17. 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. The reporting of 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 may be due to an infected (or contaminated) transfusion or infection that 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 UK (excluding Scotland) and the Republic of Ireland by the National Blood Authority and the Health Protection Agency Communicable Disease Surveillance Centre in October 1995. Reported data from England, Wales and Northern Ireland are included in this report.

A similar collation of reports of cases investigated by Scottish blood centres has been in place in Scotland since October 1998.

Methods

Participating blood centres in England, Wales and Northern Ireland reported all post-transfusion infections of which they had been informed to the NBS/Health Protection Agency Infection Surveillance. 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/Deoxyribonucleic acid 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 Hepatitis A virus (HAV), HBV, HCV, Epstein-Barr virus 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.)

and d) the case did not involve human T-cell leukaemia virus (HTLV) infections diagnosed in recipients who had received transfusions in the UK prior to August 2002 when screening for anti-HTLV was first implemented. As a result of screening the NBS has begun a national 'lookback' programme to identify any recipients of blood donated by anti-HTLV positive donors before the introduction of testing. Any post-transfusion HTLV infections identified through the 'lookback' are excluded from this report (see c above) but will be reported to the NBS and analysed and published elsewhere, as was done previously with HCV 'lookback'.

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 31/3/2003 about incidents of transfusion-transmitted infections initially reported by blood centres between 01/10/2001 and 31/12/2002 are included in this report. Data received about incidents reported during the previous six years of the surveillance system are included in a cumulative table (table 43).

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.

Blood centres in Scotland reported all cases to the Microbiology Reference Unit of the Scottish Blood Transfusion Service where they were investigated, and the details and conclusion of each case was then provided to the SHOT system.

Results

Between 01/10/2001 and 31/12/2002, 34 post-transfusion infections were reported by blood centres in the UK, 28 from blood centres in England, Wales and Northern Ireland and 6 from Scotland (figure 33).

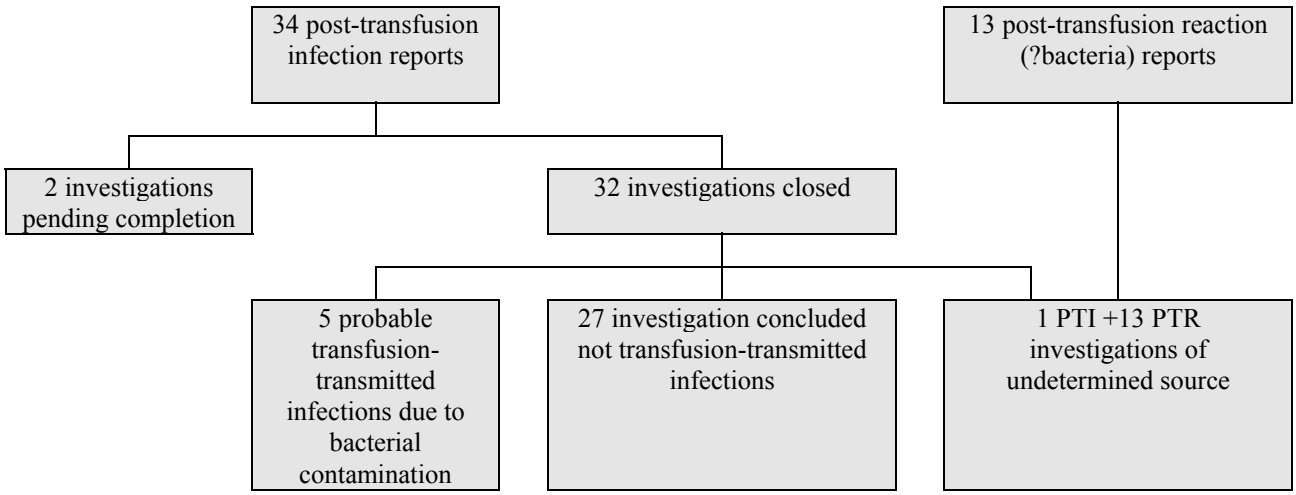
Of the 28 PTI reports received from blood centres in England, Wales and Northern Ireland, 1 HCV infection (4%) was classified as a post-transfusion infection of undetermined source due to inconclusive investigation of the donation(s) implicated as the source of infection. For 20 (71%) PTI reports (10 bacteraemia, 6 HBV infections, 3 HCV infections, 1 HIV infection), investigation was completed and there was no evidence to implicate transfusion as the source of infection. A possible source of infection other than transfusion was known for 5 of these infections: 1 HBV was born and lived in Pakistan; 1 HBV had received a transfusion 36 years ago; 1 HBV had received a transfusion in Shanghai; 1 bacteraemia due to enterocolitis and 1HIV due to maternal transmission. Five (19%) PTI reports were classified as transfusion-transmitted infections due to bacterial contaminations, 4 were transfused in 2001, and one during 2002. Two (7%) PTIs are still under investigation (1 HBV and 1 HCV).

An additional 13 reports were received for post-transfusion reactions that were suspected to be due to bacteria but had no evidence of bacterial infection (or endotoxin) that could have caused the reaction in either the recipient or the implicated component.

Reports from blood centres in England, Wales and Northern Ireland were received from 8 of the total 12 centres; donations made at these 8 centres represent approximately 70% of all donations tested each year in England, Wales and Northern Ireland.

Blood centres in Scotland reported 6 post-transfusion infection investigations during the report year. Two post-transfusion HIV infections and 3 post-transfusion HCV infections were completed and no evidence was found to implicate transfusion as the source of infection. One post-transfusion HCV infection is still under investigation. Scottish cases reported since October 1998 have been included in the numbers of post-transfusion infections and transfusion-transmitted infections shown in the tables and figures here since the 2000/01 SHOT Annual report.

Figure 33
Classification of post-transfusion infections (and post-transfusion reactions) in the UK reported between 1/10/2001 and 31/12/2002.



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.

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

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

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

B. Infections for which donation testing is not mandatory

Bacterial contamination
Five transfusion-transmitted bacterial contaminations were reported between 1/10/2001 and 31/12/2002. All recipients had major morbidity, none died.

One recipient (61 year old female) developed rigors and restlessness after transfusion with a single 5-day old pooled platelet unit during treatment for myeloma. *Staphylococcus epidermidis* of an identical strain was cultured from the recipient's blood and the platelet pack. Three of the 4 donors who contributed to the unit were swabbed and *S. epidermidis* was cultured from all 3, and the same strain was found on the arm of one donor. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with S. *epidermidis* from the donor's arm.

One recipient (66 year old male) developed fever after transfusion with a single unit of 5-day old pooled platelets. *Staphylococcus epidermidis* was cultured from the recipient's blood and the platelet pack. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with *S. epidermidis:* no source of contamination was identified.

One recipient (28 year old female) developed tachycardia, hypotension and pyrexia immediately after transfusion with a single 5-day old unit of platelets during treatment for thrombocytopenia. *Morganella morganii* was isolated from the recipient and giving set. The probable source of the recipient's reaction was concluded to be a unit of platelets contaminated with *M. morganii:* no source of this contamination was identified.

One recipient (72 year old female) developed an acute wheeze, fever and rigors after the start of transfusion with a 3-day old unit of pooled platelets during treatment for myeloma and acute mylomonocytic leukemia thrombocytopenia. Group B *streptococcus* was isolated from the platelet pack. Culture of throat and arm swabs from the donors of this unit did not isolate any group B streptococcus. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with group B *streptococcus*: no source of this contamination was identified.

One recipient (62 year old male) developed hypertension, fever and rigors during a transfusion with a single 5-day old unit of pooled platelets during treatment for myelodysplasia. *Staphylococcus epidermidis* was cultured from the recipient's blood and the platelet pack but not from the donor's skin. Despite this, the probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with *S. epidermidis* from the venepuncture site of the donor.

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.

Previous years

During the previous reporting year (i.e. 01/10/2000 to 30/09/2001) 4 transfusion-transmitted infections were reported (see SHOT Annual Report 2000-01 for details of these cases).

The investigations of 4 post-transfusion HBV infections that were classified as pending full investigation in the 2000-01 SHOT Annual Report have subsequently been concluded to be not due to transfusion.

Table 43 shows the cumulative number of transfusion-transmitted infections reported by the end of December 2002.

Cumulative data

The cumulative number of PTI and PTR reports received by year of transfusion since October 1995 are shown in Figure 34.

Figure 34
Post-transfusion infection reports by year (Scotland included from 10/98)

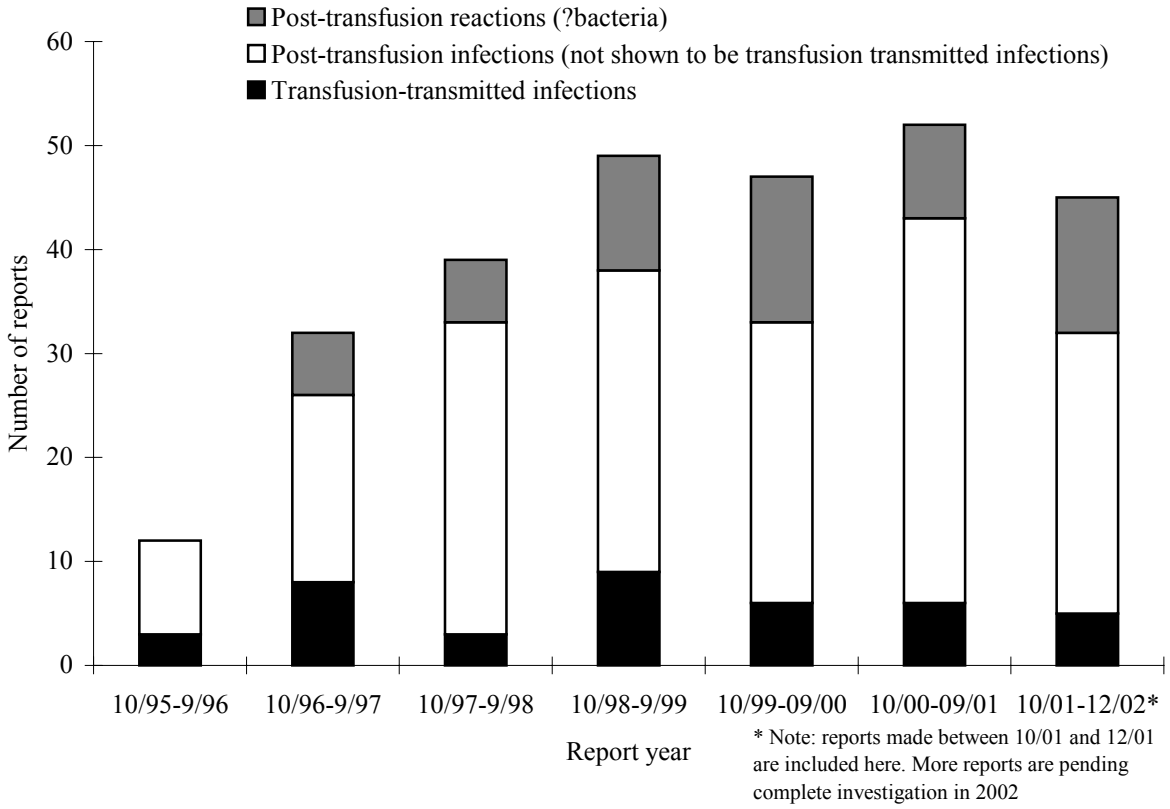


Table 43
Cumulative total transfusion-transmitted infections: reported between 1/10/1995-31/12/2002 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	Pre-1995	1995	1996	1997	1998	1999	2000	2001	2002	Total	Deaths
Infection											
HAV	-	-	1(1)	-	-	-	-	-	-	1(1)	-
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)	2(3)	1(1)	-	-	8(9)	-
HCV	-	-	1(1)	1(1)	-	-	-	-	-	2(2)	-
HIV[c]	-	-	1(3)	-	-	-	-	-	-	1(3)	-
Bacteria	-	1(1)	1(1)	3(3)	4(4)[ax2]	4(4)[a]	7(7)[ax3]	5(5)	1(1)	26(26)	6
Malaria	-	-	-	1(1)[a]	-	-	-	-	-	1(1)	1
HTLV I	1(1)	-	-	-	-	-	-	-	-	1(1)	-
Total[d]	2(2)[b]	2(2)	5(7)	6(6)[a]	5(5)[ax2]	6(6)[a]	8(8)	5(5)	1(1)	40(43)	7

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 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.

Bacterial contaminations

A summary of the species of bacteria and the type and age of the implicated components for the 26 transfusion-transmitted bacterial contaminations reported between 01/10/1995 and 31/12/2002 are shown in table 44.

Table 44
Transfusion-transmitted bacterial contaminations reported in UK between 01/10/1995 and 31/12/2002 by species and component type and age (N=26).

	Platelets Age (in days) at use							Red cells
	1	2	3	4	5	NK	All	
All species	*0*	*1*	*2*	*6*	*4*	*4*	*22*	*4*
Bacillus cereus				3[a]		1	4	
Coagulase negative Staphylococci					1		1	1 (23 days)
Enterobacter aerogenes			1[a]				1	
Escherichia coli			1[a]			1	2	
group B Streptococcus			1	1		1	3	
Morganella morganii					1		1	
Serratia liquifaciens								1
Staphylococcus aureus					1	1[a]	2	
Staphylococcus epidermidis		1[a]		2	5		8	1 (32 days)
Yersinia entercolitica								1[a] (33 days)

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

Seven of the 22 contaminated platelet units were collected by apheresis from single donors, 14 were recovered from whole blood donations (each from a pooling of four donations) and for one the source of platelets was not known. For 8 of these cases the donor's arm was confirmed by subsequent testing to have been the probable source of the contamination. For some others, investigation of donors' arms was incomplete or inconclusive but the nature of the contaminating organism was suggestive of a skin contaminant that was most likely to have been

introduced to the pack at the time of collection. For 2 cases, the donor's blood was concluded to have been the source of the contamination (i.e. endogenous bacteria, so contamination of the pack not preventable by skin cleansing or diversion).

Cumulative data about Hepatitis B virus transmissions

Since October 1995, 7 of the 8 transfusion-transmitted HBV infections reported have been concluded to be probably due to infectious blood collected from donors with acute HBV infection, with only one (reported in the first reporting year) due to infectious blood from a donor with later stage HBV infection. This is a change from that observed in earlier collations of transfusion-transmitted HBV infection. For example between 1991 and 1997 only 3 of 14 transfusion-transmitted HBV infections reported to the Health Protection Agency were found to be due to donations from donors with acute infection, with the majority being due to donations from donors with chronic infection[18]. This change has implications for the choice of strategies to further reduce the risk of transfusion-transmitted HBV infection.

COMMENTARY

- Due to the adjustment in reporting year, reports made over a 15-month period from October 2001 to December 2002 are included in this report. Despite this extended period, the numbers of post transfusion infections reported were fewer than reported in the previous report year (43 reported between October 2000 and September 2001). Reasons for this may include variation in testing, diagnosing and reporting practices for infections in transfusion recipients. The number of these that are later classified as transfusion transmitted infections, however, is unchanged and suggests consistent sensitivity in the surveillance of these.

- Reported transfusion-transmitted infections are rare: only 5 confirmed cases were recognised in the UK during this 15-month period of reporting. Investigations of a further 28 cases of post-transfusion infection were reported. The majority (86%) of the closed PTI investigations reported during this period were not caused by transfusion.

- 13 cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported (in England, Wales and Northern Ireland). 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).

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

- Most bacterial contaminations are due to skin flora entering the pack at the time of collecting the donation

- In August 2002, the NBS began screening all blood donors for HTLV. Transfusion-transmitted HTLV infection has been previously documented in UK[19]. Leucodepletion may have reduced the risk of HTLV transmission by transfusion since these cases were transfused[20]. A 'lookback' at the serological status of any infected donors and the fate of these units is to be carried out and will be reported elsewhere.

- Numbers of reported cases are small and fluctuations in reports 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 have accounted for the majority of reported transmissions by transfusion and the majority of known deaths due to transfusion transmitted infections in the cumulative data.

- The absence of any reports of transfusion transmitted HCV (or HIV) infections is consistent with the expected low risk of an HCV infectious donation entering the blood supply in the presence of the current testing of blood donations for both anti-HCV and HCV RNA (and anti-HIV).

RECOMMENDATIONS

- **Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components. These include implementation of diversion of the first few mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site) and improvements in cleansing of donors' arms. Methods for testing platelets for bacterial contamination should be evaluated. The risk of transfusion of a contaminated component can be reduced by adherence to BCSH guidelines (1999)[6] with regard to the visual inspection of units for any irregular appearance immediately prior to transfusion (particularly platelets);**

- **Hospitals should consult guidelines and the blood service about the investigation of transfusion reactions suspected to be due to bacteria. National guidelines on the investigation of these cases are available from all NBS centres. Cases that are inconclusive due to discard of the implicated pack before sampling continue to be reported, therefore particular attention should be paid to the sampling and storage of implicated units.**

- **The Standing Advisory Committee for Transfusion Transmitted Infections (SACTTI) is currently reviewing the residual risk of transfusion transmitted HBV infection to assess the need for additional screening methods, such as HBV RNA testing and/or anti-HBC.**