MEETING HELD AT THE MIDDLESEX HOSPITAL MEDICAL SCHOOL ON THURSDAY

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The current state of surveys of HTLV-3 antibody in haemophilia A patients in the U.K. was reviewed.

AIDS AND HTLV-3 ANTIBODY PREVALENCE IN HAEMOPHILIACS

Three patients with haemophilia A had so far been reported with AIDS, 2 of whom had died. Two of these were known to have been infected with HTLV-3 virus at least two years and eighteen months before they were diagnosed as AIDS. Approximately 30 patients had been reported to Dr. Craske at PHLS Manchester. Some of these were patients with the AIDS-related complex; symptomatic disease (weight loss etc); others were symptomless with thrombocytopenia. A third group had been identified with evidence of a glandular fever-like syndrome which seemed to be associated with primary HTLV-3 infection.

Overall about 30-34% of haemophilia A patients were positive for HTLV-3 antibody. Sixty per cent of haemophilia A patients had 'severe' blood coagulation defects. Fifty - 80% of those who have received one or more batches of U.S. commercial factor VIII are now HTLV-3 antibody positive. Most of these are symptomless. Retrospective testing has shown that the first sero-conversions to HTLV-3 antibody positive occurred early in 1980.

A meeting of Haemophilia Centre Directors, which had been held at the Blood Products Laboratory, Dagger Lane, Elstree, Herts., on December 10th, 1984, had decided to recommend that all patients should receive heat treated factor VIII concentrate.

Four commercial companies importing factor VIII into the U.K. were proposing to introduce heat treated factor VIII . Three were 'dry' heat preparations (Travenol, Cutter and Revlon Health) and one (∝Therapeutics Ltd) was 'wet' heat treated. The Blood Product Laboratory was also proposing to produce a 'dry' heat treated preparation which would be available in limited quantities in April 1985.

IMPLICATIONS

The change to heat treated products would produce several problems in the short term. It was likely that a considerable quantity of ~~infected~~ untreated NHS factor VIII will be available for use before the heat treated product becomes available. On present evidence this carried a low risk of HTLV-3 infection compared with the high risk untreated commercial preparations. An alternative strategy for the use of heat treated factor VIII for every class of patient might be to use un~~treated~~ treated NHS factor VIII for HTLV-3 antibody positive patients .

and heat treated concentrate for HTLV-3 negative. Commercial factor VIII was known to carry the risk of non-A, non-B hepatitis and other infections which were not eliminated by the heat treatment processes. The evidence of 3 anecdotal reports of follow up of patients after treatment with heat treated factor VIII were encouraging but formal follow up of a large group of patients was essential to confirm this observation. It was possible for instance that the substitution of heat treated commercial factor VIII for untreated NHS factor VIII ~~for untreated NHS factor VIII~~ might give rise to other side reactions associated with transfusions, e.g., non-A, non-B hepatitis in a patient who had not received commercial products before.

RECOMMENDATIONS

It was therefore decided to propose to the U.K. Haemophilia Centre Directors the following strategy for HTLV-3 serology.

The following proposals would be put to the Haemophilia Reference Centre Directors in February 1985:-

HTLV-3 ANTIBODY SURVEY PATIENTS

a) All patients treated with factor VIII and IX concentrate in U.K. Haemophilia Centres would be offered an antibody test for HTLV-3 antibody within the period February to April, 1985. This would provide a clear picture to each Director of the number of patients at risk of developing AIDS, and assist in counselling patients and their relatives, and also assist in the investigation of AIDS related disease. It would also make it easier to devise strategies for the use of NHS factor VIII concentrate during the period before heat treated factor VIII concentrate became widely available.

b) Family contacts of patients. It was also hoped to offer HTLV-3 antibody tests to relatives of patients who were found to be HTLV-3 positive. In view of the shortage of reagents, this would be better done by carrying out limited family studies to determine the risk of spread of infection before offering a test to all relatives.

c) Follow-up of sero-positive patients. It was essential that this should be carried out on a large sample of patients and that this should be related to reports of AIDS related illness to obtain an accurate picture of the prognosis of HTLV-3 infection.

d) Future HTLV-3 antibody prevalence surveys Much information might be obtained by repeating the survey in one years time to obtain an objective picture of the sero-conversion rates in one year. This would be related to treatment as reported in the Oxford returns during any year.

1) The results of these serological tests for HTLV-3 antibody so far carried out at CPHL and the Middlesex would be pooled, and a file generated at Manchester in the computer to form the basis of a register of patients with known HTLV-3 antibody status.

2) Haemophilia Centre Directors would be offered the chance of testing as many of their patients as they wished within the next three months. Haemophilia Centres would be asked to send sera to either Dr. Tedder (Middlesex Hospital) or Dr. Mortimer (CPHL) for antibody testing. Copies of each report would be sent to Dr. Craske at PHL Manchester, who would enter the results on a computer. The names, age and register number of each patient tested would be confirmed against the Oxford register to avoid confusion and mistakes due to clerical errors. A suitable request form would be generated for each request by Dr. Craske. Information concerning the presence or absence of illness possibly related to AIDS would be ~~sort.~~ sought.

3) Suitable specimen tubes could be supplied by the testing laboratories for each Haemophilia Centre. Adherence to the relevant codes of practice for the despatch of serum specimens by post would be requested, including notification of despatch of specimens from Haemophilia Centres to testing laboratories.

4) It was essential that follow up of a large enough sample of patients who are changed to heat treated factor VIII were organised to determine the precise risk, if any, of HTLV-3 infection, since no precise information was available concerning the effect of 'dry' or 'wet' heat treatment. Since the contamination rate for unheated NHS and commercial factor VIII was unknown it was important to examine as large a number of batches as possible.

5) Outline of prospective studies of heated factor VIII

		Clinical examination
Patient changed to heat treated factor VIII:		test for HTLV-3 antibody WBC and differential, including absolute lymphocyte count. Total immunoglobulins, platelet count.
Start new product:	1st batch: a)	Test positive for HTLV-3 antibody. No further follow up unless clinically indicated, e.g., patient with AIDS related disease.
	b)	Test negative for HTLV-3 antibody. Repeat test 6 weeks later also clinical examination. WBC & differential Absolute lymphocyte count, total immunoglobulins, plateletcount.
	2nd batch	repeat HTLV-3 antibody test and clinical and laboratory investigations at 0 and 6 weeks. Further specimens could be taken at other intervals, but since facilities for HTLV-3 antibody testing are limited, these will have to be tested retrospectively by arrangement with the testing laboratory.

Specimens would only be examined other than as specified above if the patient developed symptomatic illness possibly associated with HTLV-3 infection. The aim will be to study 4 or 5 patients per batch and at least 20 batches for each product. It would be open to any Haemophilia Centre Director to carry out additional studies if he wished.

Dr. J. Craske