

PLASMINOGEN ACTIVATOR PRODUCTION BY MALIGNANT HUMAN CELLS: IN VIVO AND IN VITRO STUDIES. N.A. Marsh, *M.J. Duffy and +P.J. Gaffney. Queen Elizabeth College, London W8 7AH, *St. Vincent's Hospital, Dublin, +National Institute for Biological Standards and Control, London NW3 6RB.

A link between malignancy and impaired haemostatic function has been suggested for some time. However, the clinical implication remains confused and mutually exclusive hypotheses concerning the nature of this link are in vogue. This report concerns part of a study designed to establish the nature of this association and to define whether it is causal or accidental.

Initial experiments indicated that there was no clear correlation between malignancy, transformation and plasminogen activator (PA). Indeed, cultures of the malignant cell lines Hela and Hep2 and of a transformed lung fibroblast line produced little PA while two normal lines, MRC 5 and WI38 produced very high amounts of PA. *In vivo* data were obtained from human breast tumours which had been classified into those which contained steroid binding receptors and those which did not. PA levels were measured in tumour extracts by means of two assays, a functional ^{125}I -labelled fibrin digestion technique and a radioimmuno-metric method. Enzymic activity was also screened on a range of synthetic chromogenic substrates.

PA levels were consistently lower in those breast tumours containing steroid receptors, the ratio of PA activity in receptor-negative and receptor-positive tumours ranging from 1.43 to 3.03. All samples contained small amounts of antiplasmin-like activity and some contained other haemostatic component activities including thrombin, kallikrein and Factor Xa.

Our results do not confirm the findings of other workers who have demonstrated a positive correlation between breast tumour plasminogen activator activity and the level of steroid receptors. Plasminogen activator levels may thus be of limited prognostic value in determining the hormone-responsiveness of breast tumours and cast doubt on the view that malignant cells produce increased amounts of PA.

ACQUIRED α_2 ANTIPLASMIN DEFICIENCY IN PATIENTS WITH GLOMERULAR PROTEINURIA. D. A. Taberner. Department of Haematology, Withington Hospital, Manchester, UK.

α_2 antiplasmin has been measured in the plasma of 20 patients with a glomerular proteinuria. Significantly lower levels were found as compared to eight controls. The unconcentrated urine was also examined and α_2 antiplasmin antigen was demonstrated in seven patients but in none of the controls. Deficiency of antithrombin III due to glomerular leak has been suggested as a major cause for tendency for venous thrombosis in these patients. Acquired α_2 antiplasmin deficiency also due to renal loss may tend to counterbalance this effect. Furthermore, the presence of this potent plasmin inhibitor in the urine in patients with nephrotic syndrome may be involved in other pathological mechanisms involving fibrinolysis in the renal tract.

FIBRINOLYTIC ACTIVITY IN METASTATIC TUMORS AND TUMOR THROMBI. P. Yuen and H.C. Kwaan. Department of Pediatrics, University of Hong Kong and Department of Medicine, Northwestern University Medical School and VA Lakeside Medical Center, Chicago, IL, U.S.A.

In an attempt to clarify the conflicting reports of plasminogen activator and lack of fibrinolytic activity in tumor tissues, the fibrinolytic activity of 62 metastatic tumors and 5 tumor thrombi from autopsy and biopsy specimens was studied by the fibrin slide technique. Metastatic tumors involved lymph nodes, liver, lung, brain and ovary. Tumor thrombi were mainly comprised of hepatoma thrombi in branches of either hepatic or portal veins.

The lack of fibrinolytic activity was graded according to the focal lysis time of vascular tissues within the tumor and in the case of lymph nodes, lymphatic channels. A complete lack of fibrinolytic activity was observed in metastatic tumors and tumor thrombi, a finding similar to that observed in primary tumors.

Immunofluorescent studies on the tumors revealed the presence of antigenic material identical to fibrin, platelets and α_2 plasmin inhibitor.

HYPERFIBRINOLYSIS IN A PATIENT WITH IgG-PARAPROTEINEMIA. R. Egbring, H.-G. Klingemann, N. Heimbürger*, H.E. Karges, and K. Havemann. Department of Haematology, Medizinische Universitätsklinik and *Behringwerke AG, 3550 Marburg, W. Germany.

In patients with various malignancies (prostate, thyroid, gastric), a hyperfibrinolytic syndrome has been described. We would like to give a report on a 56 year-old male patient who became clinically apparent by his spontaneous bleeding tendencies with large haematoma. Analysis of the coagulation status revealed a primary hyperfibrinolysis characterized by a prolonged TT and PTT, decreased fibrinogen (F I) and a simultaneous increase of FDP, associated with the consumption of F I. There was also a significant fall of plasminogen (Plg) and an α_2 -plasmin-inhibitor (α_2 PI) down to about 10% of the norm. However, a Plg activator as a trigger of hyperfibrinolysis could not be detected in plasma, a malignoma could not be diagnosed. However, a IgG-paraproteinemia and -uria associated with a 20% infiltration of bone marrow with plasma cells was assessed. The bleeding tendency was treated successfully with aprotinin (Antagosan®). Under the infusion (1 Mio KIU/d) a normalization of the coagulation status was observed as measured by means of the TT and PTT; simultaneously an increase of F I and the disappearance of FDP was observed. Plg and α_2 PI also rised but did not reach normal values. Based on these observations an interrelationship between hyperfibrinolysis and paraproteinemia appears to be possible.