MANAGEMENT OF HAEMOPHILIA

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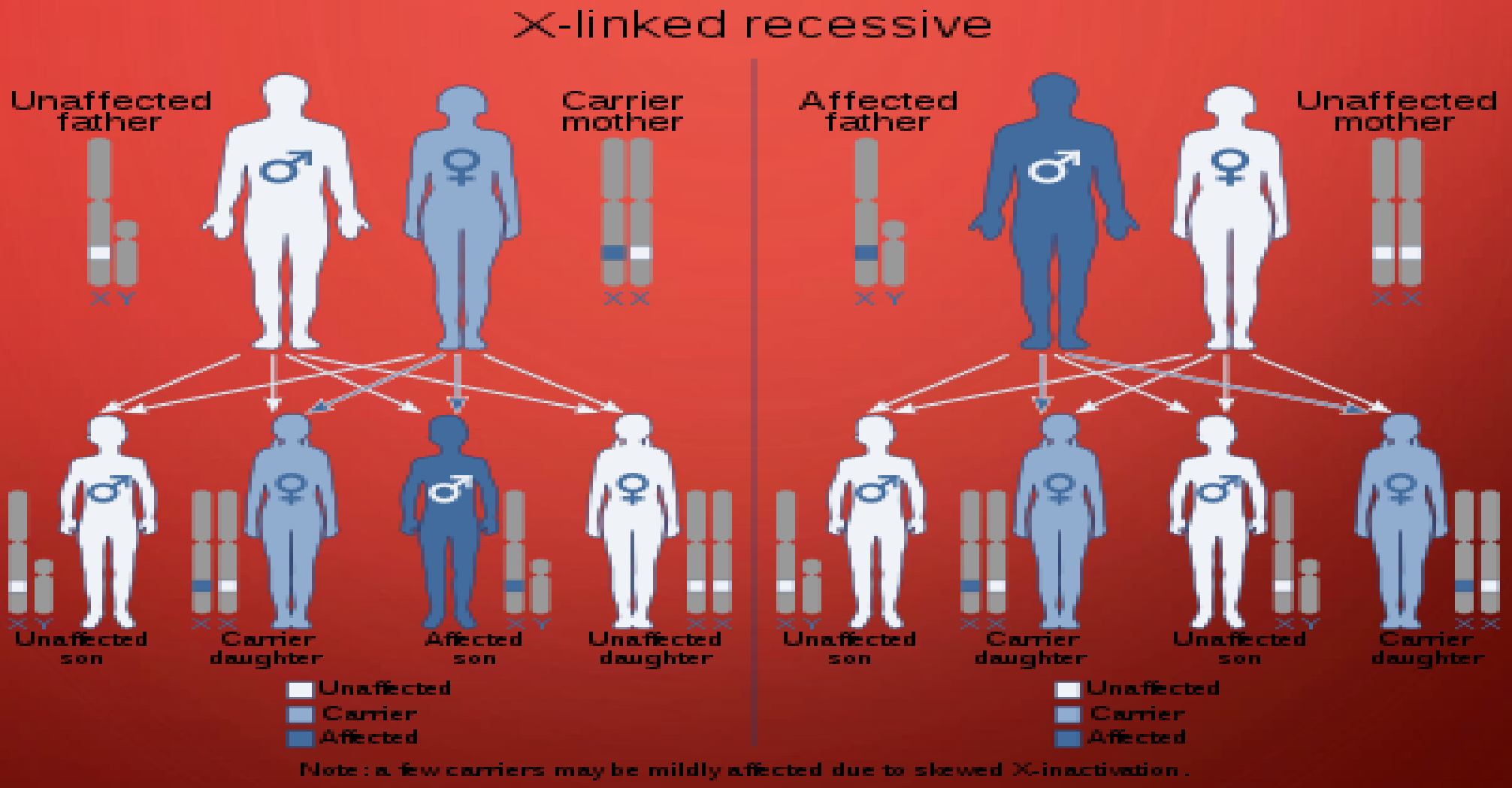
MANAGEMENT

- Introduction
- Clinical features
- Laboratory diagnosis
- Prevention of bleeds/bleeding episodes
- Home management
- Clinical treatment
- Complications
- References

INTRODUCTION

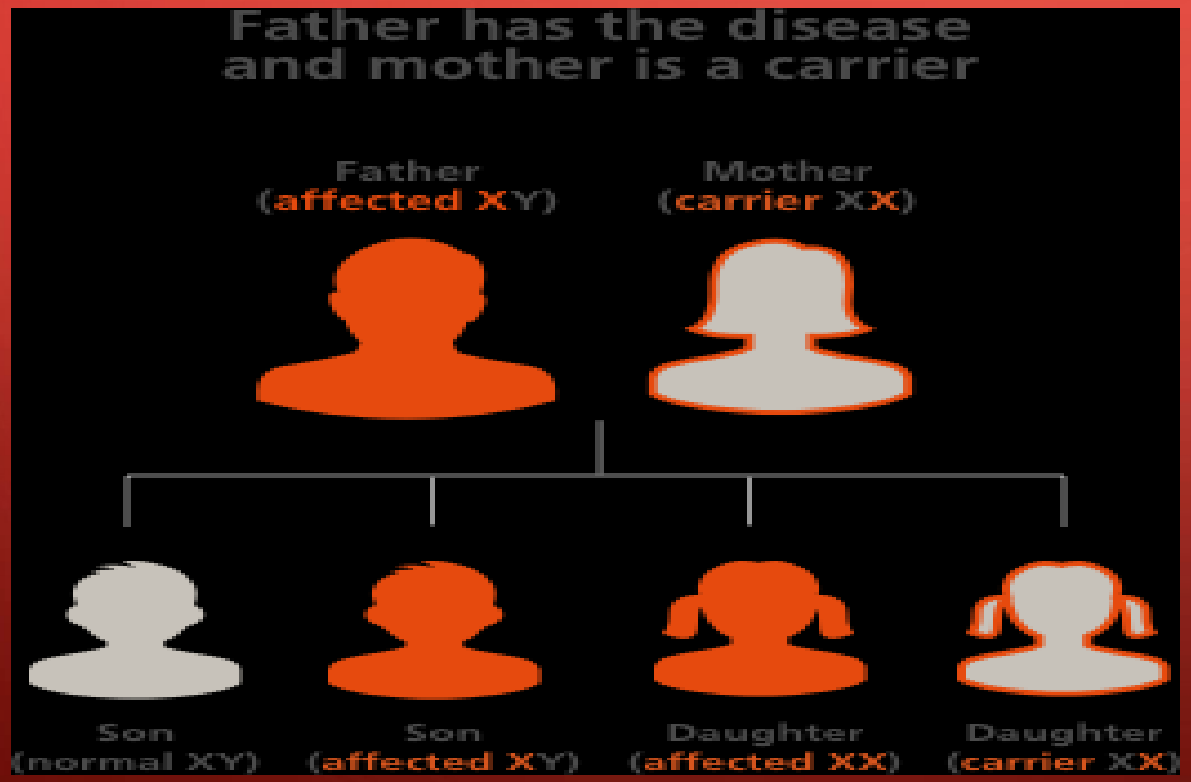
- Most common inherited bleeding disorder
- Acquired forms exist (spontaneous mutation)
- Prevalence: 30 – 100 per million population (? Nigeria)
- Haemophilia A and B
- Absence or low levels of these factors
- Pathogenesis: missense or frameshift mutation or deletions in the factor genes

INHERITANCE PATTERN – MALE HAEMOPHILIACS



INHERITANCE PATTERN – FEMALE HAEMOPHILIACS

- Affected father + carrier mother



INHERITANCE PATTERN – FEMALE HAEMOPHILIACS

- Lyionization of one X chromosome: XX(X0)
- Acquired haemophilia : antibodies

MANAGEMENT

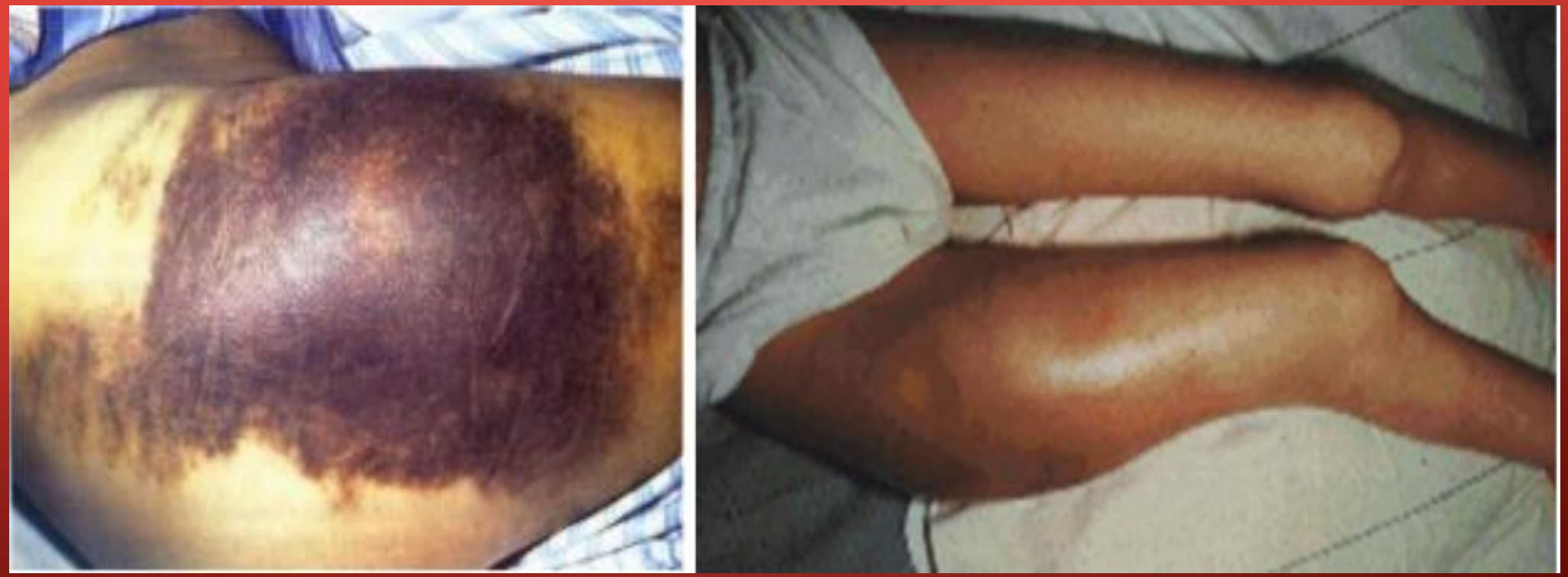
- Haemophilia treatment center
- Multidisciplinary approach
  - Core team
    - Haematologists
    - Haemophilia trained nurses
    - Physiotherapists
    - Laboratory scientists
    - Mental health specialists
  - More members
    - Dental surgeons
    - Orthopaedic surgeons
    - Obstetricians/Gynaecologists
    - Chronic pain specialists
    - Geneticists

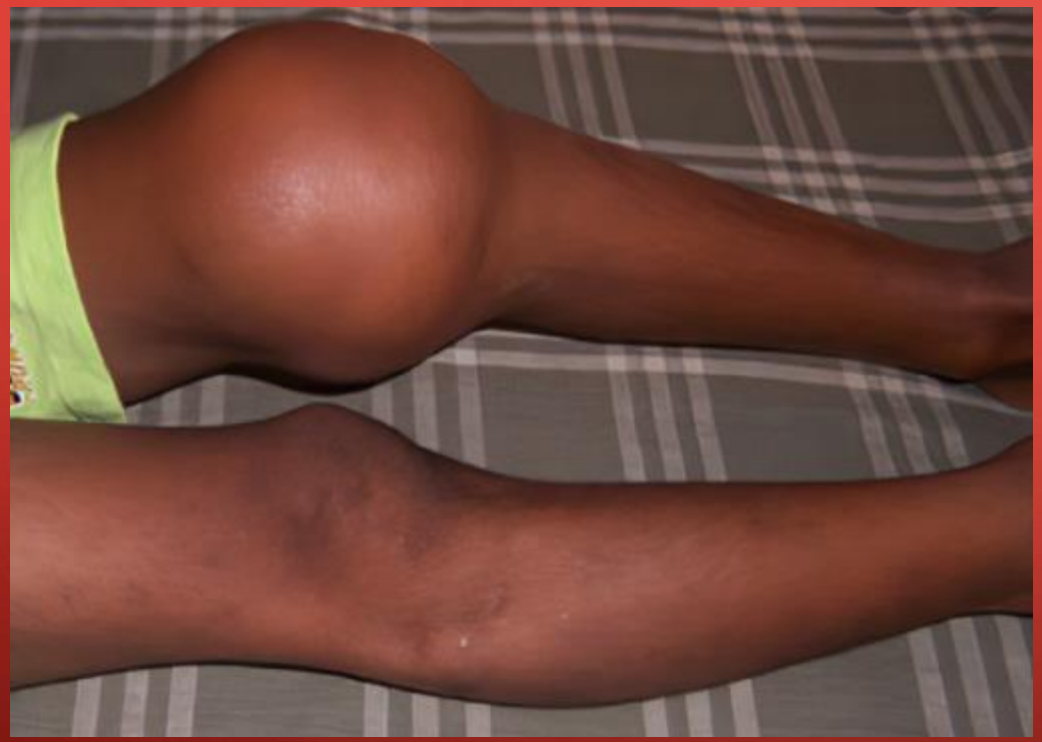
CLINICAL FEATURES

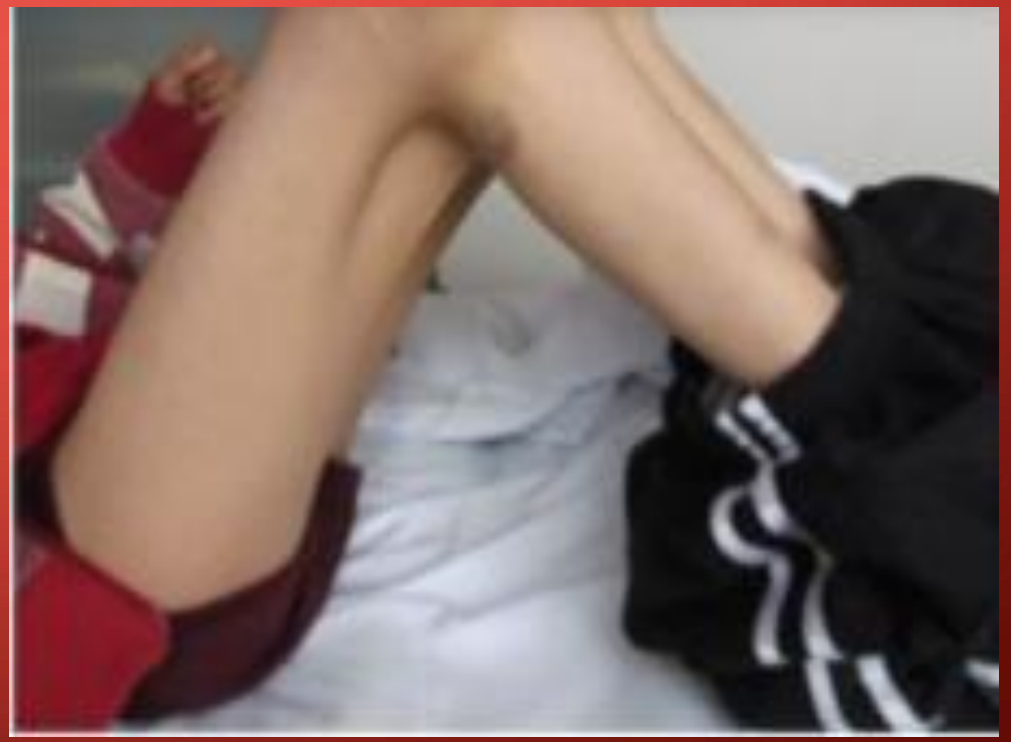
- Bleeds into/through virtually any system: starts from childhood
- Central nervous system (CNS)
- Cardiovascular system (CVS)
- Respiratory system (RS)
- Gastrointestinal system (GIT)
- Genitourinary system (GUS)
- Musculoskeletal (MSS)
- Integumentary system (IGS)

CLINICAL FEATURES CONTD

- CNS: headache, neck stiffness, vomiting etc
- CVS: vessel bleeds, tarchycardia, lethargy
- RS: epistaxis, haematoma causing airway obstruction
- GIT: hematemesis, melena, hematochezia, abdo pain
- GUS: Post circumcision bleed, hematuria, renal colic
- MSS: joint/muscle pain, tingling sensation, stiffness, warmth, limited limb movement or use, compartment syndrome, pseudotumors, haemathrosis
- IGS: haemorhage







CLASSIFICATION OF BLEEDS

- Mild (>5 – 40/50% factor activity) – bleeding following sugery or significant trauma
- Moderate (1- 5% factor activity) – bleeding following minor trauma, occasional spontaneous bleeds
- Severe (<1% factor activity) – frequent spontaneous bleeds

PREVENTION OF BLEEDS/BLEEDING EPISODES

- Avoid trauma
- Over induldging exercises
- High impact sports
- Children keeping sharp objects away
- Prophylaxis with recombinant factors

CLINICAL TREATMENT

- Hospitalisation (In-patient) : life-threatening bleeds, surgery
- Outpatient
- Factor replacement
  - Recombinant factor VIII (or IX)
  - Plasma derived factor VIII (heat and solvent detergent treated)
- Need for vascular access device

- Spontaneous mild bleeds like early hemarthrosis, epistaxis, gingival bleeds - raise factor level to 30% of normal
- Spontaneous major bleeds like late hemarthrosis, muscle bleeds - raise the facor level to 50% or more of normal
- For major surgeries, bleeding occurring at dangerous sites and lie-threatening bleeds- raise factor level to 100% and maintain above 50% when acute bleeding must have been arrested and healing has taken place
- For every unit infused per kg, factor level is raised by 20U/L


Kovaltry
500 IU Range
Antihemophilic Factor (Recombinant)
Recombinant Factor VIII
LOT 2712322
EXP 10 JUN 21
IU 576
750 IU Nominal
ELOCTATE
GRIFOLS
Factor IX Complex
Profilnine
5 mL
500 IU FIX Range
Humanitarian Use Only
Not For Resale
Bioverativ
sobi
Fresh Case

SUGGESTED DOSAGE FOR EXTENDED HALF-LIFE CLOTTING FACTOR CONCENTRATES FOR COUNTRIES WITH LIMITED RESOURCES

	Hemophilia A		Hemophilia B	
	Extended half-life products Eloctate (rFVIIIFc) (recommendation for countries where treatment products are limited)		**Extended half-life products Alprolix (rFIXFc)** (recommendation for countries where treatment products are limited)	
Type of hemorrhage	**Dosage and frequency (IU/kg)**	**Duration of therapy (Days)**	**Dosage and frequency (IU/kg)**	**Duration of therapy (Days)**
ON-DEMAND (EPISODIC) TREATMENT				
Minor/Moderate				
Early hemarthrosis, muscle bleeding or oral bleeding; serious hemorrhage in joints (extensive hemarthrosis), muscle bleeding or hematoma (iliopsoas, calf, and forearm)	**10** Repeat infusion every 24–48 hours	Until the bleeding episode is resolved	**10–20** Repeat infusion every 48 hours	Until the bleeding episode is resolved
Major (Life threatening hemorrhages)				
Intracranial, intrathoracic, gastrointestinal, and renal	**30–40** Repeat infusion every 12–24 hours	Until the bleeding episode is resolved (measure FVIII level, if level is <50–70% repeat infusion every 24 hours)	**50–60** Repeat infusion every 24 hours for the first 3 days, then repeat infuion every 48–72 hours until bleeding stops	Until the bleeding episode is resolved (approximately 7–10 days)
PROPHYLAXIS				
	10	Every 4 days	**10–20**	Every 7 days
	20	Every 7 days	**20**	Every 10 days
SURGERY				
Minor, including tooth extraction				
	20–30 Repeat infusion every 24 hours	1–3 days, depending on type of procedure	**30–40** Repeat infusion every 48 hours	At least 1 day until adequate wound healing occurs
Major				
Pre-operative	**30–40**	Every 12–24 hours for the first 48 hours or until adequate wound healing occurs, then repeat infusion every 24-48 hours for at least 7 days	**40–60**	Every 12 hours for the first 24 hours or until adequate wound healing occurs, then repeat infusion every 48 hours for at least 7 days
Post-operative	**20** After 12 hours and then every 24 hours		**20–40** Every 24–48 hours	

For further information please contact the World Federation of Hemophilia
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- Desmopressin (1-Diamino-8-D-arginine vasopressin):
  - Usually used in mild Haemophilia
  - Given intravenously or as nasal spray (0.3mcg/kg)
  - Peak effect in 30 - 60mins
  - Fluid retention is a draw back
- Antifibrinolytics – eg tranexamic acid can be used in oral bleeds to neutralize the fibrinolytic activity in the oral cavity

- Pain management- acetaminophen, opiods (oxycodone,morphine, methadone, codeine)… avoid NSAIDS and drugs which can induce or worsen bleeds
- Fresh frozen Plasma
- Inhibitors
  - Emicizumab – monoclonal antibodies (binds factors IXa and X)
  - Immune tolerance induction
  - High dose of factor VIII
  - Activated prothrombin complex concentrate
  - Activated recombinant factor VII
  - Porcine factor VIII (low crossreactivity with the antibody against factor VIII)
- Gene therapy a virus is used to introduce a copy of the gene which encodes the deficient factor

HOME TREATMENT

- R.I.C.E treatment
  - Rest affected limb
  - Ice wrapped in a cloth/towel
  - Compression – compression stockings or elastic band
  - Elevation
- Factor infusion
  - Camps (trainining on self infusion; life saving)
- Pain management
- Chart
  - Frequency of bleeds
  - Frequency of factor infusion
  - Other management procedures done

COMPLICATIONS

- Inhibitors – antibody production to factors
- Infection
- Contractures
- Walking disabilities – arthritis, joint deformity, crippling
- Psychological problems

CONCLUSION

- *Haemophilia is an important inherited bleeding disorder which can also be acquired and requires impute not just from the health sector but from family and society to ensure increased life expectancy and improve morbidity in affected patients, thereby ensuring*

- *Thank you for listening*