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

Advisory Information
Coagulation testing is highly complex, often requiring the performance of multiple assays and correlation with clinical information. For that reason, we suggest ordering AATHR / Thrombophilia Profile.

Necessary Information
1. If the patient is being treated with Coumadin, this should be noted. Coumadin will lower protein C.

2. Heparin> or =4 U/mL may interfere with this assay.

Specimen Required
See Coagulation Guidelines for Specimen Handling and Processing in Special Instructions.

Patient Preparation: Patient should be fasting

Specimen Type: Platelet-poor plasma

Collection Container/Tube: Light-blue top (citrate)

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL
Test Definition: CFX
Protein C Activity, P

Collection Instructions:
1. Centrifuge, remove plasma, and centrifuge plasma again.
2. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C, or, ideally < or =-40 degrees C.

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
0.5 mL

Reject Due To

| Gross hemolysis | Reject |
| Thawing         | Cold OK-refreeze-note to lab |
|                 | Warm reject                  |
| Gross lipemia   | Reject                        |
| Gross icterus   | Reject                        |

Specimen Stability Information

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<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Plasma Na Cit</td>
<td>Frozen</td>
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Clinical and 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 (PAI-1).

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 (PCAG / Protein C Antigen, Plasma).

**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) >4 U/mL
-Heparin (low-molecular-weight) >2 U/mL
-Hemoglobin >500 mg/dL
-Bilirubin >21 mg/dL
-Triglycerides >890 mg/dL

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

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**


**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, Bedford, MA, 12/2008)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Monday through Friday
Test Definition: CFX
Protein C Activity, P

Analytic Time
1 day

Maximum Laboratory Time
3 days

Specimen Retention Time
7 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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 U.S. Food and Drug Administration.

CPT Code Information
85303

LOINC® Information

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<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tr>
<td>CFX</td>
<td>Protein C Activity, P</td>
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