FIBRINOPEPTIDE A DETERMINATION IN CLINICAL PLASMA SAMPLES. W.B.J.Gerrits, O.Th.N.Flier and J.van der Meer. Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, The Netherlands

Since the development of radioimmunoassays for fibrinopeptide A (FPA), several studies have been reported on the levels of FPA in plasma from patients. Thus, elevated plasma levels of FPA have been described in disseminated intravascular coagulation, with or without consumption coagulopathy, venous thrombosis or pulmonary embolism. Increased levels of FPA have also been reported during pregnancy and in malignancies. In the majority of these patients, intravenous administration of heparin resulted in a normal FPA level, suggesting that the initially elevated FPA level was caused by the action of thrombin. However, in some patients heparin injection did not lead to normalization of FPA levels. The presence of thrombin in the blood circulation may lead to elevated FPA levels, but also to an accelerated in vitro generation of FPA, which occurs if an anticoagulant without heparin is used. Our studies demonstrate that an enhanced in vitro generation of FPA often occurs in blood samples from patients with elevated FPA levels, but also in samples with a normal FPA level. The mechanism responsible for the latter phenomenon is not clear. Possibly, proteases other than thrombin can lead to the generation of FPA.

QUANTITATIVE ESTIMATION OF CIRCULATING FIBRINMONOMER BY MEANS OF AFFINITY CHROMATOGRAPHY ON FIBRINOGEN-AGAROSE (FG-Ag). D.L.Heene and F.R.Matthias. Zentrum Innere Medizin, Justus Liebig University, Giessen, Germany.

The presence of circulating fibrinmonomer and fibrinmonomer-complexes indicates indirectly the intravascular action of thrombin. The analytical detection of these fibrinogen derivatives is mainly achieved by means of three methods: the ethanol test, agarose-gel-chromatography and affinity-chromatography on fibrinogen-agarose. The principle of the latter procedure is based on the property of fibrinmonomer to form complexes with fibrinogen according to the accessibility of polymerization sites. This method (Heene, Matthias: *Thrombos.Res.* 2,137,1973) was investigated in detail with regard to its application on clinical cases with hypercoagulability and DIC. Studies on plasma samples containing ^3H -labeled fibrinmonomer confirmed specific and selective adsorption on FG-ag and complete recovery following elution according to standard conditions of the chromatographic procedure. The absolute amount of fibrinmonomer in plasma of normal donors ($n = 27$) was found to be 0.7 mg/100 ml which is 0.25% of total plasma fibrinogen. In samples of patients with hypercoagulability (myocardial infarction, DIC) considerable increase of fibrinmonomer can be detected quantitatively even if other coagulation assays fail to reveal procoagulant activity. Comparative studies to the ethanol test indicate that a positive ethanol test can be expected if plasma fibrinmonomer concentration ranges from 7 to 11 mg/100 ml and above.

HIGH MOLECULAR WEIGHT FIBRIN(OGEN) COMPLEXES. N.Aikjaersig. Washington University School of Medicine, St.Louis, Missouri, U.S.A.

Plasma fibrinogen, because of catabolism of fibrinogen in vivo, exhibits biochemical heterogeneity, manifested by molecular weight and other differences between the various thrombin clottable moieties. These comprise high molecular weight fibrin(ogen) complexes (HMWFC) ranging in molecular weight from 400,000 to 1,000,000, native fibrinogen (m.w. 330,000) and derivatives of fibrinogen smaller than the native protein (m.s. 260,000 or less). These moieties may be assayed, in plasma as well as in the purified system, by gel exclusion chromatography with immunologic assay of chromatographic effluents by the Technicon Immunoprecipitator and mathematical analysis of elution profiles. The coefficient of assay variation for the individual moieties is 7%.

Normal control subjects show (mean + 1 s.d.) $7.7 \pm 6.2\%$ (18.4 + 21 mg%) of plasma fibrinogen in higher molecular weight complex form, $67 \pm 10.3\%$ monomeric fibrinogen and $25.8 \pm 6.4\%$ fibrinogen first derivative. Values for plasma HMWFC exceeding mean + 2 s.d. of normal (20% or 71 mg%) are classed as abnormal and regarded as demonstrative of enhanced fibrin formation. The hypothesis that enhanced fibrin deposition is associated with the presence of demonstrable pathology, extravascular or intravascular fibrin deposition or thrombosis, has been validated in several human disease models.