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**Lab Dept:** Coagulation

**Test Name:** PROTEIN S ACTIVITY

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***General Information***

**Lab Order Codes:** PRSA

**Synonyms:** Protein S

**CPT Codes:** 85306 – Clotting inhibitors or anticoagulants; protein S

**Test Includes:** Protein S Activity reported as a percent (%).

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***Logistics***

**Test Indications:** Protein S, a vitamin K dependent plasma protein is the cofactor of activated Protein C. It stimulates the proteolytic inactivation of Factor V and Factor VIII by Protein C, thereby stimulating its coagulation inhibiting effect. A diminished Protein S activity increases thromboembolic risk. Homozygous Protein S deficiency, like homozygous Protein C deficiency, leads to Purpura fulminans in neonates.

Functional assays should be performed first, because all types of Protein S deficiencies will be detected. The free antigen is needed only if the functional assay is decreased and the total antigen assay is needed only if the free antigen is decreased in order to determine the deficiency subtype. If the antigen assays are performed without the functional assay, patients with certain subtypes will not be detected.

**Lab Testing Sections:** Coagulation (Minneapolis Campus)

**Phone Numbers:** MIN Lab: 612-813-6280

STP Lab: 651-220-6550

**Test Availability:** Daily, 24 hours

**Turnaround Time:** 1-7 days, performed on Fridays

**Special Instructions:** Protein S is decreased in Coumadin® therapy/Vitamin K deficiency.

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***Specimen***

**Specimen Type:** Whole blood

**Container:** Light Blue top (Buffered Na citrate 3.2%) tube

<b>Draw Volume:</b>	2.7 mL blood in a 3 mL tube (Minimum: 1.8 mL in a 2 mL tube)
<b>Processed Volume:</b>	Minimum 1.8 mL (plasma).
<b>Collection:</b>	<ul style="list-style-type: none"> <li>• A clean venipuncture is essential, avoid foaming.</li> <li>• Entire sample must be collected with single collection, pooling of sample is unacceptable.</li> <li>• Capillary collection is unacceptable.</li> <li>• Patient's with a hematocrit level &gt;55% must have a special tube made to adjust for the hematocrit; contact lab for a special tube.</li> <li>• Mix thoroughly by gentle inversion. Deliver immediately to the laboratory at room temperature via courier or pneumatic tube.</li> </ul> <p><b>Off campus collections:</b></p> <ul style="list-style-type: none"> <li>• Must be tested within 4 hours.</li> <li>• Do not refrigerate.</li> <li>• If not received in our lab within 4 hours of collection, sample must be centrifuged and *platelet-poor plasma removed from cells and transferred to an aliquot tube being careful not to disturb the cell layer. Centrifuge the plasma a second time and transfer into a clean aliquot tube being careful not to include any residual platelets on the bottom of the tube. Freeze at -20°C and deliver to the lab on dry ice within 2 weeks.</li> </ul> <p><b>*Validation of your lab's centrifuge for platelet poor plasma is required.</b></p>
<b>Special Processing:</b>	<p>Lab Staff: All testing will be performed in Minneapolis.</p> <p>St.Paul Lab: Send whole blood specimens to Mpls.</p> <p>For processing via courier. Must be processed within 4 hours of collection. Contact Mpls prior to sending. If there will be a delay in delivery, the sample should be spun, plasma removed and spun again. Aliquot spun plasma into a screw-capped plastic vial and freeze at -70. Send frozen plasma.</p> <p>If the patient is being treated with Coumadin®, this should be noted.</p>
<b>Patient Preparation:</b>	Coumadin® will lower Protein S
<b>Sample Rejection:</b>	Improper tube; clotted sample; underfilled tube; mislabeled or unlabeled specimens

### ***Interpretive***

<b>Reference Range:</b>	Reference range: 70 – 130%
	Note: There are insufficient data concerning Protein S activity in normal infants, neonates and children; but normal or near normal activity probably is present by age 3-6 months.
<b>Critical Values:</b>	N/A

**Limitations:**

This test detects functionally active Protein S.

Activated Protein C resistance (e.g. heterozygosity or homozygosity for the factor V Leiden mutation) may lead to a diminished recovery of Protein S.

The antiphospholipid antibodies (e.g. Lupus anticoagulant) may be accompanied by either increased or decreased Protein S activity results.

This assay should not be performed on patients that are on hirudin or argatroban anticoagulation.

**Methodology:**

Protein C proteolytically cleaves Factor V which is generated by the activation of the coagulation cascade by Russell's Viper Venom (RVV). In this reaction Protein S acts as a cofactor, which accelerates the reaction. As a result the coagulation time increases proportionally to the activity of Protein S in the sample. The addition of deficient plasma ensures that the test mixture has a sufficient supply of fibrinogen, Factor V and other necessary coagulation factors. Coagulation is triggered at the level of Factor X by the Factor X activator of RVV. Factor X forms thrombin from prothrombin under the action of the remaining Factor V. The resulting thrombin finally converts fibrinogen to fibrin. The coagulation time is then detected optically.

**References:**

Protein S Ac Reagent package insert (May 2008) Standard Human Plasma package insert, Siemens Healthcare Diagnostics Inc., Newark, DE

Control Plasma N package insert (December 2007) Siemens Healthcare Diagnostics, Newark, DE

Control Plasma P package insert (December 2007) Siemens Healthcare Diagnostics, Newark, DE

Application Sheet for Protein S Ac on BCS and BCSXP.

Andrew M, Paes B, Milner R, et al, (1987) "Development of the Human Coagulation System in the Full Term Infant," Blood, 70(1):165-72

Thrombophilia Powerpoint presentation Kandice Kottke-Marchant M.D. PhD.

[http://aniaracorp.s3.amazonaws.com/PhyFiles/Thrombophilia2/Marchant\\_medium.wmv](http://aniaracorp.s3.amazonaws.com/PhyFiles/Thrombophilia2/Marchant_medium.wmv)

An Algorithmic Approach to Hemostasis Testing Kottke-Marchant (2008) CAP Press

**Updates:**

2/6/2012: Test moved from referral to Fairview University to being performed inhouse at Children's Laboratory.

9/15/2014: Added Off Campus collection info.