Overview

Useful For

Diagnosis of von Willebrand disease (VWD) Type 2N

Evaluation and genetic counseling of patients with mild-to-moderate hemophilia A with an atypical 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

Special Instructions

Informed Consent for Genetic Testing

Coagulation Patient Information

Informed Consent for Genetic Testing (Spanish)

Method Name

Direct Mutation Analysis by Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Specimen Required

Container/Tube:

Preferred: Yellow top (ACD solution A or B)

Acceptable: EDTA, sodium citrate

Specimen Volume: Full tube

Collection Instructions:

1. Invert several times to mix blood.

2. Send specimen in original tube.

Additional Information: If F8A / Coagulation Factor VIII Activity Assay, Plasma; VWAG / von Willebrand Factor Antigen, Plasma; and/or RIST / Ristocetin Cofactor, Plasma have been previously performed on the patient, include results of these tests when submitting specimen for testing.
Test Definition: VWD2N
von Willebrand Disease 2N (Normandy)

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. Coagulation Patient Information (T675) in Special Instructions

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

Specimen Minimum Volume
1 mL of blood in 3-mL ACD tube

Reject Due To

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<td>Lipemia</td>
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Specimen Stability Information

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Clinical and Interpretive

Clinical Information

Hemophilia A (HA) and von Willebrand disease (VWD) are bleeding disorders caused by quantitative or qualitative defects in factor VIII (FVIII) or von Willebrand factor (VWF), respectively, and constitute 2 of the most common bleeding disorders. Hemophilia A is inherited as an X-linked recessive disorder while most subtypes of VWD are inherited as autosomal dominant disorders.

VWF plays 2 essential roles in hemostasis. VWF mediates platelet adhesion to damaged blood vessel walls and VWF is a carrier protein for FVIII.

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 shortened.

Mutations within the VWF gene regions encoding for the FVIII binding domain of VWF may produce a phenotype of isolated FVIII “deficiency” associated with a clinically mild-to-moderate bleeding disorder which may be misdiagnosed as HA. This mild VWD phenotype was first described in patients from the Normandy region of France, VWD Normandy (VWD Type 2N). VWD Type 2N inheritance pattern is autosomal recessive.
In an international survey, VWD Normandy was detected in 58 (4.8%) of 1,198 patients previously diagnosed as having mild hemophilia A. Three VWF gene mutations (VWF Thr791Met, Arg816Trp, and Arg854Gln) accounted for 96% of patients with mutations in the FVIII binding domain of VWF. (3) Patients who are homozygous for 1 of the 3 common mutations have reduced levels of FVIII activity, whereas patients who are heterozygous typically have normal FVIII activity. However, patients who are heterozygous for 1 of the 3 common VWD Type 2N mutations may have decreased FVIII activity in the presence of a second (compound heterozygous) mutation in the VWF gene that typically results in a Type 1 or Type 3 VWD (quantitative defect). VWD Type 2N also has been associated with a more severe bleeding phenotype among patients who are homozygous for other mutations (VWF Glu24Lys) within the FVIII binding domain of VWF. (1,2)

Additional studies suggest that 1.5% (3/199) to 13.8% (5/36) of patients with vWD Type 1 have a FVIII binding defect. (2,4)

The diagnosis of VWD Type 2N is important for appropriate genetic counseling, because the inheritance of VWD Type 2N is autosomal recessive (as opposed to the X-linked recessive inheritance of HA).

Optimal treatment or prophylaxis of bleeding requires products containing functional VWF.

**Reference Values**

**Negative**

**Interpretation**

Interpretive report will include specimen information, assay information, background information, and conclusions based on the test results.

Clinical information and results of patient testing (factor VIII coagulant activity, von Willebrand factor antigen, and ristocetin cofactor activity) are useful for test interpretation.

**Cautions**

On-site Hemophilia Center, Special Coagulation, and/or Medical Genetics consultations are available for registered Mayo Clinic patients and may be especially helpful in complex cases. Phone consultations are available for Mayo Clinic Laboratories clients.

This test will not detect other rare mutations within the known factor VIII binding domain of the von Willebrand factor (VWF) gene or other mutations in the VWF gene.

**Clinical Reference**


Method Description
Direct mutation analysis:


PDF Report
No

Day(s) and Time(s) Test Performed
Tuesday; 1 p.m.

Analytic Time
2 days

Maximum Laboratory Time
9 days

Specimen Retention Time
Extracted DNA indefinitely, patient must opt-out.

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-VWF (von Willebrand factor) (eg, von Willebrand disease type 2N), common variants (eg, T791M, R816W, R854Q)

LOINC® Information

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## Test Definition: VWD2N
von Willebrand Disease 2N (Normandy)

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