NOT FOR PUBLICATION

COMMERCIAL IN CONFIDENCE

The Safety of Heat Treated Factor VIII

Introduction

At a meeting on AIDS held in Newcastle on February 12, Dr Peter Jones Director of the Newcastle Haemophilia Centre made a public statement that he felt heat treated Factor VIII was not safe as regards transmission of HTLVIII. He cited a case in Holland and several cases in the USA. Since then Dr Jones has written to the CSM with anecdotal evidence, particularly citing the Armour product "Factorate HT". Dr Jones' letter is included as an appendix to this paper.

The comments he makes are discussed below together with the results of discussion with physicians at the University Hospital of Amsterdam, Dr D Arenson of the Bureau of Biologics and representatives of Armour Pharmaceuticals.

1.1 Dr Jones Statement

	Product	Source of Information
"Adult haemophiliac followed for almost a year on HT material, heterosexual, no other risk factors, repeatedly tested after being seronegative.	Armour	Dr Breederveld, University of Amsterdam. Permission to quote given February 1986"

Comment

This patient has been discussed with Armour and with his physician.

The patient is a severe haemophiliac with no other apparent risk factors treated with cryoprecipitate and non-heat treated Factor VIII until 1983 when he switched to Armour heat treated material. He is getting 40-50 bottles/month of "high purity" concentrate. He was negative for HTLVIII antibody in Autumn 1984. In January 1985 he developed malaise and lymphadenopathy and was found to have seroconverted to HTLVIII antibody positive.

Over 1985 the antibody "titre" has risen from 1:200 to 1:1500 but no virus has been cultured from his cells despite repeated attempts in Holland and at the Pasteur Institute.

At present he is well and his lymphadenopathy has resolved. He is continuing treatment with the Armour product. No other patient in Amsterdam has seroconverted despite wide use of Armour material.

This patient received treatment from a batch of Factorate HT which was withdrawn because a donor to it had developed AIDS (see below).

1.2 Dr Jones Statement	Product	Source of Information
"3 haemophiliacs all reported to CDC who appear to "probably" fulfil criteria for seroconversion in one case and "possibly" fulfil criteria in 2 cases.	Not known	Dr Levine. Permission to quote given February 1986"
"Haemophiliac without other risk factors treated at Chapel Hill and reported as seroconversion after HT material.	Hyland	Reported to Professor Manucc February 1986"

Comment

Bureau of Biologics (BOB) confirm that there is a patient at Chapel Hill who seroconverted after receiving huge doses of heat treated material (Hyland) for injuries sustained in a road traffic accident. He also received red cell transfusions. This patient is a long standing intravenous drug abuser.

Dr Levine who is cited as the source of the other cases is the co-ordinator for the National Haemophilia Foundation in the USA. He is in close contact with the BOB and between them they know of no other case in the USA who has seroconverted after heat treated material.

1.3 Dr Jones Statement	Product	Source of Information
"Virus detected in material subjected to heating for less than 34 hours. One product said to cause seroconversion.	Armour	Dr Koerper, University of California, San Francisco, also quoting work of Dr Levy, December 1985."

Comment

Armour do not know of this, neither do the BOB. In fact there is no report in the literature of live virus ever being grown from Factor VIII heat treated or not.

1.4 Dr Jones Statement

"Seroconversions in the FDR were also reported to a meeting of the Haemophilia Society in November 1985.

David Watters, co-ordinator
Haemophilia Society,
London, February 1986"

Comment

I have not been able to confirm this.

2. Heat Treated Factor VIII

The status of currently used products is given below. The Hoechst material is not marketed in the UK at present.

FACTOR VIII - HEAT TREATMENT - CURRENT POSITION (FEBRUARY 1986)

Company	Wet/dry	Temperature	Duration	Screened donors
Licensed				
Armour	Dry	60°	30 hours	Yes
Alpha	Heptane Suspension	60°	20 hours	95%
Immuno Factor VIII	Dry	60°	10 hours	Yes
FEIBA	Dry	80°	10 hours	Yes
Cutter/ Miles	Dry	68°	72 hours	Yes
Hyland	Dry	60°	72 hours	Yes
Hoechst	Wet	60°	10 Hours	Yes

- All the commercial companies are carrying out spiking experiments to show the safety of their procedures.
- The PFC in Edinburgh are setting up a system to test their own procedures and those of the Elstree Centre.

4. Armour Batch Number Y69402 (Heat-Treated)

This batch was withdrawn in the UK in 1985 because a donor contributing to it had developed AIDS. The same donor also contributed to another batch given to the patient in Holland (this second batch was not distributed in the UK).

12 patients in the UK received Y69402 and are being followed up.

5 patients were HTLVIII ab +ve before treatment with Y69402.
1 patient has died from liver disease (not related to AIDS).
5 are still seronegative 1 year after treatment.

1 patient has seroconverted. Information on this patient has been obtained from his physician

The patient is a mild haemophiliac who has no other risk factors. He was tested for HTLVIII antibodies in January 1985 and found to be negative. He had received no treatment since 1980.

In February 1985 he received two bottles of batch Y69402 and HTLVIII antibodies were found in May 1985 and confirmed in November 1985. Testing was by ELISA - no Western blot has been done. T cell subsets are normal although Trosettes are said to be "slightly abnormal". The patient remains well.

5. Summary

There are three known cases of seroconversion for HTLVIII antibody after heat treated Factor VIII.

One - the American case - appears to have other risk factors. This case is associated with the Hyland product.

Two cases seroconverted after treatment with Armour material from a batch known to contain an AIDS donor.

GRO-C

4 March 1986

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