STUDY ON THE EFFECT OF DDAVP ON FACTOR VIII-RELATED PROPERTIES IN HEMOPHILIA AND VWD N. Ciavarella, S. Solinas, D. Pilolli, P. Ranieri, D. Corraro, S. Antoniocechi and G. Mariani. Institute of Clinical Medicine, University of Bari and Institute of Hematology, University of Rome, Italy.

Twenty-one patients affected by mild and moderate Hemophilia A as well as 9 patients with the classic form of vonWillebrand’s disease (vWD) were given a total of 58 infusions of DDAVP. Concerning Hemophilia a three fold mean raise (X = 3.0, sem 0.19; range of ratios post/preinfusion 1.35 – 5.55) of factor VIII:C levels was observed after the infusion of 0.3 ug/Kg b.w. A mean raise of 3.44 (sem 0.48, range 2.20 - 6.7) after the infusion of 0.4 ug/Kg was found. The difference between the two regimens is not statistically significant (p > 0.5). As to the vWD 18 infusions were given. In 6 patients the changes of factor VIII:C, VIIIIR:Ag and VIII:vWF were roughly consensual ( ratios post/preinfusion ranging from 2.2 to 4.0 for VIII:C; from 1.8 to 3.5 for VIIIIR:Ag and from 3.1 to 6.2 for VIII:vWF). In the remaining 3 patients a very strong response of VIII:C (ratios post/preinfusion 12.0, 15.1 and 6.5) was observed. Also the other properties related to factor VIII underwent to relevant increase. In one of these patients a modified electrophoretic mobility of factor VIII was found; the other two (father and daughter) had a normal factor VIII mobility after stimulation with DDAVP.

Recent experiments have shown, that PPSB (factor IX-concentrate) derived from 8-propiolactone/ultraviolet (8-PL/UV)-treated (cold sterilized)plasma is not infectious in chimpanzees in respect to hepatitis B and Non A-Non B. To answer the question whether the B-PL/UV treatment influences the tolerance and efficacy of the cold sterilized PPSB-concentrate, long term application of PPSB-Biostest was performed in chimpanzees.

After 12 applications of 25 units factor IX/kg in weekly intervals no signs of intolerance were observed by means of skin testing and observation of blood pressure during i.v. application. Determination of coagulation factor activity during the application period shows the same factor IX-recovery at the beginning and at the end of the study.

In vitro tests were demonstrated to be insufficient for the determination of the thrombogenicity of PPSB preparations with peptide substrates or the TGt50 and the NAPTT. Unequivocal determinations of the thrombogenicity of PPSB preparations are possible only up to now in vivo models. As an alternative to the up to now proposed dog or hemophila B dog models we have determined the thrombogenicity of cold sterilized PPSB in chimpanzees. PPSB isolated from 8-propiolactone treated and UV irradiated plasma was injected into the chimpanzees at a dose of approximately 100 units/Kg body weight. An FDA licensed PPSB preparation served as a control.

15 minutes, 1 h, 4 h, and 24 h after the PPSB application the following parameters were determined in the chimpanzee blood: factors II, VII, IX, X, VIII, fibrinogen, AT III, thrombin coagulase, Quick value, APTT and platelet count.

Neither the untreated control preparation nor the PPSB from 8-propiolactone treated and UV irradiated plasma showed signs of a thrombogenic effect in this chimpanzee model.