Communicable Disease Case Reporting and Investigation Protocol

ANAPLASMOSIS/EHRLICHIOSIS

I. IDENTIFICATION AND DEFINITION OF CASES

A. Clinical Description: Human anaplasmosis (HA) and human ehrlichiosis (HE) are two very similar tickborne illnesses caused by two different genera of rickettsial bacteria, *Anaplasma* and *Ehrlichia*, respectively. *Anaplasma phagocytophilum*, which causes the disease previously referred to as human granulocytic ehrlichiosis (HGE), is the only species in the genus *Anaplasma* that is known to cause disease to 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. *Ehrlichia chaffeensis*, which causes the disease previously referred to as human monocytic ehrlichiosis (HME), and *Ehrlichia ewingii* are two separate species in the genus *Ehrlichia* that have been known to cause human ehrlichioses. In 2009, a third species of *Ehrlichia* was identified in Wisconsin and Minnesota. This novel *Ehrlichia* species, referred to as *Ehrlichia muris-like* (EML), genetically resembles the *Ehrlichia muris* species that infects wild mice in Japan.

Initial signs and symptoms for both Anaplasmosis and Ehrlichiosis 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, and elevated liver enzymes. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients. Ehrlichiosis tends to be more severe than Anaplasmosis, more often involving the central nervous system and resulting in life-threatening complications.

B. Laboratory Criteria:

- **Confirmatory laboratory evidence:**
  a. Detection of DNA from an *Anaplasma/Ehrlichia* species by polymerase chain reaction (PCR) assay performed in EDTA whole blood, **OR**
  b. Fourfold change in IgG antibody titer to antigen from an *Anaplasma/Ehrlichia* species 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), **OR**
  c. Immunohistochemical (IHC) detection of antigens from an *Anaplasma/Ehrlichia* species in a skin biopsy or autopsy sample, **OR**
  d. Isolation of an *Anaplasma/Ehrlichia* species from a clinical specimen in cell culture.

- **Supportive laboratory evidence:**
  a. Serological evidence of elevated IgG (IgM antibody titer is not used independently) to an *Anaplasma/Ehrlichia* species by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays in other format, **OR**
  b. Identification of morulae in the cytoplasm of monocytes or macrophages (for Ehrlichiosis) or in neutrophils or eosinophils (for Anaplasmosis) by microscopic examination.

NOTE: Clinical signs of disease caused by these agents are similar; therefore, it is important to perform testing for all 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* and *E. chaffeensis*. There is currently no commercial IFA test available for identification of EML species. The Centers for Disease Control and Prevention (CDC) has developed an in-house IFA serology test specific for detecting EML antibodies. 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/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 (>= 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.

C. **Wisconsin Surveillance Case Definition:**

Four categories of Anaplasmosis/Ehrlichiosis should be reported for the purpose of surveillance:

a. *Anaplasma phagocytophilum* infection: Most currently referred to as human anaplasmosis (HA), was formerly called human granulocytic ehrlichiosis (HGE), OR

b. *Ehrlichia chaffeensis* infection: Formerly known as human monocytic ehrlichiosis (HME), OR

c. *Ehrlichia ewingii* infection: Formerly included in the human ehrlichiosis unspecified category, OR

d. Human anaplasmosis/ehrlichiosis-undetermined: includes

   i. Case-patients with test results demonstrating cross-reactivity or possible dual infection with more than one agent (cases with serology test results that have equivalent titers or less than a fourfold difference in titers between two different species, and that are unable to be resolved by further testing), and

   ii. Case-patients infected with novel species that have not been classified, including EML species.

**Clinically compatible illness:** Any reported fever and one or more of the following: headache, myalgia, anemia, leucopenia, thrombocytopenia, or any hepatic transaminase elevation. All positive (IgG titer >=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 four disease categories above.
- **Probable:** A clinically compatible illness that has supportive laboratory results for one of the four disease categories above.
- **Suspect:** A positive laboratory result without any clinical information (no follow-up information).

**Note:** Because Anaplasmosis is the more common infection in Wisconsin, a single IgG titer of >=1:64 to *A. phagocytophilum* meeting compatible clinical symptoms is classified as probable Anaplasmosis. 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. Since Ehrlichiosis is less common in Wisconsin, it is important to ask about travel history outside of the county of residence and out of state within 30 days of symptom onset for all *Ehrlichia* species detected.

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 (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, leucopenia, thrombocytopenia, or any hepatic transaminase elevation. All positive (IgG titer >=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 (LHD) 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:**
   1. 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 available at the DHS website: [http://www.dhs.wisconsin.gov/forms/f0/f00336.pdf](http://www.dhs.wisconsin.gov/forms/f0/f00336.pdf)
   2. Upon completion of investigation, set WEDSS disease incident process status to “Sent to State.”

IV. **PUBLIC HEALTH INTERVENTIONS AND PREVENTION MEASURES**

   B. Contact providers for clinical signs and symptoms using the *[Wisconsin Tickborne Rickettsial Disease Case Report Worksheet](http://www.dhs.wisconsin.gov/forms/f0/f00336.pdf)* 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 to reduce the risk of exposure to infected ticks, methods to prevent future infection, and how to create tick-safe zones around patient’s home.

V. **CONTACTS FOR CONSULTATION**
   A. Local health departments and tribal health agencies: [https://www.dhs.wisconsin.gov/lh-depts/index.htm](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: 1-800-862-1013

VI. **RELATED REFERENCES**


   C. Centers for Disease Control and Prevention websites:


   E. Wisconsin Tickborne Rickettsial Disease Case Report Worksheet: [https://www.dhs.wisconsin.gov/forms/f0/f00336.pdf](https://www.dhs.wisconsin.gov/forms/f0/f00336.pdf)