OUTLINE PROTOCOL OF AN EPIDEMIOLOGICAL STUDY OF THE HTLV III/LAV VIRUS BY THE BLOOD TRANSFUSION SERVICE.

It is clearly established that the transfusion of fresh blood components which are not amenable to viricidal treatments can transmit HTLV III. This study is designed to identify both blood donors and recipients who are anti-HTLV III seropositive thus allowing epidemiological study of these subjects and their close contacts (and facilitating their proper counselling and treatment when drugs become available). Donors who are found to be members of the major risk groups will not be studied further other than to try to establish why they gave blood inspite of efforts to educate them not to do so. Their treatment and counselling will be in the hands of others. Proper emphasis will be placed on the counselling of all participants of the purpose and relevance of the study and the implications to the individual and others of allowing themselves to be HTLV III antibody testing (D Miller, J Green, D J. Jeffries et al. 1986 BMJ 292: 941). Counselling beyond the resources of the study team and other specialist help will be needed by donors and patients identified by this study. Suitable services must be available within each Region before starting the study.

2. ORGANISATION OF THE STUDY.

For simplicity the organisation of the study will be divided into two phases (see figure), in the first phase index patients who have received a potentially infected donation, suitable for an epidemiological study, will be identified, in the second the epidemiological study itself will be performed. Phase two will be

started as soon as phase one provides subjects for study, the phases will overlap. Since positive donors are likely to be uncommon (1 in 45,000 on the basis of experience up to now, a maximum of 40-50 in the first year of testing) the study will embrace the whole of the UK.

Phase One.

It is expected that Donors will be recruited from two sources.

(i)Those identified as anti-HTLV III positive by screening tests carried out by RTC's. It should be possible to recruit these donors into the study during the counselling that follows a positive HTLV III antibody test. A few will also have been identified from back tracing in cases where transfused patients have developed symptomatic HTLV III/LAV infection

(ii)Those who have been identified on attendance at S.T.D. clinics or in other areas of medical specialization (drug addiction, the prison medical service) where high risk persons are seen by asking for a history of previous blood donation. This will require the c )peration of consultants in these specialties who will have to be asked to identify and recruit through appropriate counselling patients under their care who have been blood donors. Cases notified to the CDSC will also be pursued. Organ and sperm donors are also screened and relevant organisations will be approached for help. Relevant 'Gay' organisations will be asked to help with publicity for the study and to encourage participation. Regional Transfusion Directors will be asked to contact colleagues within their own Region. Explanatory documents will be provided to help with this. Details of HTLV III

antibody positive blood donors willing to participate in the study will be sent to the project's central coordinator. Printed stationary will be provided for that purpose. Arrangements will then be made for the donor to be seen by a medically qualified research assistant. This doctor will take blood for reference purposes and administer a questionaire to establish the likely duration of infectivity of that donor and enquire into their reasons for donating blood inspite of information available of the risks involved. Regional Transfusion Centres will then be asked to identify from their records the fate of blood and products prepared from previous donations (not to include B.P.L. clotting factors) together with the hospital to which they were issued. A search back over a period of up to five years or to the time at which the donors history suggests convincingly that they became infectious will be made. With the help of Hospital Haematologists patients transfused with these products will be identified. Regional Transfusion Directors will be asked to make contact with their colleagues for this purpose, explanatory documents will be provided. Worksheets to facilitate the whole process will also be provided. These worksheets will also be used to send data back to the Central Coordinator for further action.

Phase two.

Patients identified in phase one will be approached initially either by the Consultant caring for them at the time of transfusion of the putatively infectious donation or their General Practitioner. This will happen as soon as is practical after they have been

identified. The Hospital Haematologist will be asked to make contact with local colleagues for this purpose. Further action will depend on the judgement of these practioners. They represent a third set of medical professionals involved in the study. Explanatory documentation will be available for them as for the other groups involved. These patients will have to be offered testing for anti-HTLV III in the context of appropriate counselling about the test and its implications. If positive further counselling and perhaps specialist medical referral will be necessary. If it is agreed that the patient could be entered into the study their informed consent will be asked before proceeding further. They will also be asked if their sexual contacts and members of their household (that is people who have shared the same home for three months or more) including children up to the age of 12 years, might agree to enter the epidemiological study. A record of the investigation and its outcome up to this point will be sent to the project coordinator. From the patients and their close contacts, (called a 'case group') who give consent, all antibody positive case groups and a control group who proved negative will be studied further by an epidemiological research assistant (supervised from the Department of Epidemiology, Middlesex Hospital) who will administer a detailed questionaire aimed at discovering possible routes of spread of the virus (available for inspection) and take further blood samples as required. It will be necessary again to fall back on local provisions for coping with anti-HTLV III positive persons to handle any problems that arise as a result of this final part of the investigation. Any Donor identified in the first phase of the study

whose infection was due to blood transfusion could if willing be the index to a case group for the second phase.

Blood tests.

Confirmatory serology will be undertaken in one location only, The Department of Virology, Middlesex Hospital.

Confidentiality and ethics.

It is vital that all of the information obtained in the course of this study remains confidential. Providing that confidentiality is preserved the activity described presents few ethical problems. Doctors close to the patient will take the decision whether or not to pursue the possibility that they have been infected by a transfusion. They will only be tested for antibody after counselling. They will only be entered into the trial with their informed consent. It is possible that treatment able to influence the outcome of their infection will become available, patients will have to have been identified to benefit. Counselling may help prevent the spread of the virus to others. All of these factors are important to any ethical considerations.

Reference

Miller D, Green J, Jefferies D J 1986, Contempory Themes. HTLV III: Should testing be routine? BMJ 292: 941.