

# Tickborne Rickettsial Disease (TBRD) Investigation Guideline

*[Including Anaplasmosis, Ehrlichiosis,  
and Spotted Fever Rickettsiosis]*

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Ehrlichiosis/Anaplasmosis Fact Sheet (vs. 2013)	
Spotted Fever Rickettsiosis Fact Sheet (vs. 2012)	

*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:**

<b>Date</b>	<b>Replaced</b>	<b>Comments</b>
01/2016	09/2011	Combined the Anaplasmosis/Ehrlichiosis and Spotted Fever Rickettsiosis guidelines into one Tickborne Rickettsial Disease Investigation guideline. Updated Notification, Investigator Responsibilities, and Data Management sections with disease surveillance indicator targets.
12/2013	04/2009	Reformatted and added notification section.

# Tickborne Rickettsial Disease

## Disease Management and Investigation Guidelines

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### CASE DEFINITION

#### Clinical Description for Public Health Surveillance:

- Anaplasmosis and Ehrlichiosis – Any reported fever and one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation.
- Spotted Fever Rickettsiosis – Any reported fever and one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

#### Laboratory Criteria for Case Classification:

For the purposes of surveillance, the definition of a qualified laboratory assay is:

- Laboratory confirmed:
  - Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer between paired serum specimens (one taken in the first week of illness and a second 2-4 weeks later), OR
  - Detection of DNA in a clinical specimen via amplification of a specific target by PCR assay, OR
  - Demonstration of antigen in a biopsy or autopsy specimen by IHC, or
  - Isolation from a clinical specimen in cell culture.
- Laboratory supportive:
  - Has serologic evidence of elevated IgG or immunoglobulin M (IgM) antibody by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.
  - Identification of morulae in cytoplasm of neutrophils or eosinophils (for *Anaplasma phagocytophilum*), or of monocytes and macrophages (for *Ehrlichia chaffeensis*) by microscopic examination.

#### Exposure:

Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. Occupation should be recorded if relevant to exposure. A history of a tick bite is not required.

#### Case Classification:

- **Confirmed:** A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.
- **Probable:** A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results. (An “Ehrlichiosis/Anaplasmosis, undetermined” case can only be classified as probable. This occurs when a case has compatible clinical criteria with laboratory evidence to support *Ehrlichia/Anaplasma* infection, but not with sufficient clarity to definitively place it in one of the categories previously described. This may include the identification of morulae in white cells by microscopic examination in the absence of other supportive laboratory results.)
- **Suspect:** A case with laboratory evidence of past or present infection but no clinical information available (e.g., a laboratory report).

**LABORATORY ANALYSIS:**

- Clinical suspicion of any of these diseases is sufficient to begin treatment. Delay in treatment may result in severe illness and death.
- The State Public Health Laboratory does not provide testing and sends all specimens to the CDC. *Warning:* Prior consultation required from the KDHE Epidemiology Program at 1-877-427-7317. CDC does not offer routine testing – illness **MUST** meet clinical case definition.

Laboratory Findings	Anaplasmosis	Ehrlichiosis	Spotted Fever
Anemia	Mild	May occur late in illness	--
Thrombocytopenia	Yes	--	Yes
Leukopenia	Relative and absolute; lymphopenia and left shift	Absolute	--
Blood smear: morulae in cytoplasm	In granulocytes	<i>E. chaffeensis</i> : in monocytes <i>E. ewingii</i> : in granulocytes	--
Elevated Transaminase	Mild to moderate in some patients		Mildly elevated
Hyponatremia	--		Yes
Skin biopsy: DNA detection by PCR; or IHC staining of organism	--		Yes
Whole blood sample: DNA detection by PCR	Most sensitive in first week of illness; sensitivity may decrease after administration of antibiotics		Unreliable
Serology	<p>Antibodies are detectable 7–10 days after illness onset.</p> <p>The gold-standard serologic test looks for a four-fold change in IgG-specific antibody titers using immunofluorescence assay (IFA) on paired samples.</p> <p>The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later.</p>		

**NOTE:** IgM antibodies are less specific than IgG antibodies and are more likely to generate false positives. Do not use IgM results alone for laboratory diagnosis.

**NOTE:** Antibody titers are frequently negative in the first 7–10 days of illness, thus serologic tests may be falsely negative during this time period.

## EPIDEMIOLOGY

The tickborne rickettsial disease (TBRD), including Rocky Mountain Spotted Fever (RMSF), Ehrlichiosis (HME), and Anaplasmosis (HGA) are caused by *Rickettsia rickettsii*, *Ehrlichia chaffeensis*, and *Anaplasma phagocytophilum*, respectively. These pathogens are maintained in nature by interactions of wild mammals with hard-bodied (ixodid) ticks. The epidemiology of these diseases reflects the geographic distribution and seasonal activities of the vectors and reservoirs and the human behaviors that place persons at risk for tick attachment and subsequent infection. RMSF, HME, and HGA are reported each month of the year in the United States, although 90%-93% of reported cases occur during April-September during peak levels of tick feeding activity on humans. Travelers outside of the United States might also be exposed to other tick vectors in other countries that transmit related agents that result in disease after they return to the United States.

Males appear to be at higher risk for infection with all TBRD, possibly because of recreational or occupational exposures to tick habitats. Although previous studies have indicated that the highest incidences of RMSF have occurred in children aged <10 years, surveillance during 2003 demonstrates a higher age-specific incidence for RMSF among persons aged 40-64 years, compared with other age groups. For HME and HGA, the highest age-specific incidences occurred among persons aged >70 and 60-69 years, respectively. The higher frequency of disease reporting in adults might reflect greater susceptibility to recognizable disease rather than higher infection rates. Deaths from TBRD are rare, but severe complications can occur. Even in the absence of the most severe complications, hospitalizations due to these diseases are common. From 2012 through 2014, 54 to 61 percent of Kansas ehrlichiosis/anaplasmosis cases were hospitalized, and 22 to 30 percent of RMSF cases were hospitalized. (Source: [MMWR, 2006](#))

RMSF is reported as “spotted fever rickettsiosis” to allow reporting of all spotted fever cases to the CDC, including those caused by *R. parkeri* and *R. 364D*. Spotted fever cases are found throughout the contiguous U.S., but five states (North Carolina, Oklahoma, Arkansas, Tennessee, and Missouri) account for over 60% of RMSF cases. In eastern Arizona, RMSF cases associated with exposure to the brown dog tick (*Rhipicephalus sanguineus*) have recently been identified in an area where RMSF had not previously been seen.

Anaplasmosis is most frequently reported from the upper midwest and northeastern U.S. Ehrlichiosis is most frequently reported from the southeastern and south-central U.S., from the eastern seaboard extending westward to Texas. In 2009, a new *Ehrlichia* species, provisionally called *Ehrlichia muris-like* (EML) was identified among patients in the upper Midwest.

## DISEASE OVERVIEW

### A. Agent:

- *Ehrlichia chafeensis* and *E. ewingi*, gram-negative bacteria associated to human monocytic ehrlichiosis (HME). Other species, including *Ehrlichia muris-like* (EML), are also associated to human illness.
- *Anaplasma phagocytophila*, gram-negative bacteria associated to human granulocytic anaplasmosis (HGA) which was previously referred to as human granulocytic ehrlichiosis (HGE).
- *Rickettsia* species of the Spotted Fever group (obligate intracellular coccobacillus): *R. rickettsii*, *R. parkeri*, and *R. species 364D*.

### B. Clinical Description:

A tick-borne illness is characterized by acute onset of fever and may be accompanied by headache, myalgia, malaise, anemia, thrombocytopenia, or elevated hepatic transaminases. Nausea, vomiting, or rash may be present.

- Those with spotted fever rickettsiosis may have an eschar present or a macular or maculopapular rash that appears 4-7 days following onset. The rash is often on the palms and soles. The rash may be absent in 20% of patients and some people do not develop the rash until late in the disease process after treatment should have already begun.
- Those with anaplasmosis or ehrlichiosis may exhibit leukopenia and morulae may be observed in monocytes or granulocytes on blood smears.

### C. Reservoirs:

- Animal reservoirs include white-tailed deer, dogs, and small rodents. Ruminants are also considered a reservoir for anaplasmosis.
- Vectors in the United States:
  - *R. rickettsii*: *Dermacentor variabilis* (American dog tick), *Dermacentor andersoni* (Rocky Mountain wood tick), and *Rhipicephalus sanguineus* (brown dog tick).
  - *Rickettsia parkeri*: *Amblyomma maculatum* (Gulf Coast tick)
  - *Rickettsia* species 364D: *Dermacentor occidentalis* (Pacific Coast tick).
  - *E. chaffeensis* and *E. ewingii*: *Amblyomma americanum* (Lone Star tick)
  - *A. phagocytophilum*: *Ixodes scapularis* (blacklegged tick) and *Ixodes pacificus* (western blacklegged tick).

### D. Mode(s) of Transmission:

Transmission occurs from the bite of an infected tick. For RMSF, transmission can also occur by the contamination of broken skin with the crushed tissue or feces of a tick and laboratory data suggests that the tick must remain attached for 4 - 6 hours before transmission occurs.

### E. Incubation Period:

- 7-14 days for human ehrlichiosis and anaplasmosis.
- 2-21 days for spotted fever group rickettsial infections.

### F. Period of Communicability:

Not communicable person-to-person; ticks remains infective for life.

### G. Susceptibility and Resistance:

All persons are susceptible.

### H. Treatment:

Anaplasmosis, ehrlichiosis and Rocky Mountain spotted fever are treated in the same manner with doxycycline. Clinical suspicion of any of these diseases is sufficient to begin treatment. According to the CDC, it is most effective when given within the first 5 days of illness.

## NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Tickborne rickettsial disease (including anaplasmosis, ehrlichiosis, and spotted fever rickettsiosis) shall be reported within seven days:

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 STANDARD report to the Center of Disease Control and Prevention (CDC).

1. STANDARD 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 TBRD report.

## INVESTIGATOR RESPONSIBILITIES

- 1) Report all TBRD cases to the KDHE-BEPHI.
  - Initiate the case investigation within 3 days of notification of a report.
  - Complete the investigation within 7 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.
- 4) Record data, collected during the investigation, in the KS EpiTrax system under the data's associated [tab] in the case morbidity report (CMR).
- 5) 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. (This includes medical records for hospitalized patients.)
  - Did the medical provider diagnose a TBRD?
    - Yes: Record the diagnosis date [Clinical] and continue the investigation.
    - No, not diagnosed based on negative IgM testing alone: Discuss with provider that IgM results alone should not be used for diagnosis, and continue with the investigation if needed based on other findings.
    - No, not diagnosed based on other findings: Record the alternative diagnosis in the [Notes] of EpiTrax. No further investigation required. “Complete” and “Approve” the case as directed in Data Management.
  - Obtain information on any laboratory tests performed.
    - Complete blood cell counts (CBC) and differential results.
    - Liver enzyme testing results.
    - Any tickborne disease testing results that has not been reported.
  - Record onset date of first symptoms associated to this episode [Clinical]
  - Symptoms: fever, rash, headache, myalgia, anemia, leukopenia, thrombocytopenia, elevated hepatic transaminases, eschar, or other symptoms [Investigation – Symptoms].
  - Immunocompromised patient? [Investigation – Symptoms]
  - Complications: adult respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy (DIC), meningitis/encephalitis, renal failure, other or none. [Investigation – Complications]
  - Collect patient’s demographics (address, birth date, gender, race/ethnicity, primary language, and phone number(s)). [Demographic]
  - Record treatment: type of antibiotic and number of days prescribed
  - 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 TBRD based on lab criteria and clinical symptoms.
  - If any of the following situations are present the investigation can be closed as ‘Not a Case’:
    - The medical provider states it is not a case of TBRD and gives an alternative diagnosis.
    - There was no fever (subjective or measured). (Continue the investigation if the presence of fever is unknown.)
    - There was fever reported but no other TBRD symptoms were present (continue investigation if any symptoms are unknown).

- 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 to determine risk factors and transmission. [Investigation – Exposure]
  - Thirty days prior to patient’s illness onset, was there a history of a tick bite. Where was the patient when the tick bite occurred? (What county?)
  - Thirty days prior to patient’s illness onset, was there any exposure to wooded or brushy areas or exposure to animals that may have been in a wooded/brushy area?
  - Where were the wooded or brushy areas located that were associated to direct or indirect exposure during the 30 days prior to illness onset?
    - Travel to other Kansas counties? (If yes, City/County and dates)
    - Was there travel outside of Kansas?
      - Travel in the U.S.? (If yes, City/State and dates)
      - Travel internationally? (If yes, City/Country and dates)
  - Record patient’s occupation [Notes]
- 4) Examining the epidemiological information, record where the infection was most likely imported from. (Indigenous or out-of-county, state, or U.S.) [Epidemiologic]; also record the county, state, and country that was the most likely exposure [Investigation – Exposure].

### 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 infected ticks is potentially at risk.

### Isolation, Work and Daycare Restrictions

None.

### Case Management

Not required.

### Contact Management

- 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

#### ***Veterinary tick control in domestic animals:***

- 1) Domestic animals may become infected with TBRD bacteria.
- 2) Domestic animals can carry infected ticks into areas where people live.
- 3) Veterinary tick-control products help to reduce tick presence on pets.

#### ***Community-based integrated tick management strategies:***

- 1) May reduce the incidence of tick-borne infections, but limiting exposure to ticks is the most effective method of prevention

- 2) Strategies to reduce vector tick densities through area-wide application of an acaricide (i.e., chemicals that kill ticks and mites) and control of tick habitats (e.g., leaf litter and brush) have been effective in small-scale trials.
- 3) New methods under development include applying acaricide to rodents and deer by using baited tubes, boxes and deer feeding stations in areas where these pathogens are endemic.
- 4) Biological control with fungi, parasitic nematodes, and parasitic wasps may play important roles in integrated tick control efforts.

Additional measures that can assist with determining risk include:

- Entomologic surveys: Inventory and mapping of tick populations sometimes with limited testing for TBRD. This can occur as part of special studies and through monitoring at deer and other animals.
- Testing of ticks: [Kansas State University](#) (KSU) Veterinary Diagnostic Laboratory does offer a fee for use service that tests ticks for RMSF.
  - **All clinical decisions should be made based on the patient's clinical signs and symptoms not tick testing results.**
- Tick identification: Contact your local [K-state extension office](#) or the [Insect Diagnostician](#) with the K-State Department of Entomology.

### **Education**

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

- 1) It is a good idea to take preventive measures against ticks year-round, but be extra vigilant in warmer months (April-September).
- 2) 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.
- 3) Outdoor activities in tick-infested areas present opportunities for exposure.
- 4) Keep yards clear of excessive leaves, brush, and tall grasses.
- 5) Walk in the center of trails to avoid contact with tall grasses and brush.
- 6) When camping, sleep in screened tents.
- 7) Hunters should be aware of tick infestations on mammals, especially deer, and check for ticks after handling carcasses.
- 8) Keep pets free of ticks.
- 9) Frequent tick checks increase the likelihood of finding a tick before it can transmit disease.
- 10) 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 TBDR bacteria.

Additional education materials are available at: [www.cdc.gov/ticks/index.html](http://www.cdc.gov/ticks/index.html)

## 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.
  - Active case finding will be an important part of any investigation.

## 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 [Tick-Borne Rickettsial 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 the [Tick-Borne Rickettsial 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**

- A. Treatment / Differential Diagnosis:** Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.
- B. Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual (CCDM), 20th Edition. Washington, DC, American Public Health Association, 2015.
- C. Case Definitions:** CDC Division of Public Health Surveillance and Informatics, Available at: [www.cdc.gov/nndss/](http://www.cdc.gov/nndss/)
- D. Kansas Regulations/Statutes Related to Infectious Disease:** [www.kdheks.gov/epi/regulations.htm](http://www.kdheks.gov/epi/regulations.htm)
- E. Tickborne Diseases of the United States: A Reference Manual for Health Care Providers:** [www.cdc.gov/lyme/resources/TickborneDiseases.pdf](http://www.cdc.gov/lyme/resources/TickborneDiseases.pdf)
- F. Additional Information (CDC):** [www.cdc.gov/ticks/index.html](http://www.cdc.gov/ticks/index.html)