MAYO CLINIC LABORATORIES

Test Definition: ADMBU

ADAMTS13 Inhibitor Bethesda Titer

Overview

Useful For

Assisting with the diagnosis of congenital or acquired thrombotic thrombocytopenic purpura

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

Only orderable as part of a profile. For more information see ADM13 / ADAMTS13 Activity and Inhibitor Profile, Plasma.

Fluorescence Resonance Energy Transfer (FRET)

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Specimen Required

Only orderable as part of a profile. For more information see ADM13 / ADAMTS13 Activity and Inhibitor Profile, Plasma.

Patient Preparation: Fasting preferred

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

Submission Container/Tube: Plastic vials

Specimen Volume: 2 mL in 2 plastic vials each containing 1 mL

Collection Instructions:

1. Specimen must be collected prior to replacement therapy.

2. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing in Special Instructions.

3. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.

4. Aliquot plasma (1 mL per aliquot) into 2 separate plastic vials, leaving 0.25 mL in the bottom of centrifuged vial.

5. Freeze plasma immediately (no longer than 4 hours after collection) at -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. If priority specimen, mark request form, give reason, and request a call-back.

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

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Minimum Volume

2 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen (preferred)	14 days	

Clinical & Interpretive

Clinical Information

Thrombotic thrombocytopenic purpura (TTP), a rare (estimated incidence of 3.7 cases per million) and potentially fatal thrombotic microangiopathy (TMA) syndrome, is characterized by a pentad of symptoms: thrombocytopenia, microangiopathic hemolytic anemia (intravascular hemolysis and presence of peripheral blood schistocytes), neurological symptoms, fever, and renal dysfunction. The large majority of patients initially present with thrombocytopenia and peripheral blood evidence of microangiopathy, and in the absence of any other potential explanation for such findings, satisfy criteria for early initiation of plasma exchange, which is critical for patient survival. TTP may rarely be congenital (Upshaw-Shulman syndrome), but far more commonly is acquired. Acquired TTP may be considered to be primary or idiopathic (the most frequent type) or associated with distinctive clinical conditions (secondary TTP) such as medications, hematopoietic stem cell or solid organ transplantation, sepsis, and malignancy.

The isolation and characterization of an IgG autoantibody frequently found in patients with idiopathic TTP, clarified the

basis of this entity and led to the isolation and characterization of a metalloprotease called ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 motif 13 repeats), which is the target for the IgG autoantibody, leading to a functional deficiency of ADAMTS13. ADAMTS13 cleaves the ultra-high-molecular-weight multimers of von Willebrand factor (VWF) at the peptide bond Tyr1605-Met1606 to disrupt VWF-induced platelet aggregation. The IgG antibody prevents this cleavage and leads to TTP. Although the diagnosis of TTP may be confirmed with ADAMTS13 activity and inhibition studies, the decision to initiate plasma exchange should not be delayed pending results of this assay.

Reference Values

Only orderable as part of a profile. For more information see ADM13 / ADAMTS13 Activity and Inhibitor Profile, Plasma.

<0.4 BU

Interpretation

Less than 10% ADAMTS13 activity is highly indicative of thrombotic thrombocytopenic purpura (TTP) in an appropriate clinical setting. The presence of ADAMTS13 inhibition (positive inhibitor screen) with a measurable antibody titer is most consistent with an acquired TTP.

Cautions

The ADAMTS13 activity assay is an in vitro assay using a synthetic substrate peptide in a static liquid environment. The measured ADAMTS13 activity may not reflect the true in vivo biological ADAMTS13 activity.

Not all patients with a clinical diagnosis of idiopathic thrombotic thrombocytopenic purpura (TTP) have a severe ADAMTS13 deficiency. Conversely, patients with other non-TTP conditions may have a severe ADAMTS13 deficiency (< or =10%). These conditions include hemolytic uremic syndrome, hematopoietic stem cell and solid organ transplantation, liver disease, disseminated intravascular coagulation, sepsis, pregnancy, and certain medication. Therefore, TTP remains a clinical diagnosis.

Interferences of ADAMTS13 activity assay include high levels of endogenous von Willebrand factor, hyperlipidemia, hemolysis with plasma free hemoglobin greater than 2 g/L, hyperbilirubinemia (bilirubin concentration >100 micromolar), and cleavage by other protease.

Recent plasma exchange or transfusion may falsely normalize ADAMTS13 levels, thus potentially masking the diagnosis of TTP.

The impact of ADAMTS13 levels and presence of inhibitors on overall survival, ultimate clinical outcome, responsiveness

to plasma exchange, and relapse are still controversial. Therefore, clinical correlation is recommended.

Clinical Reference

1. Sadler JE: Von Willebrand factor, ADAMTS13, and thrombotic thrombocytopenic purpura. Blood. 2008 Jul 1;112(1):11-18. doi.org/10.1182/blood-2008-02-078170

2. George JN: How I treat patients with thrombotic thrombocytopenic purpura: 2010. Blood. 2010 Nov 18;116(20):4060-4069. doi: 10.1182/blood-2010-07-271445

3. Upshaw JD: Congenital deficiency of a factor in normal plasma that reverses microangiopathic hemolysis and thrombocytopenia. N Engl J Med. 1978 Jun 15;298(24):1350-1352. doi: 10.1056/NEJM197806152982407

Performance

Method Description

The ADAMTS13 activity is measured by a fluorescence resonance energy transfer (FRET)-based assay using a 73 amino-acid peptide (FRETS-VWF73) of von Willebrand factor (VWF) as substrate. The inhibitor screen and titer assay are performed by using mixing studies that are similar to the Bethesda assay. One inhibitor (Bethesda) unit is defined as the concentration of an inhibitor that is able to reduce ADAMTS13 activity of normal pooled plasma by 50%.(Kokame K, Nobe Y, Kokubo Y, Okayama A, Miyata T: FRETS-VWF73, a first fluorogenic substrate for ADAMTS13 assay. Br J Haematol. 2005 Apr;129[1]:93-100. doi: 10.1111/j.1365-2141.2005.05420.x)

PDF Report

No

Specimen Retention Time

14 Days

Performing Laboratory Location

Rochester

Fees & Codes

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 US Food and Drug Administration.

Test Definition: ADMBU

ADAMTS13 Inhibitor Bethesda Titer

CPT Code Information

85335

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
ADMBU	ADAMTS13 Inhibitor Bethesda Titer	40824-5

Result ID	Reporting Name	LOINC®
61214	ADAMTS13 Inhibitor Bethesda Titer	40824-5