

From The Medical Letter on Drugs and Therapeutics

Treatment of Lyme Disease

Most cases of Lyme disease in the US occur between May and September in the Northeastern, Mid-Atlantic, and North Central states.

The Disease

Lyme disease in the US is caused by the spirochete *Borrelia burgdorferi*, which is transmitted to humans by *Ixodes scapularis* or *I pacificus* ticks.¹ The characteristic skin lesion, erythema migrans, develops at the site of the tick bite 1-2 weeks after the tick

has detached (range 3-30 days) and expands over days to weeks. The classic skin lesion has central clearing with a bull's-eye appearance, but more often the rash is homogeneously erythematous and, rarely, necrotic or vesicular. Erythema migrans may go unnoticed because it often occurs in areas not readily visible to the patient, such as the back, buttocks, axillae or popliteal fossa, is often asymptomatic, and resolves spontaneously within weeks.

Fever, headache, malaise, arthralgia, or myalgia may accompany erythema migrans. A newly discovered species of *Borrelia*, *B mayonii* (found in the upper Midwest), may cause nausea and



Author Audio Interview at jama.com

develops at the site of the tick bite 1-2 weeks after the tick

Table. Treatment of Lyme Disease^a

	Drug	Usual Adult Dosage (Range) ^b	Usual Pediatric Dosage ^c
Tick Bite	Doxycycline ^{d,e} and/or observation	200 mg PO × 1 dose	≥8 yrs: 4 mg/kg PO × 1 dose
Erythema Migrans	Doxycycline ^e or Amoxicillin or Cefuroxime axetil or Azithromycin ^f	100 mg PO bid × 10 d 500 mg PO tid × 14 d 500 mg PO bid × 14 d 500 mg PO once/d × 7-10 d	≥8 yrs: 2 mg/kg PO bid 50 mg/kg/d PO divided tid 30 mg/kg/d PO divided bid 10 mg/kg/d PO
Neurologic Disease			
Facial nerve palsy	Doxycycline ^{e,g} or Amoxicillin	100 mg PO bid × 14 d 500 mg PO tid × 14 d	≥8 yrs: 2 mg/kg PO bid 50 mg/kg/d PO divided tid
Other neurologic disease ^h	Doxycycline or Ceftriaxone	100 mg PO bid × 14 d 2 g q24 h IV × 14 d	≥8 yrs: 2 mg/kg PO bid 50-75 mg/kg/d IV
Cardiac Disease			
Mild (first-degree AV block, PR <300 msec)	Doxycycline ^e or Amoxicillin or Cefuroxime axetil	100 mg PO bid × 14 d (14-21) 500 mg PO tid × 14 d (14-21) 500 mg PO bid × 14 d (14-21)	≥8 yrs: 2 mg/kg PO bid 50 mg/kg/d PO divided tid 30 mg/kg/d PO divided bid
More serious ⁱ	Ceftriaxone	2 g q24 h IV × 14 d (14-21)	50-75 mg/kg/d IV
Arthritis ^j			
Arthritis without neurologic disease ^k	Doxycycline ^e or Amoxicillin or Cefuroxime axetil	100 mg PO bid × 28 d 500 mg PO tid × 28 d 500 mg PO bid × 28 d	≥8 yrs: 2 mg/kg PO bid 50 mg/kg/d PO divided tid 30 mg/kg/d PO divided bid
Persistent or recurrent ^l	Ceftriaxone	2 g q24h IV × 14-28 d	50-75 mg/kg/d IV

^a Regardless of the clinical manifestation of Lyme disease, complete response to treatment may be delayed beyond the treatment duration. Relapse may occur with all of these regimens; patients who relapse may need a second course of treatment. Excessively prolonged treatment or many repeat courses of therapy are not recommended.

^b Based on severity and/or response.

^c Should not exceed adult dosage. Duration of therapy is the same as in adult patients.

^d The strongest indication for prophylaxis with doxycycline is when: 1) the attached tick can be reliably identified as an *Ixodes scapularis* tick that is estimated to have been attached for ≥36 hours based on the degree of engorgement of the tick or the time of exposure; 2) it can be started within 72 hours after tick removal and 3) the local rate of infection of *I scapularis* ticks with *Borrelia burgdorferi* is >20%.

^e Should generally not be used for children <8 y old or for pregnant or lactating women.

^f For patients unable to take beta-lactams or tetracyclines.

^g Cefuroxime axetil 500 mg bid can be substituted for patients unable to take tetracyclines.

^h Available data on European neuroborreliosis indicate that doxycycline 200 mg q24 h and ceftriaxone are equally effective in Lyme meningitis. Data are lacking on the efficacy of doxycycline in Lyme encephalitis or Lyme encephalopathy. In the absence of brain or spinal cord involvement, doxycycline may be considered an acceptable treatment option if the illness is not severe.

ⁱ Includes hospitalized patients with first-degree AV block with symptoms or with a PR interval ≥300 milliseconds, or second- or third-degree AV block. A temporary pacemaker may be necessary. Oral treatment with doxycycline, amoxicillin, or cefuroxime axetil may be substituted for IV therapy after resolution of heart block in a stable patient.

^j In late disease, the response to treatment may be delayed for several weeks or months.

^k Patients with Lyme arthritis and neurological symptoms should be treated with ceftriaxone 2g IV q 24h × 28 d.

^l Patients with mild persistent or recurrent arthritis may be treated with a second course of oral antibiotics.

vomiting as well.^{2,3} Weeks to months after initial infection, patients with untreated Lyme disease may develop early disseminated disease that can include migratory musculoskeletal pain, carditis, facial nerve palsy, ocular manifestations, or meningitis. Months to a few years after initial infection (late disease), arthritis may develop, typically of the knee.

Prophylaxis

Avoidance of ticks and use of tick repellents can reduce the risk of being bitten.⁴ Ticks found on the skin should be removed promptly; ticks must be attached for ≥ 36 hours to transmit the disease. Within 72 hours after tick removal, antibiotic prophylaxis with a single dose of doxycycline should be considered (Table); the strongest indication is when an *Iscapularis* tick from a highly endemic area is partially engorged or attached for ≥ 36 hours, but prophylaxis would also be reasonable when the duration of tick attachment or degree of engorgement is uncertain.⁵

Erythema Migrans

In patients with early Lyme disease, treatment with oral doxycycline for 10 days shortens the duration of the skin lesion and generally prevents development of late sequelae. Doxycycline is not recommended for children <8 years old or for pregnant or lactating women; amoxicillin and cefuroxime axetil (Ceftin, and generics) are effective alternatives.

Neurologic Disease

Facial nerve palsy, which may be bilateral, can be a presenting feature of early disseminated Lyme disease. For patients with isolated facial nerve palsy, oral doxycycline is effective. Patients with other neurologic involvement such as meningitis, other cranial nerve palsies, radiculopathy, or cognitive deficits are usually treated with IV ceftriaxone (Rocephin, and generics).

Cardiac Disease

Cardiac conduction abnormalities associated with Lyme disease are generally self-limited. Patients with minor cardiac involvement (first-degree atrioventricular [AV] block with a PR interval of <300 milliseconds) can be treated with oral doxycycline, amoxicillin, or cefuroxime axetil. Those with more severe cardiac involvement, such as first-degree AV block with symptoms or a PR interval ≥ 300 milliseconds, or second- or third-degree AV block, should be hospitalized and treated with IV ceftriaxone.

Arthritis

Oral treatment with doxycycline, amoxicillin, or cefuroxime axetil for 28 days is usually effective for treatment of Lyme arthritis. Arthritis that has only partially responded to oral treatment may respond fully to a second month of oral therapy. Refractory arthritis can be treated with IV ceftriaxone.

Post-Treatment Lyme Disease Symptoms

Some patients whose objective manifestations of Lyme disease resolved with antibiotic treatment report persistent subjective symptoms such as fatigue, musculoskeletal pain, or cognitive difficulties. These long-standing symptoms have not been associated with active infection and have not responded to antibiotics.⁶⁻⁸ Recurrent symptoms in previously treated patients may be due to new tick bites and reinfection.⁹

Conclusion

Use of tick repellents and early removal of ticks are the first steps in preventing Lyme disease. After an *Iscapularis* tick bite in a highly endemic area, prophylaxis with a single dose of doxycycline would be reasonable for nonpregnant adults and children ≥ 8 years old. Recommended doses of antibiotics cure almost all patients with erythema migrans and can prevent more serious manifestations of Lyme disease.

ARTICLE INFORMATION

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