Rheological and biochemical analyses on blood coagulation
~ Discovery of a new pathway under stagnant flow conditions ~

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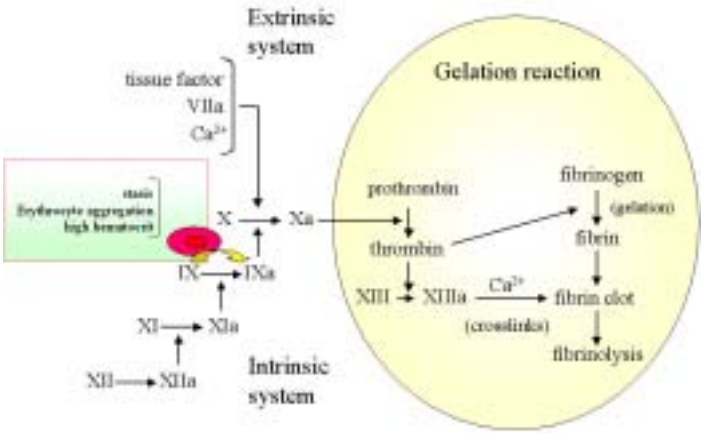
It has been considered that the enhancement of erythrocyte aggregation and high hematocrit at stasis would be risk factors for coagulation, mainly venous thrombosis. However, the relations between these erythrocyte abnormalities and thrombogenesis remain unclear. Furthermore, normal erythrocytes are considered to have no procoagulant activity. In our early study, we examined the coagulation of blood from a rheological point of view, and we speculated that an intrinsic coagulation pathway that is triggered through factor IX or X activation by erythrocytes exists, where platelets and leukocytes are little incorporated in initiating the coagulation cascade.

In this report, we show that human erythrocytes are able to directly trigger the intrinsic coagulation cascade through factor IX activation in the presence of calcium ions. We purified factor IX-activating enzyme on erythrocyte membrane. The N-terminal amino acid sequence of the enzyme was determined. The mechanism of F-IX activation by the extract was examined. Also, we examined the effects of shear rate, hematocrit and erythrocytes from different donors on F-IX activation. The present data suggest the participation of erythrocytes in the intravascular coagulation of blood under stagnant flow conditions, especially venous thrombosis, which may lead to a fatal pulmonary embolism.



Extrinsic and intrinsic pathways