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VISCOELASTIC STUDIES OF COAGULATION: CELL-PLASMA INTERACTIONS. J. Mitchell, L. Zuckerman, J.P. Vagher, and J.A. Caprini. Department of Research, Evanston Hospital, Evanston, IL.

In order to examine the cell-plasma interactions during coagulation, a thrombelastograph was modified to measure two viscoelastic properties of blood: rigidity (G) and rate of stress relaxation (S). Citrated whole blood was collected from healthy donors and centrifuged to obtain platelet-rich and platelet-poor plasma and washed red cells. The blood was reconstituted at varying hematocrits (HCT) and platelet counts (PLT) and coagulation was initiated by adding $CaCl_2$. Factor XIII (FXIII) activity was inhibited with glycine ethyl ester (GEE). In normal blood, the rigidity increases rapidly after 6-8 min following addition of $CaCl_2$ with a rate constant (k_G) of 8.2 min and a saturated rigidity (G_{sat}) of 22.3×10^3 dyn/cm^2. S decreased in a biphasic manner: the first phase (ΔS1) lasting about 15 min and accounting for a 70% fall in S and with a rate constant (k_{S1}) of 6.7 min; the second phase (ΔS2) from 15 min on with a 15% drop in S and with a rate constant (k_{S2}) of 71.4 min. Increasing PLT resulted in a linearly increasing G up to 31×10^3 dyn/cm^2 for 3×10^5 cells/mm^3. Increasing HCT had no effect on G_{sat}, but increased k_G linearly for $10 < HCT < 50\%$. Inhibition of FXIII activity by GEE had no effect on G, but inhibited ΔS2 while k_{S2} was linearly dependent on GEE concentration. In cell-free plasma, ΔS1 was about 80% in 10 min with virtually no ΔS2. With the inclusion of even a small number of platelets, ΔS1 and ΔS2 returned to that found in normal blood.

It was concluded that platelets change the configuration of fibrin in the clot and alter the kinetics of orientation and crosslinking. Red cells have little mechanical influence but do seem to have some procoagulant activity.

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INTENSITY OF THERAPEUTIC RANGE AND MEAN ANTICOAGULANT DOSAGE PRESCRIBED: AN INTERNATIONAL STUDY. L. Poller and D. A. Taberner. National (UK) Reference Laboratory for Anticoagulant Reagents and Control, Withington Hospital, Manchester, UK.

It has been suggested that anticoagulant dosage requirements vary in different parts of the world. An international survey on anticoagulant dosage involving over 500 laboratories was performed employing a questionnaire on the mean daily anticoagulant dosage of 20 stabilised patients. Replies received show a considerable variation in dosage between countries.

In order to further investigate the influence of the intensity of the therapeutic range on local dosage differences, participants were asked to assess a lyophilised human coumarin plasma sample. Most agreed that the plasma was adequately anticoagulated. However, laboratories finding the plasma overdosed were prescribing a lower mean anticoagulant dosage than those laboratories finding the plasma underdosed. This suggests that some of the differences in dosage between laboratories may be accounted for by the varying intensities of the therapeutic ranges used in the different countries.

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IMPROVEMENT OF PLASMATIC COAGULATION IN PATIENTS WITH LIVER DISEASE TO ENABLE NECESSARY DIAGNOSTIC AND THERAPEUTIC STEPS. G.E. Vogel, S. Tuchtenhagen, Ch. Komm A. Oberdorfer*, II. Medical Clinic and *Institute for Clinical Chemistry and Pathobiochemistry of the Technical University Munich, Munich, G.F.R.

Specific plasmatic concentrations of coagulation factors are necessary in endoscopic treatment e.g. slerosis of esophageal varices. Thrombotest of 35 to 40% is necessar. To correct with factor concentrates and fibrinogen is dangerous in cause of pushing DIC (disseminated intravascular coagulation). The substitution of the inhibitor AT III which is succeeded from prothrombin concentrates and fibrinogen avoid fearful consumption reactions. The AT III plasma activity was measured by chromogenic substrates in citric plasma. In 5 patients (2 female, 3 male- age 19-67) the diminished AT III-levels were increased to the normal value of 80%. After normalization of the inhibitors prothrombin complexes and if necessary fibrinogen were substituted. It was seen an assessable improvement of the plasmatic coagulation which depends on the unit concentration of the substituted factors. In the improved coagulation situation 2 laparoscopies and 3 slerosis of esophageal varices could be done without any bleeding complication.
Patients with liver diseases and coagulation disorders who were unsuitable for endoscopic and surgical treatment can be treated with this concept.

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ISOLATION AND CHARACTERIZATION OF PROCOAGULANT SUBSTANCES FROM HUMAN ASCITES. M.F.M. Johnston, J. Vargo and J.H. Joist. Departments of Pathology and Medicine, St. Louis University School of Medicine, St. Louis, Missouri, U.S.A.

The treatment of massive, medically intractable ascites by a peritoneovenous shunt (PVS) is associated with variably severe disseminated intravascular coagulation (DIC). Ascitic fluid obtained from cirrhotic patients at the time of placement of a PVS was found to shorten the partial thromboplastin time (PTT) of normal human platelet-poor plasma. This procoagulant activity which was found to reside in the cell-free fraction of ascitic fluid was heat stable and insensitive to pH change over a wide range. Chromatography on Bio-Rad Agarose 1.5 yielded one major high molecular weight component and several smaller fractions of lower molecular weight exhibiting procoagulant activity as determined by the PTT assay. The activity in the major fraction (80% total activity) coprecipitated with human fibrinogen but could be separated from fibrinogen by affinity chromatography using anti-human fibrinogen. This procoagulant did not hydrolyze chromogenic substrates S-2222 and S-2238 and was not inhibited by diisopropylfluorophosphate (DFP). Purification of a minor procoagulant fraction by aluminum hydroxide ($Al(OH)_3$) adsorption and chromatography on Sephadex G-200 yielded a fraction that clotted both citrated normal plasma (without the addition of calcium chloride) and purified human fibrinogen and induced platelet aggregation in citrated human platelet-rich plasma. Chromatography on DEAE cellulose yielded two peaks with procoagulant activity (PTT), one of which hydrolyzed S-2238 and was DFP-sensitive. These studies indicate that at least three distinct, clotting active substances are present in ascitic fluid some or all of which may be responsible for PVS-induced DIC. Further studies on purification and characterization of these ascitic procoagulants are in progress.