

# Ehrlichiosis / Anaplasmosis Investigation Guideline

## CONTENT:

## VERSION DATE:

### Investigation Protocol:

- Investigation Guideline

12/2013

### Supporting Materials found in attachments:

- Fact Sheet

12/2013

## Revision History:

Date	Replaced	Comments
12/2013	04/2009	Reformatted and added notification section.
02/2012	-	Removed references to KS-EDSS.

# Ehrlichiosis / Anaplasmosis

## Disease Management and Investigative Guidelines

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### CASE DEFINITION (CDC 2008)

#### Clinical Description for Public Health Surveillance:

Any reported fever **and** one or more of the following: rash, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

#### Laboratory Criteria for Case Classification:

For the purposes of surveillance, there are at least three species of bacteria, responsible for ehrlichiosis/ anaplasmosis in the United States: *Ehrlichia chaffeensis*, found primarily in monocytes, and *Anaplasma phagocytophilum* and *Ehrlichia ewingii*, found primarily in granulocytes. The clinical signs of disease that result from infection with these agents are similar, and the range distributions of the agents overlap, so testing for one or more species may be indicated. Serologic cross-reactions may occur among tests for these etiologic agents.

Four sub-categories of ehrlichiosis/anaplasmosis should be reported:

- 1) human ehrlichiosis caused by *E. chaffeensis*,
- 2) human ehrlichiosis caused by *E. ewingii*,
- 3) human anaplasmosis caused by *Anaplasma phagocytophilum*, or
- 4) human ehrlichiosis/anaplasmosis - undetermined.

*Cases in the fourth sub-category can only be reported as "probable" because the cases are only weakly supported by ambiguous laboratory test results.*

Problem cases for which sera demonstrate elevated antibody IFA responses to more than a single infectious agent are usually resolvable by comparing the levels of the antibody responses, the greater antibody response generally being that directed at the actual agent involved. Tests of additional sera and further evaluation via the use of PCR, immunohistochemistry, and isolation via cell culture may be needed for further clarification. Cases involving persons infected with more than a single etiologic agent, while possible, are extremely rare and every effort should be undertaken to resolve cases that appear as such via other explanations.

Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. Furthermore, IgM tests are not always specific and the IgM response may be persistent. Therefore, IgM tests are not strongly supported for use in serodiagnosis of acute disease.

#### ***Ehrlichia chaffeensis* infection (Human Monocytic Ehrlichiosis [HME]):**

- Laboratory confirmed:
  - Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer to *E. chaffeensis* antigen by indirect immunofluorescence assay (IFA) between paired serum samples (one taken in first week of illness and a second 2-4 weeks later), or
  - Detection of *E. chaffeensis* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, or
  - Demonstration of ehrlichial antigen in a biopsy or autopsy sample by immunohistochemical methods, or
  - Isolation of *E. chaffeensis* from a clinical specimen in cell culture.
- Laboratory supportive:
  - Serological evidence of elevated IgG or IgM antibody reactive with *E. chaffeensis* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-

- ELISA, or assays in other formats (CDC uses an IFA IgG cutoff of  $\geq 1:64$  and does not use IgM test results independently as diagnostic support criteria.), or
- Identification of morulae in the cytoplasm of monocytes or macrophages by microscopic examination.

***Ehrlichia ewingii* infection** (Ehrlichiosis [unspecified, or other agent]):

- Laboratory confirmed:
  - Because the organism has never been cultured, antigens are not available. Thus, *Ehrlichia ewingii* infections may only be diagnosed by molecular detection methods: *E. ewingii* DNA detected in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay.

***Anaplasma phagocytophilum* infection** (Human Granulocytic Ehrlichiosis [HGE]):

- Laboratory confirmed:
  - Serological evidence of a fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in first week of illness and a second 2-4 weeks later), or
  - Detection of *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, or
  - Demonstration of anaplasma antigen in a biopsy/autopsy sample by immunohistochemical methods, or
  - Isolation of *A. phagocytophilum* from a clinical specimen in cell culture.
- Laboratory supportive:
  - Serological evidence of elevated IgG or IgM antibody reactive with *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent Assay (ELISA), dot-ELISA, or assays in other formats (CDC uses an IFA IgG cutoff of  $\geq 1:64$  and does not use IgM test results independently as diagnostic support criteria.), or
  - Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination.

**Human ehrlichiosis/anaplasmosis – undetermined:**

- See case classification for a probable case.

**Exposure:** Defined as having been in potential tick habitats within the past 14 days before onset of symptoms. 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 no supportive laboratory results.
  - For ehrlichiosis/anaplasmosis – an 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

- The State Public Health Laboratory does not provide testing and sends all specimens to the CDC. *Warning:* Prior consultation required from the State Epidemiology Program. CDC does not offer routine testing – illness MUST meet clinical case definition.
- For additional information and/or questions concerning isolate submission, and laboratory kits call (785) 296-1620 or refer to online guidance at [www.kdheks.gov/labs/lab\\_ref\\_guide.htm](http://www.kdheks.gov/labs/lab_ref_guide.htm)

## EPIDEMIOLOGY

Because human ehrlichiosis has been recognized as a disease in North America only since the 1980's, information about the epidemiology of the disease is incomplete. Anaplasmosis is most frequently reported from the upper Midwest and northeastern U.S. in areas that correspond with the known geographic distribution of Lyme disease. Ehrlichiosis is most frequently reported from the southeastern and south-central U.S., from the eastern seaboard extending westward to Texas. The areas from which cases are reported correspond with the known geographic distribution of the lone star tick (*Amblyomma americanum*), which is associated with transmission of both *E. chaffeensis* and *E. ewingii*. Three states (Oklahoma, Missouri, Arkansas) account for 35% of all reported *E. chaffeensis* infections. Most cases of HME have been reported from south-central and southeastern states and occur during tick season, early spring to hard frost.

## DISEASE OVERVIEW

### A. Agent:

*Ehrlichia spp.* are gram-negative bacteria. Human monocytic ehrlichiosis (HME) is caused by *E. chaffeensis* and *E. ewingii* and human granulocytic ehrlichiosis (HGE) is caused by *E. phagocytophila* and *E. equi*.

### B. Clinical Description:

A tick-borne illness characterized by acute onset of fever, headache, myalgia, and/or malaise. Nausea, vomiting, or rash may be present in some cases. Clinical laboratory findings may include thrombocytopenia, leukopenia, and/or elevated liver enzymes. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

### C. Reservoirs:

The principal vector of HME is *Amblyomma americanum*, (i.e., lone star tick). The vector for HGE is unknown but believed to be the *Ixodes scapularis* (i.e., deer tick). Animal reservoirs for HME and HGE are uncertain at this point.

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

The bite of an infected tick can cause HME and HGE. Since bites from ticks are often painless and may occur on parts of the body that are difficult to observe, cases of may have no known history of a tick bite.

**E. Incubation Period:**

Range 7-21 days; average 9 days.

**F. Period of Communicability:**

Not transmissible person-to-person.

**G. Susceptibility and Resistance:**

Susceptibility is believed to be general. No data are available on immunity caused from previous infection.

**H. Treatment:**

Doxycycline, tetracycline or chloramphenicol. Preventive treatment for those who have been exposed to a tick but are not ill is not warranted.

## NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Ehrlichiosis/Anaplasmosis disease shall be designated as infectious or contagious in their nature, and cases or suspect cases 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**

As a nationally notifiable condition, confirmed and probable Ehrlichiosis/Anaplasmosis 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.
  - KDHE-BEPHI will file electronic reports weekly with CDC.
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 Ehrlichiosis/Anaplasmosis report.

## INVESTIGATOR RESPONSIBILITIES

- 1) Report all information that helps to confirm or rule-out cases to the KDHE within seven days of the initial report.
- 2) Use current case definition, to confirm diagnosis with the medical provider.
- 3) Conduct case investigation to determine the individual's at-risk activities and potential site of exposure.
- 4) Complete and report all information requested in the Kansas electronic surveillance system.
- 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 reported or ordered the testing of the case.
  - Determine what information has been released about the patient's diagnosis and identify if the needed epidemiologic data can be found in the clinical record alone.
  - If hospitalized: obtain admission/progress notes and discharge summary.
    - Record hospitalizations: reason, location and duration of stay
  - If pregnant: obtain the due date.
  - Obtain information that supports clinical findings in the case definition and information on the onset date of the symptoms, especially:
    - Clinical symptoms of fever, headache, myalgia, anemia, thrombocytopenia, leukopenia, or elevated hepatic transaminases.
    - Underlying immunosuppressive condition.
  - Obtain information on any laboratory tests performed and fax results to KDHE at 1-877-427-7318, if not previously reported.
    - Results of complete blood cell counts (CBC)
    - Results of liver enzyme testing
  - Collect case's demographic data and contacting information (birth date, county, sex, race/ethnicity, address, phone number(s))
  - Record outcomes: survived or date of death
- 2) If data found in patient charts does not provide information on risk factors, interview the case to determine source, risk factors and transmission settings.
- 3) Focus case investigation within the incubation period of the specific infectious agent, and consider:
  - Recent travel to endemic areas or history of possible exposure to ticks. List geographic location(s) and date(s).
  - Exposure to animals or pets with ticks.
  - Outdoor activities.
  - Occupational risks (e.g., laboratory worker, landscape worker, etc.).
  - Any travel 30 days prior to onset that was outside of the county

## Contact Investigation

There are no formal definitions of a contact; however, consideration should be given to individuals that were in the same geographic location as the case when exposed.

## Isolation, Work and Daycare Restrictions

None.

## Case Management

None.

## Contact Management (Information Purposes Only)

- 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.

- 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.
- 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.
- Biological control with fungi, parasitic nematodes, and parasitic wasps may play important roles in integrated tick control efforts.

## Education

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

- In tick-infested areas, the highest risk of bites 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 ticks 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.

## 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.

### B. Tick Removal Procedure:

To remove attached ticks, use the following procedure:

- Do not handle the tick with bare hands because infectious agents may enter through mucous membranes or breaks in the skin. This precaution is particularly directed to individuals who remove ticks from domestic animals with unprotected fingers. Children, the elderly and immunocompromised persons may be at greater risk of infection and should avoid this procedure.
- Use fine-tipped tweezers or shield fingers with a tissue, paper towel, or rubber gloves.
- Grasp the tick as close to the skin surface as possible and pull upward with steady, even pressure. Do not twist or jerk the tick; this may cause the mouthparts to break off and remain in the skin. If this happens, remove mouthparts with tweezers.
- Do not squeeze, crush, or puncture the body of the tick because its fluids (e.g., saliva, hemolymph, gut contents) may contain infectious organisms.
- After removing the tick, thoroughly disinfect the bite site and wash hands with soap and water.

## DATA MANAGEMENT AND REPORTING TO THE KDHE

### A. Organize and collect data.

### B. Report data via the state electronic surveillance system.

- Especially data that collected during the investigation that helps to confirm or classify a case.
- Cases will be reported using the following disease names (see case definitions):
  - Anaplasma phagocytophilum (f. HGE)
  - Ehrlichiosis / Anaplasmosis, undetermined
  - Ehrlichiosis, Ehrlichia chaffeensis (f. HME)
  - Ehrlichiosis, Ehrlichia ewingii

## ADDITIONAL INFORMATION / REFERENCES

- A. **Treatment / Differential Diagnosis:** American Academy of Pediatrics. 2009 Red Book: Report of the Committee on Infectious Disease, 28th Edition. Illinois, Academy of Pediatrics, 2009.
- B. **Epidemiology, Investigation and Control:** Heymann. D., ed., Control of Communicable Diseases Manual, 19th Edition. Washington, DC, American Public Health Association, 2009.
- C. **Case Definitions:** CDC Division of Public Health Surveillance and Informatics, Available at: [www.cdc.gov/osels/ph\\_surveillance/nndss/casedef/case\\_definitions.htm](http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm)
- D. **Animals in Public Places Compendium:**  
[www.kdheks.gov/epi/human\\_animal\\_health.htm](http://www.kdheks.gov/epi/human_animal_health.htm)
- E. **Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis --- United States (MMWR 2006):** [www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm)
- F. **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)
- G. **Additional Information (CDC):** [www.cdc.gov/health/default.htm](http://www.cdc.gov/health/default.htm)

## ATTACHMENTS

- **Fact Sheet**

*To view attachments in the electronic version:*

1. Go to <View>; <Navigation Pane>; <Attachments> – OR – Click on the “Paper Clip”  icon at the left.
2. Double click on the document to open.