Lyme Disease *(Borrelia burgdorferi)*
North Carolina 2022 Case Definition
(CSTE Position Statement 12-ID-05)

Clinical Criteria

An illness 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:

- *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 high-grade (2nd-degree or 3rd-degree) atrioventricular conduction defects that resolve in days to weeks.

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

Laboratory Criteria

For the purposes of surveillance, laboratory evidence includes:

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].

Presumptive laboratory evidence:

1. Positive IgG immunoblot[5], interpreted according to established criteria[3], without positive or equivocal first-tier screening assay.

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

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

[2] IgM 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). ***Low incidence states 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 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)

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

Criteria to Distinguish a New Case from an Existing Case

A new case is one that has not been reported within the same calendar year (January through December).**
** Using calendar year allows case counting which more closely corresponds with the seasonality of Lyme disease than using a number of months between case reports.

Case Classification

Suspect

- 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.

Probable

- A clinically compatible case that meets presumptive laboratory criteria.

Confirmed

- A clinically compatible case that meets confirmatory laboratory criteria.

Note: This CSTE case definition is intended solely for public health surveillance purposes and does not recommend diagnostic criteria for clinical partners to utilize in diagnosing patients with potential Lyme Disease.

Case Classification Comments

North Carolina is a low-incidence jurisdiction according to the definitions below. Incidence of Lyme disease varies by county in NC. All cases of Lyme disease reported for NC residents are to be classified using the low- incidence jurisdiction reporting rules regardless of county of residence or suspected State of acquisition.

High-incidence jurisdictions are those that have had an average Lyme disease incidence of ≥10 confirmed cases/100,000 population for a period of three consecutive years. At the time of CSTE position statement 21-ID-05 (spring 2021), those jurisdictions were: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, West Virginia, Wisconsin, and the District of Columbia (http://www.cdc.gov/lyme/stats/tables.html).

Low-incidence jurisdictions are those that have not had an average Lyme disease incidence of ≥10 confirmed cases/100,000 population for a period of three consecutive years. Once ≥10 confirmed cases/100,000 population have been observed in a low-incidence jurisdiction for a period of three consecutive years, they become a high-incidence jurisdiction for the purposes of surveillance and should permanently switch reporting criteria.

For determining incidence for case classification and reporting purposes, calculations should be made at the state or territory level. Case classification for reporting should not be differentially applied at the subdivision level.
A clinically compatible case is defined as a case that meets the clinical criteria defined above.

References

1. Burgdorfer, W., A. G. Barbour, S. F. Hayes, J. L. Benach, E. Grunwaldt, and J. P. Davis. 1982. Lyme disease: a tick-borne spirochetosis? Science 216:1317–1319.
2. Steere AC. Lyme disease. N Engl J Med. 1989 Aug 31;321(9):586-96. doi: 10.1056/NEJM198908313210906. PMID: 2668764.
3. Mead PS. Epidemiology of Lyme disease. Infect Dis Clin North Am. 2015 Jun;29(2):187-210. doi: 10.1016/j.idc.2015.02.010. PMID: 25999219.
4. Pritt. Bobbi S et.al. 2016. Identification of a novel pathogenic *Borrelia* species causing Lyme borreliosis with unusually high spirochaetaemia: a descriptive study. Lancet Infect Dis. 2016 Feb 5. pii: S1473-3099(15)00464-8.
5. Steere AC, Sikand VK. The presenting manifestations of Lyme disease and the outcomes of treatment. N Engl J Med. 2003 Jun 12;348(24):2472-4. doi: 10.1056/NEJM200306123482423. PMID: 12802042