

Ehrlichiosis & Anaplasmosis

Surveillance Protocol



Ehrlichiosis and anaplasmosis are tick-borne diseases that are clinically similar but differ by their epidemiology and etiology. These diseases first became reportable in the United States in 1999. In West Virginia, 41 cases of ehrlichiosis were reported between 2011–2020. The first cases (2) of anaplasmosis were reported in West Virginia during 2011. Since then, there have been a total of 13 cases. Due to the relative difficulty of differentiating between these two diseases, there is also a category called ehrlichiosis/anaplasmosis, undetermined. Since 2011, there have been 8 reported cases of this type in West Virginia.

Healthcare Provider Responsibilities

1. Report suspect and confirmed cases of ehrlichiosis and anaplasmosis (including copies of lab results) to the local health department within one week of diagnosis. Supply requested clinical information to the local health department to assist with case ascertainment.
2. Follow recommended testing guidelines for ehrlichiosis and anaplasmosis. The gold standard serologic test is indirect immunofluorescence assay (IFA) using paired serum samples taken 2-4 weeks apart. Polymerase chain reaction (PCR) and microscopic examination of blood smears may also be performed.
3. Early treatment with doxycycline is associated with improved outcomes. See <https://www.cdc.gov/ehrlichiosis/tratment/index.html> for more information.

Laboratory Responsibilities

1. Report positive laboratory results for ehrlichiosis and anaplasmosis to the local health department within one week.

Local Health Responsibilities

1. Conduct an appropriate case investigation.
 - a. Contact the healthcare provider that ordered the laboratory test to obtain the clinical information on the West Virginia Electronic Disease Surveillance System (WVEDSS) form.
 - b. If needed, contact the patient to obtain information regarding tick exposure and/or travel history.
 - c. Educate the patient and the patient's family on ehrlichiosis and anaplasmosis prevention.
 - d. Report all case data using WVEDSS.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



2. Educate the public about ehrlichiosis and anaplasmosis, especially regarding the mode of tick transmission and use of personal protection. Prevention messages for these diseases are also effective for other tick-borne diseases (e.g. Lyme disease).
3. Educate providers and laboratories to report cases of ehrlichiosis and anaplasmosis to the local health department in the patient's county of residence within one week of diagnosis.

State Health Responsibilities

1. Review completed case reports from local health departments within one week.
2. Report all confirmed and probable cases to the Centers for Disease Control and Prevention (CDC) upon confirmation of case status. Complete the supplemental case report form entitled, "Tick-Borne Rickettsial Disease Case Report" and submit to CDC upon confirmation of all confirmed and probable cases.
3. Provide training and consultation to local health departments regarding case ascertainment for ehrlichiosis and anaplasmosis.
4. Disseminate an annual Health Alert Network (HAN) message in early spring to increase awareness about ehrlichiosis and anaplasmosis (and other tick-borne diseases) among healthcare providers and local health departments.
5. Monitor tick vector distribution and density across the state.

Disease Control Objectives

1. Reduce severe complications of disease by educating healthcare providers about the occurrence of ehrlichiosis and anaplasmosis and the importance of initiating early antibiotic treatment based on clinical symptoms and patient history.

Disease Prevention Objectives

1. Reduce disease risk through public education regarding use of personal protective measures.

Disease Surveillance Objectives

1. To identify and monitor the epidemiologic characteristics of ehrlichiosis and anaplasmosis in West Virginia, including the geographic distribution of cases.

Occupational Health

None.

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Surveillance Protocol



Public Health Significance

Ehrlichiosis and anaplasmosis became nationally notifiable in 1999 and are considered emerging infectious diseases. Passive surveillance data demonstrated an increase of *Ehrlichia chaffeensis* cases from 200 in 2000 to 2093 cases in 2019.¹ The number of anaplasmosis cases also increased from 348 cases in 2000 to 5655 cases in 2019.² In addition, a new pathogenic species of *Ehrlichia* was identified in 2009 from 4 patients in Wisconsin and Minnesota. This new species is known as *Ehrlichia muris euclairensis* but are reported under the undetermined ehrlichiosis/anaplasmosis category.

Surveillance for ehrlichiosis and anaplasmosis can help to inform healthcare providers of the seasonality, incidence, and geographic distribution of these diseases. This information can be useful in facilitating appropriate diagnoses and initiating early treatment to help avoid severe complications. Surveillance data can also help identify fewer common routes of transmission including organ transplants, blood transfusions, and perinatal exposure.

Clinical Description

Initial symptoms of ehrlichiosis and anaplasmosis are non-specific and usually begin within 1-2 weeks of a bite from an infected tick. Both diseases are characterized by acute onset of fever, headache, myalgia, and malaise. Common laboratory findings include thrombocytopenia, leukopenia and evidence of hepatic injury.^{3,4} Severe complications of ehrlichiosis include fulminant multi-organ failure, central nervous system involvement (meningitis or meningoencephalitis), and respiratory distress syndrome while anaplasmosis is more commonly associated with peripheral neuropathies.

Diagnosis: The gold standard serologic test for diagnosing ehrlichiosis and anaplasmosis is the indirect immunofluorescence assay performed on paired serum samples taken 3-6 weeks apart. Because of the similarities during presentation, acute and convalescent sera should be obtained and tested for both ehrlichiosis and anaplasmosis.⁵ A summary of options for diagnosis is found in Table 1. Additional testing for other tick-borne diseases, such as spotted fever rickettsiosis, may also be considered since there are similarities in clinical presentation.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol

Table 1. Summary of Diagnostic Options for Ehrlichiosis and Anaplasmosis⁶

Test	Sensitivity	Comments
Paired IgM and IgG using immunofluorescence assay (IFA) at a 2-4-week interval	'Gold standard'	<ul style="list-style-type: none"> Acute specimen is commonly negative High rates of cross-reactivity between <i>Ehrlichia</i> and <i>Anaplasma</i> – test acute and convalescent sera for both pathogens
Blood smear staining for morulae	Low sensitivity	<ul style="list-style-type: none"> Blood smear with Wright or Giemsa stain Sensitivity is highest in the first week of infection Prior treatment reduces sensitivity
Polymerase chain reaction (PCR)	High sensitivity (first week of illness) Low sensitivity (after treatment)	<ul style="list-style-type: none"> Collect blood samples in EDTA or sodium citrate anti-coagulant Prior treatment reduces sensitivity Sole diagnostic option for <i>Ehrlichia ewingii</i>
Culture isolation	Low	<ul style="list-style-type: none"> Prior treatment reduces sensitivity Can be done postmortem
Immunohistochemistry	Low	<ul style="list-style-type: none"> Tissue (biopsy) or bone marrow required Autopsy specimen for post-mortem diagnosis Prior treatment reduces sensitivity Only available at special laboratories

While serologic testing can help confirm ehrlichiosis and anaplasmosis infections, the decision to treat should be based on clinical signs (fever with or without systemic signs), laboratory findings (thrombocytopenia, leukopenia, and elevated serum transaminase levels), and the patient's history (travel to tick-infested area or history of tick bite). Doxycycline is the antibiotic of choice for treatment of ehrlichiosis and anaplasmosis in children and adults. Because doxycycline is most effective at preventing serious complication when initiated early in the course of disease, clinicians should not wait for laboratory test results to begin treatment.

It is important to note that ehrlichiosis has been transmitted through blood transfusion and organ transplant and anaplasmosis has also been transmitted through blood transfusion and perinatal exposure. Therefore, patients with clinically compatible symptoms and laboratory findings but without a possible history of tick exposure should also be considered for ehrlichiosis and anaplasmosis testing.

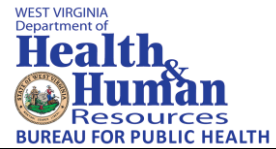
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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



Etiologic Agent

The etiologic agents of ehrlichiosis and anaplasmosis are gram-negative obligate intracellular bacteria. Three *Ehrlichia* species (*E. chaffeensis*, *E. ewingii*, and *E. muris eauclairensis*) and one *Anaplasma* species (*Anaplasma phagocytophilum*) are currently known to infect humans.

Reservoir

The bacteria that cause ehrlichiosis and anaplasmosis are thought to be maintained in nature by mammalian reservoirs. For *E. chaffeensis*, white-tailed deer are an important reservoir.⁷ Goats, dogs, and coyotes have also been found to be naturally infected with this bacterium. For *E. ewingii*, less is known about its ecological features, however, dogs and deer have been found to be naturally infected with this bacterium. White-footed mice (*Peromyscus leocopus*) are a competent reservoir for *E. muris eauclairensis* and mammalian host for its tick vector.⁸ Small mammals, such as the white-footed mouse, have shown been shown to be competent reservoir for *A. phagocytophilum*; however, other wild mammals may also be important reservoirs.⁹

Mode of Transmission

Ehrlichiosis and anaplasmosis are tick-borne diseases primarily transmitted to humans through the bite of an infected tick. Adult and nymphal ticks transmit these diseases. The lone star tick (*Amblyomma americanum*) is responsible for transmitting ehrlichiosis; the black-legged tick (*Ixodes scapularis*) and the western black-legged tick (*I. pacificus*) are responsible for transmitting anaplasmosis.

Transmission has also occurred through blood transfusions for anaplasmosis and is thought to be possible for ehrlichiosis. Patients have been infected with ehrlichiosis (*Ehrlichia chaffeensis*) through organ transplants. Perinatal transmission of anaplasmosis has also been documented.

Incubation Period

The incubation period is generally 1 to 2 weeks following a bite from an infected tick.

Period of Communicability

Person-to-person transmission usually does not occur. Humans are considered incidental hosts.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



Outbreak Recognition

There is a low likelihood of outbreaks occurring due to ehrlichiosis and anaplasmosis; however, outbreaks of ehrlichiosis and anaplasmosis could potentially occur by transfusion or transplantation of contaminated blood products. Patients who develop ehrlichiosis or anaplasmosis within one month of a blood transfusion or solid organ transplant should be reported to the Division of Infectious Disease Epidemiology (DIDE). Additionally, community outbreaks may occur if people are exposed to infected ticks in a localized geographic area. For example, in 1989, an outbreak of ehrlichiosis was reported among members of an army reserve unit who trained together in a distinct geographic area where ticks were common.¹⁰

Case Definition

The 2008 case definition is the most current version (CSTE Position Statement Number: 09-ID-15).

Subtypes

Ehrlichia chaffeensis infection (formerly Human Monocytic Ehrlichiosis [HME])

Ehrlichia ewingii infection (formerly Ehrlichiosis [unspecified or other agent])

Anaplasma phagocytophilum infection (formerly Human Granulocytic Ehrlichiosis [HGE])

Ehrlichiosis/Anaplasmosis, human, undetermined

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, history of tick bite, or recent blood transfusion from potential case.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol

Epidemiological Evidence for Transfusion Transmission

For the purposes of surveillance, epidemiologic linkage between a transfusion recipient and a blood donor is demonstrated if all the following criteria are met:

1. In the transfusion or organ recipient:
 - A. Received an organ transplant or one or more blood transfusions (plasma, red blood cell (RBC) or platelet transfusions) within one year before the collection date of a specimen with laboratory evidence of *Ehrlichia* or *Anaplasma* infection; and
 - B. At least one of these transfused blood components was donated by the donor described below; and
 - C. Transfusion-associated infection is considered at least as plausible as tick-borne transmission; and
2. In the donor:
 - A. Donated an organ or blood (plasma, RBC, or platelet components) that was transfused into the above recipient; and
 - B. The plausibility that this blood component was the source of the infection in the recipient is considered equal to or greater than that of blood from other involved donors (more than one plausible donor may be linked to the same recipient).

Ehrlichia chaffeensis: (formerly Human Monocytic Ehrlichiosis [HME])

Laboratory criteria for diagnosis

Supportive:

1. Serological evidence of elevated immunoglobulin G (IgG) or immunoglobulin M (IgM) antibody reactive with *E. chaffeensis* antigen by immunofluorescence assay (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
2. Identification of morulae in the cytoplasm of monocytes or macrophages by microscopic examination.

Confirmed:

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

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol

Ehrlichia ewingii: (formerly Ehrlichiosis [unspecified or other agent])

Laboratory criteria for diagnosis

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.

Anaplasma phagocytophilum: (formerly Human Granulocytic Ehrlichiosis [HGE])

Laboratory criteria for diagnosis

Supportive:

1. Serological evidence of elevated IgG or IgM antibody reactive with *A. phagocytophilum* antigen by IFA, 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
2. Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination.

Confirmed:

1. 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
2. Detection of *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay; or
3. Demonstration of anaplasma antigen in a biopsy/autopsy sample by immunohistochemical methods; or
4. Isolation of *A. phagocytophilum* from a clinical specimen in cell culture.

Ehrlichiosis/Anaplasmosis, human, undetermined:

See case classification below.

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. 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

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



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.

Preventive Interventions

There is no evidence that prophylactic antibiotic treatment following a tick bite is effective in preventing ehrlichiosis or anaplasmosis and may delay the onset of disease. Instead, a person bitten by a tick should be alert for symptoms suggestive of tick-borne illness and consult a physician if fever, rash, or other symptoms of concern develop. Also, there is no human vaccine for ehrlichiosis or anaplasmosis.

Avoiding tick bites is the main stay of ehrlichiosis and anaplasmosis prevention. The following are important personal protective measures that should be followed, especially for persons that live, work, or spend leisure time in an area likely to have ticks:

- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light-colored shirts, and long pants tucked into socks when weather permits.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N, N-diethyl-m-toluamide), and choose a product that will provide sufficient protection. DEET products should not be used on children <2 months of age. The following precautions should be observed when using DEET products:
 - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
 - Apply DEET on exposed skin, using only as much as needed.
 - Do not use DEET on the hands of young children and avoid applying repellent to areas around the eyes and mouth.
 - Do not use DEET over cuts, wounds, or irritated skin.
 - Wash treated skin with soap and water after returning indoors, and wash treated clothing.
 - Avoid spraying DEET products in enclosed areas.
- Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



- Check yourself, children, and pets for ticks upon returning from outdoors. Make sure to check the following areas: between the toes, back of the knees, groin, armpits, neck, along the hairline, and behind the ears.
- Promptly remove attached ticks using fine-point tweezers. Grasp the tick close to the skin and pull straight up using steady pressure; do not squeeze or twist the tick.

Environmental Measures:

Prevention of ehrlichiosis and anaplasmosis can also involve actions to keep ticks out of yards.

- Keep grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch, or gravel barrier where the lawn meets the woods, and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

If applying a pesticide outdoors, a licensed applicator experienced with tick control should be hired. In general, good tick control can be achieved with no more than two pesticide applications in any year.

Treatment

Doxycycline is the drug of choice for treating both ehrlichiosis and anaplasmosis infections in adults and children. Doxycycline is most effective at preventing severe complications if started early in the course of illness.

The use of doxycycline to treat suspected ehrlichiosis in children is standard practice recommended by both CDC and the American Academy of Pediatrics (AAP) Committee on Infectious Diseases.¹¹ Unlike older generations of tetracyclines, the recommended dose and duration of medication needed to treat ehrlichiosis has not been shown to cause staining of permanent teeth, even when five courses are given before the age of eight.

Surveillance Indicators

1. Proportion of cases with complete demographic information.

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Ehrlichiosis & Anaplasmosis

Surveillance Protocol



2. Proportion of cases with complete clinical information (i.e., presence of fever and other clinical signs meeting clinical criteria of case definition).
3. Proportion of cases with risk factor information (i.e., history of potential tick exposure through recreational or occupational activities).

Ehrlichiosis & Anaplasmosis

Surveillance Protocol

References

- (1) Annual cases of Ehrlichiosis in United States. CDC .
<https://www.cdc.gov/ehrlichiosis/stats/index.html>. 8-4-2021. 1-19-2022.
- (2) Annual cases of Anaplasmosis in United States. CDC.
<https://www.cdc.gov/anaplasmosis/stats/index.html>. 8-6-2021. 1-19-2022.
- (3) Dumler JS, Kyoung-Seong C, Garcia-Garcia JC et al. Human Granulocytic Anaplasmosis and Anaplasma phagocytophilum. Emerging Infectious Diseases 2005;11:1828-1834.
- (4) Dumler JS, Madigan JE, Pusterla N, Bakken JS. Ehrlichioses in Humans: Epidemiology, Clinical Presentation, Diagnosis, and Treatment. Clinical Infectious Diseases 2007;45:S45-S51.
- (5) Longo, Fauci, Kasper et al. Harrison's Principles of Internal Medicine. 18 ed. New York: McGraw Hill, 2012.
- (6) Clinical and laboratory diagnosis of Ehrlichiosis and Anaplasmosis. CDC.
<https://www.cdc.gov/ehrlichiosis/healthcare-providers/diagnosis.html>. 1-19-2022.
- (7) Varela-Stokes AS. Transmission of bacterial agents from lone star ticks to white-tailed deer. J Med Entomol 2007;44:478-483.
- (8) Castillo CG, Eremeeva ME, Paskewitz SM et al. Detection of human pathogen Ehrlichiamuris-like agent in Peromyscus leucopus. Ticks Tick Borne Dis 6: 155-157.
- (9) Keesing F, Hersh MH, Tibbetts M et al. Reservoir competence of vertebrate hosts for Anaplasma phagocytophilum. Emerg Infect Dis 2012;18:2013-2016.
- (10) Petersen LR, Sawyer LA, Fishbein DB et al. An outbreak of ehrlichiosis in members of an Army Reserve unit exposed to ticks. J Infect Dis 1989;159:562-568.
- (11) CDC. Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis --United States, A Practical Guide for Physicians and Other Health -- Care and Public Health Professionals. MMWR, March 31, 2006 / 55(RR04);1-27. MMWR , 1-27. 3-16-2006.

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