

Fall Is the Season for Lyme Arthritis

Diagnosing the Complex Condition

by Evren Akin, M.D.

Arthritis is a major manifestation of Lyme disease, the most common tick-borne illness in the United States. Lyme arthritis occurs as a result of untreated Lyme infection, which develops when the spirochete called *Borrelia burgdorferi*, the bacteria carried by deer ticks, is transmitted to humans and travels through the bloodstream into various areas of the body, including the joints.

Because early symptoms of Lyme disease aren't always recognized, the disease can go untreated — increasing the chances of developing Lyme arthritis. Sixty percent of untreated children infected with *Borrelia burgdorferi* develop Lyme arthritis.

Lyme arthritis usually presents symptoms during the fall season, several weeks — or even months — after the initial tick bite.

Knowing Early Symptoms Could Prevent Arthritis

The early symptoms of Lyme disease (stage 1 and stage 2) can be mild and easily overlooked. People who are aware of the risk of Lyme disease in their communities, and who don't ignore the sometimes-subtle early symptoms, are most likely to seek medical attention early enough to be assured of a full recovery. Lyme disease is often overlooked — especially in children — because some of the symptoms mimic those of influenza.

Common symptoms seen in early stages of Lyme disease are:

- Solid red or bull's-eye rash, called *erythema migrans*, usually at the bite site (present in 80 to 90 percent of all Lyme disease cases)
- Swelling of lymph glands near the bite
- Generalized achiness and headache
- Fever without upper respiratory symptoms (flu-like illness)

Because these symptoms often occur within days of the initial tick bite, testing for Lyme disease may not immediately confirm the infection. Furthermore, ticks that transmit the disease often attach to the scalp, armpits, buttocks and other inconspicuous areas, so the rash can be easily overlooked. A thorough evaluation of a patient's symptoms, and questioning the patient's whereabouts during the weeks and months prior to developing symptoms, can lead to prompt treatment and prevent the development of Lyme arthritis.

Case Study I:

A 7-year-old presents with a fever and an acutely swollen knee. She's admitted to the hospital for drainage and lavage of the knee. Complete blood count shows mild leukocytosis. Erythrocyte sedimentation rate is 28. Synovial white cell count is 30,000 milliliters. While awaiting culture results, Lyme titer comes back strongly positive at 5.4 with a positive Western blot for immunoglobulin M (IgM) (3/3 bands) and immunoglobulin G (IgG) (7/10 bands). Knee swelling resolves after four weeks of amoxicillin. The family brings a picture to the follow-up appointment, which shows the girl at a farm visit earlier that summer. Faint, circular lesions are visible on her arm.

This case demonstrates the acute presentation of Lyme arthritis. Often a preceding rash may not be remembered. Constitutional symptoms and laboratory tests may suggest septic arthritis. Lyme titer by enzyme-linked immunosorbant assay (ELISA) and Western blot will almost always be strongly positive when arthritis is the presenting sign of Lyme disease.

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Case Study 2:

An 18-month-old is noted to be clumsier than usual over the past few weeks. His pediatrician notes a swollen ankle on exam. Complete blood count and erythrocyte sedimentation rates are normal. Antinuclear antibodies are positive at 1:320 and a Lyme titer is mildly elevated at 1:1. Western blot is positive with two out of three IgM bands, but no IgG bands. Swelling and clumsiness persist despite two months of amoxicillin. The toddler develops iritis during the ensuing six months and continues treatment for juvenile rheumatoid arthritis.

This case demonstrates the difficulty in differentiating pauciarticular onset juvenile arthritis from Lyme arthritis. A false positive IgM Western blot is common in children under age 4. Without a positive IgG Western blot and a history of tick exposure, arthritis is unlikely to be the sole manifestation of Lyme disease. Continued joint swelling after appropriate antibiotic treatment should prompt rheumatology and ophthalmology follow-up.

Figure A Western blots of acute-phase sera from 25 patients with *erythema migrans*.

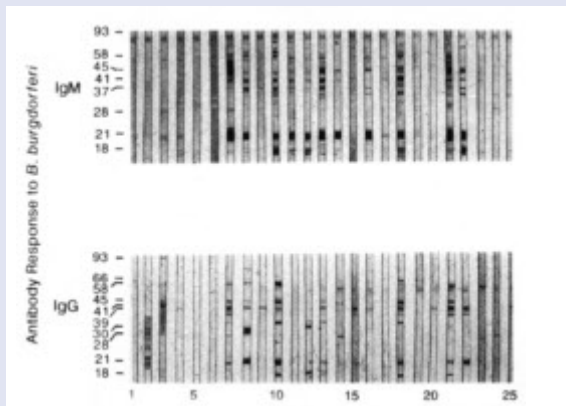
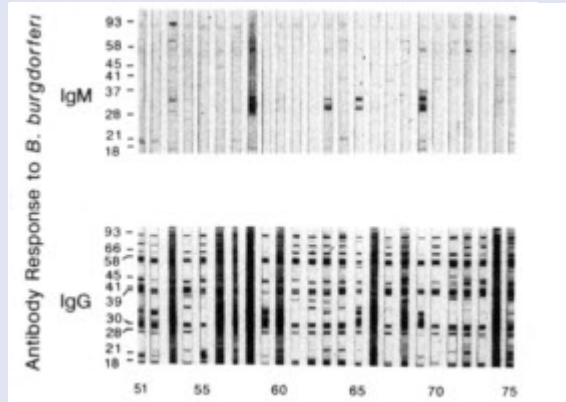


Figure B Western blots of acute-phase sera from 25 patients with Lyme arthritis.



Dressler, F., Whalen, J.A., Reinhardt, B.N., Steere, A.C. Western Blotting in Serodiagnosis of Lyme Disease, *Journal of Infectious Diseases* 167(2): 392-400, 1993

Joints Affected¹

	Number of Patients					
	First Attack			Recurrent Attacks		
	Children (39)	Adults (12)	Total (51)	Children (25)	Adults (10)	Total (35)
Knee	35	8	43 (84)*	22	8	30 (86)*
Ankle	3	2	5 (10)	5	3	8 (23)
Wrist	3	2	5 (10)	7	1	8 (23)
Temporomandibular	2	3	5 (10)	2	3	5 (14)
Shoulder	2	2	4 (8)	4	3	7 (20)
Hip	3	1	4 (8)	4	0	4 (11)
Elbow	2	1	3 (6)	10	6	16 (46)

*Percentage of patients with either or both joints affected.

¹Steere, A.C., Malawista, S.E., Syndman, D.R., et al: Lyme Arthritis: An Epidemic of Oligoarticular Arthritis in Children and Adults in Three Connecticut Communities. *Arthritis and Rheumatism* 1977; 20:7

Diagnosing Lyme Arthritis in Children

Symptoms of Lyme arthritis present months — and, in some cases, years — later. Most commonly, the arthritis intermittently attacks one or a few large joints at a time, especially the knee. Nevertheless, numerous joints can be involved, including the temporomandibular joint as originally described by Steer, et.al.¹

Children, especially younger children, may have moderate fevers and increased erythrocyte sedimentation rates. Their first attack of arthritis may last several days to weeks. Although this can mimic septic arthritis, the joint of a child with Lyme arthritis rarely is as painful as that of a child with acute arthritis. Analysis of joint fluid is rarely helpful, because the leukocyte count in synovial fluid can range from fewer than 10,000 to greater than 100,000 cells per milliliter.

Physicians often evaluate joint swelling in active individuals, and suspicion naturally falls first on a patient's activities as a likely cause. Lyme disease is rarely the initial diagnosis, particularly in a patient who recalls none of the disease's usual symptoms. A careful patient history, however, may show that the patient exercised, hiked or camped in a region where Lyme disease is endemic. In such a case, Lyme arthritis may be the initial presentation, and the physician should proceed with appropriate tests to determine proper diagnosis and treatment.

Testing for Lyme Arthritis

Children — especially those with histories of tick bites — who complain of joint pain, a mysterious summer illness, or a rash should undergo specific tests to confirm Lyme disease. Several laboratory tests help diagnose Lyme disease. The most common is the ELISA titer test, which measures the amount of antibody to the spirochete. Physicians should be aware that ELISA testing is subject to false-positive results because the spirochete shares certain antigens with other infectious agents. In younger children, false-positive ELISA results — particularly of the IgM type — are common.

Children who have equivocal or positive ELISA results should be tested by Western blot. The Western blot test identifies proteins of the spirochete to which the antibody response is directed. When patients have IgG reactivity with five or more of 10 particular spirochete proteins, it is highly likely that they have been exposed to the spirochete that carries Lyme disease. However, this test doesn't distinguish between past exposure and present illness. Therefore, results need to be evaluated in the context of clinical symptoms.

During the early stages of Lyme disease, patients often have positive IgM Western blots. Once arthritis develops, the immune response expands to include IgG antibodies, as described by Dressler, et.al. (see figures A and B). Therefore, a negative IgG Western blot in a patient with arthritis essentially rules out Lyme disease. A positive IgM titer in such a patient is likely a false positive. On the other hand, a positive IgM ELISA titer and a positive IgM Western blot can persist along with a positive IgG for months or years in patients with Lyme disease. It's important to inform patients that they will have positive test results for years (although the titers may drop) — even after they've been treated.

Treatment-Resistant Lyme Arthritis

In cases where arthritis is resistant to treatment, Polymerase Chain Reaction (PCR) testing in the joint may help differentiate non-specific inflammation from ongoing infection.

During antibiotic treatment, children may experience joint discomfort for up to eight weeks. Ibuprofen (30 mg/kg/day) or Naproxen (10-20 mg/kg/day) can be recommended for the first several weeks as adjunct therapy. Despite appropriate treatment, 10 percent of patients may have continued joint swelling more than six months after therapy. That has been termed treatment-resistant Lyme arthritis. Such patients deserve evaluation by a rheumatologist to define a further course of action.

Recommended Treatment for Lyme Disease²

Clinical Manifestation		Drug	Patient Age	Dose*
Early disease	Erythema chronicum migrans	Doxycycline**	≥ 9 yrs old	100 mg bid, po
	Isolated Bell's palsy	Tetracycline		250 mg qid, po
	Arthritis	Amoxicillin**	< 9 yrs old	25-50 mg/kg/d divided tid, po
	Mild carditis (PR < 0.3 sec)	Penicillin		25-50 mg/kg/d divided tid, po
Late disease	Persistent arthritis	Ceftriaxone**		75-100 mg/kg/d, IV
	Severe carditis	Penicillin G		300,000 u/kg/d, IV

* Duration of therapy is 10-30 days for oral regimens and 14-21 days for parenteral therapy, depending on the extent of the disease and the patient's response to therapy.

** Preferred agent

²Christy, C., Siegel, D.M.: *Lyme Disease — What It Is, What It Isn't*. Contemporary Pediatrics, 1995, Vol. 12, No. 7; 12:64-86

Author's Profile

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Evren Akin, M.D., is a pediatric rheumatologist at Gillette Children's Specialty Healthcare in St. Paul, Minn. She sees patients with juvenile arthritis and related conditions. She's also an adjunct faculty member at the University of Minnesota School of Medicine and an active member of the University's department of pediatric rheumatology.

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Most recently, Akin was assistant professor of pediatrics at Tufts University's School of Medicine in Boston, Mass. She has served as a staff pediatrician with the division of pediatric rheumatology and as a research associate in the division of rheumatology at New England Medical Center. Her particular research interest is treatment-resistant Lyme arthritis.

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Friday, December 13, 2002

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