MAYO CLINIC LABORATORIES

Test Definition: ADAMP

ADAMTS13 Activity with Reflex Inhibitor Profile, Plasma

Overview

Useful For

Assisting with the diagnosis of immune or acquired thrombotic thrombocytopenic purpura

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
ADAMS	ADAMTS13 Activity Assay, P	Yes	Yes
ADMI	ADAMTS13 Interpretation	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
ADMB	ADAMTS13 Inhibitor Titer, P	No	No
AADAM	ADAMTS13 Profile Interpretation	No	No

Testing Algorithm

Testing begins with the ADAMTS13 activity assay to evaluate the percent activity. If the ADAMTS13 activity is less than 30%, the inhibitor titer and ADAMTS13 profile interpretation will be performed.

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing
- Coagulation Patient Information

Method Name

ADAMS, ADMB: Fluorescence Resonance Energy Transfer (FRET)
ADMI, AADAM: Technical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Ordering Guidance

Order this profile when considering a diagnosis of immune thrombotic thrombocytopenic purpura (iTTP), also known as acquired thrombotic thrombocytopenic purpura (aTTP). This diagnosis should be considered in a patient presenting with hemolytic anemia and thrombocytopenia. In patients with known iTTP/aTTP, the profile (rather than the single order ADAMTS13 activity) should be ordered if wanting to monitor presence of ADAMTS13 inhibitor.

Shipping Instructions

Send both vials in the same shipping container.

Specimen Required

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 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 immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally, at -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.

Forms

1. If not ordering electronically, complete, print, and send one of the following with the specimen:

-Renal Diagnostics Test Request (T830)

-Coagulation Test Request (T753)

2. Coagulation Patient Information (T675)

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 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

ADAMTS13 ACTIVITY ASSAY
> or =70%
Although not verified, the pediatric (<1 year) reference range could be similar to or lower than that of adults.

ADAMTS13 INHIBITOR TITER
<0.5 BU

Interpretation

Less than 10% ADAMTS13 activity is highly indicative of thrombotic thrombocytopenic purpura (TTP) in an appropriate clinical setting. The presence of ADAMTS13 measurable Bethesda titer is most consistent with an acquired (autoimmune) TTP.

Cautions

This 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 the ADAMTS13 activity assay include high levels of endogenous von Willebrand factor, hyperlipidemia, hyperbilirubinemia (bilirubin concentration >30mg/dL), and cleavage by other proteases.

Specimens collected in EDTA instead of 3.2% sodium citrate will result in artificially reduced ADAMTS13 activity.

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. (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

7 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

85397
85335 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ADAMP	ADAMTS13 Act w/Inhibitor Prof, P	53622-7

Result ID	Test Result Name	Result LOINC® Value
621149	ADAMTS13 Interpretation	69049-5
621150	ADAMTS13 Interpretation	No LOINC Needed
620816	ADAMTS13 Activity	53622-7
620819	Interpretation	69049-5