THROMBIN-ANTI THROMBIN III AND PLASMIN-ANTIPLASMIN COMPLEXES AS INDICATORS OF IN VIVO ACTIVATION OF THE COAGULATION AND/OR FIBRINOLYTIC SYSTEMS. D.Collen and F.de Cock. Laboratory of Blood Coagulation, Department of Medical Research, University of Leuven, Belgium.

Both the thrombin-antithrombin III and plasmin-antiplasmin complexes contain neoantigenic structures, not present in the parent molecules, to which non cross-reacting precipitating antibodies are produced (Thromb.Res. 5, 577, 1974). This phenomenon has been used to develop immunochemical methods for the quantitation of these complexes in human blood (Thromb. Res. 7, 235, 1975). Patients with in vivo activation of the coagulation and/or fibrinolytic systems consistently showed increased levels of enzyme-inhibitor complexes (Eur.J.Clin.Invest. in press, 1977). The circulatory half-life of these complexes was estimated to be several hours (0.5 to 0.75 days).

On several occasions, increased plasmin-antiplasmin titers were observed in the presence of a normal screening hemostasis analysis, suggesting that these assays may be more sensitive indicators of in vivo activation of the coagulation-fibrinolytic systems than assays for fibrinogen degradation products.

Studies to determine the clinical value of the measurement of these enzyme-inhibitor complexes as indicators of a prethrombotic state are in progress and will be reported.

PLATELET FACTOR 4 AND β -THROMBOGLOBULIN. D.S.Peppler. Edinburgh & South-east Scotland Regional Blood Transfusion Service, Royal Infirmary, Edinburgh, Scotland.

If the prethrombotic state exists and the platelet release reaction is involved, a radioimmunoassay of any platelet specific substance which is released by physiologic stimuli would be helpful. For technical reasons we have chosen β -thromboglobulin, a protein of MW 36,000, which at present has no known function. In comparison with BTG, the PF4-RIA is technically less satisfactory, the observed levels of PF4 are 2-3 fold lower than BTG and the half-life appears to be similar. Several factors limit this general approach and are not readily calculated other than from experimental measurements. These factors include (a) the ratio of concentrations in plasma and serum (b) the half-life of the marker in vivo (c) the sensitivity and precision of the RIA. Our experience with BTG and PF4 indicates that the major limitation is the half-life (both approximately 20 minutes) and that other platelet specific substances (for instance the high molecular weight glycoprotein TSP) should be investigated to find a marker with a half-life of hours or days. The BTG test is technically trouble free and has been used by us for 3 years on patients samples. It must finally be tested however in a properly designed clinical trial, and in the case of 'prethrombotic states' this presents considerable problems of patient numbers in terms of the incidence and detection of thrombotic disease. In practice, 'false positive' elevation of the released substances can occur, apart from known coagulation mechanisms, we have observed elevated levels of BTG in patients having uraemia and bacterial infections. Nevertheless, taking all factors into consideration, the BTG/PF4-RIA tests represent a major advance in our ability to assess platelet function and we are confident that a better understanding of platelet involvement in thrombotic disease and normal processes will result.

PLATELET COAGULANT ACTIVITIES IN PATIENTS WITH THROMBOTIC DISORDERS. P.N.Walsh. Temple University, School of Medicine, Philadelphia, Pennsylvania, U.S.A.

Platelets can initiate intrinsic coagulation by two alternative mechanisms, one involving the activation of factor XII by ADP-stimulated platelets (contact product forming activity), and the other involving activation of platelet-associated factor XI by collagen-stimulated platelets (collagen-induced coagulant activity). Subsequently, platelet membrane phospholipoproteins are made available by which platelets can first promote factor-X activation (intrinsic factor -Xa forming activity) and finally prothrombin activation. Specific assay techniques for each of these platelet coagulant activities have been applied to the study of patients with thrombotic and prethrombotic disorders. We have demonstrated an association between platelet coagulant hyperactivity and the development of post-operative deep vein thrombosis in patients undergoing reconstructive surgery of the hip. In patients with acute primary retinal vein occlusion two- to three-fold elevations of platelet coagulant activities concerned with the initiation and early stages of intrinsic coagulation have been observed whereas plasma coagulation and platelet aggregation studies have been normal. In patients with transient cerebral ischemic attacks and normal serum lipids we have found two- to three-fold elevations of platelet coagulant activities concerned with the initiation and early phases of intrinsic coagulation but normal platelet factor 3 activity and normal plasma coagulation and platelet aggregation studies. These studies indicate an association between platelet coagulant hyperactivity and various venous and arterial thrombotic disorders. This association may have important pathogenetic implications.