

Transfusion-Transmitted Infections (TTI) n=3 events, 4 recipients

12

Authors: Rachael Morrison and Su Brailsford

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

Note that for the purposes of the European Union (EU) legislation, serious adverse reactions (SAR) are defined as any reactions in patients that are 'life-threatening, disabling or incapacitating, or which result in or prolong hospitalisation or morbidity.'

These must be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) (a legal requirement). This includes all confirmed transfusion-transmitted infections.

Key SHOT messages

- Bacterial screening of platelets has been shown to be useful in reducing the risk of contaminated platelets entering the blood supply, however, there is still a small residual risk that bacteria may not be detected
- The risk of transfusion-transmitted hepatitis B (HBV), hepatitis C (HCV) or human immunodeficiency virus (HIV) is very low in the United Kingdom (UK)
- 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. For example, HEV is commonly transmitted by food. Investigation includes checking records and if available, testing samples taken prior to the implicated transfusion(s) to check that the recipient did not already have the infection

Introduction

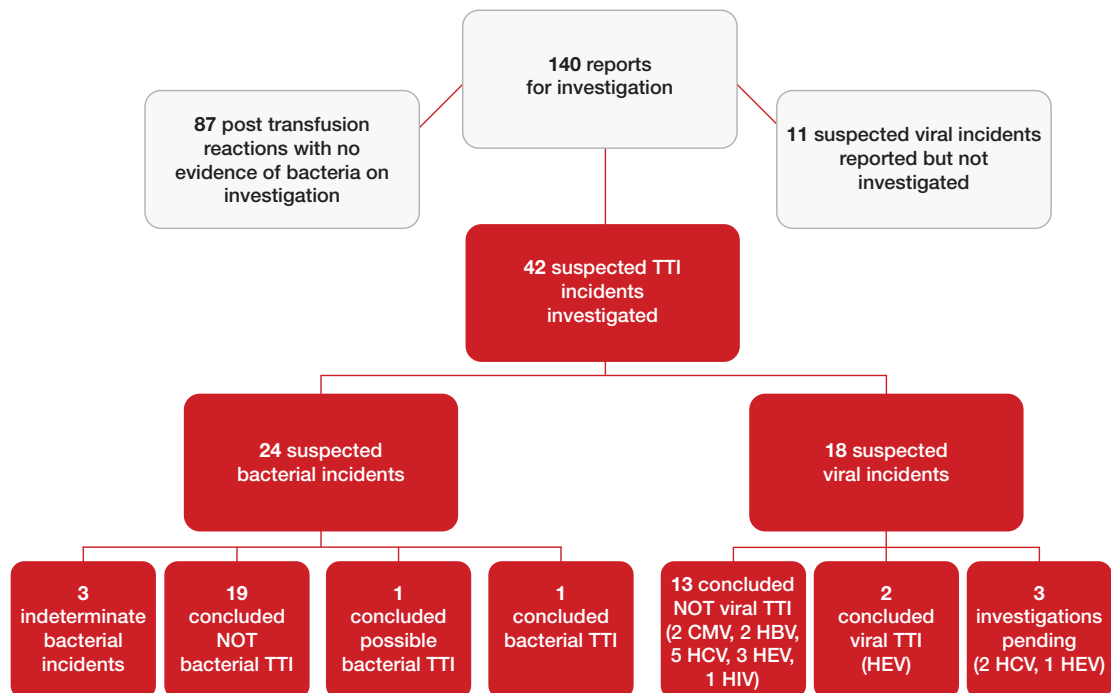
This chapter describes the possible transfusion-transmitted infection incidents investigated by the UK Blood Services and reported to the National Health Service Blood and Transplant (NHSBT)/Public Health England (PHE) Epidemiology Unit in 2015.

Summary of reports made to the NHSBT/PHE Epidemiology Unit in 2015

During 2015, UK Blood Services investigated 111 suspected bacterial cases and 18 suspected viral incidents total n=129 (Figure 12.1). An 11 additional suspected viral incidents were not investigated. From these suspected cases, there has been:

- One proven bacterial transfusion-transmitted *Staphylococcus aureus* infection
- One possible group B streptococcus transmission; although the investigation is complete, the source of infection in the patient could not be confirmed
- Two transfusion-transmitted hepatitis E virus (HEV) incidents, one following multiple transfusions between December 2014 and November 2015 and one following 2 doses of platelets and 2 doses of cryoprecipitate in July 2015

Figure 12.1:
Outcome of reports
of suspected
TTIs made to
the NHSBT/PHE
Epidemiology Unit
in 2015*



*HCV investigations where the transfusion was prior to screening are not included in this Figure

CMV=cytomegalovirus

Bacterial TTI reports 2015

In 2015, there was one proven bacterial transfusion-transmitted incident, one possible bacterial transmission (not included in Table 12.2) and no near miss incidents.

Case 12.1: Confirmed bacterial TTI

A six day old pooled platelet unit was transfused to a female neutropenic patient with acute myeloid leukaemia who was in her 70s. Fifteen minutes into the transfusion, the patient became agitated and experienced symptoms of rigors, tachycardia and pyrexia. The patient's temperature spiked at 38.7°C and continued to rise overnight reaching 40°C. The transfusion was stopped and the patient was given hydrocortisone, chlorphenamine and started on broad spectrum antibiotics, ciprofloxacin, piperacillin/tazobactam and gentamicin. The patient recovered and was well enough to be discharged from hospital.

Bacterial screening of the pooled platelet was negative at day 7; investigation revealed no obvious errors in either sampling or in the screening protocol. The same strain of Staphylococcus aureus was isolated from patient blood cultures, cultures from the almost empty pack of the transfused unit and skin swabs from one of the donors whose donation was included in the pool. The strains were compared using molecular typing and were found to be indistinguishable.

It was the good practice and quick thinking of the hospital staff which prevented further harm being caused to this patient.

Case 12.2: Possible bacterial TTI

A seven day old pooled platelet unit was transfused to a female patient in her 50s at a routine outpatient appointment as part of ongoing treatment for aplastic anaemia. The patient previously had allergic reactions to platelets and was routinely given prophylaxis with hydrocortisone and chlorphenamine. Half-way through the transfusion, the patient developed rigors and angioedema, but the blood pressure was normal. The patient was admitted overnight and treated with piperacillin/tazobactam and steroids and recovered. Bacterial screening was negative and no obvious errors were detected in sampling or screening protocol. The hospital reported that Streptococci were identified in both the pack and the patient blood culture 24 hours post transfusion.

Streptococcus agalactiae (also known as group B streptococcus) and E. coli were isolated from the returned platelet pack; although the same organism was isolated from the component and the patient it was not possible to confirm that the source of the infection was the pooled platelet.

Bacterial TTIs 1996–2015

Screening of platelet components cannot guarantee freedom from bacterial contamination. Packs are released for issue as 'negative-to-date' which may be before bacteria have multiplied sufficiently to trigger an initial screening reaction. On the other hand, an initial screen-reactive result may be a false positive result, or related to bacteria which are of low pathogenicity and unlikely to cause any noticeable reaction in the recipient. Prior to 2015 the previous documented confirmed bacterial TTI was in 2009, predating universal bacterial screening of platelets throughout the UK Blood Services (2011). There have been 4 near misses (3 in platelets) reported to the unit between 2011 and 2015. Overall, since reporting began in 1996, a total of 37/44 bacterial transfusion-transmissions to individual recipients (34 incidents) have been caused by the transfusion of platelets, and 7/44 by red cells (Table 12.2).

Viral TTI reports 2015

In 2015, there were two confirmed transfusion-transmitted hepatitis E virus (HEV) incidents.

Case 12.3: Confirmed viral TTI (1)

A male patient in the 50-60 age group (life-long vegetarian) with multifocal central nervous system lymphoma diagnosed in December 2014, underwent an autologous stem cell transplant for reversible bone marrow failure and received extensive transfusion support from June 2015. HEV testing was carried out because the patient developed persistent transaminitis. The patient eventually died with decompensated liver failure.

There were 33 donor exposures based on donations transfused in the 12 weeks prior to the first positive HEV result. Two donations from two different donors were implicated. One donation in a pooled platelet transfused with a low viral load in June 2015 (donor 1) and one apheresis platelet split with a high viral load transfused in May 2015 (donor 2) were found on retesting of the archive samples to have been HEV ribonucleic acid (RNA) positive at the time of donation. Red cells and fresh frozen plasma (FFP) had also been issued from the donation given by donor 1; neither recipient had evidence of current or past hepatitis E when tested at least 6 months after transfusion. The second platelet split from donor 2 was transfused to a paediatric liver transplant recipient, who was diagnosed with HEV, treated, and cleared the infection before the HEV-positive platelet component had been identified.

Sequencing studies showed that the recipient's virus changed over time and it cannot be said with certainty whether HEV from one or both HEV RNA positive donations was transmitted to this recipient.

The donors both cleared their HEV infection and remain on the active donor panel.

Case 12.4: Confirmed viral TTI (2)

A male patient in the 40-50 age group with non-Hodgkin lymphoma received 2 doses of platelets and 2 doses of cryoprecipitate (18 donor exposures) on 31st July 2015. On the 19th October 2015 (80 days post transfusion), he was admitted to hospital with jaundice, nausea and abdominal discomfort. He was hepatitis A virus (HAV)-, HBV- and HCV-negative, however he was HEV IgG (low) and IgM (high) positive.

Records of all donors were examined. None of the donors had reported any illness at the time of donation or subsequently. Archive samples from the 18 index donations were tested for HEV RNA. One donation which was included in one of the cryoprecipitate doses was found to be HEV RNA positive. Red cells from the same donation were transfused to a paediatric thalassaemia patient; this patient had no evidence of transfusion-transmitted HEV.

The donor cleared the infection and remains on the donor panel.

Update on viral TTI reports from 2014

There were three pending HEV and one HBV case in 2014. One HEV case was subsequently a confirmed TTI.

Case 12.5: Confirmed viral TTI

A male liver transplant recipient received blood components in the perioperative period. He was found to be significantly HEV viraemic 68 days post transplant (October 2012) whereas he was negative when assessed in June 2012. The liver donor tested negative for HEV.

On investigation, it was found that the index patient had received 5 doses of apheresis platelets, 14 units of FFP, 9 units of red blood cells, 1 platelet pool (4 donors) and 1 cryoprecipitate dose (5 donors) in August 2012. Two units of platelets transfused in 2011, prior to the patient being reported as HEV positive, were excluded from this investigation. Thirty-seven blood donor exposures were identified. Archive samples from all 37 donations were retrieved and tested for antibodies to HEV (IgG and IgM) and HEV RNA. One donor (FFP) showed evidence of active HEV infection (HEV IgM and HEV RNA positive; HEV IgG negative) at the time of donation. An additional three donors had evidence of past HEV infection (HEV IgG positive, HEV IgM and HEV RNA negative) at the time of donation. Sequence analysis showed that the sequence in the HEV RNA positive donor was a highly conserved match with the transplant patient sample.

Viral TTIs 1996–2015

The year of transfusion may be many years prior to the year in which the case is investigated and reported to SHOT because of the chronic nature, and therefore late recognition, of some viral infections. Since 1996, 29 confirmed incidents of transfusion-transmitted viral infections have been documented, involving a total of 36 recipients. HBV is the most commonly reported proven viral TTI in the UK. This is partly because the 'window period' where an infectious donation from a recently infected donor cannot be detected by the screening tests is longer than for HCV or HIV, despite nucleic acid testing (NAT).

Risks of HBV, HCV or HIV being transmitted by transfusion

The risk of a component potentially infectious for HBV, HCV or HIV being released for use in the UK is very low (Table 12.1) (PHE 2015).

	HBV	HCV	HIV
Number per million donations	0.63	0.038	0.16
95% confidence interval	0.17-1.19	0.015-0.100	0.10-0.23
At 2.3 million donations per year testing will miss a potentially infectious window period donation every:	year	16 to 17 years	2 to 3 years

**The window period is the time at the start of an infection before the tests can detect it*

Far fewer TTIs are observed in practice than estimated in Table 12.1, partly because the estimates have wide uncertainty and the model is based on the risk in all packs released. The model does not incorporate pack non-use, recipient susceptibility to infection, or under ascertainment/under reporting, for example due to recipients dying from an underlying medical condition before a chronic asymptomatic viral condition is identified, or, in the case of HBV, an asymptomatic acute infection.

HEV testing 2016

In 2015, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) recommended that HEV-screened components were required for specific patient groups:

- Allogeneic stem cell/bone marrow transplantation
- Solid organ transplantation

More details can be found here <http://hospital.blood.co.uk/products/hepatitis-e-screening>.

UK Blood Services began testing blood and apheresis donations for HEV RNA in order to supply HEV-screened components for selected patient groups from spring 2016.

Parasitic TTIs

There were no reported parasitic infections for investigation in 2015. There have been two proven malaria TTIs reported to SHOT, the last in 2003 (Table 12.2). Malaria antibody testing was not applicable at the time according to information supplied at donation, and the donor selection guidelines were updated after these incidents to minimise the risk of further malaria TTIs (Kitchen et al. 2005). The current selection guidelines on deferral and additional testing for malaria can be accessed at the UK transfusion guidelines web pages at <http://www.transfusionguidelines.org.uk/red-book>.

Variant Creutzfeldt-Jakob Disease (vCJD) 2015

There were no vCJD investigations in 2015.

vCJD 1996–2015

Three vCJD incidents (Table 12.2) took place prior to the introduction of leucodepletion and other measures taken by the UK Blood Services to reduce the risk of vCJD transmission by blood, plasma and tissue products. All these measures have been reviewed and endorsed by SaBTO (SaBTO 2013).

Risk assessment and research into vCJD continues, however currently there is no suitable blood test available for screening blood donations for vCJD.

More information can be found here https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/407681/measures-vcjd.pdf

Table 12.1:
The estimated risk of a potentially infectious HBV, HCV or HIV window period* donation entering the UK blood supply: 2012–2014

Table 12.2:
Number of confirmed TTI incidents*, by year of transfusion** with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2015 (Scotland included from October 1998)

Year of transfusion**	Number of incidents (recipients) by infection											Implicated component				
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV I	Parvovirus (B19)	Malaria	vCJD/ prion	Total	RBC	Pooled platelet	Apheresis platelet	FFP	Cryo
Pre 1996	-	-	1 (1)	-	-	-	2 (2)	-	-	-	3 (3)	3	-	-	-	-
1996	-	1(1)	1 (1)	1 (1)	-	1 (3)	-	-	-	1 (1)	5 (7)	5	1	-	1	-
1997	3 (3)	-	1 (1)	1 (1)	-	-	-	-	1 (1)	2 (2)	8 (8)	6	1	1	-	-
1998	4 (4)	-	1 (1)	-	-	-	-	-	-	-	5 (5)	2	1	2	-	-
1999	4 (4)	-	2 (3)	-	-	-	-	-	-	‡ (1)	6 (8)	5	3	-	-	-
2000	7 (7)	1 (1)	1 (1)	-	-	-	-	-	-	-	9 (9)	1	5	3	-	-
2001	5 (5)	-	-	-	-	-	-	-	-	-	5 (5)	-	4	1	-	-
2002	1 (1)	-	1 (1)	-	-	1 (1)†	-	-	-	-	3 (3)	2	1	-	-	-
2003	3 (3)	-	1 (1)	-	-	-	-	-	1 (1)	-	5 (5)	1	1	3	-	-
2004	††	-	-	-	1 (1)	-	-	-	-	-	1 (1)	1	-	-	-	-
2005	2 (2)	1 (1)	1 (1)	-	-	-	-	-	-	-	4 (4)	1	3	-	-	-
2006	2 (2)	-	-	-	-	-	-	-	-	-	2 (2)	-	1	1	-	-
2007	3 (3)	-	-	-	-	-	-	-	-	-	3 (3)	2	1	-	-	-
2008	4 (6)	-	-	-	-	-	-	-	-	-	4 (6)	-	2	4	-	-
2009	2 (3)	-	-	-	-	-	-	-	-	-	2 (3)	1	-	2	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	1 (2)	-	1 (2)	-	-	-	-	-	2 (4)	2	-	-	2	-
2012	-	-	1 (1)	-	1 (1)	-	-	1(1)	-	-	3 (3)	2	-	-	1	-
2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2014	-	-	-	-	2 (3)	-	-	-	-	-	2 (3)	1	-	-	2	-
2015	1(1)	-	-	-	2 (3)	-	-	-	-	-	3 (4)	-	2	1	-	1
Number of incidents	41	3	12	2	7	2	2	1	2	3	75					
Number of infected recipients	44	3	14	2	10	4	2	1	2	4	86	35	26	18	6	1
Death due to, or contributed to, by TTI	11	-	-	-	1	-	-	-	1	3	16					
Major morbidity	29	2	14	2	5	4	2	1	1	1§	61					
Minor morbidity	4	1	-	-	4	-	-	-	-	-	9					
Implicated component																
RBC	7	1	11	2	3	2	2	1	2	4	35					
Pooled platelet	21	2	1	-	1	1	-	-	-	-	26					
Apheresis platelet	16	-	1	-	1	-	-	-	-	-	18					
FFP	-	-	1	-	4	1	-	-	-	-	6					
Cryoprecipitate	-	-	-	-	1	-	-	-	-	-	1					

Numbers in brackets refer to recipients

*No screening was in place for vCJD, human T cell lymphotropic virus (HTLV), hepatitis A virus (HAV), HEV or parvovirus B19 at the time of the documented transmissions. In both malaria transmissions, malaria antibody testing was not applicable at the time according to information supplied at donation

** Year of transfusion may be prior to year of report to SHOT due to delay in recognition of chronic infection

† The two HIV incidents were associated with window period donations (anti-HIV negative/HIV RNA positive) before HIV NAT screening was in place. 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 2004 there was an incident involving contamination of a pooled platelet pack with *Staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely. This case was classified as 'not transfusion-transmitted'

‡ Same blood donor as one of the 1997 transmissions so counted as the same incident; note: counted as two separate incidents in previous reports

§ A further prion case died but transfusion was not implicated as the cause of death. The outcome was assigned to major morbidity instead because although there was post-mortem evidence of abnormal prion proteins in the spleen the patient had died of a condition unrelated to vCJD and had shown no symptoms of vCJD prior to death

For further information or alternative breakdown of data please contact the National Coordinator for Transfusion-Transmitted Infections via the NHSBT/PHE Epidemiology Unit at epidemiology@nhsbt.nhs.uk.

Learning points and recommendations from previous years are still relevant and can be found in the supplementary information on the SHOT website www.shotuk.org.

References

BCSH Tinegate H, Birchall J et al. (2012) **Guideline on the investigation and management of acute transfusion reactions**. Prepared by the BCSH Blood Transfusion Task Force. Br J Haematol 159(2),143-153

Department of Health (2013) **vCJD and transfusion of blood components: an updated risk assessment**. <https://www.gov.uk/government/publications/vcjd-and-transfusion-of-blood-components-updated-risk-assessment> [accessed 16 March 2016]

Hewitt PE, Ijaz S et al. (2014) **Hepatitis E virus in blood components: a prevalence and transmission study in southeast England**. Lancet 384,1766-1773

Kitchen AD, Barbara JA, et al. (2005) **Documented cases of post-transfusion malaria occurring in England: a review in relation to current and proposed donor-selection guidelines**. Vox Sang 89, 77-80

Parker S, Gil E et al. (2014) **Case report: passive transfer of hepatitis B antibodies from intravenous immunoglobulin**. BMC Infect Dis 14,99 <http://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-99> [accessed 16 March 2016]

PHE (2015) NHSBT/ PHE Epidemiology Unit: **Safe Supplies: Uncovering donor behaviour. Annual Review from the NHS Blood and Transplant/Public Health England Epidemiology Unit, 2014**. <https://www.gov.uk/government/publications/safe-supplies-annual-review> [accessed 01 December 2015]

SaBTO (2012) **Cytomegalovirus tested blood components position statement**. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/215125/dh_133086.pdf [accessed 16 March 2016]

SaBTO (2013) **Measures currently in place in the UK to reduce the potential risk of transmitting variant Creutzfeldt-Jakob disease via blood**. <https://www.gov.uk/government/publications/current-measures-to-reduce-the-risk-of-vcjd-transmission-by-blood> [accessed 16 March 2016]