MAYO CLINIC LABORATORIES

Test Definition: ADMAB

ADAMTS 13 Antibody, Plasma

Overview

Useful For
Assisting with the diagnosis and monitoring of congenital, immune, or acquired thrombotic thrombocytopenic purpura

Special Instructions
- Coagulation Guidelines for Specimen Handling and Processing

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Plasma Na Cit

Ordering Guidance
Consider ordering in patients to aid in distinguishing between congenital thrombotic thrombocytopenic purpura (TTP) and acquired autoimmune TTP.

Specimen Required
Patient Preparation:
Fasting: 8 hours, preferred
Collection Container/Tube: Light-blue top (3.2% sodium citrate)
Submission Container/Tube: Polypropylene plastic vial
Specimen Volume: 1 mL plasma
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 into a separate plastic vial, 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.
Specimen Stability Information: Frozen 21 months
Additional Information:
1. Double-centrifuged specimen is critical for accurate results.
2. Each coagulation assay requested should have its own vial.

Forms

If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.

Specimen Minimum Volume

1 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		

Clinical & Interpretive

Clinical Information

Immune thrombotic thrombocytopenic purpura (iTTP) is a rare (estimated incidence of 3.7 cases per million) and potentially fatal thrombotic microangiopathy syndrome. It is characterized by thrombocytopenia and microangiopathic hemolytic anemia (intravascular hemolysis and presence of peripheral blood schistocytes), with no apparent alternative explanation of these findings. Other clinical features may include neurological symptoms, fever, and acute kidney injury. 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 is far more commonly acquired or immune mediated. iTTP 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 iTTP 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. Normally, 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 anti-ADAMTS13 IgG antibody interferes with this cleavage resulting in circulating ultra-high molecular weight multimers, microvascular occlusion, and leads to TTP.

The initial testing for diagnosis of TTP consists of testing for ADAMTS13 activity and, if indicated, assessment of an inhibitor against ADAMTS13. However, in the appropriate clinical circumstance, the decision to initiate plasma exchange should not be delayed pending results of this assay.

Approximately 35% of antibodies to ADAMTS13 are non-neutralizing. These will not be detected by a mixing study Bethesda type of assay but may foster enhanced clearance/reduction of ADAMTS13. Enzyme-linked immunosorbent assay ADAMTS13 antibody testing may be useful in determining congenital vs. immune TTP.(1)

Cohort studies have examined the prognostic impact of presence of ADAMTS13 IgG antibody in TTP. Although there are

conflicting studies, the weight of evidence suggests that a low ADAMTS13 activity, an elevated Bethesda titer, presence of an IgG antibody and a low ADAMTS13 antigen are strong independent predictors of more severe disease, longer time to achieving remission and when present at remission a shorter time to relapse.

Reference Values

Negative: <12 U/mL
Borderline positive: 12-15 U/mL
Positive: >15 U/mL

Interpretation

Greater than or equal to 12 U/mL ADAMTS13 antibody is indicative of immune mediated thrombotic thrombocytopenic purpura in an appropriate clinical setting.

Cautions

Interferences of the ADAMTS13 antibody assay include high levels of hyperlipidemia. Lipemia can result in inconsistent to falsely elevated ADAMTS13 antibody U/mL, resulting in variable to false-positive test results using this methodology.

Recent treatment for thrombotic thrombocytopenic purpura (TTP) may reduce antibody levels; submission for testing prior to treatment is recommended.

Samples with high concentrations other than anti-ADAMTS13 autoantibodies may result in weak-positive or borderline-positive results.

Not all patients with a clinical diagnosis of TTP have a severe ADAMTS13 deficiency. Conversely, patients with other non-TTP conditions may have a moderate to 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.

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. Dainese C, Valeri F, Bruno B, Borchiellini A. Anti-ADAMTS13 autoantibodies: From pathophysiology to prognostic impact-A review for clinicians. J Clin Med. 2023;12(17):5630. doi:10.3390/jcm12175630.
2. Nakashima MO, Zhang X, Rogers HJ, et al. Validation of a panel of ADAMTS13 assays for diagnosis of thrombotic thrombocytopenic purpura: activity, functional inhibitor, and autoantibody test. Int J Lab Hematol. 2016;38(5):550-559. doi:10.1111/ijlh.12542
3. Alwan F, Vendramin C, Vanhoorelbeke K, et al. Presenting ADAMTS13 antibody and antigen levels predict prognosis in immune-mediated thrombotic thrombocytopenic purpura. Blood. 2017;130(4):446-471. doi:10.1182/blood-2016-12-758656
4. Yang S, Jin M, Lin S, Cataland S, Wu H. ADAMTS13 activity and antigen during therapy and follow-up of patients with idiopathic thrombotic thrombocytopenic purpura: correlation with clinical outcome. Haematologica. 2011;96(10):1521-1527. doi:10.3324/haematol.2011.042945
5. Masias C, Cataland SR. The role of ADAMTS13 testing in the diagnosis and management of thrombotic microangiopathies and thrombosis. Blood. 2018;132(9):903-910. doi:10.1182/blood-2018-02-791533
6. Starke R, Machin S, Scully M, Purdy G, Mackie I. The clinical utility of ADAMTS13 activity, antigen and autoantibody

assays in thrombotic thrombocytopenic purpura. Br J Haematol. 2007;136(4):649-655. doi:10.1111/j.1365-2141.2006.06471.x
7. MacArthur TA, Goswami J, Moon Tasson L, et al. Quantification of von Willebrand factor and ADAMTS-13 after traumatic injury: a pilot study. Trauma Surg Acute Care Open. 2021;6(1):e000703. doi:10.1136/tsaco-2021-000703
8. Edvardsen MS, Hansen ES, Ueland T, et al. Impact of the von Willebrand factor-ADAMTS-13 axis on the risk of future venous thromboembolism. J Thromb Haemost. 2023;21(5):1227-1237. doi:10.1016/j.jtha.2023.01.024
9. Rieger M, Mannucci PM, Kremer Hovinga JA, et al. ADAMTS13 autoantibodies in patients with thrombotic microangiopathies and other immunomediated diseases. Blood. 2005;106(4):1262-1267. doi:10.1182/blood-2004-11-4490

Performance

Method Description

Testing is performed on the Janus G3 liquid handler and BioTek microplate reader with Gen5 software using the Technoclone Technozym INH kit. The method used is an enzyme-linked immunosorbent assay.

A microtiter plate coated with a recombinant form of ADAMTS13 protease (rADAMTS13) in a 96 well polystyrene plate. Diluted patient plasma is incubated in the wells, allowing anti-ADAMTS-13 antibody in the sample to bind to the (rADAMTS13) in the wells. The plate is washed to remove unbound target. Conjugate: POX anti-human ADAMTS13 detection antibody is added to each well and incubated. After incubation, the conjugate is removed by washing. A chromogenic substrate of tetramethylbenzidine (TMB) is incubated and followed by a stopping solution of 2.5% sulfuric acid, to develop a color reaction. The intensity of the color is measured at 450 nm (reference of 620 nm) and is directly proportional to amount of ADAMTS13 antibody in the sample as determined against a reference line using assayed reference plasma.(Package insert: TECHNOZYM ADAMTS 13 INH ELISA, quantitative test for detection of human autoantibodies (IgG) in serum or plasma against ADAMTS13. Technoclone; Rev.023, 09/22/2021; Dekimpe C, Roose E, Kangro K, et al. Determination of anti-ADAMTS-13 autoantibody titers in ELISA: Influence of ADAMTS-13 presentation and autoantibody detection. J Thromb Haemost. 2021;19[9]:2248-2255. doi:10.1111/jth.15297)

PDF Report

No

Day(s) Performed

Varies

Report Available

7 to 15 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

83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ADMAB	ADAMTS 13 Antibody, P	40824-5

Result ID	Test Result Name	Result LOINC® Value
623136	ADAMTS 13 Antibody	40824-5
623272	Interpretation	69049-5