Babesiosis

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Babesiosis

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Babesiosis is an emerging infectious disease caused by protozoan parasites of the genus *Babesia* that infect red blood cells. Although more than 100 *Babesia* (*B.*) species have been reported, relatively few have caused documented cases of human infection; these include (but are not limited to) *B. microti*, *B. divergens*, *B. duncani*, and a currently unnamed agent designated MO1. Overall, most of the documented zoonotic cases of babesiosis in the world have occurred in the U.S., some have occurred in Europe, and relatively few in various other countries. Most cases of babesiosis in the U.S. are caused by the parasite *B. microti*. *B. microti* are spread in nature by *Ixodes (I.) scapularis* ticks (also called blacklegged ticks or deer ticks). Tick-borne transmission is most common in particular regions and seasons: it mainly occurs in parts of the Northeast and upper Midwest; and it usually peaks during the warm months. Other possible ways of becoming infected with *Babesia* include: receipt of a contaminated blood transfusion (currently, no *Babesia* tests have been licensed for screening blood donors); or transmission from an infected mother to her baby during pregnancy or delivery.

Many people who are infected with *B. microti* feel fine and do not have any symptoms. Asymptomatic infection may persist for months to years and remain subclinical throughout its course in otherwise healthy people, especially those < 40 years of age. Symptoms, if any, usually develop one to five weeks following a tick bite and one to nine weeks following a *Babesia* contaminated blood transfusion, but can occasionally be longer. Some people develop flu-like symptoms, such as fever, chills, sweats, headache, malaise, body aches, and loss of appetite, nausea, or fatigue. Hepatosplenomegaly with jaundice, mild to moderately severe hemolytic anemia, mild neutropenia, and thrombocytopenia may occur. Symptoms may appear or recur many months (even > 1 year) after initial exposure, particularly in the context of immunosuppression or splenectomy.

Babesiosis is sometimes fatal, particularly in the elderly, asplenic patients, infants born prematurely and patients with AIDS. In such patients, babesiosis may resemble falciparum malaria, with high fever, hemolytic anemia, hemoglobinuria, jaundice, and renal failure. ***NOTE**: Splenectomy may cause previously acquired asymptomatic parasitemia to become symptomatic.*

No vaccine is available to protect people against babesiosis; however the infection is both treatable and preventable. The use of prevention measures is particularly important for people at increased risk for severe babesiosis (e.g., people who do not have a spleen, the immunocompromised, the elderly, etc.). If possible, areas infested with ticks should be avoided, especially during warm months. If such areas cannot be avoided, use protective measures during outdoor activities as described on the CDC Babesiosis Prevention and Control page. The tiny *I. scapularis* ticks that spread *B. microti* usually must stay attached to a person for more than 36-48 hours to be able to transmit the parasite. Daily tick checks can prevent disease transmission. For a complete description of babesiosis, please refer to the following sources:

- *Control of Communicable Diseases Manual* (CCDM). 20th ed. Washington, D.C.: American Public Health Association, 2015.
- American Academy of Pediatrics. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL. American Academy of Pediatrics; 2015.
- *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 8th ed. 2015.

2011 Case Definition – Babesiosis (*Babesia* spp.)[4] (5/16)

Clinical Description

Babesiosis is a parasitic disease caused by intraerythrocytic protozoa of the *Babesia* genus (*B. 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 *B. 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.

(Continued on next page.)

Laboratory supportive:

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

(Continued on next page.)

- 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.

Information Needed for Investigation

Verify the diagnosis. What laboratory tests were conducted and what were the results? Compare results to the National Notifiable Diseases Surveillance System case definition, specifically the "**Laboratory Criteria for Diagnosis**" component provided above.

Establish the extent of the illness. Determine if household members, travelling companions, co-workers, or other close contacts are, or have been ill that have shared environmental exposures with the patient. Are there any other persons with a similar illness that may require medical evaluation? If so, urge them to contact their physician for a medical evaluation.

Obtain demographic, clinical and laboratory information on the case from the attending physician, hospital, and/or laboratory. Obtain the epidemiological information necessary to complete the Disease Case Report (CD-1) and the Babesiosis Case Report Form. The information may be obtained from the patient or a knowledgeable family member.

Determine the source of infection. Establish the occupation of the case since this information may help narrow the search for the route of exposure. Are there co-workers ill? Shared activities or exposures should be investigated for cases among family and friends. ***NOTE:*** *Risk factors include outdoor activities in areas where the disease is found* (*i.e., Northeast and upper Midwest in the U.S.*). The tick usually must stay attached to a person for more than 36-48 hours to be able to transmit the parasite.

Identify possible routes of exposure preceding the illness, did the patient report:

1. Travel outside county of residence? If yes, where?
2. Visiting known tick habitat?
3. A tick bite or attachment? ***NOTE***: *Infected people might not recall a tick bite because Ixodes scapularis nymphs are very small (about the size of a poppy seed).*
4. Receiving a blood transfusion? If, so immediately contact the District Communicable Disease Coordinator.
5. Is the index case an infant*?* ***NOTE****: In rare cases transmission from infected mother to baby (during pregnancy or delivery) has been reported.* ***COMMENT****: Sometimes the source of infection is not identified.*

Provide Babesiosis information to persons at risk of infection and the general public as needed. Efforts should be made to promote babesiosis awareness, see the CDCs' Babesiosis● Fact Sheet, Babesiosis FAQs, the Babesiosis●Provider Fact Sheet, and Tickborne Diseases of the United States for information. Additional information is available from CDC and can be found at: http://www.cdc.gov/parasites/babesiosis/prevent.html and http://www.cdc.gov/Features/StopTicks/.

Babesiosis Surveillance. Data collected from babesiosis surveillance is used to monitor geographic and temporal occurrence of disease so that clinicians can maintain a high awareness of the disease and the public kept adequately informed of their risk of contracting babesiosis and the importance of personal protective measures.

Notification

Contact the District Communicable Disease Coordinator, the Senior Epidemiology Specialist for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7).

- If a case(s) is associated with a child care center, BCDCP or the LPHA will contact the BEHS, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.
- If a case(s) is associated with a long-term care facility, BCDCP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDCP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.

Control Measures[1, 3, 5, 6]

Generally, asymptomatic individuals need not be treated unless a *Babesia* species is detected on blood smear or **PCR** for more than three months. Suspected babesiosis should not be treated if reliable blood smear and PCR results are negative. When *Babesia* is detected, symptomatic patients should be treated.[3] For additional treatment information, see the following resources: "Tickborne Diseases of the U.S., A Reference Manual for Health Care Providers" or CDC's website: Parasites – Babesiosis - Treatment. ***NOTE**: Treatment decisions should be individualized, especially for patients who have (or are at risk for) severe or relapsing infection. Health care providers may consult CDC staff about whether to treat someone who has babesiosis, what type(s) of therapy to use, how to monitor the status of the infection, and how long to treat.*

No vaccine is available to protect people against babesiosis; however people can take steps to prevent babesiosis. ***NOTE**: The use of prevention measures is particularly important for people at increased risk for severe babesiosis (e.g., people who do not have a spleen, have a weaken immune system, have serious health conditions, or are elderly).* If possible, areas infested with ticks should be avoided, especially during warm months. If such areas cannot be avoided, use protective measures during outdoor activities such as repellants and protective clothing. See the CDC Prevention and Control page for additional tips. Tick-borne disease prevention information can also be found on the MDHSS website: Tick-borne Disease and CDC's website: Avoiding Ticks. ***NOTE**: People with a known history of babesiosis should be informed that they are deferred indefinitely from donating blood.*

Laboratory Procedures[5, 6]

Diagnosis of babesiosis requires a high index of suspicion, in part because the clinical manifestations are nonspecific. For acutely ill patients, the findings on routine laboratory testing frequently include hemolytic anemia and thrombocytopenia. Additional findings may include proteinuria, hemoglobinuria, and elevated levels of liver enzymes, blood urea nitrogen, and creatinine. Diagnosis can be made by microscopic examination of blood-smears for intraerythrocytic *Babesia* parasites. For other laboratory analyses, see the **Laboratory Criteria**

for Diagnosis component provided above. ***NOTE**: If the diagnosis of babesiosis is being considered, manual (nonautomated) review of blood-smears should clearly be requested in symptomatic patients with acute infection. Babesia typically can be detected by blood-smear examination, although multiple smears may need to be examined.*[6]

The Missouri State Public Health Laboratory (MSPHL) will provide assistance in providing identification and speciation of presumptive positive blood smears for *Babesia.* If blood smears cannot be speciated microscopically, specimens are sent to the CDC for further testing. Information on specimen collection and transport to the MSPHL can be found at: http://health.mo.gov/lab/bloodparasites.php. ***NOTE**: 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. Please call ahead for detailed collection instructions: MSPHL- Microbiology Unit - 573-751-3334.*

Reporting Requirements

Babesiosis is a Category III reportable disease and shall be reported to the local public health agency or to the MDHSS within three (3) days of first knowledge or suspicion, by telephone, facsimile, or other rapid communication.

As a Nationally Notifiable Condition, all confirmed and probable cases are a **STANDARD** report to CDC. MDHSS will submit these reports to the CDC by electronic case notification (WebSurv) within the next reporting cycle.

1. For all reported cases of babesiosis complete a Disease Case Report (CD-1) and a Babesiosis Case Report Form.
2. Entry of the completed CD-1 into WebSurv negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. Send the completed Babesiosis Case Report Form to the District Health Office.
4. MDHSS will report to CDC following the above reporting criteria (see box).
5. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Surveillance Report (CD-51).
6. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

References

1. American Public Health Association. *Babesiosis*. Herwaldt BL, In: Heymann, DL (ed), *Control of Communicable Diseases Manual*. 20th ed. Washington, DC: American Public Health Association, 2015: 61-63.
2. American Academy of Pediatrics. *Babesiosis*. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, IL. American Academy of Pediatrics; 2015: 253-254.
3. Elsevier Inc. *Babesia Species.* Gelfand JA, Vannier EG In: Bennett JE, Dolin R, Blaser MJ eds. *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 8th ed. 2015: 3165-3172.

4. Centers for Disease Control and Prevention's (CDC) National Notifiable Diseases Surveillance System (NNDSS) and Case Definitions. http://wwwn.cdc.gov/nndss/conditions/babesiosis/ (5/16).
5. Centers for Disease Control and Prevention. *Babesiosis.* In: http://www.cdc.gov/parasites/babesiosis/ (5/16).
6. Tickborne Diseases of the United States - *A Reference Manual for Health Care Providers* Third Edition, 2015 U.S. Department of Health and Human Services, Center for Disease Control and Prevention http://www.cdc.gov/lyme/resources/TickborneDiseases.pdf (5/16).
7. The Merck Manual. Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ. *Babesiosis*. Pearson, RD In: *The Merck Manual Professional Edition; Merck Manual; Health Care Professionals; Professional / Infectious Diseases / Extraintestinal Protozoa. http://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/babesiosis* (5/16).