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## Lyme Arthritis: A Primer for Primary Care

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# Lyme Arthritis: A Primer for Primary Care

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## Abstract

Lyme disease is caused by a bacteria belonging to the Borreliaceae family. Wooded forests and terrains are affected, including those in the Northeastern United States. Teenage ticks are most commonly discovered on humans as those ticks need to satisfy their nutritional requirements for growth. They bite warm, moist areas of the body and take 24 to 48 hours to transmit the *Borrelia Burgdorferi* infection. Lyme disease manifests as a multisystem disorder in humans, and is known for its dermatological, neurological and rheumatological findings. For the primary care provider, Lyme disease should be on the differential in multisystem diseases. Our case is a 63 year old gentleman who presented with unilateral knee pain for the last 3 months. He initially visited the outpatient orthopedic outpatient office for this arthritic pain. Before moving forward with knee replacement he was eventually tested for Lyme Serology IgG and IgM tests. His positive results warranted Lyme Western Blot testing which confirmed the suspicion of lyme arthritis secondary to *Borrelia Burgdorferi*. He was treated with a 14 day course of doxycycline, which resulted in significant improvement of knee pain and return to baseline functionality without surgical intervention. The purpose of this report is to stress the importance of beginning doxycycline as soon as possible to avoid progression into other organ systems such as worsening rheumatologic arthritis, central nervous system neuropathies, peripheral nervous system palsies, or cardiac atrioventricular blocks. The optimal treatment is obtained with thorough history taking and physical examination.

## Keywords

Lyme, Neurology, Cardiology, Heart Block, Erythema Migrans

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## Conflict of Interest Statement

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## **Lyme Arthritis: A Primer for Primary Care**

### **Introduction**

Lyme disease is caused by a bacteria belonging to the *Borreliaceae* family. In North America, *B. burgdorferi* is the most common species known to cause infection. Wooded forests and terrains are affected, including those in the Northeastern United States.<sup>1</sup> The *Ixodes scapularis* tick transmits the spirochete through vectors such as rodents, cats and deer. Teenage ticks are most commonly discovered on humans as those ticks need to satisfy their nutritional requirements for growth. They bite warm, moist areas of the body and take 24 to 48 hours to transmit the *Borrelia burgdorferi* infection.<sup>2</sup> Lyme disease manifests as a multisystem disorder in humans, and is known for its dermatologic, neurological and rheumatological findings. The goal of this brief review is to provide a framework for primary care physicians to guide the evaluation for Lyme disease.

### **Typical Case Presentation in the Ambulatory Setting**

A 63-year old male with a past medical history notable for coronary artery disease, diabetes mellitus type 2, and obstructive sleep apnea requiring CPAP, presented with unilateral knee pain for the last 3 months. The worsening pain was associated with knee swelling, warmth and redness. The left knee arthritis affects his gait mobility and decreases his daily activities. He initially visited the outpatient orthopedic outpatient office for this arthritic pain. He was asked to visit the primary care office before x-ray or surgery consultation for knee replacement. At the primary care office, he discussed living in the countryside with two dogs, one of which was recently diagnosed with Lyme disease.

Before moving forward with knee replacement, the differential of unilateral knee swelling was evaluated, including: normal complete blood count and basic metabolic profile; negative ANA; a non-diagnostic x-ray; and an arthrocentesis, which revealed trace leukocytes, no crystals, and no purulent fluid. Gout, septic arthritis (including gonorrheal infection), osteoarthritis, and rheumatoid arthritis were ruled out. Positive tests on Lyme serology, both IgG and IgM, warranted Lyme Western Blot testing, which confirmed the suspicion of Lyme arthritis secondary to *B. burgdorferi*. He was treated with a 14-day course of doxycycline, which resulted in significant improvement of knee pain and return to baseline functionality without surgical intervention.

### **Discussion**

Lyme disease may be missed on the differential diagnosis when multiple systems are involved over time and discovering it requires a thorough history and physical. (Table) In the above case, the history of living in the countryside and outdoor activities were enough information for the caretaking physician to perform Lyme serology testing. Diagnosis can be difficult without obvious external signs, such as the classic erythema migrans rash, which was not seen in this case. Targeted history taking is paramount to avoid unnecessary procedures.

Stage	Onset Time	Manifestation
Dermatologic	Within 3 months of infection	<ul style="list-style-type: none"> <li>• Erythema Migrans</li> <li>• Borrelial lymphocytoma (rare)</li> <li>• Acrodermatitis chronica</li> </ul>
Musculoskeletal	Often after 6 months of infection	<ul style="list-style-type: none"> <li>• Muscle pain, joint pain (knee most commonly affected)</li> <li>• Chronic arthritis (patients positive for HLA-DR4/DR2 more at risk)</li> </ul>
Cardiovascular	Several weeks to months after infection	<ul style="list-style-type: none"> <li>• Conduction abnormalities, especially atrioventricular blocks</li> <li>• Exudative pericarditis</li> </ul>
Central Nervous System	Months-Years after infection	<ul style="list-style-type: none"> <li>• Bannwarth Syndrome (lymphocytic meningitis with radicular pain)</li> <li>• Radicular Pain (usually worse at night)</li> <li>• Cranial Nerve Palsy (most commonly facial nerve)</li> <li>• Visual disturbances</li> <li>• Encephalopathy</li> </ul>

<sup>a</sup>Adapted from Biesiada, et al.<sup>1</sup>

Lyme disease affects the integumentary system with the erythema migrans (EM) ‘bullseye’ rash. There is an initial uniform circular pattern of erythema from accumulation of *B. burgdorferi*. The body’s immune and inflammatory systems begin to clear away the organisms and create the central clearing seen in Lyme disease; however, the classical EM rash is not always present at the time of evaluation.<sup>2</sup> Aucott *et al.* in their retrospective analysis of a panel of patients in a community based practice found that 13% of patients diagnosed with Lyme disease did not present with a rash, and amongst those patients who did have a rash, the diagnosis of EM was initially missed in 23% of patients.<sup>3</sup>

There are at least 11 genostrains of *B. burgdorferi* currently known.<sup>4</sup> Most immunoblot testing is based on the B31 lab strain. Genetic variability among strains, including variance of outer surface proteins (Osp), in part accounts for a lack of detection on serological testing.<sup>5</sup> The CDC criteria excludes OspA and OspB, in spite of rising numbers of these variants.<sup>5</sup> This is further compounded by the introduction of genetic variants by vectors such as migratory birds.

Lyme disease commonly affects the musculoskeletal system with an arthritis of knee joints. Classically, there is involvement of one knee joint rather than bilateral swelling. In the 1970’s, lyme arthritis was first seen in an outbreak of monoarticular arthritis in children in Lyme, Connecticut.<sup>6</sup> It is a late disease manifestation, months after the initial infection, and the arthritic symptoms can last anywhere between days and many years.

Long-standing arthritis is associated with immune resistance by the organism and failure to decrease inflammation of that immune response even after Lyme disease disappears. Arthritis pathophysiology is explained by inflammation secondary to the immune system producing antibodies to phagocytize the spirochetes.<sup>6</sup> It is associated specifically with HLA-DR alleles that bind an epitope of *B. burgdorferi* outer-surface protein A (OspA) which initiates a strong T helper cell 1 response. The T cell reaction is secondary to a TLR1 polymorphism (1805GG) that is found in half of the European Caucasian population which leads to the exaggerated release of cytokines and chemokines in affected joints. In the synovial fluid of knee joints, there are lower frequencies of the FoxP3+ T cells resulting in increased duration for Lyme eradication.<sup>7</sup> Not only

are there fewer T cells, but cartilage is known to have decreased vascular supply. Therefore, immune responses take longer for synovial fluid targeting.

Lyme disease affects both the central and peripheral nervous systems. Jozefowicz-Korczynska, *et al.*, in their review of 13 cases of Lyme disease, found that central nervous system involvement, termed neuroborreliosis, may present with symptoms such as meningitis, vertigo, dizziness, tinnitus, and hearing loss.<sup>7</sup> Peripheral nerve involvement includes facial nerve Bell's palsy. A Lyme disease presentation as lymphocytic meningoradiculitis, known as Bannwarth syndrome, is almost exclusively seen in Europe.<sup>8</sup> This is most often implicated with the subtype, *B. garinii*. Bannwarth syndrome is characterized by the triad of painful radiculopathy, cranial neuropathy, and lymphocytic pleocytosis.<sup>8</sup> Diagnosis is made by cerebrospinal fluid analysis for IgG/IgM antibodies to *B. burgdorferi*. Although there is central nervous system involvement, patients commonly do not experience meningeal signs of neck stiffness, headache or vomiting. Therefore, appropriate history can lead to cerebrospinal fluid analysis to confirm Bannwarth syndrome.

Testing for Lyme disease consists of Lyme IgG and IgM Serological testing. A positive *B. burgdorferi* IgG test reports 5 or more bands of 18, 23, 28, 30, 39, 41, 45, 58, 66 or 93 kDa and a positive *B. Burgdorferi* IgM test reports 2 or more bands of 23, 39 or 41 kDa.<sup>9</sup> Positive serological testing is confirmed with Western Blot Lyme testing. Lyme IgG and IgM serological testing can be negative in up to 60% of patients with 1 week of infection, so history and physical exam direct toward correct diagnosis.<sup>10</sup> Serology for Lyme arthritis is often positive before treatment and negative after the treatment.

Treatment for Lyme disease consists of a 14 day course of doxycycline or amoxicillin. During the course of disease, a negative IgG or IgM Lyme Serology test does not stop management course due to the relatively low 60% test sensitivity.<sup>11</sup> Even with a negative test, continue doxycycline treatment for a total 14 day course and confirm with Lyme Western Blot test returns. In addition, tetracycline is teratogenic in pregnant women and should be avoided in this population.

If Lyme disease remains untreated, within 2 weeks of infection, it can progress to serious complications including heart block, neurologic symptoms and severe arthritis. For these late disease Lyme cases, starting ceftriaxone for a 14 day course can prevent further progression.<sup>12</sup> Ceftriaxone is not meant to treat current symptoms, but rather to stop 2nd degree heart blocks from converting into complete dissociation of atria and ventricles.<sup>12</sup>

Post-treatment complications are part of a symptom complex known as post-infective syndrome, also dubbed Post Treatment Lyme Disease Syndrome.<sup>12</sup> Patients may suffer from symptoms such as joint pain, insomnia, and impaired cognition even after treatment with antibiotics. These pose important implications for patients with joint pain as many individuals may go on to develop disturbances in gait, strength, and overall functionality if infections are not treated in a time- sensitive manner.<sup>12</sup>

## Conclusion

For the primary care provider, Lyme disease should be on the differential in multisystem diseases. The presentation of arthritis without EM or specific attachment of a tick warrants targeted questioning about outdoor activities and hobbies. Physical exam is useful for identifying the classical EM rash, the arthritic swelling, and nerve palsies. Begin doxycycline as soon as possible to avoid progression into other organ systems such as worsening underlying arthritis,

central nervous system neuropathies, peripheral nervous system palsies, or cardiac atrioventricular blocks. Do not change management based on serology IgG or IgM Lyme tests, but rather based on clinical suspicion, and be aware of the manifestation of Lyme disease in each system.

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