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Transfusion-Transmitted Infections Reported to the National Healthcare Safety Network Hemovigilance Module

Kathryn A. Haass [a,*], Mathew R.P. Sapiano [b], Alexandra Savinkina [a,c], Matthew J. Kuehnert [a], Sridhar V. Basavaraju [a]

[a] Office of Blood, Organ, and Other Tissue Safety, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention
[b] Surveillance Branch, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, US Centers for Disease Control and Prevention
[c] Oak Ridge Institute for Science and Education

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ABSTRACT

Transfusion-transmitted infections (TTIs) can be severe and result in death. Transfusion-transmitted viral pathogen transmission has been substantially reduced, whereas sepsis due to bacterial contamination of platelets and transfusion-transmitted babesiosis may occur more frequently. Quantifying the burden of TTI is important to develop targeted interventions. From January 1, 2010, to December 31, 2016, health care facilities participating in the National Healthcare Safety Network Hemovigilance Module monitored transfusion recipients for evidence of TTI and recorded the total number of units transfused. Facilities use standard criteria to report TTIs. Incidence rates of TTIs, including for bacterial contamination of platelets and transfusion-transmitted babesiosis, are presented. One hundred ninety-five facilities reported 111 TTIs and 7.9 million transfused components to the National Healthcare Safety Network Hemovigilance Module. Of these 111 reports, 54 met inclusion criteria. The most frequently reported pathogens were *Babesia* spp in RBCs (16/23, 70%) and *Staphylococcus aureus* in platelets (12/30, 40%). There were 1.95 (26 apheresis, 4 whole blood derived) TTIs per 100 000 transfused platelet units and 0.53 TTI per 100 000 transfused RBC components, compared to 0.68 TTI per 100 000 all transfused components. Bacterial contamination of platelets and transfusion-transmitted babesiosis were the most frequently reported TTIs. Interventions that reduce the burden of bacterial contamination of platelets, particularly collected by apheresis, and *Babesia* transmission through RBC transfusion would reduce transfusion recipient morbidity and mortality. These analyses demonstrate the value and importance of facility participation in national recipient hemovigilance using standard reporting criteria.

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Transfusion-transmitted infections (TTIs) can result in significant morbidity and mortality among recipients of blood products [1-3]. Strategies to reduce the risk of TTIs include blood donor health assessment, questionnaires to evaluate risk exposure including travel history and high-risk behaviors, and laboratory screening of donors or

* Corresponding author at: Kathryn Haass, Mail stop D26, Centers for Disease Control & Prevention, 1600 Clifton Rd Ne Atlanta, GA 30329-4027.
E-mail address: yoc0@cdc.gov (K.A. Haass).

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donations for some pathogens [4]. However, these infections can still occur when questionnaires do not identify donor risk factors or when laboratory screening methods are not available, are not used, or may otherwise not identify infection due to limitations including window period, sensitivity, or limit of detection. Quantifying the burden of TTIs is important to identify and implement targeted prevention strategies.

Since the advent of the HIV epidemic in the 1980s, intervention efforts have largely focused on prevention of transfusion-transmitted viral blood-borne pathogens. The introduction of nucleic acid testing has reduced the residual risk of HIV and HCV to approximately 1 in 2 000 000 transfusions [5-8]. Whereas the occurrence of transfusion-transmitted viral blood-borne pathogen transmission has been substantially reduced, other infections may be more likely to occur such as sepsis due to bacterial contamination of platelets and transfusion-transmitted babesiosis [2,9].

Hemovigilance plays a key role in ensuring transfusion recipient safety in the United States and internationally [10-15]. Historically, many organizations, both public and private, were involved in the collection and analysis of hemovigilance data in the United States, resulting in fragmented monitoring and reporting [16-19]. However, in 2010, the Centers for Disease Control and Prevention (CDC) began operating the National Healthcare Safety Network (NHSN) Hemovigilance Module, a voluntary, passive surveillance system [20]. The NHSN Hemovigilance Module serves as the only national surveillance platform for recipient hemovigilance that is available for use by all US health care facilities performing transfusions regardless of reaction type, blood supplier, or manufacturing deviations that affect blood product purity, potency, or effectiveness. In addition to other transfusion-related adverse reactions, participating facilities report TTIs, including the implicated blood product and pathogen [21]. Enrollment has grown from 82 facilities in 2010 to 277 facilities in 2016 of the estimated 4600 acute care facilities in the United States, with mandatory reporting for 69 facilities in the state of Massachusetts [22,23]. We present an analysis of TTIs reported to the NHSN Hemovigilance Module for 2010-2016, including estimates of the incidence rate of these infections, with additional focus on bacterial contamination of platelets and transfusion-transmitted babesiosis. Prevention interventions are also discussed.

Methods

Ethical Consideration

Data for this study were collected for surveillance and program evaluation purposes and determined to not require institutional review board review by CDC's Office of the Associate Director for Science. Individual and institutional identifiers reported to NHSN are confidential and not disclosed by CDC without consent of the participating facility.

Data Collection

From January 1, 2010, to December 31, 2016, participating facilities conducted comprehensive monitoring of transfusion recipients for evidence of TTIs and recorded the total number of units transfused by component type (whole blood, red blood cells, platelets, plasma, cryoprecipitate) and collection method (apheresis, whole blood) by month. Since 2016, facilities have further reported on total number of transfused plasma and apheresis platelet units subjected to pathogen-reduction technology (PRT). Facilities must have conducted complete surveillance for data to have been included in the study. Complete surveillance was defined as submitting TTI data (ie, zero or one or more infections) for the month and entering the corresponding number of total transfused units for the same month into the Hemovigilance Module.

Facilities that participate in the Hemovigilance Module use standard criteria for case definition, severity, and imputability for TTIs and other transfusion reactions [24]. For TTIs, facilities perform clinical monitoring of transfused patients for specific signs and symptoms of infections including rigors, fever, tachycardia, nausea, vomiting, shortness of breath, decreased blood pressure, or back pain [25,26]. If a TTI is suspected, laboratory testing is performed to identify a pathogen in the patient, the implicated unit, and the donor, in some cases [25,27]. If a pathogen is identified in the transfused patient, a definitive case definition designation is assigned. If a pathogen is not identified but clinical signs and symptoms are consistent with infection, a possible case definition designation is assigned [20,24,28]. Laboratory testing of the patient, the implicated unit, or the donor is reported as part of the TTI report. All reports with a definitive case definition designation are reviewed by CDC for a specific pathogen identified through laboratory testing. If a possible case definition is assigned, imputability designations are limited to possible, doubtful, ruled out, or not determined.

In addition to case definition criteria, all TTI reports include an imputability and severity designation that is entered into the Module by participating facilities. Facilities assign an imputability designation which indicates the likelihood that the transfusion caused the reaction [24]. This designation is based on the case definition designation, the presence of supporting clinical signs and symptoms, laboratory evidence, and other possible exposures, such as evidence of the pathogen in the transfused component, the donor at the time of donation, or concurrent components from the same donation. Imputability designations can be classified as definite, probable, possible, doubtful, ruled out, and not determined. *Severity* is defined as the level of medical intervention required to stabilize a patient and may include patient outcome [24]. Severity designations included nonsevere, severe, life threatening, death, and not determined.

For TTIs in which a platelet unit was implicated, supplemental information was collected from facilities including apheresis collection platform, when applicable, bacterial detection method, sample volume for bacterial testing, time sample was taken postcollection, and additional methods, if any, used for bacterial risk mitigation. Information related to use of a rapid test for bacterial detection and visual inspection of the product prior to issue was collected.

Descriptive analyses were conducted to calculate the total number of reported TTIs and to stratify these cases by component type, collection method, PRT treatment (when applicable), and pathogen type. Calculation of rates included only TTIs with a definitive case definition designation and a definite, probable, or possible imputability designation. TTI reports with a possible case definition designation or imputability designation of doubtful, ruled out, or not determined were excluded from rate calculations. TTI reports with a possible case definition and possible imputability designation are described. The TTI rate per 100 000 transfused units was calculated and stratified by component type, collection method, and pathogen type. Unit age (ie, number of days postcollection) at time of transfusion was calculated for implicated platelet units and stratified by severity. Seasonal occurrence was evaluated for transfusion-transmitted babesiosis by month of reaction date, which is the date the implicated unit was transfused. Transfusion-transmitted *Babesia* reports were evaluated to determine whether the blood component was donated or transfused in 1 of 9 states with the highest incidence rate of babesiosis infections in the United States according to national surveillance data from 2011 to 2014 (Connecticut, Massachusetts, Maine, Minnesota, New Hampshire, New Jersey, New York, Rhode Island, and Wisconsin) (https://www.cdc.gov/parasites/babesiosis/data-statistics/index.html) [29,30]. For this study, these 9 states were defined as *Babesia*-endemic states. In cases where more than 1 pathogen was reported for the same event, this case was counted only once (in the numerator of the rate) to estimate the rate at which a contaminated unit was transfused. The rate at which blood components were contaminated with more than 1 pathogen was not calculated. Supplemental information related to bacterial contamination of platelets was analyzed and described. Data entered into the Module as of July 31, 2017, and available on August 1, 2017, dataset were used for these analyses. All analyses were conducted using SAS, version 9.4 (SAS Institute Inc, Cary, NC).

Results

During January 1, 2010, to December 31, 2016, 308 facilities were enrolled in the NHSN Hemovigilance Module. A total of 195 health care facilities entered 111 reports of a suspected TTI and corresponding monthly transfusion totals. Between 2010 and 2016, 7 917 786 transfused components were reported to the NHSN Hemovigilance Module, which included 4 376 341 red blood cell units, 1 536 115 platelet units, and 1 301 064 plasma units. Of these 111 reports, 54 (49%) met case definition and imputability inclusion criteria for rate calculations. Fifty-seven (57/111) reports were excluded from rate calculation for not meeting inclusion criteria (Fig 1). Imputability designations for the 54 reports included in the study were definite (23/54; 43%), probable (17/54; 31%), or possible (14/54; 26%). Most (38/54, 70%) TTIs were severe, were life threatening, or resulted in death (Table 1).

Of the 54/111 reported TTIs that met inclusion criteria, 37/54 (69%) were bacterial, 16/54 (30%) were parasitic, and 1/54 (2%) was viral. The most frequently identified organism was *Staphylococcus aureus* (14/37, 38%), followed by other *Staphylococcus* species (8/37, 22%), *Streptococcus* viridans (4/37, 11%), and *Escherichia coli* (3/37, 8%). *Babesia microti* and *Babesia* spp (species not indicated) (12/16, 75%) were the only parasitic pathogens reported to the Module, and hepatitis C was the only viral pathogen. Of the total number of cases that were reported, *Staphylococcus aureus* (12/14, 86%) or gram-negative organisms (8/10, 80%) were most often implicated among platelet units. One report implicated a thawed plasma unit that was contaminated with *Bacillus* spp. Viral and parasitic pathogens were only reported with red blood cell units (Table 2).

During the study period, 5 (5/54, 9%) infections caused a life-threatening condition in the recipient and 4 (4/54, 7%) resulted in death. Of these 9 reports, 8 (8/9, 89%) implicated platelet units and 1 report implicated a red blood cell unit. Of the 4 reported deaths, 2 were definitively linked to the transfusion and 2 were considered probably caused by the transfusion (Tables 2 and 3). Of the 5 life-threatening reactions, 3 were definitively linked to the transfusion and 2 were considered probably caused by the transfusion. Pathogens were identified in both the patient and the transfused unit in 8/9 (89%) life-threatening and fatal reactions. Of the 8 reports that implicated platelets, 5 were apheresis platelet units and 3 were whole blood–derived platelet units (Tables 2, 3, and 4), and all were transfused on day 4 or 5 postcollection (Fig 2). One whole blood–derived platelet-associated death was due to *Staphylococcus aureus*. All units were leukoreduced.

Overall, 0.68 TTI was reported per 100 000 transfused components. The TTI rate was higher among platelet units than among red blood cell components (1.95 and 0.53 per 100 000 transfused components, respectively). The rate of bacterial contamination was higher among apheresis platelet components than among whole blood–derived platelets (2.43 and 0.86 per 100 000 transfused components, respectively) (Table 5). Gram-negative organisms were more often identified in apheresis platelet units (7/8, 88%) than whole blood–derived platelet units (1/8, 13%) (Table 2).

Table 1
Imputability and severity designations of transfusion-transmitted infections reported to the NHSN Hemovigilance Module, 2010-2016

	Severity					
Imputability	Nonsevere	Severe	Life threatening	Fatal	Not determined	Total
Definite	4	14	3	2	0	23
Probable	5	9	0	2	1	17
Possible	5	6	2	0	1	14
Total	14	29	5	4	2	54

Supplemental information was requested from facilities for reports of bacterial contamination of platelets meeting the protocol criteria. Of the 30 platelet units implicated, 26/30 (87%) were apheresis platelets and 4 (4/30, 13%) were whole blood–derived platelets. Of the 26 apheresis platelets, partial supplemental information was reported for 17/26 units and no supplemental information was provided for 9 units. Collection platforms include Gambro TRIMA Accel (Terumo BCT;, Lakewood, CO) (2/17, 12%) and Amicus (Fenwal, Inc, lake Zurich, IL) (1/17, 6%). The collection platform was unknown or not reported for 14/17 (82%) units. Bacterial testing was performed by the BacT/Alert 3D automated culturing system (bioMerieux, Durham, NC) (16/17, 94%) or the enhanced bacterial detection system (eBDS, Pall Corp, East Hills, NY) (1/17, 6%). Of the 16 units tested by the BacT/Alert 3D automated culturing system, sample collection time and sample volume were not reported for 15 units and 1 unit was tested 24 hours postcollection with an 8-mL sample volume. The 1 unit tested by the eBDS used a 4-mL sample volume and was tested at 24 hours postcollection. Information about visual inspection was not provided for 12/17 units and performed on 5 (5/17, 29%) units with no abnormalities observed.

Among the 4 whole blood–derived platelet units for which a septic transfusion reaction was reported, the Pall Bacterial Detection System (eBDS) was used to test 3 units at 24 hours postcollection using a 4-mL sample volume. The Pan Genera Detection test (Verax Biomedical, Inc, Worcester, MA) method was used to test 1 (1/4, 25%) unit at the time of issue. Visual inspection was performed on all 4 units, of which 3 units appeared normal. One unit contained particulate matter and was later transfused and resulted in a septic reaction. Units were transfused at day 4 postcollection (2/4, 50%) and day 5 postcollection (2/4, 50%) (Fig 2).

Fourteen of 16 transfusion-transmitted *Babesia* reports were confirmed by positive test results of the implicated unit (4/14, 29%), the donor (7/14, 50%), or both (3/14, 21%). All were in RBCs and accounted for 16/23 (70%) of RBC reports. Of the 16 infections, 13 resulted in a severe reaction. The rate of transfusion-transmitted babesiosis reported to

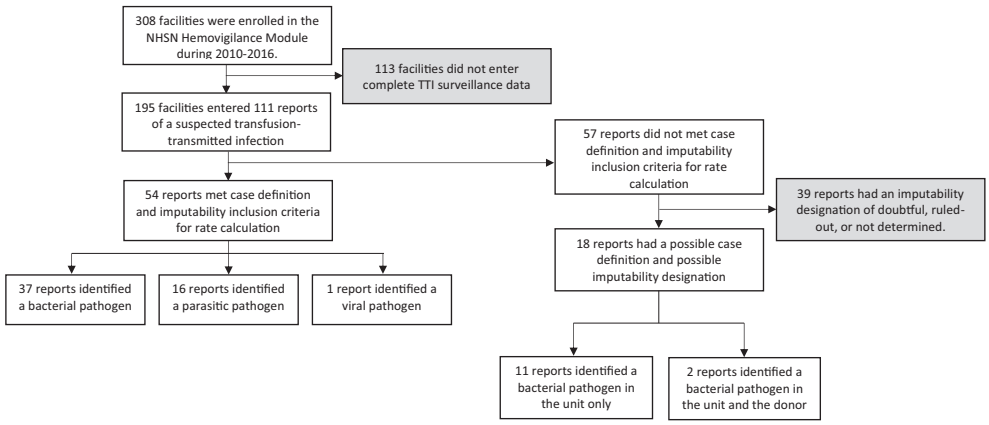

Fig 1. Flow diagram of facility participation and data inclusion for analysis of transfusion-transmitted infections reported to the NHSN Hemovigilance Module, United States, 2010 to 2016.

Table 2
Transfusion-transmitted pathogens identified by a facility in the transfused patient and the implicated unit or donor as reported to the NHSN Hemovigilance Module, 2010-2016

Infection type	Pathogen	No. of cases	No. of cases where pathogen was identified by a facility in unit or donor	Associated component type[a]			
				Red blood cell	Whole blood–derived platelet	Apheresis platelet	Plasma[b]
Bacterial	Gram-positive						
	Staphylococcus aureus	14	9	2	2	10	
	Staphylococcus, non-*aureus*[c]	8	5	1	1	6	
	Streptococcus, viridans group	4	4			4	
	Bacillus spp	1	1				1
	Corynebacterium spp	1		1			
	Enterococcus faecalis	1		1			
	Gram-negative						
	Escherichia coli	3	2	1	1	1	
	Acinetobacter spp	2	2			2	
	Achromobacter spp	1	1			1	
	Brevundimonas diminuta	1	1			1	
	Pseudomonas fluorescens	1	1	1			
	Ralstonia picketti	1	1			1	
	Gram-negative rods	1				1	
Viral	Hepatitis C virus	1		1			
Parasitic	*Babesia microti*	12	11	12			
	Babesia spp	4	3	4			

[a] No transfusion-transmitted infections reports implicated cryoprecipitate.
[b] Thawed plasma (E2701 ISBT 128 Blood Product code).
[c] *Staphylococcus*, non-*aureus* includes *Staphylococcus epidermidis*, other coagulase-negative *Staphylococcus* spp, and *Staphylococcus* spp.

the Module in endemic states was 0.88 per 100 000 transfused red blood cell units. Of the 16 transfusion-transmitted *Babesia* reports, we determined the donation location for 13 reports which included Massachusetts (7/16, 44%), Rhode Island (5/16, 31%), and Connecticut (1/16, 6%). The donation location was unknown for 3/16 (19%) reports. The transfusion location for all 16 reports was Massachusetts. There were no cases of transfusion-transmitted *Babesia* reported to the Module by facilities located in states where the risk of *Babesia* transmission is lower. More transfusion-transmitted *Babesia* reports listed a reaction date in the summer (June-August) and fall (September-November) seasons compared to winter (December-February) and spring (March-May) seasons, with a rate of 1.24 and 1.30 vs 0.70 and 0.22 per 100 000 red blood cell units transfused, respectively (Table 6).

Of the 57 (57/111, 51%) reports excluded from rate calculations, 18 (32%) reports had a possible case definition designation and a possible imputability designation. Thirty-nine (39/57, 68%) reports had an imputability designation of doubtful, ruled out, or not determined. Of the 18 reports with possible designations for case definition and imputability, 2 (2/18, 11%) reports identified the same bacterial pathogen in the implicated unit and the donor. Eleven (11/18, 61%) reports identified a bacterial pathogen in the unit only, and 5 (5/18, 28%) reports did not identify a pathogen in either the implicated unit or donor. Of the 13 reports where a bacterial pathogen was identified, pathogens included *Staphylococcus*, coagulase negative (4/13, 31%); *Staphylococcus epidermidis* (3/13, 23%); *Streptococcus mitis* (2/13, 15%); *Staphylococcus aureus* (1/13, 8%); *Staphylococcus* spp (1/13, 8%); *Micrococcus* spp (1/13, 8%); and *Corynebacterium* spp (1/13, 8%). Two (2/18, 11%) reactions were severe and 16 (16/18, 89%) reactions were nonsevere.

Discussion

Analysis of data reported to the NHSN Hemovigilance Module substantiates that TTIs are rare but often severe and can be fatal. Bacterial contamination of platelets and transfusion-transmitted babesiosis currently present the most frequent and serious transfusion-related infectious threats in the United States, which is consistent with findings from other studies reporting TTIs in the United States [31,32]. In particular, these findings suggest that bacterial contamination of apheresis platelets occurs more often than those derived from whole blood. The mechanism for this finding is unclear but has been reported previously

Table 3
Product, organism, and imputability of bacterial contamination that resulted in patient death

Products	Organism	Imputability	Patient outcome
Whole blood–derived platelets (pooled prestorage)	*Staphylococcus aureus*	Definite	Death
Apheresis platelets	*Staphylococcus*, coagulase negative	Probable	Death
Red blood cells	*Pseudomonas fluorescens*	Definite	Death
Apheresis platelets	*Ralstonia picketti*	Probable	Death

Table 4
Product, organism, and imputability of bacterial contamination that resulted in a life-threatening reaction

Products	Organism	Imputability	Patient outcome
Apheresis platelets	*Acinetobacter baumannii*	Definite	Life threatening
Apheresis platelets	*Escherichia coli*	Definite	Life threatening
Whole blood–derived platelets	*Escherichia coli*	Possible	Life threatening
Apheresis platelets	*Staphylococcus aureus*[a]	Possible	Life threatening
Whole blood–derived platelets (pooled prestorage)	*Staphylococcus aureus*	Definite	Life threatening

[a] *Staphylococcus aureus* was only identified in the transfused patient and was not identified in the implicated unit.

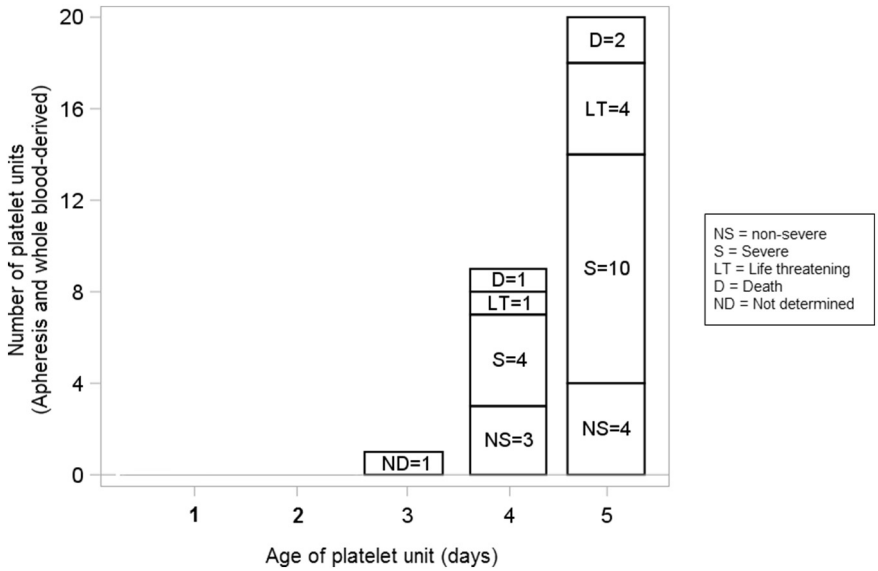

Fig 2. Number of platelet units that were contaminated with bacteria that resulted in adverse reactions by age of platelet unit stratified by the severity of the reaction.

[33]. Furthermore, we observed a very low (less than 1 in a million) risk of viral bloodborne pathogen transmission through transfusion, likely resulting from previous implementation of successful risk reduction strategies. Interventions directed at reducing the burden of bacterial contamination of platelets and *Babesia* transmission through red blood cell transfusion would reduce morbidity and mortality among transfusion recipients. Lastly, these analyses demonstrate that voluntary, passive surveillance can provide similar insight into trends observed from other types of surveillance systems.

Bacterial contamination of platelets occurred more often than contamination of other transfused components as reported to the Hemovigilance Module. Apheresis platelets were more often implicated in TTIs and more often resulted in life-threatening or fatal reactions when transfused on day 4 or 5 postcollection when compared to whole blood–derived platelets. This may be due to differences in the collection and processing of apheresis platelets, specifically the type of instrumentation used during collection [34-37]. However, the total number of apheresis and whole blood-derived platelets transfused on day 4 or 5 postcollection was not available for the present study and precluded rate calculations to assess the outcome of reaction by day of postcollection transfusion. Additionally, information about collection platform for this study was not available. The rate of bacterial contamination of platelets reported to the NHSN Hemovigilance Module is consistent with findings of other national hemovigilance systems [10-15,38]. The higher rate of TTI with apheresis platelets is consistent with other passive surveillance studies such as the current study [25,33,39,40]. However, studies that report data from active surveillance to monitor bacterial contamination of platelets more often implicate whole blood–derived platelet products [41]. Further study is required.

Currently, the most common method used in practice for mitigating risk of bacterial contamination of platelets is aerobic bacterial culture approximately 24-36 hours postcollection (ie, primary testing) performed at the blood collection center, in addition to other interventions during product collection such as skin cleansing at the venipuncture site and blood diversion pouches [42-44]. Less common strategies used include rapid testing or culture at point-of-issue after day 3 postcollection (ie, secondary culture) [45]. Despite these interventions, contaminated platelet units are still transfused because many bacteria grow well at 20-24 C (ie, room temperature), which is the main storage condition of platelet units. False-negative results of the primary culture due to a low bacterial count (due to slow growth or lag in bacterial growth) at the time of sampling and also insufficient volume of sampling are contributing factors [42,46-48]. Other interventions have been described to further reduce the risk of transfusing a contaminated platelet unit. These include PRT, minimum proportional volume sampling, larger volume delayed sampling, and delayed secondary bacterial culture [49-55]. Additionally, although anaerobic infections were not reported to the Module during the study period, these pathogens have been described and implementation of anaerobic bacterial culture has been introduced elsewhere [39,54,56-58]. Implementation of an anaerobic blood culture bottle also adds a potential increase in detection sensitivity of

Table 5
Rates of transfusion-transmitted infections per 100 000 units transfused (full and aliquot) by component type and collection method, as reported to the NHSN Hemovigilance Module, 2010-2016

		Rate, per 100 000 U of blood (n)		
Transfused blood components	Total units transfused	All transfusion-transmitted infections	*Babesia* spp[a]	Bacterial contamination
All components	7 917 786	0.68 (54)		0.47 (37)
Red blood cells[b]	4 376 341	0.53 (23)	0.37 (16)	0.14 (6)
Apheresis	467 693	0.43 (2)	0.21 (1)	0.21 (1)
Whole blood derived	3 908 648	0.51 (20)	0.38 (15)	0.10 (4)
Platelets	1 536 115	1.95 (30)		1.95 (30)
Apheresis	1 069 854	2.43 (26)		2.43 (26)
Whole blood derived	466 261	0.86 (4)		0.86 (4)
Plasma	1 301 064	0.08 (1)		0.08 (1)
Whole blood derived	1 175 540	0.09 (1)		0.09 (1)

[a] No reports of transfusion-transmitted *Babesia* infection implicated platelet or plasma units.
[b] One report indicated 3 red blood cell units, whole blood–derived and apheresis, were transfused and did not implicate a specific unit. This report was not included in the collection method rate calculation.

Table 6
Rates of transfusion-transmitted *Babesia* per 100 000 red blood cell units transfused (full and aliquot) by the date the implicated unit was transfused as reported to the NHSN Hemovigilance Module, 2010-2016

	Total red blood cell units transfused	*Babesia* spp infections	Rate, per 100 000 U of blood
All facilities reporting to the Hemovigilance Module[a]	4 376 341	16	0.37
Reporting facilities located in *Babesia*-endemic states[b]	1 827 373	16	0.88
December-February	431 223	3	0.70
March-May	448 815	1	0.22
June-August	484 389	6	1.24
September-November	462 946	6	1.30

[a] One hundred ninety-five facilities are located in 34 states.
[b] *Babesia*-endemic states are defined as (number of facilities by state reporting between 2010 and 2016) Connecticut (3), Massachusetts (72), Maine (1), Minnesota (4), New Hampshire (1), New Jersey (4), New York (4), Rhode Island (0), and Wisconsin (13).

facultative anaerobes given increased overall volume. Visual inspection of platelet units at point-of-issue continues to be an important "last line of defense" before transfusion, although, as described here, septic transfusion reactions can continue to occur despite this activity [51,59].

All reports of transfusion-transmitted *Babesia* were in endemic states and implicated whole blood–derived red blood cell resulting in severe reactions during the summer and fall seasons. This is consistent with other reports of transfusion-transmitted babesiosis nationally [60,61], although, because of donor travel and movement of blood products outside endemic areas, transfusion-transmitted babesiosis is a risk across the United States [62,63]. Additionally, although all reports in this study implicated red blood cell units, whole blood–derived platelets have been linked to transfusion-transmitted *Babesia* due to some red blood cell content within these units [63]. Since July 2010, selective laboratory screening of blood donations has been conducted by some blood collection centers located in high-risk areas of the United States under investigational protocols [64-66]. Elsewhere in the United States, blood donor screening for babesiosis is required by questionnaire only, a method shown to be ineffective [67]. In May 2015, the FDA's Blood Products Advisory Committee supported the concept of nationwide, year-round testing of blood donors by antibody-based tests and year-round testing by nucleic acid amplification (NAT) of blood donors in the highest-risk region (https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/UCM446274.pdf) [68]. In March 2018, FDA approved the first 2 tests to screen for *Babesia microti* in whole blood and plasma samples from blood donors [69].

Strategies to reduce the risk of HIV, HBV, and HCV transmission through blood transfusion, including strict donor selection and universal NAT, have been successful. With advances in laboratory screening, detected cases are now so unusual that the incidence of transfusion-transmitted viral blood-borne pathogens can only be estimated statistically [70]. The present study describes approximately 7.9 million transfused components, with the number of reported HIV and HCV transfusion-transmission cases lower than expected based on modeling estimates. Four cases of HIV transmission and many more cases of HCV transmission through transfusion have been recognized and reported to public health authorities since NAT was implemented in the United States. However, modeling data estimate more cases than the number reported which could be due to transfusion being unrecognized as the source of transmission or other statistical limitations [71]. As an additional step to monitor the blood supply, following recent changes to blood donor deferral policies, standardized data collection and analytic efforts have been undertaken for estimating and understanding ongoing viral blood-borne pathogen transmission risk such that interventions can be implemented as necessary [72]. While the findings of this study likely represent the success of safety measures, the discrepancy between these projected residual risk and the actual rates found in these analyses may also reflect the challenges of identifying transfusion-transmission of viral blood-borne pathogens in clinical settings. These can include difficulties recognizing that a transfusion was the source of transmission as patients may have multiple other risk factors to which infection is attributed. Additionally, facilities participating in the Module report reactions for patients transfused within their own institutions. Module reporting may therefore not occur given the time lag in recognition of viral blood-borne pathogen infection and diagnosis by an alternative clinician or facility. However, to improve recognition of transfusion-transmission, clinicians should ascertain transfusion history for patients diagnosed with viral blood-borne pathogens and report to public health departments.

These findings are subject to the following limitations [28]. First, data are self-reported by facilities and not independently verified, although extensive data review was conducted by the study investigators and facilities were contacted by the investigators for clarification when discrepant data were reported. The accuracy of reporting relies on the recognition and communication of the occurrence of a TTI within facilities, the availability of patient information and test results, and reporter proficiency in applying case definition, severity, and imputability criteria. Second, voluntary participation and passive surveillance may result in inconsistent self-reporting by facilities of TTIs and the total number of transfused units. These factors may have an impact on rates, resulting in under- or overestimation [73]. Third, the number of participating facilities (195) is relatively small and not a representative sample of all facilities that perform transfusions in the United States, and may not be generalizable, especially where participation is not required. Additionally, 69/195 facilities are located in the state of Massachusetts where blood banks are required to report to the NHSN Hemovigilance Module. This article describes data reported to the NHSN Hemovigilance, a voluntary, passive surveillance system, and may not be representative of the entire United States.

In summary, TTIs are rare but can result in severe reactions among transfusion recipients, despite continued efforts to reduce their occurrence. These findings are broadly consistent with facility-specific studies and hemovigilance data using active and passive surveillance. Based on data collected in the NHSN Hemovigilance Module from 2010 to 2016, bacterial contamination of platelets and transfusion-transmitted *Babesia* associated with red blood cells occur most frequently in the United States and should be targeted for additional interventions.

Disclaimers

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the authors' affiliated institutions. Use of trade names, commercial sources, or private organizations is for identification only and does not imply endorsement by the US Department of Health and Human Services and/or CDC.

Conflict of Interest

None reported.

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