

# Relapsing Fever

<b>Signs and Symptoms</b>	Occurs as soft tick-borne ( <i>Borrelia hermsii</i> , <i>parkeri</i> , or <i>turicatae</i> ), hard tick-borne ( <i>Borrelia miyamotoi</i> ) or louseborne ( <i>B. recurrentis</i> ) Fever lasting 2–7 days and terminating abruptly alternating with afebrile periods of 4–14 days. There is a risk for premature birth or pregnancy loss. May be shaking chills, sweats, headache, muscle and joint pain, nausea, rash. Less frequently, patients may have jaundice, hepatosplenomegaly, photophobia	
<b>Incubation</b>	Typically 7 days, range 2 to 18 days	
<b>Case classification (soft tick-borne relapsing fever)</b>	<b>Clinical criteria:</b> relapsing pattern of fever $\geq 102^{\circ}\text{F}$ ( $38.8^{\circ}\text{C}$ ), chills, headache, myalgia	
	<b>Confirmed:</b> clinically compatible illness in a person with: confirmatory lab OR presumptive lab and epi link	<b>Probable:</b> clinically compatible illness in a person with: presumptive lab evidence or with epi link
<b>Differential diagnosis</b>	Multiple agents depending on presentation and exposure including viral hepatitis, mononucleosis, leptospirosis, rickettsial infections, vasculitis, ehrlichiosis, tularemia	
<b>Treatment</b>	Doxycycline, tetracycline, azithromycin, erythromycin, parenteral ceftriaxone or doxycycline (if central nervous system illness), or beta-lactams. A Jarisch-Herxheimer reaction can occur; monitor patients closely following treatment.	
<b>Duration</b>	1 to 10 febrile relapses if untreated; not communicable person to person.	
<b>Exposure</b>	<p><b>Soft Tick-borne:</b> wild rodent reservoir. Vectors most commonly nymphal or adult soft tick species <i>Ornithodoros hermsii</i>, <i>O. parkeri</i>, and <i>O. turicatae</i>. Bites are often unnoticed due to rapid night feeding, painless bites, and small size of the tick. Ticks live in rodent burrows and may emerge at night to feed, such as in rodent-infested cabins or from woodpiles with rodent infestation.</p> <p><b>Hard Tick-borne:</b> wild rodent reservoirs. <i>Ixodes scapularis</i> or <i>I. pacificus</i> vectors.</p> <p><b>Louseborne:</b> human reservoir in other parts of the world. Vector is the body louse.</p>	
<b>Laboratory testing</b>	<p>Local Health Jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) can arrange testing for suspected cases.</p> <p>Washington State Public Health Laboratories do microscopy on blood smears. Serum or whole blood can be tested at CDC.</p> <p><b>Best specimens:</b> blood smear collected during febrile period; acute serum within 7 days and convalescent serum after 21 days; whole blood in EDTA prior to antibiotic treatment</p> <ul style="list-style-type: none"> <li>Keep blood smears at <b>ambient temperature</b>, serum or whole blood <b>cold</b>, ship according to PHL requirements: <a href="https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu">https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu</a></li> </ul>	
<b>Public health actions</b>	<p>LHJ can consult with CDE 877-539-4344 for investigation and to arrange testing</p> <ul style="list-style-type: none"> <li>Identify potential exposures</li> <li>Educate persons who shared exposures, particularly women who are pregnant</li> <li>Educate the property owner about rodent and tick control measures</li> <li>Determine if the person donated blood or tissues recently and if so notify CDE</li> </ul> <p><i>Infection Control:</i> standard precautions for tickborne, contact precautions while removing initial clothing of a louseborne case; infested clothing should be bagged</p>	

# Relapsing Fever

## 1. DISEASE REPORTING

### A. Purpose of Reporting and Surveillance

1. To educate potentially exposed persons about signs and symptoms of disease to facilitate early diagnosis and treatment.
2. To inform owners of potentially tick-infested property (e.g., a vacation cabin) how to reduce their risk of exposure and prevent exposure to additional persons.
3. To identify and monitor changes to endemic geographic areas within Washington state.

### B. Legal Reporting Requirements

1. Health care providers and Health care facilities: notifiable to **local health jurisdiction** within 3 business days.
2. Laboratories: *Borrelia hermsii*, *B. parkeri*, *B. turicatae*, *B. miyamotoi*, or *B. recurrentis* notifiable to local health jurisdiction within 2 business days; submission on request – specimen associated with positive result, within 2 business days.
3. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Office of 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. Begin follow-up investigation upon receipt of new case information.
2. Educate other persons exposed about the signs and symptoms of disease.
3. Provide education to eliminate the source of infection.
4. Report all *confirmed* and *probable* cases (see definitions below) to CDE. Complete the relapsing fever case report form <https://www.doh.wa.gov/Portals/1/Documents/5100/210-045-ReportForm-Relaps.pdf> and enter the data into the Washington Disease Reporting System (WDRS).

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic Agent

Soft tick-borne relapsing fever is most commonly caused by *Borrelia hermsii*, but can be caused by at least 14 other *Borrelia* species. Hard tick-borne relapsing fever is caused by the recently discovered pathogen *B. miyamotoi*. In louse-borne disease, *B. recurrentis* is the only etiologic agent.

### B. Description of Illness

Relapsing fever is a systemic spirochetal disease in which periods of fever lasting 2–7 days (average 3 days) alternate with afebrile periods of 4–14 days (average 7 days); the number of febrile relapses varies from 1 to 10 episodes without treatment. Febrile periods are often associated with shaking chills, sweats, headache, muscle and joint pain, or nausea and vomiting. Each febrile period terminates by a crisis (abrupt symptom change). Symptoms can

be severe. Acute respiratory distress syndrome (ARDS) may occur in patients with tick-borne relapsing fever.\*

Optimal management of relapsing fever requires both prompt diagnosis and careful observation during the initial phases of treatment. With appropriate treatment most patients recover within a few days and the mortality rate is very low; the mortality rate without treatment is estimated at 5–10%. Long-term sequelae are rare but include iritis, uveitis, cranial nerve and other neuropathies. Soft tick-borne relapsing fever contracted during pregnancy can cause spontaneous abortion, premature birth, and neonatal death.

\*Centers for Disease Control and Prevention. Acute Respiratory Distress Syndrome in Persons with Tickborne Relapsing Fever --- Three States, 2004–2005. MMWR 2007;56:1073–76. Available at: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5641a1.htm>.

### C. Relapsing Fever in Washington

Soft tick-borne relapsing fever is among the most common tick-borne illnesses contracted in Washington State. One to 12 cases are reported annually, with rare reports of pregnancy loss due to maternal infection. Exposures are frequently associated with overnight stays in rural cabins in mountainous areas, and usually but not always during summer months.

The agent of hard tick-borne relapsing fever, *Borrelia miyamotoi*, has been detected in field-collected ticks but not yet detected in humans exposed in WA.

The louse-borne form of this disease is not endemic to the United States and it would be rare even in travelers returning to Washington State.

### D. Vectors and Reservoirs

In soft tick-borne relapsing fever in the United States, the vectors most commonly transmitting the infection are soft tick species *Ornithodoros hermsii*, *O. turicata*, and *O. parkeri*. Locally, *O. hermsii* is typically found at higher altitudes (1500 – 8000 feet), on the eastern slopes of the Cascades and in other parts of eastern Washington, and the most common reservoirs appear to be wild rodents, such as deer mice, squirrels, chipmunks, and rats. *Ornithodoros* ticks tend to live for many years and take infrequent blood meals, but once infected from feeding on a wild rodent they harbor the pathogen for life. Either the nymphal or adult stage tick can transmit the infection. Females pass the infection to their progeny.



*Ixodes* spp. ticks, particularly *I. scapularis* and *I. pacificus* are the documented vectors for *B. miyamotoi*. *I. pacificus* are found across western WA and the eastern slopes of the Cascade Mountain Range.

The body louse (*Pediculus humanus*) is the vector for louse-borne relapsing fever. Lice become infected 4-5 days after feeding on infected humans and remain infective for their lifespan of several weeks.

### E. Modes of Transmission

In tick-borne disease, people are infected by bites of infected soft or hard ticks. Unlike hard ticks, soft ticks usually feed at night. The bites are usually unnoticed since they generally occur at night and are not painful. In addition, soft ticks are small (approximate 3 mm), feed

quickly (5–20 minutes) and then leave the host. In western states including Washington, ticks may be present in rustic cabins and woodpiles with rodent infestation. The ticks live in rodent nests, which may be under flooring or between walls. If rodents are scarce or nests are disturbed the ticks may bite other warm-blooded animals, including humans, for their blood meals. Tick-borne relapsing fever is not directly transmitted from person-to-person, but theoretically might be transmitted by blood transfusion.

Louse-borne relapsing fever is not endemic to the United States but may occur in travelers. It is acquired by crushing an infected louse so that it contaminates the bite wound or mucous membranes.

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

The incubation period is usually about 7 days but can range from 2 to 18 days.

#### **G. Period of Communicability**

Tick-borne relapsing fever is not directly transmitted person to person. Tick-infested cabins may be difficult to decontaminate and may be a source of human infection for several years; ticks may also be reintroduced from wood piles or firewood brought indoors.

#### **H. Treatment**

Relapsing fever is treated with appropriate antibiotic therapy including doxycycline, tetracycline or azithromycin/erythromycin, with parenteral ceftriaxone used for central nervous system illness. Antibiotic treatment can cause a Jarisch-Herxheimer reaction (i.e., severe chills, increased temperature, and decreased blood pressure), so patients should be monitored closely during therapy, particularly during the first 4 hours after antibiotics are administered.

### **3. CASE DEFINITIONS**

**Soft Tick-borne Relapsing Fever** (including *Borrelia hermsii*, *B. parkeri*, or *B. turicatae*)

#### **A. Clinical Criteria for Diagnosis**

An acute febrile illness with:

- Measured fever  $\geq 102^{\circ}\text{F}$  ( $38.8^{\circ}\text{C}$ )
- One or more episodes of lower measured or subjective fever AND two or more of the following: headache, myalgia, nausea/vomiting, or arthralgia

#### **B. Laboratory Criteria for Diagnosis**

*Confirmatory laboratory evidence:*

1. Isolation of *Borrelia hermsii*, *B. parkeri*, or *B. turicatae* from blood using a *Borrelia*-specific medium such as Barbour-Stoenner-Kelly (BSK) broth medium.

2. *Borrelia hermsii*, *B. parkeri*, or *B. turicatae* detection through nucleic acid testing, such as PCR, which differentiates soft-tick relapsing fever *Borrelia* spp. from other relapsing fever *Borrelia* sp.<sup>1</sup>

*Presumptive laboratory evidence:*

1. Identification of *Borrelia* spirochetes in peripheral blood, bone marrow, or cerebrospinal fluid (CSF).
2. Serologic evidence of *Borrelia hermsii*, *B. parkeri*, or *B. turicatae* infection by EIA, immunofluorescence assay (IFA), IgM or IgG western immunoblot (WB), or another method specific for relapsing fever *Borrelia* species.
3. *Borrelia hermsii*, *B. parkeri*, or *B. turicatae* detection through nucleic acid testing, such as PCR, which does not differentiate soft-tick relapsing fever *Borrelia* spp. from other relapsing fever *Borrelia* sp.<sup>2</sup>

<sup>1</sup>This includes only PCR tests that can differentiate soft-tick relapsing fever *Borrelia* spp. from hard-tick and louse-borne relapsing fever *Borrelia* spp. At the time of writing, this type of test is only available from CDC.

<sup>2</sup>This includes PCR tests that are specific to relapsing fever *Borrelia* sp. but that cannot differentiate soft-tick relapsing fever *Borrelia* spp. from hard-tick and louse-borne relapsing fever *Borrelia* spp. This does not include pan-*Borrelia* PCR tests.

### C. Epidemiologic Linkage

The habitats where relapsing fever *Borrelia* spp. are present are sympatric with that of their *Ornithodoros* spp. tick vectors. *Ornithodoros hermsi*, the vector for *B. hermsii*, is typically found in rodent nests in mountainous areas above 450 m (1,500 ft) elevation where chipmunks or squirrels are present. The vector for *B. parkeri*, *O. parkeri*, is found at lower elevations in the Southwest and inhabits burrows of prairie dogs, ground squirrels and burrowing owls. *Ornithodoros turicata*, the vector for *B. turicatae*, occurs in caves, and nests and burrows of prairie dogs and ground squirrels in the plains regions of the Southwest.

**Exposure** is defined as living in, working in, or visiting a county in which *Ornithodoros* soft ticks are present or where a confirmed autochthonous case of TBRF has been previously reported. Exposure activities include entering, sleeping, or working in cabins, caves, around firewood, or other possible soft tick habitat within 2-18 days of symptom onset.

**Epidemiologic link:** Onset of clinically compatible illness in a person who had a shared exposure location as a confirmed case with symptom onset 2-18 days after exposure.

### Case Definition (Soft Tick-borne Relapsing Fever, 2022 Western States Standardized)

*Confirmed:* A clinically compatible illness in a person with confirmatory laboratory evidence,

OR

A clinically compatible illness in a person with presumptive laboratory evidence and meets the above criteria for exposure or epidemiologic linkage.

*Probable:* A clinically compatible illness in a person with presumptive laboratory evidence of infection,

OR

A clinically compatible case who meets the epidemiologic link criteria.

*Suspect:* A clinically compatible case who meets the exposure criteria above, with no laboratory testing performed,

OR

A case with laboratory evidence of infection but no clinical, exposure, or epidemiologic linkage information available.

**Criteria to distinguish a new case of this disease from reports or notifications which should not be enumerated as a new case for surveillance:**

Case not previously reported to public health authorities and with epi linkage within one month of disease onset or laboratory support (date of collection) within four months of disease onset.

## **4. DIAGNOSIS AND LABORATORY SERVICES**

### **A. Diagnosis**

Diagnostic approaches for soft tick-transmitted TBRF have been changing. As it has been for more than a century, the most common diagnostic test for confirmation of relapsing fever is spirochete identification on a stained peripheral blood smear (either by dark field microscopy or microscopic examination of a stained thick or thin blood film) taken just before or at the height of a febrile episode. The stained blood smear cannot differentiate relapsing fever *Borrelia* species. Other bacteria, such as *Helicobacter* or *Leptospira*, may appear morphologically similar, so it is important to consider clinical and geographical characteristics of the case when making a diagnosis of TBRF based on microscopy. Moreover, with the increase in the use of automated examination of blood smears in hospitals and clinics, there are fewer opportunities for the diagnosis to be serendipitously made by an alert technician in the clinical laboratory.

CDC currently offers a PCR-based assay that can differentiate soft-tick transmitted TBRF from other relapsing fever spirochetes (e.g. the louse-borne relapsing fever agent *Borrelia recurrentis* and the hard-tick relapsing fever agent, *Borrelia miyamotoi*) as well as other PCR-based assays at commercial laboratories that can detect the relapsing fever *Borrelia* species more generally. Cultivation of the organism is possible and confirmatory, but this time-consuming diagnostic procedure is performed in few diagnostic laboratories.

Serologic detection of antibodies to the GlpQ protein, which is produced by relapsing fever *Borrelia* species, including *B. miyamotoi*, but not by the agents of Lyme disease, is available in some commercial laboratories. Assays for antibodies to the GlpQ protein of *B. miyamotoi* yield positive results with sera from patients with other forms of relapsing fever and other pathogens on the basis of cross-reactivity between GlpQ proteins of different species. Serology can be useful for surveillance, however, antibody response may not be detectable in acute samples. A negative test result may be repeated if early in disease. Antibodies stimulated by other *Borrelia* sp. infections (e.g., *B. miyamotoi*) are expected to cross-react on TBRF serologic assays. Likewise, tests for other spirochetal infections (e.g., Lyme disease) may be false-positive in a patient infected with relapsing fever *Borrelia* spp. Epidemiological information including exposure history is crucial to differentiate positive serology results.

More information regarding serologic testing can be found at:

<https://www.cdc.gov/relapsing-fever/hcp/soft-tick-relapsing-fever/index.html>

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

On request PHL will review slides for spirochetes in peripheral blood smears and will forward specimens to the CDC if additional tests are needed. Both PCR and serologic testing

are available through the CDC. All requests sent to PHL must have approval from the local health jurisdiction, which will make arrangements with Communicable Disease Epidemiology.

Note that 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 details see: <https://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-Para-Blood-V1.pdf>

### C. Specimen collection

1. **Blood smear:** any hospital or commercial laboratory can provide review.

Blood smears do not need to be submitted to PHL (Microbiology), but if additional examination is requested PHL can issue a preliminary confirmation of spirochetes then forward the slides to CDC.

2. **Serum**

Acute serum should be taken within 7 days of symptom onset and convalescent serum should be taken at least 21 days after symptoms start. Specimens should be refrigerated and transported **cold** on regular cold packs. Avoid repeated freeze-thaw cycles. If specimens are already frozen, transport on dry ice.

3. **Whole blood**

EDTA-treated whole blood collected prior to antibiotic treatment. Specimens should be refrigerated and transported **cold** on regular cold packs. Specimens must not exceed 2 freeze/thaw cycles.

4. **Shipping to PHL**

Keep blood smears at **ambient temperature**, serum or whole blood **cold**, ship according to PHL requirements: <https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu>

## 5. ROUTINE CASE INVESTIGATION

Interview the case and others who might provide pertinent information.

### A. Evaluate the Diagnosis

Using the case form, collect clinical information (e.g., onset, signs, and symptoms) about the patient. Review laboratory tests performed.

### B. Identify Potential Sources of Infection

Ask whether the patient slept outside, in a cabin, or in other places with evidence of rodents in the 18 days prior to onset. Ask about tick or insect bites, or the potential for soft tick exposure, including carrying firewood from a wood pile indoors or sitting outside at night in areas where there could be mouse habitation.

### C. Infection Control

1. Persons hospitalized for tick-borne relapsing fever should be cared for using standard precautions.

2. Persons with louse-borne relapsing fever should also be cared for using standard precautions. Staff should wear a gown and gloves when removing initial clothing of a louse-infested patient to prevent louse transmission. Infested clothing should be bagged.
3. Cases do not need to be restricted from work or child care.

#### **D. Identify Potentially Exposed Persons**

Identify persons who shared the exposure with the case (i.e., slept in the same cabin) and educate them about symptoms and treatment of relapsing fever. Determine whether any women who shared the exposure with the case are pregnant. Educate all potentially exposed persons about symptoms of relapsing fever to facilitate early diagnosis. Refer potentially exposed pregnant women to their doctor immediately to discuss prophylactic antibiotics.

Determine if the case donated blood, tissues or organs during the recent past. If so, contact Communicable Disease Epidemiology immediately and inform the blood or tissue bank of the potential exposure.

#### **E. Environmental Evaluation**

Notify local environmental health program and/or vector control of locally acquired cases. If the case was exposed on public property or in a building used by the general public, evaluate the site for evidence of rodent infestation. Work with the agency that oversees the site and make recommendations to decrease rodent and tick infestation on the site (see “Environmental Measures” below), recognizing that tick-infected rustic cabins may be difficult to decontaminate.

If the site of exposure is determined to be a tick and rodent infested human habitation, provide the following information to the owner of private property or the agency overseeing public property:

- Educate the owner about the ecology of tick-borne relapsing fever (see above).
- Recommend the removal of woodpiles from under/around the cabin to prevent rodent infestation outside the cabin.
- Recommend sealing the home (including roof, walls, doors, windows, around pipes, etc.) to prevent rodents from entering.
- Recommend placing all food in secondary containers to keep rodents from entering the cabin in search of food.
- Recommend the owner hire a professional pest control company to provide soft tick control.

Warn the owner that rodent-proofing without implementing tick control might increase the risk for tick-borne relapsing fever since the ticks can be left in the property after the rodents are removed.

## **6. MANAGING SPECIAL SITUATIONS**

Determine if the case is associated with or potentially associated with an outbreak.

**If an outbreak is suspected, notify Communicable Disease Epidemiology immediately: 1-877-539-4344.**

## 7. ROUTINE PREVENTION

### A. Immunization Recommendations: None

### B. Prevention Recommendations for Soft Tick-borne Relapsing Fever

1. Persons should avoid sleeping in rodent infested buildings.
2. Persons should rodent-proof structures to prevent future colonization by rodents and their soft ticks.
  - **Inspect** structures on a regular basis for signs of rodent activity.
  - **Eliminate** rodent nesting areas from your structure.
  - **Use** food and waste-handling practices that eliminate food sources for rodents.
  - **Rodent-proof** your cabin as follows:
    - Seal all holes in foundation and walls.
    - Place heavy gauge metal screens on windows, vents, and other openings to prevent entry of rodents.
  - Place an 18" perimeter border of gravel around the cabin. This can help prevent the movement of rodents and ticks into the cabin.

### C. Prevention Recommendations for Hard Tick-borne Relapsing Fever

When spending time outdoors in risk areas, persons should:

1. 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.
2. Wear light colored, tightly woven clothing which will allow the dark tick to be seen more easily. The tight weave makes it harder for the tick to attach itself.
3. Use tick repellent on exposed skin and clothing. Products containing DEET or permethrin are very effective. Carefully follow instructions on the label. Take special care when using repellents on children.
4. Tumble clothes in a dryer on high heat for 10 minutes to kill ticks on dry clothing after you come indoors.
5. Bathe or shower within 2 hours of outdoor activity to wash off unattached ticks and to perform a thorough tick check.
6. Check yourself, your children, pets, and gear thoroughly for ticks. If you find a tick attached to your skin, promptly remove it. 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 not crush ticks; this could result in direct inoculation of spirochetes. For more information about removing a tick, visit:  
[https://www.cdc.gov/ticks/after-a-tick-bite/?CDC\\_AAref\\_Val=https://www.cdc.gov/ticks/removing\\_a\\_tick.html](https://www.cdc.gov/ticks/after-a-tick-bite/?CDC_AAref_Val=https://www.cdc.gov/ticks/removing_a_tick.html).

7. Monitor the bite and be alert for early symptoms of tick-borne disease, e.g. fever or rash over the next month. If symptoms develop, contact your health care provider.

## **ACKNOWLEDGEMENTS**

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17<sup>th</sup> Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format of this document.

## **UPDATES**

January 2010: In Section 2D, additional vector information was added.

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. The laboratory services at PHL and submission form links were updated in Section 4B.

December 2013: The former Controlling Further Spread section was combined into section 5.

March 2017: Front page added, general updates

December 2022: Updated throughout to include hard tick-borne relapsing fever and to differentiate from soft tick-borne relapsing fever, updated case definition to 2022 Western States Standardized Case Definition for Soft Tick-borne Relapsing Fever. Updated diagnostics section to reflect current test availability. Updated reporting timeframes consistent with 2023 WAC changes.

December 2023: For 2024 WAC revision updated laboratory submission.

June 2024: CDC links updated.

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