

EHRlichiosis / ANAPLASMOSIS

(*Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Anaplasma phagocytophilum*; formerly known as: Human Monocytic Ehrlichiosis (HME), Human Granulocytic Anaplasmosis (HGA), Human Granulocytic Ehrlichiosis (HGE), and *Ehrlichia phagocytophilum*)

REPORTING INFORMATION

- **Class B:** Report by the end of the next business day in which the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
 - [Ohio Confidential Reportable Disease form](#) (HEA 3334, rev. 1/09), [Positive Laboratory Findings for Reportable Disease form](#) (HEA 3333, rev. 8/05), the local public health department via the Ohio Disease Reporting System (ODRS), or telephone.
 - The Centers for Disease Control and Prevention (CDC) [Tick-borne Rickettsial Disease Case Report form \(CDC 55.1, rev. 10/09\)](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and sent to the Ohio Department of Health (ODH). The mailing address for this form is: Ohio Department of Health, Zoonotic Disease Program, 35 E. Chestnut St, Columbus, OH 43215.
- Key fields for ODRS reporting include: date of illness onset, fields under the Signs and Symptoms section, fields in the Epidemiology Module and fields in the Travel History module.

AGENTS

Ehrlichia chaffeensis (formerly known as HME)

Anaplasma phagocytophilum, (aka *Ehrlichia equi* or *Ehrlichia phagocytophila*) (formerly known as HGA, HGE)

Ehrlichia ewingii

CASE DEFINITION

Clinical Description

A tick-borne illness characterized by acute onset of fever and one or more of the following symptoms or signs: headache, myalgia, malaise, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases. Nausea, vomiting, or rash may be present in some cases. Intracytoplasmic bacterial aggregates (morulae) may be visible in the leukocytes of some patients.

Laboratory Criteria for Diagnosis

1) ***Ehrlichia chaffeensis* infection** (formerly included in the category Human Monocytic Ehrlichiosis [HME]):

Laboratory confirmed:

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer to *E. chaffeensis* antigen by indirect immunofluorescence assay (IFA) between paired serum samples (one taken in first week of illness and a second 2-4 weeks later), *or*
- Detection of *E. chaffeensis* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, *or*
- Demonstration of ehrlichial antigen in a biopsy or autopsy sample by immunohistochemical methods, *or*
- Isolation of *E. chaffeensis* from a clinical specimen in cell culture.

Laboratory supportive:

- Serological evidence of elevated IgG or IgM antibody reactive with *E. chaffeensis* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or assays in other formats (CDC uses an IFA IgG cutoff of $\geq 1:64$ and does not use IgM test results independently as diagnostic support criteria.), *or*
- Identification of morulae in the cytoplasm of monocytes or macrophages by microscopic examination.

2) ***Ehrlichia ewingii* infection** (formerly included in the category Ehrlichiosis [unspecified, or other agent]):

Laboratory confirmed:

- Because the organism has never been cultured, antigens are not available. Thus, *Ehrlichia ewingii* infections may only be diagnosed by molecular detection methods: *E. ewingii* DNA detected in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay.

3) ***Anaplasma phagocytophilum* infection** (formerly included in the category Human Granulocytic Ehrlichiosis [HGE]):

Laboratory confirmed:

- Serological evidence of a fourfold change in IgG-specific antibody titer to *A. phagocytophilum* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in first week of illness and a second 2-4 weeks later), *or*
- Detection of *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, *or*
- Demonstration of anaplasma antigen in a biopsy/autopsy sample by immunohistochemical methods, *or*
- Isolation of *A. phagocytophilum* from a clinical specimen in cell culture.

Laboratory supportive:

- Serological evidence of elevated IgG or IgM antibody reactive with *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent Assay (ELISA), dot-ELISA, or assays in other formats (CDC uses an IFA IgG cutoff of $\geq 1:64$ and does not use IgM test results independently as diagnostic support criteria.), *or*
- Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination.

4.) **Human ehrlichiosis/anaplasmosis – undetermined**

- See case classification

Case Classification

Confirmed: A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.

Probable: A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results. For ehrlichiosis/anaplasmosis – an undetermined case can only be classified as probable. This occurs when a case has compatible clinical criteria with laboratory evidence to support ehrlichia/anaplasma infection, but not with sufficient clarity to definitively place it in one of the categories previously described. This may include the identification of morulae in white cells by microscopic examination in the absence of other supportive laboratory results.

Suspect: A case with laboratory evidence of past or present infection but no clinical information available (e.g. a laboratory report).

Comments

There are at least three species of bacteria, all intracellular, responsible for ehrlichiosis/ anaplasmosis in the United States: *Ehrlichia chaffeensis*, found primarily in monocytes, and *Anaplasma phagocytophilum* and *Ehrlichia ewingii*, found primarily in granulocytes. The clinical signs of disease that result from infection with these agents are similar, and the range distributions of the agents overlap, so testing for one or more species may be indicated. Serologic cross-reactions may occur among tests for these etiologic agents.

Four sub-categories of confirmed or probable ehrlichiosis/anaplasmosis should be reported: 1) human ehrlichiosis caused by *Ehrlichia chaffeensis*, 2) human ehrlichiosis caused by *E. ewingii*, 3) human anaplasmosis caused by *Anaplasma phagocytophilum*, or 4) human ehrlichiosis/anaplasmosis - undetermined. Cases reported in the fourth sub-category can only be reported as "probable" because the cases are only weakly supported by ambiguous laboratory test results. Problem cases for which sera demonstrate elevated antibody IFA responses to more than a single infectious agent are usually resolvable by comparing the levels of the antibody responses, the greater antibody response generally being that directed at the actual agent involved. Tests of additional sera and further evaluation via the use of PCR, IHC, and isolation via cell culture may be needed for further clarification.

Cases involving persons infected with more than a single etiologic agent, while possible, are extremely rare and every effort should be undertaken to resolve cases that appear as such (equivalent IFA antibody titers) via other explanations. Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. Furthermore, IgM tests are not always specific and the IgM response may be persistent. Therefore, IgM tests are not strongly supported for use in serodiagnosis of acute disease.

SIGNS AND SYMPTOMS

Any reported fever and one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation. Other symptoms include nausea, vomiting, or rash.

DIAGNOSIS

Testing is not currently available at the ODH Laboratory. Proper protocol is to send the sample(s) to CDC through the ODH Laboratory (ODHL). Call ODHL, 1-888-ODH-LABS (888-634-5227) select option #2- Microbiology, to arrange for shipment of specimens to CDC.

EPIDEMIOLOGY

Source

There are various mammals which serve as reservoirs for the vector ticks, including: deer, elk, wild rodents and dogs.

Occurrence

Found primarily in the South and Mid-Atlantic, North/South Central United States, and isolated areas of New England, *E. chaffeensis* is transmitted principally by the Lone Star tick, *Amblyomma americanum*. The case fatality rate is between 2% and 3%.

A. phagocytophilum is more likely to be found in the New England, North Central and Pacific States, and appears to be transmitted by the blacklegged ticks, *Ixodes scapularis* and *Ixodes pacificus*. The case fatality rate is less than 1%.

Found primarily in the South Atlantic and South Central United States with isolated areas of New England, *E. ewingii* appears to be transmitted by the Lone Star tick, *Amblyomma americanum*. No documented fatalities have been reported to the CDC.

Mode of Transmission

Humans contract Ehrlichiosis/Anaplasmosis through the bite of an infected tick.

Period of Communicability

Humans are dead-end hosts, not being able to infect ticks or other humans.

Incubation Period

The incubation period appears to be 5-14 days for *Ehrlichia chaffeensis* infection and *E. ewingii* infection and 5-21 days for *Anaplasma phagocytophilum* infection after being bitten by an infected tick.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

A history of the patient's travel and contact with ticks is obtained for the two to three weeks prior to onset. Outdoor occupational or recreational activities by the patient during April-September may provide additional information.

Treatment

Appropriate antibiotic treatment should be initiated immediately when there is a strong suspicion of ehrlichiosis through clinical and epidemiological findings. Fever generally subsides within 24-72 hours after treatment with doxycycline or other tetracyclines. In fact, failure to rapidly respond to a tetracycline antibiotic argues against a diagnosis of ehrlichiosis. **Treatment should not be delayed until laboratory confirmation is obtained.** Treatment with doxycycline or other tetracyclines is recommended for a minimal total course of 5-7 days. Patients with anaplasmosis should be treated with doxycycline for 10-14 days to provide appropriate length of therapy for possible incubating coinfection with Lyme disease.

Isolation and Follow-up Specimens

Isolation is not indicated. Convalescent specimens can be collected about 2 weeks after the acute samples and should be tested together at the same laboratory to determine a change in titer.

Contacts

Preventive and/or prophylactic treatment is not warranted. There is no vaccine for ehrlichiosis.

Prevention and Control

Community education and awareness activities should include methods used for personal protection from tick bites, reducing tick contacts, proper personal inspection and tick removal techniques, and measures that will reduce tick populations on individual properties.

What is ehrlichiosis/anaplasmosis?

Ehrlichiosis and anaplasmosis are bacterial diseases that are spread by ticks. In Ohio, *Ehrlichia chaffeensis* and *E. ewingii* are transmitted by the Lone Star tick, which is most commonly found in the southern and southeastern counties of Ohio. *Anaplasma phagocytophilia* is transmitted by the Black-legged tick which has been reported primarily from eastern and southern counties of Ohio. There are several types of ehrlichiosis that affect humans.

Who is most at risk for getting ehrlichiosis/anaplasmosis?

People who spend time in the outdoors in tick-infested environments especially woodlands and brushy areas, are at an increased risk of exposure. Dogs or other pets that frequent these types of areas may also bring infected ticks home. A few human cases of anaplasmosis and ehrlichiosis originate in Ohio each year.

How is ehrlichiosis/anaplasmosis spread?

Ehrlichiosis/anaplasmosis is acquired by the bite of an infected tick. It takes several hours of attachment for transmission of infectious organisms to occur. When a person has contact with fluids from ticks, usually as a result of crushing or improper tick removal, disease transmission may also occur. Transmission does not occur directly from person to person.

How is ehrlichiosis/anaplasmosis diagnosed?

Ehrlichiosis/anaplasmosis is diagnosed by a physician based on clinical symptoms and blood tests for antibody levels.

What are the symptoms of ehrlichiosis/anaplasmosis?

The symptoms of both *E. chaffeensis* and *A. phagocytophilia* infection are identical. Patients experience headache, fever, malaise, muscle aches, chills, sweating, nausea and vomiting. Less common symptoms include cough, joint ache, confusion and a rash anywhere on the body. Rash is more common in young patients. Severe signs of the disease may include prolonged fever, kidney failure, blood clotting disorders, respiratory distress, seizures, or coma. Death occurs in less than 3% of the cases. Symptoms of *E. ewingii* infection are similar, but no documented fatalities have been reported in the USA.

How soon do symptoms occur?

The early symptoms usually occur 5 to 11 days after the tick bite. Other symptoms may occur as late as 21 days after the tick bite.

What is the treatment for ehrlichiosis/anaplasmosis?

The disease is treated with antibiotics in the tetracycline group, administered either orally or by injection.

What can be done to prevent ehrlichiosis/anaplasmosis?

If you are in areas where ticks might be present, the following precautions can reduce the risk of acquiring ehrlichiosis or other tick-borne diseases:

- Wear light-colored, long pants, tuck pant cuffs into sock tops and spray pant legs and socks with insect repellent. Repellents containing 0.5% permethrin or 20-30% DEET are effective in repelling ticks. Follow application directions carefully.
- When possible, avoid walking in tall grass and weeds.
- Conduct visual "tick checks" on yourself and children every hour or two.
- Check pets for ticks before allowing them into the home.
- Carefully remove attached ticks as soon as possible.
- Keep yard and play areas well mowed to discourage ticks.

How should a tick be removed?

Since disease transmission occurs within hours of attachment, it is important to remove ticks as soon as possible after discovery.

To remove an attached tick, grasp it with tweezers as close as possible to the skin and pull with firm, steady pressure straight out. Do not twist or jerk the tick, as the mouthparts may break off. If tweezers are not available, protect fingers with rubber gloves or tissue paper.

- Do not handle ticks with bare hands.
- Do not squeeze, crush or puncture the body of the tick as it may contain infected fluids.
- After removing the tick, thoroughly disinfect the bite site and wash your hands.
- See or call your doctor if there is a concern about incomplete tick removal.

For more information, contact your local health department or the Zoonotic Disease Program at ODH by calling 614-752-1029.

For more information please visit these websites.

CDC Ehrlichiosis webpage - <http://www.cdc.gov/ehrlichiosis/>

CDC Anaplasmosis webpage - <http://www.cdc.gov/anaplasmosis/>

ODH Zoonotic Disease Program Tick-borne Diseases (statistics and educational materials) - <http://www.odh.ohio.gov/odhPrograms/dis/zoonoses/vbdp/vbtick.aspx>