Lyme is transmitted to humans most frequently by the blacklegged tick (*Ixodes scapularis*) (formerly called the Deer Tick), which is commonly found in the northeastern states and upper Great Lakes Region of the U.S[1,2,3,4]. Most human cases of Lyme disease are reported in these regions. Over 89,000 cases of Lyme disease were reported to CDC by state health departments and the District of Columbia in 2023. Recent estimates using other methods suggest that approximately 476,000 people may be diagnosed and treated for Lyme disease each year in the United States. [1] The Western blacklegged tick (*Ixodes pacificus*) is found in California, Oregon and Washington State[1,2,3,4, 8].

These vector tick species occur in regions of higher humidity and are non-existent in most of Arizona[1,2,3,4]. The western tick vector (*Ixodes pacificus*) has only been found in the higher elevations of the Hualapai Mountains in Mohave County in northwest Arizona, and had no evidence of carrying any pathogens[1,2,3,4]. Lyme disease is a reportable condition and has been since 1987[1,2,3,4]. To date, no confirmed cases of Lyme disease have been acquired from tick bites in Arizona. However, Arizona residents have become infected with this disease while traveling in other states where Lyme disease is endemic[1,2,3,4].

A. Agent:
Lyme disease is caused by the corkscrew-shaped spirochete bacterium *Borrelia burgdorferi*[1,2,3,4].

B. Clinical Description:
While the chronology of signs and symptoms vary significantly, there are three general stages in the clinical manifestation of Lyme disease: early localized, early disseminated, and late[1,2,3,4].

Early Localized Stage (3 to 30 days after tick bite): Symptoms tend to be nonspecific and may include: fever, fatigue, chills, headache, muscle and joint aches, and swollen lymph nodes. A red, expanding rash called erythema migrans (EM) occurs at the site of the tick bite in approximately 70-80% of cases. Typically, EM rashes present as the hallmark “bull’s-eye” pattern. The rash is often circular, warm to the touch, and can grow to a diameter of up to 30cm. The shape can be triangular, oval, or irregular[1,2,3,4].

Early Disseminated Stage: In untreated persons, multiple EM rashes may appear within 3-5 weeks after the tick bite. These secondary lesions, indicative that the infection has spread into the blood, resemble the primary lesion but tend to be smaller. Common signs include: swelling and pain of the joints, severe headaches or stiffness, and paralysis of facial muscles (Bell’s palsy). Heart palpitations and dizziness can also occur[1,2,3,4].

Late Stage (days to months after tick bite): Late disease is marked by recurrent arthritis in the knees and shoulders; other joints may also be involved. Neurological signs may include: impairment of mood, sleep disorders, memory difficulties, paralysis of facial muscles, pain or tingling sensations in the extremities and less commonly, meningitis and encephalitis. Late-stage symptoms can persist for several years and tend to resolve spontaneously[1,2,3,4].

About 10-20% of patients with Lyme disease develop post-treatment Lyme disease syndrome even after treatment with antibiotics[1,2,3,4]. There has not been evidence that this is caused by ongoing infection with the bacterium, but maybe lingering autoimmune response[1,2,3,4].

C. Reservoirs:
The disease is maintained in an enzootic transmission cycle that involves ixodid ticks and wild rodents, such as mice, squirrels, and shrews[1,2,3,4]. Deer also serve as an important mammalian maintenance host for vector tick species[1,2,3,4].

D. Mode of Transmission:
Lyme disease is spread through the bite of an infected *Ixodes* tick[1,2,3,4]. In most cases, ticks must be attached for 36-48 hours or more before the *Borrelia* bacterium can be transmitted[1,2,3,4]. Most people are infected through bites of ticks in the nymph stage[1,2,3,4]. These are small, difficult to see, and feed commonly during the spring and summer months[1,2,3,4]. Adult ticks also carry the bacterium, but are usually seen and removed before the bacteria are transmitted[1,2,3,4]. Adult *Ixodes* are most active during the cooler months of the year[1,2,3,4].

There is no evidence that Lyme disease can be transmitted from person to person, through blood transfusions, contact with infected pets (dogs and cats could get Lyme) or by eating meat of animals that could be reservoirs of Lyme (deer or squirrels) [1,2,3,4].

E. Incubation Period:
The incubation period is about 3-30 days for the early localized stage[1,2,3,4]. This is when the EM will likely appear around the site of the tick bite after exposure, on average 7-10 days. Early stages of the disease may not be as clearly noticed or the people may present with late manifestations[1,2,3,4]. The early disseminated stage can occur days to weeks post-tick bite. The late disseminated stage can occur months to years after the tick exposure[1,2,3,4].

F. Period of Communicability:
Lyme is not directly transmitted person-to-person[1,2,3,4].

G. Susceptibility and Resistance:
N/A

H. Treatment:
Amoxicillin[1,2,3,4,6], doxycycline or cefuroxime axetil are recommended for adults or children in early stages of disease. Intravenous penicillin or ceftriaxone is effective for meningitis and late stage illness[1,2,3,4,6]. For more details on the treatment of Lyme disease presenting with EM, complicated by neurologic/cardiac and rheumatologic manifestations or co-infection with other tick-borne pathogens refer to the 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease. [10]

I. Clinical Case Definition[5]:

A systemic, tick-borne disease characterized by **one of the following early or late-stage manifestations**, as reported by a healthcare provider, and in the absence of another known etiology[5].

Erythema migrans (EM)[1,5]

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[1,5]. A single primary lesion must reach greater than or equal to 5 cm in size across its largest diameter[1,5]. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM[1,5]. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent[1,5]. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure[1,5]. Local reactions to insect bites and stings are often misidentified as EM[1,5]. As a result, it is important to get additional information about the lesion, including (1) general description (shape and color), (2) was it itchy, painful, or warm to-the-touch, (3) when did the lesion first appear, (4) how many days did it persist, and (5) how much it expanded. [1,5]

Late Manifestations[1,5]

Late manifestations[1,5] occur after the acute period of illness, usually after months or years of infection. For the purposes of surveillance, late manifestations include any of the following when an alternate explanation is not found:

- Musculoskeletal system:
  Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints.

  Note: Manifestation not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis.
  - Arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.

- 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 (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis.

  Note: Headaches, fatigue, paresthesia, or mild stiff necks alone are not criteria for neurologic involvement.

- Cardiovascular system:

Acute onset of high-grade (2nd degree or 3rd degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis.

Note: Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.

J. Laboratory Criteria for Diagnosis[1,5]:

For the purposes of surveillance, the laboratory evidence includes:

Confirmatory laboratory evidence:

- A positive culture for *Borrelia burgdorferi* or *B. mayonii*; OR
- Detection of *B. burgdorferi* or *B. mayonii* in a clinical specimen by a *B. burgdorferi* group-specific NAAT assay, OR
- Detection of *B. burgdorferi* group-specific antigens by immunohistochemical assay on biopsy
- or autopsy tissues, OR
- 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 IgM, 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

- A positive two-tier test, defined as a positive or equivocal enzyme immunoassay (EIA) or immunofluorescence assay (IFA) followed by a positive IgM or IgG western immunoblot (WB) for Lyme disease

Presumptive laboratory evidence:

- A positive single-tier IgG[3] WB test for Lyme disease, without positive or equivocal first-tier screening assay.

[1]Currently, there are no serologic tests available for *B. mayonii* infection, but cross-reactivity with *B. burgdorferi* testing may occur.

[2] IgM WB is considered positive when at least two of the following three bands are present: 24kDa (OspC)*, 39 kDa (BmpA), and 41 kDa (Fla).
Disregard IgM results for specimens collected >30 days after symptom onset.

[3] IgG 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.

Case Classification
Refer to the ADHS Case Definition Manual and the ADHS Lyme Testing and Case Classification Algorithm.

K. Laboratory Testing[1,3,6]

Diagnosis of Lyme disease is based on symptoms, history of possible exposure to ticks in endemic areas, and laboratory blood tests. CDC currently recommends a two-step process when testing blood for evidence of antibodies against the Lyme disease bacteria. Both steps can be done using the same blood sample.[1,3,6].

The first step uses a testing procedure called "EIA" (enzyme immunoassay) or rarely, an "IFA" (indirect immunofluorescence assay) [1,3,6]. If this first step is negative, no further testing of the specimen is recommended. If the first step is positive or indeterminate sometimes called "equivocal", the second step should be performed. The second step uses a test called an immunoblot test, commonly, a "Western blot" test. Results are considered positive only if the EIA/IFA and the immunoblot are both positive[1,3,6].

The two steps of Lyme disease testing are designed to be done together. CDC does not recommend skipping the first test and just doing the Western blot. Doing so will increase the frequency of false positive results and may lead to misdiagnosis and improper treatment[1,3,6].

On July 29, 2019, FDA cleared several Lyme disease serologic assays with new indications for use based on a modified two-test methodology. The modified methodology uses a second EIA in place of a western immunoblot assay[9].

For specific examples of laboratory results and interpretation see our ADHS Lyme ADHS Lyme Testing and Case Classification Algorithm found in our VBZD resources page.

L. Assessing Laboratory Results:

See above.

M. Outbreak Definition:

There are no formal outbreak definitions.

N. Time Frame of Reporting:
Lyme disease is a nationally notifiable condition and should be reported by laboratories within 5 working days. See the ADHS Disease Reporting Homepage more details.[11]

O. Investigation and Reporting Formats:
Please refer to the Department-provided formats for submitting Epidemiologic Investigation Reports [Excel] for guidance on the required investigation fields and forms for the relevant morbidity. All the investigation forms can be found on the ADHS Forms for Reporting and Investigation.

P. Investigation Steps:

- **Confirm Diagnosis**
  i. Contact medical provider who reported or ordered the testing of the case and determine if the needed epidemiologic data can be found in the medical record alone.
     - If hospitalized: obtain admission/progress notes and discharge summary.
     - If pregnant: obtain the due date.
     - Collect birth date, county, sex, race/ethnicity, address, and phone number(s).
  ii. Obtain information that supports clinical findings in the case definition and information on the onset date of the symptoms, especially: 1) EM rashes greater that a diameter of 5 cm or 2) Any late manifestations: rheumatologic, neurologic, or cardiologic.
  iii. Obtain information on any laboratory tests performed and results. Investigators must obtain results of western blot to look for bands.
     - Results of EIA/IFA testing, IgM and IgG(1st tier).
     - Results of Western Blot, IgM and IgG (2nd tier)
     - Results of culture, if done.

- **Conduct Case Investigation**
  Epidemiological investigation report should be submitted in MEDSIS by filling out the full DSO and Travel Table.

  i. If data found in patient charts does not provide information on risk factors, interview the case to determine source, risk factors and transmission settings.
  ii. Focus case investigation within the incubation period of the specific infectious agent, and consider recent travel to endemic areas, history of tick attachment or possible tick exposure.
  iii. If there was no travel to an endemic area AND the confirmed case definition is met, list geographic location(s) and date(s) of:
     - Travel to higher elevations of the Hualapai Mountains in Mohave County
     - History of tick attachment or possible exposure to ticks
     - Exposure to animals or pets with ticks
     - Outdoor activities
     - Occupational risks (e.g., forestry worker, landscape worker, etc.)
     - Travel companions with risk of exposure or illness

- **Environmental Measures**

i. Community-based integrated tick management strategies may reduce the incidence of infections, but limiting exposure to ticks is the most effective prevention method.
ii. Strategies to reduce vector tick densities through area-wide application of an acaricide (i.e., chemicals that kill ticks and mites) and control of tick habitats (e.g., leaf litter and brush) have been effective in small-scale trials.
    - New methods under development include applying acaricide to rodents and deer by using baited tubes, boxes and deer feeding stations in areas where these pathogens are endemic.
iii. Biological control with fungi, parasitic nematodes, and parasitic wasps may play important roles in integrated tick control efforts.

- **Education and Prevention**
  Messages for Lyme disease prevention are similar to all tick-borne diseases. Educate on endemic areas for Lyme disease and proper prevention when outdoors, including wearing long clothing and insect repellent with DEET[1, 7]. Education should also include messaging of signs and symptoms and for ill persons to go to a healthcare provider, as well as encouraging tick prevention for their pets, and reducing potential tick-breeding sites around their home.

Q. Outbreak Guidelines:
N/A

Resources

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6. Lyme Disease Diagnosis and Testing video: https://www.youtube.com/watch?v=Dei-8na9wZU

7. CDC Lyme Disease Testing: https://www.cdc.gov/lyme/hcp/diagnosis-testing/index.html

8. CDC Tickborne Diseases of the USA: A reference Manual for Health Care Providers, Fifth Edition (2018). https://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf

9. Mead P, Petersen J, Hinckley A. Updated CDC Recommendation for Serologic Diagnosis of Lyme Disease. MMWR Morb Mortal Wkly Rep 2019;68:703. DOI: http://dx.doi.org/10.15585/mmwr.mm6832a4 https://www.cdc.gov/mmwr/volumes/68/wr/mm6832a4.htm

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