REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Guidelines for

The Appropriate Clinical Use of Blood and Blood Products

2nd Edition

May 2026

NAMBTS
donate life

TABLE OF CONTENTS

FOREWORD

The World Health Organization (WHO) defines the appropriate use of blood and blood products as the transfusion of safe blood to treat conditions associated with significant morbidity or mortality, where alternative interventions are ineffective or unavailable. The rational and responsible use of blood is a fundamental pillar of the WHO's integrated approach to blood and transfusion safety and remains a priority for national health systems.

Inappropriate blood transfusions expose patients to avoidable risks, including adverse transfusion reactions and transfusion-transmissible infections, while simultaneously placing pressure on Namibia's limited and valuable blood supply. Patient Blood Management (PBM), a patient-centered and evidence-based approach, has gained international recognition for improving clinical outcomes, enhancing patient safety, and reducing unnecessary transfusions. Despite increased awareness, inappropriate transfusion practices continue to pose challenges within the Namibian healthcare system. Addressing these challenges is essential to improving patient safety, reducing unnecessary healthcare expenditure, and advancing the efficient use of resources in line with national health sector strategies.

The revised Guidelines for the Appropriate Clinical Use of Blood (GACUB) have been developed in alignment with the Ministry of Health and Social Services' strategic priorities, including the advancement of Universal Health Coverage, strengthening of health systems, and the delivery of quality, patient-centered care. These guidelines support Namibia's commitment to safe, effective, equitable, and sustainable transfusion practices, ensuring that blood and blood products are used appropriately, efficiently, and in a manner that maximizes patient outcomes while safeguarding this critical national resource.

These guidelines further reinforce the Ministry's commitment to evidence-based clinical practice, improved quality of care, and the responsible stewardship of health resources as outlined in national health policies and strategic plans.

Namibia is privileged to operate a 100% voluntary, non-remunerated blood donation system. I commend all blood donors for their continued altruism, which underpins a safe and reliable blood supply. These guidelines apply to both the public and private healthcare sectors. I call upon all healthcare professionals to adhere to the GACUB and to participate in transfusion-related training programmes to strengthen patient safety and health system resilience.

Hon. Dr. Esperance Luvindao, MP
Minister of Health and Social Services
May 2026

Authors

Dr. Carla Van Zyl *(Medical Officer, NAMBTS)*
Mr. Israel Chipare *(Chief Executive Officer, NAMBTS)*
Dr. Kudakwashe Simba *(Specialist Physician and Clinical Haematologist, MoHSS)*
Dr. Darion Resandt *(Medical Officer, Transfusion Medicine, MoHSS)*

Acknowledgment

The authors extend their sincere gratitude to the following reviewers for their invaluable contributions to the development of this document:

Dr. Steffen Bau (Paediatrician)
Dr. Jesse Musokota Mumba (Anaesthetist)
Dr. Abdul Rashid Nashidengo (Hepatopancreaticobiliary Surgeon)
Dr. Dalitso Segula (Cardiologist)
Dr. Kaveto Andreas Sikuvi (Emergency Medicine Specialist)

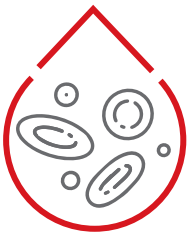
This document is formally endorsed by the Anaesthesiologists Society of Namibia (ASN).

CHAPTER 01
HAEMATOLOGICAL REVIEW

Section 1.1 - Blood

Understanding the composition of blood and the functions of its various components is essential for effectively addressing the transfusion needs of patients.

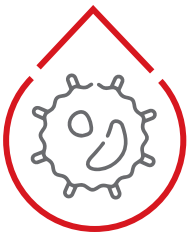
The total blood volume of an average healthy adult is approximately 5 litres. In paediatric patients, blood volume is weight-dependent and typically ranges from 65 to 90 mL/kg. The blood volume per kilogram is inversely proportional to age, with neonates and infants exhibiting higher volumes relative to body weight compared to older children. The cellular elements (red cells, white cells and platelets) accounts for 40% of the total blood volume and are suspended in plasma, which accounts for the remaining 60%.



RED CELLS (ERYTHROCYTES)

Erythrocytes are the most abundant cellular element in blood. These biconcave discs mainly contain haemoglobin, which facilitates oxygen and carbon dioxide transport between the lungs and tissues. Red cells are anucleate, exhibit constrained metabolic activity and the life span depends on the supply of glucose. The normal in vivo survival is 100 - 120 days. In vitro survival (i.e. survival of red cells in units for transfusion) is influenced by storage conditions and the type of anticoagulant-preservative solution used.

Hypoxia, low tissue oxygen levels, causes the release of erythropoietin (EPO), a glycoprotein produced in the kidneys. EPO stimulates the bone marrow, stimulating the production of erythrocytes and sometimes causing the release of reticulocytes (immature red cells) into the circulation, thereby increasing the capacity to deliver oxygen to the tissues. In a healthy person, erythropoiesis increases in response to blood loss.



WHITE CELLS (LEUCOCYTES)

Leucocytes are classified into two major types: lymphocytes and granulocytes, the latter group including eosinophils, basophils, neutrophils, and monocytes/macrophages. Lymphocytes are immunocytes along with various phagocytes, are pivotal in recognizing antigens and eliciting tailored immune responses against pathogens. This specialized function underscores their crucial role in the adaptive immunity system.

Granulocytes, comprising neutrophils, eosinophils, and basophils, are leucocytes characterized by cytoplasmic granules containing enzymes and inflammatory mediators, such as histamine, which are released during infections and

allergic reactions. Neutrophils, alongside monocytes and macrophages, act as phagocytes that engulf and digest pathogens like bacteria through the process of phagocytosis.

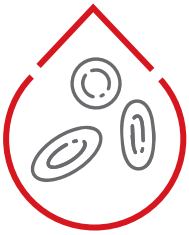
Lymphocytes survive for years in vivo and can continue to proliferate after a transfusion in the recipient. Donor T-lymphocytes may therefore, under certain preconditions, initiate an immune response against recipient lymphoid tissue causing transfusion-associated graft-versus-host disease (TA-GvHD). Irradiation of blood products prevents TA-GvHD, as it destroys the genetic material of leucocytes, ensuring that no viable lymphocytes are transfused to the recipient.

Leucodepletion of blood products is helpful in preventing some of the leucocyte-mediated adverse effects of transfusion, i.e., febrile non-haemolytic transfusion reactions.

PLATELETS (THROMBOCYTES)

Platelets are anucleate, discoid cytoplasmic fragments derived from megakaryocytes, which serve as their precursor cells within the bone marrow. Platelets are essential for primary haemostasis, as they form a plug at the site of vascular endothelial injury to prevent bleeding.

In vivo, platelets normally have a lifespan of 5 - 10 days. Due to storage of in vitro platelets at room temperature, which poses a risk of bacterial proliferation, platelet concentrate must be transfused within 7 days of donation in the presence of sterility testing.



PLASMA

Plasma is the fluid matrix of blood in which cellular elements are suspended. More than 90% of plasma is water. Proteins are the other constituent of plasma, mainly albumin that makes up about 60% of the total plasma proteins. The remaining constituents are electrolytes (sodium, potassium, chloride, hydrogen, magnesium and calcium), nutrients, waste products and dissolved gases (oxygen and carbon dioxide).

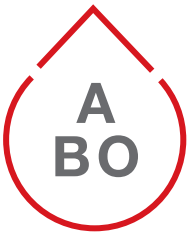
Three main functional classes of plasma proteins:

- **Coagulation Proteins:** They play an integral part to coagulation and haemostasis, especially fibrinogen and other procoagulants like thrombin and factor X.
- **Transport Proteins:** Albumin maintains osmotic pressure in the intravascular space and is the carrier protein for unconjugated bilirubin and various other substances. Others are transferrin (transports iron), haptoglobin (binds free haemoglobin) and lipoproteins (transports fat).
- **Immunological Proteins (immunoglobulins):** Antibodies or gamma globulins form part of the defence mechanism against infections and foreign antigens.

Section 1.2 - Blood Group Systems

There are currently 45 blood group systems recognized by the International Society of Blood Transfusion (ISBT) Working Party for Red Cell Immunogenetics and Blood Group Terminology containing 362 red cell antigens.

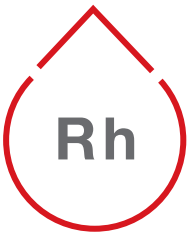
ABO, Rh, Kell, Kidd, Duffy, MNS, P, Lewis and Lutheran are the major blood group systems. Antibodies associated to antigens of some of these blood group systems like ABO, Rh, Kell, Duffy, Kidd are clinically significant as they can cause acute haemolytic transfusion reactions, delayed haemolytic transfusion reactions or haemolytic disease of the foetus and newborn. ABO and Rh systems are the most clinically significant and therefore the most important blood group systems for transfusion.



ABO BLOOD GROUP SYSTEM

The two main antigens in the ABO blood group system are A and B. The presence of one, both or neither of these antigens on the red cell membrane determines an individual's ABO blood group (A, B, AB and O).

A and B antigens are well developed at birth but their corresponding antibodies are formed from the age of 4 - 6 months. An individual always develops antibodies in his/her plasma that will react with any of the ABO antigens that are not present on his/her red cells, i.e., group A individuals thus have anti-B antibodies; group B individuals anti-A antibodies; group AB individuals have no ABO antibodies; and group O individuals have anti-A,B antibodies.



RH BLOOD GROUP SYSTEM

This system is defined by the presence of Rh antigens on the red cell membranes. The Rh system has five major Rh antigens; D, C, E, c and e. Antibodies of the Rh blood group antigens forms only after exposure to red blood cells carrying the corresponding antigens lacking in the individual and usually because of red cell transfusion or fetomaternal haemorrhage during pregnancy or delivery.

Individuals are classified as Rh positive (RhD+) if the D antigen is present on their red cells, and as Rh negative (RhD-) if the D antigen is not present. The prevalence of Rh-negative blood groups is significantly lower in Africans compared to Caucasians.

Table 1.1: Characteristics of ABO and Rh blood group systems

SYSTEM	BLOOD GROUP	ANTIGENS	ANTIBODIES	DONATE RCC TO	RECEIVE RCC FROM	DONATE PLASMA TO	RECEIVE PLASMA FROM	COMMENTS
ABO	A	A	Anti-B	A, AB	A, O	A, O	A, AB	
	B	B	Anti-A	B, AB	B, O	B, O	B, AB	
	AB	A,B	-	AB	A, B, AB, O	A, B, AB, O	AB	Universal recipient in RCC transfusion & Universal donor in plasma transfusion
	O	-	Anti-A,B	A, B, AB, O	O	O	A, B, AB, O	Universal donor in RCC transfusion & universal recipient in plasma transfusion
Rh	RhD+	D	-	RhD+	RhD+	Rh group is not considered in plasma transfusion		
	RhD-	-	-	RhD+ RhD-	RhD-			Anti-D produced after exposure to D antigen

In cases of anaemia and/or bleeding where a transfusion of blood and blood components are indicated ONLY blood group compatible units should be transfused as indicated in table 1.1.

Section 1.3 - Anaemia

Anaemia is defined as haemoglobin (Hb) concentration that is below the expected lower limit of the normal range according to the age group and gender shown in table 1.2. Anaemia results in a decreased capacity to carry oxygen to the tissues. The normal ranges for Hb according to age groups and gender are shown in table 1.2.

Anaemia is a major disease burden globally, mainly affecting young children, women of childbearing age, pregnant and postpartum women. The WHO estimated that about 40% of children aged 6–59 months, 37% of pregnant women and 30% of women of reproductive age are affected by anaemia globally. According to the WHO Global Health Observatory, Namibia reported a 46% and 25.2% prevalence of anaemia amongst children aged 6 – 59 months and women of reproductive age in 2019.

Anaemia has detrimental health consequences, especially in young children and pregnant women. In children anaemia can lead to impaired cognitive and motor developments, affecting overall academic performance. Anaemia during pregnancy is linked to adverse maternal and neonatal outcomes, including premature birth, low birth weight, and increased maternal mortality.

Hb ranges in table 1.2 can be used to investigate for the underlying causes of anaemia as indicated in table 1.3 and initiation of treatment in accordance to the specific underlying cause.

Table 1.2: WHO haemoglobin cut-offs to define anaemia severity in individuals;

Haemoglobin Concentration (g/dL)				
Population	No anaemia	Mild anaemia	Moderate anaemia	Severe anaemia
Children				
6–23 months	≥ 10.5	9.5 – 10.4	7.0 – 9.4	< 7.0
24–59 months	≥ 11.0	10.0 – 10.9	7.0 – 9.9	< 7.0
5–11 years	≥ 11.5	11.0 – 11.4	8.0 – 10.9	< 8.0
12–14 years	≥ 12.0	11.0 – 11.9	8.0 – 10.9	< 8.0
Adults				
Females	≥ 12.0	11.0 – 11.9	8.0 – 10.9	< 8.0
Males	≥ 13.0	11.0 – 12.9	8.0 – 10.9	< 8.0
Pregnancy				
1st Trimester	≥ 11.0	10.0 – 10.9	7.0 – 9.9	< 7.0
2nd Trimester	≥ 10.5	9.5 – 10.4	7.0 – 9.4	< 7.0
3rd Trimester	≥ 11.0	10.0 – 10.9	7.0 – 9.9	< 7.0

Significant haematological differences are seen in children less than 6 months of age, therefore age-specific haemoglobin values must be used.

Table 1.3: Causes of Anaemia;

INCREASED RED CELL LOSS (HIGH RETICULOCYTES)	
Blood Loss	
Acute blood loss	- Trauma, surgery, obstetric haemorrhage, gastro-intestinal haemorrhage etc.
Chronic blood loss	- Gastrointestinal, urinary or reproductive tract bleeding due to parasitic infestation, malignancy, inflammatory disorders etc.
Haemolysis (increased red cell destruction)	
Intracorpuscular Factors	- Red cell membrane defects (congenital spherocytosis) - Red cell enzyme defects (G6PD deficiency, pyruvate kinase deficiency) - Haemoglobinopathies (thalassaemia's, Hb S) - Acquired intracorpuscular defects (PNH)
Extracorpuscular Factors	- Red cell antibodies (ABO, Rh and other red cell incompatibilities; auto-antibodies including autoimmune haemolytic anaemia) - Chemicals (drugs, snake poison, arsenic, lead) - Mechanical (Burns, artificial heart valves, DIC) - Hypersplenism - Infections (malaria, Clostridium)
DECREASED PRODUCTION OF NORMAL RED BLOOD CELLS (HYPOPROLIFERATIVE ANAEMIA)	
Normochromic, normocytic anaemia (Bone marrow suppression of erythropoiesis)	
Reduced Erythropoietin	- Chronic renal failure - Hypothyroidism - Chronic inflammatory or malignant disease (IL 1 & IL 6 secretion)
Bone marrow failure	- Metastatic carcinomas (prostate, breast, lung, kidneys) - Haemopoietic tissue malignancies (lymphomas, multiple myeloma, leukaemia's) - Exposure to drugs, toxic chemicals or radiation - Others; aplastic anaemia, myelofibrosis, myelodysplastic syndrome)
Hypochromic, microcytic anaemia (decreased haemoglobin synthesis)	
Reduced Haem Synthesis	- Iron deficiency - Anaemia of chronic disease - Porphyrin synthesis abnormalities e.g. sideroblastic anaemias - α-thalassemia - β-thalassemia
Globin Synthesis Abnormalities	- α-thalassemia - β-thalassemia

Macrocytic anaemia	
Megaloblastic anaemia (low vitamin B12 and/or folate)	**Vitamin B12 deficiency** - Insufficient intake (vegetarians, vegans) - Malabsorption: • Intrinsic Factor absence (pernicious anaemia, gastrectomy, gastric epithelium damage by corrosive chemicals/malignant infiltration) • Increased utilization due to bacterial overgrowth (blind-loop syndrome) • Pathology of ileum (tuberculosis, lymphoma, coeliac disease)
	Folate deficiency - Insufficient intake (alcoholism, poor diet in the elderly) - Malabsorption (Crohn's disease, intestinal lymphoma) - Increase requirements (pregnancy, haemolytic anaemias) - Folate antagonists (trimethoprim, methotrexate, zidovudine)
Non-megaloblastic anaemia (normal vitamin B12 and folate)	- Myelodysplastic neoplasms (acquired bone marrow disorder) - Aplastic anaemia - Myelopathic process (destroying hematopoietic tissue because of direct marrow injury)

MAKING THE DECISION TO TRANSFUSE IN ANAEMIA

The decision to prescribe transfusion must be considered when anaemia is likely to cause or has already caused a reduction in oxygen supply that is inadequate to meet the patient's needs. If the body's compensatory mechanisms can sustain sufficient oxygen delivery while alternative treatments are administered, red cell transfusion should be avoided.

CRITICAL FACTORS
determining the supply of oxygen to the tissues are;

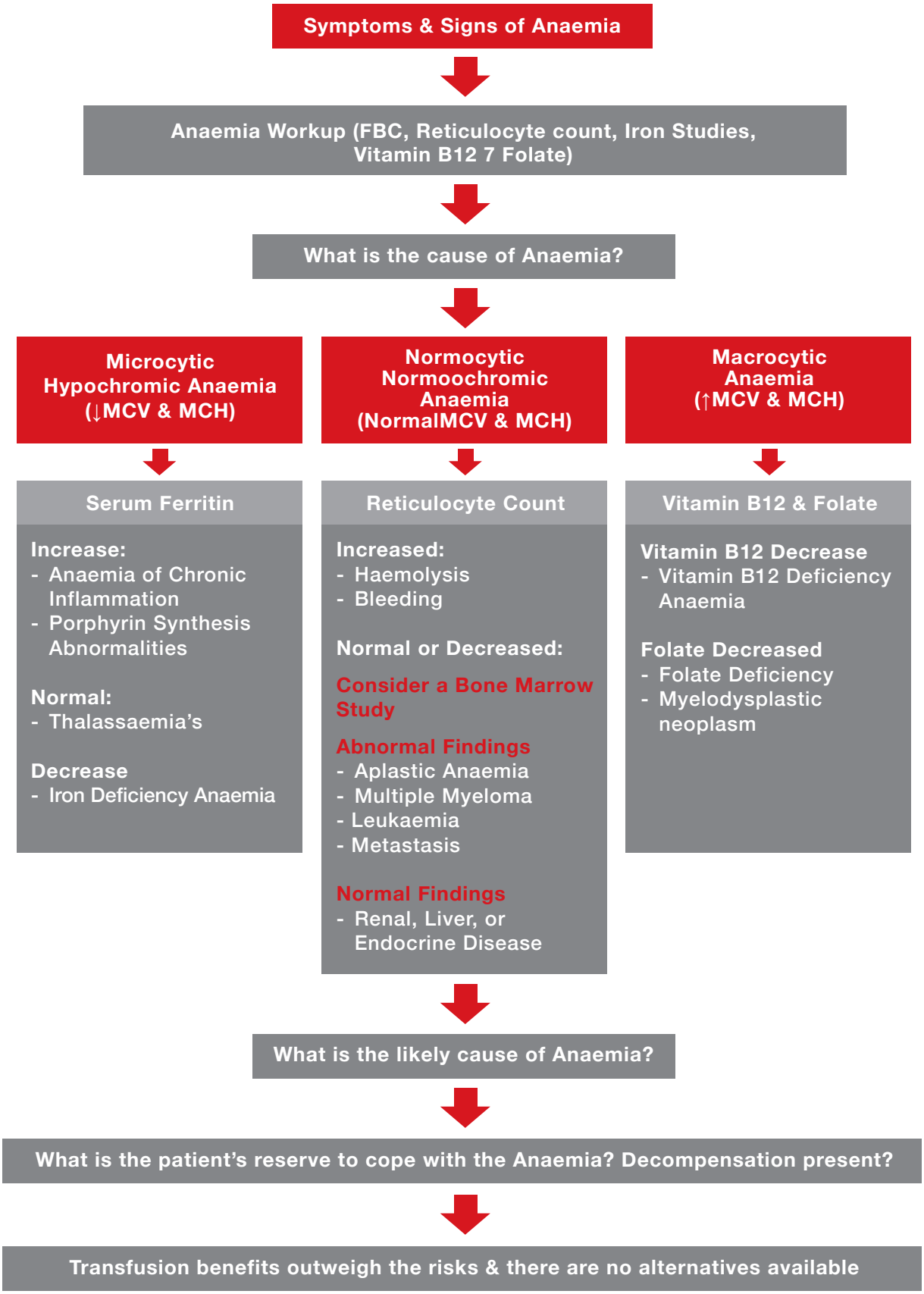
- **Hb concentration**
- **Degree of saturation of Hb with oxygen**
- **Cardiac output**

A reduced Hb level must be interpreted in context of the patient's physiological reserve to sufficiently compensate via the other variables to uphold the oxygen supply.

If signs of decompensation, i.e., mental status changes, diminished peripheral pulses, poor peripheral perfusion, cardiac failure and/or renal failure with oligo- or anuria, are present a blood transfusion is likely indicated. Restrictive transfusion strategies should still be followed to relieve the tissue hypoxia (See Chapter 3: Patient Blood Management – Restrictive Transfusion Strategies).

The approach in figure 1.1 minimizes unnecessary interventions by addressing the underlying cause of anaemia to limit the transfusions need and reduce potential complications associated with recurrent transfusions.

Figure 1.1: The following diagram should be followed in all anaemia cases, before making the decision to transfuse:



Section 1.4 - Bleeding

In a healthy individual blood loss, is limited by precisely regulated interactions between the components of the normal haemostatic system, namely vascular system, platelets and plasma coagulation proteins.

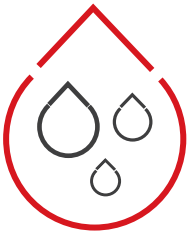
Abnormal bleeding can be due to several underlying causes, particularly platelet disorders, coagulation disorders and blood vessel wall defects as indicated in table 1.4.

Table 1.4: Causes of Abnormal Bleeding

THROMBOCYTOPENIA Decreased platelet count	**Impaired production** - Congenital disorders (i.e. TAR syndrome) - Bone marrow failure (i.e. primary haematological malignancies)
	Causes of accelerated destruction - Immunologic (i.e. ITP, HIT) - Non-immunologic (i.e. Sepsis)
	Increased consumption - Consumptive coagulopathies (i.e. TTP, DIC)
	Splenic sequestration
THROMBOCYTOSIS Increased platelet count	**Myeloproliferation** - Clonal disorders (i.e. Polycythaemia Vera) - Others (i.e. CML, myelodysplasia)
	Reactive (secondary) thrombocytosis: - Iron deficiency, haemolytic anaemias, haemorrhage syndrome)
DISORDERS OF PLATELET FUNCTION	**Disorders of adhesion** - Inherited (i.e. vWD) - Acquired (i.e. Uraemia)
	Disorders of aggregation - Inherited (i.e. Afibrinogenemia) - Acquired (i.e. Clopidogrel)
	Disorders of granule release - Inherited (i.e. gray-platelet syndrome) - Acquired (i.e. Myeloproliferative disorders, Aspirin and NSAID's)

COAGULATION DISORDERS	**Inherited Coagulation Disorders:** - Haemophilia A (factor VIII deficiency) - Haemophilia B (factor IX deficiency)
	Acquired Coagulation Disorders - Vitamin K deficiency (i.e. Liver disease) - Acquired Haemophilia A and B - Anticoagulation - DIC
VASCULAR DISORDERS	**Inherited** - Connective tissue disorders (i.e. Ehlers-Danlos syndrome) **Acquired** - Vitamin C deficiency & Immunoglobulin A–associated vasculitis - Chronic inflammatory or malignant disease (IL 1 & IL 6 secretion)

***TAR Syndrome:* is a rare genetic disorder marked by low platelet counts and absence of the radius bone in both forearms, with thumbs typically present. It is inherited in an autosomal recessive pattern and caused by mutations in the RBM8A gene.**



ASSESSMENT OF A BLEEDING PATIENT

A patient with abnormal bleeding requires a detailed personal and family history, medication review as well as a thorough physical examination, which give clues to the nature of the bleeding disorder.

- The International Society on Thrombosis and Haemostasis has developed a bleeding assessment tool BAT) to screen for bleeding disorders - *https://bleedingscore.certe.nl*
  - This standardized questionnaire consists of 14 bleeding symptom categories to aid with the assessment bleeding risk for bleeding disorders.
  - The following scores are considered to be abnormal, suggesting a bleeding disorder:
    - Children (<18 years): ≥ 3
    - Adults: ≥ 4 (males) & ≥ 6 (females)
- A medication history should always be obtained, including prescribed medications, recreational drugs, and herbal products:
  - The medication history should be in accordance to table 1.5 which list the compounds that decrease the number of platelets and/or platelet function.

Table 1.5: Compounds that Decrease Platelet Number and/or Function

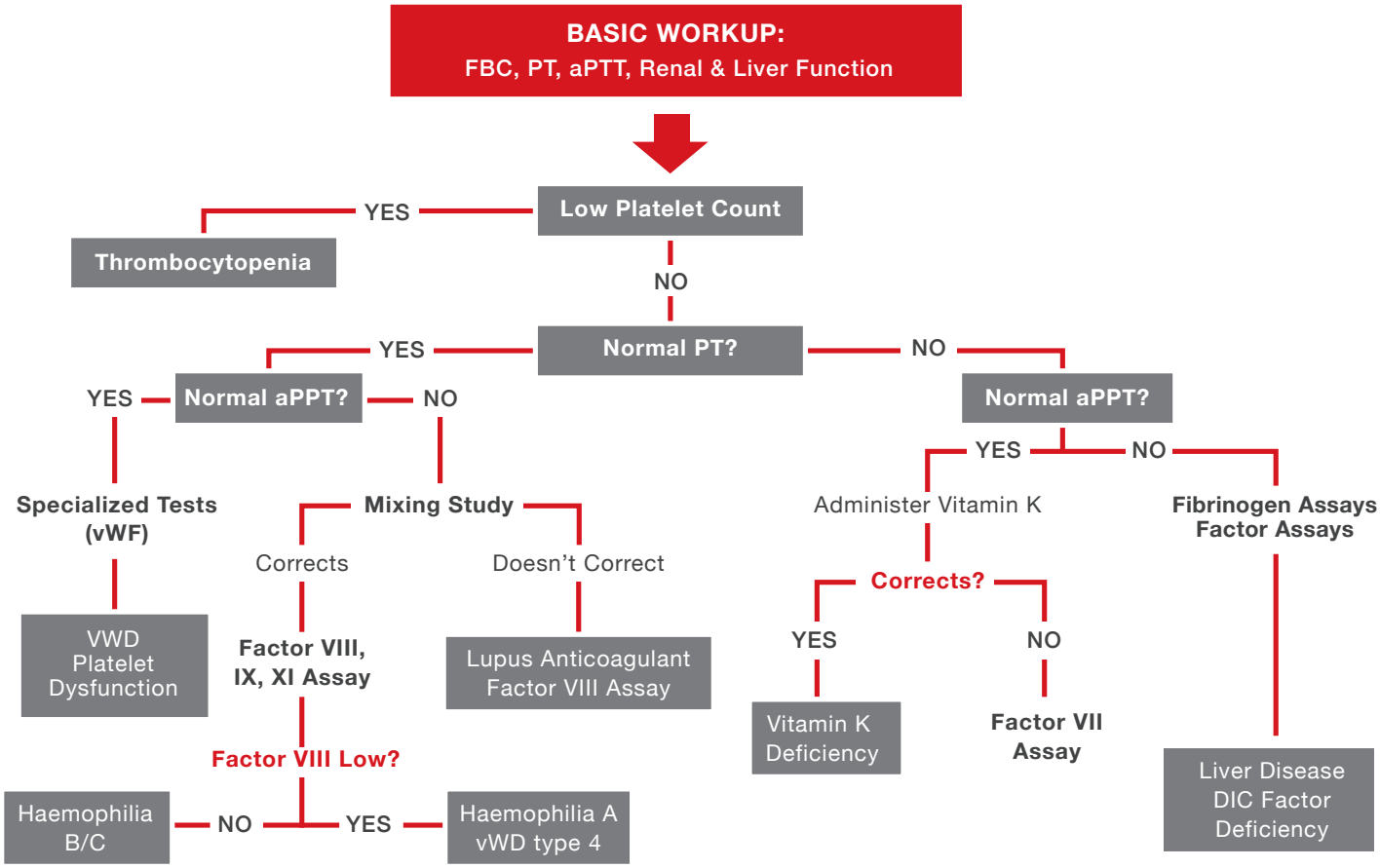
Effect	*Compound*	*Examples*
Platelet dysfunction	**COX-1 inhibitors**	Aspirin, Ibuprofen, Naproxen
	Thienopyridines	Clopidogrel
	Antibiotics	Cephalosporins, Penicillin (High dosages)
	SSRIs	Fluoxetine, Olanzapine, Citalopram, Sertraline
	Herbs & foods	Ginkgo, Garlic, Ginger, Ginseng, Black tree fungus
Decreased Platelets	**Antiepileptics**	Phenytoin, valproate, carbamazepine
	Glycoprotein inhibitors	Abciximab
	Anticoagulants	Heparin
	Herbs & foods	Quinine, white lupin, tahini, herbal tea

- Physical examination findings can suggest that the underlying condition is either a platelet (Primary Haemostasis) or coagulation disorder (Secondary Haemostasis);

Clinical Characteristic	*Platelet Defect*	*Clotting Factor Deficiency*
Site of bleeding	Skin, mucous membranes	Soft tissues, muscles, joints
Petechiae	Present	Absent
Ecchymosis	Small, superficial	Large, deep, palpable
Hemarthrosis	Rare	Common
Bleed post minor cuts	Yes	Rare
Bleed post trauma/ surgery	Immediate	Delayed

If the history and physical examination findings suggest abnormal bleeding, laboratory investigations should be done to confirm the cause of bleeding according to figure 1.2.

Figure 1.2: Laboratory investigations in patients with abnormal bleeding:



MAKING THE DECISION TO TRANSFUSE A PATIENT WITH A LOW PLATELET COUNT

A transfusion should only be considered in a patient who has a high likelihood of bleeding as indicated in table 1.6 or is actively bleeding

Table 1.6: Risk of bleeding associated with thrombocytopenia

Platelet Count	*Risk of Bleeding*
< 5 x 10^9/l	Life threatening bleeding strong possibility
5 - 20 x 10^9/l	Increased likelihood of spontaneous bleeding, particularly intracranial haemorrhage
20 - 50 x 10^9/l	Increased likelihood of bleeding with trauma, surgical procedures and specific lesions (e.g. gastric ulcer)
> 50 x 10^9/l	Bleeding rarely occurs, even in major surgery (eye/brain surgery: platelet level of > 100 x 10^9/l recommended)

PLEASE NOTE

In functional platelet disorders associated with bleeding, platelet transfusion is indicated despite normal platelet counts.

ESSENTIALS

- Results of laboratory tests are not the sole deciding factor for a transfusion.
- There is no universal “transfusion trigger”, thus all patients do not require a transfusion
- It is a good practice to consider alternatives to a transfusion and the clinical context of the patient before a blood transfusion.
- Anaemic and/or bleeding patients require thorough evaluation to identify and treat the underlying cause, minimizing transfusion needs and associated risks.
- If urgent transfusion is needed, obtain a pre-transfusion blood sample when possible to enable accurate diagnostic workup.
- Lower haemoglobin and platelet transfusion thresholds may be considered in haemodynamically stable, non-bleeding patients, depending on the clinical context and only after consultation with a clinical haematologist.

REFERENCES

- Anaemia in women and children. In: Global Health Observatory [online database]. Geneva: World Health Organization; 2019 (https://www.who.int/data/gho/data/indicators, accessed 19 July 2024).
- Girelli, G., Antoncecchi, S., Casadei, A. M., Del Vecchio, A., Isernia, P., Motta, M., Regoli, D., Romagnoli, C., Tripodi, G., & Velati, C. (2015). Recommendations for transfusion therapy in neonatology. Blood transfusion = Trasfusione del sangue, 13(3), 484–497. https://doi.org/10.2450/2015.0113-15
- Grantham-McGregor, S., Ani, C., A Review of Studies on the Effect of Iron Deficiency on Cognitive Development in Children, The Journal of Nutrition, Volume 131, Issue 2, 2001, Pages 649S-668S, ISSN 0022-3166, https://doi.org/10.1093/jn/131.2.649S.
- Guideline on haemoglobin cutoffs to define anaemia in individuals and populations. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO. ISBN 978-92-4-008854-2
- Rahman, M. M., Abe, S. K., Rahman, M. S., Kanda, M., Narita, S., Bilano, V., Ota, E., Gilmour, S., & Shibuya, K. (2016). Maternal anemia and risk of adverse birth and health outcomes in low-and middle-income countries: Systematic review and meta-analysis. American Journal of Clinical Nutrition, 103(2), 495–504. https://doi.org/10.3945/ajcn.115.107896
- Hoffbrand, A. V., Moss, P. A. H., & Pettit, J. E., 2020, Hoffbrand’s Essential Haematology, 8th ed., Wiley-Blackwell, p. 54

CHAPTER 02
LEGAL & ETHICAL ASPECTS OF BLOOD TRANSFUSION

Blood transfusion is an essential medical procedure in Namibia, serving as a vital intervention across multiple clinical disciplines within the healthcare sector. This practice, while essential, is governed by specific legal and ethical guidelines that ensure patient safety and respect for autonomy. It is imperative to consider these regulations to maintain the integrity and efficacy of transfusion services in Namibia. The legal and ethical issues related to blood transfusions are just the same as those relating to other forms of medical interventions.

All patients have the right to accept or refuse a blood transfusion as part of their medical management as stipulated in The Patient Charter of Namibia: Your Health, Our Concern. The Patient Charter is a Statement of Commitment by the MoHSS based on principles which supports high quality and people-centred health care.

Core Principles of the Patient Charter of Namibia

- **Confidentiality**
- **Empathy and Caring**
- **Honesty, Integrity and Dignity**
- **Impartiality**
- **Professionalism and Respect**
- **Transparency and accountability**
- **Innovation and creativity**
- **Customer focus**

Section 2.1 - Patient Rights

The Patient Charter of Namibia states that all patients receiving medical care under the MoHSS must;

- Be treated with dignity, respect and compassion. Diversity of culture, beliefs and values in line with clinical decision making are respected.
- Communicate openly and honestly, and provide clear, comprehensive and understandable health information and advice.
- Involve patients and their families in healthcare decision-making. Considering their preferences and values.

Section 2.2 - Responsibilities of the Blood Service and Doctors

This Code of Ethics established by the International Society of Blood Transfusion (ISBT) outlines the responsibilities of professionals involved in blood transfusion. These responsibilities are aligned to ethical principles, namely autonomy, non-maleficence, beneficence, justice and dignity.

The Blood Service, as well as clinicians have ethical responsibilities towards both donors and recipients. Their rights are of equal importance; therefore, donor safety must not be compromised in order to meet patient needs.

ETHICAL RESPONSIBILITIES OF THE BLOOD SERVICE:

The primary responsibility of a blood service is to provide a safe and sufficient supply of blood products. However, the blood service has various other ethical responsibilities towards both the blood donor & recipient;

Autonomy

- Obtain informed consent from a voluntary non-remunerated donor that the donation will be used for the purpose of transfusion.
- Ensure that all relevant documentation of donors and recipients are retained in a confidential manner.

Dignity and non-maleficence

- Apply specific evidence-based donor selection criteria to accept or defer donors appropriately to protect both the health of recipients and donors.
- Ensure structures are in place to adequately counsel and notify donors and recipients if any matters have been identified that can have undesirable health consequences.

Justice

- Ensure appropriate clinical usage of blood products to minimize wastage to improve accessibility to blood and blood products for all those in need.

ETHICAL RESPONSIBILITIES OF DOCTORS RELATED TO BLOOD TRANSFUSION

All doctors who order and/or transfuse blood & blood products have an ethical responsibility, especially towards the recipient;

Autonomy

- Provide information to potential recipients on blood transfusion, including the associated risks and available alternatives to enable shared decision-making.
- Obtain informed consent prior to a blood transfusion in a manner that is comprehensible to the recipient.

Beneficence and non-maleficence

- Ensure appropriate clinical usage of blood and blood products, namely only transfusing when clinically indicated based on best evidence-based transfusion guidelines.
- Ensure that blood is transfused to a recipient in accordance to the Standard Hospital Procedure on Blood Transfusion, including the administration, monitoring, recording of a blood transfusion and management of any transfusion adverse event

Justice

- Ensure that all recipients are treated equitably and receive the most appropriate available blood and blood products.

Section 2.3 - Informed Consent

If feasible the clinician ordering blood and blood components is responsible for obtaining informed consent prior to each transfusion from the patient in writing.

THE DOCTOR SHOULD PROVIDE INFORMATION TO THE PATIENT ON THE FOLLOWING

- Clinical reasons for transfusion and benefit thereof.
- Risks of declining transfusion.
- Risks associated with the transfusion, namely adverse transfusion events.
- Procedures employed by the blood service to ensure the safety of blood products.
- Relevant alternatives to transfusion.

The standard MoHSS “Consent to a Transfusion of Blood and/or Blood Products” form, or an equivalent, must be signed by both the doctor and the patient, or by the parent, legal guardian, or authorised representative in the case of minors or mentally incapacitated patients, as well as by a witness or translator where applicable.

In an emergency (where it is not feasible to get consent), information on blood transfusion should be provided retrospectively; the reason for transfusion and a note of consent discussion must be documented in patient’s hospital notes.

INFORMED CONSENT TO A BLOOD TRANSFUSION IN CHILDREN

The Guide to Namibia's Child Care and Protection Act 3 of 2015, Chapter 15 stipulates that a child may give consent to a medical intervention, which includes a blood transfusion, in respect of himself or herself if;

- The child is 14 years of age or older
  AND
- medical practitioner concerned is satisfied that the child has sufficient maturity and the mental capacity to understand the benefits, risks and implications of the medical intervention.

Section 2.4 - Managing a patient who declines a blood transfusion

Patients may refuse a blood transfusion for religious, personal and/or cultural reasons, such as prohibitions amongst religious groups like Jehovah's Witnesses, fear of infections, transfusion errors, previous negative experiences with transfusions or other perceived risks. Misunderstandings about the risks and benefits associated with blood transfusions also contribute to refusal.

Therefore, it is crucial for healthcare providers to educate both patients and staff about the implications and alternatives to transfusion to facilitate informed decision-making. Comprehensive education can mitigate fears and clarify the actual risks and benefits, guiding patients in making decisions that best fit their medical and personal needs. The obligation of healthcare providers extends to transparently communicating not only the benefits and risks but also the potential consequences of refusing blood and blood components. This level of transparency ensures that patient decisions are well-informed. Ultimately, informed consent is pivotal in aligning medical interventions with patient values and health requirements.

Patients facing potential life-threatening conditions may decline blood transfusions, which, despite the use of alternative treatments and the best efforts of medical teams, can lead to imminent risks such as death from haemorrhage. It is crucial that patients and their families are thoroughly informed about the critical nature of blood transfusions as potentially life-saving interventions. **Patients retain the right to reconsider their decisions regarding blood product use and should be afforded privacy to discuss these choices with healthcare providers.** The medical team must balance respect for the patient's autonomy and beliefs with the duty to **avoid undue influence from others** (i.e., Relatives/ friends).

If a patient persists in refusing blood products, their decision must be respected, as a competent adult has the legal right to refuse treatment, even if it leads to death. Additionally, it is important to provide symptom control and emotional support to both the patient and their relatives during such challenging times, ensuring that their well-being is maintained.

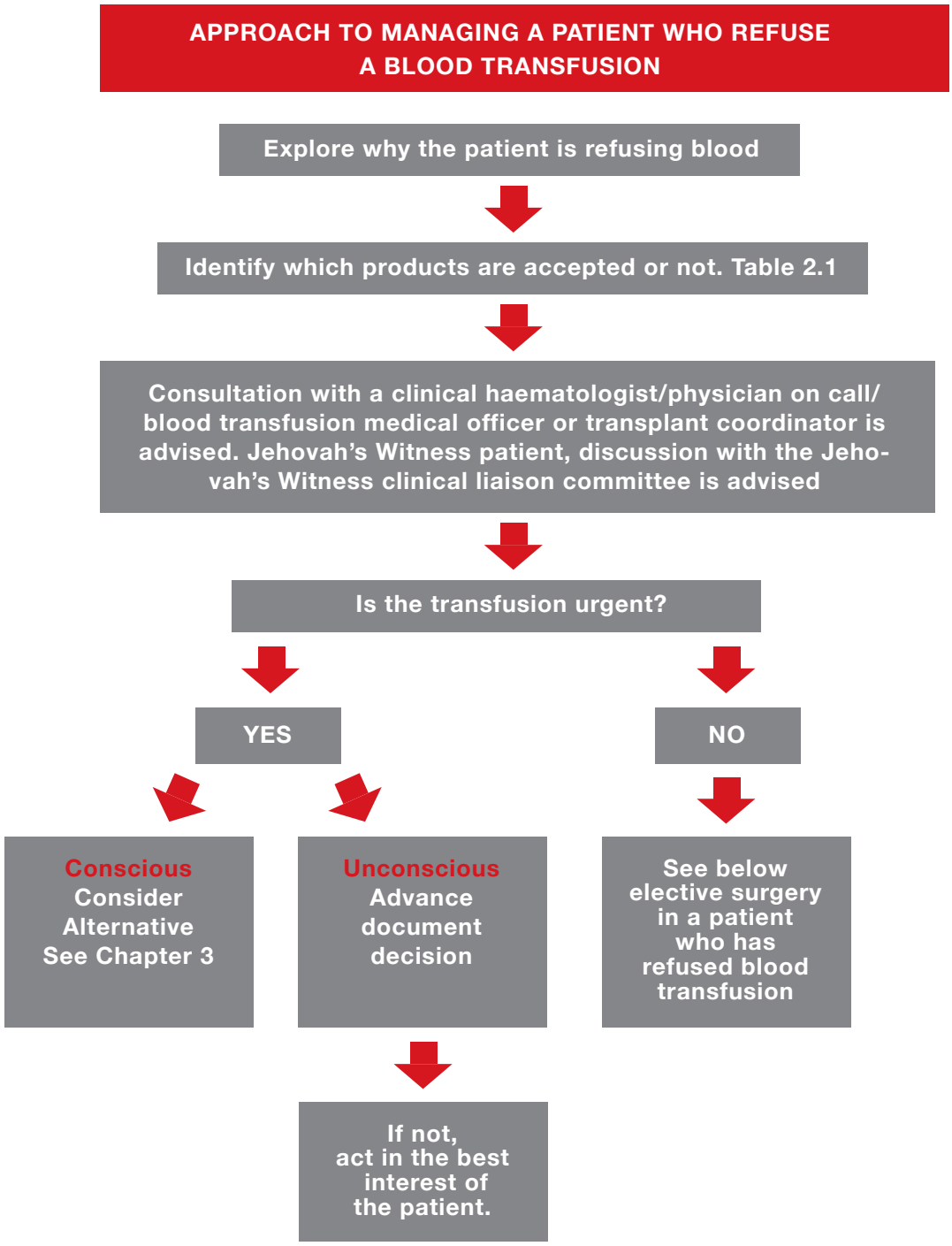


Table 2.1:

Primary components of Blood	*Derivatives of the primary blood components*	*Non-blood derived products*
1. Red Cell concentrates 2. Fresh Frozen Plasma 3. Platelets 4. Cryoprecipitate	1. Albumin 2. Immunoglobulins 3. Fibrinogen 4. Haemoglobin Hemin 5. Coagulation factors (non-recombinant)	1. Crystalloids 2. Synthethetc colloids 3. Dextrans 4. Coagulation factors (Recombinant)

ELECTIVE SURGERY IN A PATIENT WHO HAS REFUSED BLOOD TRANSFUSION

- Advance planning is required, namely a structured multidisciplinary team ap proach involving the clinical haematologist, physician with interest in transfu- sion medicine, surgeon and anaesthetist is recommended.
- Apply the principles of patient blood management (See Chapter 3, Section 3.3).
- Agree on a preoperative haemoglobin target which depends on the nature of the operation and expected blood loss.

GENERAL MANAGEMENT PRINCIPLES FOR A PATIENT WHO REFUSES A BLOOD TRANSFUSION

- **The following must be established by a medical professional in a case of refusal;**
  - That the patient is **competent**, namely not confused, under the influence and able to reason logically.
  - That **no misunderstanding** has occurrent and that the patient completely understood all information provided and the risks associated with refusal of a blood transfusion.
  - That the patient is **free to express his/her own will**, namely not overly influenced by external factors (i.e., family/members of a religious group).
  - The patients' **acceptance to other blood products**, not only red cell con centrates, and procedures. Document where possible which blood prod ucts and procedures such as cell salvage are acceptable to the patient and which are not (especially in life-saving situations) – Table 2.2 serves as an example of how an advance decision to refuse or accept a blood transfu- sion should be documented.
  - That the patient has enough **time to process information** provided by the medical professional.
- **Involve a multidisciplinary team, especially surgical/medical teams, to plan ahead in non-emergency cases;**
  - It is advisable to involve at least **two professionals** in the assessment of a patient who refused a blood transfusion.
  - Involve a **consultant haematologist** if there is any doubt.
  - It is required to **achieve consensus** amongst a multidisciplinary team and this should be documented at all times.
- **Apply principles of PBM to manage anaemia and bleeding**
  (See Chapter 3, Section 3.3 & 3.4).

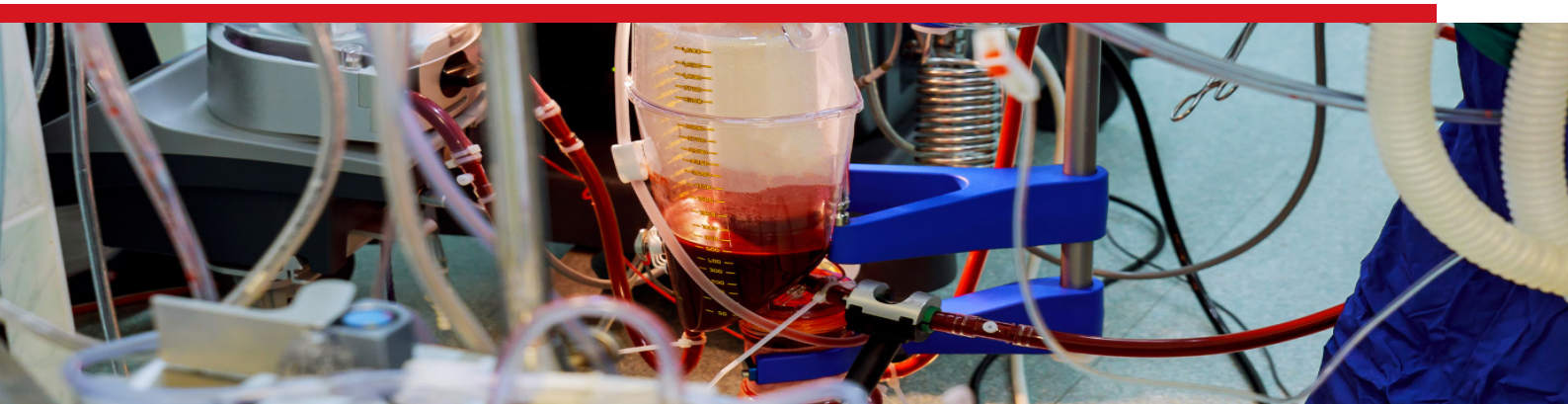


Table 2.2: Advance Decision to Refuse or Accept a Blood Transfusion

1. Patient Information:

Name & Surname: _____
Date of Birth: _____
Identification Number: _____

2. Medical Decision and Informed Consent:

I, the undersigned, having received and understood the information about the nature, purpose, risks, benefits, and alternatives to blood transfusion, hereby make the following decision regarding my medical treatment:

- ☐ I consent to receive blood transfusions as recommended by my medical team.
- ☐ I refuse all blood transfusions under any circumstances, even if refusal may result in serious harm or death.
- ☐ I consent only to the transfusion of the following specific blood product(s):
  - ☐ Red Blood Cells
  - ☐ Platelets
  - ☐ Plasma
  - ☐ Cryoprecipitate
  - ☐ Plasma-Derived Medicinal Products
  - ☐ Other: _____

3. Reason for Decision (Optional): (Please, specify religious, personal or medical reasons)

_____

4. Emergency Contact:

Name & Surname: _____
Relationship: _____
Contact Details: _____

5. Physician Statement:

I confirm that I have provided the patient with clear, comprehensible information about blood transfusion, including its risks, benefits, alternatives, and implications of refusal. The patient has had the opportunity to ask questions and has made an informed decision.

Name & Surname: _____
Signature: _____
Date: _____

6. Patient Declaration and Informed Consent Statement:

I affirm that I am of sound mind and am fully capable of making this decision. I have discussed my choices with my healthcare provider, who has provided me with the necessary information to make an informed decision regarding blood transfusions

Signature: _____ Date: _____

7. Witness Declaration:

I declare that the patient signed this document in my presence and appeared to do so voluntarily and under no duress.

Name & Surname: _____
Signature: _____ Date: _____

ESSENTIALS

- The responsibilities of a blood service and prescribing doctors must be aligned to ethical principles, such as autonomy, non-maleficence, beneficence, justice and dignity to protect both the donor and the recipient of blood.
- Informed consent MUST be obtained prior to a blood transfusion.
- All patients have the right to accept or refuse a blood transfusion.
- In all cases of transfusion refusal, it is essential to establish –
  - If the patient is competent and fully understood all information.
  - If the patient is not influenced by others (i.e., relatives/friends)
  - Which types of blood products are accepted and not.
  - What types of transfusion alternatives are available.

REFERENCES

- International Society of Blood Transfusion. A code of ethics for blood donation and transfusion. 2017. *(https://www.isbtweb.org/resource/english.html* , Accessed 21 July 2024)
- Republic of Namibia. Child Care and Protection Act of 2015. (https://namiblii.org/akn/na/act/2015/3/eng@2019-11-14, Accessed 25 July 2024)
- The Ministry of Health and Social Services of Namibia. Patient Charter *(https://mhss.gov.na/documents/146502/2041604/MOHSS+PATIENT+CHARTER+%281%29.pdf/16502fb1-7242-fa4e-3f48-8707a96afe59?t=1685540925569*, Accessed 21 July 2024)
- The Royal College of Surgeons. Caring for Patients Who Refuse Blood. 2018. *https://www.rcseng.ac.uk/standards-and-research/standards-and-guidance/good-practice-guides/patients-who-refuse-blood/*, accessed 22 July 2024)

CHAPTER 03
PATIENT BLOOD MANAGEMENT

The Blood Service faces significant challenges in maintaining an adequate supply of safe blood and blood products, particularly in the context of inappropriate blood usage. Patient Blood Management (PBM) aims to reduce unnecessary and unsafe transfusion practices, while improving clinical outcomes of patients through appropriate blood usage. PBM can also contribute to the overall efficiency and safety of healthcare delivery in Namibia.

Section 3.1 - What is PBM?

PBM is a patient-centered, systematic, multidisciplinary, evidence-based approach used to improve patient outcomes by managing and preserving a patient's own blood, while promoting patient safety and empowerment. Although, various definitions are used for PBM, the fundamentals to improve patient outcomes remain the same throughout; namely:

- **Pillar 1:** Optimization of a patient's own red cell mass
- **Pillar 2:** Reduce blood loss and bleeding
- **Pillar 3:** Optimize the patient's physiological reserve/tolerance to anaemia

These pillars of PBM were initially implemented in the surgical setting; however, elements thereof have been extended to the non-surgical setting to enhance patient outcomes by reducing unnecessary blood transfusions and associated risks, while encouraging shared decision-making and patient empowerment.

Section 3.2 - Implementation of PBM

The implementation of PBM reduced healthcare costs, while improving patient outcomes. Thus, implementing PBM in Namibia is a readily achievable strategy to reduce the financial burden on the healthcare sector while enhancing patient outcomes.

However, globally the primary challenges to the implementation of PBM are the lack of awareness and the reluctance of healthcare workers to change established and deeply ingrained transfusion practices, despite its benefits.

The Kotter's model should be considered by all healthcare facilities for the implementation of PBM. It is an eight-step model that provides clear guidance on the process of change by embracing the following accelerators.

- **Step 1:** Establish urgency for PBM
- **Step 2:** Establish a powerful PBM group
- **Step 3:** Create a vision for PBM

- **Step 4:** Communicate the PBM vision within the hospital
- **Step 5:** Empower the team & remove obstacles
- **Step 6:** Generate short-term wins
- **Step 7:** Build on the change
- **Step 8:** Anchor PBM in culture

THE IMPORTANCE OF PBM IMPLEMENTATION:

PBM significantly improve patient outcomes while contributing to more cost-effective healthcare system by reducing the utilization of resources. The implementation of PBM can address the following:

High anaemia burden –

Anaemia, an indicator of overall health remains a significant global health burden, estimated to affect about 1.89 to 1.92 billion individuals worldwide in 2021, Iron deficiency anaemia (IDA) is the most common cause of anaemia globally, estimated to affect about 1.24 to 1.46 billion individuals in 2021, particularly in low- and lower middle-income countries followed by anaemia of Inflammation.
A South African study indicated that nearly 50% elective surgery patients were anaemic, which were associated with higher in-hospital mortality and critical care unit admissions Implementing PBM will address this issue by diagnosing and treating anaemia prior to elective surgeries.

Poor patient outcomes –

PBM has proven to improve patient outcomes by reducing unnecessary transfusions after effective implementation, such as;

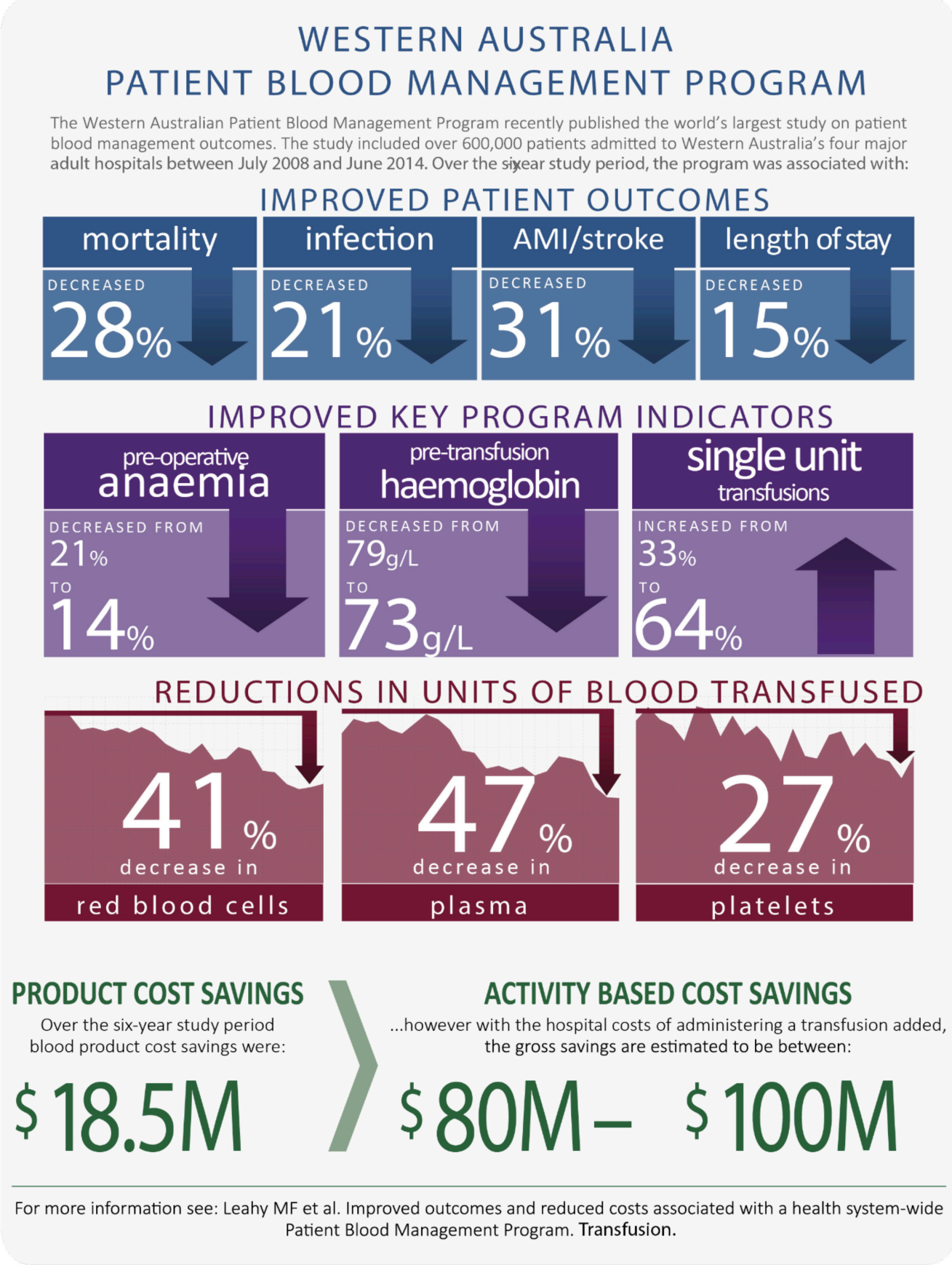
- Reduce transfusion-related adverse events (TRAEs).
- Reduce length of hospital stay & critical care admissions.
- Reduce mortality & significant morbidity, such as infections, venous thromboembolism, delayed wound healing, acute myocardial infarctions & strokes.

Utilization of healthcare resources –

PBM implementation is essential for the delivery of cost-effective healthcare, especially in a resource-limited setting, by reducing costs and resource utilization. Resources required for PBM interventions, i.e. iron supplementation, cell salvage and tranexamic acid, can be cost-effective while improving patient care and safety by means of decreasing transfusion rates, RBC utilization and length of hospital stay.

The adoption PBM as a standard of care in Namibia is currently lacking, despite evidence for improved patient outcomes and economic advantages.

Figure 3.2.1: Clinical and health economic outcomes of the Western Australia patient blood management programme, 2008–2014 (WHO):



Section 3.3 - Key Elements of PBM

Pillar 1: Optimize Red Cell Mass

Identify and correct the underlying cause of Anaemia in both surgical and non-surgical patients before considering a blood transfusion;

IDENTIFY ANAEMIA –

- All patients scheduled for an elective surgery with an expected blood loss of >500ml must be evaluated 4-6 weeks before the procedure (See Chapter 7, Section 7.2).
- All patients require an anaemia workup before a transfusion is considered which includes a FBC, reticulocyte count, peripheral blood smear, iron studies, vitamin B12 and folate levels (See Chapter 1, Section 1.3).

CORRECT ANAEMIA –

- Manage anaemia with available alternatives if possible e.g. oral/intravenous iron depending on the underlying (See Chapter 3, Section 3.4).
- Postpone all elective surgeries or invasive procedures until anaemia has been corrected (See Chapter 7, Section 7.2).
- Develop an individualized management plan for patients requiring long-term trans fusions taking the complications, namely red cell alloimmunization and iron over load into consideration (See Chapter 7, Section 7.5).

Pillar 2: Minimize Blood Loss and Bleeding:

MINIMIZE ACTIVE BLEEDING –

- Stop active bleeding immediately (pressure, elevation, tourniquets, etc.) and initi ate active fluid resuscitation if appropriate (See Chapter 3, Section 3.4)
- Assess bleeding risk, especially pre-operatively with a Bleeding Assessment Tool and avoid drug- and/or food-induced coagulopathies (See Chapter 1, Section 1.4: Bleeding)
- Employ blood-conserving techniques for surgical patients (See Chapter 7, Section 7.2).
- Use pharmacologic agents to reduce bleeding e.g. tranexamic acid.
  load into consideration (See Chapter 7, Section 7.5).

MINIMIZE IATROGENIC BLOOD LOSS –

Blood sampling result in significant blood loss in hospitalized patients, especially in ICU. An adult ICU patient lose more than 340mL of blood per week due to routine diagnostic tests, and have an 18% increase risk of anemia for each 50 mL of blood lost.

It can be reduced significantly when the following interventions are implemented;

- Avoid routine blood sampling and only do micro sampling in small volume/paediatric phlebotomy tubes if clinically indicated.
- Use arterial/ venous catheters to reduce blood wastage during sampling by returning blood or flushing lines to the patient.

Pillar 3: Optimize the physiological reserve:

OPTIMIZE CARDIOPULMONARY FUNCTION –

- Ensure optimal cardiopulmonary function by improving cardiac output (i.e., exercise, smoking cessation etc.) and oxygenation to ensure that anaemia can be tolerated.

ADOPT A SINGLE UNIT TRANSFUSION POLICY, IF THE LOCAL BLOOD BANK CAN ISSUE ON DEMAND –

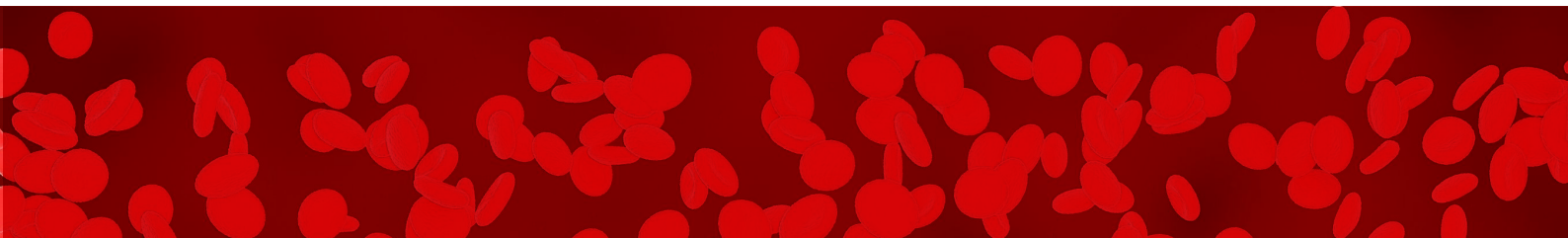
- Order only the necessary amount to address the patient's condition; for instance, if one unit of red cell concentrate alleviates hypoxia, do not order a second units.
- A single unit will often relieve acute symptoms and/or raise haemoglobin level in a stable patient to a level above the recommended transfusion threshold.
- Elderly, females and patients with renal or cardiac failure are at risk of TACO when two or more RBC units are transfused in succession.

RESTRICTIVE RBC TRANSFUSION STRATEGY –

Red Blood Cell Transfusion practices should be in accordance to the AABB Red Blood Cell Transfusion International Guidelines, 2024, as indicated below.

RBC TRANSFUSION RECOMMENDATIONS FOR ADULTS;

- Haemodynamically stable hospitalized adult patients. Consider a transfusion when the haemoglobin is **less than 7 g/dL.**
- The following haemoglobin transfusion thresholds should be considered for these subgroups of patients;
  - Haematologic/Oncologic Disorders: **7.0 g/dL**
  - Critical Care/Cardiac Surgery: **7.5 – 8 g/dL**
  - Orthopaedic Surgery/ Cardiovascular Disease: **8 g/dL**
    - *Acute myocardial infarction (AMI) or heart failure (HF): 7.0 – 8.0 g/dL, with careful monitoring of volume status and adjustment of transfusion rate to avoid transfusion-associated circulatory overload (TACO).*



RBC TRANSFUSION RECOMMENDATIONS FOR NEONATES & CHILDREN;

- **A transfusion is recommended when the haemoglobin is less than 7g/dL in;**
  - Critically ill and haemodynamically stable children at risk of critical illness without a transfusion-dependent hemoglobinopathy, cyanotic cardiac condition or severe hypoxaemia.
- **A transfusion is recommended in haemodynamically stable children with congenital heart disease (CHD) based on the cardiac abnormality and stage of surgical repair, as follows;**
  - Biventricular repair: **7 g/dL**
  - Single-ventricle palliation: **9 g/dL**
  - Uncorrected CHD: **7-9 g/dL**
- **The haemoglobin transfusion threshold in neonates born at a gestational age of 30 weeks or less of depends on the postnatal weeks and respiratory support requirements, see table 3.1;**

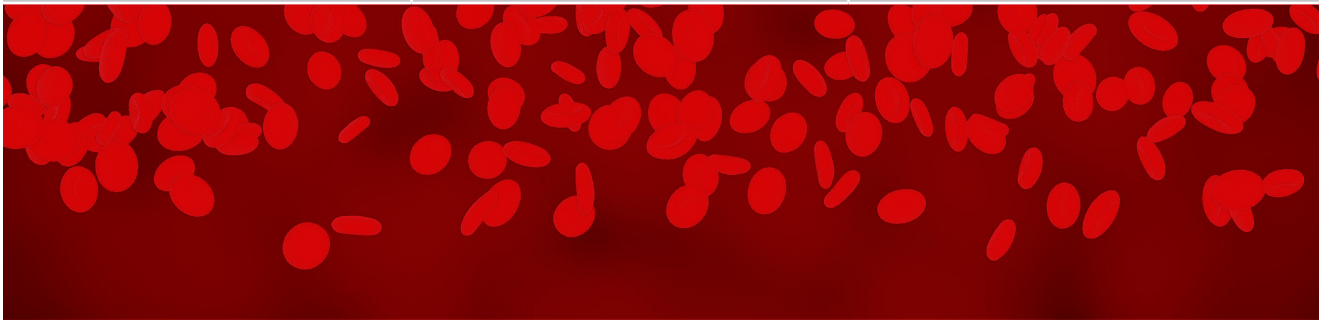
Table 3.1: Haemoglobin transfusion thresholds in neonates ≤ 30 weeks

Postnatal Week	*Require Respiratory Support or FiO2 > 30%*	*No/Minimal Respiratory Support*
1	11 g/dL	10 g/dL
2	10 g/dL	8.5 g/dL
≥3	9.0 g/dL	7.0 g/dL

Table 3.2: Patient Blood Management Pillars

Pillar 1: Optimize red cell mass	*Pillar 2: Minimise blood loss & bleeding*	*Pillar 3: Optimize the physiological reserve of anaemia*
Before a specific treatment (Pre-operative Phase)		
- Detect anaemia - Identify & manage underlying disorder(s) causing anaemia - Refer for further evaluation if required **Treat the following;** - Suboptimal iron stores - Iron deficiency - Anaemia of chronic disease - Iron-restricted erythropoiesis - Haematinic deficiencies	- Assess & manage bleeding risk - Minimise iatrogenic blood loss - Planning & rehearsal of the procedure - Autologous blood donation however not routinely recommended and must in accordance to the standards of the blood service.	- Assess & optimize the patients' physiological reserve & risk factors - Compare estimated blood loss with the patient-specific tolerable blood loss - Develop a patient-specific management plan, which is using appropriate blood conservation modalities. - Restrictive transfusion thresholds

Pillar 1: Optimize red cell mass	*Pillar 2: Minimise blood loss & bleeding*	*Pillar 3: Optimize the physiological reserve of anaemia*
During a specific treatment (Intra-operative Phase)		
- Time of surgery with haematological optimization	- Meticulous haemostasis & surgical techniques - Blood-sparing surgical techniques. - Anaesthetic blood-conserving - strategies - Autologous blood options (i.e. intraoperative cell salvage) - Use of pharmacological and/or haemostatic agents (i.e., TXA use in trauma and surgery)	- Optimize cardio-pulmonary function - Optimize oxygenation - Restrictive transfusion thresholds
After a specific treatment (Post-operative phase)		
- Stimulate erythropoiesis - Be conscious of drug interactions that can worsen anaemia	- Monitoring & management of postoperative bleeding - Avoid secondary haemorrhage - Rapid warming/maintain normothermia (unless indicated) - Autologous blood salvage - Minimize iatrogenic blood loss - Manage haemostasis & anticoagulation - Prophylaxis of upper gastro-intestinal haemorrhage - Avoid/Treat infections promptly - Be conscious of medication adverse effects	- Optimize oxygen delivery - Minimize oxygen consumption - Restrictive transfusion thresholds - Early identification and treatment of infections.



Section 3.4 - Transfusion Alternatives

A blood transfusion is generally only recommended in haemodynamically stable patients if other treatment modalities have failed. The use of transfusion alternatives must always be considered before a blood transfusion by outweighing the risks versus the benefits. The use of transfusion alternatives is of utmost importance to reduce transfusions by increasing red blood cell production, reducing the risk of bleeding and ensuring volume expansion.

3.4.1 - Intravenous Replacement Fluids

Intravenous Replacement Fluids are used to replace significant losses of blood, plasma or other extracellular fluid to mainly restore and stabilize circulatory haemodynamic's to maintain tissue perfusion and oxygenation in hypovolaemia (i.e., haemorrhagic shock).

CRYSTALLOID REPLACEMENT FLUIDS

Crystalloid solutions are employed to replace blood volume and extracellular fluid losses. Comprising of low-molecular-weight ions like Na+, K+, Cl-, and Ca2+, they maintain a sodium concentration similar to plasma, thereby restricting their entry into cells. These fluids readily traverse capillary membranes, dispersing throughout the extracellular compartment. For effective restoration of circulating blood volume, it is recommended to administer crystalloids at a volume threefold greater than the blood volume deficit.

Examples of crystalloid replacement fluids –

- Plasmalyte B
- Sodium Chloride 0,9% (Normal Saline)
- Ringer's Lactate

COLLOID SOLUTIONS

Colloids are suspensions of larger molecular weight particles, which do not pass through the capillary membranes resulting in vascular compartment retention increasing the osmotic pressure of blood.

Examples of colloid replacement fluids:

- Plasma derived colloid solutions:
  - Albumin: Only indicated in certain clinical conditions (See Chapter 6: Blood and Blood Products, Plasma Derivatives).
- **Synthetic colloid solutions:**
  - Gelatins (e.g. Haemaccel®/Gelofusine®): Contraindicated in renal failure.
  - Dextran's (e.g. Rescueflow®/Rheomacrodex®): Contraindicated in pre-existing coagulation disorders (NB may interfere with compatibility testing of blood).
  - Hydroxyethyl starches (e.g. Voluven®/Haes-Steril®): Contraindicated in pre-existing coagulation disorders and renal failure.

Table 3.3 - Differences between crystalloids and colloids

	Crystalloids	*Colloids*
Side effects	**Few side-effects, including;** - Reduce colloid osmotic pressure by dilution - Interstitial or pulmonary oedema with large volume infusions	**Many side-effects, including;** - Volume overload - Coagulation dwefects - Allergic reactions
Cost	Cheap	Expensive
Availability	Widely available	Not available in all hospitals
Duration of action	Short duration of action, plasma t1/2 is +/- 30 min	Longer duration of action, plasma t1/2 is 3-24 h.
Volume necessary	Replace 3-4 x blood volume lost	Volume for volume replacement
Pack sizes	Weighty and bulky	Less weighty and bulky
Usage	First line replacement fluid hypovolaemic shock resuscitation	No clinical evidence that more effective in resuscitation than crystalloids

3.4.2 - Haemostatic Medications

Haemostatic medications are used topically or systemically to reduce or stop bleeding by promoting coagulation. There are several classes, namely antifibrinolytics, protamine, desmopressin, fibrinogen, and blood coagulation factors. These have various mechanisms of actions such as systemic medication which induce primary coagulation by stimulating fibrin formation, promoting coagulation or inhibiting fibrinolysis, while topical medication cause vasoconstriction or promote platelet aggregation.

Topical Haemostatic Agents

Topical agents like fibrin sealants, haemostatic gelatin sponge (i.e. Surgifoam®), collagen fleece (Instat®) and cyanoacrylate glues (Dermabond®) can be used for haemostasis in an emergency or theatre setting.

Systemic Haemostatic Agents

Systemic Haemostatic Agents play a crucial role in stopping and preventing bleeding in various settings. Tranexamic acid (TXA), is the most cost-effective and widely available systemic haemostatic agent in Namibia. Clinically, TXA has been shown to exhibit beneficial haemostatic effects for a wide variety of medical and surgical indications.

TRANEXAMIC ACID (TXA)

Tranexamic acid (TXA), inhibits plasminogen activation by blocking the enzyme's lysine binding sites, preventing its interaction with plasmin and fibrin. This reduction in fibrinolysis stabilizes the fibrin

clot matrix, crucial for secondary haemostasis. Consequently, TXA is essential in maintaining clot integrity and promoting haemostasis. Studies indicate that TXA has the ability to reduce bleeding and improve clinical outcomes in a variety of haemostatic challenges. Table 3.4 shows the indications and recommended dosing regimen of TXA; however, this is just a guide therefore the prescription of TXA must still be in accordance to the product package insert.

Table 3.4 – TXA Indications and recommended dosing regimen

Indication	*TXA Dosing Regimen*	*Evidence*
Trauma-associated Haemorrhage (CRASH-2 Trial)	1.0g IV over 10 minutes then 1.0g IV over 8 hours as a continuous infusion. (Administer within 3 hours of occurrence)	Strong
Traumatic Brain Injury with a GCS >9 (CRASH-3 Trial)	1.0g IV over 10 minutes then 1.0g IV over 8 hours as a continuous infusion. (Administer within 3 hours of occurrence)	Strong
Cardiothoracic Surgery (Coronary Artery Surgery)	50 mg/kg body weight IVI more than 30 minutes after the induction of anaesthesia	Strong
Postpartum Haemorrhage (PPH) (WOMAN Trial)	1.0g IV over 10 minutes then if the bleeding continues after 30 minutes or restarts within 24 hours a 2nd 1.0g dose can be given.	Strong
Heavy Menstrual Bleeding	1.0g PO 3 times daily for 5 days during each monthly menstruation	Moderate
Orthopaedic Surgery*	10 mg/kg IV loading dose prior to incision then maintenance of 1mg/kg/hr infusion	Moderate
Intracerebral Haemorrhage (ICH) (TICH-2 Trial)	1.0g IV over 10 minutes then 1.0g IV over 8 hours as a continuous infusion. (Administer within 3 hours of occurrence)	Moderate
Haemoptysis	Variable dosages, 0.5 – 1.0g in 5 -10 mL Normal Saline nebulized 3 times daily	Moderate
Epistaxis	Cotton gauze soaked in injectable form of TXA (500mg in 5 mL)	Moderate
Hereditary Haemorrhagic Telangiectasia (HHT) with severe recurrent epistaxis	1.0 g PO 3 times daily	Moderate

Indication	*TXA Dosing Regimen*	*Evidence*
Von Willebrand Disease (vWD) (Acute bleed control & prevent bleeding risks)	20-25 mg/kg 2-3 times daily in conjunction with DDAVP/VWF containing concentrates	Moderate
Haematological Disorders (Acute Myeloid Leukaemia)	**AML related bleeding:** 1.5g IV 3 times daily if the plt count is < 20 or falling trend of < 50 until > 20 on two counts	Weak
Hereditary Angioedema	**Short-term prophylaxis:** 1g PO QID 48 hours before & after a procedure. **Long-term prophylaxis:** 1 – 1.5 g PO 2-3 times daily	Weak

* **Orthopaedic surgery includes** - bleeding prophylaxis in knee arthroplasty, spinal surgeries, & perioperatively for hip fractures.

* **Paediatric Recommended Dosing Regimen** - TXA is commonly used for traumatic bleeding at 15 mg/kg IV over 10 minutes, then 2 mg/kg/hr for 8 hours, and this regimen applies in paediatric cases for most adult indications as well. Cardiac surgery dosing differs with a 100 mg/kg IV bolus followed by 10 mg/kg/hr infusion.

Although systemic TXA helps reduce unnecessary transfusions, clinicians must consider its contraindications and cautions before prescribing, namely –

TXA Contraindications –

- Subarachnoid/ Intracranial haemorrhage
- TXA hypersensitivity reactions
- Visual disturbances (i.e., defective colour vision)
- Thrombosis (i.e., history of thromboembolism or active thromboembolic disease)

Cautions –

The most notable risks associated with TXA use is thrombosis and seizures, therefore it must be used with caution in the following;

- Advance Age
- Higher TXA dosages
- Comorbidities: Renal dysfunction, malignancy, hepatic disease/cirrhosis

OTHER SYSTEMIC HAEMOSTATIC AGENTS

Synthetic vitamin K1(Phytomenadione) –

- Konakion® (PO, IM, IV)
- Necessary for activation of coagulation factors II, VII, IX, X.
- Indications:
  - Prevention and treatment of Haemolytic Disease of the Newborn

- Reversal of warfarin effect in case of haemorrhage.
- Treatment of hypoprothrombinaemia due to factors which interfere with absorption and synthesis, malabsorption syndromes, pancreatic insufficiency, obstructive jaundice, coeliac disease, regional enteritis, ulcerative colitis, short bowel syndrome etc.

Human coagulation factor concentrates –
- See Chapter 6: Blood and Blood Components, Plasma Derivatives

Somatostatin (Octreotide, growth hormone inhibiting hormone) –
- Sandostatin® (IV)
- Reduces portal venous pressure and causes splanchnic vasoconstriction thereby reducing bleeding from oesophageal varices.
- **Indications:**
  - Management of variceal bleeding in patients
  - with cirrhosis and to protect from re-bleeding in association with endoscopic sclerotherapy.

Desmopressin (Synthetic derivative of antidiuretic hormone vasopressin) –
- DDAVP® (nasal spray, SC, IV)
- Increase plasma levels of FVIII and endothelial secretion of vWF. It has no effect on platelet count or aggregation, but enhances platelet adhesion to the vessel wall.
- **Indications:**
  - Mild haemophilia A and Type 1 vWD pre-operatively to minimize intraoperative blood loss and management of heavy menstrual bleeding in females with vWD.
  - Uraemic bleeding in patients with acute or chronic renal failure

3.4.3 - Haematinics

Haematinics are nutrients like iron, folic acid and vitamin B12, that are required by the bone marrow for haematopoiesis, the process of blood cell formation and development in the bone marrow. Deficiency of these may result in nutritional anaemias.

IRON

Iron Deficiency (ID) –

ID is the most common micronutrient deficiency and the leading contributor of anaemia globally. According to the WHO anaemia affects between 1.95–2.36 billion people globally, of whom about 1.24–1.46 billion are iron deficient. It is most prevalent amongst children younger than 5 years, women of childbearing age, and during pregnancy.

ORAL IRON THERAPY

Oral iron is usually the **first line of therapy** since it is; readily available, convenient to use, efficient and cost effective.

Treatment efficacy can be monitored by assessing the haemoglobin response:
- **Optimal response:** Hb increment of **2 g/dl** within 3-4 weeks.
- **Reasonable response:** Hb increment of **1 g/dl** within 4 weeks.

Replenish body iron stores:
- Serum ferritin **>100 g/l**
- To replenish iron stores often requires longer treatment, i.e., an **additional two to three months of treatment** after the haemoglobin has been corrected.

Examples of oral iron supplements:
- Ferrous sulphate (e.g. Ferofolic®, Ferograd®)
- Ferrous fumarate (e.g. Autrin®, Pregamal®)
- Ferrous gluconate (e.g. Ferate®, Fergon®)
- Ferrous lactate (e.g. Ferro drops®)
- Iron (III)-hydroxide polymaltose complex (e.g. Ferrimed®)

The British Society of Gastroenterology recommended ferrous salts (i.e., ferrous sulphate, fumarate or gluconate) as the first line treatment of IDA in adults.

To increase iron absorption while on oral iron therapy, the following should be adhered to;
- Take on an **empty stomach** either one hour before or two hours after a meal.
- Take oral iron with one 250 mg **vitamin C** tablet or orange juice.
- **Avoid certain medicines and food when taking oral iron, such as;**
  - Caffeinated beverages (i.e., tea & coffee)
  - Calcium containing supplements, foods and beverages
  - Antacids (i.e., take two hours before or four hours after an antacid)

Reduce gastrointestinal adverse effects by:
- Starting at a lower dose and alternate daily dosing.
- Increase gradually if tolerated
- Taking it with meals or at night

INTRAVENOUS IRON THERAPY

Intravenous iron therapy is the preferred treatment option in certain iron deficient conditions as indicated in table 3.5 below, since oral iron therapy require longer treatment courses to resolve anaemia, replenish iron stores and have a high rate of gastrointestinal adverse effects which leads to poor treatment adherence.

Examples of intravenous iron formulations:
- Low molecular weight iron dextran/ LMW ID (CosmoFer ®)
- Ferric carboxymaltose/FCM (Ferinject®)
- Iron sucrose/IS (Encifer®, Venofer®)
- Iron isomaltoside (Monofer®)

Table 3.5 - Indications for intravenous iron therapy

Indication	*Comment*
Poor tolerance, compliance or response to oral iron	**Severe intolerance to gastrointestinal side effects in IBD;** - oral iron may worsen IBD disease activity
Excessive ongoing blood loss	**Blood loss exceeds the ability of the GIT to absorb sufficient iron to meet needs;** - Heavy uterine bleeding - Hereditary haemorrhagic telangiectasia
Rapid replenishment of iron stores	**Iron Deficient patients pre-operatively;** - Require ID to be corrected for a scheduled surgery which cannot be delayed for a prolonged period (i.e., 6 weeks)
Iron malabsorption	- Surgery; Duodenal resection and gastric surgery. - Others: Active IBD, coeliac disease & Helicobacter pylori infection
Functional iron deficiencies	**Functional iron deficiencies due to underlying inflammatory conditions;** - Chronic Kidney Disease (CKD) on EPO - Malignancies
Contraindications for intravenous iron therapy:	
Known Allergy to IV Iron	**IV iron has the potential to cause allergic reactions, but life-threatening anaphylaxis is very rare;** - Higher risk in patients with previous anaphylaxis, asthma, eczema or drug allergies. **Precautionary measures:** - Administration of a test dose - Close monitoring, especially in the first 15 minutes. - Always have resuscitation equipment available.
Other:	- First trimester of pregnancy - Iron overload - Iron deficiency not proven as the cause of anaemia - Liver Cirrhosis/Hepatitis - Active Rheumatoid Arthritis - Acute Renal Failure (ARF) - Ongoing infection

Dosing for Total Dose Infusion (TDI) –

Table 3.6 - Ferric carboxymaltose (Ferinject®) Maximum: 15mg/kg/infusion			
Haemoglobin (g/dL)	**Weight (kg)**		
	< 35	**35 - 70**	**> 70**
< 10	500 mg	1500 mg	2000 mg
10 – 14	500 mg	1000 mg	1500 mg
IDWA	500 mg	500 mg	500 mg

Table 3.7 - LMW Iron Dextran (CosmoFer ®)/Iron isomaltoside (Monofer®) Maximum: 20 mg/kg/infusion		
Haemoglobin (g/dL)	**Weight (kg)**	
	50 - 70	**> 70**
< 10	1500 mg	2000 mg
> 10	1000 mg	1500 mg
IDWA	500 mg	500 mg

* Godzoni Equation for Iron Deficiency Anaemia
(https://www.mdcalc.com/calc/10139/ganzoni-equation-iron-deficiency-anemia)

**** Note: Paediatric IV iron dosing should be discussed with a paediatric haematologist or a paediatrician experienced in administering IV iron preparations.***

Preparation & Administration of IV Iron –

IV iron should **NEVER** be diluted in more than the recommended maximum diluent volume and/or give with premedication, due to the following –

- If IV Iron is diluted in a larger volume as recommended, more free iron is released into the solution which increases the risk for hypotension and non-allergic reactions.
- Premedication also increases the risk of hypotension.

Table 3.8 - Preparation & Administration of intravenous iron

IV Iron Product	Ferric Carboxymaltose Ferinject®	Low Molecular Weight Iron Dextran CosmoFer ®	Iron Isomaltoside (Monofer®)
Diluent	0.9 % Saline ONLY	0.9% Saline/5% DW	0.9 % Saline ONLY
Maximum Diluent Volume (ml)	250	500	500
Test Dose	25mg in 100 ml diluent over 15 minutes Wait for 15 minutes before the infusion can start	25mg in 100 ml diluent over 15 minutes Wait for 45 minutes before the infusion can start	25mg in 100 ml diluent over 15 minutes Wait for 60 minutes before the infusion can start
Maximum TDI	15 mg/kg/infusion	20 mg/kg/infusion	20 mg/kg/infusion
Infusion Time	15 minutes	4 – 6 Hours	15 – 60 minutes

FOLIC ACID

Folic acid is the synthetic form of folate, also known as vitamin B9. It is essential for the formation of several coenzymes of many metabolic systems, particularly for purine and pyrimidine synthesis, nucleoprotein (DNA and RNA) synthesis, and maintenance in erythropoiesis.

Folate deficiency can have significant health consequences such as –

- Poor pregnancy outcomes, including prematurity, low birth weight, and neural tube defects.
- Elevated homocysteine, increases the risk of cardiovascular disease (e.g., atherosclerosis) and neuropsychiatric conditions such as cognitive impairment, dementia, depression, and, rarely, peripheral neuropathy or subacute combined degeneration of the spinal cord.

Common causes/risk factors for folate deficiency are as follow –

- **Inadequate intake:** Alcohol abuse, inadequate diet (i.e., a diet lacking fresh fruits, vegetables, & fortified cereals) and parenteral nutrition.
- **Reduced absorption:** Gastrointestinal conditions (i.e., Coeliac Disease, Crohn Disease, Coeliac Disease, Short Bowel Syndrome and Gastric Bypass).
- **Increased demand:** Pregnancy, malignancy, exfoliative skin disorders (i.e., severe dermatitis) and/or haemolytic anaemias.
- **Prolonged medication use:** I.e., metformin, methotrexate, trimethoprim, sulphonamides, phenobarbital, phenytoin and/or oral contraceptive pills may impair folate metabolism.

Management –

Treat the underlying cause and correct the folate deficiency;

- Oral administration of folic acid is preferred. Only in certain clinical situations (e.g. patients receiving parenteral or enteral alimentation), parenteral folic acid is advocated.
- **Management of megaloblastic anaemia:**
  - **Adults:** Folic acid 1 - 5mg per os daily until clinical symptoms and haematological parameters

normalize. (If the cause is undetermined, rule out vitamin B12 deficiency before starting folic acid to avoid worsening vitamin B12 neuropathy.
  - **Paediatrics:** Dosing is age-dependent: neonates receive 0.05 mg daily; children under 4 years, 0.1–0.25 mg/kg daily; and those 4 years and older, 0.5–1 mg/kg daily.
- Prophylactic folic acid is given to patients with chronic haemolysis (5mg weekly) and pregnant women.

VITAMIN B12

Vitamin B12 (cyanocobalamin) is vital for the formation of red blood cells, as well as for the proper functioning and health of nerve tissue.

Common causes/risk factors for vitamin B12 deficiency are as follow –
- **Inadequate intake:** Alcohol Abuse and vegans/strict vegetarians (limit intake of animal products).
- **Reduced ileal absorption:** Crohn Disease, ileal resection, coeliac disease, bacterial overgrowth and tapeworm infections,
- **Absent/reduced intrinsic factor:** Atrophic gastritis, pernicious anaemia and/or post-gastrectomy Syndrome (Roux-en-Y gastric bypass).
- **Prolonged medication use:** Histamine H2 blockers (> 12 months), proton pump inhibitors (>12 months) and metformin (> 4 months).

Management –
Vitamin B12 replacement therapy will depend mainly on the underlying cause (inadequate intake vs. malabsorption), presence of neurological symptoms and/or adherence;

Vitamin B12 Deficiency due to inadequate dietary intake –
- Oral replacement (minimum 1 mg daily) should be considered if the patient is asymptomatic.
- Intramuscular vitamin B12 injections are preferred in cases of:
  - Rapid clinical deterioration.
  - Poor adherence to oral treatment.
  - Neurological/haematological manifestations, i.e., ataxia/anaemia;
    - Neurological involvement - 1 mg OD on alternate days until no further improvement, then 1 mg every 2 months
    - No neurological involvement - 1 mg 3 times/week for 2 weeks, then 1 mg every 2-3 months
    - Paediatric Dosing - 20 mcg/kg IM daily for 1 week, followed by monthly maintenance dosing.

Vitamin B12 Deficiency due to confirmed or suspected malabsorption –
- Intramuscular vitamin B12 replacement is preferred in vitamin B12 deficiency due to malabsorption at a minimum dosage of 1mg per day.

3.4.4 - Recombinant Human Erythropoietin (r-HU-EPO)

Erythropoietin is a glycoprotein mainly produced by the renal cortex in response to hypoxia. It stimulates proliferation and differentiation of erythroid precursor cells to more mature erythrocytes. Recombinant human erythropoietin (r-Hu-EPO) is an erythropoiesis-stimulating agent which is synthetically produced by recombinant DNA technology for the treatment of anaemia. Erythropoietin is not on the Namibia Essential Medicines List, but can be obtained by specialist request as buy-out.

The following erythropoiesis-stimulating agents are available in Namibia:

- **Epoetin beta**
  Recormon® (short acting) or Mircera® (long acting)

Table 3.9 - Erythropoiesis-Stimulating Agents (ESA's)

General Principles	- **Lack effectiveness due to the following reasons;**
	  - Common: Iron deficiency and chronic inflammation, i.e., due to uraemia, advanced metastatic cancer, and chemotherapy.
	  - Others: chronic blood loss, haemolysis, bone marrow fibrosis, Vitamin B12 and folate deficiencies.
	  - ESA's always require iron to be completely efficient
	- Require time to treat, monitoring & dose adjustments.

Indications	**Medical** - Treatment of anaemia in patients with Chronic Renal Failure (CKD). - Treatment of anaemia in patients with non-myeloid malignancies on chemotherapy. - Prevention of anaemia in preterm infants. **Surgical** - Increase autologous blood yield from patients in the pre-donation programme. - Increase the perioperative haemoglobin in patients who are at high risk for perioperative blood loss from elective surgery.
Contraindications	- Uncontrolled Hypertension - Hypersensitivity to mammalian-derived cell products, albumin, any component of the product. - History of pure red cell aplasia from previous ESA's. - Patients who cannot receive treatment for a thromboembolic event or patients enrolled in a pre-donation programme who had a stroke, myocardial infarction, unstable angina pectoris in the preceding month or has a history of a thromboembolic event.
Precautions	- Give the first dose under medical supervision due to the risk of anaphylaxis and resuscitation equipment must be available. - Cautious use in patients with a history of seizures and medical conditions, which predispose them to seizures due to an increased risk of seizures especially during the first 90 days. - Pre-existing elevated blood pressure, cardiovascular disease and a previous myocardial infarction/stroke
Side Effects	**Nervous System** - Headaches (common) **Cardiovascular System** - Hypertension/Hypertensive Crisis with/without encephalopathy. **Haematological System** - Neutropenia, thrombocytosis & pure red cell aplasia. **Immune System** - Hypersensitivity Reactions

ESA Dosage & Monitoring –

- **Dosage –**
  - The dosage for ESA for the various indications thereof MUST be in accordance to the product package insert.

- **Monitoring –**
  - Baseline haemoglobin and iron studies must be done prior to the initiation on ESA's.
  - Monthly monitoring of haemoglobin is recommended, and the dosing and administration frequency should be adjusted based on the treatment response according to the product package insert.

ESSENTIALS

- The implementation of PBM is essential to reduce the high anaemia burden, improve patient outcomes and improve the utilization of healthcare resources.
- **PBM consist of three pillars –**
  - **Pillar 1 –** Investigate the underlying cause of all anaemia cases and treat the underlying cause accordingly with available alternatives to a blood transfusion if possible (i.e., intravenous iron and/or EPO-stimulating agents depending on the underlying cause).
  - **Pillar 2 –** Minimize active bleeding and iatrogenic anaemia by means such as use of haemostatic agents (i.e., TXA) in patients at risk for bleeding and avoiding routine blood sampling or large volumes.
  - **Pillar 3 –** Optimize a patient's cardiopulmonary reserve to improve tolerance to anaemia/ blood loss and implement restrictive transfusion strategies.
    - **Restrictive transfusion thresholds** (Hb: 7 - 8 g/dL) has a similar 30-day morbidity and mortality compared to liberal transfusion thresholds (Hb: 9 – 10 g/dL), while reducing unnecessary blood transfusions.
- **The use of transfusion alternatives must always be considered before a blood transfusion by outweighing the risks versus the benefits.**
- **Blood transfusion alternatives commonly used, include intravenous fluids, haemostatic agents, haematinics (i.e., iron, vitamin B12, Folic acid) and erythropoietin stimulating agents. Usage hereof depends on the patient's specific underling condition.**
- **Tranexamic Acid (TXA) –**
  - **CRASH-2, CRASH-3 and WOMAN trials** indicated that the optimal effect of systemic TXA is achieved when administered early (< 3 hours).
  - **TXA dose above 1g IV** had an unremarkable dose-response for surgical blood loss.
  - **TXA is not recommended for the empirical treatment of GI bleeding –**
    - **HALT-IT Trial showed** TXA did not reduce mortality from GI bleeding, but was associated with and increase risk for VTE & seizures.
- **Intravenous Iron Therapy –**
  - Is preferred in certain iron deficient conditions, such as functional iron deficiencies, iron malabsorption, excessive ongoing blood loss, require rapid replenishment of iron stores, poor tolerance, compliance or response to oral iron.
  - Should **NEVER** be diluted in more than the recommended maximum diluent volume and/or give with premedication.

REFERENCES

- World Health Organization. (2021). The urgent need to implement patient blood management: policy brief. Genève, Switzerland: World Health Organization.

- Marsicano D, Hauser N, Roodt F, et al. Preoperative anaemia and clinical outcomes in the South African surgical outcomes study. S Afr Med J. 2018;108(10):839-846. doi:10.7196/SAMJ. 2018. v108i10.13148

- Carson JL, Stanworth SJ, Guyatt G, et al. Red Blood Cell Transfusion: 2023 AABB International Guidelines. JAMA. 2023;330(19):1892–1902. doi:10.1001/jama.2023.12914

- Deschmann E, Dame C, Sola-Visner MC, et al. Clinical Practice Guideline for Red Blood Cell Transfusion Thresholds in Very Preterm Neonates. JAMA Netw Open. 2024;7(6):e2417431. doi:10.1001/jamanetworkopen.2024.17431

- Relke, N., Chornenki, N. L. J., & Sholzberg, M. (2021). Tranexamic acid evidence and controversies: An illustrated review. Research and practice in thrombosis and haemostasis, 5(5), e12546. *https://doi.org/10.1002/rth2.12546*

- Cai J, Ribkoff J, Olson S, et al. The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. Eur J Haematol. 2020; 104: 79–87. *https://doi.org/10.1111/ejh.13348*

- Patient blood management. Association for the Advancement of Blood & Biotherapies. *https://www.aabb.org/newsresources/resources/patient-blood-management*

- Gastro Foundation. (2022). Practical Aspects of Iron Therapy [Video]. YouTube. Retrieved August 15, 2024, from *https://www.youtube.com/watch?v=2NbJI2VILmM*

- Carson, J. L., Brooks, M. M., Hébert, P. C., et. al., & MINT Investigators. (2023). Restrictive or liberal transfusion strategy in myocardial infarction and anemia. The New England Journal of Medicine, 389(26), 2446–2457. *https://doi.org/10.1056/NEJMoa2312323*

CHAPTER 04
ORDERING OF BLOOD & BLOOD PRODUCTS

In line with the Standards for the Practice of Blood Transfusion in Namibia, no blood and/or blood product may be issued without a completed Requisition for Blood Products Form which is signed by a registered Medical Practitioner prescribing the blood product or a person acting on his/her instructions.

Section 4.1 - Completion of the NAMBTS Blood Requisition Form

All blood products, including freeze-dried plasma (FDP), must be ordered from the blood bank on the NAMBTS blood requisition form.

To ensure the correct identification of the patient, it is a requirement that all the patient details on the blood requisition form correspond to the details on the crossmatch specimen label. If this is not the case, the blood bank will return the blood requisition form to the hospital and discard the crossmatch specimen.

The following must be indicated on the form by the prescribing medical practitioner:

- Patient details: surname, first name, date of birth, gender & cell phone number
- Destination of the blood consignment: Hospital, ward & hospital number
- Diagnosis: Indicate the underlying aetiology of anaemia & thrombocytopenia. The clinical diagnosis should be in accordance to the ICD10 Classification.
- Patient history relevant to transfusion: medical, obstetric & transfusion history.
- Category: surgery, internal medicine, oncology, paediatrics, trauma or obstetrics & gynaecology
- Requested blood product: type & quantity of products requested.
- Extent of compatibility testing: group & screen, stand-by, standard, emergency, none (See table 4.1)
- Time and date blood and/or blood products are requested & needed
- Other instructions: any additional information which needs to be conveyed to the blood bank, i.e., leucode pletion request, notification of a massive transfusion etc.
- Doctor's details: surname, first name, cell phone number & signature

ESSENTIALS

- The blood service cannot accept any legal responsibility if they are not supplied with sufficient information to identify the patient.
- All plasma-derived products (except freeze-dried plasma) must be ordered from the hospital pharmacy.

Section 4.2 - Positive Patient Identification

Patient identification is one of the most important steps in the blood transfusion process and MUST take place during the completion of the blood requisition form, sample collection and before commencement of the transfusion;

Steps to take for Positive Patient Identification –

- **Conscious patients** must be asked to identify themselves, which requires the patient to give their full name and date of birth.
- **Unconscious, sedated or confused patients, babies and small children and any other patients unable to communicate verbally** must be identified by the information given on their identification band and must be verified by another member of staff, relative or caregiver.
- All identification information MUST correspond to the patient's information on the identification band and/or any other associated hospital records, blood requisition form and label of the sample.

Why is Positive Patient Identification during completion of the blood requisition form and sample collection important –

- Patient identification immediately before the sample collection ensures that the sample is collected from the right patient and labelled with the right patient identification information. Labelling the sample with another patients' details is a 'wrong blood in tube' incident, which could result is an ABO incompatible transfusion.
- The risk for a **'wrong blood in tube' incident** increases when the patient is not identified at the bedside before the sample is collected, the sample is not labelled at the bedside and/or not immediately labelled by the person collecting the sample.

Section 4.3 - Extent of compatibility testing when blood is ordered

Clinicians need to be aware of the various options with regard to the extent of compatibility testing (Group & Screen, Stand-by, Standard, Emergency, None), when they are prescribing blood transfusions for their patients.

Table 4.1 - A full crossmatch entails the following steps:		
Step 1	**ABO Group**	The patient's specimen is tested for the full ABO Group
Step 2	**Rh (D) Group**	The patient's specimen is tested for D antigen
Step 3	**Antibody Screen**	The patient's specimen is tested for irregular red cell antibodies. If irregular antibodies are found, **an antibody identification** is done.
Step 4	**Crossmatch**	The patient's specimen is tested with donor blood to ensure compatibility

GROUP & SCREEN/ "GROUP & HOLD"

- **Step 1, 2 & 3:** The ABO group, Rh type and irregular antibody screen is done. The blood is only crossmatched and issued once blood is requested by the doctor.
- **When:** A transfusion might be required during admission or a surgery.
- **Note:** The blood products and number of units are now requested telephonically.

STAND-BY

- **Steps 1 – 4 & issued on request:** Full crossmatching is done & only issued upon telephonic request. The units are kept in storage for 72 hours until the doctor telephonically requests issue thereof.
- **When:** A transfusion is highly likely, especially during a surgery where significant blood loss is anticipated.
- **Note:** Always indicate the blood product type and number of units on the blood requisition form. If not used within 72 hours, the blood units are returned into blood bank stock and a new crossmatch sample must be submitted to the blood bank.

STANDARD

- **Steps 1 - 4 & issue immediately:** Full crossmatching is done & issued immediately. It requires about 1-2 hours to be issued, depending on the blood bank's workload.
- **When:** A transfusion is planned during admission or surgery.
- **Note:** Always indicate the blood product type and number of units on the blood requisition form.

EMERGENCY

- **Step 1& 2 before issue:** The patient's ABO group, Rh type and partial compatibility testing is done within 10 - 15 minutes before issuing the requested units.
  Steps 3 and 4 after issue: Full compatibility testing is completed while blood is issued. In case of any incompatibility, the requesting doctor will be informed telephonically.
- **When:** Group specific blood is always preferred to uncrossmatched O emergency units.
- **Note:** A crossmatch sample must be collected for full compatibility testing, before group specific units or blood form the emergency fridge is transfused.

NONE

- **Blood group O units are issued without crossmatching or taken from the emergency blood fridge:** No compatibility testing is done prior to transfusion of group O Rh-negative or group O Rh-positive red cell units taken from the emergency blood fridges.
- **When:** Blood is urgently required in patients who are actively bleeding and haemodynamically unstable.
- **Note:**
  - No antibody identification has been done on the patient's serum and these units have not been crossmatched to the patient's blood, which increase the risk for transfusion reactions. Thus, **it should be used as the last resort and the number of units transfused should be minimized (i.e., maximum of 2 units).**
  - A **blood requisition form must still be completed** for each patient receiving such blood for the purpose of haemovigilance and lookback investigations;
  - The pack identification number of each emergency blood unit removed from the fridge must be recorded on the form in the area under **OTHER INSTRUCTIONS** using the barcode number stickers on the red cell unit and the blood requisition form' white and yellow sheets must be left at the fridge.

ESSENTIALS

- All requests for blood and blood products MUST be accurate, complete and legible to ensure –
  - Unequivocal identification of the recipient.
  - The right quantity and type of blood product is available to the right patient, at the right time, for the reason and in the right place.
- Positive patient identification is one of the most important steps in the blood transfusion process and MUST take place during the completion of the blood requisition form, sample collection and before commencement of the transfusion.
- The timing of a blood transfusion determines the extent of compatibility testing that can be performed. However, in emergency cases uncrossmatched blood transfusions MUST be minimized as much as possible to reduce the associated risks for adverse events.

REFERENCES

- Australian and New Zealand Society of Blood Transfusion, Australian College of Nursing. Pretransfusion Testing. 2018. h*ttps://www.nzblood.co.nz/healthcare-professionals/transfusion-medicine/transfusion-medicine-handbook/3-guide-to-good-transfusion-practice/3-7-pretransfusion-testing/* Accessed 6 July, 2024.
- NHS Blood and Transplant. Blood Essentials. Administration: Sampling & Request. 2024. *https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/33257/blood-essentials-v1-april-2024.pdf* Accessed 8 July 2024.
- Standard Hospital Procedures on Blood Transfusion. Filling in the blood requisition form. Page 7 -9. 2013.

CHAPTER 05
ADMINISTRATION OF BLOOD AND BLOOD PRODUCTS

The administration of blood involves various steps to ensure the safety of the recipient at all times. In most cases where the safety of a recipient is compromised one or more of these steps were not followed in accordance to available guidelines and the Standard Hospital Procedures on Blood Transfusion.

It is recommended that the guidance provided on the following MUST be followed to ensure safety of the blood recipient;

- Preparation of the patient for transfusion
- Correct identification and verification of the patient and blood component to be transfused
- Examination of the blood product before transfusion
- Handling and administration of blood products
- Cautious monitoring and recording during a transfusion

- **Additional transfusion safety measures;**
  - Aseptic Technique
  - Changing of blood administration sets
  - Concurrent medication & fluid administration
  - Warming of blood products

Section 5.1 - Preparation of the patient for transfusion

PREPARATION OF A PATIENT INCLUDES:

- Ensure that informed consent has been obtained (See Chapter 2, Section 2.3).
- Ensure that the patient understands the entire blood transfusion procedure.
- Encourage the patient to alert the responsible medical professional if he/she is feeling unwell during the transfusion.
- Ensure positive identification of the patient
- Establish adequate IV access under aseptic conditions +/- priming of the administration set before commencement of the transfusion

PRIMING OF THE ADMINISTRATION SET;

Priming of the correct blood administration set prior to administration;
- Prior to use mix the blood product thoroughly by gentle inversion.
- Prime the blood administration set with the blood product, however it may be primed with 0.9% sodium chloride.
- Follow the manufacturer's recommendations for priming of administration sets.

Section 5.2 - Identification & verification of the patient & blood product

POSITIVE PATIENT IDENTIFICATION

Patient identification is the most crucial step in the blood transfusion process and MUST take place during the following to ensure recipient safety:

- Collection of the crossmatch sample
- Completion of the blood requisition form
- Commencement of the transfusion

Requirements for the final positive identification of the patient prior to commencement of the transfusion;

- It MUST be made at the patient bedside, where the patient must state his/her full name and date of birth (See Chapter 4 – Ordering of Blood & Blood Products).
- It MUST be made by **two individuals,** of which one must be a registered nurse or a medical practitioner.
- MUST be **verified** against accompanying medical records and the blood unit label.

If any discrepancy is found during the identification process, it must be resolved before proceeding with the transfusion.

ESSENTIALS FOR POSITIVE PATIENT IDENTIFICATION

NO POSITIVE PATIENT IDENTIFICATION = NO BLOOD TRANSFUSION

It is recommended that all patients MUST have an identification wristband on at all times, especially unconscious patients.

Section 5.3 - Examination of the blood product before a transfusion

All blood units **MUST** be carefully examined prior to insertion of the blood administration set by the medical practitioner and/or registered nurse responsible for the transfusion **AND** the witness to prevent errors.

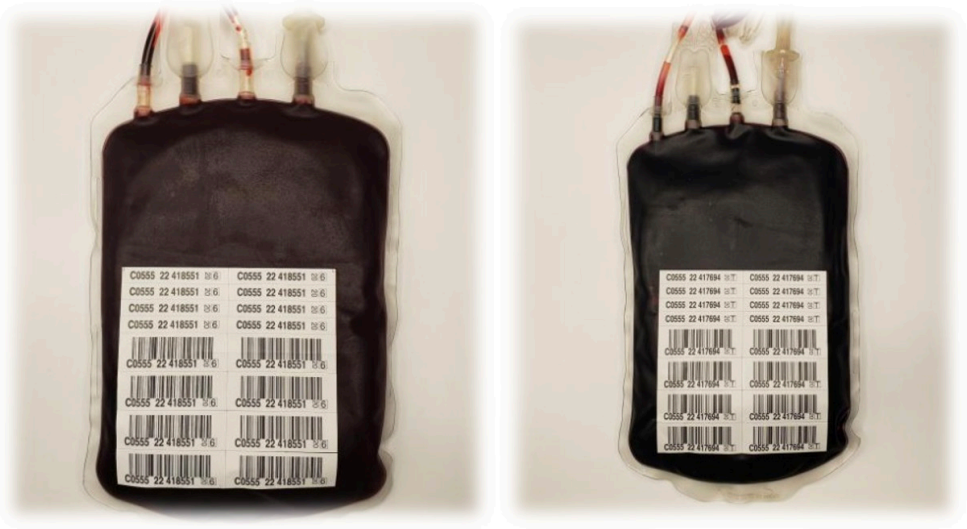
THE BLOOD UNIT MUST BE EXAMINED/CHECKED FOR THE FOLLOWING –

- **EXPIRY DATE –**
  - A unit may not be issued beyond the date of expiry.
  - **NEVER TRANSFUSE A UNIT WHICH HAS PASSED THE EXPIRY DATE**

- **LEAKAGE –**
  - Always suspect leakage if the blood unit is stained with blood.

- Gently squeeze the unit to look for leakage at the tubing, seals & joints.
- **NEVER** transfuse if a leakage has been detected due to a risk of bacterial contamination.

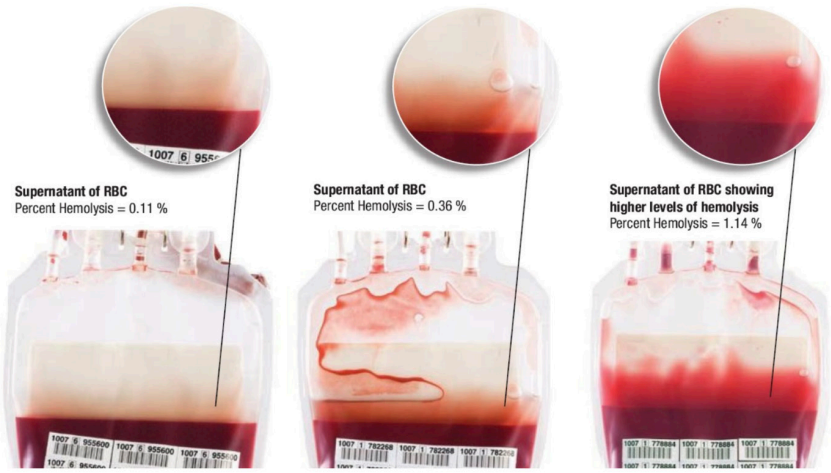
- **ABNORMAL COLOR –**
  - *WB/RCC:* Normally dark red in color (NOT PURPLE/BLACK)
  - *FFP:* Normally yellow to orange in color
  - *Platelet Concentrate:* Normally straw-colored



Source: Visual Assessment Guide - Canadian Blood Services: RCC discoloration due to bacterial contamination

- **CLOTS –**
  - Examine for any visible clots, especially in the plasma of a whole blood unit.
  - **NEVER** transfuse if clots are identified.

- **HAEMOLYSIS –**
  - Examine the supernatant plasma or suspending solution for a pink or red discoloration.
    NEVER transfuse if haemolysis is suspected.
    HOW - If the units stand for a period, the plasma or suspending solution separates
  - from the red blood cells and must be examined for haemolysis at the line separating the plasma and red blood cells.



Source: Visual Assessment Guide - Canadian Blood Services: Haemolysis

If any doubts with regards to the blood unit after inspection, consult with your local blood bank prior to commencement of the transfusion.

Section 5.4 - Handling & Administration of blood products:

Table 5.1 - Overview of handling and administration of blood products

Blood Product	RCC Whole Blood	Thawed FFP	Platelet Concentrate
Storage & Temperature	**Transport box:** 1 - 10°C **Blood fridge:** 1 - 6°C	**Transport box:** 1 - 10°C **Blood fridge:** 1 - 6°C	Transfuse immediately Do not store in wards Only stored on a platelet agitator; at 22°C ± 2 °C
Warming	Only when indicated	Only when indicated	Not indicated
Administration Set	Standard blood administration set with a 170-260-micron filter supplied by the hospital	Standard blood administration set with a 170-260-micron filter supplied by the hospital	Platelet administration set with a smaller area 170-260-micron filter & shorter line supplied by blood bank
Time limit to start infusion	Within 1 hour of removing unit from cold storage	As soon as possible after receiving unit in hospital ward; FFP expires 4 hours after thawing	Immediately after receiving unit in hospital ward
Maximum Infusion Time/Unit	4 hours/unit	30 min/unit	30 min/unit

To minimize the severity of possible transfusion reactions, the first 25 – 50 ml of each blood product should be transfused slowly and cautiously monitor the patient.

ORDER OF BLOOD AND BLOOD PRODUCT ADMINISTRATION:

The order at which blood and blood products are administered is essential to ensure that the maximum transport time of units are not exceeded, especially when multiple products have to be transfused (i.e., massive transfusions)

The order of transfusing multiple products is as follows –

1. Cryoprecipitate
2. Platelet Concentrate
3. Fresh Frozen Plasma
4. Red Cell Concentrate

Section 5.5 - Cautious monitoring & recording of a blood transfusion:

The risk of a transfusion reaction is 1-3% globally. Therefore, all recipients of blood products **MUST** be cautiously monitored during the transfusion to promptly identify and manage possible transfusion reactions.

Acute transfusion reactions may have detrimental consequences like haemolysis which can be fatal, but these can usually be prevented by stringent adherence to standard monitoring procedures before, during and after blood transfusion.
The majority of severe transfusion reactions occur within the first 15 – 30 minutes after commencement of a transfusion, therefore all recipients MUST be monitored closely during this period.

STAGES OF MONITORING –

- Baseline (before transfusion)
- 15 min after commencing transfusion
- 30 min after commencing transfusion
- ½ hourly throughout transfusion
- At the end of transfusion
- 4 h after completing transfusion
- 12 – 24 h after completing the transfusion if at risk of circulatory overload

WHAT PARAMETERS REQUIRES MONITORING –

- General appearance
- Blood Pressure
- Pulse
- Respiratory Rate
- Temperature
- Skin Changes

One should always be alert to any sudden change in these parameters. Once a sudden change in any of these parameters have been identified a doctor should be immediately alerted to initiate management as soon as possible.

Record all patient parameters at all stages on the MoHSS ½ hourly monitoring sheet or comparable alternative. Good documentation of all steps taken during a blood transfusion is of utmost importance, especially for look-back or legal investigations.

Section 5.6 - Additional transfusion safety measures:

5.6.1 - Aseptic Technique

Meticulous skin care and aseptic techniques is of utmost importance in transfusion medicine, as blood acts as an ideal culture medium for bacterial proliferation.

PROCEDURE FOR ASEPTIC NON-TOUCH TECHNIQUE (ANTT) CANNULATION –

- **Hand decontamination –**
  - Wash hands with soap and water.
- **Skin preparation –**
  - Clean the venepuncture site with the recommended hospital antiseptic solution from clean to dirty areas in a circular motion (inside to outside). Avoid re-palpation of the vein after the skin preparation.
- **Donning –**
  - While the antiseptic solution is drying, decontaminate hands and put on gloves.
- **Cannulation –**
  - Insert the appropriate size cannula in a suitable peripheral vein, preferably in the forearm and cover the transfusion site with a transparent dressing to ensure early identification of inflammation or infiltration
- **Waste management & Doffing –**
  - Ensure that waste is appropriately disposed.
  - Remove gloves and decontaminate hands.

5.6.2 - Changing of Blood Administration Sets:

CHANGING OF BLOOD ADMINISTRATION SETS MUST BE DONE IN THE FOLLOWING CIRCUMSTANCES TO ENSURE BLOOD RECIPIENT SAFETY –

- **Every 12 hours or after every 4 units, whichever comes first –**
  - Minimize the risk of bacterial proliferation, since aggregates and debris of the blood product can be trapped in the administration set filter and reduce blood flow, providing sufficient time for bacteria to proliferate.
- **Between red cell concentrates of different ABO groups and different blood products –**
  - Increases the risk of antigen-antibody reactions.
- **Immediately with the occurrence of a transfusion reaction –**
  - Prevent that harmful blood continue to enter the recipient's circulation.
- **Prior to the infusion of other intravenous fluids which contain calcium and/dextrose**
  - See Concurrent medication and fluid administration below.

5.6.3 - Concurrent medication & fluid administration:

THE CO-ADMINISTRATION OF FLUID AND/OR MEDICATION TO ANY BLOOD UNIT OR ADMINISTRATION SET IS NOT RECOMMENDED BECAUSE OF –

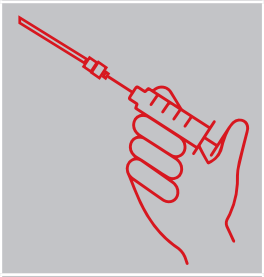
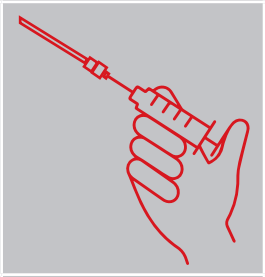
- Increased risk of bacterial proliferation
- Increased risk for interactions between the medication and additive solution/anticoagulant in the blood or blood component (i.e., Calcium or dextrose containing intravenous fluids)

MEDICATION –

Intermittent co-administration of morphine, pethidine or ketamine diluted only in 0.9% sodium chloride through the same IV line may ONLY be considered in cases where urgent administration is of these medications is required and no other IV access can be established.

Co-administration of these medications are ONLY then acceptable if the following procedure is followed:

Table 5.2 – Procedure for co-administration of medicines

1	2	3	4	5
				
STOP the transfusion	**Flush** the line with 0.9% sodium chloride	**Administer** the medication	**Flush** the line with 0.9% sodium chloride	**Continue** the blood transfusion

INTRAVENOUS FLUIDS –

ACCEPTABLE INTRAVENOUS FLUIDS –

The only intravenous fluids that may be administered concurrently through the administration set of a red cell transfusion are –

- **Normal Saline / 0.9% Sodium Chloride (THE ONLY UNIVERSAL COMPATIBLE IV FLUID)**
- Calcium-free Fluids (i.e., Plasmalyte-B / modified Ringer's lactate)
- Plasma protein fractions (i.e., Albumin 4% / Globulins)
- ABO-compatible plasma

UNACCEPTABLE INTRAVENOUS FLUIDS –

- Calcium-containing fluids (i.e., Hartmann's solution/Ringers Lactate) – The calcium in these fluids may cause citrated blood to clot.
- Dextrose containing fluids (i.e., 5% dextrose in water) & Hypotonic sodium solutions – These may cause lysis or aggregation of red cells.

If concurrent medication and intravenous fluid needs to be administered it is BEST TO OPT FOR AN ALTERNATIVE ACCESS SITE, however if this cannot be achieved the following should be done;

- Insert a multi-lumen access device (i.e. Y-piece) near the junction of the insertion of the transfusion cannula. If a continuous IV infusion is required and a multi-lumen access device is not available a second IV access must be obtained.

ESSENTIALS

The administration of two blood products concurrently via separate IV access lines is not recommended, because in case of a transfusion reaction the responsible blood product cannot be ascertained. However, this situation may arise in the setting of critical bleeding.

5.6.4 - Warming of Blood Products:

Warming of blood components are not routinely indicated and cold blood may be administered at a slow rate without causing harm. However, in cases where a rapid transfusion is required the warming of blood is recommended to prevent complications such as cardiac arrhythmias.

INDICATIONS FOR WARMING OF BLOOD –

- **Rapid transfusions**
  - >50 mL/kg/hour in adults
  - >15 mL/kg/hour in children
- **Exchange transfusions/procedures**
  - Neonatal exchange transfusions
  - Therapeutic plasma/red cell exchange
- **Patient re-warming is required**
  - Cardiopulmonary bypass surgery rewarming phase
  - Core-rewarming in severe trauma with hypothermia
- **Patients with clinically significant cold agglutinins**
  - Cold agglutinins are antibodies that cause the red blood cells to clump together at cold temperatures.
  - The blood bank will inform the prescribing medical practitioner if this is the case

HOW TO WARM BLOOD –

Blood MUST only be warmed with a blood warmer specifically designed and approved for this purpose.

GENERAL BLOOD WARMER/WARMING RECOMMENDATIONS –

- Require a visible temperature-monitoring device and an audible alarm.
- Require priming of administration sets as for normal blood transfusions.
- Require recording of the blood warmer operating temperature on the blood transfusion record.
- NEVER warm blood above 37°C, since it can cause extensive haemolysis of red cells which can be fatal.

INCORRECT warming of blood & blood products may result in adverse reactions which can compromise recipient's safety, therefore –

- **NEVER WARM BLOOD PRODUCTS IN WARM WATER (I.E., IMPROVISED WATER BATH) –**
  - Ineffectual as only the outermost layer of the red cells is warmed.
  - Increases the risk for haemolysis due to overheating.

  - Increases the risk of bacterial contamination of the unit, as the ports of the blood bag might become contaminated.
- **NEVER WARM BLOOD PRODUCTS IN A MICROWAVE –**
  - Warming of blood in a microwave will result in extensive haemolysis of the red cells which can be fatal for the recipient.
- **NEVER WARM BLOOD PRODUCTS BY RUBBING THE UNIT –**
  - Increases the risk of haemolysis of the outermost layer of red cells due to the friction.

ESSENTIALS

- **Identification & verification of the patient and the blood product(s) is the most crucial step before administration to ensure that the good transfusion practice of transfusing the RIGHT BLOOD to the RIGHT PATIENT at the RIGHT TIME is followed.**
- **The Maximum infusion time of blood and blood products MUST NEVER be exceeded therefore it must be transfused in the following order; cryoprecipitate, platelet concentrate, fresh frozen plasma then red cell concentrate.**
- **Co-administration of fluid and/or medication to any blood unit or administration set is NOT RECOMMENDED.**
- **Warming of blood is only recommended in certain situations and may ONLY be warmed with a blood warmer.**

REFERENCES

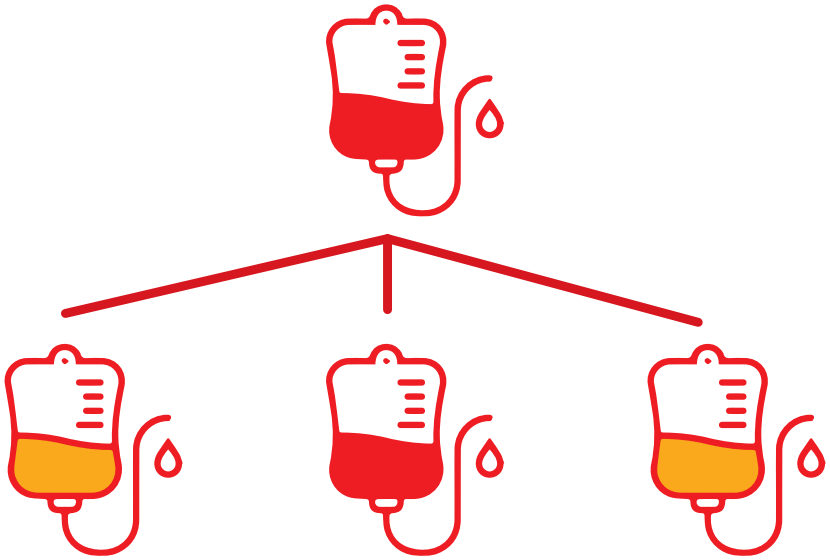
- Australian and New Zealand Society of Blood Transfusion Australian College of Nursing. Guidelines for the Administration of Blood Products, 3rd Edition, 2024. Accessed 22 September 2024. https://anzsbt.org.au/wp-content/uploads/2024/02/Guidelines-for-the-Administration-of-Blood-Products-revised-Feb-2024.pdf
- The South African National Blood Service and the Western Cape Blood Service. Clinical guidelines for the use of blood products in South Africa, 6th Edition, 2023. Accessed 15 August 2024. https://www.wcbs.org.za/wp-content/uploads/2023/09/Clinical-Guidelines-of-appropriate-use-for-the-use-blood-and-blood-products-in-South-Africa-6th-edition-2023-FINAL.pdf
- Canadian Blood Services. Professional Education. Transfusion: Visual Inspection Tool. 2024. Accessed 20 August 2024. https://professionaleducation.blood.ca/en/visual-inspection-tool

CHAPTER 06
BLOOD PRODUCTS & INDICATIONS

A WHOLE BLOOD DONATION CAN BE PROCESSED INTO DIFFERENT COMPONENTS. COMPONENT THERAPY IS RECOMMENDED, SINCE BLOOD COMPONENTS –

- Have different indications, which may only require a specific component transfusion.
- Component separation ensures **treatment of several patients** with a single whole blood donation, thus, ensuring maximum utilization of blood product.
- Are stored under different conditions to **preserve the function** of the constituents to ensure therapeutic efficacy.
  - I.e., if whole blood is stored at 4°C, only a few platelets will remain viable and labile coagulation factors, such as factor V and VIII, will decrease.

WHOLE BLOOD



Platelet Components
- Platelet Concentrates

Red Cell Components
- Red Cell Concentrate (RCC)
- Leucodepleted RCC
- Washed RCC
- Cryopreserved (Frozen) (RCC)
- Irradiated RCC

Plasma Components
- Fresh Frozen Plasma (FFP)
- Freeze dried Plasma
- Cryoprecipitate
- Plasma Derived Medicinal Products (PDMP's)

Section 6.1 - Whole Blood:

Whole blood, is blood obtained from a standard blood donation where none of its components are separated or removed. Whole blood contains red blood cells, white blood cells and platelets which are all suspended in plasma.

Whole blood transfusions are usually limited, since RCC are more appropriate in most clinical situations which require an increase in oxygen-carrying capacity.

PRODUCT DETAILS –

- **Volume/unit:** 468 - 558 ml including ± 60 ml of citrate, phosphate, and dextrose (CPD) anticoagulant-preservative solution, which contains 0.2 g citrate.
- **Storage temperature:** 1 - 6°C
- **Max. storage time:** 21 days (calculated from the day of collection)

INDICATIONS FOR FRESH WHOLE BLOOD TRANSFUSIONS (LESS THAN 5 DAYS OLD)–

Neonatal exchange transfusion –

- Exchange transfusion for clinically significant anaemia +/- hyperbilirubinaemia due to haemolytic disease of the foetus or newborn (HDFN) or other causes.

Intrauterine transfusion –

- Also known as foetal blood transfusion, is a therapeutic procedure performed in the prenatal period where whole blood is transfused intravascularly through the umbilical vein under ultrasound guidance to treat severe foetal anaemia.

Massive haemorrhage –

- Large volume blood loss, especially in major trauma where a massive transfusion and rapid correction of anaemia, coagulopathy, acidosis, and hypothermia are required.
- This is supported by studies in military trauma where fresh (<24 hours) whole blood units are transfuse, however this is not recommended amongst civilians. Alternatively, where fresh < 24 hours whole blood is not available, component therapy in a 1:1:1 ratio for the management of massive haemorrhage is strongly recommended.

REQUIREMENTS –

Whole blood for neonatal exchange and intrauterine transfusions, MUST be –

- **Compatible** (Group O Negative or Compatible with maternal plasma antibodies)
- **Fresh** (< 5 days old)
- **Low Titre & have no irregular antibodies** (Contain no high titres of anti-A & anti-B, and also have no other irregular antibodies).
- **Leucodepleted & CMV negative** (Optimal removal of leucocytes with pre-storage filtration to minimize cytokine release & CMV transmission).

THERAPEUTIC EFFECT/UNIT –

- Haemoglobin increment of **1 g/dl** in an average 70 kg patient.
- No effect on haemostasis, due to non-functional platelets & deterioration of labile clotting factors, especially factors V and VIII.

RECONSTITUTED WHOLE BLOOD ESSENTIALS
It is recommended for exchange transfusion in severe RhD HDFN!

- A compatible red blood cell unit which is leukocyte reduced is washed to remove additive solution before reconstituting it in thawed AB plasma.
- Reconstituted whole blood is immunologically safer and better than whole blood for exchange transfusion.
- Reconstitution of whole blood can take about 3 hours to prepare & expires within 24 hours.

Section 6.2 - Red Cell Products:

Red cells concentrate is the commonest transfused blood component and the major driver of blood transfusion within Namibia. Red cell components are mainly used to restore the oxygen carrying capacity in patient with clinically significant anaemia and blood loss where alternatives to a transfusion is ineffective or inappropriate.

6.2.1 – Standard Red Cell Concentrate (in additive solution):

PRODUCT DETAILS –

- **Volume/unit:** 230 - 330 ml including ± 111 ml of preservative solution that contains saline, adenine, glucose and mannitol additive solution (SAG-M).
- **Storage temperature:** 1 - 6°C
- **Max. storage time:** 42 days (calculated from the day of collection)

INDICATIONS FOR TRANSFUSION –

Red blood cell transfusions should not be based on haemoglobin level alone as it is of little value in patients with acute blood loss and/or those with anaemia with a reduced oxygen carrying capacity which compromise oxygen delivery.

ACUTE BLOOD LOSS –

- An acute blood volume loss of > 30% (+/- 1500 mL in an adult) mainly due to traumatic, gastrointestinal and obstetric haemorrhage will require red cell transfusions.
- There should be no delay in ordering and administration of red cell concentrates as an acute blood loss of >30% of the total blood volume can cause life-threatening circulatory failure.
- Red cell transfusion is crucial in patients with acute blood loss if there are symptoms and signs of anaemia, hypoxia, haemorrhagic shock and presence or risk for ongoing blood loss (See Chapter 7, Section 7.6).

ANAEMIA WITH A REDUCED OXYGEN CARRYING CAPACITY COMPROMISING OXYGEN DELIVERY –

- Usually indicated if Hb falls to **< 7 g/dL** in patients **without any cardiovascular risk factors** (See Chapter 3, Section 3.3)

- **Factors other than haemoglobin to take into consideration for transfusion –**
  - **Acute vs. Chronic Anaemia** – Better anaemia tolerance is seen in chronic anaemia due to the development of long-term compensatory mechanisms.
  - **Cause of anaemia** – The presence or risk for ongoing blood loss requires a higher haemoglobin target.
  - **Physiological reserves** – Patients with a normal cardiopulmonary reserve, namely a normal cardiac output and oxygenation, will tolerate anaemia better.

The appropriate principles of Patient Blood Management must be applied in all patients BEFORE a red cell component transfusion is considered.
(See Chapter 3)

ESSENTIALS

- **Do NOT TRANSFUSE RCC's** to an asymptomatic, non-bleeding in-patient with a Hb above 7 g/dL.
- When possible, transfuse **ONE UNIT** at a time and reassess the patient if not actively bleeding.

DOSAGE & THERAPEUTIC EFFECT/UNIT

Factors other than haemoglobin to take into consideration for transfusion

Volume (mL)=(Target Hb (g/dL)-Actual Hb(g/dL))×weight (kg)×4 (Transfusion Factor)

Repeat the haemoglobin (Hb) 1 – 4 hours after the completion of the red cell transfusion to determine the increment –

- A single RCC results in a Hb increment of **1 – 1.5 g/dl** in an average 70 kg patient.

RED CELL TRANSFUSION COMPATIBILITY –

Red cell transfusions must ALWAYS be ABO and Rh-D compatible. However, in an emergency a Rh-D incompatible transfusion may be issued to males or elderly women or women who do not plan to have children in the future. Rh-D-positive red cells may be transfused to a Rh-D-negative patient provided that the patient has not been sensitized previously, i.e., have Rh-D-antibodies. Rh-D incompatible transfusions can result in complications such as haemolytic transfusion reactions, alloimmunization and potential haemolytic disease of the fetus and newborn (See Chapter 8, Section 8.2)

Rh-D incompatible red cell transfusions MUST be AVOIDED in –

- Rh-D-negative girls and women of childbearing age
- Rh-D-negative men and women of non-childbearing age who were previously sensitized through Rh-D incompatible transfusion, childbirth, miscarriages or abortions.

Table 6.1 Blood group compatible red cell transfusion:	
Patient's Blood Group	**ABO Compatible RCC's**
A+	A+, A-, O+ or O-
A-	A- or O-
B+	B+, B-, O+ or O-
B-	B- or O-
AB+	AB+, AB-, A+, A-, B+, B-, O+ or O-
AB-	AB-, A-, B- or O-
O+	O+ or O-
O-	O-

6.2.2. - Special Red Cell Products

Some red cell products are only available on special request for specific clinical indications, namely –

- Leucodepleted RCC
- Washed RCC
- Cryopreserved (Frozen) RCC
- Irradiated RCC

LEUCODEPLETED RCC

RCC's are leucodepleted when leucocytes are removed to a level below 5×10^6 per RCC. The filtration to reduce leucocytes should be performed within 5 days of blood donation also known as pre-storage leuco-filtration. Leucodepleted products reduce the frequency and/or severity of febrile non-haemolytic transfusion reactions (FNHTRs), HLA-alloimmunization, CMV transmission and infections associated with immunomodulation (TRIM) in patients who are chronically transfused.

Product Details –

- **Volume/unit:** 85% - 100% of a standard RCC depending on amount of RCC lost during leucodepletion.
- **Storage temperature:** 1 - 6°C
- **Max. storage time:** 42 days (calculated from the day of donation)

Indications –

- All paediatric patients less than 1 year of age, especially if born prematurely and in the early neonatal period (first 28 days of life) and intrauterine transfusions.

- Patients on chronic transfusion regimens, i.e. Aplastic & Sickle Cell Anaemia.
- Haematological malignancies, i.e. Leukaemia, Lymphoma etc., especially when a stem cell/ bone marrow transplant is required.
- Patients with End-Stage Renal Disease requiring a renal transplant.
- Patients with severe autoimmune diseases, i.e. Systemic Lupus Erythematosus (SLE) & Autoimmune Haemolytic Anaemia.
- Immunocompromised patients at risk of CMV transmission
- Patients with recurrent Febrile Non-Haemolytic Transfusion Reactions (FNHTR)

Therapeutic effect/Unit –

- Same clinical outcome as a standard RCC which results in a Hb increment of 1 g/dl in an average 70 kg patient.

WASHED RCC

Washed red blood cells are when the residual plasma is removed from a standard red cell concentrate and replaced with 0.9% normal saline to reduce the risk of adverse reactions associated with plasma proteins, potassium levels or antibodies in the plasma. The preparation of washed red blood cells can be done either through manual or automated methods, however NAMBTS only make use of the manual preparation.

Product Details –

- **Volume/unit:** 85% - 100% of a standard RCC depending on amount of RCC lost during washing.
- **Storage temperature:** 1 – 6 °C
- **Max. storage time:** Expires 24 hours after washing of red cells.

Indications –

- Patients with recurrent severe allergic transfusion reactions, regardless of IgA status.
- Patients with IgA deficiency when IgA deficient donors are not available.
- Neonates with T-cell activation due to exposure of the red cell T-crypt antigens by a bacterial infection, typically necrotizing enterocolitis, which results in immune-mediated haemolysis when RCC's containing plasma are transfused to these patients as all human plasma contain antibodies to T-crypt antigens.
- Patients who are at risk of severe hyperkalaemia as an alternative to fresh standard red cells concentrates (ONLY IF FRESH RCC's ARE UNAVAILABLE).

Therapeutic effect/Unit –

- Same clinical outcome as a standard RCC which results in a Hb increment of **1 g/dl** in an average 70 kg patient.

CRYOPRESERVED (FROZEN) RCC

Cryopreserved RCC, also known as frozen RCC are prepared by freezing red cells in a cryoprotective solution which consist of 40% glycerol, to prevent damage to red blood cells during freezing and thawing. RCC are cryopreserved to store RCC for a long period of time.

Product Details –

- **Storage temperature:** - 60°C to - 82°C
- **Max. storage time:**
  - Up to 10 years from date of donation if storage temperature is continuously maintained below

- 65°C. However, some blood services may extend to the maximum storage time of up to 30 years if stored at – 80°C, since there is no published evidence to suggest adverse effect with extended storage.
- Once thawed and washed to remove the cryoprotectant, it expires after 24 hours.

- Only available from Rare Donor Blood Banks (i.e., in Durban, South Africa).

Indications –

- Patients with antibodies against high-frequency red cell antigens.
- Patients with complex and multiple antibodies
- Patients with extremely rare blood groups.
- Future autologous blood transfusions

Therapeutic effect/Unit –

- Same clinical outcome as a standard RCC that results in an Hb increment of 1 g/dl in an average 70 kg patient.

IRRADIATED RCC

Irradiation of red cell concentrates is the only method available for prevention of transfusion associated Graft vs. Host Disease (TA-GvHD), however this is **not currently available in Namibia.** Although this is a rare condition it can occur under certain circumstances, such as when the patient is immunosuppressed, i.e., due to T-lymphocyte immunodeficiency syndromes, or when during organ transplant. TA-GvHD may also occur when a patient receives blood components from a donor who shares an HLA haplotype with the patient, i.e., in the case where the blood donor is a first or second-degree relative of the patient (a directed donation between close relatives).

TA-GvHD occurs when residual lymphocytes in the blood unit engraft and proliferate in the recipient after the transfusion, which causes cellular interactions between donor T lymphocytes and recipient cells causing the donor T lymphocytes to mount an immune response against the recipient cells leading to cellular and organ damage. Although the incidence of TA-GvHD is extremely rare it is usually fatal, with a mortality rate of 98 – 99%.

Indications –

- Severe congenital T-lymphocyte immunodeficiency syndromes
- Intrauterine transfusions and neonatal exchange transfusions, especially infants or children with a previous history of intrauterine transfusions.
- Recipients of cellular components from first- and/or second-degree relatives.
- Patients undergoing bone marrow or peripheral blood progenitor cell transplantation
- Patients with Hodgkin's disease, leukaemia, or lymphoma and/or those undergoing intensive chemotherapy or immunosuppressive therapy.
- Patients with chronic graft-versus-host disease and/or on continued immunosuppressive treatment is required.

6.2.3 - Paediatric Red Cell Concentrate

PRODUCT DETAILS –

- Volume/unit: 80 -120 ml including ± 38 ml of additive solution, since a single paediatric RCC unit is prepared by dividing one standard adult RCC unit into 3 paediatric RCC units.
- Storage temperature: 1 - 6°C
- Max. storage time: 42 days (calculated from the day of collection)

INDICATIONS FOR TRANSFUSION –

The indications for paediatric RCC transfusions are similar to that of standard RCC transfusions, however the haemoglobin thresholds for RCC transfusions vary with age and the clinical condition of the patient (See Chapter 7, Section 7.1).

DOSAGE & RATE OF TRANSFUSION –

Dosage –

The usual paediatric dose for red cell transfusions is **10 – 20 ml/kg**, however an initial dose of 15ml/kg is ideal. The ideal volume for transfusion in premature infants and neonates is **5 – 15 ml/kg** due to the association of large volume transfusions in very low birth weight infants with necrotizing enterocolitis.

Transfusion volumes in paediatric patients should be determined as follow

Volume (mL)=(Target Hb (g/dL)-Actual Hb(g/dL))×weight (kg)×4 (Transfusion Factor)

Rate –

- **Initial Rate:** 1 ml/kg/hr (Start slow for the first 15 minutes)
- **Administration Rate:** 5 ml/kg/hr, up to a maximum rate of 150ml/hr

THERAPEUTIC EFFECT/UNIT –

- Each 10 – 15 ml/kg red blood cells transfused results in a Hb increment of about **1 – 2 g/dl**

PAEDIATRIC RED CELL TRANSFUSION COMPATIBILITY –

Red cell transfusions in paediatric patients under 4 months of age must ALWAYS be ABO and Rh-D compatible to both the mother and child;

Why?

- Neonates do not produce their own red cell antibodies during the first 4 months of age.
- Maternal antibodies cross the placenta into fetal circulation from the second trimester of pregnancy onwards. Therefore, compatibility must be determined against the mother's antibodies which are in the infant.

Section 6.3 - Platelet Products

Platelet transfusions are used mainly for management of platelet-related bleeding disorders. The underlying cause for bleeding should ALWAYS be identified and addressed accordingly before a platelet concentrate transfusion is considered, since it still carries a risk for transfusion adverse events and is costly.

6.3.1 - Standard Platelet Concentrates (for adult patient transfusion)

PLATELET PRODUCTS DETAILS –

Two types of platelet products –

Random Donor Pooled Platelets –

- Are platelets which are derived from the buffy coat of 4 - 5 whole blood donations of the same ABO group and suspended in either in 100% plasma or +/- 30% plasma & +/- 70% Platelet Additive Solution (PAS).
- All pooled platelets supplied by NAMBTS are leucodepleted. Leucodepletion of the platelet concentrates by leuco- filtration is performed at the time of pooling using a special leucocyte filter. Leucodepletion reduces white blood cells to 10x105 per platelet concentrate bag.

Single Donor Apheresis Platelets –

- Are platelets collected from a single donor by means of an apheresis procedure. The apheresis machine separates the donor blood in components, and remove the platelets and different amounts of plasma from the donor blood and return the remaining blood components back to the donor.
- These platelets extracted from the donor are then suspended in either 100% plasma or in +/- 30% plasma & +/- 70% PAS.
- NAMBTS currently suspend all platelets components in PAS (30% plasma & 70% PAS). Suspending platelets in PAS as opposed to 100% plasma reduces the incidence of transfusion reactions which usually caused by excessive plasma or white blood cells such as allergic reactions and TRALI (transfusion related acute lung injury).
- Leucodepletion of platelet concentrates is part of the apheresis collection procedure.
- A single donation with a high platelet yield can be split into 2 or 3 platelet products to benefit more than one adult patients.

Currently NAMBTS provides leucodepleted platelets products for all patients.
However, apheresis platelets are provided for specific indications (See Table 6.2)

The following is the same for both pooled and apheresis platelet products;

- **Volume:** 200 – 300 ml/unit
- **Platelet Count/Yield per unit:** 2.4 – 4.8 x 10^{11}/L (Indicated on the label of the platelet bag)
- **Storage Temperature:** 20 – 24 ^{0}C
- **Maximum Storage Time:** 5 – 7 days (calculated from the day of collection) on a platelet agitator. The platelet storage time may only be extended to 7 days with sterility testing of platelets due to the increased risk for bacterial contamination.

INDICATIONS –

A platelet transfusion is mainly used for prophylactic or therapeutic management of platelet related bleeding, due to a reduced platelet count or dysfunctional platelets (See Chapter 1: Table 1.4). A platelet transfusion is ONLY indicated to prevent and/or stop platelet related bleeding.

Recommendation regarding platelet transfusions in adults, table 6.2, have been adopted from the British Society for Haematology and AABB guidelines. These recommendations for platelet transfusions should only be used as a guide and clinicians are still expected to take the clinical condition of the patient, setting and alternatives to a platelet transfusion (i.e., TXA) into consideration.

Table 6.2 – Indications for Platelet Transfusions in Adults

Indication	Platelet count threshold above which transfusion is not indicated
Prophylactic use (No bleeding or WHO grade 1) One Adult dose required	
- Reversible bone marrow failure (BMF) including allogeneic stem cell transplant	10 x 10^9/L
- Reversible BMF with autologous stem cell transplant (Consider no prophylaxis)	10 x 10^9/L
- Critical Illness	10 x 10^9/L
- Chronic (irreversible) BMF receiving intensive therapy	10 x 10^9/L
- Chronic (irreversible) BMF to manage persistent bleeding of WHO grade >2	Count Variable
- Chronic stable BMF, dysfunctional platelets, platelet consumption/destruction (I.e. DIC/TTP) or immune thrombocytopenia (ITP, HIT, PTP)	Not Indicated
Prophylactic use in the presence of risk factors for bleeding (i.e., Sepsis, antibiotic treatment, haemostasis abnormalities)	
- Reversible/Chronic BMF or critical care	10 – 20 x 10^9/L
- Platelet dysfunction, platelet consumption/destruction, immune thrombocytopenia	Not Indicated
Prophylactic pre-procedure platelet transfusion (i.e. Surgery or Invasive Procedures)	
- Venous Central Line Insertion (Inserted by experienced staff and USG)	20 x 10^9/L
- Minor Surgery thrombocytopenia	30 x 10^9/L

Indication	Platelet count threshold above which transfusion is not indicated
- Lumbar Puncture	40 - 50 x 10^9/L
- Major Non-Neuraxial Surgery	50 x 10^9/L
- Percutaneous Liver Biopsy	50 x 10^9/L
- Insertion/Removal of an Epidural Catheter	80 x 10^9/L
- Neurosurgery/Ophthalmic Surgery of the posterior segment of the eye	100 x 10^9/L
- Peripheral central catheter insertions, Traction removal of tunnelled central venous catheters, Bone marrow aspirates or trephine biopsies & Cataract surgeries	Not Indicated
**Indications for pre-procedure prophylaxis in specific clinical conditions – see below*	
Therapeutic Platelet Transfusion (WHO grade 2 or more)	
- Severe bleeding	Maintain > 50 x 10^9/L
- Multiple trauma, brain or eye trauma, spontaneous intracerebral haemorrhage	Maintain >100 x 10^9/L
- Bleeding (WHO grade >2) but not severe or life-threatening	Consider if < 30 x 10^9/L
**Bleeding in specific clinical conditions – see belowNot Indicated*	
Specific Clinical Conditions	
Platelet Dysfunction: - **Congenital** – Pre-procedure or therapeutic use. Consider when alternative pharmaceuticals are contraindicated or ineffective or there is a high risk of bleeding. - **Acquired –** (anti-platelet agents/ uraemia in renal failure) – only indicated for severe bleeding.	Count Variable

Specific Clinical Conditions	
Disseminated Intravascular Coagulopathy: - Pre-procedure or therapeutic use. - These usual threshold counts may not be achievable and individual case review is required.	Use pre-procedure or therapeutic threshold as guide
Thrombotic Thrombocytopenic Purpura: - A platelet transfusion is contraindicated unless life-threatening bleeding	Count Variable
Immune Thrombocytopenia (ITP, HIT, PTP): - Pre-procedure uses only when other therapy is contraindicated or ineffective, or the procedure is urgent. - Therapeutic when there is severe bleeding. - These usual threshold counts above may not be achievable or unnecessary and individual case review is required.	Use pre-procedure or therapeutic threshold as guide

NOTE

AABB recommends a prophylactic platelet transfusion in hospitalized adult patients with a platelet count of ≤ 10 x 10^9/L to reduce the risk of spontaneous bleeding. Each case must be reviewed on a case-to case basis considering the patients clinical condition and one's setting.

Possible alternatives to platelet transfusion:

- ***Surgical Patients:***
  - Give TXA if not contraindicated for procedures with an EBL of > 500ml.
  - Apply compression after superficial procedures.
  - Correct surgical causes of bleeding.
- ***Trauma Patients:***
  - Give TXA to trauma patients with severe bleeding/ bleeding risk.
  - Replace fibrinogen in patients with severe bleeding if the plasma value is < 1.5 g/L
- ***Medical Patients:***
  - Consider TXA in chronic (irreversible) BMF.
  - Consult a haematologist and consider desmopressin in patients with inherited platelet functional disorders.
  - Discontinue anti-platelet agents or if require an urgent procedure/bleeding use TXA.

DOSAGE-

The minimum platelet dosage per single unit in Namibia is 2.4 x 10^11 platelets per unit. Studies that demonstrated that low-dose prophylactic platelet transfusions have the same clinical outcome as high-dose with a lower risk of adverse events.

If a platelet transfusion is indicated, it is recommended to transfuse ONLY a single unit per transfusion episode –

- More than a single unit of platelets per transfusion episode should only be considered in patients with severe thrombocytopenia and critical site bleeding (i.e., CNS & eyes).
- **A single unit platelet transfusion approach is preferred for several reasons, namely –**
  - Reduce transfusion associated risks, such as transfusion circulatory overload by avoiding over transfusion.
  - Avoid unnecessary platelet transfusions, as a single unit is usually sufficient.
  - Platelets need to be stored on a platelet agitator to prevent platelet aggregation and maintain optimum functioning.

THERAPEUTIC EFFECT –

Repeat the platelet count between 10 – 60 minutes after the completion of the transfusion to determine the platelet increment –

- A single platelet transfusion typically results in an increment of **30 – 50 x 10^9/L.**

The most accurate way to determine the outcome of a platelet transfusion is by determining the corrected count increment (CCI) as follow -

$$CCI = \frac{\text{(Platelet increment} \times \text{body surface area (m}^2\text{))}}{\text{(Platelet dose (x } 10^{11}\text{)}}$$

Platelet increment is the difference between the pre- and post-transfusion platelet count.
https://www.mdcalc.com/calc/4034/corrected-count-increment-cci-platelet-transfusion

- Platelet count in Namibia is on **average 3 x 10^{11} platelets** per unit:
  - The platelet dose is indicated on the label of the unit.
- **An undesirable platelet increment based on the following CCI's indicate possible platelet transfusion refractoriness:**
  - 1-hour post transfusion: < 7.5
  - 18 – 24 hours post transfusion: < 4.5

Platelet Transfusion Refractoriness:

Platelet refractoriness is a recurrent suboptimal response to platelet transfusions when the post-transfusion platelet count increments are lower than expected due to a reduced survival of platelets in the recipients' circulation caused by immune and non-immune mediated factors as indicated in table 6.3.

Table 6.3: Causes of Platelet Refractoriness	
Immune-mediated (10 – 25%)	**Non-immune mediated (60 – 80 %)**

- Antibodies against HLA Class 1
  - Most commonly implicated
  - HLA alloimmunization occur typically due to pregnancy, blood transfusions or transplants.
- ABO-mismatched platelets
- Antibodies against Human Platelet Antigen (HPA)
- Antibodies against drug-platelet glycoprotein complex
	- Infection/Sepsis
	- Haemorrhage
	  - Increased platelet consumption
	  - DIC
	- Microangiopathic haemolytic anaemia
	- Splenic Sequestration
	- Drug-induced (i.e., Amphotericin B, Vancomycin, Heparin, Interferons etc.)

ABO-compatible and leucodepleted platelets can eliminate potential variables which cause platelet refractoriness –

- **ABO-compatible Platelets:**
  - ABO-compatible platelets have a better platelet increment than ABO-incompatible platelets in patients with high titres of Anti-A or Anti-B antibodies which result in clearance of donor platelets with the same ABO antigens. However, the risk is reduced in platelets suspended in PAS due to the fact that the antibodies are removed along with plasma.

- **Leucodepleted Platelets:**
  - Leucodepleted platelets are associated with a reduction in HLA alloimmunization and/or reactions due to the removal of most residual white blood cells which cause the formation of antibodies against HLA.

PLATELET COMPATIBILITY –

Platelet transfusions or patients with platelet refractoriness, should ideally be given crossmatched platelets which are compatible with anti-HPA antibodies.

6.3.2 - Paediatric Platelet Concentrate

PLATELET PRODUCTS DETAILS –

Paediatric apheresis platelets products are prepared by dividing a single mega unit apheresis platelet into 2 to 3 units which is routinely leucodepleted as part of the apheresis collection procedure.

Product details;

- ***Volume:*** 40 - 60 ml/unit
- ***Platelet Count/Yield per unit:*** > 6.0 x 10^10/L (Indicated on the unit bag)
- ***Storage Temperature:*** 20 – 24 ^{0}C
- ***Maximum Storage Time:*** 5 – 7 days (calculated from the day of collection) on a platelet agitator.

INDICATIONS –

Paediatric transfusions are complex due to a wide age range and a lack of literature in the paediatric population. Therefore, these recommendations for paediatric platelet transfusions in table 6.4 are drawn from adult literature and clinical expertise. In addition, it is advised to consult a paediatrician.

Platelet transfusions in neonates –

Table 6.4 – Indications for Platelet Transfusions in Neonates

Indication	Platelet Threshold
- Neonates with no bleeding (including those with NAIT if not bleeding and no family history of ICH)	< 25 x 10^9/L
- Neonates with bleeding, coagulopathy, prior to surgery, or infants with NAIT and a previously affected sibling with ICH,	< 50 x 10^9/L
- Neonates with major bleeding or requiring major surgery	< 100 x 10^9/L

***NAIT – neonatal alloimmune thrombocytopenia, ICH – Intracranial Haemorrhage**

Prophylactic transfusion should be considered in all neonates with a platelet count of less than 30 x 10^9/L, but consider less than 50 x 10^9/L if –

- Clinically unstable
- Premature neonates < 1000kg or < 1 week
- Bleeding, including intraventricular haemorrhage in neonates
- Coagulopathy, including the use of medication that can alter platelet function.
- Prior to a surgery or invasive procedure, including exchange transfusions.

The suggested platelet thresholds in table 6.4 can be used for both preterm and term neonates, especially in term neonates admitted in the intensive care setting. More liberal thresholds are often considered in unstable preterm neonates than stable term neonates, due to thrombocytopenia and increased associated risk of intra- and periventricular haemorrhage.

Neonatal Alloimmune Thrombocytopenia (NAIT)

NAIT is caused by maternal HPA 1a and 5b antibodies against antigens on the foetal platelets. It results in thrombocytopenia in an otherwise healthy neonate which commonly results in bruise or petechiae, but can also cause severe intracranial haemorrhage in the early neonatal period.

It is recommended to maintain the platelet count in these neonates above 30 x 10^9/L if there is an associated bleeding risk by transfusing the baby with HPA-compatible platelets and administer

intravenous gamma globulins. **HPA-compatible platelets can be obtained from the mother by means of an apheresis collection,** however it must be suspended in PAS with minimal plasma in the unit. Irradiation of the maternal platelets are also recommended to prevent TA-GvHD, however this is not a service currently available in Namibia.

Platelet transfusions in older children –

In older children adult guidelines are often resorted to due to the lack of literature, especially for prophylactic platelet transfusions. A prophylactic platelet transfusion is usually recommended if the platelet count is less than 10 x 10^9/L in stable children, except for those with ITP, TTP, HUS, and HIT who should only be transfused therapeutically if they present with severe or life-threatening bleeding. Therapeutic platelet transfusions are generally indicated in any child with thrombocytopenia and active bleeding (See table 6.2).

DOSAGE –

If a platelet transfusion is indicated, it is recommended to transfuse 10 – 20 ml/kg –

- It should be transfused with a standard platelet administration set over 30 minutes, typically at a rate of 10 – 20ml/kg/hr.

THERAPEUTIC EFFECT –

Repeat the platelet count between **10 – 60 minutes after the completion** of the transfusion and calculate the **corrected count increment (CCI)** as discussed under adult platelet concentrates to determine the outcome of the transfusion.

PLATELET COMPATIBILITY –

See under adult platelet compatibility.

Section 6.4 - Plasma Products & Derivatives

Plasma components and derivatives are used mainly for the management of a patient who is bleeding or undergoing an invasive procedure with coagulation factor deficiencies. These products containing coagulation factors are prepared either from whole blood, i.e., Fresh Frozen Plasma, or by plasma fractionation, i.e., plasma derived medicinal products (PDMP's).

6.4.1 - Fresh Frozen Plasma (FFP)

PLASMA PRODUCTS DETAILS –

Fresh frozen plasma (FFP) is the most commonly used plasma product and can be prepared by means of centrifugation of a whole blood and separation from red cells and buffy coat using specialized equipment. FFP may also be collected from a donor using an apheresis procedure similar to the one for platelets. Once prepared from whole blood or apheresis procedure, the FFP is frozen within 6 - 18 hours to preserve the function of labile coagulation factors, such as factor V and VIII.

FFP product details;

- **Volume: 220 – 350 ml/unit** including about 60 ml anti-coagulant preservative solution.
- **Storage Temperature:** below minus (-) 25 ^{0}C
- **Maximum Storage Time:** It can be stored for up to 1 years if stored below minus (-) 20oC or up to 3 years if stored below minus (-) 25 ^{0}C (all calculated from the day of whole blood or plasma collection).

NOTE

Once plasma has been thawed it may be stored at 1 – 6 ^{0}C for a maximum of 24 hours. Ideally FFP should be transfused within 4 hours of thawing, due to labile coagulation factors that deteriorate with extended storage.

All FFP units issued by NAMBTS is donor-retested plasma, which means that no unit will be released until the donor has a subsequent Transfusion Transmissible Infection (TTI) negative donation, to minimize the risk of transmitting TTIs during the window-period stage of the infectious disease.

INDICATIONS –

Fresh Frozen Plasma (FFP) transfusions are mainly recommended for the replacement of multiple coagulation factor deficiency. FFP transfusions in adult patients are therefore recommended in accordance to table 6.5.

Table 6.5 – Indications for FFP in adult patients

Indication	Comment
Single Coagulation Factor Deficiencies	- Only when specific factor concentrate is unavailable, inappropriate or contraindicated.

Multiple Coagulation Factor Deficiency	- **Massive Blood Transfusion;**
	  - Dilutional coagulopathy with clinically significant haemostasis abnormalities and coagulation screening tests.
	  - Empirically as part of the Massive Transfusion Protocol (MTP) at a ratio of 1:1:1(RCC: FFP: platelet), due to a reduction in the risk of multi-organ failure and death.
	- **Disseminated Intravascular Coagulopathy (DIC);**
	  - Only indicated when the consumptive coagulopathy is complicated by active bleeding to maintain the PT/aPTT around 50% or the norm and fibrinogen > 1.5 g/L.
	  - Cryoprecipitate is indicated if the fibrinogen is severely reduced to less than 1.5 g/L.
	- **Liver Disease;**
	  - Appropriate in the presence of active bleeding and abnormal coagulation screening tests, or prophylactic prior to an invasive procedure.

Indication	Comment
	- Patients with liver disease are at increased risk for volume overload, therefore precautionary measures should apply with large volume plasma transfusions.
Reversal of Warfarin Effect	- Only when prothrombin complex concentrate is unavailable, inappropriate or contraindicated.
Thrombotic Thrombocy-topenic Purpura (TTP)	- FFP as replacement fluid in a therapeutic plasma exchange procedure as management of TTP as for other autoimmune diseases as per available guidelines. - Cryo-poor FFP is preferred (if available).

The use of FFP is not justified nor recommended as a replacement fluid in haemorrhagic or hypovolaemic shock.

DOSAGE –

The recommended dosage is 10 – 15 ml/kg. Subsequent doses should depend on the clinical response of the recipient and guided by frequent laboratory tests.

THERAPEUTIC EFFECT –

A standard dose of 10 - 15 ml/kg in adults, will increase the clotting factors by at least 20%

PLASMA COMPATIBILITY –

The rules for plasma compatibility differ from that of red blood cell transfusions, i.e., blood group AB are universal plasma donors since they lack anti-A and anti-B in their plasma. Any blood group can therefore receive AB plasma, but a recipient who is an AB blood group can only receive type AB plasma.

The routine use of AB plasma for all recipients are generally not recommended, since AB plasma is an extremely scarce resource with only 4% AB group prevalence in the general Namibian population. Plasma transfusions should therefore ideally be ABO compatible as that of the recipient in accordance to table 6.6.

Table 6.6 - Blood group compatible plasma transfusion:

Patient's Blood Group	ABO Compatible Plasma
A	A or AB
B	B or AB
AB	AB
O	O, A, B or AB

ABO incompatible plasma may be issued in certain situations, if the plasma component is of low titre anti-A or anti-B as it poses a lower risk for haemolysis when transfused compared to those of high titre.

6.4.2 - Paediatric Fresh Frozen Plasma

PAEDIATRIC PLASMA PRODUCTS DETAILS –

Paediatric FFP is prepared by means of apheresis or when this is not possible by means of separating the plasma from a single whole blood donation from a group AB donor into two paediatric units of approximately 150 ml each.

Product details;

- **Volume:** 100 - 150 ml/unit
- **Storage Temperature:** below minus (-) 25 ^{0}C
- **Maximum Storage Time:** It can be stored for up to 1 years if stored below minus (-) 25 ^{0}C or up to 3 years if stored below minus (-) 25 ^{0}C (all calculated from the day of whole blood or plasma collection).

INDICATIONS –

The main indication for any plasma transfusion is to correct deficiencies of clotting factors which results in active bleeding.

Indications for FFP in paediatric patients –

- **Therapeutic Indications –**
  - Clinically significant bleeding, including massive haemorrhage.
  - Significant risk of bleeding in those who have an abnormal coagulation profile, defined by PT/ aPTT significantly above the normal reference range.
  - Inherited coagulation factor deficiencies, where specific factor concentrates are not available or the specific factor deficiency has not been identified.
  - Haemorrhagic disease of the newborn, while waiting for response to Vitamin K.
- **Prophylactic Indications –**
  - Prophylactic FFP transfusion should not be done in children who are not actively bleeding with minor prolongation of the PT/aPTT, including prior to surgery.
  - However, it can be considered for surgical procedures to critical sites.

DOSAGE –

If a plasma transfusion is indicated, it is recommended to transfuse ONLY 10 – 20 ml/kg –

- It should be transfused with a standard blood-administration set.

THERAPEUTIC EFFECT –

Repeat the coagulation screen (i.e. INR/PT) within 60 minutes after the completion of the transfusion –

- A standard dose of 10 - 20 ml/kg in children, will increase the clotting factors by 20 – 30% in the absence of consumptive coagulopathy.

PLASMA COMPATIBILITY –

See adult FFP compatibility.

6.4.3 - Cryoprecipitate

Cryoprecipitate is prepared from a single plasma unit by slowly thawing FFP at 0 – 4 ^{0}C for a maximum of 14 hours. It is the centrifuged at low temperature and the supernatant is then removed and suspending the paste in a small volume of plasma and then immediately frozen. Cryoprecipitate may be made from a pool of plasma from up to 12 FFPs.

This precipitate is rich in the following coagulation factors –

- Factor VIII
- von Willebrand factor (vWF)
- Fibrinogen
- Fibronectin
- Factor XIII

PRODUCT DETAILS;

- **Volume:** 10 - 20 ml/unit
- **Storage Temperature:** below minus (-) 25 ^{0}C
- **Maximum Storage Time:** It can be stored for up to 1 years if stored below minus (-) 25 ^{0}C or up to 3 years if stored below minus (-) 25 ^{0}C (all calculated from the day of whole blood or plasma collection). After thawing cryoprecipitate must be transfused immediately.

INDICATIONS & DOSAGE –

Table 6.7 – Indications & Dosage of Cryoprecipitate:

Adults	- It is mainly indicated for the management of congenital or acquired hypofibrinogenaemia and dysfibrinogenaemia, namely –
	  - Massive haemorrhage in obstetrics, trauma or surgery when the fibrinogen is less than 1.5 g/L.
	  - DIC with a fibrinogen level of less than 1.5 g/L.
	- It may also be used for the management if hereditary factor XIII deficiency.
	- It may be used as prophylaxis before an invasive procedure or surgery where there is a significant risk of bleeding when a patient has a fibrinogen level of less than 1 g/L.
	- The standard adult dose for transfusion is 1-unit cryoprecipitate/10kg body weight via a standard blood-administration set.

Paediatrics	- It is mainly indicated for the management of congenital or acquired hypofibrinogenaemia/afibrinogenaemia, most commonly DIC. - It may also be used for the management if factor XIII deficiency with active bleeding or prior to an invasive procedure if recombinant factor XIII concentrate is unavailable. - The standard paediatric dose is 5 – 10 ml/kg body weight.

6.4.4 - Freeze Dried Plasma (FDP)

Bioplasma FDP is prepared from pooled plasma donations which are subjected to pathogen inactivation and then freeze dried. It is preserved in a powder form by a process called lyophilisation.

After reconstitution with water for injection, each 200 ml contains –

- 8 – 12 g plasma proteins with a similar concentration of albumin, immunoglobulins, coagulation and clotting factors, and their inhibitors as a standard unit of FFP.
- At least 0.4 IU/mL clotting factors (Factor II, V, VIII, IX and XI)

PRODUCT DETAILS;

- **Volume:** 200 ml/unit
- **Storage Temperature:** below 25 ^{0}C
- **Maximum Storage Time:** Up to 3 years from the date of manufacturing.

INDICATIONS & DOSAGE –

- The indication for the use of Bioplasma FDP is similar to that of standard FFP's, however the use FDP's are **reserved for emergency or peripheral settings** where immediate access to FFP's are limited.
- Initial dosage of **15 – 20 ml/kg** body weight via a standard blood-administration set, with subsequent dosage determined by the clinical condition of the patient and coagulation tests.

6.4.5- Plasma-Derived Medicinal Products (PDMP's)

PDMP's are medicinal products manufactured from large volumes of pooled plasma, usually 2000 – 5000 units, by a process of fractionation. PDMP's include products such as albumin, specific coagulation factor concentrates and immunoglobulins, which are used to manage a variety of medical conditions.

Plasma Expanders (Albumin)

Albumin solutions are mainly used to restore the intravascular colloid osmotic pressure. Table 6.8 provides and overview of the indications and contraindications of Human Plasma Albumin Solutions –

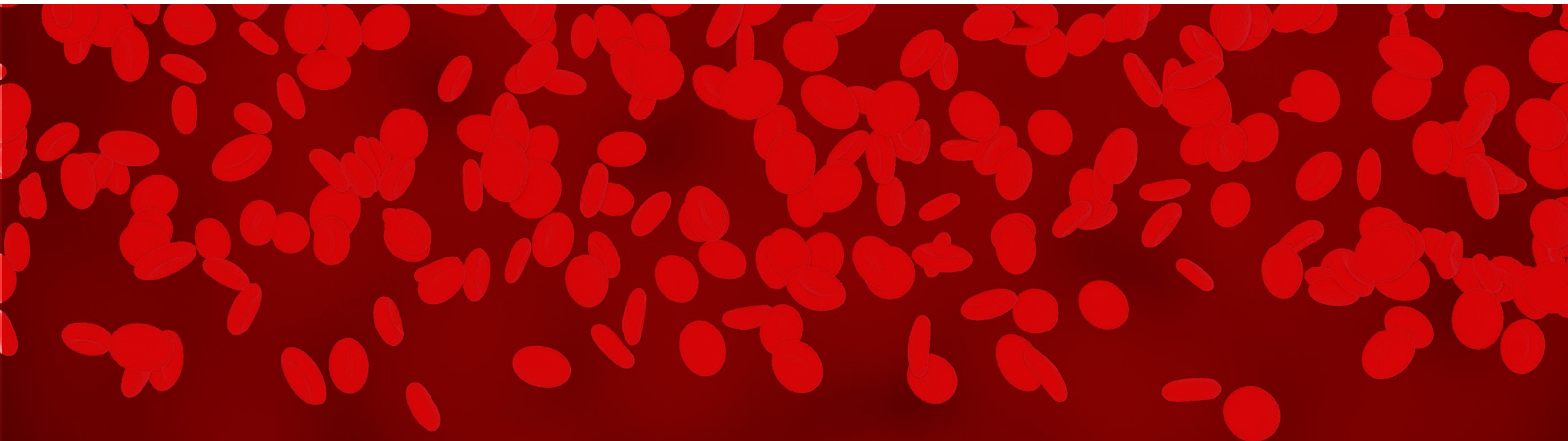


Table 6.8– Human Plasma Albumin Solutions

Product	Indications	Contraindicated

Examples of available products:
 	
- Albusol 4%
- Albusol 20%
	Recommended as an Acute Volume Replacement –
	- In burn patients after 24 hours.
	- In liver transplantation.
	- To balance volume withdrawal in plasmapheresis.
	
	Hypoalbuminemia Treatment –
	- **Administration recommended in liver failure patients with –**
	  - Spontaneous Bacterial Peritonitis
	  - Hepatorenal Syndrome (combined with vasoconstrictor therapy)
	- Recommended as plasma expander post paracentesis if volume of ascitic fluid is ≥ 6L.
		Albumin solutions are not recommended –
		- In patients with a known allergy to human proteins.
		- In Malnutrition, cirrhosis & chronic nephrotic syndrome.
		- To increase haemodynamic stability of patients –
		  - In Cardiac surgery/ ICU or perioperative phase,
		  - With traumatic brain injury, or patients with coagulopathy.
		
		Contraindicated in any patient in a hypervolemic state or who is at risk of volume overload –
		- Congestive Heart Failure
		- Pulmonary Oedema
		- Renal or post-renal anuria

COAGULATION FACTOR CONCENTRATES

Coagulation factor concentrates, such a Factor VIII and IX Concentrates in table 6.9, are either derived from human plasma or recombinant, to mainly correct specific coagulation factor deficiencies in conditions such as Haemophilia A, Haemophilia B and Von Willebrand's Disease.

Table 6.9 – Human Coagulation Factor Concentrates

Product Examples	Content	Units	Indications
Haemosolvate® Factor VIII 300 IU (NBI)	- Factor VIII/vWF	- 300 IU factor VIII - >300 IU vWF	- Therapeutic & prophylactic use in coagulation factor defects of Haemophilia A and vWD
Haemosolvate® Factor VIII 500 IU (NBI)	- Factor VIII/vWF	- 500 IU factor VIII - >500 IU vWF	
Haemosolvex® Factor IX	- Factor IX, factor II, factor VII, factor X	- 500 IU factor IX	- Therapeutic & prophylactic use in coagulation factor defects of Haemophilia B and warfarin – induced bleeding

Specific dosage and treatment should be based on guidelines locally available or available in South Africa (www.haemophilia.org.za).

IMMUNOGLOBULINS

Immunoglobulin preparations are a concentrated form of immunoglobulins which are derived from large pools of human plasma. Various immunoglobulin preparations exist namely –

Specific Immunoglobulins –

- **Polyvalent Human Normal Immunoglobulin (IVIG, Polygam etc.) –**
  - It contains mainly IgG with a broad spectrum of antibodies against infectious agents and may restore abnormally low IgG levels to norm. It also has an immunomodulation effect.
- **Indications (Table 6.10) –**

Table 6.10 - Polyvalent Human Normal Immunoglobulin Indications

Replacement therapy in immunodeficiency	- Primary immunodeficiency (e.g. congenital agammaglobulinaemia) - Secondary immunodeficiency (e.g. CLL, multiple myeloma)
Immunomodulation	- Idiopathic/Immune thrombocytopenic purpura (ITP) - Kawasaki disease - Guillain Barré syndrome

Table 6.10 - Polyvalent Human Normal Immunoglobulin Indications	
Allogeneic bone marrow transplantation	- Treatment of infections and prophylaxis of graft versus host disease. - Persistent immunosuppression

- **Precaution –**
- Should be used with caution in patient with antibodies to IgA or IgA deficiency, as Polygam contains some IgA which may cause sensitization that may lead to a severe allergic reaction.

- **Human Anti – D Immunoglobulin (RhoGAM, ImmunoRho etc.) –**
  - Anti-D prevents an active immune response to the RhD red cell antigen in RhD negative individuals exposed to RhD positive blood.

- **Human Hepatitis B Immunoglobulin (HBIG, Hebagam, ImmunoHBs etc.) –**
  - HBIG confers passive immunity against HBV, mainly for prophylaxis to accidental exposure to HBV, i.e. needle stick injury.

- **Human Rabies Immunoglobulin (RIG, Rabigam) –**
  - RIG contains a high titre of antibodies to the rabies virus and confers positive immunity against rabies, mainly prophylaxis in non-immunized individuals with known or suspected exposure to the rabies virus, i.e. an animal bite from a rabid animal.

- **Human Tetanus Immunoglobulin (TIG, Tetagam etc.) –**
  - TIG contains a high titre of antibodies to the tetanus toxin and confers passive immunity against tetanus, mainly for post-exposure prophylaxis in individuals with wounds likely to be contaminated by Clostridium tetani.

- **Human Varicella Zoster Immunoglobulin (VZIG) –**
  - VZIG contains a high titre of Varicella zoster antibodies and confers positive immunity against VZV, mainly for prophylaxis in immunocompromised individuals exposed to chickenpox

SUMMARY OF BLOOD AND BLOOD PRODUCTS			
Blood Product	**Product Details**	**Indications**	**Dosage & Therapeutic Effect**
Whole Blood	- **Volume/unit**: 468 - 558 ml including ± 60 ml anticoagulant-preservative solution. - **Storage temperature:** 1 - 6°C - **Max. storage time:** 21 days (calculated from the day of collection)	- Neonatal exchange transfusion - Intrauterine transfusion - Massive haemorrhage – component therapy is recommended in civilians.	- **Dosage** – - Based on available clinical guidelines as per indication for transfusion. - **Therapeutic Effect –** - Hb increment of 1 g/dl in an average 70 kg patient.

Blood Product	Product Details	Indications	Dosage & Therapeutic Effect
Adult RCC	- **Volume/unit:** 230-330 ml including ± 111 ml of preservative solution (SAG-M). - **Storage temperature:** 1 - 6°C - **Max. storage time:** 42 days (calculated from the day of collection)	- Acute blood loss - Anaemia with a reduced oxygen carrying capacity compromising oxygen delivery.	- **Dosage –** - Consider single-unit transfusions for adults (or equivalent volumes calculated based on weight). - **Therapeutic Effect –** - Hb increment/unit of 1 – 1.5 g/dl in an average 70 kg patient (1-4 hours post transfusion)
Leucodepleted RCC	- **Volume/unit:** 230-330 ml - **Storage temperature:** 1 - 6°C - **Max. storage time:** 42 days (calculated from the day of donation)	- Patients < 1 year of age, i.e., neonatal exchange & intrauterine transfusion. - Immunocompromised patients - Patients on chronic transfusion regimens - Haematological malignancies, especially when a stem cell/ bone marrow transplant is required. - Patients with ESRD requiring a transplant. - Patients with severe autoimmune diseases - Patients with recurrent FNHTR - Prevention of alloimmunization to HLA antigens for potential transplant patients	- **Dosage –** - Consider single-unit transfusions for adults (or equivalent volumes calculated based on weight). - **Therapeutic Effect –** - Hb increment/unit of 1 g/dl in an average 70 kg patient (1-4 hours post transfusion)
Washed RCC	- **Volume/unit:** As appropriate for the system used - **Storage temperature:** 1 – 6 °C - **Max. storage time:** Expires 24 hours after washing of red cells.	- Recurrent severe allergic transfusion reactions, regardless of IgA status. - Those with IgA deficiency when IgA deficient donors are not available. - Neonates with T-cell activation	- **Dosage –** - Consider single-unit transfusions for adults (or equivalent volumes calculated based on weight). - **Therapeutic Effect –** - Hb increment/unit of 1 g/dl in an average 70 kg patient (1-4 hours post transfusion)

Blood Product	Product Details	Indications	Dosage & Therapeutic Effect
Washed RCC		- Patients whom are at risk of severe hyperkalaemia as an alternative to fresh standard red cells concentrates (ONLY IF FRESH RCC's ARE UNAVAILABLE).	
Cryopreserved (Frozen) RCC	- **Storage temperature:** - 60°C to - 82°C - **Max. storage time:** - Up to 10 years from date of donation if storage temperature is continuously maintained below - 65°C - Once thawed and washed to remove the cryoprotectant, it expires after 24 hours. - Only available from **Rare Donor Blood Banks (i.e., in Durban, South Africa).**	- Patients with antibodies against high-frequency red cell antigens. - Patients with complex and multiple antibodies - Patients with extremely rare blood groups. - Future autologous blood transfusions	**- Dosage –** - Consider single-unit transfusions for adults (or equivalent volumes calculated based on weight). **- Therapeutic Effect –** - Hb increment/unit of 1 g/dl in an average 70 kg patient (1-4 hours post transfusion)
Irradiated RCC	- **Storage temperature:** 1 – 6 °C - **Max. storage time:** Standards recommend that it must be transfused within 14 days after irradiation, and within 28 days after collection.	- Congenital t-lymphocyte immunodeficiency syndromes - Neonatal exchange & Intrauterine transfusions - Recipients of cellular components from first- and/or second-degree relatives. - Patients undergoing marrow or peripheral blood progenitor cell transplantation - Patients with haematological malignancies and/or those undergoing intensive chemo-or immunosuppressive therapy.	**- Dosage –** - Consider single-unit transfusions for adults (or equivalent volumes calculated based on weight). **- Therapeutic Effect –** - Hb increment/unit of 1 g/dl in an average 70 kg patient (1-4 hours post transfusion)

Blood Product	Product Details	Indications	Dosage & Therapeutic Effect
		- Patients with chronic graft-versus-host disease and/or on continued immunosuppressive treatment is required.	
Paediatric Red Cell	- **Volume/unit:** 80 -120 ml including ± 38 ml of additive solution. - **Storage temperature:** 1 - 6°C - **Max. storage time:** 42 days (calculated from the day of collection)	- Similar to that of adult RCC transfusions, however Hb thresholds vary with age and the clinical condition of the patient (See Chapter 7, Section 7.1).	- **Dosage –** - 10 – 20 ml/kg, however an initial dose of 15ml/kg is ideal. - **Therapeutic Effect –** - Each 10 – 15 ml/kg red blood cells transfused results in a Hb increment of about 1 – 2 g/dl
Adult Platelet Concentrate	- **Volume:** 200 – 400 ml/unit - **Platelet Count/Yield per unit:** 2.4 – 4.8 x 10 ¹¹/L (Indicated on the unit bag) - **Storage Temperature:** 20 – 24 °C - **Maximum Storage** Time: 5 – 7 days (calculated from the day of collection) on a platelet agitator.	- Indicated for the prophylactic or therapeutic management of platelet related bleeding, i.e., to prevent or stop this bleeding. - Indications to transfuse platelets are stipulated in **table 6.2** in accordance to the British Society for Haematology and AABB guidelines. - AABB recommends a prophylactic platelet transfusion in hospitalized adult patients with a platelet count of **≤ 10 x 10^9/L** to reduce the risk of spontaneous bleeding	- **Dosage –** - Single unit transfusions are recommended, more than one unit per transfusion episode may only be considered in patients with severe thrombocytopenia and/or critical site bleeding (i.e., CNS & eyes). - **Therapeutic Effect –** - Platelet count increment/unit of 30 – 50 x 10^9/L (10 – 60 min after the completion). - The outcome of a transfusion is most accurately determined by the CCI.
Paediatric Platelet Concentrate	- **Volume:** 40 - 60 ml/unit - **Platelet Count/Yield per unit:** > 6.0 x 10^10/L (Indicated on the unit bag) - **Storage Temperature:** 20 – 24 °C	- Indications for paediatric platelet transfusions are drawn from adult literature and clinical expertise, therefore see table 6.2 and 6.4.	- **Dosage –** - 10 – 20 ml/kg with a standard platelet administration set over 30 minutes. - **Therapeutic Effect –** - Determined by the CCI as discussed under adult platelet concentrates

Blood Product	Product Details	Indications	Dosage & Therapeutic Effect
	- **Maximum Storage** Time: 5 – 7 days (calculated from the day of collection) on a platelet agitator.		
Adult FFP	- **Volume:** 220 – 350 ml/ unit including about 60 ml anti-coagulant preservative solution. - **Storage Temperature:** below minus (-) 25 ^{0}C - **Maximum Storage** Time: It can be stored for up to 3 years (calculated from the day of collection), if stored below minus (-) 25 ^{0}C.	- Are mainly recommended for the replacement of multiple coagulation factor deficiency (i.e., massive haemorrhage, DIC, Liver disease etc.) - Single coagulation factor deficiencies and reversal of warfarin effect when specific factor concentrate/ PCC is unavailable, inappropriate or contraindicated. - FFP as replacement fluid in a therapeutic plasma exchange procedure as management of TTP as for other autoimmune diseases	**- Dosage –** - 10 – 15 ml/kg, and subsequent dosages should depend on clinical response and laboratory investigations. **- Therapeutic Effect –** - A standard dose of 10 - 15 ml/kg in adults, will increase the clotting factors by at least 20%
Paediatric FFP	- **Volume:** 100 - 150 ml/unit - **Storage Temperature:** below minus (-) 25 ^{0}C - **Maximum Storage** Time: It can be stored for up to 3 years (calculated from the day of collection), if stored below minus (-) 25 ^{0}C.	- **Therapeutic Indications** - Clinically significant bleeding, or risk of bleeding in those who have an abnormal coagulation profile. - Inherited coagulation factor deficiencies - HDN, while waiting for response to Vitamin K. - **Prophylactic Indications –** - Prophylactic FFP transfusion should not be done in children who are not actively bleeding with minor prolongation of the PT/aPTT.	**Dosage –** - 10 – 20 ml/kg **Therapeutic Effect –** - A standard dose of 10 - 20 ml/kg in children, will increase the clotting factors by 20 – 30% in the absence of consumptive coagulopathy.

Blood Product	Product Details	Indications	Dosage & Therapeutic Effect
Cryoprecipitate	- **Volume:** 10 - 20 ml/unit - **Storage Temperature:** below minus (-) 25 ^{0}C - **Maximum Storage Time:** It can be stored for up to 3 years (calculated from the day of collection), if stored below minus (-) 25 ^{0}C. After thawing cryoprecipitate must be transfused immediately.	- The indications for cryoprecipitate transfusions are indicated in table 6.9.	**Dosage –** - The standard adult dose for transfusion is 1-unit cryoprecipitate/10kg body weight via a standard blood-administration set. - The standard paediatric dose is 5 – 10 ml/kg body weight.

This is only a summary and additional information relating to blood and blood products are mentioned within this chapter or require additional reading of the below listed literature.

REFERENCES

- Basu D, Kulkarni R. Overview of blood components and their preparation. Indian J Anaesth. 2014 Sep;58(5):529-37. doi: 10.4103/0019-5049.144647. PMID: 25535413; PMCID: PMC4260297.
- Hardwick, J. (2008), Blood processing. ISBT Science Series, 3: 148-176. https://doi.org/10.1111/j.1751-2824.2008.00195.x
- Valeri CR, Ragno G, Pivacek LE, Cassidy GP, ey R Sr, Hansson-Wicher M, et al. An experiment with glycerol-frozen red blood cells stored at -80 degrees C for up to 37 years. Vox Sang 2000; 79:168-74
- Cohn CS. Platelet transfusion refractoriness: how do I diagnose and manage? Hematology Am Soc Hematol Educ Program. 2020 Dec 4;2020(1):527-532. doi: 10.1182/hematology.2020000137. PMID: 33275694; PMCID: PMC7727584.
- European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS). Guide to the preparation, use and quality assurance of blood components. 20th Edition. European Directorate for the Quality of Medicines & HealthCare.
- Australian and New Zealand Society of Blood Transfusion. Guidelines for the Prevention of Transfusion-Associated Graft-Versus-Host Disease (TA-GVHD). 2nd Edition, 2024. https://anzsbt.org.au/wp-content/uploads/2024/02/TAGVHD-Guideines-2024.pdf
- Estcourt LJ, Birchall J, Allard S, et al. Guidelines for the use of platelet transfusions. Br J Haematol. 2017;176(3):365-394. doi:10.1111/bjh.14423
- Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern Med. 2015;162(3):205-213. doi:10.7326/M14-1589

CHAPTER 07
BLOOD TRANSFUSION IN CLINICAL PRACTICE

This chapter focuses on the application of appropriate blood transfusion practices in various clinical settings, including paediatrics, surgery, obstetrics etc. In order to improve patient care for those in need of a blood transfusion, it is of utmost importance to follow an evidence-based, multidisciplinary approach.

Section 7.1 – Transfusion in Paediatrics

Blood transfusions in the paediatric population is a complex area of medicine, due to various reasons such as vascular access, risk for volume overload, immunological immaturity, presence of maternal antibodies and the wide age range.

The requirements for transfusion safety in neonates and paediatrics are similar to that of adults, in addition it is critical that the following actions be considered –

- **Minimize Blood Loss –**
  - Avoiding unnecessary laboratory testing for monitoring and use of micro-techniques for blood sampling reduces iatrogenic anaemia in neonates by minimizing the volume of blood drawn, as it requires a significant number of red blood cell transfusions.
- **Minimize Donor Exposure –**
  - Clinicians must always aim to minimise donor exposure when requesting blood transfusions. This can be achieved by asking the blood service to reserve additional paediatric units from a single standard adult red cell concentrate for potential future transfusions. This approach forms part of the Paediatric Split Transfusion Programme (also known as the Limited Donor Exposure Programme), which support safer transfusion practices.

TRANSFUSION IN NEONATES

Red Cell Transfusions in Neonates –

The normal blood volume at birth varies due to the gestational age and timining of the cord claming. The estimated blood volume (EBV) is between 100 – 120 ml/kg in extremely premature infants, whilst it is between 80 – 85 ml/kg in a term infant. In neonates the volume of blood to be transfused is calculated using the following formula –

TRANSFUSION VOLUME IN NEONATES;

Transfusion Volume (ml) = Patient weight (kg) x EBV (ml/kg) x desired Hb (g/dL) – patient Hb (g/dL)/Hb of donor unit

The erythropoiesis of a neonate is not as rapid as in an adult, therefore any uncorrected blood loss can rapidly lead to anaemia.

Common indications for neonatal transfusions are –

- **Anaemia of Prematurity (AOP) –**
  - AOP is common amongst extremely premature neonates due to impaired red blood cell production and iatrogenic blood loss due to frequent sampling.
- **Anaemia associated with in utero causes –**
  - Other than haemolytic causes, non-haemolytic causes such as fetomaternal haemorrhage, maternal infections, twin anaemia polycythaemia sequence (TAPS) and genetic disorders can also contribute to fetal anaemia.

Transfusion thresholds for neonates –

The Hb transfusion threshold in neonates born very prematurely, 32 weeks or less, depends on the postnatal age and cardiopulmonary support requirements as indicated in table 7.1.

Table 7.1- Suggested Hb (g/dL) Transfusion Thresholds

Postnatal Age	Ventilated	On Oxygen/ NIPPV	Off Oxygen
First 24 hours	<12	<11	<10
≤ Week 1 (D1 – 7)	<12	<10	<10
Week 2 (D8 – 14)	<10	<9.5	<7.5*
≥ Week 3 (≥ D15)	<10	<8.5	<7.5*

NIPPV – Non-invasive Positive Pressure Ventilation
***A Hb Transfusion Threshold of 8.5 g/dL may be accepted by clinicians depending on the clinical condition of the patient.**

A transfusion is usually not recommended for critical ill and haemodynamically stable neonates who do not require cardiopulmonary support or oxygen supply, unless the haemoglobin level is less than 7.0 g/dL.

The pre-transfusion testing, transfusion volume, administration rate, and therapeutic effect of a red cell concentrate transfusion in paediatrics is discussed in Chapter 6 – Blood and Blood Products.

Recommended RCC Product –

Leucodepleted RCC is recommended for neonates (See Chapter 6, Section 6.2.2). It is also recommended that arrangements are made with the blood service for neonates that will require multiple transfusions to limit exposure to various donors. This reduces the residual infectious risk and exposure to various red cell antigens.

Platelet and Fresh Frozen Plasma Transfusion in Neonates –

See Chapter 6, Section 6.3.2 & 6.4.2

Transfusion in Neonatal Sepsis & T-activation –

T-activation may occur in neonates with neonatal sepsis, especially necrotizing enterocolitis (NEC). Those with NEC might be systemically infected with neuraminidase-producing organisms, such as *Clostridium perfringens*. Neuraminidase produced by the infective organism strips the sialic acid from the red blood cell surface which expose the T-cryptantigens. These cryptantigens make the red blood cells more susceptible to haemolysis by normal human plasma, since it contains natural occurring antibodies against these cryptantigens.

If a transfusion is required for neonates with T-activation and/or haemolysis is observed after a previous blood transfusion, washed RCC's, low-titre anti-T FFP's and platelets suspended in 100% platelet additive solution are recommended. To obtain these special products, arrangements must be made with the blood service.

TRANSFUSION IN INFANTS, CHILDREN AND ADOLESCENTS

Red Cell Transfusions in Infants, Children and Adolescents –

Older children (> 1 year of age) without any cardiopulmonary compromise are able to tolerate a lower haemoglobin level better, therefore **a haemoglobin transfusion threshold of 7 g/dL is usually recommended.** The indications for red cell transfusions in infants, children and adolescents are similar to that of adults, however the haemoglobin transfusion threshold may vary depending on the underlying diagnosis of the patient and haemodynamic stability.

Table 7. 2 - Hb Transfusion Thresholds in various clinical settings and diagnosis

Diagnosis/Setting	Hb Transfusion Threshold	Comment
Cancer	Hb Threshold of **7 – 8 g/dL** is recommended if critical ill or at risk for critical illness & haemodynamically	**Transfusion in children with cancer depends on –** - Haemodynamic stability - Likelihood of Hb to rise or fall with treatment
Congenital Heart Disease (CHD)	**Recommended Hb Thresholds for transfusion in haemo-dynamically stable children with CHD –** - Biventricular repair: **7 g/dL** - Single ventricle palliation: **9 g/dL** - Uncorrected CHD: **7 – 9 g/dL**	Transfusion in children with a CHD depends on – - Haemodynamic stability - Cardiac Abnormality - Stage of surgical repair

Blood Product	Product Details	Indications
Critical Ill admitted in PICU	Recommended Hb threshold for critically ill children or those at risk for critical illness who are haemo-dynamically stable is **7 g/dL.**	Transfusion in critical ill children depends on the overall clinical status of the patient – - symptoms, signs, physiological markers and laboratory results
Perioperative Setting	Hb threshold of **7 g/dL** if stable without any major comorbidity or bleeding. (See Section 7.2)	Recommended to investigate and treat the underlying cause of anaemia pre-operatively in all elective surgical cases.
Pure Red Cell Aplasia	Hb threshold of **7 g/dL** is rec-ommended in those with chronic anaemia. To reduce the risk of iron overload,	Patients might rely on chronic transfusion if they are unrespon-sive to other treatments; however, they are at risk for iron overload.
Sickle Cell Disease (SCD)	**Transfuse if:** - Hb **< 5 – 6 g/dL** with symptoms, or if there is a sudden drop of **> 2 g/dL** from baseline. - Persisting sickle crisis despite hyperhydration and oxygenation, even if Hb exceeds the thresh-old.	**Transfusion in children with SCD is recommended –** - In acute sickle complications (i.e., splenic sequestration, aplastic crisis, priapism, acute chest syndrome with hypoxia) and acute ischaemic stoke. - The goal is to reduce HbS to < 30% and maintain it at <30%. - Choice of simple vs exchange transfusion depends on indica-tion (e.g., exchange often pre-ferred for stroke, severe ACS, or hyperviscosity risk).

A dose of 10 – 20 ml/kg is usually recommended in infants and children. Older children more than 40kg will often require more than one standard adult RCC unit to increase the haemoglobin above the target concentration. The following formula should be used to calculate the volume of RCC required for transfusion, while taking the pre-transfusion Hb in relation to the Hb transfusion threshold into consideration. The targeted post-transfusion Hb should be no more than 2 g/dL above the transfusion threshold in haemodynamically stable children

TRANSFUSION VOLUMES IN PAEDIATRIC PATIENTS SHOULD BE DETERMINED AS FOLLOW

Volume (mL)=(Target Hb (g/dL)-Actual Hb(g/dL))×weight (kg)×4 (Transfusion Factor)

Transfusion Factor – typically refers to the estimated increase in haemoglobin from a unit of blood or blood product.

Infants and children are at an increased risk for volume overload, especially when normovolaemic and multiple products are transfused during a single transfusion episode. Therefore, furosemide (1 mg/kg) may be given to prevent volume overload.

Platelet Transfusion in infants, children and adolescence –

Guidelines for adult transfusions are often resorted to, especially for prophylactic platelet transfusions, which is usually recommended if the platelet count **is less than 10 x 10^9/L in stable children.** Therapeutic platelet transfusions are indicated in a child with thrombocytopenia and active bleeding (See Chapter 6, Section 6.3.1 - Table 6.2).

Fresh Frozen Plasma Transfusion in infants, children and adolescence –

The indications for FFP transfusions are similar to that of adults and done to correct coagulation factor deficiencies in children who are actively bleeding or at risk of active bleeding (See Chapter 6, Section 6.4.2).

FFP has the highest rate of serious adverse reactions of all blood components and must always be transfused if there is a clear indication. The use of FFP for correction of minor clotting disorders prior to an interventional or surgical procedure is not advised.

Section 7.2 – Transfusion in Surgery

The South African Surgical Outcome Study indicated that about 50% of patients who present for elective surgery had anaemia, and were associated with poorer outcomes such as in-hospital mortality and critical care admissions. Therefore, during the perioperative period surgeons and anaesthesiologists play a crucial role in the management of a patient, by applying the principles of Patient Blood Management (PBM) (See Chapter 3, Section 3.3).

Generally, the best departments to start the implementation of PBM strategies are orthopaedic and cardiac surgery services, due to high prevalence of preoperative anaemia and potential for significant blood loss. *ONTraC: A 20-Year History of Successfully Coordinated Provincewide Patient Blood Management Program: Lessons Learned and Goals Achieved trail,* conducted in multiple Canadian hospitals from 2002 to 2020 established a significant reduction in blood and blood components usage amongst surgical patients after the implementation of a PBM programme. The RCC transfusion rates during this study period decreased from 25% to 0.4% for knee replacement surgeries and from 60% to 27% for coronary artery bypass graft (CABG) surgeries, while improving the surgical outcome of the patient.

STANDARD PERIOPERATIVE PATIENT BLOOD MANAGEMENT (PBM) STRATEGIES:

The following general strategies should be implemented as standard of care for all surgical patients throughout the perioperative period to optimize outcomes, reduce transfusion requirements, and improve patient safety:

Preoperative Period –

- **Optimize red cell mass –**
  - **Screen all elective surgical patients with expected blood loss ≥ 500 mL for anaemia and nutritional deficiencies 2–4 weeks preoperatively and manage accordingly;**

- Investigate and treat based on the underlying cause if the Hb is < 13 g/dL regardless of sex.
- Target a preoperatively Hb of ≥ 13 g/dL to minimize perioperative transfusion risk and optimize surgical outcomes.
- Postpone elective surgery until anaemia is corrected when possible.

- **Early detection and treatment of anaemia (2–4 weeks preoperatively) is strongly recommended. Late correction (3–5 days before surgery) may be less effective but still beneficial;**
  - **In orthopaedic surgery, IV Iron and ESA 1 – 3 days preoperatively:**
    - Reduced RCC transfusion rate from 37 to 24%
    - Decreased nosocomial infections from 12 to 8 %
    - Shortened hospital stay from 11.7 to 10.7 days.
  - **In cardiac surgery, IV Iron, ESA, Vitamin B12 and Folic Acid 1 day preoperatively:**
    - Reduced median RCC usage from 1 unit to 0, with similar secondary outcomes as to controls.

- **Treatment Preferences:**
  - IV iron is preferred for moderate-to-severe anaemia or when surgery cannot be delayed (See Chapter 3: Haematinics, Section 3.4.3 for indications and dosing).
  - ESAs may be considered selectively but require caution due to:
    - Increased risk of thromboembolic events; thromboprophylaxis (e.g., LMWH) is essential due to an elevated baseline thrombotic risk in surgical patients.
    - Avoidance or cautious use in high-thrombotic-risk surgeries such as cardiac bypass without adequate prophylaxis (See Chapter 3, Section 3.4.3)

- **Institutional Protocols and PBM Clinics:**
  - Hospitals are encouraged to develop institution-specific anaemia management protocols (e.g., University Hospital of Zurich protocol, Table 7.3).
  - Establish multidisciplinary preoperative Patient Blood Management (PBM) clinics to optimize individual patient care and reduce transfusion requirements.

Table 7.3 - Anaemia Management Preoperatively

Investigations						Treatment
Hb	**Ferritin**		**TSAT**	**CCL**	**CRP**	
< 13 g/dL	< 100 ng/ml	or	< 20 %			IV Iron:20mg/kg ♦■ Vitamin B12: 1mg ♣ Folic acid PO: 5mg ◘
< 13 g/dL	≥ 100 ng/ml	and	≥ 20 %	< 50 ml/min		SC ESA ⋆ IV Iron: 20mg/kg ♦ Vitamin B12: 1mg ♣ Folic acid PO: 5mg ◘
< 13 g/dL	≥ 100 ng/ml	and	≥ 20 %		>5 mg/L	SC ESA ⋆ IV Iron: 20mg/kg ♦ Vitamin B12: 1mg ♣ Folic acid PO: 5mg ◘
≥ 13 g/dL	< 100 ng/ml	or	< 20 %			IV Iron:20mg/kg ♦

♦ Maximum dosage needs to be respected according to the manufacturer's instructions ■ Time of surgery is less than 5 days add ESA ⁎ ESA dosage according to manufactures instructions ♣ Route of administration according to Vitamin B12 formulation ◘ Until the day of surgery

CCL – Creatinine clearance, CRP – C- reactive protein, Hb – Haemoglobin, IV – Intravenous, PO – by mouth, SC – Subcutaneous, TSAT – Transferrin saturation.

- Minimizing bleeding and blood loss –

- All elective surgical patients should undergo a bleeding risk assessment using a standardized Bleeding Assessment Tool (See Chapter 1, Section 1.4: Bleeding).
- **Anticoagulant and Antiplatelet Management:**
  - Reversal of anticoagulants and withdrawal of antiplatelet agents should be performed preoperatively.
  - Timing of withdrawal should be guided by drug's pharmacokinetics, surgical bleeding risk, and patient-specific factors such as hepatic or renal impairment, which requires longer discontinuation periods.
- **Antiplatelet Agents –**
  - ***Aspirin:***
    - Discontinue at least 5 days pre-op in all non-cardiac surgeries.
    - In high-bleeding-risk surgeries (e.g., spinal, certain neuro or ophthalmic procedures), stop at least 7 days pre-op.
    - May be continued for CABG surgery, per select guidelines.
  - ***Clopidogrel:***
    - Discontinue 7 days preoperatively to minimize bleeding risk.
- **Vitamin K- dependent anticoagulants –**
  - Stop Warfarin and bridge with LMWH until the INR is ≤ 1.5.
  - Stop the LMWH at least 12 hours preoperatively.
- **Non-Vitamin-K oral anticoagulants (NOAC's) –**
  - Stop NOACs at least 48 hours before surgery.
  - Extend to 96 hours in patients with renal impairment (based on creatinine clearance).
  - In urgent cases administer reversal antidote for the specific NOAC. If not available administer Prothrombin Complex Concentrate.

Intraoperative Period –

Surgical Strategies –

- **Surgical techniques to Minimize Blood Loss –**
  - ***Meticulous haemostasis*** should be a core surgical objective to reduce intraoperative blood loss and transfusion requirements.
  - ***Minimally invasive techniques*** (e.g., laparoscopy) are preferred in general surgery where feasible, as they significantly reduce blood loss compared to open procedures.
  - ***Adjunctive haemostatic methods*** such as diathermy and topical agents (e.g., fibrin sealants, gelatin-thrombin matrices, oxidized cellulose) should be used to enhance haemostasis during surgery.

- **Tourniquet Usage –**
  - Tourniquets are widely used in orthopaedic limb surgery.

- However, multiple studies have indicated that although it reduces intraoperative blood loss there is no difference in overall blood loss.

- **Drain Usage –**
  - Surgical drains are commonly used to prevent haematoma and surgical site infections; however, multiple studies show no clear benefit of drain insertion over no drain.
  - In orthopaedic surgery, conventional suction drains may increase postoperative blood loss. Therefore, routine use of drains should be critically evaluated, particularly in specialties where they are standard practice.

- **Antifibrinolytic Usage –**
  - TXA is recommended in all surgeries were the expected blood loss exceeds 500 mL.
  - Strong evidence supports TXA in reducing blood loss and transfusion requirements, particularly in cardiac, spinal, orthopaedic, prostate, and obstetric surgeries (e.g., caesarean section, hysterectomy).
  - In orthopaedic surgery, TXA can reduce transfusions needs by up to 69% after a hip and knee surgery, without increasing complications.
  - TXA can be administered intravenously, intra-articularly, or in combination.
  - A combined IV and intra-articular regimen is especially effective in total knee arthroplasty (TKA), reducing blood loss for up to 7 days postoperatively

- **Intraoperative Cell salvage (ICS) and re-transfusion –**
  - ICS is an effective PBM strategy that collects, processes, and reinfuses the patient's own blood lost during surgery. It reduces the need for allogeneic transfusion and should be standard in surgeries with high expected blood loss.
  - ICS is recommended for procedures with anticipated blood loss >500–1000 mL, including cardiac, major orthopaedic, vascular, trauma, transplant, obstetric emergencies, and selected cancer surgeries where safe.
  - Benefits include up to 54% reduction in allogeneic transfusion exposure, improved haemoglobin preservation, lower infection risk, better outcomes, and cost-effectiveness.
  - ICS should be routinely available in high-blood-loss theatres, supported by institutional protocols and trained personnel. It can be used alongside other PBM strategies for optimal effect.

- **Acute normovoluemic haemodilution (ANH) –**
  - Consider ANH where appropriate and resources permit.
  - Particularly useful in cardiac surgery patients with significantly elevated haemoglobin or haematocrit levels.
    - Avoid excessive haemodilution during cardiopulmonary bypass (CPB); use techniques such as retrograde autologous priming (RAP), reduced CPB priming volume, and ultrafiltration.
    - ANH should be performed only by experienced clinicians with careful volume management to prevent fluid overload.

Anaesthetic techniques –

- **Patient Positioning –**
  - IS a simple and effective method to reduce intraoperative blood loss.
  - I.e., Reverse Trendelenburg reduces blood loss in endoscopic sinus surgery; lateral position benefits hip arthroplasty patients.
- **Central Neuraxial Anaesthesia –**
  - Central Neuraxial Blockade, such as subarachnoid or epidural anaesthesia, which blocks the

preganglionic sympathetic nerve fibres reduces arterial and venous oozing from the surgical site by causing arterial hypotension and reducing peripheral venous pressures.

- **Hypothermia Avoidance –**
  - Mild hypothermia increases blood loss by 16% and transfusion risk by 22%.
  - ***Strategies to avoid intraoperative hypothermia include –***
    - Frequent temperature monitoring (i.e., every 30 minutes).
    - Ambient theatre temperature ≥ 21^0C.
    - Use of air warming devices and intravenous fluid warming.
- **Ventilation strategies –**
  - Use positive pressure ventilation with minimal positive end-expiratory pressure (PEEP) and low tidal volumes if permitted, to increase venous return.
- **Improving Anaemia Tolerance –**
  - Optimize cardiac output, ventilation, oxygenation, and haemoglobin concentration based on evidence-based transfusion thresholds (See Chapter 3: Patient Blood Management – Restrictive Transfusions)

Postoperative Period –

- **Optimize red cell mass –**
  - Stimulate erythropoiesis with IV Iron and ESA if anaemia persist or worsen.
  - Identify and manage drug interactions, infections, or inflammation contributing to functional iron deficiency.
  - Recognize the role of surgical stress and inflammation in suppressing erythropoiesis.

- **Minimize postoperative bleeding and blood loss –**
  - Remain vigilant and actively monitor for bleeding, and intervene promptly to stop bleeding.
  - Optimize postoperative anticoagulation management to reduce bleeding risk.
  - Limit diagnostic blood sampling and use micro-sampling techniques to avoid iatrogenic anaemia (See Chapter 3, Section 3.3).
  - ICU patients may lose up to 300 mL/week from phlebotomy alone.
  - Consider postoperative cell salvage with reinfusion of blood from surgical drains, especially in major orthopaedic procedures.

- **Improve tolerance to anaemia –**
  - Support oxygen delivery by optimizing cardiac output and oxygenation, while reducing oxygen consumption.
  - ***Restrictive transfusions and single unit transfusion approach –***
    - In the majority of patients, the same transfusion threshold as the intraoperative threshold of 7 g/dL is appropriate if haemodynamically stable.
    - In patients with an underlying cardiovascular disease including acute coronary syndrome a higher transfusion threshold of 7.5 – 8 g/dL is recommended.
    - Apply a single-unit transfusion policy in haemodynamically stable, non-bleeding patients to minimize unnecessary transfusion, with reassessment before administering additional units.

GI BLEEDING AND PBM: SURGICAL AND TRANSFUSION CONSIDERATIONS

Gastrointestinal bleeding frequently necessitates urgent surgical or endoscopic intervention. While transfusion can be lifesaving, liberal transfusion strategies have been associated with increased rebleeding and mortality in certain patient groups. Within the framework of Patient Blood Management (PBM), transfusion strategies for surgical patients with GI bleeding must carefully balance maintaining haemodynamic stability, achieving effective bleeding control, and optimizing tolerance to anaemia.

Restrictive vs. Liberal Transfusion in GI Bleeding –

Restrictive transfusion strategy is preferred in most surgical settings involving GI bleeding, including perioperative management, emergency laparotomy, or endoscopic control.

- **Recommended transfusion threshold –**
  - Hb 7–8 g/dL in haemodynamically stable surgical patients.
  - Based on strong evidence (Villanueva et al., NEJM 2013), restrictive transfusion improves survival, reduces rebleeding, and decreases adverse outcomes.
  - Recommended in non-variceal UGIB, stable patients, and those without ischemic heart disease.

- **When to Consider a Liberal Strategy (Use with Caution) –**
  - Active cardiac ischemia (e.g., ACS, unstable angina)
  - Massive haemorrhage requiring ongoing resuscitation
  - Symptomatic anaemia with signs of tissue hypoxia or end-organ hypoperfusion
  - In these cases, consider individualized thresholds (Hb 8–9 g/dL), guided by clinical judgement and frequent reassessment.

Surgical Considerations in GI Bleeding –

- **Upper GI Bleeding (UGIB) –**
  - Early endoscopy (within 24 hours) is critical to:
    - Establish diagnosis
    - Achieve endoscopic haemostasis
    - Reduce transfusion requirements and mortality
  - For variceal bleeding, combine endoscopic therapy with vasoactive agents (e.g., octreotide) and prophylactic antibiotics.

- **Lower GI Bleeding (LGIB) –**
  - Most cases self-resolve; however:
    - Early colonoscopy (within 24–48 hours) is advised once stabilized.
    - Use a restrictive transfusion strategy unless ongoing haemorrhage or instability.
  - For persistent bleeding –
    - Escalate to angiographic embolization or surgical resection.

GI bleeding requiring surgical or procedural intervention must still adhere to PBM-aligned transfusion thresholds, with transfusions guided by haemodynamic status and risk profile, not solely haemoglobin levels.

Section 7.3 – Transfusion in Obstetrics'

Managing transfusion in obstetric patients requires careful consideration of the physiological changes of pregnancy and the high risk of haemorrhage. The goal is to optimize blood volume and red cell mass while minimizing blood loss to ensure favourable maternal and fetal outcomes.

The most common conditions requiring transfusion in obstetrics include –

- **Antepartum Haemorrhage (APH)**, i.e., placenta previa, placental abruption etc.
- **Intrapartum Haemorrhage**, i.e., obstetric trauma due to perineal, vaginal, or cervical lacerations from delivery.

- **Postpartum Haemorrhage (PPH)** is the most common cause requiring transfusion, i.e., uterine atony (most common), retained placenta, uterine rupture and placenta accrete.
- **Disseminated Intravascular Coagulation (DIC)**, triggered by conditions like severe haemorrhage, amniotic fluid embolism, sepsis, preeclampsia/eclampsia or HELLP syndrome.
- **Haemolysis-related conditions** which causes severe anaemia in pregnant women, i.e., sickle cell disease or thalassemia.
- **Chronic or severe anaemia,** most commonly nutritional deficiency anaemia's, depending on the haemoglobin level, clinical status and treatment response;
  - Hb <7 g/dL with symptoms (e.g., tachycardia, dyspnoea, weakness).
  - Hb <6 g/dL regardless of symptoms, especially in late pregnancy.
  - Failure to respond to oral or IV iron therapy in iron deficiency anaemia (IDA).

Patient blood management in Obstetrics –

The implementation of patient blood management in obstetric patients is essential to reduce the need for transfusion, minimize transfusion-related risks, and optimize maternal outcomes (See Chapter 3, Section 3.3).

Peripartum Strategies: Optimisation of haemoglobin in the antenatal period –

Nutritional Interventions –

- **Screening and Early Diagnosis –**
  - *Routine Hb Monitoring in pregnancy –*
    - WHO and RCOG recommends checking Hb levels at the first antenatal visit and again at 28 weeks gestation. Women with multiple pregnancies should have an additional full blood count done at 20-24 weeks.
    - If anaemia is detected, further tests include:
      - Serum ferritin (iron stores indicator)
      - Total iron-binding capacity (TIBC)
      - Serum folate and Vitamin B12 levels (if macrocytic anaemia is suspected)

- **Lifestyle and Dietary Modifications to address or prevent nutritional deficiencies –**
  - **Iron Deficiency –**
    - Iron-Rich Diet
    - *Oral Iron Supplementation –*
      - Iron is essential for erythropoiesis, and iron deficiency anaemia (IDA) is the most common cause of low Hb in pregnancy.
      - *Recommended Dosage:*
        - The WHO recommends 30–60 mg of elemental iron daily for pregnant women in areas with a high prevalence of anaemia.
        - If anaemia is diagnosed (Hb <11 g/dL in the first trimester, <10.5 g/dL in the second/third trimester and Hb <10.0g/dL postpartum), a higher dose (e.g., 100-200 mg daily) is recommended until Hb normalizes.
    - *Intravenous Iron Therapy –*
      - It is recommended in when severe anaemia is present in pregnancy, i.e., Hb < 8 g/dL in the second or third trimester and a poor response to oral iron due poor tolerance, compliance or absorption. It is also indicated in severe IDA with malabsorption syndromes (e.g., coeliac disease, inflammatory bowel disease).
      - If IV iron is required, the iron deficit should be taken into consideration when the dose is calculated (See Chapter 3, Section 3.4.3).

- **Folate deficiency –**
  - *Folate Supplementation –*
    - Folic acid is crucial for DNA synthesis and erythropoiesis.
    - WHO recommends 400 mcg/day of folic acid supplementation to prevent neural tube defects and support Hb levels.
    - In megaloblastic anaemia, higher doses (e.g., 5 mg/day) may be needed.
  - **Vitamin B12 and Other Micronutrient deficiencies –**
    - Vitamin B12 deficiency can contribute to macrocytic anaemia, especially in vegetarians.
    - Vitamin A plays a role in erythropoiesis and iron metabolism.
    - Zinc and copper deficiencies are linked to anaemia.

- **Managing underlying conditions that can contribute to anaemia –**
  - Treat parasitic infections, i.e., hookworm infections and malaria.
  - Manage chronic diseases, i.e., chronic kidney disease and hypothyroidism.

Other Interventions –

- **Erythropoiesis Stimulating agent (ESA) –**
  - ESA should not be routinely used in obstetric patients; it is however used in cases of renal disease-related anaemia or in women who cannot tolerate iron.
  - WHO suggests recombinant human erythropoietin (rHuEPO) therapy in selected cases, in combination with iron supplementation to support erythropoiesis.
  - Overcorrection should be avoided as a Hb of more than increases the thrombotic risk. The Hb target should therefore be 10 – 11 g/dL.
  - The standard dosage regimen according to the indication for ESA therapy is indicated in table 7.4 below;

Table 7.4 – ESA standard dosage regimens

Condition	EPO Type	Dosage	Route	Frequency
CKD-related anaemia	rHuEPO (epoetin alfa/beta)	50–100 IU/kg	SC/IV	1–3 times per week
Iron-refractory anaemia	Darbepoetin alfa	0.45 mcg/kg	SC	Once weekly
Severe postpartum anaemia	rHuEPO (epoetin alfa)	40,000 IU	SC	Weekly for 2–3 weeks

Intrapartum Strategies: Minimizing Blood Loss During Delivery –

- Active Management of the Third Stage of Labour (AMTSL)
- Routine Uterotonics (e.g., Oxytocin, Carbetocin, Misoprostol)
- ***Delayed Cord Clamping***
  - Beneficial for neonates but can slightly increase maternal blood loss.
  - Should be avoided in cases of severe maternal anaemia.

- ***Surgical & Procedural Techniques***
  - Minimize invasive techniques for Caesarean Delivery
  - Use blunt vs. sharp uterine entry, single-layer closure, and uterine exteriorization to reduce bleeding.
  - Balloon Tamponade (i.e., Bakri Balloon)
  - Used to control uterine bleeding before resorting to surgery.
- ***Tranexamic Acid (TXA)***
  - Given before or during delivery in high-risk women to reduce blood loss and prevent PPH.
  - Recommended dose: 1 g IV over 10 minutes, can be repeated after 30 minutes if necessary.

Postpartum Strategies: Reducing Need for Transfusion –

- ***Postpartum Iron & Erythropoietic Support –***
  - High-dose oral or IV iron therapy for postpartum anaemia.
  - Erythropoietin (EPO) to stimulate RBC production in severe cases.
- ***Restricted Transfusion Thresholds –***
  - Avoid unnecessary transfusions; transfuse only when Hb is <7 g/dL or symptomatic anaemia is present.
  - Use single-unit transfusions and reassess before giving additional units.

Alternative Strategies for Blood Conservation –

In maternity patients, other non-obstetric interventions can be applied to minimize maternal blood loss in the peripartum period, such as intra-operative cell salvage, radiological interventions etc.

Intraoperative Cell Salvage (IOCS) –

IOCS involves the collection, filtering and reinfusion of washed maternal blood lost during surgery, especially during high-risk caesarean sections where the anticipated blood loss is likely to result in a transfusion (See Section 7.2). The following must always be considered before IOCS can be performed in obstetric cases;

- Anti-D immunoglobulin should be administered following the reinfusion of salvaged red cells, if it is performed in Rh-D negative maternity patients where the cord blood group is confirmed as Rh-D positive.

Interventional Radiology (IR) –

IR involves iliac balloon catheters and transcatheter arterial embolism to block the main vessels supplying the uterus. This is however not as efficient in obstetric patients compared to other groups due to the extensive collateral pelvic vascular in pregnancy.

Risk of transfusing uncrossmatched Blood (i.e., from an emergency blood fridge) and Importance of compatibility in pregnancy (See Chapter 4, Section 4.3) –

Emergency blood transfusion is often required in obstetric emergencies, especially in PPH. However, using uncrossmatched emergency blood carries significant risks, namely –

- *Haemolytic Transfusion Reactions (HTR) –*
  - Women with previous transfusions or multiple pregnancies, are more likely to have pre-existing antibodies, which increases their risk for acute or delayed haemolytic transfusion reactions.
  - Crossmatching before a transfusion is ensures that corresponding antigen-negative blood is used for patients with alloantibodies.

- *Other Transfusion Reactions –*
  - The use of emergency uncrossmatched blood, increases the risk of other transfusion reactions suck as Transfusion-Related Acute Lung Injury (TRALI). The risk for TRALI increases, especially with the use of plasma-containing products like FFP or whole blood (See Chapter 8, Section 8.1).

- *Alloimmunization and Haemolytic Disease of the Foetus and Newborn (HDFN) –*
  - Rh-negative mothers receiving Rh-positive emergency blood may develop anti-D antibodies, leading to alloimmunization, which can result in HDFN (See Chapter 8, Section 8.2).
  - An Indirect Coombs Test (ICT) and antibody screen to detect maternal alloantibodies (anti-D, anti-Kell, anti-Duffy, anti-Kidd, etc.) antenatal care booking and at 28 Weeks.

Therefore, compatibility testing in maternity patients are critical for ensuring maternal and fetal safety in both emergency and planned transfusions. Blood samples for cross matching needs to be taken prior to starting any emergency blood units.

Section 7.4 – Transfusion in People Living with HIV/AIDS (PLWH)

Namibia is experiencing a generalized HIV epidemic, with an estimated adult prevalence of 12.6% (15.7% in females and 9.3% in males) as of 2017, according to Namibia Population-Based HIV Impact Assessment (NAMPHIA). Despite this, viral load suppression was 77.4% in this group. Blood and blood components are more frequently prescribed in PLWH due to common haematological complications, particularly cytopaenia's.

ANAEMIA IN PLWH

It is estimated that about 18–32% of people living with HIV (PLWH) without AIDS and 48–85% of those with AIDS have mild anaemia. **The causes of anaemia in PLWH are as follow, however they are often multifactorial or overlapping –**

- Reduced red blood cell production due to bone marrow infiltration, nutritional deficiencies (iron, B12, folate), or drug-induced suppression.
- Anaemia of chronic disease/inflammation caused by HIV itself, opportunistic infections, or HIV-associated malignancies.
- Autoimmune haemolysis from immune dysregulation related to HIV.

The following should be considered in the management of anaemia in PLWH before a blood transfusion is prescribed –

- **Anti-retroviral Therapy (ART) –**
  - Initiating ART as soon as possible, as the majority of PLWH will have resolution of anaemia after 12 months of ART without requiring any additional interventions.
  - In patients already on ART, consider drug-induced anaemia, particularly from Zidovudine (AZT); switching to an alternative ART regimen may reduce recurrence.

- **Positive direct anti-globulin test (DAT) complicate compatibility testing –**
  - A positive DAT almost always indicate autoimmune haemolytic anaemia (AIHA), however it may be

absent in some cases. About 20 – 40% of PLWH has a positive DAT.
- AIHA is common in PLWH which complicate compatibility testing. This may delay a blood transfusion, since serological investigations have to be done to rule out alloantibodies due to the fact that red blood cell autoantibodies may mask clinically significant alloantibodies. A haemolytic reaction is unlikely in patients with a positive DAT and indirect anti-globulin (IAT) once alloantibodies have been excluded.
- Issuing of least incompatible blood may be the best option for these patients, however must ALWAYS be transfused with caution.
- The underlying cause of AHIA must be investigated and managed accordingly, i.e., with ART, steroids, and IVIG therapy before a red cell transfusion is indicated.

- **Indications and dosage of RCC transfusion –**
  - Transfusion indications for PLWH are the same as for HIV-negative individuals. However, PLWH may have impaired bone marrow function requiring temporary haematological support until ART improves marrow recovery.
    - Chronic anaemia is common and often well-tolerated; avoid transfusion unless clinically necessary due to associated risks.
    - A maximum of 1 – 2 units RCC should be given slowly to patients who are severely symptomatic for anaemia, especially if they are critical ill due to the risk of fluid overload.

THROMBOCYTOPAENIA IN PLWH

Thrombocytopenia is common in PLWH and increases with disease progression. The commonest aetiology is Immune thrombocytopenia (ITP).

ITP occurs in up to 30% of PLWH and is due to HIV-induced autoantibodies which is directed against platelet-associated antigens. PLWH may present with ITP as the first manifestation of their disease and similar to AIHA, it is associated with a poor prognosis.

The following should be considered in the management of thrombocytopaenia in PLWH before a platelet transfusion is considered –

- **Anti-retroviral Therapy (ART) –**
  - Initiate on ART as soon as possible, to reduce the prevalence of thrombocytopenia and its associated complications in PLWH.

- **Platelet count –**
  - The underlying cause of thrombocytopenia in all cases must be investigated and managed accordingly.
  - Patients with a platelet count more than 10 x 10^9/L generally do not require a prophylactic platelet transfusion, since they generally do not bleed spontaneously. Except in in the following circumstances
    - Prematurity or neonatal thrombocytopaenia
    - Intracranial pathology or has increased risk for an intracranial bleed
    - Functional platelet disorder
    - Non-compressible site bleeding

- **Management of confirmed ITP cases –**
  - Recommended to be managed by a haematologist.
  - ***High dose steroids and/or IVIG must be considered in confirmed ITP cases before a transfusion;***
    - Initiate on high dose corticosteroids until the platelet count has stabilized at a level of 100 x 10^9/L, followed by dose tapering depending on the protocol used.

  - Initiate the patient on IVIG Therapy with or without steroids, if the platelet count is less than 30 x 10^9/L, presence of active bleeding and a rapid response is required. Except in patients with has haemophilia or those who are on anticoagulant therapy, where IVIG therapy should be initiated if the platelet drops below 50 x 10^9/L.
  - Initiate the patient on IVIG Therapy with or without a low dose Rituximab when there is a high risk of bleeding or presence of bleeding.
- **A platelet transfusion should be reserved for patients with active bleeding or those at immediate risk for bleeding;**
  - The therapeutic effect of platelet transfusion in ITP is often suboptimal due to the rapid destruction of transfused platelets by circulating autoantibodies.
  - Repeated transfusions may result in alloimmunization, leading to the development of platelet refractoriness. A condition where patients exhibit poor or no response to platelet transfusions, thereby reducing the efficacy of future transfusions.

- **Indications & dosage of platelet concentrate transfusions –**
  - The indications for platelet concentrate transfusion in PLWH are usually the same as for people who does not have HIV. The same principles of a single mega-unit approach must apply.

Section 7.5 – Chronically Transfused

Chronic red blood cell transfusions are commonly required in individuals experiencing persistent anaemia resulting from ineffective erythropoiesis. This condition characterised by the continuous need for RBC transfusion is often due to various haematological disorders, including:

- Bone marrow failure syndromes, such as myelodysplastic syndromes, myelofibrosis, and aplastic anaemia.
- Inherited haemoglobinopathies, including sickle cell disease and thalassemia.
- Congenital and acquired dyserythropoietic anaemias.

These haematological conditions necessitate frequent red blood cell transfusions to manage and alleviate symptoms. However, it is crucial to note that long-term transfusion therapy can lead to several complications, as detailed in Table 7.5 of the guideline.

Table 7.5 – Complications of chronic transfusions

Complication	Comment

Iron Overload	- Excessive iron is deposited in organs throughout the body which has significant health consequences –
	  - Liver (Liver cirrhosis leading to hepatocellular carcinoma)
	  - Heart (Cardiomyopathies & irregular heart rhythms)
	  - Endocrine Organs (“bronze” diabetes, hypothyroidism & hypogonadism)

Complication	Comment
Alloimmunization	- Chronic transfusions result in the formation of alloantibodies against specific donor red cell antigens which can complicate subsequent blood transfusions, as it can interfere with cross match testing and therefore a delay in obtaining compatible blood.
Infection Risk	- Donor exposure must be minimized in patients on chronic transfusion regimens, as the residual risk for transfusion transmissible infections increase with the amount of blood products transfused.
Psychosocial Burden	- Red cell transfusions provide temporarily improvement in the overall health of these patients. However, chronic transfusions are costly, inconvenient and contributes to psychological problems such a mild to severe depression and anxiety.

The main goals of transfusion patients who require chronic transfusion regimens are to alleviate acute and chronic symptoms of anaemia, prevent serious complications and to improve functional outcomes. Therefore, no clear-cut transfusion threshold for these various conditions, however the following transfusion thresholds in table 7.6 has been suggested –

Table 7.6– Suggested transfusion thresholds for different aetiologies which require chronic transfusions

Aetiology	Transfusion Hb Threshold
Myelodysplastic Syndromes	- The REDDS pilot trail indicated that in MDS on chronic transfusion regimens a restrictive transfusion approach (Hb 8.0 g/dL, to maintain the Hb between 8.5 – 10 g/dL) is feasible.
Myelofibrosis	- Limited studies are available to determine a definitive transfusion threshold; however, some suggested a Hb transfusion threshold of < 8.0 g/dL in symptomatic patients. - Clinical discretion should be applied for transfusion on a case to case basis to alleviate symptoms and reduce the risk of complications.
Aplastic Anaemia	- Limited studies are available to determine a definitive transfusion threshold; therefore, it should be individualized on a case to case basis (i.e., clinical situation, co-morbidities and risk of complications. - A restrictive transfusion threshold of less than 7.0 g/dL is advised for stable adult patients, except for those with cardiovascular disease, where the threshold is less than 8.0 g/dL. This recommendation is made in the absence of extensive data as the guidelines aim to balance transfusion necessity against potential risks.

Aetiology	Transfusion Hb Threshold
Sickle Cell Disease (SCD)	- **The transfusion thresholds and haemoglobin targets generally vary in patients with SCD depending on the clinical indication for transfusion –** - **Acute indications** (i.e., acute stroke, severe acute chest syndrome, multi-organ failure, acute sickle cell hepatic/splenic sequestration, patients undergoing moderate to severe risk surgery) – - The general Hb transfusion threshold is < 7 g/dL with a target Hb of 9 – 10 g/dL, especially in an acute stroke. - **Chronic indications** (i.e., stroke prophylaxis, silent infarcts, recurrent acute chest syndromes/painful episodes in clinically asymptomatic) – - The general Hb transfusion threshold is < 7g/dL or is the baseline Hb falls ≥ 2 g/dL.
Thalassemia	- **Transfusion-dependent Thalassemia should be managed on a regular transfusion programme where a transfusion is administered every 2 – 4 weeks to maintain the –** - Pre-transfusion Hb between 9.5 – 10.5 g/dL - Post-transfusion Hb of 13.0 – 15.0 g/dL - A higher Hb of 10.5 or 11.0 g/dL must be maintained in special circumstances, such as during a growth spurt for children or individuals with evidence of extramedullary haematopoiesis, leg ulcers, or heart failure.

Additional recommendations for chronic transfusions –

For patients who require chronic red cell transfusions, it is of utmost importance to maximize the survival of the transfused red cells, minimize the occurrence of transfusion reactions and alloimmunization as much as possible. Therefore, these additional recommendations have been made for red cell transfusions if available –

- Attain a red cell genotype or extended red cell phenotype for all patients who will likely require chronic transfusion, ideally prior to the first blood transfusion.
- Transfuse RCC which is genotypically or phenotypically matched for the following antigens: Rh (D, C, c, e) and K.
- Transfuse fresh RCC's (<5 days)
- Transfuse leucodepleted RCC's

Transfusion of emergency uncrossmatched blood is discouraged in patients on chronic transfusion regimens as it increases the risk of alloimmunization (See Chapter 8, Section 8.2).

Section 7.6 – Massive Transfusion

Massive blood loss is a critical emergency encountered in various clinical situations, including trauma, major surgeries, gastrointestinal bleeding, and obstetric haemorrhage. If not recognized early and managed promptly, it remains a leading cause of preventable death.

Trauma is a major cause of morbidity and mortality in Namibia and globally, with uncontrolled haemorrhage causing many early deaths. Rapid recognition of severe bleeding and timely transfusion based on clinical signs and injury mechanism are vital. Indications include:

- Signs of haemorrhagic shock (hypotension, tachycardia, altered mental status, cold/clammy skin, weak pulses)
- Bleeding unresponsive to crystalloid fluids
- High-risk injuries (pelvic fractures, abdominal trauma)
- Blood loss over 30% of total volume

The Trauma-Associated Severe Haemorrhage (TASH) Score helps predict the need for massive transfusion after trauma. Managing major bleeding involves activating a Massive Transfusion Protocol (MTP) to restore volume, oxygen delivery, and coagulation while minimizing complications like coagulopathy and hypothermia. Balancing intravascular volume and vascular tone is crucial in traumatic shock.

Permissive hypotension, limiting fluids and using norepinephrine to maintain a MAP of 40–60 mm Hg or cerebral perfusion pressure of 60–70 mm Hg, reduces blood loss and coagulopathy while ensuring organ perfusion. It is contraindicated in traumatic brain or spinal injuries, where systolic pressure must be maintained above 80–90 mm Hg.

Balanced Component Therapy and the PROPPR Study

The Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) study demonstrated that using a 1:1:1 ratio of Red Cell Concentrates (RCC), Fresh Frozen Plasma (FFP), and Platelets led to better haemostasis and lower 24-hour mortality compared to a 1:1:2 ratio. This balanced transfusion strategy, improves the coagulation profile, reduces early exsanguination and is the recommended approach for massive haemorrhages and MTPs.

In the Namibian healthcare context, this balanced component therapy should be standard in all cases where MTP is activated (see Figures 7.1 and 7.2 for algorithmic guidance).

Definitions of Massive Haemorrhage/Transfusion

Traditional (retrospective) definitions still guide the activation of MTPs in clinical practice as indicated in table 7.7.

Table 7.7: Definitions for Massive Haemorrhage/Transfusion	
Adults	**Paediatrics**
- Loss of ≥ 1 total blood volume (TBV) within 24 hours or ≥ 50% of TBV in 3 hours. - Blood loss of > 1500 mL in a 70kg adult. - Ongoing blood loss of > 150ml/min - Transfusion of > 10 units RCC in 24 hours or > 4 units in 1 hour.	- Loss of ≥ 1 TBV within 24 hours, ≥ 50% of TBV in 3 hours or ≥10% of TBV per minute. - Blood loss of > 30 ml/kg and ongoing bleeding - Transfusion of > 40 ml/kg in 24 hours.

These retrospective definitions are often difficult to apply in acute clinical situations; therefore, the trend is to use a more anticipatory or dynamic approach which is based on the clinical status, physiology and response to fluid resuscitation therapy (i.e., SBP, Pulse, RR etc.) as indicated in figure 7.1 and 7.2. However, paediatric patients have a good physiological reserve and can maintain their arterial pressure even after a 20 – 40% blood volume loss. Therefore, the clinical signs and symptoms of hypovolaemia might not be a good indicator of early haemorrhage as in adult patients.

FIGURE 7.1 – ADULT MASSIVE TRANSFUSION PROTOCOL

CRITERIA FOR MTP ACTIVATION

MAIN CLINICAL CRITERIA

Hemorrhage (any one of):

- Total Blood Volume (TBV) loss in 24 hrs. OR >50% TBV loss in 3 hrs.
- Ongoing blood loss > 150 ml/min (e.g., 3L in 20 min)
- Blood loss >1500 ml in 70 kg adult male
- Transfuse >10 RCC in 24 hrs. OR >4 units RCC in 1 hr.

Hemorrhagic Shock:

- SBP <70 mmHg + HR >120/min + RR >30/min + Urine output <20 ml/h + Hypothermia (temp <34°C)
- SBP <80 mmHg + >3 L crystalloid resuscitation ± inotropes without improvement

SUPPORTING LABORATORY CRITERIA

Coagulation indices:			
INR	> 1.5	PTT	> 60 sec
PT	> 18 sec	Fibrinogen	< 1.5 g/L
FBC:			
Hb	< 4 g/dl	Hct	< 30%
Blood gases:			
pH	< 7.1	Calcium	< 1.1 mmol/L
Base Excess	< -8		
U&E:			
Lactate	> 4 mmol/L	Potassium	> 7 mmol/L or ECG changes

INITIATE MTP

IMMEDIATE ACTIONS

- Identify the cause of bleeding & control as soon as possible.
- **Attend to ABC –**
  - Administer Oxygen
  - Gain IV Access (2 large bore peripheral/central access)
  - Do baseline blood tests: Crossmatch, FBC, U&E, ABG, C oagulation Screen (INR, PT, aPTT)
  - Fluid Resuscitation with crystalloids/colloids: warmed, controlled/restrictive.
  - Transfuse a maximum of 2 units of O-Negative RCC from the emergency blood fridge, if crossmatched blood will not be available within 15–20 minutes.
- Avoid Hypothermia

Order 1st Massive Transfusion Pack (MTP 1) –
4 RCC & 4 FFP

BLEEDING CONTROLLED? YES →

NO ↓

Order 2nd Massive Transfusion Pack (MTP 2)
4 RCC, 4 FFP & 1 mega-unit Platelets

BLEEDING CONTROLLED? YES →

NO ↓

Order 3rd Massive Transfusion Pack (MTP 3)
4 RCC (2 RCC if cryo/fibrinogen not available), 4 FFP (2 FFP if cryo/fibrinogen not available) and if available: Cryoprecipitate (1 unit/5-10kg)/ Fibrinogen (50mg/kg)

BLEEDING CONTROLLED? YES →

NO ↓ (Loop 2-3 x, then proceed)

Consider Recombinant Factor VIIa (5mg)

TERMINATE MTP

TEAM LEADER ROLE (CONSULTANT/SENIOR DOCTOR)

- Initiate and terminate MTP
- Continual patient assessment and ABC management
- **Delegate team roles:**
  - Communication with clinical & support services
  - Transport of samples & blood components
  - Secure IV access
  - Patient identification and consent

DO Blood Tests or TEG/ROTEM (if available)

- Baseline and repeat blood tests every 60 minutes or after every 4 units of blood.
- Repeat Crossmatch after 72 hours or on blood bank request

TARGETS FOR CORRECTION

Coagulation		FBC	
INR PT PTT Fibrinogen	< 1.5 < 18 sec < 35 sec > 1.5 - 2 g/L	Hb Plalets	7 - 9 g/dl > 50 × 10^9/L (> 100 CNS injury)
Blood gases		**U&E**	
pH Base Excess Calcium	> 7.2 > -6 mmol/L > 1.1 mmol/L	Potassium Lactate Temperature	< 5 mmol/L < 4 mmol/L ≥ 35 °C

ADJUNCT THERAPIES

Tranexamic Acid (TXA) in bleeding patients or high risk of bleeding, especially trauma and acute obstetric haemorrhage:

Administer TXA within 3 hours (No benefit if administered after 3 hours of bleeding onset)

- 1g bolus slowly infused over 10 minutes
- Then 1g infusion over 8 hours

Coagulant reversal required

Patient on Warfarin:

- Vitamin K 10 mg IV stat PLUS Prothrombin complex concentrate (PCC) - for PCC dosage see below;
- INR 2-3.9 give 25 IU/kg; INR 4-5.9 give 35 Ili/kg; INR >6.0 give 50IU/kg

Patient on Heparin:

- Protamine 25-50 mg IV slowly over 10 minutes (1mg protamine reverses 100 units heparin)

Reversal of new Anticoagulants:

- Discuss with a haematologist

Correct Hypocalcaemia

10% Calcium Chloride:

- 10 ml IV if ionized calcium < 1.1 mmol/L or after every 4 units of RCC

Prevent Hypothermia

- Use a fluid/blood warming device – Routinely warm all fluids and blood
- Use a forced air warming device

Correct Hypofibrinogenaemia

To raise Fibrinogen by 1g/L (approximately):

- FFP 4 units or cryoprecipitate 1 single/ 5 – 10 kg or fibrinogen concentrate 3 – 4 g

FIGURE 7.2 – PAEDIATRIC MASSIVE TRANSFUSION PROTOCOL

CRITERIA FOR MTP ACTIVATION

MAIN CLINICAL CRITERIA

Hemorrhage (any one of):

- > 1 TBV loss in 24 hours or > 50% TBV loss in 3 hours
- Blood loss > 10% TBV/min
- Blood loss > 80ml/kg in 24 hrs., 40 ml/kg in 3 hrs., or 2 – 3 ml/kg/min.
- Transfusion of > 40 ml/kg blood products

Hemorrhagic Shock:

- Lethargy, altered mental status, capillary refill > 2 sec, narrow pulse pressure, increased HR, hypotension, systolic murmur, increased RR, reduced urine output & hypothermia.

SUPPORTING LABORATORY CRITERIA

Coagulation indices:			
INR	> 1.5	PTT	> 60 sec
PT	> 18 sec	Fibrinogen	< 1.5 g/L
FBC:			
Hb	< 7 g/dl	Hct	< 30%
Blood gases:			
pH	< 7.3	Calcium	< 1.1 mmol/L
Base Excess	< -8		
U&E:			
Lactate	> 4 mmol/L	Potassium	> 6.5 mmol/L or ECG changes

INITIATE MTP

IMMEDIATE ACTIONS

- Identify the cause of bleeding & control as soon as possible
- **Attend to ABC –**
  - Administer Oxygen
  - Gain IV Access (intraosseous if peripheral not possible)
  - Do baseline blood tests: Crossmatch, FBC, U&E, ABG, Coagulation Screen (INR, PT, aPTT)
  - Fluid Resuscitation (crystalloids): warmed, restrictive (maximum 2 x 20ml/kg, 4x 10ml/kg boluses in trauma) and avoid a rapid infusion rate that can dislodge a clot.
  - Transfuse 20 ml/kg emergency O Negative RCC
- Avoid Hypothermia

Order 1st Massive Transfusion Pack (MTP 1) –

Children < 10 kg – RCC 25ml/kg, FFP 20 ml/kg, 1 paeds platelets 15ml/kg

Children 10 - 15 kg – 1 adult RCC (25ml/kg), 1 adult FFP (20 ml/kg), 2 paeds platelets (15ml/kg)

Children 16 -25 kg – 2 adult RCC (25ml/kg), 2 adult FFP (20 ml/kg), 1 adult platelets (15ml/kg)

Children 26 - 50 kg – 3 adult RCC (25ml/kg), 3 adult FFP (20 ml/kg), 1 adult platelets (15ml/kg)

Children > 50 kg – 4 adult RCC (25ml/kg), 4 adult FFP (20 ml/kg), 1 adult platelets (15ml/kg)

BLEEDING CONTROLLED? YES

NO

Order 2nd Massive Transfusion Pack (MTP 2) –

RCC and FFP as in MTP 1 PLUS Cryoprecipitate 4ml/kg (No platelets in MTP 2, ONLY cryoprecipitate to be added)

BLEEDING CONTROLLED? YES

NO (Loop 2-3 x, then proceed)

Consider Recombinant Factor VIIa (90 – 120 pg/kg)

TERMINATE MTP

TEAM LEADER ROLE (CONSULTANT/SENIOR DOCTOR)

- Initiate and terminate MTP
- Continual patient assessment and ABC management
- **Delegate team roles:**
  - Communication with clinical & support services
  - Transport of samples & blood components
  - Secure IV access
  - Patient identification and consent

DO Blood Tests or TEG/ROTEM (if available)

- Baseline and repeat blood tests every 60 minutes or after every 4 units of blood.
- Repeat Crossmatch after 72 hours or on blood bank request

TARGETS FOR CORRECTION

Coagulation		FBC	
INR PT & PT < 1.5 x normal Fibrinogen	< 1.5 PT < 18 sec PTT <50 sec > 1.5 - 2 g/L	Hb Plalets	8 - 9 g/dl > 50 x 10⁹/L (> 100 CNS injury)
Blood gases		**U&E**	
pH Base Excess Calcium	> 7.2 > -6 mmol/L > 1.1 mmol/L	Potassium Lactate Temperature	< 5 mmol/L < 3.5 mmol/L > 36 °C

ADJUNCT THERAPIES

Prevent Coagulopathy in trauma with TXA

Administer Tranexamic Acid within 3 hours
(TXA has no benefit if administered after 3 hours of bleeding onset)
- 15 – 20 mg/kg bolus slowly over 10 minutes
- Then infuse 2 mg/kg/hr. (maximum 125mg/hr.) over 8 hours

Correct Hypocalcaemia

10% Calcium Chloride:
- 0.2ml/kg IV if ionized calcium < 1.1 mmol/L over 30 minutes (Maximum of 10 mL)

Prevent Hypothermia
- Use a fluid/blood warming device – Routinely warm all fluids and blood and Use a forced air warming device

Correct Hypofibrinogenaemia

To raise Fibrinogen by 1g/L (approximately):
- FFP 15-20ml/kg or cryoprecipitate 1 unit/ 5 -10 kg or fibrinogen concentrate 70 mg/kg (safety and efficiency not established in children < 12) & beware of fluid overload

Correct Acidosis
- Sodabic if airway well supported & normal pCO2 at extremely slow infusion rates in neonates

PAEDIATRIC CIRCULATORY PARAMETERS & EBV

Calculating Estimated Blood Volume in Paediatric Patients
Premature: 90 – 100 ml/kg, < 3 Months: 80 – 90 ml/kg, > 3 Months: 70 ml/kg, Obese: 65 ml/kg

Important Values		
	Hypotension:	Urine Output:
Neonates (≤ 28 days): Infants (1 mo. – 1 yr.): Children ≤10 years: Children > 10 years:	< 60 mmHg < 70 mmHg < 70 + (age in years x 2) < 90 mmHg	3 ml/kg/hr. 2 ml/kg/hr 1 – 2 ml/kg/hr. 0.5-1 ml/kg/hr.

ESSENTIALS

- Transfusion of blood and blood product are not always straight forward and depend on multiple factors, i.e., underlying medical condition, clinical status, laboratory investigations and response to treatment.
- As indicated in this chapter the principles of PBM can be applied across multiple disciplines, and are not only limited to surgery.
- Transfusion MUST always be based on latest evidence-based practices to ensure the best possible outcome for the recipient.

REFERENCES

- Mokhtar, G., et al. Egyptian Pediatric Clinical Practice Guidelines Committee (EPG) 2024. Transfusion of blood components in pediatric age groups: an evidence-based clinical practice guideline adapted for the use in Egypt using 'Adapted ADAPTE'. Annals of hematology, 103(4), 1373–1388. https://doi.org/10.1007/s00277-024-05657-4
- Deschmann E, Dame C, Sola-Visner MC, et al. Clinical Practice Guideline for Red Blood Cell Transfusion Thresholds in Very Preterm Neonates. JAMA Netw Open. 2024;7(6):e2417431. doi:10.1001/jamanetworkopen.2024.17431
- Marsicano, D., et al. Preoperative anaemia and clinical outcomes in the South African Surgical Outcomes Study (2018). South African medical journal, (10), 839–846. https://doi.org/10.7196/SAMJ.2018.v108i10.13148
- Spahn, D. R., Muñoz, M., Klein, A. A., Levy, J. H., & Zacharowski, K. 2020. Patient Blood Management: Effectiveness and Future Potential. Anesthesiology, 133(1), 212–222. https://doi.org/10.1097/ALN.0000000000003198
- Pavenski, K., et al. ONTraC: A 20-Year History of a Successfully Coordinated Provincewide Patient Blood Management Program: Lessons Learned and Goals Achieved. 2022. Anesthesia and analgesia, 135(3), 448–458. https://doi.org/10.1213/ANE.0000000000006065
- van den Berg K, et al. A review of the use of blood and blood products in HIV-infected patients. South Afr J HIV Med. 2012 Jun;13(2):87-104. doi: 10.4102/sajhivmed.v13i2.146, PMCID: PMC5419681, https://pmc.ncbi.nlm.nih.gov/articles/PMC5419681/
- McLornan DP, Psaila B, Ewing J, Innes A, Arami S, Brady J, et al. The management of myelofibrosis:

A British Society for Haematology Guideline. Br J Haematol. 2024; 204(1): 136–150. https://doi.org/10.1111/bjh.19186

- Kulasekararaj A, Cavenagh J, Dokal I, Foukaneli T, Gandhi S, Garg M, et al. Guidelines for the diagnosis and management of adult aplastic anaemia: A British Society for Haematology Guideline. Br J Haematol. 2024; 204(3): 784–804. https://doi.org/10.1111/bjh.19236

- Davis, B.A., Allard, S., Qureshi, A., Porter, J.B., Pancham, S., Win, N., Cho, G., Ryan, K. and (2017), Guidelines on red cell transfusion in sickle cell disease Part II: indications for transfusion. Br J Haematol, 176: 192-209. https://doi.org/10.1111/bjh.14383

- Association for the Advancement of Blood and Biotherapies (AABB). Association Bulletin. Pretransfusion Hemoglobin Thresholds for Chronic, Nonemergent RBC Transfusions in Beta Thalassemia. 2023. https://www.aabb.org/docs/default-source/default-document-library/resources/association-bulletins/ab23-02.pdf

- Farmakis D, Porter J, Taher A, Domenica Cappellini M, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. Hemasphere. 2022 Jul 29;6(8):e732. doi: 10.1097/HS9.0000000000000732. PMID: 35928543; PMCID: PMC9345633

- National Blood Authority (NBA) (2014). Patient Blood Management Guidelines: Module – Obstetrics and Maternity. NBA, Canberra, Australia. https://www.blood.gov.au/module-5-obstetrics-and-maternity-patient-blood-management-guidelines

- Kidson-Gerber, G., Kerridge, I., Farmer, S., Stewart, C.L., Savoia, H. and Challis, D. (2016), Caring for pregnant women for whom transfusion is not an option. A national review to assist in patient care. Aust N Z J Obstet Gynaecol, 56: 127-136. https://doi.org/10.1111/ajo.12420

- Shah, A., Palmer, A. J. R., & Klein, A. A. 2020. Strategies to minimize intraoperative blood loss during major surgery. The British journal of surgery, 107(2), e26–e38. https://doi.org/10.1002/bjs.11393

- Melesse, D. Y., Admass, B. A., & Admassie, B. M. 2024. Perioperative Blood Transfusion Strategies in Orthopaedic Surgery: A Comprehensive Review and Analysis. Open Access Surgery, 17, 55–62. https://doi.org/10.2147/OAS.S430812

- Stanworth, S. J., Dowling, K., Curry, N., Doughty, H., Hunt, B. J., Fraser, L., Narayan, S., Smith, J., Sullivan, I., Green, L., & Transfusion Task Force of the British Society for Haematology (2022). Haematological management of major haemorrhage: a British Society for Haematology Guideline. British journal of haematology, 198(4), 654–667. https://doi.org/10.1111/bjh.18275

- Villanueva, C., et al. (2013). Transfusion strategies for acute upper gastrointestinal bleeding. The New England journal of medicine, 368(1), 11–21. https://doi.org/10.1056/NEJMoa1211801

CHAPTER 08
TRANSFUSION ADVERSE EVENTS

A blood transfusion always carries the risk of an adverse event, and doctors prescribing blood or blood products must be cautious. Weighing up the benefits of a transfusion versus the risks is a major consideration by the prescribing doctor before requesting blood. A significant risk of blood transfusion is when a patient receives an 'incorrect blood component'. Strict adherence to correct sampling, compatibility testing and administration procedures is therefore of paramount importance, even in an emergency.

Table 8.1 – Definitions of Adverse Events	
Adverse Event	Any unintended and undesirable occurrence before, during and after a transfusion of blood and blood components. Adverse events may be due to an error or incident which may or may not result in a transfusion reaction. **Examples –** - Alloimmunization - Infectious disease transmission
Incident	Any transfusion error or deviation from standard operating procedures which led to the transfusion of blood and blood components that do not meet the requirements for transfusion, or that was intended for another patient. It may or may not result in a transfusion reaction. **Examples –** - Transfusion of wrong blood to the wrong patient/ wrong blood in tube. - Inappropriate monitoring of blood fridges which result in cold chain challenges.
Near miss	A subset of incidents that are discovered before the start of a transfusion that could have led to a wrongful transfusion or a transfusion reaction. **Example –** - Transport box containing blood units delivered to the wrong ward, but detected before transfusion was administered
Transfusion Reaction	An undesirable response or effect in a patient temporarily associated with the administration of blood or blood components. It may or may not be the result of an incident. **Example –** - Acute haemolytic transfusion reaction - Allergic transfusion reactions

Section 8.1 - Transfusion Reactions

CLASSIFICATION OF TRANSFUSION REACTIONS

Transfusion reactions are classified according to timing, severity and pathophysiology as indicated in table 8.2 below –

Table 8.2 – Classification of Transfusion Reactions

Timing and speed of onset (i.e., acute or delayed)	
Acute Transfusion Reactions	- Occurs **within 24 hours** after the commencement of the transfusion. - The onset of severe acute transfusion reactions are usually within minutes after the commencement of the transfusion (i.e., acute haemolytic transfusion reaction)
Delayed Transfusion Reactions	- Occur **24 hours after** the transfusion, and usually up to 28 days. - Some may only become evident after many years (i.e., iron overload in chronically transfused patients)
Severity (i.e., non-severe, severe, life-threatening & death)	
Minor Transfusion Reactions	- Resolves without or with non-invasive intervention (i.e., symptomatic treatment)
Severe Transfusion Reactions	- Resulted in hospitalization or prolongation of hospitalization AND/OR - Resulted in persistent/ significant disability or incapacity, OR - Require an intervention to prevent permanent damage/ impairment of a body function.
Life-threatening Transfusion Reactions	- Requires major intervention after the transfusion to prevent a fatal outcome (i.e., intensive care admission, intubation, vasopressors etc.)
Pathophysiology (i.e., immune vs. non-immune mediated)	
Immunological Transfusion Reactions	- Occur due to antigens (Ag) that are recognized by a corresponding antibody (Ab). As all cellular components of blood (red cells, leucocytes and platelets) carry antigens on their surface membranes, they can all be involved in immune-mediated transfusion reactions - These include haemolytic transfusion reactions, transfusion-related acute lung injury (TRALI) etc.

Nonimmunological Complications	- These are usually caused by the physical effects of blood components or the transmission of disease. - These include haemolysis due to inappropriate blood warming, circulatory overload, iron overload etc.

SYMPTOMS AND SIGNS OF TRANSFUSION REACTIONS

Patients who receive a blood transfusion must be monitored closely for symptoms and signs of a transfusion reaction during and after the transfusion. However, the symptoms and signs are often overlapping and non-specific, it is thus of utmost importance that the transfusing healthcare professionals are able to differentiate between the symptoms and signs of various reactions as indicated in table 8.3, to ensure timely and appropriate investigation as well as management thereof.

Urticaria (hives), rash, pruritis, fever, rigors and chills are common symptoms and signs observed during a transfusion reaction, which are often self-limiting or require minimal intervention. However, restlessness, respiratory distress, hypotension, tachycardia or bradycardia, generalized pains, oliguria, anuria and haemoglobinuria indicate a more serious transfusion reaction.

INITIAL MANAGEMENT OF A TRANSFUSION REACTION

Once an acute transfusion reaction is suspected, one should always **err on the side of caution and take immediate action.** The following steps must be followed in all cases where a transfusion reaction is suspected –

- Stop the transfusion immediately.
- Remove the blood bag and the blood administration set.
- Maintain venous access with Normal Saline (0.9% NaCl).
- Call for help, by informing other nursing staff or a doctor.
- Do a clerical check to verify the patient and product details, to rule out a wrong blood to patient incident.
- Take the patient's vital signs and observations and record them regularly.
- Manage the acute symptoms and stabilize the patient.
- Notify the local blood bank staff telephonically immediately.
- **Once the patient has been stabilized, send the following to the local blood bank –**
  - The completed transfusion reaction report form (FRM/LAB/038)
  - The suspected container of blood and the blood administration set
  - All previous containers of transfused blood and blood administration sets
  - All unused blood units issued for the patient
  - **Collect and forward the following samples to the blood bank;**
    - Immediate post-transfusion clotted blood sample (5 ml into red top tube) taken from the vein opposite infusion site
    - Immediate post-transfusion EDTA blood sample (5 ml into purple top tube) taken from the vein opposite infusion site
    - Immediate post-transfusion urine sample (20ml)

All these actions MUST be done for all suspected transfusion reactions, followed by the specific management as indicated in table 8.3 for the specific transfusion reaction.

Table 8.3 – Transfusion Reactions/Adverse Events

Reaction	Cause/Description	Symptoms/Signs	Specific Management (in addition to the initial management of a transfusion reaction)
Acute Transfusion Reactions			
Febrile Non-Haemolytic Transfusion Reaction (FNHTR)	- Patient leucocyte antibodies bind to corresponding leucocyte antigens on donor leucocytes resulting in the release of cytokines and pyrogens. - Leucoreduction reduces the incidence of FNHTR, but does not eliminate it. - FNHTR is a diagnosis of exclusion. Thus, an acute haemolytic transfusion reaction, bacterial contamination and underlying cause unrelated to the transfusion must be excluded before the diagnosis can be made.	- Occurs during or within 4 hours after the cessation of the transfusion. **Common symptoms/ signs include –** - Present with a fever, i.e., a body temperature of ≥38 °C, or an increase of more than 1 °C compared with that before the transfusion or the presence of headache, nausea, myalgia, malaise, chills and rigors among other symptoms.	**Management:** - Give an antipyretic and observe the patient for signs of an infection or haemolysis. Antipyretic's prior to a transfusion does not decrease the incidence of FNHTR in most patients, and is thus not recommended. - Notify blood bank & transfusion reaction specimens, to rule out an AHTR **Prevention:** - Pre-storage leucodepleted RCC for recurrent FNHTR.
Allergic Transfusion Reaction (ATR)	- Type I hypersensitivity reaction to donor plasma proteins, namely IgG, albumin, haptoglobin etc., or the passive transfer of allergens, namely that to drugs or food, to a sensitized patient. - ATR are usually mild in nature, but can progress to a severe, life-threatening or anaphylactic reaction.	- Occurs within minutes after commencement and up to 24 hours post cessation of the transfusion. **Common symptoms/ signs include –** - Present with mucocutaneous symptoms and signs, such as pruritus, maculopapular rash, urticaria, generalized flushing and angioedema. - No fever	**Management:** - Administer an antihistamine for symptomatic relief.
Anaphylactic Transfusion Reaction	- It occurs mainly in a patient with IgA deficiency who makes antibodies against IgA and then receives blood products containing IgA.	- Occurs suddenly, usually within 5 - 15 minutes of commencement of the transfusion.	**Management:** - Managements depends on the severity of the symptoms (adrenaline, antihistamine, glucocorticoids, bronchodilators etc.). - Test to rule out an IgA deficiency

	- IgA or haptoglobin deficiencies the main causes of recurrent anaphylactic transfusion reactions. - Similar to a mild allergic reaction, more severe or life-threatening.	**Common symptoms/ signs include –** - Present with mucocutaneous (see allergic transfusion reactions) and cardiopulmonary symptoms, such as hypotension, shock, dyspnoea, bronchospasm, and stridor etc. - It may lead to cardiac arrest/death.	**Prevention:** - Future transfusions must be with washed RCC that are plasma free products. - Request for platelets only suspended in PAS - Consider giving factor concentrates etc. instead of plasma
Acute Haemolytic Transfusion Reaction (AHTR)	**Immune-mediated AHTR:** - It is caused by a transfusion of incompatible donor red cells, mainly ABO incompatible, which can lead to complement activation and severe intravascular haemolysis. - Commonly seen in incidents where wrong blood is transfused to a wrong patient (i.e., WBTP or WBIT incidents). **Non-immune mediated AHTR:** - It occurs when haemolysed red blood cells are transfused to a patient. This is caused by concurrent incompatible fluid administration (i.e., 5% dextrose solution), incorrect storage or administration of blood (i.e., the use of a malfunctioning blood warming device that cause overheating of the blood).	- Occurs within minutes after commencement and up to 24 hours post cessation of the transfusion. **Common symptoms/ signs include –** - Fever, pain (back/ flank/loin/infusion site), discomfort, feelings of 'impending doom', anxiety, flushing, hypotension, chills and rigors, 'Coca-Cola' urine/haemoglobinuria **Laboratory evidence –** - Decreased haemoglobin and haptoglobin - Increased LDH and bilirubin - Haemoglobinuria on urinalysis **Complications –** - Renal failure (oliguria/ anuria) - DIC (abnormal bleeding, oozing at IV site, epistaxis) - Death	**Management:** - Maintain intravascular volume and urine output with crystalloids, 0.9% Normal Saline at 400 ml/h in adults to maintain. - Maintain renal function and sufficient diuresis. The use of diuretics, furosemide 120 mg IVI, could be considered to limit renal damage. - In case of renal failure, consider urine alkalinization and/or renal dialysis. - In acute serious cases, consider exchange RBC transfusion. - Observe coagulation profile and consult a haematologist to manage abnormal bleeding. **Prevention:** - Follow procedures on positive patient identification during critical steps of sample collection and transfusion.

	AHTR due to other red cell antibodies - It is caused by the presence of antibodies to other blood groups other than ABO, i.e., anti-D, anti-E and anti-K. These usually results in less severe haemolytic reactions.		
Transfusion Related Acute Lung Injury (TRALI)	- TRALI is characterized by the development of non-cardiogenic pulmonary oedema due to an antibody-mediated reaction, where the pulmonary vasculature is damaged from human neutrophil antigen (HNA) or human leukocyte antigen (HLA) antibodies in the donor blood which bind to antigens of the recipient. - It is associated with the transfusion of plasma-containing products. - Individuals with underlying sepsis, trauma or organ failure are at an increased risk.	- Occurs during or within 6 hours of the cessation of the transfusion. **Common symptoms/ signs include –** - Present with an acute onset respiratory distress (dyspnoea, cyanosis, hypoxaemia, saturation < 90 %, $PaO_2/FiO_2 \leq$ 300mmHg), hypotension, fever, no features of volume overload. **Radiological evidence** - Bilateral pulmonary oedema or infiltrates with a normal sized cardiac silhouette on CXR	**Management**: - Fluid support to maintain blood pressure and cardiac output. - Supplemental oxygen or ventilatory support as indicated. - Diuretics are not indicated. **Prevention:** - Exclusion of donors with a high incidence of HNA and HLA, such as multiparous or donors who had a previous transfusion. Thus, the use of plasma from male donors only have been suggested.
Transfusion Associated Circulatory Overload (TACO)	- TACO is circulatory overload as a result of the infusion of blood or blood product volumes that exceed the patient's circulatory capacity, either due to the infusion of large volumes or a rapid infusion rate.	- Occurs during or within 6 hours of the cessation of the transfusion. **Common symptoms/ signs include –** - Present with acute or worsening of respiratory distress and/or evidence of pulmonary oedema with features of volume overload, such as tachycardia,	**Management:** - Administration of diuretics, which is both diagnostic and therapeutic. - Sit the patient up and give supplemental oxygen if required. **Prevention:** - Slow administration of a unit over 4 hours in at-risk patients.

	- Individuals of extreme ages, i.e., neonates or elderly, and those with congestive heart failure, chronic pulmonary disease, renal dysfunction are at an increased risk.	hypertension, widened pulse pressure, Jugular Venous Distension, enlarged cardiac stilhouette and peripheral oedema **Laboratory/Radiological evidence –** - Elevated BNP - Cardiomegaly and signs of pulmonary oedema.	
Transfusion Associated Dyspnoea (TAD)	- Any respiratory distress that does not meet the diagnostic criteria of TRALI, TACO or an allergic transfusion reaction and that cannot be explained by an underlying condition or other cause. - TAD remains a clinical diagnosis and a diagnosis of exclusion.	- Onset of dyspnoea within 24 hours of the commencement of the transfusion. **Common symptoms/ signs include –** - Present with dyspnoea, hypoxaemia and less frequently a cough, rigors and chills with no other associated signs of TRALI, TACO or other underlying causes or condition.	**Management:** - Supportive management
Bacterial Contamination (Septic Transfusion Reaction)	- Blood components may become contaminated (mainly platelet concentrates) due to various factors such as non-adherence to aseptic techniques, asymptomatic bacteraemia in the donor, improper handling and storage of blood components.	- Occurs usually rapid after commencement of the transfusion and within 1 hour of cessation of the transfusion. **Common symptoms/ signs include –** - Present with fever, chills, rigors, hypotension, shock, nausea or vomiting. - Usually if fever is persistent or unresponsive to symptomatic measures (i.e., antipyretics).	**Management:** - Inspect the unit for any discoloration, clots or signs of leakage. No abnormalities do not exclude bacterial contamination. - Obtain blood cultures on the unit (done at blood bank) and from the patient, then initiate the patient on broad-spectrum antibiotics. - Manage potential complications (i.e., DIC, shock). **Prevention:** - Strict adherence to aseptic techniques throughout the blood collection, processing and transfusion process.

Hypotensive Transfusion Reaction	- Isolated hypotension not due to any of the other acute transfusion reactions (e.g. AHTR, TRALI, anaphylactic TR) is caused by disturbance of the bradykinin metabolism. - The contact of plasma with negatively charged surfaces (e.g. blood transfusion tubing, dialysis membranes and some bedside leucodepletion filters) as well as ACE-inhibitors are contributory factors	- Occurs during usually within minutes after commencement or within 1 hour after cessation of the transfusion. **Common symptoms/ signs include –** - Present in adults as a drop in SBP ≥ 30 mmHg and/or SBP ≤ 80 mmHg. Infants, children and adolescents > 25% drop in SBP from baseline. - Symptoms/Signs such as facial flushing, dyspnoea, abdominal cramps are possible.	**Management:** - Immediately stop the transfusion and provide supportive treatment if required (i.e., vasopressors). - Usually respond within 10 minutes after the transfusion has been stopped.
Delayed Transfusion Reactions			
Delayed Haemolytic Transfusion Reaction (DHTR)	- Transfusion of incompatible donor RBCs after prior sensitization to RBC alloantigen's due to a previous transfusion or a feto-maternal haemorrhage in the presence of an atypical antibody (i.e. anti-Kell, anti-Duffy)	- Occurs typically between 2 – 10 days after the transfusion, however severe cases (due to anti-Kell) can present 24 hours after the transfusion. **Common symptoms/ signs include –** - Present with a fever, mild anaemia and jaundice. In severe reactions the symptoms are similar to an AHTR, but milder. **Laboratory evidence –** - Positive DAT between 24 hours – 28 days after the transfusion - Positive antibody screen in the patient. - Inadequate rise of post-transfusion Hb or a rapid decline of the Hb to the pre-transfusion level.	**Management:** - Mild reactions usually do not require any treatment. - Severe reactions must be managed supportively in accordance to the patient's clinical condition. **Prevention:** - All blood transfusions in the future must be antigen-negative for the implicated antibody.

Post Transfusion Purpura	- Patient platelet antibodies (alloantibodies) are directed against the corresponding antigen on the donor platelets with consequent destruction of the transfused as well as the patient's own platelets. - It is usually seen in woman with a history of RCC/platelet concentrate transfusion.	- Occurs typically 5 – 10 days after the transfusion. **Common symptoms/ signs include –** - Present with a rapid onset of thrombocytopenia (fall from normal ranges to less than 10 x 10^9/L), with or without widespread purpura or mucosal bleeding.	**Management:** - Infuse intravenous immunoglobulins. - Steroids can also be beneficial in some cases. - If a platelet transfusion is indicated it should be HPA-compatible if available. **Prevention:** - Transfuse washed or HPA-compatible blood components.
Transfusion Associated Graft vs. Host Disease (TA-GvHD)	- It occurs when residual lymphocytes in the blood unit engraft and proliferate in the recipient after the transfusion which causes cellular interactions between donor T lymphocytes and recipient cells causing the donor T lymphocytes to mount an immune response against the recipient cells leading to cellular damage. - The incidence of TA-GvHD is rare, but is usually fatal (98 – 99%. mortality rate).	- Occurs typically 10 - 12 days after the transfusion. **Common symptoms/ signs include –** - Present with fever, maculopapular skin rash, generalized wasting, diarrhoea, pancytopenia, hepatitis or hepatic dysfunction.	**Management:** - Elimination of clone of engrafted lymphocytes by chemotherapy at a specialist oncology unit, but it is usually ineffective. **Prevention:** - Use of irradiated cellular blood components (not currently available in Namibia) - Avoid transfusions from close relatives (i.e., directed donations from a first or second degree relative).
Iron overload / Hemosiderosis	- It is associated with chronic RCC transfusions in patients with transfusion-dependent chronic anaemia. Chronic transfusion exceeding ten RCC units significantly increases the risk of iron overload	- Organ damage, especially of the liver (i.e., cirrhosis or hepatocellular carcinoma) and heart (i.e., congestive cardiomyopathy) due to excess iron deposition. - Endocrine dysfunction due to damage to endocrine structures is the earliest evidence of iron toxicity in patients with iron overload, namely pancreas (diabetes mellitus), anterior pituitary (growth hormone deficiency) etc.	**Management/Prevention:** - Minimize transfusions as far as possible and consider the use of alternative treatments. - Continuous monitoring and screening for iron overload in transfusion-dependent patients (i.e. ferritin measurements/ MRI for assessment of cardiac and liver iron status). - Manual RBC exchange transfusion, especially for SSD patients. - Chelation therapy with iron-binding agents to prevent and treat iron overload in transfusion-dependent patients.

Section 8.2 - Alloimmunization

Alloimmunization, an adverse event of transfusion, is an immune system response against foreign antigens, specifically those on the surface of the cellular components of blood, which leads to the production of antibodies. It can be against red blood cell antigens, HLA antigens (present on white blood cells and platelets), human platelet antigen (present on platelets).

CAUSES OF ALLOIMMUNIZATION –

- It can be elicited by blood transfusions, organ/tissue transplants or pregnancy when the foetal blood enters the maternal circulation.

ALLOIMMUNIZATION CONSEQUENCES –

The production of alloantibodies can result in various transfusion related complications, namely –

- **Acute and Delayed Haemolytic Transfusion Reactions –**
  - Acute haemolytic transfusion reactions are rarely the result of alloimmunization, and almost always due to ABO incompatibility (See table 8.3).
- **Alloimmune Haemolytic Disease of the Foetus and Newborn (HDFN) –**
  - HDFN, is as a result a maternal immunoglobulin G(IgG) which destroyed the red blood cells of the foetus or newborn when it crosses the placenta into foetal circulation. These maternal antibodies develop when a red blood antigen not expressed in the mother enters maternal circulation, either during pregnancy or transfusion.
- **Transfusion Refractoriness –**
  - It is a repeated unsatisfactory response to a transfusion, particularly to platelet transfusions, namely platelet refractoriness due to HLA or HPA alloimmunization (See Chapter 6, Section 6.3).

Section 8.3 - Transfusion Transmissible Infections

A Transfusion Transmissible Infection (TTI) is an infection that is transmitted from donated blood through a blood transfusion to the recipient thereof. A TTI may be bacterial, viral, or other such as prions, protozoa and filaria.

TO ENSURE A SUFFICIENT SAFE AND SUSTAINABLE SUPPLY OF BLOOD TO THOSE IN NEED THE WHO RECOMMENDS SEVERAL STRATEGIES, NAMELY –

- Establishment of an efficient national level coordinated blood service that can supply safe blood and blood products in a sufficient and timely manner to the population in need.
- Blood collections from voluntary non-remunerated donors with a low TTI risk.
- Screening of donations for TTI, namely HIV, hepatitis B, hepatitis C, syphilis, and other relevant infections depending on local epidemiological evidence that may pose a risk to blood safety, including blood group and compatibility testing.
- Appropriate clinical use of blood and blood products to avoid unnecessary transfusions and minimize transfusion associated risks, as well as adherence to safe clinical transfusion procedures.
- Development and implementations of effective quality systems (i.e., quality management, quality standards, documentation systems, staff training programmes etc.), which are assessed on a regular basis.

STRATEGIES IMPLEMENTED BY THE BLOOD SERVICE TO MINIMIZE THE RISK OF TTI'S, INCLUDE –

- Safe donor recruitment, i.e., identifying and recruiting donors from low risk populations, continuous education of donors on TTI's, high risk behaviour, and the importance of voluntary, non-remunerated blood donation.
- Surveillance for emerging pathogens which might have transfusion transmission potential.
- Stringent screening and selection of potential donors, i.e., pre-donation donor screening via a donor history questionnaire and a focused general health examination, to identify potential safety risks.
- Strategies and procedures for quality-assured blood products, i.e., Strict adherence to aseptic non-touch techniques during blood collection and use of blood bags with divergent pouch to minimize bacterial contamination of units.
- High quality screening tests, i.e., nucleic acid and serology tests, for infectious diseases, including sterility testing for platelet concentrates.
- Meticulous cold chain maintenance and monitoring of blood from collection to transfusion.
- Visual inspection of a blood component for bacterial contamination during issuing and administration.

RESIDUAL RISK FOR TRANSFUSION TRANSMISSIBLE INFECTIONS IN NAMIBIA –

The residual risk for transfusion transmissible infections in collected blood and blood components is defined as the probability of collecting a donation from an asymptomatic viremia donor infected with a blood borne virus not being detected by routine screening assays. Such an undetected blood donation has the potential to transmit the infection to a recipient if the blood components are not pathogen inactivated. Non-detection of the infection may be caused by assay failures or by donors being in the diagnostic window period, which refers to the time between infection and seroconversion, i.e., when testing can reliably detect the virus.

Estimation of the residual risks of TTI's is essential for the blood service to monitor blood safety and assist transfusing clinicians and patients to make informed decisions when discussing transfusion versus other treatment options. The current residual risk for HIV, hepatitis B and hepatitis C in Namibia is shown in table 8.4;

Table 8.4 – Residual Risk (RR) per million donors with ID-NAT screening assay

Donor Category	HIV RR	HBV RR	HBV adjusted	HCV RR
Repeat Donor	6.97	46.25	124.53	7.84
First Time Donor	20.90	138.76	373.59	23.51
All Donors	9.30	61.79	166.36	10.47

***HBV adjusted RR – An incident adjustment factor that consider the undetected cases due to the transient nature of the antigenaemia and viraemia of HBV needs to be applied for an accurate HBV incidence.**

Table 8.4 indicates that the adjusted residual risk for HBV in a first-time donor is 373.59, meaning that HBV could have been undetected in about 373.59 first time donors out of a million donors (0.04%), either due assay failures or donations made during the window period. If these units were transfused it may have the potential to infect a recipient with HBV.

ESSENTIALS

- A transfusion ALWAYS carries a risk for an adverse event, clinicians should thus always outweigh the risk versus benefit before prescribing a transfusion and transfuse with caution.
- Transfusing healthcare professionals MUST be able to differentiate between the symptoms and signs of various reactions, to ensure timely and appropriate recognition, investigation and management thereof.
- Transfusion reactions can be FATAL, therefore if a reaction is suspected one must always err on the side of caution and initiate management immediately.
- Transfusing clinicians must ALWAYS discuss adverse events of a transfusion with patients to ensure that appropriate INFORMED CONSENT has been obtained.

REFERENCES

- Suddock JT, Crookston KP. Transfusion Reactions. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482202/
- Heddle, NM., Blajachman, M.A., Meyer, R.M., Lipton, J.H., Walker, I.R., Sher, G.D., et. al. 2002. A randomized controlled trial comparing the frequency of acute reactions to plasma -removed platelets and prestorage WBC-reduced platelets. Transfusion, 42, 556-66.
- Sanders, R.P., Maddirala, S.D., Geiger, T.L., Pounds, S., Sandlund, J.T., Ribeiro, R.C., et. al. 2005. Premedication with acetaminophen or diphenhydramine for transfusion with leucoreduced blood products in children. British Journal of Haematology, 130, 781-87.

- Hirayama, F. 2013. Current understanding of allergic transfusion reactions: incidence, pathogenesis, laboratory tests, prevention and treatment. British Journal of Haematology, 160(4), 434-44.

- Stainsby, D., Williamson, L., Jones, H., Cohen, H. 2004. 6 Years shot reporting – its influence on UK blood safety. Transfusion and Apheresis Science, 31(2), 123-31.

- Andrzejeewski, C. Jr., Casey, M.A., Popovsky, M.A. 2013. How we view and approach transfusion-associated circulatory overload: Pathogenesis, diagnosis, management, mitigation and prevention. Transfusion, 52, 160-65.

- Evan M. Bloch, Peter J. M. van den Burg, Young Ae Lim, Veera S. Nadarajan, Arwa Z. Al-Riyami and David J. Roxby. International Society of Blood Transfusion: Adverse effect of Transfusion. Accessed on 20 October 2024. https://www.isbtweb.org/resources/educational-modules-on-clinical-use-of-blood/adverse-effects-of-transfusion.html

- Shah FT, Porter JB, Sadasivam N, Kaya B, Moon JC, Velangi M, et al. Guidelines for the monitoring and management of iron overload in patients with haemoglobinopathies and rare anaemias. Br J Haematol. 2022; 196: 336–50.

CHAPTER 09
HAEMOVIGILANCE SYSTEM

Section 9.1 - Scope of a Haemovigilance System

A haemovigilance system consist of a set of surveillance procedures covering all transfusion activities in the transfusion chain from the vein of the donor to the vein of the recipient (vein-to-vein), including transfusion adverse events. (See Chapter 8 – Transfusion Adverse Events)

A haemovigilance system does not only involve the monitoring, reporting, investigation and analysis of adverse events related to the donation and transfusion of blood, but it also monitors the efficiency and efficacy of the entire transfusion chain. Thus, it provides an overview of all transfusion activities, which drive continuous quality improvement of transfusion practices through the implementation of preventative and corrective measures.

Section 9.2 - Haemovigilance System Stakeholders Responsibilities

The success of a haemovigilance system significantly depends on accurate and consistent reporting of all activities related to blood donation, processing and transfusion, especially of adverse events. This is mainly the responsibility of the blood service and transfusing healthcare facilities and professionals. **The main responsibility of transfusing healthcare facilities and professions, as indicated in table 9.1, is to identify and report adverse transfusion events to the local blood bank, blood service or haemovigilance officers.**

Table 9.1 – Haemovigilance System Stakeholder Responsibilities

Stakeholder	Responsibilities
Blood Donor	- The BTS must have policies and procedures in place to ensure that blood donors report the following - - Delayed adverse reactions post donation to the blood service. - Positive TTI test results, if diagnosed within 3 months post donation to initiate a donor triggered lookback investigation
Hospitals/Transfusion Facilities & Professionals	- Complete all information on the blood requisition form (e.g. haemoglobin value to monitor transfusion appropriateness) - Identify and accurately report all adverse events associated with a blood transfusion to the hospital blood banks, crossmatching laboratories, blood service and/or haemovigilance officer(s), including suspected cases of seroconversion due to a TTI, to initiate a recipient triggered lookback investigation.

Stakeholder	Responsibilities
	- Establish HTC's to monitor and evaluate all transfusion activities within a facility.
Hospital Blood Banks / Crossmatching Laboratories	- Forward all forms, specimens and blood units from transfusion facilities and professionals to the Blood Service for investigation of adverse transfusion events, and/or capturing and analysis of blood recipient data (i.e., blood usage, clinical indications, appropriate usage etc.). - Forward all incidents and near misses which may compromise recipient safety to the blood service to be investigated and addressed.
Blood Service	- Coordinate haemovigilance activities amongst stakeholders of the haemovigilance system. - Maintain a record of all transfusion activities related to the collection, testing and transfusion of blood for data analysis, including adverse events. - Compile an annual haemovigilance report from data collect and analyze from the database, hospitals and hospital blood banks. - Circulate the annual haemovigilance report to all stakeholders.
MoHSS	- Review the annual haemovigilance report and ensure that any critical issues compromising donor/ recipient safety identified through the haemovigilance system, but lie outside the direct responsibility of Blood Service, are evaluated and resolved. - Ensure that the haemovigilance report has been circulated to all stakeholders.
Blood Recipient	- Report all delayed transfusion reaction and suspected seroconversion to the responsible transfusing healthcare facility or professional to notify the blood service to initiate a recipient triggered lookback investigation

Section 9.3 - Lookback Investigations

A lookback investigation must be undertaken in all cases of a possible transfusion related transmission of disease and can be either a donor- or recipient-triggered lookback investigation as indicated in table 9.2 below.

Table 9.2 – Lookback Investigations

Donor-triggered	Recipient-triggered
- A process to trace all possible donations which occurred during the time period after exposure and before seroconversion and identify the recipients of those implicated donations so that they can be notified, counselled and/or treated.	- The process that identifies donors whose donations may have been the source of a TTI seroconversion, or to exclude blood transfusion as the mode of disease transmission in a recipient.
- It is initiated when a donor has a confirmead reactive result for a TTI, the donor has notified NAMBTS of a possible TTI, reactive test result at another facility or have been exposed to a high-risk situation which may compromise the blood recipient's health.	- It is initiated when a blood product recipient is reported to have seroconverted to a TTI, or reported to have been infected with any other organism, possibly as a result of receiving a contaminated unit.

Seroconversion means that one or more of the routine TTI markers (i.e., for HIV 1&2, hepatitis B and C, and syphilis) which were previously negative are now positive. Any other infection (i.e., malaria), where a blood transfusion could be implicated, also needs to be investigated under this programme.

Section 9.4 - Content of the Haemovigilance Report

The content of the haemovigilance report should cover all aspects of the transfusion chain, specifically the following, but are not limited to these –

- Blood donor and donation trends.
- Performance of blood donation activities to meet set targets
- Blood safety levels in terms of TTI prevalence, incidents rates and residual risk assessments.
- Performance of blood safety interventions to meet set goals.
- Blood components quality levels and status of good manufacturing practices (GMP) implementation in the production of blood components.
- Blood demand, and supply trends and assessment of appropriateness of blood usage in transfusing healthcare facilities.
- Blood wastage trends and interventions to meet set goals.
- Adverse events related to blood collection and transfusion, such as donor adverse events, recipient adverse events, incidents and near misses.

Section 9.5 - Benefits of a Haemovigilance System

Table 9.3 indicated the various benefits an effective haemovigilance system has to offer all the stakeholders.

Table 9.3 – Benefits of a Haemovigilance System

Stakeholder	Impact/Outcome
Blood Donor	- Improve donor safety by reducing the frequency and severity of adverse events related to blood donation.
Blood Service	- Improve donor retention and return. - Improve blood supply management, namely matching blood demand and supply. - Improve the quality of services and products provided. - Early detection of gaps and weaknesses to ensure quality improvement of transfusion services through the implementation of certain measures.
Hospitals/ Transfusion Facilities & Professionals	- Improve identification and mitigation of transfusion associated risks. - Reduce harm from adverse events and improve health care outcomes by reducing transfusion associated risks. - Improve transfusion guidelines and practices, including appropriate clinical usage of blood and blood products. - Reduce wastage of resources by improving transfusion appropriateness.
Blood Recipient	- Improve recipient safety by reducing transfusion associated adverse events.

Section 9.6 - Haemovigilance System Limitations & Weaknesses

Regardless of the success of a haemovigilance system, all have some limitations and weaknesses which needs to be addressed to improve the quality of the transfusion chain. These especially include the following;

- Poor participation
- Failure to identify adverse events
- Incomplete and underreporting
- Poor record keeping resulting in traceability failure.

Transfusing healthcare facilities and professionals play a crucial role in addressing these limitations and weaknesses in the National Haemovigilance System of Namibia, through active participation, proper record keeping, prompt identification and accurate reporting of transfusion associated adverse events.

ESSENTIALS

- Namibia is one of the 49% of countries in 2018 who has a haemovigilance system in place, although it is not fully effective and efficient.
- An effective haemovigilance system requires the collaboration of ALL INVOLVED in the transfusion chain.
- The recognition, reporting and thorough investigation of transfusion associated adverse events are of significant importance for the effectiveness of a haemovigilance system.
- Continuous education needs to be provided at transfusing healthcare facilities to healthcare professionals to improve the recognition of transfusion reactions, since the symptoms are often non-specific and can be difficult to recognize in sick patients.

UNABLE TO RECOGNIZE = UNDERREPORTING

REFERENCES

- de Jonge, L., Wiersum-Osselton, J., Bokhorst, A., Schipperus, M., & Zwaginga, J. (2022). Haemovigilance: current practices and future developments. Annals of Blood, 7. doi:10.21037/aob-22-2
- World Health Organization. A Guide to the Establishing a National Haemovigilance System. 2016. Available online: *http://apps.who.int/iris/handle/10665/250233* (Accessed 22 October 2024)

ABBREVIATION LIST

AABB	Organization advancing transfusion and cellular therapies worldwide
Ab	Antibody
ACE	Angiotensin-converting enzyme
ADAMTS13	Von Willebrand factor cleaving protease
AfSBT	Africa Society for Blood Transfusion
Ag	Antigen
AHTR	Acute haemolytic transfusion reaction
Anti-HCV	Hepatitis C antibody
aPCC	Activated prothrombin complex concentrate
aPTT	Activated partial thromboplastin time
AZT	Azidothymidine
BCSH	British Committee for Standards in Haematology
BP	Blood pressure
CDC	Centres for Disease Control and Prevention
CKD	Chronic kidney disease
CML	Chronic myeloid leukaemia
CMV	Cytomegalovirus
CVP	Central venous pressure
DAT	Direct anti-globulin test
DHTR	Delayed haemolytic transfusion reaction
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid
ECG	Electrocardiogram
EDTA	Ethylene-diamine-tetra-acetic acid
EPO	Erythropoietin
ESA	Erythropoiesis-stimulating agent
FDP	Freeze dried plasma
FFP	Fresh frozen plasma
FMH	Feto-maternal haemorrhage
FNHTR	Febrile non-haemolytic transfusion reaction
GACUB	Guidelines for the Clinical Use of Blood and Blood Products
GIT	Gastrointestinal tract
Hb	Haemoglobin
HBsAg	Hepatitis B surface antigen
HBIG	Human hepatitis B immunoglobulin
HBV	Hepatitis B virus

HCV	Hepatitis C virus
Hct	Haematocrit
HDN	Haemolytic disease of the newborn
HIT	Heparin-induced thrombocytopenia
HIV	Human immunodeficiency virus
HIV 1&2	HIV 1&2 antigen/antibody ELISA combination test
HOD	Head of Department
HRIG	Human rabies immunoglobulin
HTC(s)	Hospital Transfusion Committee(s)
HTIG	Human tetanus immunoglobulin
HTR	Haemolytic transfusion reaction
HVIG	Human varicella zoster immunoglobulin
IBD	Inflammatory bowel disease
ICH	Intracerebral haemorrhage
Ig	Immunoglobulin
IL	Interleukin
IM	Intramuscular
INR	International normalized ratio
ISBT	International Society of Blood Transfusion
ITP	Immune thrombocytopenic purpura
IU	International unit
IV	Intravenous
IVIG	Intravenous immunoglobulin
LDH	Lactate dehydrogenase
LFT	Liver function test
MoHSS	Ministry of Health and Social Services
MSBOS	Maximum Surgical Blood Ordering Schedule
MTP	Massive Transfusion Protocol
NAIT	Neonatal alloimmune thrombocytopenia
NAMBTS	Blood Transfusion Service of Namibia
NAT	Nucleic acid testing
NIP	Namibia Institute of Pathology
NSAIDs	Non-steroidal anti-inflammatory drugs
PCC	Prothrombin complex concentrate
PCR	Polymerase chain reaction
PDMP's	Platelet-derived microparticles
PI	Prothrombin index
PT	Prothrombin time
PTP	Posttransfusion purpura

HCV	Hepatitis C virus
Hct	Haematocrit
HDN	Haemolytic disease of the newborn
HIT	Heparin-induced thrombocytopenia
HIV	Human immunodeficiency virus
HIV 1&2	HIV 1&2 antigen/antibody ELISA combination test
HOD	Head of Department
HRIG	Human rabies immunoglobulin
HTC(s)	Hospital Transfusion Committee(s)
HTIG	Human tetanus immunoglobulin
HTR	Haemolytic transfusion reaction
HVIG	Human varicella zoster immunoglobulin
IBD	Inflammatory bowel disease
ICH	Intracerebral haemorrhage
Ig	Immunoglobulin
IL	Interleukin
IM	Intramuscular
INR	International normalized ratio
ISBT	International Society of Blood Transfusion
ITP	Immune thrombocytopenic purpura
IU	International unit
IV	Intravenous
IVIG	Intravenous immunoglobulin
LDH	Lactate dehydrogenase
LFT	Liver function test
MoHSS	Ministry of Health and Social Services
MSBOS	Maximum Surgical Blood Ordering Schedule
MTP	Massive Transfusion Protocol
NAIT	Neonatal alloimmune thrombocytopenia
NAMBTS	Blood Transfusion Service of Namibia
NAT	Nucleic acid testing
NIP	Namibia Institute of Pathology
NSAIDs	Non-steroidal anti-inflammatory drugs
PCC	Prothrombin complex concentrate
PCR	Polymerase chain reaction
PDMP's	Platelet-derived microparticles
PI	Prothrombin index
PT	Prothrombin time
PTP	Posttransfusion purpura

PTT	Partial thromboplastin time
RNA	Ribonucleic acid
RBC	Red blood cell
RCC	Red cell concentrates
r-HU-EPO	Recombinant human erythropoietin
SC	Subcutaneous
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TA-GVHD	Transfusion-associated graft-versus-host disease
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TEG	Thromboelastography
TR(s)	Transfusion reaction(s)
TRALI	Transfusion-related acute lung injury
TRIM	Transfusion-related immunomodulation
TTI's	Transfusion-transmissible infections
TTP	Thrombotic thrombocytopenic purpura
TXA	Tranexamic acid
U&E	Urea and electrolytes
USG	Ultrasonography
vWD	Von Willebrand disease
VTE	Venous thromboembolism
WB	Whole blood
WHO	World Health Organization

The Blood Transfusion Service of Namibia (NamBTS)
35 Tal Street, Windhoek
Tel: 083 378 7000