THE NATURAL HISTORY OF "INHIBITORS" TO FACTORS VIII AND IX IN HEMOPHILIACS. C.E.C. HARRIS. St. Mary's Hospital, Montreal, Quebec, Canada.

Since 1954 an increasing number of adult hemophiliacs have been followed and "inhibitors" have been found in a minority of patients. A retrospective study was made of 40 factor-VIII and of 9 factor-IX cases who have attended with sufficient regularity for adequate documentation. The presence of this complication was, until recently, suspected because of failure clinically to respond to replacement therapy and confirmed by the original Biggs' technique in the laboratory. In the past 4 years, this has been replaced by her method using serial dilutions at room temperature and at 37°C., incubated for 1 hour. In addition, studies have been made of factor recovery and survival following infusions.

In no case were immuno-suppressive agents used. There were no deaths. Life-threatening crises were met by conservative measures, including hypothermia, and by the use of porcine factor-VIII. Instances when in vivo survival of infused concentrate was shortened were usually managed successfully by more frequent administration of equal or lesser dosage quantities; it was exceptional in such cases to witness enhancement of "inhibitor" potency as a consequence.

In no less than 6 of the 9 patients would it seem that the "inhibitor" has disappeared and full clinical response is now being obtained with standard dosage schedules. The nature of "inhibitors" would not seem to be well understood.

DIAGNOSTIC AND THERAPEUTIC PROBLEMS IN A PATIENT WITH FACTOR VIII INHIBITOR. G. Sas, I. Pető, M. Csörgő, Á. Köves and L. Kun. Postgraduate Medical School, Budapest, Hungary.

An old man was admitted to our hospital with the suspicion of acute abdomen. Sonography was used to visualize the psoas haematoma which accounted for the severe abdominal pain and made it possible to avoid an explorative laparatomy. We found a circulating anticoagulant against factor VIII /4 Bethesda units per ml plasma/. The antibody belonged to the IgG class. The patient was treated repeatedly by transfusions of fresh blood, large doses of cryoprecipitate and prednisolone. The improvement of the haemorrhagic symptoms was slow and a long term immuno - suppressive therapy was introduced. After a symptom-free year a massive bleeding occured in the thigh and in the psoas muscle. FEIBA therapy was introduced /plus prednisolone & azathioprine/. At first 15 units of FEIBA/kg were administered but the long clotting time did not change. In the following days the quantity of the FEIBA was gradually increased up to 60 units/kg but the coagulation time did not shorten significantly. The PTT became longer, the antithrombin III level decreased. At the same time a definite clinical improvement was observed.

In our case sonography has proved a very useful tool in the diagnosis of psoas haematoma. However, the value of therapy applied could not be judged just as unequivocally.

HUMAN FACTOR VIII CONCENTRATES IN HEMOPHILIAC DOGS. Jessica H. Lewis, Ute Hasiba and Joel A. Spero University of Pittsburgh School of Medicine and Central Blood Bank of Pittsburgh, PA, U.S.A.

Human factor VIII corrects the clotting defect in dog hemophilic plasma in vitro. The present studies were undertaken to see if this happened in vivo and to look for and document the development of an inhibitor. Four hemophiliac dogs were infused with factor VIII concentrates, the first two on five occasions, the others three times. Factor VIII:C, VIIIR:Ag (defined with antibody to human VIII) and VIIIR:vW were followed at pre, 10 minutes, 2 and 24 hours post infusion. The pre-infusion VIII:C (assayed with human substrate) averaged 0.23 U/ml compared to 6.93 U/ml for normal dogs; VIIIR:Ag was absent in both. VIIIR:vW was low but variable. Following the first injection, all four dogs responded in VIII:C about as calculated. The amounts of VIIIR:Ag and vW were much greater than VIII:C in the concentrates and in the post-first infusion samples from the dogs. On subsequent infusions rises in VIIIR:Ag were not detected and increases in VIII:C and VIIIR:vW were minimal. Precipitating anti-human VIII was found on the third infusion and thereafter. After the first infusion reactions were marked. Vomiting and diarrhea occurred in all, and one dog died in anaphylactic shock about one hour after the third infusion. Lack of response in VIIIR:Ag occurred before anti-VIII could be demonstrated in vitro. This rapid development of an inhibitor suggests that prolonged cross-species VIII therapy will not be successful. The ability of the precipitating anti-VIII elicited in the dogs to destroy VIII:C, VIIIR:Ag and VIIIR:vW is analagous to the in vitro effects of heterologous anti-VIIIs (rabbit and goat).