UTAH DEPARTMENT OF HEALTH

EHRLICHIOSIS/ANAPLASMOSIS

Disease Plan

Quick Links

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Questions about this disease plan?

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✓ WHY IS EHRLICHIOSIS IMPORTANT TO PUBLIC HEALTH?

Ehrlichiosis is the general name used to describe several bacterial diseases that affect animals and humans. Ehrlichiae are transmitted to humans by the bite of an infected tick. Ehrlichiosis is a serious illness that can be fatal if not treated correctly, even in previously healthy people, making it an important public health concern. Ongoing surveillance is needed to establish the burden of disease and better define the epidemiology of the various infections caused by Ehrlichia and Anaplasma species. This information will be used to better inform medical professionals about the disease and tailor prevention messages for the public.

Clinical Description

The human granulocytic anaplasmosis (HGA), formerly known as human granulocytic ehrlichiosis (HGE) and human monocytic ehrlichiosis (HME), agents infect different white blood cells, but the signs, symptoms, and clinical courses of the two diseases are similar. Both cause sudden illness, with fever being the predominant sign. The clinical illness is similar to the early phase of Rocky Mountain spotted fever (RMSF), although patients more often have low white blood cell counts and less often develop rash. In addition to fever, patients may have headache, malaise, chills, muscle and joint aches, nausea, vomiting, and loss of appetite. Patients with HGE rarely have a rash, while about 40% with HME develop a rash. Many people with HGE or HME may be asymptomatic or may have a very mild, self-limited illness. Antibiotics are used to treat both infections. Response to treatment is usually apparent within 24-48 hours. Severe complications are associated with delayed treatment, older age, or with the case being immunocompromised or having diabetes. These complications may affect the lungs, bone marrow, brain, meninges (linings of the brain and spinal cord), kidneys, and blood. Fatal infections have been reported. Coinfections with other tickborne agents, such as the agents of Lyme disease and babesiosis, may complicate the clinical picture.

Causative Agent

Human granulocytic anaplasmosis (HGA) is a bacterial infection caused by *Anaplasma phagocytophilum* (formerly *Ehrlichia phagocytophila*). Human monocytic ehrlichiosis (HME) is caused by the bacterium *Ehrlichia chaffeensis*. The etiologic agents are rickettsiae and intracellular pathogens.

Differential Diagnosis

Rocky Mountain Spotted Fever, Lyme disease, babesiosis, sepsis, toxic shock syndrome, gastroenteritis, meningoencephalitis, tickborne encephalitis, tularemia, Colorado Tick Fever (CTF), leptospirosis, hepatitis, typhoid fever, murine typhus, and blood malignancies should be considered along with ehrlichiosis.

Laboratory Identification

Ehrlichiosis is typically identified serologically, and requires evidence of an increase in titer between acute and convalescent sera, as antibodies are slow to appear. Immunohistology is specific but not sensitive. PCR is sensitive but not widely available.

Buffy coat examination — Intracytoplasmic inclusions (morulae) are characteristic of ehrlichiosis. They are seen in the cytoplasm of neutrophils in 20-80% of patients with HGA and in mononuclear cells in a minority of HME patients (1-20%).

Polymerase chain reaction — PCR-based testing is available for both HME and HGA. While not yet standardized, these techniques are becoming more widely used for the diagnosis of ehrlichiosis and are available from the CDC and some state public health and commercial laboratories. Sensitivity and specificity of assays vary from laboratory to laboratory. The reported sensitivity of PCR for HGA varies from 60-70%; more variable results have been reported in studies of patients with HME (52-87% sensitivity). Most clinicians use PCR in association with serologic tests for the diagnosis of ehrlichiosis. Doxycycline therapy may decrease the sensitivity of nucleic acid detection assays

Immunohistochemical stains — A few cases of ehrlichiosis and anaplasmosis have been diagnosed by staining bone marrow tissue or autopsy tissue such as spleen, lymph nodes, liver, or lung.

Treatment

There have been no controlled trials examining the efficacy of antimicrobial therapy in either HME or HGA. Treatment recommendations are based on clinical case series and in vitro data. Both tetracycline and chloramphenicol appear to be effective clinically. Doxycycline is the drug of choice for adults and children. Rifampin has been used for HGA in pregnant and pediatric patients. Quinolones have activity, but clinical efficacy data is limited. The optimal duration of therapy is unknown. Seven to 10 days of therapy is commonly recommended and relapses have not been described with this treatment duration.

Adult Guidelines - Doxycycline can be given either orally or intravenously at a dose of 100 mg twice daily. Doxycycline treatment for ehrlichiosis should be continued in adults for 10 days or for three to five days after defervescence. Patients who have intolerance or allergy to tetracyclines can be treated with rifampin (300 mg twice daily) for 7-10 days, but careful follow-up and monitoring of such patients is recommended, as there is only anecdotal information on the efficacy of this agent.

Child Guidelines - Children weighing more than 45 kg should receive the adult dose of doxycycline; smaller children should receive 4 mg/kg per day in two divided doses (up to a maximum of 100 mg per dose).

All tetracyclines can cause dental staining in children; however, the risk of such staining after use of doxycycline is minimal if a short course of therapy is administered.

Children ≥8 years can be treated with a 10-day course of doxycycline. For severely ill children <8 years of age without concomitant Lyme disease, a treatment course of 4-5 days (or three days after resolution of fever) is recommended by the Infectious Disease Society of America guidelines. Careful follow-up and monitoring of children treated with this short course is recommended. If co-infection with Lyme disease is documented, then amoxicillin (50 mg/kg per day in three divided doses [maximum of 500 mg per dose]) or cefuroxime axetil (30 mg/kg per day in two divided doses [maximum of 500 mg per dose]) should be started at the end of the short course doxycycline treatment to complete a 14-day course of therapy.

Pregnancy Guidelines: At present, no guidelines exist for the treatment of ehrlichiosis in pregnancy. Although doxycycline is not recommended for use in pregnancy, some experts believe that, in cases when the infection is considered life-threatening, doxycycline might be warranted in the treatment of HME or HGA. Doxycycline has been used successfully and safely in a few cases in pregnant women with HME or HGA.

An alternative to doxycycline is rifampin, which is both active and bactericidal against HGA in vitro. Rifampin has been effective in small numbers of pregnant women with HGA

Case Fatality

Severe complications are associated with delayed treatment, older age, or with the case being immunocompromised or having diabetes. These complications may affect the lungs, bone marrow, brain, meninges (linings of the brain and spinal cord), kidneys, and blood. Fatal infections have been reported, with a case fatality rate of 2-3%.

Reservoir

The vector of HGA is the deer tick, *Ixodes scapularis,* which is the same tick associated with Lyme disease and babesiosis. Deer ticks may be co-infected with, and capable of transmitting, more than one disease agent at the same time. Deer, elk, and wild rodents are likely reservoirs for HGA.

The primary vector of HME is the lone star tick, *Amblyoma americanum*. This tick is named for the prominent white spot or “star” on the back of the adult female. The lone star tick is predominantly found in the southeastern U.S. Lone star ticks infected with *E. chaffeensis* have been found in Connecticut and Rhode Island. White-tailed deer are a major host of lone star ticks, and appear to represent a natural reservoir for *E. chaffeensis.* Another important reservoir appears to be dogs.

Transmission

Anaplasma phagocytophilum, the agent responsible for HGA, is transmitted through the bite of an infected deer tick. *E. chaffeensis*, the agent responsible for HME, is transmitted through the bite of an infected lone star tick. Limited data suggest that the longer an infected tick remains attached, the higher the likelihood of successful transmission of *A. phagocytophilum* or *E. chaffeensis*. Since tick bites are often painless and may occur on parts of the body that are difficult to observe, cases of HGA and HME may have no known history of tick bite.

Although ehrlichiosis is primarily a tick-borne disease, transmission by other means has been suggested, such as maternal-child transmission, blood transfusion, and through direct contact with slaughtered deer. People who have ehrlichiosis/anaplasmosis should not donate blood or bone marrow for 6 months after their illness.

Susceptibility

Susceptibility is believed to be general; older or immunocompromised individuals are likely to suffer a more serious illness. No data are available on protective immunity in humans due to infections caused by these organisms. Reinfection is rare, but has been reported.

Incubation Period

The period between exposure to infection and the first symptoms of HME or HGA ranges from 7-14 days.

Period of Communicability

HGA and HME are not communicable from person to person.

Epidemiology

The epidemiologic features of human monocytic ehrlichiosis (HME) and human granulocytic anaplasmosis (HGA) are similar. In 2010, US cases attributed to E. chaffeensis, the causative agent of HME, declined almost 22%, whereas those cases attributed to A. phagocytophilum, the causative agent of HGA, increased by 52%. Most cases occur in the spring and summer months. In Utah, ehrlichiosis was just recently added to our list of reportable diseases in 2000. There have been no cases since that time

Human monocytic ehrlichiosis – HME is most often reported in the southeastern and southcentral states, reflecting the range of its tick vector. The average reported annual incidence of HME in the U.S. was 3.2 cases per million population in 2012, with wide variations in incidence by state. The total number of cases of HME reported annually to the CDC quadrupled from 2000 to 2008. However, these numbers likely underestimate the actual incidence of the disease as many cases are not confirmed by laboratory testing and current surveillance systems rely on voluntary reporting by clinicians. Tick bites, exposure to wildlife, and golfing have been associated with an increased risk of infection.

Human granulocytic anaplasmosis – In the U.S., HGA is most often reported in the northeastern and upper-midwestern states. HGA is more frequently reported than HME in the U.S., with an average reported annual incidence of 6.3 cases per million population during 2008 to 2012. The number of cases of HGA reported to the CDC increased more than threefold from 2000 to 2008 (from 351 to 1053 cases). Regional estimates of HGA vary significantly by locale; states with the highest incidence are Rhode Island (36.5 cases per million), Minnesota (3.9 to 12.3 cases per million), Connecticut (8.1 to 15.9 cases per million), Wisconsin (8.8 to 9.5 cases per million), New York (2.3 to 2.7 cases per million), and Maryland (1.6 cases per million).

✓ PUBLIC HEALTH CONTROL MEASURES

Public Health Responsibility

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.

Prevention

Managing Special Situations: Response to a Tick Bite

The longer a tick remains attached to someone, the higher the likelihood of disease transmission. Individuals should promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted, but grasped close to the skin and pulled straight out using steady pressure. Whenever an attached tick is removed from the body, one should monitor one's health for the appearance of rash, fever, or flu-like symptoms, and should immediately seek the advice of a health care provider should any symptoms occur, especially if the tick was attached for more than 24 hours. It may be helpful to save the tick after removal for two reasons: 1) if the person who was bitten goes on to develop signs or symptoms such as fever, flu-like symptoms, or a rash, it may be helpful for the physician to know the type of tick; and 2) depending on the circumstances of the bite (i.e., when a person was bitten, the type of tick, how long it was attached), a physician may choose to treat the person who was bitten. The tick may be kept either securely sealed in a small plastic bag or attached, with clear tape, to a piece of paper. For individuals who do not wish to keep the tick, it can be either drowned in alcohol or flushed down the toilet.

Preventive Measures

Environmental Measures

Prevention of diseases spread by ticks, involves making the yard less attractive to ticks.

- 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 an individual chooses to use a pesticide to reduce the number of ticks on his/her property, he/she should be advised to hire a licensed applicator who is experienced with tick control. A local landscaper or arborist may be a licensed applicator. In general, good tick control can be

achieved with no more than two pesticide applications in any year. Advise individuals to ask, when selecting an applicator, if they will provide:

- A written pest control plan that includes information on the pesticide to be used.
- Information about non-chemical pest control alternatives.
- Signs to be posted around the property after the application.

Personal Preventive Measures/Education

There is no human vaccine for Ehrlichiosis. If someone lives, works, or spends leisure time in an area likely to have ticks, they should be advised of the following:

- The single most important thing one can do to prevent a tickborne disease is to check oneself for ticks once a day. Favorite places ticks like to go on the body include areas between the toes, back of the knees, groin, armpits, neck, along the hairline, and behind the ears. Remember to check children and pets too. Promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted but grasped close to the skin and pulled straight out using steady pressure.
- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light-colored shirts, and long pants tucked into socks.
- 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 for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. 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. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

Chemoprophylaxis

None.

Vaccine

None.

Isolation and Quarantine Requirements

Isolation: None.

Hospital: None.

Quarantine: None.

✓ CASE INVESTIGATION

Reporting

Report all suspect and confirmed cases of Ehrlichiosis. Report any illness to public health authorities that meets any of the following criteria:

1. Any person with clinical and laboratory evidence of infection with *Ehrlichia chaffeensis, Ehrlichia ewingii, Anaplasma phagocytophilum*, or Ehrlichiosis/anaplasmosis undetermined species.
   Ehrlichia ewingii or *Anaplasma phagocytophilum*. Laboratory evidence of infection includes any of the following:
   a) A fourfold change in *E. chaffeensis* or *A. phagocytophilum* -specific immunoglobulin G (IgG) antibody titer by indirect immunofluorescence assay (IFA) between paired serum samples
   b) Elevated IgG antibody reactive with *E. chaffeensis* or *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays
   c) Elevated IgM antibody reactive with *E. chaffeensis* or *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays
   d) Detection of *E. chaffeensis, E. ewingii*, or *A. phagocytophilum* -specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)
   e) Demonstration of *E. chaffeensis* or *A. phagocytophilum* –specific antigen in a biopsy or autopsy sample by immunohistochemical methods
   f) Isolation of *E. chaffeensis* or *A. phagocytophilum* from a clinical specimen in cell culture
   g) Identification of morulae in monocytes, granulocytes, or macrophages by microscopic examination.

2. A person whose healthcare record contains a diagnosis of ehrlichiosis or anaplasmosis.

3. A person whose death certificate lists ehrlichiosis or anaplasmosis as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases of ehrlichiosis and anaplasmosis should be reported.
- Reporting should be on-going and routine.
- Frequency of reporting should follow the state health department's routine schedule.

Table A. Table of criteria to determine whether a case should be reported to public health authorities

Criterion	Reporting	
Clinical Presentation		
Fever	C	
Headache	C	
Myalgias	C	
Anemia	C	
Leukopenia	C	
Thrombocytopenia	C	
Elevated Hepatic Transaminases	C	
Nausea	C	
Vomiting	C	
Rash	C	
Healthcare record contains a diagnosis of Ehrlichiosis or Anaplasmosis		S
Death certificate lists Ehrlichiosis or Anaplasmosis as a casue of death or a significant condition contributing to death		S
Laboratory Findings		
A fourfold change in *Ehrlichia chaffeensis* specific immunoglobulin G (IgG) antibody titer by indirect immunofluorescence assay (IFA) between paired serum samples	O	
Detection of *Ehrlichia chaffeensis*-specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	O	
Demonstration of *Ehrlichia chaffeensis* antigen in a biopsy or autopsy sample by immunohistochemical methods	O	
Isolation of *Ehrlichia chaffeensis* from a clinical specimen in cell culture	O	
Elevated IgG antibody to *Ehrlichia chaffeensis* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dotELISA, or other assays	O	
Elevated IgM antibody to *Ehrlichia chaffeensis* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dotELISA, or other assays	O	
Detection of *Ehrlichia ewingii*-specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	O	

A fourfold change in *Anaplasma phagocytophilum*-specific immunoglobulin G (IgG) antibody titer by indirect immunofluorescence assay (IFA) between paired serum samples	O	
Detection of *Anaplasma phagocytophilum*-specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	O	
Demonstration of *Anaplasma phagocytophilum* antigen in a biopsy or autopsy sample by immunohistochemical methods	O	
Isolation of *Anaplasma phagocytophilum* from a clinical specimen in cell culture	O	
Elevated IgG antibody to *Anaplasma phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays	O	
Elevated IgM antibody *Anaplasma phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dotELISA, or other assays	O	
Identification of morulae in monocytes, granulocytes, or macrophages	O	
Epidemiological Risk Factors		
History of having been in potential tick habitat in the 14 days prior to the onset of illness	C	
History of a tick bite	C	

Notes:
S = This criterion alone is sufficient to report a case
O = At least one of these “O” criteria in each category in the same column (e.g., clinical presentation and laboratory findings) is required to report a case.
C = This finding corroborates (e.g., supports) the diagnosis of—or is associated with—Ehrlichiosis, but is not included in the case definition and is not required for reporting.
A requisition or order for any of the “S” laboratory tests is sufficient to meet the reporting criteria. A requisition or order for any of the “O” laboratory tests—in conjunction with at least one of any “O” criteria in the other non-laboratory categories in the same column—is sufficient to meet the reporting criteria.

Case Definition

Ehrlichiosis

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.

Epidemiologic evidence
A history of having been in a tick habitat in the 14 days before illness onset; history of a tick bite is not required. Consider occupation if relevant to exposure, and consider travel in the past 14 days, including location of travel.

Laboratory evidence
For the purposes of surveillance:

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, *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 Anaplasmosis [HGA])

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 below

Exposure

Exposure is defined as having been in potential tick habitats within 14 days before onset of symptoms. A history of a tick bite is not required.

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).

Comment

There are at least three species of bacteria, all intracellular, responsible for ehrlichiosis/ anaplasmosis in the U.S.: *E. chaffeensis*, found primarily in monocytes, and *A. phagocytophilum* and *E. 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 *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 associated with 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.

Table B. Proposed table of criteria to determine whether a case is classified as confirmed, probable, or suspected.

Criterion	Confirmed	Probable	Suspected
Clinical Presentation			
Fever	N	N	
Headache	O	O	
Myalgias	O	O	
Anemia	O	O	
Leukopenia	O	O	
Thrombocytopenia	O	O	
Elevated Hepatic Transaminases	O	O	
Nausea	C	C	
Vomiting	C	C	
Rash	C	C	
Laboratory Findings			
A fourfold change in *E. chaffeensis* specific immunoglobulin G (IgG) antibody titer by indirect immunofluorescence assay (IFA) between paired serum samples	O1		O1

Detection of *E. chaffeensis* - specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	O1		O1
Demonstration of *E. chaffeensis* antigen in a biopsy or autopsy sample by immunohistochemical methods	O1		O1
Isolation of *E. chaffeensis* from a clinical specimen in cell culture	O1		O1
Elevated IgG antibody to *E.* chaffeensis antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays		O1	O1
Elevated IgM antibody to *E. chaffeensis* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays		O1	O1
Detection of *E. ewingii* -specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	N2		O2
A fourfold change in *A. phagocytophilum* -specific immunoglobulin G (IgG) antibody titer by indirect immunofluorescence assay (IFA) between paired serum samples	O3		O3
Detection of *A. phagocytophilum* - specific nucleic acid in a clinical specimen by polymerase chain reaction (PCR)	O3		O3
Demonstration of *A. phagocytophilum* antigen in a biopsy or autopsy sample by immunohistochemical methods	O3		O3
Isolation of *A. phagocytophilum* from a clinical specimen in cell culture	O3		O3
Elevated IgG antibody to *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays		O3	O3
Elevated IgM antibody *A. phagocytophilum* antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or other assays		O3	O3
Identification of morulae in monocytes, granulocytes, or macrophages	C1,C2,C3	C1,C2,C3,N4	O4

Epidemiological risk factors			
History of having been in potential tick habitat in the 14 days prior to the onset of illness	C	C	
History of a tick bite	C	C	

Notes:
N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to classify a case. A number following an “N” indicates that this criterion is only required for a specific clinical presentation
O = At least one of these “O” criteria in each category in the same column (e.g., clinical presentation and laboratory findings)—in conjunction with all other “N” criteria in the same column—is required to classify a case. A number following an “O” indicates that this criterion is only required for a specific clinical presentation.
C = This finding corroborates (e.g., supports) the diagnosis of—or is associated with—Ehrlichiosis, but is not included in the case definition and is not required for classification. A number following a “C” indicates that this criterion is compatible with a specific clinical presentation.
1 = Ehrlichia chaffeensis infection
2 = Ehrlichia ewingii infection
3 = Anaplasma phagocytophilum infection
4 = Human ehrlichiosis/anaplasmosis – undetermined

Case Investigation Process

- Fill out morbidity form.
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and implement measures to eliminate it.

Outbreaks

More than one case of Ehrlichiosis in a one month period of time would constitute an outbreak.

Identifying Case Contacts

None.

Case Contact Management

None.

✓ REFERENCES

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✓ VERSION CONTROL

Updated. Dec 15, 2016: Updated swimlanes.

Updated. Apr 22, 2016: Updated and added information to treatment, laboratory identification, and epidemiology.

Updated. Apr 19, 2016: General update to formatting (split tick-borne diseases into their own separate disease plans).

Updated. Apr 19, 2016: Added the importance to public health section.

Updated. Apr 19, 2016: Added reporting information (narrative and swimlanes).

✓ UT-NEDSS Minimum/Required Fields by Tab

Demographic
- ☑ County
- ☑ State
- ☑ Street
- ☑ City
- ☑ Zip Code
- ☑ Date of Birth
- ☑ Birth Gender
- ☑ Race
- ☑ Ethnicity
- ☑ First Name
- ☑ Last Name
- ☑ Phone Number

Clinical
- ☑ Date of Death
- ☑ Hospitalized
- ☑ Died
- ☑ Disease
- ☑ Onset Date
- ☑ Pregnant
- ☑ Clinician
- ☑ Diagnostic Facility
- ☑ Specific Disease Being Reported
- ☑ Did the patient have an underlying immunosuppressive condition?
- ☑ Did the patient experience any of the following life-threatening complications in clinical course of illness?
- ☑ Was the patient treated with antibiotics?

Laboratory
- ☑ Organism
- ☑ Specimen Source
- ☑ Test Result
- ☑ Test Type

Epidemiological
- ☑ Imported From

Investigation
- ☑ List date 14 days prior to disease onset
- ☑ Was patient bitten by a tick during the above time period?
- ☑ Was patient in a wooded, brushy or grassy area (potential tick habitat) <30 days prior to onset of symptoms?
- ☑ Was the patient camping during exposure period?
- ☑ Was the patient hunting during exposure period?
- ☑ Did the patient visit any parks during exposure period?
- ☑ Did the patient traveled outside of Utah during exposure period?

Contacts
- ☑ Last Name
- ☑ First Name
- ☑ Date of birth

Reporting
- ☑ Date first reported to public health

Administrative
- ☑ Outbreak Name
- ☑ Outbreak Associated
- ☑ State Case Status