PROSPECTIVE STUDY OF THE INCIDENCE OF ACUTE AND CHRONIC HEPATITIS IN HAEMOPHILIACS AS A RESULT OF FIRST EXPOSURE TO FACTOR VIII CONCENTRATE OR CRYOPRECIPITATE.

INTRODUCTION

The hepatitis surveillance programme at Oxford has shown that the group of haemophiliacs with the highest incidence of acute hepatitis are those patients exposed to freeze dried concentrate for the first time.(1) Most of these are mild haemophiliacs who usually require few transfusions, usually of cryoprecipitate only. Since the risk of chronic hepatitis following an acute attack of non-A, non-B hepatitis after a transfusion of factor VIII concentrate is between 20 and 40%, it is important that an accurate estimation should be made of the incidence of transfusion hepatitis in this group. A further problem is the risk of transmission of acute hepatitis B to household contacts of haemophiliacs, especially adults who contract factor VIII or IX associated hepatitis B.(2) Some of the operative or treatment procedures covered by concentrate transfusion are minor, and it seems possible that some could be carried out with the use of alternative methods of treatment.

OBJECT

To assess the risk of acute B and in B hepatitis after transfusion of freeze dried factor VIII or IX concentrate and of chronic sequelae.

METHOD

i) Patients at the Oxford Haemophilia Centre who have received less than 2 transfusions of factor VIII concentrate in the past year will be considered for this study.

Categories of patient who will be considered are:-

1) Newly diagnosed haemophiliacs, Christmas patients and Von Willebrand's disease patients.

2) Haemophiliacs, carriers of the haemophilia gene, Christmas Disease or Von Willebrand's Disease patients who are about to undergo an elective treatment procedure which will require cover with concentrate.

ii) Procedure. Patients who attend the Oxford Haemophilia Centre during the course of the study who are into the categories given in (1) will be admitted to the project. The objects of the project will be explained to them, and their consent, or that of their parents if under 18 years of age obtained.

a) Prior to the start of factor VIII or IX treatment, they will undergo clinical examination, and blood will be taken for hepatitis B serology, full blood count and liver function tests before treatment is started. If the patient is seen as an emergency, than as many tests will be performed as is compatible with the clinical situation.

b) Patients will be followed for 12 months after their operation. Liver function tests and hepatitis B serology will be carried out at weeks 1, 2, 4, 8, 12, 16, 20, 26, 28, 32 and 52 post operatively. If a patient develops evidence of acute hepatitis, his liver function tests and hepatitis B serology will be followed fortnightly until his condition resolves, or three months after the onset and then monthly for six months. Follow-up after this will be six monthly.

DEFINITION OF HEPATITIS

A patient will be considered to be suffering from acute hepatitis if he develops overt clinical symptoms and signs as in appendix I, or shows an increase at least two and a half times the upper limit of normal serum enzyme levels having previously had normal values.

Hepatitis will be classified as acute icteric (raised serum bilirubin)
" acicteric
" symptomless

This may be of 2 varieties: hepatitis B or non-A, non-B. Hepatitis A, cytomegalovirus infection, glandular fever and toxoplasmosis will be eliminated by appropriate laboratory tests. Tests will also be carried out using a gel precipitin test, possibly associated with non-A, non-B hepatitis. (2)

FOLLOW-UP

Patients whose liver function tests remain elevated 6 months after the acute attack or become carriers of hepatitis B virus will be considered for referral to Dr. Trowell's Liver Clinic. Patients will be reviewed 3 - 6 monthly as in the Chronic Hepatitis Study.

TRANSFUSION RECORDS

Detailed transfusion records will be kept for all patients followed in the project, which will last for 18 months.

HOUSEHOLD CONTACTS

These contacts will be investigated prospectively. Serum specimens for Hepatitis A and B serology and liver function tests will be obtained from adult household contacts of haemophiliacs, subject to informed consent on entry of each patient to the project. These will be repeated at 3 and 6 months after the index patient received his first transfusion of concentrate. If the patient contracts hepatitis then serum specimens will be taken monthly for liver function tests for the next 3 months. Cases of overt hepatitis will be investigated as required. If possible, faecal specimens will be obtained from household contacts if the index patient develops hepatitis while at home.

SAMPLE SIZE

If possible, 40 - 50 patients will be studied.

RESULTS

At the end of the period the incidence of acute hepatitis, both B and non-A, non-B will be assessed in relation to:-

1) Type of product transfused

2) Transfusion history of each patient

3) Disease category and severity of coagulation defect.

4) Ratio of symptomless to overt hepatitis for B and non-A, non-B hepatitis

5) Age of the patients

6) The number of units of factor VIII transfused

7) The type of procedure for which the treatment was given.

J. Craske 2.7.1980.

Dept. of Virology,
Withington Hospital,
Manchester.

REFERENCES

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2) Second Annual Report to the D.H.S.S. of the Oxford Factor VIII and IX Associated Transfusion Hepatitis Project.

3) Hopkins, R., (1980) In Preparation.