RECENT REDUCTION IN THROMBOGENIC ENZYME CONTENT OF PROTHROMBIN COMPLEX CONCENTRATES. H.S. Kingdon, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA.

In previous studies of prothrombin complex concentrates, it was demonstrated that there was a high content of potentially thrombogenic enzymes in the products from certain manufacturers, and that the enzyme content correlated closely with in vivo assays for thrombogenicity and with the observed incidence of thrombotic episodes following infusion (Thromb. Diath. Haemorrh. 33, 617, 1975). Subsequently, it was shown that the thrombogenic enzymes could be generated by prolonged contact with DEAE-cellulose or calcium ions during preparation or later handling (Blood, 49, 159, 1977). In view of these observations, efforts have been made to reduce the contact time of plasma fractions with either DEAE-cellulose or calcium ion during purification of these fractions for therapeutic use. In vitro assays for thrombogenic enzymes using the nonactivated partial thromboplastin time (NAPTT) were recently repeated on some of the currently available therapeutic materials. Assays were standardized and compared with previous results by using a provisional standard provided by Dr. David Aronson, Bureau of Biologics, USFDA. In the 1975 study, one manufacturer was identified as making a concentrate virtually free of thrombogenic enzyme. The concentrate currently being made by this manufacturer still does not significantly shorten the NAPTT. In the 1975 study, 2 manufacturers were shown to be making concentrates with high titers of thrombogenic enzyme. The current products of these two manufacturers contain detectable but significantly lower levels of thrombogenic enzymes. Thus it appears that for these two manufacturers, minor changes in production procedures have led to a product containing less potentially thrombogenic material.

RESULTS OF LIVER BIOPSIES, RATE OF ICTERIC HEPATITIS, AND FREQUENCY OF ANTI-HBs AND HBs-ANTIGEN IN PATIENTS OF THE HEIDELBERG HEMOPHILIA CENTER. Kl. Schimpf, K. Zimmermann, J. Rüdel, G. Thamer, and P. Zeltsch. Rehabilitation Hospital and Hemophilia Center Heidelberg, Rehabilitation Foundation, Heidelberg, West-Germany.

With the opening of the hemophilia center in Oct. 1972 an intensive replacement therapy with clotting factor concentrates was started the first time for many patients. Concerning the induced liver damages, three years later the following resume could be drawn. From 113 examined patients 17 (19%) acquired an icteric hepatitis (i.h.). Excluding 2 cases the interval between beginning of intensive clotting factor substitution and outbreak of i.h. was found to be 46 days in the average (13-117). 10 827 u (1 800-27 990) of clotting factor concentrates had been injected until to this moment. (The average consumption by the 113 examined patients from Oct. 1972 to Oct. 1975 was 57 186 u per patient and year.) In Oct. 1975 the distribution of Anti-HBs and HBs-Ag positive patients (radio immune assay) was: Frequently transfused cases (more than 15 000 u per year): Anti-HBs 86%, HBs-Ag 8% (total 94%); less frequently transfused cases: Anti-HBs 71,5%, HBs-Ag 9,5% (total 81%). In 18 patients (not identical to those with i.h.) liver biopsies could be performed with the following results: chronic hepatitis: 9, subsided hepatitis without activity: 4, alcoholic liver damages: 3, acute dystrophia: 1, cholangiolitis: 1.

LIVER DISEASE IN HEMOPHILIA. Joel A. Spero, Jessica H. Lewis, and Ute Hasiba. University of Pittsburgh School of Medicine and Central Blood Bank of Pittsburgh, Pittsburgh PA, U.S.A.

Abnormal liver function tests (LFTs) in patients with Hemophilia A and B who have been treated with commercial factor concentrates have been observed since 1973. One hundred and seventeen of these had had LFTs performed at least twice and at least six months apart. Of these, 13 were chronically Hb_sAg positive and the rest anti-Hb_s positive. Forty percent of the anti-Hb_s group had persistently abnormal LFTs for greater than 6 months, the majority for more than two years. Owing to the uncertain relationship of this "transaminitis" with true liver pathology, especially in the anti-body positive patients, seven closed liver biopsies were performed without incident under high coverage with factor VIII replacement. All patients were asymptomatic at the time of biopsy. One had a prior episode of illness probably related to subclinical hepatitis. An eighth patient underwent an open liver biopsy as part of a staging laparotomy for Hodgkins Disease. Six biopsies showed varying degrees of chronic persistent hepatitis (CPH). One was not evaluable owing to changes related to a retrospectively obtained history of ETOH intake. Finally, the individual with previous clinical liver disease had post-necrotic cirrhosis. Fluorescent studies with anti-Hb_s and anti-Hb_c as well as electron microscopy were done on the seven closed biopsy specimens. The biopsy results suggest that the "transaminitis" found in transfused hemophiliacs represents histologic liver disease. In the majority of patients studied, CPH, a relatively benign entity, was present; and this does not justify withdrawal of concentrate therapy at this time.