POTENTIATION OF HEPARIN BY DEXTRAN AND ITS CLINICAL IMPLICATION. M. Atik, M.D. Drew Postgraduate Medical School, University of California. Los Angeles, California, U.S.A.

The different mechanisms underlying the antithrombotic effects of heparin and dextran are known. To document the clinically suspected potentiation effect when the two agents are used together, the following study was undertaken:

In 20 patients with peripheral vascular disease, the Ivy bleeding time, the Lee-White clotting time and the platelet adhesiveness by Hellem method, were determined at control periods and at 1 and 3 hours following infusion of various doses of heparin alone. These were repeated on separate days after infusion of 500 ml of dextran in combination with same doses of heparin.

While dextran alone had no effect on the clotting time, it produced a marked and statistically significant potentiation of heparin effect ($P<0.01$). The mean clotting time one hour after infusion of 10,000 u of heparin was increased from 36 min. with dextran to 69 min. with dextran. This effect persisted at 3 hours. The mean clotting time after 5,000 u of heparin with dextran was almost the same as after 10,000 u of heparin with dextran. The potentiation was slight at 2.500 u of heparin. Heparin did not affect platelet adhesiveness. Dextran suppressed it when it was abnormally high, but did not reduce it below the normal value of 41 ± 9%. There was no demonstrable changes in the bleeding time by either dextran or heparin at the dosage given.

Our clinical experience and reports of other investigators suggest the desirability of the use of the two drugs in certain circumstances. To be effective and yet safe, it is recommended that whenever heparin is used in patients receiving dextran the dosage should be reduced to a half or a third of the usual.

INCREASED VON WILLEBRAND FACTOR AND DEFECTIVE RISTOCETIN-INDUCED PLATELET AGGREGATION IN LIVER DISEASE. S.Maragall, A.Ordinas, C.Clemente, F.Casals, J.Profitós and R.Castillo. Facultad de Medicina. Hospital Clínico y Provincial. Barcelona. Spain.

Increased concentrations of factor VIII-related antigen (VIIIR:AG), factor VIII procoagulant activity (VIII:C) and factor VIII von Willebrand activity (VIIIR:WF) were found in plasma of patients with evidence of advanced hepatic cirrhosis. There was no correlation among the three plasmatic activities of factor VIII complex as opposed to those existing in normal individuals. The mobility of the (VIIIR:AG) as detected by crossed electrophoresis was normal.

On the other hand, washed platelets from those patients showed a defective Ristocetin-induced aggregation with normal platelet poor plasma (PPP). The platelet (VIIIR:AG) was quantitatively and qualitatively normal.

THE MICROEMBOLISM SYNDROME. Tom Saldeen, Department of Forensic Medicine, University of Uppsala, Sweden.

Clinical, autopsy and experimental investigations in parallel have revieled the existence of a microembolism syndrome where respiratory insufficiency is the main finding. In the early, usually benign form of the syndrome, transient pulmonary microemboli give rise to transitory pulmonary dysfunction. There is a phase of bronchiolar constriction, probably due to platelet release of prostaglandins. In the delayed, often malignant, form of the syndrome persistent pulmonary microemboli result in a progressive respiratory insufficiency. Three important factors in the pathogenesis of the delayed syndrome are fibrin, a delayed fibrin elimination from the lungs and a fibrin degradation product (FDP) which causes an increased vascular permeability. The delayed fibrin elimination is mainly caused by a fibrinolysis inhibitor, which primarily inhibits plasminogen activation. The inhibitor has been isolated in serum from patients with the delayed syndrome by affinity chromatography. The liver synthesis of this inhibitor can be prevented by nicotinic acid, probably due to a decreased release of free fatty acids. Dextran decreases the effect of this inhibitor. The contact time between the permeability increasing FDP and the pulmonary endothelium is much longer in a state of delayed fibrin elimination than during normal fibrin elimination where the FDP are rapidly swept away from the lungs. During the last years there has been a drop in the number of deaths in this syndrome, probably due to new prophylactic measures, especially those decreasing the degree of intravascular coagulation and inhibition of fibrinolysis.