Overview

Useful For
Diagnosis of von Willebrand disease (VWD) type 2N

Evaluation of patients diagnosed with mild-to-moderate hemophilia A with an autosomal inheritance pattern

Evaluation of hemophilia A patients with a shortened survival of infused factor VIII (FVIII) (not caused by a specific FVIII inhibitor)

Evaluation of female patients with low FVIII activity and no prior family history of hemophilia A

Evaluation of patients with Type 1 or Types 2A, 2B, or 2M VWD with FVIII activity discordantly-lower than the von Willebrand factor antigen level

Highlights
This test is the most cost effective test for diagnosis of von Willebrand Factor (VWF): Factor VIII (FVIII) binding defects.

Genetic tests screening for variants that cause von Willebrand disease (VWD) type 2N are available. Limitations of genetic testing include expense and the potential for variants causing VWD 2N in regions not covered by the molecular assays.

Special Instructions

• Coagulation Studies

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Plasma Na Cit

Additional Testing Requirements
VWAG / von Willebrand Factor Antigen, Plasma; VWFX / von Willebrand Factor Activity, Plasma and F8A / Coagulation Factor VIII Activity Assay, Plasma are recommended to supplement results of this test.

Necessary Information
If performed at another laboratory, forward the results of the following tests with the specimen:

- von Willebrand factor (VWF) antigen

- VWF activity (ristocetin cofactor, latex immunoassay etc)

- Factor VIII (FVIII) activity
These results aid in the interpretation of this test.

**Specimen Required**

See [Coagulation Studies](#): Guidelines for Specimen Handling and Processing in Special Instructions.

**Specimen Type:** Platelet-poor plasma

**Collection Container/Tube:** Light-blue top (3.2% sodium citrate)

**Submission Container/Tube:** Polypropylene vial

**Specimen Volume:** 1 mL

**Collection Instructions:** Centrifuge, remove plasma, and centrifuge plasma again.

1. Aliquot plasma into a separate tube leaving 0.25 mL in the bottom of the centrifuged vial.

2. Freeze plasma immediately (no longer than 4 hours after collection) at < or = -20 degrees C, or, ideally < or = -40 degrees C.

**Additional Information:**

1. Double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.

2. Each coagulation assay requested should have its own vial.

**Forms**

If not ordering electronically, complete, print, and send a [Coagulation Test Request](#) (T753) with the specimen.

**Specimen Minimum Volume**

0.5 mL

**Reject Due To**

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**Specimen Stability Information**

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**Clinical and Interpretive**

**Clinical Information**

von Willebrand disease (VWD) is a bleeding disorder due to quantitative or qualitative defects in von Willebrand factor (VWF), which results from pathogenic alterations in the VWF gene. VWD constitutes 1 of the 2 most common
bleeding disorders. Most subtypes of VWD are inherited as autosomal dominant traits, although autosomal recessive variants occur.

In hemostasis, there are 2 essential roles for VWF. The first is its ability to promote platelet adhesion to damaged vessel walls, and the second is to function as a carrier protein for Factor VIII (FVIII). Thus, noncovalent binding of FVIII to VWF is necessary for normal survival of FVIII in the blood circulation. In patients with severe VWD the circulating half-life of endogenous or infused FVIII is shorter than expected. Pathogenic alterations within the FVIII binding domain of VWF may result in an isolated deficiency of FVIII associated with a clinically mild to moderate bleeding disorder which may be misdiagnosed as Hemophilia A (HA).

Abnormal binding of FVIII to VWF can be detected with a binding assay. Since its initial description in patients from the Normandy region of France, more recent studies suggest that VWD type 2N or Normandy (VWD2N) has been associated with a more severe phenotype among patients who are homozygous for pathogenic alterations within the FVIII binding domain of VWF.

In an international survey, FVIII binding defect was detected in 58/1198 (4.8%) of patients with mild HA. Other studies confirm these findings and reveal that 1.5% to 16.6% of patients with VWD Type 1 have the FVIII binding defect. The diagnosis of VWD2N has 2 main implications: 1) genetic counseling differs considerably from that for X-linked recessive HA since the inheritance of VWD2N is autosomal recessive; and 2) optimal treatment or prophylaxis of bleeding requires factor replacement therapy with products containing functional VWF.

**Reference Values**

68-106%

Pediatric reference ranges have not been established for this assay but likely achieve adult reference range by 18 years of age.

**Interpretation**

A reduced capacity of patient’s von Willebrand factor (VWF) to bind to recombinant factor VIII (FVIII) is consistent with von Willebrand disease (VWD) type 2N (Normandy).

A mild to moderate decrease of the VWF:FVIIIB ratio suggests the presence of a VWD Type 2N due to heterozygous variants in the FVIII binding domain of VWF. If clinically indicated, DNA sequence analysis of the FVIII binding domain of VWF may provide useful information.

Results do not exclude other variants of congenital VWD, eg, type 1, 2A, 2B or 2M or congenital hemophilia A. Clinical correlation should be made between patient and family bleeding history and results of VWF antigen, factor VIII and VWF activity assays.

**Cautions**

The presence of anti-rabbit antibodies in certain subjects may lead to aberrant results.

A von Willebrand Factor (VWF) antigen level greater than or equal to 15% is necessary for a good interpretation of VWF:FVIIIB results.

**Clinical Reference**


Performance

Method Description

The von Willebrand Factor (VWF):Factor VIII B (FVIIIB) assay utilizes enzyme linked immunosorbent assay (ELISA) technology. A diluted plasma sample adjusted to 10 IU dL of VWF:Antigen (Ag) is incubated with a rabbit antihuman VWF F(abâ€™)2, which is coated on the internal walls of the microplate wells. The factor VIII of the tested plasma dissociated during the incubation is washed away. Recombinant FVIII is then added, which binds to VWF. Next, mouse monoclonal anti-human FVIII antibody coupled with peroxidase binds to the remaining free antigenic determinants of the bound FVIIIr. Bound FVIIIr is quantified using a peroxidase-conjugated mouse antihuman FVIII monoclonal antibody. The intensity of the color is directly proportional with the concentration of VWF:FVIIIB initially present in the plasma sample.(Package Insert: Asserachrom VWF:FVIIIB. Diagnostica Stago, Parsippany, NJ, Revised March 2014)

PDF Report

No

Day(s) and Time(s) Test Performed

Thursday; 8 a.m.

Analytic Time

1 day

Maximum Laboratory Time

7-10 days

Specimen Retention Time

7 days

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81401  

**LOINC® Information**

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