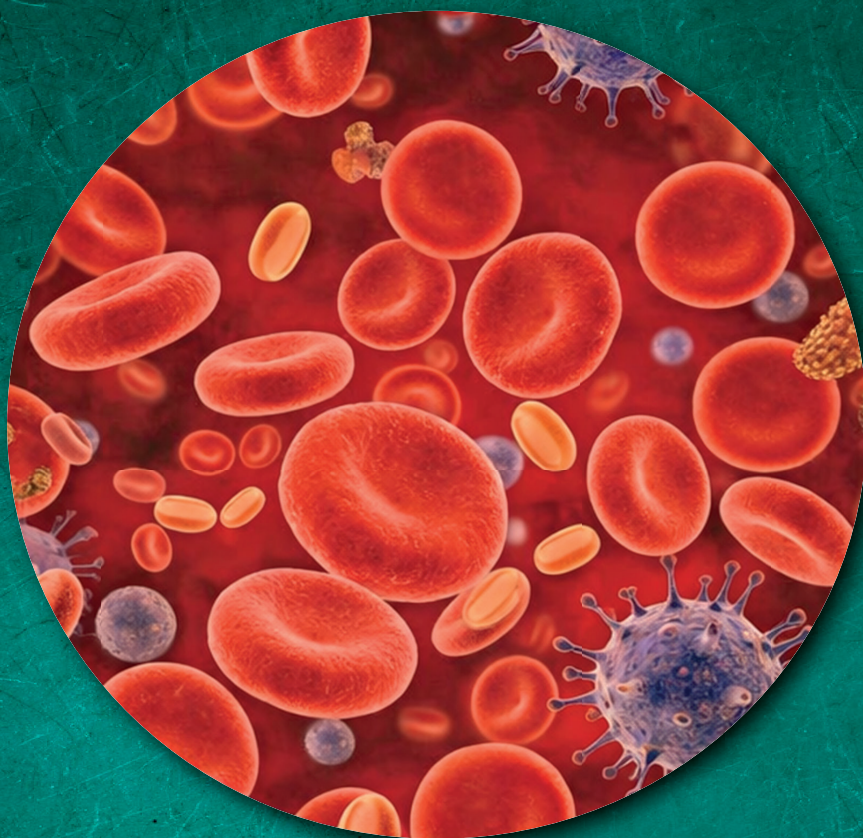




NATIONAL GUIDELINE FOR MANAGEMENT OF HAEMOPHILIA

Directorate General of Health Services
Government of the People's Republic of Bangladesh

First Edition, 2026





National Guideline for **MANAGEMENT OF HAEMOPHILIA**

First Edition, 2026

DIRECTORATE GENERAL OF HEALTH SERVICES
Mohakhali, Dhaka



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Disclaimer: This guideline is based on the 'WFH Guidelines for the Management of Haemophilia, 3rd edition, 2020', and adapted for the healthcare context of Bangladesh. While every effort has been made to ensure the accuracy of the recommendations, clinical judgment should be exercised based on the individual patient's needs and available local resources. This guideline will be updated periodically on the DGHS website to align with evolving international standards.

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Director General
Directorate General of Health Services (DGHS)
Mohakhali, Dhaka

Message

Haemophilia is a rare inherited bleeding disorder that can be life-threatening and requires uninterrupted and timely access to clotting factor replacement therapy. In the absence of adequate treatment, affected individuals may suffer from severe disability, irreversible organ damage, chronic morbidity, and premature mortality. In resource- constrained settings, these challenges are further compounded by delayed diagnosis, limited awareness, and insufficient access to essential therapies. Bangladesh continues to face these challenges despite important progress in recent years.

The Government of Bangladesh remains firmly committed to ensuring improved health outcomes and quality of life for people living with haemophilia. In line with this commitment, and under the leadership of the Ministry of Health and Family Welfare (MoH&FW), the Non-communicable Disease Control (NCDC) Wing of the Directorate General of Health Services (DGHS), in partnership with the World Federation of Hemophilia (WFH) PACT Programme, the Haemophilia Society of Bangladesh, and the Haematology Society of Bangladesh, has initiated key efforts to develop practical national guidelines and enhance access to treatment services. However, the current availability of clotting factors in the country remains critically insufficient, covering only about 16–17% of the estimated national need, underscoring the urgent requirement for structured and standardized management.

This guideline marks a significant collaborative milestone between DGHS and the World Federation of Hemophilia (WFH). By introducing standardized protocols at the Upazila Health Complex (UHC) level, the initiative seeks to decentralize specialized care and extend it to the community level, ensuring that individuals with haemophilia and other bleeding disorders receive timely, appropriate, and quality care within the national health system.

I extend my sincere appreciation to all contributors involved in the development of this guideline. It is hoped that effective implementation at the primary healthcare level will facilitate early identification of undiagnosed cases and ensure standardized management, ultimately improving outcomes and enhancing the quality of life for people living with haemophilia.

Professor Dr. Pravath Chandra Biswas
Director General
Directorate General of Health Services





Director (Disease Control)
Directorate General of Health Services (DGHS)
Mohakhali, Dhaka

Message

The development of the "National Guideline for Management of Haemophilia" marks an important step towards strengthening the prevention, diagnosis, treatment, and long-term management of haemophilia in Bangladesh. As a rare inherited bleeding disorder, haemophilia poses significant challenges not only to affected individuals and their families but also to the healthcare system, particularly in ensuring timely diagnosis and equitable access to quality care.

Over the years, Bangladesh has made commendable progress in expanding services for noncommunicable diseases and other chronic health conditions. However, haemophilia and other inherited bleeding disorders have often remained under-recognized, resulting in delayed diagnosis, preventable complications, disability, and reduced quality of life. The availability of standardized national guidance is therefore essential to promote evidence-based practices and ensure a coordinated approach to care across all levels of the health system.

This guideline has been developed through a collaborative effort involving the Directorate General of Health Services (DGHS), the Haematology Society of Bangladesh, the Haemophilia Society of Bangladesh, and other national experts. It provides practical recommendations for healthcare providers on early detection, referral, emergency management, comprehensive care, and follow-up of patients with haemophilia and related bleeding disorders.

From a disease control perspective, our priority is to strengthen service delivery, improve case detection, enhance the capacity of healthcare providers, and facilitate access to essential medicines and clotting factor replacement therapy. The introduction of standardized protocols at primary and secondary healthcare facilities will contribute significantly to reducing morbidity, disability, and preventable deaths associated with haemophilia.

I commend all individuals who have contributed to the preparation of this guideline. Their dedication and technical expertise have resulted in a valuable resource that will support healthcare professionals throughout the country. I am confident that the effective implementation of this guideline will strengthen haemophilia care services, promote earlier diagnosis of undetected cases, and improve the health and well-being of people living with haemophilia in Bangladesh.

Together, let us work towards ensuring that no person with haemophilia is left undiagnosed, untreated, or deprived of the care and support necessary to lead a healthy and productive life.

Professor Dr. Md. Halimur Rashid
Director (Disease Control)
Directorate General of Health Services (DGHS)



Preface



Haemophilia is a rare inherited bleeding disorder that can result in life-threatening complications and chronic disability if not diagnosed and managed appropriately. In Bangladesh, over 4,055 individuals with haemophilia have been registered to date, while the estimated total number of affected people is around 24,000. This suggests that a large proportion of cases remain unidentified and therefore are not receiving appropriate diagnosis or treatment. Limited awareness, delayed diagnosis, and inadequate availability of clotting factors continue to pose major challenges, particularly in resource-constrained settings.

Recognizing these realities, the *National Guideline for Management of Haemophilia* has been developed as a practical and context-responsive framework to strengthen haemophilia care in Bangladesh. The guideline emphasizes evidence-based yet feasible approaches to diagnosis, treatment, prevention, rehabilitation, and long-term management that are sustainable within the country's healthcare system.

This document is intended to serve as the national reference for healthcare professionals, programme managers, and policymakers involved in haemophilia care. By promoting standardized, quality, and patient-centered care, the guideline aims to reduce complications, prevent disability, and improve the survival, well-being, and long-term quality of life of persons living with haemophilia in Bangladesh.

I would like to express my deep appreciation to all the experts, professionals, and partner organizations who have contributed their time, expertise, and dedication to the development of this guideline. Their collaborative efforts, technical insight, and commitment to improving haemophilia care have been instrumental in shaping this important document. This collective endeavor reflects a shared vision to strengthen health services and ensure better outcomes for individuals living with bleeding disorders across the country.

A handwritten signature in black ink, appearing to read 'Syed Zakir Hossain'.

Prof. Dr. Syed Zakir Hossain

Coordinator- NCDC Team &

Former Line Director, Non-Communicable Disease Control (NCDC)

Directorate General of Health Services (DGHS)



Message From **The Haematology Society of Bangladesh**



Professor Dr. Amin Lutful Kabir
President



Dr. Md. Adnan Hasan Masud
General Secretary

The Haematology Society of Bangladesh takes great pride in being actively involved in the development of this comprehensive National Haemophilia Guideline. As the professional body representing haematologists across the country, our mission has always been to advance the standard of care for blood disorders, and this guideline marks a historic milestone in that journey.

Managing haemophilia in a resource-limited setting such as Bangladesh presents unique and formidable challenges. For decades, patients have faced restricted access to life-saving clotting factor concentrates, a critical shortage of specialized care centres, and substantial out-of-pocket expenditures that place families under severe financial strain. Diagnosis is frequently delayed, and the delivery of consistent, evidence-based treatment has remained difficult to sustain across all levels of the healthcare system.

Yet within these challenges lies the opportunity for meaningful, structured change. This guideline is our scientific & social response to those longstanding gaps. Meticulously developed by leading national experts, it offers practical, evidence-based, and resource-adapted recommendations designed to reflect the realities of our healthcare environment. Our core objective is to standardize haemophilia care across Bangladesh - ensuring that every clinician, whether practising at a tertiary referral centre or a district-level facility, has a clear and reliable roadmap for safe and effective patient management.

We extend our sincere gratitude to all contributors, reviewers, and stakeholders who dedicated their time and expertise to this undertaking. A guideline, however carefully crafted, derives its true value from implementation. We therefore call upon the Government of Bangladesh, healthcare providers at all levels, and our international partners to embrace and operationalize these recommendations. Together, we can meaningfully close the gap in haemophilia care and secure a safer, healthier future for every individual living with this condition in Bangladesh.

Professor Dr. Amin Lutful Kabir

Professor Dr. Md. Adnan Hasan Masud



Message From **The Hemophilia Society of Bangladesh**



Najmul Alam
President



Abu Sayeed Arif
General Secretary

For the thousands of individuals and families living with hemophilia in Bangladesh, every day is a battle against pain, uncertainty, and physical disability. As the national patient organization, we have witnessed firsthand the immense struggles of our community – the desperation of a parent looking for factor concentration during a bleeding crisis, the young lives interrupted by joint damage, and the heavy financial burden of an expensive lifelong condition.

In a country where healthcare resources are limited, hemophilia has long been a neglected suffering. For years, our cry has been for recognition, structured care, and affordable treatment. We are well aware that advanced, modern treatments available abroad are still completely out of reach for patients in Bangladesh. We do not have access to the latest therapies that make managing this condition easier, meaning our patients must fight harder just to survive and maintain basic mobility with the limited treatment we have.

The publication of the National Hemophilia Guideline fills our hearts with immense hope. For the first time, the patient community feels truly seen and heard. This document is not just a medical text; to us, it is a promise of better care, safer treatment protocols, and a more organized healthcare system using the resources available to us right now.

We are deeply grateful to all the doctors & contributors who worked tirelessly to create this guideline. Your expertise gives us a fighting chance at a normal life.

An accurate guideline is the first step, but our ultimate dream is to see it put into action in every hospital across Bangladesh. We hope this document serves as a powerful tool for advocacy, encouraging policymakers to ensure a steady, reliable supply of basic clotting factors and comprehensive care. We stand ready to walk hand-in-hand with our medical community to turn the words of this guideline into a reality for every patient.

Najmul Alam

Abu Sayeed Arif



Message From **National Haemophilia Guideline Development Committee**

Haemophilia is a genetic disorder characterized by deficiency of clotting factors VIII or IX. The standard of treatment in haemophilia is replacement of factors, regularly and prophylactically, i.e., before bleeding starts. Factor replacement is a very costly treatment worldwide. Without factor replacement, haemophilia patients are destined to die from major abnormal bleeding, or to survive with complications of bleeding in various organs, like deformed joints, muscle atrophy, etc. In Bangladesh, as of October 2025, 4,055 people with haemophilia are registered with the Haemophilia Society of Bangladesh. The availability of factors in Bangladesh has been consistently scarce. It is estimated that, supply of factors in this country is only 16-17% of total demand. Moreover, most of the patients treated with factors got those on donation. Since the year 2020, approximately >80% of the donations are received as a support from the World Federation of Haemophilia (WFH) Humanitarian Aid Program, and the remaining are procured by the Government of the People's Republic of Bangladesh. To ensure a healthy life for individuals with haemophilia, Non-communicable Disease Centre (NCDC) of Directorate General of Health Services (DGHS) of Bangladesh and the Path to Access to Care and Treatment (PACT) programme of the World Federation of Hemophilia (WFH) are in an agreement to develop a concise guideline practically applicable in this country. This guideline is principally based on the '*WFH Guidelines for the Management of Haemophilia*, 3rd edition, 2020', along with recommendations from other guidelines suitable for our country.

Adequate and effective treatment allows haemophilia patients to participate in many activities without major bleeding and to maintain a good quality of life. However, this scenario is different in resource-poor countries like Bangladesh due to late diagnosis and inadequate factor replacement therapy. To ensure proper treatment at the grassroot levels in Bangladesh, especially in low socio-economic condition, the NCDC in collaboration with Haematology Society of Bangladesh (HSB) declared a committee on August 3, 2025. The committee consists of representatives from NCDC, haematologists, paediatric haemato-oncologists, internists, transfusion medicine specialists, physiatrists, orthopaedic surgeon and dental surgeons. The main purpose of this committee was to establish guidelines for diagnosing haemophilia among people with bleeding disorders and for maintaining a registry at the Upazila Health Complex (UHC) levels. The committee arranged several workshops with open and elaborate discussions among the specialists, patients and caregivers.

The "*National Guideline for Management of Haemophilia*" will provide essential guidance to physicians in Bangladesh on the primary assessment of bleeding disorders and primary level management of haemophilia, which includes the treatment of specific haemorrhages, comprehensive care, prophylaxis in haemophilia and recommendations in special situations. This guideline will also cover the management of musculoskeletal complications, the use of haemostatic agents and genetic assessment. This guideline will be available on the DGHS website (<https://dghs.gov.bd>), and it will be regularly updated and modified to align with the WFH guidelines.



Acknowledgement by Managing Editor



The Non-communicable Disease Control (NCDC) unit of the Directorate General of Health Services (DGHS), in collaboration with the World Federation of Haemophilia (WFH) under the Path to Access to Care and Treatment (PACT) programme, is providing strategic leadership, stewardship, and governance in addressing the challenges of haemophilia in Bangladesh. In light of the persistent shortage of clotting factors—currently meeting only 16–17% of the national requirement—the national programme has identified the development of the “*National Guideline for Management of Haemophilia*” as a top priority. This guideline is intended to equip physicians at all tiers of the health system, including those serving at Upazila Health Complexes (UHCs), with standardized and practical clinical guidance.

Although the initiative started in 2022, it gained significant momentum in 2025. We sincerely acknowledge the valuable multidisciplinary contributions of the committee constituted on August 9, 2025. The committee comprised Haematologists, Paediatric Haemato-oncologists, Internists, Transfusion Medicine Specialists, Physiatriests, Orthopaedic Surgeons, Dental Surgeons, Haemophilia Society of Bangladesh, and Haematology Society of Bangladesh, who took a leading role in this initiative. Their collective expertise was pivotal in formulating comprehensive guidance on diagnosis, establishing and maintaining a national registry, and addressing complex musculoskeletal complications associated with haemophilia. We also convey our heartfelt congratulations to all members of the National Haemophilia Guideline Development Committee for their commitment, diligence, and exemplary teamwork.

Special appreciation is extended to the World Federation of Haemophilia and the Haemophilia Society of Bangladesh for their sustained support and for facilitating humanitarian assistance that continues to benefit many of our patients.

We also express our sincere gratitude to the Ministry of Health and Family Welfare (MoHFW) and the Directorate General of Health Services (DGHS) for their continued guidance and support throughout the preparation and finalization of this document.

A handwritten signature in black ink, consisting of stylized loops and a long horizontal stroke.

Dr. Md. Nurul Islam
Deputy Director & Former Program Manager-1
NCDC, DGHS



Aims of this Guideline

The main purpose of this guideline is to provide a clear, practical guidance for managing haemophilia in Bangladesh, with particular attention to resource-limited settings.

The objectives include:

1. **Standardizing Diagnosis:** Developing protocols for the identification of haemophilia among individuals with bleeding disorders and ensuring the maintenance of a registry at the Upazila Health Complex (UHC) level.
2. **Improving Clinical Management:** Offering guidance to physicians on initial assessment and treatment, including comprehensive care, management of specific bleeding episodes, and prophylactic therapy.
3. **Addressing Complications:** Establishing frameworks for the management of musculoskeletal issues, chronic synovitis, and inhibitor development.
4. **Enhancing Quality of Life:** Ensuring effective and timely treatment to help patients engage in daily activities while minimizing morbidity and mortality.
5. **Providing Contextual Solutions:** Recommending “lower-dose” clotting factor replacement strategies adapted to the socio-economic realities of Bangladesh.
6. **Strengthening the Haemophilia Registry System:** Ensuring the establishment and systematic maintenance of a comprehensive Haemophilia Registry at all levels of the health system—from UHCs to tertiary centres—to enable accurate case identification, continuity of care, monitoring of treatment outcomes, and evidence-based planning for resource allocation and policy development.



To Whom this Guideline is Intended

This guideline is intended for primary care physicians, specifically those working at the grassroots level, such as the UHC, for initial assessment and registry maintenance.

Following persons may get benefitted from this guideline for quick consultation, though reference texts might be more helpful.

1. Haematologists and Paediatric Haemato-oncologists: For specialized diagnosis and management.
2. Medical Officers/Internists: For general medical management and emergency care.
3. Physical Medicine & Rehabilitation Specialists (Physiatrists) and Physiotherapists/Occupational Therapists: For managing musculoskeletal health and rehabilitation.
4. Surgeons (Orthopaedic, Dental, General, and Paediatric)
5. Laboratory Specialists and Transfusion Medicine Specialists: For accurate factor assays and provision of safe blood components.
6. Nurse Coordinators: For care coordination and patient education.
7. Support Staff: Psychosocial counsellors, social workers, and school staff who support the patient's integration into the community. Separate booklets in local language would be more beneficial.
8. Patients and Caregivers: To serve as an educational resource for self-management, bleed recognition, and home therapy. Separate text in local language and demonstrations are strongly recommended.



Methodology for Developing This Guideline

While this document is a practically applicable concise guideline for Bangladesh, it is principally anchored in international standards:

Primary Source: This guideline is based on the 'WFH Guidelines for the Management of Haemophilia, 3rd edition, 2020'.

Contextual Adaptation: Recommendations have been modified to be suitable for resource-limited countries.

Expert Consensus: Clinical protocols were developed through several workshops and open discussions among a multidisciplinary committee of specialists, including haematologists, paediatric haemato-oncologists, internists, transfusion medicine specialists, physiatrists, orthopaedic surgeon, dental surgeons as well as patients and caregivers.

Practice Patterns: It specifically includes a "*Lower-dose practice pattern*" for CFC replacement, which is recommended for effectiveness in low-resource settings like Bangladesh.



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Abbreviations and Acronyms

ABR	Annual Bleeding Rate
ADL	Activities of Daily Living
AF	Atrial Fibrillation
AFO	Ankle-Foot Orthosis
APCC	Activated Prothrombin Complex Concentrate
APTT	Activated Partial Thromboplastin Time
AROM	Active Range of Motion
ASA	AcetylSalicylic Acid
BD	Bis in Die (twice a day)
BT	Bleeding Time
BU	Bethesda Unit
CBC	Complete Blood Count
CFC	Clotting Factor Concentrate
CKD	Chronic Kidney Disease
CNS	Central Nervous System
COX2	Cyclo-Oxygenase 2
CT	Computed Tomography
DDAVP	Desmopressin
DGHS	Directorate General of Health Services
DIC	Disseminated Intravascular Coagulation
dL	DeciLitre
DM	Diabetes Mellitus
EACA	Epsilon AminoCaproic acid
EHL	Extended Half-Life
FFP	Fresh Frozen Plasma
FI	Clotting Factor I
FII	Clotting Factor II
FIX	Clotting Factor IX
FIXc	Activity of Factor IX
FV	Clotting Factor V
FVII	Clotting Factor VII
FVIII	Clotting Factor VIII
FVIIIc	activity of Factor VIII
GI	GastroIntestinal
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HMWK	High Molecular Weight Kininogen
HSB	Haematology Society of Bangladesh
HTC	Haemophilia Treatment Centre



HTN	Hypertension
ICU	Intensive Care Unit
ID	IntraDermally
IFT	InterFerential Therapy
IM	IntraMuscular
ITI	Immune Tolerance Induction
IU	International Unit
IV	IntraVenous
LBW	Lean Body Weight
LLLT	Low Level LASER Therapy
KAFO	Knee-Ankle-Foot Orthosis
MRI	Magnetic Resonance Imaging
MSK	Musculoskeletal
MSK US	Musculoskeletal Ultrasonogram
NCDC	Non-Communicable Disease Centre
NMES	NeuroMuscular Electric Stimulations
NSAID	Non-Steroidal Anti-Inflammatory Drug
NV	NeuroVascular
OD	Omne in Die (once a day)
OP	Orthotist & Prosthetist
POLICE	Protection, Optimum Loading, Ice, Compression, Elevation
Pre-K	Pre-kallikrein
PRICE	Protection, Rest, Ice, Compression, Elevation
PROM	Passive Range of Motion
PL	Phospho Lipid
PT	Prothrombin Time
rFVIIa	Recombinant Activated clotting Factor VII
RICE	Rest, Ice, Compression and Elevation
ROM	Range of Motion
RVVT	Russel Viper Venom Time
SC	SubCutaneously
SHL	Standard Half-Life
SOP	Standard Operating Procedure
TENS	Transcutaneous Electric Nerve Stimulation
TT	Thrombin Time
UHC	Upazila Health Complex
UST	Ultrasonic Therapy
VAS	Visual Analogue Scale
VTE	Venous ThromboEmbolism
vWD	von Willebrand Disease
vWF	von Willebrand Factor
WBAT	Weight Bearing as Tolerated
WFH	World Federation of Hemophilia



National Guideline for MANAGEMENT OF HAEMOPHILIA

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CHAPTER 01 Comprehensive Care of Haemophilia

1.1. Introduction

- a) Haemophilia is a rare X-linked congenital bleeding disorder. It affects mostly males.
- b) It is caused by deficiency of either coagulation factor VIII (also known as FVIII) or coagulation factor IX (also known as FIX). Bleeding disorders resulting from deficiency of FVIII is called haemophilia A, and that from deficiency of FIX is called haemophilia B.
- c) The factor deficiencies are the result of pathogenic variants (Mutations) in the *F8* and *F9* clotting factor genes.
- d) As of 2019, the worldwide prevalence of Haemophilia is estimated to be 1,125,000, with the majority being undiagnosed, including about 418,000 males with severe Haemophilia.

1.2. Haemophilia A and B

- a) Haemophilia A is estimated to account for 80%-85% of all haemophilia cases, and haemophilia B is estimated to account for 15%-20%.
- b) Estimated prevalence at birth:
 - i. Haemophilia A (all severities): 24.6 cases per 100,000 male birth (9.5 cases for severe Haemophilia A).
 - ii. Haemophilia B (all severities): 5.0 cases per 100,000 male birth (1.5 cases for severe Haemophilia B).
- a) In 30% of all cases, and over 50% of newly diagnosed severe cases, there is no family history, and these cases mostly come from new mutations in *F8* or *F9* gene.
- b) Haemophilia typically affects only males who inherit an affected maternal X chromosome but may also occur in a proportion of female.

1.3. Clinical Diagnosis

Haemophilia should be suspected in individuals presenting with a history of any of these symptoms since childhood:

- a) Easy bruising.
- b) Spontaneous bleeding (bleeding for no apparent/known reason), particularly into the joints, muscles, and soft tissues.
- c) Excessive bleeding following trauma or surgery.
- d) Early symptoms of joint bleeds in children at a very young age are a key indicator of severe Haemophilia.
- e) Abnormal bleeding on the background of abnormal or unexplained bleeding in any siblings or maternal male relatives.

1.3.1. Relationship of Bleeding Severity to Clotting Factor Level

The severity of bleeding manifestations generally correlates with the degree of the clotting factor deficiency.



Table 1 Relationship of Bleeding Severity to Clotting Factor Level

Severity	Clotting factor level	Bleeding Episodes
Severe	<1 IU/dL or <1% of normal factor activity	Spontaneous bleeding into joints or muscles, predominantly in the absence of identifiable haemostatic challenge
Moderate	1-5 IU/dL or 1-5% of normal factor activity	Occasional spontaneous bleeding; prolonged bleeding with minor trauma or surgery
Mild	>5-40 IU/dL or >5-40% of normal factor activity	Severe bleeding with major trauma or surgery; rare spontaneous bleeding

- * People with mild Haemophilia may not necessarily have abnormal or prolonged bleeding problems until they experience serious trauma or undergo surgery.

1.3.2. Sites of Bleeding in Haemophilia

People with severe Haemophilia most commonly experience bleeds into the joints, muscles, and internal organs.

Table 2 Sites of Bleeding and Frequency Haemophilias

Site of bleeding	Approximate frequency	Notes
Joints	70-80%	More common in hinged joints: ankles, knees, elbows. Less common in multi-axial joints: shoulders, wrists, hips.
Muscles	10-20%	
Other sites (major bleeds)	5-10%	Intracranial, neck/throat & gastro-intestinal bleedings are uncommon but life-threatening bleedings.
Central nervous system	<5%	

1.3.3. Bleeding Manifestations in Newborns and Children

In newborns and children of less than 2 years of age with severe haemophilia, common types of bleeding include:

- Soft tissue and intramuscular bleeding.
- Bleeding is associated with a medical procedure (e.g., venipuncture, central line placement, circumcision, neonatal heel prick).
- Mucocutaneous bleeding (e.g. oral, nasal).
- Extracranial bleeding.

1.4. Laboratory Diagnosis and Monitoring

Diagnosis of Haemophilia is based on the following three principles:

- Understanding the clinical features of Haemophilia and the appropriateness of the clinical diagnosis;



- b) Using screening tests such as prothrombin time (PT) and activated partial thromboplastin time (APTT) or bleeding time and platelet function tests to identify the potential cause of bleeding (while keeping in mind that normal screening test results do not exclude the possibility of a clinically relevant bleeding disorder being present); and
- c) Confirming the diagnosis by factor assays and other appropriate specific investigations.

1.5. Comprehensive Care

- a) Comprehensive Haemophilia care involves multidisciplinary medical services necessary for the diagnosis, treatment, and management of the condition and its complications.
- b) These services are typically delivered by a Haemophilia Treatment Centre or Haemophilia Comprehensive Care Centre.

1.5.1. Aim of Comprehensive Care

Comprehensive care promotes physical health, psychosocial well-being, and quality of life for people with haemophilia and reduces morbidity and mortality. It is much more than treatment of acute bleeding.

1.5.2. Key Components of Comprehensive Care (Priorities in Treatment)

Priorities in Haemophilia treatment and care include:

- a) Provision of safe blood components such as fresh frozen plasma (FFP) and cryoprecipitate if adequately screened, tested, and/or virus-inactivated where Clotting Factor Concentrates (CFCs) are not available;
- b) Prevention of bleeding and joint damage;
- c) Prompt management of bleeding episodes including physical therapy and rehabilitation after joint bleeds;
- d) Pain management;
- e) Management of musculoskeletal complications;
- f) Prevention and management of inhibitors;
- g) Management of comorbidities;
- h) Dental care;
- i) Quality-of-life assessments and psychosocial support;
- j) Counselling; and
- k) Ongoing patient/family caregiver education and support.

1.5.3. Emergency Care Requirements

Emergency care should be available at all times, with the following essential services and resources:

- a) Coagulation laboratory services with the capacity to perform accurate and precise clotting factor assays including inhibitor testing;
- b) Provision of CFCs (virus-inactivated plasma-derived or recombinant), as well as other haemostatic agents such as desmopressin (DDAVP) and antifibrinolytic agents (tranexamic acid or epsilon aminocaproic acid [EACA]) where available;
- c) Provision of safe blood components (FFP and cryoprecipitate) if adequately screened, tested, and/or virus-inactivated where CFCs are not available; and
- d) Casting and/or splinting and mobility/support aids, as needed.



1.5.4. Comprehensive Care Team (Multidisciplinary Team)

The wide-ranging needs of people with Haemophilia and their families are best met by a multidisciplinary team of healthcare professionals with expertise and experience in haemophilia, in accordance with accepted protocols and practices.

Core Members of **Comprehensive Care Team**:

- a) Medical director,
- b) Nurse coordinator,
- c) Physical Medicine & Rehabilitation specialist, and
- d) Orthopaedic surgeon.

Table 3 Composition of a Comprehensive Care Team

Role	Qualification	Responsibilities
Medical Director	Normally a paediatrician and/or adult haematologist or a physician with training and expertise in managing Haemophilia.	Oversees patient management including ordering diagnostic laboratory tests, prescribing treatment, and monitoring patient health and medical needs.
Nurse Coordinator	Have training in the management of patients with bleeding disorders.	Coordinates care by the multidisciplinary team; Educates patients and families; Provides training for home therapy and other care aspects; Assesses patients' and institutes' initial care where appropriate.
Musculo-skeletal specialists	Physical medicine and rehabilitation specialist, orthopaedic surgeons.	Provide treatment for specific musculoskeletal conditions.
Allied Professionals	Physiotherapist, Occupational therapist.	Educates on preventive measures; Facilitates complete functional recovery after each bleed; Counsels on preserving musculoskeletal health.
Laboratory Specialist	Medical laboratory specialist.	Performs specialized blood tests to establish diagnosis and to monitor therapy, including blood coagulation tests, factor assays, and inhibitor assays.
Psychosocial Counsellor	Preferably a social worker or psychologist.	Conducts psychosocial assessments & provides counselling and/or referrals to community resources.
Other Specialists	Internal Medicine specialist, Transfusion medicine specialist, General Surgeon, Gynaecologist/obstetrician, Paediatric surgeon, Dental Surgeon, Psychiatrist, Chronic pain specialist, Pharmacist, Geneticist, Hepatologist, infectious disease specialist, Immunologist and vocational counsellor.	Dentists with haemophilia experience. Other specialists as needed to address specific medical and health-related issues.
Other Key Members	The patient and family caregivers, Medical social workers & voluntary organizations.	

**Detailed clinical management protocols are essential to ensure continuity of care in the event of personnel changes within the comprehensive care team.*



1.6. Functions of a Comprehensive Care Programme

1.6.1. Coordination and Provision of Care

- a) Enables centralized coordination of care from across multidisciplinary specialties, services, and facilities.
- b) Provides inpatient care (hospital stays) and outpatient care (checkups and other clinic visits) to patients and their families.
- c) People with Haemophilia require periodic monitoring and assessment of their condition and circumstances at least once per year (every 6 months for children).
- d) Referrals to other services (e.g., dentistry, surgery, obstetrics & gynaecology) are arranged through the programme, helping ensure optimal care from specialists with appropriate Haemophilia expertise.
- e) Ongoing collaboration with patients and family caregivers is essential to develop, audit, and refine the comprehensive care management plan.
- f) Smaller centres and family physicians can provide primary care and manage some complications of Haemophilia by infrequent consultation with the Haemophilia comprehensive care centre, especially for patients who live a long distance from the nearest Haemophilia treatment centre.

1.6.2. Patient/ Caregiver Education and Support

People with Haemophilia and family/primary caregivers must receive comprehensive education on Haemophilia care on:

- a) Prevention of bleeds;
- b) Training on essential skills for self-management, including bleed recognition, self-treatment, record-keeping, dental care, and risk management;
- c) Education and training on prophylactic home therapy;
- d) Issues with schooling and/or employment;
- e) Psychosocial and mental health issues;
- f) Bleeding problems and reproductive issues in carriers;
- g) In collaboration with patient organizations, the program helps promote and/or facilitate Haemophilia support groups, educational workshops, and recreational activities such as Haemophilia camps.



1.6.3. Patient Registry and Data Collection

The comprehensive care program facilitates centralized patient registry and data collection. A proposed data sheet is as follows:

General Information
• Name / Age / Sex: • Type of Haemophilia – A / B • Severity – Mild / Moderate / Severe (Factor level %) • Body Weight:
History of Bleeding
• Date & Age of 1st Bleeding: • Bleeding pattern – Spontaneous / Traumatic • Bleeding per year (Annual Bleeding Rate – ABR): • Target Joint (knee / ankle / elbow, etc.): • Other involved joints: • Muscle bleed history (iliopsoas, calf, forearm, etc.) • Recent bleeding episode:
Treatment History
• Type of treatment: On-demand / Prophylaxis • Factor replacement history: • Any history of Factor VIII inhibitor (Yes/No): • Blood transfusion history:
Surgical & Hospital History
• Previous Dental procedure/ Circumcision/ Synovectomy/ Arthrodesis/ Arthroplasty • Any ICU or repeated admission for hemarthrosis
Comorbidity Screening
• HCV / HBV / HIV status, • Other disease: HTN, DM, CKD
Home Facilities
• Ice pack availability • Axillary crutches • Factor VIII / IX • Crepe bandages • Paracetamol and Tranexamic acid • Use of High Commode/Chair commode • Management of Chronic Stage



1.7. Home Therapy and Self-Management

Require Hands-on Training of The Patients and/ or Caregivers.

1.8. Adjunctive Management

1.8.1. Role of Adjunctive Care

- a) Supports factor treatment (CFCs/DDAVP).
- b) Important when factor supply is limited, helping to lessen the product required.

1.8.2. First-Aid for Joint/ Muscle Bleeds (Established Protocols)

- a) **PRICE:** Protection, Rest, Ice, Compression, Elevation.
- b) **POLICE:** Adds Optimum Loading (early, controlled mobilization) instead of full Rest to prevent stiffness.

1.8.3. Other Key Therapies

- a) Antifibrinolytic Drugs
- b) Physical Therapy
- c) Pain Management

1.8.4. Fitness and Physical Activity

Regular physical activity is recommended.

Focus: Bone health, muscle strength, coordination, healthy weight, and positive self-esteem.

Table 4 Low Risk and High-risk Activities

Recommended (Low-Risk)	Avoid (High-Risk)
Non-Contact Sports (e.g., Swimming, Walking, Cycling).	Collision/High-Contact (e.g. Running Football, cricket, Wrestling).

1.8.5. Safety Protocols

- a) **Consult physical therapy specialist:** Always talk to a physical therapy specialist before starting a new activity.
- b) **Prophylaxis & Gear:** Discuss required factor coverage and protective equipment (braces/splints) for target joints.
- c) **Education:** Ongoing education is crucial for informed choices and self-management.

1.9. Pain Management Steps

Avoid aspirin, ibuprofen, naproxen or other conventional NSAIDs.



Table 5 Drugs Used in Pain Management in Haemophilias

Steps	Medication	Notes
Step 1: First Line	Paracetamol/ Acetaminophen.	In children: 10-15 mg/kg per dose, 4-6 hourly. Adults: 500-1000 mg, 4-6 hourly. Max. 4 gm/d. if body weight <50 kg, max. 3 gm/d. Suspensions/Syrup: 120 mg/5 ml. Drops: 80 mg/ml. Tablets 500 mg. Suppositories: 60/125/250/500 mg.
Step 2: If Step 1 is Not Effective (Choose One)	Option A: Selective COX-2 Inhibitor (e.g., celecoxib, meloxicam).	Celecoxib: 100 mg OD to 200 mg BD. Children (>2 year): 10-25 kg: 50 mg 12 hourly. >25 kg: 100 mg 12 hourly. Meloxicam: 15 mg/d. Children > 2 years, max. 7.5 mg/d.
	Option B: Paracetamol/ Acetaminophen plus Codeine (3-4 times/day).	Not available in our country. Codeine is contra-indicated in age <12 year.
	Option C: Paracetamol/ Acetaminophen plus Tramadol (3-4 times/day).	1-2 tab 6 hourly, maximum 5 days. Not in children.
Step 3: Strong Opioid	Fentanyl patches, buccal tablet, Pethidine IV; Nalbuphine, Morphine.	Morphine: Use a slow-release product for baseline pain. Supplement with a rapid-release product as an 'escape' (breakthrough) analgesic. If rapid-release is used 4 times/day, increase the slow-release dose. Fentanyl patches: costly, but available. Should be advised by specialist.

1.10. Dental Care and Management**1.10.1. Primary Goal**

- Maintain good oral health (prevent gingivitis, caries, and periodontal disease).
- Why:** To prevent serious gum bleeding and avoid the need for major dental surgery.

1.10.2. Key Principles

- Priority Group:** People with Haemophilia are a priority for preventive dental care due to the *risk of severe/ life-threatening complications from prolonged bleeding after treatment.*
- Access to Expertise:** Ensure access to dental treatment and regular preventive care at a designated centre with expertise in managing haemophilia.



1.10.3. Oral Care

Table 6 WFH Oral Hygiene Recommendations

WFH Oral Hygiene Recommendations	Action
All people with Haemophilia	Brush twice daily using a soft/medium brush and fluoridated toothpaste.
Technique	"Spit, but don't rinse" after brushing to maximize fluoride benefit.
Plaque removal	Encourage use of dental floss or interdental brushes.
Adaptations	Use modified or electric toothbrushes if joint restrictions are present.
Children less than 6	Require parental/caregiver supervision of toothbrushing.

1.10.4. Dental Surgery and Invasive Procedures: *Managing Bleeding Risk*

Table 7 WFH Recommendations for Dental Procedures

Intervention	Action
Antifibrinolytics (e.g., Tranexamic Acid)	Effective adjunct pre- and post-operative to reduce the need for factor replacement .
Local Measures (Extractions)	Use wound suture, topical antifibrinolytics, oxidized cellulose, and fibrin sealant. Maintain a soft diet and undertake careful brushing around the wound site for a minimum of 3-5 days postoperatively to avoid disturbing the clot. Restorative work (e.g., fillings) and professional cleanings typically do not require factor replacement .
Local anaesthesia	Essential part of pain and anxiety management. Most dental injections pose a low risk when - delivered by a dental care professional - with a vasoconstrictor - delivered slowly with a single-use fine-gauge needle. Higher-risk intramuscular oral injections should follow systemic haemostatic measures preoperatively.
Antibiotics	Prescribe only if clinically indicated.

1.11. Transition From Paediatric to Adult Care

1.11.1. Core Goal

Support young patients to develop **self-management knowledge and skills** before transferring to adult care.

1.11.2. Adherence Risks

Challenge: Adherence to prophylaxis often drops in adolescence/young adulthood (ages 13-30).



1.11.3. Key Barriers

Low perceived risk (from prior good care), desire to be "normal," forgetfulness, and high treatment burden.

1.11.4. Care Team Strategy

- a) **Structure:** Use a **structured transition plan** and readiness assessments.
- b) **Skills:** Provide targeted education on **prophylaxis adherence** and self-infusion skills (e.g., via Haemophilia camps).
- c) **Collaboration: Joint visits** with paediatric and adult haematologists are encouraged to ensure a smooth hand-off.



CHAPTER 02 Laboratory Diagnosis and Monitoring

2.1. Diagnosis of Haemophilia as a Bleeding Disorder

- a) Abnormal bleeding versus normal bleeding
- b) Inherited defect vs. acquired defect
- c) Coagulation or secondary haemostatic defect (e.g. Haemophilia) vs primary haemostatic defect
- d) Gender predominance
- e) Family history and inheritance pattern in most (75%-85%) instances.
- f) Laboratory confirmation

2.2. Abnormal Bleeding

- a) Any bleeding without any trauma or cannot be objectively appropriated with degree of trauma.
- b) Can be overt (from body orifices, cut injury) or covert (petechiae, ecchymosis, bruise, haematoma, haemarthrosis, brain, gut wall, etc.). Haematoma or haemarthrosis in bleeding disorder, e.g., Haemophilia, continue to expand with increasing pain and may develop after a reasonable time gap after a minor trauma unlike normal traumatic haematoma which is immediate.
- c) Almost invariably from multiple sites except few cases of vascular anomaly (e.g., hereditary haemorrhagic telangiectasia).
- d) Recurrent iron deficiency anaemia without apparent inadequate nutrition or localized site of chronic blood loss. Or requiring hospitalization or blood transfusion after a procedure (e.g., circumcision, dental extraction) or minor cut requiring surgical intervention.
- e) Some subtle bleeding may require objective assessment by appropriate scoring system warrant referral to specialized centre to mark as abnormal.

2.3. Inherited Bleeding

- a) Inherited bleeding is invariably recurrent
- b) Generally, symptoms are from early childhood

2.4. Coagulation Defect

- a) Haemophilias are defect of coagulation, also called, secondary haemostatic defect; more specifically that of intrinsic pathway of coagulation.
- b) Coagulation defects are distinct from primary haemostatic defects related to platelet number or platelet or vascular function.

Table 8 Differences Between Coagulation Defects and Primary Haemostatic Defects

Character	Coagulation defects	Primary haemostatic defects
Onset of symptom in relation to trauma	Generally delayed	Invariably immediate
Deep seated bleeding like haematoma, haemarthroses	Common	Uncommon
Superficial bleeding like petechiae, ecchymosis, bleeding from minor scratch	Uncommon	Common
Family history	Common	Uncommon

However, these distinctions may be blurred, especially in young children.



2.5. Gender Predominance

- a) As X-linked recessive disorders, haemophilias generally affect males.
- b) However, females rarely have haemophilia in certain circumstances. Females with such suspicion should be referred to specialized centre/HTC for further evaluation.

2.6. Family History and Inheritance

- a) History of affected male relative(s) in maternal kindred – maternal grandfather, maternal uncles, male maternal cousins (sons of mother's sister).
- b) Consanguinity is insignificant except in certain females with haemophilia.
- c) Affected children with non-affected consanguineous parent indicate autosomal recessive disorders like coagulation disorders other than haemophilia, platelet functional disorder and most types of von Willebrand disease.

2.7. Laboratory Confirmation

2.7.1. Basic Coagulation Tests

Laboratory diagnosis is the most important part of diagnosis of Haemophilia and other bleeding disorders. Basic coagulation laboratory facility is essential for initial diagnosis of Haemophilia and other categories of bleeding disorders. Basic coagulation tests include -

- a) CBC (for platelet count): $>50,000/\text{cmm}$ is haemostatically adequate in absence of any surgical challenge.
- b) Bleeding time: Normal value <8 minutes in modified Ivey's method.
- c) Prothrombin Time (PT): Normal value is 12 - 15 seconds, established by individual laboratories.
- d) Activated Partial Thromboplastin Time (APTT): 28 - 33 seconds, established by individual laboratories.

PT & APTT are clotting times. Other clotting times are Thrombin Time (TT), Russel Viper Venom Time (RVVT), etc. These clotting times test integrity and abnormality of certain specific pathway or portions of pathway of coagulation cascade and are quite different from crude whole blood clotting time, popularly known as CT. For understanding the abnormalities of clotting times easily following diagram (Figure 1) to be kept in mind.

2.7.2. Typical Pattern of Basic Coagulation Test Results in Haemophilias

In haemophilias, there is defect in intrinsic pathway of coagulation.

Platelet count	: Haemostatically adequate
Bleeding time	: Normal
PT	: Normal
APTT	: Prolonged

This pattern is also seen in Factor XI deficiency (sometimes called hHaemophilia C). In cases with above scenario, reduced activity of Factor VIII (FVIIIc) and of Factor IX (FIXc) indicate Haemophilia A and Haemophilia B respectively. It should be noted that, factor assay usually means factor *activity* assay, factor *level* measurements are not usually done.



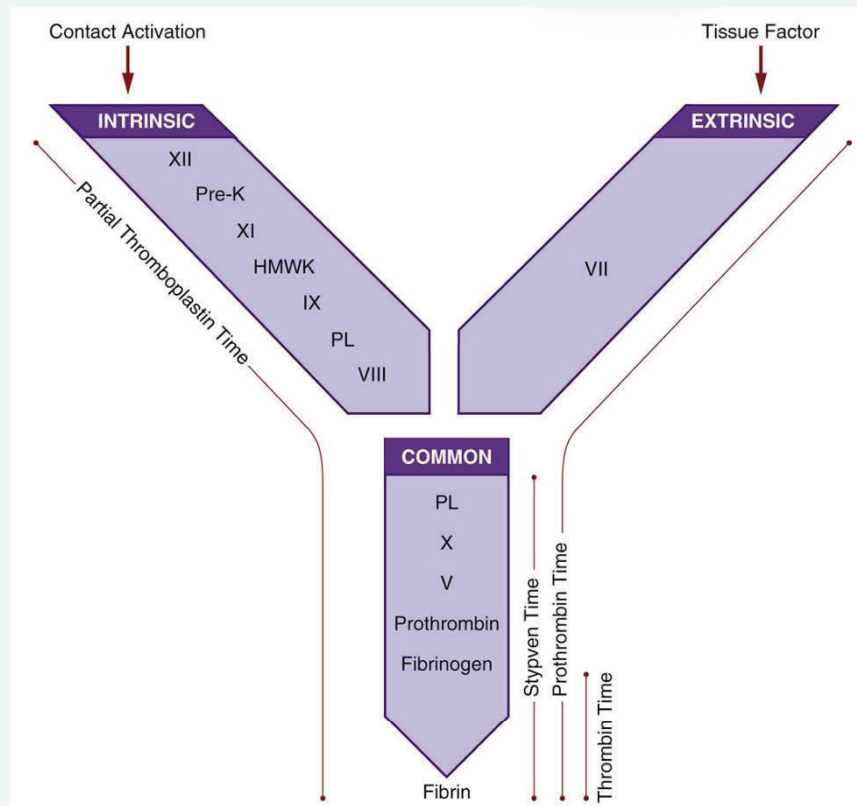


Figure 1: Coagulation Pathways

2.7.3. Interpretation of Some Other Pattern

Table 9 Basic Coagulation Test Patterns in Some Conditions Other Than Haemophilias

Test Patterns		Interpretation
Platelet count	: Haemostatically adequate	Abnormality in common pathway: Fibrinogen (FI), Prothrombin (FII), Factor V or Factor X.
Bleeding time	: Normal	
PT	: Prolonged	
APTT	: Prolonged	
Platelet count	: Haemostatically adequate	Abnormality in extrinsic pathway: Factor VII. This pattern is also common in early liver disease.
Bleeding time	: Normal	
PT	: Prolonged	
APTT	: Normal	
Platelet count	: Haemostatically adequate	Quantitative defect of vWF: Type 3 or relatively severe type 1.
Bleeding time	: Prolonged	
PT	: Normal	
APTT	: Prolonged	
Platelet count	: Low	Disseminated intravascular coagulation (DIC)
Bleeding time	: NA*	
PT	: Prolonged	
APTT	: Prolonged	

*BT is non-contributory in low (haemostatically inadequate) platelet count.

2.8. Inhibitor Screening

- a) Inhibitor against factors VIII and IX are neutralizing antibodies and they are time dependent inhibitor.
- b) Please see the section 'Management of Inhibitor' to see when patient's blood is to be tested for presence of inhibitor.
- c) All inhibitor positive cases should undergo Bethesda assay for inhibitor titre.

2.9. Laboratory Monitoring of Treatment with Factor Concentrates

- a) Laboratory monitoring of treatment with factor concentrate is recommended to
 - i. Asses therapeutic efficacy, especially while on intensive therapy, such as following surgery, acute bleed, etc.
 - ii. To look at the possibility of development of inhibitor. Decreased factor recovery in comparison to previous experience may be the 1st sign of inhibitor.
- b) Monitoring is done by peak level and/or trough level of factor.

2.9.1. Technical Aspect for Test Validity

- a) Bleeding time test is contraindicated, hence non-contributory while platelet count is <20,000/cmm.
- b) Bleeding time to be done in modified Ivey's method following Standard Operating Procedure (SOP) strictly by a technologist experienced to do that test.
- c) Fasting is not necessary before collection of blood for investigation of possible bleeding disorders.
- d) Whenever possible, patients should avoid medications that can affect test results such as acetylsalicylic acid (ASA), which can severely affect platelet function for 7-10 days.
- e) Levels of factor VIII (FVIII) and von Willebrand factor (vWF) may be temporarily elevated by strenuous exercise, stress, or inflammation enough to affect the accuracy of diagnosis. Factor VIII/vWF levels increase during pregnancy.

2.9.2. Sample Collection, Preservation and Transportation

- a) The sample should preferably be collected near the laboratory to ensure quick transport so that, test can be performed within 4 hours of sample collection. It should remain capped during transport.
- b) Results of tests can change according to the interval between collection and testing and according to sample storage conditions. Higher temperatures (>25°C) lead to loss of FVIII activity over time, whereas cold storage (2-8°C) may lead to cold activation of several proteolytic systems. Storage of blood samples at 2-8°C before processing can lead to loss of FVIII and vWF sufficient to cause unaffected patients to be misdiagnosed with von Willebrand disease (vWD).
- c) The sample must be collected within 1 minute of tourniquet application without prolonged venous stasis.
- d) Blood should be withdrawn into a plastic syringe or an evacuated collection system. The needle should be 19-21 gauge for adults and 22-23 gauge for small children. Collection through peripheral venous catheters or non-heparinized central venous catheters can be successful for many haemostasis tests.



- e) Blood from an indwelling catheter should be avoided for some coagulation tests, particularly if platelet aggregation testing is being performed.
- f) Frothing of the blood sample should also be avoided. It is only necessary to discard the first 2 mL of blood collected if blood is collected through a catheter. The sample should be collected in citrate tubes containing 0.105 M - 0.109 M (c3.2%) aqueous trisodium citrate dihydrate, maintaining the proportion of blood to citrate at a 9:1 ratio. If the tube contains less than 90 % of the target volume, results may be adversely affected, and prolongation of PT and APTT is expected when tubes contain less than 80 % of target volume.

2.9.3. Referral to Advanced Coagulation Laboratory Facility / HTC

- a) For FVIIIc and FIXc assay to identification and severity assessment of Haemophilia A and Haemophilia B,
- b) For further precise diagnosis of other haemostatic abnormality patterns except DIC,
- c) All suspected female patients with Haemophilia,
- d) Suspected patient with inhibitor when inhibitor screening facility is not available at local laboratory,
- e) For Bethesda assay in inhibitor screened positive cases.



CHAPTER 03 Haemostatic Agents and Regular Prophylaxis in Haemophilia

The mainstay of treatment is the correction of factor deficiency and, therefore, bleeding tendency. There are two main therapeutic aims:

- a) Prophylaxis is aimed at **prevention** of spontaneous bleeds and excessive bleeding with trauma and surgery, thus altering the clinical phenotype (normalizing or reducing severity) of the disorder. Treatment for bleeding or impending bleeding, without regular prophylaxis, is called on-demand treatment.
- b) Management of **acute** bleeds, which may be spontaneous or traumatic.

In this guideline, prophylaxis is discussed first because it is the universal standard of management of Haemophilia. Management of acute bleeds, in the patients on prophylaxis or patients without prophylaxis, is discussed in the next chapter.

To treat and prevent bleedings in Haemophilia patients, different types of pharmacological agents are used. Those can be classified into the following types. Some of them are used in both types of haemophilias.

3.1. Haemostatic Agents

- a) **Clotting Factor Concentrates (CFCs)** (used for both prophylaxis and acute bleeds. Can be natural, i.e., derived from plasma, or artificial, i.e., manufactured in laboratory by recombinant technology. The natural ones should be viral-inactivated.)
 - i. Standard half-life (SHL) FVIII CFCs
 - ii. Extended half-life (EHL) FVIII CFCs
 - iii. Standard half-life (SHL) FIX CFCs
 - iv. Extended half-life (EHL) FIX CFCs
- b) **Bypassing Agents**
 - i. Recombinant activated factor VIIa (both in haemophilias A and B, **very costly**)
 - ii. Activated Prothrombin Complex Concentrate (**aPCC**) (both in haemophilias A and B, **not easily available**)
- c) **Other Plasma Products**
 - i. Cryoprecipitate (only in haemophilia A)
 - ii. FFP
- d) **Other Pharmacological Options**
 - i. Desmopressin (DDAVP) (only in moderate haemophilia A)
 - ii. Tranexamic acid
 - iii. Epsilon aminocaproic acid
- e) **Non-Factor Replacement Therapies**
 - i. Emicizumab – Factor VIII mimetic (used only as *prophylactic* in haemophilia A)



3.2. Prophylaxis in Person with Haemophilia

- Regular prophylaxis describes the institution of regular treatment with replacement or non-replacement therapies to prevent spontaneous bleeding.
- Regular prophylaxis is superior to on-demand treatment (Table X) (treatment of bleeds and during surgery), and it represents the current standard of care for patients with severe Haemophilia.

Table 10 Summary Table: Prophylaxis vs On-Demand

Treatment Aspect	Prophylaxis	On-Demand Treatment
Bleed Prevention	Prevents most bleeds	Treats after bleeds occur
Joint Health	Preserves joints, prevents arthropathy	Progressive joint damage
Quality of Life	Comparable to non-haemophilic	Reduced due to disability, pain
Risk of Severe Bleed	Markedly reduced	Not reduced
Endorsement	Universal standard of care	Accepted only where factor is limited

3.2.1. Prophylaxis Types on the Basis of Agents Used

- Clotting Factor Concentrates (CFCs) (also called regular replacement therapy): It is given regularly to prevent bleeding, unlike episodic or on-demand therapy, which is only given during a bleed or surgery.
- Non-Factor Therapies (*only for haemophilia A*): New treatments like Emicizumab (HEMLIBRA) subcutaneous injections are redefining prophylactic therapy.

3.2.2. Prophylaxis Types on the Basis of Time of Initiation of Prophylaxis

Table 11 Prophylaxis Types on the Basis of Time of Initiation of Prophylaxis

Prophylaxis Types	Application
Primary prophylaxis	Regular continuous prophylaxis started in the absence of documented joint disease, determined by physical examination and/or imaging studies, and before the second clinically evident joint bleed and 3 years of age.
Secondary prophylaxis	Regular continuous prophylaxis initiated after 2 or more joint bleeds but before the onset of joint disease; this is usually at 3 or more years of age.
Tertiary prophylaxis	Regular continuous prophylaxis initiated after the onset of documented joint disease. Tertiary prophylaxis typically applies to prophylaxis commenced in adulthood.



3.2.3. Special Consideration Regarding Prophylaxis

Table 12 Special Consideration Regarding Prophylaxis

When to start?	Prophylaxis with FVIII or FIX is initiated after the first spontaneous bleed or in the second year of life
Aimed to keep trough levels (lowest level between infusions)	• Around 1% • Recent guidance has recommended trough levels of 3- 5% to reduce joint damage further
Venous access	For regular intravenous infusions, especially in the very young and older patient groups, may be an issue. Various strategies – including venous access devices, e.g. Portacath or permanent arterio-venous fistulae.
Will prophylaxis ensure bleeding-free life?	No. With a well-planned prophylactic regimen, patients can expect to have 0-2 spontaneous bleeds in a year.

3.2.4. Prophylaxis with Replacement Therapy

Table 13 Conventional Factor Prophylaxis with Standard Half-life (SHL) Clotting Factor Defined According to its Intensity

Prophylaxis intensity	Haemophilia A	Haemophilia B
High-dose prophylaxis	25-40 IU FVIII/kg thrice per week (>4000 IU/kg per year)	40-60 IU FIX/kg twice per week (>4000 IU/kg per year)
Intermediate-dose prophylaxis	15-25 IU FVIII/kg twice per week (1500-4000 IU/kg per year)	20-40 IU FIX/kg twice per week (2000-4000 IU/kg per year)
Low-dose prophylaxis (with escalation of dose intensity, as needed)	10-15 IU FVIII/kg every 2-3 days (1000-1500 IU/kg per year)	10-15 IU FIX/kg twice per week (1000-1500 IU/kg per year)

It is not as yet determined what constitutes high-, intermediate-, and low-dose prophylaxis with Extended half-life (EHL) CFCs and whether these definitions should be revised.



CHAPTER 04 Treatment of Specific Haemorrhages and Surgical Prophylaxis

4.1. Introduction

Prolonged or excessive bleeding is the principle clinical problem of Haemophilia. In general, bleeding is proportional to extent of deficiency of factors, though individual variation exists. The main treatment for bleeding episodes in patients with severe Haemophilia is prompt clotting factor replacement therapy and rehabilitation. However, different types of bleeds and bleeding at particular anatomical sites may require more specific management with additional measures. It is important to consult the appropriate specialists for the management of specific haemorrhages. The amount and type of haemostatic agent used for bleeding and duration of treatment depends on the site and severity of bleeding.

On the other hand, surgical prophylaxis is also an on-demand treatment, different from regular prophylaxis discussed in the previous chapter. That is why it is also discussed in this chapter.

4.2. Families Should be Told:

- a) Early treatment and follow-up can prevent most long-term complications.
- b) Keep ice pack and necessary clotting factors in refrigerator for emergency use at home.
- c) Keep a record of every bleed and treatment episode.
- d) Never use aspirin or over-the-counter NSAIDs.
- e) Seek medical help early for new joint swelling, muscle pain, or soft tissue masses.

Table 14

Specific Haemorrhage Site and Immediate Actions to be Taken for That Even Before Factor Replacement

Type of Haemorrhage	Immediate actions
1. Joint haemorrhage	PRICE/POLICE approach (see page 20.), Table 15
2. Central nervous system and intracranial haemorrhage	Hospitalization and evaluation
3. Throat and neck haemorrhage	Hospitalization and evaluation Consult specialist
4. Gastrointestinal/abdominal haemorrhage	Hospitalization Endoscopy if clinically indicated
5. Renal haemorrhage/haematuria	Adequate hydration & bed rest. No antifibrinolytics
6. Ophthalmic haemorrhage	Refer to an ophthalmologist
7. Oral haemorrhage	Apply direct pressure and/or sutures and use antifibrinolytics
8. Epistaxis/nose bleed	Elevate the head and apply cold compression to the nasal area
9. Lacerations and abrasions	Suture the wound if appropriate and provide haemostatic coverage for suture removal
10. Soft tissue haemorrhage	Evaluate for severity, possible neurovascular involvement



Table 15 Management of Joint Haemorrhage

Target joint	A single joint in which 3 or more spontaneous bleeds have occurred within a consecutive 6-month period.
The onset of bleeding into a joint	Often experienced by patients as a sensation “Aura”, - described as a tingling sensation and tightness within the joint that precedes the appearance of clinical signs. A joint haemorrhage (haemarthrosis) is defined as an episode characterized by a combination of any of the following: • Increasing swelling or warmth of the skin over the joint • Increasing pain or • Progressive loss of range of motion or difficulty in using the limb as compared with baseline
Management	
Clotting factor replacement therapy	Severe haemarthrosis – should be treated immediately with IV clotting factor concentrate replacement infusion(s) until there is bleed resolution. Moderate or mild joint bleeding – Patient should be given one IV infusion of clotting factor concentrate, repeated if clinically indicated, depending on the resolution of the bleed.
Pain management	Pain management is discussed in Table 5, page 8.
Adjunctive care and Rehabilitation (Please see page 37 for further details)	A key element of managing the symptoms of hemarthrosis has been RICE (rest, ice, compression and elevation). Immobilization contributes to improvement of joint bleeds. Therefore, PRICE, which includes P for “protection” of the injured area, is often recommended. To avoid prolonged immobility and its complication (e.g., flexion deformity), POLICE, where R (rest) replaced by OL (‘optimal loading’), is advised now-a-days. Application of ice should not be direct and only for 15-20 minutes after bleeding. Weight bearing should be postponed until patient is comfortable to weight bear without significant pain. Physical therapy/exercises under clotting factor coverage should begin as soon as the pain symptoms stop.
Arthrocentesis	Arthrocentesis is recommended only if there is a tense, painful hemarthrosis or suspicion of infection. Routine arthrocentesis is not advised.
Definitions of response to treatment	
Excellent	Complete pain relief and/or complete resolution of signs of continuing bleeding after the initial infusion within 8 h and not requiring any further factor replacement therapy within 72 h after onset of bleeding.
Good	Significant pain relief and/or improvement in signs of bleeding within approximately 8 h after a single infusion but requiring more than 1 dose of factor replacement therapy within 72 h for complete resolution.
Moderate	Modest pain relief and/or improvement in signs of bleeding within approximately 8 h after the initial infusion and requiring more than 1 infusion within 72 h but without complete resolution.
None	No or minimal improvement, or condition worsens, within approximately 8 h after the initial infusion.



Table 16 Management of Central Nervous System (CNS) and Intracranial Haemorrhage

	It is a Medical Emergency • CNS bleeds or bleed-related symptoms, clotting factor replacement therapy should be administered immediately before investigations are performed. • If a bleed is confirmed, maintain the appropriate factor level for 10-14 days. • Immediate medical evaluation and hospitalization are required, including a computed tomography (CT) scan or magnetic resonance imaging (MRI) of the brain, including neurological consultation. Ultrasound examination may be considered in children.
Factor replacement therapy	
Secondary prophylaxis	Secondary prophylaxis is recommended to prevent bleed recurrence.

Table 17 Management of Throat and Neck Haemorrhage

	It is a Medical Emergency • Gently elevate the head to help reduce airway obstruction due to the haemorrhage. • Treat immediately with CFC to raise the patient's factor level. • Protective factor levels should be maintained until symptoms resolve. • Patients with throat and neck bleeding and local infection, antifibrinolytics should be started to treat the bleed and antibiotics to treat the infection.
Factor replacement management	

Table 18 Management of Gastrointestinal/abdominal Haemorrhage

	It is a Medical Emergency
Presentation	Acute gastrointestinal (GI) haemorrhage may present as haematemesis, haematochezia (rectal passage of fresh blood), or melaena depending on level of bleeding. Abdominal pain, tenderness, unexplained shock may be presentation of concealed GI bleeding.
Management	• All patients with GI bleeds should be hospitalized. • Must be treated as soon as possible following injury and/or the onset of the earliest symptoms with Clotting Factor Concentrate (CFC) replacement therapy. Continue CFC support until haemorrhage has stopped. • Antifibrinolytics are often effective adjunctive therapy for both haemophilias. Concurrently, Activated Prothrombin Complex Concentrate (APCC) may be used. • Treat the origin of the haemorrhage, monitor vitals and haemoglobin levels confirmation of regularly, and treat anaemia or shock as needed.
Diagnosis	• Perform a clinical assessment of the patient with a physical examination, pain assessment, and history taking including bleed history. • Perform endoscopy, if clinically indicated, in any patient with dropping haemoglobin levels or deteriorating vitals. • An ultrasound and/or CT scan can identify the site and extent of abdominal bleeding. Consult with a specialist.



Table 19 Management of Renal Haemorrhage/ Haematuria

Clinical features	• Uncommon but can occur spontaneously or following trauma. • May be associated with pain/dysuria. • Often due to local lesions. • Anaemia may be significant.
Management	
Check for urinary tract infection	1. In mild haematuria without significant pain, Adequate hydration (3 L/sq.m body surface area/day). 2. Avoid DDAVP when hydrating intensively. 3. If bleeding is severe (gross haematuria/clot colic/significant anaemia) or mild but persistent (>3 days) factor replacement (to achieve 20-40% level repeated every 12-24 hours, as necessary) may be required. 4. Urology opinion & radiology. 5. Blood transfusion may be needed if anaemia is severe.
No Antifibrinolytic Drugs should be used	

Table 20 Management of Ophthalmic Haemorrhage

Management	• Bleeding in the eye is uncommon unless associated with trauma or infection. • Should be treated immediately and maintain until the aetiology of the bleed can be defined, treatment with consultation with a specialist. • Regular physical examination should be carried out every 6-8 hours.
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Table 21 Management of Oral Haemorrhage

Aetiology	Common causes • Dental extraction • Gingival bleeding • Trauma Less common causes • Self-injury • Shedding of deciduous (baby) teeth • Recent dental surgery.
Management	In dental bleeding, direct pressure should be applied on the tooth socket using a damp gauze swab and maintained for at least 15-30 minutes. In oral bleeding, the site of bleeding should be identified and direct pressure and/or sutures applied, if possible.



Table 21 Management of Oral Haemorrhage (Cont'd)

(Cont'd) Management	If persistent oral bleeding: • Systemic treatment e.g., CFC replacement, DDAVP (in Haemophilia A). • Continue direct pressure on the area with gauze soaked with antifibrinolytics. • Local anaesthesia with adrenaline/epinephrine to aid local vasoconstriction. • Sutures for wound closure. • Application of local haemostatic agents, e.g., oxidized cellulose, thrombin, fibrin sealant. • Oral or topical antifibrinolytics as a mouthwash or paste. • Monitoring of vital signs. • Treatment for anaemia, if required. If haemostasis is achieved, advise: • Use systemic and/or topical antifibrinolytic agents for 5-7 days. • Avoid sports and intensive exercises for 3-5 days. • Eat a soft diet with no vigorous mouth rinsing for 3-5 days. • Avoid or reduce smoking for at least 24 hours. • Consider use of a soft splint to protect the wound.
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Table 22 Management of Epistaxis

General management	Epistaxis can occur with injury or irritation to the nasal mucous membrane. Clotting factor replacement therapy is often not necessary unless bleeding is severe or recurrent. • Head should be elevated and cold compression applied to the Little's area of the nose. • Nasal packing should be avoided as it can cause bleeding when removed.
Acute epistaxis	• Place the patient's head in a forward position to avoid swallowing of blood and have the patient gently blow out weak clots. • Apply firm continuous pressure with a gauze soaked in ice water to the anterior nasal septum, i.e., Little's area, for 5-10 minutes. • An antifibrinolytic agent applied locally using a soaked gauze is helpful. • Antihistamines and decongestant medications. • For infection administer antibiotics. • If epistaxis is prolonged or occurs frequently, evaluate for anaemia. • In severe and recurrent nosebleeds – specialist consultation. • Increasing the humidity of the environment. • Applying gels (e.g., petroleum jelly or saline drops/ gel) to the nasal mucosa.
Preventive measures	• Saline spray. • Medications such as antihistamines, decongestant medications, and antibiotics as directed.



Table 23 Management of Soft Tissue Haemorrhage

Site of involvement	Muscles, ligaments, tendons and subcutaneous spaces.
Management	• Application of firm pressure and ice may be helpful. • Clotting factor replacement therapy may not be necessary for most of the superficial soft tissue bleeding. • Immediate clotting factor replacement therapy is required in open compartmental haemorrhage, such as in the retroperitoneal space, scrotum, buttocks, or thighs. • Local application of ice and adjunct treatment to reduce pain, inflammation should be continued.

4.3. Practice Patterns in CFC Replacement

Two types of practices are followed:

- Lower-dose practice pattern
- Higher-dose practice pattern

Lower-dose practice pattern can be followed in low resource countries like Bangladesh.

Table 24 Practice patterns in CFC Replacement for Haemorrhages

Type of haemorrhage	Haemophilia A		Haemophilia B		Remarks
	Peak factor FVIII level (IU/dL)	Treatment duration in Days	Peak FIX level (IU/dL)	Treatment duration (d)	
Joint	10-20	1-2	10-20	1-2	
Superficial muscle/no NV compromise (except iliopsoas)	10-20	2-3	10-20	2-3	
Iliopsoas or deep muscle with NV injury or substantial blood loss					
Initial	20-40	1-3	15-30	1-3	
Maintenance	10-20	8-14	10-20	8-14	
Throat and neck					
Initial	30-50	1-3	30-50	1-3	
Maintenance	10-20	4-7	10-20	4-7	
Gastrointestinal					
Initial	30-50	1-3	30-50	1-3	
Maintenance	10-20	4-7	10-20	4-7	
Renal/haematuria	20-40	3-5	15-30	5-7	Do NOT use anti-fibrinolytics
Deep laceration	20-40	5-7	15-30	5-7	
Intracranial Bleeding	50- 80	1-3	50- 80	1-3	
Initial	30-50	4-7	30-50	4-7	
Maintenance	20-40	8-14	20-40	8-14	

*Lower CFC replacement levels require much closer observation for effectiveness of bleeding control, with a potentially greater chance of requiring additional CFC replacement to achieve the target plasma level as well as the haemostatic and musculoskeletal outcomes. Abbreviations: CFC- clotting factor concentrate; NV- neurovascular.



4.4. Before Surgery: Preoperative Assessment and Planning

4.4.1. Stepwise Approach

- a) **Confirm Diagnosis:** Always verify type and severity of Haemophilia (Haemophilia A or B) with laboratory tests before any surgery. Never depend solely on past records.
- b) **Inhibitor Testing:** Check if the patient has or ever had inhibitors (antibodies) against factor VIII or IX, as this dictates the treatment plan.
- c) **Comorbidity Review:** Assess for liver, kidney, or cardiac problems, and check for drugs/supplements that increase bleeding risk (e.g., NSAIDs, aspirin, fish oil, herbal supplements) and try to stop them 7-14 days before surgery.
- d) **Access to Treatment:** Ensure the centre where surgery is planned has ready access to Clotting Factor Concentrates (CFCs), or alternatives like FFP/cryoprecipitate if CFCs unavailable. Haematologist input is essential for complex or major surgeries.
- e) **Patient and Family Preparation:** Counsel about risks, bleeding signs, and infusion plans. For those not able to self-infuse, arrange for IV access and support post-surgery.
- f) **Make a haemostasis Plan:** Write down and circulate a clear, simple plan:
 - i. Diagnosis and inhibitor status
 - ii. Type of surgery
 - iii. Doses and timing of factor or other agents pre/during/post-op
 - iv. Monitoring schedule (labs and clinical)
 - v. Referral contacts for emergencies

4.4.2. Preoperative Management

- a) **Minor Surgery (including uncomplicated dental extraction):**
 - i. 50 to 80 IU/dL (or % of normal).
 - ii. A single dose may be sufficient; repeat as needed after 24 to 48 hours until bleeding stops, and healing is achieved.
- b) **Major Surgery**
 - i. 60 to 100 IU/dL (or % of normal).
 - ii. Consider repeat dosing after 6 to 10 hours, then every 24 hours for the first 3 days.

4.4.3. During Surgery: Practical Points

- a) Always schedule surgeries early in the day/week to ensure access to labs and blood bank if more support is needed.
- b) Ensure factor products or alternatives ready in theatre.
- c) Have infusion/IV access ready at all times.
- d) Close attention to gentle handling—avoid unnecessary IM injections, use padding for joints, and minimize mucosal trauma during airway interventions.
- e) For detailed protocols, consult your local haemophilia comprehensive care centre or WFH-aligned guidance.
- f) Always individualize plans based on patient, procedure, and available resources.



4.4.4. Postoperative Care

- Continue Clotting Factor support for several days depending on procedure (see tables above). Taper as healing progresses.
- Watch for delayed bleeding – educate staff and family on warning signs.
- Early Mobilization and Physiotherapy – start as soon as haemostasis is stable. Factor infusions may be timed before physiotherapy to reduce risk.

Table 25 Practice Patterns in CFC Replacement for Surgeries

Surgical condition	Haemophilia A		Haemophilia B		Remarks
	Peak factor FVIII level (IU/dL)	Treatment duration in Days	Peak FIX level (IU/dL)	Treatment duration (d)	
Surgery (major)					
Pre- operative	60-80	--	50- 70	--	Within 2 hours of surgery
Post- operative	30-40	1-3	30-40	1-3	
	20-30	4-6	20-30	4-6	
	10-20	7-14	10-20	7-14	
Surgery (minor)					
Pre-operative	40-80	--	40-80	--	Within 2 hours of surgery
Post-operative	20-50	1-5	20-50	1-5	

4.4.5. General Guideline on Dosing and Intervals of CFC Replacement

The dosing and intervals for Factor VIII and Factor IX replacement depends on formulations of the factors.

As a general guide, dosage calculation for plasma-derived or recombinant standard half-life (SHL) Factor VIII is done by multiplying the patient's weight in kilograms by the desired FVIII level in IU/dL, then multiplying by 0.5 .

For example, in a severe haemophilia A patient (factor VIII level <1%) of 50 kg weight, if the desired FVIII level is 40IU/dL, the dose will be $50 \text{ kg} \times 40 \text{ (IU/dL level desired)} \times 0.5 = 1000 \text{ IU}$ of FVIII. As the half-life of FVIII is 8-12 hours, the dose should be repeated 12 hourly.

On the other hand, standard half-life (SHL) Factor IX dose is calculated directly by multiplying the haemophilia B patient's weight in kilograms by the desired FIX level in IU/dL As the half-life of FIX is 18-24 hours, the dose should be repeated daily.



CHAPTER 05 Management of Inhibitors

5.1. Definition

- a) **IgG alloantibodies to exogenous clotting factors** VIII (FVIII) or IX (FIX) that neutralize the function of infused Clotting Factor Concentrates (CFCs).
- b) Measured by the technique **Bethesda assay or Nijmegen-modified Bethesda assay**.
- c) **One Bethesda unit (BU)**: amount of antibody that will destroy 50% of the coagulation factor activity in 2 hours.
- d) **Positive inhibitor**: ≥ 0.6 Bethesda units (BU) for FVIII and ≥ 0.3 BU for FIX.

5.2. When to Suspect

Should be suspected in any haemophilia patient who fails to respond clinically to adequate CFC replacement therapy, particularly in previously responsive patient.

5.3. Types

- a) **Low-responding inhibitor < 5.0 BU**: Transient, drops below the definition threshold within 6 months of initial documentation, without any change in treatment regimen and despite antigenic challenge with CFCs.
- b) **High-responding inhibitor ≥ 5.0 BU**: Persistent, may fall or become undetectable after a long period without CFC exposure; however, they increase 3-5 days after re-challenge with CFCs (anamnestic response).

5.4. Incidence of Inhibitors

- a) For Haemophilia A, approximately 30% of the patients will develop inhibitors sometime in their lifetime. Among the patients who develop inhibitor, 79% develop that within the first 20 exposures of factor and almost all patients develop inhibitors within the first 75 exposures. (This is corrected because, total incidence rate was missed, and if 79% patients with inhibitor develop inhibitor in the first 20 exposures, the remaining 21% develop inhibitor from the 21st to the 75th exposure).
- b) For Haemophilia B, incidence rate of inhibitor development is not $> 10\%$, and most inhibitors occur after a median of 9-11 exposures, and before 20 exposures, typically before 2 years of age.

5.5. Inhibitor Screening

Initially every 6 months, and then annually for newly diagnosed Haemophilia A and Haemophilia B.

5.6. Indications for Inhibitor Testing

- a) After intensive factor exposure, e.g., daily exposure for more than 5 days.
- b) For recurrent bleeds or target joint bleeds, despite adequate CFC replacement therapy.
- c) For failure to respond to adequate CFC replacement therapy.
- d) For suboptimal clinical or laboratory response to CFC replacement therapy
- e) Before surgery.
- f) For suboptimal post-operative response to CFC replacement therapy.



5.7. Haemophilia A and FVIII Inhibitors

5.7.1. Management of Bleeding

5.7.1.1. For low-responding inhibitors with Acute bleeds

- FVIII CFC replacement therapy is preferred; **rFVIIa or aPCC** is given if haemostatic response is poor.
- Loading dose of FVIII:** $[\text{body weight (kg)} \times 80 \times [(1 - \text{haematocrit}) \times \text{antibody titre (BU)}]]$
- An additional 50 IU/kg above loading dose is added to achieve a measurable FVIII activity
- FVIII levels should be measured 15 minutes after completion of the bolus, and adjustment to reach target levels is necessary because there is substantial individual variation.

5.7.1.2. For high-responding inhibitors with Acute bleeds

- Bypassing agent therapy (rFVIIa or aPCC) or porcine FVIII.
- High-responding inhibitors whose titres have fallen to undetectable or low levels, standard FVIII CFC replacement may be used in an emergency for up to 3-5 days followed by bypass agent.
- If haemostasis is unsatisfactory with rFVIIa or aPCC as single agents, each may be alternated every 6 hours.

5.7.2. Prophylaxis

- Emicizumab** prophylaxis is preferred over bypassing agents (rFVIIa or aPCC), but it is *not used to treat active bleeds*.
- For Breakthrough Bleeds:** FVIII concentrates for low-responding inhibitors and bypassing agents for high-responding inhibitors; rFVIIa is preferred over aPCC due to the risk of thrombotic microangiopathy.

Table 26 Treatment of Acute Bleeds in Haemophilia A Patients with Inhibitors

Haemophilia A	Low- responding inhibitors	High- responding inhibitors
Agent	FVIII	rFVIIa or aPCC, or FVIII
Monitoring	FVIII activity (FVIII:C) assay	Thromboelastography or thrombin generation assay

5.7.3. Surgery and Invasive Procedures

- Inhibitor testing is recommended** for all Haemophilia patients before surgery or invasive procedures.
- Low-responding inhibitors:** higher and more frequent FVIII dosing during surgery due to short half-life of FVIII.
- High-responding inhibitors: bypassing agents** (rFVIIa or aPCC).
- If one bypassing agent fails, alternating or combining rFVIIa and aPCC can be used.
- Continuous infusion with daily dose adjustments is another option during surgery or procedures.
- After stable haemostasis for 3-5 days, treatment can be tapered over 1-3 weeks.

5.7.4. Inhibitor Eradication by Immune Tolerance Induction (ITI)

- Inhibitor eradication* by ITI therapy is successful in 70%-80 % of patients with severe Haemophilia A, but less effective in moderate/mild Haemophilia A.
- The best ITI regimen is still unclear, but a high-dose regimen (200 IU/kg daily) is preferred.



- c) If patients on ITI have frequent bleeding, they may receive prophylaxis with bypassing agents (rFVIIa, aPCC) or emicizumab.
- d) Successful ITI means a persistently negative Bethesda titre with normal pharmacokinetics, including factor recovery >66% and a half-life >6 hours for standard FVIII concentrates.
- e) Once successful ITI is achieved, FVIII prophylaxis may be initiated or resumed.
- f) ITI failure is the inability to achieve tolerance within 2–3 years of starting therapy.
- g) For patients who fail ITI, emicizumab prophylaxis is preferred over bypassing agents.

5.8. Haemophilia B and FIX Inhibitors

5.8.1. Introduction

- a) Developing an FIX inhibitor is the most serious complication in Haemophilia B.
- b) About 50 % of Haemophilia B patients with inhibitors experience anaphylaxis.
- c) In Haemophilia B patients who have anaphylaxis to FIX therapy, screening for an FIX inhibitor is recommended, as the allergic reaction may be the first sign.

5.8.2. Management of Acute Bleeding

- a) **For low-responding inhibitors:** FIX CFCs, if there is no history of allergic reaction.
- b) **For high-responding inhibitors:** rFVIIa is preferred over aPCC, because aPCC contains FIX and may trigger or worsen an allergic reaction.

5.8.3. Prophylaxis

rFVIIa, or, in the absence of an allergic/ anaphylactic reaction to FIX, aPCC.

Table 27 Treatment of Acute Bleeds in Haemophilia B Patients with Inhibitors

Haemophilia B	Low- responding inhibitors	High- responding inhibitors
Agent	FIX	rFVIIa or aPCC
Monitoring	FIX activity (FIX:C) assay	Thromboelastography or thrombin generation assay

5.8.4. Surgery and Invasive Procedures

- a) **For low-responding inhibitors:** more frequent dosing is recommended due to the short FIX half-life.
- b) **For high-responding inhibitors or those with past allergic reactions to FIX products:** rFVIIa is preferred over aPCC since aPCC contains FIX and may trigger or worsen allergy.
- c) Once haemostasis is achieved and maintained on a bypass agent regimen for 3-5 days, use of these agents may be tapered over a week or more.

5.8.5. Immune Tolerance Induction

- a) For patients with Haemophilia B and inhibitors, the WFH is unable to make a recommendation on the use of immune tolerance induction, as experience with ITI in Haemophilia B is limited.
- b) The principles of treatment are similar to those in Haemophilia A (i.e. high-dose factor replacement protocols), but the success rate is lower.



CHAPTER 06 Management of Special Situations

6.1. Carriers

6.1.1. Definitions

A Haemophilia carrier is typically a female who carries a genetic change (mutation) in the factor VIII or factor IX gene on one of her X chromosomes.

6.1.1.1. Obligate Carriers

- a) Any biological daughter of a father with Haemophilia;
- b) Any biological mother of a child with Haemophilia who also has at least one other family member with Haemophilia or who is a known carrier of Haemophilia;
- c) Any biological mother of two or more children with Haemophilia.

6.1.1.2. Potential Carriers

- a) Any biological daughter, sister, mother, maternal grandmother, aunt, niece, or female cousin of a carrier of Haemophilia;
- b) A biological mother of a child with Haemophilia and no known family history of Haemophilia or carriers of Haemophilia.

6.1.2. Common Manifestations Among Symptomatic Carriers

- a) Menorrhagia,
- b) Dysmenorrhea,
- c) Postpartum haemorrhage,
- d) Perimenopausal bleeding, and
- e) Abnormal bleeding alone, following trauma, or after medical interventions.

6.1.3. Bleeding Management

- a) Carriers of Haemophilia with low factor levels *should be treated and managed the same as males* with Haemophilia.
- b) Carriers who exhibit a greater bleeding tendency than would be predicted by their factor level, as in males, may have a second coagulation defect, (i.e. VWF) or a congenital platelet defect.
- c) All potential and obligate carriers of Haemophilia should have their FVIII/FIX levels measured to establish their baseline levels prior to major procedures, surgery, or pregnancy.
- d) Hormonal therapy is useful in managing heavy menstrual bleeding. Oral antifibrinolytics, e.g., tranexamic acid (15-25 mg/kg every 6-8 hours), may also be helpful.

6.1.4. Pregnancy and Prenatal Planning

- a) During pregnancy, FVIII levels in carriers can rise and may become normal in later stages. Levels of FIX, do not usually change significantly.



- b) Pregnant carriers of Haemophilia should have their FVIII/ FIX levels assayed in the third trimester of pregnancy to assess their bleeding risk during delivery and in the postpartum period.
- c) Regional block anaesthesia (epidural) is not contraindicated if the coagulation screen is normal and the relevant factor level is above 50 IU/dL or raised to above 50 IU/dL by prophylactic treatment.
- d) Factor replacement therapy, if required, should be administered to maintain factor levels >50 IU/dL during labour and delivery and maintained in the normal range for at least 3 days after vaginal delivery and at least 5 days after caesarean delivery.
- e) Delivery of infants known or suspected to have Haemophilia must be atraumatic, regardless of whether it is by vaginal or caesarean delivery, to decrease the risk of bleeding complications.
- f) Some recommend caesarean delivery to reduce the risk of intracranial bleeding in infants with severe Haemophilia.
- g) Forceps, vacuum extraction, and invasive foetal procedures (like scalp sampling or internal electrodes) should be avoided.
- h) Pregnant Haemophilia carriers should deliver in a hospital with access to Haemophilia specialists.

6.1.5. Postpartum Care

- a) FVIII level of carrier falls off fairly rapidly after delivery, usually returning to baseline levels in 7-10 days.
- b) It is important to monitor and maintain factor levels post-delivery as carriers are at increased risk of primary and secondary postpartum haemorrhage.
- c) If postpartum haemorrhage occurs, factor replacement therapy, anti-fibrinolytics (tranexamic acid), and hormonal therapy are the first-line therapies for its management.
- d) Prophylactic hormonal therapy may be started immediately after delivery and continued for one month in selected carriers deemed to be at higher risk of bleeding.
- e) Haemoglobin levels in carriers at risk of late postpartum haemorrhage should be checked before discharge from hospital.
- f) Follow-up to monitor postpartum bleeding for approximately 1-2 months may be appropriate.

6.1.6. Newborn Testing

- a) Cord blood should be collected from all male newborn infants of carriers of Haemophilia to assess APTT or factor levels for early identification and management of Haemophilia.
- b) Infants who may be mildly affected will require repeat screening at 3-6 months of age.

6.1.7. Miscarriage Management

- a) Surgical management of spontaneous abortion is preferred.
- b) Adequate haemostatic treatment is required in accordance with the recommended perioperative protocols (i.e. CFC replacement, adequate obstetric management).



6.2. Circumcision

- a) Plasma factor level should be raised to 80-100 IU/dL just prior to the procedure.
- b) Intraoperative care should be taken to cauterize all bleeding vessels.
- c) If continued clotting factor replacement is required, the goal would be to maintain factor levels >50 IU/dL for the first 3 days, and >30 IU/dL for the subsequent 4-8 days.
- d) Consider inhibitors and other causes in case of intractable bleeding after surgery.
- e) Non-dissolvable stitches (if used) should be removed 10-14 days post-surgery; the inevitable bleeding should be managed with clotting factor replacement.
- f) Adjunct and supportive therapy should be used.

6.3. Vaccinations

- a) Routine vaccines should be administered.
- b) Preferable route: subcutaneously (SC) rather than intramuscularly (IM) or intradermally (ID).
- c) If IM injection must be the route, single dose of 30 IU/kg CFC should be given 30 minutes before, and the smallest gauge needle available (25-27 gauge) should be used.
- d) There has been no evidence that vaccinations result in inhibitor development.

6.4. Sexuality

Adult patients with Haemophilia should be assessed for sexual health issues as part of routine care.

6.5. Psychosocial Issues

For patients with severe Haemophilia, provision of psychological and social support as part of comprehensive Haemophilia care is recommended.

6.6. Cancer / Malignancy

- a) For diagnosis and treatment of malignancy in patients with Haemophilia, provision of adequate factor replacement is necessary to minimize bleeding risk.
- b) Antineoplastic treatments should be the same as recommended for the general population.
- c) If chemotherapy or radiotherapy is accompanied by severe long-lasting thrombocytopenia, continuous prophylactic replacement therapy is recommended.

6.7. Atrial Fibrillation (AF)

- a) For patients with severe or moderate Haemophilia and atrial fibrillation (AF), clinical management is based on basal FVIII/ FIX levels and stroke risk.
- b) For patients with AF at high risk of bleeding and thromboembolism, left atrial appendage occlusion is recommended, particularly if long-term replacement therapy is not feasible.
- c) For patients whose AF-associated stroke is high or outweighs the risk of bleeding complications, careful consideration of the use of anti-coagulants is recommended.
- d) The choice between direct oral anticoagulants and vitamin K antagonists depends on the local protocols.
- e) Most experts suggest maintaining trough levels of ≥ 15 -30 IU/dL while on anticoagulant therapy for atrial fibrillation.
- f) In Haemophilia patients with inhibitors, anticoagulant therapy is generally contraindicated.



6.8. Venous Thromboembolism / Thrombosis (VTE)

- a) Therapeutic anticoagulants can be given when clotting factor levels are kept above 30 IU/dL or at least 15 IU/dL.
- b) For high-risk surgery, mechanical thromboprophylaxis (i.e. graduated compression stockings) is preferred over pharmacological methods.
- c) Pharmacological thromboprophylaxis should be used only after achieving haemostatic control with adequate replacement therapy.
- d) In patients without inhibitors, who develop acute VTE, short-term high-intensity anticoagulation is recommended with clotting factor coverage and close monitoring.
- e) This recommendation does not apply in presence of inhibitors, since anticoagulants are generally contraindicated in these cases.

6.9. Metabolic Syndrome

Obese patients should have FVIII/IX replacement therapy based on lean body weight (LBW) after individual pharmacokinetic assessments.

- $LBW \text{ (men)} = 0.407 \times \text{weight [kg]} + 0.267 \times \text{height [cm]} - 19.2$
- $LBW \text{ (women)} = 0.252 \times \text{weight [kg]} + 0.473 \times \text{height [cm]} - 48.3$

6.10. Diabetes Mellitus

- a) Same screening and management strategies is recommended as for the general population.
- b) Subcutaneous insulin can be administered without bleeding and without the need for factor replacement.

6.11. Renal Disease

- a) Haemodialysis using heparin and a single dose of CFC before and after each procedure is often preferred.
- b) Before placement of central venous line, factor levels should be 80-100 IU/dL and then maintained between 50 and 70 IU/dL for 3 days after the procedure.

6.12. Osteoporosis

- a) All patients should be encouraged to engage in regular physical activity and to have adequate calcium and vitamin D intake.
- b) Bisphosphonates should be considered for patients with demonstrated osteopenia. A dental evaluation should be carried out before initiating long-term bisphosphonate therapy.
- c) Osteoporosis, fragility fractures, or increased fracture risk should be treated with individually adjusted anti-osteoporotic medications.

6.13. Hypertension

Management is same as that applied in the general population.



6.14. Coronary Artery Disease

- a) Same cardiovascular risk screening and management as for general people, with added clotting factor correction as needed.
- b) In patients with high-responding inhibitors, antithrombotics should be used only when the risk of untreated thrombosis is greater than the bleeding risk.
- c) Maintain trough levels at $\geq 15\text{--}30$ IU/dL during dual antiplatelet therapy and $\geq 1\text{--}5$ IU/dL during single antiplatelet therapy.
- d) For patients without inhibitors undergoing percutaneous coronary intervention (PCI), keep clotting factor levels at 80–100 IU/dL while therapeutic antithrombotic are used.
- e) For patients without inhibitors undergoing coronary artery bypass grafting (CABG), keep clotting factor levels at 80–100 IU/dL before, during, and after surgery until wounds heal.
- f) Thrombolytic therapy (after myocardial infarction (MI)) should be used only after full correction of haemostasis with clotting factor replacement.
- g) For heart valve replacement, choose a bioprosthetic valve to avoid lifelong anticoagulation.

6.15. Hypercholesterolaemia

The management of hypercholesterolemia is the same as for the general population.



CHAPTER 07 Musculoskeletal Complications of Haemophilic Patients

7.1. Terminology

- Acute bleeds – evidenced by recent (few min to h) aura with bleeding with warm, swelling with sudden loss of ROM (Range of Motion) within days to week (up to);
- ADL – ‘Activities of Daily Living’ are the essential self-care tasks that a person must be able to perform to live independently. i.e., eating, grooming, brushing, bathing, toileting, transfer, mobilization;
- ROM – Range of motion
- AROM – Active Range of motion
- Arthrocentesis – aspiration from joint;
- Aura – a joint bleed as an episode characterized by an unusual sensation (aura) in the joint in combination with any of the following:
 - increasing pain
 - increasing swelling/warmth of the skin over the joint
 - progressive loss of ROM
- Chronic stage – old joint bleed associated with structural changes in X-ray with chronic synovitis, commonly in 2nd or 3rd decade of life;
- Chronic synovitis – Persistent (> 3 months) inflammation and hypertrophy (thickening) of synovial membrane following repeated joint bleeds, swelling with doughy (boggy) feeling but usually not intensely hot or painful;
- Contracture – permanent tightening or shortening of muscles, tendons, skin and nearby tissues;
- Deformity – irreversible joint damage with loss of ROM, muscle atrophy. E.g., Fixed Flexion Deformity (FFD), ankylosing, valgus/ varus, etc.;
- Expert Occupational Therapist (OT) – allied health professional who has at least 3 months exposure to give occupational therapy on haemophilia patients concerned with improvement of hand function and ADL activities;
- Expert Physiotherapist – allied health professional who has at least 6 months exposure to give physical therapy on haemophilia patients concerned with improving ROM, muscle strengthening and gait;
- Haemarthrosis – bleeding into joint;
- Haemophilic arthropathy – chronic degenerative joint disease caused by repeated bleeding into joints characterized by chronic synovitis, cartilage destruction, bone erosion and/or deformity (stage IV-V in X-ray);
- Intermittent prophylaxis – on demand treatment or treat bleed after it occurs; e.g., treating bleeding events during physical therapy;
- Joint at risk – 1st time massive bleeding, 2nd time bleeding within 2 months;
- MSK US – Musculoskeletal Ultrasonogram;



- Orthotist & Prosthetist (OP) – allied health professional who design, measure, fabricate and fit custom medical devices externally or replacing body parts;
- Physiatrist – specialist in Physical Medicine & Rehabilitation;
- PROM – Passive ROM;
- PWH – people with Haemophilia;
- QoL – Quality of Life;
- Rebleed – worsening of the condition either on treatment or within 72 hours after stopping treatment;
- Rehabilitation – set of structured, goal-oriented interventions designed to restore, maintain or improve functional ability and QoL for individuals who have experienced a loss of function due to an injury, diseases or medical treatment;
- Subacute stage – early arthropathy but before chronic stage (3 weeks to 3 months);
- Synovectomy – removal of diseased or inflamed synovium;
- Target joints – joint that bled ≥ 3 times within 6 months;
- VAS-Visual Analogue Scale.

7.2. General Information

Most common joint bleed area: Knee, Elbow and Ankle

7.2.1. Assessment

7.2.1.1. Symptoms: Pain, swelling and warm with feeling of aural sensations.

7.2.1.2. Signs:

- Doughy feeling,
- Tenderness,
- Positive patellar tap/fluctuation test,
- Limited ROM,
- Contracture, joint deformity.

7.2.1.3. Imaging Tools:

- X-ray-** Affected joints, Standing x-ray of both knee joint antero-posterior view.
- Grey-scale Musculoskeletal (MSK) Ultrasonography (US)-** If available, use to see synovial hypertrophy, vascularity, collection, osteophyte, cartilage, bone erosion, etc. by Grey scale (black & white).

7.3. Common MSK Complications:

- Acute haemarthrosis,
- Chronic haemophilic arthritis,
- Muscle haematoma,
- Flexion contracture,
- Osteonecrosis of femoral head,
- Pseudotumor.



7.4. Radiological Staging

Radiologically, five stages of haemophilic arthropathy are recognized:

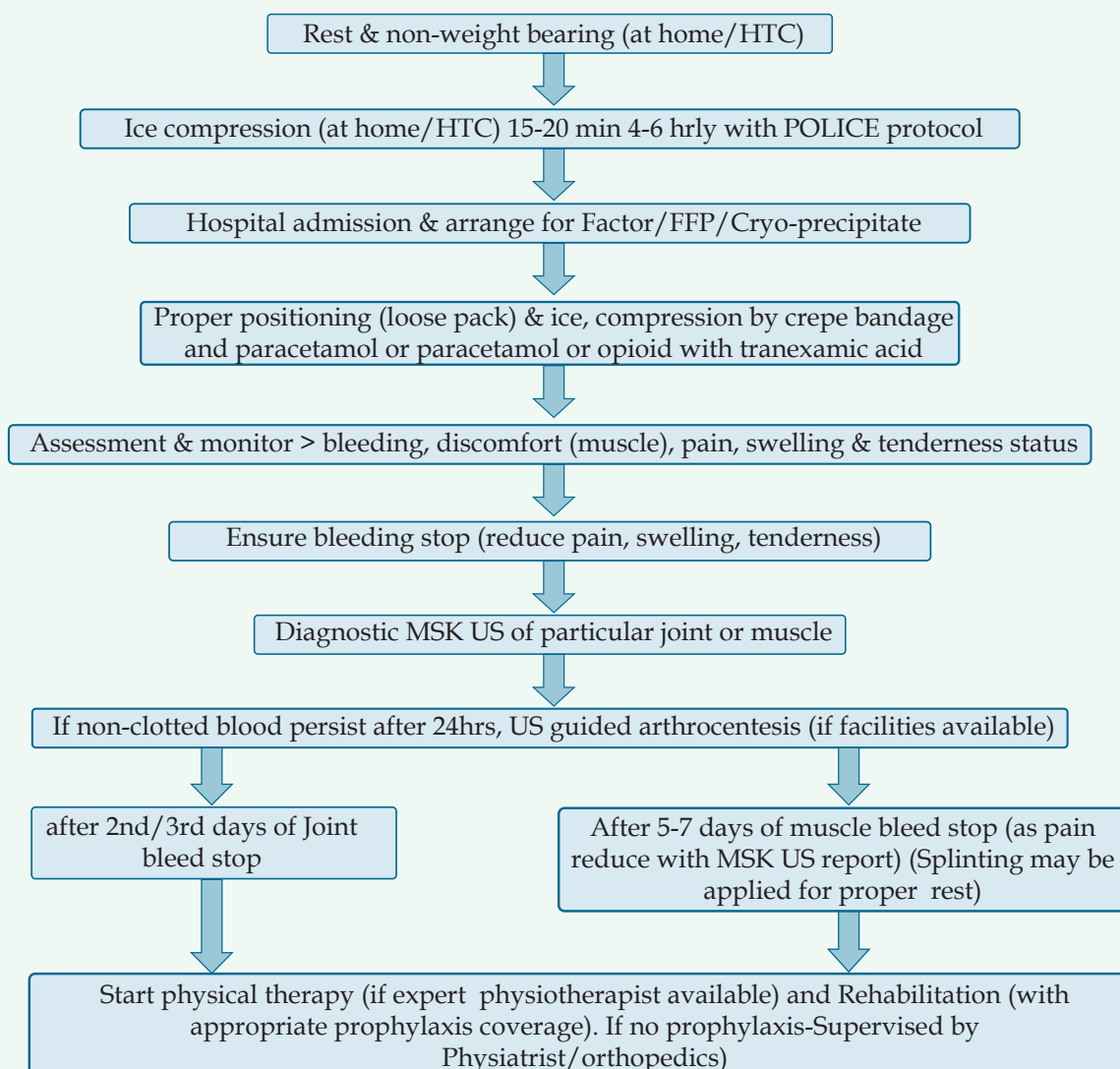
- a) **Stage 1:** Soft tissue swelling of the joint and adjacent tissues.
- b) **Stage 2:** Osteoporosis due to inflammatory hyperaemia, especially in knee and elbow.
- c) **Stage 3:** Joint disorganization due to osseous lesions.
- d) **Stage 4:** Cartilage destruction and secondary joint space narrowing.
- e) **Stage 5:** Complete loss of cartilage spaces with bone erosion.

7.5. Data Sheet of Haemophilic Patient

Completing and updating a data sheet for haemophilic patient is part of musculoskeletal treatment. Please see Annex 1.

7.6. Management of Acute Joint Bleeds (Please see Table 15, Page 20)

7.6.1. Flowchart:



7.6.2. Rehabilitation

Guided by experienced Physiatrist or Orthopaedic surgeon (if Physiatrist not available) and done by trained Physiotherapist/ Occupational Therapist/ Orthotist.

7.6.2.1. POLICE

- a) P – Protection from trauma (use orthosis, if available or care during movement or transfer);
- b) OL – Optimum loading weight bearing as tolerated (WBAT). First 7 days – axillary crutch in weight bearing joint, wheelchair – in upper limb joint and iliopsoas haemorrhage;
- c) I – Ice* (First 2 days, 20 min 4 hourly- 2 days until acute bleeding stop)
- d) C – Compression (by crepe bandage in figure of “8” with 10% stretch) for until bleeding stops;
- e) E – elevation.

**Avoid direct contact*

7.6.2.2. Physical Therapy: with icing prior (5 min) and post therapy (10 min)

For details of physiotherapy, see Annex 2.

7.6.2.3. Exercise

a) Initial 1-2 days:

Position: Loose pack position of particular joint.

Exercise **is not recommended** during bleeding period.

b) After 2-3 days:

- AROM exercise - mild, gentle, pain free
Dose- 5 repetition/joint, 3 times/day
- Isometric strengthening exercise
Dose: 5 repetition/muscle, 3 times/day

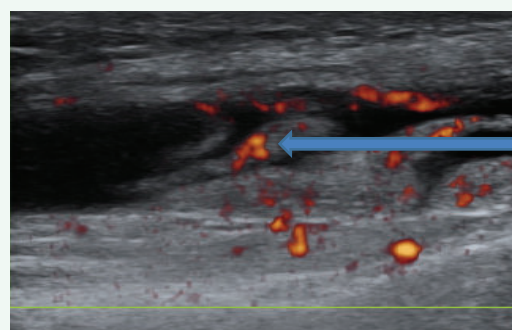
Caution: Regular evaluation of the patient for pain during physical therapy or exercise which may suggest re-bleeding.

7.6.2.4. Arthrocentesis

- a) Not routine but supplemental;
- b) If initial factor treatment does not lead to rapid improvement in a very tense, painful joint after 24 hrs of conservative treatment;
- c) It should be performed under factor level at least 30-50 IU/dl for 48-72 hrs.
- d) It is best done soon after stopping of bleeding in aseptic precaution;
- e) Evidence of neurovascular compromised of limb;
- f) A large bore needle (16/18 gauze)



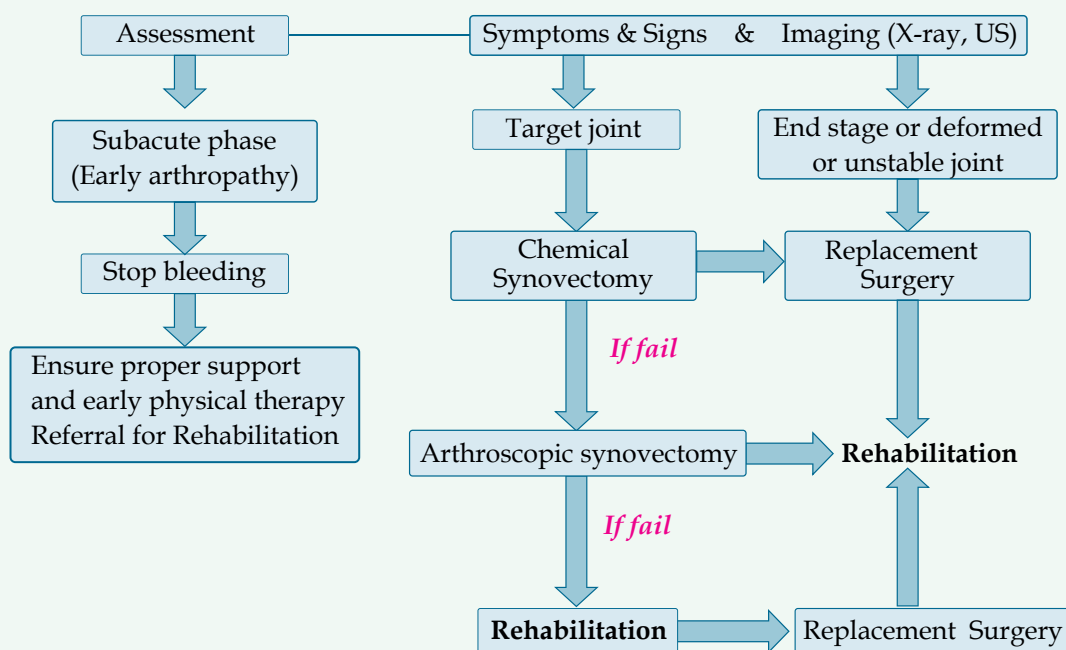
7.7. Management of Chronic Stage



Synovial hypertrophy with vascularity

Figure 2. Chronic Synovitis (inflammatory)

7.7.1 Flowchart



7.7.2. Rehabilitation

- Guided by experienced Physiatrist or Orthopaedic surgeon (if Physiatrist not available) and done by trained Physiotherapist/ Occupational therapist/ Orthotist;
- With factor coverage (**if supported**), experienced physical therapist can start physical therapy;
- Without factor coverage (**if not available**), Rehabilitation process should be supervised by Physiatrist or Orthopaedic surgeon;
- Emphasis physical therapy on gradual decrease joint pain & swelling with increase ROM with or without intermittent prophylaxis;
- Increase muscle strength by exercise;
- Increase WBAT by planned withdrawal of support;
- Activities of Daily Living (ADL) for joint protection technique;
- Focusing rehabilitation for optimum functional mobility and connectivity with HTC centre.



7.7.2.1 Physical Therapy: Icing prior (5 min) and post therapy (10 min)

For details of physiotherapy, see Annex 3.

7.7.2.2. Exercise: Icing for 10 min after exercise session

For details of exercise, see Annex 4.

7.7.2.3. Occupational Therapy: Task specific exercises, Adaptation to the home, school or work environment to allow participation in community activities and employment and to facilitate ADL (done by Occupational therapist).

7.7.2.4. Orthosis - serial casting for correction of Fixed flexion deformity (up to less than 60) e.g.: Ankle-foot orthosis (AFO), Knee-ankle-foot orthosis (KAFO) with or without hinge, knee orthosis, foot orthosis (insoles), static volar orthosis, Gaiter, etc. (made by Prosthetist & Orthotist)

7.7.2.5. Assistive Devices and Others

- a) **Mobility aids:** Axillary crutch, Elbow crutch, four footed cane, 3 footed cane, single footed cane, walker, wheelchair;
- b) **Adaptive equipment:** Long handled reachers, dressing aids (sock aids, button hooks), grab bars, elevated seats or raised high commode, chair commode, built -up handles, etc.

7.7.2.6. Education: Lifestyle modification or learning safety technique for affected joints during work.

7.7.2.7. Chemical Synovectomy

For details, please see Annex 5

7.8. Muscle Haemorrhage

Common sites:

Lower limb: Iliopsoas, quadriceps, Calf muscles.

Upper limb: Forearm flexors, Deltoid, Biceps, Triceps.

7.8.1 Evaluation

7.8.1.1 Clinical

- a) **Symptoms:** Discomfort, pain, swelling, warm;
- b) **Signs:** Swelling, warm, tenderness, adjacent joint ROM may or may not be affected.

7.8.1.2 Imaging: MSK US, MRI.

7.8.1.3. Monitor: VAS, muscle bulk.

7.8.1.4. Iliopsoas Haemorrhage:

- a) Pain on extension & groin, lower abdomen/back;
- b) Other hip rotation normal;
- c) Quadriceps weakness;
- d) Abnormal sensation along medial aspect thigh;
- e) May mimic appendicitis.

7.8.2. Complications: Contracture, nerve palsy (femoral/post tibial/deep peroneal), pseudotumor.

Caution: Volkman Ischemic contracture in flexor forearm.

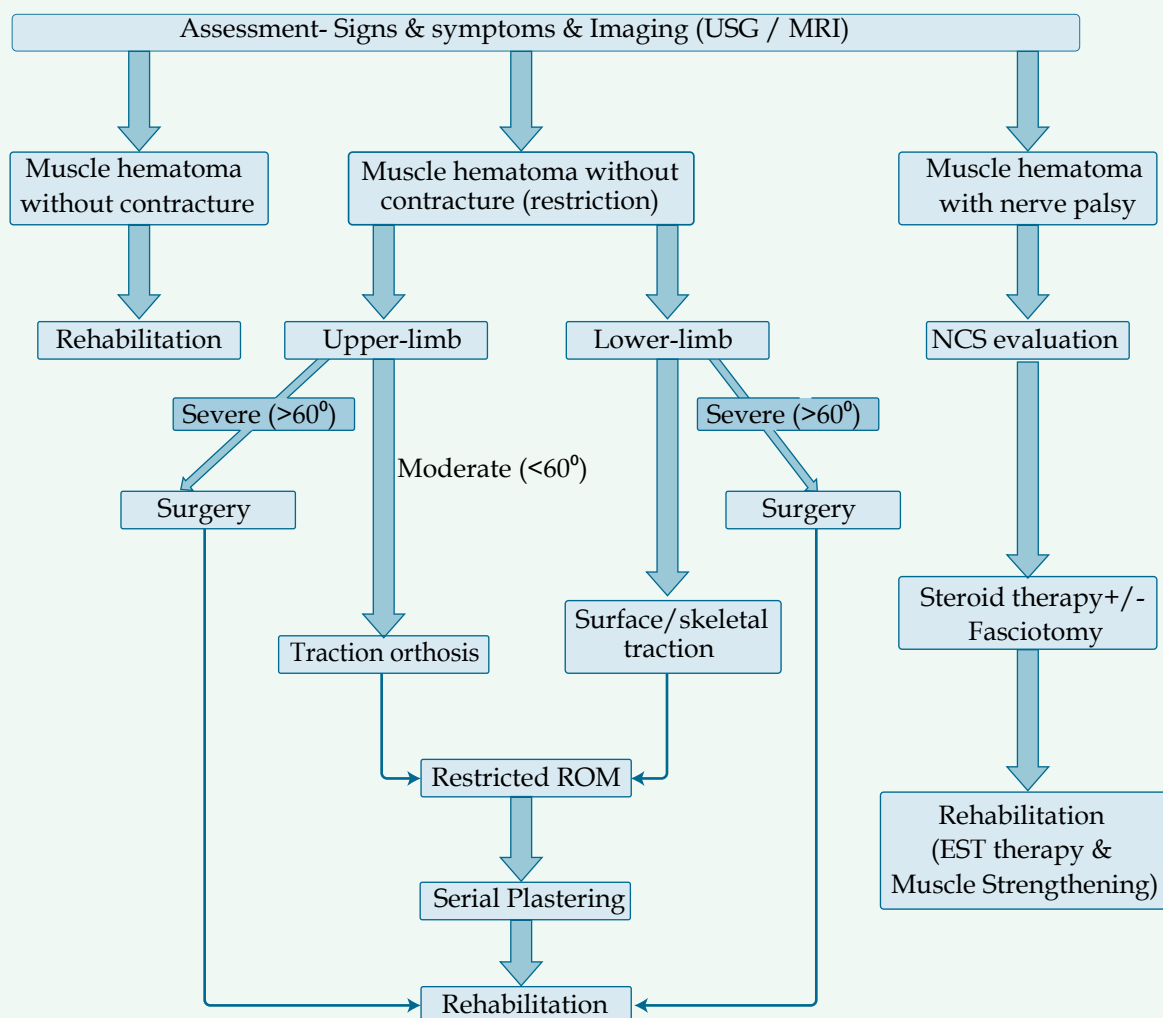




Figure 3. Haematoma Seen in Ultrasonogram

7.8.3. Management

7.8.3.1. Flow Chart for Management



7.8.3.2. Factor

- a) Ensure Prophylaxis coverage;
- b) In settings without factor coverage, physiotherapy may be performed during the rehabilitation period if the treatment is coordinated by an experienced interdisciplinary team with musculoskeletal expertise like physiatrist or orthopaedic specialist.

7.8.4. Rehabilitation

- a) Police or cryotherapy apply in acute stage, with or without splinting for. absolute rest, 15-20 min 4-6 hourly until bleeding stop or pain subside.
- b) Usually, physical therapy in muscle bleeds start after 1 week of bleeding stop (3-4 days later in comparison to joint bleed).
- c) Ensure ambulation by axillary crutch (except iliopsoas) for lower limb or wheel chair for upper limb cases.

Caution: Regular evaluate the patient for pain during physical therapy or exercise which may suggest re-bleeding.

7.8.5. Ultrasonography guided aspiration:

- a) The early removal of blood should theoretically reduce its damaging effect;
- b) It is best done soon after stopping of bleeding in aseptic precaution;
- c) It should be performed under factor level at least 30-50 IU/dl for 48-72 hrs
- d) A bleeding sense, painful joint after 24 hrs of conservative treatment;
- e) Evidence of neurovascular compromised of limb;
- f) A large bore needle (16/18 gauze).

7.9. Articular Deformity:

For details, please see Annex 6.



CHAPTER 08 Counselling of Haemophilia Patients

8.1. Disease Education

Explain definition, severity, inheritance, lifelong nature, outcomes.

Haemophilia is a disease of blood clotting. It is a genetic disease, which means you have acquired this from your parents or some permanent changes have occurred in genes inside the cells of your body. Genetic diseases usually are not cured easily, but can be controlled to much extent. Interestingly, Haemophilia disease is almost always suffered by males. What may happen to your offsprings will be discussed later on.

As a patient of Haemophilia, your blood doesn't clot properly. That is why when there is a trauma or surgery happened upon your body there is prolonged bleeding in your body. The swellings in your joint or some other parts, and the redness under your skin is due to poorly clotted blood. To avoid these unusual bleeding, you must be very careful from getting injured and seeking treatment from any medical personnel for any disease.

Extent of abnormal bleeding in Haemophilia depends on severity. The most severely affected people may notice bleedings since early childhood even without any perceived trauma. On the other hand, least severely affected people may remain undiagnosed till adulthood. Severity depends on extent of lack of a protein in your blood, the protein that is crucial for blood clotting. According to your blood report, the protein deficient in your case is Factor, and you are a Haemophilia patient.

Most common sites affected due to unusual bleeding in Haemophilia are joints and muscles, these comprises 9 out of 10 bleeding sites. Some other sites uncommon but dangerous, are brain, neck and abdomen. In many cases untreated Haemophilia is an incapacitating disease, because of repeated joint bleeds leading to joint deformity and poor quality of life. But if you and your caregiver follow the instructions properly, it is possible to lead a successful life.

8.2. Treatment Counselling

Discuss factor therapy, non-factor therapy, inhibitors.

As it is already said, your blood deficient of a protein that is crucial for blood clotting, the protein in your case is Factor Worldwide the treatment for this disease is factor replacement in the venous route. Unfortunately, factor is a very costly drug, and it does not persist inside the body for not even a day. So, many people even in the developed country, and almost all people in the developing countries cannot get adequate factor as needed. Ideally, upon diagnosis, a Haemophilia patient is supposed to get regular factor replacement even before any serious bleeding occur, it is called primary prophylaxis. If life-long regular prophylactic therapy can be ensured, the person may lead an almost normal life. But due to high cost and unavailability, in our country most of the time patients receive factor during bleeding or before surgery, which is called on-demand therapy. We will gradually learn what should we do to prevent bleeding, and what should be done if a bleeding has occurred or suspected.

Besides drugs, i.e., factors, some other measures must be taken during acute bleeding, we will discuss those in a step-by-step fashion. Moreover, in absence of optimum prophylaxis, which unfortunately occurs in most of the patients in our country, repeated bleeding into joints make the joints prone to permanent damage. Physiotherapy and, in more advanced stages, orthopaedic surgery, are of much benefit in Haemophilia.



Now-a-days some newer types of drugs, for prophylaxis only, are available which are much costlier, but much beneficial over factor replacement therapies. Emicizumab available as the brand name HEMLIBRA. For acute treatment purpose, some less effective or adjunct drugs are available, namely, cryoprecipitate, fresh frozen plasma and tranexamic acid.

As factors are large protein molecules introducing into the body of the patients, they can produce antibodies in the patient. These antibodies are called inhibitors because they minimise effectiveness of the factors by time. If inhibitors appear in your blood, higher doses of factors or different factors or drugs other than factors might be necessary to stop bleeding. That treatment will be much costlier.

8.3. Bleeding Recognition

Symptoms and first response steps.

As I have mentioned 9 out of 10 bleeding in Haemophilia occur in joints or muscles. Among the joints, knees, ankles and elbows are mostly affected. On the other hand, muscles inside the abdomen and upper and lower limb muscles are mostly affected. Bleeding usually starts with a tingling sensation and tightness within the joint, which is called 'aura'. The best thing you can do at this time is, keep the joint or the muscle in complete rest, in a relaxed, least painful and elevated position. Any movement or attempt for movement will hamper clot formation. It is advisable to keep ice in the freezer of the house of the patient or of the neighbour. Application of ice helps reduce blood flow, bleeding and swelling, but it should not be maintained for more than 20 minutes, because it also hampers clot formation at a later stage. Compression by crepe bandage is good to reduce bleeding and swelling.

As we know, worldwide the treatment for this disease is factor replacement in the venous route, all Haemophilia patients should have factors stored in their or nearby refrigerator, and accessories and training to receive the factor intravenously. You will learn how to calculate factor requirement in each type of bleeding condition, but infuse the factor dose available at your hand as soon as possible. A full list of factor requirements is available this guideline. If full dose of factor is not readily available, oral or injectable tranexamic acid 500 mg to 1000 mg, every 8 hours can be added to the emergency treatment. Tranexamic acid must not be taken if there is blood with urine.

Bleeding within the abdomen may lead to bleeding with stool or vomiting. Stool may be red or black depending on the site of bleeding in the bowel. If outside bowel, bleeding in the abdomen may be represented by abdominal swelling, pain or discomfort. Any severe headache, especially after head injury, may the symptom of fatal bleeding inside the head. Bleeding inside the neck or chest may present as coughing out of blood or pressure effect.

This is very important to note down any bleeding episode, treatment achieved and outcome of the treatment in a 'Bleed records'.

8.4. Lifestyle and Activity Counselling

Safe vs. avoidable activities.

Lifestyle and activities of a haemophilic patient depend on prophylactic treatment you are getting. If you are getting high-dose prophylaxis, you can lead a normal life, with additional doses during expected collision or high-contact activities including sports. But it will be certainly very very costly. On the other hand, if you adopt on-demand factor replacement, i.e., only during a bleeding episode or before surgery, you must be very careful about your movement and minor injuries. No way you can think yourself useless or handicapped. Try your best to cope with your bleeding tendency and be habituated to adopt the lifestyle. High risk and low risk activities are listed in the guideline.



8.5. Pain Management

Use paracetamol, avoid NSAIDs.

Management of pain is important for starting activity early. Rest is mandatory during active bleeding, but prolonged rest causes joint movement restriction, contracture and ultimately permanent disability. Best painkiller is paracetamol, but it is only mildly effective. Step by step stronger painkillers like tramadol, morphine and some injectable drugs are added for pain relief. We will prescribe the drugs with trade names and dosage. One group of drugs commonly used as painkillers is NSAID. This should be avoided in Haemophilia and that is why you must disclose about your condition to any physician, pharmacist or drug sellers attending you.

8.6. Dental and Surgical Counselling

Dental precautions, antifibrinolytics, pre-operation plans.

Teeth are very vascular organs and diseases, and treatment of dental diseases often leads to uncontrollable bleeding. That is why, take a good care of teeth. Brush teeth twice daily with soft brushes and fluoridated toothpaste and consult your dental surgeon at the earliest problem with teeth. If any bleeding occurs, immediately factor and tranexamic acid should be started. Additionally tranexamic acid-soaked gauze can be applied at the bleeding point. After brushing, spit but don't rinse, to maximize fluoride benefit of the toothpaste.

8.7. Psychosocial Counselling

Address fear, school issues, stigma, employment.

As already mentioned, the recommended treatment worldwide is life-long prophylactic factor replacement, which is costly for everybody. Haemophilia is an incurable disease, like diabetes or hypertension. It may hamper your physical activities, but your mental strength will help you to be educated, skilled for a handsome income and a successful in life. You must not feel bad for things beyond your control. A lot of people around are living more miserable lives. Your sincerity, honesty and good behaviour will help you to adjust with your surroundings during study period and professional life.

8.8. Emergency Counselling

Red flags, emergency steps.

I need you and your caregiver to clearly understand that Haemophilia can sometimes cause life-threatening bleeding, even without a major injury. Some bleedings are emergencies, and in those situations you must act immediately.

Bleeding involving the head or brain, neck or throat, chest, abdomen, back (iliopsoas muscle), eyes, or spinal cord is always an emergency. If you develop severe headache, repeated vomiting, unusual sleepiness, confusion, seizures, swelling in the neck, difficulty in breathing, severe abdominal pain or swelling, blood in vomit or stool, sudden pain in the back or groin, or weakness of any limb, you must consider this dangerous.

In any suspected serious bleeding, factor replacement must be given immediately. You should not wait for scans, blood tests, or doctor confirmation. Delay in factor infusion can lead to death or permanent disability.

If factor is available at home, give the factor first, then immediately go to the nearest emergency department or Haemophilia Treatment Centre (HTC).

You must always carry a Haemophilia emergency card with you. This card should clearly mention your diagnosis, severity, inhibitor status, usual treatment, and contact details of your HTC. When you reach the emergency department, you or your caregiver must clearly tell the doctors that factor treatment should not be delayed for investigations.

Please remember this very clearly: any head injury, even if it looks minor at first, requires urgent factor infusion and medical evaluation.



8.9. Genetic and Family Counselling

Inheritance, carrier testing, prenatal testing.

Now I want to explain how Haemophilia runs in families. Haemophilia is an X-linked genetic condition. Almost all patients are male, while females usually carry the gene without severe symptoms.

If a mother is a carrier, in each pregnancy there is a 50% chance of having an affected son and a 50% chance of having a carrier daughter. This is why family counselling is very important.

I advise that all families receive genetic counselling so that everyone understands the inheritance pattern, future risks, and implications for other family members. Female relatives—especially mother, sisters, and daughters—should be offered carrier testing, using factor level testing and genetic testing where available.

Some carriers have low factor levels and may also experience bleeding problems. Therefore, carriers need medical advice, particularly before surgery, dental procedures, pregnancy, or delivery.

Prenatal diagnosis is available in specialized centres. If you wish to discuss this, I will explain the options in a non-directive and ethical way. My role is to give you correct information so you can make your own informed decision. I will not pressure you toward any choice.

Please be assured that genetic counselling is confidential, supportive, and non-judgmental.

8.10. Adolescents and Transition Counselling

Self-management, infusion training, sexual health.

As you grow into adolescence, you will gradually start taking responsibility for your own treatment. This period is very important. The transition from paediatric care to adult care should be planned, slow, and well supported, and it should start early.

I will help you learn how to recognize bleeding early, give factor by yourself, keep proper records, store medicines correctly, and respond in emergencies. If treatment is missed or delayed during this phase, it can lead to permanent joint damage and other complications.

During counselling, we will also talk openly about risk-taking behaviour, treatment adherence, peer pressure, school or work challenges, and emotional stress. We will discuss sexual health, safe relationships, and family planning in a way that is respectful, age-appropriate, and culturally sensitive.

My goal is to help you become independent, but at the same time I will ensure that you continue to receive support from your family and the HTC team. Poor transition often leads to loss of follow-up and worse long-term outcomes, and we want to avoid that.

8.11. Documentation Standards

Document all counselling points discussed.

Finally, I want you to know that everything we discuss during counselling is important and must be properly recorded. I will document the education provided, treatment plans, emergency instructions, lifestyle advice, psychosocial issues, and genetic or family counselling in your medical record.

Details of each bleeding episode, factor usage, response to treatment, inhibitor status, complications, and adherence issues should be recorded carefully. I will also encourage you and your caregiver to maintain bleed logs and treatment diaries, because these help us make better treatment decisions.

Proper documentation ensures continuity of care, improves quality of treatment, supports review and audit, and protects both you and the healthcare team. It also helps different doctors and emergency services understand your condition quickly when needed.



হিমোফিলিয়া রোগীদের কাউন্সেলিং (পরামর্শ দান)

রোগ সম্পর্কে অবহিতকরণ ও সচেতনতা

হিমোফিলিয়া হলো একটি আজীবন স্থায়ী, বংশগত রক্ত তঞ্চন (রক্ত জমাট বাঁধা) জনিত ত্রুটি, যা মূলত পুরুষদের আক্রান্ত করে। শরীরে প্রয়োজনীয় ক্লোটিং ফ্যাক্টর বা রক্ত জমাট বাঁধার উপাদানের ঘাটতি থাকায় আঘাত, অস্ত্রোপচার, এমনকি কখনও কখনও দৃশ্যমান কারণ ছাড়াই (তীব্র মাত্রার রোগের ক্ষেত্রে) দীর্ঘ সময় ধরে অস্বাভাবিক রক্তপাত হতে পারে। বেশিরভাগ রক্তপাতই (৯০%) জোড় বা জয়েন্ট এবং পেশিতে ঘটে, যা চিকিৎসা করা না হলে স্থায়ী বিকলাঙ্গতার রূপ নিতে পারে। তবে সঠিক ব্যবস্থাপনার মাধ্যমে একটি সুস্থ জীবনযাপন করা সম্ভব।

চিকিৎসা

এই রোগের মূল চিকিৎসা হলো শিরাপথে (Venous route) কৃত্রিম ক্লোটিং ফ্যাক্টর প্রতিস্থাপন করা। উন্নত দেশগুলোতে রক্তপাত প্রতিরোধের জন্য নিয়মিত "প্রাইমারি প্রোফাইল্যাক্সিস" অর্থাৎ 'রক্তপাত প্রতিরোধী চিকিৎসা' দেওয়া হলেও, বাংলাদেশের মতো উন্নয়নশীল দেশগুলোতে অতিরিক্ত খরচের কারণে সাধারণত রক্তপাত শুরু হলে বা অস্ত্রোপচারের আগে "অন-ডিমান্ড থেরাপি" (প্রয়োজনভিত্তিক চিকিৎসা) দেওয়া হয়। বর্তমানে আরও উন্নত ও ব্যয়বহুল প্রোফাইল্যাক্সিস ওষুধ (যেমন: Efficizumab, এমিসিজুম্যাব) ব্যবহৃত হচ্ছে। এছাড়াও, এবং সহযোগী ওষুধ (যেমন: ট্রান্সেস্লামিক অ্যাসিড, প্লাজমা) ব্যবহৃত হয়। দীর্ঘদিন ফ্যাক্টর নেওয়ার ফলে রোগীদের শরীরে "ইনহিবিটরস" (অ্যান্টিবডি) তৈরি হতে পারে, যা ফ্যাক্টরের কার্যকারিতা কমিয়ে দেয় এবং চিকিৎসার খরচ বাড়িয়ে দেয়।

রক্তপাত শনাক্তকরণ

রক্তপাত শুরু হওয়ার আগে সাধারণত জয়েন্টে এক ধরনের কিম্বিকিম অনুভূতি বা টানটান ভাব (যাকে 'Aura' বলা হয়) অনুভূত হয়। এমন হলে তাৎক্ষণিক করণীয় পদক্ষেপগুলো হলো:

- আক্রান্ত জয়েন্ট বা পেশিকে সম্পূর্ণ বিশ্রামে রাখা এবং উঁচুতে রাখা।
- বরফ দেওয়া (সর্বোচ্চ ২০ মিনিট) এবং ক্রেপ ব্যান্ডেজ দিয়ে চেপে বেঁধে রাখা।
- দ্রুততম সময়ের মধ্যে হাতের কাছে থাকা ফ্যাক্টরের ডোজ শরীরে প্রবেশ করানো।
- একটি বিস্তারিত "ব্লিড রেকর্ড" বা রক্তপাতের খাতা বজায় রাখা।

বিশেষ দৃষ্টব্য: শরীরের ভেতরের রক্তপাত (যেমন: পেট, মাথা বা গলা) অত্যন্ত ঝুঁকিপূর্ণ এবং এর জন্য হাসপাতালে জরুরি চিকিৎসার প্রয়োজন।

জীবনযাত্রা

যেসব রোগী অন-ডিমান্ড থেরাপির ওপর নির্ভরশীল, ছোটখাটো আঘাত এড়াতে তাদের উচ্চ-ঝুঁকিপূর্ণ বা শারীরিক সংস্পর্শে আসার খেলাধুলা থেকে সতর্কতার সাথে দূরে থাকতে হবে।

ব্যথানাশক ওষুধের ব্যবহার

ব্যথানাশক হিসেবে প্যারাসিটামল সবচেয়ে নিরাপদ। প্রয়োজন অনুযায়ী চিকিৎসকের পরামর্শে আরও তীব্র ব্যথানাশক ওষুধ দেওয়া যেতে পারে, তবে রক্তপাতের ঝুঁকি বাড়ায় বলে NSAID (যেমন: আইবুপ্রোফেন, ডাইক্লোফেনাক ইত্যাদি) জাতীয় ওষুধ সম্পূর্ণ পরিহার করতে হবে। স্থায়ীভাবে জয়েন্ট জট লেগে যাওয়া বা বিকলাঙ্গতা রোধ করতে দীর্ঘ দিন সম্পূর্ণ বিশ্রামে থাকা নিরুৎসাহিত করা হয়।



দাঁত ও অস্ত্রোপচার সংক্রান্ত পরামর্শ

দাঁত অত্যন্ত রক্তনালী-সমৃদ্ধ হওয়ায় রোগীদের দাঁতের যত্নে অত্যন্ত যত্নবান হতে হবে যাতে দাঁতের বড় কোনো অপারেশনের প্রয়োজন না হয়। নরম ব্রাশ দিয়ে দিনে দু'বার ব্রাশ করতে হবে এবং টুথ পেস্টে থাকা ফ্লুরাইডের কার্যকারিতা বাড়াতে ব্রাশ করার পর কুলকুচি না করে শুধু থুতু ফেলতে হবে। দাঁত থেকে রক্তপাত হলে অবিলম্বে ফ্যাক্টর এবং ট্র্যান্সেন্জামিক অ্যাসিড শুরু করতে হবে।

মনস্তাত্ত্বিক পরামর্শ

মনস্তাত্ত্বিক দিক থেকে, রোগীদের মানসিক শক্তি বৃদ্ধি করতে হবে, যাতে তারা সামাজিক প্রতিবন্ধকতা কাটিয়ে একটি স্মার্ট জীবন ও নিরাপদ কর্মসংস্থান বেছে নিতে পারে।

জরুরি অবস্থার কাউন্সেলিং

মাথা, গলা, বুক, পেট, পিঠ (ইলিওসোয়াস পেশি), চোখ বা মেরুদণ্ডের রক্তপাত জীবন সংশয়কারী জরুরি অবস্থা হিসেবে গণ্য করা হয়। তীব্র মাথাব্যথা, বারবার বমি হওয়া, অস্বাভাবিক ঘুম ঘুম ভাব, মানসিক বিভ্রান্তি এবং হঠাৎ হাত-পা দুর্বল হয়ে যাওয়া - এগুলো হলো বিপদের লক্ষণ।

জরুরি নিয়ম: যেকোনো মারাত্মক রক্তপাতের সন্দেহ হলে সময়সাপেক্ষ পরীক্ষা-নিরীক্ষা বা ডাক্তারের রিপোর্টের জন্য সময় নষ্ট না করে অবিলম্বে ফ্যাক্টর প্রতিস্থাপন করতে হবে। ফ্যাক্টর দেওয়ার ক্ষেত্রে বিলম্ব হলে মৃত্যু বা স্থায়ী পঙ্গুত্ব হতে পারে। রোগীদের সবসময় একটি "হিমোফিলিয়া ইমার্জেন্সি কার্ড" সাথে রাখা উচিত।

জিনগত ও পারিবারিক কাউন্সেলিং

হিমোফিলিয়া একটি এক্স-লিঙ্কড (X-linked) জেনেটিক রোগ। আক্রান্ত মায়েরা (যারা ক্যারিয়ার বা বাহক) প্রতি গর্ভাবস্থায় ৫০% ঝুঁকিতে থাকেন একজন আক্রান্ত পুত্রসন্তান জন্ম দেওয়ার এবং ৫০% ঝুঁকিতে থাকেন একজন বাহক কন্যাসন্তান জন্ম দেওয়ার। তাই পারিবারিক কাউন্সেলিং অত্যন্ত গুরুত্বপূর্ণ। নারী আত্মীয়দের ক্যারিয়ার টেস্ট করা উচিত, কারণ কিছু বাহকের শরীরেও ফ্যাক্টরের মাত্রা কম থাকতে পারে এবং অস্ত্রোপচার বা সন্তান প্রসবের আগে তাদের বিশেষ চিকিৎসার প্রয়োজন হতে পারে। বিশেষায়িত কেন্দ্রে গোপনীয়তার সাথে প্রসবপূর্ব (Prenatal) রোগ নির্ণয়ের সুবিধাও রয়েছে।

প্রাপ্ত বয়সে পদার্পণ

কিশোর বয়সীদের ধীরে ধীরে নিজেদের চিকিৎসার দায়িত্ব নেওয়া শিখতে হবে; যেমন - রক্তপাতের পূর্বাভাস ('aura') চেনা, নিজে নিজে ফ্যাক্টর পুশ করা এবং জরুরি অবস্থায় সিদ্ধান্ত নেওয়া।

চিকিৎসা সংক্রান্ত নথি সংরক্ষণ

সবশেষে, চিকিৎসার যাবতীয় তথ্য সঠিকভাবে লিপিবদ্ধ করা অত্যন্ত জরুরি। রোগীদের প্রতিটি রক্তপাতের ঘটনা, ব্যবহৃত ফ্যাক্টরের পরিমাণ এবং কার্যকারিতার সঠিক হিসাব (bleed log, ব্লিড লগ) রাখতে হবে, যা জরুরি অবস্থায় চিকিৎসকদের দ্রুত সঠিক সিদ্ধান্ত নিতে সাহায্য করবে।



ANNEXURE

ANNEX 1 Data Sheet for Haemophilic Patient

General Information

- Name / Age / Sex:
- Type of Haemophilia – A / B
- Severity – Mild / Moderate / Severe (Factor level %)
- Body Weight:

History of Bleeding

- Bleeding per year (Annual Bleeding Rate – ABR):
- Target Joint (knee / ankle / elbow)
- Joint at risk:
- Other involved joints:
- Muscle bleed history (iliopsoas, calf, forearm etc.)
- Recent bleeding episode:

Treatment History

- Type of treatment: On-demand / Prophylaxis
- Factor replacement history:
- Any history of Factor VIII inhibitor (Yes/No)

Home Facilities

- Ice pack availability
- Axillary Crutch
- Factor VIII / IX
- Crepe bandage
- Paracetamol, Tranexamic acid
- Use of High Commode/ Chair commode
- Management of Chronic Stage



ANNEX 2 Physical Therapy in Acute Joint Bleeds

- a. **TENS- Transcutaneous Electric Nerve Stimulation-high frequency low intensity as patient tolerated**
 - Dosimetry: frequency - 80-150 hz
 - Intensity- sensory threshold
 - pulse width-50-125 μ s (microsec)
 - Session time- 15-30 min, can be repeated in multiple times in a day
 - Duration- 3 times/week for 2- 4 weeks
- b. **Interferential Therapy (IFT)**
 - Dosimetry- low intensity-sensory threshold only,
 - Beat frequency-90-150hz (high), carrier frequency-4000hz, electrode placement – quadripolar (criss-cross) duration 15-20 min
- c. **Low Level LASER Therapy (LLLT)-**
 - Area- 4-6 points in large joint, 1 min20 sec in each point
 - Dosimetry: wavelength- 780-980nm
 - Energy-4-12 J/cm²
 - session- 8-15 min
 - Duration: 3 times/week for 2- 4 weeks

ANNEX 3 Physical Therapy in the Management of Haemophilic Arthropathy

- a. **Low Intensity Pulsed Ultrasonic (UST) Therapy**
(dosimetry - intensity - 0.1 to 3.0 w/cm², frequency-1 mghz (deep), 3 Mghz (superficial) duration-5-10 min),
- b. **NMES - (Neuromuscular Electric Stimulations)-**
High – motor level, Frequency- 35-50 hz, duration (width)-200- 400 μ s (microsec), duty cycle -on:off ratio-1:3 to 1:5 (eg. 10 sec on, 30-50 sec off), Ramp up time 2-4 sec, time-10-15 mi
- c. **Transcutaneous Electric Nerve Stimulation (TENS) -**
Dosimetry: frequency-80-150 hz
Intensity- sensory threshold
Pulse width-50-125 μ s (microsec)
Session time- 15-30 min, can be repeated in multiple times in a day
Duration- 3 times/week for 2- 4 weeks
- d. **Hot Moist Compression: 10 min followed by exercise**
Note: if any doubt, apply ice urgently and share with your local haematologist/physician/physiatrist/therapist



ANNEX 4 Exercise in the Management of Haemophilic Arthropathy

Position: Avoid loose pack position of particular joint. Keep affected limb as straight as possible.

- a. AROM exercise - mild, gentle, pain free
Dose- 5-10 repetition/joint, 3-5 times/ day
- b. PROM exercise - mild, gentle, pain free
Dose- 5-10 repetition/joint 2 times/ day
- c. Isometric strengthening exercise
Dose:5- 10 repetition/ muscle, 3-5 times/ day
- d. Multi-angle isometric exercise-
Dose-5-10sec/ angle, 2 times/ day
- e. Stretching* exercise- Gentle, soft, slow ex. following hot moist compression**
Dose-10-20 sec, 5 -10 repetitions/ group of muscles

***By expert Physiotherapist**

****Prior hot moist compression for exercise session.**

Caution: Regular evaluate the patient for pain during physical therapy or exercise which may suggest re-bleeding.

ANNEX 5 Chemical Synovectomy in the Management of Haemophilic Arthropathy

- Drug- Either Rifampicin or Oxy-tetracycline chlorhydrate
- Dose - once weekly injection for 4-5 weeks until synovitis is controlled with one dose of CFC per treatment.
- The joint should be immobilized with compression bandaging (by crepe) at least 24 hours followed by progressive rehabilitation.
- Caution: The minimum interval between repeated treatments in the same joint is 6 months





According to Radiological stage (I-IV):

- Correction of biomechanics by shoe modification
- Knee off-loading brace

Deformity correction-Radiological stage (V):

- Non-operative treatment:
Flexor contracture-up to 60 degree
Improvement at least 5 degree/week or 10 degree/2 weeks
- Operative treatment:
Failure of conservative treatment for at least 4-6 weeks

Rehabilitation after Total knee Replacement Surgery

Management:

Maintaining adequate factor levels is the most critical element to allow for safe and effective rehabilitation.

- Pre- and Perioperative: High factor levels (e.g., 80-100 IU/dl for Factor VIII, 60-80 IU/dl for Factor IX) are required for major surgery like Total Knee Arthroplasty (TKA).
- Postoperative Tapering: Factor levels are typically maintained at a high level initially (e.g., 50 IU/dl) and then gradually tapered over several weeks (20-40%).

- Factor concentrate should be administered prior to physical therapy sessions, especially in the early, more intensive stages, to maintain a safe level and prevent joint or muscle bleeding.

Rehabilitation

- Rehabilitation aims for early and progressive mobilization while carefully
 - managing pain and swelling.
- Pain Management: Use of regional anaesthesia (like epidural or peripheral nerve blocks) with careful attention to factor levels to prevent spinal/epidural hematoma.
- Cryotherapy, Compression & Elevation: Continuous or frequent use of cooling devices (cryotherapy) and full-length compression.
- Out of Bed: Within 24 hours of surgery and begin walking with physical therapy guidance as medically stable.
- The physical therapy program is structured but must be adapted to the individual's pre-operative condition, factor coverage, and pain/swelling status.
- Initial Focus (Inpatient/Early Outpatient):
- Range of Motion (ROM): Focus on achieving knee extension and progressively increasing flexion (often targeting >90° circ by 4 weeks).
- Therapeutic Exercise: Start with Active/Active Assisted/Passive ROM (A/AA/PROM) exercises, isometric quadriceps and hamstring exercises, and soft tissue mobilization.
- Weight Bearing (WB): Follow the surgeon's weight-bearing restrictions, often progressing toward Weight Bearing as Tolerated (WBAT) with an assistive device.
- Progression (Weeks 1-4 and beyond): Advanced ROM: Use a stationary bicycle (low or no resistance) for ROM and endurance.
- Strengthening: Progress to closed-chain exercises (e.g., mini-squats with support) once pain control and strength allow. Avoid exercises with heavy weights or resistance initially.
- Functional Training: Focus on transfers, stair climbing, balance, and proprioception.
- Long-Term Goals: Return to recreational activities like walking, swimming, golf, and biking. Activities that involve repetitive high impact, heavy lifting, or high-level torsion/twisting are usually not recommended (e.g., difficult hiking, aggressive skiing, or repetitive aerobic stair climbing).
- Psychosocial role:
 - Psychological support
 - Social support
 - Chronic pain has more impact on patient & family members> Social isolation.
- Environmental:
 - Train occupational staff
 - Child: school staff- train about acute & post-acute care, Do or do not
- Recommendations:
 - Children: 6 monthly thorough assessment
 - Adult: Yearly thorough assessment



- Prevention:
 - Good Prophylaxis-Pilot study
 - Identify “joint at risk”
 - Prevention of risk of development Inhibitors-Haematologist concern
 - Adherence to Haematologist & Rehab team.
 - Lifestyle modification



SUBCOMMITTEES FOR DEVELOPING THIS GUIDELINE

SUBCOMMITTEE 1	Comprehensive Care of Haemophilia
CONTRIBUTORS	LEAD: Prof Dr. Md. Belayet Hossain Head, Dept. of Paediatric Haemato-Oncology Bangladesh Shishu Hospital & Institute, Dhaka. MEMBERS Dr. Chowdhury Shamsul Haque Kibria Associate Professor, Department of Paediatric Haematology & Oncology, Bangladesh Medical University, Dhaka. Dr. Shakhawat Hossain Associate Professor, Oral & Maxillofacial Surgery Department, Dean, Faculty of Dentistry, Bangladesh Medical University, Dhaka. Dr. Jannatul Ferdous Associate Professor & Head, Department of Transfusion Medicine Mugda Medical College & Hospital, Dhaka. Dr. Mirza Golam Sarwar Associate Professor of Haematology Shaheed Suhrawardy Medical College, Dhaka.
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SUBCOMMITTEE 4	Inhibitors to Clotting Factors & Management of Special Situations
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গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
প্রাথমিক স্বাস্থ্য পরিচর্যা
স্বাস্থ্য অধিদপ্তর
মহাখালী, ঢাকা -১২১২।
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তারিখঃ ০১/০৭/২০২৬ইং।

বরাবর,
অধ্যাপক ডা. সৈয়দ জাকির হোসেন
ওএসডি, সাবেক লাইন ডাইরেক্টর
নন কমিউনিকেশনাল ডিজিজ কন্ট্রোল প্রোগ্রাম
স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।

বিষয়ঃ “National Guideline for Management of Haemophilia” শীর্ষক গাইডলাইনটি কারিকুলাম কমিটি কর্তৃক অনুমোদন প্রসঙ্গে।

স্বাস্থ্য অধিদপ্তরের নন কমিউনিকেশনাল ডিজিজ কন্ট্রোল প্রোগ্রামের তত্ত্বাবধানে এবং বাংলাদেশ হেমাটোলজি সোসাইটির সহযোগিতায় **National Guideline for Management of Haemophilia** শীর্ষক -গাইডলাইনটি পর্যবেক্ষণের জন্য কমিটির ০১/০৮/২০২৬ইং তারিখের সভায় পর্যালোচনা ও সংশোধন করে সর্বসম্মত ভাবে অনুমোদন করা হলো। মার্চ পর্যায়ে বাস্তবায়নের মাধ্যমে অভিজ্ঞতার আলোকে পরবর্তীতে উক্ত গাইড লাইনটি সংশোধন, পরিমার্জন ও পরিবর্ধন করা যেতে পারে।

Kamul

(ডাঃ সৈয়দ কামরুল ইসলাম)

পরিচালক

প্রাথমিক স্বাস্থ্য পরিচর্যা

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সভাপতি, কারিকুলাম অনুমোদন কমিটি

স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।

স্মারক নং- স্বাঃঅধিঃ/পরিঃ/পিএইচসি/ কারিকুলাম/২০১৭/

তারিখঃ ০১/০৭/২০২৬ইং।

অনুলিপি সদয় অবগতি জন্যঃ

১. মহাপরিচালক, স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা। দৃষ্টি আকর্ষণঃ সহকারী পরিচালক (সমন্বয়)।
২. অতিরিক্ত মহাপরিচালক (প্রশাসন/পরিকল্পনা ও উন্নয়ন), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৩. পরিচালক (প্রশাসন ও গবেষণা), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৪. পরিচালক (অর্থ) স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৫. পরিচালক (হাসপাতাল ও ক্লিনিক সমূহ) স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৬. পরিচালক (রোগনিয়ন্ত্রণ), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৭. পরিচালক, এমআইএস, স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা- (ডিজিএইচএস এর ওয়েব সাইটে প্রকাশের অনুরোধসহ)।
৮. চীফ (কোঅর্ডিনেশন / এইচ আর আই এস), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
৯. উপ-পরিচালক (পিএইচসি), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
১০. উপ-পরিচালক (ইনসিটু), পিএইচসি, স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।
১১. প্রধান, স্বাস্থ্য শিক্ষা বুরো, স্বাস্থ্য শিক্ষা অধিদপ্তর, মহাখালী, ঢাকা।
১২. মেডিকেল অফিসার (কোঅর্ডিনেশন / এইচ আর আই এস), স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা।

(ডাঃ সৈয়দ কামরুল ইসলাম)

পরিচালক

প্রাথমিক স্বাস্থ্য পরিচর্যা

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সভাপতি, কারিকুলাম অনুমোদন কমিটি

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