INCREASED HEPARIN CLEARANCE IN EXPERIMENTAL PULMONARY EMBOLISM. W.G. van Aken, H. Chiu, J. Hirsh, E. Regoeczi and A.A. Horner. Dept. of Path., McMaster Univ., Hamilton, Canada and Dept. Physiol., Univ. of Toronto, Toronto, Canada.

Patients with pulmonary embolism (PE) have been reported to have a shortened heparin half-life ($t_{1/2}$). Heparin clearance was investigated in rabbits to explore the possible contribution of platelets in increased heparin clearance in acute PE. Heparin clearance was measured by a protamine titration (heparin activity) assay and by ^{35}S radioactivity. Both assay methods gave comparable results and showed a shortened heparin $t_{1/2}$ in PE. Heparin $t_{1/2}$ was significantly shorter in PE (12.0 min) than in venous thrombosis (VT) (18.2 min) and in control rabbits (20.0 min) when a dose of heparin 50 U/kg was injected. Heparin $t_{1/2}$ was not reduced in animals with PE that were treated with heparin 200 U/kg and in animals that were embolized with polyether urethane coated-glass pellets. No significant absorbance of ^{35}S heparin to the surface of PE or VT was found. The heparin $t_{1/2}$ was shortened to the same extent in severely thrombocytopenic animals (platelet count $< 30,000/\text{mm}^3$) with PE as in non-thrombocytopenic animals with PE (12.8 min compared to 12.0 min) and was significantly shorter than in thrombocytopenic, VT and control animals ($p < 0.005$). In addition, platelet survival was uninfluenced by PE and there was no increase in antiheparin activity in plasma after PE. It is concluded that the mechanism for the shortened heparin $t_{1/2}$ is not platelet mediated, that it is influenced by the nature of thromboembolic material and that this effect on heparin $t_{1/2}$ appears to be dose dependent.

POSTER SYMPOSIUM IX

Coagulation: Variants of Von Willebrand's Disease.

REDUCED POLYMERIZATION OF WILLEBRAND FACTOR IN A FAMILY OF PIGS WITH A VARIANT OF VON WILLEBRAND'S DISEASE. D. N. Fass and E. J. W. Bowie, Mayo Clinic and Foundation, Rochester, Minnesota, U.S.A.

Sodium dodecyl sulfate electrophoresis on 2% agarose allows the separation of porcine Willebrand factor into multiple macromolecular complexes from 1.5 million to 21 million molecular weight. In non-denaturing buffers these forms are resistant to alteration by 10^{-4}M mercaptoethanol, reduced glutathione, or cysteine. At sulfhydryl concentrations of 10^{-4}M both dithiothreitol (DTT) and dithioerythritol (DTE) seem to catalyze disulfide interchange evidence by the appearance of very high molecular weight polymers. Both DTT and DTE in the absence of detergent or other denaturants lowered the average complex size at sulfhydryl concentration of 10^{-3}M . Concomitant with the reduction in average polymer size there was a loss of ristocetin-Willebrand factor activity. A severe reduction of average molecular weight was found to be a characteristic of the Willebrand factor found in a genetically determined variant of the porcine model of von Willebrand's disease. These observations provide a molecular basis for a qualitative version of the porcine disease in contrast to all previously described affected pigs which suffer a quantitative deficiency of Willebrand factor activity and antigen.