MAYO CLINIC LABORATORIES

# Test Definition: AVWPQ

von Willebrand Disease Profile Interpretation

## Overview

### Useful For

Interpretation of testing performed as part of a profile for detection of deficiency or abnormality of von Willebrand factor (VWF) and related deficiency of factor VIII coagulant activity

Interpretation of testing performed as part of a profile for subtyping von Willebrand disease (VWD) as type 1 (most common), type 2 variants (less common), or type 3 (rare)

This test is **not useful** for detection of hemophilia carriers.

This test is **not useful** for differentiating type 2A versus 2B VWD or platelet-type VWD (pseudo-VWD).

### Method Name

Only orderable as a reflex. For more information see AVWPR / von Willebrand Disease Profile, Plasma.

Medical Interpretation

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma Na Cit

### Specimen Required

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| Gross icterus | Reject |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Plasma Na Cit | Frozen | 14 days | |

## Clinical & Interpretive

### Clinical Information

von Willebrand factor (VWF) is synthesized by the endothelial cell and megakaryocyte and is present in these cells, as well as in platelets, subendothelial tissue, and plasma.

VWF serves as an adhesive protein important in adhering platelets to subendothelial tissue at the site of vascular injury and for adhering platelets to each other (aggregation). Platelet adhesion and aggregation are essential to form a mechanical hemostatic "plug" and as the focus for interaction of clotting factors and phospholipid required for the formation of the fibrin platelet clot. VWF also stabilizes plasma factor VIII by binding it and protecting it from proteolysis and serves as a carrier protein for that clotting factor.

VWF circulates in the blood in 2 distinct compartments. Plasma VWF mainly reflects VWF synthesis and release from vascular endothelial cells. Platelet VWF (about 10% of the blood VWF) reflects VWF synthesis by bone marrow megakaryocytes with storage primarily in the alpha granules of circulating platelets.

Plasma VWF circulates normally in multimeric forms with molecular weights ranging from 500,000 to as much as 20,000,000. The high-molecular-weight (HMW) forms of VWF are the most effective components for interaction with platelets. This primary activity of plasma VWF is measured in the laboratory with the VWF activity assay, whereas VWF antigen testing measures the amount of VWF protein, and factor VIII coagulant activity indirectly reflects VWF interaction with factor VIII. VWF multimer analysis visualizes the distribution of VWF multimers and is useful as a reflexive test for subtyping von Willebrand disease (VWD).

Levels of factor VIII, VWF antigen, and VWF activity may vary greatly within each individual over time and also with blood type (normal type "O" individuals may have VWF lower than normals of other blood groups). VWF levels (and factor VIII) can be elevated in liver disease, pregnancy, estrogen therapy, inflammation, and after exercise (acute-phase reactant). VWF levels in hemophilia are normal.

VWF antigen measurement assesses the mass of plasma VWF protein, but does not reflect VWF functions or platelet VWF. The function of VWF (mediating platelet-platelet or platelet-vessel interaction) is most commonly assessed by measurement of plasma VWF activity.

VWD is the most common inherited bleeding disorder, affecting up to 1% of the population. It can also occur as an acquired bleeding disorder. Bleeding symptoms in all types of VWD are primarily mucosal, including epistaxis, menorrhagia, gastrointestinal bleeding, and ease of bruising, but surgical or posttraumatic bleeding can also occur.

Subtypes of inherited VWD are:

Type 1 VWD:
VWF plasma levels (antigen and activity) typically are both concordantly reduced in type 1 VWD. Because of this reduction, the level of coagulation factor VIII is often secondarily reduced also. Type 1 VWD is the most common VWD variation, representing 70% to 80% of clinical VWD. It is typically inherited in autosomal dominance fashion, although recessively inherited VWD also occurs (eg, type 3 VWD). Clinical severity ranges from mild or minimal to a moderately severe bleeding diathesis, and tends to correlate most closely with VWF activity. Severe type 1 disease is also called type

3 VWD, but the distinction between the 2 may sometimes be difficult.

Type 2 VWD:
Type 2 VWD variants represent 20% to 30% of clinical VWD, typically autosomal dominant in inheritance. There are 4 subtypes of type 2 VWD: 2A, 2B, 2M, and 2N. Abnormal plasma HMW VWF function and multimeric structure with decreased or absent HMW multimers are characteristic of types 2A and 2B, but are normal in type 2M or 2N.

VWF activity is decreased in types 2A, 2B, and 2M, and typically is discordantly lower than VWF antigen. Type 2N (Normandy) has substantially decreased factor VIII coagulant activity (typically 5%-30% of mean normal), with normal VWF antigen and activity and normal VWF multimers with clinical manifestation as autosomally inherited mild hemophilia (in contrast to classical X chromosome-linked hemophilia A).

Type 2A is the most common of the 4. Type 2B manifests thrombocytopenia, either persistent or transient, and is distinguished from type 2A by abnormally heightened aggregation response of patient platelets and plasma to low dose ristocetin stimulation. Type 2M typically demonstrates hypofunctional VWF with decreased VWF activity discordantly lower than VWF antigen not due to loss of HMW multimers. One variant of type 2M, Vicenza variant VWD, has ultralarge VWF multimers in plasma.

Type 3 VWD:
VWF is absent or markedly decreased in type 3 VWD (VWF antigen and activity either undetectably low or below 5% to 10% of mean normal, with secondary decrease of factor VIII coagulant activity (5%-30%). VWF multimers may be undetectable or, if present, have a normal distribution. Platelet VWF may also be absent.

Acquired VWD:
VWD can also occur on an acquired basis by a variety of mechanisms not well understood. Disorders associated with acquired VWD include certain myeloproliferative or lymphoproliferative disorders, plasma cell dyscrasias including monoclonal gammopathy of undetermined significance, autoimmune disorders (eg, rheumatoid arthritis, systemic lupus erythematosus), and a variety of other diseases. In some cases, no associated disorder is detected. Laboratory testing currently cannot distinguish between congenital and acquired VWD; clinical correlation is required.

## Reference Values

Only orderable as part of a profile. For more information see AVWPR / von Willebrand Disease Profile, Plasma.

An interpretive report will be provided.

## Interpretation

An interpretive report will be provided when testing is complete, noting presence or absence of von Willebrand Disease.

## Cautions

Testing should be performed prior to and in the absence of recent transfusion or von Willebrand factor (VWF) replacement therapy, (eg, Humate P or DDAVP [desmopressin]). If the patient has received any such therapy, this information should be provided. von Willebrand disease (VWD) patients receiving Humate P therapy may have a VWF activity level 10% to 20% lower than the VWF ristocetin cofactor activity level. Low normal levels of VWF antigen or activity do not exclude possible diagnosis of VWD (repeat testing may be indicated). Use of estrogens may result in a mild increase in VWF levels, thus, masking a diagnosis of mild VWD.

Borderline low or slightly decreased levels of VWF antigen or activity may be observed in clinically normal individuals of blood group "O."

This test is not useful for differentiating type 2A versus 2B VWD or platelet-type VWD (pseudo-VWD). This differentiation requires ristocetin-induced platelet aggregation testing, which must be performed using freshly obtained patient platelets and plasma.

Clinical correlation is required for differentiating acquired from congenital (hereditary) forms of VWD. Repeat testing may be helpful for confirming or evaluating low or borderline low levels of VWF (antigen and activity), especially when there is strong suspicion of VWD.

The milder forms of the disease, especially type 1 VWD, can be difficult to diagnose or exclude, reflecting the variability of baseline VWF levels. In addition to demonstration of persistently decreased levels of VWF, clinical correlation is required for diagnosis of all VWD subtypes, especially mild type 1 VWD.

### Clinical Reference

1. Federici AB, Mannucci PM. Advances in the genetics and treatment of von Willebrand disease. Curr Opin Pediatr. 2002;14(1):23-33
2. Budde U, Schneppenheim R. von Willebrand factor and von Willebrand disease. Rev Clin Exp Hematol. 2001;5(4):335-368
3. Kumar S, Pruthi RK, Nichols WL. Acquired von Willebrand disease. Mayo Clin Proc 2002;77(2):181-187
4. Favaloro EJ and Lippi G. eds. Hemostasis and Thrombosis, Methods and Protocols. Humana Press 2017

## Performance

### Method Description

A coagulation expert (clinician or hematopathologist) reviews the laboratory data and an interpretive report is issued.

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

7 to 12 days

### Performing Laboratory Location

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

Not Applicable

## CPT Code Information

85390-26 Special Coagulation Interpretation

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| AVWPQ | von Willebrand Disease Interp | 48595-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 603179 | Reviewed by | 18771-6 |
| 603186 | von Willebrand Disease Interp | 48595-3 |