Boletim Hemorreologia nº 1/2002
Pista: Bolet-H3

# Low Level of Circulating Activated Protein C Is a Risk Factor for Venous Thromboembolism

**Francisco España[1], Amparo Vayá[2], Yolanda Mira[2], Pilar Medina[1], Amparo Estellés[1], Piedad Villa[2], Cristina Falcó, Justo Aznar**

[1] *Research Center and the*
[2] *Department of Clinical Pathology, "La Fe" University Hospital, Valencia, Spain*

**(Thromb Haemost (2001); 86: 1368-1373)**

**Abstract**

The levels of circulating activated protein C (APC) reflect in vivo protein C activation. The aim of this study was to determine whether a low APC level is an independent risk factor for venous thromboembolism (VTE). We measured APC in 160 patients with a history of VTE and without recognized thrombophilic defects, and in 199 healthy individuals. The mean (±SD) APC level was lower in patients (0.99±0.44 ng/ml) than in controls (1.19±0.41 ng/ml) ($p < 0.0001$), and showed a different distribution in the two groups. Thirty--eight patients (23.7%) had APC levels below the 5th percentile of the control group (<0.69 ng/ml) and 57 patients (35.6%) had APC levels below the 10th percentile (<0.77 ng/ml). APC levels <0.69 ng/ml increased the risk of a single or recurrent episode of VTE 4.2-fold (95% confidence interval, 2.0-9.0) or 6.9-fold (2.6-17.9), respectively, and APC levels <0.77 ng/ml increased these risks 3.4-fold (1.9-6.2) or 5.1-fold (2.3-11.2) respectively, compared with controls. Familial studies revealed that in some cases the low APC phenotype seems to be hereditary. We conclude that a low level of circulating APC in individuals without any of the most recognized thrombophilic defects is a prevalent, independent risk factor for VTE, and that it predisposes to recurrent VTE.

**Key-words:** Thromboembolism, protein C, activated protein C, venous thrombosis, risk factor.

Correspondence to: Dr. Francisco España, Hospital La Fe.
Centro de Investigación. Av·. Campanar. 21 46009 Valencia, Spain
Phone: 34-96- 3862797, Fax: 34-96-3868718.
E-mail: espanya_fra@gva.es

# Complexes between Activated Protein C and Protein C Inhibitor Measured with a New Method

## Comparison of Performance with other Markers of Hypercoagulability in the Diagnosis of Deep Vein Thrombosis

**Karin Strandberg[1], Jan Astermark[2], Ola Björgell[3], Charlotte Becker[1], Paul E. Nilsson[3], Johan Stenflo[1]**

[1] *Department of Clinical Chemistry, University Hospital, Malmö, Lund University, Malmö, Sweden,*
[2] *Department of Coagulation Disorders, University Hospital, Malmö, Lund University, Malmö, Sweden,*
[3] *Department of Diagnostic Radiology, University Hospital, Malmö, Lund University, Malmö, Sweden*

**(Thromb Haemost (2001); 86: 1400-1408)**

**Abstract**

A first clinical evaluation has been made of the performance of a newly devised immunofluorometric assay for measuring plasma concentrations of activated protein C (APC) in complex with protein C inhibitor (PCI). The method was compared with testing for other markers of hypercoagulability in a case-control study comprising 123 patients with clinical suspicion of deep vein thrombosis (DVT). The diagnosis was confirmed by ascending phlebography, and the thrombotic burden estimated with a newly developed scoring system. Receiver operating characteristics (ROC) curves calculated to demonstrate the discriminatory capacity of the methods, showed the area under the curves (AUCs) to be similar for the APC-PCI and D-dimer methods. However, in contrast to the D-dimer method, the APC-PCI method measures a well-defined analyte, a prerequisite for reliable comparisons of future clinical studies. The APC-PCI method appears to be particularly useful as a marker for detection of recently developed proximal thrombi.

**Key-words:** APC-PCI complex. immunofluorometric assay,· deep vein thrombosis. case-control study, hypercoagulability markers.

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Correspondence to: Dr. J. Stenflo. Dept. of Clinical Chemistry. University Hospital Malmö. Lund University, S-20502 Malmö, Sweden
Tel.: +46403314421:
Fax: +46640929023: E-mail: johan.stenflo@klkemi.mas.lu.se