Babesiosis

Clinical criteria for case classification
Babesiosis is a parasitic disease caused by intraerythrocytic (living inside red blood cells [RBCs]) 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 (no spleen), advanced age, and other causes of impaired immune function or serious health conditions (e.g., HIV, malignancy, corticosteroid therapy, liver or kidney disease). Some immunosuppressive therapies or conditions may cause the patient to be afebrile. Severe cases can be associated with marked thrombocytopenia, disseminated intravascular coagulation, low or unstable blood pressure, acute respiratory distress, myocardial infarction, renal failure, hepatic compromise, altered mental status, and death. Recurrence can occur, particularly in those who are or become immunosuppressed.

Laboratory criteria for case classification
Confirmatory:
One or more of the following:
- Identification of Babesia organisms within RBCs by light microscopy in a Giemsa, Wright, or Wright-Giemsa–stained blood smear;
- Or detection of B. microti DNA in a whole blood specimen by polymerase chain reaction (PCR);
- Or detection of Babesia species genomic sequences in a whole blood specimen by PCR;
- Or isolation of Babesia organisms from a whole blood specimen by animal inoculation.

Presumptive:
One or more of the following:
- Indirect fluorescent antibody (IFA) titer ≥1:256 for B. microti total immunoglobulin (Ig) or IgG antibody,
- Or IFA titer ≥1:64 for B. microti total Ig or IgG antibody in epidemiologically linked blood donors and recipients,
- Or positive IgG immunoblot for B. microti,
- Or IFA titer ≥1:256 for B. divergens total Ig or IgG antibody,
- Or IFA titer ≥1:512 for B. duncani total Ig or IgG antibody.
Epidemiological criteria for case classification

Either of the following:
- A person who spent time in tick habitats in endemic areas (northeastern, north central, or western U.S. states) at least one week and to up to a year prior to identification and reporting of clinical criteria
- Or transfusion-linked epidemiologic criteria: evidence of transfusion transmission between a blood donor and recipient where either the donor or recipient is a confirmed or probable babesiosis case and all of the following are met:
  - Transfusion recipient:
    - Received one or more 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 tick-borne transmission.
  - 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

Confirmed:
A person with any clinical criteria (fever, anemia, thrombocytopenia, chills, sweats, headache, myalgia, or arthralgia), epidemiologic criteria, and confirmatory laboratory evidence.

Probable:
Either of the following:
- A person with objective clinical criteria (fever, anemia, or thrombocytopenia), epidemiologic criteria, and presumptive laboratory evidence
- Or a blood donor or recipient meeting the transfusion-linked epidemiologic criteria with any laboratory evidence.

Suspect case:
A person with any laboratory evidence and no clinical information available (no medical record or patient interview).

Criteria to distinguish a new case from previous reports
Not applicable.

Comments
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. Obtaining travel history for the past year is essential for either disease.
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.

*B. 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 plausibility of blood- and tick-borne transmission.

▶ **Whole blood (purple top tube) and unstained whole blood smear from all confirmed cases must be sent to the Bureau of Public Health Laboratories for confirmation.**

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