Ehrlichiosis/Anaplasmosis

Ehrlichia spp./*Anaplasma phagocytophilum*

DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS

Per N.J.A.C. 8:57, healthcare providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of ehrlichiosis and anaplasmosis to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at http://localhealth.nj.gov.

If the health officer is unavailable, the healthcare provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.

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1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Ehrlichiosis and anaplasmosis are tickborne rickettsial (intracellular bacterial) diseases that share similar clinical features yet are epidemiologically and etiologically distinct. Spotted Fever Group Rickettsiosis (including Rocky Mountain Spotted Fever) are another group of tickborne rickettsial disease and are described separately.

Ehrlichiosis: In the United States, three *Ehrlichia* species are known to cause symptomatic human infection. *Ehrlichia chaffeensis,* the cause of human monocytic ehrlichiosis, was first described in 1987 and is the most common agent of human ehrlichiosis. *Ehrlichia ewingii* was first reported in 1999 and *Ehrlichia murus*-like *(EML* agent*)* ehrlichiosis was first described in 2011. To date, EML agent has only been identified in a small number of persons living or residing in Minnesota and Wisconsin.

Anaplasmosis: Anaplasmosis is caused by the bacterium *Anaplasma phagocytophilum* and is also known as human granulocytic anaplasmosis (HGA), *formerly* human granulocytic ehrlichiosis (HGE).

B. Clinical Description

Tickborne rickettsial diseases commonly have nonspecific symptoms early in the course of disease, but the frequency of certain symptoms varies. Ehrlichiosis and anaplasmosis are characterized by an acute onset of illness, often presenting with fever, headache, malaise, and myalgia. Common laboratory findings include leukopenia, thrombocytopenia, increased hepatic transaminase levels, hyponatremia, and anemia.

Ehrlichiosis: Persons infected with *E. chaffeensis* often report gastrointestinal (GI) symptoms, including nausea, vomiting, and diarrhea. In addition, a rash is present in 30% of adults and 60% of children appearing usually 5 days after illness onset. The rash affects the trunk and extremities, but can affect the palms, soles, and face. The presentation of the rash can vary in character from petechial or maculopapular to diffuse erythema. Cough or respiratory symptoms are reported in about 1/3 of patients and neurologic manifestations, including meningitis and meningoencephalitis, are present in 20% of patients. With *E. ewingii* and anaplasmosis infections, however, GI symptoms, rash, and neurological symptoms are uncommon.

Severe, life-threatening complications can occur in persons not treated early in the disease. These complications can include renal failure, respiratory failure, myocarditis, encephalopathy and coagulopathy. Fatal infections have been reported but are rare (3% case-fatality rate for *E. chaffeensis*, <1% for anaplasmosis).

Anaplasmosis: In persons with anaplasmosis, rash is rarely reported and the presence of a rash may signify that the patient has a coinfection with another pathogen, such as the agents of Lyme disease and babesiosis.

Treatment

CDC recommends doxycycline as the drug of choice for treatment of all tickborne rickettsial diseases in patients of all ages, including children aged <8 years (https://www.cdc.gov/mmwr/volumes/65/rr/rr6502a1.htm?s_cid=rr6502a1_w).

C. Vectors and Reservoirs

Ehrlichiosis: The primary vector of *E. chaffeensis and E. ewingii* is the lone star tick (*Amblyomma americanum)*. The lone star tick is a very aggressive human biter. The adult female is easily distinguished by a white dot or "lone star" on her back. Lone star tick saliva can be irritating; redness and discomfort near a tick bite does not necessarily indicate an infection. White-tailed deer is a major host of the lone star tick and is thought to be an important reservoir for *E. chaffeensis.* Dogs and small rodents may also be reservoirs.

Anaplasmosis: In New Jersey, the primary vector for anaplasmosis is the blacklegged or deer tick (*Ixodes scapularis*). *I. scapularis* is the same tick associated with Lyme disease, babesiosis, and Powassan. The natural animal reservoir for anaplasmosis is not known but are most likely small rodents.

D. Modes of Transmission

Ehrlichiosis and anaplasmosis are acquired from a bite from an infected tick. The duration of time the tick must remain attached before the transmission of infectious organisms occurs is unclear. Because tick bites may be painless and may occur on parts of the body that are difficult to observe, unrecognized tick bites are common in patients who are later confirmed to have a tickborne rickettsial disease.

Transmission of anaplasmosis and ehrlichiosis via blood transfusion and organ transplantation has been reported infrequently.

E. Incubation Period

Symptoms generally appear 1-2 weeks after a tick bite.

F. Period of Communicability or Infectious Period

Because these bacteria infect the white blood cells and circulate in the blood stream, there is a risk of transmission via blood transfusion and organ transplantation. Infected donors who are asymptomatic or in the pre-symptomatic period pose the greatest risk to the blood supply and may not be identified through routine blood donation screening.

G. Epidemiology

The epidemiology of each tickborne rickettsial disease reflects the geographic distribution and seasonal activities of the tick vectors and vertebrate hosts involved in the transmission of these pathogens, as well as the human behaviors that place persons at risk for tick exposure, tick attachment, and subsequent infection. Cases have been reported in each month of the year, although most cases are reported during April–September, coincident with peak levels of tick host-seeking activity

Ehrlichiosis: During 2008–2012, the average annual incidence of ehrlichiosis was 3.2 cases per million persons, which is more than twice the estimated incidence during 2000–2007. Incidence generally increases with age, with the highest age-specific incidences occurring among persons aged 60–69 years. Case-fatality rates are highest among children aged <10 years and adults aged ≥70 years, and an increased risk for death has been documented among persons who are immunosuppressed. Most cases of ehrlichiosis have traditionally been reported from south-central and southeastern states, which corresponds to the geographic distribution of the lone star tick. States with the highest reported incidence rates include Arkansas, Delaware, Missouri, Oklahoma, Tennessee, and Virginia. In 2016, New Jersey had the 6th highest number of reported *E. chaffeensis* infections (75 cases). From 2000-2013, Atlantic and Hunterdon counties had the highest incidence rates in New Jersey.

Anaplasmosis: During 2008–2012, the average annual incidence of anaplasmosis was 6.3 cases per million persons. Age-specific incidence of anaplasmosis is highest among those aged ≥60 years. The reported case-fatality rate during 2008–2012 was 0.3% and was higher among persons aged ≥70 years and those with immunosuppression. Incidence is highest in the northeastern and upper Midwestern states, and the geographic range of anaplasmosis appears to be expanding. States with the highest number of reported cases in 2016 were Massachusetts, New York, and Minnesota. New Jersey had the 8th highest number of reported anaplasmosis cases (109). From 2000-2013, Sussex, Warren, and Hudson counties had the highest incidence rates in New Jersey.

2 CASE DEFINITION

The NJDOH Infectious & Zoonotic Disease Program follows the current case definition as published on the CDC National Notifiable Disease Surveillance System (NNDSS) website.

Ehrlichiosis and Anaplasmosis Case Definition:
https://wwwn.cdc.gov/nndss/conditions/ehrlichiosis-and-anaplasmosis/

Case definitions enable public health to classify and count cases consistently across reporting jurisdictions and should not be used by healthcare providers to determine how to meet an individual patient's health needs.

A. Clinical Description

- Clinical description: A tick-borne illness characterized by acute onset of fever and one or more of the following symptoms: headache, myalgia, malaise, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases.

B. Laboratory Criteria (*E. chaffeensis, E. ewingii* or *A. phagocytophilum)*

Confirmed:

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

Supportive:

- Serological evidence of elevated IgG or IgM antibody reactive with antigen by IFA, ELISA, dot-ELISA, or assays in other formats **OR**
- Identification of morulae in the cytoplasm of monocytes or macrophages by microscopic examination

C. Case Classification

Cases should be classified in CDRSS as Ehrlichiosis/Anaplasmosis with one of the following subgroups:

- *Anaplasma phagocytophlum*
- *Ehrlichia chaffeensis*
- *Ehrlichia ewingii*
- Undetermined

CONFIRMED
A clinically compatible case that is laboratory confirmed

PROBABLE
A clinically compatible illness that has supportive laboratory results

NOTE: 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. An

example of an undetermined case is when the only available test is the visualization of morulae in leukocytes by microscopic examination (blood smear) since a smear cannot distinguish between ehrlichiosis and anaplasmosis.

POSSIBLE

A case with laboratory evidence but no clinical information available (e.g., a laboratory report)

3 LABORATORY TESTING

Laboratory confirmation of ehrlichiosis and anaplasmosis requires serologic, molecular, or culture-based methods. Organisms may also be observed in blood smears, but microscopic identification can't definitively distinguish between ehrlichiosis and anaplasmosis or speciate within Ehrlichia species.

Microscopic identification: The bacteria responsible for ehrlichiosis/anaplasmosis are intracellular - *E. chaffeensis* is found primarily in monocytes, and *A. phagocytophilum* and *E. ewingii*, are found primarily in granulocytes. They tend to multiply and form clusters of bacteria called morulae that can be identified through microscopic identification (blood smear) during the first week of illness in about 20% of patients.

Nucleic acid testing: During the acute phase of illness, whole blood can be tested by PCR methods. PCR is most sensitive in the first week of illness and quickly decreases in sensitivity after the administration of antibiotics.

Serology: It usually takes 7-10 days after symptom onset to develop detectable antibody titers, so a negative test during this time does not rule out infection. The gold standard serologic test for diagnosis of ehrlichiosis is the indirect immunofluorescence assay (IFA), performed on paired serum samples to demonstrate a significant (four-fold) rise in antibody titers. The first sample should be taken as early in the disease as possible, preferably in the first week of symptoms, and the second sample should be taken 2 to 4 weeks later. In most cases, the first IgG IFA titer is typically low, or "negative," and the second typically shows a significant (four-fold) increase in IgG antibody levels. IgM antibodies usually rise at the same time as IgG near the end of the first week of illness and remain elevated for months or longer. Also, IgM antibodies are less specific than IgG antibodies and more likely to result in a false positive. For these reasons, physicians requesting IgM serologic titers should also request a concurrent IgG titer.

Serologic tests based on enzyme immunoassay (EIA) technology are available, but are qualitative rather than quantitative, meaning they only provide a positive/negative result, and are less useful to measure changes in antibody titers between paired specimens. Furthermore, some EIA assays rely on the evaluation of IgM antibody alone, which may have a higher frequency of false positive results.

Antibodies may remain elevated for months or longer after the disease has resolved, or may be detected in persons who were previously exposed to antigenically related organisms. Therefore, if only one sample is tested it can be difficult to interpret, while paired samples taken weeks apart

demonstrating a significant (four-fold) rise in antibody titer provides the best evidence for a correct diagnosis.

Culture: Culture is only available at specialized laboratories and is not widely used.

The Division of Public Health and Environmental Laboratories (PHEL) does not provide testing for ehrlichiosis or anaplasmosis, but testing is available at commercial laboratories.

4 PURPOSE OF SURVEILLANCE AND REPORTING

- To better understand the local epidemiology of infection with *E. chaffeensis, E. ewingii, and A. phagocytophilum*
- To recognize areas in New Jersey where incidence of disease has changed (increased or decreased)
- To focus preventive education

5 CASE INVESTIGATION

A. Investigation

Local health departments are asked to investigate ehrlichiosis and anaplasmosis reports and close cases in CDRSS within 3 months of case creation. Cases that remain open for three months or more and have no investigation or update notes will be closed by NJDOH. The NJDOH Rickettsial Disease Investigation Worksheet may be used to help guide the patient or physician interview. All information collected using the worksheet should be documented in CDRSS. Worksheets should not be sent to NJDOH.

A minimum of 3 attempts should be made to obtain information. After 3 attempts, enter what is known into CDRSS, including attempts to obtain information (dates and results of the attempts), and classify/close the case according to the case definition.

B. Key CDRSS Fields Specific for Ehrlichiosis and Anaplasmosis

CDRSS Screen	Required Information
Patient Info	• After reviewing laboratory tests, select subgroup: ○ *Anaplasma phagocytophilum* ○ *Ehrlichia chaffeensis* ○ *Ehrlichia ewingii* ○ Undetermined

CDRSS Screen	Required Information
Clinical Status	• Enter date of initial health care evaluation, initial diagnosis, all medical facility and hospitalization dates, and all treatment information (including dosage and dates).
Signs/Symptoms	• In addition to asking about clinical symptoms, ask healthcare provider about other lab work, specifically anemia, leukopenia, thrombocytopenia, and elevated liver enzymes.
Risk Factors	• Enter complete information about risk factors (i.e., known tick exposures) to facilitate study of ehrlichiosis in New Jersey. Focus on one to three weeks before onset and note tick bite and travel history (exposure history). • Ask about receipt of blood transfusion or solid organ transplant in the month prior to symptom onset. Include dates and hospital where blood/organ products were received. Notify CDS by email.
Laboratory Evaluation	• If there is only a single serological test result, ask healthcare provider if an acute (or convalescent) test was ordered; request that negative test results be sent to LHD, and then enter into CDRSS

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements/Protection of Contacts of a Case

There are no isolation or quarantine restrictions.

B. Managing Special Situations

Transfusion/Transplant-Associated Cases

If a blood transfusion or organ transplant was received in the month prior to symptom onset, notify CDS by telephone or email. CDS will reach out to the blood center for further investigation.

Removing a Tick

Ticks should be removed as soon as they are found on the skin. Fine-tipped tweezers should be used to firmly grasp the tick very close to the skin. Using a steady motion, the tick's body should be pulled away from the skin. Efforts should be made to not twist or jerk the tick - this can cause the mouth-parts to break off and remain in the skin. If this happens, the mouth-parts should be removed with tweezers. If they can't be removed, it isn't cause for concern. Once the mouthparts are removed from the rest of the tick, it can no longer transmit the bacteria. After the tick is removed, the bite area should be cleaned with rubbing alcohol, an iodine scrub, or soap and water.

Dispose of a live tick by submersing it in alcohol, placing it in a sealed bag/container, wrapping it tightly in tape, or flushing it down the toilet. Never crush a tick with fingers.

Petroleum jelly, a hot match, nail polish, or other products should not be used to remove a tick. The date of tick attachment should be documented so if symptoms develop, this information can be relayed to a healthcare provider.

Tick Testing and Identification:

Tick testing of individual ticks is not useful because:

- If the test shows that the tick contained disease-causing organisms, that does not necessarily mean that the person has been infected.
- If someone has been infected, s/he will probably develop symptoms before results of tick testing are available. Treatment should not be delayed while waiting for tick testing results.
- Negative results can lead to false assurance. For example, the person concerned may have been unknowingly bitten by a different tick that was infected.

Tick identification may be of value when discussing tick bite exposures with a healthcare provider. County mosquito control agencies or agricultural extension offices may offer tick identification services. The TickEncounter Resource Center has tick identification resources online: http://www.tickencounter.org/tick_identification.

C. Preventive Measures

Preventing ticks in the yard: Prevention of tickborne disease involves keeping wildlife out of the backyard and making it less attractive to ticks.

- Clear tall grasses and brush around homes and at the edge of lawns.
- Place a 3-ft wide barrier of wood chips or gravel between lawns and wooded areas and around patios and play equipment. This will restrict tick migration into recreational areas.
- Mow the lawn frequently and keep leaves raked.
- Stack wood neatly and in a dry area (discourages rodents that ticks feed on).
- Keep playground equipment, decks, and patios away from yard edges and trees and place them in a sunny location, if possible.
- Remove any old furniture, mattresses, or trash from the yard that may give ticks a place to hide.
- When using acaricides (tick pesticides) around the home, always follow the label instructions and never use near streams or other bodies of water.

Preventing ticks on pets: Pets can bring infected ticks into the home or yard. For these reasons, it's important to use a tick preventive product for dogs.

Preventing tick bites on people: The best preventive measure is to avoid tick-infested areas. In areas where contact with ticks may occur, individuals should be advised to do the following:

- Wear long-sleeved shirts and long, light-colored pants tucked into socks or boots.
- Stay on trails when walking or hiking and avoid high grass.
- Use repellent that contains 20 percent or more DEET, picaridin, or IR3535 on exposed skin for protection that lasts several hours. Always follow product instructions. Parents should apply this product to their children, avoiding hands, eyes, and mouth.
- Use products that contain permethrin on clothing. Treat clothing and gear, such as boots, pants, socks and tents with products containing 0.5% permethrin. It remains protective through several washings.
- Bathe or shower as soon as possible after coming indoors (preferably within 2 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. Parents should check their children for ticks under the arms, in and around the ears, inside the belly button, behind the knees, between the legs, around the waist, and especially in their hair.
- 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 dry clothes in a dryer on high heat for 10 minutes to kill ticks on dry clothing after you come indoors.

Additional Information

An Ehrlichiosis Fact Sheet, Investigation Worksheet and additional information can be obtained from the NJDOH website: http://www.state.nj.us/health/cd/topics/ehrli.shtml

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