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EXPERIENCE OF CONTROL OF THE INITIATION OF COUMAROL THERAPY WITH AN AMIDOLYTIC ASSAY OF FACTOR X. N. Egberg and H. Johnsson. Departments of Blood Coagulation Disorders and Medicine, Karolinska Hospital, Stockholm, Sweden.

Most authors agree that probably any of the vitamin K dependant factors can be used for control of coumarol therapy at steady state of treatment. However, during initiation of coumarol therapy poor correlations have been found between one stage prothrombin assays and specific factor analyses (II and X) and thus the usefulness of the specific assays in the initial phase of treatment has been questioned.

Purpose of study To investigate if a specific factor X analyses could be used for control of the initiation of coumarol (warfarin) therapy.

Methods Thrombotest (Nyegaard AS, Oslo). Amidolytic factor X assay according to Bergström and Egberg.

Patients admitted to the hospital because of venous thrombosis and/or pulmonary embolism. At present 13 patients (9 men, 4 women), age 36-81 years.

Design of study Heparin therapy was started as soon as the diagnosis was assigned. Warfarin treatment was commenced on the following day. Thrombotest and factor X was determined before and daily for 6 days after coumarol therapy was started. Only the results from the factor X analyses were given to the doctor in charge of the patients for monitoring of the coumarol therapy.

Results Thrombotest and factor X values generally fell in parallell except when high concentrations of heparin in the blood samples inhibited the Thrombotest method. The correlation between Thrombotest and factor X in 10 patients was good (r 0.81-0.99, mean 0.94).(Three patients were excluded for different reasons). The doctor in the ward found it as easy to monitor coumarol treatment with the factor X assay as with the Thrombotest. No bleeding or thromboembolic complications occurred.

Conclusion The amidolytic factor X assay could be used for monitoring coumarol treatment in the initial phase of treatment. The absence of sensitivity to heparin was regarded an advantage to the Thrombotest method.

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GROUP ANALYSIS OF ABNORMAL FACTOR X MOLECULES
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Factor X lies central in blood coagulation being the point of convergence of the intrinsic and extrinsic pathways and in its activated form is the initial enzyme in the final stages of clot formation. The interaction of Factor X with its activators, cofactors and substrates suggest that there are multiple structural loci present on the surface of this molecule available for these molecular associations. Hence, abnormal molecules may reflect different specific structural defects resulting in decreased function. We analyzed 28 abnormal Factor X plasmas by four parameters: 1) antigen (Ag) measured in radioimmunoassay and activity as measured by: 2) prothrombin time (PT), 3) Russell's viper venom time (RVV), and 4) activated partial thromboplastin time (APTT). Abnormal Factor X plasmas were from congenital (16), transient (2) and amyloid associated (10) deficiencies. In order to objectively determine groups of abnormal molecules we evaluated their distributions in the following manner: (1) PT activity vs Ag concentration; (2) RVV activity vs PT/Ag; and (3) APTT activity vs RVV/(PT/Ag).

A non-random distribution of plasmas was observed which could be grouped into ten classes and subclasses of abnormal Factor X molecules. These data suggest that the groups of abnormal molecules may reflect common structural defects shared among its members located at specific structural loci involved in either the activation or the function of these Factor X molecules.

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KINETIC STUDY OF FACTOR X (FX) : POTENTIAL VALUE FOR THE INITIATION OF ORAL ANTICOAGULANT TREATMENT. J.N. FIESSINGER, M. AIACH, C. NUSSAS, L. CAPRON. Chaire de Clinique Médicale et de Pathologie Vasculaire. Laboratoire d'hémostase. Hôpital Broussais, Paris, France.

FX has been claimed to be of clinical relevance in monitoring long term treatment with anticoagulants. The aim of this investigation was to study the behaviour of FX at the beginning of the treatment.

Seventeen patients under heparin therapy received a daily dose of 3 mg of Acenocoumarol. Blood samples were obtained at 1, 2, 4, 6, 8 days (D_0 - 8), after starting the treatment. Heparin was stopped when prothrombin time (PT) was less than 40 per cent of normal value. FX was evaluated using an automated amidolytic method. Factor VII (FVII) and PT were measured in a clotting assay.

The disappearance of FX from plasma could be fitted to an exponential decay pattern during 6 days in 17 patients, 8 days in 11 patients. Concerning FVII, the exponential decay was limited to the first 2 days, then a stable level was reached. The decrease rates of FVII and FX during the first two days were correlated (r = 0,76). The regression line ln (FX) = f (D) calculated from D_0, D_1, D_2 could be used for predicting FX concentration at D_6 or D_8. A highly significant linear correlation existed between the observed and predicted levels (D_8 : r = 0,97) (D_6 : r = 0,92).

These results suggest that FX amidolytic assay could be useful for monitoring the initiation of anticoagulant treatment. The decrease rate of FX could be a valuable guide for an early determination of the maintenance dose of anticoagulant.

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SIALIC ACID CONTENT AND THE BIOLOGICAL ACTIVITY OF STUART FACTOR (F X). A.M. Engel. Department of Thrombosis. Fundación Centro de Investigaciones Médicas Albert Einstein (Fundación CIMAE), Buenos Aires, Argentina.

Substantial release of sialic acid (SA) from purified F X was obtained with sialidase from Clostridium perfringens. The total SA content of F X was found to be 1.7%, in agreement with previous reports. After almost complete removal of SA, aliquots were examined by polyacrilamide disc electrophoresis and by polyacrilamide in sodium dodecyl sulphate (SDS) and the gels were stained for proteins and for glycoproteins. When SA was progressively removed from F X its clotting activity was slightly increased while its electrophoretic mobility was retarded, as expected. The tryptic activation of F X was affected by the removal of 60-70% of SA, yielding more clotting activity than the native F X. No difference was observed between the esterase activity of regular F X and asialo-X as measured by the hydrolysis of N-alpha-acetyl glycyl-L-lysyl-methyl ester acetate (AGLMe).

When asialo-X was interacted with 25% sodium citrate the kinetics were accelerated and the maximal clotting and esterase activities were obtained at 6 hours of activation while the native F X reached the peack of both activities at 24 hours. Both activation mixtures were analyzed, at the period of maximal activity, for liberation of peptidic material by thin-layer electrophoresis (TLE). TLE patterns of asialo-X varied according to the activation system used; they also differed from the ones obtained with native F X.

The data indicate that SA influences the kinetic of activation of F X and the nature and distribution of the peptidic material released during activation.