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 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.

Retrospective data were collated in Scotland for cases occurring in Scotland during this 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, (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).

One category of post-transfusion infections is not included in these data. In January 1999, a meeting of reporters agreed that HCV and 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 should be excluded from reporting. The blood service is rarely able to conduct follow-up investigation of donors implicated in these cases and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions. Numbers and details of such infections are therefore not included in this report.

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 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

Twice this year, all participating blood centres were reminded of the requirement to report, and asked to report any cases that had not yet been notified.

Data received by 31/12/99 about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/98 and 30/9/99 were included in this report. Data received about incidents reported during the previous three 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

34 initial reports of post-transfusion infections were made by blood centres during the report year. An additional 11 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 participating in the surveillance system. These 12 centres collect approximately 86% 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 34 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/98 and 30/9/99, 7 (21%) were classified, after appropriate investigation, as transfusion-transmitted infections. Table 22 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/98 and 30/9/99 by year of transfusion: Four were transfused during the report year, and 3 were transfused prior to the report year.

Figure 13
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 1/10/98 and 30/9/99.

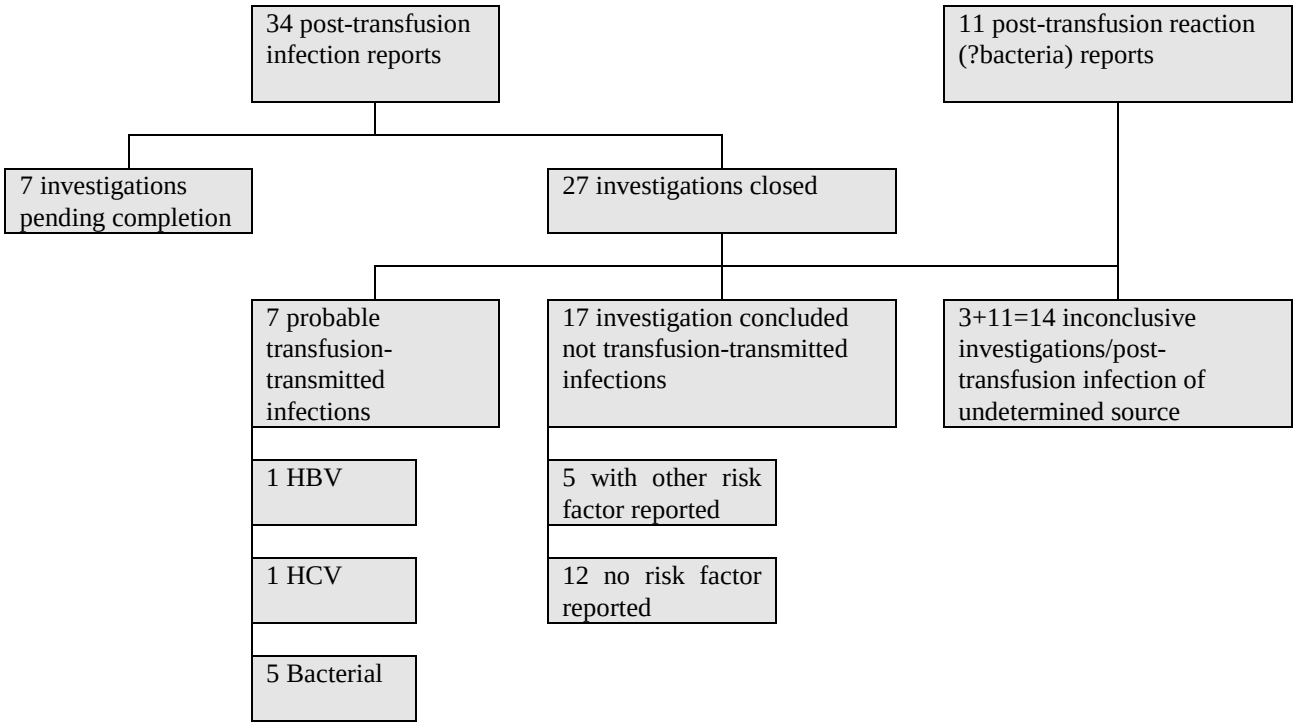


Table 22
Transfusion-transmitted infections reported between 1/10/98-30/9/99 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	1997	1998	1999 (to end Sept)	Total
Infection				
HBV	-	1(1)	-	1(1)
HCV	1(1)	-	-	1(1)
Bacteria	-	2(2) [a]	3(3) [a]	5(5) [ax2]
Total [b]	1(1)	3(3) [a]	3(3) [a]	7(7) [ax2]

Notes: [a] Infection was implicated in the death of a recipient.
[b] Additionally, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

A retrospective collation of cases investigated by blood centres in Scotland found three post-transfusion infection investigations during the report year. One recipient (72 year old male) developed pryexia and tachycardia after transfusion with red cells (23 days old, not leucodepleted). The recipient responded to antibiotic therapy and recovered. Coagulase negative *Staphyloccocus* was cultured from the red cell pack. For two post-transfusion HCV infection reports (one transfused in 1996, one in 1999) 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 known for one of these cases.

Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus

One transfusion-transmitted HBV infection was reported.

One recipient (73 year old female) was found to have markers of acute HBV infection four months after transfusion of a red cell unit (one of three units received during a month) collected from a donor who developed acute HBV infection between one and two months after donating blood. The recipient was traced after the donor's General Practitioner informed the blood service of the donor's infection status. The archive of the implicated donation was confirmed to be HBsAg negative on re-testing but was found to be HBV DNA positive by nested PCR. (DNA was not detectable by PCR on a 1 in 96 dilution). The recipient died three months after her HBV diagnosis from the underlying reason for transfusion: HBV infection was not implicated in the recipient's death.

The probable source of the recipient's HBV infection was concluded to be an HBV infectious, though HBsAg negative, donation collected from a repeat donor during early acute infection. The blood donor did not report any risk factor for HBV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

Hepatitis C virus

One transfusion-transmitted HCV infection was reported. A repeat donor was found to be anti-HCV positive and HCV RNA positive. The archived sample of the previous (first) donation from this donor was re-tested and was also anti-HCV and HCV RNA positive. The recipient (a 64 year old male) of this red cell unit was traced and tested fourteen months after transfusion and was found to be anti-HCV positive and HCV RNA positive. Investigation by the blood service found an error had occurred during the re-testing of the donation that was initially reactive to the anti-HCV test. The duplicate repeat tests were read as negative because the samples were unintentionally dispensed into blank wells that are used to fill out part plates so they can be handled by automated machinery. It had been common practice to blank these out with a black marker pen to ensure that in the event they were accidentally used for samples they would return a fail safe positive reaction. However new machinery had been introduced which read these as negative. Once the problem was identified corrective and preventative action was put in place to ensure that a different mechanism is used to ensure that blank wells will if accidentally used return a positive result and "fail safe".

The probable source of the recipient's HCV infection was concluded to be an HCV infectious, anti-HCV positive, donation from a new donor. The donation was not excluded from the blood supply because of a laboratory error during the testing process. The blood donor did not report any risk factor for HCV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

HIV

No transfusion transmitted HIV infections were reported during this year.

B. Infections for which donation testing is not mandatory

Bacteria

Five transfusion-transmitted bacteraemias were reported.

One recipient (27 year old male) developed bacteraemia after transfusion with two leucodepleted, 4 day old apheresis platelet units from the same donor. The recipient recovered and was asymptomatic one week after the transfusion. *Staphylococcus epidermidis* was isolated from the platelet packs and from the recipient (and these two isolates had identical banding patterns). *Staph. epidermidis* (with a different DNA fingerprint) was subsequently cultured from swabs of the donor's arms. *Staph. epidermidis* was not grown from swabs taken after standard skin preparation. No failure in the donor arm cleansing procedure at the time of donating the implicated donation had been noted.

The probable source of the recipient's bacteraemia was concluded to be transfusion with platelets contaminated with skin flora from the donor's arm.

One recipient (52 year old male) suffered a severe febrile reaction during transfusion of a leucodepleted, 3 day old apheresis platelet unit, and died later the same afternoon. On inspection the

next day the remainder of the platelet pack had some signs of bacterial contamination (unusual orange colouration and small specks visible when held up to the light). *Escherichia coli* was cultured from the recipient's blood and from the platelet pack (and these two isolates had identical biochemical profiles). No leaks or defects were identified in the platelet pack. An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs of the donor's arm skin were negative on culture.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with platelets contaminated with *E.coli*. No source of the contamination was identified.

One recipient (78 year old female) suffered symptoms including feeling hot, sweaty and dyspnoeic during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient subsequently recovered and was completely asymptomatic two weeks after the transfusion. Blood cultures were not taken from the recipient. *Staphylococcus epidermidis* was cultured from the platelet pack and from the red cell unit made from the same donation.
An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs from the skin of the donor's arm were negative on culture.
The probable source of the recipient's transient reaction was concluded to be transfusion with platelets contaminated with *Staph. epidermidis*. No source of the contamination was identified.

One recipient (63 year old female) developed urticaria, rigors and pyrexia during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient was pyrexial for three days after transfusion and was treated with broad spectrum antibiotics. *Bacillus cereus* was cultured from the recipient's blood and from the platelet pack (and these two isolates were both of type 29). *B cereus* (type 29) was also cultured from swabs from the skin of the donor's arm (both pre- and post- arm cleansing).
The probable source of the recipient's reaction was concluded to be transfusion with platelets contaminated with *B. cereus* from the donor's arm.

N.B. The above four cases were associated with leucocyte depleted platelets: all platelets issued in the UK since January 1999 have been leucocyte depleted. The numbers of cases are too small to detect any effect of leucodepletion on bacterial contamination of components.

One recipient (58 year old female) suffered a respiratory and cardiac arrest during transfusion of a second unit of red cells (33 day old, not leucodepleted) and died the same day. *Yersinia entercolitica* (serotype 09, biotype 3) was isolated from the patient's blood, the implicated red cell pack, the archive of the implicated donation and a fresh sample of blood taken from the donor 5 months after the donation. On follow-up the donor reported a history of diarrhoea a few weeks prior to the donation.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with red cells contaminated with *Yersinia entercolitica* from the donor's blood.

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

Three (9%) post-transfusion infections (all bacteraemias) were classified as post-transfusion infections of undetermined source due to inconclusive investigation of the transfusion(s) implicated as the source of infection. For seventeen (50%) post-transfusion infection reports (1 HAV infection, 5 HBV infections, 7 HCV infections, 2 HIV infections, 1 syphilis infection and 1 bacteraemia), 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 (HBVx1: invasive medical procedure abroad, HCVx1: renal dialysis & transplant, HCVx1: tattoo, HIVx2: sexual risk factors).

Reporting delay

For the 5 transfusion-transmitted bacterial infections, disease occurred on the same day as the transfusion. Both of the transfusion-transmitted viral infections (1 HBV and 1 HCV) were diagnosed with sub-clinical infections (130 days and 440 days after transfusion respectively) during the follow up of suspected infectious donations. Blood centres were informed of the bacteraemias suspected to be associated with transfusion on the same day (3 cases), the next day, and 7 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 124 days, 98 days, 32 days, 22 days and 12 days for the 5 clinically detected (bacterial) infections. The average interval between transfusion and the initial report (i.e. including all time intervals and reporting delays) was 135 days (n=7).

Under-reporting

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 under-reporting 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 year

During the previous reporting year (i.e. 1/10/97 to 30/9/98) 4 transfusion-transmitted infections were reported (see SHOT Annual Report 1997-98 for details of these cases). One of these was an HCV infection transmitted by transfusion prior to anti-HCV testing of blood donations: this case has now been excluded from the cumulative figures. None of the post-transfusion infections reported during the 1997-98 year that were pending full investigation at the time of the last (i.e. 1997-98) SHOT annual report have been subsequently concluded to have been transfusion-transmitted infections.

The investigations of seven post-transfusion infections that were classified as pending full investigation in the 1997-98 SHOT report have subsequently been concluded to be not due to transfusion (4 cases) or inconclusive (3 cases). One of the inconclusive cases concerned an HIV infection in a patient who had received multiple transfusions during the early 1990s and had no other risk factors for HIV infection. Investigation of the transfusions given to this patient did not identify a source of infection, however, as not all transfusions were investigated, transfusion with HIV infectious, anti-HIV tested, blood was concluded to be the probable, although unproven, source of infection.
Table 23 shows the cumulative number of transfusion-transmitted infections reported by the end of September 1999.
Figure 14 shows the number of reports received by year of transfusion since October 1995.

Table 23

Cumulative total transfusion-transmitted infections: reported between 1/10/95-30/9/99 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 (to end Sept)	Total	Deaths
Infection								
HAV	-	-	1(1)	-	-	-	1(1)	
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)-		5(5)	
HCV	-	-	1(1)	1(1)	-		2(2)	
HIV[c]	-	-	1(3)	-	-	-	1(3)	
Bacteria	-	1(1)	1(1)	3(3)	3(3)[ax2]	3(3)[a]	11(11)	3
Malaria	-	-	-	1(1)[a]	-	-	1(1)	1
Total[d]	1(1)[b]	2(2)	5(7)	6(6)[a]	4(4)[ax2]	3(3)[a]	21(23)	4

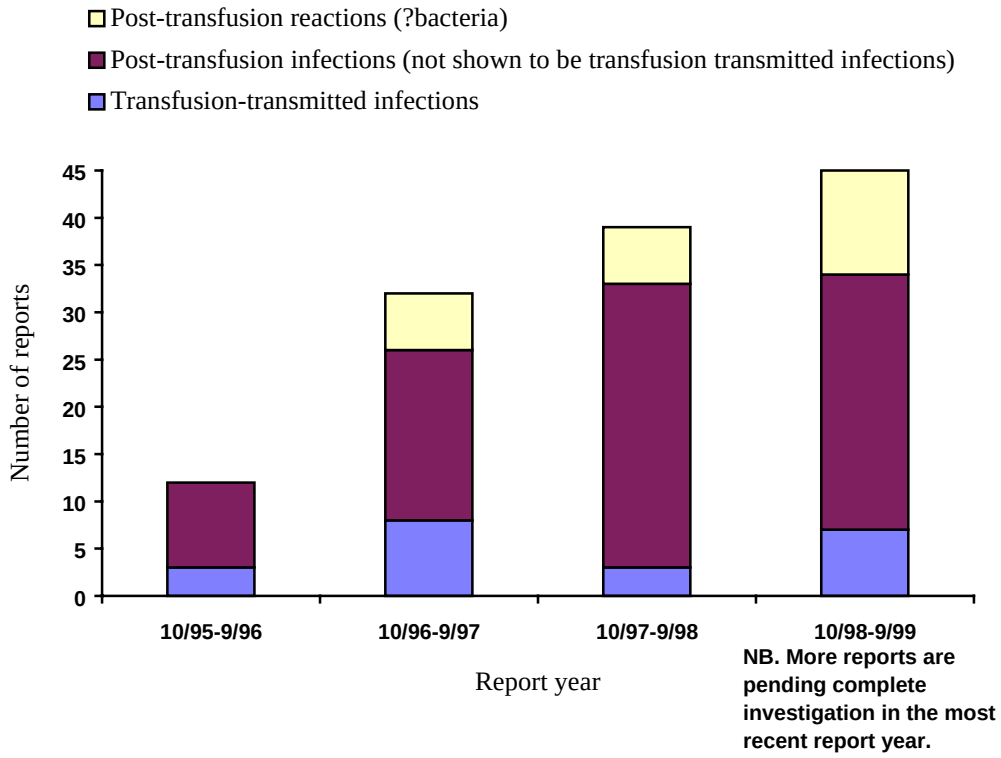
Notes: [a] Infection was implicated in the death of a recipient.

[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, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

Figure 14
PTI reports by report year



COMMENTARY

- Reported transfusion-transmitted infections are rare: only 7 confirmed cases were recognised during this 12-month period of reporting. Investigations of a further 29 cases of post-transfusion infection were reported. 50% of the PTI reports during this year have been shown not to be caused by transfusion. For 9% of the reports the investigation was inconclusive and for the remainder investigation continues. Similarly, in Scotland during this year, one probable case was recognised and two reports were shown not to be caused by transfusion.

- Eleven 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 diagnosis of transfusion-transmitted infections were long - many weeks, months or years. Infections transmitted by transfusion between 1/10/98 and 30/9/99 will continue to be ascertained by the surveillance system as diagnoses are made in the future.

- Two transfusion-transmitted viral infections (1 HBV and 1 HCV) were detected by follow-up of recipients after the detection of infections in blood donors. In one case (HCV) the donor's infection was diagnosed by the blood service by the testing of a subsequent donation, and in the other case (HBV) the donor's GP informed the blood service of the donor's infection. Neither of these transfusion-transmitted infections had caused symptomatic, diagnosed disease in the recipients. One of these transfusion-transmitted infections (HBV) was due to a donation collected from a donor during the marker negative "window period" early in a recent infection. One (HCV) was due to a laboratory error resulting in a false negative test result. Neither of these donors reported risk factors.

- Five transfusion-transmitted bacterial infections arose from donations from donors with infections for which no routine microbiology testing is performed.

- One reported transfusion-transmitted infection resulted from errors in the microbiological testing, or release, of blood donations.

- Two transfusion-transmitted infections, both bacterial, reported during this year resulted in the death of the recipient.

- Several reports have been received of components that were observed to have visual signs of bacterial contamination before use, were not transfused, were sent for bacteriological investigation and were found to contain bacteria expected to cause disease in a recipient if transfused. Inspection of components, especially platelets, detected contamination and prevented morbidity in these incidents. Such inspection should continue to be encouraged. These reports indicate "near-miss" bacterial transmissions. The investigation of the source of the contamination in these cases can be as informative as the investigation of transmissions, and the possibility of requesting and collating some information about these cases in the future is being considered.

RECOMMENDATIONS

- Careful inspection of blood components can, in some cases, detect bacterial contamination and prevent potential transmission. Components showing any unusual colour, turbidity or clumping should not be transfused, but should be returned to the Hospital Blood Bank for culture.

- Clinicians should report all post-transfusion infections diagnosed in their patients to their regional blood service 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. National guidelines (from the NBS) on the investigation of these cases are currently being revised following comments from users.

- Donors' clinicians (and donors themselves) can aid the detection of transfusion-transmitted infections, and hence their appropriate care, by communicating with the blood service about any relevant history of blood donation on patients diagnosed with blood borne infections.

- 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.