Lyme Disease

Investigative Guidelines

January 2025

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To assess trends in Lyme disease (LD) incidence.
2. To identify zoonotic sources of infection.
3. To identify endemic geographic areas.
4. To educate the public regarding the risks and prevention of tick bites.

1.2 Laboratory and Physician Reporting Requirements

1. Physicians are required to report LD cases within one working day of diagnosis.
2. Laboratories are required to report positive results.

1.3 Local Public Health Authority (LPHA) Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but *not* suspect) cases (see definitions below) to the Oregon Public Health Division (PHD) by the end of the calendar week.
2. Begin follow-up investigation within one working day, using Orpheus. (If Orpheus is unavailable, use the Lyme disease investigation form linked here, and send or fax a copy of the completed form to PHD within 7 days of initial report).

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

In the United States, *Borrelia burgdorferi*, a spirochetal bacterium. Other *Borrelia* spp. are associated with Lyme-like infections in Europe and elsewhere, but two of note in Oregon are *B. hermsii*, transmitted by *Ornithodoros hermsi* ticks, which are found in the Western U.S. at elevations of 1200–5200 feet) *B. turicatae* (transmitted by nesting O. *turicata* ticks in southwestern and south-central states and Florida) and *B. parkeri* (transmitted by *O. parkeri* ticks in southwestern states). Another spirochete, *B. recurrentis*, causes louse-borne relapsing fever (LBRF); spontaneous outbreaks of LBRF are rare outside of sub-Saharan Africa.

2.2 Description of Illness

The diagnosis of LD is complicated by its protean dermatologic, neurologic, and cardiologic manifestations. The infection may abort at any stage, with or without treatment. Definitive diagnosis is difficult; false positive and false negative test results may be common.

Early Lyme Disease (Stage I)

Early illness is usually marked by one or more non-specific signs and symptoms: fatigue, chills and fever, headache, myalgias, arthralgias, and lymphadenopathy. Erythema migrans (EM), which occurs in 60%–80% of cases, is the most common and distinctive feature of early LD and, if adequately documented, is all but pathognomonic for LD. EM lesions typically have a “bull’s eye” appearance, with partial central clearing. The rash is usually >5 cm (2 inches) in diameter but may enlarge to a diameter of 15 cm (6 inches) or more. Occasionally, EM may appear as a solid red rash with a vesicular center. EM lesions are most common at the site of a tick bite, often the thigh, groin, trunk, or armpits, but primary and satellite lesions can occur anywhere. The rash may be warm or pruritic but is generally not painful. EM develops 3–32 days after the tick bite; lesions occurring within hours of a bite are not caused by LD. Erythema migrans usually resolves spontaneously within 3–4 weeks, if untreated, and within one week if treated.

Early Disseminated Lyme Disease (Stage II)

Several weeks after the tick bite, some infected persons develop small, multiple annular lesions. Other symptoms include fatigue, malaise, regional or generalized lymphadenitis, and migratory joint, bone, and muscle pain. Lyme arthritis, which may occur weeks to months after infection is acquired, is characterized by intermittent attacks of oligoarticular arthritis in large joints, especially the knees. Neurologic symptoms develop in some persons (<20%) weeks to months after the tick bite. Bell’s palsy, painful radiculitis, cranial neuritis, or meningitis may develop. Atrioventricular (AV) block or pericarditis occurs in fewer than 10% of patients but may be the most serious complication. AV block may progress from first to second to third degree. Heart block can be expected to resolve spontaneously, but a temporary pacemaker may be required.

Late Infection (Stage III)

Distinguishing chronic LD from fibromyalgia, chronic fatigue syndrome, or other causes of encephalopathy, polyneuropathy, and rheumatic disease can be difficult. It is not clear how many s/s may be caused by persistent spirochetal infection or may be attributable to an autoimmune reaction. Mono- or polyarthritis is most common in the knees and shoulders. This may last several years, but usually resolves spontaneously. Neurologic abnormalities are varied and include encephalopathy, mood, sleep, or memory impairment; and polyneuropathy manifesting as spinal or radicular pain or distal paresthesias. Leukoencephalitis may mimic dementia or multiple sclerosis. Neuropathies can persist for ten years. Acrodermatitis chronica atrophicans (skin swelling or bluish-red discoloration at the site of the original tick bite) occurs in a few patients.

2.3 Lyme Disease and Pregnancy

Published literature on LD during pregnancy is limited. Several case reports in the 1980s suggested that LD might be transmitted transplacentally; however, small follow-up studies of pregnant women with LD have failed to demonstrate a definitive link between LD and adverse fetal outcomes, e.g., fetal death, prematurity, or congenital malformations. Pregnant women should be aware of potential risk to the fetus if LD is contracted and—like everyone else—should take precautions to minimize tick exposure. Women who acquire LD while pregnant should be treated with penicillin or erythromycin. Spontaneous abortions and stillbirths occurring in mothers treated for LD should be investigated pathologically for involvement. Newborns of mothers treated for active *B. burgdorferi* infection should be tested for LD. Placental culture should be attempted using BSK media.

2.4 Vectors and Reservoirs

From a human perspective, the principal if not only vector of LD are certain *Ixodes* ticks in the *I. ricinus* complex. In Oregon and the rest of the West, I. pacificus is the only recognized vector. In the rest of the U.S., *I. scapularis* (né *I. dammini*) is the major player. *Dermacentor* ticks, though common in Oregon, are not known to be competent vectors. *I. pacificus* is found throughout Oregon west of the Cascades and around the mouth of the Deschutes River, and has been reported from Deschutes County, but has not been found elsewhere in eastern Oregon.

B. burgdorferi is maintained in nature by complex life cycles involving hard-bodied (ixodid) ticks in the genus *Ixodes* and a variety of mammals, reptiles, and possibly birds. These life cycles may differ significantly between the western United States and other foci of LD in the U.S., Europe, and elsewhere. Natural transmission cycles in the western U.S. may include wood rats, lizards, and other *Ixodes* ticks that do not themselves feed on humans. Deer and other rodents may be of less importance here than in the eastern U.S., although this is uncertain.

The usual 2-year life cycle of the tick includes larval, nymphal, and adult stages. Larvae and nymphs typically become infected while feeding on small rodents (their preferred hosts) and remain infected as they mature (transstadial transmission). LD has a wide distribution in northern temperate regions of the world. In the United States, the reported incidence is highest in the Northeast (particularly in southern New England); in the upper Midwest (Wisconsin and Minnesota); and in northern California. Three elements are necessary for LD to be a significant threat: competent vector ticks, enough hosts to provide food for the ticks, and the presence of *B. burgdorferi* bacteria. Data are extremely limited about the co-occurrence of these elements in Oregon, although it appears that the risk of LD is highest in southwestern Oregon, notably Coos, Curry, Josephine, and Jackson counties.

2.5 Sources and Routs of Transmission

Lyme disease is acquired by tick bite. The probability of transmission is directly correlated with duration of tick attachment. Laboratory studies suggest that attachment for at least 24 hours is required for spirochete transmission to occur. Thus, prompt removal of ticks can prevent transmission. Ixodid tick bites are generally painless, and many LD patients have no recollection of a tick bite, so the absence of a tick bite history is not inconsistent with a diagnosis of LD.

In North America, most infections are acquired between May and August, when the poppy-seed-sized *Ixodes* nymphs are most active. Although all stages of *I. pacificus* can feed on humans, nymphs are probably the most important source of human infections—perhaps because they are likely to remain unnoticed on the skin for the requisite 24+ hours. Adult ticks may feed on deer or other small mammals that, although not directly involved in the life cycle of the spirochete, may be important to the survival of the ticks.

2.6 Incubation Period

A few days to a few weeks, although hard to confirm for people who do not develop EM lesions. EM lesions usually develop within 7–10 (range 3–32) days of the tick bite.

2.7 Coinfection

Coinfection with both *Babesia microti* (the causative agent of babesiosis) or *Anaplasma phagocytophilum* (the causative agent of anaplasmosis) is well documented. Anaplasmosis is especially relevant in that cases and their exposures have been reported in southwestern Oregon. Coinfection should be considered when initial symptoms are more severe than is typical of early Lyme disease (especially a high-grade fever lasting more than 48 hours despite appropriate antibiotic therapy for Lyme disease), when thrombocytopenia or lymphopenia is present, or when flu-like symptoms persist after resolution of EM lesions.

2.8 Period of Communicability

Not transmitted from person-to-person.

2.9 Treatment

If the diagnosis is suspected, either by the presence of EM, or a constellation of symptoms suggestive of LD, appropriate serology or cultures should be taken prior to treatment.

For Stage I LD:

- First-line therapies include doxycycline, amoxicillin, and cefuroxime axetil; the recommended duration of treatment is 14–21 days.

- For patients intolerant of doxycycline, cefuroxime axetil or amoxicillin, macrolide antibiotics (azithromycin, clarithromycin or erythromycin) are

the recommended second-line agents—though they are less effective than the first-line agents.

For stage II or stage III LD, 2 to 3 weeks of antibiotics (doxycycline, amoxicillin, cefuroxime, or ceftriaxone) are indicated. There is no evidence that more prolonged therapy is more efficacious, and significant side effects have been reported in patients receiving protracted courses of antibiotics.

Prophylaxis is not recommended for asymptomatic persons with histories of tick bites, unless there is novel documentation of *B. burgdorferi* infection in greater than 20% of an area's tick population (which has generally not been the case in Oregon).

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

The case definition for Lyme is restrictive and intended to enhance the specificity of surveillance data. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs. Most reportable cases will be presumptive. If a patient is treated soon after infection based on EM or other history, the patient may never seroconvert.

3.1 Confirmed Case Definition

A clinically compatible case that meets confirmatory laboratory criteria.

3.2 Presumptive Case Definition

A clinically compatible case that meets presumptive laboratory criteria

3.3 Suspect Case Definition

- A case that meets confirmatory or presumptive laboratory criteria, but no clinical information is available, **OR**
- A case of *erythema migrans* rash with no laboratory evidence of infection.

3.4 Clinical Criteria

- *Erythema migrans (EM) rash*. For purposes of surveillance, EM is defined as a skin lesion (observed by a healthcare provider) that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach a size of ≥5 cm in diameter.

  Note: Secondary lesions also may occur.

- *Musculoskeletal system.* Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints.

  Note: Objective joint swelling may sometimes be followed by chronic arthritis in one or a few joints.

- *Nervous system.* Any of the following signs that cannot be explained by any other etiology, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (unilateral or bilateral); radiculoneuropathy; or, rarely, encephalomyelitis.

- *Cardiovascular system.* Acute onset of 2nd-degree or 3rd-degree atrioventricular conduction defects that resolve in days to weeks.

  Note: Atrioventricular conduction defects may sometimes be associated with myocarditis.

3.5 Laboratory Tests for Lyme Disease

Confirmatory laboratory evidence:

1. Isolation of *B. burgdorferi* sensu stricto or *B. mayonii* in culture, **OR**
2. Detection of *B. burgdorferi* sensu stricto or *B. mayonii* in a clinical specimen by a *B. burgdorferi* group-specific nucleic acid amplification test (NAAT) assay, **OR**
3. Detection of *B. burgdorferi* group-specific antigens by immunohistochemical assay on biopsy or autopsy tissues, **OR**
4. Positive serologic tests[1] in a two-tier or equivalent format, including:
    a. Standard two-tier test (STTT): a positive or equivocal first-tier screening assay, often an enzyme immunoassay [EIA] or immunofluorescence assay [IFA] for immunoglobulin M (IgM), immunoglobulin G (IgG), or a combination of immunoglobulins, followed by a concordant positive IgM[2] or IgG[3] immunoblot interpreted according to established criteria, **OR**
    b. Modified two-tier test (MTTT): positive or equivocal first-tier screen, followed by a different, sequential positive or equivocal EIA in lieu of an immunoblot as a second-tier test.[4]

[1] Currently, there are no serologic tests available for *B. mayonii* infection, but cross-reactivity with *B. burgdorferi* testing may occur.
[2] IgM immunoblot (Western Blot [WB]) is considered positive when at least two of the following three bands are present: 24 kDa (OspC)*, 39 kDa (BmpA), and 41 kDa (Fla). Oregon should disregard IgM results for specimens collected >30 days after symptom onset. *Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDa.
[3] IgG immunoblot (Western Blot [WB]) is considered positive when at least five of the following 10 bands are present: 18 kDa, 24 kDa (OspC)*, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa. *Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDa.
[4] The MTTT algorithm should be performed using assays specifically cleared by the US Food and Drug Administration (FDA) for this purpose. (Mead et al, 2019)

Presumptive laboratory evidence:

1. Positive IgG immunoblot,[5] interpreted according to established criteria,[6] without positive or equivocal first-tier screening assay.

3.6 OSPHL Services and Tick Identification

All testing should be performed at private laboratories. Tick identification may be done at the local vector control districts depending on the local expertise available for proper identification.

4. ROUTINE CASE INVESTIGATION

Interview the case and others who might provide pertinent information. Routine case investigation should include the documentation of case demographic, laboratory and clinical data. Personal information should be collected based on people's self-reported identities and should include "REAL-D" and "SOGI" information.

During the investigation, the potential geographic exposure and the onset date of the disease are important factors in evaluating Lyme disease infections. Some patients may require acute-phase and convalescent-phase serologic analysis because of decreased sensitivity during the first weeks of infection.

4.1 Evaluate the Diagnosis

Using the case investigation form, itemize signs and symptoms. Determine if the patient has any chronic diseases that could mimic LD. Get copies of laboratory reports that support the diagnosis.

4.2 Assess the Possibility of Tick Exposure

Ask about tick bites, if any, and known or possible duration of tick attachment. For exposures that presumably occurred in Oregon, get a detailed description of the geographic location where the exposure may have occurred—good enough that the site can be found by investigators. If the exposure probably occurred outside Oregon, obtain a general description of the area. Ask whether any pets, particularly dogs, have had ticks removed recently or have exhibited symptoms of intermittent or persistent arthritis. (Other signs of LD are not seen in dogs.)

4.3 Environmental Evaluation

If a case of LD is identified and the geographic location of the tick exposure is known, OPHD may attempt to collect ticks. Consult with OPHD epidemiologists as soon as you hear about a case.

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[5] While a single IgG WB is adequate for surveillance purposes, a two-tier test is still recommended for clinical diagnosis.

[6] IgG immunoblot (Western Blot [WB]) is considered positive when at least five of the following 10 bands are present: 18 kDa, 24 kDa (OspC)*, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa. *Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDa.

5. CONTROLLING FURTHER SPREAD

The role of the LPHA is limited to providing general education to interested members of the public, as well as working with other agencies (parks departments, etc.) as indicated. There is no need for patient isolation or work or child-care restrictions, and no long-term follow-up is indicated for public health purposes.

As opportunities allow, the following general messages can be disseminated:

- In tick-infested areas, the highest risk of bites is probably between February and September.
- The use of protective clothing, including light-colored garments, long trousers tucked into socks (to prevent ticks from crawling under garments), long-sleeved shirts, hats, etc., as well as tick repellents, may reduce risk. DEET-containing formulations are effective on exposed skin or clothing, albeit somewhat unpleasant to use, and potentially neurotoxic if slathered too liberally on small children. Permethrin repellents can be used on clothing.
- Outdoor activities in tick-infested areas present many opportunities for exposure. Keep yards clear of excessive leaves, brush, and tall grasses. Walk in the center of trails to avoid contact with tall grasses and brush.
- When camping, sleep in screened tents. Hunters should be aware of tick infestations on mammals, especially deer, and check for tick attachments after handling carcasses.
- Spiroquette transmission requires a long attachment—probably more than 24 hours. Checking for and promptly removing mobile or attached ticks after spending time outdoors in tick infested areas is prudent. It is important to check the scalp, axilla, and groin areas carefully.
- Remove attached ticks intact; do not leave embedded head parts. Use gentle, direct traction with tweezers or hemostat. Other methods, such as application of a hot match or petroleum products are not effective and should not be used.

UPDATE LOG

January 2025. Updated guidelines to the national 2022 Lyme Disease Case Definition; other minor changes. (Emilio DeBess)

September 2019. Updated treatment guidelines, coinfection, etiologic agent.

June 2016. Updated minor changes.

January 2011. OSPHL no longer provides testing for Lyme disease.

December 2006. Minor tweak to purpose of reporting #1. References to “OHS” replaced by “OPHD.” Re-writing and re-formatting of Case Definition section (§3) to clarify definitions.