U.K. HAEMOPHILIA HEPATITIS WORKING PARTY

ANNUAL REPORT FOR THE YEAR 1982-3. THE COMMITTEE HAS MET THREE TIMES DURING THE YEAR. SUBJECTS CONSIDERED WERE:

a) Prospective studies of hepatitis in mildly affected haemophiliacs.

b) Evaluation of the infectivity of heat treated factor VIII or IX using a protocol based on the prospective studies described in (a)

c) Hepatitis Surveillance. Details of the years 1980 and 1981 and preliminary figures for 1982 are available.

In addition, work has been started on putting all the past patient data from the 1974-6 survey of Hemofil and Kryobulin associated hepatitis on the Regional Computer of the Oxford Regional Health Authority.

d) Hepatitis B vaccine.

e) The Acquired Immune Deficiency Syndrome.

A surveillance system for the reporting of cases was set up. Two cases have so far been reported in the U.K. which conform to the CDC criteria. This subject will be considered separately at the meeting.

a) Prospective studies of hepatitis in infrequently treated haemophiliacs

This study was started at Oxford in 1981 and the first 30 patients followed after 1 transfusion of factor VIII concentrate for at least 6 months are described in a paper which will shortly appear in the British Medical Journal. Of the 30 studies, 4 patients were excluded because they had evidence of chronic liver disease, 2 patients received cryoprecipitate and did not develop hepatitis. Of the remaining 24, 17 patients contracted non-A, non-B hepatitis, 9 after their first transfusion of factor VIII concentrate. Seven of these were after transfusion of one batch of NHS factor VIII with a pool size of between 1,200 and 2,600 plasma donations (mean 1,600). This interesting result confirms that the risk of contracting non-A, non-B hepatitis is 100% on first exposure, whether NHS or commercial factor VIII. All 5 patients treated with U.S. commercial factor VIII contracted hepatitis whether or not they had previously received factor VIII. No cases of hepatitis B were observed, although 12 patients had evidence of past hepatitis B. The incubation period of the non-A, non-B hepatitis varied from 1 - 12 weeks.

Of the patients who had hepatitis, 12 have been followed for at least 1 year and 4 of these have evidence of continuing liver disease.

b) Evaluation of the infectivity of heat treated factor VIII using a protocol based on the prospective study, since no tests for non-A, non-B hepatitis are yet available.

The recent development of new preparations of factor VIII where attempts have been made to reduce the contamination of preparations by hepatitis viruses by heat treatment has made it necessary to devise protocols for the evaluation of the residual infectivity of these preparations, since no tests of infectivity are available for non-A, non-B hepatitis viruses. A protocol drawn up by the

Working Party based on the experience of the prospective study was circulated to interested Haemophilia Centre Directors. It was hoped that a sufficient number of patients with no previous treatment with concentrate would be identified, so that formal trials could be conducted as part of collaborative evaluation of each product on the basis of exemption from a clinical trial certificate.

An internationally based trial was started with the Travenol product, and an Armour product will be available for evaluation in the next 3 months. However, the problem of AIDS has overshadowed these developments, as the ethical problem of exposing mild haemophiliacs to commercial material must be considered by each Director.

This is summarised in the enclosed discussion paper (Appendix C(i)).

c) Hepatitis Surveillance. See attached Appendix C(ii).

d) Hepatitis B vaccine

This has been shown to be immunogenic in haemophiliacs, and results of the Oxford trial are being analysed. However, problems of possible contamination of the course plasma by a putative AIDS related agent has complicated this situation. WHO recently reviewed the situation and has recommended that any vaccine derived from human plasma should include at least 2 inactivation steps, one of which should be exposure to formalin. The only vaccine which fulfills these criteria is the Merck, Sharp and Dohme vaccine, the only vaccine licensed in the U.K.

A formal follow-up of subjects who took part in the 1978 New York trial of the Merck vaccine is in progress. While there is no evidence of risk to persons who received the vaccine in the New York trial, it would be wise to exercise caution in the use of vaccine until the formal follow-up period is completed. The theoretical risk of AIDS must be balanced against the risk of contracting hepatitis B.

Recommendations regarding the use of hepatitis vaccine in Haemophilia Centres is given in Appendix C(iii).

J. Craske
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