BONE MARROW PLASMINOGEN ACTIVATOR IN MALIGNANT DISEASE. J.W. Hampton, A.S. Weidenbach, and S. Rao. Hematology Research Laboratory, Oklahoma Medical Research Foundation, 825 N.E. 13th, Oklahoma City, Oklahoma, 73104, U.S.A.

Enhanced blood fibrinolytic activity has been reported with metastatic malignancy and with primary hepatic disease. The demonstration of a plasminogen activator in a case of acute myelomonocytic leukemia prompted us to test bone marrow concentrates from healthy individuals (7), individuals with cirrhosis (3), carcinoma of the prostate (1), and with leukemia (17). Three mls of bone marrow was obtained by sternal marrow aspiration and mixed with 1 ml sodium heparin (10,000 u/ml). Using progressively smaller bore needles the particles were fractured and layered with a Ficoll-Hypaque solution. The cells are resuspended in a final concentration of 10^5 cells/ml. Using affinity-chromatographed plasminogen, 10µl of the cell suspension was added to a bovine fibrin plate. After 17 hours the diameter of the plate was measured and converted to Ploug units using a standard urokinase curve. Healthy individuals showed generally no or very low activity. The patients with cirrhosis showed 2-6.5 u/10^5 cells. The single patient with metastatic carcinoma of the prostate showed 24 u/10^5 cells. Patients with acute leukemia showed from 1-40 u/10^5 cells. There was a rough correlation between the height of activity and the percent blast cells in the marrow. Triton-X added to the marrow cells caused the release of the membrane activity in experiments with 3-22 u/10^5 cells. Immunodiffusion of bone marrow activator from a patient with leukemia showed identity with the activator from a patient with cirrhosis and with primary fibrinolysis. We conclude that the bone marrow plasminogen activator may reflect the altered stem cell associated with leukemia.

EVIDENCE FOR THE PRESENCE IN HUMAN PLASMA OF A STREPTOKINASE CO-FACTOR - SEPARABLE FROM PLASMINOGEN. K. Korsan-Bengtsen, M. Johnsen and G. Gustavsson. Blood coagulation laboratory, Department of Medicine II, Sahlgren's Hospital University of Göteborg, Sweden.

Our original observation was that plasma made plasminogen-free by lysine sepharos chromatography accelerated the streptokinase activation of purified plasminogen when measured by means of a chromogenic peptide substrate. The substance with this property is preciptable from plasma with 3-5 % polyethylenglycol (PEG), it is eluted near the front on Sepharos 6 B gelfiltration and does not move on electrophoresis at pH 8.6. The activity is not lost on heating to 65°C for 10 min. Traces of immunoglobulins, C-3, C-4, alfa and betalipoproteins present in the purified co-factor preparations were removed by means of affinity chromatography without loss of co-factor activity. The co-factor does not in itself have any proteolytic activity and it cannot be activated with streptokinase or urokinase to give proteolytic activity. It is a potent accelerator of the streptokinase plasminogen activation. One of the two tested commercial streptokinase preparations was found to be influenced more than the other by the co-factor. When this preparation was run on a Sephadex 200 column a certain fraction with a high co-factor "sensitivity" was identified. We have not been able to separate two distinct activities from the streptokinase preparation.

PROPERTIES OF PLASMINOGEN ACTIVATORS IN CIRCULATING HUMAN BLOOD AND HUMAN CADAVERIC VEINS. Michael Mackie, Bruce Bennett, Derek Ogston. Department of Medicine, Aberdeen University, Aberdeen, Scotland.

The properties of 3 partially purified plasminogen activators prepared from human blood have been compared with activator prepared from cadaveric veins and urokinase.

Circulating plasminogen activator present in blood after venous occlusion of the arm has been partially purified by gel filtration on Sephadex G-200 in phosphate buffer containing 0.15 M NaCl followed by gel filtration of active fractions on Sephadex G-200 in buffer containing 1 M NaCl.

Plasminogen activator generated from lysine-sepharose treated plasma after activation of Hageman factor by kaolin has been partially purified by elution of the activator from kaolin by 0.5 M NaCl and gel filtration on Sephadex G-200; the activator precipitated by dextran sulphate from the euglobulin supernatant prepared from lysine-sepharose treated plasma has been partially purified by similar gel filtration techniques.

Cadaveric plasminogen activator has been prepared by ammonium sulphate precipitation of the washout from cadaveric veins followed by sequentail filtration on Sephadex G-200 in (a) low and (b) high concentrations of NaCl. The properties of these 4 plasminogen activators are compared with those of urokinase in terms of their stability, susceptibility to protease inhibitors and molecular size.