February 2025

Lyme Disease

Surveillance and Investigation Protocol

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Lyme Disease

Surveillance and Investigation Protocol

I. ABOUT THE DISEASE

Lyme disease is caused by the bacteria *Borrelia burgdorferi* (and rarely *Borrelia mayonii*) and is transmitted by blacklegged ticks (*Ixodes scapularis* and *Ixodes pacificus*). It was first recognized in the United States in 1977, after an unusual outbreak of arthritis among children near Lyme, Connecticut.[1] Public health surveillance for Lyme disease began in 1980 and was nationally notifiable beginning in 1991.[1] Today, it is the most reported vector-borne disease in the United States. Cases of Lyme disease have been increasing in West Virginia in recent years. The state is now considered a "high endemic" Lyme disease state. **Suspected and confirmed Lyme disease cases should be reported to the local health department where the patient resides within one week.**

A. Clinical Presentation

This tickborne disease is characterized by a distinctive skin lesion, systemic symptoms and neurologic, rheumatologic, and cardiac involvement that occur in varying combinations over a period of months to years.[8] An initial skin lesion occurs in 60%-80% of patients and appears as a red macule or papule that expands slowly in an annular manner, often with central clearing. This distinctive skin lesion is called erythema migrans (EM) or may sometimes be referred to as a "bull's-eye rash." EM may be single or multiple. To be considered significant for case surveillance purposes, the EM lesion must be physician diagnosed and measure at least 5 cm in diameter.[9] According to the Infectious Disease Society of America (IDSA), EM is the only objective sign of Lyme disease in the United States that is characteristic enough to allow clinical diagnosis of Lyme disease in the absence of laboratory confirmation.[9]

With or without EM, early systemic manifestations of Lyme disease may include malaise, fatigue, fever, headache, stiff neck, myalgia, migratory, arthralgias and/or lymphadenopathy, all of which may last several weeks or more in untreated patients.[9]

Within weeks to months after onset of the EM lesion, neurologic abnormalities such as aseptic meningitis and cranial neuritis – including cranial nerve palsy, radiculopathy, cerebellar ataxia, motor or sensory radiculoneuritis, myelitis and, rarely, encephalitis – may develop; symptoms fluctuate, may last for months, and may become chronic. In the United States, cranial neuropathy is the most common manifestation of early neurologic Lyme disease.[9] Cardiac abnormalities (including atrioventricular block and rarely, acute myopericarditis or cardiomegaly) usually occur around 2 months after onset of EM.[9] Weeks to years after initial disease onset, intermittent episodes of swelling and pain in large joints, especially the knees, may develop and recur for several years; chronic arthritis may occasionally result. Similarly, sometimes following long periods of latent infection, chronic neurologic manifestations may develop and include

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encephalopathy, polyneuropathy or leukoencephalitis; the cerebrospinal fluid (CSF) often shows lymphocytic pleocytosis and elevated protein levels, while the electromyogram is usually abnormal.

It should be noted that in recent years, the number of cases with documented late manifestations of Lyme disease (including neurologic, rheumatologic, and cardiac complications) have appeared to decline compared with earlier reports of the prevalence of these manifestations. IDSA suggests these declines may be due to ascertainment bias in earlier studies, or more successful treatment of early Lyme disease due to better recognition of EM.[8]

B. Etiologic Agent

The bacterium *Borrelia burgdorferi* is the most common pathogen responsible for Lyme disease in North America. In 2013, *Borrelia mayonii* was identified as a Lyme disease pathogen.[10] *Borrelia mayonii* has only been found in the upper Midwest. The illness caused by *B. mayonii* appears similar to infection by *B. burgdorferi*, including fever, headache, rash, and arthritis a few weeks after illness onset. In addition, *B. mayonii* can also cause nausea and vomiting, large, widespread rashes, and a higher bacteremia in the blood than *B. burgdorferi* infection.

C. Reservoir

Ixodid ticks are reservoirs for Lyme disease through transstadial transmission, meaning *B. burgdorferi* can be transmitted from one tick stage to the next.[7] Wild rodents, especially *Peromyscus* spp. (deer mice) in the northeastern and midwestern United States and *Neotoma* spp. (pack rats) in the western United States maintain the enzootic transmission cycle. Deer serve as important maintenance mammalian hosts for vector tick species. Larval and nymphal ticks feed on small mammals and adult ticks feed primarily on deer. Most Lyme disease cases result from bites by infected nymphs.

D. Incubation Period

For EM, the incubation period ranges from 3 to 32 days (mean 7 to 10 days) after tick exposure;[7] however, the early stages of the illness may be unapparent, and the patient may present with later manifestations weeks to months after becoming infected.

E. Mode of Transmission

The most important and by far the most common mode of transmission is through the bite of an infected tick. In experimental animals, transmission by *I. scapularis* and *I. pacificus* usually does not occur until the tick has been attached for more than 36 hours; this may also be true in humans[7]. Additionally, *B. burgdorferi* can survive in blood products; therefore, patients with

suspected Lyme disease should refrain from donating blood until after completing adequate antibiotic therapy.[7,11] Information on the current criteria for blood donation is available from the American Red Cross, https://www.redcrossblood.org/donate-blood/how-to-donate/eligibility-requirements.html. Transmission from infected blood products is theoretically possible; however, to date there have been no reports of cases acquiring Lyme disease through blood products.[11]

Lyme disease acquired during pregnancy may lead to infection of the placenta and possible stillbirth; however, no negative effects on the fetus have been found when the mother receives appropriate antibiotic treatment.[11] There are no reports of Lyme disease transmission from breast milk. Although dogs and cats can get Lyme disease, there is no evidence that they spread the disease directly to their owners. However, pets can bring infected ticks into the home or yard. Consider protecting pets by using tick control products for animals.[11]

There is no evidence of natural transmission from person to person. There are rare case reports of congenital transmission.

F. Period of Communicability

Person-to-person transmission is not known to occur; however, transplacental transmission may occur.

II. DISEASE CONTROL AND PREVENTION

A. Disease Control Objectives

1. Increase the number of patients treated with antibiotics in the early stages of Lyme disease to reduce the number of patients with disseminated and late disease.

B. Disease Prevention Objectives

1. Reduce disease risk through public education by encouraging use of personal protective measures that prevent tick bites.

C. Disease Prevention and Control Intervention

1. Increase the number of patients treated with antibiotics in the early stages of Lyme disease to reduce the number of patients with disseminated and late disease.
2. Avoid potential tick habitat (such as woody, brushy, or grassy areas) when possible.
3. Minimize exposure by wearing light-colored clothing that covers legs and arms, so ticks are more easily seen; tuck pants into socks and apply tick repellent such as 20% DEET to

the skin (according to label directions) or permethrin (a repellent and contact acaricide) to pant legs and sleeves (not skin).

4. Many infections from tickborne diseases happen at home. Create tick-free zones by removing leaf litter and brush around the home and at the edges of lawns; placing wood chips or gravel between lawns and wooded areas; mowing the lawn and clearing brush regularly; and by keeping playground equipment, decks, and patios away from yard edges and trees.
5. If working or playing in potential tick habitats, search the total body area daily, including haired areas.
    a. Remove ticks promptly. Keep in mind ticks may be very small and difficult to see.
    b. Remove any attached ticks by grasping the tick with tweezers as close to the skin as possible.
    c. Pull upward using gentle, steady pressure to avoid leaving mouth parts in the skin; protect hands with gloves, cloth or tissue when removing ticks from humans or animals. Following tick removal, cleanse the attachment site with soap and water.
6. Check pets for ticks regularly; consult with a veterinarian regarding medications effective for controlling ticks.

D. Treatment

Studies have shown that most patients can be cured of Lyme disease with a few weeks of antibiotics taken by mouth. Antibiotics commonly used for oral treatment include doxycycline, amoxicillin, or cefuroxime. Patients with certain neurological or cardiac forms of illness may require intravenous treatment with drugs such as ceftriaxone.[5]

Patients treated with antibiotics in the early stages of the infection usually recover rapidly and completely. A few patients, particularly those diagnosed with later stages of disease, may have persistent or recurrent symptoms. The authors of studies sponsored by the National Institutes of Health (NIH) have concluded these patients may benefit from a second 4-week course of therapy; however, longer courses of antibiotic treatment are not beneficial. Longer courses of antibiotics have been linked to serious complications, including death.[13]

Studies of women infected during pregnancy have found there are no negative effects on the fetus if the mother receives appropriate antibiotic treatment for Lyme disease. In general, treatment for pregnant women is similar to that for non-pregnant persons, although certain antibiotics are not used because they may affect the fetus.

III. DISEASE INVESTIGATION

A. Case Definition and Case Classification

The 2022 case definition is the most current (CSTE Position Statement Number 21-ID-05).[12]

Clinical Description

A systemic, tick-borne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The most common clinical marker for the disease is erythema migrans (EM), the initial skin lesion that occurs in 60%-80% of patients.

Erythema migrans (EM) rash. For purposes of surveillance, EM is defined as a skin lesion 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 greater than or equal to 5 cm in size across its largest diameter. 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. 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. A healthcare provider must make the diagnosis of EM. Laboratory confirmation is recommended for people with no known exposure.

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. Manifestations not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, 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 unilateral or bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Headache, fatigue, paresthesia, or mildly stiff neck 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. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.

Laboratory Criteria for Diagnosis

For the purposes of surveillance, laboratory evidence includes:

Confirmatory laboratory evidence:

- Isolation of *B. burgdorferi* sensu stricto or *Borrelia mayonii* in culture, OR
- 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
- Detection of *B. burgdorferi* group-specific antigens by immunohistochemical assay of biopsy or autopsy tissues, OR
- Positive serological 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

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

[1] Currently, there are no serological 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: 24kDa (OspC),* 39 kDa (BmpA), and 41 kDa (Fla). Low incidence states should disregard IgM results for specimens collected >30 days after symptom onset.
*Depending on the assay, OspC should 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 (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 U.S. Food and Drug Administration (FDA) for this purpose.

[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
High-incidence jurisdictions (as defined in Case Classification Comments below)

- A case that meets presumptive laboratory evidence.

Probable
High-incidence jurisdictions (as defined in Case Classification Comments below)

- A case that meets confirmatory laboratory evidence.

Confirmed
High-incidence jurisdictions (as defined in Case Classification Comments below)

- N/A

Note: The Council of State and Territorial Epidemiologists (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
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 this time of CSTE position state 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 definition above.

B. Reporting Timeframe to Public Health

West Virginia Code 64CSR7 requires reporting of Lyme disease within one week of notification.

C. Outbreak Recognition

The ecology of Lyme disease is based on the presence of the vector, causative agent, and appropriate hosts. Because West Virginia is considered a Lyme disease endemic state, increased cases will be monitored for greater understanding of the geographic distribution of disease. During active tick season, bi-weekly reports will be disseminated to provide situational awareness of Lyme disease activity in West Virginia.

D. Healthcare Provider Responsibilities

1. Report suspect and confirmed cases of Lyme disease (including copies of lab results) to the local health department within one week of diagnosis.
2. Follow national guidelines for Lyme disease testing.[2,3,4,5] Appropriate Lyme disease testing includes standard two-tier testing approach that includes enzyme immunoassay (EIA) or immunofluorescence assay (IFA) screening with Western blot (WB) confirmation, modified two-tier testing that includes initial EIA/IFA screening with secondary EIA confirmation, pathogen culture, nucleic acid amplification, or immunohistochemical assay of antigen.

E. Laboratory Responsibilities

1. Report positive laboratory results for Lyme disease to the local health department within 1 week.
2. Follow national guidelines for Lyme disease testing.[2,3,4,5] Appropriate Lyme disease testing should include standard two-tier testing approach that includes an EIA or IFA screening of serum with WB confirmation, modified two-tier testing that includes initial EIA/IFA

screening with secondary EIA confirmation, pathogen culture, nucleic acid amplification, or immunohistochemical assay of antigen.

F. Local Health Responsibilities

1. Reinforce standard reporting of Lyme disease per the Reportable Disease Rule to healthcare providers.
2. Record information from paper Lyme disease paper reports into the West Virginia Electronic Disease Surveillance System (WVEDSS).
3. As of January 2022, local health departments are not expected to review incoming electronic laboratory reports or call providers for clinical signs and symptoms when a positive laboratory report is received.

G. State Health Responsibilities

1. Educate the public about Lyme disease, especially regarding the mode of tick transmission and use of personal protection. Cases of Lyme disease usually occur between April and November in West Virginia. Increased public education should be targeted during this time period with the understanding that Lyme disease may be reported year-round.
2. Educate providers and laboratories to report cases of Lyme disease to the local health department in the patient's county of residence within one week of diagnosis.
3. Auto import and review Lyme laboratory results that are received electronically.
4. Conduct an appropriate Lyme disease case investigation.
5. Educate providers and laboratories about appropriate laboratory confirmation of Lyme disease including two-tiered testing approaches (EIA/IFA screening using serum samples with WB confirmation or initial EIA/IFA screening with secondary EIA confirmation, pathogen culture, nucleic acid amplification, and immunohistochemical assays of antigens).
6. Conduct tick surveillance when ticks are most active:
    a. Monitor the density of *Ixodes scapularis* throughout West Virginia.
    b. As able, test ticks for the causative agents of Lyme disease, *Borrelia burgdorferi* and *Borrelia mayonii*.
7. Use ESSENCE to conduct weekly syndromic surveillance.
    a. Include this data in the seasonal, bi-weekly Vectorborne Disease Reports.

IV. DISEASE SURVEILLANCE

A. Public Health Significance

Lyme disease is transmitted to humans by the bite of infected blacklegged (deer) ticks.[8] In the United States, endemic foci of Lyme disease exist along the Atlantic coast and are concentrated between Massachusetts and Maryland; an expanding focus is currently concentrated in Wisconsin and Minnesota. Cases are also identified in some areas of California and Oregon. Lyme disease continues to increase nationally. In 2019, 95% of Lyme disease cases were reported from 14 states. State health departments reported 23,500 confirmed cases of Lyme disease to the Centers for Disease Control and Prevention (CDC) in 2019, compared with just over 16,200 confirmed cases in 1999.[6]

Initial infection occurs primarily during summer, with a peak in June and July, but may occur throughout the year, depending on the seasonal abundance of the tick in different geographic areas.[7] The distribution of most cases coincides with the distribution of *Ixodes scapularis* (formerly called *I. dammini*) ticks in the eastern and midwestern United States. The explosive repopulation of white-tailed deer in the eastern United States has been linked to the spread of Lyme disease in this region.[7] Reported Lyme disease cases are most common among men 55-69 years of age.[6]

B. Disease Surveillance Objectives

1. To identify and monitor the epidemiological characteristics of Lyme disease in West Virginia, including the geographic distribution of cases.

C. Surveillance Indicators

1. Proportion of cases with complete demographic information.
2. Proportion of cases with appropriate laboratory testing (as defined by CDC case definition as “Laboratory Evidence”) including copies of lab results submitted to the Division of Communicable Disease Epidemiology (DCDE).

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West Virginia Department of HEALTH

Appendix A. Lyme Disease Case Investigation Toolkit

2022 LYME DISEASE

CASE INVESTIGATION TOOLKIT

This toolkit can be used by local health department staff to facilitate Lyme disease case investigations. Items in the toolkit include:

- **Enzyme Immunoassay (EIA) Tips**
- **Interpretation IgM/IgG Western Blots**
- **Provider Quicksheet**

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Enzyme Immunoassay (EIA) Interpretation Tips

- EIA tests detect the amount of antibodies produced by the patient. Immunoglobulin M (IgM), immunoglobulin G (IgG), and combined (or quantitative) IgM/IgG EIA tests are common for Lyme disease diagnostics.
  - IgM antibodies are produced by the body *early* in an infection. The presence of IgG antibodies indicates that the patient was infected with Lyme disease *at some point* in life.

- If the Lyme disease test result you receive has numbers like "0.91"or "5.65," it is an EIA/IFA test.
  - The higher the number, the more antibodies are being produced.

- Some tests will have a reference ranges for "**positive**," "**equivocal**," and "**negative**" test results listed on the laboratory report (see example below).

- An "**indeterminate**" or "**equivocal**" result means that the level of antibodies detected in the patient's specimen is low. It could also indicate a false positive result. Either way, more information is needed to determine if the patient's immune system produced a response to an infection with Lyme disease; therefore, the EIA **and** IgM/IgG Western blot are recommended.

- "**Positive**" also means "**reactive**." "**Negative**" also means "**non-reactive**."

Sample reference ranges

≤0.90	Negative
0.91-1.09	Equivocal
≥1.10	Positive

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Interpreting IgG and IgM Western Blots

IgM Western Blot

An IgM immunoblot should be considered positive if **two of the following three bands** are present:

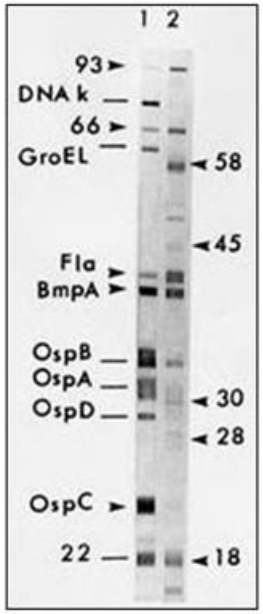
-24 kDa (OspC) band
-39 kDa (BmpA) band
-41 kDa (Fla) band

Visit the CDC's Lyme disease testing page for more information:
http://www.cdc.gov/lyme/diagnosistesting/index.html

IgG Western Blot

An IgG immunoblot should be considered positive if **five of the following ten bands** are present:

-18 kDa band
-21 kDa (OspC) band
-28 kDa band
-30 kDa band
-39 kDa (BmpA) band
-41 kDa (Fla) band
-45 kDa band
-58 kDa band
-66 kDa band
-93 kDa band



Sample Western blot

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PROVIDER QUICKSHEET: LYME DISEASE

MARCH 2022

Important Information About Selecting Laboratory Tests

1. CDC recommends a two-tier approach for testing serological specimens:
    - Standard two-tier approach using IFA/EIA antibody screen, followed by IgM[1] and IgG WB if IFA/EIA is positive or equivocal, **OR**
    - Modified two-tier approach using IFA/EIA antibody screen, followed by secondary IFA/EIA if initial IFA/EIA is positive or equivocal.
2. Other CDC recommended diagnostic assays for Lyme disease include:
    - Detection of *B. burgdorferi* or *B. mayonii* by nucleic acid amplification test, **OR**
    - Immunohistochemical stain of *B. burgdorferi* or *B. mayonii* antigen in biopsy or autopsy sample, **OR**
    - Positive culture for *B. burgdorferi* or *B. mayonii*, **OR**
    - Single positive tier IgG[2] WB test for Lyme disease.[3]

[1] IgM WB is considered positive when at least two of the following three bands are present: 24 kilodalton (kDa) outer surface protein C (OspC)*, 39 kDa basic membrane protein A (BmpA), and 41 kDa (Fla). Disregard IgM results for specimens collected >30 days after symptom onset.
[2] 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 flagellin (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa.
[3] While a single IgG WB is adequate for surveillance purposes, a two-tier test is still recommended for patient diagnosis.
*Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDA.

THE USE OF SINGLE-TIER IGM WESTERN BLOT TESTING IS NOT RECOMMENDED AND WILL NOT BE CONSIDERED CONFIRMATORY FOR PUBLIC HEALTH SURVEILLANCE PURPOSES

Resources for Patients

- CDC website has several brochures and info sheets for patients: http://www.cdc.gov/lyme/.

Resources for Healthcare Providers

- CDC has a "Resources for Clinicians" page (including clinician education modules and continuing education credit) available at https://www.cdc.gov/lyme/healthcare/clinicians.html.
- Information about two-tier testing for Lyme disease is available at https://www.cdc.gov/lyme/diagnosistesting/ /index.html.
- The Association of Public Health Laboratories (APHL) guidance and interpretation of Lyme disease serological results is available at https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf.
- Clinical practice guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR) for prevention, diagnosis, and treatment of Lyme disease located at https://www.idsociety.org/practice-guideline/lyme-disease/.

- The West Virginia Department of Health and Resources provides information about the state's Lyme disease surveillance system as well as links to useful resources available at https://oeps.wv.gov/lyme/pages/default.aspx.

- CDC has a "Tickborne Diseases of the United States" reference manual for healthcare providers located at https://www.cdc.gov/ticks/tickbornediseases/TickborneDisease-P.pdf.

- The American Academy of Family Physicians (AAFP) provides guidelines on Lyme disease diagnosis and management available at https://www.aafp.org/afp/2012/0601/p1086.html to aid healthcare providers in diagnosing Lyme disease available at http://www.aafp.org/afp/2005/0715/p297.pdf.