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INFECTED BLOOD INQUIRY

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DRAFT Dr Harris' comments in red

Dr Tyrrell's comments in bold print

MRC: IN CONFIDENCE

Informal meeting on AIDS

A meeting took place at 10.30 am on 29 July 1983 at 20 Park Crescent. Those present were Sir James Gowans, Dr M P W Godfrey, Dr D A J Tyrell, Dr E L Harris (DHSS) and Dr J E M Whitehead (PHLS). Dr Dickens was in attendance.

Sir James welcomed the visitors and said that the purpose of the meeting was to advise him as Council Secretary on what steps MRC could usefully take concerning AIDS. He drew attention to the papers circulated before the meeting and referred to his own visit to the US National Institutes of Health in March 1983. He had continued to receive papers from NIH as they were issued. He invited Dr Harris and Dr Whitehead to comment on the AIDS problem.

Dr Harris stated that DHSS maintained close contacts with the NIH in America and with the Ministries of Health of the important Western Countries. He described recent discussions with Regional Blood Transfusion Directors, including a European group who were planning to issue a Code of Practice for donors. A DHSS Code was also in preparation, for distribution to all potential blood donors - copies would be sent to the MRC when available. The object of the Code was to stress the delicate point that homosexuals or drug addicts should not volunteer donations until further notice. Dr Harris circulated a short paper by [redacted] referring to heat treatment of blood products (see Annex). He hoped that in the UK it would be possible to avoid problems encountered in the USA where many donors were homosexuals and drug addicts - groups with a high rate of chronic infection with multiple pathogens, especially viruses such as hepatitis B. There was, of course, no scientific evidence that the use of heat treatment in the preparation of blood products achieved the specific aim of preventing AIDS transmission (by inactivtion of a causative virus) and there was concern about the possible effect of heat on the subsequent activity of blood products. It was likely, however, that such a step would be added to the manufacturing process in the UK. 50% of the UK requirement for Factor VIII was manufactured at the Blood Products Laboratory at Elstree and a new building, costing £18M, should open in 18 months' time and provide for total UK needs. Dr Harris also mentioned that there was much interest on the part of the Trade Unions on

vaccination of personnel against hepatitis B who might be exposed to infections. It could cost up to £30M to vaccinate all NHS personnel who might run any risk of infection with hepatitis B; the latest demand from ASTMS had been for a categoric assurance by Ministers that such vaccination would not in itself constitute any form of enhanced risk of contracting AIDS. Close collaboration with MRC would be welcomed by DHSS concerning any forthcoming research activities and it was agreed that both parties should keep the other informed.

Dr Whitehead, for PHLS, described the AIDS national surveillance scheme organised by the Communicable Diseases Surveillance Centre at Colindale, and also a proposed new scheme of 'sentinel' STD clinics which would make weekly reports about possible causes of AIDS. Recognition of early cases was particularly important in the UK context, and protocols were currently being drafted to ensure that the epidemiological work was as soundly based as possible and carried out consistently throughout the UK; the aims of this work were to help recognition of early cases of AIDS (and thus facilitate the obtaining of specimens), to maintain surveillance of registered haemophiliac patients, to obtain data from the hospital sector to compare with those from the 'sentinel' clinics, and to survey areas where no case of AIDS had as yet been reported (eg Manchester). Copies of the propocols would be sent to the Council when they were available. It was also agreed that attention should be paid to possible early forms of AIDS, eg Extended Lymphadenopathy Syndrome (ELS).

In further dicussions about blood products, the DHSS Advisory Committee on the National Blood Transfusion Service had a Working Party on Plasma Supply chaired by Dr H H Gunson of Manchester and maintained a watch over blood product manufacture. There was also a Central Committee for Research and Development in Blood Transfusion under the aegis of the Central Laboratories (a Special Health Authority) - which was considering sponsoring research in AIDS. In Scotland the National Blood Transfusion Service was keeping a close watch on hepatitis B and AIDS.

Dr Tyrrell commented that AIDS was indeed a mysterious disease. further virological work was needed; current work in the USA was of great interest. He did not think that it would be possible for the MRC to undertake studies on all possible facets of the disease, but it would be worthwhile to concentrate on the early stages of the epidemiology and cases of early, and possibly unrecognised, infection. The aetiology could be studied, and also the disturbances to immunological function which were present; cultured cells could be looked at by various methods, including electron microscopy, and animal inoculation could be carried out; another possiblity was that there might be more than one

aetiological agent and they might interact to produce the disease picture. He suggested that the disease would spread in the UK, but not on the scale of the USA.

It was thought that some central point of reference was needed for research studies and it was agreed that the Clinical Research Centre should have a definite 'presence' in this context - it was known that Sir Christopher Booth would welcome such a development. A working party was the best way for the Council to assist the exchange of information, to maintain enthusiasm, to facilitate co-operation, and possibly to plan and promote large scale projects; it would also advise on applications to the MRC for grant support. Links with NIH should aslo be maintained, through Sir James. Animal studies were worth considering, although it had not yet been possible to transmit the infection in an animal population. As well as cases from Haiti, a worrying number had arisen in Zaire - eg 16 cases had been reported in Belgium, 14 having come directly from Zaire; it was possible that there were areas in Central or West Africa where the condition was endemic but as yet unrecognised because the infections or tumours from which the patient died were not investigated in sufficient depth. The Working Party could also be kept informed of the progress of a DHSS sutdy of the 2,100 haemophiliacs in England and Wales, with particular reference to those exposed to a possible risk of AIDS from imported American Factor VIII.

Dr Harris and Dr Whitehead then left, it having been agreed that the Council would have ready a statement in reply to press enquiries, although it would not be formally issued as a press statement. The guidelines compiled for the press were as follows:

"i) On 29 July 1983, representatives of the Medical Research Council, the Department of Health and Social Security and the Public Health Laboratory Service met to discuss the problems of AIDS and to advise the MRC Secretary on any action which should be taken in regard to research.

ii) The MRC has kept in close touch with the highly expert work being undertaken by the National Institutes of Health in the USA, and the position of the United Kingdom was reviewed against that background.

iii) The representatives of the three organisations agreed to keep in close touch in order to exchange information.

iv) The Medical Research Council is setting up a working party which will act as a forum for discussion about research on AIDS and will advise the Council in this field."

CENTRAL BLOOD LABORATORIES AUTHORITY

AIDS

Progress with heat treatment of human plasma products

Heat treatment or pasteurisation of blood products is directed towards inactivation of a group of transmissible viruses which result in sub-clinical or clinical hepatitis in a proportion of treated patients. Currently, albumin fractions are pasteurised at 60°C for ten hours to inactivate hepatitis B virus and there is the assumption that this heat process also inactivates the group of viruses responsible for non-A non-B hepatitis. Long-standing use of pasteurised albumin products without the complication of hepatitis suggests that the pasteurisation process is effective.

Pasteurisation of other blood products has not been developed to this extent because these products are not amenable to the heat treatment process:- examples are fibrinogen, factor VIII, factor IX, which are all known to transmit hepatitis B and non-A non-B viruses.

Immunoglobulin produced by ethanol precipitation in Cohn Fraction II is not pasteurised but in long-standing wide use has acquired only a marginal anecdotal association with transmission of hepatitis virus. The earlier assumption that virus in immunoglobulin would be immune-complexed and therefore inactivated is more likely to account for the lack of transmission of infection rather than the view that the virus is not fractionated in with Cohn Fraction II immunoglobulin intermediates.

Virus transmission in haemophiliacs

Hepatitis B transmission in large-pool factor VIII and factor IX concentrates is recognised in haemophilia patients but the incidence has been effectively reduced by screening of plasma to exclude source material from hepatitis B antigen carriers. The absence of markers for non-A non-B hepatitis virus does not allow for this screening of source material and epidemiological evidence suggests that large-pool concentrates are universally associated with effective transmission of non-A non-B hepatitis virus.

The severity of non-A non-B hepatitis in haemophiliacs probably associated with the co-existent impaired immune responsiveness of these patients has motivated plasma fractionation organisations to re-examine means whereby hepatitis virus can be inactivated in large-pool concentrates. Heat treatment of blood products is still primarily directed at the inactivation of transmissible viruses causing hepatitis in recipients.

AIDS

The syndrome of acquired immune deficiency currently under investigation is likely to include in its aetiology transmission of an infective virus and the possible phenomenon of reactivation of an existing virus in individuals concerned. In limited numbers, AIDS sufferers have included individuals receiving human blood-based fractions. This aetiological observation has promoted more activity in the area of blood products pasteurisation with the empirical view that a virus is involved and, as with hepatitis virus, is likely to be partially or completely inactivated by heat.

Means of heat treatment of blood products

Heat treatment represents only one pathway by which viruses may be inactivated. Nonetheless, it is the most favoured route at present. Heat treatment may take place during the process of blood product purification, i.e. during a wet process step or heating a finished freeze dried product can be attempted. Heat transfer in the wet state is more homogeneous and efficient and to satisfy reliability in manufacture is to be preferred; however, wet treatment is associated with more molecular damage of heat unstable proteins than occurs by the dry-heat route.

Wet-heat pasteurisation of blood products at BPL is now available with albumin fractions, anti-thrombin III, factor XIII, and is likely to be successful during this calendar year with factor IX. The loss of yield of factor IX incurred may be tolerated within the considerable excess of source material available to the fractionation facility.

Wet-heat of factor VIII intermediate concentrate is likely to require a longer programme of work if a satisfactory reliable method is to be developed which does not carry unacceptable penalties related to loss of yield of factor VIII activity. Progress with this procedure will be reported to the Authority.

Dry-heat: the majority of commercial manufacturers are currently depending upon dry-heat of the finished factor VIII concentrate to reduce the infectivity of the product relative to transmission of hepatitis. The associated claims (which are entirely unfounded in scientific and quality control terms) are that the heat process will inactivate the putative virus transmission causing AIDS.

Appreciating pressure under which users are currently operating in the management of haemophilia, BPL has undertaken preliminary studies to assess yield of factor VIII intermediate concentrate after dry-heat. It has been shown possible to maintain greater than 95% of factor VIII activity in the finished product after heating at 75°C for ten hours or heating at 60°C for 24 hours. Both these presentations of heat exceed the requirements established for virus inactivation by wet-heat with albumin products (60°C for ten hours).

Since this form of product treatment will allow BPL to present to clinical managers of haemophilia a product carrying equivalent weight of claims for safety as those of rival commercial organisations, this product is being advanced with high priority to enable manufacture to become routine by the late summer 1983.

To introduce the product, the full co-operation of the haemophilia directors will be required since a non-human primate testing facility is not available to BPL accepting that this system of testing may not be appropriate with regard to hepatitis or AIDS transmitting viruses.

Introduction of an extra stage in the process of purification of factor VIII may impose costly intermediate reorganisation of manufacturing and equipment for which there is no budgeted sum. It is assumed that this contingency will be met recognising the political sensitivity of AIDS transmission in the UK caused by treatment with blood products.

[redacted]

26th July 1983.