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MEDICAL RESEARCH COUNCIL

PTH 80/5

BLOOD TRANSFUSION RESEARCH COMMITTEE

king Party on Post-Transfusion Hepatitis

Minutes of the first meeting held on Thursday, 14 February 1980, at 2.00pm at 20 Park Crescent, London W1N 4AL

Present: Dr H H Gunson (Chairman) (Director, Oxford RBTC)
Dr J Craske (Secretary) (PHLS, Manchester)
Dr W J Jenkins (Director, North East Thames RBTC and Chairman of the DHSS Advisory Group on Testing for the presence of HB Ags and its Antibody)
Dr D B L McClelland (Director, Edinburgh and South East Scotland RBTC)
Dr Sheila Polakoff (PHLS, Colindale)
Dr H C Thomas, Royal Free Hospital Medical School, (representing Professor Dame Sheila Sherlock)
Dr J O'H. Tobin (Director, Oxford Regional Public Health Laboratory)
Dr Diana M Walford (DHSS)
Professor A J Zuckerman (London School of Hygiene and Tropical Medicine)

In attendance: Dr A J G Dickens

1. Membership

The Chairman welcomed the members to the WP, (PTH 80/2). An apology for absence was received from Professor Dame Sheila Sherlock, who was represented by Dr H C Thomas of the Royal Free Hospital School of Medicine.

2. Purpose of the Working Party

The Chairman opened the discussion by asking the meeting to define the function of the Working Party.

It was noted that other bodies carried out functions in the field of post-transfusion hepatitis (PTH) and the Chairman explained that it was important to define clearly the object of the Working Party (WP) so as to avoid needless duplication of effort in this field.

The DHSS Advisory Group on Testing for the presence of HB Ags and its antibody advised on methods and policy with regard to the screening of blood donations and the preparation of national standards. An ad hoc group had met at the MRC at the request of DHSS in February 1979 as a result of discussions in the Advisory Group, and this had resulted in the establishment of the MRC PTH WP. Dr Walford said that a new DHSS Advisory Group would shortly be formed to advise on the public health aspects of hepatitis.

It was agreed that the function of the MRC WP was to promote research to assess

he nature and size of the problem of PTH in the UK, with particular reference o changes in transfusion practice, eg the use of products prepared from pooled lasma from large numbers of donors and the introduction of commercial products om abroad. Studies should include (1) an assessment of any further need for research into hepatitis B, eg the need for a vaccine, (2) investigations to assess the incidence of non-A, non-B hepatitis in the UK, particularly with the risk of introducing the infection by blood transfusions, and (3) the position of research to characterise the agent(s) associated with this form of hepatitis, and to derive diagnostic tests.

3. Transmission of hepatitis by blood derivatives:

3.1 There was some discussion about the methods of selection of blood donors and testing for hepatitis B surface antigen. It was agreed that this matter would be dealt with by the Advisory Group for Hepatitis B antigen testing and its antibody.

The problems of non-A, non-B hepatitis viruses

3.2 There was a wide-ranging discussion regarding the incidence of PTH in the UK. There was agreement that the reported cases of hepatitis B were very few. No cases of non-A, non-B hepatitis related to whole blood transfusions had yet been reported despite enquiry of hospitals in London where open heart surgery was carried out. There was some evidence that acute non-A, non-B hepatitis occurred in the general community. Professor Zuckerman said that 15-20% of cases of acute hepatitis in a special study in West London were probably non-A, non-B hepatitis. Dr Craske said some cases had been identified in general practice in Manchester that were unrelated to transfusion. Six cases of non-A, non-B hepatitis had been reported to the Oxford Haemophilia Centre which were related to transfusions of cryoprecipitate since 1978. All patients had been transfused with 50-100 bags of cryoprecipitate within the previous six months.

There was a problem of non-A, non-B hepatitis related to freeze dried factor VIII and IX, both of NHS and commercial types imported from Austria and the USA. The factor VIII associated hepatitis was of short incubation in type and was followed by chronic sequelae in 20-30% of cases. Dr Thomas described a recent study at the Royal Free Hospital of 11 selected patients of whom 8 received commer concentrate, 2 NHS concentrate and 1 cryoprecipitate. Eight cases were symptom-less, the abnormal transaminase levels lasting at lease six months. There was evidence obtained by liver biopsy that a proportion of these cases might suffer chronic sequelae. Dr Craske said there was as yet no evidence that factor VIII associated hepatitis was transmitted to household contacts of haemophiliacs, although the possibility must be borne in mind. It was agreed that the importatio of blood products might result in the introduction into the general community of new viruses associated with chronic hepatitis.

Dr McClelland said work was proceeding at the South East Scotland BTC into the problem of non-A, non-B hepatitis associated with blood transfusion. He suggested that a multi-centre study might be sponsored by the WP. It was agreed, however, that this matter should be deferred until candidate laboratory tests were available.

It was decided that the following problems needed investigation: (a) The identification of donors and units of blood associated with possible cases of non-A, non-B hepatitis, (b) Research into methods of identifying the viruses associated with non-A, non-B hepatitis, and (c) Epidemiological surveys to assess the size of the problem in relation to blood transfusions.

Dr Dickens said that as a result of the meeting of the ad hoc group in February 1979 three special project grants had been approved for research into the incidence, epidemiology and clinical features of non-A, non-B hepatitis, and a fourth would probably soon be approved too. It was open to the WP to initiate fresh projects in this field.

Methods of inactivation of hepatitis viruses in blood derivatives

3.3 Professor Zuckerman described research being carried out at present by the Boyer Pharmaceutical Company into the inactivation of viruses in blood products using β-propiolactone. Dr Walford questioned whether a product subjected to such a process might not have problems in acquiring a product licence in the UK, since β-propiolactone had been shown under certain experimental conditions to act as a carcinogen.

It was agreed that more information was required by the WP regarding the inactivation of viruses in blood products. Dr Jenkins and Professor Zuckerman undertook to initiate a review of the literature for members of the WP; this would probably be undertaken by a member of Dr Jenkins' staff.

Removal of viruses from blood products by fractionation processes

3.4 Dr Craske said there was some epidemiological evidence from studies of factor VIII associated non-A, non-B hepatitis that commercial factor VIII concentrate from the USA was associated with one type of hepatitis, and that NHS factor VIII and factor IX made by Immuno Ltd. in Austria might be associated with one or more different types, distinct from those in American commercial material. The most likely explanation was that the PEG/glycine fractionation method concentrated one serotype of virus and inactivated others.

It was also noted that research was being carried out in the USA into fractionation procedures which would eliminate or decrease the concentration of virus in the product as part of the fractionation process. (1) Searle Laboratories Ltd. were carrying out a project with the Blood Products Laboratory, Elstree, using the polyelectrolyte method for the fractionation of plasma.

4. Identification of agents carrying non-A, non-B hepatitis

This subject was mostly dealt with in the discussion under item 3.2. It was agreed that Professor Zuckerman would produce a paper outlining the work with inoculation experiments in chimpanzees, detailing forthcoming plans and providing justification for the financial support requested. Experiments so far showed that there were probably 2 types of non-A, non-B hepatitis associated with factor VIII. The second type had been produced by the same batch of 'Hemofil' which was associated with the Bournemouth outbreak in 1974. Further collaborative work with Dr Craske was planned.

5. Methods of obtaining and storing material with a high content of markers of hepatitis B and non-A, non-B hepatitis viruses

Professor Zuckerman said that he had obtained approximately 100 units of HB_sAg positive plasma for use in research and the development of a hepatitis B vaccine. The WP agreed to approach Dr J W G Smith, Director of the National Institute of Biological Standards and Control, to see if he could offer space for storage of Professor Zuckerman's collection of HB_sAg positive plasma, so that it could form the nucleus of a collection to be obtained through the NBTS for future hepatitis B vaccine development. It was also agreed that it was important to obtain similar bottles of plasma

associated with cases of non-A, non-B hepatitis to form the nucleus of well documented material for research into this disease. A start had been made through the identification of infected batches of factor VIII, but it was essential to obtain individual bottles of plasma from implicated donors as there was some evidence that different viruses might be involved in factor VIII and in whole blood transfusions. Some preliminary work had already been done at the Edinburgh and South East Scotland BTC.

6. Transmission of cytomegalovirus (CMV) by blood transfusions

Dr Tobin outlined the problems and risks associated with the transmission of CMV by whole blood transfusions. Two papers had been circulated to members of the WP: the first described the proceedings of a meeting held at Oxford to discuss this problem in 1977, (PTH 80/3), and the second summarised the present position, (PTH 80/4).

The risk of transmission by transfusion of CMV occurred with transfusions of fresh blood, platelets or leucocytes. With whole blood the risk depended on the presence of viable leucocytes containing the virus and probably existed up to 10 days after the donation with blood stored at 4°C.

Problems could arise in five situations:-

(a) Exchange transfusions of neonates. In one series this was shown to occur in 24/270 patients with no CMV antibody before transfusion. There was also a risk of transmission of the infection to the infant's mother if she was susceptible to infection, and there was a small risk of resultant congenital infection if the mother again become pregnant.

(b) Transplantation. CMV infection could be acquired in i) the donor organ, ii) transfusing CMV positive blood into susceptible patients, and iii) reactivatio of latent infection in recipients through CMV positive blood acting as an allograf

(c) Open heart surgery. An infectious mononucleosis-like illness in susceptible patients after transfusion for open heart surgery was associated with CMV infection.

(d) Use of blood products, eg platelet or leucocyte transfusions, especially in children with acute lymphocytic leukaemia.

(e) Transfusion in early pregnancy

At Oxford RBTC a donor panel of approximately 5,000 CMV-free donors had been set up to provide CMV antibody negative donations for transfusion to patients in the above categories. The fluorescent antibody test had been used to screen blood donors. It was likely that radioimmunoaasay and ELISA tests would be required if large scale screening were to be employed.

Dr Tobin said that it was debatable whether every Transfusion Centre should supply CMV-free blood, but more follow-up studies should be undertaken.

7. Any other business

There was none.

8. Date of next meeting

To be arranged.