Summary Practice Guideline for **Clinicians**

# Guidelines Summary for the Prevention, Diagnosis, and Treatment of Lyme Disease

IDSA Infectious Diseases Society of America
AMERICAN ACADEMY OF NEUROLOGY
AMERICAN COLLEGE of RHEUMATOLOGY Empowering Rheumatology Professionals

This is a summary of "Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease," which was published in *Arthritis & Rheumatology*, *Arthritis Care & Research, Clinical Infectious Diseases,* and *Neurology*® online on November 30, 2020.

*Please refer to the full guideline for more information.*

## I. Which measures should be used to prevent tick bites and tick-borne infections?

### A. Personal protective measures

| Level | Recommendation |
|---|---|
| Good practice statement | 1. Individuals at risk of exposure should implement personal protective measures to reduce the risk of tick exposure and infection with tick-borne pathogens. |

### B. Repellents to prevent tick bites

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For the prevention of tick bites, we recommend N,N-Diethyl-meta-toluamide (DEET), picaridin, ethyl-3-(N-n-butyl-N-acetyl) aminopropionate (IR3535), oil of lemon eucalyptus (OLE), p-methane-3,8-diol (PMD), 2-undecanone, or permethrin. |

### C. Removal of attached ticks

| Level | Recommendation |
|---|---|
| Good practice statement | 1. We recommend promptly removing attached ticks by mechanical means using a clean fine-tipped tweezer (or a comparable device) inserted between the tick body and the skin. |
| Good practice statement | 2. We recommend against burning an attached tick (with a match or other heat device) or applying noxious chemicals or petroleum products to coax its detachment. |

## II. Which diagnostic tests should be used following a tick bite?

### A. Diagnostic tick testing

| Level | Recommendation |
|---|---|
| Good practice statement | 1. We recommend submitting the removed tick for species identification. |
| Strong recommendation, moderate-quality evidence | 2. We recommend against testing a removed *Ixodes* tick for *Borrelia burgdorferi.*<br><br>**Comment:** The presence or absence of *B burgdorferi* in an Ixodes tick removed from a person does not reliably predict the likelihood of clinical infection. |

### B) Diagnostic testing of asymptomatic patients following tick bites

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. We recommend against testing asymptomatic patients for exposure to *B burgdorferi* following an *Ixodes* spp. tick bite. |

## III. Who should receive antibiotic prophylaxis to prevent Lyme disease following presentation with a tick bite?

| Level | Recommendation |
|---|---|
| Strong recommendation, high-quality evidence | 1. We recommend that prophylactic antibiotic therapy be given to adults and children only within 72 hours of removal of an identified high-risk tick bite, but not for bites that are equivocal risk or low risk.<br><br>**Comment:** If a tick bite cannot be classified with a high level of certainty as a high-risk bite, a wait-and-watch approach is recommended. A tick bite is considered to be high-risk only if it meets the following three criteria: the tick bite was from a) an identified *Ixodes* spp. vector species, b) it occurred in a highly endemic area, and c) the tick was attached for ≥ 36 hours. |

## IV. What is the preferred antibiotic regimen for the chemoprophylaxis of Lyme disease following a high-risk tick bite?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For high-risk *Ixodes* spp. bites in all age groups, we recommend the administration of a single dose of oral doxycycline within 72 hours of tick removal over observation.<br><br>**Comment:** Doxycycline is given as a single oral dose, 200 mg for adults and 4.4 mg/kg (up to a maximum dose of 200 mg) for children. |

## V. What is the preferred diagnostic testing strategy for erythema migrans?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. In patients with potential tick exposure in a Lyme disease endemic area who have one or more skin lesions compatible with erythema migrans, we recommend clinical diagnosis rather than laboratory testing. |
| Weak recommendation, low-quality evidence | 2. In patients with one or more skin lesions suggestive of, but atypical for erythema migrans, we suggest antibody testing performed on an acute-phase serum sample (followed by a convalescent-phase serum sample if the initial result is negative) rather than currently available direct detection methods such as polymerase chain reaction (PCR) or culture performed on blood or skin samples.<br><br>**Comment:** If needed, the convalescent-phase serum sample should be collected at least 2 to 3 weeks after collection of the acute-phase serum sample. |

## VI. What are the preferred antibiotic regimens for the treatment of erythema migrans?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For patients with erythema migrans, we recommend using oral antibiotic therapy with doxycycline, amoxicillin, or cefuroxime axetil.<br><br>**Comment:** For patients unable to take both doxycycline and beta-lactam antibiotics, the preferred second-line agent is azithromycin. |

## VII. How long should a patient with erythema migrans be treated?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. We recommend that patients with erythema migrans be treated with either a 10-day course of doxycycline or a 14-day course of amoxicillin or cefuroxime axetil rather than longer treatment courses.<br><br>**Comment:** If azithromycin is used, the indicated duration is 5 to 10 days, with a 7-day course preferred in the US, as this duration of therapy was used in the largest clinical trial performed in the US.[1] |

## VIII. Should patients with the southern tick-associated rash illness (STARI) be treated with antibiotics?

| Level | Recommendation |
|---|---|
| No recommendation, knowledge gap | 1. In patients who develop an erythema migrans-like skin lesion following the bite of the lone star tick (*Amblyomma americanum*), an illness referred to as STARI, we make no recommendation for or against the use of antibiotics.<br><br>**Comment:** In certain geographic regions both STARI and Lyme disease are endemic.[2] Distinguishing single erythema migrans due to Lyme disease from STARI may not be possible clinically unless the responsible tick has been identified.[3] When STARI cannot be distinguished from Lyme disease-associated erythema migrans in areas endemic for both conditions, antibiotic therapy directed towards Lyme disease is indicated. |

## IX. What is the preferred diagnostic testing strategy for Lyme neuroborreliosis?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. When assessing patients for possible Lyme neuroborreliosis involving either the peripheral nervous system (PNS) or central nervous system (CNS), we recommend serum antibody testing rather than PCR or culture of either cerebrospinal fluid (CSF) or serum. |
| Strong recommendation, moderate-quality evidence | 2. If CSF testing is performed in patients with suspected Lyme neuroborreliosis involving the CNS, we (a) recommend obtaining simultaneous samples of CSF and serum for determination of the CSF:serum antibody index, carried out by a laboratory using validated methodology, (b) recommend against CSF serology without measurement of the CSF:serum antibody index, and (c) recommend against routine PCR or culture of CSF or serum. |

## X. For which neurologic presentations should patients be tested for Lyme disease?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. In patients presenting with one or more of the following acute disorders: meningitis, painful radiculoneuritis, mononeuropathy multiplex including confluent mononeuropathy multiplex, acute cranial neuropathies (particularly VII, VIII, less commonly III, V, VI, and others), or in patients with evidence of spinal cord (or rarely brain) inflammation, the former particularly in association with painful radiculitis involving related spinal cord segments, and with epidemiologically plausible exposure to ticks infected with *B burgdorferi*, we recommend testing for Lyme disease. |

| Level | Recommendation |
|---|---|
| Strong recommendation, low-quality evidence | 2. In patients with typical amyotrophic lateral sclerosis, relapsing-remitting multiple sclerosis, Parkinson disease, dementia or cognitive decline, or new-onset seizures, we recommend against routine testing for Lyme disease. |
| Strong recommendation, low-quality evidence | 3. In patients with neurologic syndromes other than those listed in (1) or (2), in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we recommend against screening for Lyme disease. |
| Weak recommendation, low-quality evidence | 4. In patients presenting with nonspecific magnetic resonance imaging white matter abnormalities confined to the brain in the absence of a history of other clinical or epidemiologic support for the diagnosis of Lyme disease, we suggest against testing for Lyme disease. |

## XI. Should adult patients with psychiatric illnesses be tested for Lyme disease?

| Level | Recommendation |
|---|---|
| Strong recommendation, low-quality evidence | 1. In patients with psychiatric illness, we recommend against routine testing for Lyme disease. |

## XII. Should children with developmental, behavioral, or psychiatric disorders be tested for Lyme disease?

| Level | Recommendation |
|---|---|
| Weak recommendation, low-quality evidence | 1. In children presenting with developmental, behavioral, or psychiatric disorders, we suggest against routinely testing for Lyme disease. |

## XIII. What are the preferred antibiotic regimens for the treatment of acute neurologic manifestations of Lyme disease without parenchymal involvement of the brain or spinal cord?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. In patients with Lyme disease-associated meningitis, cranial neuropathy, radiculoneuropathy, or with other PNS manifestations, we recommend using intravenous (IV) ceftriaxone, cefotaxime, penicillin G, or oral doxycycline over other antimicrobials.<br><br>**Comment:** Decisions about the choice of antibiotic among these, including the route of administration, should primarily be made based on individual factors such as side effect profile, ease of administration, ability to tolerate oral medication, concerns about compliance unrelated to effectiveness. Treatment route may be changed from IV to oral during treatment. The preferred antibiotic duration is 14 to 21 days. |

## XIV. Should patients with Lyme disease-related parenchymal involvement of the brain or spinal cord be treated with oral or IV antibiotics?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. In patients with Lyme disease-associated parenchymal involvement of the brain or spinal cord, we recommend using IV over oral antibiotics. |

## XV. Should patients with Lyme disease and facial nerve palsy receive corticosteroids in addition to antimicrobial therapy?

| Level | Recommendation |
|---|---|
| No recommendation, knowledge gap | 1. In patients with Lyme disease-associated facial nerve palsy, we make no recommendation on the use of corticosteroids in addition to antibiotics.<br><br>**Comment:** In patients age 16 or older presenting with acute facial nerve palsy but without other objective clinical or serologic evidence of Lyme disease, corticosteroid treatment should be administered within 72 hours in accordance with current facial nerve palsy guideline recommendations.[4] |

## XVI. Should all patients with early Lyme disease receive an electrocardiogram (ECG) to screen for Lyme carditis?

| Level | Recommendation |
|---|---|
| Weak recommendation, low-quality evidence | 1. We suggest performing an ECG only in patients with signs or symptoms consistent with Lyme carditis.<br><br>**Comment:** Symptoms and signs of cardiac involvement in Lyme disease include dyspnea, edema, palpitations, lightheadedness, chest pain, and syncope. |

## XVII. Which patients with Lyme carditis require hospitalization?

| Level | Recommendation |
|---|---|
| Strong recommendation, very low-quality evidence | 1. In patients with or at risk for severe cardiac complications of Lyme disease including those with significant PR prolongation (PR > 300 milliseconds), other arrhythmias, or clinical manifestations of myopericarditis, we recommend hospital admission with continuous ECG monitoring.<br><br>**Comment:** Clinical manifestations of Lyme carditis include exercise intolerance, palpitations, presyncope, syncope, pericarditic pain, evidence of pericardial effusion, elevated biomarkers (such as troponin), edema, and shortness of breath. |

## XVIII. What pacing modality should be used if needed for the management of Lyme carditis?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For patients with symptomatic bradycardia due to Lyme carditis that cannot be managed medically, we recommend temporary pacing modalities rather than implanting a permanent pacemaker. |

## XIX. What are the preferred antibiotic regimens for the treatment of Lyme carditis?

| Level | Recommendation |
|---|---|
| Weak recommendation, very low-quality evidence | 1. In outpatients with Lyme carditis, we suggest oral antibiotics over IV antibiotics. |
| Weak recommendation, very low-quality evidence | 2. In the hospitalized patient with Lyme carditis, we suggest initially using IV ceftriaxone over oral antibiotics until there is evidence of clinical improvement, then switching to oral antibiotics to complete treatment. |
| Weak recommendation, very low-quality evidence | 3. For the treatment of Lyme carditis, we suggest 14 to 21 days of total antibiotic therapy over longer durations of treatment.<br>**Comment:** Oral antibiotic choices for Lyme carditis are doxycycline, amoxicillin, cefuroxime axetil, and azithromycin. |

## XX. Should patients being evaluated for acute myocarditis/pericarditis or chronic cardiomyopathy of unknown cause be tested for Lyme disease?

| Level | Recommendation |
|---|---|
| Strong recommendation, low-quality evidence | 1. In patients with acute myocarditis/pericarditis of unknown cause in an appropriate epidemiologic setting, we recommend testing for Lyme disease. |
| Weak recommendation, low-quality evidence | 2. In patients with chronic cardiomyopathy of unknown cause, we suggest against routine testing for Lyme disease. |

## XXI. What is the preferred diagnostic testing strategy for Lyme arthritis?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. When assessing possible Lyme arthritis, we recommend serum antibody testing over PCR or culture of blood or synovial fluid/tissue. |
| Strong recommendation, moderate-quality evidence | 2. In seropositive patients for whom the diagnosis of Lyme arthritis is being considered but treatment decisions require more definitive information, we recommend PCR applied to synovial fluid or tissue rather than *Borrelia* culture of those samples. |

## XXII. What are the preferred antibiotic regimens for the initial treatment of Lyme arthritis?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For patients with Lyme arthritis, we recommend using oral antibiotic therapy for 28 days. |

## XXIII. What are the approaches to patients in whom Lyme arthritis has not completely resolved?

| Level | Recommendation |
|---|---|
| No recommendation, knowledge gap | 1. In patients with Lyme arthritis with partial response (mild residual joint swelling) after a first course of oral antibiotic, we make no recommendation for a second course of antibiotic versus observation.<br>**Comment:** Consideration should be given to exclusion of other causes of joint swelling than Lyme arthritis, medication adherence, duration of arthritis prior to initial treatment, degree of synovial proliferation versus joint swelling, patient preferences, and cost. A second course of oral antibiotics for up to 1 month may be a reasonable alternative for patients in whom synovial proliferation is modest compared to joint swelling and for those who prefer repeating a course of oral antibiotics before considering IV therapy. |
| Weak recommendation, low-quality evidence | 2. In patients with Lyme arthritis with no or minimal response (moderate to severe joint swelling with minimal reduction of the joint effusion) to an initial course of oral antibiotic, we suggest a 2- to 4-week course of IV ceftriaxone over a second course of oral antibiotics. |

## XXIV. How should post-antibiotic (previously termed antibiotic-refractory) Lyme arthritis be treated?

| Level | Recommendation |
|---|---|
| Weak recommendation, very low-quality evidence | 1. In patients who have failed one course of oral antibiotics and one course of IV antibiotics, we suggest a referral to a rheumatologist or other trained specialist for consideration of the use of disease modifying antirheumatic drugs, biologic agents, intraarticular steroids, or arthroscopic synovectomy.<br>**Comment:** Antibiotic therapy for longer than 8 weeks is not expected to provide additional benefit to patients with persistent arthritis if that treatment has included one course of IV therapy. |

## XXV. Should patients with persistent symptoms following standard treatment of Lyme disease receive additional antibiotics?

| Level | Recommendation |
|---|---|
| Strong recommendation, moderate-quality evidence | 1. For patients who have persistent or recurring nonspecific symptoms such as fatigue, pain, or cognitive impairment following recommended treatment for Lyme disease, but who lack objective evidence of reinfection or treatment failure, we recommend against additional antibiotic therapy.<br><br>**Comment:** Evidence of persistent infection or treatment failure would include objective signs of disease activity, such as arthritis, meningitis, or neuropathy. |

## XXVI. What is the preferred antibiotic regimen for the treatment of borrelial lymphocytoma?

| Level | Recommendation |
|---|---|
| Weak recommendation, low-quality evidence | 1. In patients with borrelial lymphocytoma, we suggest oral antibiotic therapy for 14 days. |

## XXVII. What is the preferred antibiotic regimen for the treatment of acrodermatitis chronica atrophicans?

| Level | Recommendation |
|---|---|
| Weak recommendation, low-quality evidence | 1. In patients with acrodermatitis chronica atrophicans, we suggest oral antibiotic therapy for 21 to 28 days over shorter durations. |

## XXVIII. Under what circumstances should a patient with Lyme disease be evaluated for co-infection with *Anaplasma phagocytophilum* or *Babesia microti*?

| Level | Recommendation |
|---|---|
| Good practice statement | 1. In patients with Lyme disease who have a high-grade fever or characteristic laboratory abnormalities, clinicians should assess for possible co-infection with *A phagocytophilum* and/or *B microti* infection in geographic regions where these infections are endemic.<br><br>**Comment:** Co-infection should be investigated in patients who have a persistent fever for greater than one day while on antibiotic treatment for Lyme disease. If fever persists despite treatment with doxycycline, *B microti* infection is an important consideration. Characteristic laboratory abnormalities found in both anaplasmosis and babesiosis include thrombocytopenia, leukopenia, neutropenia, and/or anemia. Evidence of hemolysis, such as elevated indirect bilirubin level, anemia, and elevated lactate dehydrogenase are particularly suggestive of babesiosis. |

This clinical practice guideline was endorsed by American Academy of Family Physicians , Association of Medical Microbiology and Infectious Disease Canada, Child Neurology Society, Pediatric Infectious Diseases Society, Entomological Society of America, and European Society of Clinical Microbiology and Infectious Diseases.

## References

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2. Feder HM, Jr., Hoss DM, Zemel L, Telford SR, 3rd, Dias F, Wormser GP. Southern Tick-Associated Rash Illness (STARI) in the North: STARI following a tick bite in Long Island, New York. Clin Infect Dis 2011;53(10):e142-6.

3. Wormser GP, Masters E, Nowakowski J, et al. Prospective clinical evaluation of patients from Missouri and New York with erythema migrans-like skin lesions. Clin Infect Dis 2005;41(7):958-65.



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