MAYO CLINIC LABORATORIES

Test Definition: ADM13

ADAMTS13 Activity and Inhibitor Profile, Plasma

Overview

Useful For

Assisting with the diagnosis of congenital or acquired thrombotic thrombocytopenic purpura

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
ADMFX	ADAMTS13 Activity Assay	No	Yes
ADMIN	ADAMTS13 Interpretation	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
ADMIS	ADAMTS13 Inhibitor Screen	No	No
ADMBU	ADAMTS13 Inhibitor Bethesda Titer	No	No

Testing Algorithm

Testing begins with the ADAMTS-13 activity assay to evaluate the percent activity. If the ADAMTS-13 activity is less than 30%, an inhibitor screen will be performed to look for specific ADAMTS-13 inhibition. If specific inhibition is apparent, the titer of the inhibitor will be determined.

Special Instructions

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

Method Name

Fluorescence Resonance Energy Transfer (FRET)

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Shipping Instructions

Send both vials in the same shipping container.

Specimen Required

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
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, below -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.

Forms

1. Coagulation Patient Information (T675)
2. If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-Coagulation Test Request (T753)

-Renal Diagnostics Test Request (T830)

Specimen Minimum Volume

2 mL

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	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 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 ADAMTS-13 (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 ADAMTS-13. ADAMTS-13 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 ADAMTS-13 activity and inhibition studies, the decision to initiate plasma exchange should not be delayed pending results of this assay.

Reference Values

ADAMTS13 ACTIVITY ASSAY
> or =70%

ADAMTS13 INHIBITOR SCREEN
Negative

ADAMTS13 BETHESDA TITER
<0.4 BU

Interpretation

Less than 10% ADAMTS-13 activity is highly indicative of thrombotic thrombocytopenic purpura (TTP) in an appropriate clinical setting. The presence of ADAMTS-13 inhibition (positive inhibitor screen) with a measurable antibody titer is most consistent with an acquired TTP.

Cautions

This ADAMTS-13 activity assay is an in vitro assay using a synthetic substrate peptide in a static liquid environment. The measured ADAMTS-13 activity may not reflect the true in vivo biological ADAMTS-13 activity.

Not all patients with a clinical diagnosis of idiopathic thrombotic thrombocytopenic purpura (TTP) have a severe ADAMTS-13 deficiency. Conversely, patients with other non-TTP conditions may have a severe ADAMTS-13 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 ADAMTS-13 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 transfusion may falsely normalize ADAMTS-13 levels, thus potentially masking the diagnosis of TTP.

The impact of ADAMTS-13 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

Performance

Method Description

The ADAMTS-13 activity is measured by a fluorescence resonance energy transfer-based assay using a synthetic fragment of von Willebrand factor as substrate and quantifying the cleavage of this small fragment by the ADAMTS-13 protease. The inhibitor screen and titer assay are performed 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 ADAMTS-13 activity of normal pooled plasma by 50%.(Mackie I, Mancini I, Muia J, Kremer Hovinga J, Nair S, Machin S, Baker R. 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)

PDF Report

No

Day(s) Performed

Monday through Friday, Sunday

Report Available

1 to 3 days

Specimen Retention Time

7 days

Performing Laboratory Location

Rochester

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)
85335 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ADM13	ADAMTS13 Activity and Inhibitor Profile	53622-7

Result ID	Test Result Name	Result LOINC® Value
61211	ADAMTS13 Activity Assay	53622-7
34586	ADAMTS13 Interpretation	69049-5