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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.

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 vomiting as well. 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. 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; the strongest indication is when an I. scapularis 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.

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. Recurrent symptoms in...
CONCLUSION — Use of tick repellers and early removal of ticks are the first steps in preventing Lyme disease. After an *I. scapularis* 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. ■

10. Patients with Lyme arthritis and neurological symptoms should be treated with ceftriaxone 2g IV q24h x 14 days.
11. Patients with Lyme arthritis and neurological symptoms may be treated with a second course of oral antibiotics.
12. Patients with mild persistent or recurrent arthritis may be treated with a second course of oral antibiotics.

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1. 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.
2. Based on severity and/or response.
3. Should not exceed adult dosage. Duration of therapy is the same as in adult patients.
4. The strongest indication for prophylaxis with doxycycline is when: a) 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; b) it can be started within 72 hours after tick removal and c) the local rate of infection of *I. scapularis* ticks with *Borrelia burgdorferi* is ≥20%.
5. Should generally not be used for children <8 years old or for pregnant or lactating women.
6. For patients unable to take beta-lactams or tetracyclines.
7. Cefuroxime axetil 500 mg bid can be substituted for patients unable to take tetracyclines.
8. Available data on European neuroborreliosis indicate that doxycycline 200 mg q24h 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.
9. 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.
10. In late disease, the response to treatment may be delayed for several weeks or months.
11. Patients with Lyme arthritis and neurological symptoms should be treated with ceftriaxone 2g IV q24h x 28 days.
12. Patients with mild persistent or recurrent arthritis may be treated with a second course of oral antibiotics.
Addendum: Doxycycline for Young Children?

A reader commenting on our Treatment of Lyme Disease article (Med Lett Drugs Ther 2016; 58:57) objected to a footnote in the table advising against use of doxycycline in children <8 years old. This warning has been included in the labeling of all tetracyclines since 1970 when it was recognized, after decades of use, that these drugs caused permanent staining and enamel hypoplasia of developing teeth. The CDC recently stated that short courses of doxycycline, which was first marketed in the US in 1967 and has less affinity for calcium than other tetracyclines, have not been shown to cause tooth staining. That statement was prompted by the discovery that children <10 years old have a disproportionately high fatality rate from rickettsial diseases, particularly Rocky Mountain spotted fever, for which doxycycline is the drug of choice and chloramphenicol is the only proven alternative.

The main evidence supporting the CDC’s statement was a retrospective cohort study consisting of a record review and dental examination of 271 children living on a Native American reservation. No staining was detected in any of the 58 children who had been treated with doxycycline before the age of 8 years or in any of the 213 children who had not been exposed to the drug. Enamel hypoplasia was present in 4% of children in both cohorts. Lyme disease, unlike Rocky Mountain spotted fever, is seldom fatal and can be treated with antibiotics other than doxycycline. A single dose of doxycycline is recommended for prophylaxis after a tick bite. Given the CDC’s statement about its safety, it would seem reasonable to use doxycycline for prophylaxis in all age groups. When longer treatment courses (10, 14, or 28 days) are recommended for the various clinical manifestations of Lyme disease in children <8 years old, alternative antibiotics generally could be used instead.
