

## 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

No

## 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 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. Immediately freeze plasma (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**

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**

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 (eg, warfarin) 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 to 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.

A 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 Instrument 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; 06/ 2017)

#### PDF Report

No

**Day(s) Performed**

Monday through Friday

**Report Available**

1 to 3 days

**Performing Laboratory Location**

Mayo Clinic Jacksonville Clinical Lab

**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