

## ***Babesia* Species**

### **Disease Agent:**

- In the US: *Babesia microti*, *Babesia duncani* (formerly WA1), *Babesia* variant CA1, *Babesia divergens*-like variant M01
- In Europe/Asia: *Babesia microti*, *Babesia divergens*, *Babesia* variants: EU1, KO1, TW1

### **Disease Agent Characteristics:**

- Protozoan, 1-2.5  $\mu\text{m}$  (small *Babesia* species generally infect humans; large *Babesia* species of 2.5-5  $\mu\text{m}$  occur primarily in animals with the exception of the human variant KO1 that is classified as a large *Babesia* organism)
- Order: Piroplasmidora
- Family: Babesiidae
- All are intraerythrocytic parasites with characteristic microscopic appearance similar to *Plasmodium* species

### **Disease Name:**

- Babesiosis

### **Priority Level**

- Scientific/Epidemiologic evidence regarding blood safety: Moderate/High
- Public perception and/or regulatory concern regarding blood safety: Very low, but moderate in endemic regions
- Public concern regarding disease agent: Very low, but moderate regionally

### **Background:**

- Approximately 100 species that infect mammals have been described, some of which may be synonymous; traditionally, species have been defined based primarily on morphology and host specificity.
- Emergent in the US, probably due in part to expanding range of ticks and their mammalian hosts, increased intrusion of humans into tick-infested habitats and increased awareness and testing.
- *B. divergens* is primarily a bovine parasite but human infections have been documented in Europe.
- Worldwide, cases caused by various species are increasingly being recognized.

### **Common Human Exposure Routes:**

- Tick bites
- For *B. microti*, in the US, bite of an infected nymphal stage of the tick *Ixodes scapularis* commonly known as the black-legged or deer tick; other tick species may also transmit *B. microti*. Adult ticks may also transmit.

- Tick species vary with *Babesia* species.
- Transmission occurs after a period of tick attachment that is generally at least 48 hours.
- Blood transfusion

### **Likelihood of Secondary Transmission:**

- Moderate—transmissible by transfusion with over 70 cases documented in the US
- Low—organ/tissue transplantation
- Transplacental/perinatal transmissions documented for *B. microti*.

### **At-Risk Populations:**

- Asplenic, elderly, immunocompromised adults and infants at-risk for clinically manifest infection which might be severe.
- People exposed to tick vectors during hiking, gardening, and other outdoor activities; co-infection of *B. microti* with *Borrelia burgdorferi* (agent of Lyme disease) can occur and can lead to more severe disease. Co-infection of *B. microti* with *Anaplasma phagocytophilum* (agent of human granulocytic anaplasmosis) also is possible since all 3 agents are transmitted by the same ticks.

### **Vector and Reservoir Involved:**

- *Ixodes* ticks for *B. microti*; *I. scapularis* (also referred to as *I. dammini*) in the eastern US is the most common; however, other tick species may be involved.
- White-footed mice serve as amplifying hosts for *B. microti*.
- Although white-tailed deer (*Odocoileus virginianus*) are not infected with *B. microti*, they serve as the transport and reproduction hosts for adult ticks.
- *I. ricinus* is one tick species identified as a vector for *B. divergens* in Europe.
- For some of the *Babesia* species, the tick vector and reservoir hosts have not been identified.

### **Blood Phase:**

- Intermittent parasitemia detectable for months to years during asymptomatic infection

### **Survival/Persistence in Blood Products:**

- At least 35 days in red cells based on transfusion transmission data

### **Transmission by Blood Transfusion:**

- *B. microti* documented in over 70 cases; all cases have occurred in the US, except for one case in Canada (donor was exposed in the US) and one case in Japan; potentially one case in Europe.
- *B. duncani*: 2 cases reported in the literature

- Travelers from non-endemic areas infected while visiting endemic areas, donors from babesiosis-endemic areas who donate elsewhere, and exportation of blood products are increasingly implicated in transfusion cases.
- Since fiscal year 1998, an increasing number of fatalities and Blood Product Deviations (BPDs) have been reported to the FDA. A total of 272 BPDs related to possible *Babesia* infection in donors were reported from FY 1998-2007 of which 52 were investigated as possible transfusion-transmitted *Babesia* infections. Twelve fatalities were reported since 1998, with 9 of 12 reported in the last 3-year period. Five of these patients received their transfusions in states where *Babesia* was not endemic. All recipients who died were infected with *B. microti*. Red blood cells were implicated in each case, including one frozen deglycerolized product. Each infection was diagnosed by thin peripheral blood smear; associated donors had antibody titers  $\geq 1:128$  by IFA.
- The American Red Cross reported 18 definite or probable cases of transfusion-transmitted *B. microti* from 2005-2007, including five fatalities. Seventeen antibody-positive donors were implicated including the donor of one split red cell unit that infected a 1-day old infant and a 32-year old sickle cell patient. Of the 17 antibody-positive donors, 11 were residents of *Babesia*-endemic areas, while 4 residents of non-endemic areas had a history of travel to endemic areas.

#### Cases/Frequency in Population:

- *B. microti* is endemic in Northeast as far south as New Jersey and the Upper Midwest. Seroprevalence in healthy blood donors in endemic areas ranges up to 2%, but the only seroprevalence study carried out outside of New England was in Wisconsin. Areas of hyperendemicity (up to 9%) in the general population have been reported.
- *B. duncani* and the variant CA1 are found in several western states. MO1 and other *B. divergens*-like organisms have been identified in Missouri and several other states.
- *B. divergens*, EU1, and *B. microti* found in Europe; *B. microti* reported in Japan where it was implicated in a transfusion case; KO1 in Korea; TW1 in Taiwan

#### Incubation Period:

- 1-6 weeks following tick bite
- 1-9 weeks following transfusion but may be longer depending in part on the immune status of the individual
- The 9 fatalities reported above had an approximate interval from transfusion to symptom onset of 2.5 to 7 weeks.

#### Likelihood of Clinical Disease:

- Generally produces mild and transient infection in immunocompetent hosts; however, intermittent parasitemia may be detected for months to years
- Higher likelihood of more severe clinical disease in at-risk populations

#### Primary Disease Symptoms:

- Clinical infection ranges from mild, flu-like illness to fulminant, malaria-like disease that can be fatal.
- Severe babesiosis can manifest with hemolysis, disseminated intravascular coagulation (DIC), hemodynamic instability and multiorgan dysfunction (e.g., renal failure, respiratory distress).

#### Severity of Clinical Disease:

- Absent/Low: Healthy, immunocompetent persons
- High: Asplenic, elderly, immunocompromised adults or infants

#### Mortality:

- For clinical *B. microti* infections, estimated at 5% in population-based study
- Rates may be higher among splenectomized patients

#### Chronic Carriage:

- Months to years in some people
- Self-limiting infection in most people

#### Treatment Available/Efficacious:

- Effective treatment with clindamycin and quinine, but side effects are very frequent. Clindamycin and quinine remain the standard of care for severe babesiosis.
- The combination of atovaquone and azithromycin, recently introduced, is equally efficacious with significantly fewer side effects
- Exchange transfusion may be indicated in severe cases (i.e., high-level parasitemia).

#### Agent-Specific Screening Question(s):

- Currently in use as part of Donor History Questionnaire: "Have you ever had babesiosis?"
- In endemic areas, a question on exposure to tick bites has been shown to be ineffective in distinguishing *Babesia*-infected from uninfected donors. The question lacks sensitivity and specificity.

#### Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Options for diagnostic testing include blood smear microscopy, indirect IFA (cut-off titers vary with assay and lab), EIA, western blot, NAT, and animal inoculations.

- Limited donor screening is being conducted or considered using research tests (i.e., IFA, PCR) in some endemic areas. This may enable the application of a selective algorithm for screening of blood components for transfusion to high-risk patients in endemic areas (i.e., the CMV model).

#### Currently Recommended Donor Deferral Period:

- Indefinite deferral for history of babesiosis per AABB Standard. No FDA Guidance exists.
- Consideration of deferral for donors implicated in investigations of transfusion-transmitted babesiosis or those testing positive by research/investigational tests

#### Impact on Blood Availability:

- Agent-specific screening question(s): Current question has no impact in some regions and may have minimal impact in others.
- Laboratory test(s) available: Infections are regional, and seroprevalence rates will vary. Impact could be significant in high seroprevalence areas should serologic tests be introduced.

#### Impact on Blood Safety:

- Agent-specific screening question(s): Minimal/none as current screening question as well as potential question about tick bite exposure are insensitive
- Laboratory test(s) available: Serologic testing, whether universal or selected, would likely have a high impact on blood safety.

#### Leukoreduction Efficacy:

- Unlikely to be effective because the parasite is intraerythrocytic and documented transfusion cases associated with leukoreduced products have been reported.

#### Pathogen Reduction Efficacy for Plasma Derivatives:

- No specific data are available but it is presumed that the agent should be sensitive to many measures used in the fractionation process.

#### Other Prevention Measures:

- Personal practices to avoid ticks (e.g., repellants, long pants, and long sleeves)
- Tick control measures in the environment
- Pathogen inactivation in components has been demonstrated with a variety of agents.
- Education/Awareness

#### Other Comments:

- Clinical recognition and early treatment important
- Because of the parasite's regional distribution, transfusion cases outside the endemic area may not be recognized or accurately diagnosed; however, under-recognition is a problem even in areas where babesiosis is endemic.

#### Suggested Reading:

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  14. Quick RE, Herwaldt BL, Thomford JW, Garnett ME, Eberhard ML, Wilson M, Spach DH, Dickerson JW, Telford SR 3rd, Steingart KR, Pollock R, Persing DH, Kobayashi JM, Juranek DD, Conrad PA. Babesiosis in Washington State: a new species of *Babesia*? *Ann Intern Med* 1993;119:284-90.
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