



Communicable Disease Case Reporting and Investigation Protocol **ANAPLASMOSIS**

I. IDENTIFICATION AND DEFINITION OF CASES

- A. **Clinical Description:** Human anaplasmosis is a tickborne illness caused by the rickettsial bacterium *Anaplasma phagocytophilum*. *A. phagocytophilum*, previously referred to as human granulocytic ehrlichiosis (HGE), is the only species in the genus *Anaplasma* that is known to cause disease in humans. Anaplasmosis is transmitted by *Ixodes scapularis* (commonly known as the deer or blacklegged tick) and is the second most reported tickborne disease in Wisconsin after Lyme disease.

Initial signs and symptoms for anaplasmosis generally include acute onset of fever, sweats, chills, headache, fatigue, and muscle aches. Other less common signs and symptoms may include nausea, vomiting, diarrhea, cough, joint pains, confusion, rigors, and rash. Some individuals may only experience very mild symptoms or remain asymptomatic. Clinical laboratory findings may include thrombocytopenia, leukopenia, anemia, and elevated liver enzymes. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

B. Laboratory Criteria:

- **Confirmatory laboratory evidence includes at least one of the following:**
 - a. Detection of DNA from *A. phagocytophilum* species by polymerase chain reaction (PCR) assay performed in EDTA whole blood.
 - b. Fourfold change in IgG antibody titer to antigen from *A. phagocytophilum* by indirect immunofluorescence assay (IFA) between paired serum samples (with the first collected within one week of illness onset and the second collected two to four weeks later).
 - c. Immunohistochemical (IHC) detection of antigens from *A. phagocytophilum* in a skin biopsy or autopsy sample.
 - d. Isolation of *A. phagocytophilum* from a clinical specimen in cell culture.
- **Supportive laboratory evidence includes at least one of the following:**
 - a. Serological evidence of elevated IgG (IgM antibody titer is not used independently) to *A. phagocytophilum* by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays in other format.
 - b. Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination.

NOTE: Clinical signs of disease caused by *A. phagocytophilum* are similar to those caused by *Ehrlichia species*; therefore, it is important to perform testing for all ehrlichiosis- and anaplasmosis-causing agents.

Current commercially available ELISA tests cannot evaluate changes in antibody titers. IFA serology is the most common testing employed by commercial laboratories for the detection of *A. phagocytophilum*. PCR testing is the best method for determining a diagnosis between all the rickettsial agents because it is more specific, sensitive, and does not cross-react. When performing PCR testing, an EDTA blood sample should be collected before the patient has been treated with antibiotics. Biopsy or autopsy specimens should be collected when performing IHC testing.

Serology testing (IFA) requires a fourfold titer change between two serum samples for confirmation of results. The first sample should be collected within one week of illness onset, and the second sample two to four weeks later. CDC uses an IFA IgG titer cutoff of $\geq 1:64$ as positive, but other laboratories may have their own positive cutoff. CDC does not use IgM test results independently because IgM tests may be unreliable as they lack specificity and can persist for a long time. When sera demonstrate elevated antibody responses to both *Ehrlichia* and *Anaplasma* species, the agent with the higher antibody response (at least fourfold) should be the disease agent reported. In cases where an elevated antibody response is demonstrated to both *Ehrlichia* and *Anaplasma* species, and a fourfold difference is *not* established, cases should be classified as ehrlichiosis/anaplasmosis, undetermined.

C. Wisconsin Surveillance Case Definition:

Two categories of anaplasmosis should be reported for the purpose of surveillance:

1. Anaplasmosis, *A. phagocytophilum* infection: Most currently referred to as human anaplasmosis (HA), and formerly called human granulocytic ehrlichiosis (HGE).
2. Ehrlichiosis/anaplasmosis, undetermined, which includes:
 - a. Case-patients with test results demonstrating cross-reactivity or possible dual infection with *A. phagocytophilum* and at least one *Ehrlichia* species bacterium (cases with serology results that have equivalent titers or less than a fourfold difference in titers between at least two different species, and that are unable to be resolved by further testing).
 - b. Case-patients infected with novel species that have not been classified.

Clinically compatible illness: Any reported fever and one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation. All positive (IgG titer $\geq 1:64$) laboratory results need to be accompanied with the patient's clinical information to determine case status as listed below:

- **Confirmed:** A clinically compatible illness that is laboratory confirmed for one of the two disease categories above.
- **Probable:** A clinically compatible illness that has supportive laboratory results for one of the two disease categories above.
- **Suspect:** A positive laboratory result without any clinical information (no follow-up information).

Note: If equivalent titers are present for both *Anaplasma* and *Ehrlichia* and patient meets compatible clinical symptoms, it can be classified as probable ehrlichiosis/anaplasmosis, undetermined.

II. REPORTING

- A. **Wisconsin Disease Surveillance Category II — Methods for Reporting:** This disease shall be reported to the patient's local health officer or to the local health officer's designee within 72 hours of recognition of a case or suspected case, per Wis. Admin. Code § [DHS 145.04\(3\)\(b\)](#). Report electronically through the Wisconsin Electronic Disease Surveillance System (WEDSS), or mail or fax a completed [Acute and Communicable Disease Case Report](#) (form [F-44151](#)) to the address on the form.
- B. **Responsibility for Reporting:** According to Wis. Admin. Code § [DHS 145.04\(1\)](#), persons licensed under Wis. Stat. ch. [441](#) or [448](#), laboratories, health care facilities, teachers, principals, or nurses serving a school or day care center, and any person who knows or suspects that a person has a communicable disease identified in [Appendix A](#).
- C. **Clinical Criteria for Reporting:** Any reported fever and one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation. All positive (IgG titer $\geq 1:64$) laboratory results need to be accompanied with the patient's clinical information to determine case status as described in the surveillance case definitions above.
- D. **Laboratory Criteria for Reporting:** Confirmatory or supportive laboratory findings.

III. CASE INVESTIGATION

- A. **Responsibility for case investigation:** It is the responsibility of the local health department to investigate or arrange for investigation of suspected or confirmed cases as soon as is reasonably possible. A case investigation may include information collected by phone, in person, in writing, or through review of medical records or communicable disease report forms, as necessary and appropriate.
- B. **Required Documentation:** Complete the WEDSS disease incident investigation report, including appropriate disease-specific tabs. This may be facilitated by completing the [Wisconsin Tickborne Rickettsial Disease Case Report Worksheet](#) (form [F-00336](#)). Upon completion of investigation, set WEDSS disease incident process status to "Sent to State."

IV. PUBLIC HEALTH INTERVENTIONS AND PREVENTION MEASURES

- A. In accordance with Wis. Admin. Code § [DHS 145.05](#), local public health agencies should follow the methods of control recommended in the current editions of *Control of Communicable Diseases Manual*, edited by David L.

Heymann, published by the American Public Health Association, and the American Academy of Pediatrics' *Red Book: Report of the Committee on Infectious Diseases*, unless otherwise specified by the state epidemiologist.

- B. Contact providers for clinical signs and symptoms using the [Wisconsin Tickborne Rickettsial Disease Case Report Worksheet](#) for all positive laboratory results.
- C. Once a report is determined as a confirmed or probable case, interview patients for travel history (out of county and out of state) within 30 days from onset of symptoms for exposure risk assessment.
- D. Educate patients as needed on how to reduce the risk of exposure to infected ticks, prevent future infection, and create tick-safe zones around patient's home. Offer [Anaplasmosis fact sheet](#).

V. CONTACTS FOR CONSULTATION

- A. Local health departments and tribal health agencies: <https://www.dhs.wisconsin.gov/lh-depts/index.htm>
- B. Bureau of Communicable Diseases, Communicable Diseases Epidemiology Section, vectorborne epidemiologists: 608-267-9003
- C. Wisconsin State Laboratory of Hygiene: 800-862-1013

VI. RELATED REFERENCES

- A. Heymann DL, ed. Ehrlichiosis. In: *Control of Communicable Diseases Manual*. 20th ed. Washington, DC: American Public Health Association, 2015: 183-186.
- B. Kimberlin DW, ed. *Ehrlichia, Anaplasma, and Related Infections*. In: *Red Book: 2018-2021 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics, 2018: 323-328.
- C. Centers for Disease Control and Prevention Anaplasmosis website: <https://www.cdc.gov/anaplasmosis/index.html>
- D. Centers for Disease Control and Prevention. Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis-United States. *MMWR*. 2016;65:1-44.
- E. Wisconsin Tickborne Rickettsial Disease Case Report Worksheet: <https://www.dhs.wisconsin.gov/forms/f0/f00336.pdf>
- F. Wisconsin Anaplasmosis and Ehrlichiosis Fact Sheet: <https://www.dhs.wisconsin.gov/publications/p4/p42045.pdf>