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PROTOCOL B

TRANSFUSION ASSOCIATED JAUNDICE IN HAEMOPHILIACS

SURVEILLANCE OF NHS FACTOR VIII.

Study of the incidence of jaundice after transfusion with Edinburgh Factor VIII concentrate.

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 Edinburgh Factor VIII. It is hoped to study the incidence of hepatitis after transfusion of this concentrate in designated centres. In addition it is hoped to include batches possibly associated with cases of hepatitis occurring elsewhere, which are reported to the Oxford Haemophilia Centre or the Protein Fractionation Centre, Edinburgh. Ideally all batches should be included in the survey, but owing to the large number of batches used this may not be practicable, and hence a selection may have to be made randomly for intensive study.

METHOD

1. Directors of Haemophilia Centres using Edinburgh concentrate who agree to take part in the study will be supplied with batches of concentrate by the usual method of distribution. Cases of hepatitis will be reported in the first instance to Dr. John G. Watt at the Scottish National Blood Transfusion Service, Protein Fractionation Centre, Ellen's Glen Road, Edinburgh. Cases for investigation will be referred by him to Dr. John Cash at the South East Scotland Regional Blood Transfusion Service. The results will be co-ordinated by his staff, and duplicate returns will be sent to the Oxford Haemophilia Centre for their records. The medical sickness Form C3 adapted for use with Edinburgh concentrate will be used. 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. Jaundice will be defined as that apparent on clinical examination or a serum bilirubin of more than 50umols. (SI Units). Other causes of jaundice including drug reaction should be excluded as far as possible. 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 by reverse 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. 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 for Hepatitis B.

Details of the blood products received for six months prior to the onset of hepatitis will be recorded on Form C (revised). If necessary, instances in which the diagnosis is uncertain will be clarified by correspondence with the Director of the Haemophilia Centre or reference to the patient's notes if available. An attempt will be made to collect acute and convalescent specimens for 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 will be recorded on Form 4C and returned to the Regional Transfusion Centre, Edinburgh. After co-ordination of results, copies will be sent to the Oxford Haemophilia Centre, and Dr. Watt at the Protein Fractionation Centre for his information.

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.

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.

*It may be easier to take a specimen of serum from each patient when they commence treatment with batches of Edinburgh concentrate which are to be included in this survey. A convalescent specimen can then be taken at the time that any patient develops hepatitis, and possibly specimens from patients who do not become ill whenever possible.