MAYO CLINIC LABORATORIES

Test Definition: ATTI

Antithrombin Antigen, Plasma

Overview

Useful For

Assessing abnormal results of the antithrombin activity assay (ATTF / Antithrombin Activity, Plasma), the recommended primary (screening) antithrombin assay

Diagnosing antithrombin deficiency, acquired or congenital, in conjunction with measurement of antithrombin activity

An adjunct in the diagnosis and management of carbohydrate-deficient glycoprotein syndromes

Special Instructions

- Coagulation Guidelines for Specimen Handling and Processing

Method Name

Latex Immunoassay (LIA)

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Ordering Guidance

For monitoring treatment of antithrombin deficiency disorders, including infusion of antithrombin therapeutic concentrate, order ATTF / Antithrombin Activity, Plasma.

Necessary Information

If patient is being treated with heparin, this should be noted, as heparin treatment may lower plasma antithrombin.

Specimen Required

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: 13-mm x 75-mm, 5-mL, plastic vial (polypropylene preferred)

Specimen Volume: 1 mL Platelet-poor plasma

Collection Instructions:

1. For complete instructions, see Coagulation Guidelines for Specimen Handling and Processing.
2. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.

3. Aliquot plasma into a plastic vial leaving 0.25 mL in the bottom of centrifuged vial.
4. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally, at-40 degrees C or below.

Additional Information:

1. 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

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

Specimen Minimum Volume

Platelet-poor plasma: 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Antithrombin is a member of the serine protease inhibitor (serpin) superfamily. It is the principal plasma anticoagulant serpin mediating inactivation of serine protease procoagulant enzymes, chiefly thrombin and coagulation factors Xa and IXa.(1) Heparin and certain other naturally occurring glycosaminoglycans markedly enhance antithrombin's anticoagulant activity (approximately 1000-fold) by providing a template to catalyze formation of covalently bonded, inactive complexes of serine protease and antithrombin that are subsequently cleared from circulation. Antithrombin is the mediator of heparin's anticoagulant activity.

The antithrombin gene on chromosome 1 encodes a glycoprotein of approximately 58,000 Da that is synthesized in the liver and is present in a relatively high plasma concentration (approximately 2.3 mcmol/L). The biological half-life of antithrombin is 2 to 3 days.

Hereditary antithrombin deficiency, a relatively rare, autosomal dominant disorder, produces a thrombotic diathesis (thrombophilia). Individuals with hereditary antithrombin deficiency are usually heterozygous with plasma antithrombin activity results of approximately 40% to 70%. These patients primarily manifest with venous thromboembolism (deep vein thrombosis and pulmonary embolism), with the potential of development as early as adolescence or younger

adulthood. More than 100 different variants have been identified throughout the gene, producing either the more common type I defects (low antithrombin activity and antigen) or the rarer type II defects (dysfunctional protein with low activity and normal antigen).(2) Homozygous antithrombin deficiency appears to be incompatible with life.

The incidence of hereditary antithrombin deficiency is approximately 1:2000 to 1:3000 in general populations, although minor deficiency (antithrombin activity =70% to 75%) may be more frequent (approximately 1:350 to 1:650). In populations with venous thrombophilia, approximately 1% to 2% have antithrombin deficiency. Among the recognized hereditary thrombophilic disorders (including deficiencies of proteins C and S, as well as activated protein C-resistance [factor V Leiden variant]), antithrombin deficiency may have the highest phenotypic penetrance (greater risk of venous thromboembolism). Arterial thrombosis (eg, stroke, myocardial infarction) has occasionally been reported in association with hereditary antithrombin deficiency.

Hereditary deficiency of antithrombin activity can also occur because of defective glycosylation of this protein in individuals with carbohydrate-deficient glycoprotein syndromes (CDGS).(3) Antithrombin activity assessment may be useful as an adjunct in the diagnosis and management of CDGS.

Acquired deficiency of antithrombin is much more common than hereditary deficiency. Acquired deficiency can occur due to:
-Heparin therapy (catalysis of antithrombin consumption)
-Intravascular coagulation and fibrinolysis (ICF), disseminated intravascular coagulation (DIC), or other consumptive coagulopathies
-Liver disease (decreased synthesis and/or increased consumption)
-Nephrotic syndrome (urinary protein loss)
-L-asparaginase chemotherapy (decreased synthesis)
-Other conditions(1)

In general, the clinical implications (thrombotic risk) of antithrombin deficiency in these disorders are not well defined, although antithrombin replacement in severe DIC/ICF is being evaluated.(4) Assay of antithrombin activity may be of diagnostic or prognostic value in some acquired deficiency states.

Reference Values

Adults: 80-120%
Normal, full-term newborn infants may have decreased levels (> or =35-40%) that reach adult levels by 180 days postnatal.*
Healthy, premature infants (30-36 weeks gestation) may have decreased levels that reach adult levels by 180 days postnatal.*
*See Pediatric Hemostasis References section in Coagulation Guidelines for Specimen Handling and Processing.

Interpretation

Hereditary antithrombin deficiency is much less common than acquired deficiency. Diagnosis of hereditary deficiency requires clinical correlation, testing of both antithrombin activity and antithrombin antigen, and may be aided by repeated testing and family studies. DNA-based diagnostic testing may be helpful but is generally not readily available.

Acquired antithrombin deficiency may occur in association with a number of conditions (see Clinical Information). The clinical significance (thrombotic risk) of acquired antithrombin deficiency is not well established, but accumulating information suggests possible benefit of antithrombin replacement therapy in carefully selected situations.(4)

Increased antithrombin activity has no definite clinical significance.

Cautions

Antithrombin antigen results are potentially affected by:
-Heparin (unfractionated or low-molecular-weight) greater than 4 U/mL
-Heparin therapy; may temporarily decrease plasma antithrombin antigen into the abnormal range
-Hemoglobin greater than 700 mg/dL
-Bilirubin greater than 45 mg/dL
-Lipemia; may lead to an underestimation of the antithrombin antigen level
-Rheumatoid factor greater than 800 IU/mL; may lead to overestimation of the antithrombin antigen level
-Anti-rabbit antibodies; may lead to aberrant results in certain subjects

Clinical Reference

1. Bock SC. Antithrombin III and heparin cofactor II. In: Colman RW, Hirsh J, Marder VJ, et al, eds. Hemostasis and Thrombosis. 4th ed. Lippencott Williams and Wilkins; 2001:321-333
2. Viazzer H. Hereditary and acquired antithrombin deficiency. Semin Thromb Hemost. 1999;25(3):257-263
3. Conrad J. Antithrombin activity and antigen. In: Laboratory Techniques in Thrombosis-A Manual. 2nd ed. Kluwer Academic Publishers; 1999:121-128
4. Lane DA, Bayston T, Olds RJ, et al. Antithrombin mutation database: 2nd (1997) update. For the Plasma Coagulation Inhibitors Subcommittee of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Thromb Haemost. 1997;77(1):197-211
5. Van Cott EM, Orlando C, Moore GW, et al. Recommendations for clinical laboratory testing for antithrombin deficiency; Communication from the SSC of the ISTH. J Thromb Haemost. 2020;18(1):17-22

Performance

Method Description

This assay is performed on the Instrumentation Laboratory ACL TOP using the Diagnostica Stago LIATEST AT III kit. Antithrombin antigen is determined using automated latex immunoassay (LIA) methodology. Patient plasma, containing antithrombin antigen, is combined with a latex reagent containing rabbit antihuman antibodies. An antigen-antibody reaction takes place, causing the latex particles to agglutinate and form aggregates. The aggregates form diameters greater than the wavelength of the light (405 nm) passing through causing absorption of the light. This change in absorption is measured over time and reported as delta optical density. The increase in absorption is proportional to the concentration of antithrombin antigen present in the sample.(Package insert: LIATEST AT III. Diagnostica Stago S.A.S.; Rev. 04/2018)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 to 4 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 has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

85301

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ATTI	Antithrombin Antigen, P	27812-7

Result ID	Test Result Name	Result LOINC® Value
ATTI	Antithrombin Antigen, P	27812-7