

## Lyme Carditis

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Lyme borreliosis, or Lyme disease, is a globally occurring, systemic disease caused by the spirochete *Borrelia burgdorferi* and transmitted by the *Ixodes* tick. The disease classically is divided into three stages. Stage 1, the early localized stage, generally occurs several days or up to 1 month after the initial tick bite. It is notable for an influenza-like illness and often is accompanied by the erythema migrans (EM) rash. Stage 2, the early disseminated stage, occurs weeks to months after EM. Neurologic symptoms and musculoskeletal complaints are the hallmarks of this stage. Cardiac abnormalities, predominantly involving the conduction system and myocardium, also may manifest at this time. Stage 3 occurs several months to years after EM and is characterized by a monoarthritis or oligoarthritis affecting the large joints, and the development and progression of neurologic sequelae. Steere and colleagues first described the cardiovascular complications of Lyme disease nearly 30 years ago in a retrospective report of 20 North American cases. Australian and European cases were reported in the early to mid-1980s. The principal manifestation of Lyme carditis is self-limited conduction derangement, most commonly involving the atrioventricular node. Additionally, pericarditis, endocarditis, myocarditis, pericardial effusion, myocardial infarction, coronary artery aneurysm, QT-interval prolongation, tachyarrhythmias, and congestive heart failure have been reported. Although the number of reported cases and knowledge of the disease have increased since Steere's initial case series, most reports of Lyme carditis are case reports with few large retrospective or prospective studies.

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## Epidemiology

Lyme disease, caused by the spirochete *B burgdorferi*, is transmitted by the *Ixodes* tick [1–6]. It is the most commonly reported vector-borne disease in the United States. Between 2003 and 2005, 64,382 cases were reported to the Centers for Disease Control and Prevention (CDC) [7]. The number of reported cases has remained relatively stable since 2002 (23,763 cases reported in 2002, 21,273 in 2003, 19,804 in 2004, and 23,305 in 2005) [7,8]. The overall incidence of Lyme disease in the United States in 2005 was 7.86 cases per 100,000, but, while 46 states and the District of Columbia have reported cases, there is substantial regional variation, and most cases are reported in the northeast and northern midwestern United States. In 2005, the highest rates of infection were reported in:

- Delaware (76.6 cases per 100,000 population)
- Connecticut (51.6 cases per 100,000 population)
- New Jersey (38.6 cases per 100,000 population)
- Massachusetts (36.5 cases per 100,000 population)
- Pennsylvania (34.5 cases per 100,000 population)
- New York (28.9 cases per 100,000 population)
- Wisconsin (26.3 cases per 100,000 population)
- Maryland (22.1 cases per 100,000 population)
- New Hampshire (20.2 cases per 100,000 population)
- Minnesota (17.9 cases per 100,000 population)

Lyme borreliosis is also common in forested areas in Europe, with the highest reported incidence in middle Europe and Scandinavia, particularly in Germany, Austria, Slovenia, and Sweden [6,9]. The infection also is found in Russia, China, and Japan.

The median age of infected patients in the United States was 41 years, but there was a bimodal distribution, with peaks at 5 to 9 years and 44 to 59 years. There was a slight male predominance (54% of all cases and 61% of cases among children 5 to 14 years old).

Among the 49,157 cases for which date of illness onset was available from 2003 to 2005, the summer months predominate, with a peak in July (29% of cases). This correlates with a delay from infection to presentation, as the nymph form of *Ixodes* ticks generally arises in May and June.

The most common reported symptoms from 2003 to 2005 were a history of EM (70%), arthritis (30%), facial palsy (8%), radiculopathy (3%), meningitis or encephalitis (2%), and heart block (less than 1%). This array of presenting symptoms is similar to those observed in a report from 2001 to 2002 [8]. The incidence of late manifestations of Lyme disease, such as arthritis, neurologic complications, or cardiovascular manifestations, is likely to decrease, because patients more frequently are treated with antibiotics.

The first reported cases of Lyme carditis came in 1980, when Steere and colleagues [2] described 20 North American cases. These were followed

closely by reports of Lyme carditis in Australia and Europe [3–5]. Most reports of Lyme carditis are case reports, with few large retrospective or prospective studies.

It is estimated that between 4% and 10% of patients in the United States who have untreated Lyme disease develop carditis [2,10,11], but some have estimated the prevalence of asymptomatic carditis to be as high as 30% [12]. The incidence is lower in Europe, where it is thought to be 0.3% to 4.0% [13]. The reason for this difference is unclear but may be related to a difference in virulence of the North American and European *B burgdorferi* isolates [14,15].

Some authors have suggested that the North American incidence is overestimated, and one series of 187 patients with stage 2 disease characterized by neurologic manifestations had no clinical evidence of cardiac involvement [16]. Another prospective study of 61 patients with early-localized Lyme disease who were treated with antibiotics found only one patient who developed atrioventricular block [17]. Interestingly, despite the fact that there is only a slight male-to-female predominance for Lyme disease [7], there is a 3:1 male-to-female predominance for Lyme carditis [18,19].

## Pathology and experimental evidence

### *Pathology*

*B burgdorferi* can affect all layers of the heart [20–22]. Histologically, there is typically a transmural, inflammatory infiltrate composed nearly entirely of macrophages [23–25]. Very early in the disease process, small inflammatory nodules composed primarily of neutrophils and macrophages have been reported [22]. This is followed by infiltration of lymphoid cells, which create a characteristic band-like or plaque-like pattern. Myocyte necrosis also can occur, and subsequent endocardial and interstitial fibrosis has been reported [26].

Vasculitis involving the small and large intramyocardial vessels can take place. The small vessels frequently show endothelial cell edema, whereas large vessels show adventitial infiltrates with loose reticulin and increased collagen deposition [22,27]. The latter finding is one of the distinguishing characteristics that separates Lyme carditis from myocarditis caused by *Treponema palladium*. When the heart or great vessels are involved in syphilitic disease, the arteritis, aortitis, and valvular dysfunction are more prominent [18,19,28]. Although valvular dysfunction is one of the hallmarks of rheumatic disease, valvular dysfunction-related Lyme carditis is extremely rare [29]. Also, in rheumatic myocarditis, the inflammation is more focal and granulomatous [27].

Spirochetal forms have been found in endocardial biopsy [20] and autopsy specimens [30] showing the forms inside and near cellular infiltrates, between muscle fibers, and in the myocardium [20,22,31]. They also have been cultured from biopsy specimens of several patients [21]. Whether the presence of live

spirochetes is required for continued disease or whether the disease results from immune-mediated mechanisms remains to be determined [32].

### *Mouse models and experimental evidence*

The pathophysiology of Lyme disease has been characterized best in animal models. In mice with severe combined immunodeficiency syndrome, *B burgdorferi* induces progressive polyarthritis and carditis [33–35]. Antibodies are critical for protective immunity and arthritis modulation, but immune serum resolves arthritis and not carditis, spirochetemia, or spirochete clearance from tissues [36–38].

Mice with T cell deficiency, defective B cell maturation, and absent natural killer cells are susceptible to progressive infection with *B burgdorferi*, resulting in pancarditis, synovitis, and skeletal myositis [39]. A potential deleterious role of cytokines and T cell immunity has been suggested. In one study, early infection was characterized by up-regulation of the proinflammatory cytokines interleukin (IL)-1 $\beta$  and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ). Interferon- $\gamma$  appeared after the expression of these cytokines and remained elevated for 6 weeks [40].

Another group compared *B burgdorferi* inoculation in immunocompetent and B cell-deficient mice. Results showed that immunodeficient mice developed myocarditis, implying that innate immunity mediated initial clearance of infection. Cell transfer experiments using infected knock-out mice showed that transferring naive T cells and B cells induced resolution of carditis, and infected mice reconstituted with T cells developed myocarditis. CD4<sup>+</sup> T cells were responsible for the observed immune-mediated pathology [41]. Conversely, a subsequent study reported that CD4<sup>+</sup> T cells promoted resolution, rather than exacerbation, of Lyme carditis [42].

There is evidence that autoimmunity may play a role in Lyme carditis, and that antibodies directed toward *B burgdorferi* react with myosin. This was shown in a murine model of autoimmunity and suggested that persistent symptoms among some patients with underlying autoimmune disorders may not be caused by persistent infection [43].

Because extravasation of immune cells into tissues plays a large role in inflammatory processes, it is not surprising that  $\beta$ 2 integrins, a group of adhesion molecules, play an important role in Lyme carditis. Disruption of the  $\beta$ 2 integrin pathway, however, did not abrogate the effects of *B burgdorferi* on the myocardium completely [44]. Rather, dendritic cells secrete higher levels of chemoattractant proteins in the setting of  $\beta$ 2 integrin deficiency. Thus, although  $\beta$ 2 integrins may mediate the severity of disease, they are not essential for its expression.

The importance of macrophages in the clearance of spirochetes from the myocardium is evidenced by the fact that in mice lacking the macrophage receptor CCR2, there is an increased burden of *B burgdorferi* compared with wild-type mice in resistant mouse models [23]. In contrast, in a sensitive

mouse model, the absence of CCR2 leads to a compensatory mechanism of increased neutrophil recruitment.

A mouse model has been developed to study the electrophysiologic properties of Lyme carditis. These mice exhibit conduction abnormalities that are reversible after inoculation [45]. The resolution closely parallels resolution of inflammation on pathology. It is hoped that this model will provide useful insight into the pathophysiologic mechanisms of the conduction disorders in this disease.

### Clinical findings

Lyme carditis typically occurs between June and December, with a range of 4 days to 7 months after tick bite or EM [2,28,46]. The cardiac manifestations of early disseminated Lyme disease are usually coincident with other features of the disease (eg, EM, arthritis, or neurologic disease). One series found EM in 67%, joint complaints in 51%, and early neurologic sequelae in 27% of patients who had Lyme carditis [31]. There are, however, case reports of patients presenting with complete heart block as the sole manifestation of their Lyme disease with no recollection of antecedent tick bite or rash [47]. Patients who have cardiac involvement may be asymptomatic, thus clouding the true incidence of cardiac involvement. Common complaints include light-headedness, syncope, dyspnea, palpitations, and/or chest pain. In a review by the CDC of 84 patients who had Lyme carditis, 69% reported palpitations; 19% had conduction abnormalities. Ten percent had myocarditis; 5% had left ventricular systolic dysfunction, and 21% of the patients were hospitalized [10]. The principal manifestation of Lyme carditis is self-limited conduction derangement, most commonly varying degrees of atrioventricular conduction delay. Less frequently, pericarditis, endocarditis, myocarditis, pericardial effusion, myocardial infarction, coronary artery aneurysm, QT-interval prolongation, tachyarrhythmias, and congestive heart failure have been reported.

The spectrum of disease is variable, with some patients remaining asymptomatic and unaware of any underlying cardiac dysfunction, while others experience severe manifestations, including cardiac tamponade and permanent heart block [48]. Lyme carditis is a rare cause of mortality; however, there is a report of a patient with coexistent *Babesia microtii* infection who died unexpectedly. The patient was found to have spirochetes on endomyocardial biopsy specimen and a positive serologic test for *B burgdorferi* [30]. A fatal case of Lyme carditis in an English farm worker also has been reported [26].

### *Conduction disease*

Multiple studies suggest that the conduction disturbances associated with Lyme carditis, while predominantly atrioventricular nodal in nature, are

variable and rapidly fluctuating. On occasion, patients may progress from having a prolonged PR interval to complete heart block within minutes, with alternating tachycardias and bradycardias as the signs most strongly suggestive of cardiac involvement [2]. A retrospective analysis by McAlister and colleagues [46] showed that 45 of 52 patients who had Lyme carditis had documented atrioventricular block; Wenckebach and complete heart block were present in 40% and 50% of subjects, respectively. Similar findings were reported by van der Linde [31]. In an analysis of 105 reported cases of Lyme carditis from 1977 through 1990, approximately 50% progressed to complete heart block, 13% developed bundle-branch block or intraventricular conduction delay, and 18% had rhythm disturbances, most commonly supraventricular. It was hypothesized that these supraventricular rhythm disturbances may have been secondary to pericarditis, which was observed in 16% of patients. Rarely, ventricular and fascicular tachycardias have been reported [19,49]. Seslar and colleagues [50] reported two cases of prolongation of the corrected QT-interval, a previously unreported manifestation of Lyme carditis, which resolved after 6 to 7 weeks with 4 weeks of intravenous ceftriaxone.

Classic Wenckebach periodicity has been noted in some reports, and although the preponderance of data supports that the level of conduction disturbance in Lyme carditis is most commonly at the atrioventricular node, other reports show classic Wenckebach periodicity or narrow complex escape rhythms. The lack of response of most patients to atropine sulfate administration is further suggestive of a direct effect of Lyme disease on the atrioventricular node, rather than an indirect vagotonic effect. Electrophysiologic studies performed in 19 patients from van der Linde's [31] series suggest diffuse conduction system involvement in the acute phase of the disease. Ten patients (53%) had prolonged A-H intervals, but only three (16%) had H-V prolongation, and six (31%) had increased intra-atrial, H-V, and A-H conduction times.

The aforementioned data, and reports of patients who had prolonged A-H and H-V intervals [31,51] and alternating bundle-branch blocks and escape rhythms that are wide, slow, or absent [52] highlight that, although Lyme disease can affect the conduction system diffusely, the atrioventricular node appears to be the most vulnerable.

Although there are case reports showing the need for permanent pacing for Lyme carditis despite antibiotic therapy, this is rare [13,20,46,53–55]. Complete heart block is transient and generally resolves within 1 week. Lesser conduction disturbances resolve within 6 weeks [46]. Goldings and Jericho [56] reported a need for temporary pacing in 38% of patients. In van der Linde's [31,55] retrospective study of 105 cases, temporary pacing was employed in 35% of cases. A permanent pacemaker was implanted in five patients, four of whom had complete resolution of their conduction disturbances; one patient had persistent complete heart block. Overall, 94% of patients recovered completely. A 1990 study by Peeters and colleagues

[57] suggested that despite its relative rarity, Lyme disease may be an unrecognized cause of persistent complete heart block with cases having an increased incidence of anti-*B burgdorferi* antibodies versus controls. Seropositive patients were also more likely to have resolution of their heart block with appropriate antibiotic therapy.

### *Myocardial disease*

Although nonspecific, the most common manifestation of *B burgdorferi*-induced myocardial disease is the presence of diffuse ST segment and T wave changes on surface electrocardiogram, indicating diffuse myocardial involvement. These were noted in 65% of patients in Steere's series [2]. Myocardial involvement may lead to cardiomegaly, left ventricular dysfunction, or clinical congestive heart failure and is thought to be present in 10% to 15% of patients with Lyme carditis [31,46]. In most cases, myocardial dysfunction is mild and self-limited [2,58,59].

These findings are in contrast to cardiac manifestations of Rocky Mountain spotted fever. As in Lyme carditis, dysrhythmias are common, but myocardial involvement may be extensive and fulminant [60]. *Rickettsia rickettsii* has been shown on immunofluorescent staining of the myocardial capillaries, venules, and arterioles [61]. In fatal Rocky Mountain spotted fever, interstitial mononuclear myocarditis and vascular injury-induced myocardial edema are common autopsy findings. Echocardiographically detected cardiac function abnormalities may persist after resolution of other manifestations of the disease [62].

Although relatively rare, it has been suggested that *B burgdorferi* may play a causative role in chronic heart failure. This hypothesis originated from a 1990 European case report of a 54-year-old man with a 4-year history of dilated cardiomyopathy, high levels of serum *B burgdorferi* IgG, and a *B burgdorferi* culture-positive endomyocardial biopsy specimen [21]. These same investigators studied 72 patients who had idiopathic dilated cardiomyopathy, 55 patients who had coronary artery disease, and 61 healthy controls. Positive ELISA values were present in 26.4%, 12.7%, and 8.2% of subjects, respectively [63].

Further evidence suggesting a role of Lyme disease in the subsequent development of clinical congestive heart failure came from several other observational studies by European investigators. In Italy, two patients who had idiopathic dilated cardiomyopathy grew *B burgdorferi* from endomyocardial biopsy specimens. Both had complete resolution of their myocardial dysfunction after treatment with angiotensin converting enzyme inhibitors, digoxin, and penicillin [64]. A Dutch group noted improvement in left ventricular ejection fraction in eight of nine *B burgdorferi*-seropositive patients with idiopathic dilated cardiomyopathy who were treated with antibiotics. Six of the nine subjects sustained a complete recovery of myocardial function [65].

Interestingly, the ability to grow *B burgdorferi* from biopsy specimens and clinical improvement after antibiotic treatment in seropositive patients has not been replicated in the United States. A prospective study of 175 patients in the United States who had chronic heart failure showed a high false-positive ELISA rate and no improvement in heart failure with appropriate antibiotic therapy [66]. Seropositivity was higher among patients who had severe heart failure compared with blood donor controls, although not statistically significant (8.0% versus 3.0%;  $P = .07$ ). Of 77 patients who had idiopathic dilated cardiomyopathy, 6 (7.8%) had positive ELISA tests with no significant difference according to cause of heart failure. Of these, five of six patients had negative confirmatory Western blot results. Six seroreactive patients were treated with antibiotics. None of the subjects had improvement in heart failure symptoms [46].

The different outcomes of these studies may be caused, at least in part, by differences in patient and control populations or in the serologic assays used. Additionally, as was stated previously, the causative organism of Lyme disease differs between the two regions, with infection by *B burgdorferi sensu stricto* and *B burgdorferi sensu lato* occurring more frequently in the United States and Europe, respectively.

Clinical differences in the seroreactive patients from Europe and North America may underlie the differing response to therapy. It has been proposed that the European patients may have had a self-limited illness unrelated to Lyme disease, or the North American patients may have had late-stage disease that was no longer responsive to antibiotics. The former is unlikely, given that most patients had EM, a history of tick bites, or both [66].

Further studies are warranted to clarify the role that *B burgdorferi* plays in acute and chronic congestive heart failure. Nevertheless, it is reasonable to consider *B burgdorferi* infection in the differential diagnosis of dilated cardiomyopathy. False-positive ELISA assays are common in patients who have severe cardiomyopathy; therefore confirmatory Western blot analysis should be performed. Screening and treatment should be reserved for patients who have a specific clinical history suggestive of prior Lyme disease.

## Diagnosis

Appropriately diagnosing Lyme carditis is challenging, requiring confirmation of the association between a patient's historical, clinical, and laboratory data. It is diagnosed most accurately in cases in which there is historical evidence of borreliosis (tick bite, EM, arthritis, neurologic dysfunction) accompanied by cardiac manifestations (such as electrocardiographic conduction abnormalities, cardiomegaly, and congestive heart failure) in the setting of positive serologic testing for *B burgdorferi* antibodies. As mentioned, Lyme carditis can occur in the absence of EM, and patients may not recall a rash or tick bite. Therefore, the diagnosis should be



considered in a patient who has light-headedness, syncope, dyspnea, palpitations, and chest pain, especially when seen in conjunction with neurologic sequelae and electrocardiographic or echocardiographic abnormalities.

A positive ELISA serologic test for the presence of antibodies to *B burgdorferi* supports the diagnosis of Lyme carditis, but is not sufficient. Similarly, a negative result does not rule out the diagnosis, as serologic tests can be negative in the first 6 to 8 weeks of disease [28]. Positive or equivocal results should prompt confirmatory Western blot analysis, because 5% or more of the normal population and patients who have severe heart failure are positive in many assays [17,28]. The presence of IgM (rather than IgG) antibodies is more suggestive of recent infection with *B burgdorferi*, making it the most likely etiologic agent [6].

Echocardiography may provide evidence of myocardial dysfunction, guiding management and treatment decisions [67]. Characteristic findings on endomyocardial biopsy, such as the bandlike endocardial infiltrate and isolation of *B burgdorferi* in culture may support the diagnosis in the appropriate clinical setting [22,27]. Current guidelines do not recommend routine biopsy for diagnosis given the potential focality of myocarditis and the high risk of the procedure [68]. MRI plays a supportive role in the assessment and diagnosis of Lyme carditis, typically displaying nonspecific epicardial contrast enhancement rather than the subendocardial enhancement often appreciated in acute coronary syndromes [69]. Gallium-67 myocardial scanning and Indium-111 antimyosin antibody imaging are nonspecific tests that have been used in several series to document myocardial inflammation. Diffuse, intense uptake that normalizes with resolution of the carditis has been shown [70–75].

## Treatment

Antibiotic therapy in the early stages of Lyme disease has been reported to prevent or attenuate later complications of the disease. In a retrospective study, Sanga and colleagues [76] demonstrated no increase in cardiac manifestations compared with controls in 176 patients who were treated with appropriate antibiotic therapy for Lyme disease at the time of initial presentation. Although antibiotics are recommended to clear the infection, there are no randomized controlled clinical trials that have studied the efficacy of antibiotics in the treatment of Lyme carditis, specifically.

Common antibiotic regimens for the treatment of Lyme carditis include amoxicillin 500 mg orally three or four times daily for 30 days, doxycycline 100 mg orally twice daily for 30 days, and ceftriaxone 2 g intravenously daily for 2 to 4 weeks [77]. Cefotaxime 3 g intravenously twice daily for 2 to 4 weeks is reportedly as effective as ceftriaxone in patients who have other late manifestations of Lyme disease, although its efficacy in Lyme carditis has not been proven [78,79]. Patients who have minor cardiac involvement (eg, prolongation of the PR interval no more than 0.30 seconds) and no

other symptoms should receive oral antibiotic therapy with amoxicillin or doxycycline as for early disease. Patients who have more severe conduction system disease, such as second- or third-degree atrioventricular conduction delay with a PR interval greater than 0.30 seconds, or clinical evidence of congestive heart failure should be hospitalized and administered intravenous ceftriaxone or high-dose penicillin G. A combination of intravenous and oral antimicrobial therapy should be continued for 4 weeks, although shorter courses of 14 to 21 days may be as efficacious. Some have advocated the addition of corticosteroids or salicylates if conduction disease does not improve over 24 to 48 hours [46]; however, there is no evidence that this speeds recovery of conduction disease. Additionally, steroids may precipitate recurrent central nervous system symptoms or joint symptoms or both upon withdrawal [27]. Given the increased risk of complete heart block and asystole these patients should be placed on telemetry [27]. Prophylactic transvenous pacing is not recommended. A transcutaneous pacemaker, however, should be accessible until it is clear the patient has an adequate escape rhythm [54]. Indications for pacing are the same as in other causes of heart block [54]. As mentioned, complete heart block generally resolves within 1 week, with resolution of lesser conduction disturbances within 6 weeks [46].

## Summary

Lyme disease is a globally occurring vector-borne illness caused by the spirochete *B burgdorferi*. It can affect multiple organ systems during the early disseminated phase, including the heart. The cardinal manifestation of Lyme carditis is self-limited conduction system disease at the level of the atrioventricular node. Temporary pacing may be necessary in up to one third of patients, but permanent heart block rarely develops. Myocardial and pericardial involvement also occurs commonly, but tends to be mild and self-limited. Endocarditis, pericardial effusion, myocardial infarction, coronary artery aneurysm, QT interval prolongation, tachyarrhythmias, and congestive heart failure also have been reported.

The diagnosis requires confirmation of the association between a patient's historical, clinical, and laboratory data. It is diagnosed most accurately in cases in which there is historical evidence of borreliosis (prior tick bite, EM, arthritis, neurologic dysfunction) accompanied by cardiac manifestations (such as electrocardiographic conduction abnormalities, cardiomegaly, and congestive heart failure) and symptoms (such as chest pain, palpitations, syncope, and dyspnea). The presence of *B burgdorferi* antibodies in serologic studies can support the diagnosis in the appropriate clinical setting. Given the significant false-positive ELISA rate in patients with chronic congestive heart failure and the unclear benefit of antimicrobial therapy, however, confirmatory Western blot analysis is recommended. Echocardiography and MRI may be useful in selected circumstances.

Endomyocardial biopsy revealing bandlike endocardial infiltrate and isolation of *B burgdorferi* in culture may support the diagnosis further, but should be reserved for patients who have a clear history of antecedent Lyme disease or tick bite, given the inherent risks of the procedure. No treatment has been proven to attenuate or prevent the development of Lyme carditis. Mild carditis generally is treated with oral antibiotics and severe carditis with intravenous antibiotics in an effort to eradicate the infection and prevent late complications of Lyme disease. The clinical course of Lyme carditis is usually benign, with most patients recovering completely. In rare instances, death from Lyme carditis has been reported.

## References

- [1] Weinstein A, Bujak DI. Lyme disease: a review of its clinical features. *N Y State J Med* 1989; 89(10):566–71.
- [2] Steere AC, Batsford WP, Weinberg M, et al. Lyme carditis: cardiac abnormalities of Lyme disease. *Ann Intern Med* 1980;93(1):8–16.
- [3] Stewart A, Glass J, Patel A, et al. Lyme arthritis in the Hunter Valley. *Med J Aust* 1982;1(3): 139.
- [4] Houwerzyl J, Root JJ, Hoogkamp-Korstanje JA. A case of Lyme disease with cardiac involvement in the Netherlands. *Infection* 1984;12(5):358.
- [5] Cornuau C, Bernard M, Daumas PL, et al. Cardiac manifestations of Lyme disease. Apropos of 2 cases). *Ann Cardiol Angeiol (Paris)* 1984;33(6):395–9 [in French].
- [6] Steere AC. Lyme disease. *N Engl J Med* 2001;345(2):115–25.
- [7] Lyme disease—United States, 2003–2005. *MMWR Morb Mortal Wkly Rep* 2007;56(23): 573–6.
- [8] Lyme disease—United States, 2001–2002. *MMWR Morb Mortal Wkly Rep* 2004;53(17): 365–9.
- [9] O’Connell S, Granstrom M, Gray JS, et al. Epidemiology of European Lyme borreliosis. *Zentralbl Bakteriol* 1998;287(3):229–40.
- [10] Ciesielski CA, Markowitz LE, Horsley R, et al. Lyme disease surveillance in the United States, 1983–1986. *Rev Infect Dis* 1989;11(Suppl 6):S1435–41.
- [11] Schmid GP, Horsley R, Steere AC, et al. Surveillance of Lyme disease in the United States, 1982. *J Infect Dis* 1985;151(6):1144–9.
- [12] Woolf PK, Lorsung EM, Edwards KS, et al. Electrocardiographic findings in children with Lyme disease. *Pediatr Emerg Care* 1991;7(6):334–6.
- [13] Mayer W, Kleber FX, Wilske B, et al. Persistent atrioventricular block in Lyme borreliosis. *Klin Wochenschr* 1990;68(8):431–5.
- [14] Anderson JF, Barthold SW, Magnarelli LA. Infectious but nonpathogenic isolate of *Borrelia burgdorferi*. *J Clin Microbiol* 1990;28(12):2693–9.
- [15] Stanek G, Wewalka G, Groh V, et al. Differences between Lyme disease and European arthropod-borne *Borrelia* infections. *Lancet* 1985;1(8425):401.
- [16] Hansen K, Lebech AM. The clinical and epidemiological profile of Lyme neuroborreliosis in Denmark 1985–1990. A prospective study of 187 patients with *Borrelia burgdorferi*-specific intrathecal antibody production. *Brain* 1992;115(Pt 2):399–423.
- [17] Rubin DA, Sorbera C, Nikitin P, et al. Prospective evaluation of heart block complicating early Lyme disease. *Pacing Clin Electrophysiol* 1992;15(3):252–5.
- [18] Steere AC. Lyme disease. *N Engl J Med* 1989;321(9):586–96.
- [19] Vlay SC, Dervan JP, Elias J, et al. Ventricular tachycardia associated with Lyme carditis. *Am Heart J* 1991;121(5):1558–60.

- [20] de Koning J, Hoogkamp-Korstanje JA, van der Linde MR, et al. Demonstration of spirochetes in cardiac biopsies of patients with Lyme disease. *J Infect Dis* 1989;160(1):150–3.
- [21] Stanek G, Klein J, Bittner R, et al. Isolation of *Borrelia burgdorferi* from the myocardium of a patient with longstanding cardiomyopathy. *N Engl J Med* 1990;322(4):249–52.
- [22] Duray PH. Clinical pathologic correlations of Lyme disease. *Rev Infect Dis* 1989;11(Suppl 6):S1487–93.
- [23] Montgomery RR, Booth CJ, Wang X, et al. Recruitment of macrophages and polymorphonuclear leukocytes in Lyme carditis. *Infect Immun* 2007;75(2):613–20.
- [24] Ruderman EM, Kerr JS, Telford SR III, et al. Early murine Lyme carditis has a macrophage predominance and is independent of major histocompatibility complex class II-CD4+ T cell interactions. *J Infect Dis* 1995;171(2):362–70.
- [25] Barthold SW, Beck DS, Hansen GM, et al. Lyme borreliosis in selected strains and ages of laboratory mice. *J Infect Dis* 1990;162(1):133–8.
- [26] Cary NR, Fox B, Wright DJ, et al. Fatal Lyme carditis and endodermal heterotopia of the atrioventricular node. *Postgrad Med J* 1990;66(772):134–6.
- [27] Cox J, Krajden M. Cardiovascular manifestations of Lyme disease. *Am Heart J* 1991;122(5):1449–55.
- [28] Sigal LH. Early disseminated Lyme disease: cardiac manifestations. *Am J Med* 1995;98(4):25S–8S [discussion: 28S–29S].
- [29] Canver CC, Chanda J, DeBellis DM, et al. Possible relationship between degenerative cardiac valvular pathology and Lyme disease. *Ann Thorac Surg* 2000;70(1):283–5.
- [30] Marcus LC, Steere AC, Duray PH, et al. Fatal pancarditis in a patient with coexistent Lyme disease and babesiosis. Demonstration of spirochetes in the myocardium. *Ann Intern Med* 1985;103(3):374–6.
- [31] van der Linde MR. Lyme carditis: clinical characteristics of 105 cases. *Scand J Infect Dis Suppl* 1991;77:81–4.
- [32] Sigal LH. Immunopathogenesis of Lyme borreliosis. *Clin Dermatol* 1993;11(3):415–22.
- [33] Barthold SW, Sidman CL, Smith AL. Lyme borreliosis in genetically resistant and susceptible mice with severe combined immunodeficiency. *Am J Trop Med Hyg* 1992;47(5):605–13.
- [34] Schaible UE, Gay S, Museteanu C, et al. Lyme borreliosis in the severe combined immunodeficiency (scid) mouse manifests predominantly in the joints, heart, and liver. *Am J Pathol* 1990;137(4):811–20.
- [35] Schaible UE, Kramer MD, Museteanu C, et al. The severe combined immunodeficiency (scid) mouse. A laboratory model for the analysis of Lyme arthritis and carditis. *J Exp Med* 1989;170(4):1427–32.
- [36] Barthold SW, Feng S, Bockenstedt LK, et al. Protective and arthritis-resolving activity in sera of mice infected with *Borrelia burgdorferi*. *Clin Infect Dis* 1997;25(Suppl 1):S9–17.
- [37] McKisic MD, Barthold SW. T cell-independent responses to *Borrelia burgdorferi* are critical for protective immunity and resolution of Lyme disease. *Infect Immun* 2000;68(9):5190–7.
- [38] Barthold SW, Hodzic E, Tunev S, et al. Antibody-mediated disease remission in the mouse model of Lyme borreliosis. *Infect Immun* 2006;74(8):4817–25.
- [39] Defosse DL, Duray PH, Johnson RC. The NIH-3 immunodeficient mouse is a model for Lyme borreliosis myositis and carditis. *Am J Pathol* 1992;141(1):3–10.
- [40] Kelleher Doyle M, Telford SR III, Criscione L, et al. Cytokines in murine Lyme carditis: Th1 cytokine expression follows expression of proinflammatory cytokines in a susceptible mouse strain. *J Infect Dis* 1998;177(1):242–6.
- [41] McKisic MD, Redmond WL, Barthold SW. Cutting edge: T cell-mediated pathology in murine Lyme borreliosis. *J Immunol* 2000;164(12):6096–9.
- [42] Bockenstedt LK, Kang I, Chang C, et al. CD4+ T helper 1 cells facilitate regression of murine Lyme carditis. *Infect Immun* 2001;69(9):5264–9.
- [43] Raveche ES, Schutzer SE, Fernandes H, et al. Evidence of *Borrelia* autoimmunity-induced component of Lyme carditis and arthritis. *J Clin Microbiol* 2005;43(2):850–6.

- [44] Guerau-de-Arellano M, Alroy J, Huber BT. Beta2 integrins control the severity of murine Lyme carditis. *Infect Immun* 2005;73(6):3242–50.
- [45] Saba S, VanderBrink BA, Perides G, et al. Cardiac conduction abnormalities in a mouse model of Lyme borreliosis. *J Interv Card Electrophysiol* 2001;5(2):137–43.
- [46] McAlister HF, Klementowicz PT, Andrews C, et al. Lyme carditis: an important cause of reversible heart block. *Ann Intern Med* 1989;110(5):339–45.
- [47] Kimball SA, Janson PA, LaRaia PJ. Complete heart block as the sole presentation of Lyme disease. *Arch Intern Med* 1989;149(8):1897–8.
- [48] Bruyn GA, De Koning J, Reijsoo FJ, et al. Lyme pericarditis leading to tamponade. *Br J Rheumatol* 1994;33(9):862–6.
- [49] Greenberg YJ, Brennan JJ, Rosenfeld LE. Lyme myocarditis presenting as fascicular tachycardia with underlying complete heart block. *J Cardiovasc Electrophysiol* 1997;8(3):323–4.
- [50] Seslar SP, Berul CI, Burklow TR, et al. Transient prolonged corrected QT interval in Lyme disease. *J Pediatr* 2006;148(5):692–7.
- [51] Rey MJ, Zimmermann M, Adamec R, et al. Intrahisian 2:1 atrioventricular block secondary to Lyme disease. *Eur Heart J* 1991;12(9):1048–51.
- [52] Rosenfeld ME, Beckerman B, Ward MF, et al. Lyme carditis: complete AV dissociation with episodic asystole presenting as syncope in the emergency department. *J Emerg Med* 1999;17(4):661–4.
- [53] Artigao R, Torres G, Guerrero A, et al. Irreversible complete heart block in Lyme disease. *Am J Med* 1991;90(4):531–3.
- [54] Nagi KS, Thakur RK. Lyme carditis: indications for cardiac pacing. *Can J Cardiol* 1995;11(4):335–8.
- [55] van der Linde MR, Crijns HJ, de Koning J, et al. Range of atrioventricular conduction disturbances in Lyme borreliosis: a report of four cases and review of other published reports. *Br Heart J* 1990;63(3):162–8.
- [56] Goldings EA, Jericho J. Lyme disease. *Clin Rheum Dis* 1986;12(2):343–67.
- [57] Peeters AJ, Dijkmans BAC, Sedney MI. Lyme borreliosis: a hidden cause of heart block in pacemaker treated males. Presented at IV International Conference on Lyme borreliosis. Stockholm, Sweden, 1990.
- [58] Horowitz HW, Belkin RN. Acute myopericarditis resulting from Lyme disease. *Am Heart J* 1995;130(1):176–8.
- [59] Midttun M, Lebech AM, Hansen K, et al. Lyme carditis: a clinical presentation and long time follow-up. *Scand J Infect Dis* 1997;29(2):153–7.
- [60] Helmick CG, Bernard KW, D'Angelo LJ. Rocky Mountain spotted fever: clinical, laboratory, and epidemiological features of 262 cases. *J Infect Dis* 1984;150(4):480–8.
- [61] Walker DH, Paletta CE, Cain BG. Pathogenesis of myocarditis in Rocky Mountain spotted fever. *Arch Pathol Lab Med* 1980;104(4):171–4.
- [62] Marin-Garcia J, Mirvis DM. Myocardial disease in Rocky Mountain spotted fever: clinical, functional, and pathologic findings. *Pediatr Cardiol* 1984;5(2):149–54.
- [63] Stanek G, Klein J, Bittner R, et al. *Borrelia burgdorferi* as an etiologic agent in chronic heart failure? *Scand J Infect Dis Suppl* 1991;77:85–7.
- [64] Lardieri G, Salvi A, Camerini F, et al. Isolation of *Borrelia burgdorferi* from myocardium. *Lancet* 1993;342(8869):490.
- [65] Gasser R, Dusleag J, Reisinger E, et al. Reversal by ceftriaxone of dilated cardiomyopathy *Borrelia burgdorferi* infection. *Lancet* 1992;339(8802):1174–5.
- [66] Sonnesyn SW, Diehl SC, Johnson RC, et al. A prospective study of the seroprevalence of *Borrelia burgdorferi* infection in patients with severe heart failure. *Am J Cardiol* 1995;76(1):97–100.
- [67] Vujisic-Tesic B, Simin N, Petrovic M, et al. [The role of echocardiography in the evaluation of cardiac damage in Lyme disease.] *Glas Srp Akad Nauka [Med]* 1993;(43):241–3 [in Serbian].
- [68] Wu LA, Lapeyre AC III, Cooper LT. Current role of endomyocardial biopsy in the management of dilated cardiomyopathy and myocarditis. *Mayo Clin Proc* 2001;76(10):1030–8.

- [69] Munk PS, Orn S, Larsen AI. Lyme carditis: persistent local delayed enhancement by cardiac magnetic resonance imaging. *Int J Cardiol* 2007;115(3):e108–10.
- [70] Alpert LI, Welch P, Fisher N. Gallium-positive Lyme disease myocarditis. *Clin Nucl Med* 1985;10(9):617.
- [71] Jacobs JC, Rosen JM, Szer IS. Lyme myocarditis diagnosed by gallium scan. *J Pediatr* 1984; 105(6):950–2.
- [72] Reznick JW, Braunstein DB, Walsh RL, et al. Lyme carditis. Electrophysiologic and histopathologic study. *Am J Med* 1986;81(5):923–7.
- [73] Rienzo RJ, Morel DE, Prager D, et al. Gallium avid Lyme myocarditis. *Clin Nucl Med* 1987; 12(6):475–6.
- [74] Veluvolu P, Balian AA, Goldsmith R, et al. Lyme carditis. Evaluation by Ga-67 and MRI. *Clin Nucl Med* 1992;17(10):823.
- [75] Sarda L, Assayag P, Palazzo E, et al. 111Indium antimyosin antibody imaging of primary myocardial involvement in systemic diseases. *Ann Rheum Dis* 1999;58(2):90–5.
- [76] Sangha O, Phillips CB, Fleischmann KE, et al. Lack of cardiac manifestations among patients with previously treated Lyme disease. *Ann Intern Med* 1998;128(5):346–53.
- [77] Olson LJ, Okafor EC, Clements IP. Cardiac involvement in Lyme disease: manifestations and management. *Mayo Clin Proc* 1986;61(9):745–9.
- [78] Sigal LH. Current recommendations for the treatment of Lyme disease. *Drugs* 1992;43(5): 683–99.
- [79] Rahn DW, Malawista SE. Lyme disease: recommendations for diagnosis and treatment. *Ann Intern Med* 1991;114(6):472–81.