



## Communicable Disease Case Reporting and Investigation Protocol **EHRlichiosis**

### I. IDENTIFICATION AND DEFINITION OF CASES

- A. **Clinical Description:** Human ehrlichiosis is a tickborne illness caused by at least three different *Ehrlichia* species of rickettsial bacteria: *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, and *Ehrlichia muris eauclairensis* (formerly *E. muris*-like or EML). Ehrlichiosis caused by *E. chaffeensis* (previously referred to as human monocytic ehrlichiosis or HME) and ehrlichiosis caused by *E. ewingii* are spread by the lone star tick (*Amblyomma americanum*) and are endemic to the southeastern and south-central United States. Ehrlichiosis caused by *E. muris eauclairensis* (EME), however, is transmitted by the blacklegged (deer) tick (*Ixodes scapularis*). EME is an emerging pathogen discovered in 2009, and to date, has only been diagnosed in residents of or travelers to Wisconsin and Minnesota.

Initial signs and symptoms of ehrlichiosis typically present five to 14 days after a tick bite and include acute onset of fever, chills, sweats, headache, myalgia, and fatigue. Other less common signs and symptoms include nausea, vomiting, diarrhea, cough, arthralgia, confusion, rigors, and rash. Some individuals may only experience very mild symptoms or remain asymptomatic. Clinical laboratory findings commonly include thrombocytopenia, leukopenia, mild anemia, and mildly elevated liver enzymes. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes, particularly monocytes, of some patients. Ehrlichiosis may also progress to involve the central nervous system, resulting in life-threatening complications.

#### **Clinical Criteria:**

- **Objective:** fever as reported by patient or health care provider, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation
- **Subjective:** chills/sweats, headache, myalgia, nausea/vomiting, or fatigue/malaise

#### **B. Laboratory Criteria:**

##### **1. Confirmatory laboratory evidence:**

- Detection of *E. chaffeensis*, *E. ewingii*, *E. muris eauclairensis*, unspiciated *Ehrlichia*, or other *Ehrlichia* species (spp.) DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, nucleic acid amplification tests (NAAT), or other molecular testing, **or**
- Serological evidence of a four-fold or greater change in IgG-specific antibody titer to *Ehrlichia* spp., *E. chaffeensis*, or *E. ewingii* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in the first two weeks after illness onset and a second taken two to 10 weeks after acute specimen collection)<sup>1</sup>, **or**
- Demonstration of *Ehrlichia* spp. antigen in a biopsy or autopsy sample by immunohistochemical methods, **or**
- Isolation of *E. chaffeensis*, *E. ewingii*, *E. muris eauclairensis*, unspiciated *Ehrlichia* spp., or other *Ehrlichia* spp. from a clinical specimen in cell culture with molecular confirmation (for example, PCR or sequencing).

##### **2. Presumptive laboratory evidence:**

- Serological evidence of elevated IgG antibody reactive with *Ehrlichia* spp., *E. chaffeensis*, or *E. ewingii* antigen by IFA at a titer  $\geq 1:128$  in a sample taken within 60 days of illness onset, **or**
- Microscopic identification of intracytoplasmic morulae in leukocytes in a sample taken within 60 days of illness onset.

**Note:** IgM test results are not used as confirmatory or presumptive laboratory evidence for case classification. Positive IgG results with a titer  $< 1:128$  (for example, IgG titers equal to 1:64) in a single specimen do not meet laboratory evidence for case classification. A positive IgG titer  $< 1:128$ , however, may be used as one of a paired serum sample to demonstrate a four-fold or greater change in IgG-specific antibody titer.

#### **C. Wisconsin Surveillance Case Definition:**

1. **Confirmed:** For the purpose of surveillance, confirmed ehrlichiosis cases are classified with one of four disease names.
  - **Ehrlichiosis, *E. muris eauclairensis* (EML):** Meets the confirmatory laboratory evidence specific to *E. muris eauclairensis* (through a molecular method such as PCR or sequencing) and has at least one of the objective or subjective clinical criteria.
  - **Ehrlichiosis, *E. chaffeensis*:** Meets the confirmatory laboratory evidence specific to *E. chaffeensis* (through a molecular method such as PCR or sequencing) and has at least one of the objective or subjective clinical criteria.
  - **Ehrlichiosis, *E. ewingii*:** Meets the confirmatory laboratory evidence specific to *E. ewingii* (through a molecular method such as PCR or sequencing) and has at least one of the objective or subjective clinical criteria.
  - **Ehrlichiosis, species undetermined:** Meets the confirmatory laboratory evidence for *Ehrlichia* spp. and has at least one of the objective or subjective clinical criteria.
2. **Probable<sup>2</sup>:** For the purposes of surveillance, all probable ehrlichiosis cases should be reported as **Ehrlichiosis, species undetermined.**
  - Meets presumptive laboratory evidence with fever as reported by the patient or health care provider, and at least one other objective or subjective clinical evidence criterion (excluding chills/sweats); **or**
  - Meets presumptive laboratory evidence without a reported fever, but with chills/sweats **and:**
    - At least one objective clinical evidence criterion; **or**
    - Two other subjective clinical evidence criteria.
3. **Suspect:** Meets confirmatory or presumptive laboratory evidence with no or insufficient clinical information to classify as a confirmed or probable case (for example, a laboratory report only).

<sup>1</sup> A four-fold or greater change in titer is equivalent to a change of at least two dilutions (for example, 1:64 to 1:256, or 1:128 to 1:512). A four-fold rise in titer should not be excluded as confirmatory laboratory evidence if the acute and convalescent specimens are collected within two weeks of one another.

<sup>2</sup> A patient should not be classified with cases of both anaplasmosis and ehrlichiosis based on serologic evidence alone. See III. D for details.

#### D. Criteria to Distinguish a New Case:

Reinfection with *Ehrlichia* is possible, but rare, and individuals with ehrlichiosis may continue to test positive for IgG antibodies years after infection has resolved. Therefore, a person previously reported as a probable or confirmed case may be counted as a new case when there is an episode of new clinically compatible illness with confirmatory laboratory evidence.

## 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:** A clinically compatible disease.
- D. **Laboratory Criteria for Reporting:** Any laboratory test result positive for *Ehrlichia* including intracytoplasmic morulae in leukocytes.

## 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 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. For cases with confirmatory or presumptive laboratory evidence, complete the following sections:
    - The clinical signs and symptoms questions on the lab/clinical tab in WEDSS.
    - The travel history, occupation, outdoor activity, tick exposure, and blood and organ recipient questions on the risk tab in WEDSS.
    - The treatment, and blood and organ donation questions on the intervention tab in WEDSS.
    - For all confirmed cases of **Ehrlichiosis, E. muris eauclairensis (EML)** and confirmed cases of **Ehrlichiosis, species undetermined**, complete the domestic animal exposure and wildlife exposure questions on the risk tab in addition to all the above sections.
  2. Upon completion of investigation, set the WEDSS disease incident process status to “Sent to State.”
- C. **Additional Investigation Responsibilities:** If a patient has a history of blood, blood product, or organ donation in the 30 days before their illness onset, or a history of receipt of blood, blood products, or organs in the 60 days before their illness onset, call Bureau of Communicable Diseases staff within one business day.
- D. **Case Enumeration for Patients with Positive Antibody Results for Both *Anaplasma* and *Ehrlichia* Species:** Clinical signs of disease caused by *Ehrlichia* spp. are similar to those caused by *Anaplasma phagocytophilum*. Additionally, *Anaplasma* and *Ehrlichia* bacteria are closely related genera and antibodies against *Anaplasma* and *Ehrlichia* can cross-react in serologic tests. Many patients suspected of having a tickborne illness are tested using serologic panels that include targets for species in both genera. A patient with positive antibody results for both *Anaplasma* and *Ehrlichia*, for the same disease event, should **not** be classified as cases of both anaplasmosis and ehrlichiosis. Instead, the agent with a four-fold or higher antibody titer compared to the other titer should be the disease agent reported. In cases where an elevated antibody titer is demonstrated against both *Anaplasma* and *Ehrlichia* species, and a four-fold difference is not demonstrated (equivalent titers or titers with only a two-fold difference), case investigators should classify the case as anaplasmosis for surveillance purposes. Anaplasmosis is significantly more common than ehrlichiosis in Wisconsin with approximately 25 times more reports of confirmed anaplasmosis cases compared to confirmed ehrlichiosis cases during 2017–2022.

#### 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 the *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. Because *Ehrlichia* infection can be acquired through blood transfusion or organ transplantation, ascertain whether patient recently received or donated blood or blood products or recently received or donated an organ.
- C. Patient education as needed to minimize future risk of exposure to infected ticks.

#### 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: 608-267-9003
- C. Wisconsin State Laboratory of Hygiene: 1-800-862-1013

## VI. RELATED REFERENCES

- A. Heymann DL, ed. Ehrlichiosis. In: *Control of Communicable Diseases Manual*. 21st ed. Washington, DC: American Public Health Association, 2022: 190-193.
- B. Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Ehrlichia, Anaplasma, and Related Infections. In: *Red Book: 2021-2024 Report of the Committee on Infectious Diseases*. 32nd ed. Itasca, IL: American Academy of Pediatrics, 2021: 308-311.
- C. Wisconsin Department of Health Services website: <https://www.dhs.wisconsin.gov/tick/ehrlichiosis.htm>
- D. Centers for Disease Control and Prevention website: <https://www.cdc.gov/ehrlichiosis/index.html>