Test Definition: ADM13  
ADAMTS13 Activity and Inhibitor Profile

Overview

Useful For
Assisting with the diagnosis of congenital or acquired thrombotic thrombocytopenic purpura

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>ADMFX</td>
<td>ADAMTS13 Activity Assay</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>ADMIN</td>
<td>ADAMTS13 Interpretation</td>
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Reflex Tests

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<tr>
<td>ADMIS</td>
<td>ADAMTS13 Inhibitor Screen</td>
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<tr>
<td>ADMBU</td>
<td>ADAMTS13 Inhibitor Bethesda Titer</td>
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</table>

Testing Algorithm
Testing begins with ADAMTS13 activity assay to evaluate the percent activity. If the ADAMTS13 activity assay is less than 30%, an inhibitor screen will be performed to look for specific ADAMTS13 inhibition. If specific inhibition is apparent, the titer of the inhibitor will be determined.

Special Instructions
- Coagulation Studies
- Coagulation Patient Information

Method Name
ADMFX: 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
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Patient Preparation: Fasting preferred

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

Submission Container/Tube: Plastic vials

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

Collection Instructions:
1. Specimen must be drawn prior to replacement therapy.
2. Spin down, remove plasma, and spin plasma again.
3. 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.

Forms
1. Coagulation Patient Information (T675) in Special Instructions

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

<table>
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<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
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<tbody>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
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<tr>
<td>Gross icterus</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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<tr>
<td>Plasma Na Cit</td>
<td>Frozen</td>
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**Clinical and 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**

**ADAMTS13 ACTIVITY ASSAY**

> or =70%

**ADAMTS13 INHIBITOR SCREEN**

Negative

**ADAMTS13 BETHESDA TITER**

<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**


**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, et al: FRETS-VWF73, a first fluorogenic substrate for ADAMTS13 assay. Br J Haematol 2005 Apr;129[1]:93-100)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Sunday; Varies

**Analytic Time**

ADAMTS13 Activity Assay: 24 hours/ADAMTS13 Inhibitor Assay: 1-3 days/ADAMTS13 Bethesda Titer: 1-3 days

**Maximum Laboratory Time**

3 days

**Specimen Retention Time**

7 days

**Performing Laboratory Location**

Rochester

**Fees and Codes**
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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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
85397-ADAMTS13 activity assay
85335-ADAMTS13 inhibitor screen assay (if appropriate)
85335-ADAMTS13 Bethesda titer (if appropriate)

LOINC® Information

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