Babesiosis
Investigation Guideline

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Fact Sheet

Attachments can be accessed through the Adobe Reader’s navigation panel for attachments. Throughout this document attachment links are indicated by this symbol ; when the link is activated in Adobe Reader it will open the attachments navigation panel. The link may not work when using PDF readers other than Adobe.
**Revision History:**

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CASE DEFINITION

Clinical Criteria (for the purposes of public health 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 purposes of public health surveillance):
- Laboratory confirmed:
  - 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 (≥) 1:256 (or ≥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 (≥) 1:256; OR
  - Demonstration of a *Babesia duncani* IFA total Ig or IgG antibody titer of greater than or equal to (≥) 1:512.

Epidemiologic Linkage (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).

LABORATORY ANALYSIS:

1) Detailed laboratory diagnosis information is available at [www.cdc.gov/dpdx/babesiosis/dx.html](http://www.cdc.gov/dpdx/babesiosis/dx.html)

2) Blood smears: The Kansas Health and Environmental laboratory (KHEL) will facilitate parasite identification on stained thin blood smears working with CDC’s DPDx telediagnosis network and by referring specimens (including unstained blood smears and blood specimens) to CDC’s Division of Parasitic Diseases and Malaria.
   - Multiple thick and thin smears may be necessary to identify a blood parasite and differentiate between *Plasmodium* and *Babesia* organisms.
   - If a determination cannot be made from a smear, CDC may choose to perform species-specific PCR.
   - Contact the KHEL at 785-296-3718 before sending any specimens.

3) Serological testing: Not available at KHEL, but is available through various commercial laboratories or can be arranged at special request though KHEL for testing at CDC. The provider must be sure to request testing for total Ig or IgG, as opposed to IgM alone.
   - A positive *Babesia* IFA result for IgM is insufficient for diagnosis and case classification 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, collect a follow-up blood specimen drawn at least one week after the first. If the IgG 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 magnitude of \textit{Babesia} titters (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).

• Serologic and molecular tests available for \textit{B. microti} infection do not typically detect these other \textit{Babesia} agents.

4) Blood-borne transmission of \textit{Babesia}, laboratory testing: The epidemiologic linkage criteria for transfusion transmission described in the case definition (IgG antibody titer of $\geq 1:64$ in epidemiologically linked blood donors or recipients) provides 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.

• Without an epidemiologic linkage for IgG antibody titers $\geq 1:64$ but $<1:256$ or $<1:512$ (for \textit{B. duncani}), the classification is “not a case” and no further investigation will occur.

• A potential epi link will result in a transfusion investigation that will entail laboratory testing for evidence of \textit{Babesia} infection in recipients and donors as well as epidemiologic assessments of the plausibilities of blood- and tick-borne transmission.

\section*{EPIDEMIOLOGY}
\textit{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 \textit{Babesia} agents include \textit{B. duncani} (formerly the WA1 parasite) and related organisms (CA1-type parasites) in several western states as well as parasites characterized as "\textit{B. divergens} like" (MO1 and others) in various states.

Blood-borne transmission of \textit{Babesia} is not restricted by geographic region or season.

\section*{DISEASE OVERVIEW}
\begin{itemize}
  \item \textbf{A. Agent:}
  Hemoprotozoan parasite of genus \textit{Babesia}, most commonly \textit{B. microti} but also including \textit{B. duncani} (formerly WA1), which was first described from Washington State, and \textit{B. divergens}-like agents identified in the United States

  \item \textbf{B. Clinical Description:}
  Illness can be asymptomatic; symptoms include fever, chills, myalgia, arthralgia, enlarged spleen or liver, jaundice and hemolytic anemia, with more severe illness in the elderly, asplenia, and immunocompromised. Laboratory findings may include thrombocytopenia, proteinuria, hemoglobinuria, and elevated levels of liver enzymes, blood urea nitrogen, and creatinine.
\end{itemize}
C. Reservoirs:
   Deer mice (Peromyscus leucopus) and other small mammals for B. microti in
   the United States; cattle for B. divergens in Europe; not definitively established
   for other zoonotic Babesia species.

D. Mode(s) of Transmission:
   Transmission is usually through bites of infected Ixodes ticks; person-to-person
   transmission is by transfusion or, more rarely, transplacentally.

E. Incubation Period:
   Variable, probably 1-8 weeks for tickborne transmission, and from weeks to
   months for bloodborne transmission. Symptoms may appear or recrudesce
   many months (even >1 year) after initial exposure, particularly in the context of
   immunosuppression.

F. Period of Communicability:
   Communicable through transfusion, parasitemia may occur months to >1 year
   after infection; asymptomatic, undiagnosed parasitemia may be protracted.

G. Susceptibility and Resistance:
   Susceptibility assumed to be universal. Persons who are asplenic, elderly,
   immunocompromised, or otherwise debilitated are at increased risk.

H. Treatment:
   Most asymptomatic persons do not require treatment. 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. Treatment decisions should be individualized, especially for
   patients who have (or are at risk for) severe or relapsing infection.
   (www.cdc.gov/parasites/babesiosis/health_professionals/index.html#tx)

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Suspected cases of tickborne rickettsial disease (including anaplasmosis,
ehrlichiosis, and spotted fever rickettsiosis) shall be reported 24 hours, except if
the reporting period ends on a weekend or state-approved holiday, the report shall
be made by 5:00 p.m. on the next business day after the 24-hour period:
1. Health care providers and hospitals: report to the local public health
   jurisdiction.
2. Local public health jurisdiction: report to KDHE-BEPHI (see below).
3. Laboratories: report to KDHE-BEPHI (see below).

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)
Phone: 1-877-427-7317 Fax: 1-877-427-7318
**Further responsibilities of state and local health departments to the CDC:**

As a nationally notifiable condition, confirmed and probable cases require a ROUTINE report to the Center of Disease Control and Prevention (CDC).

1. ROUTINE reporting requires KDHE-BEPHI to file an electronic report for within the next reporting cycle.

2. **Local public health jurisdiction** will report information requested as soon as possible, ensuring that the electronic form is completed within 7 days of receiving a notification of a report.

**INVESTIGATOR RESPONSIBILITIES**

1) **Report** all Babesiosis cases to the KDHE-BEPHI.
   - Initiate the case investigation within 3 days of notification of a report.
   - Complete the investigation within 14 days of the notification.

2) Contact medical provider to collect additional information and confirm diagnosis using current **case definition**. For all diagnosed cases:
   - Collect all information requested in **Step 1** of case investigation.
   - Ensure that case/proxy is aware of the diagnosis.

3) Conduct a **case investigation** to determine the individual’s risks of exposure and potential geographical location of exposure.
   - Identify exposures eight weeks prior to symptom onset or diagnosis (use earliest date), consider travel, tick bites, and exposure to tick habitats.
   - Identify if the case-patient’s infection was transfusion associated.
   - Use the **CDC case form** as a guide.

4) Conduct contact investigation to identify additional cases, as needed.
   - If a potential blood transfusion or donation occurred within the last year, work with KDHE-BEPHI to test all blood donors or recipients associated with the case-patient.

5) Initiate any needed control and prevention measures.
   - No isolation or restrictions apply.
   - Case must defer donating blood for life.
   - Educate those sharing a case’s exposure about signs and symptoms of babesiosis and encourage them to seek care if illness develops

6) **Record** data, collected during the investigation, in the KS EpiTrax system under the data’s associated [tab] in the case morbidity report (CMR).

7) As appropriate, use the disease **fact sheet** to notify the case, contacts and other individuals or groups.
STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who ordered testing of the case and obtain the following information. (Request medical records for hospitalized patients.)
   • If the case-patient was identified through an IgG serological titer that is less than 1:256, identify if the case-patient received any blood products or organ donations the year before the specimen collection date.
     - Yes, blood products received or organ donation occurred: continue on with the investigation.
     - No blood products or organ donation received and titers <1:256: No further investigation required. Record findings and “Complete” and “Approve” the case as directed in Data Management.
   • Did the medical provider diagnose a Babesiosis?
     - Yes: Record the diagnosis date [Clinical] and continue the investigation.
     - No, not diagnosed because of other findings: Record the alternative diagnosis and findings in the [Notes] of EpiTrax. Unless a potential transfusion association was identified, no further investigation should be required. “Complete” and “Approve” the case as directed in Data Management.
   • Obtain information on any laboratory tests performed and fax results to KDHE at 1-877-427-7318, if not previously reported.
     - Blood Smear
     - IFA testing, IgM and IgG
     - Immunoblot or PCR
   • Record onset date of first symptoms associated to this episode [Clinical]
   • Symptoms: [Investigation – Symptoms].
     - Objective symptoms: fever, anemia and/ or thrombocytopenia
     - Subjective: headache, chills, sweats, myalgia, and arthralgia.
   • Immunocompromised patient? [Investigation – Symptoms]
     - Any underlying medical conditions: immune suppression or asplenia (record date of splenectomy)
   • Complications: [Investigation – Complications]
     - Any complications: acute respiratory distress, congestive heart failure, disseminated intravascular coagulation, myocardial infarction, renal failure
   • Collect patient’s demographics (address, birth date, gender, race/ethnicity, primary language, and phone number(s)). [Demographic]
   • Record treatment: [Clinical]
   • Record hospitalizations: location and duration of stay [Clinical]
   • Record outcomes: survived or date of death [Clinical]
   • Record pregnancy status for women. [Clinical]

2) Establish if the patient’s illness is clinically compatible to Babesiosis based on lab criteria and clinical symptoms.
3) If a continued investigation is needed and the patient charts do not provide information on the following risk factors or travel, interview the case-patient to determine risk factors and transmission. [Investigation – Exposure]
   - Identify exposures eight weeks prior to symptom onset or diagnosis (use earliest date.
   - Travel out of county, state, or country: record dates and location
     – Especially make note of any travel to malaria endemic areas.
   - Engage in outdoor activities, describe
   - Spend time outdoors in or near wooded or brushy areas
   - Any tick bites: geographic location where tick was acquired and when
   - Occupational risks (e.g., laboratory worker, landscape worker, others)
     – Record patient’s occupation [Epidemiologic]
4) Examining the epidemiological information, record where the infection was most likely imported from. (Indigenous or out-of-county, state, or U.S.) [Epidemiologic].
5) Lost to follow-up: After several unsuccessful attempts to obtain needed information, fill out as much of the Babesiosis report as possible. Note why you could not obtain further information.

**Contact Investigation**

Not usually required, these diseases cannot be transmitted from person-to-person, but an individual living in the same household, travel companions, co-workers, and anyone else who might be exposed to ticks is potentially at risk.

Exceptions:
1) Pregnant babesiosis cases require follow-up to report birth outcomes
2) Possible transfusion or organ transplant transmission; situation will be evaluated by the KDHE-BEPHI to determine if a potential contact investigation is necessary.

**Isolation, Work and Daycare Restrictions**

No restrictions except permanent exclusion of a case-patient from blood donation.

**Case Management**

Ensure education has occurred on preventing further tick exposures and on refraining from blood donation.

**Contact Management (Informational purposes)**

1) Preventive treatment is not warranted.
2) Instruct those exposed to a tick to monitor themselves for symptoms. Treatment is necessary only if symptoms develop.
3) Those who exhibit any signs or symptoms compatible with tick-borne illness should be referred to their medical provider for evaluation.
Environmental Measures

Community-based integrated tick management strategies may reduce the incidence of tick-borne infections, but limiting exposure to ticks is the most effective method of prevention.

Education

As opportunities allow, the following general messages should be distributed:

- In tick-infested areas, the highest risk of bites is occurs from March-July.
- The use of protective clothing, including light-colored garments, long pants tucked into socks, long-sleeved shirts, hats, as well as tick repellents, may reduce risk.
- Outdoor activities in tick-infested areas present opportunities for exposure.
- Keep yards clear of excessive leaves, brush, and tall grasses. Walk in the center of trails to avoid contact with tall grasses and brush.
- When camping, sleep in screened tents.
- Hunters should be aware of tick infestations on mammals, especially deer, and check for tick attachments after handling carcasses.
- Keep pets free of ticks.
- Transmission requires a long attachment. Check for ticks at regular intervals while outdoors and after spending time outdoors in tick infested areas.
- Remove attached ticks intact, do not leave embedded head parts. Use gentle, direct traction with tweezers or hemostat. Other methods, such as application of a hot match or petroleum products to the tick, are less reliable. Do not crush ticks as this may result in direct inoculation of infectious agent.
MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:
   • There are no formal outbreak definitions; however, the investigator may consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.
   • Notify KDHE immediately, 1-877-427-7317.

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the [Administrative] tab.

B. Organize and collect data, using appropriate data collection tools including:
   • The CDC Case Report Form can be used to collect information.
   • Alternatively, investigators can collect and enter all required information directly into EpiTrax [Investigation], [Clinical], [Demographics], [Epidemiological] tabs.
   • During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.

C. Report data collected during the course of the investigation via EpiTrax.
   • Verify that all data requested on CDC Case Report Form has been recorded on an appropriate EpiTrax [tab], or that actions are completed for a case lost to follow-up as outlined below.
   • Some data that cannot be reported on an EpiTrax [tab] may need to be recorded in [Notes] or scanned and attached to the record.
   • Paper report forms do not need to be sent to KDHE after the information is recorded and/or attached in EpiTrax. The forms should be handled as directed by local administrative practices.

D. If a case is lost to follow-up, after the appropriate attempts to contact the case have been made:
   • Indicate 'lost to follow-up' on the [Investigation] tab with the number of attempts to contact the case recorded.
   • Record at least the information that was collected from the initial reporter.
   • Record a reason for 'lost to follow-up' in [Notes].

E. Once the investigation is completed, the LHD investigator will record the date the investigation was completed on the [Administrative] tab and click the “Complete” button. This will trigger an alert to the LHD Administrator so they can review the case before sending to the state.
   • The LHD Administrator will then “Approve” or “Reject” the CMR.
   • Once a case is “Approved” by the LHD Administrator, BEPHI staff will review and close the case after ensuring it is complete and that the case is assigned to the correct event, based on the reported symptoms reported. (Review the EpiTrax User Guide, Case Routing for further guidance.)
ADDITIONAL INFORMATION / REFERENCES


C. Case Definitions: CDC Division of Public Health Surveillance and Informatics, Available at: www.cdc.gov/nndss/

D. Kansas Regulations/Statutes Related to Infectious Disease: www.kdheks.gov/epi/regulations.htm


F. CDC Babesiosis web page: https://www.cdc.gov/parasites/babesiosis/