

## 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:** Polypropylene plastic vial

**Specimen Volume:** 1 mL

**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.

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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. A 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**

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

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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) or disseminated intravascular coagulation (DIC), and 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 by 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) >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. 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. 02/2015)

### **PDF Report**

No

### **Day(s) Performed**

Monday through Friday

### **Report Available**

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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             |