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:**
  - The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the [Ohio Confidential Reportable Disease Form](#) (HEA 3334).
  - 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 the form should be uploaded under the Administration module in ODRS.
- 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**

**Clinical presentation:** 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.

**Clinical evidence:** Any reported fever and one or more of the following: headache, myalgia, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation.

**Exposure**

History of having been in potential tick habitat in the 14 days prior to the onset of illness or history of tick bite.

**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 ≥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, *E. 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 anaplasmal 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 ≥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**

- **Suspected**: A case with laboratory evidence of past or present infection but no clinical information available (e.g. a laboratory report).
**Probable:** A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results. An undetermined ehrlichiosis/anaplasmosis case can only be classified as probable. This occurs when a case has compatible clinical criteria with laboratory evidence to support *Ehrlichia* or *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.

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

*This case classification can be used for initial reporting purposes to ODH as CDC has not developed a classification.*

**Comments**

There are at least three species of bacteria, all intracellular, responsible for ehrlichiosis and anaplasmosis in the United States: *E. chaffeensis*, found primarily in monocytes, and *E. ewingii* and *A. phagocytophilum*, 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 and anaplasmosis should be reported: 1) human ehrlichiosis caused by *E. chaffeensis*, 2) human ehrlichiosis caused by *E. ewingii*, 3) human anaplasmosis caused by *A. 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, immunohistochemistry, 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, malaise, chills, confusion, conjunctival injection (red eyes), anemia, confusion, leukopenia, thrombocytopenia, or any hepatic transaminase elevation. Other symptoms include nausea, vomiting, diarrhea or rash.
Comment
Skin rash is not considered a common feature of ehrlichiosis and should not be used to rule in or rule out an infection. *E. chaffeensis* infection can cause a rash in up to 60% of children but is reported in fewer than 30% of adults. Rash is not commonly reported in patients infected with *E. ewingii*. The rash associated with *E. chaffeensis* infection may range from maculopapular to petechial in nature and is usually not pruritic (itchy). The rash usually spares the face, but in some cases may spread to the palms and soles. A type of rash called erythroderma may develop in some patients. Erythroderma is a type of rash that resembles sunburn and consists of widespread reddening of the skin that may peel after several days. Some patients may develop a rash that resembles the rash of Rocky Mountain spotted fever making these two diseases difficult to differentiate on the basis of clinical signs alone.

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 ODH Zoonotic Disease Program, 614-752-1029, 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* and *E. ewingii* are transmitted principally by the lone star tick, *Amblyomma americanum*. The white-tailed deer is a major host of all stages of lone star ticks and an important natural reservoir for *E. chaffeensis* and *E. ewingii*. Lone star ticks are among the most commonly encountered ticks in the southeastern United States. The case fatality rate is between 2% and 3% for *E. chaffeensis*. No documented fatalities from *E. ewingii* have been reported to the CDC.

*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 *Ix. pacificus*. The case fatality rate is less than 1%.

Mode of Transmission
Humans contract ehrlichiosis or anaplasmosis through the bite of an infected tick. In rare cases, *A. phagocytophilum* as well as *Ehrlichia* species can be transmitted through blood transfusions. These bacteria have been shown to survive for more than a week in refrigerated blood. Patients who develop ehrlichiosis or anaplasmosis within a month of receiving a blood transfusion or solid organ transplant should be reported to the Ohio Department of Health for prompt investigation.

Period of Communicability
There is no evidence of direct person to person transmission.

Incubation Period
The incubation period appears to be 5-14 days for *E. chaffeensis* infection and *E. ewingii* infection and 5-21 days for *A. 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

Doxycycline is the first line of treatment for adults and children of all ages and should be initiated immediately whenever ehrlichiosis or anaplasmosis is suspected. Appropriate antibiotic treatment (doxycycline or other tetracyclines) should be initiated immediately when there is a strong suspicion of ehrlichiosis or anaplasmosis through clinical and epidemiological findings. If a patient is treated within the first 5 days of the disease, fever generally subsides within 24-72 hours. In fact, failure to rapidly respond to a doxycycline argues against a diagnosis of ehrlichiosis or anaplasmosis. Treatment should not be delayed until laboratory confirmation is obtained. Patients with ehrlichiosis or anaplasmosis should be treated with doxycycline for at least 3 days after the fever subsides and until there is evidence of clinical improvement. Standard duration of treatment for anaplasmosis is 10 to 14 days. Standard duration of treatment for ehrlichiosis is 5-7 days. Some patients may continue to experience headache, weakness and malaise for weeks after adequate treatment.

The use of doxycycline to treat suspected ehrlichiosis or anaplasmosis in children is standard practice recommended by both CDC and the AAP Committee on Infectious Diseases. Unlike older generations of tetracyclines, the recommended dose and duration of medication needed to treat ehrlichiosis or anaplasmosis has not been shown to cause staining of permanent teeth, even when five courses are given before the age of eight. Healthcare providers should use doxycycline as the first-line treatment for suspected ehrlichiosis or anaplasmosis in patients of all ages.

Isolation and Follow-up Specimens

Isolation is not indicated. Convalescent specimens can be collected 2 to 4 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 or anaplasmosis.

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.

Vector Investigation

For advice on vector assessment, contact the ODH Zoonotic Disease Program (ZDP) at (614) 752-1029, option 1.
Tick Bite Avoidance

The best way to prevent ehrlichiosis and anaplasmosis infection is to avoid tick bites. Prevention tips are similar to those for other diseases transmitted by ticks, such as Lyme disease or Rocky Mountain spotted fever:

- Avoid direct contact with ticks by avoiding woody or busy areas with high grass and leaf litter and walking in the center of trails.
- Use insect repellent registered with the U.S. Environmental Protection Agency (EPA) on exposed skin. Always follow the directions on the package. When using both sunscreen and insect repellent, apply the sunscreen first then the repellent.
- Wear long sleeves, pants and socks if feasible.
- Wear permethrin-treated clothing to repel and kill ticks.
- Bathe or shower as soon as possible after coming indoors (preferably within two hours) to wash off and more easily find ticks that are crawling on you.
- Conduct a full-body tick check using a hand-held or full-length mirror to view all parts of your body upon return from tick-infested areas.
- Examine gear and pets. Ticks can ride into the home on clothing and pets, then attach to a person later, so carefully examine pets, coats and day packs.
- Tumble clothes in a dryer on high heat for an hour to kill remaining ticks. (Some research suggests that shorter drying times may also be effective, particularly if the clothing is not wet.)
What are ehrlichiosis and anaplasmosis?
Ehrlichiosis and anaplasmosis are bacterial diseases that are spread by ticks. In Ohio, *E. 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 blacklegged tick which has been reported primarily from eastern and southern counties of Ohio, but is likely to occur in suitable wooded, brushy habitats throughout the state.

Who is most at risk for getting ehrlichiosis or 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 areas may also bring infected ticks home. A few human cases of ehrlichiosis and anaplasmosis originate in Ohio each year.

How are ehrlichiosis and anaplasmosis spread?
Ehrlichiosis and anaplasmosis are spread 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 are ehrlichiosis and anaplasmosis diagnosed?
Ehrlichiosis and anaplasmosis are diagnosed by a physician based on clinical symptoms and blood tests.

What are the symptoms of ehrlichiosis and anaplasmosis?
The symptoms of *E. chaffeensis*, *E. ewingii* 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 for *E. chaffeensis* and *A. phagocytophilia*. No documented fatalities have been reported in the USA due to *E. ewingii* infection.

How soon do symptoms occur?
The early symptoms usually occur 5 to 11 days after a bite from an infected tick. Other symptoms may occur as late as 21 days after the tick bite.

What is the treatment for ehrlichiosis and anaplasmosis?
These diseases are treated with antibiotics.

What can be done to prevent ehrlichiosis and anaplasmosis?
If you are in areas where ticks might be present, take the following steps to reduce the risk of ehrlichiosis, anaplasmosis and 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/](http://www.cdc.gov/ehrlichiosis/)

CDC Anaplasmosis webpage - [http://www.cdc.gov/anaplasmosis/](http://www.cdc.gov/anaplasmosis/)

ODH Zoonotic Disease Program Tick-borne Diseases (statistics and educational materials) - [http://www.odh.ohio.gov/ticks](http://www.odh.ohio.gov/ticks)