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Treatment of Lyme Disease

Lyme disease in North America is caused by the spirochete *Borrelia burgdorferi*, which is transmitted to humans by *Ixodes scapularis* or *pacificus* ticks. These ticks may also carry other pathogens; coinfection with *Babesia microti* or *Anaplasma phagocytophilum* (formerly *Ehrlichia*) has been reported.¹ In 2001 and 2002, 12 states (CT, DE, ME, MD, MA, MI, NH, NJ, NY, PA, RI, WI) reported about 95% of all the Lyme disease in the US, but cases occurred in all states except HI, MT and OK.² Most Lyme disease in North America occurs between May and September.

THE DISEASE — About 70-80% of patients infected by *B. burgdorferi* develop the characteristic skin lesion, erythema migrans, which occurs at the site of the tick bite 3 to 30 days after the tick has detached.³ Fever, headache, malaise, arthralgias and myalgia usually accompany early disease. Multiple (secondary) skin lesions occur in about 15% of patients. Patients with untreated Lyme disease may develop cardiac involvement, neurologic disease or migratory musculoskeletal pain. Late manifestations of Lyme disease include arthritis, typically of the knee, and various neurologic conditions, including peripheral neuropathy and subtle encephalopathy with cognitive defects. Clinical manifestations of the disease are somewhat different in Europe because other borrelia species cause human infection there.⁴

DIAGNOSIS — In endemic areas, Lyme disease is diagnosed by recognition of erythema migrans. IgG antibodies to *B. burgdorferi* are usually detectable 4 to 6 weeks after the initial infection. If an enzyme-linked immunosorbent assay (ELISA) or immunofluorescent assay (IFA) is positive or equivocal, the specimen should also be tested with a standardized Western blot.⁵

PROPHYLAXIS — No vaccine is currently available to prevent Lyme disease in humans. Avoidance of

ticks and use of tick repellents such as DEET or picaridin, or the insecticide permethrin on clothing can prevent Lyme disease.⁶ Since transmission of *B. burgdorferi* is more likely with prolonged tick attachment, prompt removal of ticks can also prevent disease.⁷ Whether early antibiotic prophylaxis is indicated after a tick bite is controversial; the strongest indication is in a highly endemic area when an engorged tick is attached for 48 hours or more. In one study of 482 patients who had removed an attached *I. scapularis* tick, a single 200-mg dose of doxycycline (*Vibramycin*, and others) within 72 hours of tick removal was 87% effective in preventing development of erythema migrans at the site of the bite.⁸ In another prophylactic study, 10 days of amoxicillin (*Amoxil*, and others) appeared to be effective (no treated patients developed the disease), but the incidence of infection in the placebo group was too low to permit any conclusions.⁹

ERYTHEMA MIGRANS — Oral antibiotic therapy shortens the duration of the rash and generally prevents development of late sequelae. Among the 3 drugs used for this indication, only doxycycline is also effective against *A. phagocytophilum* infection; it should not be used in pregnant women or children less than eight years old. One double-blind controlled trial in 180 patients with erythema migrans showed that 10 days treatment with doxycycline was as effective as 20 days. Some patients remained symptomatic at the end of antibiotic therapy, but they continued to improve after treatment at the same rate regardless of whether they were treated for 10 or 20 days. One patient in the 10-day group developed meningitis.¹⁰

Amoxicillin is as effective as doxycycline and is preferred for children less than 8 years old and pregnant or lactating women. Cefuroxime axetil (*Ceftin*) is also effective, but much more expensive. Macrolides such as azithromycin (*Zithromax*) have been less effective in controlled trials.¹¹ Patients in whom bacterial cellulitis cannot be excluded could be treated with cefuroxime axetil or amoxicillin/clavulanic acid (*Augmentin*), since these

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TREATMENT OF LYME DISEASE¹

	DRUG	ADULT DOSAGE	PEDIATRIC DOSAGE ²
ERYTHEMA MIGRANS	Doxycycline ³ (<i>Vibramycin</i> , and others)	100 mg PO bid x 10-21d	≥8 yrs; 1-2 mg/kg bid
	or Amoxicillin (<i>Amoxil</i> , and others)	500 mg PO tid x 14-21d	25-50 mg/kg/d divided tid
	or Cefuroxime axetil (<i>Ceftin</i>)	500 mg PO bid x 14-21d	30 mg/kg/d divided bid
NEUROLOGIC DISEASE			
Facial nerve palsy	Doxycycline ³	100 mg PO bid x 14-21d	≥8 yrs; 1-2 mg/kg bid
	or Amoxicillin	500 mg PO tid x 14-21d	25-50 mg/kg/d divided tid
More serious disease	Ceftriaxone ⁴ (<i>Rocephin</i>)	2 g/d IV once/d x 14-28d	75-100 mg/kg once/d IV
CARDIAC DISEASE			
Mild (first degree AV block)	Doxycycline ³	100 mg PO bid x 14-21d	≥8 yrs; 1-2 mg/kg bid
	or Amoxicillin	500 mg PO tid x 14-21d	25-50 mg/kg/d divided tid
More serious disease ⁵	Ceftriaxone ⁴	2 g once/d IV x 14-21d	50-100 mg/kg once/d IV
ARTHRITIS⁶			
	Doxycycline ³	100 mg PO bid x 28d	≥8 yrs; 1-2 mg/kg bid
	or Amoxicillin	500 mg PO tid x 28d	25-50 mg/kg/d divided tid
	or Ceftriaxone ⁴	2 g once/d IV x 14-28d	50-100 mg/kg once/d IV

1. Regardless of the clinical manifestation of Lyme disease, complete response to treatment may be delayed beyond the treatment duration. Relapse has occurred with all of these regimens; patients with objective signs of relapse may need a second course of treatment.
2. Should not exceed adult dosage.
3. Should not be used for children less than eight years old or for pregnant or lactating women.
4. Or cefotaxime (*Claforan*) 2 g IV q8h x 14-28d for adults and 150-200 mg/kg/d in 3-4 doses for children.
5. A temporary pacemaker may be necessary. Oral treatment may be substituted for IV therapy after resolution of the heart block in a stable patient.
6. In late disease, the response to treatment may be delayed for several weeks or months.

drugs are active against Lyme disease as well as *Streptococcus pyogenes* and most community-acquired strains of *Staphylococcus aureus*. Fluoroquinolones are ineffective against *B. burgdorferi*.

NEUROLOGIC DISEASE — For patients with facial nerve palsy alone, oral doxycycline or amoxicillin may be effective. Patients with other neurologic involvement, such as meningitis, other cranial nerve palsies, radiculopathy or cognitive deficits, should be treated with IV ceftriaxone (*Rocephin*) or cefotaxime (*Claforan*).¹²

CARDIAC DISEASE — Cardiac conduction abnormalities associated with Lyme disease are generally self-limited. Patients with minor cardiac involvement (first-degree atrioventricular block) can usually be treated with oral doxycycline or amoxicillin. Those with more severe cardiac involvement should receive IV ceftriaxone or cefotaxime.

ARTHRITIS — Oral therapy with doxycycline or amoxicillin for 28 days is usually effective for treatment of Lyme arthritis. Patients who have not responded to oral treatment may respond to a second one-month course of oral therapy or to IV therapy with ceftriaxone or cefotaxime. One trial found similar efficacy in eradicating signs and symptoms with 14 and 28 days of ceftriaxone in patients with late Lyme disease, the majority of whom had Lyme arthritis.¹³

POST-LYME DISEASE SYNDROME — Some treated patients whose objective manifestations of Lyme disease

have resolved with antibiotic treatment report subjective symptoms such as fatigue, musculoskeletal pain or cognitive difficulties of varying intensity that may persist over prolonged periods. Microbiologic evaluation of these patients has failed to find evidence of either persistent *B. burgdorferi* infection or of co-infection with another tick-borne pathogen. Two controlled studies, one in 78 patients seropositive for IgG antibodies to *B. burgdorferi* and another in 51 seronegative patients, both with a history of treated Lyme disease and persistent symptoms for at least 6 months, compared 1 month of IV ceftriaxone plus 2 additional months of oral doxycycline with placebo and found no clinical benefit of antibiotic therapy.¹⁴

CONCLUSION — Use of repellents and avoidance and early removal of ticks are the first steps in prevention of Lyme disease. In highly endemic areas, when an engorged *Ixodes scapularis* tick is attached for at least 48 hours, prophylaxis with a single dose of doxycycline would be reasonable in adults and children at least 8 years old. With a less compelling indication, it would be reasonable not to prescribe antibiotics unless erythema migrans develops. Recommended doses of antibiotics cure almost all patients with erythema migrans without complications. Antibiotic therapy is not recommended for patients with a history of appropriately treated Lyme disease and persistent subjective symptoms. □

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