THE COMBINED EFFECTS OF 2,3-DIPHOSPHOGLYCERATE AND PHOSPHOLIPASE-A ON PLATELET AGGREGATION INDUCED BY ADP, EPINEPHRINE, NOREPINEPHRINE AND COLLAGEN. M.F. Asterita, P.G. Iatridis, S.G. Iatridis, R. Torrella, B.H. Ragatz, J. Gadarowski, and S.G. Markidou. Northwest Center for Medical Education, I.U. School of Medicine, Gary, Indiana, U.S.A. and School of Medicine, University of Athens, Greece.

It has been shown recently, that under specific conditions, phospholipase-A (Phl-A) or 2,3-diphosphoglycerate (2,3-DPG) can inhibit human platelet aggregation induced by ADP, epinephrine, norepinephrine or collagen. In this report, by using a dual channel Payton Aggregometer, the effects of 2,3-DPG and Phl-A on platelet aggregation were further studied. When 2,3-DPG (2μM) was added in human platelet rich plasma with Phl-A (200μU), 30, 60, 120 or 300 sec. before the addition of ADP (0.5-2.0μM), epinephrine (2-5μM) or norepinephrine (2-5μM) an enhancement of platelet aggregation was observed, whereas the same concentration of 2,3-DPG alone or Phl-A alone, inhibited both the rate and extent of the second phase of platelet aggregation induced by the same aggregating substances. The combined effects of 2,3-DPG and Phl-A on collagen induced platelet aggregation remained inhibitory. Aspirin on the other hand abolished the enhancement of platelet aggregation induced by 2,3-DPG and Phl-A. These combined effects of 2,3-DPG and Phl-A were both a concentration and a time dependent response. The results indicate that the combined effects of 2,3-DPG and Phl-A were probably mediated through prostaglandin formation. Since Phl-A is a physiological platelet enzyme which releases arachidonic acid, then we may postulate that 2,3-DPG probably activates the synthetases and/or cyclooxygenases which are the enzymes necessary for the formation of the important platelet aggregating substances, namely the endoperoxides and thromboxanes. Supported by USPHS HL-15425.

STUDIES ON HUMAN SERUM INHIBITORS OF PLASMIN, UROKINASE AND PLASMA KALLIKREIN USING CHROMOGENIC SUBSTRATES. M.J. Gallimore and E. Fareid. Institute for Thrombosis Research, Rikshospitalet, Oslo, Norway.

Human serum inhibitors of plasmin, urokinase and kallikrein were studied using chromogenic substrate assays, (Plasmin substrate, S-2251, Kabi, Sweden; Urokinase substrate, Chromozyme -UK and Plasma Kallikrein substrate, Chromozyme -PK, Pentapharm, Basle, Switzerland). In whole serum both "immediate" and "time dependent" inhibition of plasmin and kallikrein was observed, whilst only very weak inhibition of urokinase was detected. When serum samples were fractionated by Sephadex G-200 gel-filtration the "immediate" plasmin inhibitors were identified as α_2-macroglobulin and low molecular weight antiplasmin whilst α_2-macroglobulin and C^1-esterase inhibitor were immediate inhibitors of kallikrein. "Time-dependent" inhibition of both enzymes was observed in the α_1-antitrypsin containing fractions.

THROMBOEMBOLIC PROPHYLAXIS AND VISCOSITY REDUCTION WITH ANCROD. G.D.O. Lowe, C.D. Forbes, C.R.M. Prentice, J.C. Barbenel. University Department of Medicine, Royal Infirmary, and Department of Bio-Engineering, University of Strathclyde, Glasgow, Scotland.

Blood and plasma viscosity were measured at high shear rates in 10 patients receiving intravenous ancrod and 9 patients receiving subcutaneous ancrod. In both groups significant viscosity reduction accompanied fibrinogen depletion and there was no significant fall in haematocrit. Blood and plasma viscosity were also significantly reduced in 28 patients after operation for fractured hip, who were given daily subcutaneous injections of ancrod to reduce the mean plasma fibrinogen to 1G/L. Dose ranging studies suggest a suitable regime to be a total of 560 units ancrod, given in five daily doses starting immediately after surgery. No significant viscosity changes were observed in 14 control patients after hip surgery although the haematocrit fall was similar in both groups. No significant changes occurred in 13 patients receiving intravenous heparin. Viscosity reduction during ancrod therapy does not depend on haematocrit reduction or anticoagulation, and is probably due to depletion of plasma fibrinogen. Subcutaneous ancrod appears feasible and safe, and merits trial as a thromboembolic prophylactic agent.