

FIBRINOGEN/FIBRIN INTERACTION WITH PLATELETS. D. Michaeli and K. Orloff. University of California, San Francisco, California, U.S.A.

There is considerable evidence that fibrinogen is involved in ADP-induced platelet aggregation. On the basis of fluorescent probe experiments, it was concluded that fibrinogen increases the exposure of hydrophobic regions on the platelet membrane. A proposal was made that fibrinogen enhancement of ADP-induced aggregation is mediated via a thrombin-fibrinogen interaction leading to the formation of fibrin bridges between platelets. Evidence militating against this mechanism will be reviewed.

Platelets are capable of interacting with nascent fibrin, which in turn induces the aggregation and release reactions. Platelets can similarly react with fully polymerized fibrin. Fragment D inhibited these interactions, probably due to its binding to fibrin, and thereby blocking sites on fibrin that are involved in its interaction with platelets.

STUDIES ON THE POLYMERIZATION SITES IN FIBRINOGEN. J.L. York, B. Blombäck and B. Hessel. University of Arkansas College of Medicine, Little Rock, Arkansas (U.S.A.), and Karolinska Institutet, Stockholm, Sweden.

A microcolumn assay has been developed for the quantitation of the affinity of various soluble fragments of fibrin and fibrinogen for fibrinmonomer-Sepharose. The assay involves a study of the concentration dependence of the substance in question on the inhibition of the binding of thrombin activated  $^{125}\text{I}$ -N-DSK (amino terminal disulfide knot) to the fibrinmonomer-Sepharose (Fbm-Seph). Presumably the same surface orientated sites involved in the affinity binding are also involved in polymerization; consequently, this approach provides a method for evaluating specific regions of the fibrin molecule as possible polymerization sites. Thrombin activated N-DSK (N-DSK<sub>A</sub>) binds to Fbm-Seph. at one non-interacting site, but unactivated N-DSK does not. Iodination of N-DSK prevents binding. Specifically, increased iodination of B $\beta$  Tyr<sub>117</sub> of N-DSK is correlated with a decreased affinity for Fbm-Seph. On the other hand,  $\gamma$  chain tyrosines 18 and 32 are not susceptible to iodination and therefore cannot play a role in polymerization. Amidination of the lysines of activated N-DSK does not inhibit binding to Fbm-Seph. The isolated chains of N-DSK were poor inhibitors of  $^{125}\text{I}$ -N-DSK<sub>A</sub> binding as were the fibrinopeptides. N-DSK activated with Reptilase and thrombin activated plasmin fragment E had only half the affinity of thrombin activated N-DSK. The tryptic core, DS-4 of N-DSK was a poor inhibitor of N-DSK<sub>A</sub> binding. Iodinated fibrinogen, although 98% clottable, forms a very weak clot and iodinated N-DSK<sub>A</sub> isolated from this iodinated fibrinogen has poor affinity for the Fbm-Seph. These results imply that one or more major polymerization sites occur in the N-DSK portion of the fibrin molecule.

PHYSIOLOGICAL AND CLINICAL SIGNIFICANCE OF FIBRIN POLYMERIZATION. E.A. Beck. Central Hematology Laboratory, Inselspital, 3010 Berne, Switzerland.

The physiological importance of fibrin polymerization is not well understood in man. In fact, severe disorders of fibrin polymerization (e.g. in congenital dysfibrinogenemia) are mostly "laboratory diagnoses" without clinical implications. Pathophysiologically, fibrin polymerization may be rated either as "favorable" or "unfavorable": fibrin deposition supports hemostasis, promotes wound healing and confines activated coagulation enzymes mechanically, but participates in thrombosis, favors serous mucosal adhesions and may block phagocytosis. In many diseases, the balance between favorable and unfavorable effects of fibrin polymerization is delicate. Therapeutically, fibrin polymerization should probably be inhibited more often than promoted.