Ehrlichiosis/Anaplasmosis

Merlin disease code=08381 Anaplasmosis, HGA (A. phagocytophilum)
Merlin disease code=08382 Ehrlichiosis, HME (E. chaffeensis)
Merlin disease code=08383 Ehrlichiosis (E. ewingii)
Merlin disease code=08384 Ehrlichiosis/Anaplasmosis, Undetermined
Case report form (CRF): Tick-Borne Rickettsial Disease CRF
PAPER CRF REQUIRED

Background
A tick-borne illness 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.

Clinical criteria for case classification
Both of the following:
• Acute onset of fever
• And one or more of the following:
  o Rash,
  o Or headache,
  o Or malaise,
  o Or myalgia,
  o Or nausea,
  o Or vomiting,
  o Or anemia,
  o Or leukopenia,
  o Or thrombocytopenia,
  o Or elevated hepatic transaminases.

Laboratory criteria for case classification

*Ehrlichia chaffeensis* infection, human monocytic ehrlichiosis (HME)
Confirmatory:
One or more of the following:
• Serological evidence of a fourfold change in IgG-specific antibody titer to *E. chaffeensis* antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (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 polymerase chain reaction (PCR),
• Or demonstration of *E. chaffeensis* antigen in a biopsy or autopsy specimen by immunohistochemistry (IHC),
• Or isolation of *E. chaffeensis* from a clinical specimen in cell culture.

Presumptive:
Single elevated IgG antibody reactive with *E. chaffeensis* antigen by IFA, enzyme immunoassay (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).

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

**Confirmatory:**
One or more of the following:
- Serological evidence of a fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by IFA in paired serum specimens (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 PCR,
- Or demonstration of anaplasmal antigen in a biopsy/autopsy specimen by IHC,
- Or isolation of *A. phagocytophilum* from a clinical specimen in cell culture.

**Presumptive:**
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 ≥1:64 and does not use IgM test results independently as diagnostic support criteria).

**Human ehrlichiosis/anaplasmosis, undetermined**

**Presumptive:**
Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination.

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**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 clinically compatible illness in a person with confirmatory laboratory evidence.

**Probable:**
A clinically compatible illness in a person with presumptive laboratory evidence.

**Suspect:**
A person with confirmatory or presumptive laboratory evidence but no clinical information available.

For ehrlichiosis/anaplasmosis undetermined, cases 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 place it definitively 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 evidence.

**Criteria to distinguish a new case from previous reports**

Not applicable.

**Comments**

There are at least three species of bacteria, all intracellular, responsible for ehrlichiosis/anaplasmosis in the U.S.: *E. chaffeensis* (found primarily in monocytes), *A. phagocytophilum*, 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.
Four sub-categories of confirmed or probable ehrlichiosis/anaplasmosis should be reported: 1) human ehrlichiosis caused by *E. chaffeensis*, 2) human ehrlichiosis caused by *E. ewingii*, 3) human anaplasmosis caused by *A. phagocytophilum*, or 4) human ehrlichiosis/anaplasmosis, undetermined. Cases reported in the undetermined 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, 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.

✉️ **Acute and convalescent sera from reported and suspect cases should be acquired on all cases and sent to the Bureau of Public Health Laboratories.**

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