

Lec 17: Hemophilia

Hemophilia is a genetic bleeding disorder in which the blood does not clot properly due to a deficiency of clotting factors

Hemophilia types and Diagnosis

Types of Hemophilia

1.Hemophilia A (Classic Hemophilia)

- Cause: Deficiency of Factor VIII.
- Prevalence: Most common type (80–85% of cases.)
- Inheritance: X-linked recessive (primarily affects males.)
- Symptoms:
 - Prolonged bleeding from injuries or surgery.
 - Joint and muscle bleeding (hemarthrosis).
 - Spontaneous bruising.

2.Hemophilia B (Christmas Disease)

- Cause: Deficiency of Factor IX.
- Prevalence: Less common (15–20% of cases.)
- Inheritance: X-linked recessive (similar to Hemophilia A.)
- Symptoms: Same as Hemophilia A, but due to Factor IX deficiency.

3.Hemophilia C

- Cause: Deficiency of Factor XI.
- Prevalence: Very rare, more common in Ashkenazi Jewish populations.
- Inheritance: Autosomal recessive (affects both males and females.)
- Symptoms: Milder bleeding tendencies, especially after surgery or trauma

Diagnosis of Hemophilia

1. Clinical Evaluation

- Family history of bleeding disorders.
- Symptoms like prolonged bleeding, easy bruising, and joint swelling.

2. Laboratory Tests

a) Screening Tests

- **Prothrombin Time (PT):** Normal in hemophilia.
- **Activated Partial Thromboplastin Time (aPTT):** Prolonged (because factors VIII, IX, and XI belong to the intrinsic pathway.)
- **Platelet Count & Bleeding Time:** Normal (platelet function is not affected.)

b) Specific Clotting Factor Assays

- **Measures Factor VIII** (Hemophilia A), **Factor IX** (Hemophilia B), or **Factor XI** (Hemophilia C) levels.
- **Mild Hemophilia:** Factor levels 5–40% of normal.
- **Moderate Hemophilia:** Factor levels 1–5% of normal.
- **Severe Hemophilia:** Factor levels <1% of normal.

c) Genetic Testing

- Identifies mutations in the F8 gene (Hemophilia A) or F9 gene (Hemophilia B.)
- Used for carrier detection in females and prenatal diagnosis.

Lec 18: Von Willebrand Disease (vWD)

Functions of vWF

Von Willebrand factor (vWF) is a large glycoprotein involved in hemostasis (blood clotting). Its main functions include:

1. Platelet Adhesion: vWF helps platelets adhere to damaged blood vessel walls by binding to exposed collagen and platelet receptors (GPIb-IX-V complex).
2. Platelet Aggregation: It supports platelet-platelet interactions, promoting clot formation.
3. Carrier for Factor VIII: vWF stabilizes and transports clotting Factor VIII in the bloodstream, protecting it from degradation and ensuring proper clot formation.

Importance of vWF

- vWF is essential for normal blood clotting and preventing excessive bleeding.
- Deficiencies or dysfunction in vWF can lead to bleeding disorders.

Disorders Related to vWF

1.Von Willebrand Disease (VWD)

- The most common inherited bleeding disorder, affecting vWF quantity or function.

• Types of VWD:

- Type 1 (Mild Deficiency): Reduced vWF levels; mild bleeding tendencies.
- Type 2 (Dysfunctional vWF): Normal quantity but impaired function.
- Type 3 (Severe Deficiency): Nearly absent vWF; severe bleeding.

2.Acquired von Willebrand Syndrome (AVWS)

- Caused by underlying conditions like heart disease, autoimmune disorders, or cancer.

Diagnosis of vWF Disorders

1.Bleeding History & Family History – Helps identify potential hereditary bleeding disorders.

2.Laboratory Tests:

- vWF Antigen Test – Measures vWF levels.
- vWF Activity (Ristocetin Cofactor) Test – Assesses vWF function.
- Factor VIII Activity Test – Evaluates associated clotting factor levels.
- Multimer Analysis – Determines vWF structure and subtype.
- Platelet Function Assays – Tests platelet adhesion ability.

Conclusion

vWF is crucial for normal clotting, and disorders affecting it can lead to excessive bleeding. Early diagnosis and appropriate treatment (such as desmopressin or clotting factor concentrates) can help manage vWF-related conditions effectively.