INTRAPEITONEAL ACTIVITY OF HEPARIN DURING PERITONEAL DIALYSIS. E.O. Gossens, R.I. Farnan, and J. Hooker. Department of Hematology, School of Pathology and Pharmacology, University of the Witwatersrand, Johannesburg, S.A. In order to study intraperitoneal heparin was studied in 11 patients undergoing maintenance peritoneal dialysis. Heparin was administered by adding dialysate to central plasma and the volume of heparin was determined by the resulting increase in the activated partial thromboplastin time (A-PTT). It was observed that the A-PTT was prolonged in proportion to the amount of heparin in the peritoneal fluid. The decay of this activity was relatively slow, with the mean T 1/2 in the peritoneal cavity being 10.78 ± 0.98. Systemic blood coagulation was unaffected by single 10,000 U intraperitoneal doses of heparin in that plasma A-PTT’s were not lengthened over the ensuing 6 hours. Anti- thrombin III assessed by immunological and functional procedures was present in low concentrations in residual peritoneal fluid aspirated prior to commencing dialysis. Generally this was less than 1/3 of normal plasma values, and with the repeated dilution and outflow sequences of dialysis, the cofactor concentrations fell to negligible levels, usually below 1% by the end of the second cycle. These results indicate therefore that despite the persistence and slow decay of heparin within the peritoneal cavity, the prophylactic efficacy of heparin is unlikely to be achieved except in cases where adequate cofactor might be introduced as a result of massive intraperitoneal hemorrhage.

FUNCTIONAL PROPERTIES AND IN VIVO SURVIVAL OF NORMAL AND ASIALO HUMAN FACTOR VIII/VON WILLEBRAND PROTEIN. J.M. Sadek, S.V. Pizza and P.A. McLean, Duke University Medical Center, Durham NC, U.S.A. Recent evidence suggests that the molecular defect in von Willebrand’s disease resides in the carbohydrate moiety of Factor VIII/von Willebrand factor (FVIII/vWF). In light of this, we have examined and compared certain properties of normal and asialo FVIII/vWF. Purified human FVIII/vWF was desialylated using a protease-free neuraminidase. At various incubation times, asialo acid release, ristocetin-induced platelet aggregating activity (RPA) and procoagulant activity (PCA) were assayed. Asialo FVIII/vWF was assayed with increasing amounts of asialo acid released. The desialylated samples were then completely desialylated (95%), only 35 ± 10% of the initial RPA was retained. In contrast, PCA remained constant with up to 80-85% asialo acid removed. Normal and asialo FVIII/vWF displayed similar immunological reactivity to normal and rabbit anti-human antibodies. However, insulin electrophoretic results clearly indicated a reduced ability to be bound to FVIII/vWF relative to normal. Normal and asialo FVIII/vWF were then radiolabeled with 125I, infused in rabbits and the circulation time measured. Asialo FVIII/vWF was cleared from circulation at a rate 50-fold greater than that observed for normal FVIII/vWF. This clearance was accompanied by quantitative appearance of radioactivity in the liver. In addition, simultaneous infusion of human asialo IgG glycoprotein, a protein known to bind to hepatic asialoglycoprotein receptors, competitively inhibited asialo FVIII/vWF clearance. These results indicate that desialylation of FVIII/vWF does not alter PCA, decreases RPA and, as observed with other plasma glycoproteins, increased hepatic clearance. Understanding these properties of asialo FVIII/vWF should be important initial step towards defining a possible carbohydrate defect as a cause for von Willebrand’s disease.

A STUDY OF ANTIITHROMBIN III LEVELS IN HEALTHY MALE AND FEMALE SUBJECTS TESTED MONTHLY FOR ELEVEN MONTHS BY FOUR METHODS. M.S. Sirridge and R. Shannon, U.M.R.C. School of Medicine, Kansas City, Missouri, U.S.A. Because of the increased interest in the role of Antithrombin III as a physiological coagulation inhibitor and because of some previous problems we encountered in sequential measurement of this protein, the present study was designed to answer three questions: 1) Which of four methods (2 functional activity methods and 2 immunologic methods) is the most practical, accurate and reproducible? 2) Do normal subjects have relatively constant levels when tested sequentially by these methods? 3) What is the range of Antithrombin III levels in young healthy male and female subjects? A serum pool was tested by each of the 4 serum methods at least 20 different times throughout the study. The von Kaulla functional activity method gave the lowest standard deviation and coefficient of variation. In the group of 29 subjects this method proved to be the most practical and also gave very low coefficients of variation for individual subjects when they were tested from 11 to 16 times (range 0.023-0.054). The other methods did not give such low coefficients of variation for individual subjects. The range of levels was 77 to 110% on 364 samples tested by the von Kaulla method with a mean of 92.8% and a standard deviation of 6.4%. The standard deviations for the pool and for individual subjects were greater but quite satisfactory for all methods.