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0766 ANTICOAGULATION KINETICS FOLLOWING BOLUS HEPARIN INJECTIONS. L.F. Mockros, S.D. Hirsch, L. Zuckerman*, J.A. Caprini, W.P. Robinson and J.P. Vagher; Northwestern University, Evanston Hospital, Evanston, Illinois, U.S.A.

Anticoagulation (AC) levels were monitored simultaneously in dogs by 3 whole blood (WB) and 2 plasma (P) clotting assays. Three levels of heparin (50,100 and 200 U/kg were tested in 26 experiments by intravenous injection. Blood was sampled at 10 and 30 min then repeated every 30 min for 4 hours. The WB clotting tests provided more sensitivity with respect to the kinetics of neutralization of the heparin than did the P assays. The levels of AC determined by each assay method was fit to exponential curves using a computerized iterative least squares method. The points were weighted inversely with the variance and the censored data was used by fitting the known values to a gamma distribution and deriving the average and SEM of the series. The coagulation curves were dependent upon the heparin dose and test methods. Extrapolated levels of initial AC demonstrate from 3 to 67 fold increases in relative clotting times for 50 and 200 U/kg dosages respectively, depending on the assay method. The AC half lives ($T_{\frac{1}{2}}$) with the three WB assays varied from 15 to 41 min for the low dosage and 24 to 34 min and 27 to 30 min for 100 and 200 U/kg dosages respectively. The shortness of these $T_{\frac{1}{2}}$ is a consequence of using data acquired at 10 to 30 min post injection. Reanalysis of our data using sampling periods >60 min significantly prolonged the derived $T_{\frac{1}{2}}$. Finally there was a marked post heparin shortening (less than preheparin values) of the WB assays at 2-4 hours. The values appeared to be dose dependent, as the shortest values occurred in those animals receiving the highest heparin dose. Therefore, intravenous heparin can be associated with high initial AC followed within 2-4 hours by a quicker than normal clot time.

P6-110 0767 VISCOELASTIC STUDIES OF SURFACE LAYERS OF HEPARIN-FIBRINOGEN SYSTEMS AND THE ANTITHROMBOTIC ACTION OF HEPARIN OTHER THAN ANTICOAGULATION

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Decreased rigidity of torque values of surface layers (SL) of heparin plasma was reported by us (Thromb.Res.1,1,1972). In subsequent viscoelasticity studies of SL of fibrinogen (Fg) systems we found lowering of viscosity (ηM) and of elasticity (γM) with some heparin preparations (HP). No relationship was found between these decreased values and the antithrombin activity (AA) of the HP. Certain HP, whether fractionated or not, markedly decreased ηM and γM, although their AA was very low. The antithrombotic action (ATA) of HP is therefore not necessarily dependent upon their AA. Since Copley & Robb discovered that HP can clump platelets in vitro & in vivo (Am.J. Clin. Path.12,416,563,1942), the ATA of HP could hitherto be explained only by AA. Our new findings are explained by Copley's concept on initial thrombus formation (Biorheol.8,79,1971), in which Fg forms gels without thrombin action (Copley & King, Thromb.Res. 8, Suppl.II,393,1976). Such production of Fg gels can no longer be doubted, as found by Tooney & Cohen (J.Molec.Biol. 110,363,1977). Conclusion. The ATA of HP is twofold: (1) further growth of formed thrombi is inhibited by AA; (2) formation of new thrombi is prevented by inhibition of Fg gelation due to constituent, if present, of HP.