Inherited coagulation factor disorders

- **Hemophilia A and B**
- **Von Willebrand disease (vWD)**

Learning Objectives

At the end of lecture student should be able to know :

- *How to approach to a child who have hemophilia or VWD through:*
  - *Clinical history and physical examination*
  - *Laboratory investigations and its interpretation*
  - *Important lines of treatment*

Hemophilia A and B

- The most common hereditary coagulation disorders after vWD
- X-linked recessive bleeding disorder
- Decreased blood levels or lack of factor
  VIII (**called Hemophilia A**)
  IX Christmas factor (called Hemophilia B)

- The incidence of hemophilia A is probably 1 per 5,000 live male births
- Hemophilia A accounts for 80-85% of cases of hemophilia, with hemophilia B accounting for the remainder
- Normal factor VIII or IX level = 50-150%

Relationship of Factor Levels to Severity of Clinical Manifestations of Hemophilia A and B :

Type	% factor VIII / IX	Type of hemorrhage
Severe	**<1**	**Spontaneous; hemarthroses and deep soft tissue hemorrhages**
Moderate	**1-5**	**Gross bleeding following mild to moderate trauma; some hemarthrosis; seldom spontaneous hemorrhage**
Mild	**>5**	**Severe hemorrhage only following moderate to severe trauma or surgery**

Common Sites of Hemorrhage in Hemophilia

- **Hemarthrosis**
- **Intramuscular hematoma**
- **Hematuria**
- **Mucous membrane hemorrhage: mouth,dental,epistaxis**
- **High-risk hemorrhage(life threatening)**
  - Central nervous system : Intracranial , Intraspinal
  - Retropharyngeal
  - Retroperitoneal
  - Iliopsoas muscle
- **Hemorrhage causing compartment syndrome/ nerve compression**
  - Iliopsoas muscle

Neither factor VIII nor factor IX crosses the placenta; thus, bleeding symptoms may be present from birth

Laboratory evaluation

- Hemophilia A and B is easily identified by a markedly **prolonged PTT** and the absence or reduced level of FVIII or FIX
- (Platelet count, bleeding time, prothrombin time, and thrombin time) are normal.

Treatment of Hemophilia

- Replacement of missing clotting protein
  - On demand
  - Prophylaxis
- **On demand treatment** :
  - When bleeding occurs, the factor VIII level must be raised to hemostatic levels (35–50%) or for life-threatening or major bleeds to 100%

☐ **Dose of FVIII(IU) =**

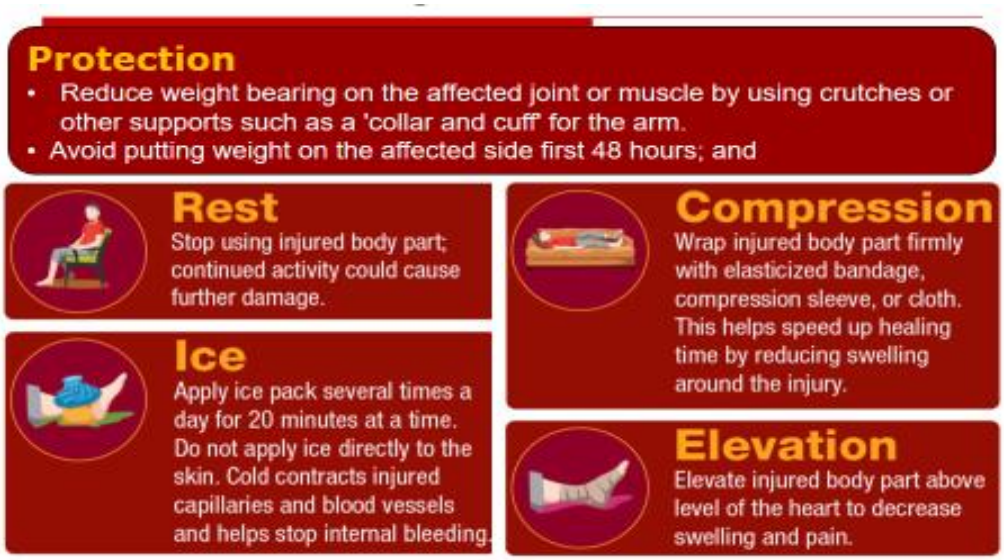
Desired rise in FVIII X Body W.t(Kg) X 0.5

☐ **Dose of FIX (IU) =**

Desired rise in plasma FIX X Body W.t(Kg) X 1.3

- **Prophylaxis:**
  - Prophylaxis should be considered optimal therapy for children with severe hemophilia
  - Treatment is usually provided every 2-3 days to maintain a measurable plasma level of clotting factor (1-2%) when assayed just before the next infusion

- **Adjuvants therapy:**
  - **Desmopressin acetate / Stimate**
  - in patient with mild hemophilia ,the patients endogenously produced FVIII can be released by administration of DDAVP
  - **Antifibrinolytic Agents**
  - **Supportive measures:** Non pharmacological therapy **(P.R.I.C.E therapy)** which represent the following:

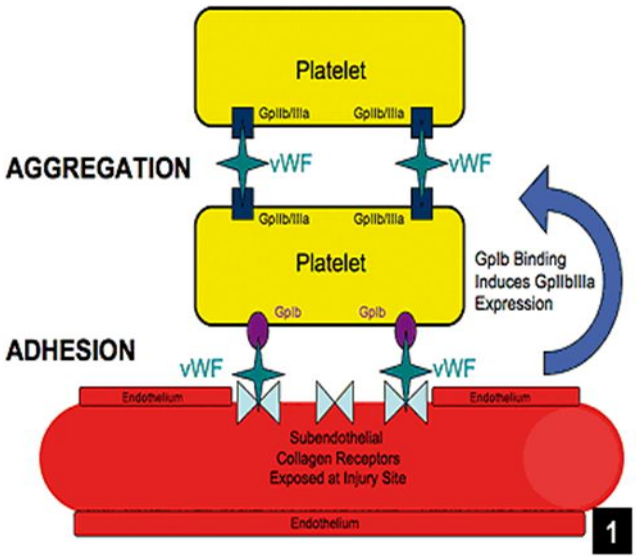


Long term complications of joint bleeding

- **Chronic arthropathy**
  As further hemorrhages occur into the same joint, the patient is said to have developed a "target" joint for future bleeds
- **Inhibitors antibodies to FVIII or FIX**
  are antibodies that the immune system develops against infused factor VIII or IX and are suspected clinically when patients become less responsive to replacement therapy:
  Treatment of inhibitors
  1.Desensitization programs(ITI), in which high doses of factor VIII or factor IX are infused in an attempt to saturate the antibody and to permit the body to develop tolerance.
  2. Activated prothrombin complex concentrates
  3. Factor VIIa

Von Willebrand disease (vWD)

- Von Willebrand disease (vWD) is an autosomally inherited congenital bleeding disorder
- **vWF has two functions:**
  - It plays an integral role in mediating adherence of platelets at sites of endothelial damage, promoting formation of the platelet plug.
  - It binds and transports FVIII, protecting it from degradation by plasma proteases



Von Willebrand disease (vWD)caused by a :

- Deficiency of vWD (**type 1**)
- Dysfunction of vWD (**type 2**)
- Complete absence of vWF (**type 3**)

Clinical manifestations:

- Epistaxis , ecchymosis, menorrhagia
- Post operative bleeding particularly after mucosal surgery e.g. tooth extraction ,tonsillectomy
- Rarely large hematoma , hemartherosis except in type 3

Laboratory finding

- Prolong bleeding time
- Prolong PTT.
- vWf antigen, vWf activity

Treatment

- von Willebrand factor concentrates
- Desmopressin, which increases the amount of circulating VWF by release from storage. thus use for treatment of type 1
- Antifibrinolytics : Aminocaproic acid or Tranexamic acid

References

- **Nelson Textbook of Pediatrics**
- **Nelson essentials Textbook of Pediatrics**
- **Illustrated textbook of pediatrics**