

ANAPLASMOSIS/EHRlichIOSIS

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I. IDENTIFICATION

- A. **CLINICAL DESCRIPTION:** Human anaplasmosis (HA) and human ehrlichiosis (HE) are two very similar tick-borne illnesses caused by two different genera of bacteria, *Anaplasma* and *Ehrlichia*, respectively. *Anaplasma phagocytophilum*, 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) ticks and is the second most reported tickborne disease in Wisconsin. *Ehrlichia chaffeensis*, 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 new species of *Ehrlichia* was identified in WI and MN. This novel *Ehrlichia* species referred to as *Ehrlichia muris*-like (EML) genetically resembles the *Ehrlichia muris* species that infects wild mice in Japan.

Historically, ehrlichiosis is less common in Wisconsin because the tick vector (*Amblyomma americanum*, commonly known as the lonestar tick) is usually not found in the state. Since 2008, there has been an increase in reports of probable *E. chaffeensis* cases. One confirmed *E. chaffeensis* case with WI exposure to ticks was reported in 2010. From 2009-2010, the new EML species was identified in eight human cases, two pools of *I. scapularis* ticks, and one white-footed mouse (*Peromyscus leucopus*) in the northwest region of WI. *Ehrlichia ewingii* infections are usually not seen in WI.

Initial signs and symptoms for both infections 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 be 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 infection tends to be more severe than anaplasmosis infections, more often involving the central nervous system and resulting in life-threatening complications.

Four categories of anaplasmosis/ehrlichiosis should be reported for the purpose of surveillance:

- ***Anaplasma phagocytophilum***: most currently referred to as human anaplasmosis (HA), was formerly called human granulocytic ehrlichiosis (HGE), **or**
- ***Ehrlichia chaffeensis***: formerly known as human monocytic ehrlichiosis (HME), **or**
- ***Ehrlichia ewingii***: formerly included in the human ehrlichiosis unspecified category, **or**
- ***Human anaplasmosis/ehrlichiosis - undetermined***: includes
 - 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 four-fold difference in titers between two different species, and that are unable to be resolved by further testing),
 - Case-patients infected with novel species that have not been classified, including EML species.

B. REPORTING CRITERIA: Confirmatory or supportive laboratory findings in an individual with a clinically compatible illness.

C. LABORATORY CRITERIA FOR CONFIRMATION:

Laboratory confirmed:

- Detection of DNA from an *Anaplasma/Ehrlichia* species by polymerase chain reaction (PCR) assay performed in EDTA whole blood, **OR**
- Fourfold change in IgG antibody titer to antigen from an *Anaplasma/Ehrlichia* species by indirect immunofluorescence assay (IFA) between paired serum samples (one collected in the first week of illness and second collected 2-4 weeks later), **OR**
- Immunohistochemical (IHC) detection of antigens from an *Anaplasma/Ehrlichia* species in a skin biopsy or autopsy sample, **OR**
- Isolation of an *Anaplasma/Ehrlichia* species from a clinical specimen in cell culture.

Laboratory supportive (probable):

- 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**
- 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. 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 four-fold titer change between two serum samples for confirmation of results. The first sample should be collected within 1 week of illness onset, and the second sample 2-4 weeks later. CDC uses an IFA IgG titer cutoff ($\geq 1:64$) 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 a four-fold) should be the disease agent reported.

D. WISCONSIN CASE DEFINITION: In 2008, the Wisconsin Division of Public Health adapted the CSTE/CDC Anaplasmosis and Ehrlichiosis 2008 surveillance case definition.

Clinical criteria for the purpose of surveillance:

Any reported fever and one or more of the following: headache, myalgia, anemia, leucopenia, thrombocytopenia, or any hepatic transaminase elevation. All positive (IgG titer $\geq 1:64$)

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laboratory results need to be accompanied with the patient's clinical information to determine case status as listed below:

- **Confirmed anaplasmosis/ehrlichiosis:** A clinically compatible illness that is laboratory confirmed for one of the four disease categories above.
- **Probable anaplasmosis/ehrlichiosis:** A clinically compatible illness that has supportive laboratory results for one of the four disease categories above.
- **Suspect anaplasmosis/ehrlichiosis:** 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 $\geq 1:64$ 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 reported.

II. ACTIONS REQUIRED / PREVENTION MEASURES

A. WISCONSIN DISEASE SURVEILLANCE CATEGORY II:

Report to the patient's local health department either electronically through the Wisconsin Electronic Disease Surveillance System (WEDSS), by mail or fax using an Acute and Communicable Disease Case Report ([F-44151](#)), or by other means within 72 hours upon recognition of a case or suspected case.

B. EPIDEMIOLOGY REPORTS REQUIRED:

- *Electronically* – Report through WEDSS, including appropriate disease-specific tabs
OR
- *Paper Copy* – Acute and Communicable Diseases Case Report ([F-44151](#)) **AND**
The Wisconsin Tickborne Rickettsial Disease Case Report

C. PUBLIC HEALTH INTERVENTIONS:

In accordance with Wisconsin Administrative rule DHS 145.05, local public health should follow the methods of control recommended in the current edition of *Control of Communicable Diseases Manual*, edited by David L. Heymann, published by the American Public Health Association.

- Contact providers for clinical signs and symptoms using the WI Tickborne Rickettsial Disease case report worksheet for all positive laboratory results.
- 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.
- Educate patient 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.

III. CONTACTS FOR CONSULTATION

A. LOCAL HEALTH DEPARTMENT – REGIONAL OFFICES – TRIBAL AGENCIES:

Wisconsin Division of Public Health Communicable Disease Surveillance Guideline

<http://www.dhs.wisconsin.gov/localhealth/index.htm>

- B. BCDER / COMMUNICABLE DISEASE EPIDEMIOLOGY SECTION: Diep (Zip) Hoang Johnson, Vectorborne Coordinator at (608) 267-0249, email: diep.hoangjohnson@wi.gov
- C. WISCONSIN STATE LABORATORY OF HYGIENE: Serology (608) 262-0248

IV. RELATED REFERENCES

- Heymann DL, ed. Ehrlichioses In: *Control of Communicable Diseases Manual*. 19th ed. Washington, DC: American Public Health Association, 2008: 212-215
- Pickering LK, ed. Ehrlichia and Anaplasma Infections. In: *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2009: 284-287
- Centers for Disease Control and Prevention. Nationally notifiable infectious conditions, United States 2010
http://www.cdc.gov/osels/ph_surveillance/nmdss/phs/infdis.htm
- Centers for Disease Control and Prevention. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis- United States. *MMWR*. 2006;55:1-27