18. Transfusion-Transmitted Infection (TTI)

Definition

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

- The recipient had evidence of infection following transfusion with blood components, and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection;

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 contain the agent of infection.

DATA SUMMARY

Total number of incidents	**2**	*Implicated components*		*Mortality/morbidity*	
Total number of recipients	**3**	Red cells	**1**	Deaths due to transfusion	**1**
		FFP	**0**	Deaths in which reaction was implicated	**0**
		Platelets	**2**	Major morbidity	**2**
		Other (specify)	**0**		

Gender		*Age*		*Emergency vs. routine and core hours vs. out of core hours*		*Where transfusion took place*	
Male	**3**	18 years+	**2**	Emergency	**0**	ED	**0**
Female	**0**	16 years+ to 18 years	**0**	Routine	**3**	Theatre	**0**
Unknown	**0**	1 year+ to 16 years	**0**	Not known	**0**	ITU/NNU/HDU/Recovery	**0**
		28 days+ to 1 year	**1**			Wards	**3**
		Birth to 28 days	**0**	In core hours	**2**	Community	**0**
		Unknown	**0**	Out of core hours	**1**	Outpatient/day unit	**0**
		Total	**3**	Not known/applicable	**0**	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 Epidemiology Unit. From here, data are included in the SHOT report. A number of reports were also received from SHOT via the MHRA's online reporting system for Serious Adverse Blood Reactions and Events (SABRE).

Incidents are included for the year in which they were reported, even if the investigation is not yet complete, as the investigation into some suspected viral TTIs can take several months.

During 2009, 39 suspected TTI incidents were reported by blood centres and hospitals throughout the UK. A number of ATRs were reported which did not meet the criteria for TTI, either because there was no evidence of infection in the recipient or because an alternative source of infection was identified. Many of these cases were reported to the NHSBT/HPA Epidemiology Unit only and not to SHOT. It is recommended that such reactions be reported to SHOT and it is likely that most cases could be recorded as febrile reactions.

Two incidents (both bacterial, described below) were confirmed as TTIs according to the above definition. Thirty investigations were concluded as not TTI, including 11 hepatitis B (HBV) incidents, 1 vCJD investigation, 1 hepatitis C (HCV), 3 HIV, 1 herpes simplex virus, and 13 bacterial incidents.

There were 4 undetermined TTI investigations in 2009 – 3 bacterial and 1 HIV. In 2 of the bacterial cases clinical suspicion was that bacterial contamination was not the cause of the reaction, but it could not be ruled out. In 2 cases there was growth from the patient blood cultures but the transfused packs had been discarded and so were not available for culture. In the third case, coagulase negative staphylococci were isolated from a unit of transfused platelets at the hospital microbiology laboratory, but environmental contamination of the pack during testing could not be ruled out, and the packs were not returned to the blood services for investigation. Patient blood cultures were negative, but these had been taken 4 days after the patient had been started on antibiotics.

The undetermined HIV investigation was a complex case involving a large number of donors (116). All but 1 of the donors (115/116) were re-tested; none was found to have markers of HIV infection. It was not possible to trace the remaining donor (donor has possibly left the country); however, it was subsequently discovered that the recipient was exposed to another risk of HIV infection (sexual contact), which was thought more likely to have been the source of infection.

Three incidents reported in 2009 are pending complete investigation (1 HTLV, 1 HBV and 1 HCV).

Confirmed Incidents

Report of transfusion-transmitted *Streptococcus pneumoniae*

An un-issued, expired unit of apheresis platelets was referred for microbiological testing after routine quality monitoring found the pack to have a low pH and abnormal colouration. *Streptococcus pneumoniae* was isolated from the unit. Four associated units had been transfused into 2 patients with acute myeloid leukaemia (AML) – 1 unit to an adult and 3 neonatal units to a baby.

Retrospective investigations revealed that both patients had experienced transfusion reactions (including a fever of 39.8°C in the adult patient and 40.5°C in the baby), but these were thought at the time to have been related to the patients' underlying conditions. All of the transfused packs had been discarded but a blood sample taken from the adult patient yielded *S. pneumoniae*. Blood cultures from the neonatal patient were negative, but the patient was on antibiotics at the time of transfusion.

The organisms isolated from both the contaminated index pack and the adult patient were compared using molecular techniques (Pulse Field Gel Electrophoresis, Multi Locus Sequence Typing, and Variable Number Tandem Repeat analyses) and were found to be indistinguishable from one another. Nose and throat swabs taken from the donor were negative; however, *S. pneumoniae* is known to be difficult to culture from swabs.[47,48] Approximately 4–8% of adults carry *S. pneumoniae*.[48,49] It is thought that the organism may have originated from the throat of the donor or donor carer and been transferred from there to the venepuncture site by fingers or a cough/sneeze or from an underlying asymptomatic bacteraemia in the donor.

Report of transfusion-transmitted *Pseudomonas koreensis*

Three units of red cells were transfused into an elderly man receiving palliative care for cancer of the rectum and liver cirrhosis. Approximately 2 hours into transfusion of the third unit the patient became unwell with hypotension, fever (39.6°C), and abdominal pain and vomiting; he died later the same day.

Pseudomonas koreensis was cultured from the remains of the red cell unit at the microbiology laboratories of both the hospital and the blood service, and also from the patient blood cultures. All 3 isolates were found to be indistinguishable on molecular typing. *P. koreensis* is associated with cold temperatures and it was thought that contamination of the unit may have occurred within a cold storage room or processing area at the blood service or the hospital. Skin carriage of *P. koreensis* is rare. The donor was recalled and swabs were taken from the arms but these were negative. The donor was thought unlikely to have been the source of the contaminating bacteria. Despite extensive environmental sampling

of processing and cold storage areas at the hospital and blood services, the source of the contamination could not be identified. The red cell pack was pressure tested but this did not reveal any holes or defects and so it is unclear how the bacteria may have entered the pack. The incident has led to an extensive review of cold room cleaning protocols within processing and issues areas.

Other Incidents

Near Miss

Staphylococcus aureus was isolated from 2 of 3 un-issued, 4-day-old units of apheresis platelets after visible clumps/aggregates were noted in the packs. The donor was sampled and *S. aureus* was isolated from the nose, throat and venepuncture site pre arm-cleansing. Coagulase negative staphylococci were isolated from the venepuncture site post cleansing. The isolates identified from the donor and platelet packs were found to be a single clonal type. In light of the results of the swabs taken from the donor it was agreed that he should be permanently deferred from the panel due to *S. aureus* colonisation. Carriage of this organism varies. It is suggested that between 20 – 40% of the population carry it in their nose.[50] Increased carriage of *S. aureus* on the skin is associated with eczema and other dermatological conditions.

Investigations reported as pending in previous years

The investigations reported as pending in 2008 are now complete (1 HBV, 2 HCV). No donor was found to have evidence of infection, therefore all 3 incidents were concluded as not transfusion-transmitted infection.

Cumulative Data

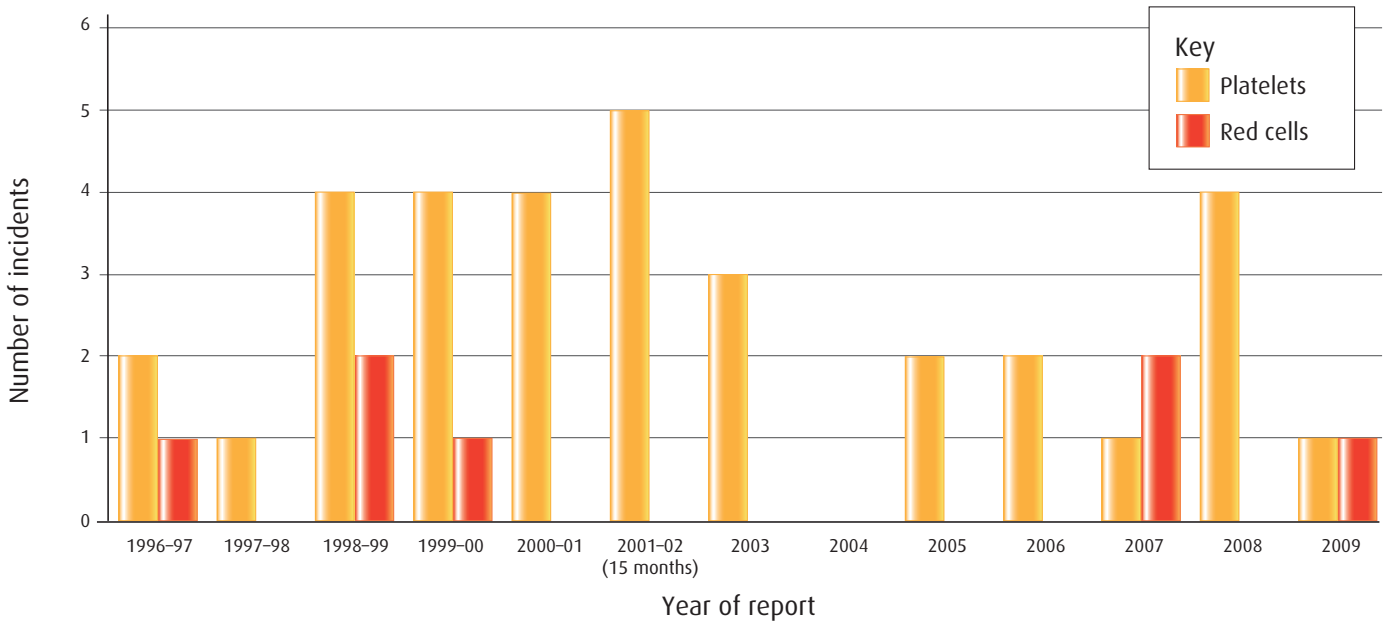
Bacterial TTIs

Since 1996, 40 bacterial TTI incidents have been confirmed involving a total of 43 recipients (Figure 21 and Table 45), 11 of whom died (death due to infection or in which transfusion reaction was implicated). A total of 33 incidents have related to the transfusion of platelets whereas only 7 have related to the transfusion of red cells.

In Figure 21:

- The histogram shows the number of incidents, not infected recipients identified. For 2 incidents in 2008, and 1 in 2009, 2 infected recipients were identified.
- In 2004 there was a further incident (not included in Figure 21) involving the contamination of a pooled platelet pack with *S. epidermidis* which did not meet the TTI definition because transmission to the recipient was not confirmed, although it was likely.

Figure 21
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from 10/1998)



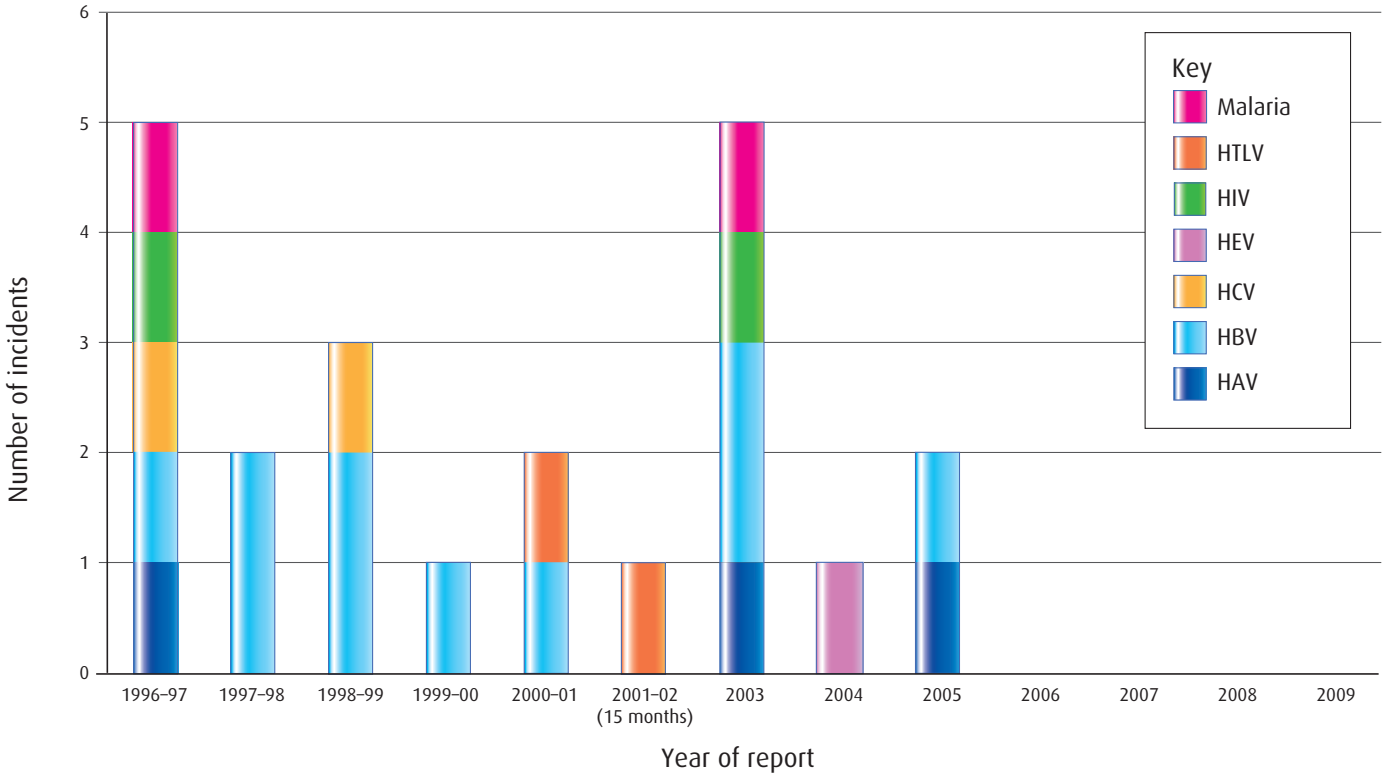
Viral and parasitic TTIs

Since 1996, 22 confirmed incidents of transfusion-transmitted viral and parasitic infections have been reported, involving a total of 25 recipients (Figure 22 and Table 45), 1 of whom died (malarial transmission). There have been no confirmed transfusion-transmitted viral or parasitic infections in recent years – the last confirmed incident was in 2005.

In Figure 22:

- 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 viral infections. Figure shows number of *incidents*, not infected recipients identified. For 1 incident in 1996–97 (HIV), and 1 in 1999–2000 (HBV), 3 and 2 infected recipients were identified respectively.
- 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 22).
- No screening was in place for the following TTIs at the time of transfusion: HAV, HEV, HTLV.

Figure 22
Number of viral and parasitic TTI incidents, by year of report and infection type (Scotland included from 10/1998)



Variant Creutzfeld Jakob disease (vCJD)

There was 1 vCJD investigation in 2009 which was concluded not TTI due to blood components. A person with haemophilia was found to have evidence of abnormal prion protein in his spleen at postmortem. The patient received red cell transfusions between 1998 and 2007, but had also been treated with multiple batches of UK sourced clotting factors in the 1990s, including 2 batches of Factor VIII that were manufactured using plasma from a donor who went on to develop vCJD. It was thought that Factor VIII was the most likely source of infection.[51]

To date, there have been 4 incidents involving the transmission of vCJD/prion infection via red cell transfusion. Reporting of suspected vCJD transmissions differs from that of other infections: the cases reported were among a small group of recipients 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 (MB-FFP) obtained outside the UK for children under 16 years old (2002)
- importation of plasma for fractionation (1998)
- imported solvent detergent (SD) treated FFP for adult patients with thrombotic thrombocytopenic purpura (TTP) (2006)[39]
- exclusion of donors who have received a blood transfusion in the UK since 1980 (2004).

Table 45
Number of confirmed TTI incidents, infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2009 (Scotland included from October 1998)
NB No screening in place for the following TTIs at the time of transfusion: HAV, HEV, HTLV, vCJD/prion

Infection	Number of Incidents	Number of Infected Recipients	Death due to, or contributed to, by TTI	Major morbidity	Minor morbidity
Bacteria	40	43	11	28	4
HAV	3	3	0	2	1
HBV	10	11	0	11	0
HCV	2	2	0	2	0
HEV	1	1	0	0	1
HIV	2	4	0	4	0
HTLV-I	2	2	0	2	0
Malaria	2	2	1	1	0
Prion	1	1	0	1	0
vCJD	3	3	3	0	0
Total	**66**	**72**	**15**	**51**	**6**

COMMENTARY

Currently the greatest risk of transfusion-transmitted infection is associated with bacterial contamination, although there is likely to be under-reporting of both viral and bacterial incidents. A BCSH guideline on the management of acute transfusion reactions is currently in preparation, and a revised protocol is being devised by NHSBT. One of the confirmed bacterial incidents in 2009 was revealed only upon retrospective investigation after an expired unit of platelets was found to have a low pH and abnormal colouration, when the fate of associated components was investigated. This case demonstrates that acute transfusion reactions can be difficult to recognise, particularly when patients have other underlying symptoms and/or are taking antibiotics, which may mask their symptoms. This case was also the first known report of transfusion-transmitted *Streptococcus pneumoniae* infection in the UK.

If bacterial contamination is suspected, staff should report the incident to the blood services as soon as possible, in order to facilitate the return of implicated packs and the recall of any associated units. A BCSH guideline on the management of acute transfusion reactions is currently in preparation, and a revised protocol is being devised by NHSBT. Attention should be paid to the sampling and storage of implicated units or their residues to avoid environmental contamination of the pack. Guidance for English hospitals can be found at: http://www.blood.co.uk/hospitals/library/request_forms/aer/. For other services please contact the local blood supply centre.

The most likely source of the organism in the *Pseudomonas koreensis* case was thought to have been environmental contamination within a cold storage room or issues area. While the MHRA's 'Orange Guide' includes recommendations on standards of environmental cleanliness for 'clean' rooms (where sterile conditions are maintained),[28] there are no guidelines covering acceptable levels of cleanliness within cold storage areas. Nonetheless, cleaning protocols for such areas should be reviewed regularly and compliance with these should be audited.

Strategies to reduce the bacterial contamination of blood components should be under continual review. At a meeting in July 2009, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) did not recommend the adoption of pathogen inactivation (PI) of platelets at present, until further data on the cost benefit and safety of this method become available. Most of the UK blood services already screen platelet donations for bacterial contamination and this is planned for introduction in England in early 2011. It should be noted that the effectiveness of screening is influenced by the methodology used and data from a number of studies have shown that bacterial screening is unlikely to prevent all transmissions.[52] The UK Standing Advisory Committee on Transfusion Transmitted Infection (SACTTI) have tasked a subgroup to recommend how bacterial screening should be performed.

The current estimated risks of transmission of HBV, HCV, HIV and HTLV via blood transfusion are low (1.09 per million donations for HBV, 0.01 per million for HCV, 0.19 for HIV and 0.04 for HTLV-1).[53]

Learning point

Clinicians investigating suspected viral TTIs should explore all possible risk exposures (e.g. surgery, or discuss with the patient any sexual risks, injecting drug use, occupational exposure) in parallel with the blood service investigations, as highlighted by the undetermined HIV investigation this year.

RECOMMENDATIONS

- Staff should maintain a high index of suspicion for bacterial causes when managing acute transfusion reactions. Symptoms may appear to be related to the patient's underlying condition, and temperature rises may be small or absent altogether.

  Action: Hospital Transfusion Teams

- Processing and issues teams at the UK blood services and hospital transfusion teams should be vigilant to any abnormalities or clumps present in packs prior to transfusion, as highlighted by the Near Miss case in 2009.

  Action: Hospital Transfusion Teams, UK blood services

- Cleaning protocols for cold rooms and processing and storage areas should be reviewed regularly. Compliance with these should be audited.

  Action: Hospital Transfusion Teams, UK blood services

- Clinicians investigating suspected viral TTIs should explore all possible risk exposures in parallel with the blood service investigations, in order to determine the patient's most likely source of infection.

  Action: Clinicians, UK blood services

Recommendations still active from previous years, with modifications

Year first made	Recommendation	Target	Progress
2008	Staff must maintain a high index of suspicion of bacterial causes when managing acute transfusion reactions. Symptoms may appear to be allergic in nature, but cultures must still be performed whenever bacterial contamination is a possibility.	**Hospital transfusion teams**	A BCSH guideline on the management of acute transfusion reactions is in preparation.
2005, 2008, 2009	Where bacterial contamination is suspected, staff should report the incident to the blood services as soon as possible in order to facilitate the return of implicated packs and the recall of any associated units. Attention should be paid to the sampling and storage of implicated units or their residues to avoid environmental contamination of the pack.	**Hospital transfusion teams, UK blood services**	Guidance for English hospitals can be found on the NHSBT hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer/ For other services please discuss with the local blood supply centre.
2003, 2008	Strategies to reduce bacterial contamination of blood components should continually be reviewed. 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 - Consideration of bacterial screening interventions and/or pathogen inactivation - Adherence to BCSH guidelines (2009) with regard to the visual inspection of blood components for any irregular appearance immediately prior to transfusion.	**UK blood services, SaBTO, 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 all possible incidents of post-transfusion infection via appropriate local and national reporting routes.	**Hospital transfusion teams**	Serious Adverse Reactions must be reported under the terms of the BSQR 2005. Reporting to SHOT is required for compliance with HSC/2002/009 'Better Blood Transfusion' and is a standard for the Clinical Negligence Scheme for Trusts in England.