Nebraska Department of Health and Human Services

Health Alert Network

UPDATE

May 1, 2024

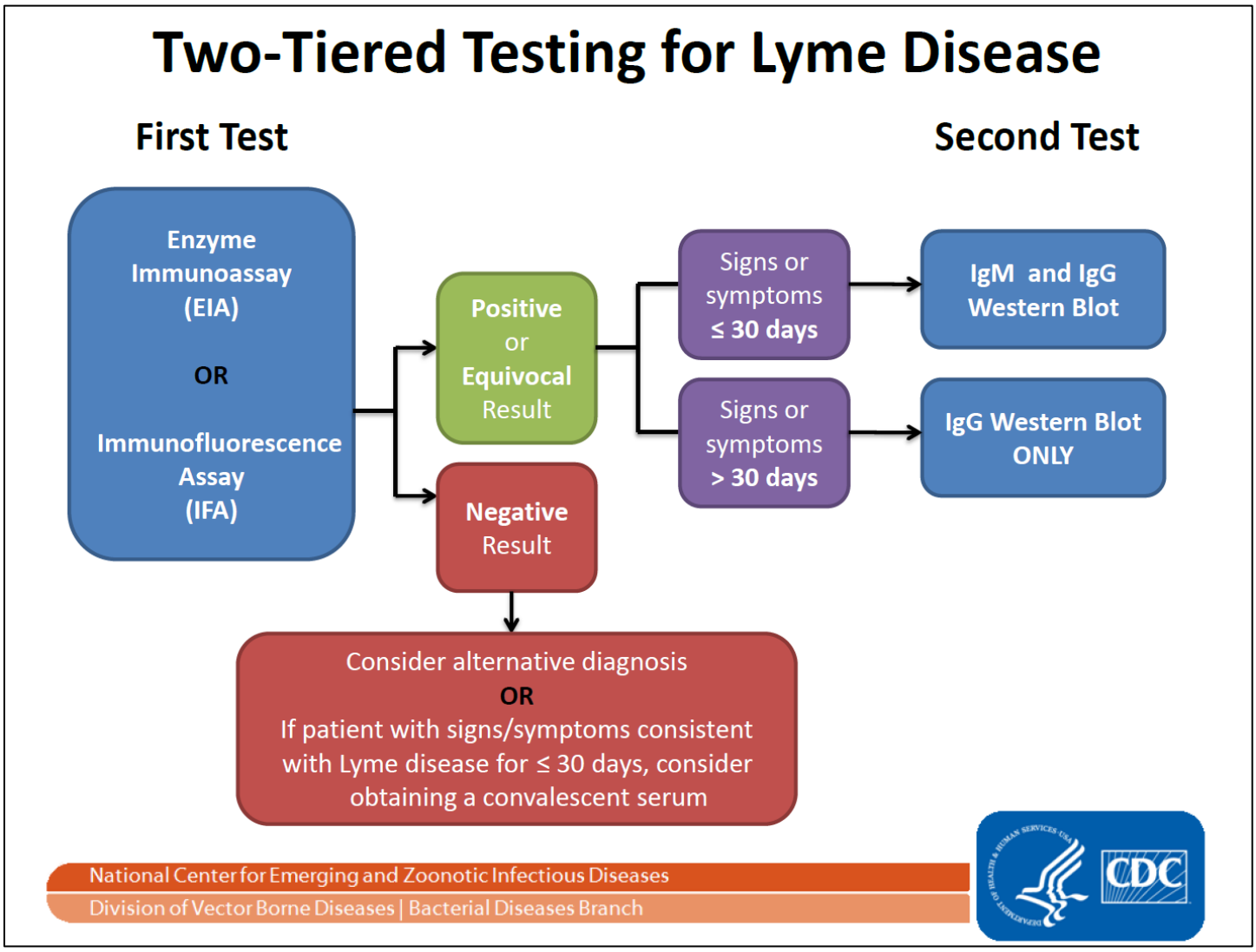
Lyme Disease in Nebraska

Lyme disease is transmitted by the tick *Ixodes scapularis* (black-legged tick or deer tick). In 2019, established populations of this tick were identified in Douglas, Sarpy, and Saunders counties. In 2021, as part of an epidemiological investigation into a cluster of Lyme disease cases, an established population was detected for the first time in Thurston County. The ticks collected from Thurston County were tested and positive for *Borrelia burgdorferi*, the bacteria that causes Lyme disease. This was the first time the *B. burgdorferi* has ever been detected in ticks collected in Nebraska. **The local identification of both the vector and pathogen of Lyme disease, in association with documented Lyme disease cases, demonstrates that *B. burgdorferi* can be acquired in eastern Nebraska. However, Nebraska will likely remain a low prevalence state for Lyme disease.** Tick surveillance efforts are continuing through partnerships with several state agencies and universities to determine human health risk in Nebraska.

Lyme disease is highly regional in the United States, with most cases reported from the Northeast and Upper Midwest. Over the last five years (2019-2023), Nebraska has reported an average of 7.6 cases per year to CDC. Nebraska is in a zone where the tick vector appears to be expanding further**, providers suspecting Lyme disease must be vigilant and obtain thorough patient histories including: any travel 30 days prior to symptom onset, reported tick attachments/bites, reported exposure to tick habitat (e.g., tall grass or wooded areas), etc. Additionally, providers should take great care to order the correct serologic tests in the correct order**.

Standard Two-Tier Serological Testing of Lyme Disease

Serologic testing for Lyme disease is currently the best method for diagnosis. The standard method **requires a strict two-step process.** The first required test is either an enzyme immunoassay (EIA) or immunofluorescence assay (IFA). If this test is negative and the patient is within 30 days from symptom onset, the provider may treat the patient and follow up with a convalescent serum. If this test is negative and the patient is more than 30 days from symptom onset, the provider should consider an alternative diagnosis. If the first test yields positive or equivocal results, two options are available: 1) if the patient has had symptoms for less than or equal to 30 days, an IgM and IgG Western blot is performed; 2) if the patient has had symptoms for more than 30 days, the IgG Western blot is performed. **The IgM should not be used if the patient has been ill for more than 30 days**. Positive serologic evidence **requires both the EIA (or IFA) and Western blot to be positive**. This testing algorithm optimizes sensitivity and specificity in untreated patients (https://www.cdc.gov/lyme/healthcare/index.html).



Understanding the EIA and IFA Test

Several types of first-tier Lyme disease screening tests exist. In most scenarios these validated, and FDA-approved tests quantify a person's potential total IgM/IgG antibody to the VlsE1/pepC10 antigen of the *Borrelia burgdorferi* bacteria that causes Lyme disease. These tests are designed to be ultra "sensitive," meaning that when they are used properly, almost everyone with Lyme disease will test positive. It is also possible, however, to test positive with an EIA or IFA test even when you do not have Lyme disease. This can occur because of other medical conditions, including but not limited to:

- Tick-borne relapsing fever
- Syphilis
- Anaplasmosis (formerly known as granulocytic ehrlichiosis)
- Leptospirosis
- Some autoimmune disorders (e.g., lupus)
- Bacterial endocarditis
- Infection with *Helicobacter pylori*, Epstein Barr virus, or *Treponema denticola* (bacteria found in the mouth that can cause gum disease and/or infection after dental procedures)

For this reason, providers should verify any "positive" or "equivocal" (indeterminate) results by performing an immunoblot test such as a Western blot. The Western blot or other FDA-approved type of immunoblot can help distinguish patients who have Lyme disease from those with other conditions.

Understanding the Immunoblot Test

The immunoblot is a second-tier confirmatory laboratory test that looks for antibodies the body makes against a variety of antigens, that are part of the *B. burgdorferi* bacteria. Western blots were the first type of immunoblot developed for Lyme disease testing. Later, a striped type of immunoblot was approved by the FDA that does not require human interpretation of bands.

Practically speaking, the test produces something that looks like a bar code used on grocery items, with several lines or "bands." Each line represents antibodies to a different component of the bacteria. As with bar codes, the presence of any one or two lines is not particularly meaningful. Instead, it is the combination of multiple, specific lines that identifies the infection as being due to *B. burgdorferi*.

Immunoblot tests for Lyme disease testing can detect two different classes of antibodies: IgM and IgG. IgM antibodies are made sooner, so testing for them can be helpful for identifying patients during the first few weeks of infection. The downside of testing for IgM antibodies is that they are **more likely to give false positive results**. Tests for IgG antibodies are more reliable but can take 4-6 weeks for the body to produce in large enough quantities for the test to detect them. Just remember the following:

- The immunoblot **should not** be run without first performing an EIA or IFA.
- The immunoblot **should not** be run if the EIA or IFA tests are negative.
- A positive IgM immunoblot is only meaningful during the first 4 weeks of illness.
- If a patient has been ill for longer than 4-6 weeks and the IgG immunoblot test is negative, it is unlikely that he or she has Lyme disease, even if the IgM immunoblot is positive.

Note on test result interpretation: It is not correct to interpret a test result that has only some bands that are positive as being "mildly" or "somewhat" positive for Lyme disease. The criterion that requires at least 5 IgG bands reflects the fact that people with Lyme disease have at least 5 antigens (specific molecules) detectable.

Modified Two-Tier Serologic Testing of Lyme Disease

In 2019 **CDC updated its recommendations** regarding serologic diagnosis of Lyme disease to include a modified standard method in addition to the standard two-tier system, where two different FDA approved EIAs are performed either sequentially or concurrently without the use of immunoblots. The first-tier again quantifies a person's potential total IgM/IgG antibody to the VlsE1/pepC10 antigen of the *B. burgdorferi*. If the first-tier test is negative no further testing is needed. If there is strong clinical suspicion of Lyme disease after a negative first-tier test and it has been ≤ 30 days, collection of a convalescent specimen should be considered several weeks later. If the first-tier result is equivocal or positive, individual second-tier EIAs are run to distinguish between the IgM and IgG class antibodies. Many commercial reference labs are transitioning or have already transitioned to this being their preferred Lyme disease test due to it being easier to run while still having similar sensitivity and specificity when compared to the standard two-tier serologic Lyme disease test.

Laboratory Tests that are Not Recommended

Some laboratories offer Lyme disease testing using assays whose accuracy and clinical usefulness have not been adequately established. Examples of unvalidated tests include:

- Capture assays for antigens in urine
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- "Reverse Western Blots"
- In-house criteria for interpretation of immunoblots
- Measurements of antibodies in joint fluid (synovial fluid)
- IgM or IgG Western Blot tests without a previous ELISA/EIA/IFA

Treatment of Lyme Disease per CDC Guidance

Erythema Migrans Rash:

- People treated with appropriate antibiotics in the early stages of Lyme disease usually recover rapidly and completely. Early diagnosis and proper antibiotic treatment of Lyme disease can help prevent late Lyme disease.

Table 1. Treatment Regimens for Erythema migrans Rash

Age Category	Drug	Dosage	Maximum	Duration, Days*
Adults	Doxycycline OR	100 mg, twice per day orally	N/A	10-14
	Amoxicillin OR	500 mg, three times per day orally	N/A	14
	Cefuroxime	500 mg, twice per day orally	N/A	14
Children	Doxycycline OR	4.4 mg/kg per day orally, divided into 2 doses	100 mg per dose	10-14
	Amoxicillin OR	50 mg/kg per day orally, divided into 3 doses	500 mg per dose	14
	Cefuroxime	30 mg/kg per day orally, divided into 2 doses	500 mg per dose	14

*When different durations of antibiotics are shown to be effective for treatment of Lyme disease, the shorter duration is preferred to minimize adverse effects, including infectious diarrhea and antimicrobial resistance.
Note: For people intolerant of amoxicillin, doxycycline, and cefuroxime- azithromycin may be used, although it is less effective. People treated with azithromycin should be closely monitored to ensure that symptoms resolve.

Neurologic Lyme Disease:

- In patients with facial palsy who are unable to close one or both eyes, eye drops, or an eye patch may be needed to prevent dry eyes.
- Neurologic symptoms do not necessarily indicate central nervous system infection in a patient with Lyme disease.
- Two-step serologic testing for Lyme diseases is the recommended diagnostic test for neurologic Lyme disease.
- CSF analysis is not necessary to diagnose Lyme meningitis but can help exclude other causes of illness such as bacterial meningitis.
- Consider Lyme radiculoneuritis in patients who report sever limb or truncal radicular pain without preceding trauma who live in or who traveled to Lyme-endemic areas.

Table 2. Treatment Regimens for Facial Palsy

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Doxycycline	100 mg, twice per day orally	N/A	14-21
Children (any age)	Doxycycline	4.4 mg/kg per day orally, divided into 2 doses	100 mg per dose	14-21

Table 3. Treatment Regimens for Lyme Meningitis or Radiculoneuritis

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Doxycycline OR	200 mg per day orally, divided into 1 or 2 doses	N/A	14-21
	Ceftriaxone*	2 grams intravenously, once a day	N/A	14-21
Children (any age)	Doxycycline OR	4.4 mg/kg per day orally, divided into 1 or 2 doses	100 mg per dose	14-21
	Ceftriaxone*	50-75 mg/kg intravenously once a day	2 g per day	14-21

*Oral therapy can be substituted when the patient is stabilized or discharged to complete the course.

Lyme Carditis:

- Ask all patients with suspected Lyme disease about cardiac symptoms, e.g., palpitations, chest pain, light headedness, fainting, shortness of breath, and difficulty breathing with exertion.
- Ask all patients with acute, unexplained cardiac symptoms about possible tick exposure and symptoms of Lyme disease.
- Treat patients with suspected Lyme carditis with appropriate antibiotics immediately – do not wait for Lyme disease test results. **Patients with suspected severe Lyme carditis require immediate hospitalization for cardiac monitoring and intravenous antibiotics.**

Table 4. Treatment of Mild Lyme Carditis (1st degree AV block with PR interval <300 milliseconds)

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Doxycycline OR	100 mg, twice per day orally	N/A	14-21
	Amoxicillin OR	500 mg, three times per day orally	N/A	14-21
	Cefuroxime	500 mg, twice per day orally	N/A	14-21
Children (any age)	Doxycycline OR	4.4 mg/kg per day orally, divided into 2 doses	100 mg per dose	14-21
	Amoxicillin OR	50 mg/kg per day orally, divided into 3 doses	500 mg per dose	14-21
	Cefuroxime	30 mg/kg per day orally, divided into 2 doses	500 mg per dose	14-21

Table 5. Treatment of Severe Lyme Carditis (symptomatic, 1st degree AV block with PR interval ≥300 milliseconds)

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Ceftriaxone*	2 grams intravenously, once a day	N/A	14-21
Children (any age)	Ceftriaxone*	50-75 mg/kg intravenously once a day	2 g per day	14-21

*After resolution of symptoms and high-grade AV block, consider transitioning to oral antibiotics to completed treatment course (see Table 4).

Lyme Arthritis:

- Antibody-based Lyme disease tests have excellence sensitivity in patients with Lyme arthritis. PCR can be used as an adjunctive diagnostic test to identify DNA in synovial fluid but should not be the first lab test used.
- Lyme arthritis can be mistaken for septic arthritis, especially in children. Whereas septic arthritis may require surgical intervention, Lyme arthritis generally does not.

Table 6. Oral Antibiotic Treatment Regimens for Lyme Arthritis*

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Doxycycline OR	100 mg, twice per day orally	N/A	28
	Amoxicillin OR	500 mg, three times per day orally	N/A	28
	Cefuroxime	500 mg, twice per day orally	N/A	28
Children (≥8 years old)	Doxycycline OR	4.4 mg/kg per day orally, divided into 2 doses	100 mg per dose	28
	Amoxicillin OR	50 mg/kg per day orally, divided into 3 doses	500 mg per dose	28
	Cefuroxime	30 mg/kg per day orally, divided into 2 doses	500 mg per dose	28

Age Category	Drug	Dosage	Maximum	Duration, Days
Children (≤8 years old)	Amoxicillin OR	50 mg/kg per day orally, divided into 3 doses	500 mg per dose	28
	Cefuroxime	30 mg/kg per day orally, divided into 2 doses	500 mg per dose	28

*For patients with an initial episode of Lyme arthritis, a full course of oral antibiotics is recommended. For patients with improving but persistent symptoms after an initial course of oral antibiotics, a second course of the same oral antibiotic or observation alone can be considered.

Table 7. Parenteral Antibiotic Regimens for Lyme Arthritis^

Age Category	Drug	Dosage	Maximum	Duration, Days
Adults	Ceftriaxone*	2 grams intravenously, once a day	N/A	14-28
Children (any age)	Ceftriaxone*	50-75 mg/kg intravenously once a day	2 g per day	14-28

^Intravenous ceftriaxone is the preferred regimen for the second course of antibiotics for patients without any response after the initial course of antibiotics.

Post-Treatment Lyme Disease Syndrome

Lyme disease is caused by infection with the bacterium *B. burgdorferi*. Although most cases of Lyme disease can be cured with a 2- to 4-week course of oral antibiotics, patients can sometimes have symptoms of pain, fatigue, or difficulty thinking that lasts for more than 6 months after they finish treatment. This condition is called Post-Treatment Lyme Disease Syndrome (PTLDS).

Why some patients experience PTLDS is not known. Some experts believe that *B. burgdorferi* can trigger an "auto-immune" response causing symptoms that last well after the infection itself is gone. Auto–immune responses are known to occur following other infections, including campylobacter (Guillain-Barré syndrome), chlamydia (reactive arthritis), and strep throat (rheumatic heart disease). Other experts hypothesize that PTLDS results from a persistent but difficult to detect infection. Finally, some believe that the symptoms of PTLDS are due to other causes unrelated to the patient's *B. burgdorferi* infection.

Unfortunately, there is no proven treatment for PTLDS. Although short-term antibiotic treatment is a proven treatment for early Lyme disease, studies (https://www.niaid.nih.gov/diseases-conditions/lyme-disease-antibiotic-treatment-research) funded by the National Institutes of Health (NIH) have found that long-term outcomes are no better for patients who received additional prolonged antibiotic treatment than for patients who received placebo. Long-term antibiotic treatment for Lyme disease has been associated with serious, sometimes deadly complications, as described in the links below.

Patients with PTLDS usually get better over time, but it can take many months to feel completely well. If you have been treated for Lyme disease and still feel unwell, see your healthcare provider to discuss additional options for managing your symptoms. If you are considering long-term antibiotic treatment for ongoing symptoms associated with a Lyme disease infection, please talk to your healthcare provider about the possible risks of such treatment.

Southern Tick-Associated Rash Illness (STARI)

An erythema migrans-like rash has also been described in humans following bites of the Lone Star Tick (*Amblyomma americanum*). The condition associated with these ticks has been named Southern Tick-Associated Rash Illness (STARI). Although the rash may be accompanied by flu-like symptoms, long-term sequelae have not been reported. Because the cause of STARI is unknown, diagnostic blood tests are not available.

The Lone Star Tick is found from Central Texas and Oklahoma eastward across southern states, along the Atlantic coast as far north as Maine. In Nebraska, this tick is found in areas of eastern and central Nebraska and typically, one of the two most collected ticks in the state. It is a very aggressive tick at all life stages readily biting humans.

It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians often treat patients with the same antibiotics recommended for Lyme disease.

For More Information Please Visit

APHL Suggested Reporting, Interpretation, and Guidance Regarding Lyme Disease Serologic Test Results: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf

CDC Lyme Disease Page: https://www.cdc.gov/lyme/

CDC Treatment of Lyme Disease Page: https://www.cdc.gov/lyme/treatment/index.html

CDC Southern Tick-Associated Rash Illness (STARI) Page: https://www.cdc.gov/stari/index.html

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

IDSA, AAN, and ACR Guidelines Summary for the Prevention, Diagnosis, and Treatment of Lyme Disease: https://www.idsociety.org/globalassets/idsa/practice-guidelines/lyme/idsa_aan_acr-lyme-disease-guideline---clinician-summary.pdf

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