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Appendix C

REPORT ON THE WORKING PARTY ON CHRONIC LIVER DISEASE IN HAEMOPHILIA

UK REGIONAL HAEMOPHILIA CENTRE DIRECTORS

Chairman : Professor F E Preston

Dr C R Rizza
Dr G Dusheiko
Dr D R Triger
Dr P Mortimer

The members of the Working Party met in July 1990. The following items were discussed:-

a) Results of UK Haemophilia Centre Directors questionnaire.
b) Surveillance of chronic liver disease in haemophilia.
c) HCV antibody testing in consorts.
d) Hepatocellular carcinoma.

Results of UK Haemophilia Centre Directors Questionnaire

A questionnaire was circulated to all of the UK Haemophilia Centre Directors. Responses have been received from 74 Centres.

In response to the question relating to the frequency of ALT testing in haemophiliacs, 40% of Centre Directors tested once annually. 35% tested twice annually. 12% tested three times annually. 8% tested four times annually and 4% more than four times annually.

The following clinical features of chronic liver disease were reported-

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Hepatomegaly	54
Splenomegaly	82
Spider Naevi	20
Oesophageal varices	16
Ascites	7
Jaundice	3
Portal hypertension	1
Liver failure	1

During the past three years 128 deaths were reported from 44 Centres. Autopsies were performed in 12 Centres. Of the 42 patients on whom autopsies were performed, liver disease was found to be present in 16, ie in 38%.

Surveillance of Chronic HCV Liver Disease in Haemophilia

Most haemophiliacs who have been treated with clotting factor concentrates are likely to have been infected by HCV. In view of the known tendency of this virus to produce chronic liver disease it is recommended that all haemophiliacs should be investigated for evidence of previous exposure to HCV and the development of chronic HCV hepatitis. This will include clinical examination, measurement of ALT/AST and determination of HCV antibody status. When appropriate tests become available, positive HCV-antibody tests should be confirmed by appropriate confirmatory tests. Patients who are HCV antibody negative should be re-tested at least annually but preferably at six-monthly intervals. Since it is likely that newer tests for HCV antibody and HCV RNA will become available, aliquots of serum samples tested for HCV antibody status should be stored frozen.

Patients who are HCV antibody positive and those who are HCV antibody negative but have abnormal liver enzymes, should have their liver enzymes determined at 3-4 monthly intervals. Serum ALT is possibly a more sensitive index of hepatic dysfunction than serum AST, although it is recognised that both enzymes are not available in many Centres.

Since alcohol may have a deleterious on the progression of chronic viral hepatitis, it is recommended that patients should be advised to restrict their alcohol intake to less than 40 gms daily. It is also advisable to limit the usage of paracetomol to a maximum of 4 gms daily.

The progression of chronic non-A, non-B hepatitis to cirrhosis is not easy to detect since cirrhosis is a histological diagnosis and liver biopsy is not as a rule performed in patients with haemophilia. The identification of cirrhosis therefore has to rely on clinical parameters such as firm hepatomegaly, splenomegaly. ascites or possibly oesophageal varices. A CT-scan may show a small shrunken liver, ascites, splenomegaly and collateral circulation. Endoscopy may reveal oesophageal varices. These investigations should be undertaken if clinically indicated but it should be appreciated that the observations may be imprecise. In haemophilia, splenomegaly may be present in the absence of either chronic liver disease or HIV infection, its presence therefore should be interpreted with caution.

Hepatocellular Carcinoma

In patients with cirrhosis due to chronic hepatitis C there may be progression to hepatocellular carcinoma. It may therefore be advisable to screen patients who have clinical evidence of cirrhosis or who are known to be cirrhotic for the presence of this tumour. The risk of HCC increases progressively with the duration of cirrhosis and also with increasing age of the patient. We suggest that serum alpha-fetoprotein be determined in all patients who have had cirrhosis for at least ten years and those with cirrhosis irrespective of its duration in patients who are 40 years of age or older. Any suspicious increase in serum alpha-fetoprotein should be checked and repeated within one month.

HCV Antibody Testing in Consorts

There is some suggestions of sexual transmission of HCV. In view of the high prevalence of HCV antibody in patients with haemophilia it is possible that transmission may occur between patients with haemophilia and their sexual partners. If sexual transmission does occur, it is still not known whether this will produce a similar pattern of acute and chronic liver disease as that which occurs following HCV transmission by blood products. Currently the Working Party is exploring the possibility of establishing a prospective study of possible sexual transmission of HCV.

Hepatitis B in Haemophilia

Chronic hepatitis B infection is rarely a problem in haemophiliacs in the UK although high prevalence rates occur in many other countries. Like HCV, chronic HBV infection frequently leads to progressive liver damage at a variable rate and usually without symptoms until late stages of the disease. The long-term sequelae of HBV infection are similar to those of HCV.

HBV vaccination is safe and apart from in immuno compromised patients, is highly effective. HBV vaccination is therefore strongly recommended for all individuals with familial bleeding disorders who do not have antibodies to hepatitis B. Attention is drawn particularly to those patients with only mild or moderate abnormalities of haemostasis.. They may therefore be seen only infrequently at their Haemophilia Centres.

Patients who are HBeAg positive and have elevated (greater than twice normal) serum transaminases should be considered for interferon therapy. After a 16 week course of interferon about 40% of patients sero convert from HBeAg to anti HBe and this is accompanied by a sustained reduction in liver inflammation. A small proportion also seroconvert from HbsAg to anti HBs.