IS FIBRINOLYSIS A CONTINUOUS LOW LEVEL MECHANISM IN NORMAL ADULTS? E.F. Plow and T.S. Edgington. Scripps Clinic and Research Foundation, La Jolla, California, U.S.A.

Continuous fibrino(geno)lysis by plasmin has been suggested as a primary pathway for fibrinogen catabolism and as a means of compensating for ongoing low levels of blood coagulation and fibrin formation. The cleavage-associated neoantigen, fg-D_{neo} , provides an incisive immunochemical marker for assessment of this hypothesis since it is expressed in an equimolar fashion by all major physiologic cleavage fragments (X, Y and the D:E complex) of fibrinogen and fibrin. In previous studies (J. Clin. Invest. 52:273, 1973), fg-D_{neo} expression was not detected in normal plasma, but the sensitivity of the described assay was not sufficient to exclude low levels of these derivatives. In the present study, utilizing sequential radioimmunoassay procedures, preincubation of the competing antigen with anti- fg-D_{neo} prior to addition of the ^{125}I -ligand (fg-D), the sensitivity of the assay exceeded $1 \times 10^{-11} \text{ M}$ ($< 2 \text{ ng fg-X/ml}$). In this system, 20 plasmas from healthy adults were found to contain no detectable fg-D_{neo} activity. On the basis of assay sensitivity, less than one molecule of degradation product is present per 100,000 fibrinogen molecules in normal plasma. In separate studies, it was established that the initial cleavage of the amino-terminal aspects of the B β chain of fibrinogen were required for exposure of fg-D_{neo} . A α chain cleavage alone was insufficient as high solubility fibrinogen fractions 1-8 and 1-9 failed to express fg-D_{neo} . On this basis, it is concluded that fibrinolysis and fibrinogenolysis sufficient to produce fragment X or later plasmic derivatives do not represent significant normal physiological pathways.