13. TRANSFUSION-TRANSMITTED INFECTIONS

Definition
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

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 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 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.
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, 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, and to reveal any systematic errors or deficiencies in the blood service testing. 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 similar collation of reports of cases investigated by blood centres in Scotland found that four post-transfusion infections were investigated during the report year. One post-transfusion HCV infection was found to be not due to transfusion. One post-transfusion Q fever (*Coxiella burnetii*) infection was investigated when a recipient developed acute Q fever confirmed by compliment fixation tests. No evidence of *Coxiella burnetii* infection was found in any of the donations given to the recipient (all tested with IgG and IgM ELISAs, followed - if reactive - by immuno-flourscence tests). One post-transfusion HBV infection is awaiting complete investigation. Two recipients (57 year old male and 30 year old male) developed acute HBV infection 9 months (this recipient was on chemotherapy) and 4 months after transfusion with platelets and red cells respectively from the same donation. The implicated donation was HBsAg negative by PRISM and Murex and was anti-HBc negative and

HBV DNA negative by PCR. A donation 8 months later from the implicated donor was anti-HBc positive, anti-HBs (>1000 IU/l) and anti-HBe positive. The probable source of both recipients' HBV infections was concluded to be an HBV infectious, HBsAg negative, donation from a donor in the early incubation period of an acute HBV infection.

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, (see exception below) 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).

and c) the case did not involve HCV or HIV infections diagnosed in recipients who had received transfusions in the UK that were not tested for anti-HCV (i.e. pre September 1991) or anti-HIV (i.e. pre October 1985) respectively. (These cases have been excluded because the blood service is rarely able to conduct follow-up investigation of all donors implicated and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions.)

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)

Data received by 31/12/2000 about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/1999 and 30/9/2000 were included in this report. Data received about incidents reported during the previous four 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

Twenty-six initial reports of post-transfusion infections were made by blood centres during the report year. An additional 14 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 10 of the 17 blood centres participating in the surveillance system. These 10 centres collect approximately 86% of the donations tested by blood centres participating in the surveillance system.
Figure 20 shows the classification of reports during the report year.
Of the 26 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/1999 and 30/9/2000, 4 (14%) were classified, after appropriate investigation, as transfusion-transmitted infections. Table 37 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/1999 and 30/9/2000 by year of transfusion: all were transfused during the report year.

Figure 20
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 1/10/1999 and 30/9/2000.

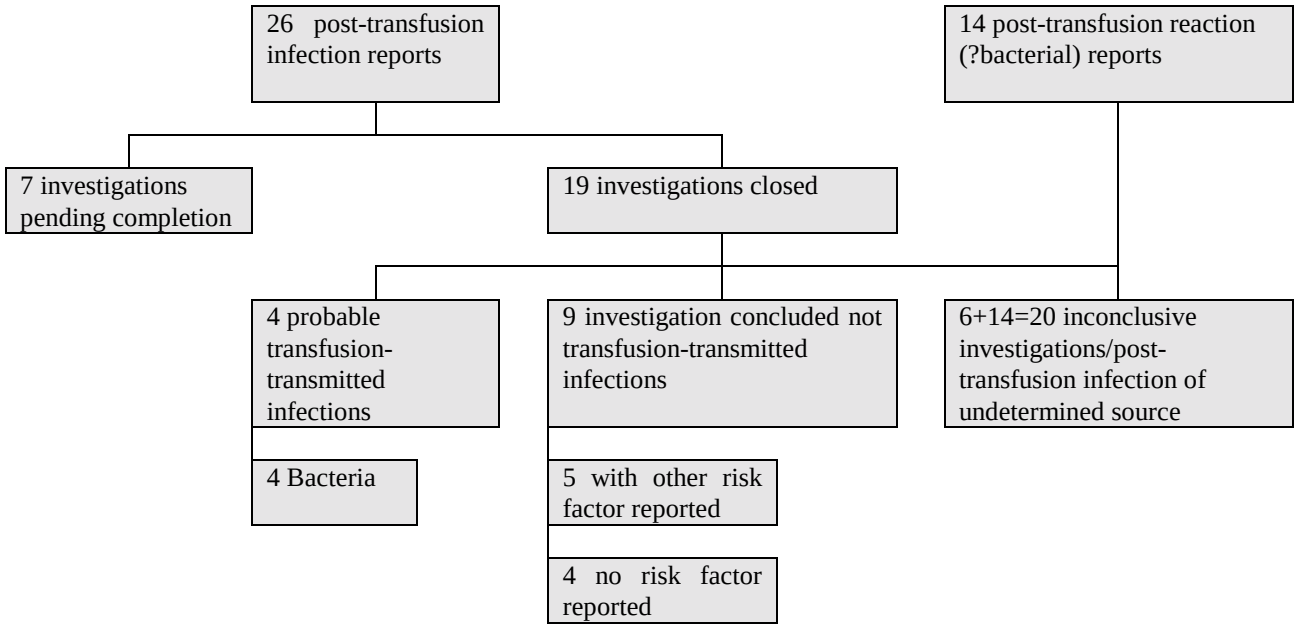

Table 37
Transfusion-transmitted infections reported between 1/10/1999-30/9/2000 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	1999	2000 (to end Sept)	Total[b]
Infection			
Bacteria	1(1)	3(3) [a]	4(4) [a]
Total	1(1)	3(3) [a]	4(4) [a]

Notes: [a] Infection was implicated in the death of a recipient.
[b] Additionally, reports in Scotland included one donation shown to have transmitted HBV infection to 2 recipients, transfused during 1999.

Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus
No transfusion transmitted HBV infections were reported during this year. One post-transfusion HBV infection reported during the previous year was concluded during this year to be due to transfusion. (See details of case reported in Scotland included in Introduction.)

Hepatitis C virus
No transfusion transmitted HCV infections were reported during this year.

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

B. Infections for which donation testing is not mandatory

Bacteria
Four transfusion-transmitted bacteraemias were reported.

One recipient (83 year old female) felt unwell and flushed after transfusion with a 3 day old apheresis platelet pack. The condition subsequently worsened and the recipient suffered a cardiac arrest and died. *Enterobacter aerogenes* was cultured from the platelet pack. Follow-up swabs of the donor's venepuncture site were culture negative.

One recipient (79 year old female) suffered a bacteraemia after transfusion with 32 day old red cells. Identical isolates of *Staphylococcus epidermidis* were cultured from the recipient's blood and from the red cell pack. The donor was not further investigated.

One recipient (66 year old male) developed rigors and fever after transfusion with a 5 day old pooled platelet pack. Coagulase negative *Staphylococci* with the same antibiotic sensitivities were cultured from the recipient's blood and the platelet pack. The donors were not further investigated.

One recipient (female child) suffered pyrexia, rigors, abdominal pain and vomiting after transfusion with a 5 day old pooled platelet pack. *Staphylococcus epidermidis* was isolated from the recipient's blood and from the platelet pack. The two *Staph epidermidis* isolates had different antibiotic sensitivities reported, however as this apparent inconsistency could not be investigated by further molecular typing (isolates were destroyed), and the other evidence was strong, the recipient's reaction was concluded to be due to transfusion transmission of *Staph. epidermidis*. The donors were not further investigated.

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

Six (21%) post-transfusion infections (3 bacteraemias, 2 HCV infections and 1 CMV infection) were classified as post-transfusion infections of undetermined source due to inconclusive investigation of the transfusion(s) implicated as the source of infection. For nine (35%) post-transfusion infection reports (1 bacteraemia, 3 HBV infections, 3 HCV infections, 2 HIV infections), 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 5 of these infections (HBVx2: invasive medical procedure (one abroad), HCVx1: renal dialysis & previous transfusion, HCV x1: tattoo, HIV x1: sexual risk).

Reporting delay

For the 4 transfusion-transmitted bacterial infections, serious clinical events occurred on the same day as the transfusion. Blood centres were informed of the bacteraemias suspected to be associated with transfusion 4 days, 7 days, 22 days and 54 days after transfusion. The intervals between the blood centre being informed and the completion of the initial surveillance report form (i.e. reporting delay) were 17 days, 37 days, 96 days and 97 days for the 4 bacterial infections. The average interval between transfusion and the initial report (i.e. including all time intervals and reporting delays) was 83 days (N=4:21,59,104, 150).

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 be inconsistent 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 are all key variables.

Previous year

During the previous reporting year (i.e. 1/10/98 to 30/9/99) 7 transfusion-transmitted infections were reported (see SHOT Annual Report 1998-99 for details of these cases). One post-transfusion HBV infection reported during the 1998-99 year that was awaiting full investigation at the time of the last (i.e. 1998-99) SHOT annual report has subsequently been concluded to have been a transfusion-transmitted HBV infection. A recipient (49 year old female) was tested for markers of HBV infection while receiving dialysis treatment and was found to be negative for HBsAg at the start of her red cell transfusion treatment and to be HBsAg and HBeAg positive four months later. The donor of one of the implicated red cell donations was found subsequently to be anti-HBc and anti-HBs positive and the archive of the implicated donation was anti-HBc negative and had weak levels of anti-HBs. The probable source of the recipient's HBV infection was concluded to be an HBV infectious, HBsAg negative donation collected from a donor who was in the early stages of an HBV infection at the time of donating.

The investigations of five post-transfusion infections that were classified as awaiting full investigation in the 1998-99 SHOT report have subsequently been concluded to be not due to transfusion (2 cases of HBV infection) or inconclusive (3 cases: 2 HCV infections, 1 bacteraemia).

Table 38 shows the cumulative number of transfusion-transmitted infections reported by the end of September 2000.

Figure 21 shows the number of reports received by year of report since October 1995.

Table 39 lists some summary details of the 15 bacterial cases reported between October 1995 and September 2000.

Table 38
Cumulative total transfusion-transmitted infections: reported between 1/10/1995-30/9/2000 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	1999	2000 (to end Sept)	Total	Deaths
Infection									
HAV	-	-	1(1)	-	-	-	-	1(1)	
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)	1(1)	-	6(6)	
HCV	-	-	1(1)	1(1)	-	-	-	2(2)	
HIV[c]	-	-	1(3)	-	-	-	-	1(3)	
Bacteria	-	1(1)	1(1)	3(3)	3(3)[ax2]	4(4)[a]	3[a]	15(15)	4
Malaria	-	-	-	1(1)[a]	-	-	-	1(1)	1
Total[d]	1(1)[b]	2(2)	5(7)	6(6)[a]	4(4)[ax2]	5(5)[a]	3	26(28)	5

Notes: [a] Infection was implicated in the death of a recipient.
[b] One household member who was caring for the recipient has been diagnosed with acute HBV.
[c] One additional investigation, initially reported during 97-98 and concluded during 98-99, failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.
[d] Additionally, reports in Scotland found one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, and one donation shown to have transmitted HBV infection to 2 recipients, transfused during 1999.

Figure 21
Post transfusion infections (PTI) reports by report year

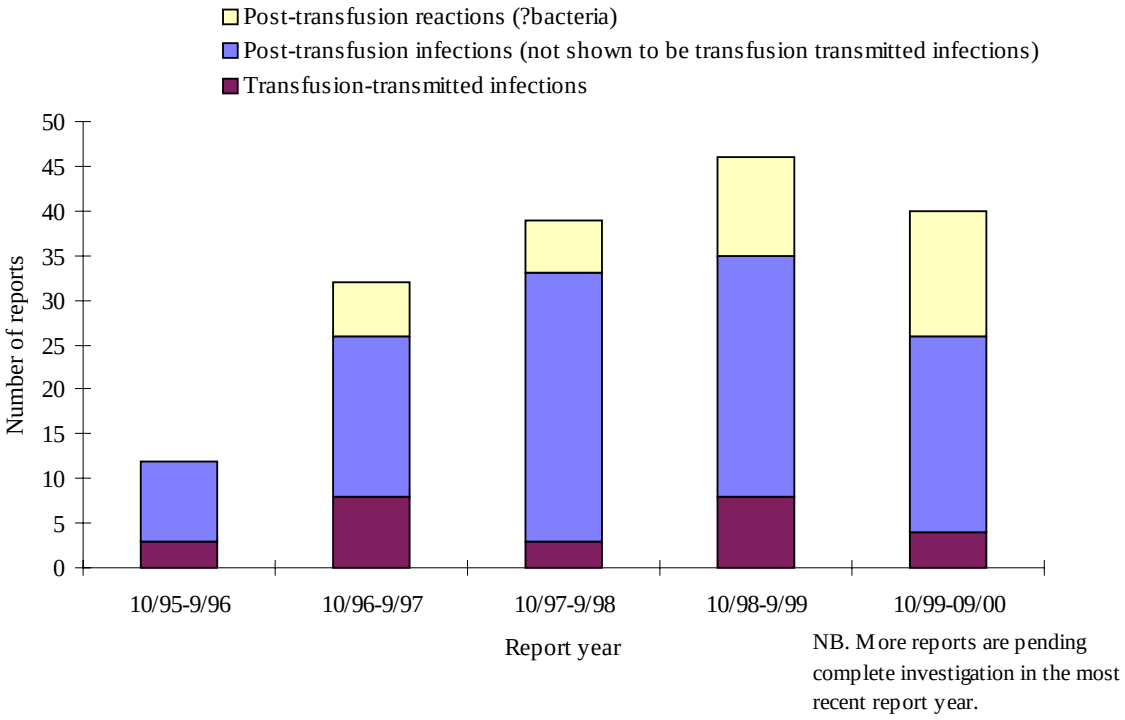

Table 39
Cumulative total transfusion-transmitted bacterial infections: reported between 1/10/1995-30/9/2000.

Year of transfusion	Organism	Component type	Source	Morbidity in recipient
1995	Bacillus cereus	Pooled platelets	Donor's arm	Death (other causes)
1996	group B Streptococcus	Pooled platelets	Donor's blood	Major morbidity
1997	Serratia liqufaciens	Red cells	None identified	Major morbidity
1997	Bacillus cereus	Pooled platelets	Donor's arm	Major morbidity
1997	Escherichia coli	Apheresis platelets	None identified	Major morbidity
1998	Staphylococcus aureus	Pooled platelets	Donor's arm	Death attributed to infection
1998	Staphylococcus epidermidis	Apheresis platelets	Donor's arm	Major morbidity
1998	Escherichia coli	Apheresis platelets	None identified	Death attributed to infection
1999	Staphylococcus epidermidis	Red cells	None identified	Major morbidity
1999	Staphylococcus epidermidis	Pooled platelets	None identified	Major morbidity
1999	Yersinia entercolitica	Red cells	Donor's blood	Death attributed to infection
1999	Bacillus cereus	Pooled platelets	Donor's arm	Major morbidity
2000	Staphylococcus epidermidis	Pooled platelets	None identified	Major morbidity
2000	Coagulase negative Staphylococci	Pooled platelets	None identified	Major morbidity
2000	Enterobacter aerogenes	Apheresis platelets	None identified	Death attributed to infection
15		12/15=platelets		5 fatalities

COMMENTARY

- Transfusion-transmitted infections are rare: only 4 confirmed cases were recognised during this 12-month period of reporting. Investigations of a further 22 cases of post-transfusion infection were reported. Half (47%) of the closed PTI investigations reported during this year have been shown not to be caused by transfusion. For 32% (6) of closed investigations the investigation was inconclusive. Additionally, in Scotland during this year, one confirmed case (with two infected recipients) was recognised, one incident was shown not to be caused by transfusion, and one investigation is pending completion.

- Fourteen 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. 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).

- Cases of transfusion transmitted bacterial infections have continued to be reported following the introduction of universal leucodepletion.

- There were no transfusion transmitted viral infections amongst the concluded reports initially received during this year. One HBV transmission was concluded in a case reported in the previous year. Other reports are awaiting complete investigation and cases transfused during this year may accrue over the next year, and at later stages in the course of the infection.

- One transfusion-transmitted infection from a platelet transfusion (*Enterobacter*) reported during this year resulted in the death of the recipient.

- Numbers of reported cases are small and fluctuations in reports from year to year are to be expected. Also, the reporting system is probably biased towards infections that cause rapid onset of acute disease. However, it should be noted that bacteria account for the majority of reported transmissions by transfusion and the majority of known deaths due to transfusion transmitted infections - not only in this year's cases, but also in the cumulative data since the inception of SHOT.

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.**

- **Clinicians should report all post-transfusion infections diagnosed in their patients to the blood service (via their regional blood centre) for appropriate investigation. Blood centres should, in turn, complete an initial report form as soon as possible.**

- **The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. Hospitals should consult guidelines and the blood service about the investigation of such cases, including the sampling and storage of implicated units. (A NBS guidance document entitled *Bacteriological investigation of adverse reactions associated with transfusion* has been agreed in consultation with the PHLS and the Association of Medical Microbiologists (AMM), and distributed to blood centres.) and is reproduced in appendix 9.**

- **Strategies to prevent transfusion transmitted bacterial infections should be given appropriate priority in efforts to reduce the infectious risks of transfusion.**