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 from several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in a particular year can 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 within days of 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.

Post-transfusion infections (PTI) may be due to an infected (or contaminated) transfusion or 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, thus confirming the infection as transfusion-transmitted (TTI). Alternatively, the need to investigate other possible sources of infection may be identified. 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. A parallel system is in place in Scotland; no confirmed cases were reported in Scotland during this report year.

Methods

Participating blood centres (see above) 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 in the recipient had been confirmed (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. (PTI report forms are in Appendix 5).

A post-transfusion infection was classified as a transfusion-transmitted infection (TTI) 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 31/12/98, about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/97 and 30/9/98, were included in this report. Data received about incidents reported during the previous two years of the surveillance system are included in a cumulative table.

Unless the investigation was closed due to the identification of a probable source of infection other than transfusion, investigations that were closed without being able to conclusively investigate the source of the post-transfusion infections were classified as post-transfusion infections of undetermined source.

Results

Thirty-five initial reports of post-transfusion infections were made 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 implicated component (i.e. the incidents did not satisfy the criteria for a post-transfusion infection as stated above, but may have been reactions of bacterial origin). Reports were received from 12 of the 21 blood centres (between 1-7 cases each) participating in the surveillance system. These 12 centres collect approximately 87% of the donations tested by blood centres participating in the surveillance system.

Figure 13 shows the classification of reports during the report year. Of the 35 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/97 and 30/9/98, 4 (11%) were classified, after appropriate investigation, as transfusion-transmitted infections. Table 20 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/97 and 30/9/98 by year of transfusion: Two were transfused during the report year, and 2 were transfused prior to the report year.

Figure 13
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 1/10/97 and 30/9/98

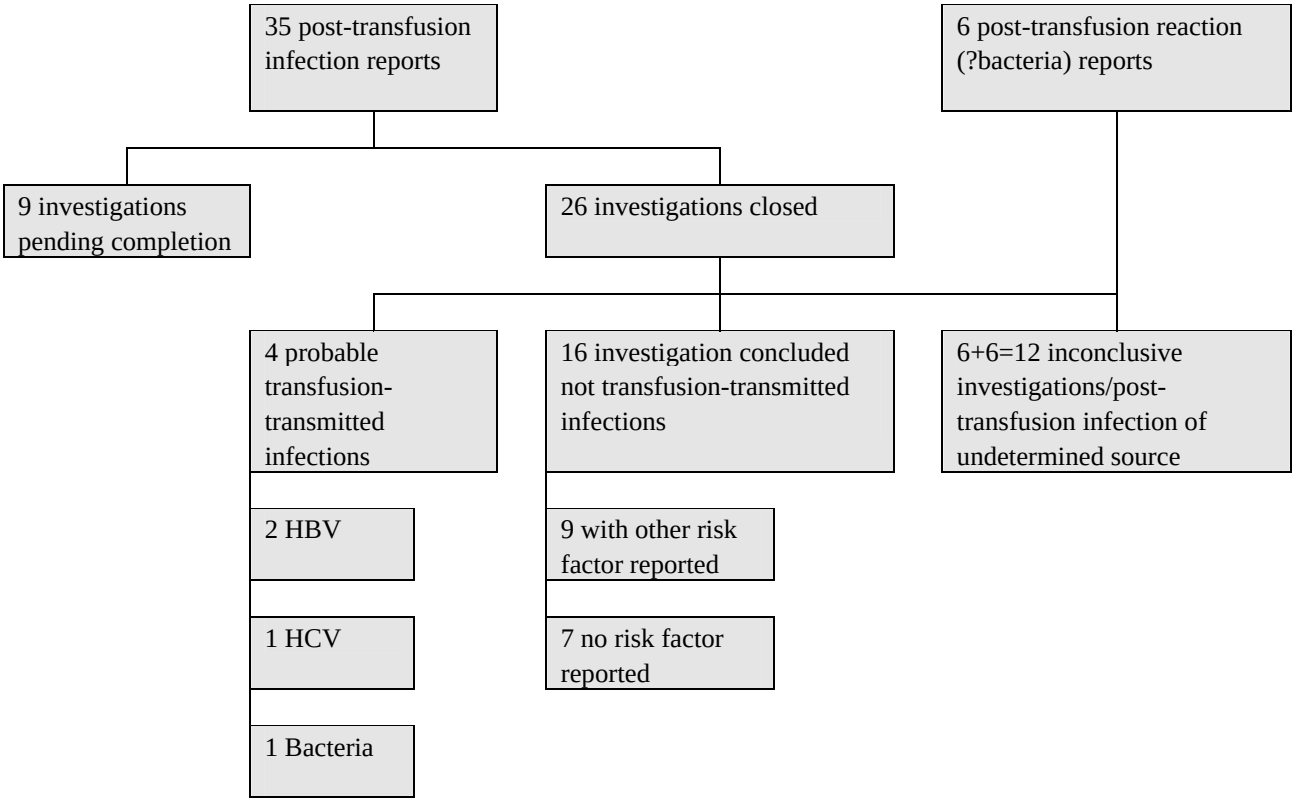


Table 20
Transfusion-transmitted infections reported between 1/10/97-30/9/98 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	pre-1997	1997	1998 (to end Sept)	Total
Infection				
HBV	1(1)[a] [1991]	1(1)	-	2(2)
HCV	1(1) [1970-85]	-	-	1(1)
Bacterial	-	-	1(1)[b]	1(1)
Total	2(2)	1(1)	1(1)	4(4)

Notes [a]One household member who was caring for the recipient has been diagnosed with acute HBV.
[b]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

Two transfusion-transmitted HBV infections were reported. One recipient (26 year old male) had acute HBV infection five months after transfusion of a red cell unit (one of 14 red cell units given over a year) that was found, by testing of the archived sample of the donation, to be anti-HBc negative but HBV DNA positive. At the time of the investigation, the donor recalled having viral symptoms and abdominal pains 5 months post-donation and was found to be anti-HBs positive. The probable source of the recipient's HBV infection was concluded to be an HBV infectious, though HBsAg and anti-HBc negative donation collected from a repeat donor during early acute infection.

One recipient (59 year old male) was found to be an HBsAg and HBeAg positive HBV carrier 6 years after transfusion with 8 red cell units. One of the donors was found to have markers of resolved HBV infection and it was also discovered that this donor had developed acute HBV (confirmed by the local laboratory) 3 months after donating the implicated donation. No archived sample of the donation was available for further testing. The probable source of the recipient's HBV infection was concluded to be an HBV infectious, but HBsAg negative, donation collected from a new donor during acute infection. Secondary transmission seems to have occurred as a household member who was caring for the infected recipient was diagnosed with acute HBV at the same time as the recipient's diagnosis.

Both of the donations implicated in these two transfusion-transmitted HBV infections were collected from donors who subsequently disclosed risk factors for HBV infection that should, according to donor selection criteria in place at the time, have been recognised as making them ineligible for blood donation. Further investigation is needed to identify the reasons why these donors were not recognised as ineligible for donation.

Hepatitis C virus

One transfusion-transmitted HCV infection was reported. A patient (52 year old male) was found to be anti-HCV and HCV RNA positive during investigation of chronic liver disease. The patient had been transfused with at least 4 red cell units more than 7 years prior to the introduction of anti-HCV testing of blood donations in September 1991. One of the donors was found to be anti-HCV positive when a subsequent donation was tested at another blood centre. This donor's previous donations were entered into the HCV lookback programme and at the start of the lookback process one red cell unit was identified as a component involved in this post-transfusion infection investigation. The probable source of the recipient's HCV infection was concluded to be an HCV infectious donation collected from a repeat donor prior to anti-HCV testing.

HIV

No transfusion-transmitted HIV infections were reported during this year.

B. Infections for which donation testing is not mandatory

Bacteria

One transfusion-transmitted bacteraemia was reported. One recipient (32 year old female) developed a bacteraemia after transfusion with red cells and platelets and died two days after the transfusion. *Staphylococcus aureus* was isolated from the recipient and from skin and nasal swabs from one of donors who contributed to the platelet pool.

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

Six (17%) post-transfusion infections (1 bacteraemia, 1 HBV infection, 4 HCV infections) were classified as post-transfusion infections of undetermined source due to incomplete investigation of the transfusion(s) implicated as the source of infection. For sixteen (46%) post-transfusion infection reports (9 HBV infections, 5 HCV infections, 1 dual HBV and HCV infection and 1 HIV infection), investigation was completed and no evidence was found to implicate transfusion as the source of infection. A possible source of infection other than transfusion was known for 9 of these infections (HBV: previous transfusion (details incomplete), surgery (x2), travel to country of high endemicity, birth in country of high endemicity, liver transplant; HCV: birth & travel in country of high endemicity, transfusion abroad, injecting drug use).

Time to reporting

For the 4 transfusion-transmitted infections, the intervals between transfusion and diagnosis of the infection in the recipient was 1 day (*Staphylococcus aureus*), 17 weeks (acute HBV), 6 years (HBV carriage) and 12 years (HCV). The intervals between diagnosis and blood centres being informed that the infection was suspected to be associated with transfusion were 2 days, 72 days, 110 days and 30 days. The intervals between the blood centre being informed and the completion of the initial surveillance report form were 40 days, 44 days, 63 days and 214 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. The proportion of post-transfusion infections that are reported each year may vary as other factors such as testing performed on transfusion recipients, awareness of transfusion as a possible source of infection, reporting of information to blood centres and reporting of information from blood centres to the surveillance centre vary. In June 1998 all participating blood centres were contacted and asked to confirm that the number of reports they had made to the surveillance system was the total number of post-transfusion infections that they had been informed about, or to report outstanding reports as soon as possible.

Previous year

During the previous reporting year (i.e. 1/10/96 to 30/9/97) 8 transfusion-transmitted infections were reported (see SHOT Annual Report 1996-97 for details of these cases). None of the post-transfusion infections reported during the 1996-97 year that were pending full investigation at the time of the 1996-97 SHOT annual report have been subsequently concluded to have been transfusion-transmitted infections.

One post-transfusion HCV infection investigation that was initially reported in the 1995-96 report year, and was classified as undetermined at the time of the 1996-97 SHOT report was, during the 1997-98 report year, updated to become a transfusion-transmitted infection when an untraced donor returned to donate blood in another region and was found to be anti-HCV positive. This donor's previous donations were entered into the HCV lookback programme and at the start of the lookback process one component was identified as a component involved in this post-transfusion infection investigation.

Table 21 shows the cumulative number of transfusion-transmitted infections reported by the end of September 1998.

Figure 14 shows the number of reports received by year of report since October 1995.

Table 21

Cumulative total transfusion-transmitted infections: reported between 1/10/95-30/9/98 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

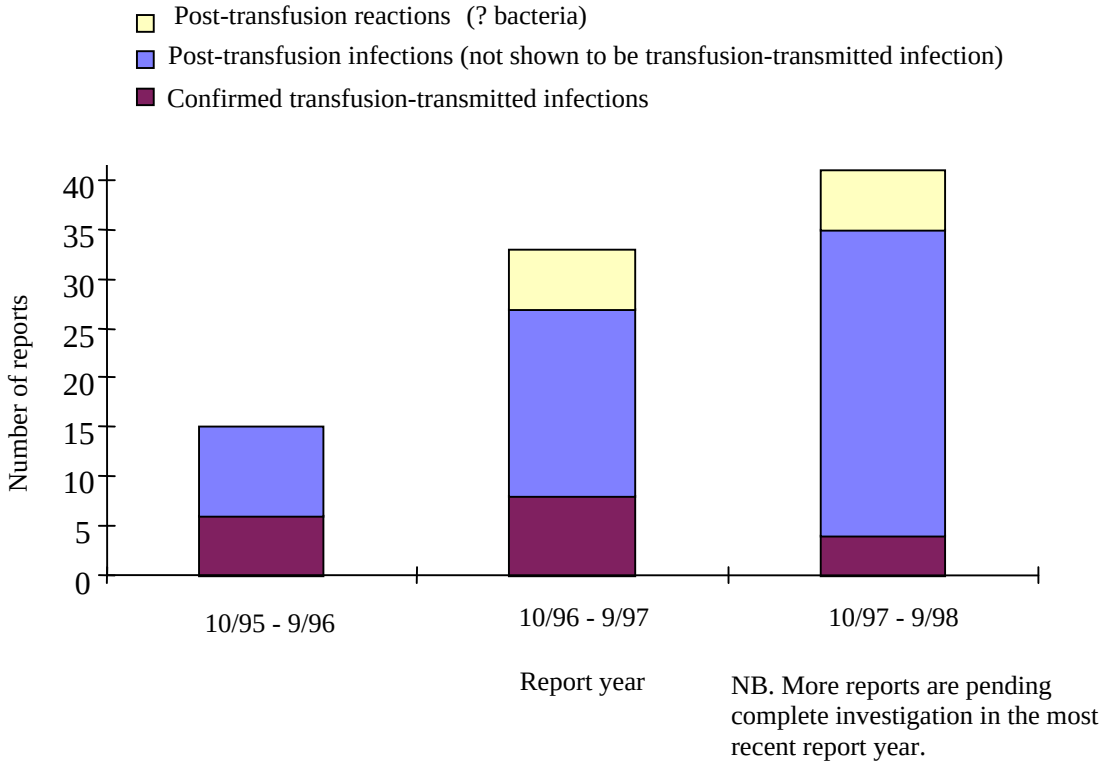
Year of transfusion	pre-1995	1995	1996	1997	1998 (to end Sept)	Total
Infection						
HAV		-	1(1)	-	-	1(1)
HBV	1(1)[a]	1(1)	1(1)	1(1)	-	4(4)
HCV	4(4)[b]	-	5(5)	-	-	5(5)
HIV		-	1(3)	-	-	1(3)
Bacterial		1(1)	1(1)	3(3)	1(1)[c]	6(6)
Malaria		-	-	1(1)[c]		1(1)
Total	5(5)	2(2)	5(7)	5(5)	1(1)	18(20)

Notes: [a]One household member who was caring for the recipient has been diagnosed with acute HBV.

[b] Transfusions prior to anti-HCV testing of blood donations.

[c] Infection was implicated in the death of the recipient.

Figure 14 : PTI reports by report year



NB. More reports are pending complete investigation in the most recent report year.

Comments

- Reported transfusion-transmitted infections are rare, and only 4/35 (11%) suspected cases were confirmed during this 12-month period of reporting. A further 31 cases of post-transfusion infection were reported to have been investigated. Almost half (46%) of the PTI reports during this year have been shown to not be caused by transfusion; for 17% of the reports the investigation was inconclusive and for the remainder (26%) the investigation is still ongoing.

- Six cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported. Conclusive 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. This means that absence of evidence of an infection (or toxin), in donations given to recipients who had post-transfusion reactions that were suspected (on clinical presentation) to be due to bacteria does not equate with evidence of absence of a transfusion-transmitted infection (or toxin).

- The intervals between transfusion and diagnoses of transfusion-transmitted infections were long - many weeks, months or years. Infections transmitted by transfusion between 1/10/97 and 30/9/98 will continue to be ascertained by the surveillance system as diagnoses are made in the future.

- The intervals between blood centres being informed of post-transfusion infections and completing an initial report form were long and should be reduced in order to ensure that information reaches the surveillance centre as soon as possible.

- Two transfusion-transmitted infections (2 HBV infections) were due to donations collected from donors during marker negative “window periods” following recent infection. Both donors had risk factors for acute HBV that should have led to their exclusion from blood donation.

- Two transfusion-transmitted infections (1 HCV infection, 1 bacterial) were due to collection of a donation from a donor with an infection for which no routine microbiological testing was in use routinely at that time.

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

- One transfusion-transmitted infection reported during this year resulted in the death of the recipient.

Recommendations

- National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge.

- All post-transfusion infections diagnosed in patients should be reported by the clinician to the local blood centre for appropriate investigation. Blood centres should, in turn, complete an initial report form as soon as possible.

- National guidelines for the bacteriological investigation of adverse reactions associated with transfusion are available for hospitals. Hospitals should not destroy blood components implicated in post-transfusion reactions suspected to be due to bacteria, and should consult these guidelines and the local blood centre about the investigation of such cases.

- Methods and criteria used to exclude those individuals who have risk factors for transfusion transmissible infections from donating blood warrant continuing evaluation and development. Investigation of the reasons for non-exclusion of ineligible donors is also warranted.

- Staff handling blood components should familiarise themselves with their normal range of appearance, and inspect packs for leaks or unusual colour/turbidity which might suggest bacterial contamination. Components which appear unusual in any way should NOT be transfused, but returned to the blood bank[9].