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

The effect of temperature on soluble fibrinogen complexes was studied using 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, anocrod, thrombin in 2M ione, or anocrod plus Arg-10042 diontortrix venon. Thrombin removes fibrinopeptides A and B, anocrod removes fibrinopeptide A, while A. contortrix enzymes remove first fibrinopeptide B, followed by A. Complexes containing neither fibrinopeptide A or B, formed by digestion of fibrin produced by thrombin, or by anocrod plus Arg-10042 diontortrix enzymes, were stable at 37°C. In contrast, complexes which retained fibrinopeptide B, formed from fibrin produced by anocrod or by thrombin in 2M ione, were unstable at 37°C. Fibrin polymerization was necessary for the stability of fibrinogen complexes. Complexes from plasmin digests of fibrin produced by anocrod plus A. contortrix enzyme in 2M ione, 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 anocrod-fibrin did not. A second set of polymersization sites in fibrinogen are proposed, distinct from the R-DEK 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.C. Serri, Serri, G.P. Genesini, B. Abbate, R. Prisco, G. Muggiani and S. Pavilla, 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) (Serri et al 1970, Harker and Sliechter 1972) could suggest a hypercoagulable state. We investigated 25 MIP, 15 CVP and 51 controls for circulating high molecular weight fibrinogen complexes (HMWC) by gel-filtration (agarose 4%,100-500 n,m column 1.5 x 50 cm, buffer Tris-Cl-citrate pH 7,6, flow 13 ml/hour, recording of OD at 280 um) on plasma beta-alanine precipitated. HMWC are eluted in a peak at an elution volume corresponding to the void volume of the column, at which values globular proteins of M, over 1 million are eluted. HMWC concentration was in the controls 2.08±1.32 % of the fibrinogen, eluted in MIP 8.27±2.0 % (P<0.01) and in CVP 7.43 ±1.9 % (P<0.01). When HMWC concentration was higher than 6-7 %, P5A electrophoresis of the eluted complexes (after mercaptoethanol reduction) allowed to detect gamma-gamma dimers, so indicating the cross-linkage of HMWC. Herperin treatment (10,500 I U x 2) markedly lowered the concentration of HMWC and made gamma-gamma dimers undetectable. These results indicate that in MIP and in CVP a hypercoagulability frequency exists.

SOLUBLE FIBRINOGEN-FIBRIN COMPLEXES IN OBSTETRICAL CONDITIONS. C.A. Mckillop, P.W. Howie, C.D. Forbes and C.B.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 staphyloccocal 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.