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FACTOR IX RELATED ANTIGEN IN HEMOPHILLA B. H.C. Yang and P.H. Levine. The Memorial Hospital and the University of Massachusetts Medical School, Worcester, Massachusetts, U.S.A.

The presence of Factor IX related antigen (FIXRA) was studied in 15 hemophilia B patients, 20 normals, 2 obligate carriers of hemophilia B, 10 hemophilia A patients and 2 patients on coumadin therapy. A monospecific rabbit antiserum for factor IX was used in a counterimmunoelectrophoresis (CIEP) system. Only 3 out of the 15 hemophilia B patients, representing 3 of 10 pedigrees, had a Factor IX related antigen as demonstrated by a precipitin line in CIEP, the other 24 subjects all had demonstrable FIXRA. The presence of FIXRA in hemophilia B did not correlate with the factor IX procoagulant level. The hemophilia B group with FIXRA could partially neutralize a human inhibitor to Factor IX. Hemophilia B is a heterogeneous disease in which a minority have a factor IX related antigen.

The procoagulant (PCGF) and the platelet aggregating (PAF) activities of bovine F. VIII were studied in order to establish their relation to the antigens A1 and A2, antigens similar to those synthesized by von Willebrand and hemophilia A patients respectively. Studies of antibody to different agents (temperature, EDTA, thrombin, etc.) allowed us to establish that FVIII (PCGF) and FVIII (PAF) are not mutually dependent. An homogenous antibody of low specificity against human F. VIII binds specifically with A1 (A2) antigenic moiety of bovine F.VIII. The complex so formed is purified by gel filtration and has FVIII (PAF) activity but not FVIII (PCGF) activity indicating that FVIII (A1) and FVIII (PCGF) activities associate. Another complex, formed by bovine factor VIII and a rabbit antibody against the FVIII (A1) moiety, was prepared. This complex has FVIII (PCGF) activity but not FVIII (PAF) activity, indicating that FVIII (A2) and FVIII (PAF) associate. The complex and its procoagulant activity sediment in the same way and may be recovered by suspension of the precipitate. The following scheme showing the relationship between the antigenic moieties and the activities of bovine factor VIII is proposed: FVIII (A1+PCGF) (A2+PAF).

THE large SCALE PREPARATION OF CLOTTBABLE FIBRINOGEN-FREE, HIGH PURITY, HIGH POTENCY FACTOR VIII CONCENTRATE. L.P. Pohlke, V.L. Wilson, and R.L. High. Bay Area Hematology, Santa Monica, Ca, USA.
Crude Factor VIII was initially extracted from plasma as cryoprecipitate. This crude concentrate was treated with high molecular weight polymer F-45 to remove the bulk of fibrinogen. The yield of Factor VIII at this point was 6% theoretical and 4% actual (the starting plasma contained 6% Factor VIII). Total protein in the cryoprecipitate was 2.8 gms and 0.93 gms after removal of fibrinogen bulk. The next step was addition of a thrombin-like enzyme, at a concentration of 0.5 units, with the resultant removal of remaining fibrinogen. After clotting out residual fibrinogen, resultant fibrin strands were removed by high speed centrifugation. The final product gave a theoretical yield of 6% and an actual yield of 2%; thus, 6% of the initial Factor VIII was recovered in the final product. Prior to lyophilization, the final product was stabilized with albumin. After lyophilization, the final product was subjected to a high speed centrifugation. Protein electrophoresis analysis revealed 70% in the alpha-1 globulin region, 25% in the alpha-2 globulin region, and 2% in the beta-2 globulin region. Total protein was normal negative and icosemicurin test were 1+4. Plasminogen and plasminogen were undetectable and fibrinogen (Fg) degradation products were 80 ug/mL. The large scale preparation of this fibrinogen-free Factor VIII concentrate may prove highly useful in sparing the hemophillate patient fibrinogen deposits in the kidneys and other organs, a complication of existing concentrates. In addition, much higher potency in much less volume may be achieved with this material. The cost for large scale preparation of this material should be the same as for existing concentrates.