12 APR 1977

PUBLIC HEALTH LABORATORY SERVICE

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7th April, 1977.

Dear Dr. d'A. Maycock, 16/4.

I enclose a revised version of the protocol for the study of jaundice after transfusion of Elstree Factor VIII. If you have any comments perhaps you would let me know in due course.

We hope to start this study in August or September, and I shall write to you again when the details have been finalised.

Kindest regards,

Yours sincerely,

GRO-C

J. Craske.
Consultant Virologist

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SURVEILLANCE OF N.H.S. FACTOR VIII

PROTOCOL A

TRANSFUSION ASSOCIATED JAUNDICE IN HAEMOPHILIACS

Study of incidence of jaundice after transfusion with Elstree Factor VIII.

OBJECT

Following the study of the incidence of hepatitis after transfusions of Hemofil[1,2], it has been decided to undertake a study of different preparations of Factor VIII in an effort to find out how the incidence and type of hepatitis observed in recipients compares with that observed after "NHS intermediate concentrate" i.e. prepared either at Protein Fractionation Centre, Edinburgh ("Edinburgh Concentrate"), Blood Products Laboratory, Elstree ("Elstree Concentrate"), or Plasma Fractionation Laboratory, Oxford ("Oxford Concentrate").

This protocol is concerned with the surveillance of batches of Elstree Factor VIII. So many batches of this concentrate are now issued that it was decided to study a number of specified batches in designated centres rather than try to study a large number on a nationwide basis. In addition it is hoped to include batches possibly associated with cases of hepatitis reported to the Oxford Haemophilia Centre.

METHOD

1) Directors of Haemophilia Centres who agree to take part in the study will be supplied with batches from the Blood Products Laboratory, Lister Institute, Elstree (Director, Dr. W.d'A. Maycock) via the appropriate RTC or direct. Cases of hepatitis possibly associated with the use of these products will be reported to the Oxford Haemophilia Centre using Form C3, the medical sickness form. Cases will be only considered as hepatitis which are reported as having had three or more symptoms or signs positive other than abnormal LFT's as shown on the medical sickness Form C3. A serum aspartic or alanine aminotransferase level of more than twice the normal value of the local hospital biochemistry laboratory will be considered as evidence of abnormal liver function.

Cases of hepatitis will be classified as "B" or "Non-B". A patient will be considered as suffering from hepatitis B when a serum specimen is positive for Hepatitis B surface antigen byreverse passive haemagglutination (RPHA) or radioimmunoassay within one month of the onset of acute hepatitis. Serum specimens taken before this should be negative by one of these tests.

Alternatively seroconversion to a positive serum antibody test for Hepatitis B surface antibody (Anti HB_s) or Hepatitis B core antibody (Anti HB_c) or both will indicate recent Hepatitis B. Non-B hepatitis will be defined as cases of acute hepatitis where tests for recent Hepatitis B infection as defined above are negative.

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Asymptomatic cases of Hepatitis B will be defined as patients who become positive for HB_sAg or seroconvert by both of the antibody tests, without overt symptoms or signs of acute hepatitis.

Patients who are known carriers of HB_sAg will be excluded from assessment. Details of the blood products received for six months prior to the onset of hepatitis will be recorded on Form C (revised). If a diagnosis of hepatitis is suspected, it is requested that Dr. Craske at the Manchester Public Health Laboratory should be consulted concerning the range of laboratory tests to be carried out and the number of blood samples to be taken. Forms, containers and packaging can be obtained on request. If necessary, instances in which the diagnosis is uncertain will be clarified by correspondence between Dr. Craske and the Director of the Haemophilia Centre or reference to the patient's notes if available. The Haemophilia Centre Director should attempt to collect acute and convalescent specimens from as many cases as possible.

2) At the end of each year each Haemophilia Centre will be asked to complete a record of transfusions giving the numbers of batches transfused to each patient and the dates administered for each designated batch of Factor VIII. These transfusions will be recorded on Form C, one or more forms being used for each batch, and returned to the Oxford Haemophilia Centre. Transfusion records for batches of Elstree Factor VIII other than those designated will be included if they are associated with cases of hepatitis.

3) At the end of a two year period the results will be analysed to obtain the following data:

1) The number of B and Non-B hepatitis cases related to each batch.

2) The attack rates for each type of hepatitis related to age, batch, severity of Factor VIII deficiency. They will be initially classified as B or Non-B hepatitis.

3) The mortality and incidence of chronic sequelae related to the above factors.

4) The incidence of Hepatitis B associated with the results of tests for HB_sAg on each batch of concentrate.

5) Whether any of the above factors are related to the incidence of hepatitis observed in the haemophiliacs.

6) Whether the age of first transfusion with Elstree Factor VIII affects the incidence of hepatitis.

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References

1) Craske J., et al (1975) ii 221.

2) Hemofil associated hepatitis in the U.K. 1974/75. A retrospective survey. J. Craske and P. Kirk.
Report to Haemophilia Centre Directors, 1977.

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