HAEMOPHILIA CENTRE DIRECTORS ORGANISATION

AIDS Advisory Document

At a recent meeting of Reference Centre Directors the following observations were discussed and recommendations made in consultation with Drs. Richard Lane, John Cash, Harold Gunson, Phillip Mortimer, Richard Tedder, John Craske and others.

Background

1. In U.S.A. There are over 6,000 cases of AIDS including 52 haemophiliacs.

   In U.K. There have been 102 cases with three reported haemophiliacs. No doubt other cases are developing in the haemophilic population.

2. Tests for HTLV III antibody are available for haemophiliacs via:
   Dr. Phillip Mortimer
   Central Public Health Laboratory Service
   175 Colindale Avenue
   Colindale, London NW9 5HT.

   Dr. Richard Tedder,
   Department of Virology
   School of Pathology,
   The Middlesex Hospital Medical School,
   Riding House Street,
   London W1P 7LD.

   Antibody positivity probably correlates with exposure to imported concentrates but there have been two notable recent episodes concerning U.K. concentrates.

3. Antibody tests indicate prior infection but do not imply immunity as antibodies may not be neutralising. Infective carriers can be antibody positive and there may also be a variable period of antigen positivity before seroconversion occurs.

   Antibody positive persons should therefore be considered at risk of transmitting or developing AIDS but antibody negativity does not exclude infectivity.

General Precautions

Donors

(a) the BTS is making increased efforts to ensure exclusion of donors at risk by questionnaires or leaflets or both.

(b) HTLV antibody tests either commercial or home grown should become available during 1985 but cannot be instantaneously implemented. Equipment, space and staff may be needed at Regional Transfusion Centres.

It seems probable that HTLV III has been incorporated into at least one BPL and one Scottish batch of factor VIII. Recipients are being followed up.

Concentrates

Factor VIII. Evidence is accruing that HTLV is heat labile but the data from "spiked" concentrate is entirely related to U.S. concentrates and is minimal. It seems that in concentrates HTLV III is inactivated by dry heat at 68°C for 24 hours. It is unlikely that this process completely inactivates Non A Non B hepatitis . Loss of yield is 15% for dry heat. Wet heat with stabilisers is probably more effective but evidence is lacking and loss of yield is up to 50%. Of current products heat treated Koate HT and Factorate HT are dry heated and sell at 12p a unit. Travenol Hemofil T is dry heat treated and sells at 15p a unit. Alpha Profilate (heated) is wet-treated (14p a unit). Immuno also have heated preparations.

Factor IX Profilnine (heated) (Alpha), heated Konyne (Cutter) and Immuno (heated Prothromplex) are available at prices up to 20p a unit but the effects on efficacy and thrombogenicity are unpublished. Since AIDS and laboratory changes seem (controversially) to be less common in Christmas disease than haemophilia A no firm recommendation can be given on heated factor IX.

Heated Feiba is also available from Immuno at 30p a unit but is probably not cost-effective.

BPL Factor VIII BPL can dry heat 30% of its output available from January 30th, 1985 and the rest in two months time when two more ovens are installed to supplement the existing one. The process produces an acceptablein vitro product but extensive clinical trials have not been undertaken.

Edinburgh From now on all Scottish factor VIII will be dry heated to supply Scotland and N. Ireland.

Options in probable decreasing order of safety from AIDS for Haemophilia A

1. Heated U.K. concentrate (note: still NANB hepatitis risk)
2. Single donor cryo. or FFP
3. Heated imported conc. (note: still NANB hepatitis risk)
4. Unheated U.K. conc.
5. Unheated imported conc - almost certain to be contaminated.

Note: Heated concentrates may still transmit hepatitis. Some of the distinctions e.g. between 3 and 4 are debatable and the long-term effects (e.g. immunogenicty) of using heated plasma proteins in this way are unknown. Even pasteurised albumin is not given as frequently to individuals as will be factor VIII.

RECOMMENDATIONS

1. Concentrate is still needed; bleeding is the commonest cause of disability and death.

2. Use DDAVP in mild Haemophilia A and vWd if possible.

3) For Haemophilia A needing blood products

(a) "Virgin" Patients those not previously exposed to concentrate, and childre use cryo or heated NHS factor VIII (if available).

(b) Severe and Moderate haemophiliacs previously treated with factor VIII use heat treated NHS factor VIII, if available or heat treated US commercial.

4) Haemophilia B

(a) Mild Christmas Fresh frozen plasma if possible (otherwise NHS Factor IX.

(b) "Virgin" Patients and those not previously exposed to concentrate use fresh frozen plasma (or NHS factor IX concentrate if essential)

(c) Severe and Moderate Christmas Disease previously exposed to factor IX concentrate continue to use NHS factor IX.

In individual patients there may need to be a choice. In general heated concentrate appears to be the recommendation of virologists consulted but individual Directors may wish to make up their own minds. This is particularlytrue of unheated NHS material. The evidence that heated U.S. factor VIII is safer than unheated NHS is debatable and some Directorsmay wish to continue using unheated NHS material until all supplies are heated. This is valid for carefully selected patients but must be on individual decision based on the assumption that some batches of NHS materials will be contaminated with HTLVIII. The argument that HTLV III positive patients have already beeninfected and could receive unheated American material is probablyscientifically true but this material would pose an additional risk to staff and families and its continued use would pose logistic problems.

Supplies

It seems that as from January 30th, 1985 a limited supply of BPL heat treated British factor VIII will be available. Preference will be given (a) to treat patients defined in recommendation 3a above and possibly (b) to those willing to participate in clinical trials.

NOTES

1. The Blood Products Laboratory cannot take back for reissue unused unheated concentrate. Do not ask your BTS to order more of this than you are willing to use because this would prejudice supplies of heated material later in the year.

2. If the bill for heated commercial concentrate is heavy at first it can be put to your Authority that increasedsupplies of heat treated BPL material could be available later in the Summer asstockpiled unheated material at BPL is heated.

3. Funding will need to be negotiated at local level although strong representations are being made to DHSS for central funding if needed. Please inform the Chairman (Prof A.L. Bloom) and Secretary (Dr. C.R Rizza) if you are experiencing difficulties. They cannot promise individual help but the information will be useful.

4. The need for elective surgery etc., should be assessed in the light of supplies of heated concentrate.

ANTIBODY TESTING

It is recommended that patients be HTLV III Ab tested.

Test should be repeated if positive.

Ab positive people should be informed, reassured and counselled regarding transmission to spouses etc., including the possible use of barrier contraception. This seems to be the most practical method available. Facilities are only available at present for HTLV III Ab studies on contacts as part of organised projects. Please note that sample bottles of serum must be leak-proof. The Laboratory Directors would prefer to liase with a small number of haemophilia doctors. Thus where possible samples should be chanelled through Reference Centres or the nearest large Haemophilia Centre from where suitable sample bottles may be obtained.

ORDINARY LABORATORY TESTING

Samples from patients with AIDS or PGL will be subject to the regulations promulgated by the AdvisoryCommittee on Dangerous Pathogens. Although very restrictive draft instructions have been circulated in an unauthorised fashion in various quarters we were assured that the definitive document is less so. Careful safety auditing of laboratory procedures is recommended. The recommendations apply to AIDS and high suspect patients. The rules for samples from healthy HTLV III Ab positive patients have not been specifically addressed but presumably these are also potentially dangerous.

CLINICAL

Plastic aprons could be used for preparing and administering all treatments (including home treatment). Home treatment procedures should be reviewed. Use of butterfly needles may be safer than ordinary syringe and needle as the risk of 'walk on' injury is reduced.

In the wards patients with AIDS or high risk thereof should be nursed in single rooms. Gloves and aprons should be worn by nurses when carrying out practical procedures. In general hepatitis B-like precautions should be taken. HTLV III Ab pos. patients should be dealt with for Dental care as for hep. BAg pos. In case of needle injuries virological advice from PHLS at Colindale should be obtained after applying the usual first aid measures. Aerosols and casual contacts do not constitute a risk and there is no need to isolate routinely HTLV III Ab positive patients.

STAFF

HTLV III Ab testing of staff is not recommended routinely but it could be useful to have organised studies in certain larger centres.

These recommendations will obviously need to be modified in the light of rapidly changing experience.

December 14th, 1984