Poster Board P5-045

0320 FIBRINOGEN SEATTLE: A HERITABLE DISFIBRINOGEN WITH AN ISOLATED IMPAIRMENT IN FIBRINOPEPTIDE B RELEASE

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The slow clotting, asymptomatic, fibrinogen Seattle first described in a patient with tetralogy of Fallot has been traced through four generations as an autosomal dominant with 70% penetrance. The dysfibrinogen was indistinguishable from normal fibrinogen by radial immunodiffusion and immunoelectrophoresis. Transamidation and plasmin digestion studies gave no evidence of abnormality. Thrombin and botroxobin monomer reprolymerization followed turbidometrically (A_{350}) disclosed a shorter lag phase, a more acute maximal slope, and a lower maximal turbidity. Electron microscopy revealed that thrombin incubated fibrinogen Seattle more readily formed clots with aperiodic fibers than comparable controls. By amino acid analysis the final yield of fibrinopeptide B was slightly more than half normal (54% at 2 hours with 2.5 NIH units/ml). The dysfibrin manifested evidence of retention of fibrinopeptide B as equal quantities of chains with Bβ and β charge mobility were demonstrated on low pH (2.7) polyacrylamide electrophoresis in 2M urea. A distinction is made between fibrinogen Seattle and fibrinogen Detroit both with disordered fibrinopeptide B release on the basis of the patterns of fibrinopeptide release, immunoelectrophoretic mobility, botroxobin monomer aggregation, chronometric fibrinogen concentration, and clinical symptomatology. No other dysfibrinogens have been shown to manifest disordered release of fibrinopeptide B alone.

P5-046

0321 POLYMERISATION DEFECT OF FIBRINOGEN LONDON

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In the present study further work has been carried out on fibrinogen that has been isolated from a patient with a coagulation defect tentatively designated fibrinogen London. The dysfibrinogenemia was characterised by normal polypeptide chains on SDS gel electrophoresis, normal release of fibrinopeptide A and a delayed polymerisation of fibrin monomers. The polymerisation defect was pH and ionic strength dependent and partially corrected by protamine sulphate and Ca^{++} ions. Studies on the NH2 and COOH terminal polymerisation domains were carried out using insolubilised fibrin monomers prepared from patient and normal fibrinogen (Kudryk et al, Thromb.Res., 9,25, 1976). High MW fragment D, prepared by plasmin digestion of normal fibrinogen, bound to both normal and patient fibrin monomer and was eluted with 8M urea indicating no gross malfunction of the NH_2 terminal polymerisation domain. Also purified fibrinogens from normal and patient plasma bound to normal fibrin monomer sepharose, suggesting that the COOH terminal domain is capable of binding to the NH_2 terminal domain of normal fibrin. These results suggest that the polymerisation defect of fibrinogen London is different in character to that of fibrinogen Detroit, where the NH_2 terminal domain does not bind to the normal COOH terminal domain.

P5-047

0322 FIBRINOGEN LOGROÑO. A NEW FIBRINOGEN MOLECULAR VARIANT

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We present a new molecular variant of fibrinogen. The majority of biological tests were normal except prolonged prothrombin and thrombin times, fibrinogen deficiency as quantified by a colourimetric method, and the polymerization of fibrin's monomers. Normal thrombin times were obtained by addition of normal plasma, bovine thrombin, $CaCl_2$, and by changes in pH and ionic strength.

The study of the purified fibrinogen showed normal fibrinopeptides' liberation and sialic acid and hexosamine levels. Fibrin stabilization, coagulability index = 64%, electrophoretic mobility, pI = 5.4 (N = 5.8), and $S_{20,w}$ = 10 (N = 8.2), were abnormal.