Test Definition: ADMB

ADAMTS13 Inhibitor Bethesda Titer, Plasma
(Non-Orderable)

Overview

Useful For

Only orderable as a reflex. For more information see ADAMP / ADAMTS13 Activity with Reflex Inhibitor Profile, Plasma.

Assisting with the diagnosis of congenital, immune or acquired thrombotic thrombocytopenic purpura as a part of a profile

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

Only orderable as a reflex. For more information see ADAMP / ADAMTS13 Activity with Reflex Inhibitor Profile, Plasma.

Fluorescence Resonance Energy Transfer (FRET)

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Specimen Required

Only orderable as a reflex. For more information see ADAMP / ADAMTS13 Activity with Reflex Inhibitor Profile, Plasma.

Specimen Type: Platelet-poor plasma
Patient Preparation:
Fasting: 8 hours, preferred but not required
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: Polypropylene plastic vials
Specimen Volume: 2 mL Platelet-poor plasma in 2 plastic vials, each containing 1 mL
Collection Instructions:
1. Specimen must be collected prior to factor replacement therapy.
2. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing.
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. Immediately freeze plasma (no longer than 4 hours after collection) at -20 degrees C or, ideally, -40 degrees C or

below.

Specimen Stability Information: Frozen 2 years

Additional Information:

1. A 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.

Specimen Minimum Volume

See Specimen Required

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen		

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 kidney dysfunction. A 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 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.

ADAMTS13 and inhibitor Bethesda titer results can have an impact on overall survival, ultimate clinical outcome, responsiveness to plasma exchange, and relapse are still controversial in recent literature. Therefore, clinical correlation is essential.

Reference Values

Only orderable as a reflex. For more information see ADAMP / ADAMTS13 Activity with Reflex Inhibitor Profile, Plasma.

<0.5 BU

Interpretation
Assisting with the diagnosis of congenital, immune or acquired thrombotic thrombocytopenic purpura as a part of a profile

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, hyperbilirubinemia (bilirubin concentration >30mg/dL), and cleavage by other proteases.

Recent plasma exchange or plasma 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;112(1):11-18. doi:10.1182/blood-2008-02-078170
2. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. Blood. 2010;116(20):4060-4069. doi:10.1182/blood-2010-07-271445
3. Upshaw JD Jr. Congenital deficiency of a factor in normal plasma that reverses microangiopathic hemolysis and thrombocytopenia. N Engl J Med. 1978;298(24):1350-1352. doi:10.1056/NEJM197806152982407
4. Chiasakul T, Cuker A. Clinical and laboratory diagnosis of TTP: an integrated approach. Hematology Am Soc Hematol Educ Program. 2018;2018(1):530-538. doi:10.1182/asheducation-2018.1.530
5. Mackie I, Mancini I, Muia J, et al. International Council for Standardization in Haematology (ICSH) recommendations for laboratory measurement of ADAMTS13. Int J Lab Hematol. 2020;42(6):685-696. doi:10.1111/ijlh.13295

Performance

Method Description
The ADAMTS13 activity is measured by a fluorescence resonance energy transfer-based assay using a synthetic fragment

of von Willebrand factor as substrate. Cleavage of this small fragment by the ADAMTS13 protease generates fluorescence that is directly proportionate to the quantification of ADAMTS13 activity. The Bethesda titer assay is performed using mixing studies. 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%.(Package insert: ATS-13 ADAMTS13 Activity Assay 2.0. Immucor; 08/2023)

PDF Report
No

Day(s) Performed
Monday through Friday, Sunday

Report Available
1 to 3 days

Specimen Retention Time
14 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
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
85335

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ADMB	ADAMTS13 Inhibitor Titer, P	40824-5

Result ID	Test Result Name	Result LOINC® Value
620817	ADAMTS13 Inhibitor Titer	40824-5