

Time
16.00
cont.

0841 CANCER CELL PROCOAGULANT ACTIVITY

H.R. Gralnick, National Institutes of Health, Bethesda, Md. USA

Studies of the procoagulant activity (PA) of human acute leukemia cells (ALC) has demonstrated that acute lymphocytic leukemia (ALL) had approximately 25-50% of the PA of normal human granulocytes, while lymphoid leukemias had increased PA. Acute promyelocytic leukemia (APL) had approximately 4-8 times the activity of normal granulocytes while acute myeloblastic leukemia (AML) cells had the same activity as normal. The PA was characterized as tissue factor (TF). Two correlations of the TF activity in ALC is the incidence of the fibrinogen kinetics and intravascular coagulation. We have done fibrinogen survivals on 15 patients with AL. The results of these kinetic studies have revealed that in 5 patients with ALL the T/2 is $2.94 \pm .31$ days; fraction catabolic rate (FCR) $29.8 \pm 4.3\%/day$ were slightly different from the control of T/2 3.69 ± 0.45 days; FCR $22.1 \pm 2.5\%/day$. In 3 patients with AML, the T/2 was 1.92 ± 0.79 days; FCR $44.2 \pm 20.6\%/day$. In patients with APL, the fibrinogen survival revealed a T/2 of 0.069 ± 0.25 days; FCR $160. \pm 62.7\%/day$. The use of anticoagulants in APL markedly decreases death from hemorrhage. In other investigations we have studied the effect of anticoagulation on the spread of peripheral sarcomas in man. Warfarin anticoagulation was used as an adjunct to amputation of sarcomas. The results of these studies are quite encouraging in that the patients appear to have a longer remission and to have better overall survival.

0842 PATHWAYS OF BLOOD CLOTTING INITIATION BY CANCER CELLS.

N. Semeraro, Istituto di Ricerche Farmacologiche "Mario Negri", Milan, Italy.

Although available information indicates that cancer cells may activate blood coagulation the precise mechanism remains still uncertain. A procoagulant with characteristics of tissue thromboplastin has been found in human benign and malignant tissues and in some experimental tumors. On the other hand it has been reported that extracts from malignant tissues directly activate coagulation factor X, due to the presence of a serine protease. We have investigated the procoagulant activity of cells from some experimental tumors isolated in culture or as single cell suspension from ascitic fluid. Cells from Lewis lung carcinoma (primary and metastasis), Ehrlich carcinoma ascites and JW sarcoma ascites were able to shorten markedly the recalcification time of normal, factor VIII and factor VII-deficient, not of factor X-deficient human plasma. The same cells did generate thrombin when mixed with a source of prothrombin and factor X, absorbed bovine serum (as a source of factor V), phospholipid and $CaCl_2$. Cells from Sarcoma 180 ascites were completely inactive in both test systems. It was concluded that cells from some experimental tumors, similarly to normal platelets, possess the capacity to directly activate coagulation factor X. This suggests the existence of an alternative "cellular" pathway in blood clotting initiation distinct from both the intrinsic and extrinsic mechanisms.

(Supported by Italian CNR and NIH, NCI, USA).

0843 PLASMINOGEN ACTIVATOR RELEASED FROM MALIGNANT TUMOURS

B. Astedt, Department of Gynecology and Obstetrics and the Coagulation Laboratory, University of Lund, MAS, Malmö, Sweden.

Urokinase-like plasminogen activators are released from carcinomas in vitro and in vivo. In organ or cell culture of ovarian carcinoma three forms of plasminogen activators with molecular weights of about 90,000, 54,000 and 31,000 daltons are released with mainly the high molecular weight forms in early cultures and low molecular weight forms in late cultures. They are inactivated by diisopropylfluorophosphate and resemble urokinase in respect of active site and immunologic determinants. Based on the cross-reaction between urokinase and tumour plasminogen activator a radioimmunoassay was devised using urokinase of 30,000 daltons and monospecific antiserum against this fraction, and applied for determination of tumour plasminogen activator.

Tumour activator and urokinase are neutralized by the naturally occurring inhibitors alpha₂-antiplasmin, alpha₁-antitrypsin and alpha₂-macroglobulin. An inhibitor derived from placenta inhibits the tumour plasminogen activator and urokinase, but not the tissue plasminogen activator.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.