

# Overview of the clinical manifestations of *Borrelia burgdorferi* infection

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**RJ DATTWYLER, BJ LUFT. Overview of the clinical manifestations of *Borrelia burgdorferi* infection. Can J Infect Dis 1991;2(2):61-63.** Lyme disease, caused by the spirochete *Borrelia burgdorferi*, has classically been divided into three stages: erythema migrans; neurological or cardiac involvement; and arthritis. Rather than defining a set disease pattern, however, one should, more logically, conceptualize a progressive infection that may be localized or disseminated, acute or chronic. Erythema migrans, the earliest and most easily recognized manifestation of *B burgdorferi* infection, is an expanding annular erythematous skin lesion with a central clearing that develops soon after the bite of an infected ixodes tick. Musculoskeletal manifestations are common, with approximately one-half of untreated individuals developing arthritis. Of these, only 10% have chronic arthritis. Invasion of the central nervous system occurs as the infection disseminates hematogenously, with encephalitis, myelitis and meningopolyneuritis being the most severe results. Acute cardiac involvement is recognized in up to 8% of adult patients, and less often in children. Early antibiotic treatment of the infection is highly effective.

**Key Words:** Clinical manifestations, Disease stages, Lyme disease, Progressive infectious disease

## Aperçu des manifestations cliniques de l'infection à *Borrelia burgdorferi*

**RESUME:** La maladie de Lyme est provoquée par le spirochète *Borrelia burgdorferi* et se déclare en trois étapes: un érythème chronique migrateur, suivi par des manifestations neurologiques ou cardiaques, puis articulaires. Mais plutôt que de définir une évolution pathologique établie, il est plus logique de conceptualiser une infection progressive qui peut être localisée ou disséminée, aiguë ou chronique. L'érythème chronique migrateur, la manifestation précoce et la plus aisément reconnue de l'infection à *B burgdorferi*, est une lésion cutanée érythémateuse annulaire qui s'étend avec un blanchissement central et qui se développe peu après la piqûre du tique *Ixodes*. Les manifestations articulaires sont courantes et une arthrite se déclare chez environ la moitié des personnes non traitées. Parmi celles-ci, 10 % seulement souffrent d'arthrite chronique. L'atteinte du système nerveux central survient tandis que l'infection se dissémine par voie hémotogène; l'encéphalite, la myélite, la méningoencéphalite et les multinévrites en sont les résultats les plus sévères. Des atteintes cardiaques aiguës sont reconnues chez 8 % des patients adultes et moins fréquemment chez l'enfant. L'antibiothérapie administrée au stade précoce de l'infection semble efficace.

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CLASSICALLY, LYME DISEASE HAS BEEN DIVIDED INTO three distinct stages: erythema migrans; neurological or cardiac involvement; and arthritis. Viewing the disease in this way insinuates that organ system involvement proceeds in a fairly orderly fashion. This is not the case. Rather than conceptualizing Lyme disease as a disease in which organ systems become involved in a set pattern, one should conceptualize *Borrelia burgdorferi* infection as a progressive infectious disease. Infection begins locally, with dissemination to multiple organs and tissues occurring early in the course of infection in a high percentage of patients. It seems more logical, therefore, to consider whether the infection in each of its manifestations, is localized or disseminated, acute or chronic.

### OVERVIEW

Erythema migrans is the earliest and most easily recognized manifestation of *B burgdorferi* infection (1). This characteristic skin lesion is observed in approximately two-thirds of patients, and usually develops a few days to a few weeks following the bite of an infected ixodes tick. Initially the spirochete is localized to the skin lesion, and most individuals are asymptomatic. As the infection progresses, one or more systemic signs or symptoms – fever, malaise, headache, stiff neck, fatigue – develop, often heralding the systemic spread of this pathogen. The clearest evidence of this early dissemination is the appearance of multiple areas of erythema migrans, with most series reporting an 8 to 15% incidence of multiple lesions. The infectious load increases rapidly in this early phase. With acute hematogenous dissemination, major organ systems including the heart, brain, liver and synovium may become involved. Acute meningitis, meningoencephalitis, neuropathies, myocarditis with or without common block abnormalities, hepatitis, myositis and, less commonly, frank arthritis, are the most dramatic manifestations of the acute disseminated phase of infection.

As the immune response gains control of the infection, the number of spirochetes appears to drop and the disease enters a more chronic phase. Although multiple organ systems can be involved concomitantly, localized inflammatory processes tend to predominate. Constitutional signs and symptoms are generally few. The skin, nervous system and musculoskeletal system are the major systems involved during the chronic phase.

### DERMATOLOGICAL MANIFESTATIONS

Erythema migrans is classically described as an expanding annular erythematous skin lesion with central clearing (1). However, variations are relatively common and include uniformly erythema-

tous and target-like lesions. Erythema migrans can be associated with mild local pruritus, dysesthesia or mild local discomfort (2). Accompanying signs and symptoms can be noted in about 40% of patients at presentation (1-3). Signs and symptoms can be quite diverse, ranging from mild and transitory symptoms to profound fatigue, lethargy, mild encephalopathy, meningeal irritation, migratory musculoskeletal pain, hepatitis, generalized lymphadenopathy or splenomegaly, pharyngitis, pleurisy and myocarditis. Patients with notable signs and symptoms probably have dissemination of the pathogen from the local site. Erythema migrans clears spontaneously within one to four weeks in the overwhelming majority of untreated patients, and recurrence is rare.

### MUSCULOSKELETAL MANIFESTATIONS

Musculoskeletal manifestations are common (4). In acute disseminated infection, pain in joints, tendons, bursas, muscle or bones is noted by the majority of patients. True arthritis, usually involving large joints such as the knee, is rarely noted. Characteristically only one or two sites at a time are affected, and symptoms last from a few hours to several days.

In North America, approximately one-half of untreated individuals develop arthritis as the infection progresses. This arthritis, characteristically episodic in nature, primarily involves the large joints. The knee is the most commonly involved joint. Most series report a 90% or greater incidence of knee involvement. The arthritis usually follows a benign course, with only 10% of patients developing chronic arthritis. Even in such patients there tend to be spontaneous remissions. Small joint involvement is uncommon.

### NERVOUS SYSTEM MANIFESTATIONS

Invasion of the central nervous system occurs as *B burgdorferi* disseminates hematogenously (4). As reported by Steere et al (3), signs and symptoms referable to the nervous system are common in patients with erythema migrans. In that study, 80% of all patients with erythema migrans experienced malaise, fatigue and lethargy; 64% experienced headaches; and 48% experienced neck stiffness (3).

Meningitis, cranial neuritis (most commonly seventh nerve) or painful radiculitis occurs in approximately 15% of patients within the first three months of infection. Patients with a cranial neuropathy can have significant cerebrospinal fluid abnormalities in the absence of obvious signs of meningitis; therefore, a lumbar puncture and examination of cerebrospinal fluid are required for appropriate evaluation of these patients or any

patient suspected of having central nervous system involvement.

Chronic nervous system disease is more difficult to assess. Although there has recently been a great deal of speculation as to the full range of neurological manifestations of the chronic phase of this infectious disease, it should be remembered that *B burgdorferi* causes unifocal or multifocal areas of inflammation in the brain and spinal cord, and that in the absence of objectively measurable abnormalities, the diagnosis should only be made with a great deal of caution, if at all.

Encephalitis, myelitis and meningopolyneuritis represent the most severe examples of nervous system involvement observed in disseminated *B burgdorferi* infection (5). More commonly, with sensitive neurophysiological techniques, 40% or more of patients with late disease are shown to have demonstrable abnormalities. The peripheral nervous system also has a wide spectrum of abnormalities, ranging from the severe, painful and debilitating meningopolyneuritis (Garin, Bujadoux, Bannwarth syndrome) to a milder but much more common neuropathy in patients with chronic infection. Peripheral neuropathies may be distributed symmetrically or asymmetrically, and paresis of involved extremities can be associated with neuritis. Nerve conduction studies demonstrate that the abnormalities are secondary to axonal involvement and not demyelination. Fatigue is noted by many patients with Lyme disease. However, fatigue in the absence of objectively measurable abnormalities is unlikely to be related to *B burgdorferi* infection, regardless of the serological status of the patient.

## CARDIAC MANIFESTATIONS

Acute cardiac involvement, manifested by varying degrees of atrioventricular block, is recognized in up to 8% of adult patients, and less often in children (4). Myocarditis or pericarditis is ob-

served in approximately 65% of patients with cardiac involvement. Although left ventricular dysfunction can be documented in almost 50% of these patients, it is usually not clinically significant. Late cardiac manifestations remain to be fully defined; there may be chronic carditis and cardiomyopathy.

## TREATMENT

Few prospective randomized trials have been published. Still fewer have studied antibiotic regimens selected on the basis of the in vitro sensitivity of the organism. In a recent trial in patients with erythema migrans, both amoxicillin plus probenecid and doxycycline were demonstrated to be highly effective (6). In contrast to earlier studies (7), none of the patients developed an objectively measurable abnormality post treatment, and none required retreatment. Other agents including oral cephalosporins and the new macrolide, azithromycin, are currently under study; however, the role these agents should play in the treatment of *B burgdorferi* infection remains to be defined.

Ceftriaxone and penicillin have established roles in the treatment of disseminated infection (8,9). Ceftriaxone has been shown to be more effective than penicillin (8,9). Other third generation cephalosporins may also be efficacious, but they remain less well studied. Oral regimens have not been shown to provide adequate levels of antibiotic within the central nervous system and cannot be recommended when the nervous system is involved.

No published data demonstrate that prolonged antibiotic therapy has any increased efficacy over conventional treatment regimens. Some patients with chronic disease (10 to 15%) appear to be refractory to antibiotic therapy and may have a post infectious immune-mediated disorder, the treatment of which has yet to be established.

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