

Overview

Useful For

As an initial test for evaluating patients suspected of having congenital protein C deficiency, including those with personal or family histories of thrombotic events

Detecting and confirming congenital type I and type II protein C deficiencies

Detecting and confirming congenital homozygous protein C deficiency

Identifying decreased functional protein C of acquired origin (eg, due to oral anticoagulant effect, vitamin K deficiency, liver disease, intravascular coagulation and fibrinolysis/disseminated intravascular coagulation)

Special Instructions

- [Coagulation Guidelines for Specimen Handling and Processing](#)

Method Name

Chromogenic

NY State Available

Yes

Specimen

Specimen Type

Plasma Na Cit

Ordering Guidance

Coagulation testing is highly complex, often requiring the performance of multiple assays and correlation with clinical information. For that reason, consider ordering AATHR / Thrombophilia Profile, Plasma and Whole Blood.

Necessary Information

1. If the patient is being treated with Coumadin, this should be noted. Coumadin will lower protein C.
2. Heparin (unfractionated or low molecular weight) 2 U/mL or more may interfere with this assay.

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.
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****Physiology:**

Protein C is a vitamin K-dependent anticoagulant proenzyme. It is synthesized in the liver and circulates in the plasma. The biological half-life of plasma protein C is approximately 6 to 10 hours, similar to the relatively short half-life of coagulation factor VII.

Protein C is activated by thrombin, in the presence of an endothelial cell cofactor (thrombomodulin), to form the active enzyme activated protein C (APC). APC functions as an anticoagulant by proteolytically inactivating the activated forms of coagulation factors V and VIII (factors Va and VIIIa). APC also enhances fibrinolysis by inactivating plasminogen activator inhibitor.

Expression of the anticoagulant activity of APC is enhanced by a cofactor, protein S, another vitamin K-dependent plasma protein.

Pathophysiology:

Congenital homozygous protein C deficiency results in a severe thrombotic diathesis, evident in the neonatal period and resembling purpura fulminans.

Congenital heterozygous protein C deficiency may predispose to thrombotic events, primarily venous thromboembolism; arterial thrombosis (stroke, myocardial infarction, etc.) may occur. Some individuals with hereditary heterozygous protein C deficiency may have no personal or family history of thrombosis and may or may not be at increased risk. Congenital heterozygous protein C may predispose to development of coumarin-associated skin necrosis. Skin necrosis has occurred during the initiation of oral anticoagulant therapy.

Two types of hereditary heterozygous protein C deficiency are recognized:

- Type I (concordantly decreased protein C function and antigen)
- Type II (decreased protein C function with normal antigen level)

Acquired deficiencies of protein C may occur in association with:

- Vitamin K deficiency
- Oral anticoagulation with coumarin compounds
- Liver disease
- Intravascular coagulation and fibrinolysis/disseminated intravascular coagulation (ICF/DIC)

The clinical hemostatic significance of acquired protein C deficiency is uncertain.

Assay of protein C functional activity is recommended for the initial laboratory evaluation of patients suspected of having congenital protein C deficiency (personal or family history of thrombotic diathesis), rather than assay of protein C antigen.

Reference Values

70-150%

Interpretation

Values below 60% to 70% may represent a congenital deficiency state, if acquired deficiencies can be excluded.

Protein C activity (and antigen) is generally undetectable in individuals with severe, homozygous protein C deficiency.

Oral anticoagulant therapy (warfarin, Coumadin) decreases protein C activity, compromising the ability to distinguish between congenital and acquired protein C deficiency. Concomitant measurement of the activity of coagulation factor VII (or factor X) may aid in differentiating congenital deficiency state from acquired protein C deficiency due to oral anticoagulant effect, but the ratio of the activities of protein C:factor VII (or factor X) has not been demonstrated to provide certainty about this distinction.

The clinical significance of acquired protein C deficiency and of increased protein C is unknown.

Cautions

Protein C activity result may be affected by:

- Heparin (unfractionated) > or =2 U/mL

- Heparin (low molecular weight) >2 U/mL
- Hemoglobin >500 mg/dL
- Bilirubin >21 mg/dL
- Triglycerides >890 mg/dL

Lipemia may interfere with functional protein C assay. Blood specimens for protein C functional assay should be drawn in the fasting state, if possible.

Protein C functional assay using a venom activator and a chromogenic peptide substrate has the potential of not detecting certain congenital protein C variants that might be detectable using clot-based assay of protein C function.

Clinical Reference

1. Mannucci PM, Owen WG: Basic and clinical aspects of proteins C and S. In: Bloom AL, Thomas DP, eds. *Haemostasis and Thrombosis*. 2nd ed. Churchill Livingstone; 1987:452-464
2. Marlar RA, Mastovich S. Hereditary protein C deficiency: a review of the genetics, clinical presentation, diagnosis and treatment. *Blood Coagul Fibrinolysis*. 1990;1(3):319-330
3. Marlar RA, Montgomery RR, Broekmans AW. Diagnosis and treatment of homozygous protein C deficiency. Report of the Working Party on Homozygous Protein C Deficiency of the Subcommittee on Protein C and Protein S, International Committee on Thrombosis and Haemostasis. *J Pediatr*. 1989;114(4 Pt 1):528-534
4. Miletich J, Sherman L, Broze G Jr. Absence of thrombosis in subjects with heterozygous protein C deficiency. *N Engl J Med*. 1987;317(16):991-996
5. Pabinger I, Allaart CF, Hermans J, Briet E, Bertina RM. Hereditary protein C-deficiency: laboratory values in transmitters and guidelines for the diagnostic procedure. Report on a study of the SSC Subcommittee on Protein C and Protein S. Protein C Transmitter Study Group. *Thromb Haemost*. 1992;68(4):470-474
6. Cooper PC, Pavlova A, Moore GA, Hickey KP, Marlar RA. Recommendations for clinical laboratory testing for protein C deficiency, for the subcommittee on plasma coagulation inhibitors of the ISTH. *J Thromb Haemost*. 2020;18(2):271-277
7. Baron JM, Johnson SM, Ledford-Kraemer MR, Hayward CP, Meijer P, Van Cott EM. Protein C assay performance: an analysis of North American specialized coagulation laboratory association proficiency testing results. *Am J Clin Pathol*. 2012;137(6):909-15. doi:10.1309/AJCP8MWU4QSTCLPU
8. Roshan TM, Stein N, Jiang XY. Comparison of clot-based and chromogenic assay for the determination of protein C activity. *Blood Coagul Fibrinolysis*. 2019;30(4):156-160. doi:10.1097/MBC.0000000000000806

Performance

Method Description

This Protein C activity assay is performed using the HemosIL Protein C kit on the Instrumentation Laboratory ACL TOP. Protein C in plasma is activated by a specific enzyme (protein C activator) from copperhead snake venom (*Agkistrodon contortrix contortrix*). The amount of activated protein C is determined by the rate of hydrolysis of the chromogenic substrate, S-2366 (pyroGlu Pro-Arg-pNA-HCL). The pNA release is measured kinetically at 405 nm and is directly proportional to the protein C level in the plasma.(Package insert: HemosIL Protein C. Instrumentation Laboratory; 03/2016)

PDF Report

No

Day(s) Performed

Monday through Friday

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

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

85303

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|-----------------------|--------------------|
| CFX | Protein C Activity, P | 27818-4 |

| Result ID | Test Result Name | Result LOINC® Value |
|-----------|-----------------------|---------------------|
| CFX | Protein C Activity, P | 27818-4 |