

Babesiosis (*Babesia* spp.)

2011 Case Definition- CSTE Position Statement10-ID-27

Clinical Description

Babesiosis is a parasitic disease caused by intraerythrocytic protozoa of the *Babesia* genus (*Babesia microti* and other species). *Babesia* are transmitted in nature through the bites of infected ticks but can also be acquired through contaminated blood components from asymptomatic parasitemic donors or, more rarely, transplacentally. *Babesia* infection can range from subclinical to life-threatening. Clinical manifestations, if any, can include hemolytic anemia and nonspecific influenza-like signs and symptoms (e.g., fever, chills, sweats, headache, myalgia, arthralgia, malaise, fatigue, generalized weakness). Splenomegaly, hepatomegaly, or jaundice may be evident. In addition to signs of hemolytic anemia, laboratory findings may include thrombocytopenia, proteinuria, hemoglobinuria, and elevated levels of liver enzymes, blood urea nitrogen, and creatinine. Risk factors for severe babesiosis include asplenia, advanced age, and other causes of impaired immune function (e.g., HIV, malignancy, corticosteroid therapy). Some immunosuppressive therapies or conditions may mask or modulate the clinical manifestations (e.g., the patient may be afebrile). Severe cases can be associated with marked thrombocytopenia, disseminated intravascular coagulation, hemodynamic instability, acute respiratory distress, myocardial infarction, renal failure, hepatic compromise, altered mental status, and death.

Clinical Criteria

For the purposes of surveillance:

- Objective: one or more of the following: fever, anemia, or thrombocytopenia.
- Subjective: one or more of the following: chills, sweats, headache, myalgia, or arthralgia.

Laboratory Criteria for Diagnosis

For the purposes of surveillance:

Laboratory confirmatory:

- Identification of intraerythrocytic *Babesia* organisms by light microscopy in a Giemsa, Wright, or Wright-Giemsa–stained blood smear; **OR**
- Detection of *Babesia microti* DNA in a whole blood specimen by polymerase chain reaction (PCR); **OR**

- Detection of *Babesia* spp. genomic sequences in a whole blood specimen by nucleic acid amplification; **OR**
- Isolation of *Babesia* organisms from a whole blood specimen by animal inoculation.

Laboratory supportive:

- Demonstration of a *Babesia microti* Indirect Fluorescent Antibody (IFA) total immunoglobulin (Ig) or IgG antibody titer of greater than or equal to (\geq) 1:256 (or \geq 1:64 in epidemiologically linked blood donors or recipients); **OR**
- Demonstration of a *Babesia microti* Immunoblot IgG positive result; **OR**
- Demonstration of a *Babesia divergens* IFA total Ig or IgG antibody titer of greater than or equal to (\geq) 1:256; **OR**
- Demonstration of a *Babesia duncani* IFA total Ig or IgG antibody titer of greater than or equal to (\geq) 1:512.

Epidemiologic Linkage

Epidemiologic evidence for transfusion transmission.

For the purposes of surveillance, epidemiologic linkage between a transfusion recipient and a blood donor is demonstrated if all of the following criteria are met:

- In the transfusion recipient:
 - Received one or more red blood cell (RBC) or platelet transfusions within one year before the collection date of a specimen with laboratory evidence of *Babesia* infection; **AND**
 - At least one of these transfused blood components was donated by the donor described below; **AND**
 - Transfusion-associated infection is considered at least as plausible as tickborne transmission; **AND**
- In the blood donor:
 - Donated at least one of the RBC or platelet components that was transfused into the above recipient; **AND**
 - The plausibility that this blood component was the source of infection in the recipient is considered equal to or greater than that of blood from other involved donors. (More than one plausible donor may be linked to the same recipient.)

Case Classification

Suspected

A case that has confirmatory or supportive laboratory results, but insufficient clinical or epidemiologic information is available for case classification (e.g., only a laboratory report was provided).

Probable

- a case that has supportive laboratory results and meets at least one of the objective clinical evidence criteria (subjective criteria alone are not sufficient); **OR**
- a case that is in a blood donor or recipient epidemiologically linked to a confirmed or probable babesiosis case (as defined above) **AND**:
 - has confirmatory laboratory evidence but does not meet any objective or subjective clinical evidence criteria; **OR**
 - has supportive laboratory evidence and may or may not meet any subjective clinical evidence criteria but does not meet any objective clinical evidence criteria.

Confirmed

A case that has confirmatory laboratory results and meets at least one of the objective or subjective clinical evidence criteria, regardless of the mode of transmission (can include clinically manifest cases in transfusion recipients or blood donors).

Comments

The validity of the diagnosis of babesiosis is highly dependent on the laboratory that performs the testing. For example, differentiation between *Plasmodium* and *Babesia* organisms on peripheral blood smears can be difficult. Confirmation of the diagnosis of babesiosis by a reference laboratory is strongly encouraged, especially for patients without residence in or travel to areas known to be endemic for babesiosis.

A positive *Babesia* IFA result for immunoglobulin M (IgM) is insufficient for diagnosis and case classification of babesiosis in the absence of a positive IFA result for IgG (or total Ig). If the IgM result is positive but the IgG result is negative, a follow-up blood specimen drawn at least one week after the first should be tested. If the IgG result remains negative in the second specimen, the IgM result likely was a false positive.

When interpreting IFA IgG or total Ig results, it is helpful to consider factors that may influence the relative magnitude of *Babesia* titers (e.g., timing of specimen collection relative to exposure or illness onset, the patient's immune status, the presence of clinically manifest versus asymptomatic infection). In immunocompetent persons, active or recent *Babesia* infections that are symptomatic are generally associated with relatively high titers (although antibody levels may be below the detection threshold early in the course of infection); titers can then persist at lower levels for more than a year. In persons who are immunosuppressed or who have asymptomatic *Babesia* infections, active infections can be associated with lower titers.

Babesia microti is the most frequently identified agent of human babesiosis in the United States; most reported tick-borne cases have been acquired in parts of northeastern and north-central regions. Sporadic U.S. cases caused by other *Babesia* agents include *B. duncani* (formerly the WA1 parasite) and related organisms (CA1-type parasites) in several western states as well as parasites characterized as "*B. divergens* like" (MO1 and others) in various states. Serologic and molecular tests available for *B. microti* infection do not typically detect these other *Babesia* agents.

Blood-borne transmission of *Babesia* is not restricted by geographic region or season. The epidemiologic linkage criteria for transfusion transmission that are described here provide a low threshold for asymptomatic donor or recipient cases to be considered probable cases for surveillance purposes and are not intended to be regulatory criteria. Transfusion investigations entail laboratory testing for evidence of *Babesia* infection in recipients and donors as well as epidemiologic assessments of the plausibilities of blood- and tick-borne transmission.