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MULTICENTRIC SPANISH STUDY OF BIOLOGICAL CAUSES OF DEEP VEIN THROMBOSIS. J.Felez,R.Rodriguez-Pinto,A. Oliver,F.Velasco,I.de Diego,J.L.Steegmann,S.Martin. GRUPO ESPAÑOL DE HEMOSTASIA Y TROMBOSIS (GEHT)

305 unselected patients under long-term oral anticoagulation treatment for having presented one o more episodes of deep vein thrombosis and/or pulmonary embolism, have been studied for the following anomalies: Dysfibrinogenemia, Lupus anticoagulant, Antithrombin-III deficiency,Protein C, Protein S, Heparin Cofactor II, and anomalies in the fibrinolytic components t-PA PAI and Plasminogen. Protein C antigen and activity as well as free Protein S antigen levels have been related to those found in a control group at different intensities of oral anticoagulant.

As shown in the table this study, performed on unselected patients from the clinical point of view, has not only confirmed the presence of a previously known congenital defect in 16 patients (5%) but also has permiteed the identification of a previously unkown defect in 45 patients (15%).

	PAI	P.C	P.S	AT.III	LUP.	DFg.	DPg.	HC-II
known	-	8	-	3	4	1	-	-
unknown	17	5	9	6	5	1	1	1
TOTAL	17	13	9	9	9	2	1	1

Since the identification of a congenital abnormality permits to prevention of new thrombotic episodes and the identification of the afected members, these results support the convenience of performing such systematic biological studies in patients suffering from thrombosis.

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FAMILY STUDIES OF PATIENTS WITH RECURRENT VENOUS THROMBOSES AND INHERITED DISORDERS OF BLOOD COAGULATION OR FIBRINOLYSIS. V. Hach-Wunderle, R. Walter-Fincke, K.H. Beck, I. Scharrer. Center of Internal Medicine, University Hospital, Frankfurt, West Germany

Several defects of the coagulation and/or fibrinolytic system have been found to be associated with venous thromboembolism. In young patients with recurrent thromboses or a positive family history, an inherited disorder should be excluded.
535 young patients with venous thromboses, phlebitis and/or pulmonary embolism were investigated from 1980 until 1986. The first thrombotic event had occurred at an age of less than 45 years. An inborn disorder of the blood coagulation or fibrinolytic system was found in 18 families. Most of them (n=13/18) had a positive family history. In all families either thromboses had occurred in at least one member (n=12/18) and/or the defect could be detected in one of them (n=12/18).
Most often we found a deficiency of antithrombin III (n=6). A deficiency of protein C (type I) was detected in 3 and a deficiency of protein S in 5 families. In one patient a combined deficiency of antithrombin III, protein C and protein S was found. Extensive family studies revealed a deficiency of antithrombin III in the grandmother of the patient, who suffered from arterial thrombosis. A deficiency of plasminogen and an abnormal plasminogen molecule were detected in 2 other families. Defective release of t-PA could be demonstrated in 3 members of one investigated family up to now.
Some family members with either defects of protein C, protein S or plasminogen as well as a defective release of t-PA lack thrombotic events. Furthermore thromboses of mesenteric veins occurred in 2 of 6 patients with antithrombin III deficiency and in 1 of 5 patients with protein S deficiency. Superficial vein thromboses were mainly found in patients with protein C- or protein S-deficiency.

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PREVELANCE OF PRIMARY COAGULATION DEFICIENCIES IN PATIENTS WITH DEEP VENOUS THROMBOSIS. B. Grossman and A. Duncan. Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Grady Hospital, Atlanta, GA., U.S.A.

Hereditary causes of thrombosis are becoming more evident as assays (and antibodies) for antithrombin III, protein C, and protein S become more widely available. From March 1986 to January 1987, ninety-nine patients with venous thrombosis were referred to our laboratory for evaluation. This included 55 males and 42 females (age ranges: <1- 79 years). In 79 patients protein C antigens and activities were performed and 24 abnormally low values were obtained. Fourteen of these patients had multiple low values of other vitamin K dependent coagulation factors, reflecting warfarin therapy. Ten patients (12.7%) had isolated protein C deficiency with the other vitamin K dependent factors being within our normal ranges. Of 75 free protein S antigens performed there were 32 abnormally low values. Thirteen (17.3%) were isolated deficiencies. Of 62 antithrombin III antigens and activities measured, there were 8 (12.9%) abnormally low values. The prevelance of these hereditary deficiencies are higher in our referral population than previously reported. This may represent a true increase prevelance in our referral population or reflect a selection bias because of our careful screening of the patient's history prior to performing the test, or an increased availability of the test to the clinicians. These test should be performed routinely in young patients with venous thrombosis and without predisposing risk factors. These results confirm that all patients with thrombosis should have a comprehensive evaluation done. Not only will the etiology be determined but given the cost of these evaluations, it is more efficient to profile rather than to order isolated request for one factor, as has often been the habit in the past.

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INCIDENCE OF DEFECTIVE T-PA RELEASE IN 158 UNRELATED YOUNG PATIENTS WITH VENOUS THROMBOSIS IN COMPARISON TO PC-, PS-, AT III-, FIBRINOGEN- AND PLASMINOGENDEFICIENCY. I. Scharrer, V. Hach-Wunderle, H. Heyland, C. Kühn. Department of Internal Medicine, University Hospital, Frankfurt, West Germany

The incidence of defective T-PA release in 158 young unrelated patients (< 45 years old) with deep vein thrombosis was studied and compared to that of PC-, PS-, AT III-, fibrinogen- and plasminogen deficiency. Thrombotic episodes were documented using venography with contrast medium. Venous occlusion test (VO) over 20 min. was performed in all patients, 8-12 weeks after thrombosis. T-PA antigen (Biopool kit), T-PA activity (on fibirnplates) and PAI (T-PA-inhibitor, Biopool kit) were measured before and after VO in the fasting morning samples. Furthermore we investigated the functional and immunologic levels of PC,PS,AT III, fibrinogen and plasminogen. We detected 28 patients (15 females, 13 males) = 17.7% with abnormal T-PA release. In these patients the VO test was repeated three times in an interval of 6-8 weeks. Release of T-PA activity and T-PA-Ag was diminished in all these patients. PAI levels were enhanced in 12 of these 28 patients. The rate of recurrency of thrombosis was 52%. A family history of thrombosis was reported only in 20%.
The incidence of PC def. was 9.4%, of PS def. 6.3%, of AT III def. 5%, of dysfibrinogenemia 0.6% and of plasminogen def. 1.2%. No combined defect of abnormal T-PA release with other known hereditary coagulation or fibrinolysis disorders could be detected.
In 11 healthy volunteers we investigated 4 different time periods of VO, 5, 10, 15 and 20 min. in an interval of 10 days in order to find the suitable time for VO. It was striking that T-PA activity (on fibrin plates) did not decrease to the same extent as T-PA-Ag. The different behaviour is demonstrated on table 1. Decrease in % is compared to the values of 20 min. VO.

Table 1

	T-PA activity (fibrin plate)	T-PA-Ag
VO over 5'	- 59.3%	- 82%
VO over 10'	- 33.7%	- 60%
VO over 15'	- 26%	- 42%

Therefore we recommend a time period of at least 15' for exact detection of T-PA Ag release.