Test Definition: AATTA

Antithrombin Summary Interpretation

Overview

Useful For

Diagnosis of antithrombin deficiency, acquired or congenital

Monitoring treatment of antithrombin deficiency disorders, including infusion of antithrombin therapeutic concentrate

Testing Algorithm

If the antithrombin activity assay is normal or elevated, a computer-generated interpretive comment will be provided indicating antithrombin antigen and the antithrombin summary interpretation are not indicated and will not be performed.

If the antithrombin activity assay is low, a computer-generated interpretive comment will be provided indicating results of activity and reflexed antithrombin antigen and antithrombin summary interpretation.

Method Name

Only orderable as a reflex. For more information see AATTF / Antithrombin Activity, with Reflex to Antithrombin Antigen, Plasma.

Technical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Specimen Required

Only orderable as a reflex. For more information see AATTF / Antithrombin Activity, with Reflex to Antithrombin Antigen, Plasma.

Reject Due To

Gross hemolysis	Reject
Thawing**	Cold reject; Warm 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 the anticoagulant activity of antithrombins (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 anticoagulant activity of heparin.

The antithrombin gene on chromosome 1 encodes a glycoprotein with a molecular weight of approximately 58,000 D, which 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 alterations 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%-75%) may be more frequent (approximately 1:350-650). In populations with venous thrombophilia, approximately 1% to 2% of individuals 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) or disseminated intravascular coagulation (DIC), and other consumptive coagulopathies

-Liver disease (decreased synthesis and/or increased consumption) or with nephritic 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 disseminated intravascular coagulation/intravascular coagulation and fibrinolysis (DIC/ICF) is being evaluated.(4) Assay of antithrombin activity may be of diagnostic or prognostic value in some acquired deficiency states.

Reference Values

Only orderable as a reflex. For more information see AATTF / Antithrombin Activity, with Reflex to Antithrombin Antigen, Plasma.

An interpretive report will be provided.

Interpretation

Antithrombin deficiencies due to inherited causes are much less common than those due to acquired causes (see Clinical Information). Diagnosis of hereditary deficiency requires clinical correlation, with the prospect of repeat testing (including antithrombin antigen assay), and family studies (with appropriate counseling). DNA-based diagnostic testing may be helpful, see GNANT / Antithrombin Deficiency, *SERPINC1* Gene, Next-Generation Sequencing, Varies.

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)

Antithrombin deficiency, acquired or congenital, may contribute to the phenomenon of "heparin therapy resistance" (requirement of larger heparin doses than expected for achievement of therapeutic anticoagulation responses). However, it may more often have other pathophysiology, such as "acute-phase" elevation of coagulation factor VIII or plasma heparin-binding proteins.

Increased antithrombin activity is of unknown hemostatic significance. Direct factor Xa inhibitors, rivaroxaban (Xarelto), apixaban (Eliquis), and edoxaban (Savaysa) may falsely elevate the antithrombin activity and mask a diagnosis of antithrombin deficiency.

Cautions

Antithrombin functional result is affected by:
-Heparin (unfractionated or low-molecular-weight) >4 U/mL
-Alpha-1-antitrypsin >4 mg/mL
-Alpha-2-macroglobulin >10 mg/mL
-Heparin cofactor II >4 U/mL
-Hemoglobin >500 mg/dL
-Bilirubin >40 mg/dL
-Triglycerides >2300 mg/dL

Heparin therapy may temporarily decrease plasma antithrombin activity into the abnormal range.

Antithrombin activity in serum specimens may be significantly lower than in plasma.

Antithrombin antigen results are potentially affected by:
-Heparin (unfractionated or low-molecular-weight) >4 U/mL
-Hemoglobin >7 g/L
-Bilirubin >500 mg/L
-Lipemia; may lead to an over-estimation of the antithrombin antigen level
-Rheumatoid factor (RF) >800 IU/mL; may lead to overestimation of the antithrombin antigen level
-Anti-rabbit antibodies in certain subjects leads to aberrant results
-Heparin therapy may temporarily decrease plasma antithrombin antigen into the abnormal range

Clinical Reference

1. Lane DA, Olds RJ, Thein SL. Antithrombin and its deficiency. In: Bloom AL, Forbes CD, Thomas DP, eds. Haemostasis and Thrombosis. 3rd ed. Churchill Livingstone; 1994:655-670
2. 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 Haesmostasis. Thromb Haemost. 1997;77(1):197-211
3. Young G, Dricsoll MC. Coagulation abnormalities in the carbohydrate-deficient glycoprotein syndrome: case report and review of the literature. Am J Hematol. 1999;60(1):66-69. doi:10.1002/(sici)1096-8652(199901)60:1<66::aid-ajh11>3.0.co;2-d
4. Mammen EF. Antithrombin: its physiological importance and role in DIC. Semin Thromb Haemost. 1998;24(1):19-25. doi:10.1055/s-2007-995819
5. Yohe S, Olson J. Thrombophilia: Assays and Interpretation. In: Kottke-Marchant Wiley K, ed. Laboratory Hematology Practice. Blackwell Publishing; 2012:492-508
6. 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. doi:10.1111/jth.14648

Performance

Method Description

A technologist evaluates the testing performed and a computer-generated summary interpretive report is provided.

PDF Report

No

Day(s) Performed

Monday through Saturday

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

Not Applicable

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AATTA	Antithrombin Summary Interp	No LOINC Needed

Result ID	Test Result Name	Result LOINC® Value
AATTA	Antithrombin Summary Interp	69049-5