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 cases	**0**	**There were no *proven* cases of TTIs reported in 2010**

Most reports of suspected viral and bacterial 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 2010, 48 suspected TTI incidents were reported by Blood Services and hospitals throughout the UK. A number of ATRs (over 50) were reported and investigated which did not meet the criteria for TTI, either because there was no evidence of infection in the recipient or the packs or because an alternative source of infection was identified. Some of the English 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.

No incidents were confirmed as TTIs according to the above definition. A total of 39 investigations were concluded as not TTI, including 2 hepatitis B virus (HBV) incidents, 5 hepatitis C virus (HCV), 1 human immunodeficiency virus (HIV), 1 parvovirus and 30 bacterial incidents.

There were 3 undetermined bacterial TTI investigations in 2010.

In the first case, 1 unit of red cells was transfused into a patient following a lower limb amputation. Approximately 1 hour after the start of the transfusion the patient developed tachycardia, chest and abdomen pain, and a very slight temperature rise to 37.4ºC. The patient was on clarithromycin at the time of the transfusion and no additional antibiotics were given after the reaction, from which the patient recovered quickly. Blood cultures taken 2 days after the transfusion reaction were negative. *Bacillus cereus* was cultured from the remains of the red cell unit at the microbiology laboratories of both the hospital and the Blood Service, and these isolates were indistinguishable by molecular typing. However, it appears that the pack was sampled using a needle directly through the pack and the pack was leaking on arrival at the Blood Service. Samples from the donor taken after arm cleansing were negative. It was

therefore difficult to establish whether the bacteria entered the pack prior to transfusion or whether it was introduced during the microbiological sampling. Bacillus is a ubiquitous environmental organism and therefore, although unlikely to be a TTI, both scenarios are possible.

In the second case a patient received 2 units of red cells and 1 unit of platelets, after which the patient collapsed with hypotension, tachycardia and pyrexia. Blood cultures from the patient grew viridans streptococci. However, the empty transfused packs were discarded locally and were therefore unavailable for further investigation.

The third case involved 1 unit of apheresis platelets transfused to a patient who suffered a reaction within 10 minutes of completion of the transfusion. This initiated a recall of associated components (2 additional apheresis platelet components) that had been issued to two different hospitals. Clinical follow up of all 3 patients confirmed that transfusion related adverse reactions occurred in all 3 patients. At notification of this transfusion reaction, BacT/ALERT was negative for this component and was negative at completion of testing. Testing was repeated and extended for 7 days with negative results. Bacteriology investigations were instigated locally at two of the hospitals and both identified *Staphylococcus aureus* from the platelet residues, as well as other microbes that did not concur. Bacteriological investigations by the Blood Service on returned residues did identify bacteria but not *S. aureus*. BacT/ALERT was subsequently challenged with eight different isolates of *S. aureus* and all were detected. Samples of the bacteria identified by the hospitals were forwarded to a reference laboratory, which reported that the *S. aureus* identified by the two hospitals were similar but not identical. Review of the previous donation history of the donor indicated that the donor had been implicated in previous suspected transfusion reactions. On review, these previous investigations had revealed no evidence of bacterial contamination or any HLA-related issues with the recipients. There was no evidence of anti-IgA, HLA or platelet antibodies, although a granulocyte antibody was detected. Although bacterial contamination cannot be completely excluded, it is more likely that the cause of the transfusion reactions was the presence of a granulocyte antibody in the donor.

Six incidents reported in 2010 are pending complete investigation (1 CMV, 1 HBV, 2 HCV, 1 HIV and 1 bacterial case).

Confirmed incidents

There were no confirmed TTIs reported in 2010.

Other incidents

Near miss

There were 3 near miss incidents reported in 2010. In 2 separate incidents *S. aureus* was isolated from 2 unissued apheresis platelets after visible clumps/aggregates were noted in the packs, 1 at 3 days and 1 at 5 days. Neither donor had evidence of Staphylococcus species post arm cleansing. Both donors were therefore returned to the panel. In the third incident, organisms initially identified as *Klebsiella oxytoca* were isolated from an apheresis pack returned to the Blood Service by the hospital after it was noticed the contents of the pack looked 'odd'. On return, a large aggregate was observed in the pack with no evidence of holes or other damage to the pack. After further investigation at the Health Protection Agency reference laboratory the organism was identified as *Raoultella planticola*, a close relative of *Klebsiella*. Samples from the donor did not show Klebsiella-like organisms pre or post cleansing.

Investigations reported as pending or undetermined in 2009

There were 3 investigations reported as pending in 2009 (1 Human T-cell lymphotropic virus (HTLV), 1 HBV and 1 HCV). The reported HTLV infection was not confirmed and the investigation closed. In both the HBV and HCV cases no donor was found to have evidence of infection, and they were concluded as not due to TTI.

One HIV incident reported as undetermined in 2009 has now been completed. The last remaining donor was found to have no evidence of infection and therefore this incident was not a TTI.

Cumulative data

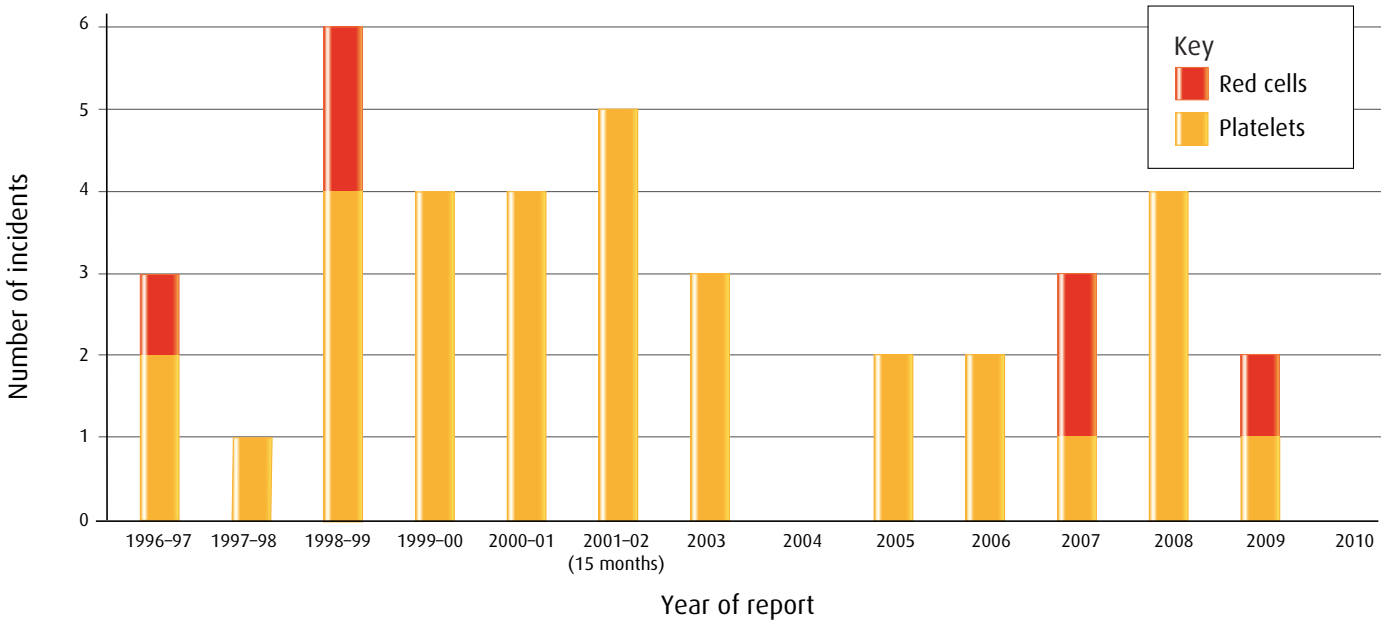
Bacterial TTIs

Since 1996, 40 bacterial TTI incidents have been confirmed, involving a total of 43 recipients (see Figure 18 and Table 48), 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 18:

- 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 each incident.
- In 2004 there was a further incident (not included in Figure 18) involving the contamination of a pooled platelet pack contaminated with *S. epidermidis*. This incident did not meet the TTI definition as transmission to the recipient, although likely, could not be confirmed.

Figure 18
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from 10/1998)



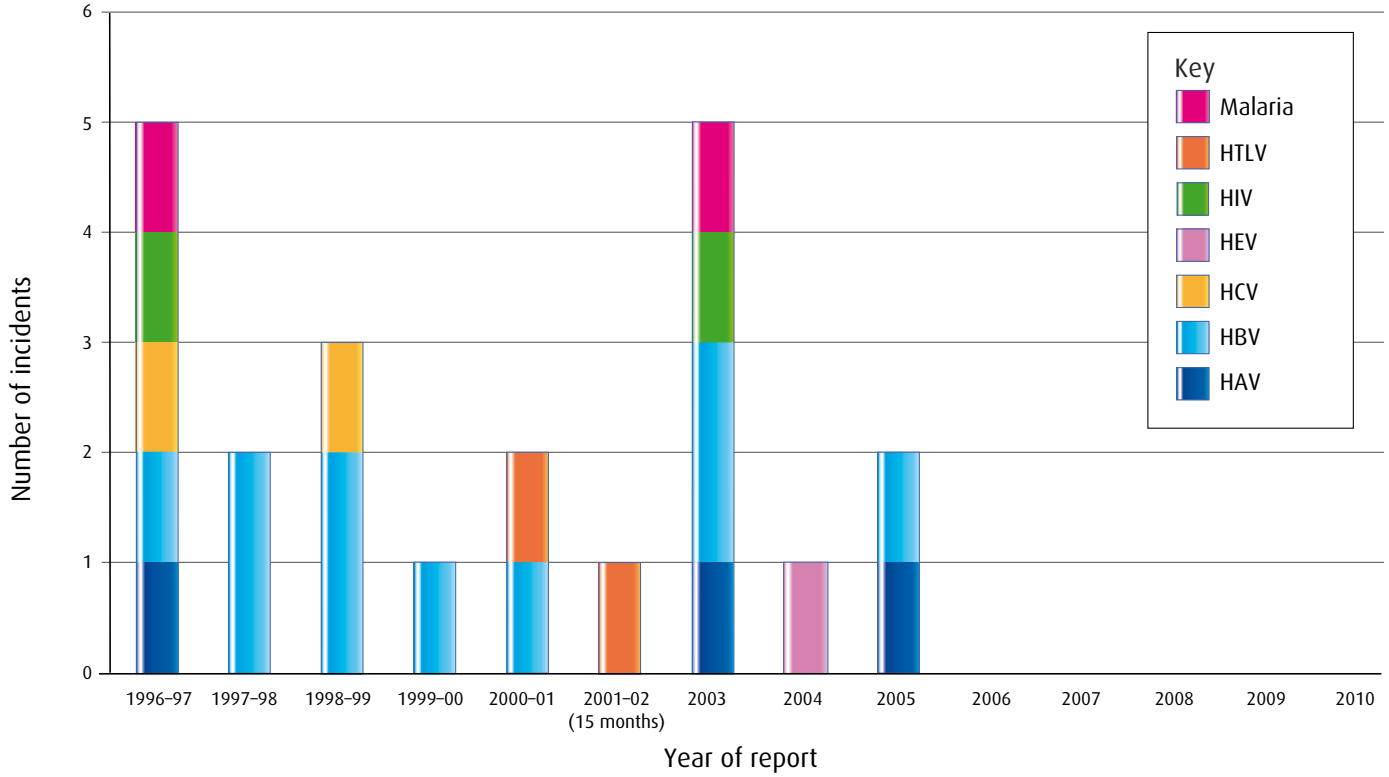
Viral and parasitic TTIs

Since 1996, 22 confirmed incidents of transfusion-transmitted viral and parasitic infections have been reported, involving a total of 25 recipients (see Figure 19 and Table 48); 1 incident resulted in a fatal transfusion reaction (malarial transmission). There have been no confirmed transfusion-transmitted viral or parasitic infections in recent years – the last confirmed incident was in 2005. Three of the incidents were related to the transfusion of platelets, including the 2005 hepatitis A virus (HAV) incident, while the remaining 19 incidents were related to the transfusion of red cells.

In Figure 19:

- The year of transfusion may have been many years prior to the year in which the case is investigated and reported in SHOT because of the chronic nature of some viral infections. The figure shows the number of incidents, not infected recipients identified. For 1 incident in 1996–97 (HIV) and 1 in 1999–2000 (HBV), 3 and 2 recipients were identified, respectively.
- The 2 HIV incidents were associated with anti-HIV negative/HIV RNA positive donations, i.e. window period donations. A third window period donation in 2002 was transfused to an elderly patient, who died soon after surgery. The recipient's HIV status was therefore not determined and not included in Figure 19.
- No screening was in place for the following TTIs at the time of transfusion: HAV, hepatitis E virus (HEV) and HTLV.

Figure 19
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 were no vCJD investigations in 2010.

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 non-leucodepleted RBCs between 1996 and 1999 from blood donors later diagnosed with vCJD.

Since 1997, the UK Blood Services have introduced a number of precautionary measures:[1]

- 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 treated FFP (SD-FFP) for adult patients with TTP (2006).
- Exclusion of donors who have received a blood transfusion in the UK since 1980 (2004).

Work to develop a test for vCJD is at a very early stage of development. The UK Blood Services are involved in the work to develop further a possible test. However, there is currently no screening test for vCJD available for use in blood donors.

Table 48
Number of confirmed TTI incidents, infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2010 (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	No. of incidents	No. 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
HTLV1	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

In 2010 there were no proven reports of TTI. This reflects the continuing high working standards and improvements based on the learning outcomes from previous investigations into contamination incidents.

Currently the greatest risk of TTI 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 ATRs is currently in preparation (expected 2011).

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. The Blood Services provide comprehensive bacterial testing and where isolates are available from the recipient and pack will arrange typing of strains. However, if sampling the pack locally, attention should be paid to the sampling and storage of implicated units or their residues to avoid contamination of the pack. It is suggested that an unused administration port is swabbed with 70% ethanol and left to dry before inserting a sample site coupler spike with needle injection site or equivalent into the port. This will enable the bag to be sampled with a sterile hypodermic needle and syringe, but still maintain the integrity of the bag. The coupler spike should also be swabbed, as before, prior to sampling. Where possible, any organisms isolated in local laboratories should also be returned to the Blood Service reference laboratory to allow the completion of the investigation. The investigation of possible TTIs forms part of the quality and governance framework.

If viral or parasitic contamination is suspected staff should, before reporting, attempt to ensure that the infection is confirmed and was not present prior to the transfusion. For example, testing for antibodies to hepatitis B core in samples taken prior to transfusion can help to rule out reactivation of past HBV infection in immunocompromised patients. As the risks of TTI are so low, other identified possible sources of infection should be investigated without waiting for the outcome of the Blood Service investigation.

Guidance and reporting forms for suspected bacterial, viral or parasitic TTIs for hospitals served by NHSBT can be found at http://www.blood.co.uk/hospitals/library/request_forms/aer/. For other services please contact the local blood supply centre.

Strategies to reduce the bacterial contamination of blood components are under continual review. Most of the UK Blood Services already screen platelet donations for bacterial contamination and this was introduced in NHSBT in early 2011.

It should be noted that bacterial screening is unlikely to prevent all transmissions and the current high standards of collection, processing and vigilance should be maintained.[2]

The current estimated risks of transmission of HBV, HCV, HIV and HTLV via blood transfusion are low (1.50 per million donations for HBV, 0.01 per million for HCV, 0.20 for HIV and 0.06 for HTLV-1).[3]

Learning points

- If sampling packs for bacterial testing, use ports rather than breaching the pack to minimise environmental contamination of the pack post transfusion.
- Retain suspected bacterially contaminated packs even if near empty for return to the Blood Service as these can be washed out and the residue cultured.
- Testing for antibodies to hepatitis B core in samples taken prior to transfusion can help rule out reactivation of past HBV infection in immunocompromised patients.

Recommendations

- Attention should be paid to the sampling and storage of implicated units or their residues to avoid sampling or environmental contamination of the pack.

  Action: Hospital microbiology laboratories

- Even if TTI is excluded in a case of ATR, the case should still be reported to SHOT as an ATR.

  Action: HTTs, clinicians

- 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. This includes checking records and testing samples taken prior to the implicated transfusion(s) to check that the recipient was not infected prior to transfusion.

  Action: Clinicians, UK Blood Services

For active recommendations and an update on their progress, please refer to the SHOT website.