

SIMULTANEOUS MEASUREMENT OF PLATELET FACTOR 4 (PF4) AND β -THROMBOGLOBULIN (β TG) RELEASE AND FIBRINOPEPTIDE A (FPA) CLEAVAGE. K.L. Kaplan and H.L. Nossel. Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, U.S.A.

Platelet activation and fibrin formation occur in thrombo-embolism, arterial disease, and intravascular coagulation. Selective involvement in certain disease entities and combined involvement in others has been suggested on the basis of turnover studies. The development in this laboratory of sensitive and specific radioimmunoassays for two released platelet proteins, PF4 and β TG, and the availability of the radioimmunoassay for FPA as an index of fibrin formation have allowed studies of the physiologic basis for differential involvement of platelets and fibrin formation. Simultaneous measurement of platelet activation, monitored by radioimmunoassay for PF4 and β TG as well as aggregometry and 3 H-serotonin (5HT) release, and FPA cleavage were carried out in citrated platelet rich plasma, whole blood and gel-filtered platelets. Collagen and ADP aggregated platelets and released 5HT, PF4 and β TG without detectable FPA cleavage indicating that thrombin action on fibrinogen is not involved in aggregation or release induced by these agents. Thrombin cleaved FPA at concentrations 100-fold less than those required for platelet protein release, and platelet protein release could be detected at lower thrombin concentrations than 5HT release. This might be due to greater sensitivity of the PF4 and β TG assays in detecting release or to different mechanisms of release of the proteins and 5HT. These results suggest that, in clinical samples, elevated FPA with normal PF4 and β TG might be due to concentrations of circulating thrombin sufficient to cleave FPA but too low to induce platelet release, and that the converse situation, with elevated PF4 and β TG but normal FPA might imply platelet activation by exposed subendothelial collagen with no thrombin action.

THE EFFECT OF THE FIBRINOGEN CONCENTRATION AND WHITE CELL COUNT ON INTRAVASCULAR FIBRIN DEPOSITION. Victor Gurewich and Boguslaw Lipinski. St. Elizabeth's Hospital, Tufts University School of Medicine, Boston, Massachusetts, U.S.A.

The relationship between blood fibrinogen concentration and intravascular fibrin deposition was examined in EACA-treated rabbits infused with a standard amount of thrombin or simplastin sufficient to produce fibrin monomer (FM) but not defibrination. Fibrin in organs was measured by a previously described quantitative technique using 125 I-fibrinogen. A significant ($p < 0.01$) positive correlation was found between the baseline fibrinogen concentration and fibrin deposition 3 hours after infusion. By contrast, in vitro there was an inverse relationship between fibrinogen concentration and enzymatic clotting as well as non-enzymatic fibrin formation from soluble FM. When HN2-treated leukopenic rabbits were infused, fibrin deposition was inhibited despite the fact that the animals' fibrinogen concentration was substantially increased by the HN2 treatment. When leukocytosis was induced by pretreatment with endotoxin, fibrin deposition was potentiated. It is concluded that fibrin deposition from circulating FM is facilitated by a raised fibrinogen concentration by a mechanism that cannot be explained by the well known in vitro interaction between FM and fibrinogen. Secondly, white cells appear to participate in the intravascular precipitation of circulating soluble FM complexes.

FIBRINOPEPTIDE A (FPA) LEVELS IN VENOUS THROMBOSIS AND PULMONARY EMBOLISM BEFORE AND DURING ANTICOAGULANT THERAPY. I. Yudelman, H.L. Nossel, K.L. Kaplan and J. Hirsh. Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, U.S.A., and Department of Pathology, McMaster University Medical Centre, Hamilton, Ontario, Canada.

FPA levels were measured in 60 patients subjected to venography and to lung scan for symptoms suggestive of venous thromboembolism. In all 23 patients with negative venography and/or lung scan, FPA levels were in the normal range (< 1.3 pmol/ml, mean 0.6 pmol/ml). The FPA levels were elevated in 34 of the 37 patients with a positive lung scan and/or venogram. The range was 0.4 – 112 pmol/ml, median 6.2 pmol/ml. The FPA levels were measured serially in patients with confirmed thromboembolism who were treated with heparin. In 14 of the 15 patients there was a marked drop in FPA levels in the first 15 minutes after the initial dose of heparin. In 1 patient the FPA levels only reached the normal range after 48 hours of heparin therapy. FPA levels were measured daily in 10 patients while on anticoagulant therapy. In 4 patients FPA levels became normal and remained so and no symptoms recurred. In the other 6 patients there were 13 episodes of FPA elevations. 10 of these were preceded by a recurrence of the initial symptoms. In one patient FPA elevations occurred in the absence of symptoms while the repeat lung scan showed new lesions. Suboptimal anticoagulation and/or the transition from heparin to Coumadin preceded the recurrence of symptoms in 6 out of 10 episodes. FPA levels were frequently normal in asymptomatic patients with evidence of venous thrombosis as shown by 125 I fibrinogen uptake scan. These results suggest that FPA measurements may be useful in the diagnosis and in monitoring therapy of symptomatic thromboembolism.