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UK Transmission of HIV 1 by 'Window Phase' Blood Donation

The finding of anti-HIV in a UK blood donation is a rare event. By December 31st., 1996, over 30 million donations had been screened of which only 325 (0.001%) were confirmed as anti-HIV positive (National Blood Authority and Scottish National Blood Transfusion Service). HIV infection in the UK continues largely to be restricted to well-defined groups[1] who are instructed to exclude themselves from blood donation; and because of this and other safeguards, it is believed that the risk of transfusion-transmitted HIV infection in the UK is negligible. Nevertheless, almost one-half of anti-HIV positive donations detected are from repeat donors, and many subsequently admit to HIV-risk behaviours. This suggests that some are regularly donating blood as a means of monitoring HIV status. Repeat donors are more likely than new ones to donate in the 'window' between infection and development of an anti-HIV response when the current screening tests will be negative. We report here such a case, only the second recognised in the UK[2].

A multiply-transfused patient, tested for anti-HIV in preparation for a transplantation procedure, was reactive in an anti-HIV 1/2 assay. Further tests confirmed the presence of anti-HIV 1, HIV 1 proviral DNA and neutralisable p24Ag in two separate specimens. Direct sequencing of PCR product from the *gag* gene indicated a clade B virus. The patient's sexual partner, of 6 years standing, was anti-HIV negative. A serum specimen collected from the patient the month before transfusion (113 units) was anti-HIV, HIV RNA and p24Ag negative. Records showed that some donors who had contributed to the transfusion had donated again, and all of these were again anti-HIV negative. Aliquots (250 µl) of archived serum from the other 72 donors were screened by a sensitive anti-HIV 1/2 assay different to that employed to screen the donations. None contained anti-HIV. RT-PCR for HIV RNA was done on eight pools of nine donations (30µl of each pooled; RNA extracted from 200µl). HIV 1 *env*-specific RT primers were used to prepare cDNA which was subjected to nested PCR. The products were electrophoresed, ethidium bromide stained, and examined for a band of the expected size (500 base-pairs). As one pool yielded this band, its components (50µl of each) were tested singly. One was RT-PCR positive. Phylogenetic analysis of PCR-

amplified *gag* and *env* sequences from this donor's and the index case's HIV showed them to be closely related in clade B [**Figure**]. The RT-PCR positive donation was unreactive in the anti-HIV assay originally employed to screen it (OD/COs: 0.051 & 0.034), as well as in assays for IgM, IgA and IgG anti-HIV and Western blot. However, it contained 150-200 pg/ml of HIV p24 Ag (ICD protocol; neutralisable). The index case had received the platelets from this donation. Archived aliquots of five previous donations from the implicated donor, the most recent given 119 days before, were negative for anti-HIV, p24Ag (specimen diluted 1 in 3) and HIV RNA. When traced, this donor admitted that he knew, when donating, that he should have excluded himself. A blood sample drawn at interview contained anti-HIV 1 and HIV proviral DNA (Roche Amplicor).

These findings are consistent with the index case having contracted HIV from the anti-HIV negative, RT-PCR and p24Ag positive donation from which two others also received components. The red cell recipient had died from unrelated causes, but a pre-mortem serum contained anti-HIV 1. The plasma recipient was anti-HIV 1 and HIV proviral DNA (Roche Amplicor) positive. It was decided, as there are rare reports of the interval between exposure and anti-HIV seroconversion exceeding 6 months[3], to seek to test recipients of the donation collected 110 days previously. The surviving recipient was anti-HIV negative.

This incident reveals that, despite strenuous efforts by the NBS to discourage it, donating blood to check HIV status continues. Those who do this apparently believe, erroneously, that laboratory screening guarantees the safety of their donation. Means of increasing the impact of donor education on each donor, and ready access to confidential HIV testing are needed to minimise these inappropriate donations. The practice of archiving an aliquot of each donation was crucial to investigating this incident, enabling us to show that the infectious donation contained HIV p24Ag and viral RNA. Busch *et al* suggest that the seroconversion window is reduced by about 6 days by adding p24 Ag screening to a 'third generation' anti-HIV EIA[4]. They forecasted 0.4-0.8 anti-HIV negative/ p24Ag positive US donations per million screened (p24Ag screening of North American donors began in the Summer of 1996) . In the UK, where HIV infection is rarer in blood donors, the frequency would be lower and the substantial cost of p24Ag screening might not be justified, especially when the knowledge that more sensitive screening was available

in Blood Centres might attract 'at risk' donors. Detection of HIV RNA has the advantages over p24Ag testing of closing the window further and acting as a check of anti-HIV screening. Moreover, through mini-pooling, accurate and timely PCR screening of blood components may soon become feasible and affordable[5].

In the meantime the importance of impressing upon all donors the necessity of self-exclusion whenever they have put themselves at risk of HIV infection as defined in the leaflet 'DO NOT GIVE BLOOD Without Reading this Leaflet' (DoH G78/036 3666 1P 3m Dec 95 (12)), provided to all donors, cannot be overemphasised. Alone, no laboratory screening test for HIV infection can ever be regarded as infallible.

References

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