AIDS Scientific and Technical Working Group

Summary of the 1st Meeting, Friday, May 2nd 1986, held at NIBSC

Present

Dr. R.J. Perry, Dr. B. Cuthbertson	Edinburgh PFC
Dr. D.B.L. McClelland	Edinburgh BTS
Dr. R.S. Lane, Dr.P. Harrison	BPL, Elstree
Dr. P. Feldman	PFL, Oxford
Dr. A. Smithies, Dr. F. Rotblat	DHSS
Dr. G.C. Schild (Chairman), Dr. D.P. Thomas,)	
Dr. T.W. Barrowcliffe, Dr. R. Thorpe,)	NIBSC
Dr. A.J. Garrett, Mr. P. Jacobs)	

Introduction

Dr. Schild welcomed everyone to NIBSC and outlined the scope of the group. The aim was to share information and, where appropriate, scientific and technical resources among the plasma fractionation laboratories and NIBSC. The group would cover all aspects of virological safety, though initial focus of attention would be on LAV/HTLV III.

Ongoing activities

Each group outlined its current activities and immediate future plans.

Dr. Cuthbertson reported that his laboratory had already obtained data on viral inactivation during the fractionation process, using model viruses, and are currently awaiting results of spiking experiments using LAV/HTLV III virus. These experiments are in collaboration with Edinburgh University and the Chester Beatty Institute. Initial conclusions from model virus studies were that pepsin at pH 4 is a very effective viricidal step and that presence or absence of antibody may modify the degree of virus kill.

Dr. Lane reported that BPL are not duplicating the Edinburgh experiments with HTLV III. Experiments are being carried out in chimpanzees in the USA to test the safety of Factor VIII and i.v. IgG products for NANB hepatitis. Preliminary results indicate that treatment of IgG with pepsin at pH 4 may render it non-infective for NANB. Current data from a clinical trial of heated Factor VIII ('8Y' product) show no seroconversion to HTLV III Ab, and no alteration of liver enzymes to date.

Dr. Thorpe and Dr. Garrett described their work on serological tests. They have set up lymphocyte cultures for growth of HTLV III virus, and are using an inactivated viral antigen preparation for Western blotting, with a monoclonal anti-IgG. Of many batches of i.m. and i.v. IgG tested for anti-HTLV III by Western blotting, only a few were positive, and these were also positive by ELISA. However, Dr.

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McClelland presented serial data on two patients in whom a positive Western blot had been found before being detected by the ELISA method. Western blotting gave more information than ELISA about the characteristics of the antibody, and had been used to study the virus isolates from two cases of AIDS at Northwick Park Hospital. These two viruses gave immunoblot patterns identical to those of the prototype LAH/HTLV III virus.

Work has also been done on evaluation of HTLV III Ab kits, and an international collaborative study is being organised by NIBSC in which a group of samples will be sent to about 20 expert laboratories for evaluation by ELISA and immunoblotting.

Dr. Smithies was mainly concerned with the efficiency of current screening procedures for blood donors. Initial testing of kits from five manufacturers by PHLS had led to selection of the Wellcome and Organon kits. Recently, a further five manufacturers' kits had been evaluated. After the first 3 months of testing in the BTS, 300 samples had been referred to PHLS for further testing and 16 of these were confirmed positive. These samples are being further evaluated by four different kits in a central laboratory (Dr. Tedder). The group felt strongly that these samples should also be tested by immunoblotting, using a technique such as that developed by Dr. Thorpe and Dr. Garrett at NIBSC.

Suggestions for collaborative work

Screening of blood donors Dr. McClelland expressed his concern about current screening procedures. Recent data from BTS centres indicated inconsistent detection of known positive samples and it was not clear whether this was due to differences between kit batches or problems of internal quality control. Dr. Lane pointed out that, in the hepatitis B screening programme, administrative errors rather than technical failure were responsible for most of the incorrect results.

It was agreed that the group should liaise with PHLS regarding quality control, and should find out what measures were being used by the manufacturers to ensure batch-to-batch consistency of kits. The group would also like to be involved in confirmatory testing, especially by immunoblotting.

Surveillance of recipients It was agreed that this topic should be discussed at a separate meeting, involving Dr. C.D. Forbes, who was co-ordinating data for haemophiliacs, and the PHLS. Dr. McClelland stressed the need for more surveillance of recipients of IgG, and suggested that blood donors who had received normal IgG could be checked. Dr. Smithies said that funds were available from MRC for epidemiological studies of this kind.

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Collaborative studies and standards Dr. Garrett would send samples from his collaborative study to both Edinburgh laboratories and to Elstree. There was a need to standardise assays for HTLV III infectivity but as yet these assays were still being developed. It was thought that the most useful standards at the moment would be an HTLV III Ab positive IgG and a standard HTLV III antigen preparation for immunoblotting.

The group also considered the evidence for the safety of immunoglobulins. After full discussion, the group concluded that:

1. There is no epidemiological evidence associating the administration of intramuscular immunoglobulin with seroconversion for antibodies to LAV/HTLV III or the subsequent development of AIDS, and there is no reason to believe that intramuscular immunoglobulin, both normal and specific, is anything other than a safe product. Furthermore, several studies have now shown that patients who received immunoglobulins containing anti-LAV/HTLV III antibodies have not subsequently seroconverted.

2. While the epidemiological evidence for the safety of intravenous immunoglobulins prepared by conventional Cohn fractionation is somewhat less secure, there is no convincing evidence that such preparations transmit LAV/HTLV III infection. However, certain products have been demonstrated to transmit non-A, non-B hepatitis.

3. Current evidence suggests that the LAV/HTLV III virus does not survive cold ethanol plasma fractionation during the preparation of immunoglobulins. At least six laboratories have demonstrated, in spiking experiments, that the virus is inactivated or removed during Cohn fractionation for immunoglobulins. However, it was also noted that partition of virus during Cohn fractionation poses substantial GMP considerations for plasma fractionators, who should be encouraged to incorporate an additional downstream step which demonstrably inactivates viruses.

4. The group did not consider that the recall of distributed batches of immunoglobulins for intramuscular use prepared from unscreened donors was warranted on the basis of the available evidence.

The group also noted that the National Blood Transfusion Service, as an added safety measure, has adopted a policy of not issuing immunoglobulins manufactured from a plasma pool to which a donor contributed who subsequently developed anti-LAV/HTLV III antibodies. Currently, all immunoglobulins (both i.m. and i.v.) that are subject to batch release by NIBSC under the Medicines Act are examined by immunoblotting, and any batch that is positive is not released for distribution. The group was informed by Dr. Rotblat that all licensed immunoglobulins will be prepared from plasma derived from screened donors by the end of June, 1986.

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