

Central Blood Laboratories Authority

Minutes of the first meeting of the Working Group on AIDS in relation to Blood Transfusion, held on 14 October, 1983 in the Board Room, The Crest.

PRESENT: Dr H H Gunson (in the Chair)
Dr J Craske
Dr I A Fraser
Dr R S Lane
Dr A MacMillan
Dr D B L McClelland
Dr P Mortimer
Dr D Onions
Dr R Tedder
Dr T Wallington

1. Membership of The Working Group

The Chairman confirmed that the CBLA had formed the Central Research Committee for Research and Development in Blood Transfusion which, at its first meeting in June, had agreed that this ad-hoc Working Group should be set up to consider the problem of AIDS in relation to the transfusion of blood and blood products.

The Chairman informed members of the Working Group that the MRC had set up a similar Committee on AIDS and said that he had spoken with Dr Katherine Levy, the Senior Medical Officer involved with the MRC Committee, who had expressed the view that a link between the two groups should be established. It was noted that the MRC Group had held its first meeting on 10 October and the Chairman said that Professor A Bloom, already a member of the Research and Development Committee, was also a member of the MRC Group and could provide the link between the two groups if this was considered acceptable. This was unanimously endorsed, and it was agreed that Professor Bloom should be invited to the next meeting of the Working Group. It was agreed also that it would be beneficial for the Working Group and the MRC Committee to exchange minutes of meetings, and Dr Gunson would pursue this with the MRC.

2. Apologies for Absence

There were no apologies for absence.

3. Possible Areas for Investigation into AIDS

3.1. The Donor Population

3.1.1. The Leaflet 'AIDS and how it concerns blood donors'

The Chairman commented that the issuing of the above leaflet was, at present, the only practical step being taken by the Transfusion Service. Approximately one-half of the RTC's were distributing the leaflet with the call-up card/letter whilst others were either having the leaflets available on sessions or

actively handing them to donors on sessions. In general, the Group considered that a uniform system of distribution would be advantageous and it was noted that RTC's had been asked by the DHSS to report on the distribution at the end of November 1983.

Dr Lane expressed the view that persons experienced in marketing/advertising would be able to give advice on getting the information to the public and their methods may be more effective.

It was agreed that:

- (a) Special clinics should be included in the distribution
- (b) Health Education Councils should be approached
- (c) Gay Societies should be contacted
- (d) Comments on the leaflets from donors might be invited

With respect to the content of the leaflet itself, it was considered that the important message as far as the blood donor was concerned, i.e. not to give blood if they were in a high risk group, should be highlighted in some way.

It was agreed that the above matters would be raised at the DHSS on Monday 17th October 1983, when the Advisory Committee on the N.B.T.S. met.

3.1.2. The Use of Surrogate Tests

It was generally agreed that if investigation into surrogate tests was to be carried out it would be preferable to investigate the use of anti-HBc screening rather than the TPHA.

With respect to anti-HBc screening, the Working Group learnt that in the Bristol region, 10,000 donor blood samples had been screened for anti-HBc and 75 positives were found (incidence 0.75%) whilst in North London the incidence was 2.6% after screening 25000 donor blood samples. The latter screening was still in progress and the results of 5000 tests would be available in the near future.

It was apparent that regional variations of anti-HBc positives may be considerable and a discussion took place on the possibilities of a pilot study. One area of concern was with respect to the follow-up of the donors and the ethical considerations involved.

It was agreed that Dr B McClelland would collate the information that had already been obtained on anti-HBc screening and Drs. Fraser and Tedder agreed that the results of their studies would be made available in confidence to the Working Group.

Having considered the value of the available data, Dr McClelland would submit outline proposals for a prospective study in time for the next meeting early in 1984.

The Chairman stressed that economical considerations could not be ignored if it was concluded that an additional test for screening blood donors was proposed. It was noted that a monoclonal reagent was available and this may help to reduce the cost of the testing.

It was agreed that other surrogate tests such as the detection of α -thymosin, α -interferon and β_2 -microglobulin were not suitable yet for large-scale screening, but they may be of value in a study for examining blood samples of anti-HBc positives.

3.1.3. T-lymphocyte Studies

Dr Onions presented a short discussion on the importance of HTLV in relation to AIDS. (A paper is attached as an appendix to the minutes).

3.2 Blood Transfusion Practices

3.2.1. Use of plasma Pools Containing Smaller Numbers of Donors

Dr Lane outlined the investigations with respect of infectivity to non-A, non-B hepatitis with the use of pools of plasma containing donations obtained by apheresis for the preparation of Factor VIII concentrate. He commented that the preliminary results were encouraging. Also, he explained the outline of two further studies to be undertaken at Bristol and Sheffield RTC's using filtration plasmapheresis in which the Factor VIII obtained from the plasma would be used to treat patients with haemophilia A who had not previously been exposed to blood products.

If one could extrapolate from results with respect to non-A, non-B hepatitis to those which may be expected for AIDS the concept of small donor-pool material, with a group of donors where there was a greater chance to obtain more information, might have considerable advantages. It was noted, however, that this would, if implemented, require a reconsideration of plasma supply for self-sufficiency in blood products.

It was agreed that the protocols for the two studies mentioned above would be made available, in confidence, to the Group. Dr Craske suggested that evidence for transmission of viruses in the Herpes Group might be helpful.

3.2.2. Treatment of Blood Products to eliminate micro-organisms

The only aspects of this subject discussed were:

- (a) It was noted that, with respect to non-A, non-B hepatitis the dry-heat treatment of Factor VIII and Factor X had not initially been encouraging from the studies on chimpanzees. Wet-heat treatment appeared successful in the case of the albumin solutions and Dr Lane expressed the opinion that further work was necessary and that such products should be subjected to evaluation before accepted.
- (b) The fractionation process itself may be inhibitory to viruses and it was agreed that there was no evidence that intramuscular immunoglobulin prepared by Cohn fractionation was unsafe with respect to virus transmission, although the base material (fractions II and III) may not always be so.

Such observations had considerable implications and were being studied at BPL.

Items on the use of blood substitutes, immunological sequelae of the transfusion of blood and products and autotransfusion were deferred until the next meeting.

4. Date and Time of Next Meeting

It was agreed that the next meeting would be held at Elstree on the 27th January, 1984, at 11.00 a.m.

WORKING GROUP ON AIDS IN RELATION TO BLOOD TRANSFUSION1. Epidemiological Features of HTLV Infection

The epidemiological features of AIDS suggest that an infectious agent is responsible for the condition but as yet no aetiological factor has been unequivocally associated with the disease. Amongst the viruses that have been considered, the human T-cell leukaemia virus (HTLV) has drawn particular attention. This is for two reasons: first HTLV, a virus known to be associated with certain T-cell malignancies, belongs to the retrovirus group which have the general properties of leukaemogenicity and immunosuppression. For instance, it is known that infection of cats with the related feline leukaemia virus (FeLV) more frequently results in death of these animals from immunosuppression than from leukaemia.

Secondly, a limited sero-epidemiological survey indicated that about 25% (19/75) of American male homosexual AIDS patients had evidence of HTLV infection, whilst only 1 of 81 matched homosexual controls had anti-HTLV antibody. This study (Essex et al., Science 220, 859-862) employed indirect immunofluorescence of patients' sera against HTLV infected cell lines. Confirmation of the specificity of the reaction was based on immunoprecipitation of ³⁵S-methionine labelled proteins from HTLV infected cells. Sixteen of 20 'immunofluorescent positive' sera precipitated the major internal antigen of HTLV (p24). In addition, these sera precipitated a protein P61 which is coded for or induced by HTLV.

HTLV infection in AIDS patients has been demonstrated directly in a number of instances either by virus isolation (Gallo et al., Science 220, 865-867) or by detection of integrated proviruses. Gelman et al. (Science 220, 862-864) found 2 of 33 patients had detectable proviruses in peripheral blood lymphocytes and that the infected cells represented a monoclonal or oligoclonal population.

An important observation was that on subsequent sampling HTLV sequences were no longer detectable in one of these patients. Both the Gelman and Gallo 'isolates' have been of subgroup I. Recently two variant viruses have been found in association with a few AIDS patients. Chermann *et al.* (Science 220, 868-871) have described a retrovirus isolated from a French homosexual patient with lymphadenopathy. Recent evidence suggests that this virus is distinct from HTLV and may be related to the non-oncogenic virus of horses, known as equine infectious anaemia virus (Montagnier. Pers. Comm.). A virus related to HTLV but distinct from HTLV1 and HTLV11 has recently been demonstrated in proviral form in a few AIDS patients (Phillips Pers. Comm.).

2. Significance of HTLV Infection in AIDS Patients

The inherent difficulty in interpreting the significance of HTLV infection in AIDS patients is that these individuals are highly susceptible to a wide range of opportunistic infections, a category into which HTLV might fall. Furthermore the establishment of infections requiring intimate contact is likely to be favoured in populations with a high degree of sexual promiscuity, a social culture which appears to be common in AIDS victims. In this regard it is noticeable that AIDS patients have a higher prevalence of antibodies to hepatitis A virus and treponema pallidum and higher titres of antibody to cytomegalovirus and Epstein-Barr virus than do control groups (Rodgers *et al.*, Task Force on AIDS. Ann. Intern. Med. 103).

A second problem associated with ascribing an aetiological role to HTLV in AIDS is the apparent absence of the condition in the HTLV endemic areas of Japan. To sustain an argument in favour of the role of HTLV in AIDS one would require to argue that either genetic resistance to immunosuppression occurs in the Japanese population, or more likely, that variants of HTLV, rather than HTLV-1 are

involved in the induction of the condition. The variant proviruses detected by Mullins and his colleagues may, therefore, be of particular importance.

A further factor for consideration is the absence of HTLV antibody and HTLV-1 proviral sequences in the majority of AIDS patients. In HTLV associated malignancy the majority, but not all, patients have demonstrable anti-HTLV antibody. Most of the screening for HTLV infection in AIDS has been carried out with HTLV-1 infected cells or HTLV-1 probes, and if a variant virus is involved this may not always be detected. For instance HTLV-1 and HTLV-11 show relatively weak cross hybridisation although immunological cross reaction of their internal antigens is retained. It is also possible that HTLV infection results in elimination of the $OkT4^+$ population and therefore of the HTLV infected cells. The decline in the detectable HTLV sequences reported by Gelman might have occurred in this fashion. A speculative model for this process has been proposed as follows.

The $OkT4^+$ lymphocyte is the natural target for HTLV infection and it is this population that is ablated in AIDS patients. Infection of the $OkT4^+$ cells leads to the expression of viral envelope proteins on the cell surface which mimic HLA Class 1 antigens (Mann et al., Nature 305, 58-60). The apparently novel HLA expression on these cells could then induce their immune destruction.

3. Importance of HTLV Screening in the United Kingdom

Resolution of the significance of HTLV or other infections in AIDS would be facilitated by a prospective survey. Within the United Kingdom we are well placed to conduct such surveys. In contrast to the United States we are probably only in the early stages of an AIDS 'epidemic'. Secondly, it is possible to obtain a high degree of cooperation of likely susceptible groups, a feature which would be essential for any successful prospective survey.

Finally the background HTLV infection rate in the United Kingdom is likely to be low and largely restricted to persons of Carribean origin.

Screening tests have already been developed by Dr. Richard Tedder in collaboration with Dr. Robin Weiss, and are based on a competition radioimmunoassay. The solid phase consists of plastic bound, polyclonal anti-HTLV-1 antibody to which HTLV-1 is in turn bound. Patients' sera is then allowed to compete with radiolabelled anti-HTLV-1 antibody for binding to the antigen. Sera positive by this assay have been reassayed using the pseudotype neutralisation and syncitium inhibition assays developed by Dr. Weiss. Several HTLV risk groups are being screened including, tropical area donors, male homosexuals, lymphadenopathy and AIDS patients. Preliminary results have not revealed a high prevalence of HTLV antibody in the latter two groups.

Dr. McMillan presented information on an Edinburgh-based group of male, homosexuals from whom serial samples have been obtained and stored for a number of years. The high repeat attendance of this group at routine screening clinics for venereal disease suggests that they may consent to and form a useful cohort for a prospective study of putative AIDS associated agents.