

Rationale & Scope

Lyme disease is caused by an infection with a spirochete bacterium called *Borrelia burgdorferi*. In Ohio, *B. burgdorferi* is transmitted to humans through the bite of an infected blacklegged tick. Lyme disease cases are increasing in Ohio as the range of blacklegged tick populations continues to expand in the state and encounters with this tick occur more frequently, particularly in the forest habitats preferred by this tick. Most humans are infected through the bites of immature ticks called nymphs. Nymphs are tiny (less than 2 mm) and difficult to see. They feed during the spring and summer months.

The incidence of Lyme disease in Ohio has significantly increased, from 45 cases in 28 counties in 2008 to 388 cases in 48 counties as of August 2024, with the highest concentration in the eastern half of the state, including Cuyahoga County. The guidelines focus on accurate diagnosis, appropriate testing, effective treatment, and preventive measures against Lyme disease, tailored to the specific epidemiological context of northeastern Ohio. They serve as a practical guide for licensed healthcare providers, ensuring that patient management is based on the best available scientific evidence and local epidemiological data.

Summary of Key Management Statements

- The **clinical manifestations of Lyme disease** are divided into three stages: early localized, early disseminated, and late manifestations. **Early localized** disease is the most common in children and is characterized by a distinctive lesion called erythema migrans (EM). **Early disseminated** Lyme disease presents with multiple EM lesions, cranial neuritis, meningitis, radiculitis, or carditis. The most common **manifestation of late disease** is joint arthritis, most frequently in the knee.
- Most cases of early localized and early disseminated Lyme disease occur between April and October, with a peak in June and July. The incidence is highest among children ages 5 through 9 years but can affect people of all ages. Most children that develop Lyme disease do not recall a tick bite.
- **Testing:** Testing is unnecessary for classic EM and will often be negative early in the disease course. Treat with empiric antibiotics without testing; two-tier serologic with reflex confirmatory testing is recommended for non-classic symptoms.
- **Treatment:** Preferred treatment regimen depends on disease category. Single dose prophylactic doxycycline for engorged ticks attached for ≥ 36 hours and removed within 72 hours, symptomatic treatment for persistent symptoms.
- **Prevention:** Wear protective clothing, use tick repellent, perform regular tick checks, and promptly remove attached ticks.

Inclusion and Exclusion Criteria

- This guideline is intended for providers involved in the diagnosis and management of Lyme disease.
- Diagnosis of Lyme disease rests first and foremost on the recognition of a compatible clinical illness in people who have had plausible geographic exposure; see section on diagnosis below.
- No absolute exclusions to this guideline; however, patients with Lyme disease can be infected simultaneously with agents of babesiosis, anaplasmosis, and hard tick-borne relapsing fever. (See section on differential diagnosis below)

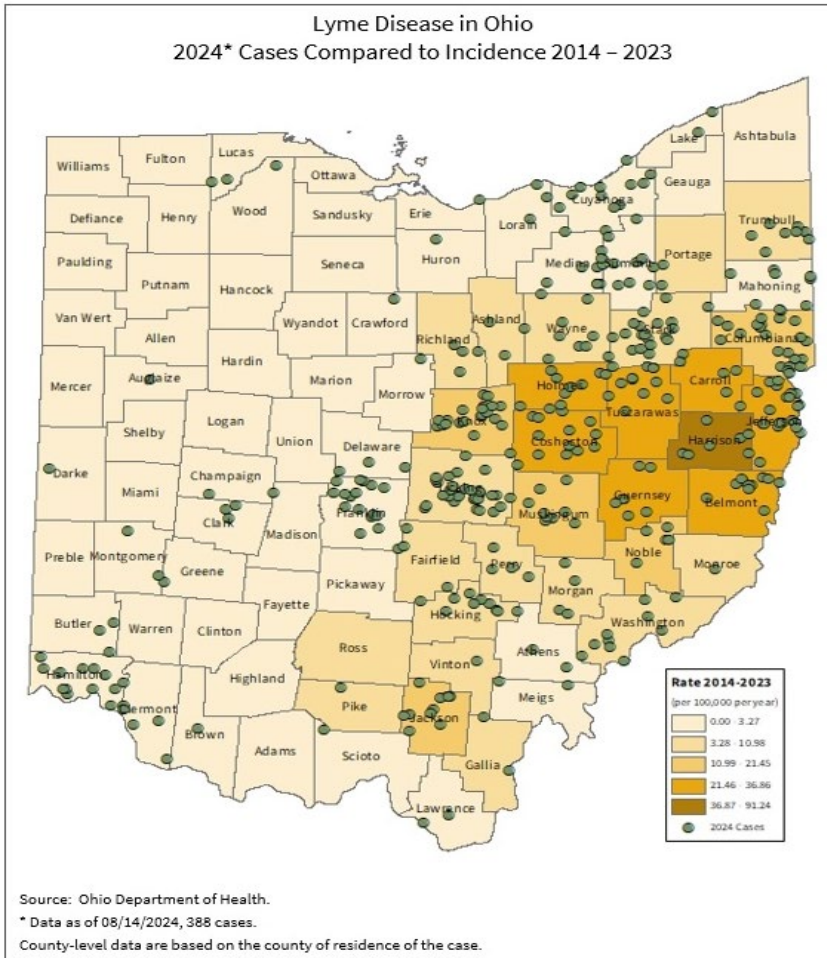
INCLUSION CRITERIA

- a. All pediatric patients that meet clinical diagnosis for Lyme disease

EXCLUSION CRITERIA

- a. No absolute exclusion

Geographic Incidence in Ohio



Source: <https://odh.ohio.gov/know-our-programs/zoonotic-disease-program/media/lyme-disease-map>; Last Accessed: October 13, 2024

Clinical Manifestations

- **Erythema Migrans:** appears at the site of tick bite days to weeks later, beginning as a red macule or papule that usually expands to form a large (≥ 5 cm in diameter) annular, erythematous lesion, classically with central clearing creating a bull's-eye pattern. The lesion typically is painless and nonpruritic.
- EM lesions can vary greatly in size and shape and can be confused with other skin conditions (eg, cellulitis or ring worm).

Lyme Disease Stage	Symptoms	Time Since Tick Bite
Early Localized	Erythema migrans (EM) at site of bite Can have general symptoms of fever, malaise, headache, myalgia and arthralgia	1-2 weeks from bite
Early Disseminated	Multiple EM Cranial nerve palsies, ophthalmic conditions, meningitis Carditis Other systemic symptoms	2-4 weeks from bite
Late Disease	Arthritis Peripheral neuropathy or other central nervous system disease	Months after bite

"Bull's-eye" or target lesion



NOTE: Dog tick and lone star tick do not transmit Lyme disease. However, they may transmit other tick-borne illnesses that are not within the scope of this guideline.

For more images of Lyme disease related rashes, visit: <https://www.cdc.gov/lyme/signs-symptoms/lyme-disease-rashes.html>

Tick Guide Source: <https://odh.ohio.gov/know-our-programs/zoonotic-disease-program/resources/tick-id-card>

Diagnosis, Differential Diagnosis, and Testing

- In patients with **classic symptoms** (erythema migrans with the correct exposure), **testing is unnecessary** and will often be negative early in the disease course. Empiric treatment is recommended.
- The **diagnosis of non-classic symptoms** (extracutaneous Lyme disease, including late-stage disease) requires a typical clinical illness, plausible geographic exposure, and a positive serologic test result with the **standard 2-tier serologic method**.
 - 1st Step:** Test for general Lyme antibody. (NOTE: Do not order Lyme Disease, PCR. This is not the correct screening test).
 - 2nd Step:** Reflex IGG and IGM via Elisa following positive Lyme antibody test.
 - At UH labs in EPIC, order: "LYME (B. BURGDORFERI) AB MODIFIED 2-TITER TESTING, WITH REFLEX TO IGM AND IGG BY ELISA",
 - If using lab outside of UH, may need to order separately. The 1st Step may be termed, "LYME (B. BURGDORFERI) serum antibody testing".
- If serum antibodies (1st step) are negative: no further testing needs to be done**, and this is interpreted as a negative result.
 - However, if symptom onset is < 1 month and symptoms persist, consider repeat serum antibody testing ~ 14 days later.
- On reflex, IgM alone has a high false positive rate and is unreliable alone.**
 - If a patient has had symptoms for more than 1 month and only IgM is positive, then this is **likely a FALSE positive** and it is unlikely the patient has Lyme Disease. Alternative diagnosis for symptoms should be considered.
- Providers that need additional guidance in testing interpretation should contact RBC Pediatric Infectious Diseases for assistance.

Treatment Recommendations

- Chemoprophylaxis.**
 - Prophylactic antibiotic can be considered for patients with high-risk tick bite, occurring in area of high endemicity, believed to be from blacklegged tick, and attached greater than 36 hours. Prophylactic antibiotic should be given within 72 hours of tick removal.
 - 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.
 - Dosing: single prophylactic dose of doxycycline 4.4 mg/kg PO up to a maximum dose of 200 mg.



- **Antimicrobial Treatment of Lyme Disease in Children.** See the table below which summarizes recommendations published jointly by the Infectious Diseases Society of America, American Academy of Neurology, and American College of Rheumatology.

Disease Category	Antibiotics and Dose
Erythema migrans (single or multiple) (any age) (also termed early localized disease)	1 st line: Doxycycline: 4.4 mg/kg per day, orally, divided into 2 doses (max 200 mg/day) for 10 days, OR
	1 st line: Amoxicillin: 50 mg/kg per day, orally, divided into 3 doses (max 1.5 g/day) for 14 days, OR
	1 st line: Cefuroxime: 30 mg/kg per day, orally, in 2 divided doses (max 1 g/day) for 14 days, OR
	2 nd line for patient unable to take a beta-lactam or doxycycline: Azithromycin, a 10 mg/kg/day, orally, once daily for 7 days (max 500mg/dose) <i>(NOTE: due to concerns of lower efficacy, azithromycin should be reserved for patients in whom other antibiotics are contraindicated. It has not been sufficiently studied for Lyme disease other than erythema migrans.)</i>
Isolated facial palsy	Doxycycline: 4.4 mg/kg per day, orally, divided into 2 doses (max 200 mg/day), for 14–21 days
Arthritis	An oral agent used for early localized disease; prescribe for duration of 28 days
Persistent arthritis after first course of therapy	Re-treat using an oral agent as for first-episode arthritis for an additional 28 days, OR
	Ceftriaxone: 50–75 mg/kg intravenously once a day (max 2 g/day) for 14–28 days
Atrioventricular heart block or carditis	An oral agent used for early localized disease; prescribe for 14 days (range 14–21 days)
	Ceftriaxone: 50–75 mg/kg, intravenously once a day (max 2 g/day) for 14 days (range 14–21 days for a hospitalized patient); oral therapy (using an agent as for early localized disease) can be substituted when the patient is stabilized or discharged, to complete the 14- to 21-day course
Meningitis	Doxycycline: 4.4 mg/kg per day, orally, divided into 1 or 2 doses (max 200 mg/day) for 14–21 days
	Ceftriaxone: 50–75 mg/kg, intravenously, once a day (max 2 g/day) for 14–21 days

- **Persistent post-treatment symptoms.** This is mistakenly called “*chronic Lyme disease.*” Some patients have persistent symptoms after treatment is completed. Additional antimicrobial agents in this scenario have not been shown to offer benefit. Symptoms may respond to symptomatic treatment and recovery may be gradual.

When to Refer to Infectious Diseases

- Recommend referral to pediatric infectious diseases for the following:
 - Any patient whose testing is unclear
 - Patient with central nervous system disease other than cranial nerve palsy (or suspected)
 - Patient with carditis or concern for carditis (should also be followed by Pediatric Cardiology)
 - Patient with arthritis

Prevention

- General protective measures to reduce exposure to ticks should be followed.
- **Dress Appropriately:** Ticks prefer wooded, grassy areas. When playing outside, children should be encouraged to wear clothing that covers the head, arms, legs, and other exposed skin. Tucking in shirts, pants into socks, and closed shoes may reduce risks.
- **Spray:** Permethrin can be sprayed on clothes and gear. Use of insect repellent with DEET (20%) can also repel ticks.
- **Tick checks:** Parents or caregivers should perform “tick checks” to inspect themselves and children’s bodies, clothing, and equipment during and after possible tick exposure. Special attention should be given to exposed regions of the body including head, neck, and behind ears. Ticks may also attach at areas of tight clothing (sock and belt line, axilla, groin). Bathing after coming indoors may be effective at locating ticks.
- **Tick Removal:** Ticks should be removed as soon as they are discovered. Fine-tipped forceps should be used to grasp close to the skin and gently pull straight out. Wash the bite site with soap and water to reduce the risk of secondary skin infections.

Major References

1. Lyme Disease. Red Book: 2024-2027 Report of the Committee on Infectious Diseases 33rd edition. P 549-556. https://doi.org/10.1542/9781610027373-S3_011_006
2. Paul M Lantos, Jeffrey Rumbaugh, Linda K Bockenstedt, Yngve T Falck-Ytter, Maria E Aguero-Rosenfeld, Paul G Auwaerter, Kelly Baldwin, Raveendhara R Bannuru, Kiran K Belani, William R Bowie, John A Branda, David B Clifford, Francis J DiMario, John J Halperin, Peter J Krause, Valery Lavergne, Matthew H Liang, H Cody Meissner, Lise E Nigrovic, James (Jay) J Nocton, Mikala C Osani, Amy A Pruitt, Jane Rips, Lynda E Rosenfeld, Margot L Savoy, Sunil K Sood, Allen C Steere, Franc Strle, Robert Sundel, Jean Tsao, Elizaveta E Vaysbrot, Gary P Wormser, Lawrence S Zemel, 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, Clinical Infectious Diseases, Volume 72, Issue 1, 1 January 2021, Pages e1–e48, <https://doi.org/10.1093/cid/ciaa1215>
3. Lyme Disease. Ohio Department of Health. <https://odh.ohio.gov/know-our-programs/zoonotic-disease-program/diseases/lyme-disease>. Last accessed Oct 13, 2024.

How was this Guideline Developed?

- This guideline was developed by pediatric infectious diseases and the antimicrobial stewardship program with input from pediatric primacy care.
- This guideline is an adoption of the recommendations jointly published by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR) which is also reflected in the AAP Red Book chapter on Lyme Disease.

Acronyms and Abbreviations

EM	Erythema Migrans
IGG	Immunoglobulin G
IGM	Immunoglobulin M

Disclaimer: Practice recommendations are based upon the evidence available at the time the clinical practice guidance was developed. Clinical practice guidelines (including summaries and pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his/her independent judgement in the management of any specific patient and is responsible, in consultation with the patient and/or the patient’s family to make the ultimate judgement regarding care. If you have questions about any of the clinical practice guidelines or about the guideline development process please contact the Rainbow Evidence Practice Program at RainbowEBPprogram@uhhospitals.org

Initial Approval (toolkit) March 2019
Revised Nov 2024