

Babesiosis

Surveillance Protocol

Provider Responsibilities

1. Report suspect and confirmed cases of babesiosis (including copies of lab results) to the local health department within one week of diagnosis.
2. Share clinical and laboratory findings with local health departments.
3. Follow national guidelines for ordering babesiosis testing (http://wwwn.cdc.gov/nndss/document/2012_Case%20Definitions.pdf#page=14).

Laboratory Responsibilities

1. Report positive laboratory results for babesiosis to the local health department within one week.
2. Follow national guidelines for performing babesiosis testing (http://wwwn.cdc.gov/nndss/document/2012_Case%20Definitions.pdf#page=14).

Local Health Responsibilities

1. Conduct an appropriate case investigation. For each case:
 - a. Contact the physician that either reported the case or ordered babesiosis testing
 - b. Using the WVEDSS Babesiosis Report Form, collect the clinical and laboratory information necessary to perform case ascertainment.
 - c. Educate the patient and the patient's family on tickborne disease prevention.
 - d. Report all case data using WVEDSS.

State Health Responsibilities

1. Send case status notifications to CDC.
2. Publish health alerts and advisories during tickborne disease season (May to September).
3. Public surveillance data related to tickborne diseases regularly during tickborne disease season.
4. Conduct tick surveillance when ticks are most active:
 - a. Determine areas of West Virginia where *Ixodes scapularis* are located
 - b. As able, test ticks for the causative agent of human babesiosis, *Babesia microti*.

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Disease Prevention Objectives

1. Reduce disease risk through public education by encouraging use of personal protective measures that prevent tick bites.
2. Educate the public about locations of *I. scapularis* habitats in West Virginia.

Disease Control Objectives

1. Increase the number of patients treated with appropriate medications in the early stages of babesiosis to reduce the parasite load early and prevent disseminated and late disease.
2. If a case is reported, prevent additional cases by:
 - a. Investigating transfusion-associated cases and alerting blood and tissue banks.

Disease Surveillance Objectives

1. To identify and monitor the epidemiologic characteristics (including demographics and risk factors) of Babesiosis in West Virginia.
2. To identify areas potentially endemic for Babesiosis in West Virginia.

Public Health Significance

Babesiosis was historically believed to be a disease of animals until 1957, when a single human case was diagnosed in Yugoslavia. The disease was first identified in the United States in 1969, when a small outbreak occurred in Nantucket, MA⁵. Public health surveillance for babesiosis began individually at the state level in the mid to late 2000's, and national surveillance began in 19 jurisdictions (18 states and one city) in January 2011³.

Cases of babesiosis are primarily concentrated in the Northeast, particularly in parts of New England, New York, and New Jersey, including both inland and coastal areas and neighboring islands. In the upper Midwest, cases have been concentrated in Wisconsin and Minnesota. A few cases have been identified as far west as California and Washington; however, these were caused by other *Babesia* species for which no vector or reservoir host has been identified.²

Tickborne transmission cases occur primarily from late spring to autumn, with peak symptoms appearing from June to August; transfusion cases can occur year-round. The distribution of cases typically mirrors the distribution of *Ixodes scapularis* ticks (commonly called black-legged

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or deer ticks). Unlike Lyme disease, however, Babesiosis shows little association with white-tail deer populations, as deer are not infected with *B. microti*. Reporting remains fairly new, with case ages ranging from <1 to 98 years and a median of 62 years³. Males tend to make up more of the cases than females at a rate of almost 2:1³. Incidence rates are still widely varied by county, as this disease only recently became nationally notifiable.

Asymptomatic donors can carry the infection for up to 12 months after they initially acquire the infection, and currently no tests have been licensed for donor screening. Individuals with a known diagnosis of babesiosis are ineligible to donate blood. Information on the current criteria for blood donation is available on the Red Cross website:

<http://www.redcross.org/donate/give/>.

Clinical Description

This tickborne disease is often asymptomatic, although severe and life-threatening onset can occur in patients who are immunocompromised, elderly, or asplenic. Clinical manifestations, if any, include fever, hemolytic anemia, and non-specific influenza-like signs and symptoms. In general, symptom onset occurs gradually and persists for several weeks to months without treatment. Laboratory findings may include thrombocytopenia, proteinuria, hemoglobinuria, and elevated levels of liver enzymes, blood urea nitrogen, and creatinine. Immunosuppressed patients may experience modulated clinical manifestations, and severe cases may present with disseminated intravascular coagulation, hemodynamic instability, acute respiratory distress, hepatic compromise, altered mental status, renal failure, myocardial infarction, or death. Splenectomized patients typically present with more severe symptoms, including pyrexia, chills, muscular pain, prostration, and jaundice.

Etiologic Agent

The agent that causes babesiosis, *Babesia*, is an intraerythrocytic protozoan. There are over 100 known species of *Babesia* in the world. Human babesiosis in the United States has been primarily linked to *B. microti*, although four to five other species of *Babesia* have been found in isolated human cases.

Reservoir

Ixodid ticks are the vector for human babesiosis through transstadial transmission, meaning *B. microti* can be transmitted from one tick stage to the next⁴. In the US, wild rodents, particularly

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the white-footed mouse (*P. leucopus*) and meadow vole (*Microtus pennsylvanicus*), maintain the enzootic cycle. Deer serve as important maintenance mammalian hosts for vector tick species, although they themselves do not carry *B. microti*. Larval and nymphal ticks feed on small mammals, and adult ticks feed primarily on deer. Human Babesiosis cases result from the bite of infected nymphs.⁴

Mode of Transmission

The most common mode of transmission is through the bite of infected ticks. The protozoan is not passed from the nymph to the adult tick, so only nymphal stages can infect humans. Sporozoites enter the erythrocytes of human hosts and undergo asexual replication. Multiplication of the blood-stage parasites produces the observed clinical manifestations. Because of the extensive protozoan lifecycle, nymphal ticks must remain attached to human hosts for 36-48 hours to completely transmit the parasite¹.

Approximately ten cases of transfusion transmitted babesiosis have been reported in the US³. Only one confirmed case of congenital transmission (from infected mother to infant during pregnancy or delivery) has occurred in the US.

Many animals can get babesiosis from *Babesia* species that have been shown to infect humans. Cattle have been reported to carry *B. divergens*, but no direct transmission from animal to human has ever been reported⁴. Domestic pets can bring infected ticks into domestic environments, so tick prevention products should be used on companion animals.

There is no evidence of natural transmission from person-to-person.

Incubation Period

The incubation period from tick bite to symptom onset ranges from 7 to 28 days⁴ in most cases, but can be several months in milder cases².

Outbreak Recognition

Outbreaks would be recognized as an increase in the usual number of cases clustered in place and time.

Case Definition

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This surveillance case definition was developed for national reporting of babesiosis; it is not intended to be used in clinical diagnosis⁷.

Clinical Presentation

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 Evidence for Diagnosis

For the purposes of surveillance:

1. Objective evidence is defined as one or more of the following: fever, anemia, or thrombocytopenia.
2. Subjective evidence is defined as one or more of the following: chills, sweats, headache, myalgia, or arthralgia.

Epidemiological 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:

1. In the transfusion recipient:
 - a. 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

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- b. At least one of these transfused blood components was donated by the donor described below; and
 - c. Transfusion-associated infection is considered at least as plausible as tickborne transmission; and
2. In the blood donor:
 - a. Donated at least one of the RBC or platelet components that was transfused into the above recipient; and
 - b. 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.)

Laboratory Criteria for Diagnosis

For the purpose of surveillance:

1. Laboratory Confirmatory
 - a. Identification of intraerythrocytic *Babesia* organisms by light microscopy in a Giemsa, Wright, or Wright-Giemsa–stained blood smear; or
 - b. Detection of *Babesia microti* DNA in a whole blood specimen by polymerase chain reaction (PCR); or
 - c. Detection of *Babesia* spp. genomic sequences in a whole blood specimen by nucleic acid amplification; or
 - d. Isolation of *Babesia* organisms from a whole blood specimen by animal inoculation.
2. Laboratory Supportive
 - a. 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
 - b. Demonstration of a *Babesia microti* Immunoblot IgG positive result; or
 - c. Demonstration of a *Babesia divergens* IFA total Ig or IgG antibody titer of greater than or equal to (\geq) 1:256; or
 - d. Demonstration of a *Babesia duncani* IFA total Ig or IgG antibody titer of greater than or equal to (\geq) 1:512.

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It should be noted that *B. microti* is the most frequently identified agent of human babesiosis in the United States, although sporadic U.S. cases caused by other *Babesia* agents have occurred. As a result, serologic and molecular tests available for *B. microti* infection do not typically detect these other *Babesia* agents.

Case Classification Confirmed

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

Probable

1. 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
2. A case that is in a blood donor or recipient epidemiologically linked to a confirmed or probable Babesiosis case (as defined above) and:
 - a. has confirmatory laboratory evidence but does not meet any objective or subjective clinical evidence criteria; or
 - b. has supportive laboratory evidence and may or may not meet any subjective clinical evidence criteria but does not meet any objective clinical evidence criteria.

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).

Preventive Interventions

The primary control method for babesiosis is to reduce the opportunity for interaction between vector ticks and their human hosts. This can be accomplished using techniques similar to those outlined in the Lyme disease prevention interventions, listed below:

1. Avoid potential tick habitat (such as woody, brushy, or grassy areas) when possible.
2. Minimize exposure by wearing light-colored clothing that covers legs and arms so that ticks are more easily seen; tuck pants into socks and apply tick repellent such as 20%

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DEET to the skin (according to label directions) or permethrin (a repellent and contact acaricide) to pant legs and sleeves (not skin).

3. Many infections from tickborne diseases happen at home — create tick-free zones. Remove leaf litter and brush around your home and at the edges of lawns. Place wood chips or gravel between lawns and wooded areas. Mow the lawn and clear brush regularly. Keep playground equipment, decks and patios away from yard edges and trees.
4. If working or playing in potential tick habitats, search the total body area daily, including haired areas. Remove ticks promptly. Keep in mind ticks may be very small and difficult to see.
5. Remove any attached ticks by grasping the tick with tweezers as close to the skin as possible. Pull upward using gentle, steady pressure to avoid leaving mouth parts in the skin; protect hands with gloves, cloth or tissue when removing ticks from humans or animals. Following tick removal, cleanse the attachment site with soap and water.
6. Check pets for ticks regularly; consult with a veterinarian regarding medications effective for controlling ticks.

Treatment

It is often difficult to distinguish *Babesia* from malaria parasite by blood-smear examination, and Babesiosis symptoms can be very non-specific; the accurate diagnosis of babesiosis should be confirmed before treatment is administered¹.

It is generally recommended that cases without a life-threatening condition receive either oral Clindamycin and quinine or atovaquone with azithromycin for 7 to 10 days, although the latter therapy has been shown to result in fewer adverse effects. For severely ill patients, an intravenous clindamycin and oral quinine combination remains the standard of care. Exchange blood transfusions may be considered for critically ill patients, especially for those with parasitemia concentrations 10% or greater².

Surveillance Indicators

1. Proportion of cases with complete demographic information.
2. Proportion of cases with complete clinical information
3. Proportion of cases with appropriate laboratory testing (as defined by the CDC case definition as “Laboratory Evidence”) including copies of lab results submitted to DIDE.

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