13. TRANSFUSION-TRANSMITTED INFECTIONS

Introduction

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. The onset of symptoms related to a transfusion-transmitted viral infection may occur several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in a particular year therefore accrue over the subsequent year(s). The number of cases ascertained by the end of any period of time is therefore expected to be an incomplete picture of the infections transmitted during that period. Acute infections, such as bacteraemias, that tend to be clinically apparent and diagnosed soon after receipt of the infectious transfusion, may be relatively complete but chronic viral infections will be underrepresented.

In addition, the occurrence of disease, or the observation of serological markers of infection, in individuals who have donated blood can lead to the ascertainment of transfusion-transmitted infections by tracing and testing of recipients exposed to components collected from donors during potentially infectious periods. Recipients may be asymptomatic at this time and only identified by this investigation.

Infections presenting weeks, months or years following a transfusion are termed post-transfusion infections (PTI). These may indeed be due to an infected (or contaminated) transfusion, but equally, infection may have been acquired from another source. Investigation of markers of infection in an implicated donation, or in subsequent samples from the donors of implicated donations, can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. The blood service must therefore be informed about implicated transfusions so that investigations can be conducted to confirm or refute the suspicion that the implicated transfusion(s) may have been infectious. This is essential to prevent further transmission(s) by other components and/or by chronically infected donors. Such investigations may involve microbiological testing of many donors and may take several months to complete.

A surveillance system to collect standardised information about infections suspected to have been transmitted by transfusion was introduced in the British Isles (excluding Scotland) and the Republic of Ireland by the National Blood Authority and the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) in October 1995.

Methods

Participating blood centres reported all post-transfusion infections, of which they had been informed, to the NBA/PHLS CDSC infection surveillance system. The criteria for identifying infections eligible for reporting as post-transfusion infections were either: a) the receipt of the transfusion had been confirmed and the infection had been confirmed in the patient (by detection of antibody, antigen, RNA/DNA or culture) and there was no evidence that the recipient was infected prior to transfusion, or, b) the receipt of the transfusion had been confirmed and the recipient had acute clinical hepatitis of no known cause (including no evidence of acute HAV, HBV, HCV, EBV or CMV infection in post-transfusion samples to date). If other possible sources of infection were known for a post-transfusion infection, an initial report was still requested.

Information about the recipient, the recipient's infection and the transfusion(s) implicated as the possible source of infection formed the basis of the initial report. Subsequently, after appropriate investigations had been completed, details about the findings of the investigation, were reported. (The report form is shown in Appendix 4).

A post-transfusion infection was classified as a transfusion-transmitted infection if the following criteria were met at the end of the investigation:

- the recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion
  and, either
- at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection,
  or
- at least one component received by the infected recipient was shown to have been contaminated with the agent of infection.

Data received by 31/12/97, about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/96 and 31/9/97, are included in this report. Data received about incidents reported during the previous (first) year of the surveillance system are also briefly described.

Incomplete investigations were classified as post-transfusion infections of undetermined source, unless the investigation was closed due to the identification of a probable source of infection other than transfusion.

Results

Twenty-five reports of post-transfusion infections were initiated by blood centres during the report year. An additional 6 reports were received about post-transfusion reactions that were suspected to be due to bacteria but for which no evidence of bacterial infection (or endotoxin) that could have caused the reaction was sought and found in the recipient or in the implicated component (i.e. although the reaction did not satisfy the criteria for a post-transfusion infection as stated above, it may have been of bacterial origin). Reports were received from eight of the 21 blood centres (between 1-6 cases each) participating in the surveillance system. These eight centres collect approximately 60% of the donations tested by blood centres participating in the surveillance system. One hospital (one clinician) reported two post-transfusion infections.

Of the 25 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/96 and 30/9/97, 8 (32%) were classified, after appropriate investigation, as transfusion-transmitted infections. None of the 6 post-transfusion reactions suspected to be due to bacteria were clearly shown to be due to transfusion-transmitted bacteria. For 4 of the 6 post-transfusion reactions suspected to be due to bacteria, details about microbiological testing of samples from the recipient were not available. Table 15 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/96 and 30/9/97 by year of transfusion: 4 were transfused during the report year, and 4 were transfused prior to the report year.

Table 15: Transfusion-transmitted infections reported between 1/10/96-30/9/97 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	1995	1996	1997 (to end Sept)	Total
Infection				
HAV	-	1(1)	-	1(1)
HBV	-	1(1)	-	1(1)
HCV	-	1(1)	-	1(1)
HIV	-	1(3)	-	1(3)
Bacteria	-	-	3(3)	3(3)
Malaria	-	-	1(1)[a]	1(1)[a]
Total	-	4(6)	4(4)	8(10)

Notes: [a] Infection was implicated in the death of the recipient.

Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory.

Hepatitis B virus

One transfusion-transmitted HBV infection was reported. This investigation was initiated because the recipient had acute HBV infection five months after transfusion of three red cell units. One of the donors was found to have markers of resolved HBV infection eleven months after donating the implicated donation. An HBV infectious, HBsAg negative (and anti-HBc negative), donation collected from a repeat donor during acute (asymptomatic) infection was concluded to be the probable source of the recipients HBV infection.

Hepatitis C virus

One transfusion-transmitted HCV infection was reported. This investigation was initiated because a repeat donor was shown to have seroconverted for anti-HCV between donations. The recipient was traced and tested for HCV infection, seven months after transfusion with a red cell unit from this donor.

The pre-seroconversion donation was subsequently shown by testing of the archived sample to be HCV RNA positive. An HCV infectious, anti-HCV negative, donation collected from a repeat donor during acute (asymptomatic) infection was concluded to be the probable source of HCV infection for the recipient.

HIV

One transfusion-transmitted HIV infection was reported. This investigation was initiated because the recipient developed clinical features consistent with HIV infection, and was found to be anti-HIV positive. This recipient had received over 100 units of red cells and platelets over a seven month period. The archived sample of one donation (giving rise to a platelet unit transfused to the patient), from a repeat donor who had not donated subsequently, was found to be HIV DNA positive. The donor was subsequently found to be anti-HIV positive. An HIV infectious, anti-HIV negative, donation collected from a repeat donor during acute (asymptomatic) infection was concluded to be the probable source of the recipient's HIV infection[27]. The recipients of the red cells and the fresh frozen plasma produced from the infectious donation were subsequently shown to have also been infected with HIV by transfusion (one recipient had died of non-HIV-related causes by the time of the follow-up).

B. Infections for which donation tested is not mandatory.

Hepatitis A

One transfusion-transmitted HAV infection was reported. This investigation was initiated after a donor reported HAV infection that developed ten days after donation. The recipient was traced and tested for HAV infection, one month after transfusion with three red cell units. An HAV infectious donation collected from a donor during acute (asymptomatic) infection was concluded to be the probable source of HAV infection for this recipient[28]. The recipient of the platelets from the implicated donation was found to be non-immune and not infected.

Bacteria

Three transfusion-transmitted bacteraemias were reported.

One recipient developed endotoxic shock after transfusion with a red cell unit. The red cell unit was subsequently found to be haemolysed and was shown to contain *Serratia liquifaciens*. No evidence of infection was found in the donor by arm swabbing and by testing blood for antibodies. The source of the contamination was not identified.

One recipient suffered a bacteraemia after transfusion with a platelet unit. *Escherichia coli* was cultured from the pack and from the patient. No damage to the pack or source of the contamination was identified.

One recipient suffered a bacteraemia after transfusion with a leucodepleted pooled platelet unit. The pack and an arm swab from one of the four donors were both yielded *Bacillus cereus*, serotype H29.

Malaria
One transfusion-transmitted malaria (*Plasmodium falciparum*) infection was reported. The recipient developed cerebral malaria two weeks after transfusion with two red cell units and died within two weeks of diagnosis. One new donor was found to have malarial antibodies when a subsequent sample was tested.

Details of post-transfusion infections not concluded to be transfusion-transmitted infections

Four (16%) post-transfusion infections (1 bacteraemia, 1 HBV infection, 2 HCV infections) were eventually classified as 'post-transfusion infections of undetermined source' due to incomplete investigation of the transfusion(s) implicated as the source of infection. One post-transfusion bacteraemia was classified as "undetermined" because the blood pack was destroyed at the hospital and was therefore not available for testing. For 7 (28%) other post-transfusion infection reports (5 HBV infections, 2 HCV infections), investigation was completed and no evidence was found to implicate transfusion as the source of infection. A probable source of infection other than transfusion was identified for 4 of these infections (HBV: surgery at a time and place associated with other cases, household and sexual contact with infection; HCV: renal dialysis, previous transfusion prior to anti-HCV testing of donations in UK).

Reporting delay

For the 8 transfusion-transmitted infections, the median interval between the transfusion and the diagnosis of the infection in the recipient was 44 days (range 0 days for the three bacteraemias to 224 days for the HCV detected by tracing the recipient after observing seroconversion in the donor). The median interval between diagnosis and blood centres being informed that the infection was suspected to be associated with transfusion was 1 day (range 0 days for the 3 bacteraemias to 98 days for the HBV infection). The median interval between the blood centre being informed and the completion of the initial surveillance report form was 54 days (range 7 days to 194 days). The median interval between the transfusion and completion of the initial surveillance report form was 134 days (range 29 days to 361 days).

Underreporting

The cases ascertained by this surveillance system were diagnosed, suspected to be attributable to transfusion, communicated to the blood service, and reported by a blood centre to the surveillance centre. At any one of these steps, other post-transfusion infections may have been missed and the extent of underreporting of post-transfusion infections is therefore unknown. More widespread testing of transfusion recipients, a heightened awareness of transfusion as a possible source of infection and improved reporting of information to blood centres and from blood centres to the surveillance centre would improve case ascertainment.

Previous year

During the first year of this surveillance system for post-transfusion infections (1/10/95-30/9/96), 15 post-transfusion infections were reported. Five were classified, after investigation, as transfusion-transmitted infections (1 HBV infection, 2 HCV infections and 2 bacteraemias: 1 group B streptococcus and 1 *Bacillus cereus*[29]). Two post-transfusion infections (1 HBV infection, 1 HCV infection) were classified as post-transfusion infections of undetermined source due to incomplete investigation of the transfusion(s) implicated as the source of the infection. For 8 (53%) post-transfusion infection reports (4 HBV infections, 4 HCV infections), investigation into the case was completed and no evidence was found to implicate transfusion as the source of infection. A probable source of infection other than transfusion was identified for 4 of these infections. Table 16 shows the cumulative number of transfusion-transmitted infections reported up till the end of September 1997.

Table 16: Cumulative total of transfusion-transmitted infections reported between 1/10/95-30/9/97 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	1980's (i.e. pre anti-HCV testing)	1995	1996	1997 (to end Sept)	Total
Infection					
HAV		-	1(1)	-	1(1)
HBV		1(1)	1(1)	-	2(2)
HCV	2(2)	-	1(1)	-	3(3)
HIV		-	1(3)	-	1(3)
Bacteria		1(1)	1(1)	3(3)	5(5)
Malaria		-	-	1(1)[a]	1(1)[a]
Total	2(2)	2(2)	5(7)	4(4)	13(15)

Notes: [a] Infection was implicated in the death of the recipient.

Comments

- Reported transfusion-transmitted infections are rare incidents, with only 8 confirmed cases recognised during a 12-month period. One transfusion-transmitted infection (malaria) resulted in the death of the recipient. A further 17 post-transfusion infections could not be clearly linked to a transfusion, as well as 6 post-transfusion reactions suspected to be due to bacteria. Infections transmitted by transfusion between 1/10/96 and 30/9/97 will continue to be ascertained by the surveillance system as diagnoses are made during future years.

- Two of the transfusion-transmitted infections (1 HAV, 1 HCV) were identified by the blood service after the diagnosis of an infection in a blood donor.

- Three transfusion-transmitted infections (1 HBV infection, 1 HCV infection, 1 HIV infection) were due to donations collected from donors during marker negative "window periods" following recent infection. All 3 were in 'repeat' donors.

- Five transfusion-transmitted infections (1 HAV infection, 1 malaria infection, 3 bacteraemias) were due to collection of donations from donors with infections for which no routine testing of donations is performed. One bacteraemia was due to contamination of the blood pack from the donor's arm; two bacteraemias were due to contamination of the blood pack from an unidentified source. The numbers of cases are too small to draw any conclusions about the risks of leucocyte depleted platelet concentrates.

- Thorough investigation of a suspected bacteraemia in a transfusion recipient relies heavily on the collection and handling of relevant samples at the hospital where the transfusion was performed. In 4 of 6 post-transfusion reactions suspected to be due to bacteria reported this year the lack of appropriate samples prevented proper investigation.

- The malaria transmission related to a donor who had been resident in a malarious area as a child. Donor selection criteria have now been amended to exclude such individuals permanently as cell donors, unless they have been shown to be negative for malaria antibodies.

- No reported transfusion-transmitted infections were due to errors in the performance of microbiological testing, or in the release, of blood donations.

Recommendations

- National collation of data arising from these cases needs to continue over several years to build up a picture of the extent and nature of the infectious complications of transfusion.
- Clinicians should report all post-transfusion infections diagnosed in their patients to their supplying blood centre, without delay.
- Hospitals should not destroy blood components implicated in post-transfusion reactions suspected to be due to bacteria, and should consult the blood service about the investigation of such cases.
- Standard protocols for investigating post-transfusion infections should be developed and used.
- Methods and criteria used to exclude those individuals who have risk factors for transfusion transmissible infections from donating blood deserve continuing evaluation and development.