Time
10.15 **0447** BINDING OF MYELOMA MONOCLONAL IMMUNOGLOBULIN WITH FIBRINOGEN AND FIBRIN.

Andrei Z. Budzynski*, Stephanie A. Olexa and Bharat V. Pandya,
Temple University, Health Sciences Center, Philadelphia, PA 19140, U.S.A.

Blood and plasma clots are frequently abnormal in patients with multiple myeloma as evidenced by the prolongation of clotting time, formation of bulky and gelatinous clots and inhibition of clot retraction. It has been demonstrated in several multiple myeloma cases that the isolated immunoglobulin inhibited clot formation in normal plasma and decreased the rate of fibrin polymerization. In this work a hypothesis was tested whether these phenomena originate from binding of multiple myeloma immunoglobulin with fibrinogen and fibrin. Blood was obtained from a patient (J.I.) having IgAλ gammopathy with prolonged clotting time and abnormal clot retraction. Washed plasma clots contained large amount of monoclonal IgAλ demonstrated by precipitation with anti-α or anti-λ antibodies and by the presence of heavy (65,000) and light (25,000) polypeptide chains. This myeloma IgA was incorporated into clots regardless of crosslinking and was extractable. Affinity chromatography of serum or heated plasma on insolubilized fibrin monomer resulted in recovery of large amount of myeloma monoclonal IgA, but not IgG, IgM or IgD. The isolated fibrin-specific IgA was taken up by clots obtained from normal plasma or purified fibrinogen. Insolubilized fibrinogen bound myeloma monoclonal IgA from plasma. Two-dimensional agarose/polyacrylamide slab gel electrophoresis demonstrated the presence of a fibrinogen-IgA complex in patient's plasma. The results indicate that a myeloma monoclonal immunoglobulin binds with fibrinogen and fibrin, probably forming an antibody antigen complex, implying the formation of autoantibodies against these proteins.

Plasminogen – Plasmin System

Hungerford Room

09.00 **0448** VARIANT PLASMINOGENS IN PATIENTS WITH A HISTORY OF VENOUS THROMBOSIS

K. C. Robbins,* R. C. Wohl, and L. Summaria, Michael Reese Research Foundation, Chicago, Illinois, U.S.A.

Kinetic methods will be described for measuring plasminogen and for studying plasminogen activation in human plasma, using specific synthetic substrates, with different activator species. These studies resulted in the discovery of several patients plasmas containing variant, or abnormal, plasminogen molecules; these plasmas showed lower observable activation rates. Plasminogen isolated from these plasmas activated with identical catalytic rate constants to normal plasminogen, by different activator species, but the apparent Michaelis constants were 10- to 100-fold higher. These data lead to the conclusion that the binding properties of the activator species to the variant plasminogens have been impaired. The interpretation of the data in two patients with venous thrombosis was possible only in terms of homogeneous populations of plasminogen molecules. These individuals have to be considered homozygous with respect to their plasminogens, and family studies indicate the possibility of an autosomal dominant hereditary transmission. The urokinase activation data with the variant plasminogens point to an activation mechanism identical to that proposed for streptokinase, namely the activation of plasminogen by a plasminogen·urokinase complex, analogous with the plasminogen·streptokinase complex.