VON WILLEBRAND DISEASE COMBINED WITH FACTOR V DEFICIENCY: VARIANT BARI. N. Ciavarella, F.A. Soaraggi, M. Petronelli, M. Coviello, A. Oreste, V. De Mitrio, M. Schiavoni, L. Bonomo. Hemophilia Centre, 2nd Institute of Clinical Medicine, University of Bari, ITALY.

We report a new variant of the von Willebrand disease combined with a deficiency of Factor V. A 35 yr. old woman presented a history of severe hemorrhagic diathesis with prolonged epistaxis, gum bleeding and menorrhagias, one of which caused hysterectomy. PT 24"/15", aPTT 70"/33", F.V 8%; Template Ivy Bleeding Time (BT) 15'-10'; VIIIC 7%, VIIIRAG 76%, VIIINF 48%; Platelet Retention (PR) 95%; Ristocetin-Induced Platelet Aggregation (RIPA) >2.0 mg/ml; Electrophoretic mobility was normal. Other plasmatic and platelet assays were normal. The propositus has two female children. One presented: BT 5'30"-6'30"; F.V 137%; VIIIC 54%, VIIIRAG 66%, VIIINF 56%. The other: BT 5'-8'; F.V 107%; VIIIC 29%, VIIIRAG 38%, VIIINF 37%. One of her two sisters has F.V 53%. The other was normal. One of her two brothers has VIIIC 84%, VIIIRAG 65%, VIIINF 52%. The other was normal. As her father died of a severe hemorrhagic episode, we studied her three aunts. One has VIIIC 44%. Another has BT 7'30" and F.V borderline. The third has F.V borderline. In all the subjects presented PR was normal, while in all but two RIPA was reduced. This new variant may represent a genetical link between the von Willebrand disease and a combined deficiency of F.VIII and F.V.

IMMUNOLOGIC STUDIES IN PATIENTS WITH VON WILLEBRAND'S DISEASE. D.Böttcher, K. Hasler and A.H.Sutor. Department of Internal Medicine and Department of Pediatrics, University of Freiburg, Germany.

An abnormal electrophoretic mobility of factor VIII related antigen (VIIIRag) is a well known finding in patients with variants of von Willebrand's disease (vWd), but it has also been described in patients with typical vWd. We have studied 12 patients with vWd and 5 members of a family with a variant of the disease, characterized by normal factor VIII activity and normal VIIIRag but low or absent ristocetin cofactor activity. The electrophoretic mobility of VIIIRag as measured by two dimensional immunoelectrophoresis at pH 8.6 was grossly abnormal in all patients with a variant of vWd corresponding to the bleeding tendency. This correlation between clinical symptoms and abnormal electrophoretic mobility of VIIIRag was not found in those patients with vWd, in whom the mobility of VIIIRag was also grossly abnormal. Chromatography of cryoprecipitate from patients with the described variant of vWd revealed a delayed elution of VIIIRag with a characteristic pattern, whereas the patients with typical vWd but abnormal electrophoretic mobility of VIIIRag had normal elution patterns. It is suggested that an abnormal electrophoretic mobility of VIIIRag is a common finding also in patients with typical vWd.

AUTOSOMAL FACTOR VIII DEFICIENCY IN RABBITS: SIZE VARIATIONS OF RABBIT FACTOR VIII. R. E. Benson and W. J. Dodds. Division of Laboratories and Research, New York State Department of Health, Albany, New York, U.S.A.

Many rabbits from our Flemish Giant-Chinchilla colony have moderate to severely reduced levels of factor VIII coagulant activity (FVIII-C). Some have shown prolonged bleeding after venipunctures and gastrointestinal and intramuscular hemorrhages. Genetic studies indicate autosomal inheritance. Gel filtration of plasma from these rabbits by the method of Rick et al. (Blood, 49, 209, 1977) at 25°C, pH 6.8 revealed two distinct peaks of FVIII-C; the majority of activity eluting as high molecular weight (HMW) material at the void volume (V⁰) followed by a much smaller low molecular weight (LMW) peak eluting close to that of fibrinogen. By contrast, filtration of plasma from New Zealand (NZ) rabbits produced threefold greater protein at the V⁰ and equal amounts of HMW and LMW FVIII-C. Increasing the pH to 7.4 had little effect on FVIII-C recovery, although filtration at 4°C virtually abolished the HMW FVIII-C peak of NZ plasma. Rat antiserum (AS) to rabbit HMW FVIII-C, absorbed with precipitate low in FVIII-C, detected precipitating antigen in both HMW and LMW fractions. After absorption with rabbit fibrinogen, the AS no longer detected HMW V⁰ material. The antigenic relationship between HMW and LMW FVIII-C and fibrinogen thus remains unclear. The differences in amount of HMW protein and the ratio of HMW to LMW FVIII-C suggest that in comparison to NZ rabbits our animals have a variant factor VIII molecule as well as low FVIII-C.