Rwanda Biomedical Centre
Healthy People, Wealthy Nation

RESULTS FOR DEVELOPMENT

EDUCATION AND TRAINING MATERIALS FOR BLOOD TRANSFUSION

RWANDA

September 2024

PREFACE

During the last 20 years, Rwanda's health system has made remarkable improvements as evidenced by various health outcomes. Most importantly, life expectancy has increased from 50 to 70 years in the last 2 decades, under-5 mortality has dropped to 45 deaths per 1,000 live births, and maternal mortality has dropped from 1,071 to 203 per 100,000 live births while 96% of births are assisted by a skilled healthcare provider. In the last decade, primary and secondary care has been strengthened and services have been brought closer to the population, which by extension, has also increased access to specialty services most of which call for safe Blood transfusion.

It is therefore with great pleasure and anticipation that I present the newly developed educational materials on Transfusion Medicine, meticulously crafted for both pre-service training in higher institutions of learning and in-service training for healthcare providers. These materials are a significant stride in our ongoing mission to elevate the standards of healthcare education and practice in Rwanda.

Blood transfusion is a cornerstone of modern healthcare, indispensable for the treatment of a wide range of medical conditions. Ensuring the safety, efficacy, and accessibility of transfusion services is essential for improving patient outcomes and saving lives.

These comprehensive educational resources are designed to address and bridge the knowledge gaps observed in transfusion medicine among healthcare providers and students transitioning from school to professional practice.

For pre-service students in higher institutions of learning, these materials provide a solid foundation in transfusion medicine. They encompass crucial topics such as blood group serology, blood collection, processing, testing, and the clinical application of blood products. By integrating these materials into our educational curricula, we aim to equip our future healthcare professionals with the knowledge and skills necessary to conduct transfusion procedures with the utmost safety and efficacy.

For in-service healthcare providers, these resources offer valuable opportunities for continuous professional development. The dynamic and evolving nature of transfusion medicine necessitates that our practitioners remain up-to-date with the latest advancements and best practices. These materials will support our healthcare workforce in maintaining their competencies and ensuring the delivery of high-quality transfusion services.

The creation of these educational materials is the result of a collaborative effort involving experts in transfusion medicine, educators, and healthcare professionals. I extend my heartfelt gratitude to all who contributed their expertise and time to this important project. Your dedication is instrumental in advancing healthcare education and practice in Rwanda.

I would like to extend special appreciation to Results for Development (R4D) for their generous technical and financial support towards Rwanda's blood safety initiatives in general, and specifically for the development of these educational materials. Your partnership and commitment have been invaluable in making this project a reality.

In conclusion, I am confident that these educational materials will play a pivotal role in enhancing the quality of transfusion medicine education and practice across Rwanda. They will help us build a more knowledgeable and skilled healthcare workforce, ultimately leading to better patient care and outcomes. I encourage all educators, students, and healthcare providers to utilize these resources to further their understanding and proficiency in transfusion medicine.

Together, we can ensure that Rwanda continues to uphold the highest standards in transfusion medicine, contributing to a healthier and stronger nation.

Dr. Sabin NSANZIMANA
Minister of Health

ABBREVIATIONS AND ACRONYMS

°C	Degree Celsius
AABB	Association for the Advancement of Blood & Biotherapies
ACD	Acid Citrate Dextrose
ACOG	American College of Obstetricians and Gynaecologists
ADCC	Antibody-dependent cellular cytotoxicity
ADP	Adenosine diphosphate
AIHA	Autoimmune hemolytic anemia
AKI	Acute Kidney Injury
aPCC	Activated prothrombin complex concentrates
aPTT	Activated partial thromboplastin time
AS	Additive solution
ATP	Adenosine triphosphate
BC	Buffy coats
BCR	B cell receptor
BTD	Blood Transfusion Division
BTR	Blood transfusion reaction
BU	Bethesda Unit
Ca	Calcium
CAP	College of American Pathologists
CBC	Complete Blood Count
CD	Cluster of differentiation
CMV	Cytomegalovirus
COVID-19	Coronavirus disease 2019
CPD	Citrate Phosphate Dextrose
CPDA-1	Citrate Phosphate Dextrose Adenine 1
CRT	Capillary refill time
DAT	Direct antiglobulin test
DAT	Direct Antiglobulin Test
DDAVP	Desmopressin
DHTR	Delayed Hemolytic Transfusion Reaction
DVT	Deep vein Thrombosis
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
FBC	Full Blood Count
FDA	Food and Drug Administration
FDPs	Fibrin degradation products
FFP	Fresh Frozen Plasma
FIFO	First-in, first-out
FPPs	Fractionated plasma products
FY	Duffy System
G-CSF	Granulocyte colony stimulating factor
G	Gram
GBS	Guillain-Barré Syndrome
GP	Glycoprotein
GYP	Glycophorins
Hb	Hemoglobin
HBOC	Hemoglobin-Based Oxygen Carriers
HbS	Hemoglobin S
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDFN	Hemolytic disease of the fetus and newborn
HF	Healthcare facilities
HIT	Heparin-induced thrombocytopenia
HIV/ AIDS	Human immunodeficiency virus /acquired immunodeficiency syndrome
HLA	Human Leucocyte Antigen
HSCs	Hematopoietic stem cells
HTLV	Human T-lymphotropic virus type
HTR	Hemolytic Transfusion Reaction
HTR	Hemolytic Transfusion reaction
HUS	Hemolytic uremic syndrome

DIC	Disseminated intravascular coagulation
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DOACs	Direct Oral Anticoagulants
Dr	Doctor
INR	International Normalized Ratio
ITP	Immune thrombocytopenic purpura
IUT	Intrauterine transfusions
IV	Intravenous
JK	Kidd System
KCL	Potassium chloride
KEL	Kell System
Kg	Kilogram
Lab	Laboratory
LE	Lewis System
LFT	Liver function test
LMWH	Low Molecular Weight Heparin
LR	Leucocyte Reduction
LU	Lutheran System
MAC	Membrane Attack Complex
MBTP	Massive Blood Transfusion Protocol
MCA-PSV	Middle cerebral arterial- peak systolic velocity
mEq	Milliequivalent
MODS	Multiple organ dysfunction syndrome
MoM	Multiple of Median
MT	Massive transfusion
NAT	Nucleic acid testing
NHS	National Health Service
NK	Natural Killer
NTDT	Non-transfusion dependent thalassemia
OSTHEO	Orthopedic Surgery Transfusion Hemoglobin European Overview
PAS	Platelet Additive Solutions
IAT	Indirect Antiglobulin Test
ICT	Indirect Coombs Test
ID	Identification
Ig	Immunoglobulin
IL	Interleukin
RBC	Red Blood Cell
RCA	Root cause analysis
RCBT	Regional Center for Blood Transfusion
RDT	Rapid Diagnostic Test
RDTs	Rapid diagnostic tests
RFDA	Rwanda Food and Drugs Authority
RFT	Renal function test
RH	Rhesus
RhD	Rhesus D
RNA	Ribonucleic acid
SAGM	Saline-Adenine-Glucose-Mannitol
SCD	Sickle cell disease
SLC14A1	Solute carrier family 14 member 1 (Kidd blood group)
TA-GVHD	Transfusion-associated graft-versus-host disease
TACO	Transfusion-associated circulatory overload
TACO	Transfusion-Associated Circulatory Overload
TBV	Total blood volume
Tc	Cytotoxic T cell
TCT	Thrombin clotting time
TDT	Transfusion-dependent thalassemia
TF	Tissue factor
TGF	Transforming growth factor
Th	T helper
TNF	Tumor necrosis factor
TRALI	Transfusion Related Acute Lung Injury
Tregs	Regulatory T Cells
TS	Transfusion service

PBS	Peripheral Blood Smear
PBSC	Peripheral blood stem cell
PCR	Polymerase chain reaction
PE	Pulmonary Embolism
PFCs	Perfluorocarbons
pH	Potential of Hydrogen
PLT	Platelet
PRBCs	Packed Red Blood Cells
PRP	Platelet-Rich Plasma
PT	Prothrombin time
TTI	Transfusion-Transmitted Infection
TTP	Thrombotic thrombocytopenic purpura
UFH	Unfractionated Heparin
UK	United Kingdom
USA	United States of America
UV	Ultraviolet
VWD	Von Willebrand Disease
vWF	von Willebrand factor
WHO	World Health Organization
µg	Microgram

Contents

1. HISTORY OF TRANSFUSION MEDICINE

1.1. Learning objectives

- Explore the evolution of transfusion medicine, from ancient blood beliefs to key contributors and milestones like blood typing, first blood banks, and advancements in transfusion techniques.
- Understand how World War II and HIV/AIDS reshaped blood transfusion practices.

1.2. Transfusion medicine history

Introduction

Transfusion Medicine, a cornerstone of modern medicine, with rich and complex history from ancient times when people believe in mystical powers of blood to the development of advanced transfusion techniques, the journey of blood transfusion highlights human creativity, determination and scientific progress.

Ancient Beliefs and Practices: In ancient civilizations such as Egypt, Greece, and Rome, blood was considered as a symbol of life and vitality. Ritualistic bloodletting (a practice of withdrawing blood from a patient) ceremonies were performed in the belief that it could purge the body of diseases and restore balance. While these practices lacked scientific merit, they laid the groundwork for early experimentation with blood transfusion.

Pioneering Experiments: The first documented attempts at blood transfusion date back to the 17th century. In 1665, English physician Richard Lower successfully transfused blood between dogs, laying the foundation for future human transfusion experiments. However, early attempts at human-to-human transfusion were fraught with challenges and often ended in failure or fatal outcomes.

Fig. 1. Richard Lower: English physician

Breakthroughs and Discoveries: Despite initial setbacks, pioneers in the field such as James Blundell (an English Obstetrician) and Karl Landsteiner (Austrian-American biologist and physician) made significant strides in advancing the practice of blood transfusion. Blundell's successful transfusion to treat postpartum hemorrhage in 1,818 demonstrated the therapeutic potential of blood transfusion in clinical settings. Blundell used blood from the patient's husband. Landsteiner's discovery of the ABO blood group system in 1,901 revolutionized transfusion medicine by enabling safe blood typing and matching.

Fig.2. James Blundell: English Obstetrician

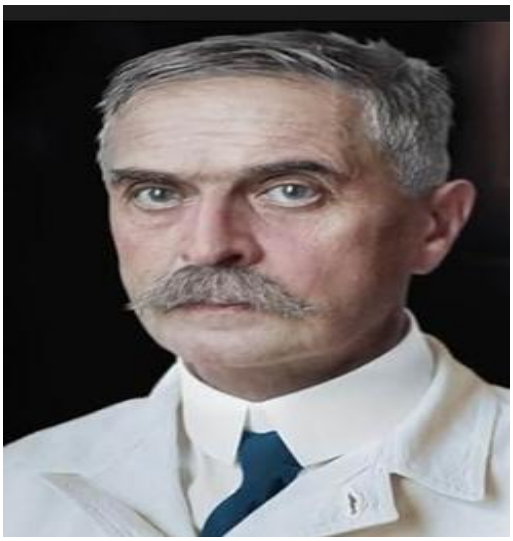

Fig. 3. Karl Landsteiner: Austrian-American biologist and physician

During the 1800s, several progresses were made in the development of blood collection devices, particularly in the context of bloodletting practices that were prevalent at the time. While some of these devices had been in use for centuries, the 19th century saw improvements and refinements in their design. Here are a few notable examples:

Scarificators: Scarificators were mechanical devices equipped with multiple blades arranged in a circular pattern. When triggered, the blades would rapidly puncture the skin, creating small incisions for bloodletting. In the 1800s, scarificators underwent improvements in their mechanisms, making them more efficient and reliable for medical practitioners.

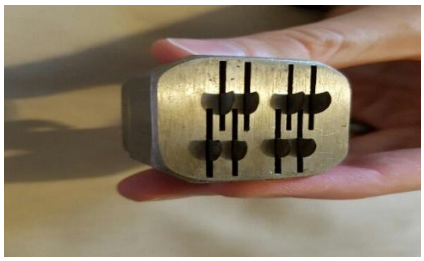

Fig. 5. Scarificators

Fleams: were handheld instruments resembling knives or lancets, often with a single sharp blade. They were used to make controlled incisions in the skin for bloodletting purposes. While fleams had been in use for centuries, progress in metallurgy and manufacturing techniques during the 19th century likely led to improvements in their design and performance.

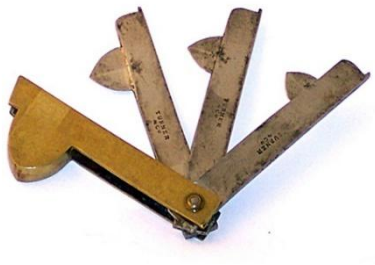

Fig. 6. Fleams

Spring Lancets: Spring lancets were handheld devices with a spring-loaded mechanism that allowed for quick and precise incisions. These devices were particularly popular among medical practitioners for bloodletting procedures, as they offered greater control and ease of use compared to traditional lancets.

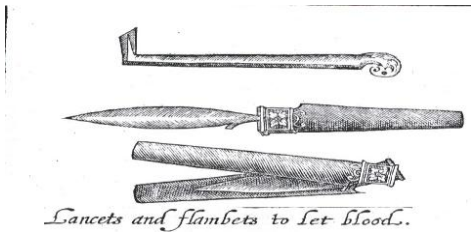

Fig. 7. Lancets and flambets to let blood

Cupping Sets: Cupping therapy, which involved creating a vacuum on the skin to draw blood to the surface, remained a popular practice during the 19th century. Cupping sets typically included glass or metal cups of various sizes, along with a pump or other device to create the vacuum. While the basic principles of cupping remained unchanged, improvements in materials and design likely enhanced the effectiveness and safety of cupping sets during this period.

Fig. 8. Cupping sets

Improved Leech Jars: Leeches were commonly used for bloodletting in the 1800s, and specialized containers called leech jars were used to store and transport them. These jars were typically designed with perforated lids or mesh inserts to allow for ventilation while preventing the escape of the leeches. While the basic design of leech jars remained relatively unchanged, advancements in glassmaking and container design may have led to improvements in their durability and functionality.

Overall, the 19th century saw continued innovation and refinement in the design of blood collection devices, driven by ongoing practices of bloodletting and related therapies. These advancements played a significant role in the evolution of medical instrumentation and the broader context of healthcare during the period.

World War I: The demand for blood transfusions surged during World War I, leading to improvements in blood collection, storage, and transfusion techniques. Blood banks were established to collect and store donated blood for use in military hospitals, saving countless lives on the battlefield.

World War II: The use of blood transfusions became even more widespread during World War II, with progress in blood typing, cross-matching, and the introduction of blood component therapy. Blood banks played a crucial role in providing lifesaving transfusions to wounded soldiers.

Post-World War II: After World War II, blood transfusion technology continued to evolve rapidly. The development of blood fractionation techniques allowed for the separation of blood into its component parts, such as red blood cells, plasma, and platelets, enabling more targeted treatments for patients with specific medical conditions.

The Era of Blood Banking: The establishment of the first blood banks in the early 20th century marked a turning point in transfusion medicine. Led by visionaries like Lawrence Bruce Robertson, these institutions pioneered techniques for blood collection, storage, and distribution on a large scale. World War II further accelerated progress in blood banking, saving countless lives on the battlefield and driving innovations in transfusion technology. Today, blood transfusions are a routine medical procedure used to treat a wide range of conditions, including trauma, surgery, anemia, and cancer. Blood banks play a critical role in maintaining an adequate supply of blood and blood products to meet patient needs while ensuring safety and quality standards.

Challenges and Ethical Considerations: Despite its life-saving potential, blood transfusion has not been without controversy. Ethical concerns surrounding donor and receipt safety, informed consent, and equitable access to blood products have prompted ongoing debate and research. The emergence of infectious diseases such as HIV/AIDS in the 20th century underscored the importance of strict safety measures and quality control in blood transfusion practices.

Forward: As we progress, the future of blood transfusion holds promises and challenges as well. Advances in technology, including the development of synthetic blood substitutes and stem cell-based therapies, offer new alternatives for improving transfusion safety and accessibility. However, the persistent need for adequate blood supply, coupled with emerging infectious threats and ethical dilemmas, reminds us of the ongoing importance of vigilance, innovation, and collaboration in the field of transfusion medicine.

Conclusion

The history of blood transfusion is evidence to human curiosity, innovation, and resilience towards the search for knowledge. From ancient to modern medical practices the story of blood transfusion reminds us of the profound impact that scientific discovery can have on the health and well-being of humanity.

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2. PRINCIPLES OF IMMUNOHEMATOLOGY

2.1. Learning objectives:

- Understand the fundamental principles of antigens and antibodies complex.
- Describe the molecular structure and functions of antigens and antibodies.
- Identify different types of antigens and antibodies and their clinical significance.
- Analyze the mechanisms of antigen-antibody interactions.
- Differentiate between various immune responses.
- Discuss the production and regulation of antibodies.
- Evaluate the diagnostic applications of antigen-antibody reactions.

2.2. Antigen and Antibody

Introduction

Antibodies are key components of the immune system, playing crucial roles in defending the body against foreign substances and pathogens. Antigens are molecules that can induce an immune response, while antibodies are proteins produced by the immune system in response to specific antigens.

A. Structure and Function

Antigens: Antigens can be proteins, polysaccharides (carbohydrates), glycoproteins, glycolipids, nucleic acids or other macromolecules. They have specific molecular structures that allow them to interact with components of the immune system, such as antibodies and immune cells. Antigens can be derived from pathogens like bacteria, viruses, and parasites, as well as from non-pathogenic substances like pollen, dust, and certain foods. Antigens stimulate the immune system to produce antibodies or activate specific immune cells, leading to the elimination of the foreign invader.

Antibodies: Antibodies, also known as immunoglobulins, are Y-shaped proteins produced by specialized white blood cells called B lymphocytes in response to exposure to antigens. Each antibody molecule consists of four polypeptide chains—two heavy chains and two light chains—connected by disulfide bonds. Antibodies have variable regions that bind specifically to antigens and constant regions that mediate effector functions. The main functions of antibodies include neutralizing pathogens, opsonization (marking pathogens for phagocytosis by immune cells), activating the complement system, and facilitating antibody-dependent cellular cytotoxicity (ADCC).

Production of Antibodies

Antibodies are produced by B cells through a process called somatic recombination. B cells undergo genetic rearrangement of their antibody genes to generate diverse antibody molecules

with unique antigen-binding specificities. Upon encountering antigens, activated B cells differentiate into plasma cells, which secrete large quantities of antibodies:

- **B Cell Activation**: B cells recognize antigens through their B cell receptors (BCRs) and undergo activation, leading to their proliferation and differentiation into plasma cells.
- **Plasma Cell Differentiation**: Plasma cells are specialized B cells that produce large quantities of antibodies with the same antigen specificity as the original B cell receptor.
- **Class Switching and Affinity Maturation (antibody synthesis)**: B cells can undergo class switching, where they change the class of antibody they produce (e.g., from IgM to IgG), and affinity maturation, where antibodies with higher affinity for the antigen are selected over time.

Regulation of antibody production: cytokines, T cell help, negative feedback mechanisms

The regulation of antibody production involves several key mechanisms, including the roles of cytokines, T cell help, and negative feedback mechanisms. Here's a summary of each component:

Cytokines:

- Cytokines are signalling molecules that are crucial in the regulation of the immune response. They can promote or inhibit various aspects of antibody production.
- Key cytokines involved in antibody production include IL-4, IL-5, IL-6, IL-10, and IFN-γ.
- IL-4 and IL-5 are important for the proliferation and differentiation of B cells into plasma cells, which are responsible for antibody production.
- IL-6 and IL-10 can enhance B cell maturation and antibody secretion.
- IFN-γ can influence the class switching of antibodies, affecting the type of antibody produced.

T Cell Help:

- T helper (Th) cells are critical for effective antibody production. They provide essential signals to B cells through direct cell-to-cell contact and the secretion of cytokines.
- Th cells express CD40L, which binds to CD40 on B cells, providing a necessary signal for B cell activation and class switching.
- The interaction between T cells and B cells often occurs in germinal centers within lymphoid organs, where B cells undergo somatic hypermutation and affinity maturation to produce high-affinity antibodies.

B. Negative Feedback Mechanisms:

- To prevent overproduction of antibodies and maintain immune homeostasis, several negative feedback mechanisms are in place.

- Regulatory T cells (Tregs) can suppress B cell activity and antibody production through the release of inhibitory cytokines like TGF-β and IL-10.
- The presence of high levels of antibodies can signal B cells to reduce antibody production through a process known as antibody-mediated feedback inhibition.
- Fc receptors on B cells can bind to antibodies and transmit inhibitory signals to the B cell, reducing further antibody production.

These mechanisms ensure a balanced and regulated antibody response, preventing excessive or insufficient production, which could lead to immune disorders.

Types of Antigens and Antibodies

- **Antigen Types**: Antigens can be classified as foreign antigens (exogenous: from outside the body) or self-antigens (endogenous: from within the body). Foreign antigens include those derived from pathogens, while self-antigens are molecules produced by the body's own cells and tissues.
- **Antibody Types**: Antibodies are categorized into five main classes: IgG, IgA, IgM, IgD, and IgE. Each class has distinct structural and functional properties, as well as roles in different aspects of the immune response. IgG is the most abundant antibody in the blood and is involved in long-term immunity. IgM is the first antibody produced during an immune response. IgA is predominantly found in mucosal secretions and helps prevent pathogen entry through mucosal surfaces. IgD is present on the surface of B cells and functions in B cell activation. IgE is involved in allergic reactions and defense against parasitic infections.

C. Antigen-Antibody Interaction

The interaction between antigens and antibodies is highly specific and forms the basis of the immune response. When an antibody encounters its specific antigen, it binds to the antigen, forming an antigen-antibody complex. This interaction triggers various immune mechanisms including:

- **Neutralization**: Antibodies bind to antigens, preventing them from interacting with host cells and neutralizing their harmful effects.
- **Agglutination**: Antibodies cross-link multiple antigens, leading to the formation of antigen-antibody complexes, which are then cleared by phagocytic cells.
- **Precipitation:** Soluble antigens and antibodies form insoluble complexes, which are then removed by phagocytosis.
- **Complement activation**: Antibodies activate the complement system, resulting in the lysis of pathogens, opsonization, and inflammation.
- **Opsonization**: Antibodies coat pathogens, facilitating their recognition and ingestion by phagocytic cells.
- **ADCC (Antibody-Dependent Cellular Cytotoxicity):** Antibodies bound to target cells activate immune effector cells, such as natural killer cells, leading to the destruction of the target cells.

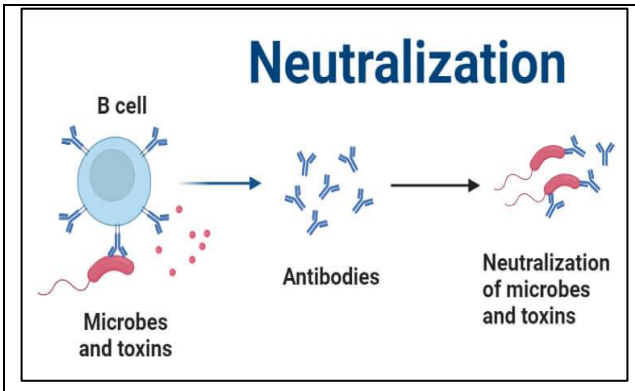

Fig. 9. Neutralization

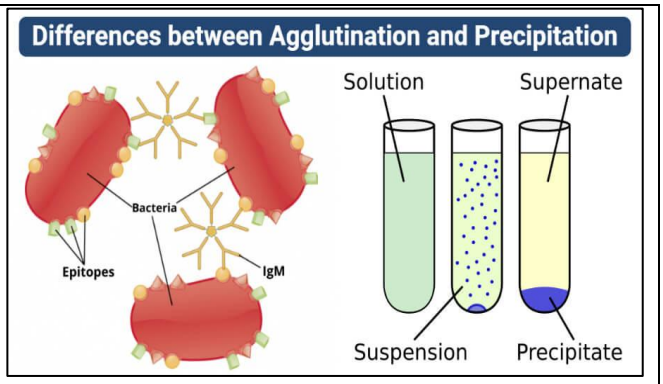

Fig. 10. Difference between agglutination and precipitation

D. The complement system

The complement system: It involves three pathways namely classical pathway, alternative pathway and mannose binding lectin pathway. The funnel depicts the complement system and the common aim of the three pathways is to yield C3 convertase. The classical and lectin pathway, upon binding to their respective activation subcomponents, cleaves C4 and C2 to C4a/b and C2a/b respectively. C4b and C2b form a complex i.e. C3 convertase. This convertase facilitates the cleavage of C3 which in turn cleaves C5 to yield C5b. C5b hence forms a complex with C6, C7, C8 and C9 to form C5b-9, also known as the Membrane Attack Complex (MAC) that leads to lysis of the target cells.

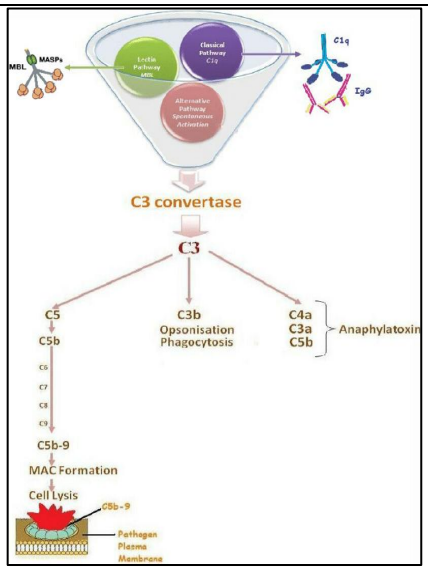

Fig. 11. Diagram illustrating the three pathways of the complement system

Mechanism of action of the complement system

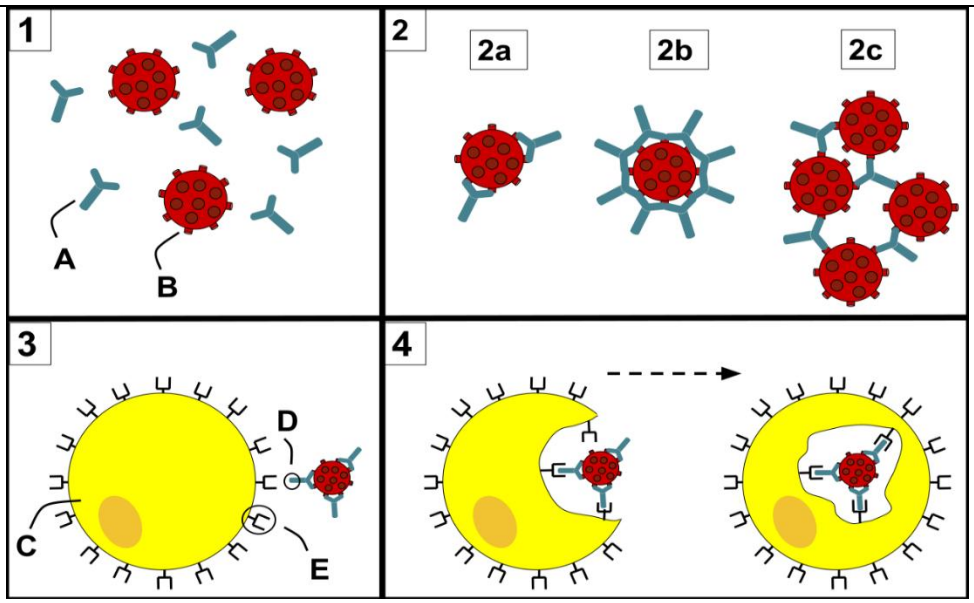

Fig. 12. Diagram illustrating mechanism of action of the complement system

- Antibodies (A) and pathogens (B) free roam in the blood.
- The antibodies bind to pathogens, and can do so in different formations such as: opsonization (2a), neutralization (2b), and agglutination (2c).
- A phagocyte (C) approaches the pathogen, and the Fc region (D) of the antibody binds to one of the Fc receptors (E) of the phagocyte.
- Phagocytosis occurs as the pathogen is ingested.

Antibody-dependent cellular cytotoxicity

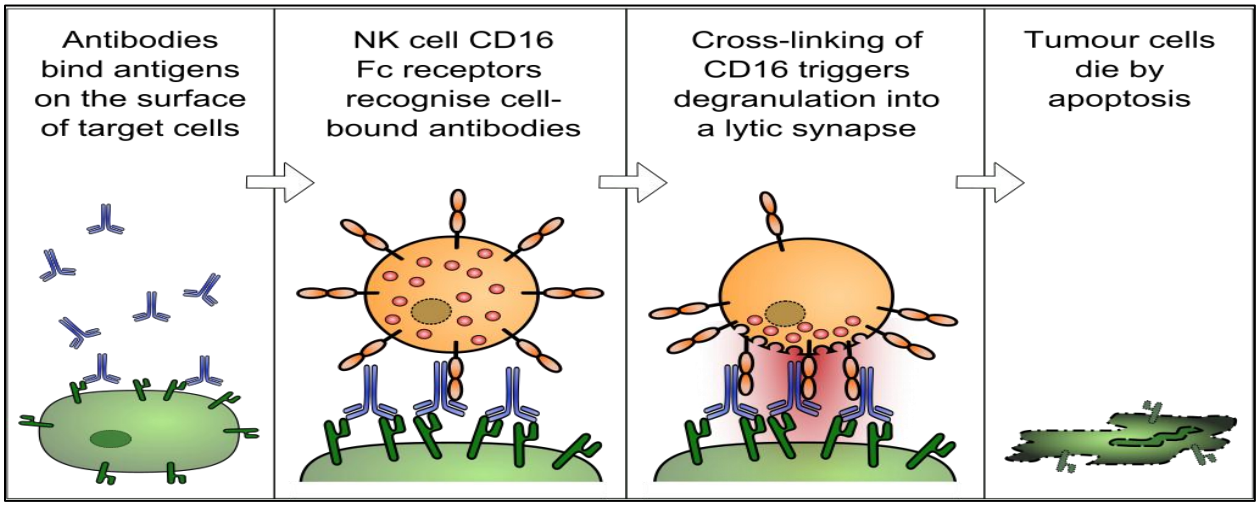

Fig. 132. Antibody-dependent cellular cytotoxicity

Types of Immune Response

The immune system can mount two types of responses:

- **Innate Immune Response**: this is the first line of defences against pathogens and involves nonspecific mechanisms, such as physical barriers (skin, mucous membranes), phagocytic cells (neutrophils, macrophages), and the complement system.
- **Adaptive Immune Response**: this is a highly specific response that develops upon exposure to specific antigens. It involves the activation of lymphocytes (B cells and T cells), which produce antibodies and generate memory cells for long-term immunity.
- **Humoral Immunity**(antibody-mediated): mediated by antibodies, humoral immunity primarily targets extracellular pathogens and toxins.
- **Cellular Immunity** (T cell-mediated): mediated by immune cells such as T cells, cellular immunity targets -intracellular pathogens and infected cells.
- **Primary vs. secondary immune response**: focusing on the role of memory B cells and T cells, and the immunoglobulins IgG and IgM:

Primary Immune Response

- **Initial Exposure**: Occurs when the body encounters an antigen for the first time.
- **Activation of Naive Cells**: Naive B cells and T cells are activated since they have not previously encountered the antigen.
- **Latency Period**: There is a delay before a detectable level of antibodies appears because the immune system needs time to recognize the antigen and activate the appropriate cells.
- **IgM Production**: IgM is the first antibody produced during the primary response. It appears early and is effective in forming antigen-antibody complexes.
- **Memory Cell Formation**: Some B cells and T cells differentiate into memory cells, which persist after the infection is cleared.
- **Characteristics**: The response is slower and less robust, with lower antibody titers that take longer to reach their peak.

Secondary Immune Response

- **Re-exposure**: Triggered when the body encounters the same antigen again.
- **Activation of Memory Cells**: Memory B cells and T cells, formed during the primary response, are quickly activated.
- **Rapid and Strong Response**: The secondary response is faster and more robust. Memory B cells rapidly differentiate into plasma cells to produce antibodies.
- **IgG Production**: IgG is the predominant antibody in the secondary response. It appears more quickly and in higher amounts compared to IgM, providing more effective and longer-lasting immunity.
- **Higher Affinity Antibodies**: Due to affinity maturation, antibodies produced during the secondary response have higher affinity for the antigen.

- **Characteristics**: This response features a shorter lag phase, higher antibody titers, and faster antigen clearance.

Role of Memory B Cells

- **Rapid Differentiation**: Quickly differentiate into plasma cells to produce antibodies upon re-exposure to the antigen.
- **Higher Affinity Antibodies**: Produce higher affinity antibodies due to prior somatic hypermutation and selection.

Role of Memory T Cells

- **Enhanced Functionality**: Include both memory helper T cells (Th) and memory cytotoxic T cells (Tc), which can rapidly perform their respective functions.
- **Quick Proliferation**: Rapidly proliferate and enhance the immune response more efficiently than naive T cells.

Role of IgG and IgM

- **IgM**:
  - **Primary Response**: The first antibody produced. It forms pentamers, making it effective in agglutination and initial defense.
  - **Secondary Response**: Produced in smaller amounts compared to IgG.
- **IgG**:
  - **Primary Response**: Appears later in the response and in lower amounts.
  - **Secondary Response**: Predominant antibody, produced in larger quantities and more rapidly. It provides long-term immunity and better opsonization and neutralization of antigens.

In summary, the primary immune response is characterized by the initial activation of naive cells and IgM production, while the secondary response is faster and more robust, driven by memory B and T cells and dominated by IgG production.

Alloantibodies vs autoantibodies

Alloantibodies

Alloantibodies are immune antibodies that are only produced following exposure to foreign red blood cell antigens.

- Produced by exposure to foreign red cell antigens which are non-self-antigens but are of the same species.
- They react only with allogeneic cells.
- Exposure occurs through pregnancy or transfusion.
- Examples include anti-K and anti-E.

Autoantibodies

Some people develop antibodies that react with their own red blood cells. This autoimmune process can be a primary idiopathic condition or a secondary condition in patients with other conditions such as certain infections or lymphomas. Autoantibodies can be clinically significant and result in in vivo hemolysis, though many are considered benign. Autoantibodies typically react with all reagent cells as well which can cause serological complications during antibody screening procedures by masking any underlying alloantibodies.

- Produced in an autoimmune process and directed against one's own red cell antigens.
- React with patient's own cells and typically all cells tested.
- It is very important to make sure that no underlying significant antibodies are present if an autoantibody is suspected.
- A positive direct antiglobulin test (DAT) or auto control could indicate the presence of an autoantibody.
- Examples include cold auto (P or I) or warm auto (Rh specificity).

An **auto-control** is the patient's red blood cells mixed with their plasma/serum. A positive auto-control suggests that the patient may have an autoantibody that is binding with their own red blood cell antigen. If the patient has an alloantibody, the auto-control would remain negative.

Diagnostic Application

Antibodies are widely used in diagnostic assays for the detection of antigens or antibodies associated with specific diseases. Techniques such as enzyme-linked immunosorbent assay (ELISA), western blotting, and immunofluorescence rely on the specific binding of antibodies to antigens for disease diagnosis.

- **Serological Tests**: Enzyme-linked immunosorbent assay (ELISA), Western blot, and indirect immunofluorescence are common serological tests used to detect the presence of antigens or antibodies in patient samples.
- **Rapid Diagnostic Tests (RDTs):** These tests provide quick and easy detection of antigens or antibodies and are commonly used for infectious diseases such as HIV, malaria, and COVID-19.
- **Blood Typing:** Antibodies are used in blood typing and cross-matching to determine blood compatibility for transfusions.
- **Monitoring antibody levels**: in autoimmune diseases and immunodeficiency disorders.

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3. BLOOD GROUP SYSTEMS

3.1. Learning objectives

With the following learning objectives, learners will develop a thorough understanding of blood group systems, with a focus on the ABO blood group system, and its clinical, genetic, and societal implications.

- Define the concept of blood group systems and their significance in transfusion medicine.
- Identify major blood group systems, including ABO, Rh, Kell, Duffy, and others.
- Explain the genetic basis of blood group systems and inheritance patterns.
- Describe the ABO blood group system and its importance in blood transfusion.
- Describe the clinical significance of Major and Minor blood group system

3.2. Blood group systems

Introduction

Blood group systems are classifications of blood based on the presence or absence of specific antigens on the surface of red blood cells. These systems categorize blood into different types, which are important for blood transfusions and organ transplants. There are several blood group systems, but the most clinically significant ones include:

- ABO system
- Rh system (also known as the Rhesus system)
- Kell system
- Duffy system
- Kidd system
- MNSs system

Blood group antigens are inherited traits encoded by genes located on chromosomes. Understanding the genetic basis of blood groups helps predict the likelihood of specific blood types in offspring based on parental genotypes.

Population Distribution: The distribution of ABO blood types varies among different populations and ethnic groups. For example, type O is more common in some populations, while type A or type B may predominate in others. (According to BTD annual report 2023, the donations per Blood group was at 51.2%, 25.8%, 19,2% and 4.3% for Group O, A, B and AB respectively assuming it represents the distribution of ABO Blood types among Rwandan population).

Antigen-Antibody Reactions: Blood group antigens can trigger immune responses when they come into contact with antibodies that recognize them as foreign. This can lead to adverse reactions, such as hemolytic transfusion reactions, if incompatible blood is transfused.

Emerging Blood Group Systems: Ongoing research continues to discover new blood group antigens and systems. These discoveries contribute to advancements in transfusion medicine, forensic science, and anthropology.

3.2.1. Major Blood Group System

3.2.1.1.ABO Blood Group System:

The ABO blood group system classifies blood into four main types based on the presence or absence of specific antigens on the surface of red blood cells. The four blood types are A, B, AB, and O. Understanding the ABO blood group system is crucial for healthcare professionals involved in blood banking, transfusion medicine, obstetrics, and genetics. It ensures safe and effective blood transfusions and contributes to better patient care and outcomes.

The ABO blood group is determined by the presence or absence of A and B alleles inherited from parents. The A allele codes for the A antigen, the B allele codes for the B antigen, and the O allele codes for neither antigen.

Antigens and Antibodies:

- Type A blood has an antigen on the surface of red blood cells and anti-B antibodies in the plasma.
- Type B blood has B antigens on the surface of red blood cells and anti-A antibodies in the plasma.
- Type AB blood has both A and B antigens on the surface of red blood cells and no anti-A or anti-B antibodies in the plasma.
- Type O blood has no A or B antigens on the surface of red blood cells and both anti-A and anti-B antibodies in the plasma.

Table 1 Summery Of Blood ABO Blood Group and the Presence of theAntigines and Antibodies in respective RBC cell

ABO blood group	Antigen(s) present on red cell	Antibodies present in plasma
Group O	-	anti-A and anti-B
Group A	A antigen	anti-B
Group B	B antigen	anti-A
Group AB	A and B antigens	-

3.2.1.2.RH System

Rh factor is an inherited protein found on the surface of red blood cells. The most clinically significant antigen is D as it has a propensity to stimulate antibody production (immunogenic) and has strong reactions with its corresponding antibody (antigenic). If the RBC has this surface

protein, then referred to as Rh positive. If the RBC doesn't have the protein, referred to as Rh negative. The Rh status referred as the "+" or "–" to describe Rh positive or Rh negative.

Determination of the RH factor done using 'Anti D' and the procedure is similar to the ABO grouping system. The presence of the D antigen is considered Rh-positive. In contrast, the absence of D antigen after agglutination reaction with antiserum D is Rh negative.

The Rh system is particularly important in pregnancy due to the risk of haemolytic disease of the fetus and new-born (HDFN). If a patient develops an Rh antibody, they are more likely to form other blood group antibodies due to sensitization. It is for this reason that some patient groups require Rh matched red cells, to try to reduce risk of this occurring.

Compatibility

A transfusion of an incompatible ABO group can cause fatal reactions within minutes, the patient's ABO antibodies attack the donor red blood cells and cause intravascular hemolysis via co It is preferable for patients to receive red cells and platelets of the same ABO and RH group. However, if ABO and RH identical products are not available, a patient may be offered an alternate compatible product.

Therefore, ABO blood typing and cross-matching are essential before blood transfusions to ensure compatibility between donor and recipient blood types. A mismatch can lead to a potentially life-threatening immune reaction known as a hemolytic transfusion reaction.

Table 2. ***Donor and Recipient ABO Blood Type Compatibility***

Blood Type	Antigens on RBCs	Antibodies in Blood	Safe Transfusions	
			To	From
A	A	Anti-B	A, AB	A, O
B	B	Anti-A	B, AB	B, O
AB	A, B	-	AB	A, B, AB, O
O	-	Anti-A, Anti-B	A, B, AB, O	O

- Type A Blood: Compatible with type A and type O blood for transfusion (can receive blood from type A or type O donors).
- Type B Blood: Compatible with type B and type O blood for transfusion (can receive blood from type B or type O donors).
- Type AB Blood: Universal recipient; compatible with type A, type B, type AB, and type O blood for transfusion (can receive blood from any blood type).
- Type O Blood: Universal donor; compatible with type O blood for transfusion (can donate blood to any blood type).

Table 3 ***RH type and Compatibility***

Patient RH type	Best option	OK to use	Never use
RH negative	RH negative	-	RhPositive
RH positive	RH positive	RH negative	-

Clinical Significance:

- ABO blood typing is routinely performed in healthcare settings for blood transfusions, organ transplants, and prenatal care.
- ABO blood type can influence susceptibility to certain diseases and conditions, such as infectious diseases and autoimmune disorders.
- ABO blood group discrepancies, where the blood type determined by different methods is inconsistent, require careful investigation to prevent transfusion errors.

ABO mismatch in blood transfusions can lead to potentially severe consequences due to immune reactions triggered by the recipient's immune system recognizing the transfused blood as foreign. Here are the main consequences:

1. **Hemolytic Transfusion Reaction (HTR)**: ABO incompatibility can result in an immune-mediated hemolytic transfusion reaction, where antibodies in the recipient's plasma attack and destroy transfused red blood cells. This can lead to hemolysis (breakdown of red blood cells), releasing hemoglobin into the bloodstream and causing symptoms such as fever, chills, chest or back pain, hematuria (blood in urine), hypotension (low blood pressure), and in severe cases, acute kidney injury, disseminated intravascular coagulation (DIC), and shock. HTRs can be life-threatening and require immediate medical intervention.
2. **Delayed Hemolytic Transfusion Reaction (DHTR)**: In some cases, the immune response to ABO-incompatible transfusions may be delayed, with symptoms appearing hours to days after the transfusion. DHTRs are characterized by the gradual destruction of transfused red blood cells and can present with symptoms similar to acute HTRs, including fever, jaundice, and hematuria. Although less immediately severe than acute HTRs, DHTRs can still lead to complications and require medical attention.
3. **Acute Kidney Injury (AKI)**: Severe hemolysis resulting from ABO mismatch can lead to the release of hemoglobin and its breakdown products into the bloodstream. These substances can cause damage to the kidneys, potentially leading to acute kidney injury (AKI). AKI may manifest as decreased urine output, fluid retention, electrolyte imbalances, and changes in kidney function tests.
4. **Disseminated Intravascular Coagulation (DIC)**: In some cases of severe hemolysis, the release of cellular debris and activation of clotting factors can lead to a widespread activation of the coagulation system, resulting in disseminated intravascular coagulation (DIC). DIC is

a life-threatening condition characterized by abnormal blood clotting followed by excessive bleeding, which can lead to multi-organ failure and death if not promptly treated.

5. **Shock and Organ Failure**: In the most severe cases of ABO-incompatible transfusions, the combination of hemolysis, DIC, and other complications can lead to shock and multi-organ failure, requiring intensive care management and supportive measures to stabilize the patient's condition.

To prevent these consequences, ABO compatibility between donor and recipient blood must be carefully ensured through proper blood typing and cross-matching procedures before transfusions.

3.2.2. Minor Blood Group System

a. **Kell System (KEL)**

- **Antigens**: K (Kell) and k (Cellano), along with others.
- **Clinical Significance**: Kell antigens are highly immunogenic. Anti-K antibodies can cause severe haemolytic transfusion reactions (HTR) and haemolytic disease of the foetus and newborn (HDFN).
- **Genetics**: The KEL gene on chromosome 7 encodes the Kell glycoprotein.

b. **Duffy System (FY)**

- **Antigens**: Fya and Fyb.
- **Clinical Significance**: Anti-Fya and anti-Fyb antibodies can lead to mild to moderate HTR and HDFN. The absence of Duffy antigens (Fy (a-b-)) is associated with resistance to Plasmodium vivax malaria.
- **Genetics**: The FY gene on chromosome 1 encodes the Duffy glycoprotein.

c. **Kidd System (JK)**

- **Antigens**: Jka and Jkb.
- **Clinical Significance**: Anti-Jka and anti-Jkb antibodies are known for causing delayed HTR and HDFN.
- **Genetics**: The SLC14A1 gene on chromosome 18 encodes the Kidd glycoprotein.

d. **MNS System**

- **Antigens**: M, N, S, and s.
- **Clinical Significance**: Anti-M and anti-N are generally cold-reactive and not clinically significant. Anti-S and anti-s can cause HTR and HDFN.
- **Genetics**: The GYPA and GYPB genes on chromosome 4 encode glycophorins A and B.

e. **Lutheran System (LU)**

- **Antigens**: Lua and Lub.

- **Clinical Significance**: Anti-Lua and anti-Lub antibodies are rare but can cause mild HTR and HDFN.
- **Genetics**: The LU gene on chromosome 19 encodes the Lutheran glycoprotein.

f. **Lewis System (LE)**
- **Antigens**: Lea and Leb.
- **Clinical Significance**: Lewis's antibodies (anti-Lea and anti-Leb) are usually not clinically significant as they are typically IgM and react at cold temperatures.
- **Genetics**: The FUT3 gene on chromosome 19 encodes the Lewis glycosyltransferase.

Clinical Implications of minor Blood group system

1. **Transfusion Medicine**
   - Importance of extended blood typing and crossmatching to prevent HTR.
   - Use of phenotypically matched blood for patients with known antibodies.

2. **Pregnancy**
   - Risk of HDFN due to antibodies against minor blood group antigens.
   - Monitoring and management of pregnant women with clinically significant antibodies.

Understanding minor blood group systems is essential for safe transfusion practices and management of HDFN. Though less prominent than ABO and Rh systems, these minor systems can significantly impact clinical outcomes.

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4. BLOOD TYPING AND COMPATIBILITY TESTING

4.1. Learning Objectives:

- Explore the processes of ABO and Rh typing.
- Understand the methods of crossmatching and their significance.
- Learn about the Indirect Antiglobulin Test (IAT) and Direct Antiglobulin Test (DAT).
- Apply knowledge of ABO blood groups to interpret blood typing results and identify compatible blood products for transfusion
- Identify challenges in compatibility testing.

Introduction

Blood group systems have important clinical implications in transfusion medicine. Therefor determination of blood system is of critical importance including

- **Blood typing**: Identifying a person's blood type (e.g., A, B, AB, O) for safe transfusions.
- **Rh compatibility**: Determining Rh factor (positive or negative) to prevent Rh sensitization in Rh-negative individuals.
- **Compatibility testing**: Determining donor-recipient compatibility before blood transfusions or organ transplants to prevent adverse reactions. Compatibility testing is crucial to avoid hemolytic transfusion reactions, which can be life-threatening.

4.2. Blood Typing

Blood typing determines an individual's ABO blood group by testing for the presence or absence of A and B antigens on the surface of red blood cells and the presence of anti-A and anti-B antibodies in the plasma. Blood typing is typically performed using agglutination tests, such as the forward and reverse typing methods:

A. Forward Typing:

- Patient's red blood cells (RBCs) are mixed with anti-A serum and anti-B serum separately.
- Agglutination (clumping) of RBCs indicates the presence of A or B antigens on the RBC surface.
- Interpretation: Agglutination with anti-A serum indicates type A blood; agglutination with anti-B serum indicates type B blood.

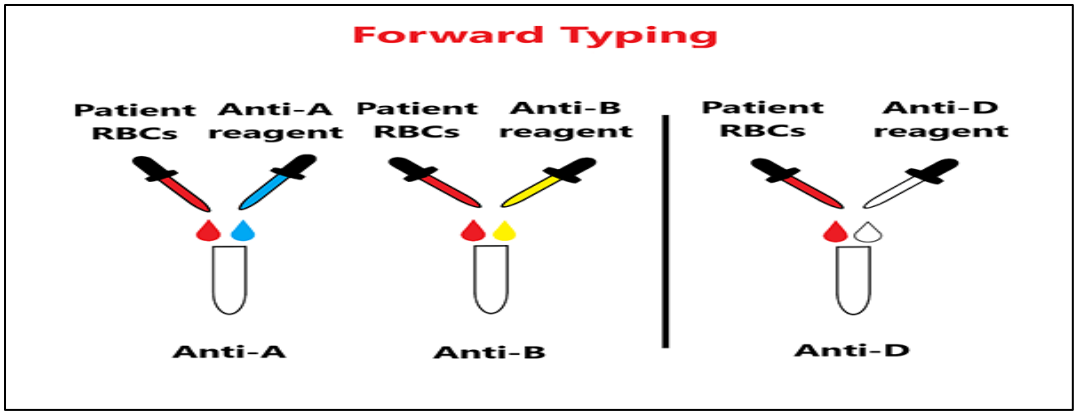

Fig. 3. Forward blood typing

B. Reverse Typing:

- Patient's plasma is mixed with type A and type B RBCs separately.
- Agglutination of RBCs indicates the presence of anti-A or anti-B antibodies in the patient's plasma.
- Interpretation: Agglutination with type A RBCs indicates the presence of anti-A antibodies in the patient's plasma; agglutination with type B RBCs indicates the presence of anti-B antibodies.

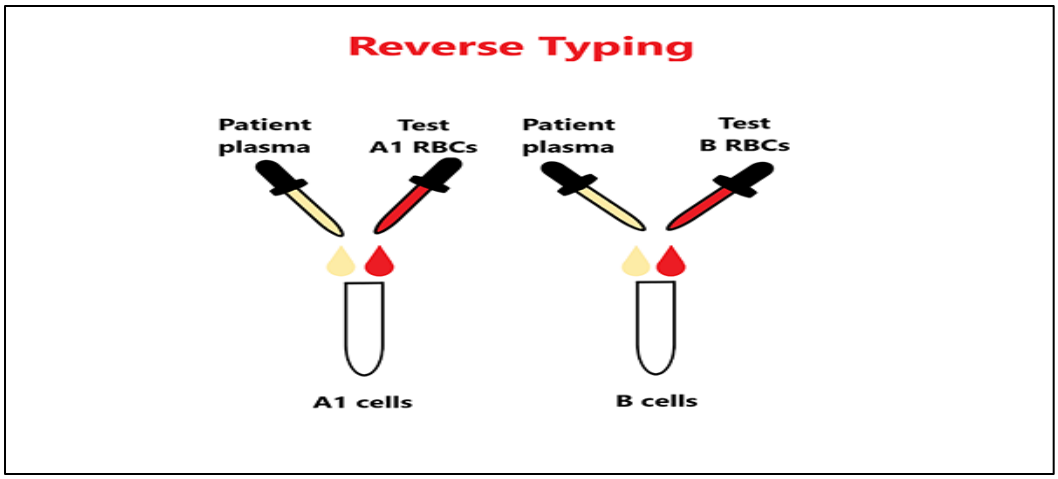

Fig. 4. Reverse blood typing

Rh Typing:
Detects the presence or absence of the D antigen on red blood cells using anti-D antiserum.

Note: for details about the above testing methods, students should go to the laboratory for practical session(s).

Table 4. ABO and Rh Typing methods and interpretation

Test	Method	Interpretation
Forward Typing	Red cells + anti-A, anti-B	Determines A, B antigens
Reverse Typing	Plasma + A cells, B cells	Determines anti-A, anti-B
Rh Typing	Red cells + anti-D	Determines Rh status (positive / negative)

Table 5 Summery of ABO and RH determination

ABO/Rh group	Forward Typing			Reverse Typing	
	Anti-A	Anti-B	Anti-D	A1 cells	B cells
O neg	0	0	0	4+	4+
O pos	0	0	4+	4+	4+
A neg	4+	0	0	0	4+
A pos	4+	0	4+	0	4+
B neg	0	4+	0	4+	0
B pos	0	4+	4+	4+	0
AB neg	4+	4+	0	0	0
AB pos	4+	4+	4+	0	0

4.3. Compatibility Testing

1. Identifying Compatible Blood Products:

- Type A Blood: Compatible with type A and type O blood for transfusion (can receive blood from type A or type O donors).
- Type B Blood: Compatible with type B and type O blood for transfusion (can receive blood from type B or type O donors).
- Type AB Blood: Universal recipient; compatible with type A, type B, type AB, and type O blood for transfusion (can receive blood from any blood type).
- Type O Blood: Universal donor; compatible with type O blood for transfusion (can donate blood to any blood type).

Note:

The transfusion should be done in accordance to the following principles:

- The transfusion should be iso-group and Iso-Rhesus,
- Type O Rh Neg is the 1st Choice for Universal donor.
- Type O Rh Pos is considered to be the 2nd choice for Universal donor.

2. Cross-Matching:

In addition to ABO typing, cross-matching is performed before transfusions to ensure compatibility between donor and recipient blood. Cross-matching involves mixing donor red

blood cells with recipient plasma (**major crossmatch**) and recipient red blood cells with donor plasma (**minor crossmatch**) to detect any antibodies that could cause transfusion reactions.

a. Major Cross-Match:

- Donor RBCs is mixed with recipient plasma.
- Observation for agglutination indicates the presence of donor-specific antibodies in the recipient's plasma.
- Agglutination indicates incompatibility between donor and recipient blood.

b. Minor Crossmatch:

- Recipient RBCs are mixed with donor plasma.
- Observation for agglutination indicates the presence of recipient-specific antibodies in the donor's plasma.
- Agglutination indicates incompatibility between recipient and donor blood.

Cross matching Type	**Procedure**:	Interpretation
Major Cross Matching	– Mix recipient plasma with donor red cells. – Incubate and observe for agglutination or hemolysis	– No agglutination/hemolysis: **Compatible**. – Agglutination/hemolysis: **Incompatible**
Minor Cross Matching	– Mix donor plasma with recipient red cells. – Incubate and observe for agglutination or hemolysis	– No agglutination/hemolysis: **Compatible**. – Agglutination/hemolysis: **Incompatible**

Compatibility is confirmed when there is no agglutination in both major and minor crossmatches, whereas incompatibility suggests the presence of donor-specific antibodies in the recipient or recipient-specific antibodies in the donor, indicating potential risks of transfusion reactions

3. Special Considerations:

- Rh compatibility: In addition to ABO compatibility, Rh factor (positive or negative) must be considered to prevent Rh sensitization in Rh-negative recipients.
- Subgroup typing rare subgroups within ABO blood groups, such as weak or variant antigens, may require specialized testing for accurate blood typing and compatibility assessment.

Note: for details about the above testing methods, students should go to the laboratory for practical session(s).

Table 6. ABO &Rh blood component transfusion Compatibility

RECIPIENT'S BLOOD TYPE	POSSIBLE DONOR BLOOD TYPE				
	pRBC	FFP	Random donor platelets (Whole blood derived platelets)	Single Donor Platelets (Apheresis)	CryoprecipitatE
O	O	Any Type	0	Any Type	Any Type
A	A or O	A or AB	A	A or AB	A or AB
B	B or O	B or AB	B	B or AB	B or AB
AB	Any Type	AB	AB	AB	AB
Rh+	Pos. or Neg.	Pos. or Neg.	Pos. or Neg.	Pos. or Neg.	Pos. or Neg.
Rh-	Negative	Pos. or Neg.	Neg.	Pos. or Neg.	Pos. or Neg.

4.4. Antiglobulin Testing

Antiglobulin testing, also known as the Coombs test, is an immunology laboratory procedure used to detect the presence of antibodies against circulating red blood cells (RBCs) in the body, which induce hemolysis. The destruction of these red blood cells (RBCs) by antibodies directed against them is described diagnostically as autoimmune hemolytic anemia (AIHA). Many etiologies fall under this classification.

Antiglobulin testing can be either direct antiglobulin testing (DAT) or indirect antiglobulin testing (IAT). The principle of DAT is to detect the presence of antibodies attached directly to the RBCs, which takes place by washing a collected blood sample in saline to isolate the patient's RBCs; this procedure removes unbound antibodies that may otherwise confound the result. IAT, by contrast, is used to detect unbound antibodies to RBCs, which may be present in the patient's serum.

Direct antiglobulin testing adds a monospecific or polyspecific reagent to the washed RBCs to detect bound IgG and/or complement C3. In practice, many laboratories first use the polyspecific reagent that can detect both IgG and C3; a positive result is followed by monospecific testing to characterize the antibody further. For indirect antiglobulin testing, serum from a blood sample gets isolated, and native RBCs are removed.

The isolated serum sample then gets incubated with foreign RBCs of known antigenicity. Antiglobulin reagent is then added, and the presence of agglutination indicates a positive result.

4.4.1. Indirect Antiglobulin Test (IAT)

Purpose: The indirect antiglobulin test (IAT), also known as the indirect Coombs test, detects antibodies in the serum or plasma that are capable of reacting with RBC antigens in vitro.

Indications

- IAT indications include pre-transfusion testing, antibody screening, and identifying clinically significant antibodies in pregnant women or patients with a history of transfusions.

Procedure:

– Mix recipient plasma with donor red cells.
– Add antihuman globulin (Coombs reagent).
– Observe for agglutination.

Note: for details about the above testing methods, students should go to the laboratory for practical session(s).

4.4.2. Direct Antiglobulin Test (DAT)

Purpose: The direct antiglobulin test (DAT), also known as the direct Coombs test, detects antibodies or complement proteins bound to the surface of red blood cells (RBCs) in vivo.

Indications

- DAT is performed to diagnose autoimmune hemolytic anemia, hemolytic disease of the newborn (HDN), drug-induced hemolytic anemia, and transfusion reactions.

Procedure:

– Mix patient's red cells with antihuman globulin (Coombs reagent).
– Observe for agglutination.

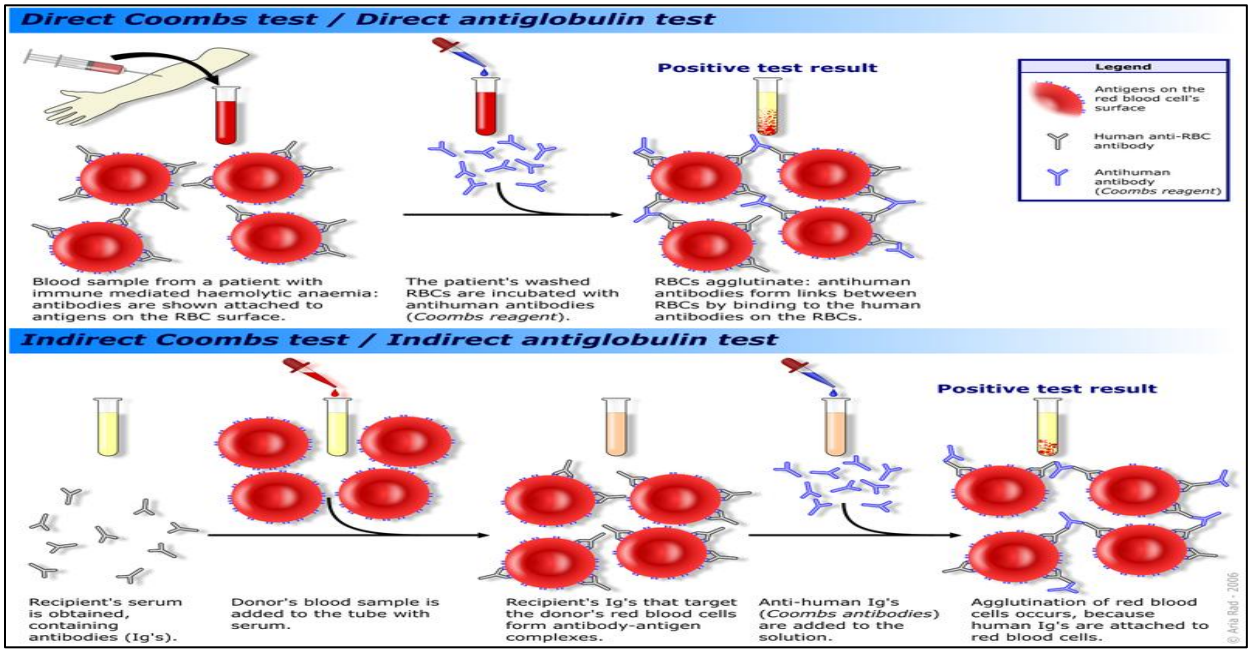

Fig. 5. Direct Antiglobulin Test and Indirect Antiglobulin Test

4.5. Compatibility Testing Challenges

- **Alloimmunization**: Development of antibodies against foreign antigens due to previous transfusions or pregnancies.
- **Autoantibodies**: Presence of antibodies that react with the individual's own red cells, complicating compatibility testing.
- **Variant Antigens**: Rare blood group antigens that may not be routinely screened for, leading to incompatibility.

Table 7. Challenges in Compatibility Testing

Challenge	Description	Mitigation Strategies
Alloimmunization	Development of antibodies due to prior exposures	Extended antigen matching, antibody screening
Autoantibodies	Antibodies against self-antigens	Autoantibody identification, adsorptions
Variant Antigens	Rare antigens not routinely screened	Specialized testing, antigen typing

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5. Blood Donation and Transfusion:

5.1. Learning Objectives

- Understand and recognize blood donation's vital role in ensuring a sustainable, safe supply for medical treatments, and emphasize voluntary donation's significance in preventing infections and maintaining reliable, safe blood products.
- Understand various blood donation types and assess the advantages and limitations of allogeneic donor recruitment, autologous blood banking, and directed donation campaigns for effective blood supply management.
- Explain the screening and eligibility criteria for blood donors
- Recognize the ethical considerations and regulatory guidelines governing blood donation practices
- Understand the role of interdisciplinary teams that develop effective blood donation policies, procedures, and quality assurance protocols aimed at enhancing donor safety, satisfaction, and retention.

5.2. Introduction to Blood Donation

Introduction

These notes cover the essential aspects of blood donor recruitment and retention, providing a comprehensive guide for understanding the process, criteria, and strategies involved.

Blood donation is a voluntary procedure where a person donates blood for medical use. Blood donation includes blood donor recruitment, blood donation process and blood donor retention. It is essential for surgeries, cancer treatment, chronic illnesses, and traumatic injuries. One donation can save multiple lives as it can be separated into different components including red cells, platelets, Fresh frozen plasma and cryoprecipitate.

Blood donor recruitment

- **Awareness Campaigns**: Use social media, community events, and partnerships with organizations to raise awareness.
- **Blood collection preparation:** meet with the local leaders and blood donor representatives at that specific site.
- **Recognition**: occasional Offer small tokens of appreciation like T-shirts, mugs, or certificates.
- **Feedback and Communication**: Regularly update donors on how their donations have helped.

Blood Donation Process

- **Pre-donation talks: emphasize more on eligibility criteria to ensure the safety of blood. Common criteria include:**
  - Age: Generally, from 18-60 years.
  - Weight: Minimum 50 kg.
  - Health: Free from infections or diseases like HIV
  - Medical history: No history of certain diseases like hepatitis.
  - Lifestyle: No recent tattoos, piercings, or risky behaviors

- **Registration:** Donor provides personal details and health history.
- **Blood donor selection:** Includes a brief medical history, vital signs, hemoglobin level check, the review of the questionnaire if eligible sign the consent form.

Phlebotomy procedure: The actual blood draw takes about 10-15 minutes.

- **Recovery period:**
  - Donor rests and receives refreshments to help recover.
  - Avoid strenuous activities for the rest of the day.
  - Drink plenty of fluids.
  - Monitor for any adverse reactions and seek medical attention if necessary.

- **Post-Donation follow up:**
  - Notification of laboratory results to all blood donors
  - Blood donor Counselling in case of a reactive results.

- **Retention strategies**

Blood Donation notification: Education and notify and encourage the blood donor the next date of blood donation.

  - Awareness Campaigns: Use social media, community events, and partnerships with organizations to raise awareness.
  - Feedback and Communication: Regularly update donors on how their donations have helped.
- .

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6. Quality management system BTD

6. BLOOD DONATION PROCESS AND TESTING

6.1. Learning objectives

Learning objectives for blood donation testing encompass the essential knowledge and skills necessary for ensuring the safety and quality of donated blood:

- Understand various blood donation types and assess the advantages and limitations of allogeneic donor recruitment
- **Blood Donation Eligibility and Donor Screening**: Identify criteria for blood donation eligibility, including age, weight, health status, and risk factors for infectious diseases.
- **Blood Collection Techniques**: Describe the various methods of blood collection, such as whole blood donation, apheresis (platelet, plasma, or red cell donation), and autologous donation.
  - Demonstrate proficiency in performing blood collection techniques and donor phlebotomy.
- **Blood Processing and Component Preparation**: Explain the process of blood processing, including centrifugation, separation of blood components (red cells, plasma, platelets), and leukoreduction.
  - Understand the principles of blood component preparation and storage to maintain the quality and integrity of blood products.
- **Understand the principle of apheresis and its mechanisms.**
- **Blood Donation Testing**:
  - Identify the purpose of blood donation testing, including screening for infectious diseases, blood typing, and compatibility testing.
  - Describe the laboratory tests used in blood donation testing, such as serological tests, nucleic acid testing (NAT), and antigen-antibody assays.
- **Quality Assurance and Regulatory Compliance**: Understand the principles of quality assurance in blood donation testing, including quality control measures, proficiency testing, and adherence to regulatory standards (e.g., RFDA regulations, AABB standards).
- Understand and recognize blood donation's vital role in ensuring a sustainable, safe supply for medical treatments, and emphasize voluntary donation's significance in preventing infections and maintaining reliable, safe blood products**.**
- Demonstrate awareness of ethical considerations and patient confidentiality in blood donation testing practices

6.2. Blood donation process and testing

Introduction

Blood donation testing plays a crucial role in ensuring the safety and quality of donated blood, which is vital for transfusion medicine and patient care. Before donated blood can be used for transfusions, it undergoes a series of rigorous tests to screen for TTIs, determine blood type compatibility, and verify its suitability for transfusion.

The primary purpose of blood donation testing is to safeguard the health and well-being of both blood donors and transfusion recipients. By screening donated blood for infectious agents and other potential hazards, blood donation testing helps prevent the transmission of diseases such as HIV, hepatitis B and C, syphilis, and other emerging infections (West Nile virus, Zika virus, etc.) through transfusion.

Additionally, blood donation testing includes blood typing and compatibility testing to ensure that donated blood matches the recipient's blood type and is compatible for transfusion. This helps minimize the risk of adverse reactions and transfusion-related complications.

6.3. Blood donation eligibility and donor screening

Blood donation eligibility and donor screening are critical steps in ensuring the safety and suitability of donated blood for transfusion:

6.3.1. **Blood Donation Eligibility**

- Donors must meet specific eligibility criteria to donate blood safely. These criteria may vary slightly depending on local regulations and blood bank policies.
- Common eligibility criteria typically include age (usually 18-60 years old, although this may vary), weight (usually above a certain threshold, e.g. 50 Kg), general health status, and absence of certain medical conditions.
- Donors must also meet minimum hemoglobin levels to ensure they can safely tolerate blood donation without experiencing adverse effects such as anemia.
- Certain medical conditions, recent illnesses, surgeries, or medications may disqualify individuals from donating blood temporarily or permanently.

6.3.2. Donor Screening

- Donor screening involves a comprehensive assessment of the donor's health history, lifestyle factors, and potential risk factors for infectious diseases.
- Donors are typically asked to complete a detailed medical questionnaire that gathers information about their medical history, recent illnesses, travel history, medications, and high-risk behaviors.

- The screening medical questionnaire may also include questions related to specific exclusion criteria, such as recent tattoos or piercings, recent blood transfusions, pregnancy, or recent exposure to infectious diseases.
- Trained healthcare professionals review the donor questionnaire with the donor to clarify any responses and assess the donor's eligibility based on their responses and medical history.
- Donor screening also involves a physical examination, including measurement of vital signs (such as hemoglobin, blood pressure, pulse, and temperature), and assessment of the general health status.

6.4. Blood Collection Techniques

Blood collection is a crucial step in the process of obtaining blood for transfusion or medical purposes. Several methods are used to collect blood, depending on the intended use, the type of blood component needed, and the preferences of the blood bank or healthcare provider.

6.4.1. **Whole Blood Donation**:

- Whole blood donation involves collecting a single unit of whole blood from a donor, which contains red blood cells, white blood cells, platelets, and plasma.
- The most common method of whole blood donation is venipuncture, where a sterile needle is inserted into a vein in the donor's arm, and blood is collected directly into a blood bag containing anticoagulants to prevent clotting.
- After collection, the donated whole blood can be separated into its individual components (red blood cells, plasma, platelets and cryoprecipitate) through a process called blood component separation.

6.4.2. **Apheresis Donation**:

- Apheresis, also known as automated or automated blood component collection, involves separating specific blood components from the donor's blood using a specialized machine called apheresis machine.
- During apheresis donation, blood is drawn from the donor's arm through a sterile needle, and the desired blood component (e.g., platelets, plasma, red blood cells) is separated using centrifugation or filtration within the apheresis machine.
- The remaining blood components are then returned to the donor's circulation, allowing for multiple blood components to be collected in a single donation session.
- Apheresis donation allows for targeted collection of specific blood components, such as platelets for patients with bleeding disorders or plasma for transfusion or plasma-derived products.

6.4.3. **Directed Donation**:

- Directed donation involves collecting blood from a specific donor designated by the recipient or their family for a particular patient.
- This method is often used in situations where a patient requires repeated transfusions or specific blood components that may be difficult to obtain from volunteer donors.
- Directed donors undergo the same screening and testing procedures as volunteer donors to ensure the safety and compatibility of the donated blood.

6.4.4. **Autologous Donation**:

- Autologous donation involves collecting and storing a patient's own blood for future use during planned medical procedures, such as surgery or chemotherapy.
- The collected blood is typically stored and reserved for the patient's use, reducing the risk of transfusion reactions and transfusion-transmitted infections associated with allogeneic (donor) blood transfusions.
- Autologous donation may involve preoperative donation, where blood is collected before surgery, or intraoperative blood salvage, where blood lost during surgery is collected, processed, and reinfused into the patient.

6.4.5. **Cord Blood Donation**:

- Cord blood donation involves collecting blood from the umbilical cord and placenta of newborn infants immediately after birth.
- Cord blood contains hematopoietic stem cells, which can be used in hematopoietic stem cell transplantation to treat various blood disorders, cancers, and immune disorders.
- Cord blood donation is typically collected using a sterile collection kit and processed and stored in a cord blood bank for future use by transplant recipients.
- Each method of blood collection has its advantages and is used based on the specific needs of patients, healthcare providers, and blood banks.

6.4.6. **Donor Phlebotomy Technique**:

- Follow established protocols and procedures for donor phlebotomy, including donor eligibility screening, preparation, and post-donation care.
- Ensure a clean and sterile environment for donor phlebotomy, adhering to infection control guidelines and safety precautions.
- Monitor donors during and after phlebotomy for signs of adverse reactions or complications, providing prompt intervention and assistance as needed.
- Document the blood collection process accurately, recording to relevant information such as donor identification, sample collection details, and any observed reactions or incidents.

6.5. Blood Processing and Component Preparation

6.5.1. Concept in blood component separation and preparation

Below are some specific techniques commonly used in blood processing and component preparation:

1. **Centrifugation:** This technique involves spinning blood unit at high speeds to separate its components based on density. For example:

– red blood cells settle at the bottom,
– plasma rises to the top, and
– platelets are found in the middle layer.

Centrifugation is used to prepare packed red blood cells; platelet concentrates and plasma products.

2. **Leukoreduction:** This process involves removing white blood cells from blood components to reduce the risk of transfusion-related reactions and infections. Leukoreduction can be achieved using filtration methods or specialized centrifugation techniques.
3. **Apheresis:** Apheresis is a procedure that allows specific blood components to be selectively collected or removed from a donor or patient while returning the remaining components to the circulation. This technique is used to collect platelets, plasma, red blood cells, or specific cell populations for therapeutic purposes.
4. **Pathogen inactivation:** Pathogen inactivation methods are used to reduce the risk of transfusion-transmitted infections by inactivating pathogens, such as viruses, bacteria, and parasites, in blood products. Common techniques include photochemical treatment and solvent/detergent treatment.
5. **Cryopreservation:** Cryopreservation involves freezing blood components at ultra-low temperatures to extend their shelf life and preserve their viability. Cryopreserved products, such as cryoprecipitate and frozen plasma, are stored in specialized freezers until needed for transfusion.
6. **Fractionation:** Fractionation is a process used to isolate and purify specific blood proteins or factors from plasma, such as albumin, clotting factors, and immunoglobulins. These purified products are used for therapeutic purposes in patients with specific medical conditions.
7. **Cross-matching:** Cross-matching is a laboratory procedure performed to determine compatibility between donor and recipient blood samples before transfusion. It involves mixing donor red blood cells with recipient plasma to detect any incompatible reactions that could lead to transfusion reactions.
8. **Quality control:** Quality control measures are implemented throughout the blood processing and component preparation process to ensure the safety, purity, and efficacy of blood products. This includes monitoring for contamination, conducting regular testing for blood-borne pathogens, and maintaining proper storage conditions.

6.5.2. Processing of Whole Blood to Components:

Guidelines from different countries variously define a Whole Blood donation as 450-500mL (±10%) of blood collected into citrate anticoagulant also containing phosphate and dextrose.

The clinical indications for transfusion of whole blood are limited to intrauterine/neonatal exchange transfusion and increasingly in some countries such as the United States, massive

transfusion. Thus, the vast majority of collected whole blood is processed into components- red cells, plasma and platelet concentrates. Whole blood-derived plasma is suitable for fractionation to plasma derivatives, freezing as transfusable plasma or further manufacture into cryoprecipitate and cryoprecipitate-depleted plasma. Whole blood donations from which platelets are to be harvested must be held and processed at 20-24 °C. Some countries permit overnight holding of whole blood at 20-24 °C prior to component production, yielding components of acceptable quality, allowing the production of platelets from the majority of collections and obviating the need for multiple manufacturing shifts.Top of Form

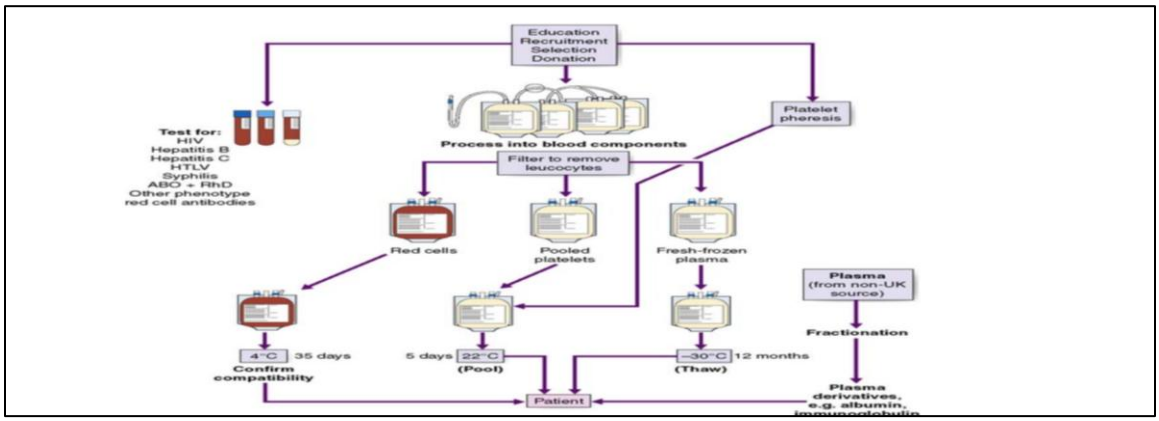

Fig. 6. Red Blood Cell Production and Storage

A. RBCs processing

Red cells may be produced either from whole blood donations or by Apheresis. For the vast majority of red cell components, an additive solution (such as Saline-Adenine-Glucose-Mannitol SAGM, or AS-3, to provide nutrients, stabilize pH, and prolong RBC viability during storage), is introduced following separation to achieve a haematocrit of 50-70% and extend storage from 21-28 days to 35-42 days.

RBC Storage

Red cell storage temperatures start at 1-2 °C, extending through 6 °C, with allowance during transport up to 10 °C. To minimize the possibility of bacterial proliferation and maintain viability, red cells should be removed from refrigeration as little as possible.

The most important changes occurring during storage are progressive extracellular leakage of potassium and decline in red cell recovery to 75-85% of transfused cells at end-expiration. Red cells used for intrauterine transfusions (IUT) and exchange transfusion of neonates are normally stored or reconstituted in compatible plasma. Typically, clinicians will request freshly collected or washed units for potassium-sensitive patients to avoid levels as high as 95mEq/L of supernatant (5-6 mEq per bag) at the end of storage.

For patients who require red cells and have a history of severe or recurrent allergic reactions or immunoglobulin A (IgA) deficiency with anti-IgA, red cells are washed and resuspended in saline or an approved additive solution. This removes >95% of plasma proteins, removing donor antigens to which patients have performed antibodies.

Red cells from donors with rare phenotypes or autologous units from patients with one rare or multiple common red cell alloantibodies, for whom provision of compatible donor blood is extremely difficult, can be stored frozen for 10 years or longer. Prior to transfusion, frozen red cells are thawed and washed to remove the cryoprotectant used to preserve them.

B. Platelet Processing

Platelets may be separated from whole blood donations and subsequently pooled, or collected by Apheresis. Platelet production from whole blood requires two centrifugation steps which differ in their intermediate. In some places, pooled buffy coats (BC) are generated by 'bottom and top' processing, while in others, Platelet-Rich Plasma (PRP) is the intermediate.

BC and Apheresis platelets yield similar increments after transfusion while PRP platelets tend to produce lower post-transfusion increments. This has been attributed to harsher centrifugation against a plastic surface and consequent increased activation for PRP platelets compared to the softer red cell cushion against which BC platelets are concentrated. An adult therapeutic dose of platelets ($>2.5\times10^{11}$) can be consistently manufactured from four or more whole blood donations. In contrast, with the appropriate selection of donors, 1- 3 adult therapeutic doses ($2.5\text{-}11\times10^{11}$) can be harvested from a single donor during one Apheresis collection procedure.

Platelets Storage

Platelets are stored under agitation at 20-24 °C for five days, which may be extended to seven days if an approved method to detect or inactivate bacterial pathogens is used. With pre-storage Leucocyte Reduction (LR), modern storage plastics, platelets stored for seven days in plasma maintain their in vitro function, with 15-20% reductions in recovery compared with five-day stored platelets.

During storage, platelets undergo a fall in PH due to accumulation of Lactic Acid, show increased surface expression of activation markers and lose their normal shape. PH remains the only quantitative change that must be monitored routinely and must be above 6.2 – 6.4 at out-date. Visual inspection to look for the 'Swirling' effect of discoid platelets has been recommended, but this is highly subjective and changes only when the platelets have been grossly damaged. For patients with severe allergic reactions, usually due to plasma proteins, it is possible to wash platelets. This results in the loss of >20% of platelet number but does ameliorate reaction rates far more than simple plasma volume reduction.

Platelet Additive Solutions (PAS) are available worldwide for Apheresis platelets and in some countries, whole blood-derived platelet pools. These solutions contain Sodium Chloride, Acetate, Citrate, Phosphate or Gluconate buffers ± Potassium and Magnesium. Platelets stored in 65%

PAS and 35% plasma are available in a number of countries and can be stored for 5-7 days. This strategy makes more plasma available for transfusion or fractionation, appears to reduce allergic reactions, but may result in lower platelet increments, depending on the additive used.

C. Plasma Processing

Fresh Frozen Plasma (FFP) from a whole blood donation must be prepared and frozen as soon after collection as possible, within eight hours and preferably within six. Usual unit volumes are 200-300mL. FFP can also be derived from Apheresis collections in 300-600mL volumes. FFP is commonly used as a source of multiple coagulation factor replacement of massive transfusion, disseminated intravascular coagulation, warfarin-induced bleeding and liver disease. It can also be used for plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP) or serve as a single source of one or more deficient factors for which no concentrates are available.

Plasma Storage

The permitted shelf-life (three months to seven years) depends on the storage temperature (≤ -18 to ≤ -65 °C). In some countries, FFP must be monitored for levels of factor VIII. FFP is thawed in a protective overwrap in a water bath, a purpose-designed microwave oven or dry heat source. Once thawed, FFP should be used as soon as possible since levels of labile coagulation factors decline during further storage. Most countries permit thawed plasma to be stored refrigerated for at least on day and up to five days in some if it is relabelled as ‘thawed plasma’.

In some countries such as the USA, liquid plasma is collected from whole blood, stored between 1°C to 6 °C and expires in 26 – 40 days, depending on the base anticoagulant into which it is collected. Whereas use in Europe and North America is generally limited to 7-14 days because of progressive factor loss. The clinical indication for liquid plasma is limited to initial treatment of massively transfused patients with life-threatening haemorrhage. As a never-frozen product with viable lymphocytes, to prevent Transfusion-associated graft-versus-host disease (TA-GVHD), irradiation is recommended.

D. Cryoprecipitate Processing

Cryoprecipitate is made by slowly thawing single units of FFP at 1- 6 °C. Cryo-protein precipitates of factors VIII and XIII, vWF, Fibrinogen and Fibronectin are concentrated 2-9-fold compared with plasma.

Cryoprecipitate Storage

Cryoprecipitate can be stored for 1-3 years, depending on temperature and local regulations. Thawed cryoprecipitate has a shelf-life of 4-6 hours depending upon open or closed system processing. Although originally developed for factor VIII deficiency (Haemophilia A), most cryoprecipitate is now prescribed to treat acquired hypofibrinogenemia, usually in the context of massive transfusion, DIC or Liver disease. An adult dose of 5-10 bags is generally indicated once the fibrinogen level falls below 1.0 – 1.5g/L.

E. Granulocyte Production

The transfusion of granulocyte concentrates is uncommon. They are presently indicated only for severely neutropenic patients (count <0.5 x 10^9/L) with bacterial of fungal infections refractory to appropriate antimicrobial therapy. Granulocytes are primarily collected by Apheresis, with buffy coat separation from whole blood as an alternative source. Most regulatory agencies require and adult dose of ≥ 1 x 10^{10} granulocytes, which is usually infused daily. To achieve such doses, Apheresis donor's peripheral counts are increased with steroids ± granulocyte colony stimulating factor (G-CSF).

G-CSF mobilization with ≈ 5µg/kg G-CSF plus oral dexamethasone 8mg, 12-24 hours prior to Apheresis results in collections of 6-8 x 10^{10} granulocytes, a dose sufficient to elevate patients' circulating counts. Some countries transfuse buffy coat as a source of granulocytes. A dose of 1 x 10^{10} can be achieved from 10 buffy coats.

Granulocytes should be transfused as soon as possible after collection due to their 24-hour shelf-life and onset of significant functional deficiency within six hours of collection. Granulocytes must be ɣ-irradiated to prevent TA-GVHD and never Leucocyte reduced.

Granulocytes Storage

Granulocytes should be kept at 20-24 °C without agitation. Because of red cell contamination, a cross-match should be performed. Substantial numbers of platelets are also present in granulocytes, usually >2.5×10^{11}. Granulocytes should not be kept for more than 24hrs

6.6. Collection of Blood Components by Apheresis

Apheresis is a blood donation procedure where specific blood components such as platelets, plasma, or red blood cells are collected, and the remaining components are returned to the donor. This method is highly efficient in collecting concentrated quantities of desired blood components

The collection of blood components by apheresis involves a specialized procedure that allows specific blood components to be selectively collected or removed from a donor or patient while returning the remaining components to the circulation. Apheresis technology permits the collection of multiple transfusable doses of components from desired ABO and RhD-specific groups. This is not possible with whole blood collections which yield a single red cell, plasma and partial platelet dose of the same blood type. Therefore, the collection of two O+, O-, A- or B- red cells or two to three A or AB plasmas and/or two or three full-dose platelets may be obtained.

The frequency of Apheresis component donations differs in different countries. Double red cell donation requires longer inter-donation intervals (as well as higher hemoglobin cut-offs) while platelet-pheresis allows collection of 1-3 adult doses per procedures often as 24 times per year. Total allowable plasma loss varies by jurisdiction and donor blood volume, but is always less than 15 liters per year.

6.6.1. Principle of Apheresis

6.6.1.1.Procedure Steps

1. **Preparation**: The donor is seated comfortably, and their vital signs are checked.
2. **Venipuncture**: A needle is inserted into a vein in one arm, and blood is drawn into an apheresis machine.
3. **Separation**: The apheresis machine uses centrifugation to separate the blood into its components.
4. **Collection**: The desired component (e.g., platelets, plasma) is collected into a sterile bag.
5. **Return**: The remaining blood components are returned to the donor through a needle in their other arm.

6.6.1.2.Health Conditions and Eligibility Criteria for Apheresis Donation

A. General Health Requirements

1. **Age**: Typically, donors should be between 18 and 60 years old (varies by country and organization).
2. **Weight**: Donors should generally weigh at least 50 kg.
3. **Health Status**: Donors must be in good health, without any active infections or chronic illnesses that could pose a risk.
4. **Haemoglobin Levels**: Donors must have acceptable haemoglobin levels to ensure they can safely donate without becoming anaemic.

B. Specific Health Conditions to Consider

1. **Cardiovascular Health**:
   - Donors should not have a history of heart disease or uncontrolled hypertension.
   - Blood pressure and heart rate are checked before donation to ensure they are within safe limits.
2. **Medications**:
   - Certain medications may disqualify a donor from apheresis. For example, donors taking anticoagulants or blood thinners may be deferred.
   - Donors should disclose all medications they are taking to the healthcare provider.
3. **Infections**:
   - Donors should not have any active infections at the time of donation.
   - History of infectious diseases such as hepatitis or HIV may disqualify a donor.
4. **Chronic Conditions**:
   - Chronic illnesses like diabetes must be well-controlled, and donors should not have complications that could be exacerbated by the donation process.
5. **Allergies and Reactions**:
   - Donors with a history of severe allergic reactions or adverse reactions to blood donation should be evaluated carefully.
6. **Recent Surgeries or Procedures**:

- Donors should be fully recovered from any recent surgeries or medical procedures.
- There may be specific deferral periods depending on the nature of the surgery.

6.6.2. Advantages of Apheresis

1. **Targeted Collection**: Allows for the collection of specific blood components in larger quantities compared to whole blood donation.
2. **Efficient Use**: Beneficial for collecting platelets and plasma, which are in high demand for patients undergoing treatments such as chemotherapy or suffering from clotting disorders.
3. **Frequent Donations**: Donors can donate platelets more frequently (every 7-14 days) compared to whole blood donations

Apheresis blood donation Process

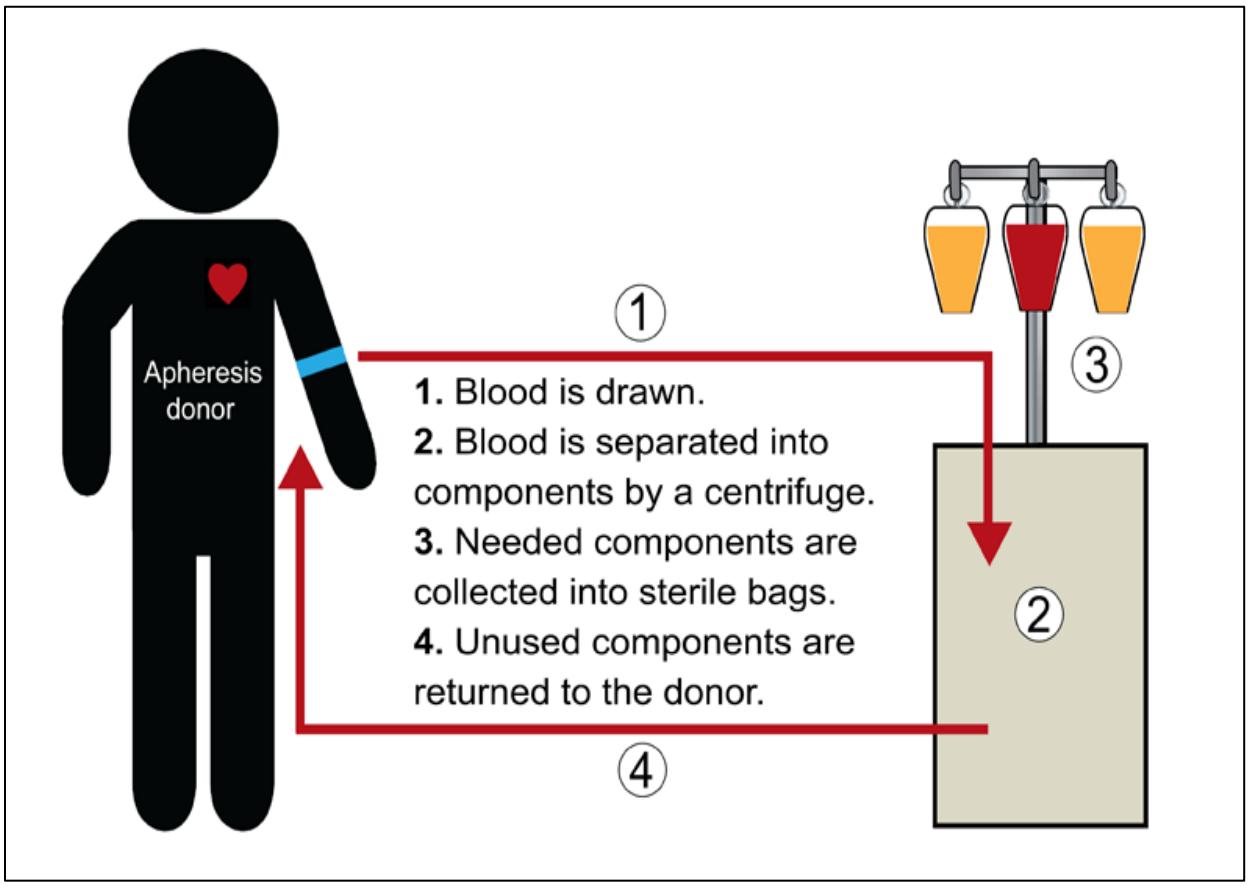

Fig. 7. Apheresis blood donation Process

6.6.3. Types of Apheresis

1. **Plasmapheresis**: Removal of plasma from the blood.
2. **Plateletpheresis**: Removal of platelets from the blood.
3. **Leukapheresis**: Removal of white blood cells from the blood.

4. **Erythrocytapheresis**: Removal of red blood cells from the blood.
5. **Photopheresis**: A type of apheresis where blood is treated with a photosensitizing agent and then exposed to UV light.

6.6.4. Clinical Applications

Donor Apheresis:

Collection of blood components from healthy donors for transfusion purposes.

Examples: Platelet donation, plasma donation, peripheral blood stem cell collection.

The process of Apheresis can be summarized with the following overview:

1. **Donor or Patient Preparation:** Before the apheresis procedure, the donor or patient is typically screened for eligibility, which may include medical history assessment, physical examination, and laboratory tests. They are then positioned comfortably for the procedure, usually in a reclining chair.
2. **Vascular Access:** A vascular access device is established to allow blood to be withdrawn and returned during the apheresis procedure. Common access sites include peripheral veins in the arm or central veins accessed through a catheter inserted into the subclavian, jugular, or femoral vein.
3. **Blood Processing System Setup:** The apheresis machine, also known as a cell separator, is programmed based on the desired blood component to be collected or removed. The machine is equipped with disposable tubing sets and centrifugation chambers specific to the procedure.
4. **Blood Separation:** The apheresis machine continuously draws blood from the donor or patient through the vascular access device and into the centrifugation chamber. Inside the chamber, centrifugal forces separate the blood into its various components based on their density and size.
5. **Component Collection:** The desired blood component is selectively collected by the apheresis machine while the remaining components, including red blood cells and plasma, are returned to the donor or patient. The collected component may include platelets, plasma, red blood cells, or specific cell populations, depending on the therapeutic purpose.
6. **Anticoagulation and Blood Return:** Anticoagulants are often infused into the bloodline to prevent clotting during the apheresis procedure. The processed blood components are returned to the donor or patient through the same vascular access device, typically in a continuous or intermittent manner.
7. **Monitoring and Adjustments:** Throughout the apheresis procedure, the donor or patient is closely monitored for vital signs, symptoms, and adverse reactions. The apheresis machine continuously monitors blood flow rates, anticoagulant levels, and other parameters to ensure the safety and efficacy of the procedure.

8. **Post-procedure Care:** After the apheresis procedure is complete, the vascular access device is removed, and the donor or patient may be observed for a brief period to monitor for any **immediate complications.** They are provided with post-procedure instructions and may be advised to hydrate adequately and rest.

By utilizing apheresis technology, healthcare providers can efficiently collect specific blood components for therapeutic purposes while minimizing donor exposure and maximizing the yield of valuable blood products.

6.7. Stem Cell Donation

Stem cell donation is a critical procedure in the treatment of various hematological and oncological conditions. Hematopoietic stem cells (HSCs) are collected either from the bone marrow, peripheral blood, or umbilical cord blood. Peripheral blood stem cell (PBSC) collection is the most common method due to its less invasive nature and higher stem cell yield.

6.7.1. Protocol for the Mobilization of Stem Cell Collection

Mobilization involves stimulating the bone marrow to release stem cells into the bloodstream, making them easier to collect.

6.7.1.1.Chemotherapy and Growth Factors

- **Chemotherapy Agents**: Cyclophosphamide or etoposide may be used in combination with growth factors to enhance mobilization.
- **Growth Factors**: Granulocyte colony-stimulating factor (G-CSF) such as filgrastim is commonly used.
- **Plerixafor**: Used in combination with G-CSF for patients with poor mobilization.

6.7.1.2.Protocol

- **G-CSF Administration**: Typically given subcutaneously at a dose of 10 µg/kg/day.
- **Duration**: Administered for 4-5 days before the collection begins.
- **Combination with Chemotherapy**: When used, chemotherapy is administered several days before the growth factor.

6.7.1.3.Waiting Time

- After the administration of G-CSF, stem cells usually peak in the bloodstream around the 4th to 5th day.
- **Plerixafor**: Given 11 hours before apheresis if needed.

6.7.1.4.Collection

1. **Peripheral Blood Stem Cell Collection (Apheresis)**
    - **Procedure**: Blood is drawn from the donor, passed through an apheresis machine that separates the stem cells, and the remaining blood components are returned to the donor.
    - **Duration**: Typically lasts 4-6 hours per session.
    - **Sessions**: May require 1-2 sessions depending on the stem cell yield.
2. **CD34+ Stem Cell Dosage**
    - **Target Dose**: 2-5 x 10^6 CD34+ cells per kilogram of the recipient's body weight.
    - **Assessment**: The number of CD34+ cells in the peripheral blood is monitored to decide the optimal time for collection.

6.7.1.5.Storage

Cryopreservation

- **Method**: Collected stem cells are cryopreserved using a controlled-rate freezer.
- **Cryoprotectant**: Dimethyl sulfoxide (DMSO) is used to protect cells during freezing.
- **Storage Temperature**: Stored at -196°C in liquid nitrogen.
- **Viability**: Stem cells can be stored for many years while maintaining viability.

6.7.1.6.Considerations and Safety

1. **Donor Safety**
    - **Pre-donation Evaluation**: Comprehensive health assessment to ensure donor suitability.
    - **Monitoring**: Regular monitoring during mobilization and collection to manage side effects.

2. **Adverse Effects**
    - **G-CSF**: Bone pain, headache, fatigue.
    - **Apheresis**: Hypocalcemia, hypotension, citrate reactions.

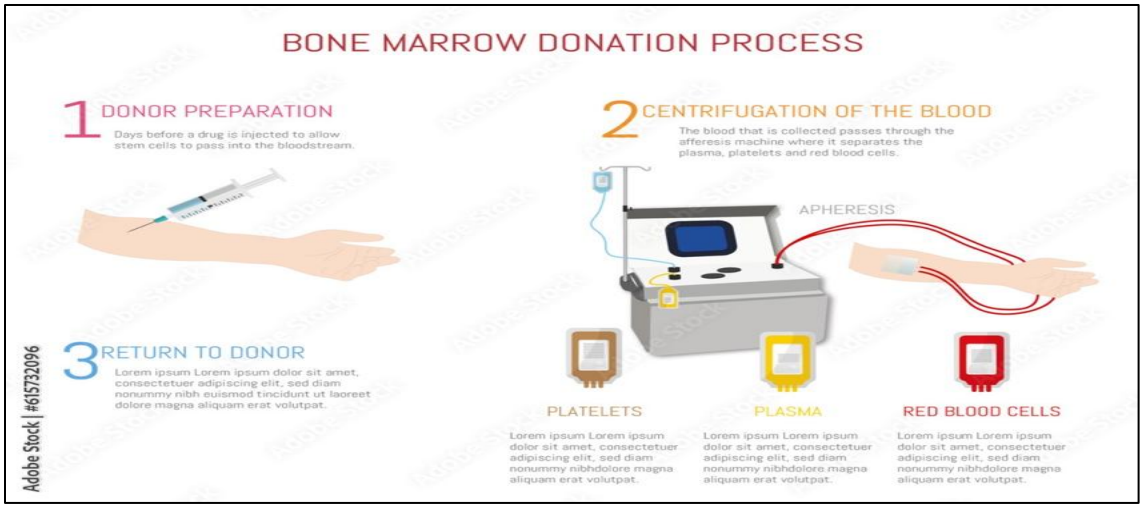

Fig. 8. Bone marrow donation process

6.8. Therapeutic Apheresis

Used to treat various medical conditions by removing pathological components from the blood:

Examples: Treatment of autoimmune diseases (e.g., myasthenia gravis, Guillain-Barré syndrome), Neurological disorders (e.g., multiple sclerosis), Hematological disorders (e.g., thrombotic thrombocytopenic purpura, sickle cell disease), Metabolic disorders (e.g., familial hypercholesterolemia), reduction of high antibody levels, removal of toxins or pathogenic substances.

Table 8. Apheresis types and their uses

Type	Component Removed	Common Uses
Plasmapheresis	Plasma	Autoimmune diseases, TTP, myasthenia gravis
Plateletpheresis	Platelets	Donation for platelet transfusions
Leukapheresis	White Blood Cells	Treatment of hyperleukocytosis, collection for stem cell transplantation
Erythrocytapheresis	Red Blood Cells	Sickle cell disease, severe malaria
Photopheresis	Various	Cutaneous T-cell lymphoma, graft-versus-host disease

Apheresis, used in various clinical scenarios, is often categorized by the urgency and priority of its application:

Grade I: First Choice

1. **Guillain-Barré Syndrome (GBS)**

    - **Application**: Plasmapheresis
    - **Description**: Plasmapheresis is used to remove antibodies thought to be responsible for the nerve damage in GBS. It is often used when the patient is unable to walk independently.
    - **Emergency Use**: Rapid progression to respiratory failure.

2. **Thrombotic Thrombocytopenic Purpura (TTP)**

    - **Application**: Plasma exchange
    - **Description**: Plasma exchange is crucial for removing large von Willebrand factor multimers and autoantibodies against ADAMTS13.
3. **Emergency Use**: Acute episodes with neurological symptoms or renal impairment.

Grade II: Second Choice

1. **Sickle Cell Anemia**

    - **Application**: Red cell exchange
    - **Description**: Used to reduce the concentration of sickle hemoglobin and decrease the risk of vaso-occlusive events.
    - **Emergency Use**: Acute chest syndrome or stroke.

2. **Cryoglobulinemia**

    - **Application**: Plasmapheresis
    - **Description**: Removal of cryoglobulins from the blood to reduce vasculitis and other symptoms.
    - **Emergency Use**: Rapidly progressive glomerulonephritis or severe systemic symptoms.

3. **Autoimmune Hemolytic Anemia**

    - **Application**: Plasmapheresis
    - **Description**: Used to remove autoantibodies responsible for hemolysis.
    - **Emergency Use**: Severe hemolysis not responsive to steroids.

Grade III: Third Choice

1. **Malaria**

    - **Application**: Exchange transfusion

- **Description**: Reduces parasitemia in severe cases.
- **Emergency Use**: Severe malaria with high parasitemia and complications.

2. **Burn Shock**

- **Application**: Plasma exchange
- **Description**: Used to manage capillary leak syndrome and reduce inflammatory mediators.
- **Emergency Use**: Severe burn shock with circulatory instability.

3. **Dilated Cardiomyopathies**

- **Application**: Immunoadsorption
- **Description**: Removal of autoantibodies that may be contributing to the disease.
- **Emergency Use**: Severe heart failure refractory to standard treatments.

4. **Inflammatory Bowel Disease**

- **Application**: Leukocytapheresis
- **Description**: Removal of activated leukocytes contributing to inflammation.
- **Emergency Use**: Severe, refractory inflammatory bowel disease with complications.

Emergency Scenarios

1. **Leukocyte Count > 500 (Hyperleukocytosis)**

- **Application**: Leukapheresis
- **Description**: Rapid reduction of white blood cell counts to prevent leukostasis.
- **Emergency Use**: Acute myeloid leukemia or chronic myeloid leukemia with hyperleukocytosis.

2. **High Titer Antibodies Post-Transplant**

- **Application**: Plasmapheresis or immunoadsorption
- **Description**: Removal of donor-specific antibodies to prevent graft rejection.
- **Emergency Use**: Acute antibody-mediated rejection post-transplant.

Table 9. Therapeutic Apheresis Indications and Benefits

Condition	Apheresis Type	Clinical Benefits
Myasthenia Gravis	Plasmapheresis	Removes circulating antibodies

Thrombotic Thrombocytopenic Purpura (TTP)	Plasmapheresis	Removes ADAMTS13 autoantibodies and ultralarge von Willebrand factor multimers
Guillain-Barré Syndrome	Plasmapheresis	Reduces recovery time, improves symptoms
Sickle Cell Disease	Erythrocytapheresis	Reduces sickle hemoglobin, prevents vaso-occlusive crises

6.9. Quality Control and Monitoring of Apheresis Donors

Quality Control Measures:

- Regular maintenance and calibration of apheresis machines.
- Adherence to standard operating procedures (SOPs).
- Continuous monitoring of donor health and response to apheresis.

Monitoring:

- Pre-donation screening: Medical history, physical examination, and laboratory tests.
- During donation: Monitoring of vital signs and apheresis process.
- Post-donation follow-up: Monitoring for any adverse reactions or complications.

Post-Apheresis Care

Immediate Care:

- Monitor vital signs and overall condition immediately after the procedure.
- Ensure the donor or patient is stable before discharge.
- Provide refreshments and ensure proper hydration.

Follow-Up Care:

- Schedule follow-up appointments to monitor for any delayed adverse reactions.
- Provide guidelines on activity restrictions and signs to watch for potential complications

Table 10. Post-Apheresis Care Guidelines

Aspect	Care Guidelines
Hydration	Encourage fluid intake
Activity Restrictions	Avoid strenuous activities for 24 hours
Monitoring	Observe for signs of dizziness, fatigue, or bleeding
Follow-Up	Schedule follow-up visits for ongoing monitoring

6.10. Ethical and Social Considerations

Ethical considerations play a significant role in various aspects of blood group testing, donor recruitment, and blood transfusion practices. Here are some key ethical considerations:

Informed Consent:

- Donors should provide voluntary and informed consent before blood donation. They should understand the purpose of blood group testing, the risks and benefits of donation, and how their blood will be used.
- Recipients should also receive information about the risks and benefits of blood transfusion, including potential complications and alternatives, to make informed decisions about their healthcare.

Confidentiality and Privacy:

- Donor and recipient confidentiality must be maintained throughout the blood donation and transfusion process. Personal health information, including blood group test results, should be protected from unauthorized disclosure.
- Blood banks and healthcare providers should adhere to data protection regulations and best practices to safeguard donor and recipient privacy.

Equitable Access:

- Blood donation and transfusion services should be accessible to all individuals regardless of socioeconomic status, race, ethnicity, religion, gender, or sexual orientation.
- Efforts should be made to address disparities in access to blood transfusion services, particularly in underserved communities and regions with limited healthcare resources.

Safety and Quality Assurance:

- Donor screening and blood testing procedures should prioritize safety and quality to minimize the risk of transmitting infectious diseases through blood transfusions.
- Blood banks and transfusion services should adhere to regulatory standards and guidelines for blood collection, testing, processing, storage and distribution.

Donor Recruitment Practices:

- Donor recruitment should be conducted ethically and responsibly, without coercion or undue influence.
- Recruitment efforts should focus on educating potential donors about the importance of blood donation, altruism, and the impact of their contributions on patient care.

Avoidance of Commercialization:

- Blood donation and transfusion should not be driven by profit motives or commercial interests. Donors should not be compensated financially for their blood donations, as this can undermine voluntary donation and raise ethical concerns about the commodification of blood.

Ethical Use of Blood Products:

- Blood products should be used judiciously and ethically, prioritizing patient safety and clinical need.
- Healthcare providers should ensure appropriate transfusion practices, including adherence to evidence-based transfusion guidelines, to minimize unnecessary transfusions and reduce the risk of adverse reactions.

Research Ethics:

- Ethical principles should guide research involving blood transfusion, including informed consent, protection of participant rights, and rigorous ethical review by institutional review boards (IRBs).

Researchers should adhere to ethical guidelines and regulations governing human subjects research to ensure the integrity and ethical conduct of research studies

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7. ANTICOAGULATION AND PRESERVATION IN TRANSFUSION

7.1. Learning Objectives

1. Understand the concept of anticoagulation and preservation in the context of blood transfusion.
2. Define the purpose of anticoagulants in preventing coagulation during blood storage.
3. Identify common anticoagulants used in blood collection and storage.
4. Analyze the impact of anticoagulants on blood components during storage.
5. Evaluate the significance of proper anticoagulation and preservation techniques in transfusion medicine.

7.2. Anticoagulation and preservation

Introduction

Blood anticoagulants and preservatives are critical for maintaining the viability and functionality of blood components during storage. They prevent clotting and provide nutrients to preserve red blood cells (RBCs). The most common solutions used in blood banking are ACD, CPD, and CPDA-1.

7.3. Definition and Purpose

- Anticoagulation in transfusion refers to the process of adding anticoagulants to collected blood to prevent clot formation during storage.
- The purpose of anticoagulants in transfusion is to maintain the viability and functionality of blood components (red blood cells, platelets, plasma) for transfusion by preventing coagulation.

7.4. Common Anticoagulants

7.4.1. ACD (Acid Citrate Dextrose)

Mode of Action

- **Acid Citrate**: Binds calcium ions, preventing blood coagulation by inhibiting the calcium-dependent steps in the clotting cascade.
- **Dextrose**: Provides a source of glucose to maintain RBC metabolism during storage.

Preservation Time

- **21 days**: ACD preserves blood components for up to 21 days when stored at 1-6°C.

Best Indication for a Specific Blood Component

- **Whole Blood**: ACD is primarily used for the preservation of whole blood, particularly in situations requiring the rapid use of collected blood, such as during apheresis or immediate transfusion.

Quantity in the Bag

- **450 mL bag**: Typically contains about 63 mL of ACD solution.
- **500 mL bag**: Typically contains about 70 mL of ACD solution.

7.4.2. CPD (Citrate Phosphate Dextrose)

Mode of Action

- **Citrate**: Binds calcium ions to prevent coagulation.
- **Phosphate**: Helps maintain the pH of the blood, ensuring better RBC metabolism.
- **Dextrose**: Provides a glucose source to sustain RBC energy and viability.

Preservation Time

- **21 days**: CPD preserves blood components for up to 21 days when stored at 1-6°C.

Best Indication for a Specific Blood Component

- **Whole Blood and Red Blood Cells**: CPD is commonly used for the storage of whole blood and RBCs, providing a balance of anticoagulation and nutrient support.

Quantity in the Bag

- **450 mL bag**: Typically contains about 63 mL of CPD solution.
- **500 mL bag**: Typically contains about 70 mL of CPD solution.

7.4.3. CPDA-1 (Citrate Phosphate Dextrose Adenine 1)

Mode of Action

- **Citrate**: Prevents coagulation by binding calcium ions.
- **Phosphate**: Helps maintain pH and supports RBC metabolism.
- **Dextrose**: Provides glucose for RBC energy needs.

- **Adenine**: Supports the production of ATP, crucial for maintaining RBC viability and function during extended storage.

Preservation Time

- **35 days**: CPDA-1 extends the preservation of blood components up to 35 days when stored at 1-6°C.

Best Indication for a Specific Blood Component

- **Red Blood Cells**: CPDA-1 is particularly effective for the extended storage of RBCs, making it ideal for blood banks that need to store RBCs for longer periods before transfusion.

Quantity in the Bag

- **450 mL bag**: Typically contains about 63 mL of CPDA-1 solution.
- **500 mL bag**: Typically contains about 70 mL of CPDA-1 solution.

7.4.4. Heparins:

Heparin inhibits thrombin and factor Xa, preventing clot formation. It is used in specialized situations such as apheresis procedures or in platelet concentrates.

Types of Heparins

1. **Unfractionated Heparin (UFH)**
    - **Description**: A mixture of glycosaminoglycans with varying molecular weights.
    - **Usage**: Commonly used in hospital settings for immediate anticoagulation.
2. **Low Molecular Weight Heparin (LMWH)**
    - **Examples**: Enoxaparin, dalteparin, tinzaparin.
    - **Description**: Derived from UFH, with more predictable pharmacokinetics and a longer half-life.
3. **Other Heparins**
    - **Heparinoids**: Synthetic or semi-synthetic compounds with similar properties to heparin.

Mode of Action

1. **Unfractionated Heparin (UFH)**
    - **Mechanism**: Binds to antithrombin III, enhancing its ability to inactivate thrombin (factor IIa) and factor Xa, leading to anticoagulation.
    - **Onset**: Rapid, within minutes of intravenous administration.
2. **Low Molecular Weight Heparin (LMWH)**

- **Mechanism**: Primarily inhibits factor Xa, with a lesser effect on thrombin due to its smaller size.
- **Onset**: More predictable anticoagulant response, with subcutaneous administration.

Preservation Time

1. **Unfractionated Heparin (UFH)**
   - **Half-life**: Short, approximately 1-2 hours when administered intravenously.
   - **Preservation**: Blood samples anticoagulated with UFH should be processed within a few hours to maintain stability.
2. **Low Molecular Weight Heparin (LMWH)**
   - **Half-life**: Longer, about 4-6 hours with subcutaneous administration.
   - **Preservation**: Allows for longer intervals between doses and more stable anticoagulation in stored samples.

Best Indications for Specific Blood Components

1. **Unfractionated Heparin (UFH)**
   - **Indications**: Acute settings requiring rapid anticoagulation, such as during surgery or in patients with acute thromboembolic events.
   - **Blood Components**: Ideal for fresh whole blood and plasma collection, particularly when immediate processing is required.
2. **Low Molecular Weight Heparin (LMWH)**
   - **Indications**: Long-term anticoagulation, prevention of venous thromboembolism in surgical and medical patients.
   - **Blood Components**: Suitable for situations where longer preservation of anticoagulated samples is needed, such as during transport or delayed processing.

Quantity in the Bag

1. **Unfractionated Heparin (UFH)**
   - **Dosage**: Typically, 10-20 units of heparin per milliliter of blood.
   - **Bag Quantity**: For a standard 500 mL blood collection bag, 5,000-10,000 units of heparin may be used.
2. **Low Molecular Weight Heparin (LMWH)**
   - **Dosage**: Lower quantities required due to more potent activity.
   - **Bag Quantity**: Usually adjusted based on the specific LMWH used and the required anticoagulation level.

7.4.5. EDTA (Ethylenediaminetetraacetic acid):

EDTA is a widely used anticoagulant in hematology for collecting and preserving blood samples. It is particularly valuable for its ability to preserve the cellular components of blood for various diagnostic tests

Mode of Action

- **Calcium Chelation**: EDTA acts by binding to calcium ions in the blood. Calcium is a crucial factor for the coagulation cascade; by chelating calcium, EDTA effectively prevents the blood from clotting.
- **Mechanism**: The chelation process is achieved through EDTA's ability to form stable complexes with calcium ions, thus inhibiting the calcium-dependent coagulation pathways.

Preservation Time

- **Preservation for Hematological Testing**: EDTA preserves the blood components well for up to 24 hours at room temperature, making it suitable for most routine hematological tests.
- **Extended Storage**: When stored at 2-8°C, EDTA-anticoagulated blood samples can be stable for up to 48 hours for most hematological analyses, though some specific tests may require fresher samples for optimal accuracy.

Best Indication for a Specific Blood Component

- **Complete Blood Count (CBC)**: EDTA is the anticoagulant of choice for CBCs, which include measurements such as white blood cell count, red blood cell count, haemoglobin, haematocrit, and platelet count.
- **Blood Smears**: Ideal for preparing blood smears for microscopic examination, as it preserves cell morphology effectively.
- **Molecular Testing**: EDTA tubes are also used in certain molecular biology techniques where DNA or RNA analysis is required.

Quantity in the Bag

- **EDTA Tubes**: Blood collection tubes containing EDTA are available in various sizes, typically ranging from 2 mL to 10 mL. The amount of EDTA in each tube is precisely calibrated to the volume of blood it is designed to hold.
    - **2 mL tube**: Contains about 1.5-2.0 mg of EDTA.
    - **5 mL tube**: Contains about 7.5-10.0 mg of EDTA.
    - **10 mL tube**: Contains about 15-20 mg of EDTA.
- **Blood Bags**: For blood collection in larger volumes, such as for transfusions or research, the specific quantity of EDTA can vary. However, these are less common compared to other anticoagulants like CPD or CPDA-1.

Clinical Implications

1. **Accurate Haematological Results**: EDTA is crucial for obtaining reliable results in haematological tests by preventing clotting and preserving cell integrity.
2. **Blood Sample Quality**: Proper mixing of blood with EDTA immediately after collection is essential to prevent microclots and ensure sample quality.

Handling and Storage

- **Mixing**: Gently invert the EDTA tube several times (usually 8-10 times) immediately after collection to ensure thorough mixing of the blood with the anticoagulant.
- **Storage**: Store EDTA tubes at room temperature if testing within 24 hours or refrigerate at 2-8°C if testing is delayed.

Conclusion

EDTA is an essential anticoagulant in clinical laboratories, particularly for hematological testing. Its ability to preserve blood cell morphology and prevent clotting makes it invaluable for accurate diagnostic testing.

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8. ADVANTAGES AND RISKS OF AUTOLOGOUS BLOOD DONATION:

8.1. Learning Objectives

1. Understand the advantages of autologous blood transfusion compared to allogeneic blood transfusion.
2. Identify the key benefits of autologous blood transfusion in various clinical settings.
3. Recognize the importance of considering autologous blood transfusion as an alternative to allogeneic blood transfusion.
4. Highlight risks of autologous blood donation

8.2. Advantages of Autologous Blood Donation

8.2.1. Elimination of immunological risks

- Autologous blood transfusion eliminates the risk of transfusion reactions, including
- hemolytic reactions, non-febrile hemolytic reactions,
- Alloimmunization: Autologous blood transfusion avoids the risk of alloimmunization, where the recipient's immune system develops antibodies against foreign antigens present in allogeneic blood.
- Autologous blood transfusion minimizes the risk of allergic reactions, such as those caused by plasma proteins or preservatives present in allogeneic blood products.

8.2.2. Reduced Risk of Infections:

- Since autologous blood comes from the patient, there is a significantly reduced risk of transfusion-transmitted infections (TTIs) compared to allogeneic blood transfusion, where the blood comes from donors.

8.2.3. Improved Compatibility:

- Autologous blood is inherently compatible with the patient's immune system, reducing the risk of immune-mediated reactions and alloimmunization.

8.2.4. Conservation of Blood Supply:

- Utilizing autologous blood helps conserve the limited supply of allogeneic blood, ensuring that donated blood is available for patients who cannot undergo autologous donation. Autologous blood follows all the protocol for testing and screening.

8.2.5. Psychological Comfort:

– Autologous blood transfusion may provide psychological comfort to patients, knowing that they are receiving their own blood rather than blood from external donors, reducing anxiety associated with transfusion.

8.3. Risks associated with autologous blood transfusion

- Clerical error while the blood is stored in a blood bank, hence can be issued to a different recipient.
- Insufficient quantity in case the needs during or post-surgery exceed the donation
- Limited shelf life: If the elective surgery timing should respect the shelf life.
- Unnecessary donation, in case there is no indication for surgery

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9. BLOOD STORAGE, MATERIALS, DISTRIBUTION AND LOGISTIC

9.1. Learning Objectives

1. Understand the optimal storage conditions for different blood components.
2. Importance of blood warmers during massive transfusion.
3. Identify the necessary storage equipment in various hospital departments.
4. Discuss the challenges of the short shelf life of blood products.
5. Learn the transport conditions required for blood components.
6. Explore strategies for harmonizing transport from the laboratory to departments.
7. Improve communication between healthcare facilities (HFs) and services like Zipline.

9.2. Storage Conditions of Each Component

- **Whole Blood**:
    - Temperature: 1-6°C
    - Shelf Life: Up to 35 days with anticoagulants
- **Red Blood Cells (RBCs)**:
    - Temperature: 1-6°C
    - Shelf Life: 35-42 days, depending on the additive solution used
- **Platelets**:
    - Temperature: 20-24°C with continuous gentle agitation
    - Shelf Life: 5-7 days
- **Plasma**:
    - Frozen Temperature: ≤ -18°C
    - Shelf Life: 1 year
    - Thawed Temperature: 1-6°C
    - Shelf Life: 24 hours
- **Cryoprecipitate**:
    - Frozen Temperature: ≤ -18°C
    - Shelf Life: 1 year

9.3. Blood Warmers

Blood warmers are used to prevent hypothermia in patients receiving large volumes of cold blood. Without blood warmers, the risk of adverse reactions increases, particularly in trauma patients. Ensure availability and proper functioning of blood warmers in transfusion areas.

9.3.1. Storage Equipment in Departments

- **Refrigerators**: For storing whole blood, RBCs, and thawed plasma at 1-6°C.
- **Freezers**: For storing frozen plasma and cryoprecipitate at ≤ -18°C.
- **Platelet Agitators**: For storing platelets at 20-24°C with agitation.
- **Temperature Monitors**: Continuous monitoring to ensure compliance with storage conditions.
- **Backup Power Supplies**: To maintain storage conditions during power outages.

9.3.2. Short Shelf Life of Distributed Blood Products

- Blood components have varying shelf lives, necessitating careful inventory management.
- Implement a first-in, first-out (FIFO) system to use older stock first.
- Regularly review inventory levels to prevent wastage due to expiration.

9.3.3. Transport Conditions of Blood Components

- **Temperature Control**: Use insulated containers and coolants to maintain required temperatures.
  - RBCs, Whole Blood, and Thawed Plasma: 1-10°C
  - Platelets: 20-24°C
  - Frozen Plasma and Cryoprecipitate: Maintain frozen state (≤ -18°C)
- **Handling**: Minimize agitation, especially for RBCs and platelets, to prevent damage.
- **Documentation**: Proper labeling and tracking of blood components during transport.

9.3.4. Harmonization of Transport from Lab to Departments

- **Standardized Equipment**: Use the same types of containers and coolants for consistency.
- **Protocols**: Develop and implement uniform protocols for the transport process.
- **Training**: Ensure all staff involved in transport are trained on protocols and equipment use.
- **Delivery:** Enhance delivery channels between healthcare facilities and services like Zipline.
  - Use technology for real-time tracking and updates.
  - Schedule regular meetings to review and improve delivery processes.

References

- World Health Organization. Blood Cold Chain Management Guidelines.
- American Association of Blood Banks (AABB). Standards for Blood Banks and Transfusion Services.
- National Blood Authority. Blood Storage and Transportation Guidelines.
- Zipline. Improving Blood Delivery in Rural Areas: Case Studies and Best Practices.

10. BLOOD TRANSFUSION IN CLINICAL PRACTICE

10.1. Learning Objectives:

1. Understand the indications for the use of different blood components in therapy.
2. Learn about the blood components available in Rwanda.
3. Explore the concept and management of massive transfusion.
4. Understand the storage requirements for blood components.
5. Identify stable blood components and their applications.
6. Identify specific indications and contraindications for each blood product.
7. Understand the role of coagulation in the prevention of bleeding.
8. Learn the coagulation cascade and its components.
9. Identify common coagulation disorders.
10. Interpret a coagulation profile and its significance in transfusion practice.

10.2. Blood Components Therapy

10.2.1. Indications for Blood Components Therapy

Red Blood Cells (RBCs):

- Indications: Anemia, acute blood loss, perioperative management.
- Purpose: Increase oxygen-carrying capacity.

Platelets:

- Indications: Thrombocytopenia, platelet function disorders, massive transfusion.
- Purpose: Prevent or control bleeding.

Fresh Frozen Plasma (FFP):

- Indications: Coagulopathy, liver disease, disseminated intravascular coagulation (DIC), massive transfusion.
- Purpose: Replace deficient clotting factors.

Cryoprecipitate:

- Indications: Hypofibrinogenemia, von Willebrand disease, haemophilia A.
- Purpose: Provide fibrinogen and factor VIII.

Table 11. Indications for blood components available in Rwanda

Component	Indications	Purpose
Red Blood Cells	Anemia, acute blood loss, perioperative management	Increase oxygen-carrying capacity

Platelets	Thrombocytopenia, platelet function disorders	Prevent or control bleeding
Fresh Frozen Plasma	Coagulopathy, liver disease, DIC	Replace deficient clotting factors
Cryoprecipitate	Hypofibrinogenemia, von Willebrand disease	Provide fibrinogen and factor VIII

10.2.2. Stable Blood Components

- **Definition**: Blood components that have a longer shelf life and can be stored for extended periods.

Examples:

- **Lyophilized Plasma**: Plasma that has been freeze-dried for extended storage.
- **Pathogen-Reduced Plasma**: Plasma treated to reduce the risk of transfusion-transmitted infections.

Applications:

- Used in remote or resource-limited settings.
- Ideal for military use or emergency preparedness.

Diagram: Stable Blood Components

10.3. Blood Products Indications and Contraindications

10.3.1. Indications and Risks of Blood Products

10.3.1.1. RED BLOOD CELLS (RBCS)

Indications:

- Anemia with symptoms (e.g., fatigue, shortness of breath)
  - Hemoglobin <7 g/dL in stable patients.
  - Hemoglobin <8 g/dL in patients with cardiovascular disease.
- Acute blood loss (e.g., trauma, surgery).
  - Hemoglobinopathies (e.g., sickle cell disease, Thalassemia).
  - Bone marrow failure syndrome (aplastic anemia…)

Risks:

- Transfusion reactions (e.g., febrile non-hemolytic, hemolytic).
- Iron overload with repeated transfusions.
- Alloimmunization (formation of antibodies against transfused blood).

Contraindications:

- Volume overload risk (e.g., heart failure).
- Hemochromatosis
- Hyperleucocytosis

- Severe anaphylactic reaction

10.3.1.2. PLATELETS

Indications:

- Thrombocytopenia (low platelet count) with bleeding or risk of bleeding.
- Platelet function disorders (e.g., Glanzmann thrombasthenia).
- Massive transfusion protocols.
- Platelet count <10,000/µL in asymptomatic patients.
- Platelet count <50,000/µL before invasive procedures.
- Essential thrombocythemia with bleeding (PLT > 800,000/ul)

Risks:

- Alloimmunization.
- Bacterial contamination leading to sepsis.
- Transfusion-related acute lung injury (TRALI)
- Allergic reactions

Contraindications:

- Thrombotic thrombocytopenic purpura (TTP) without severe bleeding.
- Heparin-induced thrombocytopenia (HIT) without bleeding.
- Hemolytic uremic syndrome in pediatric

10.3.1.3. FRESH FROZEN PLASMA (FFP)

Indications:

- Coagulation factor deficiencies (when specific concentrates are unavailable).
- Liver disease with coagulopathy.
- Disseminated intravascular coagulation (DIC).
- Massive transfusion protocols.
- Active bleeding with PT or aPTT >1.5 times normal.
- Warfarin overdose
- Protein replacement in severe immunodeficiency
- Thrombotic thrombocytopenia purpura (TTP)

Risks:

- Allergic reactions.
- Volume overload, especially in patients with heart failure.
- TRALI
- TTI

Contraindications:

- Volume expansion in patients without coagulopathy.
- Specific factor replacement if concentrates are available.

10.3.1.4. CRYOPRECIPITATE

Indications:

- Fibrinogen deficiency (e.g., afibrinogenemia, hypofibrinogenemia: <100 mg/dL with active bleeding).
- von Willebrand disease (when specific concentrates are unavailable).
- Factor XIII deficiency.
- DIC
- Haemophilia A patient

Risks:

- Allergic reactions.
- Transmission of infections.
- Volume overload in susceptible patients

Contraindications:

- When specific factor concentrates are available.
- Risk of volume overload in patients with heart failure.

10.3.1.5. SPECIAL BLOOD COMPONENTS

IRRADIATED RED BLOOD CELLS

Preparation

- Blood products should be gamma irradiated between 25Gy to 50 GY
- Shelf life: 28 days
- Blood bank should have a specific policy related to irradiated blood products.
- All irradiated blood products must be labelled appropriately

Indications

- Premature infant of less than 1.2kg
- Hodgkin's lymphoma
- Patients treated with purine analogue
- Patient post bone marrow transplant at risk of GVHD
- Fetus receiving intrauterine transfusion
- Patients with T cell deficiency other HIV

- Stem cell transplant patients
- Umbilical cord blood transplant patients

10.3.1.6. CYTOMEGALOVIRUS (CMV) NEGATIVE BLOOD PRODUCTS

CMV is a common virus that can be dangerous for immunocompromised persons. However, with the universal leucodepletion CMV negative may no longer be required.

Indications

- Neonates up to 28 days
- Low weight babies
- Intrauterine transfusion

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10.4. COAGULATION FOR TRANSFUSION PRACTICE

10.4.1. Prevention of Bleeding

- **Hemostasis**: The process of stopping bleeding, involving vascular constriction, platelet plug formation, and coagulation.
- **Primary Hemostasis**: Platelet adhesion, activation, and aggregation forming a temporary platelet plug.
- **Secondary Hemostasis**: Activation of the coagulation cascade leading to the formation of a stable fibrin clot.

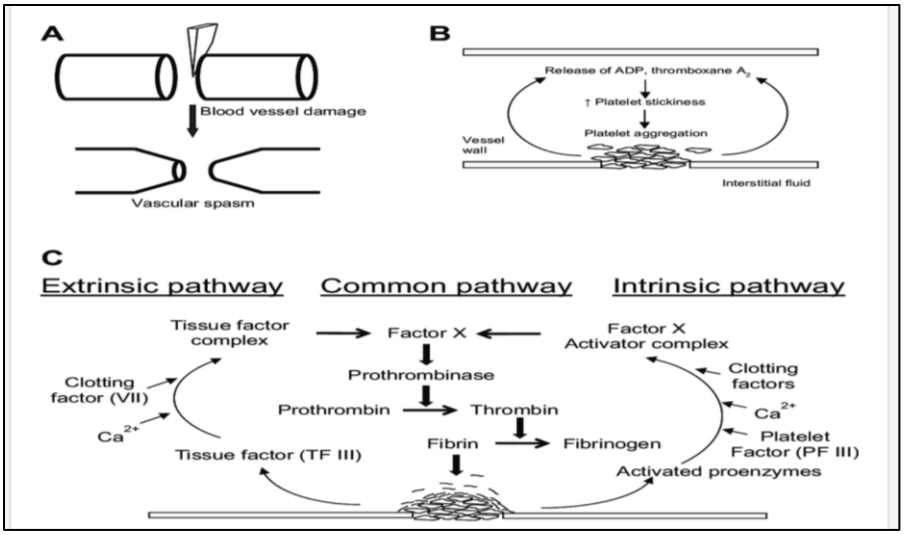

Fig. 9. Diagrammatic representation of the three phases involved in hemostasis.

A: Vascular phase: Endothelial smooth muscle cells contract after injury.
B: platelet phase: Platelets attach to the endothelial surface, exposed collagen, and each other, promoting chemically mediated platelet activation and further platelet aggregation and vascular spasm.
C: coagulation phase: This is a series of complex steps, initiated by intrinsic or extrinsic pathways, leading to the formation of factor X and finally culminating in the production of a fibrin network, which traps blood cells and platelets, resulting in the formation of a blood clot.

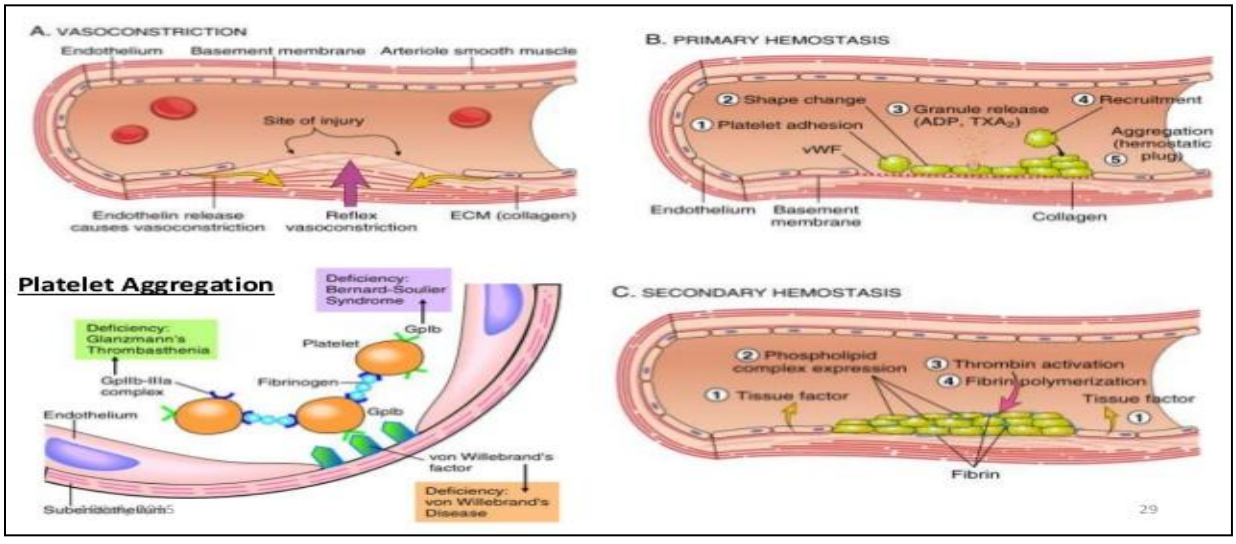

Fig. 10. Schematic representation of phases of hemostasis

10.4.2. Coagulation Cascade

- **Intrinsic Pathway**:

  - Activated by damage to the blood vessel and exposure of collagen.
  - Involves factors XII, XI, IX, VIII.
  - Measured by Activated Partial Thromboplastin Time (aPTT).
- **Extrinsic Pathway**:
  - Activated by external trauma leading to blood exposure to tissue factor (TF).
  - Involves factor VII.
  - Measured by Prothrombin Time (PT).
- **Common Pathway**:
  - Convergence of intrinsic and extrinsic pathways.
  - Involves factors X, V, II (prothrombin), I (fibrinogen), XIII.
  - Results in the conversion of fibrinogen to fibrin, stabilizing the clot.

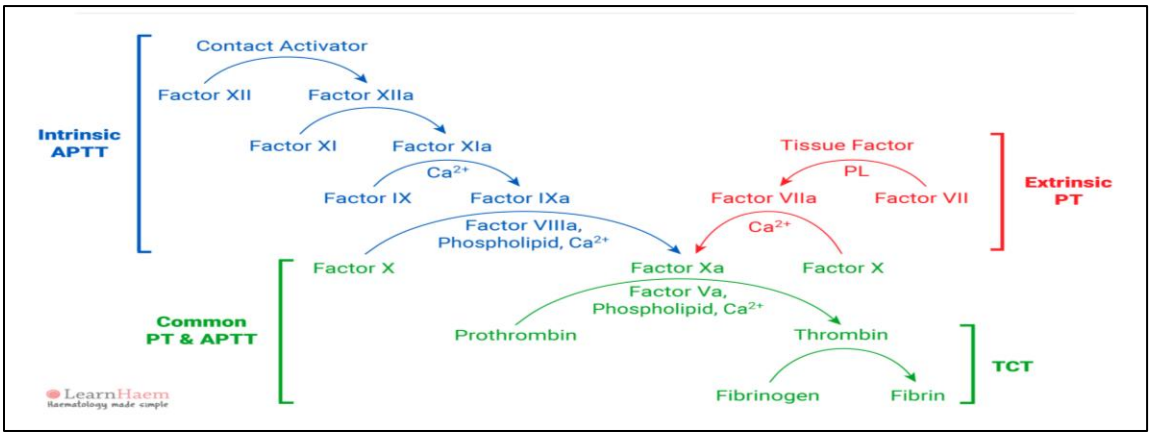

Fig. 11. Coagulation Cascade Diagram

- APTT: this is a reflection of the intrinsic pathway. Isolated prolongations of APTT should prompt considerations of factor VIII, IX, XI or XII deficiency. Of these, factor VIII (haemophilia A) and IX (haemophilia B) deficiencies can cause severe bleeding tendencies depending on the factor levels. Factor XI deficiency (haemophilia C) has a variable phenotype ranging from asymptomatic to severe bleeding. Factor XII deficiency is not associated with a bleeding disorder.
- PT: this is a reflection of the extrinsic pathway. Isolated prolongations of the PT are most often due to factor VII deficiency.
- Common pathway: deficiencies in factors V, X, thrombin and fibrinogen prolong both the APTT and the PT, as they are in the common pathway.
- TCT: this is a measure of the final step in the coagulation pathway, the conversion of fibrinogen to fibrin via the action of thrombin. It is hence sensitive to deficiencies in fibrinogen and drugs such as direct and indirect thrombin inhibitors.

10.4.3. Bleeding Disorders

A. Hemophilia

- **Haemophilia A (Factor VIII Deficiency):**
  - X-linked recessive disorder
  - Spontaneous bleeding into joints (hemarthrosis), muscles, and soft tissues
  - Prolonged bleeding after injuries or surgeries
- **Haemophilia B (Factor IX Deficiency):**
  - Also known as Christmas disease
  - X-linked recessive disorder
  - Similar clinical presentation to Haemophilia A with spontaneous bleeding and prolonged bleeding after trauma
- **Haemophilia C (Factor XI Deficiency):**
  - Autosomal recessive disorder
  - Milder bleeding tendency compared to Haemophilia A and B
  - Common in Ashkenazi Jewish population
  - Bleeding often occurs after surgery or trauma

Lab Investigations:

- **Haemophilia A:**
  - Prolonged activated partial thromboplastin time (aPTT)
  - Normal prothrombin time (PT)
  - Reduced Factor VIII levels
- **Haemophilia B:**
  - Prolonged aPTT
  - Normal PT
  - Reduced Factor IX levels
- **Haemophilia C:**
  - Prolonged aPTT
  - Normal PT
  - Reduced Factor XI levels

Treatment:

- **Haemophilia A and B:**
  - Replacement therapy with recombinant or plasma-derived Factor VIII (Haemophilia A) or Factor IX (Haemophilia B)
  - Desmopressin (DDAVP) for mild Haemophilia A
  - Antifibrinolytic agents (tranexamic acid)
- **Haemophilia C:**
  - Fresh frozen plasma (FFP) or Factor XI concentrates during bleeding episodes or before surgery

Complications:

- Development of inhibitors (antibodies) against Factor VIII or IX
- Joint damage from repeated hemarthrosis
- Increased risk of infections from plasma-derived products

B. Von Willebrand Disease (VWD)

Clinical Presentation:

- Most common inherited bleeding disorder
- Mucocutaneous bleeding (e.g., nosebleeds, gum bleeding)
- Menorrhagia in women
- Prolonged bleeding after injuries or surgeries

Lab Investigations:

- Prolonged bleeding time
- Normal to slightly prolonged aPTT
- Reduced von Willebrand factor (vWF) antigen and activity
- Reduced Factor VIII levels in some cases

Treatment:

- Desmopressin (DDAVP) to release vWF stored in endothelial cells
- vWF-containing Factor VIII concentrates
- Antifibrinolytic agents for mucosal bleeding
- Hormonal therapy for menorrhagia

Complications:

- Excessive bleeding during surgical procedures
- **Disseminated Intravascular Coagulation (DIC)**: Widespread activation of coagulation, leading to bleeding and thrombosis.

C. Disseminated Intravascular Coagulation (DIC)

Clinical Presentation:

- **Acute DIC:**
  - Widespread bleeding (e.g., from gums, venipuncture sites)
  - Organ dysfunction (e.g., renal failure, respiratory distress)
  - Shock in severe cases
- **Chronic DIC:**
  - Milder bleeding tendencies
  - Thrombosis leading to organ ischemia

Lab Investigations:

- Prolonged Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT)
- Low fibrinogen levels
- Elevated D-dimer and fibrin degradation products (FDPs)
- Thrombocytopenia (low platelet count)

Treatment:

- Treat the underlying cause (e.g., infection, malignancy, trauma)
- Supportive care with blood products (platelets, fresh frozen plasma, cryoprecipitate)
- Anticoagulants (heparin) in cases with predominant thrombosis

Complications:

- Severe bleeding leading to hemorrhagic shock

- Microvascular thrombosis causing multiple organ dysfunction syndrome (MODS)

D. Bernard-Soulier Syndrome

Clinical Presentation:

- Autosomal recessive disorder
- Severe mucocutaneous bleeding (e.g., epistaxis, gum bleeding, menorrhagia)
- Presence of large platelets on blood smear (macrothrombocytopenia)

Lab Investigations:

- Prolonged bleeding time
- Normal PT and aPTT
- Reduced platelet aggregation in response to ristocetin
- Flow cytometry showing absence or decreased expression of GPIb-IX-V complex on platelets

Treatment:

- Platelet transfusions during bleeding episodes or before surgical procedures
- Antifibrinolytic agents (e.g., tranexamic acid)
- Recombinant activated Factor VII (rFVIIa) in refractory cases

Complications:

- Increased risk of bleeding during surgeries or trauma
- Possible alloimmunization to transfused platelets

E. Glanzmann Thrombasthenia

Clinical Presentation:

- Autosomal recessive disorder
- Mucocutaneous bleeding (e.g., petechiae, purpura, epistaxis)
- Prolonged bleeding from minor cuts or surgical procedures

Lab Investigations:

- Prolonged bleeding time
- Normal PT and aPTT
- Absent or reduced platelet aggregation in response to all agonists except ristocetin
- Flow cytometry showing absence or decreased expression of GPIIb/IIIa complex on platelets

Treatment:

- Platelet transfusions for severe bleeding episodes or prior to surgery
- Recombinant activated Factor VII (rFVIIa) for acute bleeding episodes
- Antifibrinolytic agents (e.g., tranexamic acid)

Complications:

- Recurrent severe bleeding episodes
- Risk of alloimmunization to transfused platelets

Table 12. Common Coagulation Disorders

Disorder	Deficient Factor(s)	Key Features
Haemophilia A	Factor VIII	X-linked, spontaneous bleeding

Haemophilia B	Factor IX	X-linked, similar to Haemophilia A
Haemophilia C	Factor XI	X- Linked
Berbard soulier sybdrome	Abnormal platelets	Deficiency of the glycoprotein Ib-IX-V complex (GPIb-IX-V),
Glanzamann Thrombasthenia	Abnormal platelets	Deficiency of the platelet integrin alpha IIb beta3.
Von Willebrand Disease	von Willebrand factor	Autosomal, mucocutaneous bleeding
Disseminated Intravascular Coagulation (DIC)	Multiple factors	Thrombosis and bleeding, secondary to other conditions
Liver Disease	Multiple factors	Impaired synthesis due to liver dysfunction
Vitamin K Deficiency	Factors II, VII, IX, X	Dietary deficiency or warfarin use

10.4.4. Coagulation Profile

A coagulation profile is a series of tests used to evaluate the blood's ability to clot properly. It is essential for diagnosing bleeding disorders, monitoring anticoagulant therapy, and assessing patients before surgeries.

A. Full Blood Count (FBC)

Purpose:

- Quantifies platelets and other blood components (red blood cells, white blood cells).

Clinical Relevance:

- **Thrombocytopenia:** Low platelet count indicating potential bleeding disorders, bone marrow diseases, infections, or drug effects.
- **Thrombocytosis:** High platelet count indicating potential clotting disorders, inflammatory conditions, or bone marrow diseases.

B. Peripheral Blood Smear

Purpose:

- Assesses the size, shape, and color of platelets and other blood cells.

Clinical Relevance:

- **Macrothrombocytes:** Large platelets indicative of disorders like Bernard-Soulier syndrome.
- **Hypogranular Platelets:** Indicate conditions like myelodysplastic syndromes.

Bleeding Time

Purpose:

- Assesses platelet function qualitatively.

Clinical Relevance:

- **Prolonged Bleeding Time:** Indicates platelet function disorders such as Von Willebrand disease or Glanzmann thrombasthenia.

C. Prothrombin Time (PT)

Purpose:

- Assesses the extrinsic and common coagulation pathways by measuring the time it takes for blood to clot.

Clinical Relevance:

- **Prolonged PT:** Can indicate liver disease, vitamin K deficiency, or the effects of warfarin therapy.

International Normalized Ratio (INR)

Purpose:

- Standardizes PT results to monitor oral anticoagulant therapy (e.g., warfarin).

Clinical Relevance:

- **High INR:** Indicates increased risk of bleeding.
- **Low INR:** Indicates increased risk of clotting.

D. Activated Partial Thromboplastin Time (aPTT)

Purpose:

- Assesses the intrinsic and common coagulation pathways.

Clinical Relevance:

- **Prolonged aPTT:** Can indicate haemophilia, heparin therapy, or presence of lupus anticoagulant.

E. Fibrinogen Levels

Purpose:

- Measures the quantity of fibrinogen, a key protein in clot formation.

Clinical Relevance:

- **Low Levels:** Indicate DIC, liver disease, or congenital fibrinogen deficiency.
- **High Levels:** May be seen in inflammation, pregnancy, or certain cancers

F. D-dimer

Purpose:

- Indicates fibrin degradation products and is used in diagnosing DIC and thromboembolic disorders.

Clinical Relevance:

- **Elevated Levels:** Can indicate the presence of clot breakdown products, useful in diagnosing conditions like DVT, PE, and DIC

G. Factor Assay

Purpose:

- Quantifies specific coagulation factors (e.g., Factor VIII, IX).

Clinical Relevance:

- Essential for diagnosing specific factor deficiencies such as haemophilia A (Factor VIII deficiency) and haemophilia B (Factor IX deficiency).

H. Bethesda Assay

Purpose:

- Quantifies factor inhibitors.

Clinical Relevance:

- Detects and measures inhibitors in patients with haemophilia, particularly those who develop antibodies against Factor VIII or IX.

I. IVon Willebrand Activity Assay

Purpose:

- Tests for Von Willebrand factor (vWF) antigen, ristocetin cofactor activity, and Factor VIII levels.

Clinical Relevance:

- Diagnoses and characterizes Von Willebrand Disease (VWD), the most common inherited bleeding disorder.

J. Platelet Aggregometry

Purpose:

- Measures the ability of various agonists to induce in vitro platelet activation and platelet-to-platelet aggregation.

Clinical Relevance:

- Diagnoses platelet function disorders like Glanzmann thrombasthenia and Bernard-Soulier syndrome.

Table 13. Coagulation Profile Tests

Test	Pathways Assessed	Normal Range	Clinical Significance
FBC (Full Blood Count)	Quantifies blood cells: red blood cells (RBCs), white blood cells (WBCs), and platelets	• **RBC:** 4.5-6.0 million cells/µL (male), 4.0-5.5 million cells/µL (female) • **WBC:** 4,000-11,000 cells/µL • **Platelets:** 150,000-450,000 cells/µL • **Hemoglobin:** 13.8-17.2 g/dL (male), 12.1-15.1 g/dL (female) • **Hematocrit:** 40.7-50.3% (male), 36.1-44.3% (female)	• **Anemia:** Low RBC, hemoglobin, and hematocrit. • **Leukocytosis:** High WBC count, indicating infection or inflammation. • **Leukopenia:** Low WBC count, indicating bone marrow disorders or autoimmune conditions. • **Thrombocytopenia:** Low platelet count, indicating bleeding disorders. • **Thrombocytosis:** High platelet count, indicating clotting disorders or inflammation
PBS (Peripheral Blood Smear)	Morphology of blood cells: RBCs, WBCs, and platelets.	• **RBC Morphology:** Biconcave, uniform size, and shape. • **WBC Morphology:** Normal differential count with typical appearance. • **Platelet Morphology:** Small, uniformly sized with no clumping	• **Anisocytosis:** Variation in RBC size, seen in anemia. • **Poikilocytosis:** Variation in RBC shape, seen in hemolytic anemia. • **Macrothrombocytes:** Large platelets, indicative of Bernard-Soulier syndrome. • **Hypersegmented Neutrophils:** Seen in megaloblastic anemia
Prothrombin Time (PT)	Extrinsic, Common	11-13.5 seconds	Prolonged in liver disease, warfarin use
Bleeding time			
International Normalized Ratio (INR)	Standardized PT	0.8-1.2	Monitors warfarin therapy

Bleeding time			
International Normalized Ratio (INR)	Standardized PT	0.8-1.2	Monitors warfarin therapy

Activated Partial Thromboplastin Time (aPTT)	Intrinsic, Common	25-35 seconds	Prolonged in haemophilia , heparin therapy
Fibrinogen Levels	Common	200-400 mg/dL	Decreased in DIC, liver disease
Factor assay	Specific coagulation factors (e.g., Factor VIII, IX).	**Factor VIII:** 50-150% of normal activity. **Factor IX:** 50-150% of normal activity	• **Haemophilia A:** Low Factor VIII. • **Haemophilia B:** Low Factor IX. • **Liver Disease:** Decreased levels of multiple coagulation factors
Bethesda assay	measures the activity of inhibitors against specific coagulation factors, particularly Factor VIII. It quantifies the level of inhibitors (antibodies) that neutralize the activity of coagulation factors, which is critical in managing haemophilia	• **<0.6 BU:** No significant inhibitor activity. • **0.6-1.0 BU:** Low-level inhibitor activity. • **>1.0 BU:** Significant inhibitor activity	**Haemophilia A and B:** • **Development of Inhibitors:** Patients with haemophilia, especially those with severe forms, can develop inhibitors against replacement clotting factors (e.g., Factor VIII or IX). The presence of these inhibitors complicates treatment, as standard factor replacement therapies become ineffective. **Management of Haemophilia:**

	patients who develop such inhibitors		• **Inhibitor Surveillance:** Regular monitoring using the Bethesda assay is crucial for haemophilia patients receiving replacement therapy. Detecting inhibitors early allows for adjustments in treatment strategies. • **Treatment Adjustments:** High titer inhibitors (>5 BU) may require bypassing agents such as recombinant activated Factor VII (rFVIIa) or activated prothrombin complex concentrates (aPCC). Low titer inhibitors might be managed with higher doses of factor concentrates or immune tolerance induction therapy. **Non-Haemophilic Acquired Inhibitors:** • **Autoimmune Conditions:** Occasionally, non-haemophilic individuals can develop inhibitors due to autoimmune conditions, malignancies, or postpartum states. The Bethesda assay helps in diagnosing and monitoring these rare conditions

Von willebrand activity assay	Von Willebrand factor (vWF) function and quantity, ristocetin cofactor activity, and Factor VIII levels	• **vWF Antigen:** 50-150% of normal. • **Ristocetin Cofactor Activity:** 50-150% of normal. • **Factor VIII:** 50-150% of normal activity	• **Von Willebrand Disease (VWD):** Low vWF levels or activity. • **Haemophilia A:** Low Factor VIII in some cases of VWD
Platelet aggregometry	Platelet function by measuring aggregation in response to various agonists (e.g., ADP, collagen, ristocetin)	Normal aggregation response to ADP, collagen, and ristocetin	• **Glanzmann Thrombasthenia:** Absent or reduced aggregation with all agonists except ristocetin. • **Bernard-Soulier Syndrome:** Reduced aggregation with ristocetin. • **Aspirin Therapy:** Reduced aggregation with arachidonic acid
D-dimer	Fibrinolysis	<500 ng/mL	Elevated in DIC, thromboembolism

11. MANAGEMENT OF MAJOR HEMORRHAGE AND MASSIVE BLOOD TRANSFUSION:

11.1. Learning Objectives:

- Understand the principles and strategies for managing major hemorrhage.
- Learn about massive blood transfusion protocols.
- Describe procedures in transfusing blood while treating PPH.
- Identify the complications associated with massive hemorrhage and transfusion.

11.2. Major Hemorrhage:

Major hemorrhage is a life-threatening condition characterized by the rapid loss of a significant amount of blood that compromises hemodynamic stability and tissue oxygenation.

Medically major hemorrhage is defined as:

- Loss of more than one blood volume in 24 hours (70ml/kg)
- 50% of total blood volume in 3 hours
- 150ml/minute of blood loss

Causes of major hemorrhage can be obstetric hemorrhage, Trauma, major surgery, or gastrointestinal bleeding.

Obstetric hemorrhage is excessive blood loss during or after childbirth. Severe blood loss after birth is called postpartum hemorrhage (PPH) and is a major cause of maternal mortality.

11.3. Massive Blood Transfusion

Massive blood transfusion (MBTP) is a term used to describe the rapid transfusion of large volumes of blood products. While there's no universally accepted definition, a common guideline for adults is the transfusion of more than 4 units of packed red blood cells (PRBCs) within 1 hour or 10 PRBCs within 24 hours.

For children, definitions of MBT often involve blood transfusion volumes relative to total blood volume (TBV). Some examples include:

- Transfusion of >50% TBV in 3 hours
- Transfusion >100% TBV in 24 hours
- Transfusion support to replace ongoing blood loss of >10% TBV/minute

Definitions that use a 24-hour timeframe may not be as useful during active bleeding. **Dynamic definitions** focusing on the rapid blood transfusion are more practical for day-to-day clinical practice.

11.3.1. Rationale for Massive Blood Transfusion Protocol

In cases of massive bleeding, transfusing fresh whole blood might seem ideal. However, the time needed for safety testing and preparation of whole blood can lead to significant depletion of coagulation factors and platelets. Given that each blood component has specific storage requirements, administering RBCs, coagulation factors, and platelets separately can help maintain the physiological balance of blood and prevent deficiencies in any individual component.

A well-implemented Massive Blood Transfusion Protocol ensures blood components' safe and efficient use. This protocol often involves:

- Rapid assessment of the patient's condition and blood loss
- Calculation of blood product requirements
- Prioritization of blood components based on the patient's needs
- Continuous monitoring of vital signs, coagulation parameters, and electrolyte levels
- Management of potential complications such as transfusion reactions, fluid overload, and disseminated intravascular coagulation (DIC)

11.3.2. When to activate massive transfusion Protocol

A treating Doctor activates MBTP when

- A patient is having massive bleeding, and she/he expects to transfuse the Patient more than 4 units of PRBCs within one hour:
- There is an ongoing Blood loss rate of 150 ml/min.
- 10 RBCs transfused over 24 hours or from the time of ED admission to ICU transfer

Other indications for Transfusion in Major Hemorrhage

- **Red Blood Cells (RBCs)**:
  - Hemoglobin <7 g/dL in stable patients.
  - Hemoglobin <10 g/dL in patients with cardiovascular disease or ongoing bleeding.
- **Fresh Frozen Plasma (FFP)**:
  - INR >1.5 with active bleeding.
  - Replacement of clotting factors during massive transfusion.
- **Platelets**:
  - Platelet count <50,000/μL in the presence of active bleeding.
  - Platelet count <100,000/μL in patients with severe trauma or undergoing major surgery.
- **Cryoprecipitate**:

- Fibrinogen <100 mg/dL with active bleeding.

11.3.3. Quantity of Blood to Transfuse during Massive Transfusion

- Transfuse RBCs to maintain hemoglobin levels around 7-9 g/dL.
- In massive transfusion protocols, use a 4:4:1 ratio for RBCs, FFP, and platelets.
- Adjust based on patient's clinical condition and laboratory results.: See the flowchart below

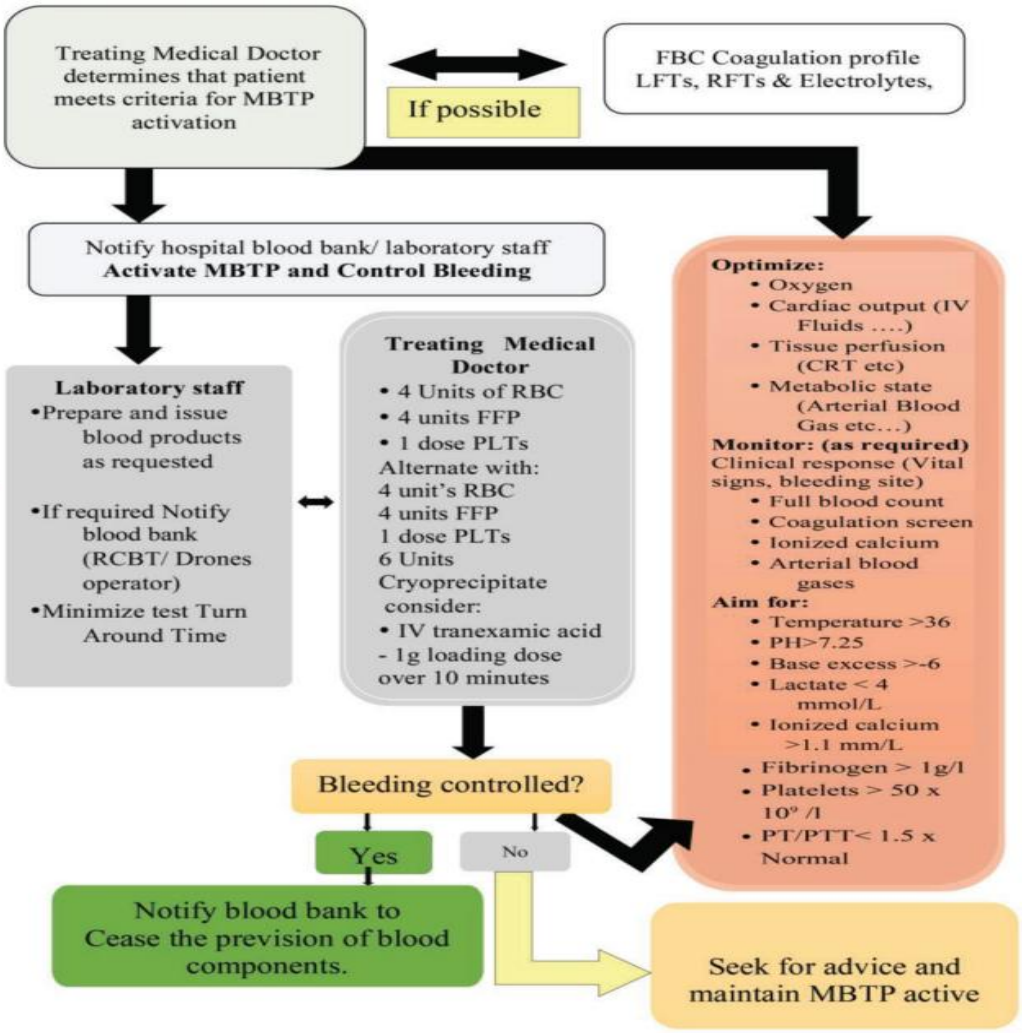

Fig. 1. Massive Blood Transfusion Protocol in Rwanda

Table 1. Indications for blood components

Component	Indication	Threshold
Red Blood Cells	Anemia, ongoing bleeding	Hemoglobin <7-10 g/dL
Fresh Frozen Plasma	Coagulopathy, massive transfusion	INR >1.5
Platelets	Thrombocytopenia with bleeding	Platelet count <50,000/µL
Cryoprecipitate	Hypofibrinogenemia	Fibrinogen <100 mg/dL

11.3.4. Blood transfusion in PPH

In the context of postpartum hemorrhage (PPH), careful consideration of red blood cell (RBC) transfusion is imperative, particularly in distinguishing active and non-active bleeding. In instances of active bleeding during the acute phase of PPH, the timely administration of RBC transfusion is often critical for preserving life. The criteria for transfusion should encompass the estimation of blood loss, evaluation of hemodynamic status and tissue oxygenation levels (e.g., lactate), monitoring of hemoglobin (Hb) and hematocrit (Ht), and prediction of PPH severity (e.g., through fibrinogen measurement). While Hb/Ht levels hold significance, relying solely on these parameters may lead to inaccurate assessments and delayed transfusions. Therefore, additional clinical criteria, particularly hemodynamic aspects, should be considered for comprehensive monitoring. According to the European Society of Anesthesiology, repeated measurements of Hb/Ht, base deficit, and serum lactate are recommended for evaluating tissue perfusion and oxygenation during hemorrhage and resuscitation.

A base deficit within the range of up to -3 is deemed physiological owing to metabolic compensation in pregnancy. Nevertheless, a concurrent rise in the base deficit and serum lactate signifies hypoperfusion often attributable to hypovolemia. In the later stages of PPH, post cessation of bleeding, exclusion of internal blood loss, and confirmation of the patient's hemodynamic stability and compensation, a more conservative approach to RBC transfusion criteria is warranted. Typically, RBC transfusion is indicated when Hb levels fall below 6 g/dL. However, in hemodynamically stable scenarios with an Hb of 8 g/dL or higher, transfusion is seldom necessary. In cases where Hb levels range between 6 and 8 g/dL, the decision to transfuse should be founded upon the clinical situation and the patient's symptoms. Intravenous iron

treatment may serve as a viable alternative to RBC transfusion for expediently elevating Hb levels and alleviating clinical symptoms, particularly when iron stores are depleted.

Blood transfusion is widely recognized as a critical component in the management of postpartum hemorrhage, especially in the presence of substantial blood loss. Nonetheless, the prudent and judicious use of blood transfusions with other appropriate measures is pivotal. The following comprises key considerations for blood transfusion in PPH:

1. **Evaluation of the need for transfusion:** This involves assessing the severity of blood loss using clinical evaluation, Hb/Ht levels, and other laboratory tests. It also involves considering hemodynamic status, tissue oxygenation, and determining the risk for hypovolemic shock or other complications.
2. **Selection of suitable blood products:** Packed red blood cells (PRBCs) are typically the primary blood product used in PPH to replenish lost red blood cells. Fresh frozen plasma (FFP) may be warranted to address coagulation disorders linked to PPH, while platelets may be necessary in the presence of thrombocytopenia or platelet dysfunction.
3. **Rigorous monitoring:** Continuous monitoring of the patient's vital signs, hemoglobin levels, and coagulation parameters, coupled with diligent observation for signs of transfusion reactions such as fever, chills, or respiratory distress.
4. **Contemplation of alternative strategies:** non-blood transfusion strategies, including the administration of uterotonics to induce uterine contraction and control bleeding, manual removal of retained placental fragments, and surgical interventions (e.g., uterine artery ligation, hysterectomy), may prove advantageous in specific scenarios.
5. **Preempting complications:** Recognizing the potential for transfusion-related complications (e.g., TRALI, TACO) and instituting measures to mitigate these risks, such as the warming of blood products, meticulous management of fluid balance, and vigilant monitoring for signs of transfusion reactions, is vital.

Note: It is priority to acknowledge that blood transfusion should not serve as a substitute for addressing the underlying cause of PPH.

11.4. Complications of massive transfusion and their management

Massive transfusion (MT) is a vital intervention for hemorrhagic shock, but it can also be associated with significant complications. The lethal triad of acidosis, hypothermia, and coagulopathy, often seen in MT, is linked to a high mortality rate.

Other complications include:

- **Hypothermia:** Cold blood products can lead to hypothermia, which can impair coagulation and exacerbate acidosis.
    - **Management:** Warming all IV fluids (not more than 40- degrees Celsius) and by the use of forced air convection warming blankets to reduce radiant heat loss
- **Dilutional coagulopathy**: loss, consumption, or dilution of coagulation factors and occurs when blood is replaced with fluids that do not contain adequate coagulation factors.
    - **Management**: Fresh frozen plasma, platelet concentrate, and cryoprecipitate are considered the mainstay hemostatic therapies
- **Acid-base derangements:** Hemorrhagic shock and massive transfusion can lead to metabolic acidosis or respiratory acidosis.
    - **Management:** adequate fluid resuscitation and correction of electrolyte abnormalities
- **Electrolyte abnormalities:** Hypocalcemia, hypomagnesemia, hypokalemia, and hyperkalemia can occur due to blood loss, transfusion, and the use of citrate anticoagulants.
    - **Management:**
        - **Hypocalcemia:** Slow IV injection of calcium gluconate 10% (5ml) over 10 minutes
        - **Hypomagnesaemia**: IV magnesium 2g in 1 hour
        - **Hyperkalemia**: Potassium shifting
        - **Hypokalemia:** IV KCL 40meq in one hour and then reassess
- **Citrate toxicity:** Excessive citrate administration can lead to hypocalcemia and metabolic alkalosis.
    - **Management:**
        - treat life-threatening hypocalcemia with IV calcium (either calcium gluconate or chloride)
        - optimize cardiac output and liver function to enhance citrate clearance.
        - consider RRT to correct metabolic derangement and enhance citrate clearance.

- **Disseminated Intravascular Coagulation (DIC)**: A condition characterized by widespread activation of the coagulation cascade, leading to the formation of blood clots in small vessels and subsequent bleeding.
    - **Management**
        - Treat the underlying cause.
        - Supportive care with blood products as needed (FFP, platelets, cryoprecipitate).
- **Transfusion-Associated Circulatory Overload (TACO):** A condition caused by volume overload due to transfusion, leading to pulmonary edema and heart failure.
    - **Management**:
        - Slow the rate of transfusion.
        - Administer diuretics.
        - Provide supportive care with oxygen.
- **Transfusion-Related Acute Lung Injury (TRALI)**: A rare but serious reaction characterized by acute lung injury within 6 hours of transfusion.
    - **Management**:
        - Immediate cessation of transfusion.
        - Supportive care with oxygen and mechanical ventilation if needed.

Table 2. Differentiation of TACO and TRALI

Feature	**TACO**	**TRALI**
Cause	Volume overload	Donor antibodies
Onset	Within 6 hours of transfusion	Within 6 hours of transfusion
Symptoms	Dyspnea, orthopnea, hypertension	Acute respiratory distress, hypoxia
Chest X-ray Findings	Pulmonary edema	Bilateral pulmonary infiltrates
Management	Slow transfusion, diuretics, oxygen	Stop transfusion, supportive care

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1. AABB (Association for the Advancement of Blood & Biotherapies). Technical Manual.
2. World Health Organization. Guidelines on Blood Transfusion.
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12. TRANSFUSION PRACTICE IN SPECIAL CONDITIONS

12.1. Learning objectives

1. Understand special conditions requiring special consideration during blood transfusion
2. Understand indications of blood transfusion related to special conditions
3. Identify blood type components used in special conditions
4. Understand transfusion protocols specific to special conditions

12.2. Transfusion practice

Certain patient groups have special requirements regarding the selection of blood and components for transfusion. Clinical teams should be made aware of these requirements through the use of guidelines supported by education. Appropriate alerts for special requirements should be used within the transfusion laboratory. Serious Hazards of Transfusion (SHOT) hemovigilance has highlighted the relative frequency of errors in this area of transfusion practice.

12.2.1. Transfusion Practice in Oncology

Indications for Transfusion in Oncology
***Anaemia*:** Common in oncology patients due to chemotherapy, radiation, and the cancer itself.

Blood transfusion should be initiated if:

- Hemoglobin <7 g/dL in asymptomatic patients.
- Hemoglobin 7-10 g/dL in symptomatic patients (e.g., dyspnea, fatigue, chest pain).

***Thrombocytopenia*:** Caused by bone marrow suppression from chemotherapy.

Blood transfusion (platelets) should be initiated if:

- Platelet count <10,000/µL to prevent spontaneous bleeding.
- Platelet count <20,000/µL if bleeding, high grade fever
- Platelets count <50,000 uL prior to an invasive procedure

***Coagulopathy*:** Resulting from liver involvement by cancer or disseminated intravascular coagulation (DIC).
Blood transfusion should be initiated if:

- Prolonged PT/INR and / or aPTT or reduced Fibrinogen with active bleeding or before invasive procedures.

Neutropenia: Severe cases may require transfusion support with granulocyte transfusions.

Blood transfusion (Granulocytes) should be initiated if:

- Severe infections unresponsive to antibiotics in neutropenic patients.

TYPES OF BLOOD COMPONENTS

Red Blood Cells (RBCs)

- **Indications**: Anemia due to chemotherapy, radiation, or the cancer itself.
- **Administration**: Typically given to maintain hemoglobin levels >7-8 g/dL or higher if symptomatic.

Platelets

- **Indications**: Thrombocytopenia due to bone marrow suppression.
- **Administration**: Single donor platelets or pooled platelets, depending on the patient's need.

Fresh Frozen Plasma (FFP)

- **Indications**: Coagulopathy with active bleeding or before invasive procedures.
- **Administration**: Given to correct deficiencies in coagulation factors.

Cryoprecipitate

- **Indications**: Hypofibrinogenemia or factor XIII deficiency.
- **Administration**: Provides fibrinogen and factor XIII in concentrated form.

Granulocytes

- **Indications**: Severe neutropenia with infections not responding to antibiotics.
    - **Administration**: Typically reserved for patients with severe infections and neutropenia.

12.2.1.1. Transfusion Protocols in Oncology

Pre-transfusion Testing:

- ABO and Rh typing.
- Crossmatching for RBC transfusions.
- Antibody screening.

Transfusion Reactions:

- Monitoring for signs of transfusion reactions (e.g., fever, chills, rash, dyspnea).
- Pre-medication with antihistamines or corticosteroids in patients with a history of reactions.

Documentation and Monitoring:

- Documentation of transfusion indications, type of blood product, and patient response.
- Regular monitoring of blood counts and coagulation parameters.

Table 14. Summary of Blood Components and Indications in Oncology

Blood Component	Indications	Administration
Red Blood Cells (RBCs)	Anemia due to chemotherapy, radiation, or cancer	Maintain hemoglobin >7-8 g/dL or higher if symptomatic
Platelets	Thrombocytopenia due to bone marrow suppression	Single donor or pooled platelets, depending on need
Fresh Frozen Plasma (FFP)	Coagulopathy with active bleeding or before invasive procedures	Correct deficiencies in coagulation factors
Cryoprecipitate	Hypofibrinogenemia, factor XIII deficiency	Provides fibrinogen and factor XIII in concentrated form
Granulocytes	Severe neutropenia with infections not responding to antibiotics	Reserved for severe infections and neutropenia

References

1. AABB (Association for the Advancement of Blood & Biotherapies). Technical Manual.
2. World Health Organization. Guidelines on Blood Transfusion.
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12.2.2. Transfusion Practice in Hemoglobinopathies:

12.2.2.1. Hemoglobinopathies Overview

Sickle cell disease (SCD) and thalassemia are complex hemoglobinopathies. Although they are grouped here together, their clinical manifestations and treatment modalities are different. Red blood cell (RBC) transfusion is a cornerstone for the management of patients with SCD and thalassemia. Transfusion in SCD patients can be for acute indications where transfusion can be life-saving, or for regular long-term therapy. These indications range from those in which transfusion is strongly recommended to those where it is unproven or controversial, and therefore requiring individualized decision.

Sickle Cell Disease (SCD):

- Genetic disorder caused by a mutation in the beta-globin gene leading to the production of abnormal hemoglobin S (HbS).
- Symptoms: Chronic anemia, pain crises, acute chest syndrome, stroke.

Thalassemia:

- Alpha Thalassemia: Deletion or mutation in alpha-globin genes.

- Beta Thalassemia: Mutation in beta-globin genes resulting in reduced or absent beta-globin production.
- Symptoms: Severe anemia, growth retardation, skeletal deformities, organ damage.

A. General Comments to Consider in Hemoglobinopathies

- An extended RBC phenotype should be performed for all patients with SCD and thalassemia using a pre-transfusion specimen. This ideally should be performed in the first year of life before the start of a regular transfusion program.
- If the patient has been recently transfused, DNA-based methods can be used to determine the predicted phenotype.
- A full cross-match and antibody screen of new antibodies should be performed before each transfusion. In centers that meet regulatory requirements, an electronic cross match can be performed.
- Every patient should have a complete record of antigen typing, antibodies, and transfusion reactions.
- Components provided need to be phenotype matched based on existing guidelines and recommendations.
- If allo-antibodies (s) are identified, RBCs used for transfusion should be negative for the corresponding antigen(s) and cross match compatible.
- RBC units for patients with SCD should be sickle test negative.
- It is recommended to provide fresh units (less than 7-14 days old) if possible, for SCD and thalassemia patients, as fresher units may reduce frequency of transfusion.
- Before first transfusion, a course of hepatitis B vaccination should be started and completed if possible. Serologic testing for hepatitis A, B, C and HIV should be performed as baseline measures, and all patients who do not have serologic immunity to hepatitis B virus should start a vaccination program and show evidence of immunity before the start of the transfusion.
- Cytomegalovirus negative components are recommended for potential candidates for stem cell transplantation.
- Chronic transfusion is associated with the risk of iron overload and related complications including cardiac, hepatic and endocrine. This necessitates monitoring of iron overload and appropriate chelation therapy initiated.

B. General Indications for Transfusion In Hemoglobinopathies

Chronic anemia:

- Regular transfusions to maintain hemoglobin levels and prevent complications.

Acute anemia:

- Acute episodes of severe anemia due to hemolysis or sequestration crisis.

Prevention of complications:

- Stroke prevention in SCD.
- Prevention of complications during surgery.

Acute complications:

- Acute chest syndrome.
- Severe vaso-occlusive crisis.

Indications of Transfusion in sickle cell disease

Chronic Transfusion:

- Stroke prevention in children with abnormal transcranial Doppler ultrasound.

- **Acute Transfusion**:
  - Acute chest syndrome.
  - Severe anemia.
  - Major surgery requiring anesthesia.
  - **Splenic and hepatic sequestration**
  - **Severe SCD crisis**
  - **Severe sepsis**
  - **Acute Priapism**

Indication for blood transfusion in Thalassemia:

"Transfusion-dependent thalassemia, TDT" who require regular transfusion from infancy to sustain life and suppress ineffective erythropoiesis, and "non-transfusion dependent thalassemia, NTDT" who have moderate haemolytic anaemia but maintaining a haemoglobin (Hb) level that is sufficient for growth and development without transfusion support.

- **Regular Transfusions**:
  - Thalassemia major to maintain pre-transfusion hemoglobin levels around 9-10 g/dL.
- **Occasional Transfusions**:
  - Thalassemia intermedia during periods of rapid growth, infection, or other stressors.

BLOOD COMPONENTS USED

Red Blood Cells (RBCs):

- **Indications**:
  - Chronic transfusion therapy in thalassemia major to maintain hemoglobin levels.
  - Acute transfusion for severe anemia in SCD.
- **Administration**:
  - Typically transfused to maintain hemoglobin >7-8 g/dL or higher if symptomatic.

Platelets:

- **Indications**:
  - Thrombocytopenia due to bone marrow suppression.
  - Bleeding disorders associated with hemoglobinopathies.
- **Administration**:
  - Single donor or pooled platelets as needed.

Fresh Frozen Plasma (FFP):

- **Indications**:
  - Coagulopathy with active bleeding.
  - Preparation for surgery or invasive procedures.
- **Administration**:
  - Corrects deficiencies in coagulation factors.

Cryoprecipitate:

- **Indications**:
  - Hypofibrinogenemia.
  - Factor XIII deficiency.
- **Administration**:
  - Provides fibrinogen and factor XIII in concentrated form.

- **Exchange Transfusion**:
  - **Indications**:
    - Acute chest syndrome.
    - Stroke prevention and management.
    - Severe vaso-occlusive crises.
  - **Administration**:
    - Reduces the proportion of sickle cells and prevents complications.

Table 15. Summary of Blood Components and Indications in Hemoglobinopathies

Blood Component	Indications	Administration
Red Blood Cells (RBCs)	Chronic anemia, acute anemia, surgery preparation	Maintain hemoglobin >7-8 g/dL or higher if symptomatic
Platelets	Thrombocytopenia, bleeding disorders	Single donor or pooled platelets, depending on need
Fresh Frozen Plasma (FFP)	Coagulopathy with active bleeding or before invasive procedures	Correct deficiencies in coagulation factors
Cryoprecipitate	Hypofibrinogenemia, factor XIII deficiency	Provides fibrinogen and factor XIII in concentrated form
Exchange Transfusion	Acute chest syndrome, stroke prevention, severe vaso-occlusive crises	Reduce sickle cell proportion, prevent complications

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13. BLOOD TRANSFUSION ALTERNATIVES

13.1. Learning Objectives

1. Understand the concept of transfusion alternatives and exemplary stewardship in the management of blood and blood products.
2. Identify available alternatives to blood transfusion and their indications in clinical practice.
3. Explore the concept of bloodless surgeries and their role in minimizing blood transfusion requirements.
4. Discuss the ethical and legal implications of refusal of blood transfusion, including considerations related to patient beliefs and autonomy.
5. Recognize the ethical dilemmas faced by healthcare professionals when patients refuse blood transfusions and strategies for addressing them.

13.2. Available Alternatives:

- **Volume expander:** Administration of crystalloid, colloid solutions to replace volume loss in cases of hemorrhage.
- **Pharmacological Agents**: Use of medications such as erythropoietin, iron supplements, to manage anemia or promote hemostasis, Vitamins vit. B12 and folate Recombinant Erythropoietin agents
- **Cell Salvage:** Collection and reinfusion of a patient's own blood lost during surgery or trauma.

Blood substitutes are developed to mimic the functions of biological blood, particularly in oxygen delivery, with the aim of addressing limitations in blood supply and transfusion safety. Despite progress, no artificial blood has yet fully replaced normal blood, and many products remain experimental

13.3. Types of Artificial Blood

- **Haemoglobin-Based Oxygen Carriers (HBOC)**
  - **Description**: Derived from purified haemoglobin from human or animal sources.
  - **Function**: HBOCs are designed to carry and release oxygen similar to normal haemoglobin, circulating in the bloodstream and delivering oxygen to tissues.
  - **Risks**: Potential for kidney injury and hypertension
- **Perfluorocarbon Emulsions (PFC)**
  - **Description**: Synthetic compounds capable of dissolving large amounts of gases, including oxygen and carbon dioxide.

- **Function**: PFCs carry oxygen through emulsification, releasing it to tissues.
- **Risks**: PFCs need to be properly emulsified for efficacy, and their effectiveness can be limited.

- **Stem Cell-Derived Red Blood Cells**

  - **Description**: Researchers are exploring the use of stem cells to produce red blood cells in the laboratory.
  - **Function**: These lab-grown red blood cells aim to replicate the oxygen-carrying capacity of natural red blood cells.

Advantages of Artificial Blood

1. **Universal Compatibility**
   - **Description**: Artificial blood can potentially be used across different blood types, eliminating the need for blood type matching.
2. **Disease-Free**
   - **Description**: Being synthetic or lab-produced, artificial blood eliminates the risk of blood-borne diseases.
3. **Longer Shelf Life**
   - **Description**: Artificial blood products can often be stored for longer periods than donated human blood, reducing waste and improving supply management.
4. **Immediate Availability**
   - **Description**: Artificial blood can be readily available in emergency situations, without the delays associated with blood donor availability.

13.4. Experimental Status and Challenges

1. **HBOCs**
   - Despite promising functions, HBOCs have encountered issues with side effects such as kidney injury and hypertension, leading to cautious progress in their development.
2. **PFCs**
   - PFC emulsions have shown potential in carrying and delivering oxygen, but their need for proper emulsification and limited efficacy have been significant challenges.
3. **Stem Cell-Derived Red Blood Cells**
   - Research is ongoing to produce functional red blood cells from stem cells. While this technology holds promise for a consistent and safe blood supply, it is still in experimental stages.

While artificial blood products offer promising alternatives to traditional blood transfusions, they are not yet fully capable of replacing natural blood. Continuous research and development are needed to overcome the current limitations and bring these technologies to clinical application.

Surgical techniques:

1. Minimally Invasive Procedures: such as laparoscopy or robotic surgery
2. Interventional radiology techniques for controlling bleeding or managing vascular anomalies without open surgery.
3. **Hemostatic Agents:** Application of topical agents, such as fibrin sealants and hemostatic sponges, to control bleeding.

- Autologous blood donation: This can be done in preoperative or in perioperative

Indications of Alternatives:

- Alternatives to blood transfusion may be indicated in patients with religious objections (Jehovah witnesses), alloimmunization, or medical conditions that contraindicate blood transfusion
- They may also be used in elective surgeries or procedures to minimize transfusion requirements and reduce the risk of transfusion-related complications.

Bloodless Surgeries:

- Bloodless surgeries, also known as blood conservation surgeries, are procedures performed without the use of donor blood transfusion.
- Techniques include preoperative optimization of hemoglobin levels, intraoperative hemostasis, and meticulous surgical techniques to minimize blood loss.

Surgical techniques:

1. Minimally Invasive Procedures: such as laparoscopy or robotic surgery
2. Interventional radiology techniques for controlling bleeding or managing vascular anomalies without open surgery.
3. Hemostatic Agents: Application of topical agents, such as fibrin sealants and hemostatic sponges, to control bleeding.

Refusal of Blood Transfusion:

- Some patients, based on religious beliefs (e.g., Jehovah's Witnesses) or personal preferences, may refuse blood transfusion.
- Healthcare professionals must respect patients' autonomy and provide alternative treatment options while ensuring patient safety.

Legal Implications & Beliefs on Refusal of Blood:

- Refusal of blood transfusion may raise legal and ethical considerations, particularly in cases involving minors or patients lacking decision-making capacity.
- Healthcare professionals should be aware of legal frameworks and guidelines governing patient refusal of medical treatment, including blood transfusion.
- Patient should sign the refusal of medical treatment

Ethical Dilemma vs. Blood Transfusion Refusal:

- Healthcare professionals may face ethical dilemmas when patients refuse blood transfusions, balancing respect for patient autonomy with concerns for patient safety.
- Strategies for addressing ethical dilemmas include patient education, shared decision-making, and involvement of ethics committees or consultation services.
- Talk about risks/benefits of blood transfusion

13.5. FRACTIONATED PLASMA PRODUCTS (FPPS)

Fractionated plasma products are therapeutic proteins extracted and purified from human plasma. These products are derived through a process called fractionation, which separates the plasma into its various components.

Types of FPPs:

- **Albumin**: Used for volume expansion and in hypoalbuminemia.
- **Immunoglobulins**: Used for immune deficiencies and autoimmune diseases.
- **Clotting Factors**: Factor VIII, Factor IX, used for haemophilia treatment.
- **Fibrinogen Concentrates**: Used for bleeding disorders.
- **Antithrombin**: Used for hereditary antithrombin deficiency.
- **C1 Esterase Inhibitor**: Used for hereditary angioedema.

Understanding Alternatives and Uses of FPPs

Alternatives to FPPs:

- **Recombinant Products**: Synthetic versions of plasma proteins produced using recombinant DNA technology.
- **Synthetic Volume Expanders**: Such as hydroxyethyl starch, used instead of albumin.
- **Direct Oral Anticoagulants (DOACs)**: Used in place of some clotting factors for specific indications.

Uses of FPPs:

Albumin:

- Volume expansion in shock and burns.
- Treatment of hypoalbuminemia in liver disease.

Immunoglobulins:

- Primary immune deficiency syndromes.
- Autoimmune disorders (e.g., ITP, Guillain-Barré syndrome).

Clotting Factors:

- Haemophilia A (Factor VIII deficiency).
- Haemophilia B (Factor IX deficiency).

Fibrinogen Concentrates:

- Congenital fibrinogen deficiency.
- Massive bleeding and trauma.

Antithrombin:

- Prevention of thrombosis in patients with hereditary antithrombin deficiency.

C1 Esterase Inhibitor:

- Acute attacks of hereditary angioedema.

Table 16. Common Fractionated Plasma Products and their uses

Product	**Indications**
Albumin	Volume expansion, hypoalbuminemia
Immunoglobulins	Immune deficiencies, autoimmune diseases
Factor VIII	Haemophilia A
Factor IX	Haemophilia B
Fibrinogen Concentrates	Bleeding disorders, congenital fibrinogen deficiency
Antithrombin	Hereditary antithrombin deficiency
C1 Esterase Inhibitor	Hereditary angioedema

13.6. Economic Impact and Sustainability

Economic Impact:

- **Cost-Effectiveness**: FPPs can be cost-effective in treating specific conditions, reducing hospital stays, and preventing complications.
- **Health Economics**: The use of FPPs can lead to significant healthcare savings by reducing the need for more expensive treatments or extended hospitalizations.

Sustainability:

- **Supply Chain Management**: Effective supply chain management ensures the availability and affordability of FPPs.
- **Blood Transfusion Systems**: FPPs contribute to the sustainability of blood transfusion systems by optimizing the use of donated plasma and providing critical therapies.
- **Regulation and Quality Control**: Ensuring high standards in the production and distribution of FPPs is crucial for safety and efficacy.

Diagram: Economic Impact of FPPs

Table 17. Economic Benefits of FPPs

Aspect	Benefit
Cost-Effectiveness	Reduces overall treatment costs
Prevention of Complications	Decreases the need for expensive interventions
Reduced Hospital Stays	Lowers hospital admission and length of stay
Optimized Use of Plasma	Enhances the utility of donated plasma

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14. COMPLICATIONS OF BLOOD TRANSFUSION

14.1. Learning objectives:

1. Understand the common complications associated with blood transfusion.
2. Identify various adverse transfusion reactions.
3. Learn strategies for preventing transfusion complications.
4. Understand the importance of patient education in the context of transfusion
5. Learn about reporting and monitoring systems for transfusion-related complications.

14.2. Blood transfusion complications

An adverse transfusion reaction is an unexpected or unintended effect resulting from blood transfusion. Often patients who receive blood transfusion experience no adverse reaction However minor to severe complication do occasionally occur and need prompt action.

Healthcare providers should be trained to recognize and respond promptly to suspected BTRs. Immediate actions may include stopping the transfusion, assessing the patient's vital signs, administering supportive care, and notifying appropriate personnel.

Comprehensive documentation of the transfusion process, including patient information, blood product details, and transfusion reactions, is essential for tracking and investigating BTRs. Timely reporting of BTRs to transfusion services, regulatory agencies, and other relevant stakeholders is necessary for monitoring and improving transfusion safety.

Root cause analysis (RCA) is a systematic process used to identify underlying causes and contributing factors of adverse events, including BTRs. RCA aims to identify opportunities for process improvement and prevent future occurrences of BTRs.

The complications of blood transfusion can be conveniently divided into acute and delayed immunological and non-immunological categories.

Adverse Transfusion Reactions classification (Adjusted to acute and delayed)

1. Immune-Mediated Reactions:

Acute:

- Acute hemolytic reaction.
- Febrile non-hemolytic reaction.
- Allergic reaction.

- Anaphylactic reaction.
- TRALI.

Delayed

- Delayed hemolytic reaction.
- Transfusion associated graft versus host disease
- Post transfusion Purpura
- Alloimmunization

2. Non-Immune-Mediated Reactions:

Acute

- TACO.
- Transfusion related sepsis
- Non immune hemolysis

Delayed

- Iron overload

Table 18. Types and management of Adverse Transfusion Reactions

Reaction Type	Cause	Symptoms	Management
Acute Immune Medicated reactions<24 hours			
Acute Hemolytic Transfusion Reaction	ABO incompatibility	Fever, chills, back pain, dark urine	Stop transfusion, IV fluids, supportive care
Febrile Non-Hemolytic Transfusion Reaction	Cytokines, leukocyte antibodies	Fever, chills	Stop transfusion, antipyretics
Allergic Reaction	Plasma protein antibodies	Urticaria, itching	Stop transfusion, antihistamines, corticosteroids (severe)
Anaphylactic Reaction	Severe allergic reaction	Hypotension, angioedema, respiratory distress	Stop transfusion, epinephrine, corticosteroids
TRALI	Donor anti-leukocyte antibodies	Acute respiratory distress, hypoxia	Stop transfusion, oxygen therapy, ventilation if need
Delayed Immune Medicated Reactions > 24 hours			
Delayed Hemolytic Transfusion Reaction	Alloantibodies	Mild fever, jaundice, decreased hemoglobin	Monitor hemoglobin, supportive care

Reaction Type	Cause	Symptoms	Management
Transfusion associated graft versus host disease	Engraftment and multiplication of donor lymphocytes in the recipient leading to host tissue destruction	Rash, watery diarrhoea, fever, anorexia, vomiting, abnormal liver function tests, bone marrow failure	Corticosteroids; cytotoxic agents; irradiation of cellular blood components
Post transfusion Purpura	Antibodies against platelet specific antigens	Thrombocytopenia, purpura, bleeding	Steroids; IVIG; plasmapheresis; avoid platelets
Alloimmunization	Immune response to red cells, platelets, leukocytes antigens	Haemolytic disease of fetus and newborn, delayed serologic	Rational use of blood components; leukofiltered blood

		reaction, platelet refractoriness	
Acute Non-Immune Mediated Reactions <24 hours			
TACO	Volume overload	Dyspnea, hypertension, pulmonary edema	Stop transfusion, diuretics, oxygen
Septic Transfusion Reaction	Bacterial contamination	High fever, chills, hypotension, septic shock	Stop transfusion, antibiotics, supportive care
Non immune hemolysis	Physical/mechanical/ chemical destruction of blood (in vitro haemolysis)	Features of intravascular haemolysis of red cells, namely, haemoglobinuria, haemoglobinemia	Symptomatic treatment
Delayed Non-Immune Mediated Reactions > 24 hours			
Iron overload	Iron deposition in a multi-transfused patient	Diabetes, Cardiomyopathy, Cirrhosis	Iron chelating agents

14.3. Reporting and Monitoring

1. **Reporting Systems:**

- Immediate reporting of adverse reactions to the transfusion service and treating physician.
- Completing an adverse reaction report form.

2. **Monitoring:**

- Pre-Transfusion: Baseline vital signs and patient assessment.
- During Transfusion: Regular monitoring of vital signs and patient status.
- Post-Transfusion: Continued monitoring for delayed reactions, follow-up tests as needed.

Post- transfusion reaction investigations:

- ABO blood grouping and cross-match (pre and post transfusion sample)
- Direct Antiglobulin Test (DAT) and IAT (indirect antiglobulin test)
- Liver and Renal Function tests
- Complete blood count (CBC) and coagulation profile.
- Blood cultures for suspected septic reactions.
- Chest X-ray for TRALI and TACO.

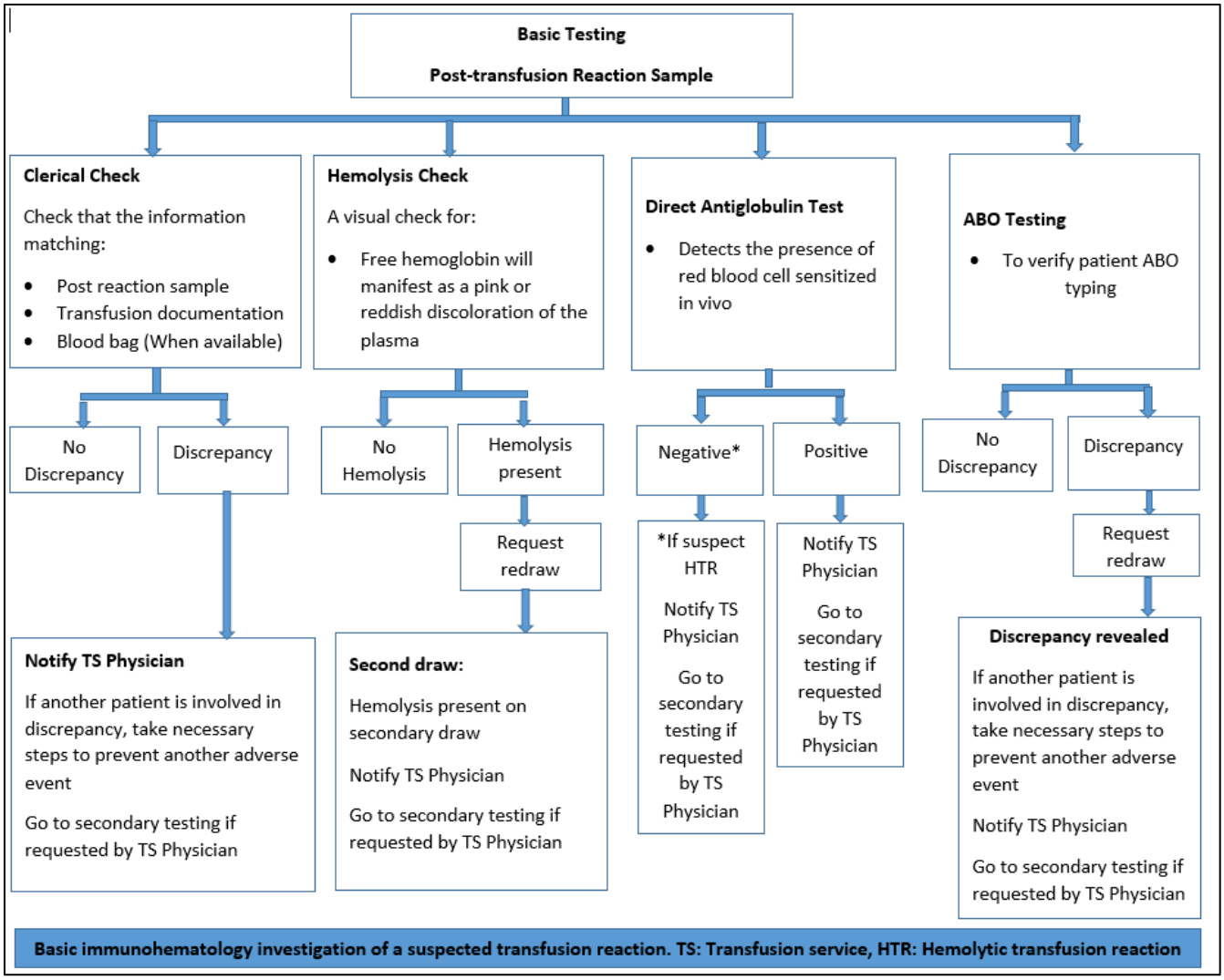

Fig. 12. Basic immunohematology investigation of a suspected transfusion reaction

Reporting and Documentation:

- Document all reactions in the patient's medical record.
- Report to the blood bank and relevant regulatory authorities.
- Conduct a root cause analysis to prevent future occurrences.

Way Forward

- **Education and Training**: Regular training for healthcare providers on the identification and management of transfusion reactions.
- **Improved Screening and Testing**: Enhanced blood screening techniques to reduce the risk of transfusion-transmitted infections.
- **Patient Monitoring**: Close monitoring of patients during and after transfusions.

- **Research and Development**: Ongoing research to develop safer blood products and transfusion practices.

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15. TRANSFUSION TRANSMISSIBLE INFECTIONS :

15.1. Learning objectives:

1. Understand the significance of transfusion-transmissible infectious diseases (TTIs) in blood transfusion.
2. Identify common TTIs and their impact on blood safety and public health.
3. Explore screening and testing protocols for TTIs, including testing technologies (Serology testing and NAT) and donor notification procedures.
4. Discuss legal and ethical considerations related to TTIs in blood transfusion.
5. Recognize emerging threats in the field of TTIs and strategies for addressing them.

15.2. Transfusion-transmissible infectious diseases

Transfusion-transmissible infectious diseases (TTIs) are infections that can be transmitted through blood transfusion. A myriad of agent can potentially be transmitted through blood transfusion, including bacteria, viruses, fungi and parasites. Of these, bacteria are the most commonly transmitted.

These diseases pose a risk to both blood donors and recipients and can have severe consequences if not properly managed.

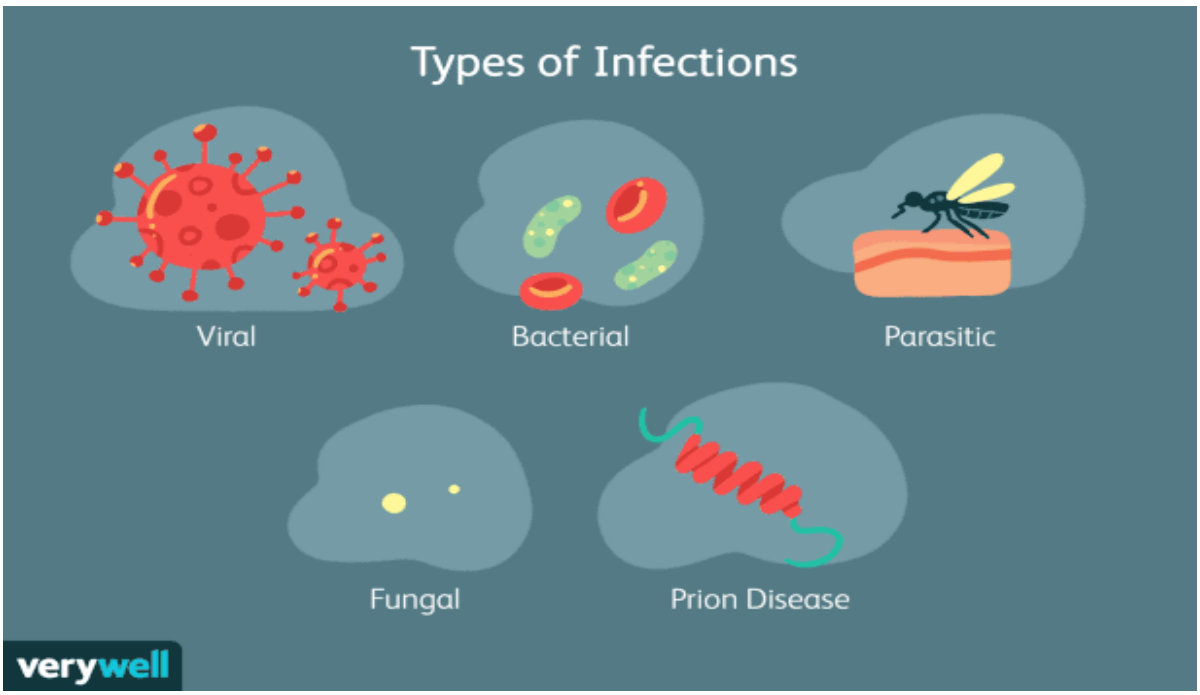

Fig. 13. Common TTIs

15.3. Common Transfusion-Transmissible Infectious Diseases:

Even if multiple TTIs can be transmitted through blood transfusion, below are the most common TTIs that are screened in all blood donors in Rwanda

1. **HIV/AIDS:**
   - Caused by the Human Immunodeficiency Virus (HIV), which attacks the immune system.
   - Transmitted through exposure to infected blood, sexual contact, or vertical transmission from mother to child during childbirth or breastfeeding.
   - Prevalence varies by region, with sub-Saharan Africa being disproportionately affected.

2. **Hepatitis B and C:**
   - Hepatitis B and C viruses (HBV and HCV) primarily affect the liver and can lead to chronic infection, cirrhosis, and liver cancer.
   - Transmitted through exposure to infected blood, contaminated needles, or sexual contact.
   - Chronic hepatitis B and C infections are major contributors to liver disease burden worldwide.

3. **Syphilis:**
   - A bacterial infection caused by Treponema pallidum.
   - Transmitted through sexual contact or exposure to infected blood.
   - Can progress through several stages if left untreated, leading to serious complications such as neurological damage and cardiovascular disease.

4. **Malaria:**
   - A parasitic infection caused by Plasmodium species.
   - Transmitted through the bite of infected mosquitoes or, less commonly, through blood transfusion.
   - Common in regions with high malaria transmission rates, particularly sub-Saharan Africa.

Screening and Testing Protocols:

- Donor screening and testing protocols are crucial for preventing the transmission of TTIs.
- Screening tests typically include serological assays for detecting antibodies or antigens associated with specific infectious agents (such as HIV, hepatitis B and C, syphilis).
- Nucleic acid testing (NAT) is increasingly used to detect viral nucleic acids in donated blood, enhancing the sensitivity of screening protocols.

- Screening algorithms and criteria for donor eligibility are established based on the prevalence of TTIs in specific populations.

Testing technologies:

- **Enzyme-linked immunosorbent assay (ELISA**) is commonly used for screening blood donors for infectious diseases.
- **Polymerase chain reaction (PCR)** is used for nucleic acid testing to detect viral DNA or RNA in donated blood.
- **Rapid diagnostic tests (RDTs)** are also used in some settings for quick screening of infectious diseases.
- **For vulnerable population such as Immunosuppressed patient, Newborns, additional precautions technologies (Leucocyte-reduction, Irradiation of blood components) should be used.**

Donor Notification:

- Donors who test positive for infectious diseases are typically notified in a sensitive and confidential manner.
- Counseling and support services may be offered to donors following notification of positive test results.

Look-back program:

Lookback programs are designed to identify and notify recipients who may have received blood products from a previously negative, screened donor who has now become positive for an infectious agent. Lookback programs represent an attempt to reduce further blood-borne transmission of the infectious agent and to provide a chance for the infected recipients to seek medical attention.

As per blood transfusion guidelines in Rwanda, once a blood bank identifies a new positive blood donor who previously donated blood, it must do the following:

- Perform a confirmatory test after a positive screen to confirm the diagnosis
- Quarantine/destroy the blood products, if any, from the newly diagnosed, TTI-positive donor
- Inform the hospitals where the patient has donated blood previously (12 MONTHS).
- The informed hospitals must look up their records and identify the patients who received blood products from that particular donor. Once the recipients are identified, the current attending physician or the physician who initially ordered the blood product must be made aware. The informed physician has the responsibility to follow up with the recipients and notify them and provide adequate medical care.

Legal and Ethical Considerations:

- Legal frameworks govern blood donation and transfusion practices, including regulations related to infectious disease screening and donor notification.
- Ethical considerations include maintaining donor confidentiality, ensuring informed consent, and protecting the rights of both donors and recipients.

Emerging Threats:

- Emerging infectious diseases, such as Zika virus and Ebola virus disease, West Nile Virus, T. Cruzi and Chagas disease pose potential threats to blood safety and require vigilant surveillance and response measures.
- Antimicrobial resistance is also a growing concern, affecting the efficacy of treatment for infectious diseases transmitted through blood transfusion.
- Surveillance, research, and response strategies are essential for addressing emerging threats and ensuring the safety of the blood supply.

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16. RED BLOOD CELL ALLOIMMUNIZATION AND HDFN

16.1. Learning Objectives

1. Understand the concept of red blood cell (RBC) alloimmunization and its clinical significance
2. Learn about different blood groups and the antigens present on RBCs.
3. Recognize the significance of antigen-antibody reactions and compatibility in blood transfusions.
4. Identify the complications associated with RBC alloimmunization.
5. Understand the pathophysiology and prevention of Hemolytic Disease of the Fetus and Newborn (HDFN).
6. Understand the signs and symptoms, of HDFN, diagnosis and Management

16.2. Red cell alloimmunization

RBC alloimmunization is a common, undesirable outcome of blood transfusion that occurs as a response of the recipient's immune system to foreign RBC antigens, particularly in chronically transfused patients. These antibodies may be clinically significant, leading to hemolytic transfusion reaction (HTR) or hemolytic disease of the fetus and newborn (HDFN) . RBC alloantibodies may also cause some technical issues and result in difficulty and delay in providing compatible blood. Therefore, RBC alloantibody detection and identification are critical in transfusion practice to provide antigen-negative blood to patients.

Blood Groups:

- Human blood is classified into different blood groups based on the presence or absence of specific antigens on the surface of RBCs.
- The ABO blood group system and the Rh (Rhesus) blood group system are the most clinically significant blood group systems.

Antigen and Antibody:

- Antigens are molecules present on the surface of RBCs that can stimulate the immune system to produce antibodies.
- Antibodies are proteins produced by the immune system in response to specific antigens. They may react with foreign antigens, leading to immune responses.

Compatibility:

- Blood compatibility refers to the compatibility between the antigens present on donor RBCs and the antibodies present in the recipient's plasma.

- Compatibility testing, including crossmatching, is essential to ensure compatibility between donor and recipient blood products. Incompatible blood transfusions can lead to adverse reactions, including hemolytic transfusion reactions.

Complications:

- RBC alloimmunization occurs when a recipient develops antibodies against antigens present on donor RBCs, often as a result of transfusion or pregnancy.
- Complications of RBC alloimmunization include hemolytic transfusion reactions, delayed hemolytic transfusion reactions, and hemolytic disease of the fetus and newborn (HDFN).

Signs and Symptoms:

- Signs and symptoms of hemolytic transfusion reactions may include fever, chills, dyspnea, hemoglobinuria, jaundice, hypotension, and renal failure.
- Signs and symptoms of HDFN may include anemia, jaundice, hepatosplenomegaly, and hydrops fetalis in severe cases.

Management:

- Management of RBC alloimmunization involves careful selection of compatible blood products for transfusion.
- For pregnant women at risk of HDFN, close monitoring of maternal antibodies and fetal well-being is essential.
- For pregnant women at risk of HDFN, close monitoring of maternal antibodies and fetal well-being is essential, with possible interventions such as intrauterine transfusions or early delivery.
- Add prevention using Anti D gamma globulin is key in Africa context where monitoring is not an option

16.3. HDFN And Management Of Rh-Negative Pregnancies

Alloimmune haemolytic disease of the fetus and newborn (HDFN) may occur when a pregnant woman has an antibody against an antigen on the fetal red cells which has been inherited from the father. Many antibodies to red blood cell antigens can cause HDFN, including those from the ABO, Rh and other blood group systems. Women can develop antibodies either through previous pregnancy or transfusion. The maternal antibodies may cross the placenta and bind to the antigen on the fetal red blood cells, triggering their destruction or suppressing erythropoiesis in fetal bone marrow. HDFN presentation ranges from asymptomatic, to jaundice, anemia and, in its worst-case

scenario, death (can be life-threatening for the fetus or newborn). The risk for HDFN can be identified by testing the mother with a group and screen during the pregnancy.

Causes of HDFN

The main cause of HDFN is due to Rhesus Incompatibility, other causes include ABO

Incompatibility which occurs when there is an incompatibility between the mother's blood type and the baby's blood type. More common but generally less severe than Rh incompatibility. It can also be a result of other Blood Group Antibodies: such as Kell, Duffy, and Kidd antibodies. These are less common but can still lead to significant hemolysis.

Table 19. The main causes of HDFN

Cause	Mechanism	Severity
Rh Incompatibility	Maternal anti-D antibodies attack fetal Rh-positive RBCs	Can be severe, leading to hydrops fetalis
ABO Incompatibility	Maternal antibodies against fetal A or B antigens	Usually mild, causing jaundice
Kell, Duffy, Kidd Antibodies	Maternal antibodies against other RBC antigens	Variable severity, can be significant

Prevention of HDFN

- Proper prenatal screening and monitoring of Rh-negative pregnancies.
- Administration of Anti-D immunoglobulin to Rh-negative mothers to suppress the mother's immune response against the fetal RhD antigen

16.4. Hemolytic Disease of The Newborn (HDN)

Indications for Anti-D Immunoglobulin

Purpose: Prevent sensitization of Rh-negative mothers to Rh-positive fetal red blood cells.

- At 28 weeks' gestation in all Rh-negative pregnant women.
- Within 72 hours postpartum if the newborn is Rh-positive.
- After any event where fetal-maternal hemorrhage may occur (e.g., miscarriage, ectopic pregnancy, abdominal trauma, amniocentesis).

Table 20. Indications for anti-D immunoglobulin

Indication	Timing
Routine prophylaxis during pregnancy	At 28 weeks' gestation
Postpartum prophylaxis	Within 72 hours of delivery
Post-miscarriage or ectopic pregnancy	Within 72 hours
After invasive procedures or abdominal trauma	Within 72 hours

Related Testing

Coombs Test (Direct Antiglobulin Test):

- **Purpose**: Detects antibodies or complement proteins bound to the surface of red blood cells.
- **Procedure**: Mix neonatal red cels with antihuman globulin (Coombs reagent).

Observe for agglutination.

Indirect Coombs Test:

Purpose: Detects antibodies in maternal serum.

Procedure:

- Mix maternal serum with Rh-positive red cells.
- Add antihuman globulin (Coombs reagent).
- Observe for agglutination.

Management of Sensitized Persons

Monitoring:

- Regular antibody screening throughout pregnancy.
- Close monitoring of fetal well-being using ultrasound and Doppler studies.

Interventions:

- Intrauterine transfusions if severe anemia is detected.
- Early delivery if fetal distress is noted.
- Postnatal treatment for the newborn, including phototherapy and exchange transfusions if necessary.

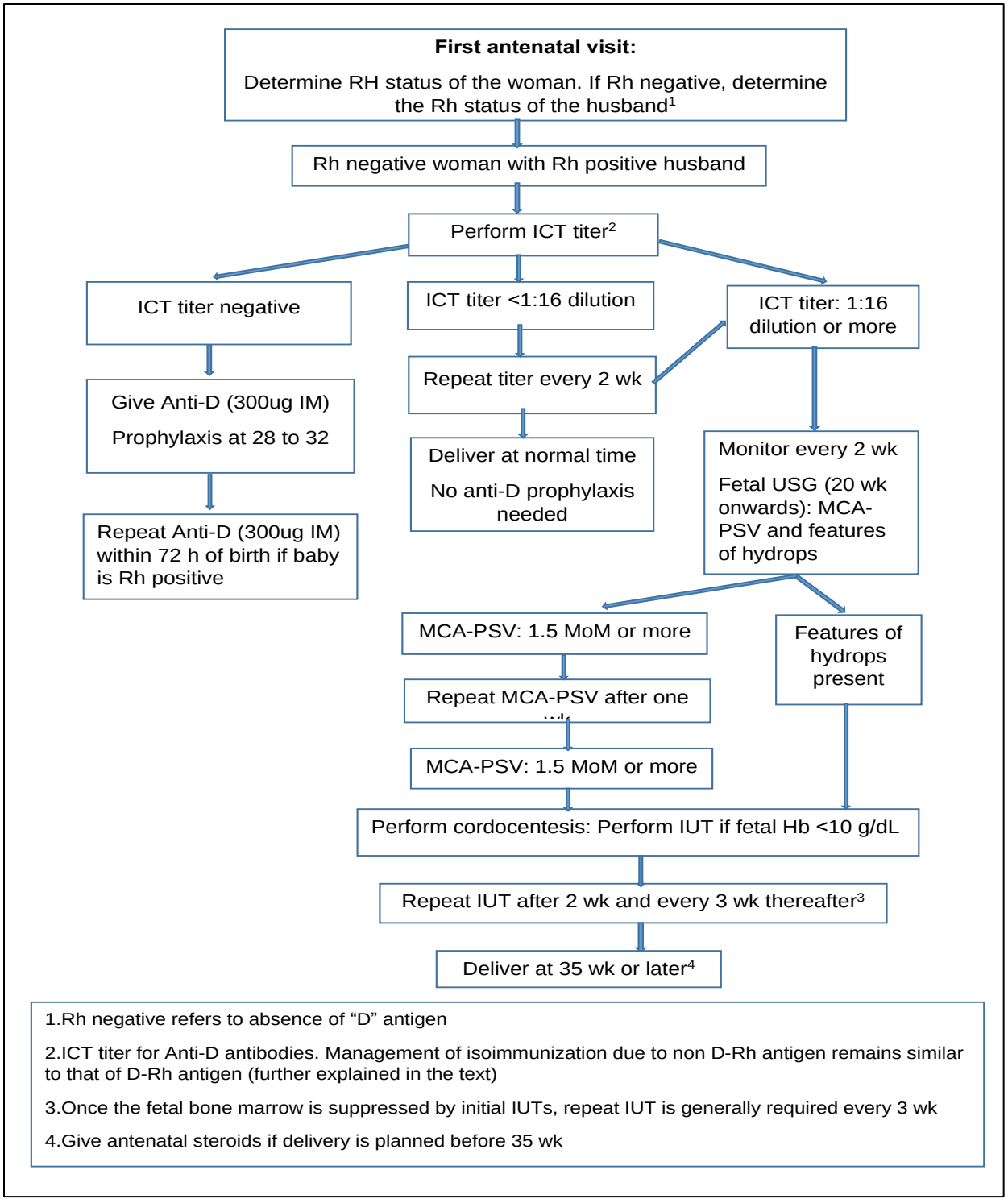

Fig. 14. The chart illustrating management of sensitized Rh-Negative Pregnancies

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17. REGULATORY ASPECTS OF TRANSFUSION MEDICINE:

17.1. Learning Objectives

1. Understanding the National guidelines in transfusion medicine.
2. Learn about the importance and components of consent forms in transfusion practice.
3. Reporting incidence and management of transfusion adverse reactions.
4. Learn about transfusion committees and its role and responsibilities in transfusion medicine.
5. Understand the principles of quality control in transfusion medicine.

17.2. Regulatory aspects

17.2.1. Consent Form

Purpose: Ensure informed consent from blood donor and recipients.

Components:

- Patient Information: Name, date of birth, Donor/Recipient's ID,
- Description of the Procedure: Explanation of the transfusion process.
- Risks and Benefits: Detailed information on potential risks and benefits.
- Alternatives: Discussion of alternative treatments.
- Consent Statement: Donor/Recipient's agreement to proceed with the transfusion.
- Signatures: Donor/Recipient's signature, date, and witness signature.

17.2.2. Incident / Adverse reaction Report Form

Purpose: Ensure reporting of incident/adverse reactions from blood donor/recipients.

Components:

- Patient Information: Name, date of birth, Donor/Recipient's ID,
- Description of the Procedure: Explanation of the transfusion process.
- Indication and time for transfusion
- Blood product received and type of reaction
- Type of incident happened
- Reporters signature and date

18. CHALLENGES OF BLOOD TRANSFUSION IN RWANDA

18.1. Learning Objectives

1. Examine cultural, social and educational factors that influences blood transfusion practices.
2. Identify the key factors contributing to blood testing, safety and supply challenges.
3. Explore the infrastructure and facility limitations impacting blood transfusion services.
4. Discuss regulatory challenges affecting blood transfusion services.
5. Evaluate training and capacity-building efforts in the field of transfusion medicine.
6. Analyze economic consideration and their implications

18.2. Educational Awareness

- Limited public awareness campaigns promoting voluntary blood donation and dispelling myths.
- Misconceptions and stigmas surrounding blood donation.
- Insufficient comprehensive educational programs targeting schools, communities, and healthcare workers.

18.2.1. Cultural and Social Factors

- Cultural beliefs and practices affecting willingness to donate blood.
- Religious beliefs influencing attitudes toward blood transfusion, particularly in certain communities.
- Gender disparities in blood donation rates due to cultural norms and societal roles.

18.2.2. Blood Testing and safety

- Limited access to quality-assured blood screening tests for TTIs
- Challenges in implementing standardized blood screening protocols across different regions.
- Shortages of skilled personnel to perform and interpret blood screening tests accurately.
- Challenges in ensuring compatibility and proper selection of blood component for transfusion.
- Insufficient resources for adverse event monitoring and reporting.

18.2.3. Blood Supply Challenges

- High prevalence of transfusion-transmissible infections (TTIs) such as Syphilis.
- Limited access to some facilities due to no-fly zone by Zipline services

18.2.4. Training and Capacity Building

- Shortage of trained personnel in transfusion medicine, including Physicians, laboratory technicians and blood bank staff.
- Limited opportunities for specialized training in blood banking and transfusion medicine.
- Insufficient funding and resources for training and capacity-building initiatives.

18.2.5. Infrastructure and Facilities

- Insufficient blood collection centers and processing centers particularly in rural areas.
- Insufficient storage capacity for blood components.
- Inadequate transportation systems for timely and safe distribution of blood products especially in health facilities in urban areas.

18.2.6. Regulatory Challenges

- Insufficient regulatory frameworks governing blood transfusion practices across health facilities.
- Lack of enforcement mechanisms leading to challenges in implementation of quality assurance standards and regulatory compliance.

18.2.7. Economic Considerations

- Financial constraints affecting blood transfusion practices, including budget limitations for equipment, supplies, and personnel.
- High costs associated with blood screening and testing, particularly for advanced diagnostic technologies.

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ANNEX 1: APA/INCIDENT REQUEST FORM:

<table>
<tr><td>RESERVED FOR QA</td><td colspan="2">Reception Date:</td><td>Index #:</td></tr>
<tr><td rowspan="2">RESERVED FOR ORIGINATOR</td><td>Originator ID:</td><td>RCBT/Service:</td><td>Date & time:</td></tr>
<tr><td colspan="3">Description: Problem/Incident/Occurrence/Near miss/Potential problem/NC*

<u>Immediate actions by Originator and/or HoS</u>

Transmitted to Head of Service on: ……..…/……..…/…….</td></tr>
<tr><td>RESERVED FOR RESPONSIBLE OF THE SERVICE HANDLING THE</td><td colspan="2">Probable causes and immediate actions to solve the issue (for temporary deviation, fill Waiver form)

Target due date:

<u>Actual Date & Signature:</u></td><td>Further actions taken to resolve the issue

Target due date:

<u>Actual Date and Signature:</u></td></tr>
<tr><td>CLOSURE OF THE ISSUE (QA)</td><td colspan="3">Were the actions taken effective?
☐ Yes, Date: ☐ No, Initiate CAPA request

CAPA request #:

Date & Signature:</td></tr>
</table>

Circle where appropriate

ANNEX 2. BLOOD DONOR ELIGIBILITY CRITERIA FOR ALLOGENIC BLOOD DONATION

N°	CATEGORY	CRITERIA/DESCRIPTION	NOTES
1	**Age**	Lower age limit is 18 years Maximum age limit is 60 years	Anyone who is more than 60 years may donate if they have certificate for fitness from their physician or BTD Medical doctor.
2	**Body weight**	The lower body weight is 50 Kg.	
3	**Whole blood volume collected**	Volume collected is 450 +/- 45mL	For AFSBT Standards the maximum volume is 10.5mL/Kg
4	**Donation interval for whole blood donation**	Minimum whole blood inter-donation intervals is 56 days for both males and females	AfSBT: 56 days
5	**Donation interval for plateletpheresis**	• At least 14 days after platelet donation and not more than 24 times in 12 months. • If a platelet donor donates a unit of whole blood, at least 8 weeks shall elapse before subsequent platelet donation. • If it becomes impossible to return the donor's red cells during apheresis, at least 8 weeks shall elapse before subsequent apheresis procedure	AFSBT Standard: The minimum interval between two apheresis collections shall be 48 hours and at most, 24 procedures shall be performed on any individual donor within a 12-month period.
6	**Pre-donation Platelet count before apheresis**	Plateletpheresis donors with a platelet count of <150,000/µl shall be deferred from	Trima accel manufacturer instructions

		plateletpheresis donation until a subsequent platelet count is at least 150,000/ µl	
7	**Pulse**	Not exceeding 100 beats/min and not less than 50 beats/min	AfSBT standard
8	**Blood pressure**	Systolic blood pressure must not be less than 100 and must not exceed 160 mmHg. Diastolic Blood pressure must not be less than 60 and must not exceed 100mmHg	AfSBT standard: • Diastolic BP limit ≤100 mm Hg • Diastolic BP limit ≤100 mm Hg
9	**Haemoglobin/hematocrit**	≥ 12.5 g/dL of Hb and 38% of Hcte for males and females	AfSBT standard
10	**Medical history and general health**	During donor qualification process, the donor must be in good health and be free of major organ diseases (eg. heart, liver, lungs, etc.), cancer, or abnormal bleeding tendency. The venipuncture site shall be free from infectious skin disease and any disease that might create a risk of contaminating the blood.	Refer to the deferral periods document

ANNEX 3: ADVERSE REACTION FORMS

Hemovigilance Incident reporting form

Name of the HF:……..
Address of the HF:……..……
Name of the MD : ..……...……
Department/ Service: ….……
Phone Number/ email of the HF Staff :
……
Patient ID:…….....

Discovery

Date of discovery: __ __ /__ __ / __ __ __ __
Time of discovery: __ __ : __ __(HH:MM) ☐ Time approximate ☐ Time unknown

At what point in the process was the incident first discovered? (check one)

☐ Product check-in ☐ Order entry ☐ Sample testing ☐ Product storage
☐ Sample collection ☐ Product manipulation ☐ Product administration
☐ Inventory management ☐ Sample handling ☐ Request for pick-up
☐ Post-transfusion review/audit ☐ Product/test request ☐ Sample receipt
☐ Product issue

☐ Other _____

How was the incident first discovered? (check one)

☐ Visual inventory review ☐ Observation by staff of nit/reagent/sample/equipment
☐ Routine audit or supervisory review ☐ Comparison of product label to patient information
☐ Comparison of product label to physician order ☐ Comparison of sample to paperwork
☐ When checking patient ID band ☐ Repeat or sample re-testing
☐ Notification or complaint from ward (Nurse, MD, etc.)
☐ Historical record/previous type check ☐ When product/units returned to lab
Communication from lab to ward ☐ Patient transfusion reaction

☐ Other (specify)

Incident summary: (500 characters max)

……
……
……
……
……

Product action: (check all that apply)

☐ Not applicable ☐ Product retrieved and returned to inventory
☐ Product retrieved and destroyed
☐ Single or multiple units destroyed?
☐ Single unit: Unit #:……..……
☐ Product issued but not transfused
☐ Product transfused
Was a patient reaction associated with this incident? ☐ Yes ☐
No
Patient
ID#(s):……

Record/other action: (check all that apply)

☐ Record corrected ☐ Attending physician notified ☐ Additional testing
☐ Patient sample re-collected
Other
(Specify)……
……..……

Investigation Results

Did this incident receive root cause analysis? ☐ Yes ☐ No

Comments (2000 characters max)
……
……
……
……
……
……
……
……
……

ANNEX 4: DONOR MEDICAL QUESTIONNAIRE

DONOR NUMBER	DONATION NUMBER

Tick where applicable ☒ Please answer the following questions correctly. This will help to protect you and the patient who receives your blood. Thank you!

Names: ……..……..……

Sex: Male ☐ Female☐ Occupation: …….
Date of Birth: ……..….. Place of Birth (District-Sector): ……

Place of Residence

District: ……..……	Sector: ……..…	Cell: ……..…	Village: ……..……
Telephone: ……..……..…		E-mail: ……	ID: ……

Are you married? ☐Yes ☐ No
Have you donated blood previously?☐ Yes ☐ No If yes, how many times? .....
What is the date of the last donation: ……Where? …….
What is your blood group?.....……
Did you have any discomfort during/after donation? ☐ Yes ☐ No

DONOR DECLARATION

I understand that I should not donate blood if:

- I consume drugs or use illegal intravenous drugs.
- I have HIV AIDS, Hepatitis B or C, Syphilis or any other sexually transmitted infections
- I have or have had sex with a partner of the same sex (Even using condom)
- My sexual partner has HIV/AIDS, hepatitis or any other Sexually Transmitted Infection.

I understand that I should wait for 6 months to donate blood if:

- I have had sex with a person who is not my spouse even using condoms
- I don't trust my partner even if I use condoms
- I have not got any HIV/AIDS test before marriage

ANNEX 5: QUESTIONS TO THE BLOOD DONOR (TICK ☒ YES OR NO THE APPROPRIATE ANSWER):

1	Are you feeling healthy and well?		
2	Are you taking any medication?		
3	Do you have any wound or cutaneous disease?		
4	Did you travel outside Rwanda recently?		
In the past 48 hours			
5	Have you taken Aspirin?		
6	Have you been bitten by insect?		
In the past 1 month:			
7	Have you had Malaria?		
8	Vaccine?		
9	Dental Extraction?		
In the past 6 months have you had:			
10	Weight loss?		
11	Repeated diarrhea?		
12	Swollen glands?		
13	Continuous low – grade fever or any disease?		
14	Tattooing or Ear piercing?		
15	Surgery or circumcision?		
16	Endoscopy?		
17	Blood transfusion?		

1	Heart Disease?		
2	Kidney Disease?		
3	Cancer?		
4	Epilepsy?		
5	Asthma?		
6	Diabetes?		
7	Tuberculosis?		
8	Abnormal bleeding tendency?		
9	Hepatitis B or C?		
10	HIV/AIDS		
11	Syphilis?		
12	Gonorrhea?		
13	A neighbor with infectious disease such as Hepatitis B, C, HIV, etc.?		
For female donors only:			
14	Are you pregnant?		
15	Do you have a child who is under 9 months		
16	Have you had abortion in the last 6 months?		

I am not donating to receive an HIV test:

I authorize the National Center for Blood Transfusion to draw, analyze and transfuse my blood. In some cases, one or more of my blood derivatives may be utilized for medical or scientific research. I know that someone may be a carrier of infection, yet have a negative test. I understand that I will be notified of my test results (HIV, Hepatitis B &C, Syphilis, etc.) whatsoever they will be.

I have carefully read education materials and answered all the questions truthfully. I understand that not being honest while answering questions on this form is a serious matter and a lie could harm another person. I understand the eventual side effects of my donation.

I have had an opportunity to ask questions and all my questions have been answered.

Date: ……..….. Donor Signature:……

ANNEX 6: MINI-PHYSICAL EXAMINATION (Filled by BT Medical Staff):

Parameters	Value	Time	Equip.ID	Initial
Weight (Kg)				
Pulse(bt/min)				
Hb(g/dl)/Hcte (%)				
BP(mmHg)				
Temperature (^{0}C)				
Height (m) (Apheresis)				
Plts (nbr/µl) (Apheresis)				

		Initials
Start time		
Stop time		
Quantity to be drawn		
Any Donor reaction?	Yes ☐ No ☐	
Used Equip. ID		

☐ Eligible ☐ Non-eligible

Reason and suspended until: _____

Comments: _____

Signature and initial of NDS: ……..……..…..…….……..

Signature of BDM&ST: ……..……..…...…….