Transfusion-Associated Babesiosis in the United States: A Description of Cases

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Background: Babesiosis is a potentially life-threatening disease caused by intraerythrocytic parasites, which usually are tickborne but also are transmissible by transfusion. Tickborne transmission of Babesia microti mainly occurs in 7 states in the Northeast and the upper Midwest of the United States. No Babesia test for screening blood donors has been licensed.

Objective: To ascertain and summarize data on U.S. transfusion-associated Babesia cases identified since the first described case in 1979.

Design: Case series.

Setting: United States.

Patients: Case patients were transfused during 1979–2009 and had posttransfusion Babesia infection diagnosed by 2010, without reported evidence that another transmission route was more likely than transfusion. Implicated donors had laboratory evidence of infection. Potential cases were excluded if all pertinent donors tested negative.

Measurements: Distributions of ascertained cases according to Babesia species and period of transfusion.

Results: 159 transfusion-associated B. microti cases were included; donors were implicated for 136 (86%). The case patients’ median age was 65 years (range, <1 to 94 years). Most cases were associated with red blood cell components; 4 were linked to whole blood–derived platelets. Cases occurred in all 4 seasons and in 22 (of 31) years, but 77% (122 cases) occurred during 2000–2009. Cases occurred in 19 states, but 87% (138 cases) were in the 7 main B. microti–endemic states. In addition, 3 B. duncani cases were documented in western states.

Limitation: The extent to which cases were not diagnosed, investigated, reported, or ascertained is unknown.

Conclusion: Donor-screening strategies that mitigate the risk for transfusion transmission are needed. Babesiosis should be included in the differential diagnosis of unexplained posttransfusion hemolytic anemia or fever, regardless of the season or U.S. region.

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Babesiosis is caused by intraerythrocytic parasites, which usually are tickborne but also are transmissible by transfusion (1–9). In the United States, 2 species—Babesia microti and B. duncani (formerly, the WA1-type parasite [10, 11])—have been associated with both transmission routes. The predominant zoonotic agent is the rodent parasite B. microti, which is transmitted by Ixodes scapularis ticks in expanding foci in the Northeast and upper Midwest of the United States, particularly during spring and summer (1–3, 12). The first described tickborne and transfusion-associated B. microti cases occurred in Massachusetts in 1969 and 1979, respectively (13–15); the first such B. duncani cases were in Washington in 1991 and 1994 (10, 16).

Regardless of the transmission route, Babesia infection can range from asymptomatic to severe, in part depending on host factors (for example, asplenia and advanced age). Clinical infection is characterized by hemolytic anemia and nonspecific flu-like symptoms (such as fever, chills, and myalgia). Complications can include multiorgan dysfunction, disseminated intravascular coagulation, and death (1–3, 6, 7). Although a history of babesiosis is an exclusion criterion for blood donation (1), persons who meet all eligibility criteria (for example, they feel well, are afebrile, and are not anemic) can have low-level parasitemia and remain infectious for months, even longer than a year (1–6, 16, 17). No Babesia assay for screening donors has been approved by the U.S. Food and Drug Administration (FDA) (1).

Posttransfusion babesiosis has been increasingly recognized (5–9, 18–29). However, national data and perspective about the U.S. burden of cases have been lacking. The Centers for Disease Control and Prevention (CDC) led a collaborative endeavor to ascertain and compile data on U.S. posttransfusion cases identified during the 3 decades since the first described case in 1979 (14). Here we summarize the transfusion-associated Babesia cases that we ascertained, including their distributions by species, time, and place.

Methods

Data Sources

Since the 1960s, the CDC’s Parasitic Diseases Laboratory has been a national reference laboratory for Babesia testing. The CDC is often contacted regarding diagnosis...
Context
Babesiosis, a parasitic infection transmitted through tick bites, can also be acquired via blood transfusion and may result in life-threatening disease. There is no U.S. Food and Drug Administration–licensed test to screen blood donors for Babesia infection.

Contribution
The risk for transfusion-associated Babesia infection may be increasing. Cases have occurred year-round and have been seen in states where Babesia species are not endemic.

Caution
Although the cases ascribed to transfusion undoubtedly represent a fraction of those that occurred, some tickborne cases inadvertently might have been included.

Implication
Improvements in the prevention and detection of transfusion-associated babesiosis are urgently needed.

—The Editors

Figure 1. Stratification of 159 U.S. transfusion-associated Babesia microti cases, 1979–2009.

By type of case (cluster vs. not; index vs. not) and by class of index case (definite, probable, or possible). This figure, in conjunction with Table 1, provides perspective about the criteria for and the tallies of cases, donors, and donations. The 159 B. microti cases include 141 index cases and 18 nonindex, cluster cases. Each index case was associated with a different donor, whether implicated (n = 118) or virtual (n = 23; see Methods section). The 61 index cases classified as definite include the index cases for the 12 multicase clusters (Table 1), which encompass 18 additional cases, for a total of 79 cases. The 3 B. duncani cases are not included in the figure.
Our minimal case criteria included receipt of 1 or more cellular blood components during 1979–2009, posttransfusion laboratory evidence of *Babesia* infection detected by 2010, and no reported evidence that another route of transmission (for example, tickborne or perinatal) was more likely than transfusion. We also required that linked (implicated) donors have laboratory evidence of infection. We excluded potential transfusion cases if all pertinent donors have laboratory evidence of infection. We excluded potential transfusion cases if all pertinent donors have laboratory evidence of infection.

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Table 1. Twelve Clusters of U.S. Transfusion-Associated *Babesia microti* Cases, 1979–2009*

| Cluster | State (Year) of Transfusion | Case Type | Case Characteristics | Data on Babesia Case† | Comments About Recipients Other Than Case Patients‡ |
|---------|----------------------------|-----------|----------------------|-----------------------|--------------------------------------------------|
| A       | RI (2004)                  | Index     | Preterm infant       | Smear/PCR-positive    | Another preterm corecipient of RBCs was treated empirically |
|         | Coreipient                 | Preterm infant | Smear/PCR-positive | –                     |
|         | Coreipient                 | Preterm infant | Smear/PCR-positive | –                     |
| B       | RI (2006)                  | Index     | Preterm infant       | Smear/PCR-positive    | No other corecipients (Lookback: recipient of RBCs donated 3 mo earlier tested negative) |
|         | Coreipient                 | Preterm infant | Smear/PCR-positive | –                     |
|         | Coreipient                 | Preterm infant | PCR-positive       | –                     |
| C       | VA (2009)                  | Index     | Preterm infant       | Smear/PCR-positive    | Platelet corecipient was asymptomatic and was not tested (Lookback: “no adverse outcomes” reported for recipients associated with 2 previous donations) |
|         | Coreipient                 | Preterm infant | Smear/PCR-positive | –                     |
|         | Coreipient                 | Preterm infant | PCR-positive       | –                     |
| D       | NY (1997)                  | Index     | Full-term infant     | Smear/PCR-positive    | Platelet corecipient (age 11 y) and 2 preterm corecipients of RBCs tested negative (Lookback >1 y earlier: RBC recipient tested negative; platelet recipient died ≤3 wk after transfusion) |
|         | Coreipient                 | Age 70 y; GI bleeding | Smear/PCR-positive | –                     |
|         | Coreipient                 | Age 70 y; GI bleeding | PCR-positive       | –                     |
| E       | NY (1999)                  | Index     | Preterm infant       | Smear/PCR-positive    | Platelet corecipient was asymptomatic and was not tested (Lookback: “no adverse outcomes” reported for recipients associated with 2 previous donations) |
|         | Coreipient                 | Age 28 y; SCD | PCR-positive       | –                     |
| F       | CT (2006)                  | Index     | Neonate              | “Proven infection”    | No additional information |
|         | Coreipient                 | Age 32 y; SCD | PCR-positive       | –                     |
| G       | MN (2008)                  | Index     | Age 92 y; asplenic   | Smear/PCR-positive    | Double RBC donation: both recipients became infected and are listed here |
|         | Coreipient                 | Age 36 y; surgery | PCR-positive      | –                     |

5 multidonation clusters

| H       | MN (1999)                  | Lookback (July donation) | Age 78 y; GI bleeding | PCR-positive | Platelet corecipient (age 70 y) tested negative about 8 mo after transfusion (Lookback: December 2001 donation tested negative) |
|         | MN (1999)                  | Lookback (September donation) | Age 80 y | PCR-positive | No corecipients |
|         | MN (1999)                  | Index (November donation) | Age 68 y; surgery | Smear/PCR-positive | No corecipients |
| J       | NY (2002)                  | Lookback (March donation) | Age 78 y; surgery | PCR-positive | (Further lookback: recipient associated with December 2001 donation tested negative) |
| K       | WI (2007)                  | Lookback (August donation) | Age 83 y; surgery | Seropositive | (Further lookback: no information about recipient of RBCs donated in August) |
| L       | MN (2008)                  | Index (August donation) | Age 83 y; GI bleeding | Smear/PCR-positive | No corecipients |
|         | MN (2008)                  | Lookforward (October donation) | Age 53 y; surgery | Seropositive | (Status of other recipients of RBCs donated in 2007: 2 died; 1 tested negative; 1 lost to follow-up) |

CT = Connecticut; FL = Florida; GI = gastrointestinal; MA = Massachusetts; MN = Minnesota; NY = New York; PCR = polymerase chain reaction; RBC = red blood cell; RI = Rhode Island; SCD = sickle cell disease; VA = Virginia; WI = Wisconsin.

* The 12 identified clusters encompass 30 cases (1 per row) linked to 19 donations by the 12 implicated donors; the 30 cases include 12 index and 18 nonindex cases (11 in corecipients, 5 detected in lookback investigations, and 2 from lookforward investigations). One case was linked to whole blood–derived platelets (cluster H; fourth donation); the other 29 were linked to RBC components. Among infants with available data, the smallest transfused volume was approximately 8 mL. In 2 multidonation clusters (J and K), case patients were identified in 2 states. In cluster J, both donations were in Maine, by a donor probably exposed in Massachusetts; in cluster K, a Wisconsin resident also donated in Florida. Five of 12 implicated donors had parasitologically confirmed infection, on the basis of testing an original unit segment (B, C, D, and G) or subsequent specimens (H); the donor linked to cluster H still had demonstrable parasitemia, by PCR analyses, 4 mo after the fourth donation, 10 mo after exposure (5). For cluster A’s donor, a segment was available but results of PCR analyses were negative.

† Seropositive is noted only for the 4 nonindex cases that were not parasitologically confirmed: The reciprocal antibody titers ranged from 256 to 1024 in *B. microti* indirect fluorescent antibody testing.

§ For recipients other than case patients, “tested negative” denotes seronegativity, at a minimum.

¶ 12 cases (13 in infants and 5 in adults); 2–3 cases per cluster.

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Table 2. Characteristics of U.S. Transfusion-Associated Babesia microti Cases, Stratified by Type and Class (159 Total Cases, Including 141 Index Cases), 1979–2009*

| Variable | All Cases (n = 159) | Stratification of All Cases, by Type (n = 159) |
|----------|---------------------|-----------------------------------------------|
|          | Index Cases (n = 141 [89%]) | Nonindex Cases (n = 18 [11%]) |
|          | Median age (range; IQR), y† | Median age (range; IQR), y† |
| Age at diagnosis, n | 157 | 139 |
| Patients aged <1 y, n (%) | 18 (11) | 11 (8) |
| Patients aged ≥1 y to <50 y, n (%) | 33 (21) | 30 (22) |
| Patients aged ≥50 y, n (%) | 106 (68) | 98 (71) |
| Male sex, n/n (%) | 78/156 (50) | 73/138 (53) |
| State of transfusion‡ | 138 (87) | 122 (87) |
| Northeast (CT, MA, NJ, NY, or RI), n | 118 | 108 |
| Upper Midwest (MN or WI), n | 20 | 14 |
| Other state, subtotal n (%) | 21 (13) | 19 (13) |
| Eastern state, n | 17 | 15 |
| Year of transfusion | 2005 (1979–2009) | 2005 (1979–2009) |
| By period, n (%) | 2000–2004 | 2005–2009 |
| 1979–1984 | 4 (3) | 3 (2) |
| 1985–1989 | 3 (2) | 3 (2) |
| 1990–1994 | 6 (4) | 6 (4) |
| 1995–1999 | 24 (15) | 19 (14) |
| 2000–2004 | 31 (20) | 26 (18) |
| 2005–2009 | 91 (57) | 83 (59) |
| Month of symptom onset or diagnosis, n§ | 128 | 114 |
| Interval from transfusion to diagnosis, n | 42 (14–230; 34–53) | 42 (14–230; 34–53) |
| Parasitologically confirmed infection, n (%¶) | 153 (96) | 139 (99) |
| Surgical splenectomy, subtotal n ** | 32 | 32 |
| Underlying condition or context for transfusion (1 per patient), n | 39 | 37 |
| Hematologic disorder, subtotal n | 14 | 14 |
| Hematologic cancer | 11 | 9 |
| Thalassemia major | 7 | 7 |
| Other hematologic disorder | 22 | 20 |
| Cardiovascular surgery or procedure | 19 | 17 |
| Gastrointestinal disease, bleeding, or surgery | 8 | 8 |
| Trauma with posttraumatic splenectomy ** | 5 | 5 |
| Other surgery, procedure, or trauma | 13 | 9 |
| Newborn or complications of prematurity | 16 | 9 |
| Carcinoma | 13 | 13 |
| Other medical reason or diagnosis | 14 | 14 |
| All-cause mortality, n (%¶¶) | 28 (18) | 27 (19) |
| Blood donor, n (%¶¶) | 136 (86) | 118 (84) |
| Parasitologically confirmed, subtotal n | 24 | 24 |

CT = Connecticut; IQR = interquartile range; MA = Massachusetts; MN = Minnesota; NJ = New Jersey; NY = New York; PCR = polymerase chain reaction; RI = Rhode Island; WI = Wisconsin.

* Data are number of cases/patients, unless otherwise noted. Diagnosis refers to babesiosis. Transfusion and blood donor refer to those associated with a case. Percentages might not total 100% because of rounding.

† Because a lower proportion of patients with index vs. nonindex cases were younger than 1 y (P = 0.001), the age distributions for index vs. nonindex patients were significantly different (P = 0.009), but not if the age comparison was limited to adults (P = 0.3).

‡ See Methods section and Figure 2. The “eastern state” category consists of Delaware, Florida, Indiana, Maryland, New Hampshire, North Carolina, Ohio, Pennsylvania, and Virginia. The “not an eastern state” category consists of California, Texas, and Washington.

§ If both were known and were different, the earlier month was specified. Data for the kidney donor (see text) were not included in analyses of month of diagnosis or interval to diagnosis.

¶ See Figure 3 regarding index patients. Among nonindex patients (Table 1), the interval to diagnosis depended on host factors, type of recipient (corecipient vs. other), and various aspects of the investigations. Although most of the ascertained nonindex patients who were adults reportedly were asymptomatic, clinical information in such regards typically was anecdotal or unspecified. In some investigations, other recipients could not be tested because they had already died.

¶¶ Data for the kidney donor (see text) were not included in analyses of month of diagnosis or interval to diagnosis.

§§ Data for the kidney donor (see text) were not included in analyses of month of diagnosis or interval to diagnosis.

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Table 2—Continued

| Definite Cases (n = 61 [43%]) | Probable Cases (n = 57 [40%]) | Possible Cases (n = 23 [16%]) |
|-------------------------------|-------------------------------|-------------------------------|
| 60                            | 56                            | 23                            |
| 69 (<1–94; 27–81)             | 65 (<1–92; 45–78)             | 67 (<1–87; 53–77)             |
| 9 (15)                        | 1 (2)                         | 1 (4)                         |
| 11 (18)                       | 16 (29)                       | 3 (13)                        |
| 40 (67)                       | 39 (70)                       | 19 (83)                       |
| 25/60 (42)                    | 33/55 (60)                    | 15/23 (65)                    |
|                               | 44 (72)                       | -                             |
|                               | 57 (100)                      | 21 (91)                       |
|                               | -                             | -                             |
|                               | 17 (28)                       | -                             |
|                               | 0                             | 2 (9)                         |
|                               | -                             | -                             |
|                               | -                             | -                             |
| 2005 (1980–2009)              | 2006 (1979–2009)              | 2005 (1993–2009)              |
| 3 (5)                         | 1 (2)                         | 0                             |
| 2 (3)                         | 1 (2)                         | 0                             |
| 1 (2)                         | 4 (7)                         | 1 (4)                         |
| 9 (15)                        | 5 (9)                         | 5 (22)                        |
| 13 (23)                       | 9 (16)                        | 4 (17)                        |
| 33 (54)                       | 37 (65)                       | 13 (57)                       |
| 56                            | 52                            | 20                            |
| Aug (Jan–Dec)                 | Oct (Jan–Dec)                 | Sep (Jan–Dec)                 |
| 53                            | 50                            | 11                            |
| 43 (22–230; 35–52)            | 42 (14–225; 34–58)            | 42 (14–54; 21–52)             |
| 61 (100)                      | 55 (96)                       | 23 (100)                      |
| 11                            | 12                            | 9                             |
| 8                             | 8                             | 1                             |
| 2                             | 2                             | 8                             |
| 1                             | 2                             | 0                             |
| 11                            | 20                            | 6                             |
| 3                             | 7                             | 4                             |
| 4                             | 5                             | 0                             |
| 3                             | 3                             | 1                             |
| 1                             | 5                             | 1                             |
| 8                             | 7                             | 5                             |
| 8                             | 6                             | 3                             |
| 2                             | 2                             | 4                             |
| 1                             | 4                             | 0                             |
| 7                             | 2                             | 0                             |
| 8                             | 1                             | 0                             |
| 5                             | 6                             | 2                             |
| 9                             | 3                             | 2                             |
| 2                             | 6                             | 1                             |
| 11 (18)                       | 12 (21)                       | 4 (17)                        |
| 61 (100)                      | 57 (100)                      | 0                             |
| 22                            | 2                             | 0                             |
| 12                            | 0                             | 0                             |

¶ Index cases were known or presumed to be parasitologically confirmed, with the exception of 2 cases classified as probable transfusion cases: the case in the kidney donor (see text) and a case diagnosed in retrospect, after recovery (30).

** The data constitute minimum numbers of case patients. Among the 12 known to have undergone splenectomy during the peritransfusion period, the contexts were trauma (n = 8) or abdominal surgery for other reasons (n = 4). The cases in the 3 patients known to have undergone posttransfusion splenectomy include 1 definite case (the index case of cluster L [25]; Table 1) and 2 probable cases, including the first described transfusion case (14).

†† Three received a kidney (living related [31], living unrelated, or cadaveric), 1 received a heart (29), and 1 underwent bilateral lung transplantation.

‡‡ Although outcome data were unavailable for some patients, we assumed that no other case patients died in the short term. The patients known to have died include 2 cluster-associated infants whose gestational ages were 23 and 24 wk, 2 (of 5) patients aged ≥90 y, and 6 (of 32) patients known to have undergone surgical splenectomy.

§§ In at least 4 case investigations, more than 1 donor had laboratory evidence of infection, typically 1 of whom was the most plausible on the basis of laboratory or epidemiologic data. However, the possibility of receipt of more than 1 contaminated unit could not be excluded.
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nors tested negative. If multiple cases were linked to the same donor, we defined the interrelated cases as a cluster, the first identified case as the index case (1 per donor), and the other cases in the cluster as nonindex cases (Figure 1 and Table 1). To facilitate bookkeeping, we defined all cases that were not cluster-associated as index cases (1 per donor).

In general, index cases were parasitologically confirmed (Table 2) (30, 31); their detection prompted a transfusion investigation; and the linked donors and nonindex cases, if any, that were identified had parasitologic or serologic evidence of infection. We defined parasitologic evidence as detection of Babesia parasites (on blood smear or by animal inoculation) or Babesia DNA (by a molecular method). Serologic evidence of B. microti infection required positive results either by indirect fluorescent antibody (IFA) testing for total immunoglobulin or IgG or by immunoblot for IgG.

Index Babesia cases that fulfilled the selection criteria were classified as definite, probable, or possible transfusion-associated cases (Figure 1). If no donor was implicated among the subset of pertinent donors who could be tested, an index case was defined as a possible case, even if transfusion was the only known risk factor for infection. All index cases that were linked to a donor were classified as definite or probable cases. An index case was defined as a definite (vs. probable) transfusion case if at least 1 of the following additional criteria was fulfilled: 1) Transfusion was the only known or plausible risk factor for infection (for example, there was no history of residence or travel in babesiosis-endemic areas); 2) a multicase cluster was identified, with at least 1 nonindex case besides the index case (Table 1); 3) the linked donor’s infection was parasitologically confirmed by testing an extant segment from the original blood unit; or 4) other donor evidence indicated active infection at the time of donation (for example, a polymerase chain reaction [PCR]–positive specimen that reflected the donor’s status at donation).

Data Analysis

We conducted univariate analyses for descriptive purposes by using Epi Info, version 3.5.1 (CDC, Atlanta, Georgia), and SAS software, version 9.2 (SAS Institute, Cary, North Carolina). Proportions were compared by using the chi-square test, or if expected cell counts were less than 5, the Fisher exact test. The Wilcoxon 2-sample test was used to compare the ranked distributions of ordinal variables. Statistical significance was defined as a 2-sided P value less than 0.05.

Unless otherwise specified, we stratified cases by period and state of transfusion (Table 2 and Figure 2) (32). We refer to 7 states with well-established foci of zoonotic transmission as “B. microti–endemic states”: 5 states in the Northeast (Connecticut, Massachusetts, New Jersey, New York, and Rhode Island) and 2 in the upper Midwest (Minnesota and Wisconsin) (1, 12). The distinction between these and other states (for example, in Figure 2) is not meant to imply that tickborne transmission occurs throughout these 7 states, that it occurred in all 7 states throughout 1979–2009, or that these are the only states in which it did or does occur. Of note, during case selection and classification, we considered the evolving focality of tickborne transmission within and among states.

Role of the Funding Source

The study received no external funding.

RESULTS

General Perspective and Summary

For the period of 1979–2009, we included 162 transfusion-associated cases: 159 B. microti cases and 3 B. duncani cases, which are described separately. The 159 B. microti cases include 12 multicase clusters encompassing 30 cases: 12 index cases (1 per cluster) and 18 nonindex cases (5, 8, 9, 20–25) (Figure 1 and Table 1). In total, 141 B. microti cases were defined as index cases: the 12 cluster-associated index cases and 129 additional cases (Table 2).

Figure 2 shows their distribution by period and state of transfusion. During the initial 11 years (1979–1989), 7 index cases occurred in 5 states (14, 17, 32–36). In contrast, during the third decade (2000–2009), 109 index cases (77% of 141) and 122 total cases (77% of 159) occurred in 18 states (5–9, 18–21, 24–29, 37–42). The associated blood donations occurred in all 12 months (Appendix Figure, available at www.annals.org); 59% were during July–October.

Overall, 122 (87%) of the index cases (138 total cases [87%]) were associated with transfusions in the 7 main B. microti–endemic states (Figure 2 and Table 2), although not necessarily in areas of endemicity. The other 19 index cases (13%) generally were attributable to interstate movements of donors or blood components (Figure 2). Various scenarios are exemplified by the 4 cases not in eastern states (Figure 2), 2 of which were attributable to donor travels: A Rhode Island resident donated while training in Washington (26), and a Texas resident donated in that state after spending the summer in Massachusetts (6). In contrast, the other case in Texas and the case in California were linked to donations in New Jersey and Maine (27), respectively. Local distributions of components collected in New Jersey also accounted for 2 cases in Pennsylvania (8, 37) and 1 in Delaware (18).

Case Characteristics

Table 2 summarizes selected characteristics of the cases, stratified by type of case (index vs. nonindex) and by class of index case (definite, probable, or possible). Table 1 provides additional perspective on the cluster-associated cases, which necessitated distinguishing between index and nonindex cases. Overall, the case patients had a median age of 65 years; 32% were either very old (33 were in the ninth or tenth decade of life) or very young (18 were infants, 13
of whom were cluster-associated). The 19 patients with hereditary blood disorders account for 73% of the 26 patients in the age range of 4 to 43 years. These 19 patients include 11 with sickle cell disease (8, 9, 28), 7 with thalassemia major (35, 43), and 1 with Diamond–Blackfan anemia (18); they account for at least 9 of the 32 patients known to have undergone surgical splenectomy. Three elderly patients with hematologic disorders underwent posttransfusion splenectomy (32, 134, or 215 days later), and their Babesia cases were diagnosed thereafter (Figure 3 and Table 2). For 2 of these patients, parasites were noted during retrospective review of presplenectomy blood smears, a finding that refocused the investigations on earlier transfusions and donors than on those initially targeted.

Five patients with transfusion cases had been transplanted with solid organs within the previous 3 months (Table 2). In addition, indirect evidence suggests that a kidney donor who received multiple transfusions the day he died served as a conduit of Babesia parasites from 1 of his blood donors to both of his kidney recipients, who developed parasitologically confirmed infection (40). No B. microti antibodies were detected by IFA testing of archived pretransplantation serum from the kidney recipients or of pretransfusion serum from the kidney donor (Table 2). However, postdonation specimens from 1 of his blood donors were seropositive (24).

The median interval from transfusion to onset of clinical manifestations was 37 days (range, 11 to 176 days) among 84 index patients with available data (Figure 3). Although babesiosis generally is considered a febrile illness, 13 (of 105) index patients were afebrile (9, 26, 32), including at least 4 adults who had cancer or were receiving immunosuppressive therapy. The median interval from symptom onset to diagnosis of index cases was 6 days (range, 0 to 54 days; n = 84). Babesiosis often was diagnosed incidentally, in some instances during routine outpatient evaluations (6), during hospitalizations for unrelated reasons, or after the patient had recovered (30) or died (data not shown). Typically, Babesia parasites were an unexpected finding when a blood smear was examined, usually in the context of a complete blood count with a manual differential (9). When intraerythrocytic ring forms were noted, malaria was the first diagnostic consideration for more than 20 index patients, at least 14 of whom were initially treated for malaria.

The minimum all-cause mortality rate among index patients was 19% (6–9, 18, 19, 32–34, 40, 44) (Table 2); Figure 3 provides various intervals to death. Some patients had a bleak prognosis even without the potential compounded effects of babesiosis. The 27 index patients known to have died include the kidney donor described earlier, whose posttrauma death on the day of transfusion clearly was unrelated to babesiosis. For other patients with available data, there was a spectrum of likelihood that by period and state of transfusion. The data are limited to the 141 B. microti index cases, 12 of which were associated with multicase clusters (Table 1). Data for the 3 B. duncani cases, which occurred in Washington (in 1994) and California (in 2000 and 2008), are not included. The x-axis includes one 6-year period (1979–1984), followed by five 5-year periods. See the Methods section for the distinction between the 7 main B. microti–endemic states and “other states”; within each category, for the tallies by state (by period), the states generally are listed in the order of their first identified case.

* Local and intraregional movements of donors and blood components were common both in the Northeast and in the upper Midwest (data not shown).† Among the 19 index cases in 12 “other states,” the North Carolina case and 1 Florida case were not linked to donors, the other Florida case was linked to a Wisconsin resident who donated blood while wintering in Florida (cluster K in Table 1), and 1 of 3 Pennsylvania cases was linked to a Pennsylvania donor who reportedly had not traveled to a known B. microti–endemic area in another state (8). Information on the donors linked to the other 15 index cases is provided in the text or the footnotes below for 7 and 8 cases, respectively.

† The donor was exposed in Massachusetts (32).§ The 4 index cases in Maryland and Virginia were linked to donations in these states. The linked donors either were or could have been exposed in the Northeast.¶ The cases in Ohio (n = 2) and Indiana (n = 1) were linked to donations in Indiana (n = 2) and Ohio (n = 1) by donors exposed in B. microti–endemic states.
B. microti encompass 136 total cases (86%) (infection was identified for 118 index cases (84%), which death often were presumptive or unclear (data not shown). babesiosis had a causal or contributory role (6, 7); causes of death often were presumptive or unclear (data not shown).

Blood Donors and Components

A linked donor with laboratory evidence of B. microti infection was identified for 118 index cases (84%), which encompass 136 total cases (86%) (Figure 1). Among the 117 linked donors whose B. microti IFA test results were known, the median reciprocal antibody titer was 256 (range, 64 to 4096; interquartile range, 256 to 1024). Twenty-four donors (20%) had parasitologically confirmed infection (Table 2). The 20 donors with positive PCR results include 12 (71%) of 17 for whom blood retained from the original donation was tested compared with 8 (14%) of 56 for whom only postdonation specimens were available (P < 0.001). The median age of the 80 donors with available data was 49 years (range, 17 to 72 years); 18 donors (23%) were at least 60 years of age. Although clinical information typically was anecdotal or unspecified, some donors had pre- or postdonation symptoms or anemia of potential relevance (5, 24–27). For example, the donor who had 4 consecutive donations linked to transmission (cluster H in Table 1) had been temporarily deferred because he was anemic when he first attempted to donate after exposure (5).

Among the 151 cases for which the type of blood component was determined, 4 cases were linked to whole blood–derived platelets (4, 5, 14) and 147 were associated with red blood cells (RBCs). The median age of liquid-stored RBCs at the time of transfusion was 16 days (range, 4 to 40 days; n = 106); 4 case patients received RBCs that were 35 to 40 days old. At least 4 patients received frozen-deglycerolized (vs. liquid-stored) RBCs (18, 35, 43). Many patients received leukoreduced RBCs (data not shown); at least 10 received irradiated RBCs.

Babesia duncanii Cases

The 3 documented B. duncanii cases were linked to RBC transfusions in Washington (in 1994 [16]) and California (in 2000 [45] and 2008). In each instance, the case patient and implicated donor lived in the same state and had parasitologically confirmed infection. The case patients include a preterm infant (45), a 59-year-old man with a hemoglobinopathy (Bloch EM, Herwaldt BL, Leiby DA, et al. Unpublished data), and a 76-year-old man with a myelodysplastic syndrome who underwent cardiac surgery (16).

DISCUSSION

Babesiosis is an uncommon but potentially life-threatening complication of transfusion that has been increasingly recognized since the first described U.S. case in 1979. Donor-screening practices do not yet include routine testing for evidence of Babesia infection. In this context, prompt detection, treatment, investigation, and reporting of Babesia cases are essential. Babesiosis should be included in the differential diagnosis of unexplained posttransfusion hemolytic anemia, with or without fever, regardless of the season or U.S. region. To enhance the abil-
Analyses, our findings underscore that irradiated, or frozen. Although we did not conduct risk
transfusions. Red blood cell components of all storage ages, component was determined were associated with RBC
survive blood bank procedures and storage conditions for
transfusions, and potential future donor screening.

Implications for diagnostic testing, transfusion investiga-
tions, and classification depended on the completeness
and accuracy of the available data.

As expected, almost all cases for which the type of
component was determined were associated with RBC
transfusions. Red blood cell components of all storage ages,
including greater than 5 weeks, were associated with trans-
mission, as were components that had been leukoreduced,
irradiated, or frozen. Although we did not conduct risk
analyses, our findings underscore that Babesia parasites can
survive blood bank procedures and storage conditions for
RBC components. The 4 identified cases linked to whole
blood–derived platelets span from 1979 (the first described
transfusion case) to 2000 and presumably were attributable
to residual RBCs or to extracellular parasites in the platelet
units (4, 5, 14, 49). These 4 cases—and the cases in infants
transfused with small RBC aliquots—underscore that small
inocula can suffice to cause infection. However, even a
segment from an implicated unit may test negative by PCR: The small volumes tested do not approximate the
volumes transfused (1, 2).

Some of the demographic and other characteristics of
the case patients reflect those of transfused patients in gen-
eral (2, 4) but may have particular importance in the con-
text of babesiosis. For example, advanced age is a risk factor
for severe babesiosis, even in otherwise healthy persons;
transfusion recipients often have comorbid conditions that
can increase their vulnerability to the compounding effects
of babesiosis and interrelated complications (such as multi-
organ dysfunction and death) (6, 7, 18, 19, 33, 34). On
the other hand, even some of the adult index patients were
afebrile, including several patients receiving immuno-
pressive therapies that may affect the host response to in-
fec tion. Although most index cases with available data were
diagnosed within 2 months of transfusion, a noteworthy
minority of cases were diagnosed months later, such as in
the context of posttransfusion splenectomy (Figure 3). These
points not only have clinical relevance but also may
affect transfusion investigations and case counts: The like-
lihood that transfusion transmission is considered and is
investigated successfully may be lower for cases with longer
intervals from the pertinent transfusion to symptom onset
or diagnosis.

The 162 transfusion-associated cases we enumerated
undoubtedly represent a fraction of those that occurred.
The extent to which cases were not detected, investigat-
ed, or reported (to the CDC, to other public health
authorities, or in publications) is unknown, both in gen-
eral and with respect to periods, regions, and various
case characteristics and outcomes. As underscored by the
 incidental diagnosis of Babesia infection, even severe
cases in babesiosis-endemic regions can be missed or
misdiagnosed, not just cases that are asymptomatic or
mild or that occur in other U.S. regions. Even if a case
is diagnosed, a transfusion investigation might not be
considered, conducted, completed, or conclusive. The
cases we included that were not linked to a donor (Fig-
ure 1 and Table 2) highlight the challenges associated
with contacting all pertinent donors and obtaining post-
transfusion specimens for testing; segments from the
original donations typically are not still available. Our
tallyes probably constitute undercounts even of docu-
mented transfusion cases (for example, those that did
not come to our attention or did not meet our selection
criteria) but inadvertently might include some tickborne
cases. As with all surveillance, case ascertainment, selec-
tion, and classification depended on the completeness
and accuracy of the available data.

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Our findings underscore the year-round vulnerability of the U.S. blood supply—especially, but not only, in and near babesiosis-endemic areas. They also highlight the importance of multiagency collaborative efforts to detect, investigate, and document transfusion cases; to assess the risks for transfusion transmission; and, thereby, to inform the scope of prevention measures. In 2009, the Transfusion-Transmitted Diseases Committee of AABB (formerly, the American Association of Blood Banks) categorized babesiosis in the highest risk level for blood safety to be prioritized for intervention (50). Donors with subclinical infection are not identified by existing measures (such as temporary deferral of persons with systemic symptoms, fever, or anemia), no Babesia assay for screening donors has been approved by the FDA, and pathogen reduction techniques for RBCs or platelets are not available in the United States (1, 2, 50). The FDA’s Blood Products Advisory Committee that was convened on 26 July 2010 supported the concept of regional donor testing for Babesia (51). The increasing recognition of transfusion cases strengthens the impetus for screening strategies that mitigate the transmission risk (1–3, 50, 51), including testing approaches implemented under FDA-approved protocols (1, 3, 51) and longer-term strategies with development of a high-throughput Babesia screening assay.

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References
1. Guibourne DM, Nakhasi HL, Mied PA, Asher DM, Epstein JS, Kumar S. Transfusion-transmitted babesiosis in the United States: summary of a workshop. Transfusion. 2009;49:2759-71. [PMID: 19821952]
2. Leiby DA. Transfusion-transmitted Babesia spp.: bull’s-eye on Babesia microti. Clin Microbiol Rev. 2011;24:14-28. [PMID: 21233506]
3. Young C, Krause PJ. The problem of transfusion-transmitted babesiosis [Editorial]. Transfusion. 2009;49:2548-50. [PMID: 20163687]
4. Cable RG, Trouen-Trend J. Tickborne infections. In: Linden JV, Bianco C, eds. Blood Safety and Surveillance. New York: Marcel Dekker; 2001:399-422.
5. Herwaldt BL, Neitzel DF, Gorlin JB, Jensen KA, Perry EH, Peglow WR, et al. Transmission of Babesia microti in Minnesota through four blood donations from the same donor over a 6-month period. Transfusion. 2002;42:1154-8. [PMID: 12430672]
6. Cangelosi JJ, Sarvat B, Sarria JC, Herwaldt BL, Indrikovs AJ. Transmission of Babesia microti by blood transfusion in Texas. Vox Sang. 2008;95:331-4. [PMID: 19138264]
7. Guibourne DM, Lucey CT, Lee KC, Conley GB, Holness LG, Wise RP. Babesia infection through blood transfusions: reports received by the US Food and Drug Administration, 1997–2007. Clin Infect Dis. 2009;48:25-30. [PMID: 19035776]
8. Tonnetti L, Eder AF, Dy B, Kennedy J, Pisciotta P, Benjamin RJ, et al. Transfusion-transmitted Babesia microti identified through hemovigilance. Transfusion. 2009;49:2557-63. [PMID: 19624607]
9. Asad S, Sweeney J, Merrel LA. Transfusion-transmitted babesiosis in Rhode Island. Transfusion. 2009;49:2564-73. [PMID: 19761547]
10. Quick RE, Herwaldt BL, Thomford JW, Garnett ME, Eberhard ML, Wilson M, et al. Babesiosis in Washington State: a new species of Babesia? Ann Intern Med. 1993;119:284-90. [PMID: 8328736]
11. Conrad PA, Kjemtrup AM, Carreno RA, Thomford J, Wainwright K, Eberhard M, et al. Description of Babesia duncani n.sp. (Apicomplexa: Babesiidae) from humans and its differentiation from other piroplasms. Int J Parasitol. 2006;36:779-89. [PMID: 16725142]
12. Herwaldt BL, McGovern PC, Gerwel MP, Easton RM, MacGregor RR. Endemic babesiosis in another eastern state: New Jersey. Emerg Infect Dis. 2003;9:184-8. [PMID: 12603988]
13. Western KA, Benson GD, Gleason NN, Healy GR, Schultz MG. Babesiosis in a Massachusetts resident. N Engl J Med. 1970;283:854-6. [PMID: 4989787]
14. Jacoby GA, Hunt JV, Kosinski KS, Demirjian ZN, Huggins C, Ekstrand P, et al. Treatment of transfusion-transmitted babesiosis by exchange transfusion. N Engl J Med. 1980;303:1098-100. [PMID: 7191475]
15. Jacoby GA. Was babesiosis transmitted by transfusion? [Letter]. N Engl J Med. 1981;304:733.
16. Herwaldt BL, Kjemtrup AM, Conrad PA, Barnes RC, Wilson M, McCarthy MG, et al. Transfusion-transmitted babesiosis in Washington State: first reported case caused by a W1-A type parasite. J Infect Dis. 1997;175:1259-62. [PMID: 9129100]
17. Wittner M, Rowin KS, Tanowitz HB, Hobsb JB, Saltzman S, Wenz B, et al. Successful chemotherapy of transfusion babesiosis. Ann Intern Med. 1982;96:601-4. [PMID: 7200341]
18. Zhao Y, Love KR, Hall SW, Beadell FY. A fatal case of transfusion-transmitted babesiosis in the State of Delaware. Transfusion. 2009;49:2583-7. [PMID: 19906041]
19. Blue D, Graves V, McCarthy L, Cruz J, Gregurek S, Smith D. Fatal transfusion-transmitted Babesia microti in the Midwest. Transfusion. 2009;49:8. [PMID: 18694463]
20. Fox LM, Wingertor S, Ahmed A, Arnold A, Chou J, Rhein L, et al. Neonatal babesiosis: case report and review of the literature. Pediatr Infect Dis J. 2006;25:169-73. [PMID: 16462298]
21. Kurkjian K, Marshall BC, Kumar P, Koch W, Mismas M, Garrett J, et al. Transmission-associated babesiosis among three neonates—Virginia, 2009 [Abstract]. In: Annual Conference of the Council of State and Territorial Epidemiologists (CSTE), Portland, OR: CSTE; 2010.
22. Dobrosetzicyj J, Herwaldt BL, Doctor F, Miller JR, Linden J, Eberhard ML, et al. A cluster of transfusion-associated babesiosis cases traced to a single asymptomatic donor. JAMA. 1999;282:927-30. [PMID: 10078490]
23. Linden JV, Kolakoski MH, Wong SJ, Carpenter JH, Kessler DA, Bianco C. Transfusion-associated babesiosis in two recipients [Abstract]. Transfusion. 2000;40 Suppl 96S.
24. Bachowski G, Kemperman MM, Skeate RC, Mair DC. Transfusion-related...
27. Wudihkarn K, Perry EH, Kemperman M, Jensen KA, Kline SE. Transmission of babesiosis in an immunocompromised patient: a case report and review. Am J Med. 2011;124:800-5. [PMID: 21683324]
26. Della-Giustina D, Laird TW Jr, Smith T. Transfusion-acquired babesiosis in a nonendemic area. Mil Med. 2005;170:295-6. [PMID: 15916297]
25. Ngo V, Given R. Babesiosis acquired through blood transfusion, California, USA. Emerg Infect Dis. 2009;15:785-7. [PMID: 19402960]
24. Cirino CM, Leitman SF, Williams E, Fedorko D, Palmore TN, Klion A, et al. Transfusion-associated babesiosis with an atypical time course after nonmyeloablative transplantation for sickle cell disease [Letter]. Ann Intern Med. 2008;148:794-5. [PMID: 18490697]
23. Lux JZ, Weiss D, Linden JV, Kessler D, Herwaldt BL, Wong SJ, et al. Babesiosis acquired through blood transfusion, California, USA. Emerg Infect Dis. 2009;15:785-7. [PMID: 19402960]
22. Marcus LC, Valigorsky JM, Fanning WL, Joseph T, Glick B. Adult respiratory distress syndrome in babesiosis. Chest. 1984;86:633-4. [PMID: 20824620]
21. Mintz ED, Anderson JF, Popovsky M, Mills L, Spielman A. Transfusion-acquired babesiosis and failure of antibiotic treatment. JAMA. 1986;256:2726-7. [PMID: 3641117]
20. Gordon S, Gordon RA, Mazdizer EJ, Valigorsky JM, Blagg NA, Barnes SJ. Babesiosis in a renal transplant recipient acquired through blood transfusion. Transplantation. 2000;70:205-8. [PMID: 10919602]
19. Smith RP, Evans AT, Popovsky M, Mills L, Spielman A. Transfusion-acquired babesiosis and failure of antibiotic treatment. JAMA. 1982;248:465-7. [PMID: 7201036]
18. Marcus LC, Valigorsky JM, Fanning WL, Joseph T, Glick B. Babesiosis: a spectrum of clinical presentations. J Clin Apher. 2010;25:358-61. [PMID: 21106022]
17. Nicholson GT, Wash CB, Madan RP. Transfusion-associated babesiosis in a 7-month-old infant after bidirectional Glenn procedure. Congenit Heart Dis. 2010;5:607-13. [PMID: 21106022]
16. Perdrizet GA, Olson NH, Krause PJ, Banevery GT, Spielman A, Cable RG. Babesiosis in a renal transplant recipient acquired through blood transfusion. Transplantation. 2000;70:205-8. [PMID: 10919602]
15. Marcus LC, Valigorsky JM, Fanning WL, Joseph T, Glick B. Babesiosis: a spectrum of clinical presentations. J Clin Apher. 2010;25:358-61. [PMID: 21106022]
14. Herman JH, Ayache S, Olkowska D. Autoimmunity in transfusion babesiosis: a spectrum of clinical presentations. J Clin Apher. 2010;25:358-61. [PMID: 20824620]
13. Mintz ED, Anderson JF, Cable RG, Hadler JL. Transfusion-transmitted babesiosis: a case report from a new endemic area. Transfusion. 1991;31:365-8. [PMID: 2021001]
12. Heerwaldt BL, de Bruyn G, Pieniazek NJ, Homer M, Loisy KH, Slmenda SB, et al. Babesia divergens–like infection, Washington State. Emerg Infect Dis. 2004;10:622-9. [PMID: 15200851]
11. Stramer SL, Hollinger FB, Katz LM, Kleinman S, Metzel PS, Gregory KR, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:1S-29S. [PMID: 19686562]
10. Butrau M, Salazar JC, Leopold H, Krause PJ. Atovaquone and azithromycin treatment for babesiosis in an infant. Pediatr Infect Dis J. 2007;26:181-3. [PMID: 17259886]
9. Pantanowitz L, Telford SR 3rd, Cannon ME. The impact of babesiosis on transfusion medicine. Transfus Med Rev. 2002;16:131-43. [PMID: 11941575]
8. Stramer SL, Hollinger FB, Katz LM, Kleinman S, Metzel PS, Gregory KR, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:1S-29S. [PMID: 19686562]
7. Luque C, Deus-Sertão AL, Serpa-Santos C, Gomes AM. The role of babesiosis in the pathogenesis of autoimmunity and anemia. J Autoimmun. 2011;36:275-82. [PMID: 21069920]
6. Stramer SL, Hollinger FB, Katz LM, Kleinman S, Metzel PS, Gregory KR, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:1S-29S. [PMID: 19686562]
5. Luque C, Deus-Sertão AL, Serpa-Santos C, Gomes AM. The role of babesiosis in the pathogenesis of autoimmunity and anemia. J Autoimmun. 2011;36:275-82. [PMID: 21069920]
4. Pantanowitz L, Telford SR 3rd, Cannon ME. The impact of babesiosis on transfusion medicine. Transfus Med Rev. 2002;16:131-43. [PMID: 11941575]
3. Stramer SL, Hollinger FB, Katz LM, Kleinman S, Metzel PS, Gregory KR, et al. Emerging infectious disease agents and their potential threat to transfusion safety. Transfusion. 2009;49 Suppl 2:1S-29S. [PMID: 19686562]
2. Luque C, Deus-Sertão AL, Serpa-Santos C, Gomes AM. The role of babesiosis in the pathogenesis of autoimmunity and anemia. J Autoimmun. 2011;36:275-82. [PMID: 21069920]
1. Pantanowitz L, Telford SR 3rd, Cannon ME. The impact of babesiosis on transfusion medicine. Transfus Med Rev. 2002;16:131-43. [PMID: 11941575]
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Appendix Figure. Distribution by month of the blood donations associated with U.S. Babesia microti transfusion cases (n = 128 of 148 total donations), 1979–2009.

The month of donation was known or estimable for 128 of 148 donations (by 141 donors) associated with transmission (Figure 1). The 19 donations by the 12 donors linked to multicase clusters occurred in 10 different months. If applicable, the month of donation was approximated by subtracting 16 days (the median age of liquid-stored red blood cells at the time of transfusion; see text) from the transfusion date. The donations linked to the 3 B. duncani cases occurred in April (n = 2) and August (n = 1); these data are not included.