Published in final edited form as:

J Am Acad Orthop Surg. 2011 February ; 19(2): 91–100.

Lyme Disease and the Orthopaedic Implications of Lyme Arthritis

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Abstract

Lyme disease is the most common tick-borne disease in the United States and Europe. Increased awareness of the clinical manifestations of the disease is needed to improve detection and treatment. In the acute and late stages, Lyme disease may be difficult to distinguish from other disease processes. The epidemiology and pathophysiology of Lyme disease are directly related to the *Borrelia burgdorferi* spirochete and its effects on the integumentary, neurologic, cardiac, and musculoskeletal systems. Lyme arthritis is a common clinical manifestation of Lyme disease and should be considered in the evaluation of patients with monoarticular or pauciarticular joint complaints in a geographic area in which Lyme disease is endemic. Management of Lyme arthritis involves eradication of the spirochete with antibiotics. Generally, the prognosis is excellent. Arthroscopic synovectomy is reserved for refractory cases that do not respond to antibiotics.

In 1977, Steere et al¹ described a mysterious arthritis epidemic that affected 39 children and 12 adults in three contiguous communities in Connecticut. The illness was characterized by recurrent attacks of asymmetric swelling and pain in large joints. The knee was the most common site of involvement. Early cases in children were misdiagnosed as juvenile rheumatoid arthritis; however, the geographic clustering of cases indicated an infectious etiology. This previously unrecognized entity was dubbed Lyme arthritis after the town of Lyme, Connecticut, where most of the first known patients lived.

The initial work of Steere et al¹ pointed toward an arthropod as the likely vector of transmission of Lyme arthritis because of the geographic clustering of the affected patients in sparsely settled, heavily wooded areas along the Connecticut shore and because the peak incidence occurred during the summer months. This hypothesis was supported by the presence of an expanding skin lesion, 1 to 24 weeks before the onset of arthritis, that was similar to erythema migrans. At the time, a vector-borne illness was the suspected etiology of erythema migrans.² Subsequent investigations into the etiology of Lyme arthritis led to the discovery of the causative agent, *Borrelia burgdorferi*, a spirochetal organism that is transmitted by the *Ixodes* tick.³

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Epidemiology

Lyme disease is the most common tick-borne illness in the United States, and its incidence continues to increase (Figure 1). In 1992, 9,908 cases were reported to the Centers for Disease Control and Prevention (CDC).⁴ By 2006, that number had increased by 101%, to 19,931 cases. Lyme disease has been reported in all 50 states and the District of Columbia, but 10 states—Maryland, Massachusetts, Minnesota, New Jersey, New York, Pennsylvania, Wisconsin, Connecticut, Delaware, and Rhode Island—account for 93% of cases each year⁴ (Figure 2). As of 2006, Connecticut had the highest average annual rate of Lyme disease, with 73.6 cases per 100,000, followed by Rhode Island, with 45.8 cases per 100,000. Lyme disease has a distinct geographic distribution, with three distinctive foci within the United States: the Northeast from Maryland to Maine, the Great Lakes region of the Midwest (Wisconsin, Minnesota, parts of Michigan), and the Pacific Northwest (Northern California, Oregon).

A bimodal age distribution exists for reported cases of Lyme disease, with average annual rates peaking in children aged 5 to 9 years and adults aged 55 to 59 years (8.6 cases per 100,000 and 7.8 cases per 100,000, respectively).⁴ Infection may occur year-round; however, most cases occur in June, July, and August (Figure 3). Children infected with *B burgdorferi* are more likely than adults to develop arthritis as an initial manifestation of Lyme disease.⁵

Pathogenesis

Lyme disease is zoonotic—that is, it is transmitted from nonhuman animals to humans. The disease is caused by the spirochete *B burgdorferi*, which is carried in the gut of the *Ixodes* tick. Mice, squirrels, shrews, and other small mammals are natural carriers of *B burgdorferi*. The *Ixodes* tick, which includes *I scapularis* in the Northeast, *I pacificus* in the Pacific Northwest, and *I ricinus* in Europe, becomes infected with the spirochete while feeding on these animals. Humans become infected when the nymphal ticks attach to the skin to obtain a blood meal. Ticks in this form are most commonly found in late spring and summer, which accounts for the seasonal distribution of reported cases of Lyme disease (Figure 4).

B burgdorferi is injected into the skin following the bite of an infected tick.⁶ Transmission of the spirochete from the tick takes approximately 48 to 72 hours; thus, ticks attached for <24 hours typically do not transmit the disease.⁷ Tick saliva, which is injected into the skin along with the spirochete, disrupts local immune mechanisms and provides a protective environment in which the bacteria replicate. The spirochetes multiply and expand within the dermis, and the characteristic erythema migrans rash is caused by the host inflammatory response.⁸ Shortly after infection, the spirochete undergoes hematogenous dissemination to multiple sites, including the skin, central nervous system, and joints,⁹ resulting in the clinical features of the disease.

Clinical Presentation

Lyme disease may be divided into three distinct clinical stages: early localized, early disseminated, and late.¹⁰ The hallmark of early localized disease is erythema migrans—the classic rash that may occur at the site of a deer tick bite (Figure 5). The rash typically begins as a red macule that develops 2 to 30 days after the tick bite and expands within days to weeks after its initial appearance to become an annular lesion measuring 5 to 60 cm in size.¹¹ Central clearing may give rise to the classic bull's-eye rash; however, rash morphology is variable. In children, the rash is most frequently found on the head and neck (26%), followed by the arms and legs (25%), back (24%), abdomen (9%), axilla (8%), groin (5%), and chest (3%).¹² Approximately one third of patients who present with a rash recall a

tick bite at the site within the month preceding onset.¹² Early localized disease may be accompanied by flu-like symptoms, including fatigue, headache, and malaise.

Early disseminated disease occurs days to months after the initial tick bite and is characterized by neurologic and cardiac manifestations. Approximately 15% to 20% of untreated children with early Lyme disease develop neurologic symptoms within months of the initial infection.¹⁰ Most children who present with neurologic symptoms have no history of erythema migrans. The most common clinical manifestations of neurologic Lyme disease are facial nerve palsy, sixth nerve palsy, and lymphocytic meningitis^{10,13} (Figure 6).

Lyme carditis is relatively rare in the initial stages of Lyme disease.¹⁴ However, one large series reported Lyme carditis in 16% of children who presented to the emergency department with early disseminated disease.¹⁵ Lyme carditis is often asymptomatic, but it may manifest as a cardiac conduction abnormality, such as second- or third-degree atrio-ventricular block. The symptomatic patient may present with syncope, fatigue, dizziness, shortness of breath, or palpitations. The prognosis is typically good, with complete resolution of conduction abnormalities following treatment.

Late Lyme Disease and Arthritis

Lyme disease is a multisystem disorder with dermatologic, cardiac, and neurologic manifestations.^{16–19} Arthritis is one of its most important features, and it is of most interest to the orthopaedic surgeon. Arthritis is the most distinguishing feature of late-stage Lyme disease. It typically develops months after disease onset in approximately 60% of untreated Lyme patients.^{20,21} Following the initial tick bite, *B burgdorferi* spirochetes disseminate and invade synovial joints, where they induce an inflammatory response in synovial tissue consisting of synovial hypertrophy, vascular proliferation, and infiltration of mononuclear cells.²² In addition, neutrophils, immune complexes, complement, and cytokines accumulate in the synovial fluid. *B burgdorferi* also has been shown to induce chondrocytes to produce matrix metalloproteinases (MMPs).²³ MMPs have several functions, including degradation of extracellular matrix proteins, collagen, and proteoglycans.²³ Elevated levels of MMPs in the synovial fluid of patients with long-standing Lyme arthritis may contribute to cartilage damage. Despite these findings, the mechanism by which *B burgdorferi* causes joint damage is not completely understood.

The host inflammatory response seen in Lyme arthritis may result in an acute clinical presentation similar to that of bacterial septic arthritis, especially in children.^{24,25} Although the mechanism by which *B burgdorferi* induces joint damage is only partially understood, Lyme arthritis is known to progress relatively slowly, and initial management is inherently different from that of bacterial septic arthritis.^{22,26} Septic arthritis is characterized by rapid destruction of articular hyaline cartilage through enzymatic release by the bacteria as well as host synovial cells and chondrocytes.^{27–29} Certain bacteria produce proteases such as collagenase, elastase, hyaluronidase, lipase, and lipoproteinase; however, *B burgdorferi* does not seem to produce its own proteolytic enzymes.²⁹ Bacterial virulence factors, such as the coagulase produced by *Staphylococcus aureus*, may contribute to joint destruction by impairing the intracapsular vascular supply as the result of small vessel thrombosis. This causes an increase in intracapsular pressure and may prevent the host immune response from adequately addressing and clearing the infection.

Typically, episodes of Lyme arthritis are brief and involve a single large joint. The knee is the most commonly affected joint, with involvement in up to 90% of patients.^{5,13,30} The elbow, ankle, hip, and wrist may be affected, as well. Joint effusions are usually large and may be out of proportion to the patient's complaints. Fever is noted in 22% to 51% of children with Lyme arthritis.^{5,13,31} Recurrence of arthritis over a period of several months to

years is seen in 50% of patients, even in those who are appropriately treated with antibiotics, with the involvement of the same or different joints.³⁰ In most patients who develop arthritis, erythema migrans never develops or goes unnoticed.

Rose et al³² described five common patterns of Lyme arthritis in children. Classic arthritis is characterized by episodic synovitis with involvement of one to four joints lasting <1 week, separated by asymptomatic periods of 2 weeks. The acute pauciarticular form is defined by continual involvement of one to four joints for <4 weeks.³² This form is also called “pseudoseptic” because of its similarity to acute bacterial septic arthritis. Classic arthritis and acute pauciarticular arthritis were the most common forms in the series by Rose et al.³² The other three forms of arthritis (ie, chronic pauciarticular, migratory, polyarticular) most closely resembled other pediatric rheumatologic disease, such as juvenile idiopathic arthritis.

Diagnosis

Diagnosis of Lyme arthritis is based on recognition of characteristic clinical findings, a history of exposure in an area in which the disease is endemic, and confirmatory serologic testing.²⁰ The CDC defines Lyme arthritis as “recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints.”³³ Serologic testing for Lyme disease consists of a two-tiered approach in which an enzyme-linked immunosorbent assay (ELISA) test is used to screen patient samples.³⁴ ELISA is sensitive but not specific to Lyme antibodies. A positive or indeterminate ELISA test is followed by confirmatory Western blot assay, which is more specific for Lyme antibodies.³⁵

Vigilance is essential when ordering and interpreting serologic tests for Lyme disease. False-positive results have been reported in 2% to 5% of asymptomatic persons who live in nonendemic areas.³⁵ Thus, the clinician must take into account the clinical indications when considering serologic testing for the disease. Current serologic testing does not accurately distinguish between active and past infection. Even after appropriate antibiotic treatment, immunoglobulin G and immunoglobulin M response may persist for many years. Testing of synovial fluid is not recommended because there is no consensus on how to interpret the results. Serologic testing for Lyme disease includes an ELISA test followed by Western blot assay; interpretation of results is based on accepted criteria.³⁵ On a Western blot assay, an immunoglobulin M immunoblot is positive when two of the following three bands are present: 24 kDa (OspC), 39 kDa (BmpA), and 41 kDa (Fla). An immunoglobulin G immunoblot is positive when five of the following 10 bands are present: 18 kDa, 21 kDa (OspC), 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa, 66 kDa, and 93 kDa.^{34,36} The diagnosis of Lyme arthritis is multifaceted and involves a thorough understanding of the common clinical and epidemiologic features of the disease along with careful understanding of the serologic tests.

Diagnostic Dilemmas

The two most common presentations of Lyme arthritis in children are the classic form, which is characterized by episodic synovitis, and the acute pauciarticular (ie, pseudoseptic) form.³² The classic presentation may be confused with inflammatory arthritides, whereas the pauciarticular form may be confused with acute bacterial septic arthritis.

The orthopaedic surgeon may be asked to evaluate a child who presents to the emergency department with an acutely swollen, tender joint as well as other Lyme disease–related symptoms that also may be indicative of bacterial septic arthritis, such as malaise or irritability with or without fever and limited weight bearing. Arthrocentesis cannot always distinguish between Lyme arthritis and bacterial septic arthritis because joint fluid analyses

frequently reveal strikingly elevated joint leukocyte counts with both diseases.^{25,37} This confusing clinical scenario can lead to unnecessary surgical joint débridement—the treatment for bacterial septic arthritis.

This clinical scenario is increasingly recognized in the literature, and retrospective reviews have been done in an attempt to distinguish acute Lyme arthritis from bacterial septic arthritis. In a retrospective review of 29 children with Lyme arthritis, Bachman and Srivastava³⁷ reported that 15 children presented with arthritis as the initial indication of Lyme disease. History of tick bite was recalled by only three patients. The average synovial fluid leukocyte count was 94,023 cells/mm³, and the average synovial fluid differential was 84% neutrophils. Seven children were initially diagnosed with septic arthritis, and six underwent surgical débridement. Willis et al²⁵ reported on 10 consecutive children who presented to the emergency department with an acutely swollen joint suspicious for bacterial septic arthritis, all of whom were eventually diagnosed with Lyme disease. No patient in this series had a history of tick bite or erythema migrans. Seven patients underwent emergent surgical débridement. Planned surgical débridement was aborted in the last three patients in the series because of the availability of a rapid test for Lyme disease at the presenting institution. However, the two-tiered serologic testing approach previously described is the only serologic test endorsed by the CDC.

Thompson et al²⁴ compared the clinical indications and laboratory results of children who presented to the emergency department with serologically confirmed Lyme arthritis with those of children who presented with septic arthritis. The patients with Lyme arthritis were more likely to have knee involvement and history of tick exposure. However, they were less likely to have a temperature >100.4°F (38.0°C), and they had a lower average erythrocyte sedimentation rate, C-reactive protein (CRP) level, joint fluid leukocyte count, and joint neutrophil percentage. Based on multivariate analysis, the authors determined the most important predictors of Lyme arthritis to be a negative history of fever, knee involvement, and normal CRP levels.

We conducted a retrospective review of children who presented to our institution with joint effusion.³¹ Compared with patients with septic arthritis, those with Lyme arthritis had a lower average peripheral white blood count, lower percentage of neutrophils in the differential, were less likely to present with a temperature >101.5°F (38.6°C), and were less likely to refuse to bear weight on the affected extremity. No statistically significant difference existed between the two groups with regard to erythrocyte sedimentation rate and CRP level (Table 1).

Lyme and septic arthritis often have similar and overlapping presentations. Thus, clinical and laboratory variables should be used as tools in the diagnostic armamentarium. Further research is warranted to better differentiate Lyme arthritis from bacterial septic arthritis in the acute setting given that a reliable, accurate, and rapid test for Lyme disease is not widely available.

Management

In general, Lyme arthritis is successfully managed with oral antibiotics.³⁸ Adults without neurologic involvement may be treated with a 28-day course of doxycycline (100 mg twice daily), amoxicillin (500 mg three times daily), or cefuroxime axetil (500 mg twice daily). For children, amoxicillin (50 mg/kg per day divided into three doses [maximum 500 mg per dose]), cefuroxime axetil (30 mg/kg daily divided into two doses [maximum 500 mg per dose]), or, if the patient is ≥ 8 years old, doxycycline (4 mg/kg daily divided into two doses) is recommended.³⁸ Oral antibiotics are easier to administer, less expensive, and associated with fewer side effects than are parenteral antibiotics. Intravenous (IV) antibiotics

traditionally have been recommended in the presence of neurologic manifestations;³⁹ however, recent data may support the use of oral antibiotics even in cases of neurologic involvement.⁴⁰ Currently, parenteral ceftriaxone for 2 to 4 weeks is the recommended course for adults with arthritis and neurologic involvement.³⁸ However, cefotaxime and penicillin G are acceptable alternatives. Ceftriaxone or cefotaxime administered intravenously is recommended for children with arthritis and neurologic involvement, but penicillin G is an acceptable alternative (Table 2). A single course of antibiotics, whether administered orally or intravenously, is sufficient to resolve symptoms in most patients.^{41,42} Figure 7 demonstrates a recommended treatment algorithm for patients with Lyme arthritis.

Patients who do not respond to an initial course of antibiotic therapy and who display objective signs of synovitis (eg, persistent or recurrent joint swelling) should repeat a 4-week course of oral antibiotics or a 2- to 4-week course of parenteral antibiotics. Oral antibiotics are recommended for patients with demonstrated improvement but without resolution of symptoms.³⁸ A course of IV antibiotics is recommended for patients whose symptoms remain unchanged.³⁸ The clinician should consider waiting several months before initiating additional antibiotic treatment because of the slow resolution of inflammation following initial treatment. Oral nonsteroidal anti-inflammatory drugs are recommended to manage symptoms during initial antibiotic treatment and before retreatment with antibiotics.

Persistent arthritis is a challenging problem. Antibiotic-refractory Lyme arthritis is defined as synovitis that persists for ≥ 2 months after completion of a course of IV antibiotics or two 4-week courses of oral antibiotics in conjunction with negative polymerase chain reaction results for *B burgdorferi* in synovial fluid or tissue samples.^{39,43} An autoimmune etiology has been proposed for antibiotic-refractory Lyme arthritis in the absence of evidence of continued infection with Lyme spirochetes. Steere et al⁴⁴ reported that patients with antibiotic-refractory Lyme arthritis are more likely to have certain human histocompatibility leukocyte antigen (HLA)-DR2 and HLA-DR4 alleles. Additionally, it has been shown that patients with certain HLA-DRB molecules that bind an epitope of *B burgdorferi* OspA are more likely to develop antibiotic-refractory Lyme arthritis.⁴⁵ Patients with antibiotic-refractory Lyme arthritis also have persistently high levels of proinflammatory cytokines in their synovial fluid despite the absence of spirochetal DNA.⁴⁶ These findings suggest that patients with antibiotic-refractory Lyme arthritis have persistent synovitis that may be caused in part by an autoimmune mechanism.

Management of antibiotic-refractory Lyme arthritis may be supportive or surgical, with no proven role for prolonged antibiotic therapy.^{41,47} Patients with persistent synovitis despite the recommended antibiotic treatment may be treated with non-steroidal anti-inflammatory drugs and intra-articular corticosteroids. Hydroxychloroquine may be used, as well; it may have antispirochetal and anti-inflammatory effects.⁴⁸ There may be a role for certain disease-modifying antirheumatic agents in the management of chronic Lyme arthritis, but experience with their use in this setting is limited.⁴⁸ Arthroscopic synovectomy is a reasonable treatment option for patients with antibiotic-refractory Lyme arthritis. McLaughlin et al⁴⁹ were the first to describe this treatment in a small series of two patients who did not respond to antibiotics. A 30-year-old man with Lyme arthritis had recurrent knee effusions despite appropriate therapy. Several years after the initial onset of symptoms, he underwent an open synovectomy and was asymptomatic at 6-year follow-up. The second patient was a 12-year-old boy with persistent knee synovitis and recurrent effusions that did not respond to nonsurgical management. He underwent arthroscopic synovectomy approximately 2 years after symptom onset and was asymptomatic at 3.5-year follow-up. Schoen et al⁵⁰ evaluated 20 patients who underwent arthroscopic synovectomy for refractory Lyme arthritis. Joint inflammation resolved during the first month of surgery or

soon thereafter in 80% of patients, and improvement was maintained at long-term (ie, 3- to 8-year) follow-up.

Long-term Prognosis and Outcomes

Lyme arthritis has an excellent prognosis with appropriate management. Up to 95% of children remain asymptomatic after a single course of oral antibiotics.^{12,13,30} In children who are not treated with antibiotics, recurrent attacks of arthritis generally decrease over time; these children rarely develop chronic arthritis.^{30,51} Adults may have a slightly increased incidence of persistent joint swelling months to years after initial infection despite appropriate antibiotic therapy.⁵² A small minority of patients may also develop chronic Lyme disease (ie, post-Lyme disease syndrome). These patients experience disabling musculoskeletal pain, neurocognitive symptoms, and/or fatigue at or soon after the onset of Lyme disease.⁵² Symptoms are similar to those of chronic fatigue syndrome and fibromyalgia, and they may persist for months or years after initial infection and management. Typically, objective evidence of persistent infection is lacking (ie, synovial fluid or tissue culture positive for *B burgdorferi*, polymerase chain reaction indicating the presence of spirochetal DNA); data supporting the use of long-term antibiotic therapy for management of post-Lyme disease syndrome are lacking, as well.^{47,52} Supportive treatment of patients with post-Lyme disease syndrome is widely accepted, however.

Summary

Lyme disease is caused by transmission of the spirochete *B burgdorferi*. The vector of transmission is the *Ix-odes* tick, which is endemic in parts of the United States and Europe. Lyme arthritis is one clinical manifestation of late-stage Lyme disease. It is characterized by recurrent episodes of monoarticular to pauciarticular joint swelling, typically in large joints, especially the knee.

Diagnosis requires objective clinical criteria that include a history of time spent in an endemic area, history of the characteristic erythema migrans rash, and findings of joint inflammation. An acute episode of joint swelling and tenderness may be confused with bacterial septic arthritis, especially in the pediatric patient. Serologic testing is used to confirm the clinical suspicion of Lyme arthritis.

Antibiotic therapy is the mainstay of treatment, and excellent results are achieved in most patients. Arthroscopic synovectomy is reserved for persistent synovitis despite appropriate management with antibiotics.

Acknowledgments

This publication was made possible by grant K24 RR022477 and Clinical and Translational Science Award grants UL1 RR024139 and KL2 RR024138 from the National Center for Research Resources and the National Institutes of Health Roadmap for Medical Research.

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Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 40 and 48 are level I studies. References 7, 23, 29, 39, and 41–43 are level II studies. References 8, 15, 24, 32, and 46 are level III studies. References 1–3, 5, 12, 13, 16–19, 25, 38, 44, 45, 47, and 49–52 are level IV studies. Reference 14 is level V expert opinion.

Citation numbers printed in **bold type** indicate references published within the past 5 years.

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Figure 1.

Graphic representation of the number of Lyme disease cases reported annually in the United States, from 1992 to 2006. For that period, a total of 248,072 cases were reported in the United States and the District of Columbia. (Reproduced with permission from Bacon RK, Kugeler KJ, Mead PS; Centers for Disease Control and Prevention [CDC]: Surveillance for Lyme disease: United States, 1992–2006. *MMWR Surveill Summ* 2008;57[10]:1–9.)

Figure 2.

Map illustrating the average rate of Lyme disease in the United States per 100,000 population by county of residence from 1992 to 2006. County of residence was available for 98.1% of cases reported in 1992 through 2006. In 2003, Pennsylvania reported 4,722 confirmed cases and 1,008 suspected cases. (Reproduced with permission from Bacon RK, Kugeler KJ, Mead PS; Centers for Disease Control and Prevention [CDC]: Surveillance for Lyme disease: United States, 1992–2006. *MMWR Surveill Summ* 2008;57[10]:1–9.)

Figure 3.

Percentage of symptoms reported by patients with Lyme disease in the United States by month of illness onset from 1992 through 2006. (Reproduced with permission from Bacon RK, Kugeler KJ, Mead PS; Centers for Disease Control and Prevention [CDC]: Surveillance for Lyme disease: United States, 1992–2006. *MMWR Surveill Summ* 2008;57[10]:1–9.)

Figure 4. Life cycle of the *Ixodes* tick. Ticks in the nymphal form most commonly transmit *Borrelia burgdorferi* spirochete to humans in late spring and summer. (Reproduced with permission from Centers for Disease Control Division of Vector-Borne Infectious Diseases: *Lyme Disease Transmission*. Available at: http://www.cdc.gov/ncidod/dvbid/lyme/ld_transmission.htm. Accessed December 13, 2010.)

Figure 5. Photograph of an erythema migrans rash following a tick bite. (Reproduced with permission from Feder HM Jr: Lyme disease in children. *Infect Dis Clin North Am* 2008;22[2]:315–326, vii <http://www.sciencedirect.com/science/journal/08915520>.)

Figure 6.

Photograph of a patient with left-sided peripheral facial nerve palsy. She could not wrinkle the left side of her forehead, close her left eye, or lift the left corner of her mouth.

(Reproduced with permission from Feder HM Jr: Lyme disease in children. *Infect Dis Clin North Am* 2008;22[2]:315–326, vii <http://www.sciencedirect.com/science/journal/08915520>.)

Figure 7.

Recommended treatment algorithm for patients with Lyme arthritis. ELISA = enzyme-linked immunosorbent assay, IgG = immunoglobulin G, IV = intravenous, NSAIDs = nonsteroidal anti-inflammatory drugs, PCR = polymerase chain reaction. (Adapted with permission from Steere AC, Angelis SM: Therapy for Lyme arthritis: Strategies for the treatment of antibiotic refractory arthritis. *Arthritis Rheum* 2006;54[10]:3079–3086.)

Table 1Lyme Arthritis Versus Septic Arthritis in Children³¹

Category	Average Lyme Arthritis (range)	Average Septic Arthritis (range)	<i>P</i> value ^a
Age	8.2 yr (1–16)	8.1 yr (0–18)	0.892
Nucleated cells (cells/mm ³)	60,200 (266–303,000)	123,000 (3,000–745,000)	0.007
Peripheral WBC count (×1,000/μL)	10.3 (3.0–19.2)	14.5 (3.2–50.8)	0.001
Serum differential	61% (29%–82%)	65% (35%–89%)	0.180
ESR (mm/h)	41 (4–121)	44 (1–91)	0.440
CRP level (mg/L)	38.5 (0.20–135)	66.8 (0.97–265)	0.075

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, WBC = white blood cell

^a*P* values were obtained using independent samples *t*-test

Table 2

Recommended Antibiotic Treatment Regimens for Lyme Disease

Drug	Adult Dosage	Pediatric Dosage
Oral regimens		
Amoxicillin	500 mg three times per day	50 mg/kg daily in three divided doses (maximum, 500 mg per dose)
Doxycycline	100 mg twice per day	Not recommended for children <8 yr. For children ≥8 yr, 4 mg/kg per day in two divided doses (maximum, 100 mg per dose).
Cefuroxime axetil	500 mg twice per day	30 mg/kg per day in two divided doses (maximum, 500 mg per dose)
Parenteral regimen		
Ceftriaxone	2 g IV once per day	50–75 mg/kg IV per day in a single dose (maximum, 2 g)
Alternative parenteral regimens		
Cefotaxime	2 g IV every 8 h	150–200 mg/kg per day IV in three to four divided doses (maximum, 6 g/day)
Penicillin G	18–24 million U per day IV, divided every 4 h	200,000–400,000 U/kg per day divided every 4 h (not to exceed 18–24 million U/day)

IV = intravenous

Adapted with permission from Wormser GP, Dattwyler RJ, Shapiro ED, et al: The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: Clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* 2006;43(9):1089–1134.