REFERENCE 6

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ABSENCE OF ANTIBODIES TO AIDS VIRUS IN HAEMOPHILIACS TREATED WITH HEAT-TREATED FACTOR VIII CONCENTRATE

SIR,—In healthy haemophiliacs treated with clotting factor VIII concentrates made from large plasma pools there is a high rate of seropositivity for the probable agent of AIDS, the retrovirus known as lymphadenopathy-associated virus (LAV) or human T-lymphotropic virus type III (HTLV-III). The prevalence of LAV/HTLV-III antibodies ranges from 34% to 74%[1,2] depending on the plasma sources (paid or unpaid donors) and treatment intensity.[3]

The Medical and Advisory Council of the National Hemophilia Foundation and the Centers for Disease Control have recommended that heat-treated factor VIII concentrates be used preferentially in haemophiliacs.[4] This recommendation is based on the fact that retroviruses are sensitive to heat inactivation in vitro[5] and on the assumption that heated concentrates carry a lower risk of transmitting the agent of AIDS. There is, however, no clinical or serological information on the reduction of LAV/HTLV-III infection in patients treated with heat-treated concentrates.

We have studied the rate of LAV seroconversion in 18 previously untreated patients with haemophilia A (7 with severe, 5 with moderate, and 6 with mild haemophilia). The patients were exclusively given a heat-treated factor-VIII concentrate ('Hemofil T', Hyland). The concentrate lots were collected and manufactured in 1982–83 and the treatment period lasted from December, 1982, to June, 1984. Clinical details are summarised in the table.

A matched control group of 29 patients, also previously untreated (20 with severe, 7 with moderate, and 2 with mild haemophilia), was chosen retrospectively because the patients had been treated with equivalent doses of various brands of non-heated commercial concentrates during the same period of time as the test group.

In the test group, blood was sampled before the first infusion and 6 and 12 months afterwards. In the controls samples were taken at least 6 months after the last infusion.

The test group had samples assayed by ELISA[6] and by either radioimmunoprecipitation assay (RIPA) (methionine), detecting antibodies to p25, or RIPA (cysteine) (L.Montagnier, unpublished), detecting antibodies to p18, p25, and membrane glycoprotein gp110. Since preliminary work[7] has shown the excellent correlation between results of tests done by ELISA and RIPA, the control group was assayed by RIPA.

None of the 18 patients in the test group were anti-LAV positive before or after treatment. 5 of the 29 controls (17%) were seropositive (see table). No patient has any symptom of AIDS or AIDS-related diseases and the 5 anti-LAV-positive controls have no risk factor for AIDS other than treatment with factor VIII concentrates.

In-vitro heat-inactivation studies[5] have shown that retroviruses are heat sensitive. Thus, any infective virion particles in the large plasma pools from which the heated concentrates were made would probably have been disrupted by the heat treatment. It is possible that precautionary measures taken by the manufacturers, such as accurate donor-screening and the avoidance of plasma collection in

CHARACTERISTICS OF TWO GROUPS OF PATIENTS TREATED WITH HEATED FACTOR VIII CONCENTRATE VERSUS NON-HEATED AND PREVALENCE OF ANTIBODIES TO LAV

	Test group (n = 18)	Control group (n = 29)
Mean age (yr) (range)	9 (0·25–58)	13 (2–50)
Factor VIII concentrate	Heated (US)	Non-heated (US)
Period of treatment	Dec 1982–June 1984	1982–1984
Mean total dose (IU) (range)	9711 (240–66 720)	7700 (1000–83 540)
Antibodies to LAV	0/18	5/29 (17%)

AIDS endemic areas, have also helped to prevent contamination of plasma pools. The absence of seroconversion to anti-LAV in the test group may therefore be due to a combination of precautionary measures and heat treatment. Long-term studies are needed to establish whether this product protects haemophiliacs treated more intensively over longer periods.

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