

THE EFFECT OF FIBRINOPEPTIDE B RELEASE ON TEMPERATURE DEPENDENT FIBRIN ASSOCIATION. W. Edgar, C.R.M. Prentice, University Department of Medicine, Royal Infirmary, Glasgow, Scotland.

The effect of temperature on soluble fibrin complexes was studied using Bio-gel filtration and chromatography on fibrinogen-sepharose 4B at 20°C and 37°C. Complexes were formed by plasmin digestion of non-crosslinked fibrin produced by thrombin, ancrod, thrombin in 2M urea, or ancrod plus Agkistrodon contortrix venom. Thrombin removes fibrinopeptides A and B, ancrod removes fibrinopeptide A, while A. contortrix enzyme removes first fibrinopeptide B, followed by A. Complexes containing neither fibrinopeptide A or B, formed by digestion of fibrin produced by thrombin, or by ancrod plus Agkistrodon contortrix, were stable at 37°C. In contrast, complexes which retained fibrinopeptide B, formed from fibrin produced by ancrod or by thrombin in 2M urea, were unstable at 37°C. Fibrin polymerization was necessary for the stability of fibrin complexes. Complexes from plasmin digests of fibrin produced by ancrod plus A. contortrix enzyme in 2M urea, where no clot formation occurred, were unstable at 37°C. Using affinity chromatography, plasmin digests of thrombin-fibrin bound to fibrinogen-sepharose at 37°C, whereas those from ancrod-fibrin did not. A second set of polymerization sites in fibrinogen are proposed, distinct from the N-DSK and carboxyterminal sites. These are activated by removal of fibrinopeptide B and require clot formation.

HIGH MOLECULAR WEIGHT FIBRINOGEN COMPLEXES IN PATIENTS WITH HISTORY OF MYOCARDIAL INFARCTION AND CEREBROVASCULAR DISORDERS. G.G. Neri Serneri, G.F. Gensini, R. Abbate, D. Prisco, C. Mugnaini and S. Favilla, University of Florence Medical School, Florence, Italy.

The increased turnover of fibrinogen and decreased platelet survival observed in many patients with history of myocardial infarction (MIP) and in patients with chronic cerebrovascular disorders (CVP) (Neri Serneri et al 1970, Harker and Slichter 1972) could suggest a hypercoagulable state. We investigated 28 MIP, 23 CVP and 31 controls for circulating high molecular weight fibrinogen complexes (HMWFC) by gel-filtration (agarose 4%, 100-200 m, column 1.5 x 90 cm, buffer Tris-Cl-citrate pH 7.6, flow 13 ml/hour, recording of OD at 280 nm) of plasma beta-alanine precipitate. HMWFC are eluted in a peak at an elution volume corresponding to the void volume of the column, at which volume globular proteins of MW over 1 million are eluted. HMWFC concentration was in the controls  $2.98 \pm 1.52$  % of the fibrinogen eluted, in MIP  $8.27 \pm 2.9$  % ( $P < 0.01$ ) and in CVP  $7.48 \pm 1.9$  % ( $P < 0.01$ ). When HMWFC concentration was higher than 6-7 %, PAA electrophoresis of the eluted complexes (after mercaptoethanol reduction) allowed to detect gamma-gamma dimers, so indicating the cross-linkage of HMWFC. Heparin treatment (12,500 U x 2) markedly lowered the concentration of HMWFC and made gamma-gamma dimers undetectable. These results indicate that in MIP and in CVP a hypercoagulability frequently exists.

SOLUBLE FIBRINOGEN-FIBRIN COMPLEXES IN OBSTETRICAL CONDITIONS. C.A. McKillop, P.W. Howie, C.D. Forbes and C.R.M. Prentice, Department of Medicine, Royal Infirmary, Glasgow, Scotland.

Soluble fibrinogen-fibrin complexes isolated by 6% agarose gel filtration (Bio-Gel A5m), were identified by the staphylococcal clumping test for the void volume polymers and radial immunodiffusion for the lower molecular weight oligomers. Women taking the oral contraceptive pill had significantly increased oligomer levels compared to non-pill controls; whilst in normal pregnancy there were small increases in both polymer and oligomer concentrations. In pre-eclampsia a marked increase in both types of soluble complex was found. This did not simply reflect the combination of hypertension and pregnancy, as soluble complex levels in pregnant women with essential hypertension did not differ from those in normal pregnancy. In pregnancies with intrauterine growth retardation there was also a small but significant increase in oligomer concentration compared with normal pregnancy.

While these results may simply reflect differing degrees of hypercoagulability, they could suggest increased local intravascular coagulation within the placenta in intrauterine growth retardation and disseminated intravascular coagulation in pre-eclampsia.