ANTIBODIES AS A CAUSE FOR PLATELET FUNCTIONAL DEFECTS. J.P. Caen, S. Levy-Toledano, C. Tobelem, H. Michel, A.T. Nurden, C. Legrand and L. Degos, Hôpital Lariboisière, 75010, Paris, (France).

The Luc. antibody occurring in a polytransfused thrombasthenic patient is an IgG which agglutinates all human platelets except thrombasthenic ones. At sub-agglutinating doses, ADP, Adrenaline, Collagen, Thrombin and arachidonic acid-induced aggregations but not ristocetin and bovine factor VIII mediated platelet aggregations are inhibited. It does not modify ADP binding to normal human platelet membranes. The antibody strongly reduced thrombus formation on rabbit aorta subendothelium. Its activity is consumed after incubation with normal human platelet membranes but not with thrombasthenic ones. It inhibits thromboxane formation with all inducers but not with arachidonic acid and PGG₂. This antibody reacts with a component present on human platelet membranes 120.000 MW.

The Por. antibody occurring in a polytransfused Bernard-Soulier patient is an IgG which agglutinates all human platelets except those of Bernard-Soulier and thrombasthenia. The activity is consumed after incubation with normal and thrombasthenic platelet membranes but not with platelet membranes of Bernard-Soulier patients. At sub-agglutinating doses only ristocetin, bovine factor VIII aggregation and adhesion of human platelets to rabbit aorta subendothelium are inhibited. Purified neuraminidase, chymotrypsin or trypsin destroy the reaction of normal platelets with this antibody. This IgG reacts with a component of human platelet membrane 155.000 MW.

FACTOR VIII (FVIII) ANTIBODIES IN HEMOPHILIA. S. S. Shapiro, Cardeza Foundation, Jefferson Medical College, Philadelphia, Pennsylvania, U.S.A.

Antibodies to FVIII arise in some 10-15% of multitransfused patients with severe Hemophilia A. Specificity of the antibody for FVIII coagulant activity can be demonstrated by coagulation assays, normal bleeding times and FVIII antigen and Ristocetin cofactor levels, as well as by inability of the antibody to interfere with Ristocetin aggregation at levels completely neutralizing FVIII coagulant activity. A genetic factor in immune responsiveness has been suggested in the past, but never proven. Recent studies lend credence to this possibility. Two groups of antibody patients can be discerned. Some patients seem capable of synthesizing only low levels of antibody and such patients can be treated with FVIII. Others are strong responders and cannot be treated successfully with FVIII at the height of their immune response, but may benefit from FIX concentrates. In hemophiliacs, the majority of antibodies tested have been of the IgG class and predominantly or exclusively of a single light-chain type. Heavy-chain typing has shown an unusual representation of the IgG₄ subclass. These observations suggest restricted heterogeneity of the immune response to FVIII. As shown by serial isoelectric focusing studies, the heterogeneity of antibody populations tends to vary markedly with time after antigenic stimulation, generally increasing with time after stimulation. This may explain some of the conflicting results in the literature on this subject. Immunosuppression has been of only limited usefulness in eliminating FVIII antibodies, and interpretation of "successful" cases is difficult because of the variable course of the antibodies.

FACTOR VIII ANTIBODIES IN VON WILLEBRAND'S DISEASE. P.M. Mannucci and N. Ciavarella, Hemophilia & Thrombosis Ctr, Univ. of Milano; and Institute of Clinical Medicine, Univ. of Bari, Italy

Precipitating antibodies (Ab) are extremely rare in congenital coagulation disorders and were not described in FVIII deficiency states. Plasma and serum of 4 multitransfused patients (pts) with severe recessive VWD were shown to react in precipitation systems with the FVIII-related antigen (VIII:R:AG) recognized by heterologous Ab. Such property was related to the IgG fraction. Plasma or IgG fractions cross reacted with plasma from a number of mammals, producing precipitation lines with partial identity with human plasma and semipurified FVIII. They also inactivate in a time-independent manner FVIII-related ristocetin cofactor (VIII:R:RCO) and inhibit platelet aggregation induced in PRP by bovine and porcine FVIII. FVIII coagulant activity (VIII:C) was inactivated by the Ab and there is evidence that this phenomenon is related to steric hindrance. Transfusion studies carried out in pts during treatment for bleeding episodes showed an impaired in vivo recovery of infused VIII:R:AG and VIII:R:RCO, and an anamnestic rise of Ab; the delayed rise of VIII:C which is usually observed in VWD patients was not shown. The findings of precipitating Ab suggest that pts with severe VWD with complete failure to synthesize FVIII have no immunological tolerance to the protein. Challenge with a totally foreign protein induced by transfusion is followed by the development of precipitating Ab. This view is supported by the observation that the properties of such homologous Ab are similar to those of the heterologous Ab raised in animals against human FVIII.