# **Tick-borne Disease, Excluding Lyme** and Relapsing Fever

(Anaplasmosis, Babesiosis, Ehrlichiosis, Tick Paralysis, Spotted Fever Rickettsiosis)

	s, babesiosis, Enrichiosis, fick Paralysis, Spotted Pever Rickettsiosis)							
Signs and	• Vary from asymptomatic to severe disease. Except in tick paralysis, symptoms							
Symptoms	often include fever, headache, myalgia, nausea; other symptoms vary							
	according to agent.							
	Babesiosis: splenomegaly, hepatomegaly, or jaundice may also be seen.							
	Spotted fever rickettsioses: eschars generally precede fever; rash and							
	lymphadenopathy can be indicative.							
	• Tick paralysis: acute, ascending, flaccid paralysis. Possible fatigue, myalgia, leg							
	numbness. Paralysis may cause respiratory failure.							
Incubation	Varies with agent; babesiosis can present after weeks or months, and may recur							
Case classification	Differs for each disease. See Section 3.							
	Babesiois							
	Ehrlichiosis							
	Anaplasmosis							
	Spotted Fever Rickettsiosis							
	Tick paralysis							
Differential	Except for tick paralysis, difficult to distinguish clinically due to overlap of							
diagnosis	symptoms; cross-reactivity and persistent IgM within etiologic agent groups may							
-	occur. Generally include: Lyme disease, malaria, bacterial or viral meningitis, other							
	rare tick-borne agents, typhoid fever.							
Treatment	For Rocky Mountain Spotted Fever (RMSF), prompt diagnosis and treatment (with							
	doxycycline) critical for preventing severe disease. Tick paralysis is treated by tick							
	removal. Others are treated with antibiotics (in combination with anti-parasite							
	drugs for babesiosis).							
Duration	Varies with agent.							
Exposure	Vector: ticks. Not person-to-person communicable, except for babesiosis and							
	anaplasmosis via blood transfusion or organ donation.							
Laboratory testing	Local health jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) can							
	arrange testing							
	Best specimens: generally whole blood collected pre-treatment, blood smears,							
	serum, biopsied skin or tissue							
	• Keep whole blood or serum cold or if already frozen keep frozen (dry ice),							
	submit to PHL for passthrough to CDC. Submit blood smear or ticks to PHL							
	Parasitology:							
	https://www.doh.wa.gov/ForPublicHealthandHealthcareProviders /							
Dublic boolth	PublicHealthLaboratories/MicrobiologyLabTestMenu							
Public health	LHJ can consult with CDE 877-539-4344 for testing							
actions	Confirm diagnosis – confirmatory testing may be needed							
	Identify potential exposures, particularly local							
	Notify CDE promptly for locally acquired cases (e.g., no out-of-state travel)							
	Babesiosis cases must defer from blood donation for life.							
	Infection Control: standard precautions							

# Tick-borne Disease, Excluding Lyme and Relapsing Fever

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# **1. DISEASE REPORTING**

#### A. Purpose of Reporting and Surveillance

- 1. To distinguish tick-borne disease infections acquired locally from those related to travel.
- 2. To understand the epidemiology of tick-borne diseases in Washington State in order to inform public health and healthcare organizations about conditions that have been diagnosed in residents and to target education and control measures.
- 3. To identify emerging tick-borne diseases in Washington
- 4. To identify common sources of exposure or risks to the blood supply.

#### **B.** Legal Reporting Requirements

- 1. Healthcare providers and Healthcare facilities: notifiable to **local health jurisdiction** within 3 business days.
- 2. Laboratories: notifiable to **local health jurisdiction** within 2 business days. Submission on request specimen associated with positive result, if available, within 2 business days.
- 3. Veterinarians: animal cases notifiable to Washington State Department of Agriculture <u>http://app.leg.wa.gov/WAC/default.aspx?cite=16-70</u>
- 4. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology (CDE) within 7 days of case investigation completion or summary information required within 21 days.

# C. Local Health Jurisdiction Investigation Responsibilities

- 1. Consult CDE about suspected endemically acquired cases or for assistance with testing.
- 2. Facilitate transport of specimens to the Washington State Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDE prior to submitting specimens (206-418-5500).
- 3. Report any case to CDE through the Washington Disease Reporting System (WDRS) as a Tick-borne Disease, including species or organism. Complete the tick-borne disease case report form (<u>https://www.doh.wa.gov/Portals/1/Documents/5100/420-214-ReportForm-Tickborne.pdf</u>) and enter the data into WDRS.

# 2. THE DISEASES AND THEIR EPIDEMIOLOGY

For information about Lyme disease and relapsing fever, see disease-specific guidelines at:

https://www.doh.wa.gov/Portals/1/Documents/5100/420-061-Guideline-Lyme.pdf

https://www.doh.wa.gov/Portals/1/Documents/5100/420-075-Guideline-RelapsingFever.pdf

#### Background

Tick-borne diseases are generally maintained in enzootic cycles involving tick vectors and mammal reservoirs. Agents include viruses, bacteria, and protozoan parasites. Only some species of ticks bite and transmit disease to people. Different species of ticks transmit different agents, but some may harbor multiple disease agents and simultaneous infections with multiple agents can occur.

Tick-borne diseases include Lyme disease (discussed separately), babesiosis, anaplasmosis, ehrlichiosis, rickettsioses, relapsing fever (discussed separately), tick paralysis, and other less common infections. Less common infections that are not included on the tick-borne diseases form can be reported under the condition "Additional Reportable Disease."

All tick-borne diseases included in this guideline were previously collected using the "Rare Diseases of Public Health Significance" form, and historical surveillance reports are summarized under this category in the Washington State Annual Communicable Disease Report:

https://www.doh.wa.gov/DataandStatisticalReports/DiseasesandChronicConditions/Com municableDiseaseSurveillanceData/AnnualCDSurveillanceReports.aspx

#### A. Etiological Agent

See Table 1 for a list of the tick-borne agents reviewed in this guideline.

#### **B.** Description of Illness

See Table 1 for a summary of symptoms for each disease. Early symptoms associated with anaplasmosis, babesiosis, ehrlichiosis, and spotted fever rickettsioses are non-specific and generally include fever, headache, myalgia, and nausea.

#### C. Tick-borne Diseases in Washington State

In contrast to Lyme disease, soft tick relapsing fever, and tularemia, for which locally acquired cases are reported each year, other tick-borne diseases are rare or have not been reported in Washington. No in-state acquired cases of ehrlichiosis or hard tick relapsing fever (*Borrelia miyamotoi*) have been reported in Washington residents. Ehrlichiosis is occasionally reported among persons with travel-related exposures. The first two cases of anaplasmosis acquired in Washington were reported in 2022 and 2023; travel-related cases are occasionally reported.

From 1990 to 2023, 18 babesiosis cases were reported, four with exposure in Washington. Of these four locally-acquired cases, three were caused by *B. duncani* and one was caused by *B. divergens*-like organism. The remaining 14 babesiosis cases were associated with travel out-of-state or blood donation from an out-of-state donor and were

confirmed or presumed to be caused by *B. microti*. To-date, tick surveillance has not identified *Babesia*-positive ticks in Washington.

Rocky Mountain spotted fever (RMSF, caused by *Rickettsia rickettsii*) was reported each year through the 1940s, after which reporting decreased to 0-4 cases per year. During 2004-2023, 25 cases were reported. Three of these cases were reported as locally acquired in 2011; however, none of these cases were confirmed and each had a single low-titer serology positive result. In 2019, a confirmed case of RMSF was reported following exposure in Spokane County and in 2020, two probable cases were reported with likely exposure in Washington state. To-date, tick surveillance has not identified *R. rickettsii*-positive ticks in Washington. Other spotted fever rickettsioses cases are reported in international travelers, including Mediterranean spotted fever (*R. conorii*) and African tick bite fever (*R. africae*).

Washington has 0-2 cases of tick paralysis reported each year, with exposures mostly in eastern Washington.

#### **D.** Vectors and Reservoirs

See Table 1 for a list of the geographical distributions and reservoirs of the relevant tick vectors. Washington has several species of ticks capable of vectoring diseases to humans including *Ixodes pacificus* (western black-legged tick), *Dermacentor andersoni* (Rocky Mountain wood tick), *D. similis* (Western dog tick), and *Ornithodorus hermsi* (soft tick).

Most ticks have four life stages: egg, larva, nymph, and adult. After hatching from the eggs, ticks must consume a blood meal at every stage to survive. Ticks that pick up pathogens from a reservoir host may spread disease to the next host, and vertical transmission of some etiologic agents (*Babesia spp., Rickettsia spp.*) has been demonstrated in many tick species.

Disease is usually spread by ticks in the nymphal stage and by adult females. Nymphs are mostly found in areas with woods, brush, or grass, and are easily overlooked due to their small size. Disease prevalence is highest during the warm months of spring and summer, coinciding with the period of highest nymph activity, but tick-borne diseases can occur at any time.

Animal hosts to hard ticks include dogs, opossums, lagomorphs, rodents, with clinical illness in dogs and some rodents.

#### E. Modes of Transmission

Tick-borne diseases are most commonly transmitted by inoculation from a tick bite. Most bites are painless and humans may not know they were bitten.

Ehrlichiosis, tick paralysis, and spotted fever rickettsioses are not known to be transmitted between persons. Transmission of anaplasmosis has been reported through blood donated from acutely infected donors.

Babesiosis is communicable via blood transfusion or from mother to infant during pregnancy or delivery.

#### **F. Incubation Period**

Varies with agent. See Table 1.

#### G. Period of Communicability

Not applicable for ehrlichiosis, tick paralysis, or spotted fever rickettsioses. Unknown for anaplasmosis. Babesiosis cases must defer from blood donation for life.

#### H. Treatment

Early diagnosis in the clinical course is critical to limit progression to severe disease and because this is the period when antibiotics are most effective. Except for tick paralysis, tick-borne diseases are treated with antibiotics, or a combination of antibiotics and antiparasite drugs (babesiosis). Doxycycline is the first line treatment for rickettsial infections including anaplasmosis, ehrlichiosis, and spotted fever rickettsioses in adults and children of all ages and should be initiated immediately whenever disease is suspected. Failure to respond to doxycycline suggests that the patient's condition might not be caused by rickettsial infection.

The treatment for tick paralysis is simply removal of the tick. This usually results in complete recovery within 24 hours.

Disease (Etiologic agent)	Vector Tick Species	Geographic Distribution of Ticks	Animal Reservoirs <sup>2</sup>	Incubation period	Common symptoms
Anaplasmosis (Anaplasma phagocytophilum )	<ul> <li>Blacklegged tick (deer tick, <i>Ixodes scapularis</i>)</li> <li>Western blacklegged tick (<i>Ixodes pacificus</i>)</li> </ul>	<ul> <li>Upper Midwest &amp; Northeastern US (<i>I. scapularis</i>)</li> <li>US West coast (<i>I. pacificus</i>)</li> </ul>	Wild rodents, cervids, ruminants, dogs	Generally 1-2 weeks (5-21 days)	Fever, headache, myalgia, malaise, nausea, abdominal pain, cough.
Babesiosis (Babesia microti, B. duncani, other rare Babesia spp.)	Blacklegged tick (deer tick, <i>Ixodes scapularis)</i> <i>Ixodes albipictus</i> for <i>B.</i> <i>duncani</i>	Upper Midwest (WI, MN) & Northeastern US. Sporadic on US West coast.	mice, voles, raccoons, deer	Variable, 1-4 weeks after tick bite and 1- 9 wks after blood transfusion	Fever, headache, sweats, myalgia, arthralgia, malaise, fatigue, nausea, splenomegaly, hepatomegaly, hemolytic anemia, jaundice.
Ehrlichiosis (Ehrlichia chaffeensis, E. ewingii, E. muris)	Lone Star tick ( <i>Amblyomma americanum</i> ) (Unknown for <i>E. muris</i> )	Southeastern & Central US	Deer, dogs, rodents, ruminants	5-14 days	Fever, headache, myalgia, malaise. Nausea/vomiting/diarrhea, confusion, rash ( $\leq 60\%$ of children, $\leq 30\%$ of adults).
Tick paralysis (Tick toxin)	<ul> <li>Western dog tick (Dermacentor similis)</li> <li>American dog tick (Dermacentor variabilis)</li> <li>Rocky Mountain wood tick (Dermacentor andersoni)</li> <li>Also seen with at least 43 tick species worldwide</li> </ul>	• Southeastern US • Northwestern US, Western Canada	n/a	4-7 days (while tick feeds)	Acute, ascending, flaccid paralysis. Possible fatigue, myalgia, numbness in the legs, and in children, flu-like symptoms. Paralysis may affect breathing muscles and cause respiratory failure.

Table 1. Geographic Distribution and Clinical Characteristics of Selected Tick-borne Diseases<sup>1</sup>

Spotted Fever Ric	kettsioses (spotted fevers)	-	-	_	-
Rocky Mountain Spotted Fever (RMSF, <i>Rickettsia.</i> <i>rickettsii</i> )	<ul> <li>Western dog tick (Dermacentor similis)</li> <li>American dog tick (Dermacentor variabilis)</li> <li>Rocky Mountain wood tick (Dermacentor andersoni)</li> <li>Brown dog tick (Rhipicephalus sanguineus)</li> </ul>	<ul> <li>East of the US Rocky Mountains, US Pacific Coast (D. similis)</li> <li>US Rocky Mountain states, SW Canada (D. andersoni)</li> <li>Transmits in SW US &amp; US-Mexico border. (R. sanguineus)</li> </ul>	Rodents	2-14 days (avg: 1 wk)	Acute onset fever, headache, myalgia, malaise, nausea/vomiting, stomach pain, anorexia, photophobia, focal neurologic deficits. Maculopapular rash 2-4 days (90% of patients), petechial rash 5+ days after fever onset.
<i>Rickettsia parkeri</i> Rickettsiosis ( <i>R. parkeri</i> )	Gulf Coast tick (Amblyomma maculatum)	Southeastern US	Rodents	2-10 days	Eschar, followed by fever, headache, myalgia, regional lymphadenopathy, rash.
Pacific Coast Tick Fever ( <i>R. philipii</i> )	Pacific Coast tick (Dermacentor occidentalis)	Western US coastline (CA, OR, WA)	Possibly jackrabbits, deer	A few days-1 week	Eschar, followed by fever, headache, myalgia, fatigue, lymphadenopathy, rash (less common).
Mediterranean Spotted Fever ( <i>R. conorii</i> )	None in U.S.	Southern Europe, southern and western Asia, Africa, India	Dogs, rodents	1-2 weeks	Rash, fever, headache, myalgia, eschar
African Tick Bite Fever ( <i>R. africae</i> )	None in U.S.	Sub-Saharan Africa, Caribbean, and Oceania	Ruminants	1-2 weeks	Fever, headache, myalgia, eschar, regional lymphadenopathy, rash

<sup>1</sup>Viral diseases caused by ticks (Colorado tick fever, Powassan) are listed in Table 1 of the arboviral disease guideline <u>https://www.doh.wa.gov/Portals/1/Documents/5100/420-046-Guideline-Arbo.pdf</u>

<sup>2</sup>Many tick species are disease reservoirs. Below adapted in part from <u>https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/rickettsial-including-spotted-fever-and-typhus-fever-rickettsioses-scrub-typhus-anaplasmosis-and-ehr</u>

# **3. CASE DEFINITIONS**

NOTE: - Lyme disease and relapsing fever are discussed in separate guidelines.

#### A. Anaplasmosis

#### 1. Background

Anaplasmosis is a tick-borne disease caused by the bacterium *Anaplasma phagocytophilum*. See Table 1 for information on vector tick distribution.

# 2. Clinical Description

Characterized by acute onset of fever and one or more of the following symptoms or signs: severe headache, myalgia, malaise, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases. Nausea, vomiting, diarrhea, anorexia, or rash may be present in some cases. Nervous system involvement, including meningoencephalitis, focal paralysis, or other neurological problems may rarely occur. If treatment is delayed, severe illness may occur, including renal or respiratory failure, peripheral neuropathies, coagulopathies, rhabdomyolysis, or hemorrhage. Persons with delayed treatment, older age, or immune compromising conditions are at higher risk of severe disease. Differential diagnoses: ehrlichiosis, spotted fever rickettsiosis, bacterial or viral meningitis, typhoid fever.

#### 3. Clinical Criteria (2024)

<u>Objective clinical evidence</u>: fever as reported by patient or healthcare provider, anemia, leukopenia, thrombocytopenia, any hepatic transaminase elevation, or elevated C-reactive protein

Subjective clinical evidence: chills/sweats, headache, myalgia, or fatigue/malaise

#### 4. Laboratory Criteria for Diagnosis (2024)

Confirmatory laboratory evidence:

- Detection of *A. phagocytophilum* DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, nucleic acid amplification tests (NAAT), or other molecular testing, **OR**
- Serological evidence of a four-fold change in IgG-specific antibody titer to *A*. *phagocytophilum* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in the first two weeks after illness onset and a second taken two to ten weeks after acute specimen collection), **OR**
- Demonstration of anaplasmal antigen in a biopsy or autopsy sample by immunohistochemical methods, **OR**
- Isolation of *A. phagocytophilum* from a clinical specimen in cell culture with molecular confirmation (e.g., PCR or sequencing)

#### Presumptive laboratory evidence:

- Serological evidence of elevated IgG antibody reactive with *A. phagocytophilum* antigen by IFA at a titer ≥1:128 in a sample taken within 60 days of illness onset, OR
- Microscopic identification of intracytoplasmic morulae in leukocytes in a sample taken within 60 days of illness onset.

#### 5. Case Classification (2024)

#### Confirmed:

• Meets confirmatory laboratory evidence AND at least one of the objective or subjective clinical evidence criteria.

#### Probable:

- Meets presumptive laboratory evidence with fever as reported by patient or healthcare provider AND at least one other objective or subjective clinical evidence criterion (excluding chills/sweats), OR
- Meets presumptive laboratory evidence without a reported fever but with chills/sweats AND
  - $\circ$  at least one objective clinical evidence criterion, OR
  - two other subjective clinical evidence criteria.

Suspect:

• Meets confirmatory or presumptive laboratory evidence with no or insufficient clinical information to classify as a confirmed or probable case (e.g., a laboratory report only).

Note: *A. phagocytophilum* is closely related to *Ehrlichia* spp. bacteria, and many patients are tested using serologic panels that include targets for both species. As a result, it is not uncommon for jurisdictions to receive positive antibody results for both *Anaplasma* and *Ehrlichia* spp. with the same collection date for a single patient. Public health agencies should use a combination of titer levels, information about the location of possible exposures, clinical manifestations, and the incidence of a particular disease in the geographic areas of exposure to help determine the appropriate disease type for individual patients. Patients should not be classified as cases for both anaplasmosis and ehrlichiosis based on serologic evidence alone.

# 6. Resources

Anaplasmosis: https://www.cdc.gov/anaplasmosis/

# **B.** Babesiosis

# 1. Background & Epidemiology

Babesiosis is a parasitic disease caused by intraerythrocytic parasites of the *Babesia* genus, most commonly *B. microti* but also *B. duncani* (formerly WA1), which was first described in Washington State, and *B. divergens*-like agents identified in the United States. *Babesia* are most commonly transmitted through bites of infected ticks but can also be acquired through contaminated blood components from asymptomatic parasitemic donors or, more rarely, transplacentally. See Table 1 for information on vector tick distribution.

# 2. Clinical Description

Clinical disease ranges in severity from asymptomatic to life-threatening. Clinical manifestations, if any, typically appear 1-4 weeks after tick bite and 1-9 weeks after blood transfusion. Common symptoms include fever, chills, sweats, headache, myalgia, malaise, and fatigue. Laboratory findings may include anemia, thrombocytopenia, and elevated levels of liver enzymes. Severe disease may include hemolytic anemia, disseminated intravascular coagulation, kidney, lung, or liver failure. Splenomegaly, hepatomegaly, or jaundice may be evident. Persons who are elderly, asplenic, or immune compromised are at risk for severe illness. Differential diagnoses: ehrlichiosis, Lyme disease, relapse of malaria, spotted fevers, typhoid fever.

# 3. Clinical Criteria (2025)

For the purposes of surveillance, a clinically compatible case is defined as follows:

- Objective: fever as reported by patient or healthcare provider, anemia, or thrombocytopenia
- Subjective: chills, sweats, headache, myalgia, or arthralgia

# 4. Laboratory Criteria for Diagnosis (2025)

For the purposes of surveillance, laboratory evidence includes:

Confirmatory:

- Identification of intraerythrocytic *Babesia* organisms by light microscopy in a Giemsa, Wright, or Wright-Giemsa–stained blood smear; **OR**
- Detection of *Babesia spp.* DNA in a whole blood specimen through nucleic acid testing such as polymerase chain reaction (PCR), nucleic acid amplification test (NAAT), or genomic sequencing that amplifies a specific target, in a sample taken within 60 days of illness onset; **OR**
- Serological evidence of a four-fold change in IgG-specific antibody titer to *B. microti* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken within two weeks of illness onset and a second taken up to 10 weeks after acute specimen collection).

#### Presumptive:

• Serologic evidence\* of an elevated IgG\*\* or total antibody reactive to *B. microti* antigen by IFA at a titer of  $\geq$  1:256 in a sample taken within 60 days of illness onset.

#### Supportive:

- Serologic evidence\* of an elevated IgG\*\* or total antibody reactive to *B*. *divergens* antigen by IFA at a titer of ≥ 1:256; **OR**
- Serologic evidence\* of an elevated IgG\*\* or total antibody reactive to *B. duncani* antigen by IFA at a titer of  $\geq$  1:512.

\*Antibodies can be indicative of active or previously resolved infections, so it is recommended that laboratory results be evaluated in conjunction with information on symptoms and exposure whenever possible. If symptom information is available, specimens meeting supportive laboratory criteria should be collected within 60 days of illness onset.

**\*\*** While a single IgG serologic test is adequate for surveillance purposes, molecular testing or blood smear are recommended for clinical diagnosis, especially in cases where species other than B. microti are suspected.

# 5. Case Classification (2025)

#### Suspected:

• Meets supportive laboratory evidence.

#### Probable:

• Meets presumptive laboratory evidence AND meets at least one of the objective clinical criteria.

# Confirmed:

• Meets confirmatory laboratory evidence AND at least one of the objective or subjective clinical criteria.

A new case of babesiosis is one that has not been previously enumerated within the same calendar year (January through December).

#### 6. Comments on Interpreting Babesiosis Laboratory Results

Diagnosis of babesiosis requires a high index of suspicion, in part because the clinical manifestations are nonspecific. The validity of the diagnosis of babesiosis is highly dependent on the laboratory that performs the testing. *Babesia* and *Plasmodium* (especially *P. falciparum*) parasites can be difficult to differentiate. Confirmation of the diagnosis by a reference laboratory is strongly encouraged, especially for patients without residence in or travel to areas known to have high incidence of babesiosis. A positive IFA result for IgM is insufficient for diagnosis in the absence of a positive IFA result for IgG or total Ig. If the IgM result is positive but the IgG result is negative, a follow-up specimen collected >1 week after the first should be tested.

7. Resources: <u>https://www.cdc.gov/dpdx/babesiosis/index.html</u>

#### C. Ehrlichiosis

#### 1. Background & Epidemiology

At least three species of obligate intracellular bacteria are responsible for ehrlichiosis in the United States: *Ehrlichia chaffeensis*, found primarily in monocytes, *E. ewingii* found primarily in granulocytes, and *E. muris eauclairensis*, with no target cell yet identified. The clinical signs of disease that result from infections with these agents are similar, and the range distributions of the agents overlap, so testing for one or more species may be indicated. Differential diagnoses: anaplasmosis, spotted fever rickettsiosis, bacterial or viral meningitis, typhoid fever.

#### 2. Clinical Presentation

Characterized by acute onset of fever and one or more of the following symptoms or signs: severe headache, myalgia, nausea, vomiting, diarrhea, loss of appetite, rash (more common in children), malaise, anemia, leukopenia, thrombocytopenia, or elevated hepatic transaminases. Severe clinical presentations may include meningitis, meningoencephalitis or other central nervous system involvement, acute respiratory distress syndrome, toxic shock or septic shock-like syndromes, renal or hepatic failure, or coagulopathies. Persons with delayed treatment, compromised immunity, or older age appear to develop more severe disease, and may also have higher case-fatality rates.

#### 3. Clinical Criteria for Diagnosis (2024)

- <u>Objective clinical evidence</u>: fever as reported by patient or healthcare provider, anemia, leukopenia, thrombocytopenia, or any hepatic transaminase elevation
- <u>Subjective clinical evidence</u>: chills/sweats, headache, myalgia, nausea/vomiting, or fatigue/malaise

# 4. Laboratory Criteria for Diagnosis (2024)

Confirmatory Laboratory Evidence:

• Detection of *E. chaffeensis*, *E. ewingii*, *E. muris eauclairensis*, unspeciated *Ehrlichia* spp., or other *Ehrlichia* spp. DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, nucleic acid amplification tests (NAAT), or other molecular method, OR

- Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer to *Ehrlichia* antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in first two weeks after illness onset and a second taken two to ten weeks after acute specimen collection)\*, OR
- Demonstration of ehrlichial antigen in a biopsy or autopsy sample by immunohistochemical methods, OR
- Isolation of *E. chaffeensis*, *E. ewingii*, *E. muris eauclairensis*, unspeciated *Ehrlichia* spp., or other *Ehrlichia* spp. from a clinical specimen in cell culture with molecular confirmation (e.g., PCR or sequence).

#### Presumptive Laboratory Evidence:

- Serological evidence of elevated IgG antibody reactive with *Ehrlichia* spp. antigen by IFA at a titer ≥1:128 in a sample taken within 60 days of illness onset, OR
- Microscopic identification of intracytoplasmic morulae in leukocytes in a sample taken within 60 days of illness onset.

\* A four-fold rise in titer should not be excluded as confirmatory laboratory criteria if the acute and convalescent specimens are collected within two weeks of one another.

#### 5. Case Classification (2024)

*Confirmed:* Meets confirmatory laboratory evidence AND at least one of the objective or subjective clinical evidence criteria.

Probable:

- Meets presumptive laboratory evidence with fever as reported by patient or healthcare provider AND at least one other objective or subjective clinical evidence criterion (excluding chills/sweats), OR
- Meets presumptive laboratory evidence without reported fever but with chills/sweats AND
  - o at least one objective clinical evidence criterion, OR
  - two other subjective clinical evidence criteria.

*Suspect:* Meets confirmatory or presumptive laboratory evidence with no or insufficient clinical information to classify as a confirmed or probable case (e.g., a laboratory report only).

Note: *A. phagocytophilum* is closely related to *Ehrlichia* spp. bacteria, and many patients are tested using serologic panels that include targets for both species. As a result, it is not uncommon for jurisdictions to receive positive antibody results for both *Anaplasma* and *Ehrlichia* spp. with the same collection date for a single patient. Public health agencies should use a combination of titer levels, information about the location of possible exposures, clinical manifestations, and the incidence of a particular disease in the geographic areas of exposure to help determine the appropriate disease type for individual patients. Patients should not be classified as cases for both anaplasmosis and ehrlichiosis based on serologic evidence alone.

#### 6. Comments on Interpretation of Results

Serologic cross-reactions may occur among tests for these etiologic agents and the IgM response may be persistent. 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. Current commercially available ELISA tests are not quantitative and hence not useful for serological confirmation.

Tests of additional sera and further evaluation via 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.

#### 7. Resources

Ehrlichiosis: https://www.cdc.gov/ehrlichiosis/

#### **D.** Tick Paralysis

# 1. Background and Epidemiology

Agent is a neurotoxin secreted in the saliva of certain ticks. If unrecognized, tick paralysis can progress to respiratory failure and may be fatal in approximately 10% of cases. Cases are rare in Washington; usually 0-1 per year and most commonly during spring months in girls (with long hair that conceals ticks) under 10 years old. Differential diagnoses: Guillain-Barré, botulism, myasthenia gravis, polyradiculoneuritis, acute peripheral neuropathy, snakebite.

# 2. Case Definition

*Confirmed:* Symptoms consistent with illness (acute, ascending, flaccid paralysis) and rapid improvement of the patient upon removal of tick.

- 3. Laboratory Diagnostics: None other than tick identification.
- 4. Resources: https://www.cdc.gov/mmwr/preview/mmwrhtml/00040975.htm

# **E. Spotted Fever Rickettsioses**

# 1. Background and Epidemiology

Spotted fever rickettsioses (SFR) are a group of tick-borne infections caused by some members of the bacterial genus *Rickettsia* and can range from mild illness to fatal disease. The most severe type in the country, Rocky Mountain spotted fever (RMSF), is caused by *Rickettsia rickettsii*. RMSF cases occur throughout the United States, but are most commonly reported from five states: NC, TN, MO, AR, and OK; which also account for >60% of SFR cases. Typically, 0-3 cases are reported annually in Washington; with most exposures out of state. Most cases occur April through September when ticks are active.

Additional SFRs occur worldwide and also result in a broad range of illnesses. The most commonly reported SFRs among Washington residents who travel internationally are African tick bite fever (*R. africae*) and Mediterranean spotted fever (*R. conorii*). Differential diagnoses: babesiosis, ehrlichiosis and anaplasmosis, bacterial or viral meningitis, drug allergy mononucleosis, measles, relapsing fever, streptococcal infection,

syphilis, toxic shock syndrome, tularemia, typhoid, typhus.

# 2. Clinical Presentation

For RMSF, illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash appears 4-7 days following onset, often present on the palms and soles. Untreated disease may lead to more severe manifestations that include encephalitis, shock, seizures, gangrene, acute respiratory and renal failure, and death. The case-fatality rate is 13-25% if untreated and 4% even with appropriate antibiotic treatment. Children frequently experience gastrointestinal symptoms, altered mental status, and edema involving hands or eyes. Petechiae are a sign of progression to severe disease and every attempt should be made to begin treatment for severe cases before petechiae develop.

Other SFRs may have similar, but milder, clinical presentation than RMSF, and may cause an eschar (ulcerated, necrotic region) at the site of tick attachment that appears before onset of fever.

# 3. Clinical Criteria (2020)

Fever as reported by the patient or a healthcare provider, AND one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

# 4. Laboratory Criteria (2020)

For the purposes of surveillance:

Confirmed:

- Serological evidence of a fourfold increase in IgG-specific antibody titer reactive with spotted fever group-*Rickettsia* (SFGR) antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (one taken in the first two weeks after illness onset and a second taken 2-10 weeks after acute specimen collection)\*, **OR**
- Detection of SFGR nucleic acid in a clinical specimen via amplification of a *Rickettsia* genus- or species-specific target by PCR assay, **OR**
- Demonstration of SFGR antigen in a biopsy or autopsy specimen by IHC, OR
- Isolation of *R. rickettsii* or other SFGR from a clinical specimen in cell culture and molecular confirmation (e.g., PCR or sequence.

# Presumptive:

• Has serologic evidence of elevated IgG antibody at a titer ≥1:128 reactive with SFGR antigen by IFA in a sample taken within 60 days of illness onset.\*\*

# Supportive:

• Has serologic evidence of elevated IgG antibody at a titer <1:128 reactive with SFGR antigen by IFA in a sample taken within 60 days of illness onset.

\*A four-fold rise in titer should not be excluded (as confirmatory laboratory criteria) if the acute and convalescent specimens are collected within two weeks of one another.

\*\*This includes paired serum specimens without evidence of fourfold rise in titer, but with at least on single titer  $\geq$ 1:128 in IgG-specific antibody titers reactive with SFGR antigen by IFA.

#### 5. Case Classification (2020)

*Suspected:* A case with confirmatory or presumptive laboratory evidence of infection with no clinical information available (e.g., a laboratory report), OR

A clinically compatible case (meets clinical criteria) that has supportive laboratory evidence.

*Probable:* A clinically compatible case (meets clinical evidence criteria) that has presumptive laboratory results.

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

#### 6. Comments on Interpretation of Results

The organism in the acute phase of illness is best detected by polymerase chain reaction (PCR) and immunohistochemical methods (IHC) in skin biopsy specimens, and occasionally by PCR in appropriate whole blood specimens taken during the first week of illness, prior to antibiotic treatment. Serology can also be employed for detection, however an antibody response may not be detectable in initial samples, and paired acute and convalescent samples are essential for confirmation.

*R. rickettsii* (RMSF) do not circulate in large numbers in the blood until the disease has progressed to a severe phase of infection. For this reason, whole blood specimens obtained during the first several days of illness are often negative when PCR or culture.

Current commercially available ELISA tests are not quantitative and hence 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.

#### 7. Resources: <u>https://www.cdc.gov/rmsf/</u>

# 4. DIAGNOSIS AND LABORATORY SERVICES

#### A. Diagnosis

Appropriate diagnostic testing depends on the suspected agent. Commercial laboratory tests may be unreliable for many of these tick-borne diseases, so confirmation by a reference laboratory may be appropriate. Any suspected cases of anaplasmosis, ehrlichiosis, babesiosis, or rickettsioses with possible acquisition in Washington should have specimens forwarded for confirmatory testing at CDC.

#### B. Tests Available at the Washington State Health Public Health Laboratories (PHL)

Consult with Communicable Disease Epidemiology (CDE) for assistance with diagnosis and testing (206-418-5500).

• PHL can identify tick species associated with any tick-borne disease and confirm *Babesia spp.* on blood smears. PHL can also arrange testing at CDC for skin or tissue

specimens, serum, and whole blood. Laboratory diagnosis does not exist for tick paralysis; ticks can be submitted for species identification. Tick or blood smear specimens should be submitted to PHL Parasitology through WAPHL LabWeb Portal:

http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLabora tories/MicrobiologyLabTestMenu

- Skin, tissue, serum, or whole blood will be forwarded to CDC for additional testing. Submit serum in red or tiger top tubes spun down and whole blood in EDTA (purple top) tubes.
- Note that Washington State Public Health Laboratories (PHL) require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.
- For appropriate collection, storage, and shipping details, see: <u>http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLabora</u> <u>tories/MicrobiologyLabTestMenu</u>

# 5. ROUTINE CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent information.

#### A. Evaluate the Diagnosis

If the case tests positive for tick-borne disease at a laboratory other than PHL or CDC, discuss the need to perform confirmatory testing with Communicable Disease Epidemiology (206-418-5500). As needed, facilitate transport of the specimen to PHL for further testing.

Determine if others are at risk through shared exposure. See Section 6 for brief descriptions of investigations for selected conditions. Consult with CDE for assistance with performing a public health investigation for other agents. The reporting form for Tick-borne Diseases is available at:

https://www.doh.wa.gov/Portals/1/Documents/5100/420-214-ReportForm-Tickborne.pdf.

#### **B.** Manage the Case

- 1. Hospitalized cases should be treated with standard precautions.
- 2. Assess evidence or risk of local transmission. Other than tick paralysis, each condition described here is very rarely reported in Washington, with the exception of ehrlichiosis, which has not been identified in Washington. Identify any travel during the patient's exposure period (including specific locations and travel dates), as well as possible exposures including: exposure to tick habitats, contact with dogs and/or wildlife, and potential tick bites with emphasis on locally acquired infection. If local exposure is suspected, collect detailed location information to facilitate potential environmental investigation.
- 3. Ask about receiving or donating blood products and about organ or tissue transplant or donation. See section 6 for disease-specific donor follow-up.

4. Controlling further spread: Educate those sharing a case's exposure about tick-borne disease and encourage them to seek care if consistent illness develops.

### 6. MANAGING SPECIFIC DISEASES

#### A. Babesiosis

Cases must defer from blood donation for life.

If the patient under investigation donated blood or organs while possibly infectious, inform the blood or tissue bank of the potential exposure risk to others. Obtain the date and location of transfusions of any products from the infected patient. Identify possible contaminated product(s) within the appropriate window. If any specimens are still available, arrange for testing. Notify other partners, including health departments in other states if blood units were transferred. Work with the blood collection facility to identify all persons who received specimens from the infected patient and ensure testing.

If the patient under investigation received blood or organs from a donor during their exposure period, obtain date(s) and location(s) of recent transfusions/transplants. Check on the availability of pre-transfusion specimens to use as baseline for testing. Acquire unit numbers, type of blood component, and associated facility for each transfusion. Notify the blood center of potential transfusion-associated infection and determine their standard procedures for donor contact and testing.

Resources:

https://www.cdc.gov/parasites/babesiosis/resources/50.153.pdf

https://www.cdc.gov/bloodsafety/pdf/Generic Transfusion Investigation form.pdf

#### **B.** Ehrlichiosis and Anaplasmosis

Doxycycline is the first line treatment for adults and children of all ages and should be initiated immediately whenever ehrlichiosis or anaplasmosis are suspected. Transfusionassociated anaplasmosis is rare but possible. Patients who develop anaplasmosis within a month of receiving a blood transfusion or solid organ transplant should be investigated as a possible transfusion-associated case. Patients who develop ehrlichiosis within a month of receiving a blood transfusion or solid organ transplant should be investigated although no cases of transmission by blood transfusion or organ donation have been confirmed.

#### C. Spotted fever rickettsiosis

Doxycycline is the first line treatment for adults and children of all ages and should be initiated immediately for all suspected rickettsial infections. Early treatment can prevent death and severe illness.

#### **D.** Tick paralysis

Carefully check patient for ticks, especially along the hairline. Prompt removal of the tick usually results in complete recovery within 24 hours.

#### E. Environmental Evaluation/Management

Consider outreach to educate the public about avoiding tick exposure. Environmental measures to reduce ticks around the home include modifying landscape to create tick-safe zones. Removing leaf litter and clearing tall grasses and brush around homes, placing

wood chips or gravel between lawns and wooded areas, and keeping play areas away from shrubs, bushes, and other vegetation may help to reduce exposures. Notify local environmental health program and/or vector control and CDE of locally acquired cases. Environmental investigation in collaboration with the public health entomologist may be pursued.

#### 7. ROUTINE PREVENTION

#### A. Immunization Recommendations

Vaccines for tick-borne diseases included in this guideline are not currently available in the United States.

#### **B.** Prevention Recommendations

When spending time outdoors in risk areas, persons should:

- 1. Treat clothing and gear with products containing permethrin.
- 2. Use EPA registered insect repellent on exposed skin, following label instructions. Products containing DEET, picaridin, IR3535, Oil of Lemon Eucalyptus, or 2undecanone are very effective. Carefully follow instructions on the label. Take special care when using repellents on children.
- 3. Wear long pants and a long-sleeved shirt. Tuck pant legs into socks or boots and shirt into pants to help keep ticks on the outside of clothing where they can be more easily spotted and removed.
- 4. Wear light colored, tightly woven clothing which will allow the darker tick to be seen more easily. The tight weave makes it harder for the tick to attach itself.
- 5. Tumble clothes in a dryer on high heat for 10 minutes to kill ticks on dry clothing after you come indoors.
- 6. Shower soon after being outdoors to wash off unattached ticks.
- 7. After potential exposures, check yourself, your children, pets, and gear thoroughly for ticks. Carefully inspect areas around the head, neck, ears, and hairline. If you find a tick attached to your skin, promptly remove it, including all mouthparts, which contain the salivary glands. Grasp the tick using tweezers as close to the skin as possible. With a steady motion, pull the tick straight out. Wash your hands and apply antiseptic to the bite. Do twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. For more information about removing a tick, visit: <a href="https://www.cdc.gov/ticks/after-a-tick-bite/index.html">https://www.cdc.gov/ticks/after-a-tick-bite/index.html</a>.
- 8. Monitor the bite and be alert for early symptoms of tick-borne disease, e.g. fever or rash over the next month.
- 9. Additional information regarding prevention of tick bites and tick repellant is available at CDC: <u>https://www.cdc.gov/ticks/prevention/index.html</u>.

#### ACKNOWLEDGEMENTS

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for developing the format of this document.

#### UPDATES

April 2018: This guideline was created based on the previous guideline for "Rare diseases of public health significance".

January 2020: The CSTE case definition for Spotted Fever Group Rickettsiosis was updated to the 2020 definition.

December 2022: For January 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B)

December 2023: For January 2024 WAC revision updated laboratory submission process.

January 2024: Updated to separate anaplasmosis and ehrlichiosis sections and updated case definitions.

December 2024: Updated section 3B with 2025 babesiosis case definition.

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