15. Transfusion-Transmitted Infections (TTI)

Definition

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection post transfusion, and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection;

and, either:

- at least 1 component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

or:

- at least 1 component received by the infected recipient was shown to contain the agent of infection.

DATA SUMMARY

Implicated Components		*Mortality / morbidity*	
Red cells	**0**	Deaths due to transfusion	**1**
FFP	**0**	Deaths in which reaction was implicated	**1**
Platelets	**6**	Major morbidity	**3**
Other *(specify)*	**0**		
Unknown	**0**		

Gender		*Age*		*Emergency vs. routine and core hours vs. out of core hours*		*Where transfusion took place*	
Male	**4**	< 18 years	**1**	Emergency	**1**	ED	**0**
Female	**2**	<16 years	**0**	Routine	**5**	Theatre	**0**
Unknown	**0**	<1 year	**0**	Not known	**0**	ITU/NNU/HDU/Recovery	**0**
		<4 weeks	**0**			Wards	**6**
				In core hours	**4**	Community	**0**
		Total	**1**	Out of core hours	**1**	Other	**0**
				Not known/applicable	**1**	Not known	**0**

Reports of suspected transfusion-transmitted infections

Most reports of suspected viral and bacterial transfusion-transmitted infections (TTIs) are received and investigated by the UK Blood Services and then reported to the NHSBT/HPA Infection Surveillance Unit. From here, data are included in the annual SHOT report. A number of reports are also received via the MHRA's online reporting system for Serious Adverse Blood Reactions and Events (SABRE).

Incidents reported in any one year to the blood services and/or MHRA are included in the same SHOT reporting year, even if the investigation is not yet complete, as the investigation into some suspected viral TTIs can take several months to complete.

During 2008, 33 suspected TTI incidents were reported by blood centres and hospitals throughout the UK.

Of these, 4 were confirmed (all bacterial, described below) according to the above definition; and among the remainder, in 1 case the bacterial report was concluded as undetermined (i.e. it was not possible to confirm or refute that the patient's infection was acquired via blood transfusion); in 2 incidents it was not possible to confirm or refute TTI because the blood unit was not available for investigation; in 23 investigations, the conclusion was not TTI (3 hepatitis B [HBV], 7 hepatitis C [HCV], 3 HIV, 1 Parvo B19, 1 toxoplasmosis, 1 chickenpox and 7 bacterial); and 3 incidents (1 HBV, 2 HCV) are pending complete investigation.

CONFIRMED INCIDENTS

Report of transfusion-transmitted *Staphylococcus epidermidis*

An elderly male patient was transfused with a unit of pooled platelets for thrombocytopenia. During the transfusion the patient developed chills, rigors, back pain and hypotension, and the transfusion was stopped. *Staphylococcus epidermidis* was isolated from patient blood cultures taken at the time of the reaction, and from the remains of the platelet pack. Four associated red cell units and 1 unit of fresh frozen plasma were recalled by the blood services but were found to be negative on culture.

All 4 donors contributing to the platelet unit were recalled. *S. epidermidis* was identified from venepuncture site samples from 2 of the donors, from pre-cleaning swabs only. Pulse field gel electrophoresis (PFGE) revealed that 1 of the strains was identical to that isolated from the remains of the platelet pack. The blood culture isolate from the patient was not available for further investigation and so it was not possible to determine whether all 3 isolates (from patient, donor and pack) were of identical strains. However, contamination of the platelet unit by skin flora from the donor venepuncture site was probably responsible for the patient's reaction. *S. epidermidis* is a common skin commensal and it is recognised that the donor arm cleansing procedure is not 100% effective.[28] Informal quality audits carried out by the blood services during 2008 suggested that the procedure could be improved, and an extensive staff re-training exercise was undertaken (see commentary).

Report of transfusion-transmitted Group G streptococcus (2 recipients)

A unit of apheresis platelets was split to produce 2 platelet doses. Pack 1 was transfused to a teenager with acute lymphoblastic leukaemia (ALL) who reacted with allergy-like symptoms. Pack 2 was transfused to a female patient in her 50s with acute myeloid leukaemia (AML) who developed chills, nausea and a feeling of impending doom. The remains of both units were returned to the blood services for investigation, with a delay in the return of pack 1 due to the initial diagnosis of an allergic reaction.

Blood cultures from both patients yielded Lancefield Group G streptococcus (GGS), as did cultures of both platelet units carried out at the blood services. GGS are known as both commensals and pathogens in animals and humans.[29] The apheresis donor denied any recent illness or change in bowel habit, but GGS was identified from their stool sample.

All 5 isolates (from both patients, both packs and the donor) were sent to a national reference laboratory for typing, and were found to be of the same strain. The likely but unproven chain of transmission was from donor gut to venepuncture site via the donor's fingers, and from there to the donated component. As with the previous case, it cannot be guaranteed that this chain of transmission would be prevented by donor arm cleansing (see commentary).

Report of transfusion-transmitted Group G streptococcus

A woman in her 50s with severe aplastic anaemia received 1 unit of pooled platelets. Within 5 minutes of starting the infusion the patient developed urticaria and pain along the access vein. She was given antihistamine and the transfusion was continued. One hour later she became pyrexial and hypotensive, requiring admission to the Intensive Therapy Unit (ITU). The transfusion was stopped and patient blood cultures were taken. These revealed Lancefield Group G streptococcus (GGS), as did cultures of the remains of the platelet pool. Four units of red cells and 1 unit of fresh frozen plasma associated with the implicated pack were recalled but cultures of these were all negative.

The donors contributing to the platelet pool were recalled; GGS was identified in stool samples provided by 3 of the 4 donors. Typing confirmed that 1 of these isolates represented the same strain as that isolated from both the patient blood cultures and the platelet unit. The donor denied any illness at or around the time of donation.

Report of transfusion-transmitted *Klebsiella pneumoniae* (two recipients)

A donation of apheresis platelets was split to produce 2 platelet doses. The first was transfused into a male neurosurgery patient (head injury) with pre-existing ischaemic bowel, liver disease and sepsis. The patient died 11 hours post transfusion and death was thought to be due the sepsis from the ischaemic bowel. As a transfusion reaction was not suspected, the transfused pack was not retained for further investigation. However, blood cultures had been taken from the patient prior to his death.

The second recipient was a male patient with AML with chemotherapy-related pancytopenia. Five minutes into the transfusion the patient became acutely unwell, requiring admission to ITU where he subsequently suffered a cardiac arrest and died. Blood cultures had also been taken from this patient prior to his death. The remains of the transfused pack were cultured at the hospital microbiology laboratory before being returned to the blood services.

Blood cultures from both patients yielded *Klebsiella pneumoniae*, as did cultures of the unit transfused to the patient with AML, and all 3 isolates were found to be of a single strain. The case was concluded as a proven incident of bacterial contamination of two platelet units with *K. pneumoniae*. This probably resulted in the death of the first patient and contributed to the death of the second. The source of the organism was most likely the donor gut, transferred to the venepuncture site and from there to the donated component. Both incidents were reported to the local Strategic Health Authority (SHA) as a Serious Untoward Incident.

OTHER INCIDENTS

Three suspected TTI investigations were undetermined in 2008. In 2 cases the blood packs transfused were not available for further investigation post transfusion to confirm or refute TTI. Similar cases appear in the Acute Transfusion Reaction (ATR) chapter in which it was not possible to confirm whether the patient's reaction was a result of bacterial contamination or due to some other cause.

Undetermined investigation: *Pantoea agglomerans*

An elderly, frail patient was transfused with 3 units of red cells for tumour related anaemia. After 200 mL of the third unit the patient developed chills, rigors, wheeze and shortness of breath, and died within an hour. The differential diagnosis included bacterial contamination, TRALI and fluid overload. The patient was not on antibiotics at the time of reaction and blood cultures were not taken.

The 2 empty packs and the remains of the third unit were returned to the blood service for investigation. The empty packs were washed out with sterile saline and cultures were set up. The exterior of the third pack was heavily contaminated with blood, and both ports had been used and blocked with spigots. Cultures were taken. This unit had been cultured at the hospital microbiology laboratory where Enterobacter species, Pantoea species and *Enterococcus faecalis* were grown. These organisms are all part of the normal intestinal flora.

Cultures of the first and second (empty) units yielded no growth and *Bacillus pumilus* respectively, while culture of the third unit yielded *Pantoea agglomerans*, consistent with the results from the cultures performed by the hospital. *Pantoea agglomerans* rarely causes infection in the normal host but is a common nosocomial isolate, arising from the endogenous intestinal flora of hospitalised patients. This recipient had metastatic carcinoma of the bowel and extensive oesophageal varices, so this organism could have originated from the patient. However, in the absence of blood cultures taken prior to the transfusion, confirmation is not possible. Similarly, it is not possible to confirm that the source of the coliform was a contaminated unit of blood, or that the coliform was the cause of, or contributed to, death.

Histopathology was inconclusive and investigation into possible TRALI is ongoing.

Undetermined investigation: blood unit not returned to blood service

An elderly patient with chronic myeloid leukaemia (CML) developed a pyrexial reaction during the second unit of a 2 unit red cell transfusion. The patient's blood cultures subsequently grew *Streptococcus sanguinis* and *Streptococcus salivarius*. The red cell unit was discarded and was not cultured. As a result, it is unknown whether this patient's infection was acquired via blood transfusion or not. The patient was treated with antibiotics and made a full recovery, and the hospital's policy on notifying the blood service of suspected TTI incidents was reviewed.

Undetermined investigation: blood unit not investigated by blood service

A male patient was transfused with 3 units of red cells for haematuria with urine retention. Five to 10 minutes into transfusion of the third unit the patient developed rigors and pyrexia. The transfusion was stopped and blood cultures were taken both after the initial reaction occurred and 12 hours later. Both cultures grew *Enterococcus faecalis*. No cultures had been taken from the patient prior to transfusion. The implicated unit was sent to the local blood centre but was not cultured for bacterial growth. Despite investigations into patient samples (culture of pre-transfusion urine and

catheter samples: both negative), an alternative source of infection was not found. It is unknown whether this patient's infection was acquired via blood transfusion or not.

Near Miss

In this category, 1 of 2 doses of apheresis platelets was returned to the blood service after blood bank staff noticed a large clump in the pack (Figure 21). The second dose was recalled and its appearance was normal. *Staphylococcus aureus* was isolated from the index pack. The donor was suspended from donation and skin, nasal and venepuncture site samples were taken. *S. aureus* was identified from the nasal sample. PFGE analysis confirmed that the isolates from the donor's nose and from the platelet unit were of the same strain. The donor did not appear to have a naturally high bacterial skin count; no *S. aureus* was detected from the skin and there was no history of skin disease. The donor was re-instated to an active donation status and requested to wash his hands and arms prior to making subsequent donations.

Figure 21
Staphylococcus aureus in apheresis platelet unit

Investigations reported as pending in previous years

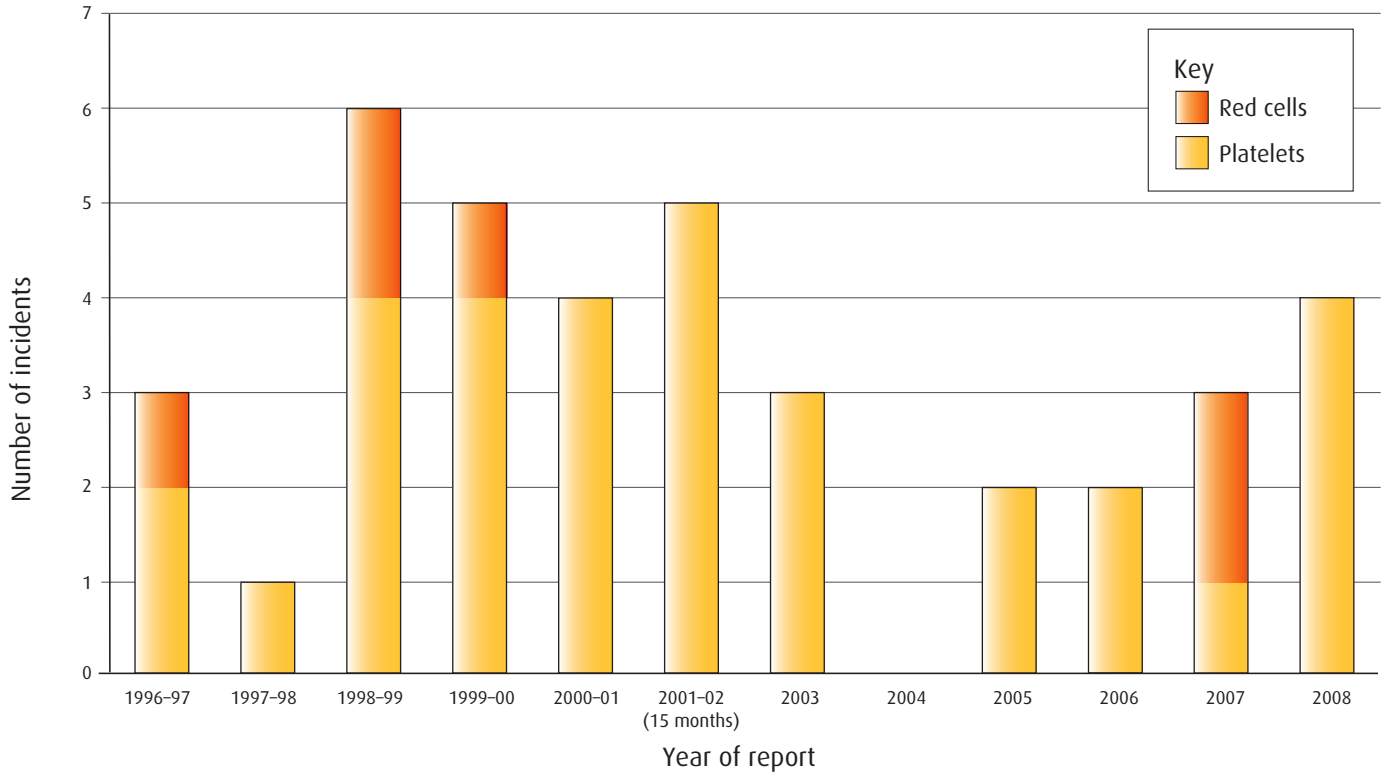
The CMV investigation pending in 2007 is now complete. No donor was found to have evidence of CMV infection, and it was concluded that there was no evidence of a transfusion-transmitted infection.

Cumulative data

Bacterial TTIs

Since 1996, a total of 38 bacterial TTI incidents have been confirmed (Figure 22), involving a total of 40 recipients (Tables 50 and 51). In total, 32 incidents have related to the transfusion of platelets and 6 have related to the transfusion of red cells. All of the confirmed cases in 2008 related to the transfusion of platelets.

Figure 22
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from October 1998)*

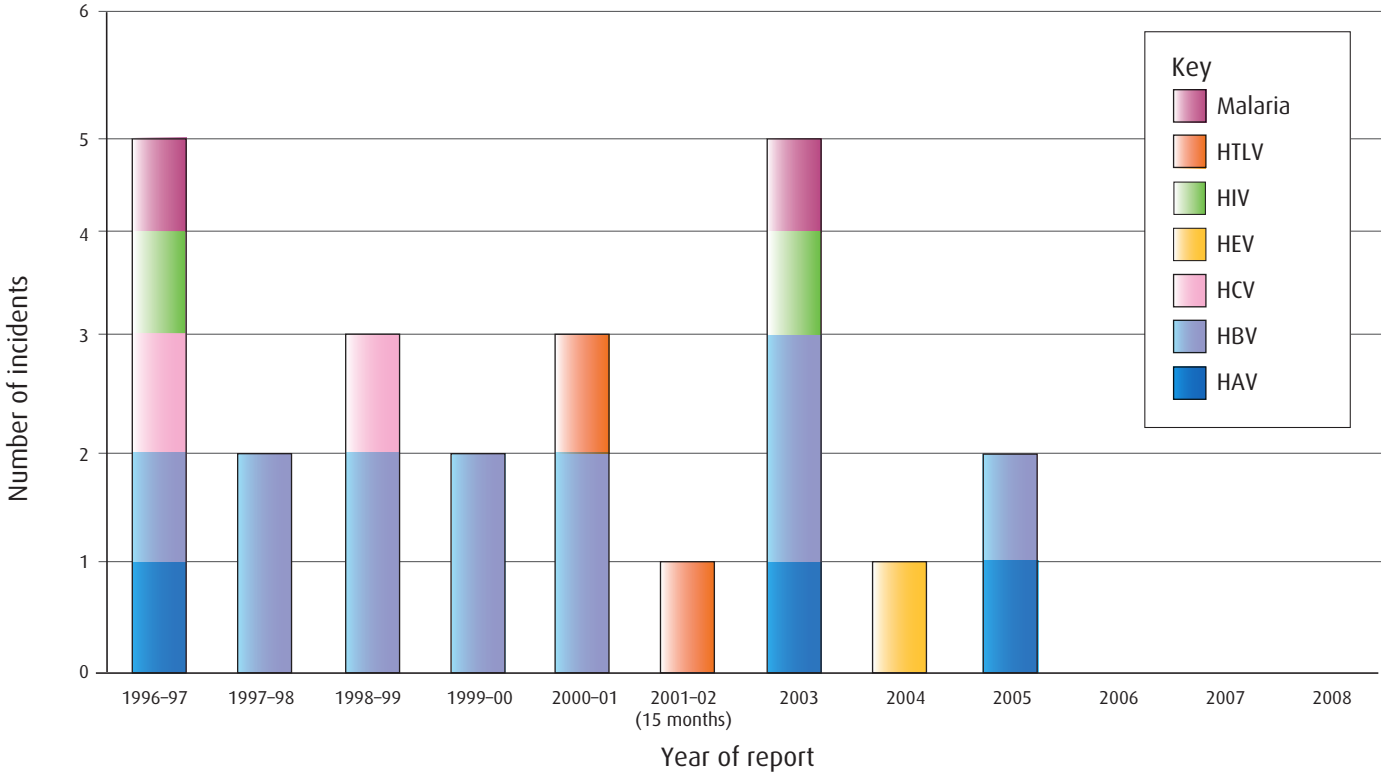


* *In 2004 there was a further incident (not included in Figure 22) involving contamination of a pooled platelet pack with S. epidermidis that did not meet the TTI definition because transmission to the recipient was not confirmed, although it was likely.*

Viral and parasitic TTIs

Since 1996, 22 confirmed incidents of transfusion-transmitted viral and parasitic infections have been reported (Figure 23), involving a total of 25 recipients. These include 10 HBV incidents (11 recipients), 3 HAV (3 recipients), 1 HEV (1 recipient), 2 HCV (2 recipients), 2 HIV (4 recipients), 2 HTLV (2 recipients) and 2 malaria (2 recipients) (Tables 50 and 51). There were no confirmed transfusion-transmitted viral or parasitic infections in 2006, 2007 or 2008.

Figure 23
Number of viral and parasitic TTI incidents, by year of report and infection type (Scotland included from October 1998)*†



* *The year of transfusion may be many years prior to the year the case is investigated and reported in SHOT, due to the chronic nature of some of these infections, leading to delay in identification of the infection.*

† *In 2003 an anti-HIV negative donation (donated in 2002) was reported HIV RNA positive on retrospective testing of a seroconverting donor. Red cells from the seronegative unit had been transfused into an elderly patient who died soon after surgery and her HIV status was not determined prior to death (not included in Figure 23).*

vCJD

To date, there have been 4 incidents involving the transmission of vCJD/prion infection via blood transfusion (no change from 2007 report, see Table 50 and Table 51 below). Reporting of suspected vCJD transmissions differs from that of other infections. The cases that have been reported were among a small group of recipients of blood who were under active surveillance because they had received blood components from donors who later developed vCJD. The 4 identified individuals had received non-leucodepleted red blood cells between 1996 and 1999.

Since 1997, the UK Blood Services have introduced a number of precautionary measures:

- leucodepletion of all blood components (1999)
- use of methylene blue virally inactivated FFP obtained outside the UK for children under 16 (2002)
- importation of plasma for fractionation (1998)
- imported solvent detergent (SD) treated FFP for adult patients with thrombotic thrombocytopenic purpura (TTP) (2006)
- exclusion of donors who have received a blood transfusion in the UK since 1980 (2004).

Table 50
Number of confirmed TTI incidents in the UK between October 1996 and December 2008, by SHOT reporting year (Scotland included from October 1998)

	10/1996–09/2001	10/2001–12/2006	2007	2008	Total
Bacteria	19	12	3	4	**38**
HAV	1	2	0	0	**3**
HBV	7	3	0	0	**10**
HCV	2	0	0	0	**2**
HEV	0	1	0	0	**1**
HIV	1	1	0	0	**2**
HTLV	1	1	0	0	**2**
Malaria	1	1	0	0	**2**
vCJD/Prion	0	4	0	0	**4**
Total	**32**	**25**	**3**	**4**	**64**

Table 51
Number of infected recipients identified and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2008 (Scotland included from October 1998)

	Number infected recipients identified	Death (due to infection)	Major morbidity	Minor morbidity
Bacteria	40	10	26	4
HAV	3	0	2	1
HBV	11	0	11	0
HCV	2	0	2	0
HIV	4	0	4	0
HEV	1	0	0	1
HTLV	2	0	2	0
Malaria	2	1	1	0
vCJD/Prion	4	3	1	0
Total	**69**	**14**	**49**	**6**

COMMENTARY

In 2008, 4 confirmed bacterial TTI incidents were reported involving the transfusion of contaminated components to 6 recipients, 4 of whom recovered and 2 of whom died (1 death due to transfusion, 1 death in which transfusion was implicated). All 4 incidents related to the transfusion of platelet units. In 2 of the 4 cases, an apheresis donation was split in 2 and transfused into 2 recipients.

Of these, 4 transfusions took place within core hours, 1 took place outside of core hours and the time of 1 transfusion was unknown. There were 5 routine transfusions and 1 emergency transfusion (patient critically ill with head injury).

It is recognised that donor arm cleansing techniques are unlikely to be 100% effective in removing bacteria from the venepuncture site.[28] However, informal quality audits in 2008 suggested that the procedure could nevertheless be improved. An extensive staff re-training exercise has been undertaken and monitoring logs were implemented

to observe and record evidence of practice standards. A national audit programme is being developed to support effective pre-donation skin preparation. The UK blood transfusion services (UKBTS) have also asked the Standing Advisory Committee on Transfusion-Transmitted Infections (SACTTI) to produce standards on how donor arm cleansing should be monitored.

The 3 undetermined investigations in 2008 were all associated with the transfusion of red cells. The first case involved a unit in which the exterior was heavily contaminated with blood. The other 2 cases related to blood units that were not cultured for bacterial growth either because the bag had been discarded by the hospital or because the bag was delayed in transit to the blood service These incidents highlight the importance of care in the handling, transport and storage of units involved in post-transfusion reaction investigations. Packs must be appropriately sealed and packaged, and internal processes must ensure the timely return of units to the blood services and to the bacteriology laboratory. If hospitals choose to culture packs locally, the pack must still be returned to the blood services for further investigation.

Two TTI incidents in 2008 involved the transfusion of an implicated donation to more than 1 recipient. Suspected cases must be reported promptly so that associated units may be recalled. Difficulties arise when it is uncertain whether the reaction was due to a bacterial cause or not.

Visual inspection of 1 platelet unit prevented the probable transmission of *S. aureus* (Near Miss incident). It is important that staff starting a transfusion visually check all components prior to doing so. However, bacterial contamination can still occur in the absence of visible features.

The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) is scheduled to discuss bacterial screening and pathogen inactivation of platelets in July 2009.

For the third consecutive year there were no confirmed viral transmissions, consistent with the very low estimated frequency of infectious donations entering the UK blood supply (2006-2007):

HIV 0.21 per million donations tested
HCV 0.02 per million donations tested
HBV 1.17 per million donations tested
HTLV 0.09 per million donations tested

For more information see www.hpa.org.uk. *(Follow the headings: infectious diseases, topics A-Z, blood borne infections in blood donors, epidemiological data.)*

Surveillance of TTIs tends to be biased towards acute cases that are immediately clinically apparent, but a high index of suspicion is required to ensure that the correct investigations are carried out. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. As a result incidents involving transfusion-related chronic infection may not be suspected and reporting may be incomplete.

RECOMMENDATIONS

New recommendations from this report

- Staff must maintain a high index of suspicion of bacterial causes when managing acute transfusion reactions. Symptoms may appear to be more allergic in nature, but cultures must still be performed whenever bacterial contamination is a possibility.

  Action: Hospital Transfusion Teams

- Staff involved in transfusion should report suspected cases of bacterial contamination to the blood services as soon as possible, in order to facilitate the return of implicated packs and the recall of any associated units, even though in some cases it may be difficult to determine whether the patient's reaction was due to a bacterial cause.

  Action: Hospital Transfusion Teams/UK Blood Services

- Strategies to reduce bacterial contamination of blood components should continually be reviewed. SHOT welcomes the involvement of SaBTO in this process.

  Action: SaBTO, UK blood services

Recommendations still active from previous years

Year first made	Recommendation	Target	Progress
2005	Hospitals should consult the blood services about the investigation of transfusion reactions suspected to be due to bacteria. Attention should be paid to the sampling and storage of implicated units or their residues and packs returned to blood services for testing.	**Hospital Transfusion Teams**	Guidance for English hospitals can be found on the NBS hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer. For other services please discuss with your supply blood centre.
2003	Efforts to prevent bacterial contamination of blood components should continue. These include: - Diversion of the first 20-30 mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site) - Enhanced donor arm cleansing using chlorhexidene - Adherence to BCSH guidelines (1999) with regard to the visual inspection of blood components for any irregular appearance immediately prior to transfusion - The UK Blood Services should continue to investigate methods to reduce bacterial contamination.	**UK Blood Services, blood collection teams, hospital transfusion laboratories, staff undertaking pre-transfusion bedside checking**	UK Blood Services have introduced enhanced donor arm cleansing and continue to monitor and evaluate the success of all possible interventions, such as bacterial screening and/or pathogen inactivation.
2003	Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately.	**Hospital Transfusion Teams**	Serious Adverse Reactions are required to be reported by hospitals under the terms of the BSQR.