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INVESTIGATION OF POSSIBLE TRANSMISSION OF HIV BY BLOOD TRANSFUSION

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ABSTRACT

Objective - To study the transmission of HIV by blood donated from individuals subsequently identified to be infected with HIV.

Design - Retrospective study of previous donations from individuals subsequently identified as infected with HIV. Investigation of donations from individuals believed to have transmitted HIV infection by transfusion. Investigation of donations transfused to recipients later found to be infected with HIV, in whom the only identified risk for infection was blood transfusion.

Setting - North London Blood Transfusion Centre and hospitals receiving blood supplies from the Centre.

Subjects - Twenty-five donors identified as HIV positive; 18 detected through routine screening at the North London Blood Transfusion Centre and 7 notified to the Centre by the donor or an outside agency. Twenty two recipients thought to have been infected with HIV through blood transfusion.

Main outcome measures - Evidence of HIV infection in the recipient of a donation originating from a donor subsequently found to be anti-HIV positive. Identification of a likely or proven HIV infected donor from whom blood or blood components had been transfused to an infected recipient.

Results - Five HIV infected recipients were identified, who had not previously been known to be infected. In addition, the RTC became aware of 2 recipients known to be anti-HIV positive but previously unreported. All infected recipients were transfused before 1985 with unscreened blood or components. Of the possible transfusion-transmitted HIV infections, one third were considered not due to transfusion, one third

thought likely (without the identification of a culprit donor) and 5 donors were identified as likely to have been responsible for 6 reported cases. One case could not be investigated through lack of records and one is still under investigation.

Conclusions - Investigations failed to reveal any infection arising after screening of blood donations commenced in 1985. Overall, 42% of identifiable recipients died within 6 months of transfusion. Eight of 32 (25%) living recipients were infected with HIV and 5 of these were newly detected through the investigation. Laboratory record keeping was generally deficient prior to 1985; accurate recording of transfusion details in patient medical records remains a conspicuous problem up to the date of the report. The investigation confirms the exceedingly small chance of transmission of HIV by transfusion of screened blood and blood components in the United Kingdom.

Introduction

In October 1985 the UK Blood Transfusion Services (BTS) commenced screening all blood donations for HIV antibodies. It was recognised that screening might reveal HIV infection in established donors whose previous (untested) donations had been transfused to recipients. Regional Transfusion Centres (RTCs) agreed to trace the fate of such donations in order to detect any recipients infected prior to the introduction of screening. This procedure is known as "look-back". Since then, screening has identified some donors who have seroconverted during their donation career. In some cases it is necessary to perform look-back on their most recent HIV seronegative donation. A third category of look-back arises when donors, not previously known to be infected with HIV, are implicated as the source of infection in a recipient of blood. Such cases have usually arisen from transfusions given before October 1985, where the donor has not subsequently returned to donate blood and whose HIV status has therefore not previously been known.

To date, there has been no report of systematic look-back on donations transfused in the UK to ascertain whether donors subsequently shown to be infected with HIV have transmitted infection to their recipients. This paper summarises the experience of one UK RTC in the investigation of possible cases of transfusion transmitted HIV infection.

Methods

Look-back when a donor is identified as seropositive

A file is opened for each donor identified as anti-HIV positive on the basis of a positive screening test at North London Blood Transfusion Centre (NLBTC) confirmed by our reference laboratory, (Dept of Virology, University College London Medical School). Note is made of any previous donations and whether they had been tested for anti-HIV. The donor is invited to see the RTC Consultant for counselling and detailed epidemiological information is obtained in order to establish when the infection may have been acquired. Where the previous donation/s has been tested for anti-HIV, laboratory worksheets are examined to ensure that the negative result was valid. If that donation was within the last 12 months and there is no clear indication of possible recent exposure to HIV, additional tests are performed on a frozen "archive" serum sample of the previous donation in order to confirm the negative status.

Look-back is initiated for all components produced from the last donation unless there is clear evidence that the donor became infected after that donation. The Consultant Haematologist in charge of each blood transfusion laboratory which received a component under investigation is asked to trace its fate. The date and cause of death are recorded for recipients who died. The clinician caring for any live recipient is informed of the possibility of HIV infection in the transfused component. Unless there are exceptional circumstances, appropriate counselling and testing of the recipient is advised. Results are logged in the donor file.

For donors who gave donations before routine anti-HIV screening, look-back is performed in a sequential fashion starting from the most recent donation, until two consecutive recipients are shown to be free of infection. If no uninfected living recipients can be

traced, look-back should be performed back to 1977 (the date when HIV infection was theoretically first present in the UK).

Investigation of possible transfusion transmitted infection

Clinicians caring for patients with suspected transfusion transmitted HIV infection complete a confidential report form for the RTC. Information is obtained about the circumstances of the original blood transfusion, the identification and date of all blood components transfused, the presence of any other risk for HIV infection, and the current clinical status of the patient. The RTC traces records relating to all donations transfused to the recipient and ascertains whether the donors have been tested for anti-HIV. Those recorded as anti-HIV negative are eliminated from the enquiry, if there are other donors who are untested. If all donors have been found anti-HIV negative then further specialised testing is performed on fresh and/or archived blood samples in order to confirm these results. Where donors have failed to attend since the introduction of routine anti-HIV screening, records are examined to establish whether there is any epidemiological information which suggests to possible risk for HIV infection. As each year passes, it becomes less likely that individuals who lapsed from donation before 1985 will be contactable since they may have either moved away, died or recognised themselves as unsuitable for donation and therefore not responded to letters from the BTS.

When all information has been gathered, it may be possible to identify a likely "culprit" donor. In these cases, a file is opened for look-back on other donations given by that donor. Where it has been impossible to identify a likely culprit, the enquiry file is left open.

Results

Between October 1985 and December 1992, 47 files were opened. Twenty two cases related to a recipient notified as being infected with HIV and in whom the possible source of infection was transfusion. The remaining 25 files related to donors possibly or probably infected with HIV. A total of 90 blood components were investigated in look-back procedures. (Table 1).

Donor investigations

A total of 25 cases were investigated (Table 2). The majority of infected donors (18) were identified through routine screening of blood donations but in 7 cases information was received from the donor or from a person acting on behalf of the donor that the individual was believed to be infected with HIV, some time after donating blood.

In all 7 cases notified by the donor him/herself or by an outside agency because the donor was thought or known to be infected, no infected recipients were identified. Of the 18 donors detected by the RTC, 14 were identified through routine screening for HIV antibodies and 4 as culprits in cases of transfusion transmitted HIV infection. During investigation of these cases, the RTC was able to identify 5 recipients not previously known to be infected with HIV. In addition, the RTC became aware of 2 recipients known to be anti-HIV positive, but not previously reported to the BTS. The reasons for the lack of reporting are unclear.

All infected recipients were transfused before 1985 with unscreened components.

Recipient notifications

Seven (32%) of the 22 recipient notifications were considered **not** transfusion transmitted infection (TTI), based either on the information supplied or on failure to reveal any HIV infection during full investigation of all the donors (Table 3). In 7 cases, mostly children or adolescents transfused in 1982 or 1983, transfusion transmitted HIV infection was thought likely, but no culprit donor could be identified. In each of these cases there was at least one donor whose anti-HIV status was unknown.

Five "culprit" donors were definitely (or highly likely) identified in 6 cases; one donor was common to 2 recipients. In 2 of these cases, investigated in 1986, a lapsed (suspected "culprit") donor was contacted and interviewed. Each donor had discontinued donation in 1983, when self-exclusion of individuals with risk behaviour for HIV was initiated. Both had subsequently been found anti-HIV positive as a result of hospital consultations, but unfortunately this information had not been forwarded to the RTC. The three "suspect" donors in the other 4 cases were not interviewed, but there was sufficient circumstantial evidence to conclude that each donor was infected with HIV at the time of the implicated donation. Two of the 5 "culprit" donors had given no other donations, but 3 had given previous donations which had been transfused and were therefore investigated. All these donations were given before 1985.

One case could not be investigated as the hospital records were unobtainable and the donations given to the recipient could not be identified. The final case is still under investigation.

Table 1 summarises the outcome of the investigations relating to 90 blood components prepared from the donations which were the subject of look-back. Some donations (particularly in the early 1980s) were issued to hospitals as whole blood; thus only one potential recipient was involved. Other donations were processed into 2, or usually 3,

components:- red cells, platelet concentrate and fresh frozen plasma (FFP) or cryoprecipitate. The FFP may have then been supplied for an individual patient, or manufactured into fractionated blood products at the Bio Products Laboratory (BPL), Elstree. For some donations therefore, there were potentially 2 or 3 identifiable recipients.

In 55 of 90 (61%) cases a blood component was traced to an individual recipient, 42% of whom had died within 6 months of transfusion. In no case was the death thought to be related to the transfusion, even with the retrospective knowledge of the possible HIV positive status of the component. A further 18 recipients (33% of those traced) were not sampled for HIV testing, despite the information from the RTC. In 4 cases the hospital could identify a named recipient who lived abroad and could not be located. Three recipients were over 80 years of age when traced and it was decided, in consultation with family doctors, to take no further action. Five recipients were known to be anti-HIV positive before information about the donor became available; two were infected before the relevant transfusion and three were identified as infected after the transfusion, although only 1 had been notified as such to the RTC. Investigations are continuing in 6 cases. Overall, therefore, 13 (48%) of the identified living recipients of previously unknown HIV status remained untested.

Blood samples were obtained from 14 identified recipients (25% of the total, 52% of the living recipients whose HIV status was unknown) in order to establish whether they had been infected. All were tested at least 6 months, and usually some years, after the transfusion in question. Nine of the 14 (64%) were seronegative and 4 were HIV seropositive. Overall, therefore, 8 of 32 (25%) living recipients were found to have been infected with HIV through the transfusion in question and 5 of these were discovered for the first time because of the RTC's investigation.

There was no identifiable recipient for over one third of the components issued from the RTC. Thirteen units of FFP were supplied for manufacture into fractionated blood products, while 10 components (11% of the total) were not transfused. The remaining 12 components (13% of the total, 34% of those not traced to an identifiable recipient) were issued by the RTC to a hospital, but the hospital was unable to trace the ultimate fate of the component. These cases usually related to the early 1980s when record-keeping was almost universally non-computerised. In all cases, RTC records could identify the destination of the component in question.

Discussion

The investigation of possible transfusion transmitted infection is extremely laborious and time consuming. Investigation must be both thorough and methodical. This involves work for the RTC, hospitals, General Practitioners and FHSAs. Meticulous checking of records at the RTC and hospital laboratory is necessary to ensure that the relevant donation is traced to the correct recipient/s and recorded in the patients' medical notes. It is not uncommon to find that a hospital laboratory has records of issuing a donation for a particular recipient, but the medical notes contain no information about the donations transfused. Such an omission obviously leaves room for doubt when investigating possible cases of transfusion transmitted infection. Hospital laboratory record keeping has generally much improved since the Health Circular relating to Record Keeping and Stock Control (HC (84)7), On the other hand, audits of blood transfusion practice continue to show gross deficits in the recording of information in medical notes (1).

The majority of cases of transfusion transmitted HIV infection arise from blood transfusions given in 1982-1984. As record keeping was not satisfactory at that time, and usually related to non-computerised systems, it can often be difficult and time consuming to retrieve information within the RTC, in the hospital laboratory and in the medical records department. Furthermore, recipients can be difficult to trace if no longer under hospital care. In many instances, recipients have moved home and are no longer registered with the General Practitioner caring for them at the time of transfusion. As contact is made first through a doctor a significant amount of time is spent in correspondence with FHSAs, to trace the appropriate GP. Sometimes the RTC has written to five or six doctors in an individual case (haematologist, surgeon, physician, referring physician, GP) without any of them wishing to take responsibility for notifying the recipient. Not only does this cause extra work, but it considerably delays the investigation. On occasion several reminder letters have been necessary before the RTC has been supplied with relevant information. The period between initiation and

completion of an investigation can be as long as one year. The more distant the transfusion, the longer the investigation will take.

The identification of recipients, not previously known to be infected with HIV, is of benefit to them and their families since awareness of HIV infection leads to the prospect of earlier and prophylactic treatments which may prolong the survival of the infected person. Furthermore, secondary transmission might be prevented. Payment from the Government to those infected with HIV through blood transfusions is an added stimulus on the Blood Transfusion Service to identify as far as possible all those individuals who may have been infected through this route. It is of continuing concern to the BTS that there is no mechanism for checking whether a lapsed donor has subsequently been reported as HIV positive through the confidential reporting system operated by the Communicable Disease Surveillance Centre. The failure of professionals to ask individuals diagnosed as infected with HIV about prior blood donation and then to notify the RTC also leads to missed opportunities to identify all recipients infected with HIV by transfusion. Our investigation of 90 individual blood components led to the identification of 5 HIV seropositive recipients who were in good health and not previously suspected to be infected. Anti-HIV screening of blood donations commenced in 1985 and it is quite likely that there are other infected recipients, transfused before 1985, who have not yet been identified. They are only likely to come to light when they develop symptoms which prompt suspicion of HIV infection.

Overall, 42% of identifiable recipients died within 6 months of transfusion. This figure is consistent with other reports (2-4). Of, the living recipients identified, 8 of 32 (25%) were infected with HIV and the RTC detected the infection in 5 of these. Two of the three infected recipients identified by hospitals were tested as part of programmes looking at multi-transfused bone marrow transplant recipients; the third was tested because of suggestive clinical symptoms. A significant number of living recipients were not tested, for a variety of reasons, although investigations are continuing in some cases. Certain

recipients could not be traced by the hospitals and in other cases the hospital medical records did not contain documentation of the transfusion given. This defect has been noted elsewhere (1).

Our investigations have failed to reveal any infection arising after screening of blood donations commenced in 1985. This confirms other reports of the very low risk of HIV infection transmitted by screened blood (5) despite the theoretical possibility of an infectious but seronegative donation being given during the "window period" of HIV infection (6).

The French national register of transfusion-transmitted infection recorded 54 reported cases of HIV infection allegedly transmitted by blood components after the implementation of donor HIV screening up to September 1990 (7) Of the 33 cases investigated, 10 were established, 18 probable and 5 presumed. All cases occurred between 1985 and 1988. The majority (11/19) of implicated donors had donated in the "window period", but 3 cases were due to erroneous release of seropositive units. A recent report from a United States multicentre study of transmission of retroviruses from seronegative donors to recipients who underwent transfusion during cardiac surgery found that 2 of 9294 recipients became infected with HIV through transfusion of a total of 120,312 units of anti-HIV screened blood and components (8). In each case a donor who had seroconverted for HIV following the donation in question was identified. In the United Kingdom, the seroprevalence of HIV in blood donors is significantly lower than in the United States and France; the risk of transmission of HIV through the transfusion of screened blood is correspondingly much lower. There has been only one such documented case in the UK since screening began (9) during which time approximately 20m units of blood and components have been transfused. Our look-back data confirms the rarity in the UK of donations being given in the "window period" of HIV infection. This information should be of use when advising potential recipients of blood donations who wish to know the current risk of HIV infection through transfusion.

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Legends for Tables

Table 1. Outcome for 90 blood components prepared from donors subsequently shown to be anti-HIV positive (1982-1992).

Table 2. Investigations of recipients for transfusion-transmitted HIV infection, following notification that the relevant donors were likely to be HIV infected.

Table 3. Notification of HIV infection in recipients.

Table 1

Total No. of components investigated = 90			
Individual recipient identified	(n=55)	No recipient or recipient untraced	(n=35)
recipient dead within 6 months of transfusion	23	plasma manufactured into fractionated blood products	13
recipient not sampled	18	fate of component not traced by hospital	12
investigations incomplete,	6		
abroad, not contactable	4	component not transfused	10
aged >80	3		
known to be anti-HIV positive post transfusion	3		
known to be anti-HIV positive pre transfusion	2		
recipient sampled	14		
anti-HIV negative	9		
anti-HIV positive	5		

Table 2

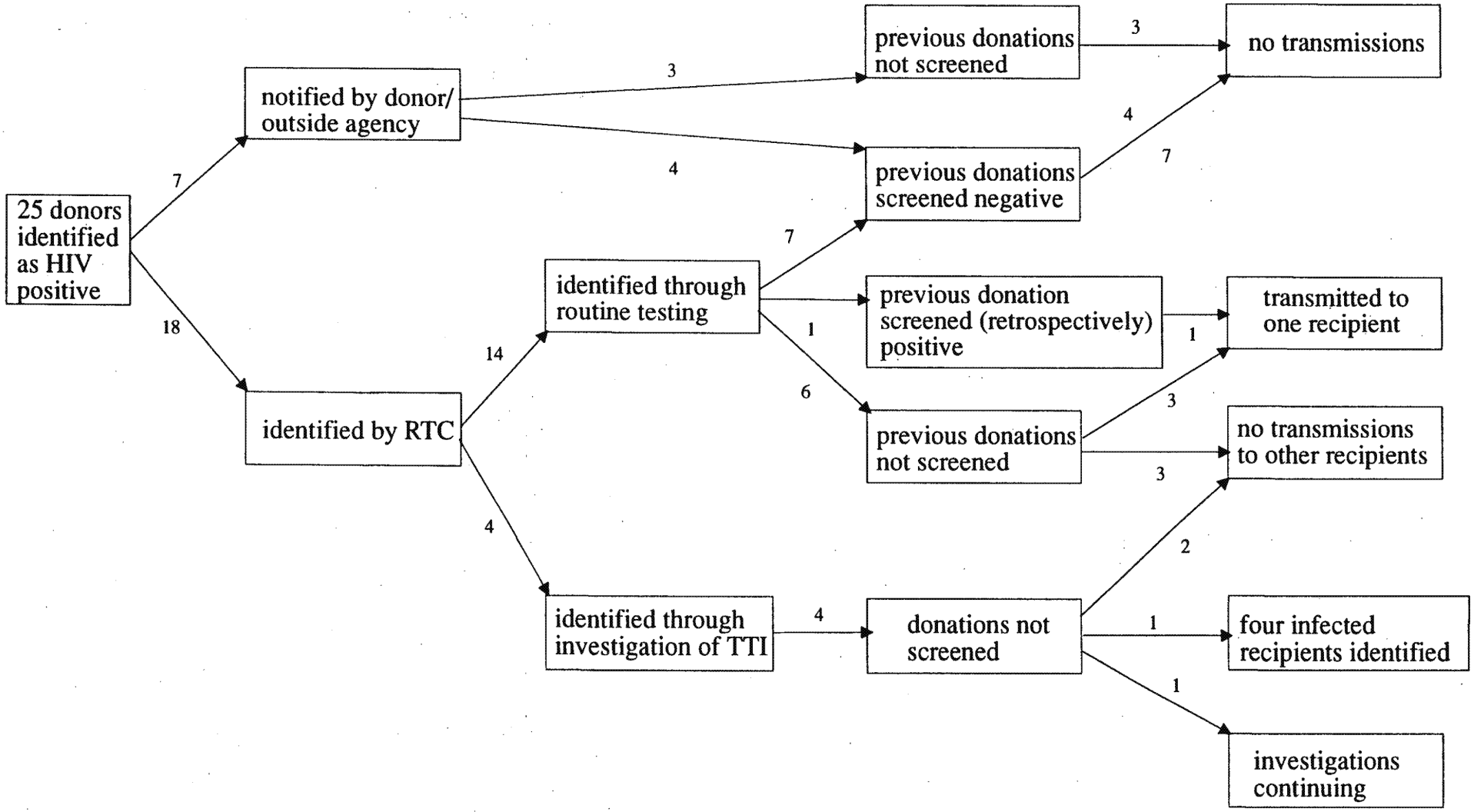

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Table 3

22 recipients -	7 cases -	not transfusion transmitted infection (TTI)
	7 cases -	likely TTI, no infectious ("culprit") donor identified
	6 cases -	culprit donor identified
	1 case -	not investigated (lack of hospital records)
	1 case -	investigation continuing

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