Hemophilia treatment

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Objectives

- Describe the drug treatment for various types of Haemophilia
- Describe the role of Desmopressin in the treatment of haemophilia

- A group of hereditary bleeding disorders in which there is a deficiency of one of the factors necessary for coagulation of blood
- People with Hemophilia bleed longer not faster.
- They are missing or have low levels of a clotting factor – this makes it difficult for the blood to form a clot

TYPES of Haemophilia

Disease	Factor deficiency	Inheritance
Hemophilia A	VIII (8)	X linked recessive
Hemophilia B	IX (9)	X linked recessive
Hemophilia C	XI (11)	Autosomal recessive
Parahemophilia	V (5)	Autosomal recessive

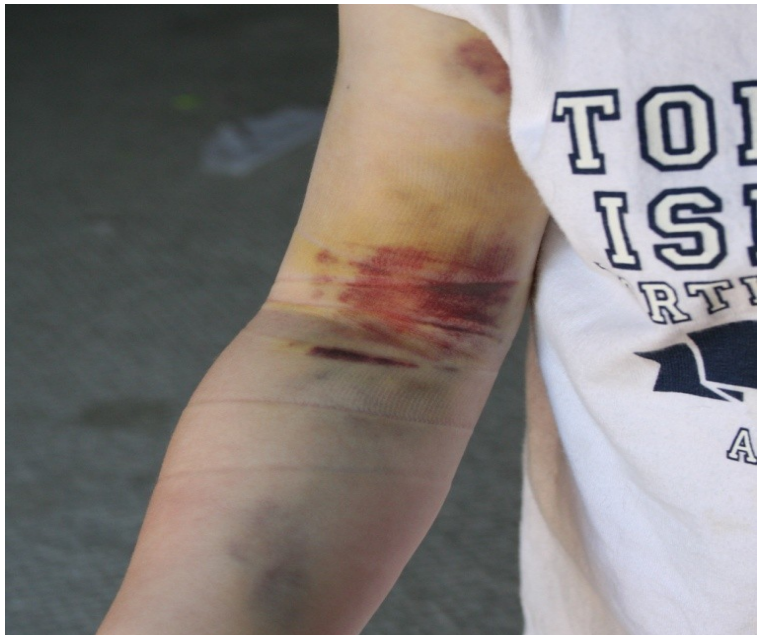
Severity

- Normal factor VIII or IX level = 50-150%
- Mild hemophilia
  - factor VIII or IX level = 6-50%
- Moderate hemophilia
  - factor VIII or IX level = 1-5%
- Severe hemophilia
  - factor VIII or IX level = <1%

Types of bleed

- Joint bleeding
- Muscle hemorrhage
- Soft tissue - bruising
- Life threatening bleeding
- Others - mouth, nose, scrapes, minor cuts

- Soft tissue bleeding is primarily characterized by bruising and hematomas (raised bruises)
- Many with hemophilia have bruising all over their bodies
- Treatment is generally not needed, but ice can help with comfort



Management Strategies

- Prevention of bleeding episodes.
- Replacement therapy.
- Gene Therapy
- Desmopressin
- Other therapies

Treatment of Bleeding Episodes

REPLACEMENT OF DEFICIENT CLOTTING FACTOR IS THE SINGLE MOST IMPORTANT STEP IN ANY INTERVENTION

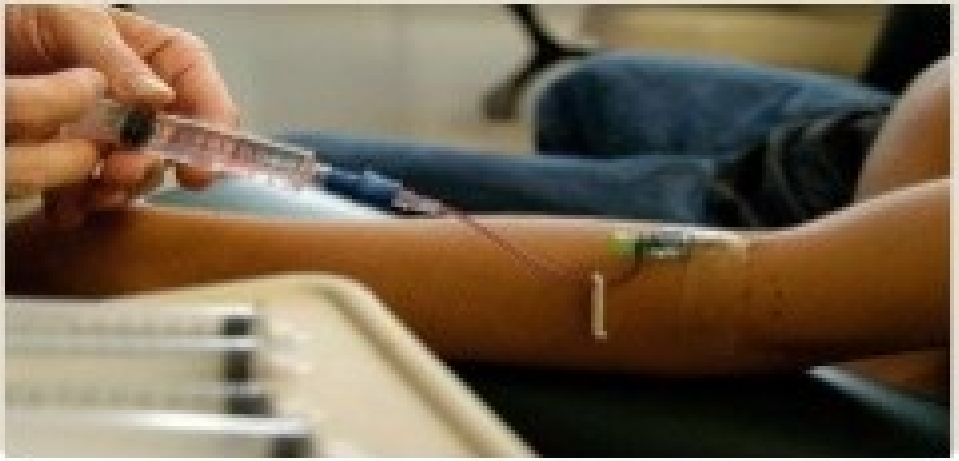
Early and appropriate treatment of each bleeding episode is critical to minimize complications.

The recognition of bleeding episodes and treating bleeds as early as possible can help prevent complications such as the lost of range of motion, arthritis and muscle atrophy

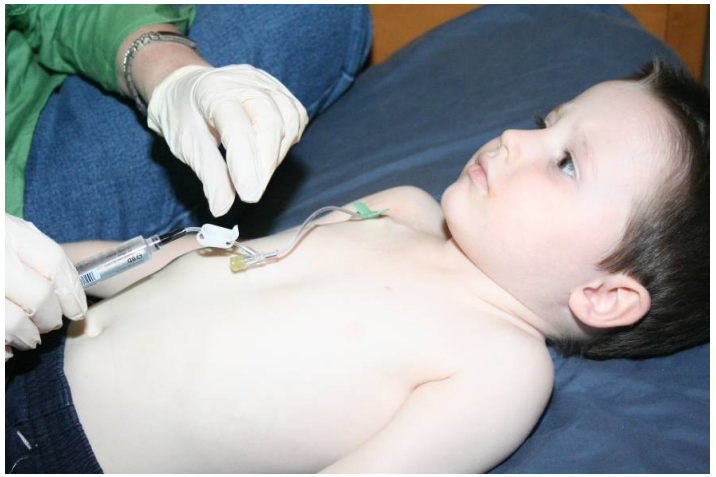
Source: Butler. *Basic Concepts of Hemophilia* 2001; 3; 3.

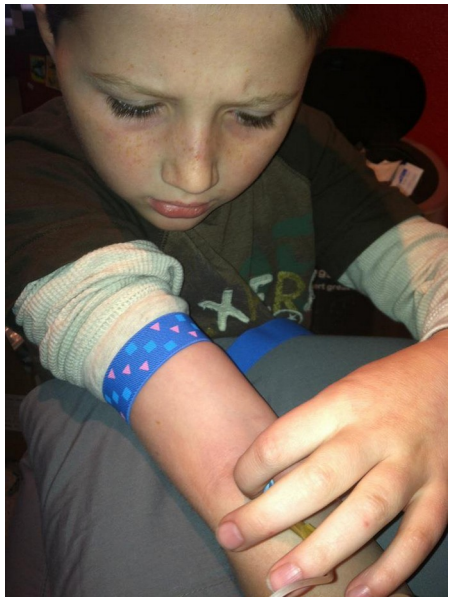
2. Replacement therapy

- Fresh whole blood
- Whole plasma
- Fresh Frozen Plasma
- Cryoprecipitate
- Factor VIII or IX Concentrate
- Recombinant Factor VII (Novo-Seven): to bypass factor VIII in the coagulation pathway



Factor Administration





- Factor concentrate is administered intravenously (IV)
- It should be administered as close to the time of the bleed as possible

Prophylaxis (or prophy)

People on prophylaxis infuse their treatment on a regular schedule to prevent bleeds from occurring. Prophylaxis is recommended for children with severe hemophilia.

- There are two types of prophylaxis:
  - Primary – This type of treatment is usually started in young children to reduce or prevent joint disease and it is continued indefinitely.
  - Secondary – This type of prophylaxis is usually short term and it is started when a bleed has occurred and continued on a regular schedule for a defined period of time.

- <u>Advantages:</u>
  - Reduced risk of joint damage
  - Ability to participate in sports and other physical activities
  - Reduced risk of spontaneous bleeding

Desmopressin (**DDAVP**)

Used to help stop bleeding in patients with von Willebrand's disease or mild **hemophilia** A.

DDAVP causes the release of von Willebrand's antigen from the platelets and the cells that line the blood vessels where it is stored.

Von Willebrand's antigen is the protein that carries factor VIII

4. Desmopressin

Action: stimulates the release of stored factor VIII and Von Willebrand factor. Von Willebrand factor carries and binds factor VIII, which then can stay in the blood stream longer.

-Administration: Injection or Nasal spray.

5. Other Treatments

EACA (ε –amino caproic acid)

Action: Antifibrinolytic → delays clot lysis

Use: Adjuvant therapy for dental procedures

Fibrin Glue:

Action: Contains fibrinogen, thrombin and factor XIII. Placed in the site of injury to stabilize clot.

Use: Dental procedures and after circumcision

Activated Prothrombin complex concentrates

- Have increased amounts of activated FVIIa, factor X & thrombin.
- APCC are effective even in patients with high titer inhibitors.
- risk of thrombosis.

Polyethylene glycol conjugation (Pegylation)

- Increases size, decreases renal excretion, extends half life.

Polysialic acid polymers

- Forms a "watery cloud" around the target molecule
- Biodegradable.

- Thank you