

Chronology of HRL Investigation of Liverpool Post-Transfusion HIV Infection (March/April 1997)

STRICTLY CONFIDENTIAL

- March 10th (Mo)** • John Craske called to indicate that a new specimen from a patient with AML, whose previous specimens of 11/96 and 2/97 had given conflicting serological findings in Liverpool and Manchester, was being sent to us
- 12th (We)** • Receipt of index case's blood specimen directly from Liverpool (97-13392; 10.3.97)
• **Biotest positive** [OD/CO: 10.0] & **Innotest positive** [OD/CO: 6.3] results
- 13th (Th)** • **GACPAT HIV 1 positive** [CO/OD: 11.1]
- 14th (Fr)** • **GACPAT HIV 2 negative** [CO/OD: 0.15]
• 'Anti-HIV 1 Detected' report telephoned to Drs Craske and Tong (Liverpool). Indicated it was very unlikely not to represent the presence of anti-HIV 1 in the specimen, but further tests were being done, including Western blot, PCR and HIV p24Ag.
- 17th (Mo)** • **IgG/IgM/IgA results. IgG anti-HIV only present** - NOT indicative of very recent seroconversion [sometimes associated with ambiguous serology]
- 19th (We)** • **Western blot findings** [p24: 1+; gp160: 1+; gp41: ??] communicated.
• First follow-up blood from index case (97-14604; 13.3.97) received.
- 20th (Th)** • **Amplicor (PCR) positive** results on 97-13392 communicated.
• Written report of findings to date issued
• **GACPAT HIV 1** [CO/OD: 3.3] result (97-14604)
• Possibility of P.T. HIV infection communicated by PPM to Angela Robinson, NBA
• Current sexual partner, and other possible sources of infection, such as HCW and cross-infection while in hospital had not been excluded at this time
• Look-back exercise instigated by NBS
- 21st (Fr)** • **HIV p24 Ag positive** result communicated (97-13392 & 97-14604)
• **Biotest** [OD/CO: 10.2] & **Innotest** [OD/CO: 6.6] **positive** results (97-14604)
• **GACPAT HIV 2 negative** [CO/OD: 0.18] result (97-14604)
• 'Anti-HIV 1 positivity confirmed' report given by telephone on basis of similar positive findings on the second specimen (97-14604)
• It is believed that the index case was informed of her HIV status on this day and that blood was indicated as a possible source
• JVP briefed Jill Dhell (MDA) on problems associated with 'antigen sandwich' assays.
• JVP briefed Vicki King (DoH) on possibility of post-transfusion HIV
- 26th (We)** • 'Anti-HIV 1 positivity confirmed' written report issued on second positive specimen (97-14604)
• Liverpool informed JVP that the sexual partner had been found to be anti-HIV negative. [At some stage in the next few days an HCW who had been involved in a percutaneous injury when treating the index case was also found to be anti-HIV negative.]
- 27th (Th)** • Pre-treatment specimen (97-16579; 09.07.96) from index case and further follow-up specimen (97-16580; 24.03.97) received.
- 28th-31st** • *Long Easter Weekend*

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- April 1st (Tu)**
- 97-16579 (09.07.96) Innotech; Biotest; IgG; IgM; IgA all unreactive
 - 97-16580 (24.03.97) Innotech; Biotest; IgG: all reactive; IgM; IgA unreactive
- 2nd (We)**
- 97-16579 (09.07.96) GACPAT HIV 1 unreactive
 - 97-16580 (24.03.97) GACPAT HIV 1 reactive
- 3rd (Th)**
- 97-16579 (09.07.96) GACPAT HIV 2 unreactive
 - 'Anti-HIV 1/2 not detected' written report issued on pre-treatment specimen (97-16579), thus indicating that infection had probably occurred during July-Nov 1996
 - 97-16580 (24.03.97) GACPAT HIV 2 unreactive
 - 'Anti-HIV 1 positivity confirmed' written report issued on final (third) positive specimen (97-16580).
 - Residual ~250µl aliquots of 72 donations given in second half of 1996 to recipient (~40 rescreened donors excluded) received at HRL (17.00hrs)
- 4th (Fr)**
- All donations screened by Biotest HIV 1/2 EIA; ONE specimen (97-17863; 880351KX) was weakly reactive
 - Biotest results telephoned to Dr Martlew; suggested weak positive result was probably not significant
- 7th (Mo)**
- Biotest reactive specimen (97-17863) found to be negative for IgG, IgM and IgA anti-HIV, confirming that the Biotest reaction was non-specific
 - Residual donor sera formed into 8 pools of 9 (30µl each)
 - 200 µl of each pool RNA extracted, reverse transcribed and PCR amplified
- 8th (Tu)**
- Pool #7 gave a PCR product of the expected size
 - Finding of an HIV RNA positive pool was communicated to Drs Martlew & Robinson and Prof. Hart (also to CDSC)
 - 50µl of the 9 sera comprising pool #7 were then extracted and tested by RT-PCR
- 9th (We)**
- A single specimen (97-17848; 679315KO) was found to contain HIV RNA
 - Finding of a single HIV RNA donor serum was communicated to Drs Martlew & Robinson and Prof. Hart (also to CDSC)
- 10th (Th)**
- Dr King (DoH) and CDSC fully briefed by JVP on all available findings to date at PHLS/DoH Liaison Meeting, PHLS HQ
- 11th (Fr)**
- Phylogenetic analysis of short gag-derived sequence showed the donor's and recipient's viruses clustering next to each other in a tree which included nearly 40 HRL-produced clade B sequences
 - Findings of phylogenetic analysis provided to Drs Martlew & Robinson and Prof. Hart (also to CDSC) and to Dr King (DoH)
- 14th (Mo)**
- Residual ~250µl aliquots of 5 previous donations from the implicated donor received from Liverpool RTC
- 15th (Tu)**
- the version of the Ortho anti-HIV 1/2 EIA in use at the time of the donation was delivered by Ortho and pilot studies including 2 seroconversion panels were performed to ensure the validity of any results
 - 50µl of the 5 previous donations and of the recipient's July 1996 (97-16579) extracted and tested by RT-PCR

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- April - 16th (We)**
- The implicated donation (97-17848; 679315KO), the donor's 5 previous donations and one of the recipient's anti-HIV positive donations from March 1997 (97-16580) and 2 seroconversion panels examined by the version of the Ortho anti-HIV 1/2 EIA in use at the time of the donation
 - **ALL** the donor's were unreactive, confirming that a technical problem at North West RTC was not the cause of the donation being released
 - RT-PCR results on the 5 previous donations and the recipient's pre-treatment bleed were all negative
- 16th (We)**
- Report of investigation of the 72 donor specimens drafted and sent to Dr Martlew, with copies to NBA Medical Director, CPHL Director, PHLS HQ, Vicki King (DoH) and CDSC
 - Second of the three recipients found to be anti-HIV positive (Liverpool)
 - PPM briefed CMO of HRL findings
- 18th (Fr)**
- HIV p24 findings on the implicated donation and 5 previous donations from the same HIV-infected donor should be available
- Further work**
- phylogenetic analysis of *env* sequences
 - serological and molecular studies of a more recent specimen from the infected donor if we can obtain the specimen
 - serological and molecular studies of the 2 other recipients of the HIV window-phase donation

HRL Contributors: *Serological studies*

**Robert Thorp
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Molecular studies

**Francisco 'Paco' Belda
Katrina Barlow
Jon Clewley**

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This summary to be copied to:

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2. Prof Peter Borriello, CPHL Director
3. Dr Barry Evans, Head HIV & STD Divn., CDSC
4. Prof Tony Hart, Academic Sub-Dean, Dept of Med Micro & GUM, Liverpool Univ
5. Dr Angela Robinson, Medical Director, National Blood Authority
6. Dr Vanessa Martlew, Consultant Haematologist, Mersey and Wales Blood Centre
7. Dr Vicki King, DoH, Wellington House