Von Willebrand Disease

Von Willebrand Disease (vWD) is caused by a decreased level of functioning **von Willebrand factor**, which plays a crucial role in primary hemostasis. Most forms of vWD follow an inherited **autosomal dominant** pattern that affects males and females equally. vWD is the most common inherited bleeding disorder and affects approximately **1% of the population** but only 1% of those with vWD have symptoms.

PATHOPHYSIOLOGY

- Qualitative defect or quantitative deficiency of vWF
- vWF needed for platelet adhesion and aggregation, and acts as a chaperone for Factor VIII, extending its half life in circulation. Thus, vWD affects both primary and secondary hemostasis
- vWF exists as a series of multimers ranging in size, with the largest being the most active in mediating platelet adhesion/aggregation
- vWF levels vary according to blood group (non-group patient patients have higher levels)

PRESENTATION

Excessive and prolonged bleeding:

- Frequent nosebleeds
- Oral mucosa bleeding
- GI bleeding
- Heavy menstrual cycles
- Easy bruising
- Prolonged bleeding after surgery or trauma

Can use the Pediatric Bleeding Questionnaire (PBQ) to assess bleeding.

DIFFERENTIAL DIAGNOSIS

- Hemophilia A, B, C
- Bernard Soulier syndrome
- Platelet disorders
- Antithrombotic therapies
- Trauma: accidental or inflicted

CLASSIFICATION

Type 1	**Mild quantitative defect** (decreased amount of vWF and proportional decrease in vWF activity)	80% of cases
Type 2	**Qualitative defect** (vWF activity disproportionally lower than quantity)	20% of cases
Type 3	**Severe total quantitative defect** (no vWF produced)	1 per million

INVESTIGATIONS

Personal and family history of bleeding with consistent labs:

- CBC, platelets, PTT
- Plasma vWF antigen levels
- vWF:Ristocetin cofactor activity (determine how well vWF binds platelets)
- Factor 8 levels

If these are abnormal consider further tests to determine subtype:

- vWF multimer distribution with gel electrophoresis
- Ristocetin-induced platelet aggregation test

TEST RESULTS

Test	Expected Result
PTT	Normal or increased
Factor VIII	Normal or decreased
Platelet Count	Normal or decreased
Ristocetin Activity	Decreased (cofactor for vWF-platelet binding)
von Willebrand antigen	Decreased
Blood group	Decreased vWF antigen in group O
vWF multimer analysis	Multimer variants

MANAGEMENT

Supportive:

- Stop the bleeding
- Ensure **hemodynamic stability**
- **Minimize trauma**
- Avoid **medications** that could worsen bleeding symptoms
- Only ~10% require long-term prophylactic therapy

Medical management:

- **Desmopressin** (ADH analogue): a long-term therapy shown to increase vWF and factor VIII
- **vWF replacement therapy**: severe deficiency, bleeding, or short-term prophylaxis for surgery
- **Estrogen therapy**: menorrhagia
- **Tranexamic acid:** dental procedure prophylaxis

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