

Slope and parallelism of APTT dilution curves: new insights

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Factor analysis with the one-stage APTT is available for factor XII, prekallikrein, high molecular weight kininogen, factor XI, factor IX and factor VIII. In the procedure dose-response curves are constructed by mixing normal plasma with factor deficient /depleted plasma.

Steep dose response curves occur for factor XII and HMWK, while for factor IX and VIII slopes are much weaker. This is related to the APTT in the deficient plasma's which is rather short for factor IX and VIII depleted plasma resulting in a smaller window of clotting times and in a less steep dose response curve, compromising accuracy

Recently, Matafonov et al (1) identified direct activity of factor XIa on factor X, which might explain the short APTT values in factor IX and VIII depleted plasma. We could demonstrate this to be the case using inhibitors of factor XIIa, kallikrein and factor XIa showing much longer APTT values in the factor IX and VIII deficient plasma's.

We further identified a significant dependence on the factor XI level of the direct activity of factor XIa on factor X. This comprises the assays precision and is a new, potential source of non-parallelism between dose response of the calibrator and patient dilutions.

Current best practice is the use of diluted substrate plasma (to reduce factor XI), with documented factor XI level, the documentation of factor XI in severe deficiencies of factor IX and VIII and the use of silica-based APTT reagents which supports the factor XIa action on factor X less than ellagic acid.

- (1) Matafonov, A., et al., *Evidence for factor IX-independent roles for factor XIa in blood coagulation.* J Thromb Haemost, 2013. 11(12): p. 2118-27.