committee comprising of clinical users of blood and representatives of the blood bank be set up to develop its own MSBOS for local use as needs of every hospital may differ.

GUIDELINES ON ESTABLISHING MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE FOR HOSPITALS

a) The Maximum Surgical Blood Ordering Schedule **(MSBOS)** is a table of elective surgical procedures, which lists the number of units of blood routinely requested and crossmatched for those procedures pre-operatively.
b) The schedule is based on retrospective analysis of actual blood usage associated with the individual surgical procedure of 6 months duration.
c) For cases where blood is unlikely to be transfused, a group screen and hold is performed.
d) Where blood is likely to be transfused, a full crossmatch is done.
e) However when antibody screen is positive, compatible blood must be made available in all cases before surgery.
f) For each procedure, indicate the number of units crossmatched and the number of units transfused.
g) In procedures where blood usage is less than 30%, GSH is sufficient while GXM is indicated when usage exceed 30%.
h) In drawing up the schedule, local factors such as expertise available in the hospital and the speed of provision of compatible blood have to be taken into account.
i) Calculation of percentage of blood usage:

$$Percentage\ of\ blood\ usage = \frac{Total\ number\ of\ units\ transfused}{Total\ number\ of\ units\ crossmatched}\ x\ 100$$

Example:

Procedure	Number of operations	Units of blood crossmatched	Units of blood transfused	Percentage of units transfused	GSH/GXM
Caesarean Section	60	120	8	6.6%	GSH indicated
Total Hip Replacement	20	60	40	66%	GXM indicated

j) **C:T Ratio (Crossmatch:Transfusion Ratio)**

- CT ratio (CTR) is an important indicator to gauge the appropriateness of blood request.
- High CTR implies that crossmatches were performed unnecessarily when a GSH would have sufficed. Ideally, CTR should be less than 2.5.
- CTR is calculated as below:

$$CT\ ratio = \frac{Number\ of\ units\ crossmatched}{Number\ of\ units\ transfused}$$

Example:

Procedure	Number of operations	Units of blood crossmatched	Units of blood transfused	CTR
Caesarean Section	60	120	8	15
Total Hip Replacement	20	60	40	1.5

k) **Transfusion index (TI)** is defined as the average number of units transfused for a given procedure.

- TI value of more than 0.5 indicates that blood needs to be crossmatched pre-operatively for that procedure as it indicative of significant blood utilization.

- TI is calculated as:

$$Transfusion\ Index = \frac{Number\ of\ units\ transfused}{Number\ of\ units\ crossmatched}$$

Procedure	Number of operations	Units of blood crossmatched	Units of blood transfused	TI	CTR
Caesarean Section	60	120	8	0.06	15
Total Hip Replacement	20	60	40	0.66	1.5

Implementation

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

*Refer **APPENDIX XIII** for example of maximum surgical blood ordering schedule (MSBOS).*

References

1. Practical Transfusion Medicine, 3rd Edition, 2009. Michael F. Murphy. Chapter 33: The principles of bloodless medicine and surgery. Aryeh Shander & Lawrence Tim Goodnough.

2. Practical Transfusion Medicine, 3rd Edition, 2009. Michael F. Murphy. Chapter 25: Good blood management: The effective and safe use of blood components. Brian McClelland & Tim Walsh.

3. A. Shokoohi S, Stanworth D, Mistry S, Lamb J, Staves & M. F. Murphy. The risks of Red Cell Transfusion for hip fracture surgery in the elderly. *Vox Sanguinis* 2012; 103 (3): 223 – 230.

4. D B L McClelland, 2007. 4th Edition Handbook of Transfusion Medicine.

5. Lenat et al. Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care. *Critical Care Medicine* 2009; 37 (12): 3124 – 3157.

6. A. M. Beliaev, R. J. Marshall, M. Gordon, W. Smith, J. A. Windsor. Clinical benefits and cost-effectiveness of allogeneic red-blood-cell transfusion in severe symptomatic anaemia. Vox Sanguinis 2012; 103: 18 – 24.

7. Hans Gombotz. Patient Blood Management: A Patient-Orientated Approach to Blood Replacement with the Goal of Reducing Anaemia, Blood Loss and the Need for Blood Transfusion in Elective Surgery. *Transfusion Medicine and Hemotherapy* 2012; 39: 67 – 72.

8. Frank, Steven M., et al. "Reducing unnecessary pre-operative blood orders and costs by implementing an updated institution-specific maximum surgical blood order schedule and a remote electronic blood release system." *The Journal of the American Society of Anesthesiologists* 121.3 (2014): 501-509.

9. Yazdi AP, Alipour M, Jahanbakhsh SS, Gharavifard M, Gilani MT. A Survey of Blood Request Versus Blood Utilization at a University Hospital in Iran. *Archives of Bone and Joint Surgery*. 2016;4(1):75-79.

10. Kuchhal, Akshat, et al. "Blood utilization practices in elective surgical patients in a Tertiary Care Hospital of Uttarakhand." *Global Journal of Transfusion Medicine* 1.2 (2016): 51.

11. Filipescu et al. “Perioperative Patient Blood Management Programme. Multidisciplinary Recommendations from the Patient Blood Management Initiative Group.” Romanian Journal of Anaesthesia and Intensive Care (2017);25(2):139 – 157.

6.0 TRANSFUSION IN CARDIOTHORACIC

The risk for blood transfusion in coronary artery bypass grafting could be due to:

a) Major bleeding.

b) Haemodilution effect of using cardiopulmonary bypass (CPB) machine. At the same time, CPB system also has a potential to cause platelet dysfunction, hyperfibrinolysis and risk for post-operative bleeding. This risk will be higher when requiring longer CPB time.

Some evidence shows that excessive transfusion in cardiac surgery causes poor long and short-term patient outcomes.

Several steps to improve transfusion in CABG patient will be discussed in separate sections below.

6.1 BLEEDING RISK ASSESSMENT

Bleeding risk assessment is important to identify subset groups of patients who are at risk for perioperative bleeding and require subsequent blood transfusion. Aggressive blood conservation intervention techniques with Patient Blood Management (PBM) concept can be implemented once the patients are categorized.

There are several main risks which are:

a) Advanced age, especially > 65 years old.
b) Low pre-operative red blood cell volume (small body size, anaemia).
c) Emergency or complex surgeries (*e.g.* redo procedures, aortic replacement surgery).
d) Pre-operative anti-thrombotic therapy.
e) Anticipated prolonged duration of CPB.
f) Significant medical co-morbidities (coagulopathy, congestive cardiac failure, renal disease).

A multidisciplinary team consisting of a surgeon, an anaesthetist, a physician and a transfusion medicine specialist should be involved in devising a multimodal perioperative blood conservation intervention for these high-risk patients.

6.2 PRE-OPERATIVE MANAGEMENT

a) Bleeding risk assessment together with baseline investigations that include peripheral blood count and coagulation profile are important in patient blood management.

b) Each patient shall be evaluated individually based on clinical judgement with consideration of symptoms & signs especially in haemodynamic instability, co-morbidity and further risk of blood loss.

c) For elective cases, patient with anaemia shall be managed early & possible cause shall be treated accordingly based on clinical diagnosis.

d) Modify anti-platelet or anti-coagulant regimens accordingly when elective surgical procedure is planned to minimize significant bleeding complications. Different drugs have different pharmacodynamics and there is variability in response to therapy. Antithrombotic therapy which is restarted post-operatively is also important for the protection of graft patency. ***(APPENDIX IX, APPENDIX X & APPENDIX XI)***

e) Request for red cells will depend on Maximum Surgical Blood Ordering Schedule (MSBOS) within the individual institution. *Refer* ***Section 5.5: Maximum Surgical Blood Ordering Schedule (MSBOS)****.*

6.3 INTRA-OPERATIVE MANAGEMENT

a) Surgical measures to minimize time and haemodilution during CPB are vital in blood conservation.

b) Intra-operative autologous blood transfusions (intra-operative blood salvage) from cardiotomy suction or cell-salvage device are potentially effective in reducing need for allogeneic blood transfusion.

c) Protamine is used for heparin reversal at the end of CPB and subsequently reduce risks of bleeding.

d) Thromboelastography (TEG) or Rotational Thromboelastometry (ROTEM) is a more accurate point of care testing and is useful to guide and help minimize transfusions in cardiac surgeries.

6.4 POST-OPERATIVE MANAGEMENT

a) Requirement of blood and blood components transfusion based on clinical condition of patient.

b) Restart antithrombotic therapy as per required clinically.

6.5 TRANSFUSION THRESHOLD FOR RED CELL

The recommended transfusion threshold for red cell are as follow:

a) Patients on CPB with haemoglobin ≤ 8 g/dL.

b) Patients on CPB with haemoglobin $\underline{\geq}$ 8 g/dL may be transfused when clinical condition takes precedence *e.g.* active and massive bleeding, high risk for end organ ischaemia or when other parameters are deranged such as haematocrit, SVO_2 or ECG/echocardiogram.

c) For stable patients with haemoglobin ≥ 10 g/dL, transfusion is unlikely to improve oxygen carrying capacity.

6.6 TRANSFUSION OF BLOOD COMPONENTS

a) Prophylactic transfusion of blood components in the absence of coagulopathy does not reduce bleeding risk in cardiac surgery. Transfusion should be based on targeted therapeutic indications.

b) Plasma transfusion might be indicated to minimize bleeding complications in situations of coagulopathy due to massive transfusion and DIC.

c) Cryoprecipitate is indicated in hypofibrinogenemia. It is recommended that fibrinogen level should be maintained above 2 g/L.

d) Platelet transfusion is usually indicated in platelet dysfunction caused by pre-operative pharmacological anti-platelet therapy that is not halted according to recommended guidelines before surgery and prolonged contact with cardiopulmonary bypass circuit.

References

1. Kilic, A., & Whitman, G. J. (2014). Blood Transfusions in Cardiac Surgery: Indications, Risks, and Conservation Strategies. *The Annals of Thoracic Surgery.* 97, 726-734.

2. Kremke, M., Hansen, M. K., Christensen, S., Tang, M., Andreasen, J. J., & Jakobsen, C.-J. (2015). The association between platelet transfusion and adverse outcomes after coronary artery bypass surgery. *European Journal of Cardio-Thoracic Surgery.* 48, e102-e109

3. Ismail A.A.C., Hussein A.R., & Ayob Y. (2018). Association of red blood cell transfusion with mortality and morbidity in post cardiac surgery patients. *Malaysian Journal of Medicine and Health Sciences.* 14, 28-33.

4. Chan Ch, Ziyadi Gm, & Zuhdi Ma. (2019). Adverse Outcomes of Perioperative Red Blood Cell Transfusions in Coronary Artery Bypass Grafting in Hospital Universiti Sains Malaysia. *The Malaysian Journal of Medical Sciences: MJMS.* 26, 49-63.

5. Bishop, C. V., Renwick, W. E. P., Hogan, C., Haeusler, M., Tuckfield, A. & Tatoulis, J. (2006). Recombinant Activated Factor VII: Treating Post-operative Hemorrhage in Cardiac Surgery. *Ann Thorac Surg,* 81(3), 875-879.

6. Engoren, M. C., Habib, R. H., Zacharias, A., Schwann, T. A., Riordan, C. J. & Durham, S. J. (2002). Effect of blood transfusion on long-term survival after cardiac operation. *The Annals of Thoracic Surgery,* 74(4), 1180-1186.

7. Ferraris, V. A., Brown, J. R., Despotis, G. J., Hammon, J. W., Reece, T. B., Saha, S. P., Song, H. K., Clough, E. R., Shore-Lesserson, L. J., Goodnough, L. T., Mazer, C. D., Shander, A., Stafford-Smith, M., Waters, J., Baker, R. A., Dickinson, T. A., FitzGerald, D. J., Likosky, D. S. & Shann, K. G. (2011). 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg,* 91(3), 944-82.

8. Royston, D. & von Kier, S. (2001). Reduced haemostatic factor transfusion using heparinase-modified thrombelastography during cardiopulmonary bypass. *British Journal of Anaesthesia,* 86(4), 575-578.

9. Santos, A. T. L., Kalil, R. A. K., Bauemann, C., Pereira, J. B. & Nesralla, I. A. (2006). A randomized, double-blind, and placebo-controlled study with tranexamic acid of bleeding and fibrinolytic activity after primary coronary artery bypass grafting. *Brazilian Journal of Medical and Biological Research,* 39, 63-69.

10. Sirlak, M., Eryilmaz, S., Yazicioglu, L., Kiziltepe, U., Eyileten, Z., Durdu, M. S., Tasoz, R., Eren, N. T., Aral, A., Kaya, B. & Akalin, H. (2003). Comparative study of microfibrillar collagen hemostat (Colgel) and oxidized cellulose (Surgicel) in high transfusion-risk cardiac surgery. *The Journal of thoracic and cardiovascular surgery,* 126(3), 666-670.

11. The Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris, V. A., Ferraris, S. P., Saha, S. P., Hessel, E. A., II, Haan, C. K., Royston, B. D., Bridges, C. R., Higgins, R. S. D., Despotis, G., Brown, J. R., The Society of Cardiovascular Anesthesiologists Special Task Force on Blood Transfusion, Spiess, B. D., Shore-Lesserson, L., Stafford-Smith, M., Mazer, C. D., Bennett-Guerrero, E., Hill, S. E. & Body, S. (2007). Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery: The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists Clinical Practice Guideline. *Ann Thorac Surg,* 83(5_Supplement), S27-86.

12. Westbrook, A. J., Olsen, J., Bailey, M., Bates, J., Scully, M. & Salamonsen, R. F. (2009). Protocol Based on Thromboelastograph (TEG) Out-Performs Physician Preference Using Laboratory Coagulation Tests to Guide Blood Replacement During and After Cardiac Surgery: A Pilot Study. *Heart, Lung and Circulation,* 18(4), 277-288.

13. Wilhelmi, M., Franke, U., Cohnert, T., Weber, P., Kaukemüller, J., Fischer, S., Wahlers, T. & Haverich, A. (2001). Coronary artery bypass grafting surgery without the routine application of blood products: is it feasible? *European Journal of Cardio-Thoracic Surgery,* 19(5), 657-661.

14. Zaidan, J. R., Johnson, S., Brynes, R., Monroe, S. & Guffin, A. V. (1986). Rate of Protamine Administration. *Anesthesia & Analgesia,* 65(4), 377-380.

7.0 SOLID ORGAN TRANSPLANT

Transfusion may influence the outcome of a transplant. Transfusion given pre-transplantation may promote sensitization and development of alloimmunization to histocompatibility antigens. This will affect the ability to obtain a compatible organ and increase the risk of graft rejections.

7.1 GENERAL PRINCIPLE OF BLOOD TRANSFUSION IN SOLID ORGAN TRANSPLANT

a) Intra-operative blood recovery (blood salvage) is important if major blood loss is expected. This method has a potential in reducing transfusion of allogeneic blood.

b) The use of pharmacological agents such as tranexamic acid may assist in reducing blood transfusion.

c) Transfusion guided by Point of Care Testing (POCT) *e.g.* Thromboelastography (TEG) or Rotational Thromboelastometry (ROTEM) could help in reducing the number of blood components transfused during surgery. TEG or ROTEM are able to test multiple arms of the coagulation cascades and results are at the point of care.

d) Early detection and proper management of concomitant pre-operative anaemia or coagulopathy can minimise the need for blood components transfusion.

7.1.1 Red cell

a) ABO identical/compatible red cell for both organ donor and recipient are needed because of the presence of A and B antigens on the vascular endothelium of the graft. Therefore, anti-A or anti-B in the recipient or transfused blood will attack the graft if incompatible blood is transfused, leading to hyperacute graft rejection. Minor ABO incompatibility can be

associated with significant haemolytic anaemia caused by ABO antibody production of passenger graft lymphocytes.

b) RhD negative recipient should receive RhD negative blood to prevent alloanti-D development especially women in childbearing age. *Refer* ***Section 9.0: Transfusion of Blood and Blood Components in RhD negative patients.***

c) Antigen negative red cell shall be provided for patients with significant red cells alloantibody.

d) Leucodepleted red cell to reduce the risk of HLA allo-immunization and risk of CMV transmission.

e) It is not necessary to irradiate red cells unless alemtuzumab (anti-CD52) has been used in the conditioning regimen.

7.1.2 Platelet

a) ABO-compatible platelets.

b) RhD positive can be safely transfused to RhD negative recipient. *Refer to* ***Section 9.4: Transfusion of Platelet Concentrate***.

c) It is not necessary to irradiate platelets unless alemtuzumab (anti-CD52) has been used in the conditioning regimen.

d) Apheresis platelet is preferred to reduce risk for platelet allo-immunization (if available).

7.1.3 Plasma components (FFP & cryoprecipitate)

a) ABO-compatible for both recipient and donor to minimize the transfer of anti-A or anti-B which is directed against the grafted organ, especially in ABO-incompatible transplantation.

7.2 RENAL TRANSPLANTATION

Pre-transplant	Recombinant erythropoietin (rEPO) is recommended to correct anaemia in patients with renal failure.
During transplant	Usually no transfusion is required. If required, blood components should be given as necessary.
Post-transplant	Usually no transfusion is required. If required, blood components should be given as necessary.

7.3 ORTHOTOPIC LIVER TRANSPLANTATION (OLT)

Pre-transplant	Most pre-existing end-stage liver disease have abnormalities in coagulation system. However, correction is not usually required unless patient has overt bleeding.
During transplant	Massive blood loss and hypocoagulability due to pre-existing liver disease and anhepatic interval during the procedure create complex problems. This result in haemodilution, platelet consumption, disordered thrombin regulation and fibrinolysis, which cause derangement of the haemostatic process and is especially severe during the anhepatic and early perfusion stage. Therefore, patients often require red cell, platelet, plasma and cryoprecipitate. Transfusion guided by TEG or ROTEM will help in reducing the number and types of blood components transfused during surgery.
Post-transplant	Post-operatively, there is a risk of hypercoagulable state that might leads to hepatic artery thrombosis. This risk may be reduced by avoiding over-transfusion of blood components.

7.4 HEART AND LUNG TRANSPLANT

Pre-transplant	Patient might need blood transfusion due to anaemia and heart failure.
During transplant	Transplant is performed using CPB machine. Cardiopulmonary bypass has a potential to cause haemodilution effect, platelet dysfunction, hyperfibrinolysis and risk for post-operative bleeding and often needs red cell, platelet and plasma products. Blood loss replacement should be given as necessary.
Post-transplant	Blood components transfusion should be given as necessary according to clinical condition of the patient.

References

1. Solves P, Carpio N, Moscardo F, Lancharro A, Cano I, Moya A, López-Andujar R, & Sanz Má. (2015). Transfusion management and immunohematologic complications in liver transplantation: experience of a single institution. 42, 8-14.

2. Burin Des Roziers N, Ibanez C, Samuel D, Francoz C, Idri S, François A, Mortelecque R, Bierling P, & Pirenne F. (2016). Rare and transient anti-D antibody response in D(-) liver transplant recipients transfused with D(+) red blood cells. *Vox Sanguinis.* 111, 107-10.

3. Sarkar, R., Philip, J., & Yadav, P. (2013). Transfusion medicine and solid organ transplant - Update and review of some current issues. *Medical Journal Armed Forces India.* 69, 162-167.

4. Gabriel, C. (2016). Choosing the right blood products for transplant patients. *ISBT Science Series.* 11, 105-110.

5. Treleaven, J., Gennery, A., Marsh, J., Norfolk, D., Page, L., Parker, A., Saran, F., Thurston, J., & Webb, D. (2011). Guidelines on the use of irradiated blood components prepared by the British Committee for Standards in Haematology blood transfusion task force. *British Journal of Haematology.* 152, 35-51.

6. Aalten, J., Bemelman, F. J., van den Berg-Loonen, E. M., Claas, F. H., Christiaans, M. H., de Fijter, J. W., Hepkema, B. G., Hené, R. J., van der Heide, J. J. H., van Hooff, J. P., Lardy, N. M., Lems, S. P., Otten, H. G., Weimar, W., Allebes, W. A. & Hoitsma, A. J. (2009). Pre-kidney-transplant blood transfusions do not improve transplantation outcome: a Dutch national study. *Nephrology Dialysis Transplantation,* **24(8),** 2559-2566.

7. Black, R. M., Poppel, D. M. & Khauli, R. B. (1991). Blood transfusions and renal transplantation: Are pretransplant blood transfusions still neededin the cyclosporine era? *Urology,* **38(5),** 397-401.

8. Ferraris, V. A., Brown, J. R., Despotis, G. J., Hammon, J. W., Reece, T. B., Saha, S. P., Song, H. K., Clough, E. R., Shore-Lesserson, L. J., Goodnough, L. T., Mazer, C. D., Shander, A., Stafford-Smith, M., Waters, J., Baker, R. A., Dickinson, T. A., FitzGerald, D. J., Likosky, D. S. & Shann, K. G. (2011). 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg,* **91(3),** 944-82.

9. Hendrickson, J. E. & Roback, J. D. (2009). Chapter 46 - Transfusion of Patients Undergoing HPC and Solid-organ Transplantation.In*:* Christopher, D. H., Md, Beth, H. S., James, C. Z., PhD and Thomas C. Abshire, M. D. (eds.), *Transfusion Medicine and Hemostasis*. San Diego: Academic Press, pp 269-274.

10. Jacob, N. (1991). Blood Transfusion Support in Liver Transplantation. *Transfusion Medicine Reviews,* **5(3),** 207-213.

11. Makroo, R. N., Raina, V., Gupta, S., Chowdhry, M., Bhanot, R. S., Arora, B. & Baburajan, L. (2008). Maximum Surgical Blood Order Schedule (MSBOS) in Liver Transplant. *Apollo Medicine,* **5(4),** 383-386.

12. Ramsey, G., Hahn, L. F., Cornell, F. W., Boczkowski, D. J., Staschak, S., Clark, R., Hardesty, R. L., Griffith, B. P. & Starzl, T. E. (1989). Low rate of Rhesus immunization from Rh-incompatible blood transfusions during liver and heart transplant surgery. *Transplantation,* **47(6),** 993-5.

13. Ross, W. B. & Yap, P. L. (1990). Blood transfusion and organ transplantation. *Blood Reviews,* **4(4),** 252-258.

14. Scornik, J. C. & Meier-Kriesche, H. U. (2011). Blood Transfusions in Organ Transplant Patients: Mechanisms of Sensitization and Implications for Prevention. *American Journal of Transplantation,* **11(9),** 1785-1791.

15. Wang, S. C., Shieh, J. F., Chang, K. Y., Chu, Y. C., Liu, C. S., Loong, C. C., Chan, K. H., Mandell, S. & Tsou, M. Y. (2010). Thromboelastography-Guided Transfusion Decreases Intra-operative Blood Transfusion During Orthotopic Liver Transplantation: Randomized Clinical Trial. *Transplantation Proceedings,* **42(7),** 2590-2593.

8.0 OBSTETRIC & GYNAECOLOGY

During normal pregnancy, physiological changes in the mother affects the reference range for haematological parameters. Knowledge of these changes helps to avoid unnecessary blood transfusion caused by misinterpretation of blood count results:

- Maternal plasma volume increases by around 50% above the non-pregnant value by the late second trimester. Red cells mass only increases by 25 – 30%, resulting in a fall in haemoglobin concentration (physiological anaemia of pregnancy).

- Up to 10% of healthy pregnant women have a platelet count below the non-pregnant reference range of 150 – 400 x 10^9/L at term (gestational thrombocytopenia). The count rarely falls below 100 x 10^9/L and there is no increase in bleeding risk.

- Many coagulation factors, including plasma fibrinogen and Factor VIII, are increased in normal pregnancy and the anticoagulant factor Protein S is reduced. This contributes to the increased risk of thrombotic complications in pregnancy.

8.1 ANAEMIA IN PREGNANCY

Prevention of anaemia in pregnancy is Important in avoiding unnecessary blood transfusion. Anaemia in pregnancy is defined as:

Haemoglobin or haematocrit value less than the fifth percentile of the distribution of haemoglobin or haematocrit in a healthy reference population based on the stage of pregnancy.

Table 8.1: WHO recommendations on antenatal care for a positive pregnancy experience (2016)

	1st trimester	2nd trimester	3rd trimester
Haemoglobin (g/dL)	< 11.0	< 10.5	< 11.0
Haematocrit (%)	< 33	< 32	< 33

Anaemia that is not due to nutritional deficiency (*e.g.* haemoglobinopathies and bone marrow failure syndromes) should be managed with a physician/haematologist.

8.2 MEASURES TO REDUCE TRANSFUSION IN OBSTETRICS

Effective management of anaemia during pregnancy:

a) Anaemia work-up at diagnosis.

b) Optimization of iron therapy in iron deficiency anaemia.

c) Oral iron should be preferred as first line treatment for iron deficiency.

d) Parenteral iron is indicated when oral iron is not tolerated, absorbed, in doubt of patient's compliance or if the woman is approaching term and there is insufficient time for oral supplementation to be effective.

e) Women should receive information on improvement of dietary iron intake and factors affecting absorption of dietary iron:

   i. 60 – 120 mg elemental iron on alternate days in single morning doses. The expected rise in haemoglobin level is at a rate of 1.0 – 2.0 g/dL per month and should be continued for 6 months after normalisation of haemoglobin. The iron storage is replenished in 6 months.
   ii. Monitoring of response: Reticulocytes response can be seen on day 3 – 5 and peaks between day 8 – 10.

f) Parenteral iron is indicated when oral iron is not tolerated, absorbed, in doubt of patient's compliance or if the woman is approaching term and there is insufficient time for oral supplementation to be effective. If this is ineffective or not tolerated, parenteral iron may be considered. It must be administered intravenously only. IV iron of 200 mg increases haemoglobin level 1.5 – 2.0 g/dL per week.

Table 8.2: Quick reference for number of ampoules (Cosmofer/Venofer) required

Increase in Hb required (g/dL) ie Target Hb minus Actual Hb								
		1g	2g	3g	4g	5g	6g	7g
Body weight (kg)	40	6	7	8	9	10	11	12
	45	6	7	8	9	10	11	12
	50	6	7	9	10	11	12	13
	55	6	8	9	10	12	13	14
	60	6	8	9	11	13	14	16
	65	7	8	10	11	13	14	16
	70	7	8	10	12	13	15	17
	75	7	9	10	12	14	16	18
	80	7	9	11	13	15	17	18
	85	7	9	11	13	15	17	19
	90	7	9	11	14	16	18	20
	95	7	10	12	14	16	19	21
	100	7	10	12	15	17	19	22

Caution: parenteral IV iron is contraindicated in first trimester

g) If no response and symptomatic, blood transfusion can be considered. The aim of the transfusion is to improve anaemic status and oxygen carrying capacity to withstand the strains of labour and blood loss during delivery.

h) Multidisciplinary approach in pregnant women with known haematological disorder *e.g.* patient in need of anti-coagulant.

8.3 RED CELL TRANSFUSION IN PREGNANCY

Clinical audits have shown that many transfusion in pregnancy especially in the post-partum period, are not clinically indicated and could be prevented by diligent antenatal monitoring and targeted use of iron supplements.

Transfusion exposes women to the risk of sensitization to red cells antigens and haemolytic disease of the foetus and newborn (HDFN) in future pregnancies. In the

absence of major haemorrhage, the decision to transfuse should be made after a thorough clinical assessment.

Clinically stable healthy women with haemoglobin > 7 or 8 g/dL can usually be managed with oral or parenteral iron.

Transfusion should be given for women with continued bleeding, severe symptoms that need immediate correction or evidence of cardiac decompensation.

8.3.1 Requirements for GSH and crossmatching

a) All pregnant women should have their blood group checked at booking and antibody screening at 28 weeks if feasible.

b) In a woman at high risk of emergency transfusion (*e.g.* placenta praevia) and with no clinically significant alloantibodies, group and screen samples should be sent and to keep blood available if necessary. Close liaison with the hospital transfusion laboratory is essential.

8.4 PLATELET TRANSFUSION IN PREGNANCY

a) Thrombocytopenia occurs in 8 – 10% of all pregnancies. The severity is classified as follows:

i. Mild : >100 x 10^9/L
ii. Moderate : 50 – 100 x 10^9/L
iii. Severe : <50 x 10^9/L

b) In pregnancy, most cases are mild and benign, but it can be associated with severe complications for mother and baby. In cases where the platelet count is <80 x 10^9/L, discussion with a consultant haematologist is advised.

Table 8.3: Possible causes of thrombocytopenia in pregnancy

Diagnosis	Proportion	Pathophysiology
Gestational Thrombocytopenia	About 75%	Physiological dilution, accelerated destruction
Immune Thrombocytopenic Purpura (ITP)	About 3%	Immune destruction, suppressed production
Thrombotic Thrombocytopenic Purpura (TTP)		Peripheral consumption, microthrombi
Haemolytic Uraemic Syndrome (HUS)		Peripheral consumption, microthrombi
Pre-eclampsia, Eclampsia, Haemolysis, Elevated liver enzymes and low platelet count syndrome (PET, HELLP)	About 15-20%	Peripheral consumption, microthrombi
Hereditary thrombocytopenia		Bone marrow underproduction
Pseudo thrombocytopenia		Laboratory artefact
Viral infections: HIV, Epstein-Barr virus		Secondary autoimmune thrombocytopenia
Medications: heparin-induced		Bone-marrow suppression
Leukaemia/Lymphoma		Failure of Platelet production, bone marrow infiltration
Severe Vitamin B12 or Folate Deficiency		Failure of Platelet production
Splenomegaly		Splenic Sequestration

Table 8.4: Safe level for intervention

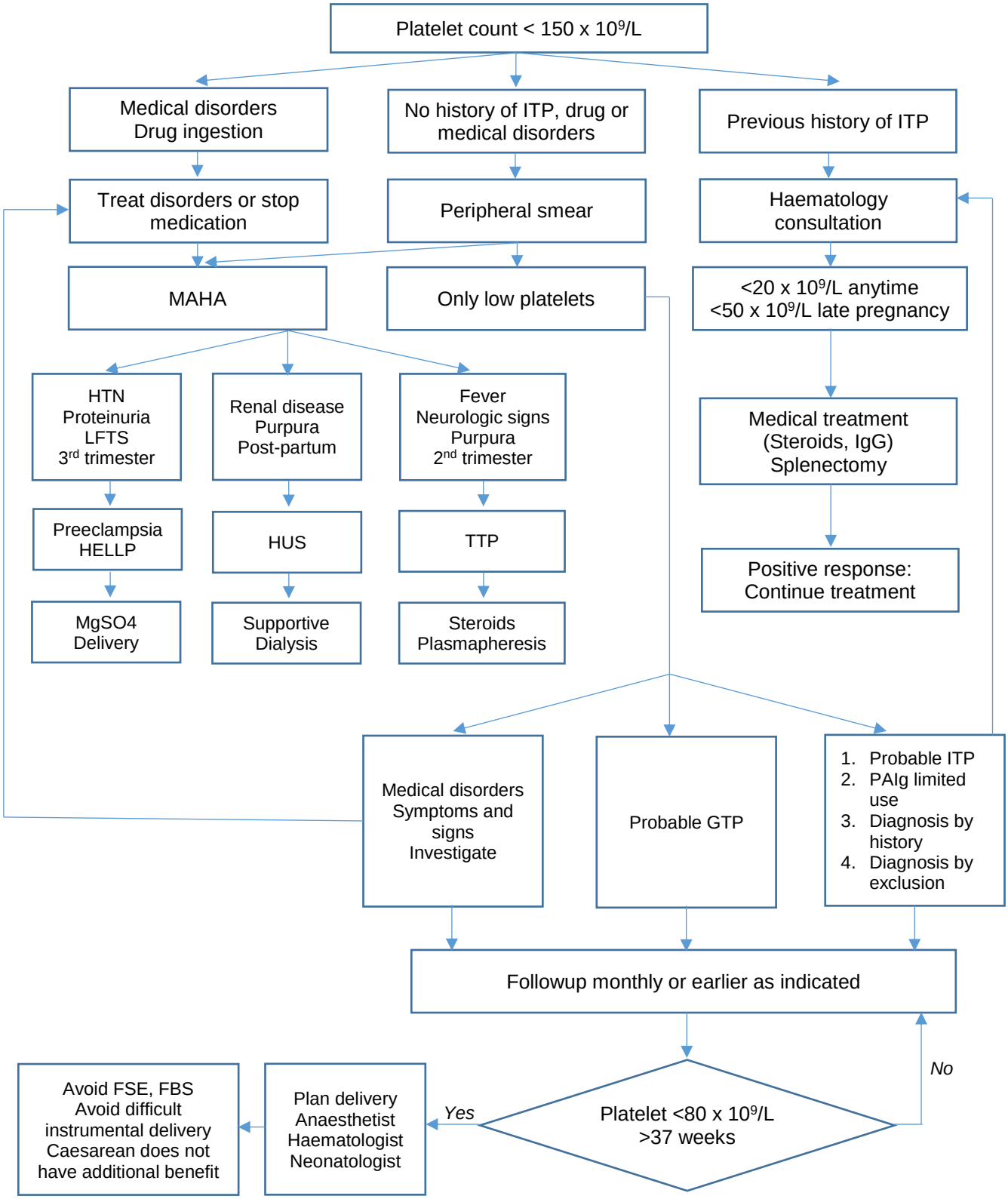
Intervention	Platelet count ($x10^9$/L)
Antenatal, no invasive procedures planned	>20
Vaginal delivery	>40
Operative or instrumental delivery	>50
Epidural anaesthesia	>80

Table 8.5: Safe platelet threshold for delivery (Grade C)

Type of Delivery	Platelet count ($x10^9$/L)
Vaginal delivery	>30
Caesarean section	>50
Epidural anaesthesia	>80

Adapted from Clinical Practice Guidelines: Management of Immune Thrombocytopenic Purpura (2006).

Figure 8.1: Process Chart for Thrombocytopenia in Pregnancy Management



Adapted from Guideline for the management of thrombocytopenia in pregnancy (GL927). NHS, October 2017.

8.5 ELECTIVE CAESAREAN SECTION

Minimum surgical blood order for elective caesarean section is as per hospital's MSBOS. This also include cases with previous scar.

8.5.1 Minimising blood loss during and after delivery

a) Prophylactic uterotonic in the management of the third stage of labour and during caesarean section is effective and safe to prevent excessive blood loss.

b) For women at increased risk of haemorrhage, it is possible that a combination of preventative measures might be superior to uterotonics alone to prevent post-partum haemorrhage.

c) Clinicians should consider the use of intravenous tranexamic acid (0.5 – 1.0 g), in addition to uterotonics, during caesarean section to reduce blood loss in women at increased risk of post-partum haemorrhage.

8.6 OBSTETRIC HAEMORRHAGE

Blood flow to the uterus is around 700 mL/minute at term. Post-partum haemorrhage can be devastating and life-threatening.

8.6.1 Massive blood loss

Massive blood loss is defined as:

- loss of 1 blood volume within a 24-hour period or
- loss of 50% blood volume in 3 hours or
- rate of loss of 150 mL/minute or
- When bleeding which leads to a heart rate more than 110 beats/min and/or systolic blood pressure less than 90 mmHg

Majority of these obstetric haemorrhages will need blood transfusion and if not properly managed may lead to morbidity and mortality.

8.6.2 Management of acute / massive obstetric haemorrhage

a) There are no firm criteria for initiating red cells transfusion. The decision to provide blood transfusion should be based on both clinical and haematological assessment.

b) Major obstetric haemorrhage protocols must include the provision of emergency blood with immediate issue of Safe O, with a switch to group-specific blood as soon as feasible and initiation of Massive Transfusion Protocol (MTP) if available.

c) Transfusion of blood components :

i. **Platelet**

- During PPH, platelet should be transfused when the platelet count is less than 75 x 10^9/L based on laboratory monitoring.

ii. **Fresh frozen plasma**

- If no haemostatic results are available and bleeding is continuing, then, after 4 units of red cells, FFP should be infused at a dose of 12 – 15 mL/kg until haemostatic test results are known.
- If no haemostatic tests are available, early FFP should be considered for conditions with a suspected coagulopathy, such as placental abruption, amniotic fluid embolism or where detection of PPH has been delayed.
- If prothrombin time/activated partial thromboplastin time is more than 1.5 times normal and haemorrhage is ongoing, volumes of FFP in excess of 15 mL/kg are likely to be needed to correct coagulopathy.
- Clinicians should be aware that these blood components must be ordered as soon as a need for them is anticipated, as there will always be a short delay in supply because of the need for thawing.

iii. **Cryoprecipitate**

- A plasma fibrinogen level of greater than 2 g/L should be maintained during ongoing PPH. Cryoprecipitate should be used for fibrinogen replacement.

d) Antifibrinoytic drugs

Consideration should be given to the use of tranexamic acid in the management of PPH.

e) The goal of transfusion in obstetric haemorrhage includes:

i. Restoring and maintaining circulating blood volume by rapid resuscitation with crystalloids to prevent tissue and organ hypoperfusion. Volume replacement must be undertaken on the basis that blood loss is often grossly underestimated.
ii. Maintenance of tissue oxygenation using red blood cells.
iii. Reversal or prevention of coagulopathy using appropriate blood components. *Refer* ***Section 10.2: Massive Transfusion***.

f) The need and assessment of outcome of blood transfusion is determined by the clinical picture and guided by laboratory results.

g) Prevention and treatment of underlying hypothermia, acidosis and hypocalcaemia will ensure optimal function of transfused coagulation factors.

8.7 DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN OBSTETRIC DISORDER

Pregnancy is associated with changes in haemostasis including an increase in the majority of clotting factors, a decrease in the quantity of natural anti-coagulants and a reduction in fibrinolytic activity.

These changes result in a state of hypercoagulability and increase the risk of thromboembolism.

8.7.1 Causes of DIC

Disseminated intravascular coagulation is associated with certain obstetric complications as tabulated in Table 8.6. It may also be triggered by massive blood loss.

Table 8.6: Common causes of DIC in obstetric

Amniotic fluid embolism
Intrauterine fetal demise
HELLP syndrome
Pre-eclampsia/eclampsia
Placental abruption and placenta praevia
Septic abortion and intrauterine infection
Postpartum haemorrhage
Acute fatty liver of pregnancy

8.7.2 Diagnosis of DIC

The diagnosis of DIC does not rely on an isolated test but interpretation of several haemostatic parameters. The characteristic findings of DIC are:

a) Prolonged prothrombin time (PT).
b) Prolonged activated partial thromboplastin time (APTT).
c) Decreasing platelet count.
d) Low fibrinogen 2 g/L.
e) Repeated measurements of D-dimer showing increasing values may be helpful.

8.7.3 Management of DIC in pregnancy

In pregnancy-associated DIC, the main management is to treat the underlying cause. Once the cause is corrected, the DIC will usually resolve. Nonetheless, additional supportive treatments that are specifically aimed at the coagulation abnormalities may be required.

Blood product therapy is given depending on the clinical condition in combination with laboratory results:

Table 8.7: Blood parameter threshold and increment level

Component	Threshold level	Increment
Platelet	< 75 x 10^9/L	5 – 10 x 10^9/L per unit (random platelet) 30 – 60 x10^9/L per unit (apheresis platelet)
Cryoprecipitate	Fibrinogen < 2.0 g/L	0.5 – 1 g/L of fibrinogen per unit (1 unit/10 kg)
Fresh frozen plasma	Prolonged PT and APTT with evidence of bleeding	>20 – 30% coagulation factors (10 – 15 mL/kg)

There is increasing evidence that antifibrinolytic agent, tranexamic acid can significantly reduce mortality in major obstetric haemorrhage. (*The WOMAN trial - http://www.thewomantrial.lshtm.ac.uk/)*. The dose of tranexamic acid used in the WOMAN trial is 1g by intravenous injection as soon as possible and a second dose is given if bleeding persists after 30 minutes or recur within the first 24 hours.

8.8 INTRAUTERINE TRANSFUSION

Intrauterine transfusion for red blood cells is usually indicated in fetal anaemia due to red cell alloimmunization, less commonly parvovirus infection or congenital red cell disorder. Intrauterine platelet transfusions are given to correct platelet alloimmunization commonly in neonatal alloimmune thrombocytopenia.

Blood products for intrauterine transfusion:

8.8.1 Red cell

a) Crossmatch-compatible with maternal plasma/serum.
b) Group O RhD positive or negative red cells, depending on maternal ABO and Rh blood group.
c) Less than or 5 days old.

d) Leucodepleted (filtered).
e) Irradiated to prevent transfusion-associated graft versus host disease (TA-GVHD).
f) Haematocrit <0.75.
g) Transfuse using blood warmer.
h) CMV seronegative (if available).

8.8.2 Platelet

a) Human platelet-specific alloantigen (HPA) compatible with maternal antibody or crossmatched platelet (if available).
b) Irradiated.

*Refer **APPENDIX XIV** for blood selection for intrauterine transfusion (IUT).*

References

1. Royal College of Obstetric and Gynaecologist, Blood Transfusion in Obstetrics, Green-Top Guideline No. 47, May 2015.

2. Patient Blood Management Guidelines Module 5, Obstetrics and Gynaecology, Australia National Blood Authority, 2015.

3. Handbook of Transfusion Medicine 5th edition 2014. Dr Derek Norfolk United Kingdom Blood Services

4. Disseminated intravascular coagulation in pregnancy – insights in pathophysiology, diagnosis and management, American Journal of Obstetrics and Gynecology, 2015

5. Prevention and Management of Postpartum Haemorrhage, Green-top Guideline No. 52, RCOG, December 2016.

9.0 TRANSFUSION OF BLOOD AND BLOOD COMPONENTS IN RHD NEGATIVE PATIENTS

9.1 INTRODUCTION

a) RhD negative red cell components is considered rare in Malaysia as less than 2% of the population is RhD negative.

b) RhD antigen is present on red cell membrane but not on platelets.

c) RhD positive cellular blood products should be avoided in RhD negative children and females of child bearing age.

9.2 CLINICAL SIGNIFICANCE

a) The probability of the production of anti-D is high when D positive red cells are transfused to a D negative individual.

b) The anti-D antibody can cause haemolytic transfusion reaction and may lead to severe morbidity and mortality.

c) Anti-D antibodies are IgG subclass which can cross the placenta and cause severe haemolytic disease of foetus and newborn.

9.3 TRANSFUSION OF RED CELLS

a) The best practice for an RhD negative patient is to transfuse red cells of the same ABO and RhD group. However, transfusion of RhD positive red cells to a RhD negative recipient might be considered in EMERGENCY settings such as:

   i. In life-threatening situations when RhD negative blood is not available.
   ii. When the patient require large volume of red cells in a short period of time.

b) The above decision shall be based on agreement between the treating clinician and the transfusion specialist.

c) Circumstances in which RhD positive red cells should be avoided:

i. Patients who have pre-existing anti-D antibody.
ii. RhD negative patients who have received RhD positive red cells transfusion and have developed anti-D antibody.
iii. RhD negative females of child bearing age.

In life threatening situations, transfusion of D positive red cells can be considered.

9.4 TRANSFUSION OF PLATELET

a) Platelets do not carry RhD antigen. However, anti-D antibody may develop in RhD negative patients who have received RhD positive platelets contaminated by red blood cells that carry RhD antigens. Each unit of platelet prepared from whole blood donation contains less than 1×10^9 (<0.1 mL) red cells. It is best to transfuse platelet prepared by apheresis.

b) Anti-D immunoglobulin prophylaxis can be given whenever the platelet concentrate is contaminated with red blood cells.

c) Refer ***APPENDIX XV*** for dosage of anti-D immunoglobulin.

9.5 TRANSFUSION OF FRESH FROZEN PLASMA (FFP) & CRYOPRECIPITATE

a) FFP and cryoprecipitate of any RhD type may be given regardless of the RhD type of the recipient.

b) Transfusion of D positive fresh frozen plasma/cryoprecipitate may not cause the development of anti-D as it contains small amount of red cell stroma and stroma is less immunogenic than intact red cells.

c) Anti-D immunoglobulin prophylaxis can be given whenever the FFP and cryoprecipitate concentrate is contaminated with red blood cells (300 µg for 2.5 mL to 15 mL red cells contamination).

9.6 DOSAGE AND ADMINISTRATION OF ANTI-D IMMUNOGLOBULIN

a) Anti-D immunoglobulin should be administered as soon as possible following events but always within 72 hours. If it is not given before 72 hours, every effort should still be made to administer the anti-D IgG, as a dose given within 10 days may provide some protection.

b) A dose of 100 IU anti-D immunoglobulin is capable to suppress primary immunization of 1 mL RhD positive red cells.

c) In any RhD negative woman who is not yet sensitised to RhD, the inadvertent treatment of D positive red cells should be done by giving a suitable dose of anti-D, *i.e.* IM anti-D IgG 125 IU/mL or IV anti-D IgG 100 IU/mL of fetal red cells. For transfusion >15 mL, IV anti-D IgG is more practical. Feto-maternal haemorrhage (FMH) testing should be carried out at 48 hours interval and further anti-D IgG given until clearance of fetal cells is achieved. When more than 2 units of RhD positive blood have been transfused, an exchange transfusion with RhD negative blood (once available) should be considered to reduce the load of RhD positive red blood cells in the circulation. This will also reduce the dose of anti-D immunoglobulin required to suppress primary immunization.

9.7 RHD IMMUNOPROPHYLAXIS IN OBSTETRICS

9.7.1 Antenatal prophylaxis

a) RhD immunoprophylaxis is given to all non-sensitised RhD negative women.

b) RhD immunoprophylaxis is not required in women who are RhD sensitised.

c) A routine 28 week antibody screening sample must be taken before administration of the first dose of anti-D immunoglobulin.

d) There are the two regimes for RhD immunoprophylaxis:

   i. Two doses of 500 IU anti-D at 28 and 34 weeks of gestation.
   ii. Single dose of 1500 IU between 28 – 30 weeks of gestation.

e) In pregnancies <12 weeks gestation, anti-D Ig prophylaxis is only indicated following ectopic pregnancy, molar pregnancy, therapeutic termination of pregnancy and in cases of uterine bleeding where it is repeated, heavy or associated with abdominal pain. The minimum dose should be 250 IU. If the bleeding is persistent, a repeated dose of Anti-D prophylaxis is recommended.

f) For potentially sensitising events between 12 and 20 weeks gestation, a minimum dose of 250 IU should be administered within 72 hours of the event.

g) For potentially sensitising events after 20 weeks gestation, a minimum anti-D immunoglobulin dose of 500 IU should be administered within 72 hours of the event. ***(APPENDIX XVI)***

h) The potential sensitising events are:

   i. Invasive prenatal diagnostic and *in-utero* therapeutic procedures.
   ii. Antepartum haemorrhage.
   iii. External cephalic inversion of the foetus.
   iv. Ectopic pregnancy.
   v. Evacuation of molar pregnancy.
   vi. Intrauterine death and stillbirth.
   vii. Miscarriage & threatened miscarriage.
   viii. Therapeutic termination of pregnancy.
   ix. Delivery (normal, instrumental or via caesarean section).
   x. Intra-operative cell salvage.
   xi. Abdominal trauma.

9.7.2 Postnatal prophylaxis

a) At least 500 IU of anti-D immunoglobulin must be given to every non-sensitised RhD negative woman within 72 hours following the delivery of an RhD positive baby.

b) A test for foetomaternal haemorrhage is recommended to guide the dosage of anti-D immunoglobulin prophylaxis. A repeat FMH test 48 – 72 hours post-prophylaxis is recommended to ensure clearance of RhD positive foetal blood from maternal circulation.

c) If the pregnancy is non-viable and no sample can be obtained from the baby, anti-D immunoglobulin should be administered to a non-sensitised RhD negative woman within 72 hours of diagnosis.

9.8 RECOMMENDATIONS

a) It is recommended that the blood collection centre keeps a list of their RhD negative donors who can be contacted in an emergency.

b) Clinicians in charge of known RhD negative patients must alert the blood bank of their patient's blood requirement at least a week prior to the required date, such as planned surgeries or expected date of delivery. This is to provide ample time for the blood collection centre to collect appropriate units of blood.

c) Monitoring of anti-D once anti-D is detected during pregnancy: Anti-D should be measured every 4 weeks up to 28 weeks of gestation and then every 2 weeks until delivery.

References

1. Qureshi, H., Massey, E., Kirwan, D., Davies, T., Robson, S., White, J.& Allard, S. (2014). BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the foetus and newborn. *Transfusion Medicine*, *24*(1), 8-20.

2. Guideline No 22: The use of Anti-D Immunoglobulin for RhD prophylaxis. Royal College of Obstetrics and Gynaecologists

3. Guidelines for the estimation of Foetomaternal Haemorrhage. Working Party of the British Committee for Standards in Haematology, Transfusion Taskforce.

4. The Management of Women with Red Cell Antibodies during Pregnancy Green-top Guideline No. 65 Royal College of Obstetrics and Gynaecologists. 2014

10.0 MASSIVE HAEMORRHAGE & MASSIVE TRANSFUSION

10.1 MASSIVE HAEMORRHAGE

Massive haemorrhage is defined as blood loss of 150 mL/min or 50% blood volume within 3 hours or loss of total blood volume in 24 hours.

10.2 MASSIVE TRANSFUSION

Massive transfusion is defined as infusion of ≥10 units of red cell within 24 hours or a transfusion of blood and blood components equivalent to or more to the patient's total blood volume if less than 24 hours or replacement of 50% or more of the estimated blood volume within 3 hours.

In children - massive transfusion is defined as the requirement of packed red cells >40 mL/kg in the first 4 hours or >80 mL/kg in the first 24 hours.

Table 10.1: Calculating blood volume

Age group	Blood volume
Neonates	80 – 95 mL/kg
Children	80 mL/kg
Adults	70 mL/kg

The main management goals in massive haemorrhage are:

a) Identify source of bleeding & securing haemostasis.
b) Restoration of circulatory volume.
c) Improving tissue oxygenation.
d) Correction of coagulopathy.
e) Consider initiating massive transfusion protocol (MTP) based on local policy.

Consider activating MTPs for:

- patients who require greater than 3 units of blood in one hour (or anticipated) – this is known as the critical administration threshold.
- patients with loss of more than 50% blood volume within 3 hours.
- if heart rate/systolic blood pressure >1.4 (shock index). *Refer also to* ***APPENDIX XVII****: Class 3 shock.*
- Those who meet criteria using a validated score. The most common is the ABC score. Consider activating MTP when 2/4 are present:
    - Penetrating mechanism
    - Systolic blood pressure <90 mmHg
    - Heart rate >120 beats per minute
    - Positive ultrasound FAST exam

High risk patients that need close monitoring:

a) Prolonged hypotension and shock predispose patients to disseminated intravascular coagulation (DIC) and acute respiratory distress syndrome (ARDS).

b) Extensive tissue damage, particularly head injuries, is associated with coagulopathy.

c) Hepatic and renal failure patients have abnormal haemostasis or plasma proteins and impaired metabolic response to citrate, potassium or glucose infused with stored blood.

Refer ***APPENDIX XVII*** *for classification of hypovolaemic shock according to blood loss.*

Refer ***APPENDIX XVIII*** *for management strategy for trauma and massive transfusion.*

10.2.1 Massive haemorrhage/transfusion protocol (MHP/MTP)

a) Massive haemorrhage/transfusion protocol is used to identify and manage patients at risk of bleeding by standardizing blood orders for component replacement during the bleeding episode. It specifies the responsibilities of the clinical team, pathology laboratory and the blood bank. It defines communication and information to be relayed.

b) The protocol should be modified for specific populations such as obstetric or paediatric patients.

c) Activation and cessation of the MHP/MTP should be clearly communicated to all relevant teams.

d) Each hospital should develop its own local MHP/MTP. A multidisciplinary team should be established to develop the protocol. Transfusion ratio of 1:1:1 recommended (4 packed cells, 4 fresh frozen plasma, 4 random platelet).

e) In developing the protocol, local resources should be taken into consideration.

f) Early communication with a transfusion specialist/haematopathologist is required.

g) Appropriate laboratory investigation is important in the evaluation and monitoring of patients with massive haemorrhage and massively transfused which includes coagulation and biochemical test.

h) In emergency situations, blood sample for blood grouping and crossmatching should be taken prior to transfusion of safe O blood.

Table 10.2: Haematology monitoring in massive transfusion

Investigation	Target Value
Haemoglobin; Haematocrit	8 g/dL; 0.25
Platelet Count	$\geq$ 50 x 10^9/L
Prothrombin Time (PT)	< 1.5 x control
Partial Thromboplastin Time (PTT)	< 1.5 x control
Fibrinogen	> 1.5 g/L

This laboratory criteria should be used in conjunction with clinical condition.

*Refer **APPENDIX XIX** for example of massive transfusion protocol in obstetric haemorrhage*.

10.2.2 Choice of blood and blood products/derivatives used in the management of massive haemorrhage

a) Crystalloids and colloids are valuable during the initial stage of resuscitation.

b) Early use of tranexamic acid is recommended.

c) Red cells

i. Red cells transfusion may be adequate during resuscitation.
ii. When bleeding continues, group-specific whole blood may be given for further management in restoring blood volume and for oxygen-carrying capacity.

d) Platelet

i. Thrombocytopenia can occur usually as a result from haemodilution and also may be due to increased consumption.
ii. It is indicated when platelet count <50 x 10^9/L in acutely bleeding patient and <100 x 10^9/L in patient with CNS injury and with continuous bleeding.
iii. Platelet transfusion should be considered early in bleeding patients especially in cardiac bypass patients (platelet functional abnormalities due to anti-platelet drugs) even with a normal platelet count.

e) Fresh frozen plasma

i. These blood components are used for the correction of coagulation abnormalities.
ii. Indicated in cases of continuous bleeding with abnormal coagulation tests (PT and APTT > 1.5 x control).

f) Cryoprecipitate

i. Most useful in massive haemorrhage as a rapid source of fibrinogen.
ii. Fibrinogen replacement can be achieved by cryoprecipitate transfusion.
iii. Fibrinogen should be maintained > 1.5 g/L.
iv. Higher levels are likely to improve haemostasis.
v. The fibrinogen level is more sensitive than PT and APTT to a developing dilutional or consumptive coagulopathy.

References

1. Transfusion of Blood Products In Trauma: An Update

2. Gustavo P. Fraga, MD, PHD,*† Vishal Bansal, MD,* and Raul Coimbra, MD, PHD, FACS*

3. *Department of Surgery, Division of Trauma, Surgical Critical Care, and Burns, University of California San Diego, San Diego, California and Division of Trauma Surgery, State University of Campinas, Campinas, Brazil

4. AU, B. K., Dutton, W. D., Zaydfudim, V., Nunez, T. C., Young, P. & Cotton, B. A. 2009. Hyperkalemia Following Massive Transfusion in Trauma. *Journal of surgical research,* 157**,** 284-289.

5. Blackall P, D. 2001. Approach to Acute Bleeding and Massive Transfusion - Handbook of Transfusion Medicine.

6. Fernández, M. C., Fuentes, G. C., Fernández, A., Vázquez, T., Aznarez, S. B. & López, A. 2011. Massive transfusion predictive scores in trauma. Experience of a transfusion registry. *Medicina Intensiva,* 35**,** 546-551.

7. Fraga, G., Bansal, V. & Coimbra, R. 2010. Transfusion of Blood Products in Trauma: An Update. *The Journal of Emergency Medicine,* 39**,** 253 -260.

8. Fries, D. 2007. *Coagulation management in massive transfusion* [Online]. [Accessed].

9. Geeraedts, L. M. G., Kaasjager C, H. A. H., Van Vugt D, A. B. & Frolke, J. P. M. 2009. Exsanguination in trauma: A review of diagnostics and treatment options. *Journal Care Injured,* 40**,** 11-20.

10. Godier, A., Ozier, Y. & Susen, S. 2011a. Massive transfusion: assessing higher plasma: blood ratios and earlier plasma administration. *European Journal of Anaesthesiology,* 28**,** 149 -151.

11. Godier, A., Ozier, Y., Susen, S. & Périopératoire', F. T. G. D. I. E. H. 2011b. Massive transfusion: assessing higher plasma: blood ratios and earlier plasma administration. *European Journal of Anaesthesiology (EJA),* 28**,** 149-151 10.1097.

12. Isaak, E. & Commitee, S. P. 2008. Massive Transfusion in Trauma.

13. Malone, D. L., Hess, J. R. & Fingerhut, A. 2006. Massive Transfusion Practices Around the Globe and a Suggestion for a Common Massive Transfusion Protocol. *The Journal of Trauma,* 60**,** 591-598.

14. Marietta, M., Pedrazzi, P., Girardis, M. & Luppi, M. 2011. Massive bleeding: Are we doing our best? *Transfusion and Apheresis Science,* 45**,** 287-290.

15. Mitra, B., Mori, A., Cameron, P. A., Fitzgerald, M., Street, A. & Bailey, M. 2007. Massive blood transfusion and trauma resuscitation. *Journal Care Injured,* 38**,** 1023-1029.

16. Mitra, B., Mori, A., Peter A, C., Fitzgerald, M., Paul, E. & Street, A. 2010. Fresh frozen plasma (FFP) use during massive blood transfusion in trauma resuscitation. *Journal Care Injured,* 41**,** 35-39.

17. National Blood Authority, C., Australia. 2011. Patient Blood Management Guidelines: Module 1. *In:* Authority, N. B. (ed.). National Blood Authority, Canberra, Australia.

18. Rahbara H, M., Foxa E, E., Del Juncoa J, D., Cottonc A, B., Podbielskic M, J., Matijevicc, N., Cohene J, M., Schreiberf A, M., Zhangg, J., Mirhajig, P., Durana J, S., Reynoldsa J, R., Benjamin-Garnerh, R. & B. Holcombc, J. 2012. Coordination and management of multicenter clinical studies in trauma:

19. Experience from the PRospective Observational Multicenter Major Trauma Transfusion (PROMMTT) Study. *Resuscitation,* 83**,** 459 - 464.

20. Rainera H, T., Anthony, M., Hob, H., Janice, H., Yeunga, H., Nai Kwong Cheunga, Raymond, S., Wongc, M., Ning Tangd, Keung, S., Lai, B., S & Abraham, C. 2011. Early risk stratification of patients with major trauma requiring massive blood transfusion. *Resuscitation,* 82**,** 724-729.

21. Rangarajan, K., Subramanian, A. & Mohan Pandey, R. 2011. Determinants of mortality in trauma patients following massive blood transfusion. *Journal of Emergency Trauma Shock,* 4**,** 58-63.

22. Scotia, P. B. C. P. N. 2010. Guidelines for Massive Transfusion in Nova Scotia. *In:* Health, N. S. (ed.). Nova Scotia.

23. Spahn, D. R., Cerny, V., Coats, T. J., Duranteau, J., Fernández, Mondéjar, Gordini, G., Stahel, P. F., Hunt, B. J., Komadina, R., Neugebauer, E., Ozier, Y., Riddez, Schultz, A., Vincent , J.-L. V. & Rossaint, R. 2007. Management of bleeding following major trauma: a European guideline. *Journal of anaesthesiology,* 11.

24. Stainsby, D., Maclennan, Thomas, S. D., Isaac, J. & Hamilton, P. J. 2006. Guidelines on the management of massive blood loss. *British Journal of Haematology***,** 634-641.

11.0 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

11.1 DEFINITION

DIC is an acquired syndrome characterized by systemic intravascular activation of coagulation leading to bleeding (due to depletion of platelets and coagulation factors) and thrombosis (due to widespread deposition of fibrin in the circulation). It is always secondary to a primary disease state which initiates the process of intravascular coagulation (Table 11.1).

Table 11.1: Clinical condition associated with DIC

Clinical condition	Causes
Sepsis	Gram-positive bacteria, Gram-negative bacteria, malaria, spirochetes, rickettsiae, protozoa, fungi, viruses
Trauma	Polytrauma, neurotrauma, fat embolism, burns
Malignancy	Solid tumors, haematological malignancies (acute promyelocytic leukaemia or monocytic leukaemia)
Obstetric complication	Postpartum haemorrhage, amniotic fluid embolism, abruptio placentae, placenta praevia, preeclampsia/eclampsia, retained dead foetus syndrome
Vascular disorder	Large vascular aneurysms, Kasabach-Merritt syndrome
Toxic reaction	Snake bites, recreational drugs
Immunologic reaction	Haemolytic transfusion reaction, transplant rejection

11.2 CLINICAL FEATURES

The clinical features of DIC varies. DIC may present with laboratory abnormalities only, haemorrhage and/or thrombosis. Most common presentations of DIC include excessive uncontrolled bleeding, bruising and oozing from puncture sites.

11.3 DIAGNOSIS

The diagnosis of DIC is based on the clinical suspicion supported by laboratory investigations in a patient with a clinical condition known to be associated with DIC. The classical characteristic laboratory findings include:

Table 11.2: Characteristic laboratory findings in DIC

Laboratory Test	Level
Platelet count	Low (<150 x 10^9/L) or decreasing trend of platelet count
Prothrombin time (PT)	Prolonged (>1.5 x PT ratio control)
Activated partial thromboplastin time (APTT)	Prolonged (>1.5 x APTT ratio control)
Fibrinogen	Low (<150 mg/dL or 1.5 g/L)
Fibrin degradation products (FDPs/D-Dimer)	Elevated

There is no gold standard diagnostic test for DIC. The International Society for Thrombosis and Haemostasis (ISTH) has recommended the use of a scoring system for overt DIC (*Refer **Table 11.3** and **Figure 11.1**)*. The presence of an underlying disorder known to be associated with DIC is a prerequisite for the use of this scoring system.

Table 11.3: ISTH Diagnostic Scoring System for DIC

Variable	Level	Score
Platelet count	>100 x 10^9/L	0
	50 – 100 x 10^9/L	1
	< 50 x 10^9/L	2
Fibrin marker (*e.g.* D-dimer, fibrin degradation products)	No increase	0
	Moderate increase	2
	Strong increase	3
Prothrombin time	< 3 seconds	0
	3 – 6 seconds	1 (INR >1.3 = 1)
	> 6 seconds	2 (INR > 1.5 = 2)
Fibrinogen level	≥ 1 g/L	0
	< 1 g/L	1

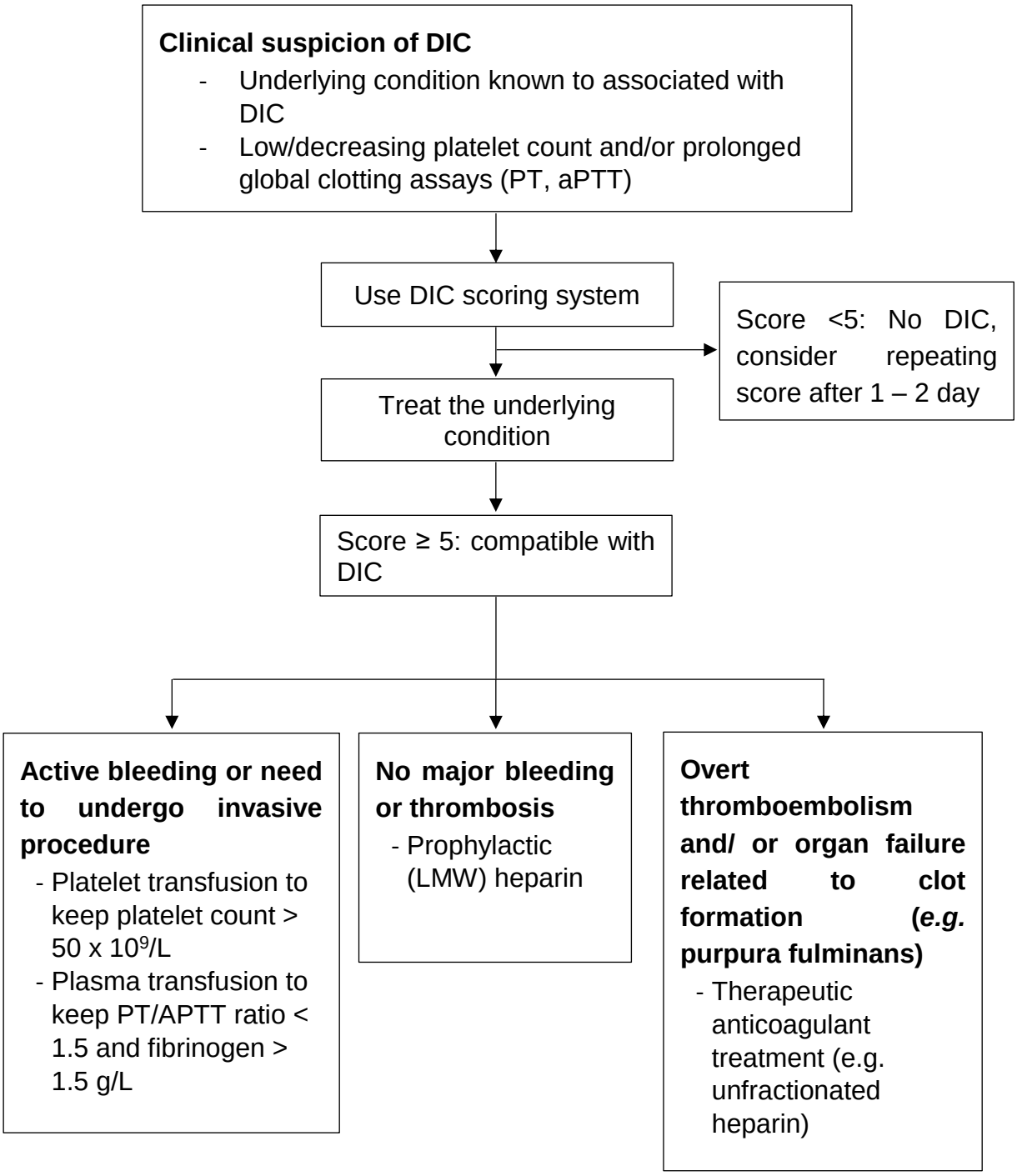


Figure 11.1: Flowchart for the diagnostic and therapeutic management of DIC

11.4 MANAGEMENT

Key to the treatment of DIC is specific and vigorous treatment of the underlying disorder.

Additional supportive treatment with blood component therapy aiming at the coagulation abnormalities may be required. However, it should not primarily be based on laboratory results and should in general be reserved for patients that present with active bleeding, requiring an invasive procedure or at risk of bleeding.

a) Platelet transfusion

   i. Platelet transfusion should be considered in:
      - DIC patients with active bleeding and platelet count <50 x 10^9/L.
      - DIC patient at high risk of bleeding (*e.g.* post-operative patients or due to undergo an invasive procedure) and a platelet count of <50 x 10^9/L.
   ii. Dosage: 1 unit of random platelet concentrate per 10 – 15 kg body weight

b) Fresh Frozen Plasma (FFP) transfusion

   i. FFP transfusion should be considered in:
      - DIC patients with active bleeding and PT/aPTT ratio >1.5 times the normal value.
      - DIC patients at high risk of bleeding (*e.g.* post-operative patients or due to undergo an invasive procedure) and PT/aPTT ratio >1.5 times the normal value.
   ii. Dosage: 15 – 20 mL/kg body weight

c) Cryoprecipitate transfusion

   i. Cryoprecipitate may be indicated in DIC and bleeding patients with plasma fibrinogen < 1.5 g/L.
   ii. Dosage : 1 unit of cryoprecipitate per 5 – 10 kg body weight
   (5 – 10 units for adult)

References

1. Papageorgion C, Jourdi G, Adjambri E, Walborn A, Patel P, Fareed J, et al. Disseminated Intravascular Coagulation: An update on pathogenesis, diagnosis and therapeutic strategies. Clinical and Applied Thrombosis/Hemostasis. 2018;24(9S):8S-28S.
2. Levi M, Scully M. How I treat disseminated intravascular coagulation. Blood. 2018 Feb;131(8):845-854.
3. Association of Surgical Technologists. Guideline for the best practices for treatment of Disseminated intravascular coagulation. 2018.
4. Tachil J. Disseminated Intravascular Coagulation: A Practical Approach. Anaesthesiology. 2016 July;125(1):230-236.
5. Wada H, Thachil J, Di Nisio M, Mathew P, Kurosawa S, Ganda S, et al. Guidance for diagnosis and treatment of disseminated intravascular coagulation from harmonization of the recommendations from three guidelines. Journal of Thrombosis and haemostasis. 2013;11:761-767.
6. Thachil J, Toh CH. Current concepts in the management of disseminated intravascular coagulation. Thrombosis Journal. 2012; 1:54-59.
7. Di Nisio M, Baudo F, Cosmi B, D'Angelo A, De Gasperi A. Diagnosis and treatment of disseminated intravascular coagulation: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISET). Trombosis Research. 2011.
8. Levi M, Meijers JC. DIC: Which laboratory tests are most useful. Blood Reviews. 2011;25:33-37.
9. Wada H, Asakura H, Okamoto K, Iba T, Uchiyama T, Kawasugi K, et al. Expert consensus for the treatment of disseminated intravascular coagulation in Japan. Thrombosis Journal. 2010;125:6-11.
10. BCSH. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Journal of Haematology. 2009;145:24-33.

12.0 TRANSFUSION IN PAEDIATRIC

12.1 INTRODUCTION

Particular attention in paediatric transfusion is important as there is a wide age range. Enhanced donor selection and screening is required for foetal, neonate and infant transfusion. Neonates and infants require repeated transfusions more frequently than older children and adults. The increase need for transfusion is usually due to:

a) Large volume phlebotomy for blood tests relative to the limited available blood volume.
b) Postnatal physiologic anaemia frequently encountered in conditions involving cardiopulmonary compromise.
c) Limited or delayed responsiveness of infant bone marrow to a variety of haematological stresses.

Transfusion in paediatrics needs to take into account that the naturally occurring antibodies (*e.g.* anti-A, anti-B) will only be fully developed when the infant is 4 months and older. Infants who are less than 4 months old may have antibodies that have been passively transferred from their mothers. Transfusion of blood and blood components presents potential risks which may have a more significant outcome for ill, high-risk infants than for older recipients. Transfusion in infants must be individualized, based on each infant's clinical status and laboratory results.

12.2 PRE-TRANSFUSION TESTING IN INFANTS LESS THAN 4 MONTHS OF AGE

Samples from both mother and infant should be obtained for initial ABO and RhD group determination. The sample to be taken from the infant shall be 1.5 mL to 2.0 mL blood in an EDTA tube. A volume of 3 mL to 5 mL blood sample in an EDTA tube shall be also be taken from the mother. Both samples shall be sent to the hospital blood bank together under a single request.

a) Investigations on the maternal sample:

   i. ABO and RhD typing.
   ii. Screening for the presence of atypical red cell antibodies.
   iii. Identification of the antibody/antibodies if the antibody screening is positive.

b) Investigation on the infant sample:

   i. ABO and RhD typing. The infant's ABO group is determined from the red cells alone (forward grouping) since the corresponding antibodies will be weak or absent in the serum.
   ii. If maternal blood is not available, the infant serum/plasma sample must be screened to exclude atypical antibodies. The serum may contain passively transferred maternal antibodies. Therefore extra sample from infant is required (3 – 5 mL). However, this is not encouraged.

c) If no antibodies detected, the red cell transfusion is ABO-compatible with the infant and the mother, and the unit is either Rh-negative or the same Rh group as the infant.

d) If unexpected red cell antibodies are detected during screening, and/or DAT is positive, investigations shall be performed to further identify the unexpected antibodies.

12.3 PRE-TRANSFUSION TESTING IN INFANTS MORE THAN 4 MONTHS OF AGE

For patients more than 4 months old, pre-transfusion testing is similar to adult. *Refer to* ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.*** The sample taken shall be between 3 mL to 5 mL of blood in an EDTA tube.

12.4 RED CELL TRANSFUSION

Blood loss due to phlebotomy or intraoperatively should be replaced when >10% of estimated blood volume (EBV) is lost, in an otherwise stable infant.

For infants, EBV = 80 – 85 mL/kg.

For preterm infants, EBV = 85 – 90 mL/kg.

Symptomatic congenital heart disease or congestive heart failure: transfuse cautiously to maintain haemoglobin >9 g/dL.

a) Infants of less than 4 months of age require red blood cell transfusion if:

   i. Haemoglobin <12 g/dL in first 24 hours of life.
   ii. Haematocrit <20% with symptoms of anaemia with low reticulocyte count.
   iii. Haematocrit <30% on oxygen therapy with FiO_2 >35%, continuous positive airway pressure or with clinical signs like apnoea, bradycardia, tachycardia and low weight gain.
   iv. Haematocrit >35% on oxygen in hood or on intermittent mandatory ventilation (IMV) with mean airway pressure (MAP) >6 cm of H_2O.
   v. Haematocrit >45% in presence of cyanotic congenital heart disease.
   vi. Blood loss >10% of estimated blood volume.

*Refer **APPENDIX XX** for suggested transfusion threshold for infants under 4 months of age.*

b) Infants of more than 4 months of age will require red blood cell transfusion if there is:

   i. Acute loss of >15% of estimated blood volume.
   ii. Hypovolaemia that is not responsive to other treatment.
   iii. Post-operative symptomatic anaemia.
   iv. Pre-operative haemoglobin <12 g/dL in presence of severe cardiopulmonary disease.
   v. Severe chronic anaemia with haemoglobin <7 g/dL.
   vi. Severe respiratory distress: transfuse to maintain haemoglobin >10 g/dL (haematocrit >40%).

vii. For stable children with non-cyanotic heart disease, a restrictive transfusion threshold of 8 g/dL following cardiopulmonary bypass (CPB) is recommended.
viii. The precise threshold will depend on the clinical situation.

*Refer **APPENDIX XXI** for management of hypovolaemia in paediatric patients.*

Table 12.1: Suggested transfusion thresholds for pre-term neonates

Postnatal age	Suggested transfusion threshold haemoglobin (g/dL)		
	Ventilated	On oxygen/ NIPPV[c]	Off oxygen
First 24 hours	<12	<12	<10
≤ Week 1 (Day 1 – 7)	<12	<10	<10
Week 2 (Day 8 – 14)	<10	<9.5	<7.5[b]
≥ Week 3 (Day 15 onwards)	<10	<8.5	<7.5[b]

a

Standard definition of pre-term is <37 weeks gestational age at birth but table applies to very pre-term neonates (<32 weeks).

b

It is accepted that clinicians may use up to 8.5 g/dL depending on clinical situation.

c

NIPPV, non-invasive positive pressure ventilation.

In actively bleeding or unstable neonates (both cyanotic and non-cyanotic) or children following CPB, a higher haemoglobin threshold may be appropriate and signs of inadequate oxygen delivery can provide additional information to support transfusion.

In haemodynamically-stable paediatrics patients (excluding neonates), evidence suggests that:

a) Haemoglobin concentration <7 g/dL, red cell transfusion is often appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.
b) Haemoglobin concentration of 7 – 9 g/dL, red cell transfusion may be appropriate. The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions.
c) Haemoglobin concentration >9 g/dL, red cell transfusion is often unnecessary and may be inappropriate.
d) Symptomatic anaemia (tachycardia and/or tachypnoea): transfuse to improve clinical parameters and treat the underlying problem.

In paediatric patients with transfusion-dependent thalassaemia, the evidence does not support any change to the current practice of maintaining a pre-transfusion haemoglobin concentration of 9 – 10 g/dL.

*Refer **APPENDIX XXII** for maintenance blood transfusion in thalassaemia.*

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

12.5 BLOOD SELECTION FOR NEONATAL TRANSFUSION

Volume of blood to be transfused is calculated based on the neonate's body weight.

$$\textit{Volume required (mL)} = \textit{Body weight (kg)} \times \textit{Haemoglobin rise required (g/dL)} \times \textit{Transfusion factor (0.4)}$$

Blood used for neonatal transfusions shall be compatible with the mother's blood.

12.5.1 Red cell transfusion

- Group O red cells are generally suitable for top-up transfusion.
- Use infant's own ABO group if crossmatching is done using infant's blood (without mother's sample).
- Fresh blood preferably not more than 5 days old.
- Leucodepleted.
- Irradiated (if available).
- Small aliquot (paedipack) for top-up transfusion.
- Blood for exchange transfusion in neonatal jaundice cases are as provided in Table 12.2 below.

12.5.1.1 Exchange Transfusion (ET)

Exchange transfusion (ET) is performed to manage a high or rapidly rising bilirubin not responsive to intensive phototherapy or IV immunoglobulin (Ig) or for severe anaemia, without hypovolaemia. The main indication for ET is to prevent neurological complication (kernicterus) caused by rapidly rising unconjugated bilirubin (severe hyperbilirubinaemia) concentration. The underlying cause is usually haemolytic disease of foetus and newborn (HDFN) due to antibodies against the baby's red cells causing haemolysis.

A single blood volume ET will remove 75% of the neonatal red cells, and a double volume (160 – 200 mL/kg depending on gestational age) up to 85 – 90% red cells, and up to 50% of circulating bilirubin. A double-volume exchange transfusion should be more successful in removing antibody-sensitized neonatal red cells and reduce the need for a subsequent ET, but there is little direct evidence.

Blood selection for ET:

- A group specific whole blood (refer to Table 12.2).
- Group O RhD positive or negative red cells, depending on maternal ABO and Rh blood group.
- Fresh (preferably not more than 5 days old).
- Leucodepleted.
- Irradiated to prevent transfusion-associated graft versus host disease (TA-GVHD) (if available).

- In hospital blood banks which do not have facilities to identify O* by performing haemolysin test, blood group O RhD positive fresh red cell suspended in fresh AB plasma can be used.
- Examples of usage:
  - For HDFN due to anti-D: use group O Rh negative.
  - For HDFN due to anti-Rh c: use group O Rh D positive that does not have the c antigen (R_1R_1, CDe/CDe).
- O* is group O RhD positive whole blood with low titres of anti-A and anti-B and negative for haemolysin.

Table 12.2: Blood for exchange transfusions in neonatal jaundice cases

		MOTHER'S BLOOD GROUP			
		O	**A**	**B**	**AB**
BABY'S BLOOD GROUP	**O**	O	O	O	O
	A	O*	A	O*	A
	B	O*	O*	B	B
	AB	O*	A	B	AB

O is group O RhD positive whole blood with low titres of anti-A and anti-B and negative for haemolysin.*

*Refer **Appendix XXIII** for guidelines for neonatal exchange transfusion.*

12.5.1.2 Intrauterine Transfusion (IUT)

Table 12.3: Products for intrauterine transfusion

Red cells and platelets	
Leucodepleted Irradiated to prevent TAGVHD	
Red cells	**Platelets**
1) Plasma reduced 2) Citrate phosphate dextrose anti-coagulant (theoretical risk of toxicity from other additive solutions) 3) <5 days old 4) Group O with low haemolysin titre (or ABO identical with the foetus) 5) RhD and red cell antigen negative for maternal alloantibodies 6) Indirect anti-globulin test crossmatch-compatible with the mother's plasma	Compatible with any maternal alloantibodies (*e.g.* anti-HPA)

*Refer **Section 8.8 Intrauterine Transfusion** and **APPENDIX XIV** for blood selection for IUT.*

12.5.2 Platelet transfusion

Platelet transfusion is indicated in patients with thrombocytopenia and abnormal platelet function when there is bleeding or bleeding is anticipated.

a) In the presence of intracranial or other life-threatening haemorrhage, platelet transfusion is usually required while other therapy is being instituted.

b) In patients undergoing surgery or invasive procedures the platelet count should be maintained above 50 x 10^9/L. For neurosurgery and eye surgery it is recommended that platelet count is above 100 x 10^9/L.

c) For plasma and platelet transfusions, infants should receive ABO-specific components whenever possible to avoid transfusing plasma antibody which is incompatible with the infant's red cell antigens.

Table 12.4: Suggested thresholds of platelet counts for platelet transfusion in children

Platelet count (× 10^9/L)	Clinical situation to trigger platelet transfusion
<10	Irrespective of signs of haemorrhage (excluding ITP, TTP/HUS, HIT)
<20	Severe mucositis Sepsis Laboratory evidence of DIC in the absence of bleeding[a] Anti-coagulant therapy Risk of bleeding due to a local tumour infiltration Insertion of a non-tunnelled central venous line
<50	Prior to lumbar puncture[b]
<50	Moderate haemorrhage (*e.g.* gastrointestinal bleeding) including bleeding in association with DIC Surgery, unless minor (except at critical sites) including tunnelled central venous line insertion
<75 – 100	Major haemorrhage or significant post-operative bleeding (*e.g.* post cardiac surgery) Surgery at critical sites: central nervous system including eyes

ALL, acute lymphoblastic leukaemia; DIC, disseminated intravascular coagulation; HIT, heparin-induced thrombocytopenia; HUS, haemolytic uraemic syndrome; ITP, immune thrombocytopenia; LP, lumbar puncture; TTP, thrombotic thrombocytopenic purpura.

a

Note: routine screening by standard coagulation tests not advocated without clinical indication; for laboratory evidence of DIC see Section 'Disseminated intravascular coagulation'.

b

It is accepted that prior to lumbar puncture some clinicians will transfuse platelets at higher counts (*e.g.* 50 × 10^9/L) in clinically unstable children, non ALL patients, or for the first LP in newly-diagnosed ALL patients to avoid haemorrhage and cerebrospinal fluid contamination with blasts, or at lower counts (≤20 × 10^9/L) in stable patients with ALL, depending on the clinical situation. These practices emphasize the importance of considering the clinical setting and patient factors.

12.6 IMMUNE THROMBOCYTOPENIA

Neonatal immune thrombocytopenia is caused by maternal anti-platelet antibodies, either auto- or alloanti-platelet antibodies, which cross the placenta and interact with foetal platelets.

a) Neonatal Alloimmune Thrombocytopenia (NAIT)

i. NAIT results most commonly from maternally derived anti-HPA-1a, anti-HPA-3a or anti-HPA-5b platelet antibodies.
ii. All neonates with NAIT (or suspected NAIT) and thrombocytopenia after birth should be discussed with a neonatologist/haematologist.
iii. Severely thrombocytopenic neonates with suspected NAIT should receive platelet transfusions at thresholds depending on bleeding symptoms or family history. *Refer* ***Table 12.5***.
iv. The suggested threshold of 25×10^9/L in the absence of bleeding is the same as that for neonates without NAIT. However, the results of diagnostic serological tests for HPA may not be available immediately.
v. A post-transfusion platelet count should be measured to check the increment.
vi. The baby should be monitored for intracranial haemorrhage (ICH) by cranial ultrasound and, if there is evidence of ICH, platelet transfusions should be given to maintain platelet counts $>100 \times 10^9$/L for the period that the baby is felt to be at highest risk of on-going haemorrhage.
vii. The treatment of choice is matched antigen-negative platelets, usually washed or re-suspended and irradiated maternal platelets.
viii. If these are not immediately available, treatment should be initiated as for thrombocytopenia due to autoantibodies.
ix. If HPA antigen-negative platelets are unavailable or ineffective in producing a platelet rise, random donor platelets (crossmatched) and/or IV Ig may be used, which may reduce the need for platelet transfusions until spontaneous recovery in platelet count occurs 1 – 6 weeks after birth.
x. For preterm neonates with very severe thrombocytopenia (platelet count below 25×10^9/L) platelet transfusions should be administered in addition to treating the underlying cause of the thrombocytopenia. Suggested threshold counts for platelet transfusions in different situations are given in **Table 12.5**.
xi. Consider intravenous immunoglobulin in NAIT refractory to platelets negative for HPA antigens or if antigen-matched platelets are unavailable.

Table 12.5: Suggested thresholds of platelet count for neonatal platelet transfusion

Platelet count (× 10^9/L)	Indication for platelet transfusion
<25	Neonates with no bleeding (including neonates with NAIT if no bleeding and no family history of ICH).
<50	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with ICH.
<100	Neonates with major bleeding or requiring major surgery (*e.g.* neurosurgery).
NAIT, neonatal alloimmune thrombocytopenia; ICH, intracranial haemorrhage.	

b) Thrombocytopenia due to maternal autoantibodies

Intravenous immunoglobulin (IVIg) 1 g/kg/day for up to 2 consecutive days, with or without steroids, is generally useful to increase the platelet count and to prolong platelet survival in this self-limiting disorder. Platelet transfusion is not indicated in the absence of life-threatening bleeding.

References

1. Authority, A. N. B. (2016). Patient Blood Management Guidelines Module 6: Neonatal and Paediatrics. *Book Patient Blood Management Guidelines Module 6 :Neonatal and Paediatrics*.

2. Avnish Bharadwaj, Mamta Khandelwal & Bhargava, S. K. (2014) In *Indian Journal of Anaesthesis*, Vol. 58, pp. 652–57.

3. Helen V. New, Jennifer Berryman, Paula H. B. Bolton-Maggs, Carol Cantwell, Elizabeth A. Chalmers, Tony Davies, Ruth Gottstein, Andrea Kelleher, Sailesh Kumar, Sarah L. Morley, Simon J. Stanworth & Haematology, a. o. b. o. t. B. C. f. S. i. (2016). Guidelines on transfusion for foetuses, neonates and older

children. *British Journal of Haematology,* Volume 175(5),784–828. doi: 10.1111/bjh.14233

4. Hussain Imam Hj Muhammad Ismail, Pak, N. H. & Thomas, . (2013). Paediatric Protocols for Malaysian Hospitals (3rd ed.): Kementerian Kesihatan Malaysia.

5. Management of anaemia in cancer patients in Europe: Findings from the Anaemia Cancer Treatment (ACT) study.

6. Nahla A. Al-Ageel a, Sinaa A. Al-Aqeel a,*, Norah O. Abanmy a, Jamal S. Alwakeel b, Alaa Sabry c,d, Khalid A. Alsaran c. Appropriateness of anaemia management in hemodialysis patients

7. Sean A Virani MSc MD FRCPC, Amit Khosla, Adeera Levin MD FRCPC. Chronic kidney disease, heart failure and anaemia

8. Massimo Franchini, Heparin –induced thrombocytopenia: an update, Thrombosis Journal, 2005.

9. 2013 Clinical Practice Guideline on the Evaluation and Management of Adults with Suspected Heparin-Induced Thrombocytopenia, American Society of Haematology

10. Dr Colin Brown Guidelines for the Management of Platelet Transfusion Refractoriness; Information Document INF139/1.1: 2011

11. Neunert C. et al, The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia, American Society of Haematology, 2011.

12. Ernest Lo, Sean Deane, Diagnosis and classification of immune-mediated thrombocytopenia, Autoimmunity review, 2014.

13. Tran, H. A., Chunilal, S. D., Harper, P. L., Tran, H., Wood, E. M. & Gallus, A. S. (2013). An update of consensus guidelines for warfarin reversal. Med J Aust, 198(4), 198-9.

14. Cushman, M., Lim, W., Zakai, N.A. Clinical Practice Guide on Antithrombotic Drug Dosing and Management of Antithrombotic Drug- Associated Bleeding Complications in Adults. ASH February 2014.

15. CPG management of dengue infection in adults (3rd edition, 2015)

16. Dengue, guidelines for diagnosis, treatment, prevention and control, new edition 2009 WHO

13.0 TRANSFUSION IN MEDICINE AND HAEMATOLOGY

Most transfusion in hospitals are given to non-surgical patients. The decision to transfuse should be based on clinical assessment supported by laboratory test result. Selection of appropriate component is essential. Where possible, appropriate alternatives should be used instead of blood such as haematinics, erythropoietin, fractionated blood products and pharmacological agents.

Blood transfusion should be avoided even in severe anaemia, unless the patient is symptomatic or has cardiovascular risks.

13.1 ANAEMIA

Anaemia is a reduction in the haemoglobin concentration of the blood below normal for age and sex.

Table 13.1: Classifications of anaemia

Microcytic, hypochromic	Normocytic, normochromic	Macrocytic
MCV < 80 fL MCH < 27 pg	MCV 80 – 95 fL MCH ≥ 27 pg	MCV > 95 fL
Iron deficiency Thalassaemia Anaemia of chronic disease Lead poisoning Sideroblastic anaemia	Many haemolytic anaemias Anaemia of chronic disease After acute blood loss Renal disease Mixed deficiencies Bone marrow failure (*e.g.* post- chemotherapy, infiltration by carcinoma, etc)	*Megaloblastic:* vitamin B12 or folate deficiency *Non-megaloblastic:* alcohol, liver disease, myelodysplasia, aplastic anaemia, myeloma and paraproteinaemia, pregnancy, neonatal, reticulocytosis, smoking, etc

13.1.1 Nutritional deficiency

The most common causes are iron deficiency, folate and vitamin B12 deficiency. The principles in the management of iron deficiency are to identify and treat the primary cause or underlying disorders which includes nutritional deficiency, menorrhagia, gastritis and malabsorption syndrome.

Iron deficiency produces microcytic red cells while folate/B12 deficiency produces macrocytic red cells. Thus, the monitoring of mean corpuscular volume (MCV) is helpful during treatment.

13.1.2 Iron deficiency

The common cause of iron deficiency is diet deficient in iron and chronic blood loss especially in woman of child bearing age.

To replenish iron stores the recommended dose of iron is:

a) Ferrous sulphate/ferrous fumarate 200 mg 3 times/day for minimum of 4 – 6 weeks (best taken before meal). The expected rise in haemoglobin level is at a rate of 0.5 – 1.0 g/dL per week. The iron store is replenished in 6 months.

    i. Monitoring of response: reticulocytes response can be seen on Day 3 – 5 and peaks between Day 8 – 10.

b) IV iron may be considered:

    i. In patients who are intolerant to oral iron preparation (*i.e.* Inflammatory bowel disease) or when oral iron is ineffective.
    ii. To support the use of erythropoiesis-stimulating agents (ESA), including in patients on renal dialysis.
    iii. Alternative to blood transfusion when a rapid rise in haemoglobin is required such as perioperative, severe anaemia in late pregnancy or postpartum.
    iv. Monitoring of response: ferritin and transferrin saturation level.

13.1.3 Folate deficiency

Folate deficiency is commonly seen in dietary deficiency, pregnancy, haemolytic anaemia and malabsorption.

The recommended dose of folic acid is 5 mg daily for 3 – 6 months.

13.1.4 Vitamin B12 deficiency

The most common cause of Vitamin B12 deficiency is failure to absorb Vitamin B12 which occurs in pernicious anaemia, gastrectomy and small intestinal (ileum) diseases.

The recommended dose of vitamin B12 (hydroxocobalamine) is IM/SC Vitamin B12, 1 mg 3 times per week for 2 weeks then IM/SC 1 mg every 3 months for life. Oral vitamin B12 is poorly absorbed from GI tract.

A blunted response to B12 is usually due to depletion of iron and/or folate stores as massive numbers of new red cells are formed, therefore a short period of iron and folate supplementation may be required.

For monitoring of response: Reticulocytosis within 1 – 2 weeks, MCV should be normalized in 8 weeks.

13.1.5 Anaemia of chronic disease

This is the second most prevalent cause of anaemia. It occurs with chronic infections (tuberculosis, osteomyelitis), inflammatory disease (rheumatoid arthritis, SLE, Crohns's disease) and malignancy.

There is a decrease in release of iron from the bone marrow to erythroblasts, insufficient erythropoietin response to anaemia and diminished red cell survival. The specific mechanism behind this is unclear but is thought to be mediated by inflammatory cytokines such as TNF-alpha, IL-1 and interferons. The diagnosis is by exclusion which includes nutritional anaemia and red cell abnormality causing chronic haemolysis.

This anaemia may respond to parenteral iron therapy. Treatment is of the underlying disorder and transfusion is rarely needed for chronic anaemia.

The principles of managing patients with anaemia of chronic disease

1. Identify and correct vitamin deficiencies.
2. Correct any identifiable causes of blood loss.
3. Treatment with erythropoeitin may be indicated.
4. Red cell transfusion is rarely needed for patients with chronic anaemia, except in decompensated situation such as:
    a) increased demand for oxygen
        i. infection
        ii. pain
        iii. fever
    b) reduction in oxygen supply
        i. acute blood loss/haemolysis
        ii. pneumonia

Signs of acute decompensation are:

a) Change in mental status.

b) Diminished peripheral pulses.

c) Congestive cardiac failure.

d) Hepatomegaly.

e) Poor peripheral perfusion (capillary refill time >2 seconds).

Management of decompensated anaemia

a) Treat infection aggressively if present.

b) Give oxygen support.

c) Correct fluid balance without overloading the patient.

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

e) Transfusion needs should be assessed on an individual basis. Single unit transfusion are generally used in patients with a low haemoglobin who are clinically stable with no active bleeding.

f) **Do not transfuse more than necessary if one unit of red cells is enough to alleviate symptoms.**

Reminder: The SINGLE unit transfusion guide can be applied to stable, normovolaemic adult patients, who do not have clinically significant bleeding, in an inpatient setting.

g) A second unit should only be considered after review of the patient which may include checking for:

   i. Clinical signs and symptoms of anaemia and excluding other causes for these symptoms, *e.g.* drug-induced dizziness.
   ii. Level of risk to patient due to anaemia.
   iii. Haemoglobin level (if appropriate).
   iv. Risk of transfusion reaction.
   v. Previous response to transfusions.
   vi. Ongoing blood loss.

h) Transfusion of 1 unit of red cells: should not exceed 4 hours.

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

13.1.6 Anaemia in renal disease

a) Anaemia affects 60 – 70% of patients with chronic kidney disease (CKD). This is mainly due to erythropoietin deficiency and reduced red cell survival. Other contributing factors which can cause anaemia usually arise through blood loss exacerbated by haemodialysis, folate deficiency, uraemia and hyperparathyroidism.

b) Haemodialysis patients tend to have more severe anaemia than those undergoing peritoneal dialysis:

   i. Greater blood loss and haemolysis.
   ii. Better removal of uncharacterized 'middle molecules' that inhibit erythropoiesis in peritoneal dialysis patients.

c) Factors contributing to anaemia:

   i. Relative deficiency of erythropoietin.
   ii. Chronic inflammation.
   iii. Hepcidin upregulation.
   iv. Iron deficiency.
   v. Reduced red cell survival.
   vi. Blood loss.
   vii. Hyperparathyroidism with marrow fibrosis.
   viii. Folate deficiency.

d) Management:

   i. Haematinics support especially folate as folate is lost during dialysis. IV iron therapy may also be required, including in combination with erythropoeitin therapy.
   ii. Erythropoietin replacement.
   iii. Transfusion is indicated only if the patient does not respond to the above and is symptomatic.

13.1.7 Haemolytic anaemia

Haemolytic anaemias are defined as anaemias that result from an increase in the rate of red cell destruction. They can be due to abnormalities affecting:

a) Red cell haemoglobin *e.g.*: haemoglobinopathies such as thalassaemia, sickle cell disease and enzymopathies such as G6PD deficiency.

b) Red cell membrane *e.g.*: spherocytosis, elliptocytosis, immune haemolysis.

c) Factors extrinsic to red cells *e.g.*: disseminated intravascular coagulation (DIC), hypersplenism, malaria and other infections, drugs and other toxin.

13.1.8 Thalassaemia

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

Approach in management of thalassaemia major

The goals of transfusion in thalassaemia major include suppression of extramedullary erythropoiesis and inhibition of increased gastrointestinal iron absorption as well as correction of anaemia.

a) Transfusion

   i. Regular transfusion to maintain pre-transfusion haemoglobin level 9 – 10 g/dL and post-transfusion haemoglobin level 1 hour after transfusion 13.5 – 15.5 g/dL. This will allow improved growth and development, reduces hepatosplenomegaly due to extramedullary haematopoeisis as well as reduces bone deformities.
   ii. Patient's red cells should be phenotyped for Rh, Kidd, Duffy and MNSs blood group before the first transfusion.
   iii. Before each red cell transfusion, it is necessary to perform screening for red cell antibodies and full crossmatch.
   iv. All thalassaemic patients should be transfused with phenotype-specific blood to avoid alloimmunization.

v. A complete and detailed record of antigen typing, red cell antibodies and transfusion reactions should be maintained for each patient and readily available if the patient is transfused at a different centre.
vi. Use leucodepleted red cells to minimize the risk of febrile non-haemolytic transfusion reaction (FNHTR), transmission of CMV and HLA alloimmunization.

b) Chelation therapy**:** An effective treatment modality in improving survival, decreasing the risk of heart failure and decreasing morbidities from transfusional iron overload.

c) Vaccination against Hepatitis B for all transfusion-dependent patients.

Refer ***APPENDIX XXII for guidelines for management of transfusion dependant thalassaemia and Paediatric Protocol for Malaysian Hospital, 4th Edition, 2018****.*

13.1.9 G6PD deficiency

G6PD deficiency is commonly asymptomatic but jaundice and anaemia are precipitated by infection, drugs and chemicals. *Refer* ***APPENDIX XXIV*** *for list of drugs and chemicals to be avoided in G6PD deficiency.*

a) Haemolysis in G6PD deficiency is self-limiting and will stop once the cells deficient in G6PD have been destroyed.

b) It is important to remove or treat any identifiable cause of haemolysis.

c) Transfusion is not required in most cases but may be life-saving in severe haemolysis when the haemoglobin level continues to fall rapidly.

13.1.10 Autoimmune haemolytic anaemia (AIHA)

AIHA is a haematologic disorder that may arise *de novo* as an idiopathic condition or in conjunction with other illnesses such as lymphoproliferative disorder or connective tissue disease.

AIHA can be classified into two major types:

- Warm antibodies reacting at 37°C (WAIHA) in 80% cases.
- Cold antibodies reacting strongly at 0 – 5°C (CAIHA) in 20% cases. However these cold antibodies are usually detected at room temperature in the laboratory.

Other types of AIHA includes mixed and drug-induced.

The autoantibody in the patient's serum usually reacts with all normal red blood cells making it almost impossible to find compatible blood. The autoantibody may mask the presence of a red cell alloantibody capable of causing a haemolytic transfusion reaction.

Table 13.2: Common investigation findings in AIHA

Test		Features
Full blood count	*Haemoglobin, haematocrit*	Normal in patient with indolent haemolysis Low in patient with fulminant haemolysis
	Reticulocyte count	Commonly high Can be low if early in diagnosis or inadequate bone marrow response
	White blood cells	Mild leucocytosis
Full blood picture (FBP)		Polychromasia, macrocytosis, nRBC, microspherocytes
Others	*Indirect bilirubin*	Increased
	Lactate dehydrogenase (LDH)	Increased
	Serum haptoglobin	Reduced
	Urine haemoglobin and haemosiderin	Positive
	Direct anti-globulin test (DAT)	Positive in 95% cases of warm AIHA

Table 13.3: Management of AIHA

Warm AIHA	Cold Agglutinin Syndrome
If bone marrow can compensate, to monitor closely.	Avoidance of cold environment.
Treat underlying cause.	Treat underlying cause.
Once anaemia developed: • Corticosteroids • Splenectomy* • Rituximab (anti CD20)* • Immunosuppression* - High dose cyclophosphamide, azathioprine, cyclosporin • Danazol* • Intravenous immunoglobulin (IVIg)	Once anaemia developed: • Corticosteroid therapy* • Cytotoxic drugs * • IVIg* • Immunosuppressive drugs* • Fludarabine* • Rituximab* • Plasma exchange* • Splenectomy*
Paroxysmal Cold Haemoglobinuria	
Supportive care. Transfusion of red cell during acute phase. Corticosteroid.	

**Under consultation and by haematologist supervision*

Transfusion in AIHA

a) Transfusion therapy in AIHA is limited to life-threatening anaemia, patients in decompensated state or severe bleeding. Avoid transfusion in haemodynamically stable patients.

b) It is often complicated by the difficulty in finding compatible blood, therefore, increases the risk of developing transfusion-related alloantibodies.

c) Red cells that are most compatible with the patient's serum is chosen in crossmatching.

d) Patient's red cells should be phenotyped for Rh, Kidd, Duffy and MNSs blood groups. These can be used to guide the exclusion of alloantibodies by indicating which antigen specificities the patient is at risk of developing.

e) Red cell transfusion if required, should be with phenotyped-match red cell.

f) Reticulocytopenia indicates a high likelihood of early need for transfusion support.

g) During transfusion, red cell should be administered slowly and monitored closely.

13.1.11 Bone marrow failure

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

Main causes of marrow failure or suppression:

i. Chemotherapy.
ii. Radiation treatment for malignant diseases.
iii. Marrow infiltration.
iv. Aplastic anaemia.
v. Infection.
vi. Toxic effects of drugs or chemicals.

Transfusion support in bone marrow failure:

a) Red cell transfusion

i. Matched ABO and RhD type.
ii. Leucodepleted and irradiated packed red cell is preferred.
iii. CMV infection can cause serious morbidity in immunocompromised CMV-negative patients. The risk can be minimised by the use of CMV-negative blood or leucodepleted red cell.
iv. Transfusion threshold for anaemia in haemato-oncology patients (chemotherapy-induced anaemia) is uncertain and depends on clinical judgement. Generally, appropriate transfusion threshold is around 7.0 – 8.0 g/dL.
v. Treatment of patients dependent on long-term transfusion (*e.g.* myelodysplasia) should aim to minimise symptoms of anaemia and improve health-related quality of life rather than achieve an arbitrary haemoglobin concentration.

b) Platelet transfusion

i. ABO compatible (ABO incompatibility can cause reduced expected increment by 10 – 30%).
ii. Leucodepleted and irradiated platelets to reduce HLA allo-immunization and transfusion associated graft-versus host disease (TA-GVHD).
iii. Maintain platelet level as stated in ***APPENDIX V.***
iv. Failure to respond to platelet transfusion may be due to:
    - Infection.
    - Splenomegaly.
    - Antibodies against HLA or platelet specific antigen.
    - Failure to control primary condition.
    - Antibiotics or antifungals therapy.
    - Disseminated intravascular coagulation.

13.1.12 Anaemia in malignancy

a) Anaemia is common in malignancy. It is due to:

i. Bone marrow suppression related to treatment.
ii. Bone marrow infiltration.
iii. Blood loss into or from tumours.
iv. Anaemia associated with chronic disease.
v. Nutritional deficiency.
vi. Impaired erythropoeisis due to inflammatory cytokines.
vii. Reduced production of the hormone erythropoietin due to kidney/liver damage.

b) Management

i. Haematinics supplementation.
ii. Erythropoietin (Epo) may benefit patients receiving myelosuppressive chemotherapy or radiotherapy especially if the anaemia is poorly tolerated. The administration of erythropoietin reduces the risk for blood transfusions and the number of units transfused in anaemic cancer patients.
iii. Red cell transfusion is indicated to alleviate symptoms of anaemia in order to improve health-related quality of life. Usually haemoglobin of 7.0 – 8.0 g/dL is required to maintain function.

13.2 THROMBOCYTOPENIA

13.2.1 Platelet refractoriness

Platelet refractoriness is defined as corrected count increment (CCI) of less than 5 x 10^9/L, using ABO-identical fresh platelets of less than 72 hours, at least on two sequential occasions, 1 hour post transfusion.

Corrected count increment is defined as body surface area (m^2) multiplied by platelet increment (per µL), divided by the number of platelet ($x10^{11}$) transfused.

$$\textit{Corrected Count Increment (CCI)} = \textit{Body surface area } (m^2) \times \textit{platelet increment (per } \mu L)$$

In practice, an increase in the patient's platelet counts of <10 x 10^9/L at between 1 and 24 hours after the transfusion can be used as a simple measure of poor response.

Platelet refractoriness can be due to non-immune ($2/3$ cases) and immune causes ($1/3$ cases). Twenty percent of cases have a combination of both immune and non-immune causes.

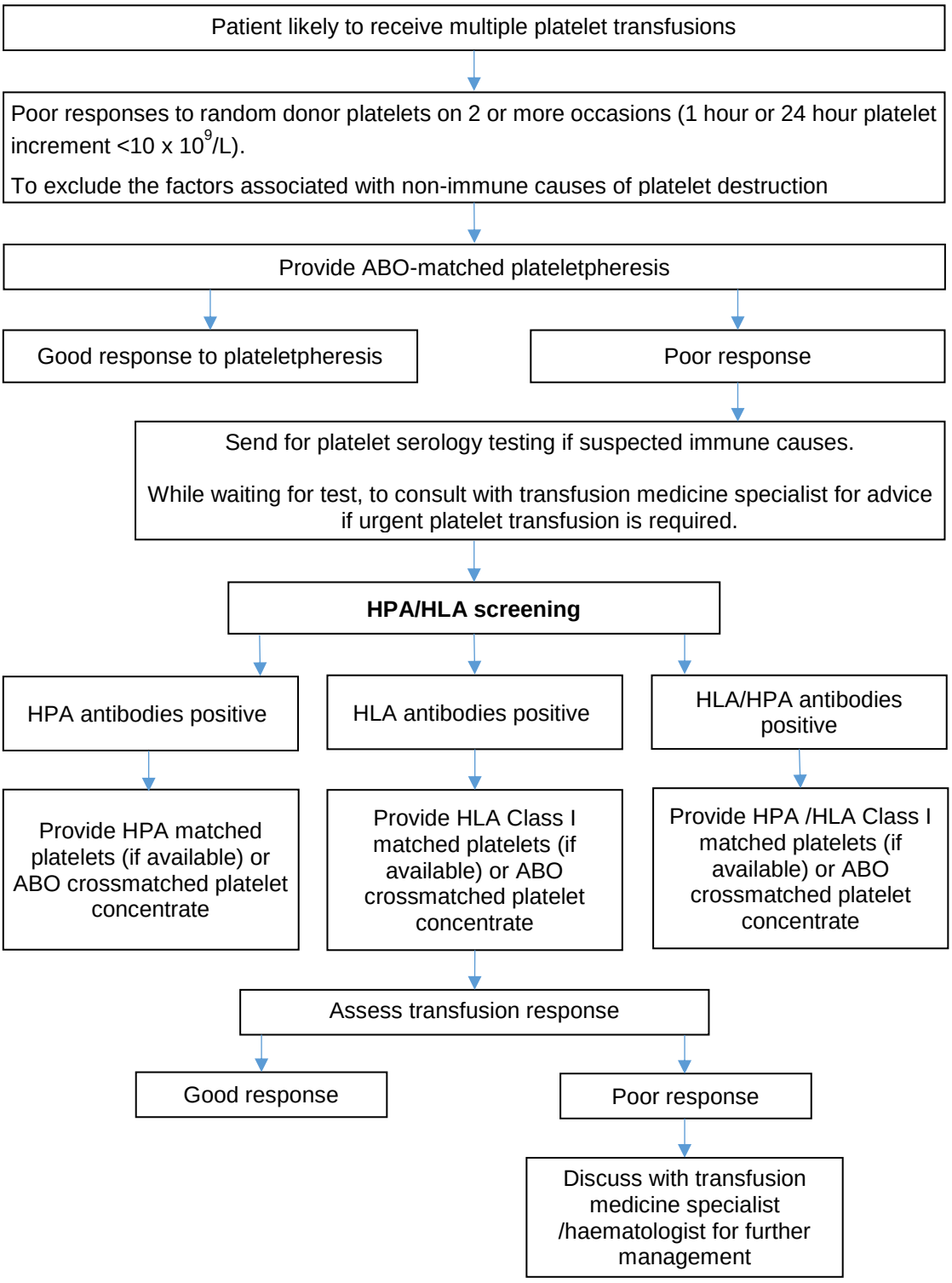
Table 13.4: Non-immune and immune causes of platelet refractoriness

Non-immune	Immune
Sepsis Fever Bleeding Splenomegaly Disseminated intravascular coagulation (DIC) Hepatic sinusoidal obstruction syndrome (hepatic veno-occlusive disease) Transfusion-associated graft-versus-host disease (TA-GVHD) Medications	Alloimmunization to human leucocyte antigen (HLA) and/or human platelet antigens (HPA)

Management of platelet refractoriness: Figure 13.1 summarizes the management of platelet refractoriness. Investigation of immune causes has to be referred to a specialized platelet laboratory. These cases require early consultation with a transfusion medicine specialist/haematologist.

Figure 13.1: Management of Platelet Refractoriness

Partially adapted with modifications to suit local management from Guidelines for the Management of Platelet Transfusion Refractoriness, UK, 2011.



13.2.2 Heparin-induced thrombocytopenia

Heparin-induced thrombocytopenia (HIT) is defined as a decrease in platelet count during or shortly following an exposure to heparin. HIT is strongly associated with thrombosis and rarely bleeding. The incidence of HIT has greatly reduced as the use of unfractionated heparin has decreased.

HIT has two distinct forms:

a) **Type 1**

i. Non-immunologic response of heparin, affecting up to 10% of patients.
ii. Usually occurs within the first two days after initiation of heparin treatment.
iii. It is characterized by a mild and asymptomatic thrombocytopenia (rarely <100 x 10^9/L) and disappears once heparin is withdrawn.

b) **Type 2**

i. Affects about 8% of heparinized patients.
ii. Due to production of antibody (IgG) towards heparin – platelet factor 4 (pf4) complexes.
iii. It can develop 5 to 10 days after exposure to heparin or 5 days after heparin withdrawal.

Management

i. Immediate cessation of heparin.
ii. Introduction of non-heparin anti-coagulants (*e.g.*: direct thrombin inhibitor: lepirudin and argatroban or Factor Xa inhibitor: danaparoid, fondaparinux). This anti-coagulation treatment is required for at least 2 to 3 months to prevent recurrence of thrombosis.
iii. Warfarin should be initiated when platelet count recovers to >150 x 10^9/L. It should be overlapped with non-heparin anti-coagulant for at least five days and until INR has reached intended target.
iv. In HIT-associated thrombosis, anti-coagulate for 3 months.
v. In HIT without thrombosis, the optimal duration is unknown. Risk of thrombosis may extend up to 4 weeks after cessation of heparin. Therefore, anticoagulation should be considered for up to 4 weeks.
vi. Platelet transfusion should be avoided in non-bleeding patients.

*Refer **APPENDIX XXV** for 4Ts score for HIT.*

13.2.3 Immune thrombocytopenia

Immune thrombocytopenia (ITP) is characterized by isolated thrombocytopenia due to antibodies formation against platelet glycoproteins. The platelet count threshold for the definition of ITP is set at 100 x 10^9/L. This in turn will lead to platelet destruction by splenic macrophages.

Table 13.5: Classification of ITP based on causes

Primary
Unknown aetiology
Secondary
1. Infection: HCV, HIV CMV, MMR, *Helicobacter pylori* 2. Autoimmune disease: systemic lupus erythematosus, antiphospholipid syndrome 3. Lymphoproliferative disease: CLL, lymphoma 4. Wiskott-Aldrich syndrome 5. Drugs: NSAIDS, cimetidines, trimethoprim-sulfamethoxazole, quinine 6. Common variable immunodeficiency

Immune thrombocytopenia usually present after an antecedent infection within the past 3 – 4 weeks in children and they tend to have more severe thrombocytopenia than adults, with platelet count <20 x 10^9/L in almost 80% of cases. For adults, ITP often has an insidious onset with no obvious triggers and follows a chronic course.

a) Management of ITP in children

i. Children with no bleeding or mild bleeding (defined as skin manifestations only, such as bruising and petechiae) can be managed with observation alone regardless of platelet count as most of them recovered spontaneously within 6 months.
ii. In cases of moderate bleeding, first line treatment:
    - Oral prednisolone 2 mg/kg/day for 14 days then taper off over 5 days (regardless of response).
    - Oral prednisolone 4mg/kg/day for 3 – 4 days.
    - IV immunoglobulin (IVIg) 0.8 g/kg/dose for a single dose
iii. Second line treatment includes dexamethasone 0.6 mg/kg/day for 4 days every 4 weeks for 6 cycles, rituximab and splenectomy.

iv. For life threatening bleeding, transfusion of larger quantities of platelets (2 – 3 times the anticipated required dose) can also be given to help stop bleeding.

Refer ***Clinical Practice Guidelines: Management of Immune Thrombocytopenic Purpura, Ministry of Health Malaysia.***

b) Management of ITP in adult

i. Most adults with ITP present with a platelet level of 30 – 50 x 10^9/L and tend to have an event-free course. However, for those with more severe thrombocytopenia, they usually require treatment.
ii. In acute life-threatening bleeding, platelet transfusion ranging from every 30 minutes to 8 hours in conjunction with a continuous infusion of IVIg has shown rapid reduction in bleeding and/or an improvement in the platelet count.
iii. First line treatment is high dose corticosteroid. If corticosteroids are contraindicated, then either IVIg 1g/kg 1 dose (or can be repeated if necessary) or anti-RhD can be used.
iv. Second line therapy should be reserved for those with persistent and symptomatic disease. This includes rituximab, immunosuppressive agents, thrombopoeitin receptor agonist and splenectomy.

13.3 COAGULOPATHY

13.3.1 Vitamin K deficiency

a) Deficiency of Vitamin K-dependent coagulation factors may be present in the following conditions:

i. Haemolytic disease of the newborn (HDN).
ii. Ingestion of coumarin anti-coagulants (warfarin).
iii. Vitamin K deficiency due to malabsorption or inadequate diet.
iv. Liver disease – Bleeding manifestations in patients with liver pathology are due to underproduction of Vitamin K-dependent factors and abnormalities due to fibrinolysis.

b) Management:

i. Treat the underlying cause of Vitamin K deficiency.
ii. Warfarin overdose - *refer* ***Section 13.3.3: warfarin reversal guidelines.***
iii. Treat malabsorption or dietary deficiency.
iv. Management of HDN.

c) Vitamin K is helpful in obstructive jaundice and all cases of vitamin K deficiency. In chronic parenchymal disease of the liver *e.g.* liver cirrhosis, vitamin K is not helpful.

d) Adult Dose:

i. IV Vitamin K 10 mg slow infusion over 10 – 15 minutes daily for 3 days.
ii. IM Vitamin K 10 mg daily for 3 days.

e) Paediatric Dose:

i. IV Vitamin K 0.2 – 0.5 mg/kg/day, slow infusion over 10 – 15 minutes for 3 days.
ii. SC/IM Vitamin K 0.2 – 0.5 mg/kg/day for 3 days.

f) Desmopressin or DDAVP has been shown to correct bleeding time in liver cirrhosis.

13.3.2 Warfarin overdose

Warfarin acts by inhibiting the biosynthesis of the vitamin K-dependent clotting factors – II, VII, IX and X.

Effect of warfarin is monitored with INR – risk of bleeding approximately doubles for each single point of increase in the INR above 3.

Guidelines for overwarfarinization are largely based on the evidence-based medicine and recommendations follow the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method by the expert panels.

a) Therapeutic interventions for reversal of warfarin

i. Withhold warfarin
- May take several days for INR to normalise (within the targeted therapeutic range).

ii. Vitamin K – reverses the effect of warfarin
- Oral route – slower (24 hours) but safer.
- IV route – faster (4 – 6 hours) but risk of anaphylactic reaction.
- High doses, though effective, may lower INR more than necessary and may lead to warfarin resistance.

iii. Prothrombin complex concentrate (PCC)
- PCC are formulated with three factors (II, IX and X) or four factors (II, VII, IX and X) with Protein C and Protein S.
- For immediate reversal, prothrombin complex concentrates (PCC) are preferred over fresh frozen plasma (FFP).
- FFP can be used only when PCC is not available.
- Advantages of PCC over FFP include rapid reconstitution into a small volume for infusion over 20 – 30 minutes, fast onset of action and minimal risk of viral transmission due to pathogen inactivation steps during manufacturing.
- Expected correction of INR will be within 30 minutes to 1 hour post-infusion of PCC.
- The suggested dose of PCC with three factors for reversal of the anti-coagulant effect of warfarin is based on initial and target INRs:

Table 13.6: Suggested dose of Prothrombinex-VF to reverse the anti-coagulant effect of warfarin according to initial and target international normalised ratio (INR)

	Initial INR			
Target INR	**1.5 – 2.5**	**2.6 – 3.5**	**3.6 – 10.0**	**> 10.0**
0.9 – 1.3	30 IU/kg	35 IU/kg	50 IU/kg	50 IU/kg
1.4 – 2.0	15 IU/kg	25 IU/kg	30 IU/kg	40 IU/kg

- If bleeding is persistent with 3-factor PCC, additional 1 unit of FFP transfusion can be considered. Alternatively, 4-factor PCC may be used (if available).

- Vitamin K 5 – 10 mg should be given intravenously with the PCC to sustain the reversal effect.

iv. Fresh frozen plasma
- FFP should not be used routinely to reverse warfarin anti-coagulation.
- However, where PCC is not available and emergency reversal is required, FFP should be used, along with vitamin K to sustain the reversal effect.

v. Recombinant factor VIIa is not recommended for emergency anticoagulation reversal.

13.3.3 Warfarin reversal guidelines

Table 13.7: Therapeutic decisions on reversal of warfarin therapy depend on the level of the INR and the presence or absence of bleeding *(Adapted from Clinical Practice Guidelines Prevention and Treatment of Venous Thromboembolism, Ministry of Health Malaysia, 2013)*

Clinical Scenario	Management
Major bleeding (Life / Limb Threatening)	For all patients, give: 1. IV vitamin K 5 mg. 2. PCC as follows: (repeat every 6 hours as needed). • INR < 5.0 give 15 IU/kg. • INR > 5.0 give 30 IU/kg. For intracranial haemorrhage, doses of up to 50 IU/kg can be given. If PCC not available, give FFP 15 to 20 mL/kg.
Non-Major Bleeding (*i.e.* haematuria, epistaxis)	Consider: Temporary discontinuation or dose reduction of warfarin (depending on clinical scenario). IV vitamin K: 1 to 3 mg.
Elevated INR (No bleeding) 1. INR > 5.0, <8.0 2. INR > 8.0	The cause for the elevated INR should be investigated. Withhold 1 to 2 doses of warfarin and reduce maintenance dose Give oral vitamin K 1 to 5 mg and withhold warfarin (as above).

13.4 TRANSFUSION IN DENGUE

13.4.1 Pathophysiology

a) The haemostatic changes that occur in dengue infection are the result of endothelial activation. This leads to thrombocytopenia and coagulation activation which are an intrinsic part of the disease. In general, these are mild and improve after fluid replacement or cease spontaneously after recovery of illness.

b) Prolonged shock can lead to acidosis and DIC resulting in occult or overt bleeding and end organ damage.

c) Thrombocytopenia and coagulation abnormalities do not reliably predict bleeding in dengue infection.

13.4.2 Management

a) Mild bleeding such as from the gums, per vagina, epistaxis or petechiae usually cease spontaneously during the recovery phase and do not require blood transfusion if the patient remains stable.

b) Transfusion of blood and blood components in dengue is indicated only when there is evidence of significant bleeding (occult or overt).

c) Significant occult bleeding can be recognised by:

   i. Haematocrit not as high as expected for the degree of shock to be explained by plasma leakage alone.
   ii. A decrease in haematocrit without clinical improvement despite adequate fluid replacement (40 – 60 mL/kg).
   iii. Refractory shock that fails to respond to consecutive fluid resuscitation of 40 – 60 mL/kg.
   iv. Persistent or worsening metabolic acidosis and end organ dysfunction despite adequate fluid replacement.

d) Transfusion of blood and component in dengue patients with significant bleeding.

i. Red cells
   - Give 5 – 10 mL/kg of red cells at an appropriate rate and observe the clinical response.
   - Consider repeating the blood transfusion if there is further blood loss or no appropriate rise in haematocrit after blood transfusion.
   - Consider blood products if in DIC or uncontrolled bleeding.
   - No significant difference in clinical outcomes and lactate recovery, when transfused with shorter-term storage red cell compared with longer-term storage red cell.

ii. Platelet and fresh frozen plasma
   - Transfusion with blood components should be administered in dengue patients with significant bleeding.
   - Prophylactic transfusion of blood components is only indicated when invasive procedure or an operation is decided.
   - Prophylactic transfusion with platelets and fresh frozen plasma do not:
     - Produce sustained changes in the coagulation status and platelet count in patients with dengue haemorrhagic fever or dengue shock syndrome.
     - Change or reduce the bleeding outcome in dengue haemorrhagic fever.
   - Inappropriate transfusion of blood components increases the risk of pulmonary oedema and transfusion-transmitted infection.

Refer ***Section 5.1.2 Treatment of thrombocytopenia and Clinical Practice Guidelines: Management of Dengue Infection in Adults. 3rd Edition. 2015.***

References

1. Helen Fellows, Ian Fellows, 2010 Elsevier 2010 Medicine 39:2, page 79-83 Anaemia and gastrointestinal (GI) tract.

2. Lian C Macdougall Anaemia and chronic renal failure, Chronic Renal Failure, (2011) Elsevier, page 425.

3. Single Unit Transfusion Guide, National Blood Authority (Australia); June 2014

4. Cappellini MD, Cohen A, Porter J, et al., editors. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT), 3rd edition. Nicosia (CY): Thalassaemia International Federation; 2014.

5. Richard Dillon, Ibrahim Momoh, Yvonne Francis, Laura Cameron, Claire N. Harrison, and Deepti Radia, “Comparative Efficacy of Three Forms of Parenteral Iron,” Journal of Blood Transfusion, vol. 2012, Article ID 473514, 3 pages, 2012. doi:10.1155/2012/473514

6. Auerbach M, Ballard H. Clinical Use of Intravenous Iron: Administration, Efficacy, and Safety. American Society of Haematology Education book 2010

7. Paediatric Protocol for Malaysian Hospital. 4th Edition; 2018.

8. Clinical Practice Guidelines: Management of Transfusion Dependent Thalassaemia (Nov 2009)

9. Kallistheni Farmaki, Ioanna Tzoumari, Christina Pappa, Oral Chelators in transfusion-dependent thalasemia major patients may prevent or reverse iron overload complications. Blood Cells, Molecules and Disease 47 (2011) 33-40 Elsevier, page 8 (dosage and route-refer thalassaemia clinical practice guidelines)

10. Agata Boncimino, Alice Bertaina, Franco Locatelli, Cord Blood Transplantation in Patients with Haemogobinopathies.Transfusion and Apheresis Science 42 (2010) 277-281, Elsevier, page 1.

11. Sigbjorn Berentsen, Geir E. Tjonnfjorn, Diagnosis and treatment of cold agglutinin mediated autoimmune haemolyticanaemia, Blood Reviews (2012) Elsevier

12. Litton Edward, Xiao Jing, Ho Kwok M. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials *BMJ* 2013

13. 5th Edition Handbook of Transfusion Medicine, Derek Norfolk, January 2014, United Kingdom Blood Services at http://www.transfusionguidelines.org.uk/transfusion-handbook

14. Das SS, Zaman RU, Safi M. Incompatible blood transfusion: Challenging yet lifesaving in the management of acute severe autoimmune haemolyticanaemia. *Asian Journal of Transfusion Science*. 2014;8(2):105-108.

15. Quentin A Hill, Robert Stamps, Edwin Massey, John D Grainger, Drew Provan and Anita Hill on behalf of the British Society for Haematology. The diagnosis and management of primary autoimmune haemolytic anaemia (2016)

16. Clinical Practice Guideline on the Evaluation and Management of Adults with Suspected Heparin-Induced Thrombocytopenia, American Society of Haematology (2013)

17. Clinical Practice Guidelines: Prevention and Treatment of Venous Thromboembolism (August, 2013)

18. Dr Colin Brown Guidelines for the Management of Platelet Transfusion Refractoriness; Information Document INF139/1.1: 2011

19. Neunert C. et al, The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia, American Society of Haematology, 2011.

20. Ernest Lo, Sean Deane, Diagnosis and classification of immune-mediated thrombocytopenia, Autoimmunity review, 2014.

21. Tran, H. A., Chunilal, S. D., Harper, P. L., Tran, H., Wood, E. M. & Gallus, A. S. (2013). An update of consensus guidelines for warfarin reversal. Med J Aust, 198(4), 198-9.

22. Cushman, M., Lim, W., Zakai, N.A. Clinical Practice Guide on Antithrombotic Drug Dosing and Management of Antithrombotic Drug- Associated Bleeding Complications in Adults. ASH February 2014.

23. Clinical Practice Guidelines: Management of Dengue Infection in Adults (3rd edition, 2015)

24. Dengue, guidelines for diagnosis, treatment, prevention and control, new edition 2009 WHO

14.0 THERAPEUTIC APHERESIS

14.1 OVERVIEW

Therapeutic apheresis is a therapeutic procedure in which blood of the patient is passed through an extracorporeal medical device which separates components of blood to treat a disease. This is a general term which includes all apheresis based procedures used therapeutically.

The goal is to remove a pathologic element from the blood. This element may be a plasma protein such as an autoantibody in myasthenia gravis (MG), red cells as in sickle cell anaemia, leucocytes as in hyperleucocytosis accompanying acute leukaemia, or platelets as in marked thrombocytosis.

Therapeutic apheresis should be carried out only where there is published evidence of efficacy or, occasionally, in very rare conditions whose pathophysiology predicts efficacy.

Apheresis therapy should have a treatment plan which should consist of the following:

a) The reasons for initiating apheresis therapy, the expected benefits and how response to apheresis should be monitored.

b) Type of apheresis procedure required and the frequency of treatment.

c) Vascular access to be used.

d) Clinical observations, as well as laboratory tests (if any), to be completed before and after each apheresis procedure.

e) Decisions on how to manage possible effects of apheresis on medications given before the procedure, and on medication that is required during procedures (*e.g.* insulin pump). Patients on anti-coagulants (*e.g.* warfarin) may require their anticoagulation adjusted or changed prior to a procedure which uses heparin.

f) Technical details of the procedure such as blood volume to be processed, replacement fluid and anti-coagulant to be used.

g) Therapy end point.

14.2 TYPES OF THERAPEUTIC APHERESIS

Procedure	Definition	Example of disease
Adsorptive cytapheresis	Activated monocytes and granulocytes are selectively adsorbed, allowing the remaining leucocytes and other blood components to be returned to the patient.	Inflammatory bowel disease (Ulcerative colitis)
Erythrocytapheresis	Red cells is separated from other components of blood. The red cells are removed and replaced with crystalloid or colloid solution, when necessary.	Polycythaemia vera; Hereditary haemachromatosis
Extracorporeal photopheresis (ECP)	The buffy coat is separated from the patient's blood, treated extracorporeally with a photoactive compound (*e.g.* psoralens) and exposed to ultraviolet A light then subsequently reinfused to the patient during the same procedure.	Cutaneous T-cell lymphoma; mycosis fungoides; Sezary syndrome (Erythrodermic)
Leukocytapheresis	The separation of white blood (e.g., leukemic blasts or granulocytes), collects the selected cells and returns the remainder of the patient's blood with or without addition of replacement fluid such as colloid and/or crystalloid solution.	Hyperleucocytosis (Symptomatic)
RBC exchange	Separation of red blood cells from other components of blood. The patient's red blood cells are removed and replaced with donor red blood cells and colloid solution.	Sickle cell disease, (Acute stroke)
Therapeutic plasma exchange (TPE)	The plasma is separated from other components of blood. The plasma is removed and replaced with a replacement solution such as colloid solution (e.g., albumin and/or plasma).	Guillain-Barre Syndrome

Procedure	Definition	Example of disease
Thrombocytapheresis	The platelets is separated and removed. The remainder of the patient's blood is returned with or without addition of replacement fluid.	Thrombocytosis (symptomatic)
Immunoadsorption (IA)	Plasma of the patient, after membrane based or centrifugal separation from the blood, is passed through a medical device (adsorber column) which has a capacity to remove immunoglobulins by binding them to select ligands on the backing matrix surface (membranes or beads) of the adsorber column.	Cryoglobulinemia (symptomatic/ severe)

Calculation of plasma and red cell volume for therapeutic apheresis

Plasma volume formula:

Estimated plasma volume (EPV) (Litre) = (1-haematocrit/100) x body weight (kg) x TBV*

* Total blood volume (TBV), male = 0.079, in female = 0.065.

Red cell volume formula:

Red cell volume (RCV) (Litre) = TBV* x haematocrit

* Total blood volume (TBV), male = 0.079, in female = 0.065.

*Refer **APPENDIX XXVI** for indication of therapeutic apheresis.*

REPLACEMENT FLUID

i. Considerations in the selection of replacement fluids include the type of procedure, the indication, and the patient's coagulation status. The recommended replacement fluid for plasmapheresis is the fluid that physiologically close to plasma.

ii. During intensive plasmapheresis with albumin replacement, depletion of other plasma proteins can occur which may require temporary use of Fresh Frozen Plasma (FFP) as a replacement fluid.

iii. FFP replacement is specifically indicated for the treatment of TTP or for the treatment of patients with coagulation factor deficiencies or bleeding risks. For patients without underlying coagulopathy who are undergoing intensive plasmapheresis, albumin can be used for the first part of the procedure and the final litre replaced with FFP. Cryosupernatant is an alternative to FFP for the treatment of TTP.

iv. Red cells are required for replacement in red cell exchange. Phenotype-matched blood for ABO, Rh and any known antibodies that are compatible are often requested in the treatment of patients with sickle cell anaemia. Fresh red cells (less than 14 days) is recommended for better outcome. Units containing either citrate-phosphate-dextrose-adenine (CPDA-1) or additive solution (AS) may be used.

ADVERSE REACTION

Adverse reaction that commonly associated with therapeutic apheresis include paraesthesia, hypotension, urticaria, nausea, vertigo, shivering, flushing, dyspnoea, arrhythmia, abdominal pain and anaphylaxis.

References

1. Blood Safety Guideline by WHO.

2. British Society of Haematology; Guideline on the clinical use of apheresis procedures for the treatment of patients and collection of cellular therapy products (2015).

3. http://www.ANZBST.org.au Australian and New Zealand Society for blood Transfusion.

4. Padmanabhan A. et al Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eight Special Issue Journal of Clinical Apheresis 31:149-162 2016.

15.0 HAEMOPOETIC STEM CELL TRANSPLANT

15.1 TRANSFUSION SUPPORT IN STEM CELL TRANSPLANT

Haemopoietic stem cell transplant (HSCT) is increasingly used as a curative therapy in haematological disorders where the recipient's bone marrow (BM) is replaced with donor haematopoietic stem cells (HSC). The major complications are caused by immunological responses triggered by the infused donor's HSCs and lymphocytes against the host. Blood support is crucial in the post-transplant period as the patient will be pancytopenic for up to 4 weeks.

Development of alloimmunization to histocompatibility antigens poses an increased risk of subsequent graft rejection. Therefore, use of blood products should be minimized including leucocyte-depleted components.

All transplanted patients are profoundly immunosuppressed. Therefore, all cellular blood components should be irradiated throughout the 1st year post transplant and longer for those with chronic graft versus host disease (GVHD) or who otherwise show signs of immunosuppression. This must be positively checked by the doctor prior to transfusion.

Where cytomegalovirus (CMV) negative blood is not available, leucodepleted blood components are considered to be "CMV reduced risk" and are equally effective in preventing transfusion associated CMV infection.

Ideally apheresis platelets should be given. Platelet transfusion may be given more frequently if platelet survival is shortened or if the patient becomes refractory.

15.2 TRANSFUSION IN ABO INCOMPATIBLE HAEMOPOIETIC STEM CELLS (HSC)

a) HSCs do not express ABO antigens; therefore HSC transplant can be performed across ABO barriers.

b) Allogeneic HSC transplant from HLA matched related donor or unrelated donors can involve ABO blood group mismatch between the donor and recipient.

c) The types of mismatch are grouped into major, minor or bi-directional according to the presence of antibody towards red cells.

Table 15.1: Categories of ABO-incompatible HSC transplant

Type	Definition	Examples
Major ABO incompatibility	The recipient's plasma contains anti-A, anti-B or anti-A, B antibodies that are incompatible with donor red cells.	Donor: A or B Recipient: O
Minor ABO incompatibility	The donor's plasma contains anti-A, anti-B or anti-A, B antibodies that can react with the recipient's red cells.	Donor: O Recipient: A or B
Bidirectional ABO incompatibility	Both the donor and recipient's plasma contain anti-A, anti-B or anti-A, B antibodies reactive with recipient and donor red cells respectively.	Donor: A Recipient: B

Table 15.2: Selection of blood component in ABO-incompatible HSC transplant in the immediate post-transplant period

	Donor	Recipient	Red Cells	Platelet	FFP
Major ABO incompatibility	A B AB AB AB	O O O A B	O O O A/O B/O	A B A A B	A B AB AB AB
Minor ABO incompatibility	O O O A B	A B AB AB AB	O O O A/O B/O	A B A A B	A B AB AB AB
Bidirectional ABO incompatibility	A B	B A	O O	B A	AB AB

d) A clear post-transplant transfusion policy should be developed for all patients undergoing HSC transplant and circulated to both clinical and laboratory

teams involved. Transfusion service shall keep detail records of the recipient's pretransplant and donor's ABO group.

e) Table 15.2 summarises the recommended ABO groups for components transfused in the immediate post-transplant period. Once conversion to donor's blood group is complete, components of donor's group can be given.

f) In RhD incompatible transplant, RhD negative red cells and platelets should be the choice of components for transfusion. However, if RhD positive platelets have to be given to unsensitised RhD negative recipients, 250 IU of anti-D immunoglobulin subcutaneously will cover up to 5 adult doses over 5 weeks.

15.3 INDICATION FOR RED CELL AND PLATELET TRANSFUSION

Red cell transfusion:

Transfusion is suggested when the haemoglobin is less than 8.0 g/dL and haematocrit is less than 25%. In adults, 1 unit of red cells increases the haemoglobin by 1.0 g/dL whereas in children the volume of blood to be transfused is derived from the formula:

Volume = Required increase in haemoglobin (g/dL) x 4 x weight (kg)

Platelet transfusion:

*Refer **APPENDIX V** for guide for the use of platelet transfusion.*

Table 15.3: Suggested indication for platelet transfusion

Platelet count threshold	Indication
10 x 10^9/L	Stable patient, for prophylaxis
20 x 10^9/L	Fever, sepsis, splenomegaly and other causes of increased platelet consumption
50 x 10^9/L	Invasive procedure *e.g.* central line insertion
Platelet transfusion should be given when there is a significant clinical bleeding irrespective of platelet count.	

HSCT recipients may develop platelet refractoriness due to the presence of antibodies against Human Leucocyte Antigen (HLA) or Human Platelet Antigen (HPA). The management of platelet refractoriness is described in ***Section 13.2 Thrombocytopenia***.

References

1. Handbook of Transfusion Medicine, 5th Edition 2013, United Kingdom Blood Services
2. AABB Technical Manual, 18th edition, AABB, Maryland, US, 2014

16.0 ADVERSE EFFECT OF TRANSFUSION

16.1 INTRODUCTION

Blood transfusion can be associated with various adverse effects. Some of these reactions are acute and arise during transfusion or within 24 hours of transfusion, but the clinical effects of others are delayed, after 24 hours, sometimes by months or years.

Adverse effects of blood transfusion range from brief episodes of fever to life threatening haemolysis. All transfusions should be carefully monitored, and adverse reactions must be appropriately investigated and managed. All personnel involved in ordering and administering transfusions must be able to recognize the symptoms and signs of transfusion reactions and to manage them.

Table 16.1: Adverse effect of transfusion

Adverse Effect of Transfusion	
Acute adverse effects (≤ 24 hours of transfusion)	**Delayed adverse effects (>24 hours of transfusion)**
Immune Acute Haemolytic Transfusion Reaction Transfusion-Related Acute Lung Injury (TRALI) Anaphylaxis/Anaphylactoid Reactions Allergic Reaction Febrile Non-Haemolytic Transfusion Reaction (FNHTR)	**Immune** Delayed Haemolytic Transfusion Reaction Transfusion Associated Graft Versus Host Disease (TA-GVHD) Post Transfusion Purpura (PTP) Immunomodulation/suppression Alloimmunization
Non-immune Transfusion Associated Circulatory Overload (TACO) Bacterial Contamination/Septic Transfusion Reaction Transfusion Associated Dyspnoea (TAD) Hypotensive Transfusion Reaction	**Non-immune** Transfusion Transmitted Infection (TTI) Transfusion Associated Haemosiderosis

16.2 SIGNS AND SYMPTOMS

Signs and symptoms that may be indicators of a transfusion reaction include:

i. Feeling of apprehension/restlessness.
ii. Fever (1°C rise in temperature from baseline).
iii. Chills with or without rigors.

iv. Pain at infusion site, chest, abdomen or flanks.
v. Hypotension or hypertension.
vi. Respiratory distress (wheezing, dyspnoea and cyanosis).
vii. Skin manifestations (urticaria, rash, flushing, pruritus and localized oedema).
viii. Nausea/vomiting.
ix. Acute onset of sepsis.
x. Anaphylaxis.
xi. Abnormal bleeding.

16.3 GENERAL MANAGEMENT OF ACUTE TRANSFUSION REACTION

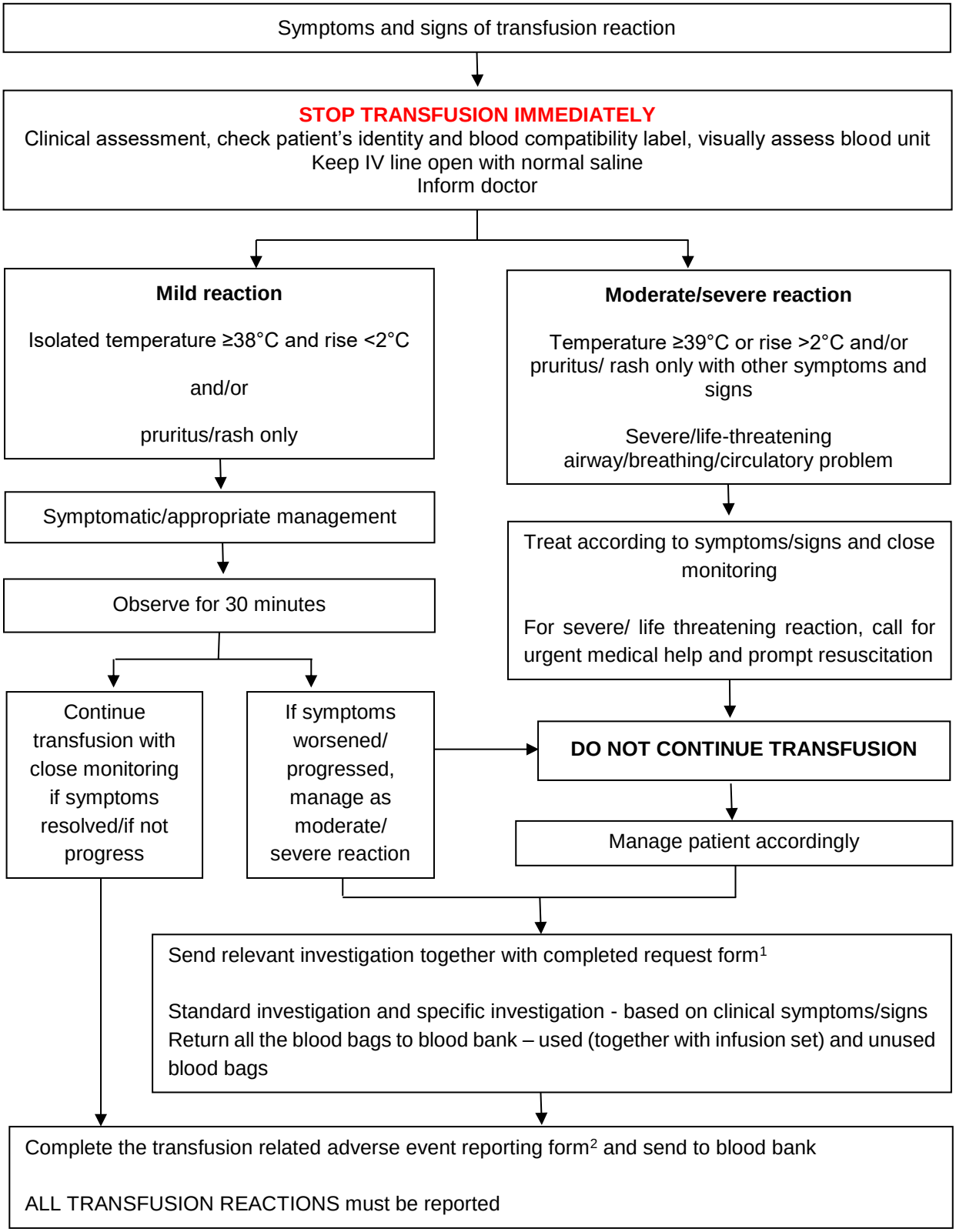
a) Standard investigations for all moderate or severe transfusion reactions:

i. 8 – 10 mL venous blood in EDTA tube for repeat blood grouping, compatibility testing, antibody screening and Direct Coomb's test.
ii. Urine examination for haemoglobin and red cell.
iii. Full blood count.
iv. Renal function test and liver function test.

b) Specific investigations depend on the type of adverse transfusion event:

i. Haemolytic transfusion reaction: standard investigations with peripheral blood picture, reticulocyte count, serum LDH, serum haptoglobin and coagulation tests.
ii. Moderate or severe allergic reaction/anaphylaxis reaction: standard investigations and serum Immunoglobulin A (IgA) level should be measured.
iii. Other immune causes: Testing the patient for human leucocyte antibodies (HLA), human platelet antibodies (HPA) or human neutrophil-specific antibodies (HNA) should be discussed with a transfusion medicine specialist or haematologist.

Figure 16.1: Flowchart for management of acute transfusion reaction



[1] Request Form for Transfusion Reaction Investigation ***(APPENDIX XXVII)***

[2] Reporting Form for Transfusion-Related Adverse Event ***(APPENDIX XXVIII)***

16.4 SPECIFIC TRANSFUSION REACTION

16.4.1 IMMUNE HAEMOLYTIC TRANSFUSION REACTION

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

ACUTE HAEMOLYTIC TRANSFUSION REACTION

a) Immediate intravascular haemolysis occurs with ABO-incompatibility.

b) The symptoms include a feeling of impending doom, agitation, flushing, restlessness, dyspnoea, pain in the abdomen, flank or chest, vomiting and diarrhoea. The signs are fever, hypotension, unexpected bleeding, dark-coloured urine and renal shutdown. In a conscious patient, even a few mL of ABO incompatible blood may cause symptoms within 1 or 2 minutes. In an unconscious/ anaesthetised patient, only the signs will be evident.

c) Investigation:

i. The compatibility label of the blood unit should be checked again to ensure that it corresponds with the patient's name, registration number/IC, blood request form and case notes.
ii. If a mistake is found, the blood bank should be informed immediately since the unit of blood intended for that patient could be transfused to another patient.
iii. Patient's blood sample should be taken immediately (post transfusion sample 1) and repeated after 24 hours (post transfusion sample 2) of reaction for the following:
    - Standard investigations.
    - Serum LDH.
    - Full blood picture.
    - Renal and liver function test.
iv. Disseminated intravascular coagulation (DIC) screening should be done to look for possible DIC.
v. Transfused blood bag together with infusion set as well as unused blood bags should be returned to the blood bank.

d) Management**:**

i. The transfusion must be stopped immediately and the doctor in charge of the patient must be informed for further management. Supportive care should be instituted immediately to manage hypotension and manage adequate renal perfusion.
ii. The airway should be maintained and high flow oxygen should be given if necessary.
iii. The blood administration set should be changed and venous access maintained using normal saline, initially 10 – 20 mL/kg to maintain blood pressure. If the patient becomes hypotensive despite adequate fluid resuscitation, an inotrope should be started.
iv. The patient's vital signs should be monitored and urine output should be maintained at >1.0 mL/kg/hr. An input/output chart should be monitored. If urine output <1.0 mL/kg/hr, fluid challenge should be given with CVP monitoring. Diuretics, *e.g.* IV Frusemide 1 – 2 mg/kg and/or Mannitol, may help to maintain urine flow.
v. IV Adrenaline (1:10,000 dilution) 0.5 mL (adult), 1 µg/kg (children) in 1 – 2 minutes should be administered and may be repeated according to clinical response.
vi. Administer IV hydrocortisone 100 – 200 mg (adult), 4 mg/kg (children).
vii. Ensure adequate hydration and obtain expert advice (nephrologist) if acute renal failure is likely. The patient may need renal replacement therapy.
viii. If DIC develops, replacement of blood components should be guided by clinical state (presence of bleeding) and coagulation results.
ix. If the patient needs further transfusion, use re-crossmatched blood. There is no increased risk of a second haemolytic reaction.

DELAYED HAEMOLYTIC TRANSFUSION REACTION (DHTR)

a) This is due to extravascular destruction of red cells caused by alloantibodies such as Kidd antibodies that are not detectable at the time of pre-transfusion testing. The patient experiences haemolysis of the transfused red cells after an interval of 24 hours up to 28 days during which an anamnestic response occurs.

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

c) Investigation:

   i. Patient's blood sample should be taken immediately (post transfusion sample 1) and repeated after 24 hours (post transfusion sample) 2) of reaction for the following:
      - Standard investigations.
      - Serum LDH.
      - Full blood picture.
      - Renal and liver function test.

d) Management:

   i. The treatment consists of monitoring the patient and providing appropriate supportive care.

e) Prevention/Recommendation:

   i. Check previous transfusion records because alloantibodies may have been identified that are no longer detectable but require transfusion of antigen-negative red cells.
   ii. In regularly transfused patients (*e.g.* thalassaemia), phenotype-matched red cell should be given to avoid alloimmunization and development of alloantibody.

16.4.2 FEBRILE NON-HAEMOLYTIC TRANSFUSION REACTIONS (FNHTR)

FNHTR is defined as a temperature increase of more or equal to 1°C associated with transfusion and without any other explanation. It is due to anti-leucocyte antibodies in those previously immunized by pregnancy or previous transfusion. FNHTR may also be the result of accumulated cytokines in a cellular blood component. The temperature rise may begin early during the transfusion or delayed in onset for up to four hours after completion. In severe cases, the symptoms may include shivering, flushing, palpitations, tachycardia, headache and rigors.

a) Management:

   i. If FNHTR occurs during transfusion, it can be managed by stopping the transfusion and giving an antipyretic if it is a mild reaction (isolated fever <2°C) *e.g.* paracetamol and transfusion may be resumed at a slower rate with close monitoring after assessing the patient 30 minutes after antipyretic.
   ii. A blood culture should be taken if bacterial contamination is suspected.

b) Prevention/Recommendation:

   If the patient had experienced two or more FNHTR:

   i. Paracetamol orally 1 hour before transfusion.
   ii. Slow transfusion.
   iii. Leucodepleted blood and blood components.
   iv. Patient who continue to react should have a trial of washed cellular blood components.

16.4.3 BACTERIAL CONTAMINATION

Contamination of blood at the source (during collection) or due to faulty storage, can lead to the development of septicaemic shock with high mortality rate in the recipient. Bacteria associated with red cell transfusion are usually cold-growing strains such as *Pseudomonas* or *Yersinia*. Skin contaminants such as staphylococci may proliferate in platelet concentrates stored at 20 – 24°C.

The signs and symptoms include high fever (often ≥2°C above the baseline), hypotension, shock, haemoglobinuria and renal failure. Vigorous treatment of septic shock and hypotension should be instituted immediately.

a) Investigation:

i. Patient's blood sample for gram stain and culture should be taken for diagnosis.

b) Management:

i. Stop transfusion.
ii. Maintain airway, provide oxygen and ventilatory support if necessary.
iii. Cardiovascular support with pressor agents as indicated.
iv. Replace giving set, hydrate to maintain urinary output.
v. Inspection of the pack may show abnormal discoloration, aggregates or offensive smell.
vi. Implicated components must be sealed to avoid leakage or contamination and returned to the transfusion laboratory for further investigation.
vii. The blood bank must be contacted immediately so that any associated components from the implicated donation can be urgently identified and withdrawn from hospital blood banks.
viii. Prompt initiation of broad spectrum intravenous antibiotic.
ix. Treatment of DIC if present.

c) Prevention/Recommendation:

i. Visual inspection of blood units for colour changes, haemolysis or clots before transfusion.
ii. Blood and blood components should be transfused within the time limit for infusion (completed within 4 hours of removal from a controlled temperature environment).
iii. One infusion set should be used only per 2 units of red cell or maximum of 4 hours.

16.4.4 ALLERGIC TRANSFUSION REACTION/ ANAPHYLAXIS

MILD ALLERGIC REACTION

Urticaria, rash, flushing or itchiness with no other symptoms. It is usually caused by hypersensitivity to allergens or plasma proteins in the transfused unit.

Management:

The transfusion should be stopped temporarily while an antihistamine (Chlorphenamine – refer Figure 16.2 for dose) is administered. The transfusion may then be resumed with slow transfusion and close monitoring if there is no progression of symptoms after 30 minutes.

MODERATE ALLERGIC REACTION

Wheezing or angioedema with or without flushing, urticaria or rash but without respiratory compromise or hypotension.

Management:

- Give antihistamine (Chlorphenamine – refer Figure 16.2 for dose) by slow intravenous injection.
- Oxygen therapy.
- IV hydrocortisone 100 – 200 mg (adult), 4 mg/kg (children) may be required.
- Salbutamol nebuliser can also be given for respiratory symptoms.

Prevention/Recommendation:

- For recipients who have had a moderate or frequent mild allergic reaction following transfusion, administering oral antihistamine 30 minutes before transfusion may be helpful.
- If antihistamine is insufficient, hydrocortisone 1 hour prior to transfusion may be helpful.

SEVERE ALLERGIC/ANAPHYLACTIC REACTION

Reactions usually begin within a few seconds or minutes after the transfusion started. Patients can present with sudden onset of severe hypotension, cough, bronchospasm (respiratory distress and wheezing), laryngospasm, angioedema, urticaria, nausea, abdominal cramps, vomiting, diarrhoea, shock and/or loss of consciousness. This may be a fatal reaction.

Mechanisms of anaphylactic transfusion reaction:

- IgA-deficient patients who have anti-IgA antibodies. Although IgA deficiency is not uncommon, fortunately most do not develop anti-IgA antibodies.
- Patient antibodies to plasma proteins (such as IgG, albumin, haptoglobin, transferrin, C3, C4 or cytokines)
- Transfusing an allergen to a sensitised patient (for example, penicillin or nuts consumed by a donor)
- Rarely the transfusion of IgE antibodies (to drugs, food, etc.) from a donor to an allergen present in the recipient.

Investigation:

a) Oxygen saturation/blood gases.

b) Chest X-ray.

c) Serum IgA level.

Management:

Treatment of severe allergic/anaphylaxis:

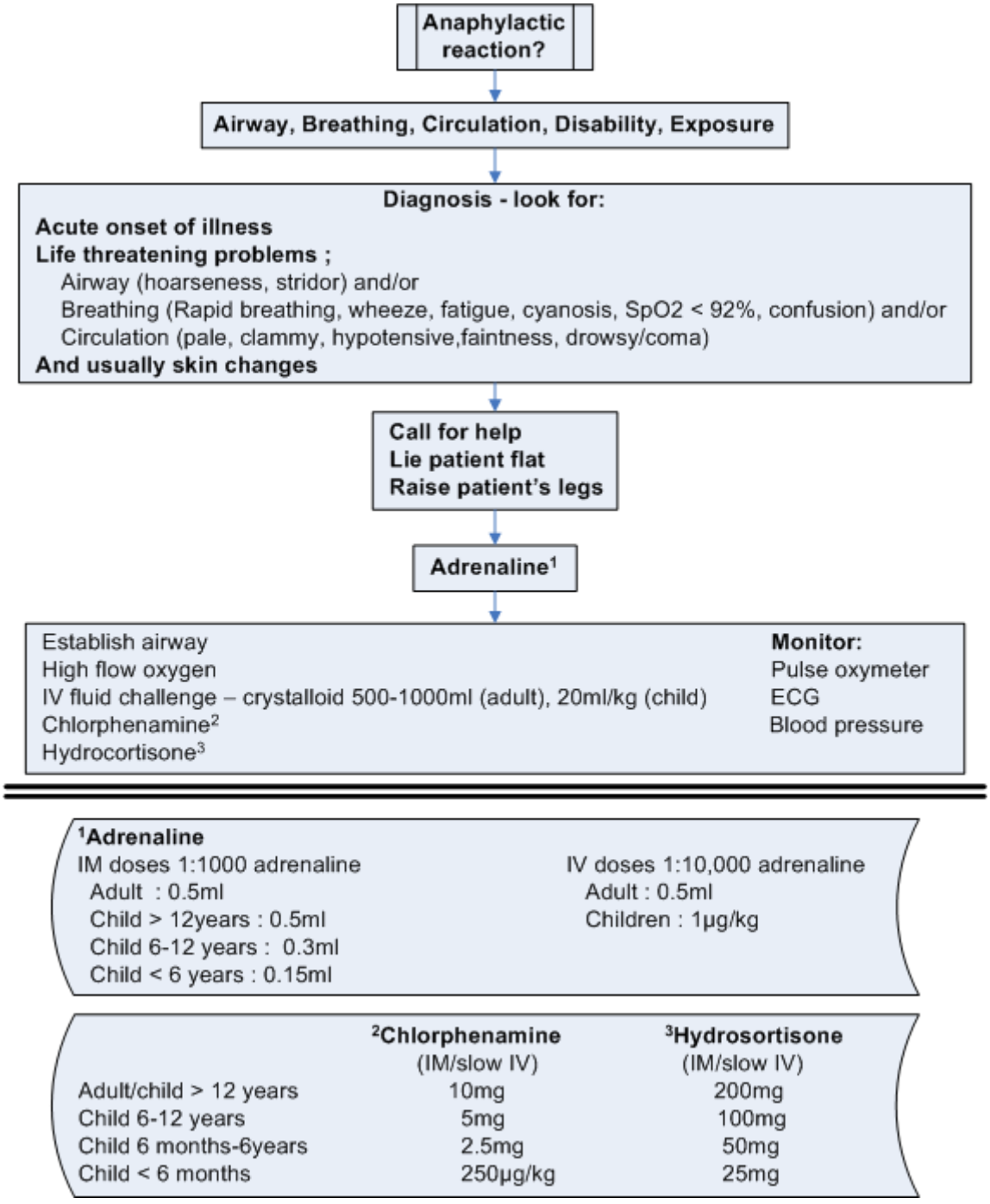
a) Stop the transfusion immediately.

b) Follow anaphylaxis management flowchart.

c) Salbutamol nebuliser can also be given if wheezing continues.

d) H2 blocker (IV Ranitidine 50 mg) may be added for severe reaction.

Figure 16.2: Anaphylaxis management flowchart *(adapted from Resuscitation council (UK), Anaphylaxis Algorithm)*



Prevention/Recommendation for severe allergic reaction:

a) Premedication with antihistamine and/or hydrocortisone 30 minutes prior to transfusion may be beneficial for patients with previous history of allergic reactions.

b) For recurrent severe allergic reaction, transfusion of washed cellular blood component should be considered.

Prevention/Recommendation for anaphylaxis:

a) Autologous blood donation for elective procedures.

b) IgA deficient patient can be given blood components from IgA-deficient donors or washed cellular blood components.

c) Premedication with hydrocortisone prior to transfusion.

16.4.5 TRANSFUSION RELATED ACUTE LUNG INJURY (TRALI)

TRALI is a serious complication of blood transfusion and is among the leading causes of transfusion-related morbidity and mortality in most developed countries. Pathophysiology of TRALI involves two-hit model where patient's condition serves as first hit and second hit is the transfusion. First hit is patient underlying factors which results in adherence of primed neutrophils to the pulmonary endothelium. Second hit is caused by mediators in transfused blood. It can be antibody-mediated or non-antibody-mediated. These mediators activate endothelial cells and pulmonary neutrophils, resulting in capillary leakage and subsequent pulmonary oedema.

Historically TRALI was attributed primarily to human leucocyte antigen (HLA) Class I and Class II and human neutrophil antigen (HNA) antibodies. However, many studies have shown that other factors in transfusion can also cause TRALI for example bioactive lipids and supernatants in stored red cells and platelets. To date, there are no biomarkers available to diagnose TRALI. Therefore diagnosis of TRALI should be made based on clinical and radiological criteria. Nevertheless, the presence of white blood cell antibodies is important for understanding the pathophysiology and evaluating TRALI risk mitigation strategies.

It is classified into two categories:

- TRALI Type I: without acute respiratory distress syndrome (ARDS) risk factor
- TRALI Type II: with an ARDS risk factor or with existing mild ARDS

ARDS risk factors:

- **Direct:** Pneumonia, aspiration of gastric contents, inhalational injury, pulmonary contusion, pulmonary vasculitis, drowning
- **Indirect:** Non-pulmonary sepsis, major trauma*, pancreatitis, severe burns, non-cardiogenic shock, drug overdose

*Major trauma is defined as multiple fractures (two or more major long bones, an unstable pelvic fracture, or one major long bone and a major pelvic fracture).

Criteria for TRALI Type I and II:

TRALI Type I:

Patients who have no risk factors for ARDS and meet the following criteria:

a) i. Acute onset

ii. Hypoxemia (P/F ≤ 300 or SpO2 < 90% on room air)

iii. Clear evidence of bilateral pulmonary edema on imaging (e.g., chest radiograph, chest CT, or ultrasound)

iv. No evidence of LAH* or, if LAH is present, it is judged to not be the main contributor to the hypoxemia

b) Onset during or within 6 hr of transfusion‡

c) No temporal relationship to an alternative risk factor for ARDS

TRALI Type II:

Patients who have risk factors for ARDS (but who have not been diagnosed with ARDS) or who have existing mild ARDS (P/F of 200-300), but whose respiratory status deteriorates§ and is judged to be due to transfusion based on:

a) Findings as described in categories a and b of TRALI Type I, and

b) Stable respiratory status in the 12 hr before transfusion

* LAH = Left atrial hypertension. Use objective evaluation when LAH is suspected (imaging, e.g., echocardiography, or invasive measurement using, e.g., pulmonary artery catheter).

‡ Onset of pulmonary symptoms (e.g., hypoxemia—lower P/F ratio or SpO2) should be within 6 hours of end of transfusion. The additional findings needed to diagnose TRALI (pulmonary edema on a lung imaging study and determination of lack of substantial LAH) would ideally be available at the same time but could be documented up to 24 hours after TRALI onset.

§ Use P/F ratio deterioration along with other respiratory parameters and clinical judgment to determine progression from mild to moderate or severe ARDS.

Classification of pulmonary edema not fulfilling TRALI criteria

- ARDS: Patients who have risk factors for ARDS, and deteriorate not due to transfusion, but as a consequence of the already present ARDS risk factors.
  a) Onset of ARDS within 6 hours after transfusion but respiratory status was deteriorating in the 12 hours before transfusion
  b) Existing ARDS of any severity that further deteriorates after transfusion where respiratory status was already deteriorating in the 12 hours before transfusion
- TRALI/TACO (Transfusion Associated Circulatory Overload) cannot be distinguished: Patients in whom TRALI cannot be distinguished from TACO or in whom both conditions occur simultaneously
  a) Clinical findings compatible with TRALI and with TACO and/or lack of data to establish whether or not significant LAH is present

---

* If pulmonary edema occurs greater than 6 hours after the transfusion, and is clinically suspicious for temporal association with transfusion, the case should be classified as Transfusion Associated Dyspnoea (TAD).

Investigations:

a) Oxygen saturation/blood gases.

b) Chest X-ray.

c) Testing donor for HLA antibodies.

d) Testing patient for HLA antigen and/or HLA antibodies.

Management:

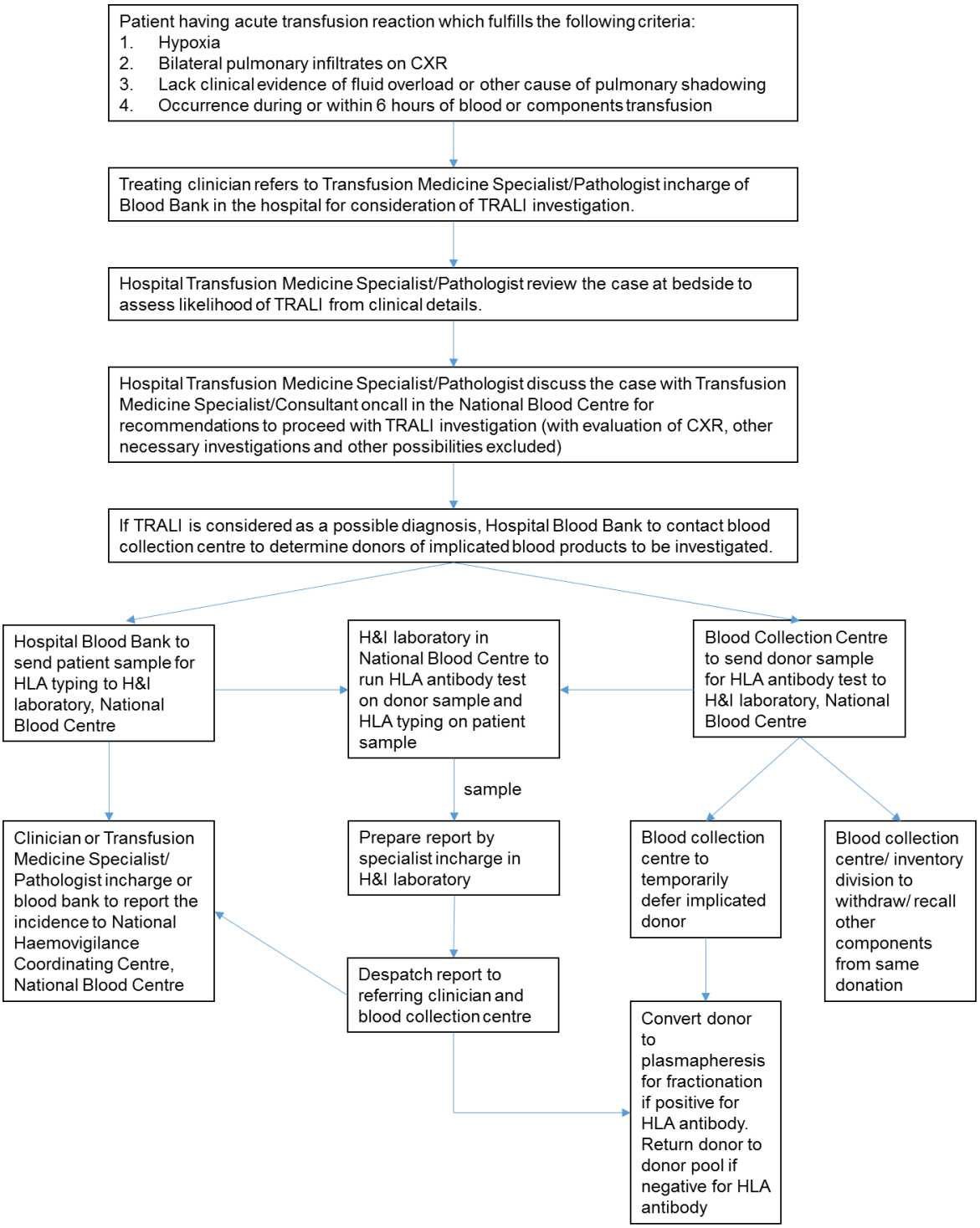
a) Patients suspected to have TRALI should be managed in critical care unit setting in which oxygen therapy and assisted ventilation are often required.

b) Hypotension should be treated with fluid administration and inotrope if necessary.

c) Steroid therapy is not effective and diuretic is not indicated (TRALI is not related to volume overload).

d) The blood bank must be informed so that the implicated donor can be tested and deferred.

Figure 16.3: Workflow on investigation for transfusion-related acute lung injury (TRALI)



16.4.6 TRANSFUSION ASSOCIATED CIRCULATORY OVERLOAD (TACO)

TACO results from circulatory overload occurred within 6 hours of transfusion and is due to the inability of the recipient to compensate for the volume of the transfused products. Main risk factors are elderly (> 70 years old) with impaired cardiovascular state or renal impairment, infant, high flow rates transfusion, large volume transfusion especially in normovolaemic patient.

It is characterized by any 4 of the following:

a) Acute respiratory distress.
b) Tachycardia.
c) Increased blood pressure.
d) Acute or worsening pulmonary edema on chest X-ray.
e) Evidence of positive fluid balance.

Investigation:

a) Oxygen saturation/blood gases.
b) Chest X-ray.

Management:

a) Upright position.
b) Maintain airway; provide oxygen and ventilator support if necessary.
c) Diuretics (IV frusemide 40 – 80 mg for adult, 1 – 2 mg/kg for children).

Prevention/Recommendation:

a) For high risk patients, the following measures can be taken:
    i. Slow transfusion (1 mL/kg/hour).
    ii. Diuretics may be given prior to/during the transfusion.
    iii. One bag of blood can be split into small bag for transfusion to reduce the volume.
    iv. Prescription of appropriate volume in millilitres (as in paediatric practice) has been recommended.

16.4.7 TRANSFUSION ASSOCIATED DYSPNOEA

Transfusion associated dyspnoea (TAD) characterized by respiratory distress within 24 hours of transfusion that does not meet the criteria of TRALI, TACO or allergic reaction. Respiratory distress should be the most prominent clinical feature and should not be explained by the patient's underlying condition or any other known cause.

Management:

a) Oxygen saturation or blood gases and chest x-ray should be performed.

b) Symptomatic treatment should be instituted.

Table 16.2: Comparison table to assist with pulmonary reaction classification						
	TRALI Type I	**TRALI Type II**	**ARDS**	**TRALI/TACO**	**TACO**	**TAD**
Hypoxemia	Present	Present	Present	Present	May be present but not required	May be present but not required
Imaging evidence of pulmonary edema	Documented	Documented	Documented	Documented	May be present but not required	May be present but not required
Onset within 6 hours	Yes	Yes	Yes	Yes	Yes	No
ARDS risk factors	None	Yes — with stable or improving respiratory function in prior 12 hours	Yes — with worsening respiratory function in prior 12 hours	None, or if present, with stable or improving respiratory function in prior 12 hours	Not applicable	Not applicable
Left Atrial Hypertension*	None/mild	None/mild	None/mild	Present or not evaluable	Present	May be present but not required
* LAH is difficult to assess. When LAH is suspected, we recommend using objective evaluation to determine if it is present. Objective criteria include imaging (e.g., echocardiography) or invasive measurement (e.g., pulmonary artery catheter pressure measurement). However, clinical judgment is often required and, if this is needed, should be used for case classification as follows: TRALI and/or TACO = respiratory insufficiency at least partially explained by hydrostatic lung edema resulting from cardiac failure or fluid overload or unable to fully assess the contribution of hydrostatic lung edema resulting from cardiac failure or fluid overload; TACO = respiratory insufficiency explained by hydrostatic lung edema resulting from cardiac failure or fluid overload.						

16.4.8 HYPOTENSIVE TRANSFUSION REACTION

This reaction is characterized by hypotension defined as a drop in systolic blood pressure of ≥ 30 mmHg occurring during or within one hour of completing transfusion and a systolic blood pressure ≤ 80 mmHg. It appears to occur more frequently in patients on angiotensin-converting enzyme (ACE) inhibitors. Most reactions do occur very rapidly after the start of the transfusion (within minutes). Hypotension is usually the sole manifestation but facial flushing and gastrointestinal symptoms may occur.

All other categories of adverse reactions presenting with hypotension, especially allergic reactions, must be excluded. The underlying condition of the patient must also have been excluded as a possible explanation for the hypotension.

Management:

a) Cessation of transfusion and supportive treatment.

Prevention:

a) Patients with recurrent hypotensive reactions may be given a trial of washed blood components.

16.4.9 POST TRANSFUSION PURPURA (PTP)

Post transfusion purpura (PTP) is characterized by thrombocytopenia arising 5 – 12 days following transfusion of cellular blood components with findings of antibodies in the patient directed against the Human Platelet Antigen (HPA) system. This antibody destroys both transfused and autologous platelet. The usual implicated antibody is anti-HPA-1a. Patients usually have a history of sensitisation by either pregnancy or transfusion with five times more female patients affected than males. The thrombocytopenia is usually severe with platelet count $<10 \times 10^9$/L and expected to last approximately 2 weeks. Bleeding from mucous membranes, gastrointestinal and urinary tracts is common.

Investigation:

a) Test for HPA antibodies.

Management:

a) For patients with active bleeding, the treatment of choice for PTP is high dose intravenous immunoglobulin (IVIg). Patients respond within 4 days, on average, and some respond within hours.

b) Platelet transfusions are usually ineffective but may be given in high doses in patients with life-threatening bleeding.

c) Steroids and plasma exchange with fresh frozen plasma may be considered in patient refractory to IVIg.

d) Antigen-negative platelets may be indicated if subsequent transfusion is required.

16.4.10 TRANSFUSION ASSOCIATED GRAFT VERSUS HOST DISEASE (TA-GVHD)

TA-GVHD is a rare complication of cellular blood product transfusion that leads to profound marrow aplasia with a mortality rate > 90%. Death typically occurring within 1 – 3 weeks of first symptoms, most commonly due to overwhelming infection. It results from viable lymphocytes from cellular blood component engrafting in an immuno-incompetent patient or in immunologically normal patients after transfusion of a relative's blood. This condition should be suspected in a patient who develops fever, skin rash, diarrhoea, elevated liver enzymes and pancytopenia within 30 days following a transfusion without any other apparent cause. Diagnosis of TA-GVHD could be made by skin biopsy or cytogenetic/HLA analysis to establish the presence of donor lymphocytes. There is no specific or successful treatment for this condition, therefore patients at high risk must be identified for appropriate prevention.

High risk group:

a) All severe T lymphocyte immunodeficiency syndromes.

b) Intrauterine transfusion and subsequent exchange transfusion.

c) Hodgkin disease.

d) Bone marrow/stem cell transplantation (both autologous and allogeneic).

e) Therapy with purine analogue drugs.

f) Aplastic anaemia patient treated with anti-tymocyte globulin.

g) Granulocytes transfusion.

h) HLA-matched transfusion.

i) Receiving directed donor blood from relatives (first or second-degree relatives).

j) On Alemtuzumab (anti-CD52).

Prevention:

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

b) TA-GVHD is preventable in high risk patient by gamma or X-irradiation of cellular blood components.

16.4.11 IRON OVERLOAD

Transfusion dependent patients such as those with thalassaemia are likely to develop iron overload. Each unit of red cells contains about 250 mg of iron. Since iron excretion is very limited, accumulation in the body causes toxic effects after 10 – 50 units have been transfused.

Management:

Refer to ***Guidelines for management of transfusion dependant thalassaemia, 3rd Edition, 2014*** and ***Paediatric Protocol for Malaysian Hospital, 4th Edition, 2018.***

References

1. Tinegate, H., Birchall, J., Gray, A., Haggas, R., Massey, E., Pinchon, D. N. D., Sewell, C., Wells, A. & Allard, BCSH (2012). Guideline on the investigation and management of acute transfusion reactions.

2. Dr Derek Norfork. Handbook of Transfusion Medicine. UK Blood Services. 5th Edition; 2013.

3. Ozment, C. P. & Turi, J. L. (2009). Iron overload following red blood cell transfusion and its impact on disease severity. Biochimia et Biophysica Acta 1790, 694-701.

4. NHS (2006). Better Blood Transfusion Level 3, Adverse Effects of Transfusion, Knowledge Base.

5. Klein, H. G. & Anstee, D. J. (2005) In Mollison's Blood Transfusion In Clinical Medicine.

6. NZBlood (2008) In Transfusion medicine Handbook 2008.

7. New York State on Human Blood and Transfusion Services (2008). Transfusion Reaction.

8. Ruhl, H., Bein, G. & Sachs, U. J. H. (2009). Transfusion-Associated Graft-Versus-Host Disease Transfusion Medicine Reviews, 23, 62-71.

9. Resuscitation Council (UK) (2012). Emergency treatment of anaphylactic reactions.

10. Faed, J. (2014). Guidelines for management of adverse transfusion reactions.

11. Triuizi, D.J. (2006). Transfusion related Acute Lung Injury(TRALI Update 2006.Transfusion Medicine Update

12. Blood Cebtre of Wisconsin (2012). Transfusion associated acute lung injury.

13. Treleaven, J., Gennery, A., Marsh, J., Norfolk, D., Page, L., Parker, A., Saran, F., Thurston, J. and Webb, D. (2011), Guidelines on the use of irradiated blood components prepared by the British Committee for Standards in Haematology blood transfusion task force. British Journal of Haematology, 152: 35–51.

14. Vlaar APJ (2019). A consensus redefinition of transfusion-related acute lung injury

15. A. L. Peters (2016). Non antibody-mediated TRALI-current understanding

16. Mark K. Fung (2014). AABB Technical Manual Eighteenth edition.

17. Guidelines for the administration of blood products, Australian & New Zealand Society of Blood Transfusion (2018).

17.0 HAEMOVIGILANCE

Haemovigilance is a surveillance programme covering adverse events occurring during the entire blood transfusion chain from the donation of blood to the follow-up of patients receiving transfusion. The ultimate goal of haemovigilance is to improve patient and donor safety through the detection, reporting, analysis of information on unexpected or undesirable effects, and implementation of corrective and preventive actions.

Transfusion safety must be ensured in every stage, starting from the donor at the time of donation, blood sampling from the patient for pre-transfusion tests as well as blood administration at patient's bedside during time of transfusion and their follow up.

17.1 HAEMOVIGILANCE REPORTING

a) All adverse events relating to blood collection, processing, testing, transfusion processes and outcome of the transfusion including near misses must be reported. Incident related to products and equipment should be included.

b) Each hospital should have a mechanism to collect, compile and analyse data of all adverse events and deviations relating to collection, processing, testing and transfusion of blood, including near misses.

c) Haemovigilance reports shall be analyse and presented to respective Hospital Transfusion Committee (HTC), the State Transfusion Committee (STC) (if applicable) and submitted to National Haemovigilance Coordinating Centre (NHCC).

d) The HTC and the STC shall take corrective and preventive actions, and facilitate allocation of adequate resources both at the hospital and at the state level for improving transfusion safety.

e) The National Blood Centre shall act as the NHCC for the Ministry of Health.

f) Confidentiality of reporting to NHCC will be maintained and the identities of the donor, patient and the reporter of the incident and the institution shall not be disclosed to a third party.

17.2 PATIENT HAEMOVIGILANCE

Transfusion process involves many important steps that are critical for patient safety. Patient haemovigilance is a surveillance system that monitors the transfusion processes in the clinical area. The process of reporting adverse events shall be as follows:

a) The treating doctor shall send a request for transfusion reaction investigation using the Request Form for Transfusion Reaction Investigation (BTS/TR/2/2016) ***(APPENDIX XXVII)*** to the hospital blood bank.

b) The hospital blood bank shall then carry out relevant laboratory investigation using the Worksheet for Investigation of Transfusion Reaction (BTS/TRW/2/2016) ***(APPENDIX XXIX)***. The findings shall be reported to the treating doctor concerned.

c) The treating doctor shall provide a detailed report using the Reporting Form for Transfusion-Related Adverse Event (BTS/HV/3/2016) ***(APPENDIX XXVIII)***. The report shall include information such as clinical findings, laboratory investigations, personnel involved and corrective actions taken if any***.*** This report shall be forwarded to the hospital blood bank within two weeks of the occurrence.

d) It shall be the responsibility of the hospital blood bank concerned to follow up with the ward and doctor concerned to diagnose the type of adverse events and to ensure that the transfusion-related adverse event report is delivered within a month to the relevant authorities. Copies of the report shall be sent to the HTC, the STC, and the NHCC. Refer ***APPENDIX XXX*** for flowchart for reporting adverse transfusion event.

e) For Incorrect Blood Component Transfused (IBCT) and Near Miss a detailed report should be submitted to NHCC with root cause analysis together with implemented corrective and preventive action (Root Cause Analysis & Action Report: Refer Guidelines on Implementation Incident Reporting & Learning System 2.0 for Ministry of Health Malaysia Hospitals).

17.3 SEROCONVERTED RECIPIENT

A seroconverted recipient is one who is confirmed positive for a particular transfusion transmitted infection (TTI) marker(s) after receiving blood transfusion, but who was negative for that infection prior to the transfusion.

a) Recipients of a transfusion may develop HIV, Hepatitis B, Hepatitis C, Syphilis infection or other possible TTI agent infection resulting from:

   i. Transfusion of blood that was donated within the window period of the infection, **OR**
   ii. Other sources not related to the blood transfusion. Assessment of the risk factors not related to blood transfusion is prudent.

b) However, it is recommended that donors of the blood that has been transfused to the patient in the 12 months period prior to the detection of the infection be contacted for testing. The hospital blood bank shall be informed to identify the blood donors and their status determined.

c) If a blood donor is identified as the source of infection, other recipients of his or her blood should be traced and investigated.

d) Blood sample are taken for the suspected infectious disease marker based on Table 17.1.

Table 17.1: Test for recipient based on type of infection

Type of infection	Test for recipient
Syphilis	RPR TPPA
Hepatitis B	HBsAg HBeAg Anti-HBe Anti-HBc Neutralization (Other supportive test *e.g.* genotyping)
Hepatitis C	Anti-HCV Line immunoassay (Other supportive test *e.g.* genotyping)
HIV	Anti-HIV Particle agglutination Line immunoassay (Other supportive test *e.g.* genotyping)

17.4 DONOR HAEMOVIGILANCE

Donor haemovigilance is a surveillance system for tracking adverse events associated with blood donation with a view to improve the safety of the donation process. This system allows the collection centres to monitor the prevalence of adverse donor events, patterns and trends, and find ways to improve blood donation process, which will result in quality donor care and safety thus better donor return.

a) All unintended reactions related to blood donation, and cases of seroconverted donors shall be reported.

b) Reporting of adverse donor events. *Refer to* ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.***

17.5 SEROCONVERTED DONOR

A seroconverted donor is one who is confirmed positive for a particular TTI in his current donation but was negative in the previous donation.

All donors found to be seroconverted with HIV, Hepatitis B, Hepatitis C or Syphilis shall first be informed and counselled by the doctors at the blood centre, and then referred to the appropriate physician for further management. *Refer to* ***Transfusion Practice Guidelines for Clinical and Laboratory Personnel (4th edition) 2016.***

Each hospital shall develop and implement a system for managing recipients that received blood or blood product from seroconverted donor. Upon notification of a seroconverted donor, recipients should be counselled by the treating specialist/consultant and may include a transfusion medicine specialist.

First counselling session with recipient should be carried out as follows (pre-test counselling):

a) Inform recipient the reason for consultation.

b) Inform and explain that the blood or blood component transfused was from a donor who recently seroconverted. As a precautionary measure, the recipient needs to be tested to ascertain whether he/ she is infected following the

transfusion of a possible window period donation. Explain that “window period” IS NOT a laboratory error.

c) Assess the risk factors of the recipient with respect to the TTI concerned. Try to identify risk factors other than blood transfusion.

d) Explain about the TTI concerned, including its mode of transmission and potential complications.

e) Explain about tests available and the interpretation of the results.

f) Take samples of blood for the implicated infection, and reassure the recipient that the probability of being infected through transfusion is low.

g) Inform about the precautions to be taken while waiting for the test results. This is to prevent potential transmission from the recipient to others.

h) Discuss with the recipient the probability of the tests outcome.

Second counselling session should be carried out as follows (post-test counselling):

a) If recipient test results is negative:

   i. Inform recipient and explain.
   ii. Reassure the recipient.
   iii. If necessary, retest after 6 months post-transfusion or implement any follow-up.

b) If test result is positive to the TTI:

   i. Inform the recipient and explain.
   ii. Further assess the risk factors other than blood transfusion. If none, explain the blood he or she received was tested negative at the time of donation.
   iii. Reassure and discuss about the treatment options.
   iv. Refer the recipient to an infectious disease physician.
   v. Report transfusion-related adverse event to NHCC using form BTS/ HV/3/2016. ***(APPENDIX XXVIII)***

17.6 NATIONAL HAEMOVIGILANCE COORDINATING CENTRE

The National Haemovigilance Coordinating Centre shall:

a) Manage the notification of adverse events reports from all hospitals.

b) Prepare annual report with recommendation of appropriate interventions for continual improvement to KKM.

c) Monitor effectiveness of corrective and preventive action taken.

References

1. Transfusion Practice Guidelines for clinical and laboratory Personnel 4th edition 2016
2. Guidelines on Implementation Incident Reporting & Learning System 2.0 for Ministry of Health Malaysia Hospitals

APPENDIX

APPENDIX I: BLOOD TRANSFUSION CONSENT FORM

BTS/TC/2/2016

CONSENT FORM FOR BLOOD OR BLOOD COMPONENT TRANSFUSION

Patient's Name: Age:

Identity Card No.: Sex: ☐ Male ☐ Female

Address:

Attending Medical Practitioner: Dr.

Identity Card No.

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

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

_____

Signature of the patient/ Signature of Attending

parent/guardian/spouse/next of kin* Medical Practitioner

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

Identity Card No. of the above :

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

_____

Signature of witness*

Name of witness :

Identity Card No.:

* delete appriopriately

** if necessary

BORANG PERSETUJUAN PEMINDAHAN DARAH ATAU KOMPONEN DARAH

Nama Pesakit: Umur:

No. Kad Pengenalan: Jantina: ☐ Lelaki ☐ Perempuan

Alamat:

Pengamal Perubatan Yang Merawat: Dr.

No. Kad Pengenalan

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

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

_____

Tandatangan pesakit/ibu bapa/ penjaga/suami/isteri/saudara terdekat

Tandatangan Pengamal Perubatan Yang Merawat

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

No. Kad Pengenalan:

Saya memperakui makluman di atas telah diterangkan kepada pesakit/ibubapa/penjaga/suami/isteri/saudara terdekat yang tanda tangannya tertera di atas. Pada hemah saya penama yang dirujuk telah memahami kandungan borang ini dan telah bersetuju untuk menerima pemindahan darah atau komponen darah secara sukarela.

_____

Tandatangan Saksi*

Nama saksi:

No. Kad Pengenalan saksi:

* potong yang tidak berkaitan

** jika perlu

APPENDIX II: BLOOD TRANSFUSION REQUEST FORM

No. Makmal:

PER-SS-BT 105
(Pind. 1/2016)

BORANG PERMOHONAN TRANSFUSI DARAH
PERKHIDMATAN TRANSFUSI PERUBATAN

(Mesti dipenuhi dalam dua salinan. Tulis dengan pen mata bulat dan sila tandakan √ dalam petak yang berkenaan.)

Nama (Tulis huruf besar)			No. Kad Pengenalan		No. Daftar
Hospital	Unit	Wad	Bangsa	Umur	Jantina
Pegawai Kerajaan Ya/Tidak	Kelas	Bayar/Percuma	Pakar Perunding		Kumpulan Darah Ada/Tiada
Diagnosa		Sebab transfusi komponen darah		Hb % atau keputusan lain yg berkaitan (Plt count etc)	
Transfusi darah masa lalu? Ya/Tidak	Jika 'ya' sebutkan tarikh transfusi darah yang terakhir			Komplikasi?	
Sekiranya pesakit seorang wanita, nyatakan →	Bil. kehamilan	Bil. Lahir Mati		Tanda-tanda "Haemolytic Disease of Newborn"	

Sampel darah diambil dan dilabel oleh:

Saya mengesahkan bahawa saya telah mengenalpasti identiti pesakit dengan bertanya secara langsung* dan memeriksa gelang pengenalan pesakit. Saya juga mengesahkan bahawa saya telah mengambil sendiri sampel darah pesakit tersebut dan melabelkannya dengan serta merta sebaik sahaja ianya diambil.

Tandatangan .....

Nama .....

Jawatan.....

Tarikh.....Waktu.....pagi/petang

* (atau ahli keluarga / penjaga untuk kes-kes pediatrik dan pesakit yang tidak sedarkan diri)

Units/ mls

- ☐ WHOLE BLOOD .....
- ☐ PACKED CELLS .....
- ☐ PAEDIPACK .....
- ☐ PLATELET CONCENTRATE .....
- ☐ CRYOPRECIPITATE .....
- ☐ FRESH FROZEN PLASMA .....
- ☐ CRYOSUPERNATANT.....

SPECIAL REQUIREMENT :

- ☐ WASHED.....
- ☐ FILTERED.....
- ☐ IRRADIATED.....
- ☐ OTHERS : .....
- ☐ GROUP, SCREEN & HOLD

Nota:-

(1) Sila hantarkan 3ml-5ml sampel darah dalam tiub EDTA. Untuk makluman, ujian keserasian memerlukan masa 2 jam.

(2) Dalam keadaan kecemasan, sila hubungi makmal transfusi darah untuk pembekalan segera berdasarkan keserasian pada peringkat awal ujian. Darah yang dibekalkan mempunyai risiko ketidakserasian yang kecil. Penggunaan darah tersebut merupakan tanggungjawab pegawai perubatan yang merawat.

(3) Darah yang tidak digunakan perlu dipulangkan dengan kadar segera ke makmal transfusi kecuali Pegawai Perubatan meminta dipanjangkan tempoh simpanannya di wad.

(4) AMARAN: Setiap transfusi darah membawa risiko infeksi.

WARNING: Every blood transfusion carries a small risk of infection.

Bekalan diperlukan

(a) Serta merta, tanpa ujian keserasian darah (safe O) (untuk menyelamatkan nyawa) ☐

(b) Segera (lihat Nota 2) ☐

(c) Pada ..... jam.....pg/ptg (Lihat Nota 3) ☐

(d) Sampel disimpan selama 24 jam. ☐

Saya mengesahkan bahawa sampel darah yang disertakan ini telah diambil daripada pesakit bernama seperti di atas dan dilabelkan mengikut prosedur kerja yang telah ditetapkan. Saya juga mengesahkan bahawa setelah diperiksa, pesakit ini memerlukan/ akan memerlukan transfusi darah.

Tandatangan: .....
Cop dan Nama
Pegawai Perubatan: .....
(Huruf besar)

KHAS UNTUK KEGUNAAN KAKITANGAN MAKMAL TRANSFUSI DARAH

Permintaan diterima	T/Tangan	Anti A	Anti B	Anti AB	Sel A	Sel B	Sel O	Rh D	Kump. Darah	T/Tangan	Tarikh & masa
Tarikh.....											
Waktu .....pg/ptg											

Serum pesakit diserasikan dengan beg darah no.	UJIAN KESERASIAN DARAH					Catatan
	R.T.	37°C	AHG	T/Tangan.	Tarikh & masa	

APPENDIX III: BLOOD/BLOOD PRODUCT TRANSFUSION CHECKLIST

HKL/ BPK/ 027

BAHAGIAN PERKHIDMATAN KEJURURAWATAN
HOSPITAL KUALA LUMPUR

BLOOD / BLOOD PRODUCT TRANSFUSION CHECKLIST

I. PATIENT DATA

NAME :		**TYPE OF COMPONENT AND BARCODE NO :**
RN :		
NEW I/C NO :		
WARD :		
DATE TRANSFUSION :		
NAME OF CONSULTANT :		

II. ADMINISTRATION OF BLOOD

A) Verify Blood / Blood Product (S) Supplied Are Compatible By Checking
i. Patient's Name ii. RN iii. IC Number IV. Blood Bag Number With:

1	Patient's case notes	Yes		No	
2	Compatibility label, blood group & expiry date	Yes		No	
3	Blood request form	Yes		No	
	Name of Doctor				
	Signature				

B) Ascertain Patient Receiving Blood / Blood Product Is Correct By Checking
i. Patient's Name ii. RN iii. IC Number IV. Blood Bag Number With:

		DOCTOR		NURSE / AMO	
		Yes	No	Yes	No
1	Patient's case notes				
2	Asking patient / relative				
3	Compatibility label , blood group , & expiry date				
4	Blood request form				

NB: DATA IN II (B) TO BE COMPLETED BY TWO PERSON

First verifier (Doctor)	*Name	
	Signature	
Counter checked by second verifier (Nurse/AMO)	*Name	
	Signature	

C) TRANSFUSION PROCEDURE

Time of commencement				
Time of completion				
Any reaction	Yes		No	
If yes, state reaction and report to blood bank medical officer no. tel : 26955542 until 9pm, public holiday 8am– 12pm				
Monitor vital signs at baseline, 15 minutes, 30 minutes and every hour until completed transfusion. Record in observation chart.	Name			
	Signature			

D) VITAL SIGNS

FREQUENCY	TIME	PULSE	B/P	T°	FREQUENCY	TIME	PULSE	B/P	T°
Baseline					Hourly				
15min					Hourly				
30min					Hourly				
Hourly					Hourly				

NB: Form are to be filled in duplicate. Put a tick (√) in the appropriate box.
** Please fill in block letters*
Original copy is to be kept in the patient's notes
Duplicate copy is to be kept in a ward file and
Each ward to send monthly analysis to the Head of Department and Unit Pengurusan Kualiti, HKL.

K02/P03/September 2010

APPENDIX IV: INSTRUCTIONS ON PROPER HANDLING OF BLOOD AND BLOOD COMPONENTS IN THE WARD

	Whole blood Red cells	**Platelet concentrate**	**Plasma component**
Supply	After crossmatch	Group specific/compatible No crossmatching required	Group specific No crossmatching required Should be thawed
Collection	Blood box with Ice	Blood box without ice	Blood box with ice
Use	As soon as possible (After reaching the ward)	Transfuse immediately	Transfuse immediately
Storage	+2°C to +6°C	Room temperature +20°C to +24°C on agitator Do not store in fridge	Should not be stored or kept in the wards
Return of unused blood to hospital blood bank	Return immediately	Return immediately	Return immediately
After use	Fill up PPDK 1 and return together with empty bag to blood bank as soon as possible	Fill up PPDK 1 and return together with empty bag to blood bank as soon as possible	Fill up PPDK 1 and return together with empty bag to blood bank as soon as possible

APPENDIX V: GUIDE FOR THE USE OF PLATELET TRANSFUSION

CLINICAL INDICATIONS	CUT-OFF VALUES OF PLATELET COUNT
HAEMATOLOGICAL MALIGNANCIES	>10 x 10^9/L is the safe limit unless: fever, bleeding, on antibiotics or coagulopathy.
PROCEDURES:	
• BONE MARROW ASPIRATION & TREPHINE	>20 x 10^9/L provided adequate surface pressure is applied.
• LUMBAR PUNCTURE, OGDS & BIOPSY, INDWELLING LINES, TRANSBRONCHIAL BIOPSY, LIVER BIOPSY, LAPARATOMY	Platelet count should be raised to at least 50 x 10^9/L.
• FOR OPERATION AT CRITICAL SITES: EYE & BRAIN, EPIDURAL	Platelet count should be raised up to at least 100 x 10^9/L.
MASSIVE TRANSFUSION:	
• ACUTE BLEEDING	Platelet count should be raised up to at least 50 x 10^9/L.
• MULTIPLE TRAUMA / CNS INJURY	Higher target level of 100 x 10^9/L.
DISSEMINATED INTRAVASCULAR COAGULATION:	
• ACUTE DISSEMINATED INTRAVASCULAR COAGULOPATHY (DIC)	Frequent estimation of platelet count and coagulation screening should be done. Aim to maintain platelet count at >50 x 10^9/L.
• CHRONIC DIC / ABSENCE OF BLEEDING	Platelet transfusion should not be given.
IMMUNE THROMBOCYTOPENIA:	
• AUTOIMMUNE THROMBOCYTOPENIA	Only for life-threatening bleeding from gastrointestinal, genitourinary, central nervous system and other conditions with severe thrombocytopenia (<10 x 10^9/L).
• NEONATAL AUTOIMMUNE THROMBOCYTOPENIA	Transfuse compatible platelet as soon as possible: HPA antigen negative. Platelet prepared from mother should be irradiated and washed.
• POST TRANSFUSION PURPURA	Platelet transfusion usually ineffective. May be used in acute phase *e.g.*: operation.
PLATELET FUNCTION DISORDERS:	
Platelet transfusion only indicated if other measures fail to control the bleeding.	

CALCULATION OF DOSE:

Random platelet	>60 x 10^9/unit (Volume of 50 mL) 1 random platelet unit increases 5 – 10 x 10^9/L of platelet level
Apheresis	>200 x 10^9/unit (Volume 200 – 300 mL) Equivalent to 4 – 6 random platelet units
Child <20 kg	10 – 15 mL/kg
Adult	$\frac{\text{Platelet increment target} \times \text{blood volume}}{\text{correction factor } (0.67)}$

****PLATELET TRANSFUSION IS CONTRAINDICATED IN:**

d) Thrombotic Thrombocytopenic Purpura (TTP)

e) Heparin-induced Thrombocytopenia (HIT)

f) Kasabach Meritt Syndrome

APPENDIX VI: REFERRAL LETTER FOR AUTOLOGOUS PREDEPOSIT

Referral letter for autologous pre-deposit (addressed to the doctor in charge of the pre-deposit programme)

Dear _____

This patient has requested autologous pre-deposit for his/her operation. I have discussed this with the patient, with appropriate reference to the Guideline for Pre-operative Autologous Donation and am of the opinion that he/she is medically suitable for the procedure.

I would be grateful if you could see him/her with a view of making the necessary arrangements.

Patient's name (Mr/Mrs/Ms): _____

Date of Birth: _____ I/C number: _____

Ward: _____ R/N: _____

Address: _____

_____

Date of admission: _____

Date of operation: _____

Planned procedure: _____

Underlying pathology: _____

Requested number of donations (maximum is 4): _____

Haemoglobin (g/dL) : _____

Additional remarks: _____

Referring consultant clinician : _____

Signature : _____

Name (BLOCK LETTER) : _____

Date : _____

APPENDIX VII: CONSENT FORM FOR AUTOLOGOUS PREDEPOSIT

Consent for autologous transfusion

The purpose of autologous transfusion has been explained to me by Dr _____ who has also explained its possible complications and hazards.

I agree to my blood being withdrawn and stored for autologous transfusion.

I understand that it may not be possible for technical reasons to return to me all or any of the units which I donate.

I understand that it may be necessary to supplement my autologous transfusion with blood from volunteer donors from the Transfusion Services.

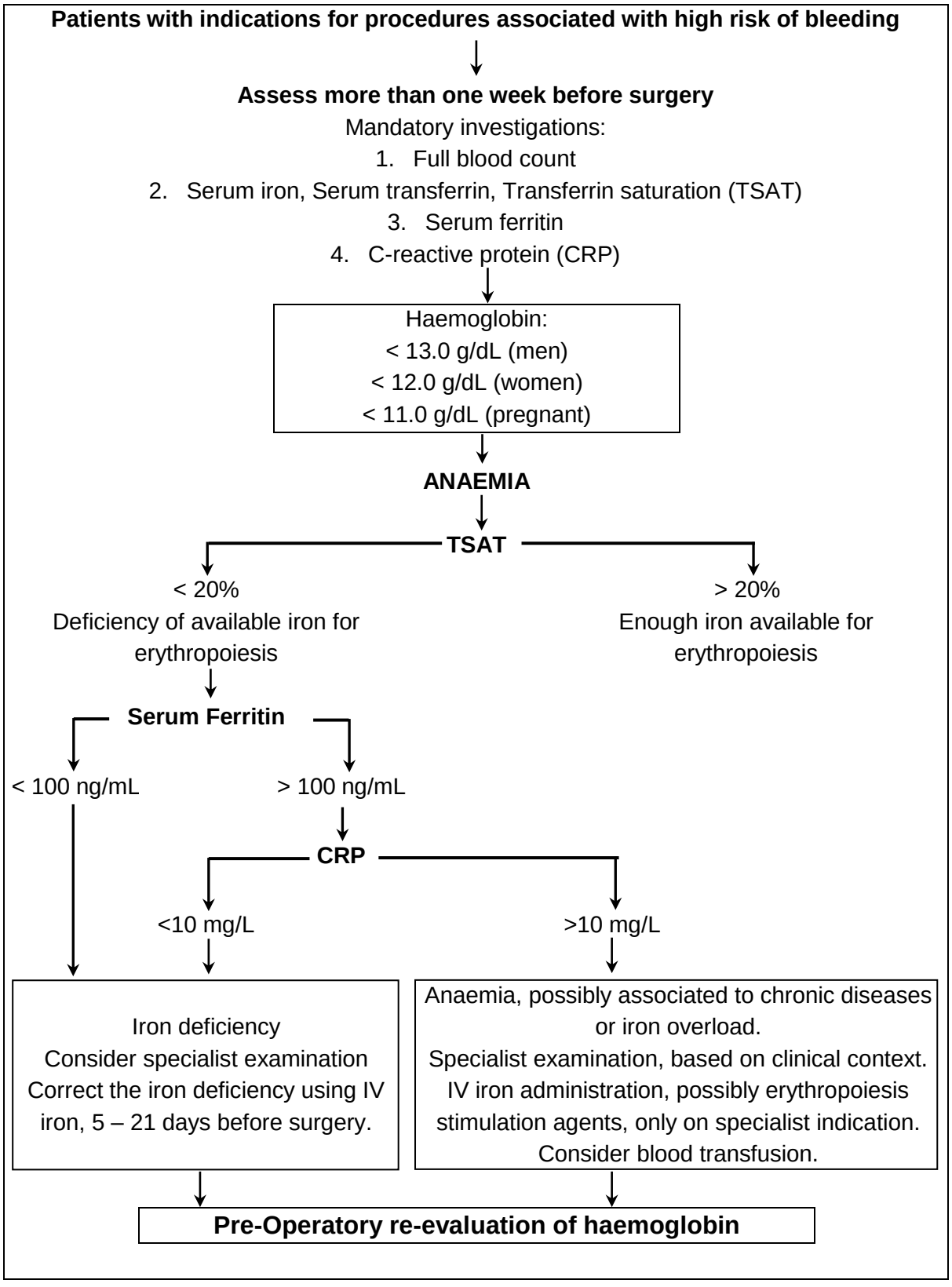
I agree to my blood being tested for HbsAg, anti-HCV, anti-HIV and RPR. In the event of a positive result in any of these tests, I agree to the clinician in charge of my case being informed.

Signature :

Date :

Witness :

APPENDIX VIII: ALGORITHM FOR PATIENT RED CELL MASS OPTIMIZATION



APPENDIX IX: MANAGEMENT FOR REVERSAL OF ANTI-COAGULANT

Anticoagulant	Non-Urgent	Urgent (Not Bleeding)	Urgent (Bleeding)
Warfarin	**Stop 5 days prior to procedure.** • **Check INR 1 – 2 days prior.** • **If INR >1.5 administer vitamin K 1 – 2 mg PO.**	If procedure can be delayed 6 – 24 hours, vitamin K 5 – 10 mg PO/IV; otherwise: • PCC or FFP prior to procedure. Repeat in 6 – 12 hours if INR >1.5 and • Vitamin K 5 – 10 mg PO/IV if sustained reversal is desired.	• ***HASHTI*** • Vitamin K 5 – 10 mg IV; repeat every 12 hours as needed • PCC or FFP, repeat every 6 hours as needed
Low molecular weight heparins (Enoxaparin, Dalteparin, Tinzaparin) and Fondaparinux	**Hold on day of procedure.** • **Once daily regimen** - **½ dose day prior** • **Twice daily regimen** - **Hold evening dose day prior**	Wait 12 – 24 hours if possible. Consider protamine sulphate if delay not possible for high bleeding risk procedure.	• ***HASHTI*** • Protamine sulphate • Consider rFVIIa
Anti-platelet (Aspirin, Dipyridamole, Clopidogrel, Ticlopidine, Prasugrel, Ticagrelor)	**Discontinue agent 5 – 10 days prior to procedure**	Consider platelet transfusion prior to high risk bleeding procedures.	• ***HASHTI*** • Platelet transfusion

Direct oral anti-coagulant (DOAC)	Direct thrombin inhibitor	Factor Xa inhibitors	
	DABIGATRAN	**RIVORAXABAN**	**APIXABAN**
Half life (hours)	12 – 17	7 – 13	8 – 15
	CrCl > 50 ml/min: Hold 1-2 days CrCl < 50 ml/min: Hold 3-5 days or longer. Unlikely the cause of bleeding if the APTT is normal Activated charcoal if ingestion less than 2 hours **May consider hemodialysis**	Hold at least 24 hours Drug presence may be assessed by anti-Xa assay. Unlikely the cause of bleeding if the PT is normal Activated charcoal if ingestion less than 8 hours	Hold 24 to 48 hours Drug presence may be assessed by anti-Xa assay Activated charcoal if ingestion less than 6 hours
Reversal of DOAC	Idarucizumab 5 g	• Andexanet-alfa 600 – 800 mg • Ciraparantag 100 mg	

General Principles of Management of Anticoagulant-Associated Bleeding

HASHTI

1. **H**old further doses of anticoagulant.
2. Consider **A**ntidote.
3. **S**upportive treatment.
    a. Volume resuscitation (intravenous fluids).
    b. Haemodynamic support (inotropes, monitoring).
4. Local or surgical **H**aemostatic measures.
    a. Anti-fibrinolytic agents can be considered (tranexamic acid).
5. **T**ransfusion.
    a. Red blood cells for severe or symptomatic anaemia.
    b. Platelets if thrombocytopenia (<50 x 10^9/L) or patient on long-acting antiplatelet agents.
6. **I**nvestigate for bleeding source.

Reference: 2011 Clinical Practice Guide on Anti-coagulant Dosing and Management of Anticoagulant – Associated Bleeding Complications in Adults, American Society of Hematology.

APPENDIX X: ANTI-COAGULANT REVERSAL AGENTS

Agent	Dose	Notes
Vitamin K	1 – 10 mg IV/PO, not subcutaneous or IM.	• Infusion reactions rare; administer over 20 – 30 minutes. • Takes 6 (IV) to 24 (PO) hours to reverse warfarin. • Large doses can cause warfarin resistance on resumption.
Protamine sulphate	12.5 – 50 mg IV - 1 mg per 90 – 100 units heparin given in previous 2 – 3 hours. *e.g.* 25 – 35 mg if 1000 – 1250 units/hour heparin infusion. - 1 mg per 1 mg enoxaparin in previous 8 hours. - 1 mg per 100 units dalteparin in previous 8 hours. - 1 mg per 100 units tinzaparin in previous 8 hours.	• Full reversal of unfractionated heparin. • 60% – 80% reversal of low molecular weight heparin. • No reversal for fondaparinux.
Prothrombin complex concentrate (PCC)	25 – 50 units/kg IV.	• Rapid INR correction in warfarin patients. • Small volume infusion over 10 – 30 minutes. • Risk of thrombosis 1.4%. • Contraindicated with history of HIT. • May need repeat dose after 6 hours • Consider adding FFP if 3-factor PCC used.
Recombinant factor VIIa (rFVIIa)	15 – 90 units/kg.	• Rapid infusion of small volume. • Risk of thrombosis 5 – 10%. • May need repeat dose after 2 hours.

Reference: 2011 Clinical Practice Guide on Anti-coagulant Dosing and Management of Anti-coagulant – Associated Bleeding Complications in Adults, American Society of Hematology.

APPENDIX XI: ANTI-PLATELET REVERSAL

Aspirin, Dipyridamole, Clopidogrel, Ticlopidine, Prasugrel, Ticagrelor

General Consideration

1. Half-lives
   a. Clopidogrel, ticlopidine, dipyridamole, prasugrel, ticagrelor: 7 – 10 hours.
   b. Low-dose aspirin (150 mg daily): 2 – 4.5 hours.
   c. Overdose aspirin (>4000 mg) : 15 – 30 hours.
2. Reversibility of anti-platelet effect
   a. Aspirin, clopidogrel, ticlopidine and prasugrel inhibit platelet function for lifetime of platelet. Inhibition takes 7 – 10 days to resolve as new platelets are generated.
   b. Ticagrelor is a reversible inhibitor, so platelet function normalizes after drug clearance.
3. Circulating drug or active metabolites can inhibit transfused platelets.
4. Must consider indication for use in decision to reverse.
   a. Risk of coronary stent occlusion (which can be fatal) within 3 months of bare metal stent implantation; period of risk is likely longer for drug-eluting stents.
   b. Consult cardiologist if uncertain.

Reversal of Anti-platelet Agents

Non-Urgent	Urgent (Not Bleeding)	Urgent (Bleeding)
Discontinue agent 5 – 10 days prior to procedure	Consider platelet transfusion prior to high risk bleeding procedures	HASHTI* Platelet transfusion

APPENDIX XII: DRUG CHART

Drug	Dosage	Notes
Haematinics	Give oral iron (ferrous sulphate 200 mg three times per day for an adult; ferrous sulphate 15 mg/kg/day for a child). **Vitamin B12** 1 mg IM twice weekly for 3 weeks. **Folic acid** 5 mg PO daily for 3 months. A higher dose of 5 mg 3 times per day may be needed if malabsorption occurs.	Continue this treatment for three months or one month after haemoglobin concentration has returned to normal. The haemoglobin level should rise by about 2 g/dL within about 3 weeks.
Erythropoietin	Haemoglobin level greater than 10 g/dL and up to 13 g/dL) 300 units/kg/day SC for 10 days before surgery, on the day of surgery, and for 4 days after OR 600 units/kg SC once weekly at 21, 14, and 7 days prior to surgery plus a fourth dose on the day of surgery; all patients should receive iron supplements and deep vein prophylaxis should be strongly considered.	
Tranexamic acid	10 mg/kg at the initiation of anaesthesia induction, followed by intravenous infusion of 1 mg/kg/hour. Adult: Slow IV 0.5 – 1 g (10 – 15 mg/kg) 3 times daily. Continuous infusion at a rate of 25 – 50 mg/kg daily.	**Contraindicated in:** Severe renal impairment. Thromboembolic disease. Intravascular clotting process. Disturbance of colour vision. Subarachnoid haemorrhage. **Precaution:** Concomitant therapy with oestrogens or thrombolytics.
Desmopressin (DDAVP)	0.3 mcg/kg over 30 minutes diluted in 50 – 100 mL NS intravenously. Doses can be repeated at 8 – 12 hours.	**Contraindicated in:** Hyponatremia or history of hyponatremia. Moderate-to-severe renal impairment.

Drug	Dosage	Notes
	If desmopressin acetate injection 4 mcg/mL is used pre-operatively, it should be administered 30 minutes prior to the scheduled procedure. No difference in dose for IV or SC administration. Mild to moderate haemophilia and vWD – Adult and child (>1 month) dose: 0.3 mcg/kg as a single dose immediately before surgery or after trauma; may be repeated at intervals of 12 hours.	Unstable angina pectoris. Decompensated cardiac insufficiency. Von Willebrand's disease type IIB. **Precaution:** Avoid fluid overload in patient taking diuretics. Monitor blood pressure and pulse during infusion.
Recombinant factor VIIa (rFVIIa)	30 to 45 mcg/kg in surgical patients. Alternatively, lower doses (10 – 20 mcg/kg) can be repeated every 15 – 30 minutes for a total of 90 – 180 mcg/kg in patients with life-threatening haemorrhage. Initially 4.5 KIU (90 mcg)/kg body weight IV bolus over 2 – 5 minutes, followed by 3 – 6 KIU (60 – 120 mcg)/kg body weight depending on type & severity of haemorrhage or surgery performed. Dosing interval: initially 2 – 3 hour to obtain haemostasis and until clinically improved. If continued therapy is needed, dose interval can be increased successively to every 4, 6, 8 or 12 hours.	**Precaution:** Thromboembolism especially in patients with known hypercoagulability. Simultaneous use of prothrombin complex concentrates, activated or not should be avoided.

References

1. *The clinical use of blood in medicine, obstetrics, pediatrics, surgery & anesthesia, trauma & burns (WHO) 2002. [Online]. Available from: http://www.who.int/bloodsafety/clinical_use/en/Handbook_EN.pdf [Accessed].*
2. *Micromedex 2.0 [Online]. Available from: www.thomsonhc.com [Accessed]*
3. *Formulari Ubat Kementerian Kesihatan Malaysia [2009].*
4. *Desmopressin [Online]. Available from: http://www.drugs.com/mtm/desmopressin.htmL [Accessed]*
5. *British National Formulary [March 2010]*

APPENDIX XIII: EXAMPLE OF MAXIMUM SURGICAL BLOOD ORDERING SCHEDULE (MSBOS)

CARDIOTHORACIC SURGERY		
No.	Procedure	Units of blood required
1	*Atrial Septal Defect*	*2*
2	*Ventricular Septal Defect*	*2*
3	*Coronary Artery Bypass*	*2*
4	*Redo CABG/ Redo Valve Replacement or Repair*	*4*
GENERAL SURGERY		
No.	Procedure	Units of blood required
1	*Anterior Resection*	*4*
2	*Hemicolectomy*	*GSH*
3	*Total Gastrectomy*	*2*
O&G		
No.	Procedure	Units of blood required
1	*Placenta Praevia Type 3 or 4*	*2 – 4*
2	*LSCS – 2 Previous Scars*	*GSH*
3	*Myomectomy*	*2*
4	*Cone biopsy*	*GSH*

* Special situation will be noted in the blood request form.

APPENDIX XIV: BLOOD SELECTION FOR INTRAUTERINE TRANSFUSION (IUT)

1. Irradiated red cells to prevent transfusion-associated graft-versus-host disease (TA-GVHD).
2. Shelf life is only 24 hours following irradiation.
3. Blood for IUT should not be transfused immediately from 4°C storage due to risks of foetal bradycardia but there are no specifically designed warming systems for the small blood volume required and the component should not be exposed to radiant heaters or sunlight as the temperature is unmonitored and there is a risk of haemolysis.
4. Transfusion volume required may be calculated based on donor and foetal haematocrits and the estimated foetoplacental blood volume. The foetoplacental volume depends on gestation and foetal weight.
5. In urgent situations, if IUT units are unavailable, acceptable alternatives are irradiated neonatal red cell exchange units or irradiated paedipacks (small-volume splits of single-donor units. Maternal blood should not be used for IUTs because of the significant risk of TA-GVHD).
6. Infants who have received IUT require to be given irradiated blood and blood components up to 6 months after the expected date of delivery *(Helen V. New et al., 2016)*

APPENDIX XV: USE OF ANTI-D IMMUNOGLOBULIN AS IMMUNOPROPHYLAXIS IN RH INCOMPATIBLE TRANSFUSION

- A dose of 250 IU anti-D immunoglobulin should be sufficient to cover up to five adult therapeutic doses of D positive platelets given within a 6-week period.
- It is not necessary to administer anti-D Ig to D negative females without childbearing potential, or males who receive D positive platelets.
- In severely thrombocytopenic patients with platelet count of ≤30 × 10^9/L, anti-D Ig should be given subcutaneously, or IV if a preparation suitable or IV route is available, to avoid the risk of IM bleed following IM injection.

Anti-D Immunoglobulin product available usage information

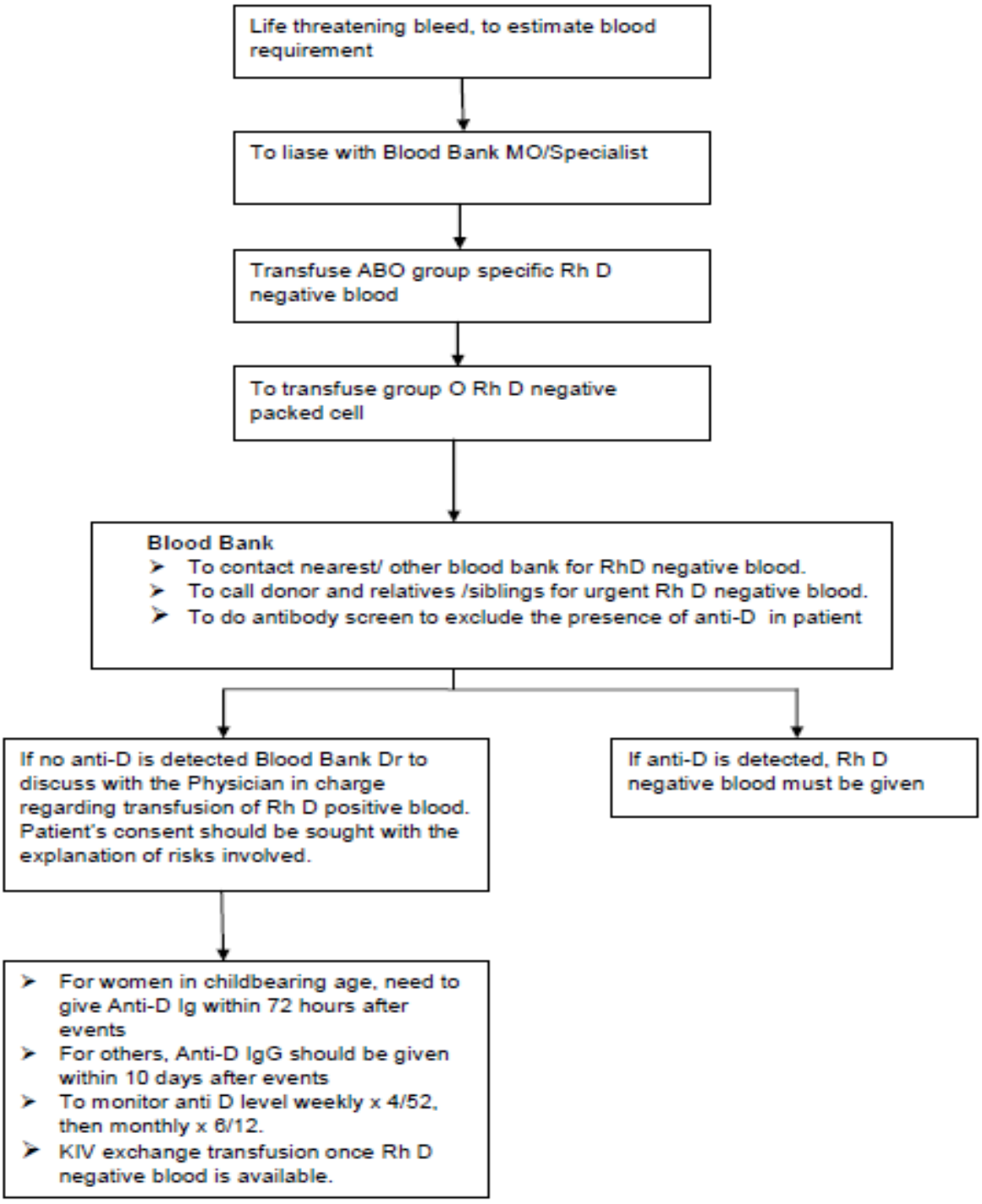
Rhogam® (300 µg/1500 IU) / **MICRhoGAM®** (50 µg/250 IU) - (IM only)
• MICRhoGAM (50 µg/250 IU) for <2.5 mL exposure of Rh incompatible red blood cells. • 300 µg (1500 IU) after 2.5 mL – 15 mL Rh-incompatible red blood cells transfusion. • If >15 mL Rh positive red cells, additional dose may be required (multiple syringes), may be given at the same time or at spaced intervals within 72 hours.
CONTRAINDICATION
• Rh positive individuals

Rhophylac® (1500 IU/300 mcg) - IM and IV use
• 20 mcg (100 IU) per 2 mL of Rh positive whole blood or 1 mL packed red cells exposure
CONTRAINDICATION
• History of anaphylactic or severe systemic reaction to human immune globulin products. • IgA deficient patients with antibodies against IgA and a history of hypersensitivity to Rhophylac or any of its components. • Newborn infant of the mother that received Rhophylac postpartum.
PRECAUTION
• Contains a small quantity of immunoglobulin A (IgA), there is a potential risk of hypersensitivity in IgA deficient individuals. • May carry a risk of transmitting infectious agents because it is made from human plasma.

ADVERSE REACTIONS

A) Injection site reactions that include swelling, induration, redness and mild pain or warmth.
B) Systemic reactions that include skin rash, body aches or a slight elevation in temperature. Patients should be observed for at least 20 minutes after administration.
C) Patients treated for Rh-incompatible transfusion should be monitored by clinical and laboratory means for signs and symptoms of a haemolytic reaction.

APPENDIX XVI: TRANSFUSION OF RHD NEGATIVE IN EMERGENCY SETTING



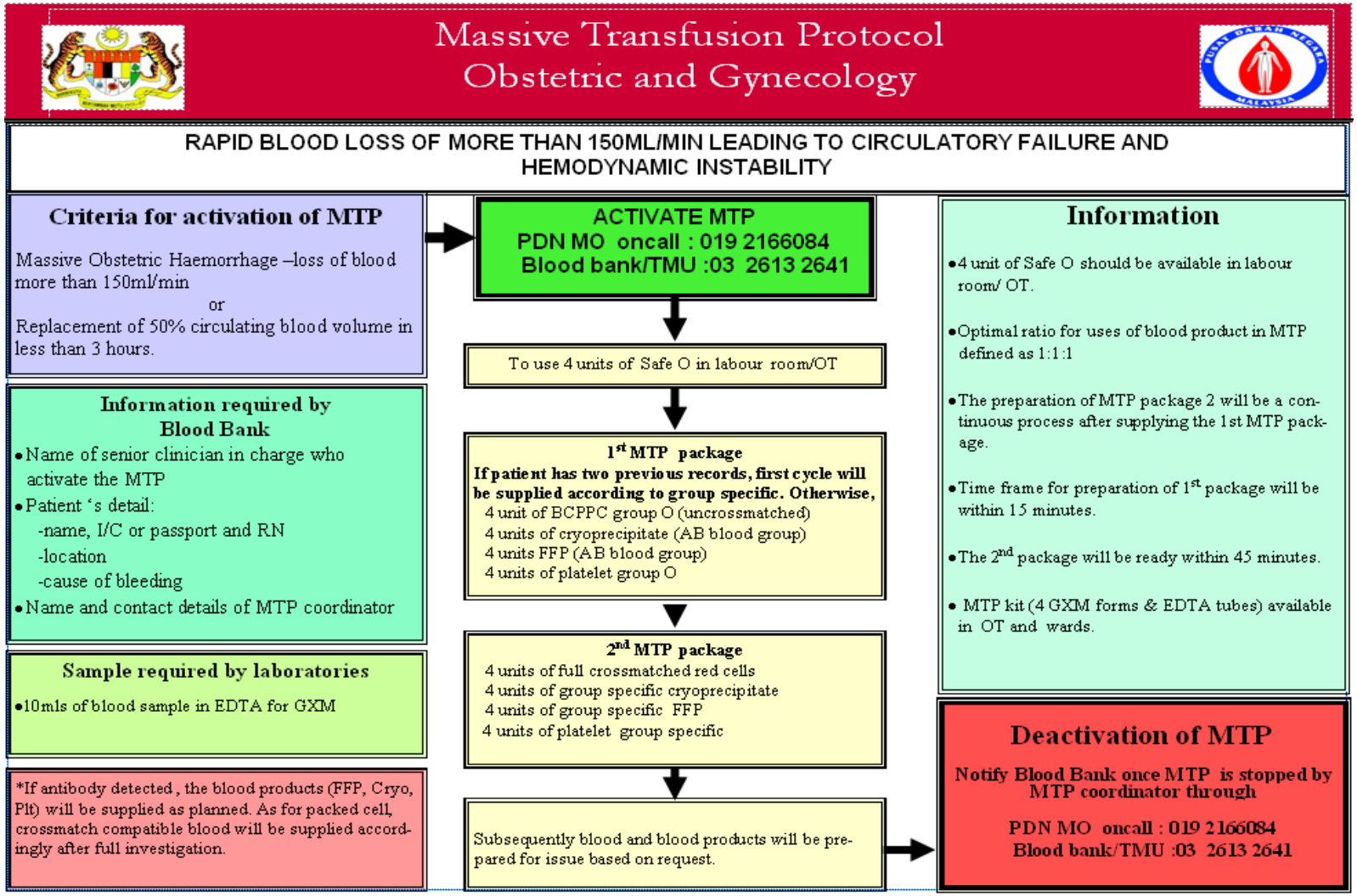
APPENDIX XVII: CLASSIFICATION OF HYPOVOLAEMIC SHOCK ACCORDING TO BLOOD LOSS

	Class I	Class II	Class III	Class IV
Blood loss (% total) (Adults & Paediatrics)	<15	15 – 30	31 – 40	>40
Blood loss (mL) (Adults)	> 750	800 – 1500	1500 – 2000	>2000
Pulse rate	Slight tachycardia	100 – 120	120 (tready)	>120 (tready)
Blood pressure Systolic Diastolic	↔	N ↓	↓ ↓	↓↓ ↓↓
Capillary refill	N	Slow > 2s	Slow > 2s	Undetectable
Respiratory rate	N	N	Tachypnoea >20/min	Tachypnoea >20/min
Urinary flow rate (mL/hr)	> 30	20 – 30	10 – 20	0 – 10
Extremities	N	Pale	Pale	Pale and Cold
Complexion	N	Pale	Pale	Ashen
Mental state	Alert	Anxious/ Aggressive	Anxious, aggressive or drowsy	Drowsy, confused or Unconscious
Management	No need for transfusion. (Transfuse if pre-existing anaemia or severe cardiorespiratory disease)	Crystalloid /colloid. (Transfuse if pre-existing anaemia or reduced cardiorespiratory reserve)	Rapid volume replacement with crystalloid/colloid. Red cell transfusion probably required.	Rapid volume replacement with crystalloid /colloid and red cell transfusion.

APPENDIX XVIII: MANAGEMENT STRATEGY FOR TRAUMA AND MASSIVE TRANSFUSION – SUMMARY OF KEY RECOMMENDATIONS (BCSH GUIDELINES)

Goals	Procedure	Comments
Restore circulating volume	Insert wide bore peripheral or central cannula. Give pre-warmed crystalloid or colloid as needed. (There was no difference in outcome and clinically equivalent when albumin and non-albumin colloids versus crystalloids were used as volume replacement). Avoid hypotension or urine output < 0.5 mL/kg/hour.	14 gauge. Monitor central venous pressure. Keep patient warm. Concealed blood loss is often Underestimated.
Contact key personnel	Clinician in charge. Consultant anaesthetist. Transfusion specialist. Early surgical or obstetric intervention. Interventional radiology.	A named senior person must take responsibility for communication and documentation. Arrange Intensive Care Unit bed.
Request laboratory investigations	FBC, PT, APTT, Thrombin time, Fibrinogen (Clauss method); blood bank sample, biochemical profile, blood gases. Ensure correct sample identification. Repeat tests after blood component infusion.	Results may be affected by colloid infusion. Ensure correct patient identification. May need to give components before results available.
Maintain haemoglobin > 8 g/dL	Assess degree of urgency. Employ blood salvage to minimise allogeneic blood use. Give red cells Group O RhD positive • In extreme emergency. • Until ABO and RhD groups known. ABO group specific • When blood group known. Fully compatible blood • Time permitting. Blood warmer and/or rapid infusion device if flow rate >50 mL/kg/hour in adult.	Further serological crossmatched not required after 1 blood volume replacement (in our setting each unit will be crossmatched at immediate spin – 15 to 30 minutes. If continue to full crossmatch – 45 minutes). For emergency crossmatch (immediate spin), transfusion laboratory will complete crossmatch after issue.
Maintain platelet count >75 X 10^9/L	Allow for delivery time from blood bank. Anticipate if platelet count <75 x 10^9/L.	Allows margin of safety to ensure platelet count >75 x 10^9/L. Keep platelet count >100 x 10^9/L if multiple or CNS trauma or if platelet function abnormal.
Maintain PT & APTT < 1.5 x mean control	Give FFP 12 – 15 mL/kg (for an adult) guided by tests. Anticipate need for FFP after 1 – 1.5 times blood volume replacement. Allow for 30 minutes thawing time.	PT/ APTT >1.5 x mean normal value correlates with increased microvascular bleeding. Keep ionised Ca^{2+} > 1.13 mmol/L.
Maintain Fibrinogen > 1.0 g/L	If not corrected by FFP give cryoprecipitate (1 unit /10 kg). Allow for 30 minutes thawing time.	Cryoprecipitate rarely needed except in DIC.
Avoid DIC	Treat underlying cause (shock, hypothermia, acidosis).	Although rare, mortality is high.

APPENDIX XIX: EXAMPLE OF MASSIVE TRANSFUSION PROTOCOL IN OBSTETRIC HAEMORRHAGE



APPENDIX XX: SUGGESTED TRANSFUSION THRESHOLD FOR INFANTS UNDER 4 MONTHS OF AGE

Transfusion	Transfusion Threshold
Transfusion of red cell	
Anaemia in the first 24 hours	Haemoglobin <12 g/dL
Neonate receiving mechanical ventilation	Haemoglobin <12 g/dL
Acute blood loss	>10% blood volume loss
Cumulative blood loss in 1 week	>10% blood volume loss
Chronic oxygen dependency (not ventilated)	Haemoglobin < 8 – 11 g/dL (depending on clinical situation)
Late anaemia, stable patient (not on oxygen therapy)	Haemoglobin < 7 g/dL
Transfusion of platelet	
Consider in all neonates	
Consider if increased bleeding risk for *e.g.*:	<30 x 10^9/L
▪ <1000 g and <1 week of age ▪ Clinically unstable (*e.g.*: labile blood pressure) ▪ Previous major bleeding (*e.g.*: grade 3 – 4 intraventricular haemorrhage) ▪ Current minor bleeding *e.g.*: petechiae) ▪ Coagulopathy	<50 x 10^9/L
▪ Planned surgery or exchange transfusion ▪ Major bleeding	<100 x 10^9/L
Transfusion of fresh frozen plasma ▪ Bleeding DIC or prior to an invasive procedure*	APTT and PT>1.5 control for age
Transfusion of cryoprecipitate ▪ Bleeding or DIC not corrected with FFP	Fibrinogen < 1 g/L

*to be transfused ½ hour before invasive procedure

APPENDIX XXI: MANAGEMENT OF HYPOVOLAEMIA IN PAEDIATRIC PATIENTS

Classification of hypovolaemia in children

	Class I	Class II	Class III	Class IV
Blood Volume	<15%	15 – 25%	25 – 40%	>40%
Pulse Rate (beats/min)	↑	>150	>150	↑or ↓
Pulse Pressure	N	↓	↓↓	Absent
Systolic Blood Pressure	N	↓	↓↓	Unrecordable
Respiratory Rate (breaths/min)	N	↑	↑	Slow sighing respiration
Capillary Refill Time	N	Prolonged	Very prolonged	Absent
Mental State	N	Irritable	Lethargic	Comatose
Urine Output	<1 mL/kg/hour	< 1 mL/kg/hour	<1 mL/kg/hour	< 1 mL/kg/hour

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

APPENDIX XXII: MAINTENANCE BLOOD TRANSFUSION IN THALASSAEMIA

Management

Regular blood transfusion and iron chelation therapy is the mainstay of treatment in patients with transfusion dependent thalassaemia.

Maintenance Blood Transfusion

BETA THALASSAEMIA MAJOR

When to start blood transfusion?

- *After* mandatory blood investigations has been taken for confirmation of diagnosis. Note that it is not necessary to wait for the confirmatory diagnosis result to be available before transfusing the patient in emergency situations, BUT blood investigations MUST be taken before transfusion.
- It is very important that Hb analysis, infection screen and RBC phenotype is done *prior* to first transfusion as failure to do so will affect the subsequent lab results and complicate the management of the patient later on.
- THAL MAJOR: Once diagnosis is confirmed or if Hb < 7g/dl on 2 occasions > 2 weeks apart (in absence other factors e.g. infection).
- THAL INTERMEDIA: Hb < 8g/dl if there is evidence of impaired growth attributed to anaemia after exclusion of other causes (dietary, constitutional).
- Bone changes (maxillary / mandibular prominence), enlarging liver and spleen, para spinal masses.

Transfusion targets

All thalassaemia major/severe E-β thal should be transfused so as to

- Maintain pre transfusion Hb level at approximately 9 -10 g/dl.
- Keep mean post-transfusion Hb at 13.5-15.5g/dl.
- Keep mean Hb 12 - 12.5 g/dl.
- The above targets allow for normal physical activity and growth, abolishes chronic hypoxaemia and reduces compensatory marrow hyperplasia which causes irreversible facial bone changes and para-spinal masses.

Transfusion interval

- Usually 4 weekly interval (usual rate of Hb decline is at 1g/dl/week).
- Interval varies depending on patients (range: 3 - 6 weekly).

Transfusion volume

- Volume: 15 – 20 mls/kg packed red cells (PRBC).
- Round-up the volume to the nearest unit of cross-matched blood provided, i.e. if calculated volume is just > 1 unit of blood, give 1 unit; or if calculated volume is just < 2 units, give 2 units.
- This strategy minimizes the number of exposure to immunological units of blood avoid wastage of donated blood.

Note:

- In the presence of cardiac failure or Hb < 5g/dl, use low volume PRBC (~ 5-10 ml/kg) at slow infusion rate over > 4 hours with IV Frusemide 1 mg/kg (20 mg maximum dose).
- It is recommended that thalassaemia patients receive leucodepleted (pre-storage, post storage or bedside leucocyte filters) PRBC of < 2 wks old.
- Leucodepletion minimizes non-haemolytic febrile reactions and alloimmunization by removing white cells in the PRBC.

Thalassaemia intermedia

- A clinical diagnosis where patients presents with less severe anaemia at > 2 years of age.
- Severity varies from being symptomatic at presentation to being asymptomatic until later adult life.
- Assessment and decision to start regular transfusion is best left to the specialist.
- All the mandatory bloods pre transfusion investigation is required as per transfusion dependent thalassaemia (refer above).

From *Paediatric Protocol for Malaysian Hospital, 4th Edition, 2019.*

APPENDIX XXIII: GUIDELINES FOR NEONATAL EXCHANGE TRANSFUSION

CALCULATIONS FOR NEONATAL EXCHANGE TRANSFUSION
Partial Exchange Transfusion for Treatment of Symptomatic Polycythaemia Replace removed blood volume with normal saline or 5% albumin $$Volume\ to\ be\ exchanged\ (mL) = estimated\ blood\ volume\ \times \frac{(patient's\ HCT - desired\ HCT)}{patient's\ HCT}$$
Two-volume Red Cell Exchange Transfusion for Treatment of Neonatal Hyperbilirubinaemia Replace calculated blood volume with whole blood or red cells suspended in 5% human albumin. $$Volume\ to\ be\ exchanged\ (mL) = estimated\ blood\ volume\ \times \frac{patient's\ HCT\ [5\%] \times 2}{HCT\ of\ transfused\ unit\ [\%]\ *}$$ * haematocrit (HCT) Whole blood 35 – 45% Red cell 55 – 75% Red cell suspension 50 – 70%

TRANSFUSION PROCEDURE

- The infant should be nil by mouth for at least 4 hours after the exchange transfusion. The stomach should be emptied if the infant was fed within 4 hours of the procedure.
- Closely monitor vital signs, blood sugar and temperature. Have resuscitation equipment ready.
- For a newborn, umbilical and venous catheters may be used and should be inserted by sterile technique (blood is drawn out of the catheter and infused through the venous catheter). Alternatively two peripheral lines may be used.
- Use pre-warmed blood only if a quality-controlled blood warmer is available. Do not improvise by using a water bath.
- Exchange 15 mL increments in full term infants and smaller volume for smaller, less stable infants. Do not allow the cells in donor unit to form a sediment.
- Withdraw and infuse blood 2 – 3 mL/kg/min to avoid mechanical trauma to the patient and donor cells.
- Give 1 – 2 mL of calcium gluconate solution I/V slowly for ECG evidence of hypocalcaemia (prolonged Q-T interval). Flush tubing with normal saline before and after calcium infusion.
- To complete two-volume exchange, transfuse 170 mL/kg for a full term infant and 170 – 200 mL/kg for a preterm infant.
- Send the last aliquot of blood drawn to the laboratory for determination of haemoglobin or haematocrit, blood smear, glucose, bilirubin, potassium, calcium and group and match.
- Prevent hypoglycaemia after exchange transfusion by continuing infusion of glucose-containing crystalloid.

APPENDIX XXIV: LIST OF DRUGS AND CHEMICALS TO BE AVOIDED IN G6PD DEFICIENCY

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

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

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

* These drugs may cause haemolysis in normal individuals if given in large doses.

APPENDIX XXV: 4Ts SCORE FOR HEPARIN-INDUCED THROMBOCYTOPENIA (HIT)

4Ts probability scoring system is useful to guide clinicians in making the diagnosis of HIT. However, it has not been compared with intuition-based diagnosis. Low probability 4T score has high negative predictive value to exclude HIT.

A clinical probability scoring system

4Ts	2 Points	1 Point	0 Point
Thrombocytopenia	Platelet count fall >50% and nadir $\geq$20 x 10^9/L.	Platelet count fall 30 – 50% or nadir 10 – 19 x 10^9/L.	Platelet count fall <30% or nadir <10 x 10^9/L.
Timing of platelet count fall	Clear onset between days 5 – 14 or platelet fall $\leq$ 1 day.	Consistent with days 5 – 14 fall, but not clear or onset after day 14 or fall $\leq$ 1 day (prior heparin exposure 30 – 100 days ago).	Platelet count fall $\leq$ 4 days without recent exposure.
Thrombosis or other sequelae	New thrombosis (confirmed); skin necrosis at heparin injection sites.	Progressive or recurrent thrombosis; non-necrotising skin lesions; suspected thrombosis (not confirmed).	None.
Other causes of thrombocytopenia	None apparent.	Possible.	Definite.

High probability 6 – 8 points; intermediate probability 4 – 5 points; low probability $\leq$ 3 points.

APPENDIX XXVI: INDICATION OF THERAPEUTIC APHERESIS

Treatment Category 1

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Acute inflammaotory demyelinating polyradiculoneuropathy (Guillain Barré syndrome)	TPE	Primary treatment	1A	TPE: Albumin or Plasma IA: NA	Frequency: Every other day or daily Volume treated: TPE: 1 – 1.5 TPV; IA: up to 3 TPV frequency
	IA	Primary treatment	1B	Duration and discontinuation/number of procedures: the typical TPE strategy is to exchange 1 – 1.5 plasma volumes 5 – 6 times over 10 – 14 days. Considerations for IA are essentially identical.	
Thrombotic microangiopathy, thrombotic thrombocytopenic purpura (TTP)	TPE		1A	Plasma or Plasma/ Albumin	Frequency : daily Volume treated : 1 – 1.5 TPV
				*Duration or discontinuation: should be based upon patient condition and response.	
Sickle cell disease, acute	Red cell exchange	Acute stroke Acute chest syndrome, severe	1C 1C	Red cell units, HbS negative, leucocyte reduced, antigen-matched (*e.g.* C/c, E/e, K)	Frequency: One procedure Volume treated: as necessary to maintain target HbS level

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Sickle cell disease, non-acute	Red cell exchange	Stroke prophylaxis	1A	Red cell units, HbS negative, leucocyte reduced, antigen-matched (*e.g.* C/c, E/e, K).	Frequency: Duration and number of RBC exchanges depend upon clinical indications; one time for pre-op, variable times for chronic pain, and life-long for stroke prevention. Volume: as needed to maintain target HbS level.
Polycythaemia vera; Erythrocytosis	Erythrocytapheresis	Polycythaemia vera	1B	Albumin, normal saline	Frequency: As needed for symptomatic relief or to reach desired HCT (usually one). Volume treated: Volume of blood processed is based on TBV, starting HCT and desired post-procedure HCT.
Hereditary haemochromatosis	Erythracytopheresis		1B	Replace at least one third to half of removed red cell volume with saline	Frequency: Every 2 – 3 weeks, keeping the pre-procedure HCT ≥30 – 36% and post-procedure HCT ≥30%. Volume treated: Erythrocytapheresis of up to 800 ml of red cells.

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Myasthenia gravis	TPE/IA	Acute, short-term treatment	1B	TPE: Albumin; IA: NA.	Frequency: Acute attack/relapse or unstable disease activity: 3 – 6 treatments over 10 – 14 days; weekly to bi-weekly individually adjusted for chronic treatment. Volume treated: 1 – 1.5 TPV with TPE; 2 – 2.5 liters for tryptophan-IA, manufacturer's recommendation; up to 2.5 TPV with regenerative immune adsorbers.
Hyperviscosity in hypergammaglobulinaemia	TPE	Symptomatic	1B	Albumin, plasma (if daily)	Frequency: Daily or every other day Volume treated: 1 – 1.5 TPV
		Prophylaxis for rituximab	1C		
Graft Versus Host Disease	ECP	Acute (aGVHD)	1C	N/A	Frequency: aGVHD, 2 – 3 treatments weekly, tapering to 2 treatments every 2 weeks. cGVHD: 2 treatments weekly for 4 weeks then 2 treatments every 2 weeks for at least 8 – 12 weeks for response assessment
		Chronic (cGVHD)	1B		

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Transplantation, renal, ABO compatible	TPE/IA	Antibody mediated rejection	1B	Albumin, plasma	Frequency: Daily or every other day Volume treated: 1-1.5 TPV
	TPE/IA	Desensitization, living donor	1B		
Transplantation, renal, ABO incompatible	TPE/IA	Desensitization, living donor	1B	Albumin, plasma	Frequency: Daily or every other day Volume treated: 1 - 1.5 TPV

Padmanabhan A. et al Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eight Special Issue Journal of Clinical Apheresis 2019;34:171–354.

Category II

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Thrombotic microangiopathy, complement mediated (atypical HUS)	TPE	Factor H autoantibody	2C	Plasma or Plasma/ Albumin	Frequency : daily Volume treated : 1 – 1.5 TPV
				* Duration or discontinuation: should be based upon patient condition and response.	
Sickle cell disease, non-acute	RBC exchange	Pregnancy Recurrent vaso-occlusive pain crisis	2B 2B	Red cell units, HbS negative, leucocyte reduced, antigen-matched (e.g., C/c, E/e, K)	Frequency: Duration and number of RBC exchanges depend upon clinical indications; one time for pre-op, variable times for chronic pain, and life-long for stroke prevention. Volume: as needed to maintain target HbS level

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Myasthenia gravis	TPE/IA	Long term treatment	2B	TPE: Albumin; IA: N/A.	Frequency: Acute attack/relapse or unstable disease activity: 3 – 6 treatments over 10 – 14 days; weekly to bi-weekly individually adjusted for chronic treatment. Volume treated : 1 – 1.5 TPV with TPE; 2 – 2.5 liters for tryptophan-IA, manufacturer's recommendation; up to 2.5 TPV with regenerative immune adsorbers.
Transplantation, haematopoietic stem cell, ABO incompatible (ABOi)	TPE	Major ABOi HPC(A) Major ABOi HPC(M)	2B 2B	TPE : Albumin, donor and recipient ABO-compatible plasma; Red cell exchange: Group O RBCs	Frequency: TPE: Daily; Red cell exchange: Once Volume treated: TPE: 1 – 1.5 TPV; Red cell exchange:1 – 1.5 red cell volume

Category III/IV

Disease	TA modality	Indication	Grade of recommendation	Technical notes	
				Replacement fluid	Course and frequency
Transplantation, haematopoietic stem cell, ABO incompatible (ABOi)	Red cell exchange	Minor ABOi HPC(A)	2C	TPE : Albumin, donor and recipient ABO-compatible plasma;	Frequency: TPE: Daily; red cell exchange: Once
	TPE	Major/Minor ABOi w/pure RBC aplasia	2C	Red cell exchange: Group O red cells	Volume treated: TPE: 1 – 1.5TPV; Red cell exchange:1 – 1.5 RBC volumes
Transplantation, haematopoietic stem cell, HLA desensitization	TPE		2C	Albumin	Frequency: Every other day Volume treated: 1 TPV
Transplantation, renal, ABO compatible	TPE/IA	Desensitization deceased donor	2C	Albumin, plasma	Frequency: Daily or every other day Volume treated: 1 – 1.5 TPV
Red cell alloimmunization, prevention and treatment	Red cell exchange	Exposure to RhD+ red cells	2C	Red cell exchange: RhD- red cell units; TPE: Albumin	Frequency: 1 – 3/week Volume treated: Red cell exchange: 1 – 2 red cell volume; TPE: 1 – 1.5 TPV
	TPE	Pregnancy, GA < 20 weeks	2C		

Category Definitions for Therapeutic Apheresis

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

IRB = Institutional Review Board

APPENDIX XXVII: REQUEST FORM FOR TRANSFUSION REACTION INVESTIGATION (BLOOD AND BLOOD COMPONENTS)

REQUEST FORM FOR TRANSFUSION REACTION INVESTIGATION (BLOOD AND BLOOD COMPONENTS)

1. When a patient has an adverse reaction to any blood or blood component, **STOP** transfusion immediately. **URGENTLY** inform the doctor in charge of the patient and the Blood Bank.

2. Report all reactions and do the following:

   2.1 Preserve the blood bag and giving set with all attached labels. Seal it securely and send immediately to the Blood Bank.

   2.2 Send the following samples for transfusion reaction investigation to the Blood Bank or relevant laboratory.

   a. Post-transfusion sample 1 (immediately)
      I. 10 mls of blood in EDTA bottle
      II. 10 mls of urine for haemoglobinuria

   b. Post-transfusion sample II (after 24 hours)
      I. 10 mls of blood in EDTA bottle
      II. 10 mls of urine for haemoglobinuria

   2.3 Please send for other appropriate investigations if necessary.

   2.4 Please refer to Section 10: Adverse effect of transfusion in Handbook on Clinical Use of Blood for details.

Hospital: ..... Ward/Clinic: .....

Patient's name: ..... IC/Passport No: .....

Race: ..... Age: ..... Sex: .....

Diagnosis.....

i. Date and time transfusion started .....

ii. Date and time of onset of reaction .....

iii. Blood/ Blood Component Serial No. .....

iv. Volume Blood/ Blood Component transfused .....

v. Blood Pressure: Before transfusion ..... After transfusion .....

vi. Temperature: Before transfusion ..... After transfusion .....

vii. Nature of Reaction: Tick off **(√)** the positive symptoms/signs.

Fever	☐	Shock	☐	Haematuria	☐
Chills /Rigors	☐	Jaundice	☐	Haemoglobinuria	☐
Urticaria	☐	Dyspnoea	☐		
Pain	☐	(Location of pain if present.....)			

viii. Solution used for starting IV drip: - N.Saline / 5% Dextrose / Others ……

ix. History of previous transfusion: Yes / No

Date of last transfusion: ……

x. History of previous transfusion reaction if any:

……

……

xi. Medication (If any, please specify):

……

……

xii. Applicable for female patients ONLY:

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

History of abortion: Yes / No No. of abortions: ……

xiii. History of transplant: ……

Date of transplant: ……

Date: …… Signature: ……

Name: ……

PLEASE SEND THIS FORM TO THE BLOOD BANK WITH ALL REQUIRED SAMPLES FOR INVESTIGATION

APPENDIX XXVIII: REPORTING FORM FOR TRANSFUSION-RELATED ADVERSE EVENT

BTS/HV/3/2016

REPORTING FORM FOR TRANSFUSION-RELATED ADVERSE EVENT
TRANSFUSION MEDICINE SERVICE
KEMENTERIAN KESIHATAN MALAYSIA

IMPORTANT INFORMATION

1. Every adverse event related to transfusion of blood or blood component shall be managed, investigated and documented accordingly.
2. The form must be completed and returned to the blood bank within 2 weeks of the incident.
3. The blood bank shall retain the completed form and send a copy to the State Transfusion Committee and the National Haemovigilance Coordinating Centre (NHCC), Pusat Darah Negara within a month.

Reported by:

Name:	Designation:
Email:	Tel. No:
Date:	Fax No:

SECTION A: PATIENT DETAILS

Name of Patient:		
NRIC/ Passport No:	Age:	Hospital:
Barcode:	Gender:	Ward:
		Department:

SECTION B: TYPE OF ADVERSE EVENTS

B1. TRANSFUSION REACTION ☐ **(Fill up section C-J)**
B2. ERROR IN TRANSFUSION PROCESS
a) INCORRECT BLOOD COMPONENT TRANSFUSED ☐ **(Fill up section C-K)**
b) NEAR MISS ☐ **(Proceed to SECTION K1 for 'NEAR MISS' on page 4)**
c) INCIDENT ☐ **(Proceed to SECTION K2 for 'INCIDENT' on page 4)**

Near Miss: Any error that has occurred but did not cause any adverse event as it was detected prior to blood transfusion.

SECTION C: ONSET OF ADVERSE EVENT

C1. IMMEDIATE (within 24 hours of transfusion) ☐
C2. DELAYED (after 24 hours of transfusion) ☐

SECTION D: BLOOD COMPONENTS IMPLICATED IN THE ADVERSE EVENT

D1.	Whole blood	☐	Irradiated:	YES / NO	Filtered:	YES / NO
D2.	Packed Cells	☐	Irradiated:	YES / NO	Filtered:	YES / NO
D3.	Apheresis Platelet	☐	Irradiated:	YES / NO	Pathogen Inactivated:	YES / NO
D4.	Random Platelet	☐	Irradiated:	YES / NO		
D5.	Fresh Frozen Plasma	☐				
D6.	Cryoprecipitate	☐			Pathogen Inactivated:	YES / NO
D7.	Cryosupernatant/ Liver plasma	☐				
D8.	Others (please specify)	_____				

SECTION E: DETAILS OF ADVERSE EVENTS

E1. Date of transfusion: (DD/MM/YY) _____/_____/_____
E2. Time transfusion started: _____am/pm
E3. Time reaction occurred: _____am/pm
E4. Volume transfused: _____ml / unit

SECTION F: RELEVANT CLINICAL HISTORY

F1. Patient's primary / provisional diagnosis: _____

F2. Indication for transfusion: _____

F3. History of pregnancy / miscarriage (if applicable): ☐ YES ☐ NO

F4. a) History of previous transfusion: ☐ YES <3 mths ☐ YES >3 mths ☐ NO ☐ UNKNOWN

b) If YES, component transfused: _____

c) Reaction towards transfusion: ☐ YES ☐ NO

d) If YES, please describe: _____

F5. Other relevant medical and/or surgical history: _____

F6. Emergency crossmatch (immediate spin) ☐ YES ☐ NO

F7. Transfusion with safe "O" or uncrossmatched group specific blood ☐ YES ☐ NO

SECTION G: SIGNS AND SYMPTOMS [Tick all that apply (✓)

G1. General: ☐ Chill ☐ Rigors ☐ Fever ☐ Nausea ☐ Haemorrhage
☐ Restlessness / Anxiety ☐ Vomiting ☐ Cyanosis
☐ Others (specify)_____

G2. Cardiovascular: ☐ Chest pain ☐ Palpitation ☐ Others (specify)_____

G3. Skin: ☐ Oedema ☐ Flushing ☐ Hives ☐ Itching ☐ Pallor
☐ Jaundice ☐ Urticaria ☐ Petechiae ☐ Rash

G4. Pain: ☐ Infusion site pain ☐ Abdominal pain ☐ Chest pain
☐ Flank pain ☐ Headache ☐ Back pain
☐ Other pain (specify)

G5. Renal: ☐ Oliguria ☐ Anuria ☐ Dark coloured urine

G6. Respiratory: ☐ Cough ☐ Hypoxia ☐ Dyspnoea
☐ Wheezing ☐ Others (specify) _____

G7. Patient's baseline observations prior to reaction: Temperature:___°C, BP:___ Pulse rate:___RR:___ SPO_2____

G8. Patient's baseline observations at time of reaction: Temperature:___°C, BP:___Pulse rate:___RR:___ SPO_2____

SECTION H: RELEVANT INVESTIGATIONS

H1. Chest X-ray findings (specify): _____

H2. Relevant **pre-transfusion** laboratory investigation results:
Full blood count: _____
Liver Function: _____
Coagulation Test: _____

H3. Relevant **post-transfusion** laboratory investigation results:
Full blood count including Reticulocyte count: _____
Liver Function: _____
Coagulation Test: _____
Red cells antibodies: _____
Haptoglobin: _____
Blood C&S Patient: POS/ NEG Organism: _____
Blood C&S Donor: POS/ NEG Organism: _____
Urine FEME: _____
☐ Haemoglobinuria ☐ Hematuria

H4. State other relevant investigations if any: _____

SECTION I : PATIENT OUTCOME FROM THE ADVERSE EVENT

I1. Recovered with no ill effects ☐
I2. Recovered with illness (morbidity) ☐
Time frame of recovery _____
Specify the morbidity _____

I3. Death ☐
I4. a) Unlikely related to transfusion ☐
b) Probable related to transfusion ☐
c) Possible related to transfusion ☐

SECTION J: TYPE OF ADVERSE EVENTS: [Tick where applicable]

Section	Events	✓	*
J1	**Incorrect Blood Component / Product Transfused (Proceed to SECTION K for 'IBCT' on page 4)**		*
	J1.1. Acute Immune Haemolytic Anaemia		*
	J1.1a. ABO incompatible		*
	J1.1b. Other red cell incompatibility (e.g. Rh positive given to Rh negative)		*
	J1.2 Blood is compatible but meant for another patient		*
	J1.3. Others :		
	J1.3a. Special requirement not met (e.g. irradiated, filtered, phenotyped)		*
	J1.3b. Inappropriate transfusion (e.g. wrong component)		*
J2	Delayed Haemolytic Transfusion Reaction		*
J3	Non-immune hemolytic reaction (due to mechanical factor, osmotic, heat, cold, etc)		*
J4	Febrile Non- Haemolytic Transfusion Reaction (FNHTR)		
J5	Allergic Reaction		
	a) Mild (Rash / Urticaria)		
	b) Moderate (Anaphylactoid)		*
	c) Severe (Anaphylactic Transfusion Reaction)		*
J6	Transfusion-Related Acute Lung Injury (TRALI)		*
J7	Transfusion-Associated Circulatory Overload (TACO)		*
J8	Transfusion-Associated Dyspnoea (TAD)		*
J9	Transfusion-Associated Graft-versus-Host Disease (TA-GvHD)		*
J10	Post-Transfusion Purpura (PTP)		*
J11	Post-Transfusion Infection : Virus (please specify) _____		*
J12	Post-Transfusion Infection : Bacteria (please specify) _____		*
J13	Post-Transfusion Infection : Parasite (please specify) _____		*
J14	Handling and storage error		*
J15	Equipment related (e.g. faulty waterbath, transfusion set, etc)		*
J16	Others , please specify :		*

*** Please send detailed report for all transfusion reaction except for FNHTR & mild allergy.**

SECTION K: ERRORS AND INCIDENTS IN TRANSFUSION PROCESS [Tick all that apply (✓)]

K1. IBCT AND NEAR MISSES IN TRANSFUSION PROCESS.

No	CLASSIFICATION OF ACTUAL ERRORS / NEAR MISS	
1.	**ERROR IN WARD**	
	a) Sampling error at time of blood taking	
	b) Labelling error at time of blood taking	
	c) Cause cannot be determined	
2.	**TESTING (BLOOD BANK)**	
	a) Technical error	
	b) Transcription error	
	c) Blood issued meant for another patient	
3.	**BLOOD ADMINISTRATION IN THE WARD**	
	a) Failure to check the blood against patient's full identity.	
	b) Others (please specify)	

K2. OTHER INCIDENTS RELATED TO TRANSFUSION PROCESS.
(Tick ✓ where applicable)

a)	Sharing same ID (IC, UNHCR, Passport)	
b)	Possible blood grouping error in other hospitals / clinics	
c)	Error in previous admission	
d)	Others (please specify)	

K3. ERROR/ INCIDENT DISCOVERED (Tick ✓ where applicable)

☐ Pre-Transfusion
☐ During Transfusion
☐ Post-Transfusion

Please describe in detail how error was discovered (additional pages to be filled if necessary):

_____

_____

_____

_____

_____

_____

Please send root cause analysis (RCA) report for all IBCTs and Near Misses.

APPENDIX XXIX: WORKSHEET FOR INVESTIGATION OF TRANSFUSION REACTION

BTS/TRW/2/2016

WORKSHEET FOR INVESTIGATION OF TRANSFUSION REACTION

Patient's name : _____ Reg. No. : _____
Ward : _____ No. of returned blood packs : _____
Date reaction was noted : _____ Date blood was returned : _____

I. RECHECK OF BLOO GROUPING	ANTI SERA				CELL			ANTI SERA	GROUP	Rh
Patient :-	A	B	AB	AC	A	B	O	D		
1. Pre-Transfusion Sample										
2. Post-Transfusion Sample I										
3. Post-Transfusion Sample II										
Donor :-										
1. Blood from Segment										

II. CHECK FOR SENSITIZATION AND ATYPICAL ANTIBODY	DIRECT COOMBS TEST ON CELLS	ANTIBODY SCREENING USING SCREENING CELLS								
		RT			37^0C/ LISS / ALBUMIN			AHG		
Patient :-		I	II	III	I	II	III	I	II	III
1. Pre-Transfusion Sample										
2. Post-Transfusion Sample I										
3. Post-Transfusion Sample II										
Donor										

III. RECHECK OF CROSSMATCHINGS:-	RT	37^0C/ LISS / ALBUMIN	AHG
1. Pre-Transfusion Sample with Donor Blood			
2. Post-Transfusion Sample I with Donor Blood			
3. Post -Transfusion Sample II with Donor Blood			

IV. URINE:-	HAEMOGLOBIN
1. Post-Transfusion Sample I	
2. Post-Transfusion Sample II	

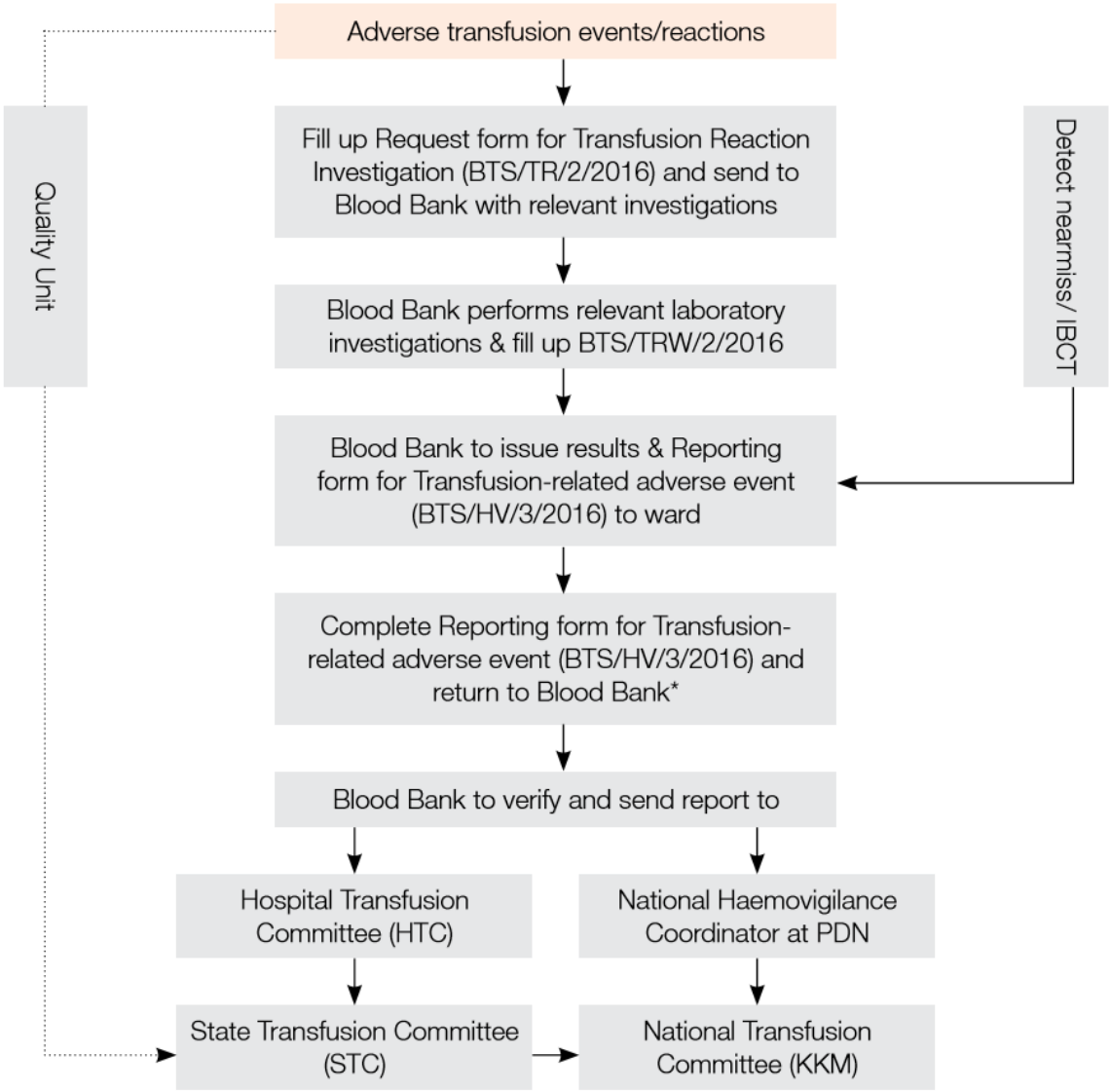
V. BLOOD CULTURE.	DATE SENT	BACTERIOLOGICAL REPORT
1. From Blood Bag		

CONCLUSION :

_____
_____
_____

Signature : _____
Name : _____
Date : _____

APPENDIX XXX: FLOWCHART FOR REPORTING OF ADVERSE TRANSFUSION EVENT



*BTS/HV/3/2016should be completed within 2 weeks after the event and sent back to Blood Bank for compilation.

Note:

1. Every case of adverse reaction must be reported.
2. If the case of adverse reaction involves a seropositive recipient, a lookback and recall procedure must be carried out.