

Merlin disease code: 08381 Anaplasmosis, HGA (*Anaplasmosis phagocytophilum*)
08382 Ehrlichiosis, HME (*Ehrlichia chaffeensis*)
08383 Ehrlichiosis (*Ehrlichia ewingii*)
08384 Ehrlichiosis/Anaplasmosis, Undetermined

[Paper case report form](#) required
No Merlin extended data

-  Acute and convalescent sera and whole blood for all cases should be sent to the Bureau of Public Health Laboratories (unless already PCR-positive)

Background

Anaplasmosis and ehrlichiosis are tick-borne illnesses characterized by acute onset of fever with headache, myalgia, nausea, vomiting, rash, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

Anaplasmosis and ehrlichiosis do not result in chronic or persistent infections. Symptoms do not last more than 30 days, even without treatment.

Clinical criteria for case classification

Confirmatory:

Both of the following lasting less than 30 days:

- Acute onset of fever
- **And** one or more of the following: rash, headache, malaise, myalgia, nausea, vomiting, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases.

Presumptive:

Confirmatory clinical criteria in the absence of a more likely diagnosis, as determined by health care provider.

Supportive:

No clinical information available (no medical record or patient interview).

Laboratory criteria for case classification

***Anaplasma phagocytophilum* infection, human granulocytic anaplasmosis (HGA)**

Confirmatory:

One or more of the following:

- Detection of *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR),
- **Or** detection of anaplasma antigen in a biopsy/autopsy specimen by immunohistochemistry (IHC),
- **Or** isolation of *A. phagocytophilum* from a clinical specimen in cell culture,
- **Or** both of the following:
 - Fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by indirect immunofluorescence assay (IFA) in paired serum specimens (one taken in first week of illness and a second 2-4 weeks later)
 - **And** absence of a negative PCR in acute whole blood specimen prior to doxycycline treatment.

Presumptive:

Either of the following:

- Single elevated IgG antibody reactive with *A. phagocytophilum* antigen by IFA, enzyme immunoassay (EIA), dot-EIA, 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.

***Ehrlichia chaffeensis* infection, human monocytic ehrlichiosis (HME)**

Confirmatory:

One or more of the following:

- Detection of *E. chaffeensis* DNA in a clinical specimen via PCR,
- **Or** detection of *E. chaffeensis* antigen in a biopsy or autopsy specimen by IHC,
- **Or** isolation of *E. chaffeensis* from a clinical specimen in cell culture,
- Or both of the following:
 - Fourfold change in IgG-specific antibody titer to *E. chaffeensis* antigen by IFA between paired serum specimens (one taken in first week of illness and a second 2-4 weeks later),
 - **And** absence of a negative PCR in acute whole blood specimen prior to doxycycline treatment.

Presumptive:

Either of the following:

- Single elevated IgG antibody reactive with *E. chaffeensis* antigen by IFA, EIA, dot-EIA, or assays in other formats (CDC uses an IFA IgG cutoff of $>1:64$ 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**

Confirmatory:

E. ewingii DNA detected in a clinical specimen via amplification of a specific target by PCR (note that the organism has never been cultured so antigens are not available).

Human ehrlichiosis/anaplasmosis, undetermined

Presumptive:

Either of the following:

- Both of the following:
 - Identification of morulae in white blood cells by microscopic examination
 - **And** absence of PCR, IHC, cell culture, and IFA testing
- **Or** all of the following:
 - *Ehrlichia* and *Anaplasma* IgG titers that are the same value,
 - **And** absence of PCR, and the geographic location of exposure includes areas where both *Ehrlichia* and *Anaplasma* are present,
 - **And** *Anaplasma* and *Ehrlichia* are present in geographic area of exposure.

Epidemiological criteria for case classification

Exposure is defined as having been in potential tick habitats within the 14 days before onset of symptoms. A history of a tick bite is not required.

Case classification

Confirmed:

A person with confirmatory clinical criteria, confirmatory laboratory criteria, and epidemiological criteria.

Probable:

A person with presumptive clinical criteria, presumptive laboratory criteria, and epidemiological criteria.

Suspect:

A person with confirmatory or presumptive laboratory criteria but no clinical information available.

Criteria to distinguish a new case from previous reports

Not applicable.

Comments

There are at least three intracellular species of bacteria responsible for anaplasmosis/ehrlichiosis in the U.S.: *A. phagocytophilum*, *E. chaffeensis* (found primarily in monocytes), and *E. 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.

Cases reported undetermined ehrlichiosis/anaplasmosis 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, IHC, 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 (equivalent IFA antibody titers) via other explanations.

Current commercially available EIA 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.

Anaplasma, *Ehrlichia*, and *Rickettsia* serologies can cross-react, resulting in false positives. Confirmatory testing and epidemiologic investigation can help determine the causative agent.

PCRs for *A. phagocytophilum* and *E. chaffeensis* may be negative with an acute infection if the specimen was collected after doxycycline treatment was given. This would be considered a false negative and serology testing is recommended. If PCR is negative in an acute whole blood specimen prior to doxycycline treatment, this would negate positive serology results.