

ANAPLASMOSIS, EHRLICHIOSIS - USA: (WISCONSIN, MINNESOTA) ALERT

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Health Advisory: Human Anaplasmosis vs. Human Ehrlichiosis in Minnesota and Wisconsin

Human anaplasmosis (HA) (agent *Anaplasma phagocytophilum*) is the 2nd most frequently reported tick-borne disease in Minnesota and Wisconsin, with recent averages of more than 250 cases reported annually in each state. *A. phagocytophilum* is transmitted by *Ixodes Scapularis* (blacklegged tick or deer tick), which also transmits the agents of Lyme disease [*Borrelia burgdorferi*] and babesiosis [*Babesia microti*].

In recent years, MDH [Minnesota Department of Health] and WDPH [Wisconsin Department of Public Health] have received increasing numbers of positive serologic reports for human ehrlichiosis (HE) (Agent *Ehrlichia chaffeensis*). These reports were unexpected, because the tick vector for HE, *Amblyomma americanum* (Lone Star tick), is uncommon in Minnesota and Wisconsin.

In 2009, Mayo Medical Laboratories detected a new species of *Ehrlichia* DNA in 4 patients (3 from Wisconsin, 1 from Minnesota) using PCR [polymerase chain reaction]. The unique nucleotide sequence is similar to *Ehrlichia muris*, a species not previously identified in North America. These patients infected with the *E. muris*-like agent (EML) presented with a febrile illness; 2 patients had a remote history of prior organ allograft. All recovered with doxycycline treatment.

The EML organism has since been found in some *I. scapularis* ticks in Wisconsin, although it is not known whether this tick serves as a vector. HA, HE, and EML infections cannot be differentiated clinically without diagnostic tests. Some cross-reactivity exists between these organisms on serologic assays, but not enough to reliably substitute one for another. For example, HA patients who are mistakenly tested only for HE using serologic tests may sometimes appear to have negative results (since not all samples will cross-react) and may ultimately be undiagnosed. In addition, some of the recent serologic reports of HE received by the MDH and WDPH may have been due to cross-reactivity with the newly identified EML organism.

Physicians need to understand the tests they are ordering and their limitations. HA tests are still sometimes called a test for "human granulocytic ehrlichiosis" by commercial laboratories, although this

terminology is outdated. Some health care providers also use this terminology and incorrectly order ehrlichiosis tests. When diagnosing HA, health care providers need to make sure the test they order detects *A. phagocytophilum* (or the agent of human granulocytic ehrlichiosis / anaplasmosis).

Since HA is the more common infection in Minnesota and Wisconsin, physicians should routinely order HA tests. However, physicians should consider the potential for locally acquired ehrlichiosis and extend testing to cover *Ehrlichia* species when appropriate.

PCR is considered the gold standard for diagnosing these infections. Currently, Mayo Laboratories offers a PCR test that can differentiate the EML organism from the agents of HA and HE. PCR is most effective when used during the 1st week of illness, and a negative PCR assay should be followed up with an IFA [immunofluorescence assay] test if clinical suspicion warrants.

A specific IFA test has not yet been developed for the EML agent and the degree of cross-reactivity of this agent with HE and HA serologic tests is unknown. Physicians suspecting infection with an *Ehrlichia* species should order serologic tests for both HA and HE. IFA IgG [Immunoglobulin G] antibody tests are preferred because IgM tests may be prone to false positives. To confirm the diagnosis, MDH and WDPH recommend that an acute serum sample should be obtained within the 1st week of illness, followed by a convalescent serum sample obtained 2-4 weeks later. A blood smear may also be conducted on specimens from acutely ill patients.

Currently, the recommended antibiotic treatment of HA, HE, and EML is the same (doxycycline for adults and children), and patients should be treated empirically. A complete course of treatment should be given, even if early diagnostic test results appear negative.

[For inquiries,] please contact MDH Vector-borne Disease Epidemiologists David Neitzel or Melissa Kemperman at (651) 201-5414, or Diep (Zip) Hoang Johnson, WDPH Vector-borne Disease Epidemiologist at (608) 267-9000. Detailed tick-borne disease information and updates are available on the MDH website: <http://www.health.state.mn.us/divs/idepc/dtopics/tickborne/index.html>, WDPH website: <http://dhs.wisconsin.gov/communicable/TickBorne/index.htm>, or CDC website: <http://www.cdc.gov/ticks/index.html>.

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