

## Ehrlichiosis/Anaplasmosis

Merlin reporting code = 08381 Ehrlichiosis/Anaplasmosis, HGE, *A. phagocytophilum*  
 = 08382 Ehrlichiosis/Anaplasmosis, HME, *E. chaffeensis*  
 = 08383 Ehrlichiosis/Anaplasmosis, *E. ewingii*  
 = 08384 Ehrlichiosis/Anaplasmosis, Undetermined

Case report form (CRF): [Tick-Borne Rickettsial Disease CRF](#)

**PAPER CRF REQUIRED**

### Clinical description

A tick-borne illness characterized by acute onset of fever and one or more of the following symptoms or signs: headache, myalgia, anemia, leukopenia, thrombocytopenia, elevated hepatic transaminases, nausea, vomiting, or rash. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

### Laboratory criteria for case classification

For the purposes of surveillance,

#### 1. *Ehrlichia chaffeensis* infection (formerly included in the category human monocytic ehrlichiosis [HME]):

##### Confirmatory:

- Serological evidence of a fourfold change in 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 polymerase chain reaction (PCR),

OR

- Demonstration of *E. chaffeensis* antigen in a biopsy or autopsy sample 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-linked immunosorbent assay (ELISA), dot-ELISA, 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).

#### 2. *Ehrlichia ewingii* infection (formerly included in the category Ehrlichiosis [unspecified, or other agent]):

##### Confirmatory:

- Because the organism has never been cultured, antigens are not available. Thus, *E. 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 PCR.

#### 3. *Anaplasma phagocytophilum* infection (formerly included in the category human granulocytic ehrlichiosis [HGE]):

##### Confirmatory:

- Serological evidence of a fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by 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 PCR,
- OR
- Demonstration of anaplasma antigen in a biopsy/autopsy sample 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-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).

**4. Human ehrlichiosis/anaplasmosis, undetermined:**

Presumptive:

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

**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. 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 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.

Suspect:

A person presumptive laboratory evidence but no clinical information available.

**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 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,

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 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.

 **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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