

# Diagnosis and Treatment of Lyme Arthritis



Sheila L. Arvikar, MD, Allen C. Steere, MD\*

## KEYWORDS

- Lyme disease • *Borrelia burgdorferi* • Lyme arthritis • Antibiotic-refractory arthritis
- Inflammatory arthritis

## KEY POINTS

- Lyme arthritis is a late disease manifestation, usually beginning months after the tick bite. Patients may not report an antecedent tick bite or erythema migrans.
- Patients have intermittent or persistent attacks of joint swelling and pain, primarily in 1 or a few large joints, especially the knee, without prominent systemic manifestations.
- The diagnosis is supported by 2-tier serologic testing for *Borrelia burgdorferi* by enzyme-linked immunosorbent assay and immunoglobulin G Western blotting.
- Initial treatment is a 30-day course of oral doxycycline or amoxicillin. For patients with an insufficient response to oral treatment, intravenous therapy with ceftriaxone is recommended.
- A minority of patients may have persistent synovitis for months or several years after oral and intravenous antibiotic therapy, which is treated with antiinflammatory agents, disease-modifying antirheumatic drugs, or synovectomy.

## INTRODUCTION/NATURE OF THE PROBLEM

### *Epidemiology*

Lyme arthritis was recognized originally because of an outbreak of monoarticular and oligoarticular arthritis in children in Lyme, Connecticut, in the 1970s.<sup>1</sup> It then became apparent that Lyme disease was a complex, multisystem illness affecting primarily skin, nervous system, heart, or joints.<sup>2</sup> Before the use of antibiotic therapy for treatment of the disease, about 60% of untreated patients developed Lyme arthritis, a late disease manifestation.<sup>3</sup> In recent years, more than 30,000 cases of Lyme disease have been reported annually to the Centers for Disease Control and Prevention (CDC), and in one-third of reported cases, arthritis was a manifestation of the disease.<sup>4</sup> However, recent CDC estimates suggest the actual number of infections with the Lyme disease spirochete may be 10-fold higher.<sup>5</sup>

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Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, Boston, MA 02114, USA

\* Corresponding author.

E-mail address: [asteere@mgh.harvard.edu](mailto:asteere@mgh.harvard.edu)

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The infection is transmitted primarily by nymphal *Ixodes scapularis* ticks, which quest in the late spring and early summer.<sup>6</sup> However, Lyme arthritis can present at any time of the year. The majority of cases occur in the northeastern United States, from Maine to Virginia.<sup>5</sup> Other affected areas in the United States include the northern mid-Western states of Minnesota, Wisconsin, and Michigan, and the West coast in northern California.

In the United States, *Borrelia burgdorferi* is the sole cause of the disease, but subtypes of *B burgdorferi* differ in pathogenicity.<sup>7,8</sup> OspC type A (RST1) strains, which account for 30% to 50% of the infections in the northeastern United States,<sup>7,8</sup> but only 3% in mid-Western states,<sup>9</sup> are particularly virulent and arthritogenic. These strains are thought to have played an important role in the emergence of the Lyme disease epidemic in the northeastern United States in the late 20th century.<sup>10</sup>

### Pathogenesis

In the northeastern United States, *B burgdorferi* strains often disseminate to joints, tendons, or bursae early in the infection.<sup>3,6</sup> Although this event is frequently asymptomatic, transient or migratory arthralgias may occur at that time. Lyme arthritis, a late disease manifestation, usually occurs months later accompanied by intense innate and adaptive immune responses.<sup>11</sup> The adaptive immune response leads to the production of specific antibodies that opsonize the organism, facilitating phagocytosis and effective spirochetal killing.

With appropriate oral and, if necessary, intravenous (IV) antibiotic therapy, spirochetes are eradicated, and joint inflammation resolves in the great majority of patients. However, in a small percentage of patients, particularly in those who were infected with highly inflammatory *B burgdorferi* RST1 strains, synovial inflammation persists for months or several years despite receiving oral and IV antibiotic therapy for 2 or 3 months, called antibiotic-refractory arthritis.<sup>12</sup> A refractory outcome is likely to require multiple factors, and may include some combination of pathogen-associated, genetic, and immunologic factors (**Box 1**).

Although antibiotic-refractory arthritis is associated with highly inflammatory strains of *B burgdorferi*, persistent infection in the postantibiotic period does not seem to play role in this outcome. Polymerase chain reaction (PCR) testing of synovial fluid for *B burgdorferi* DNA, which is often positive before treatment, is usually negative after antibiotic treatment, and both culture and PCR testing of synovial tissue have been

#### Box 1

##### Factors associated with antibiotic-refractory Lyme arthritis

###### Pathogen

- *Borrelia burgdorferi*, particularly OspC type A (RST-1) type strain<sup>8</sup>
- Possible retained spirochetal antigens<sup>18,19</sup>

###### Genetic

- Certain HLA-DR alleles that bind *B burgdorferi* outer surface protein A (OspA)<sup>14</sup>
- Toll-like receptor 1-1805 GG polymorphism<sup>17</sup>

###### Immunologic

- Endothelial cell growth factor autoantibodies<sup>20</sup>
- Decreased ratio of T-regulatory/T-effector cells among synovial fluid mononuclear cells<sup>16,17</sup>

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