Test Definition: VWD8B

von Willebrand Disease 2N (Subtype Normandy), Plasma

Overview

Useful For

Diagnosing von Willebrand disease (VWD) type 2N

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

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

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

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

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Highlights

This test is the most cost-effective test for diagnosis of von Willebrand Factor: Factor VIII 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.

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; VWACT / von Willebrand Factor Activity, Plasma; and F8A / Coagulation Factor VIII Activity Assay, Plasma are recommended to supplement results of this test.

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Necessary Information

If performed at another laboratory, forward the results of the following tests with the specimen:
-von Willebrand factor antigen
-VWF activity (ristocetin cofactor, latex immunoassay etc)
-Factor VIII activity

These results aid in the interpretation of this test.

Specimen Required

Specimen Type: Platelet-poor plasma
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions:
1. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing
2. Centrifuge, transfer all plasma into a vial, and centrifuge plasma again.
3. Aliquot plasma into a separate tube leaving 0.25 mL in the bottom of the centrifuged vial.
4. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally, less than or equal to -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

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	56 days	

Clinical & 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 disease-causing 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. Disease-causing 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 that 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 out of 1198 (4.8%) 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:
-Genetic counseling differs considerably from that for X-linked recessive HA since the inheritance of VWD2N is autosomal recessive.
-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 a 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 to factor VIII (FVIII) binding 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 antirabbit 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 to factor VIII binding ratio results.

Clinical Reference

1. Veyradier A, Caron C, Ternisien C, et al. Validation of the first commercial ELISA for type 2N von Willebrand's disease diagnosis. Haemophilia. 2011;17(6):944-951. doi:10.1111/j.1365-2516.2011.02499.x
2. Sadler JE. A revised classification of von Willebrand disease. For the Subcommittee on von Willebrand Factor of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis.Thromb Haemost. 1994;71(4):520-525
3. Mazurier C, Gaucher C, Jorieux S, et al. Evidence for a von Willebrand factor defect in factor VIII binding in three members of a family previously misdiagnosed as heamophilia A carriers: consequences for therapy and genetic counselling. Br J Haematol 1990;76(3):372-379. doi:10.1111/j.1365-2141.1990.tb06371.x
4. Schneppenheim R, Budde U, Krey S, et al. Results of a screening for von Willebrand disease type 2N in patients with suspected haemophilia A or von Willebrand disease type 1. Thromb Haemost. 1996;76(4):598-602
5. Seidizadeh O, Peyvandi F, Mannucci PM. Von Willebrand disease type 2N: an update. J Thromb Haemost. 202119(4):909-916. doi:10.1111/jth.15247

Performance

Method Description

The von Willebrand factor (VWF):factor VIII (FVIII) B assay utilizes enzyme linked immunosorbent assay technology. A diluted plasma sample adjusted to 10 IU dL of VWF:antigen is incubated with a rabbit antihuman VWF F(ab')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 (FVIIIr) is then added, which binds to VWF. Next, mouse monoclonal antihuman 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; 03/2014)

PDF Report

No

Day(s) Performed

Monthly on the third Thursday

Report Available

1 to 31 days

Specimen Retention Time

7 days

Performing Laboratory Location

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Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

85246

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
VWD8B	VWD 2N (Normandy), P	90919-2

Result ID	Test Result Name	Result LOINC® Value
607336	VWF:FVIIIB	90919-2
607337	VWF:FVIIIB Interpretation	48595-3