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# Lyme carditis: A can't miss diagnosis

Clinicians should consider a diagnosis of Lyme carditis, an early manifestation of Lyme disease, if nonspecific cardiac symptoms have been preceded by flu-like symptoms and erythema migrans, especially if the patient is young, has no history of cardiac disease, and has recently traveled to an endemic area for Lyme disease.

ABSTRACT: Lyme disease, caused by the tick-borne spirochete bacterium *Borrelia* spp., is becoming increasingly prevalent in Canada. Lyme carditis is a rare but important early disseminated manifestation of the disease, which can present with high-degree atrioventricular block in otherwise healthy young adults. Timely treatment of Lyme carditis with appropriate antibiotics can lead to complete resolution. However, patients with Lyme carditis often have missed or late diagnoses, which can result in unnecessary pacemaker implantations, complications, and even fatalities. Considering Lyme carditis in the differential diagnosis of young patients presenting with new atrioventricular blocks is critical to ensuring timely diagnosis and treatment.

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Lyme disease is the most prevalent vector-borne disease in North America and Europe. It is caused by the gram-negative spirochete bacteria *Borrelia* spp., which are transmitted by the *Ixodes* spp. tick.[1] In Canada, the number of reported cases of Lyme disease dramatically increased from 144 in 2009 to 1487 in 2018.[2] Most of this increase occurred in Eastern Canada: 88% of reported cases in 2018 were from Ontario, Quebec, and Nova Scotia.[2] In BC, the trend is reversed: the number of reported cases declined from a peak of 40 (0.8 per 100 000) in 2016 to 9 (0.2 per 100 000) in 2018.[3] Nonetheless, risk modeling suggests that the overall incidence of Lyme disease in Canada may continue to increase as migratory patterns of birds that carry *Ixodes scapularis* are affected by climate change, which could result in further dispersion of *I. scapularis* into southeastern Canada. Given that the incidence of Lyme disease has generally increased in Canada and the disease and its complications can be difficult to diagnose, it is important for clinicians to be aware of the clinical manifestations of the disease.

## Lyme disease progression

The progression of Lyme disease occurs in three stages:

**Stage 1:** Following the tick bite, there is a 3- to 32-day incubation period. Then, in 40% to 80% of cases, a localized skin infection, known as erythema migrans (EM), manifests at the site of the bite.[1] EM typically appears as a red annular skin lesion with a central clearing, and can be accompanied by a nonspecific infectious syndrome of fever, malaise, lymphadenopathy, myalgia, and headache.[1]

**Stage 2:** Early disseminated infection occurs a few weeks after the onset of Lyme disease and can include Lyme carditis, Lyme arthritis, and Lyme neuroborreliosis involvement.

**Stage 3:** Persistent infection lasts for at least 6 months and can include chronic Lyme arthritis and neuroborreliosis.[1]

This article focuses on Lyme carditis because it is often initially misdiagnosed and many patients report seeking medical attention several times before it is suspected. Misdiagnosis can lead to unnecessary implantation of permanent pacemakers in otherwise young and healthy people, which in turn can lead to a lifetime of pulse generator changes and risks of complications such as infection and lead dislodgement.[4]

## Lyme carditis pathophysiology

Lyme carditis is believed to occur as a result of direct myocardial invasion by *Borrelia* spp. followed by an exaggerated macrophagic and lymphocytic inflammatory response within the cardiac tissues.[4] *Borrelia* spp. appear to have a tropism for cardiac tissues, which often involves the atrioventricular (AV) node, as evidenced

by autopsy findings.[5] The severity of conduction abnormalities is correlated with both the number of spirochetes present in the cardiac tissues and the degree of myocardial inflammation.[6] However, typically a small number of spirochetes are present within the cardiac tissue, but there is extensive lymphocytic infiltration, which suggests that the inflammatory response in Lyme carditis is exaggerated and likely plays a significant role in the pathophysiology of Lyme carditis.[7] Furthermore, evidence suggests there is cross-reactivity between anti-*Borrelia* antibodies and cardiac tissues; therefore, autoimmunity may be a contributor to this exaggerated inflammatory response.[8]

## Lyme carditis manifestation

Compared to the cutaneous, arthritic, and neurological manifestations of Lyme disease, Lyme carditis is a relatively rare manifestation, with reported prevalence of 1.5% to 10.0% in the United States and 0.3% to 4.0% in Europe among adult patients with untreated Lyme disease.[9] Lyme carditis can be difficult to diagnose due to its rarity and nonspecific presentation. The signs of Lyme carditis are nonspecific cardiac symptoms, including syncope, presyncope, dyspnea, palpitations, and chest pain.[10] The most common electrocardiographic (ECG) manifestation of Lyme carditis is fluctuating atrioventricular block (AVB), which occurs in 90% of Lyme carditis cases, with 67% of those cases being third-degree **[Figure 1A]** or second-degree AVB **[Figure 1B, 1C]**.[4] The AVB can rapidly fluctuate from first-degree AVB **[Figure 1D]** to second- and third-degree AVB over minutes, hours, or days. Third-degree AVB can be fatal if untreated. Therefore, all Lyme carditis patients require strict cardiac monitoring.[4,9]

**Lyme carditis can be difficult to diagnose due to its rarity and nonspecific presentation.**

Lyme carditis manifests in early disseminated Lyme disease (stage 2), usually within 1 to 2 months after the onset of Lyme disease symptoms.[4] The presence of nonspecific flu-like symptoms and EM 1 to 2 months prior to the onset of nonspecific cardiac symptoms should prompt clinicians to consider Lyme carditis in their differential diagnosis. This is especially true if the patient is young, has no history of cardiovascular disease, and has recently traveled to an endemic area. Endemic areas in BC include Vancouver Island, the mainland coast across from Vancouver Island, the southern mainland, and the river valleys in southern BC.[11] Endemic areas throughout North America and Europe are shown in **Figures 2 to 4**. Similarly, history of a tick bite, especially from an endemic area for Lyme disease, that occurred 1 to 2 months prior to the onset of cardiac symptoms can be the proverbial "smoking gun" that strongly suggests the diagnosis of Lyme carditis. However, many patients do not remember being bitten, so the absence of a tick bite on history does not rule out Lyme carditis.[1]

Lyme carditis can also present with other conduction abnormalities, such as sinus bradycardia, sinus node disease, intra-atrial block, atrial fibrillation, supraventricular tachycardia, bundle branch block, ventricular tachycardia, ventricular fibrillation, and asystole.[4,10] Additionally, Lyme carditis can present as myopericarditis, myocarditis, pericarditis, and rarely, endocarditis or pancarditis.[10] Acute Lyme myopericarditis occurs in 10% of Lyme carditis cases.[10] This can lead to reduced left ventricular function, cardiomegaly, and clinical signs of congestive heart failure, though they are all reversible with appropriate treatment.[10] Lyme myopericarditis can mimic acute coronary syndrome, with ST depression or elevation,


**Figure 1.** Serial ECGs of a 27-year-old male with Lyme carditis, presenting with new onset progressive dyspnea and palpitations. Treatment with IV ceftriaxone was initiated on day 5.
(A) Third-degree atrioventricular block (AVB) with junctional escape rhythm, 41 bpm (day 1)
(B) Second-degree AVB with 2:1 conduction, 36 bpm (day 2)
(C) Second-degree AVB Mobitz I (Wenckebach), 46 bpm (day 5)
(D) First-degree AVB with PR interval of 308 ms, 37 bpm (day 8)

T wave inversion, and cardiac enzyme elevations.[4] Transthoracic echocardiogram can help distinguish between Lyme myopericarditis and acute coronary syndrome, as Lyme myopericarditis may show diffuse myocardial hypokinesis, while acute coronary syndrome would show regional wall motion abnormalities.[4] Cardiac magnetic resonance imaging or gallium-67 scintigraphy can be used for noninvasive diagnosis and monitoring of myocarditis.[10] Lyme pericarditis, which is more common in Europe (23% of Lyme carditis cases) than in the United States (2% to 5% of Lyme carditis cases), presents with signs and symptoms of pericarditis and can include complications of pericarditis such as pericardial effusion and cardiac tamponade.[10] Both Lyme endocarditis and pancarditis are very rare,[10] so they are not reviewed in this article.

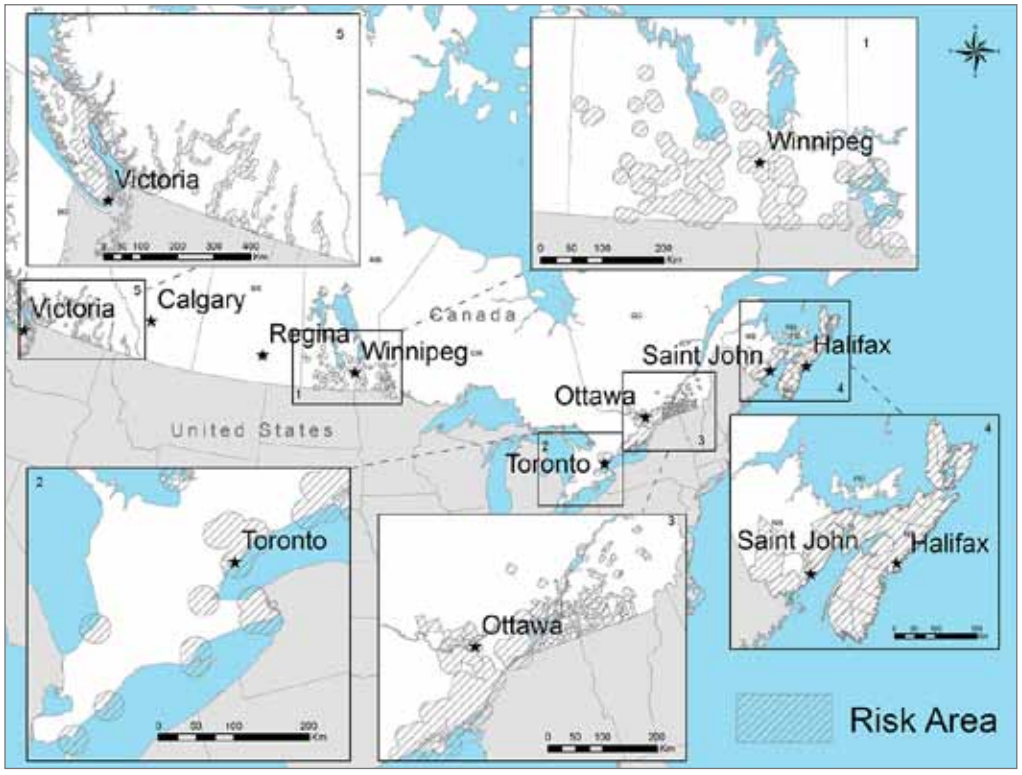


**Figure 2.** Endemic areas for Lyme disease throughout Canada. Source: Government of Canada (www.canada.ca/en/public-health/services/diseases/lyme-disease/risk-lyme-disease.html#map)

## Lyme carditis and erythema migrans

Lyme disease and Lyme carditis are often misdiagnosed due to their rarity and variable presentation. Patients report seeking medical attention numerous times before the correct diagnosis is made.[4] For localized Lyme disease (stage 1), only 40% to 80% of patients develop EM.[1,10] It is important to note that EM typically appears within 7 to 14 days after the tick bite, and should be differentiated from the initial erythematous or blistering allergic skin reaction at the site of the bite. For example, EM will continue to enlarge in the first few days after its appearance, whereas an insect bite reaction will decrease in size. Furthermore, the EM lesion does not always manifest as the typical annular lesion with a central clearing. It can also manifest as an erythematous lesion without a central clearing, or with multiple rings around it, or with a central violaceous area.[1] Indeed, in an observational cohort study of 118 cases, central clearing was seen in only 9% of cases; homogeneous lesions and central erythema were observed in 59% and 32% of patients, respectively.[12] This can make recognition of EM, and by extension, diagnosis of

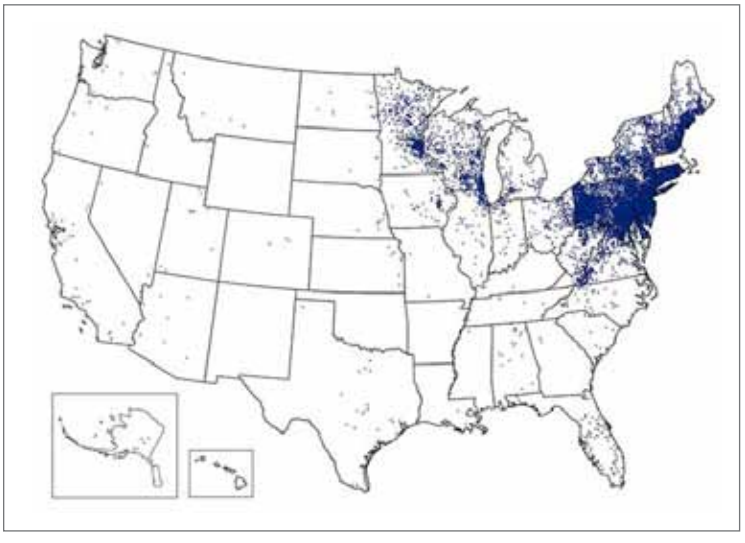

**Figure 3.** Endemic areas for Lyme disease throughout the United States. Source: US Centers for Disease Control and Prevention (www.cdc.gov/lyme/stats/maps.html)

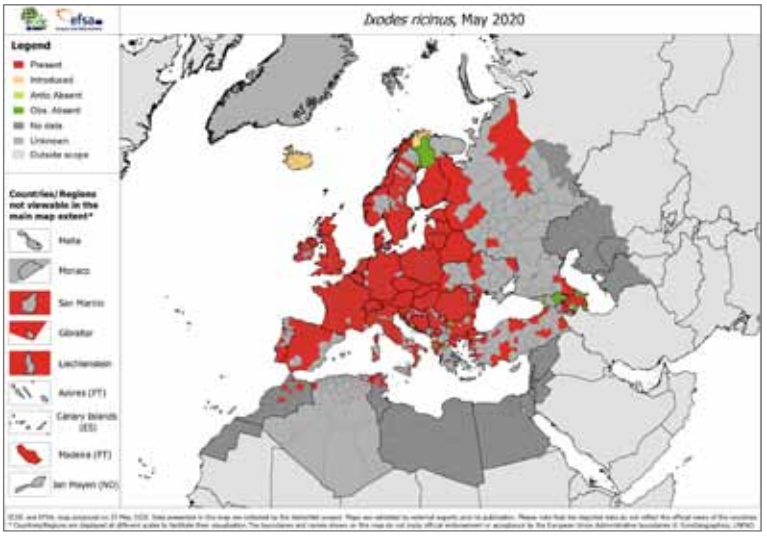


**Figure 4.** Endemic areas for Lyme disease throughout Europe. Source: European Centre for Disease Prevention and Control (www.ecdc.europa.eu/en/disease-vectors/surveillance-and-disease-data/tick-maps)

Lyme disease, difficult. As such, the cutaneous manifestations of Lyme disease are sometimes misdiagnosed as more common dermatologic diseases.[13]

Lyme carditis can also be difficult to diagnose because the preceding history of flu-like symptoms, EM, and travel usually occur 1 to 2 months prior to the cardiac presentation; therefore, clinicians may not ask about the preceding illness, and patients may not volunteer this information because it may seem irrelevant. Furthermore, the EM lesion may go unnoticed or may have resolved by the time cardiac symptoms appear. In one review of Lyme carditis patients with third-degree AVB, 40% of patients presented without EM and had syncope as the only presenting symptom.[6] Therefore, although the presence of EM is a very useful diagnostic indicator to suggest Lyme carditis, the absence of EM does not rule out Lyme carditis.

## Diagnosis of Lyme carditis

Lyme carditis diagnosis is confirmed via Lyme serology **[Figure 5]**.[4] To aid in the clinical diagnosis and empiric treatment of Lyme carditis, Besant and colleagues[14] developed and validated a highly sensitive (93%) risk stratification score called the suspicious index in Lyme carditis (SILC) score **[Table 1]**, which evaluates the pretest probability that a patient's new onset AVB is caused by Lyme carditis. The variables of the SILC score can be associated with the mnemonic CO-STAR: constitutional symptoms, outdoor activity/endemic area, sex = male, tick bite, age < 50 years, and rash (EM).[14] Patients with a high-degree AVB and a SILC score > 2 have an intermediate or high pretest probability of Lyme carditis; therefore, they should be tested for Lyme serology and begin empiric antibiotic treatment for Lyme carditis while serology results are pending.[4] Patients with a high-degree AVB and a SILC score ≤ 2 have a low pretest probability of Lyme carditis; therefore, they should undergo standard treatment for high-degree AVB and should not receive empiric antibiotic treatment.[4] These patients generally do not require Lyme serology testing, but because each clinical situation is unique, the decision to test ultimately rests with the clinical judgment of the health care team.

Lyme serology is a two-tiered test: (1) enzyme-linked immunoassay (EIA), which, if positive, is followed by (2) Western blot for confirmation **[Figure 5]**.[15] However, it is important for clinicians to note that whole cell EIA can be falsely negative in early Lyme carditis; therefore, a negative serology result does not rule out Lyme carditis.[9] If Lyme serology is negative but there is high clinical suspicion of Lyme carditis, such as a SILC score > 2, the patient should be empirically treated for Lyme carditis. In this case, a C6 peptide EIA test may be appropriate because it is a more sensitive test for early Lyme carditis than the standard

**TABLE 1. Suspicious index in Lyme carditis (SILC) score.** (Source: Besant and colleagues[14])

| Variable | Points* |
|---|---|
| Constitutional symptoms† | 2 |
| Outdoor activity or endemic area | 1 |
| Male sex | 1 |
| Tick bite | 3 |
| Age < 50 years | 1 |
| Erythema migrans | 4 |

* 0–2: Low pretest probability of Lyme carditis
3–6: Intermediate pretest probability of Lyme carditis
7–12: High pretest probability of Lyme carditis
† Fever, malaise, arthralgia, dyspnea

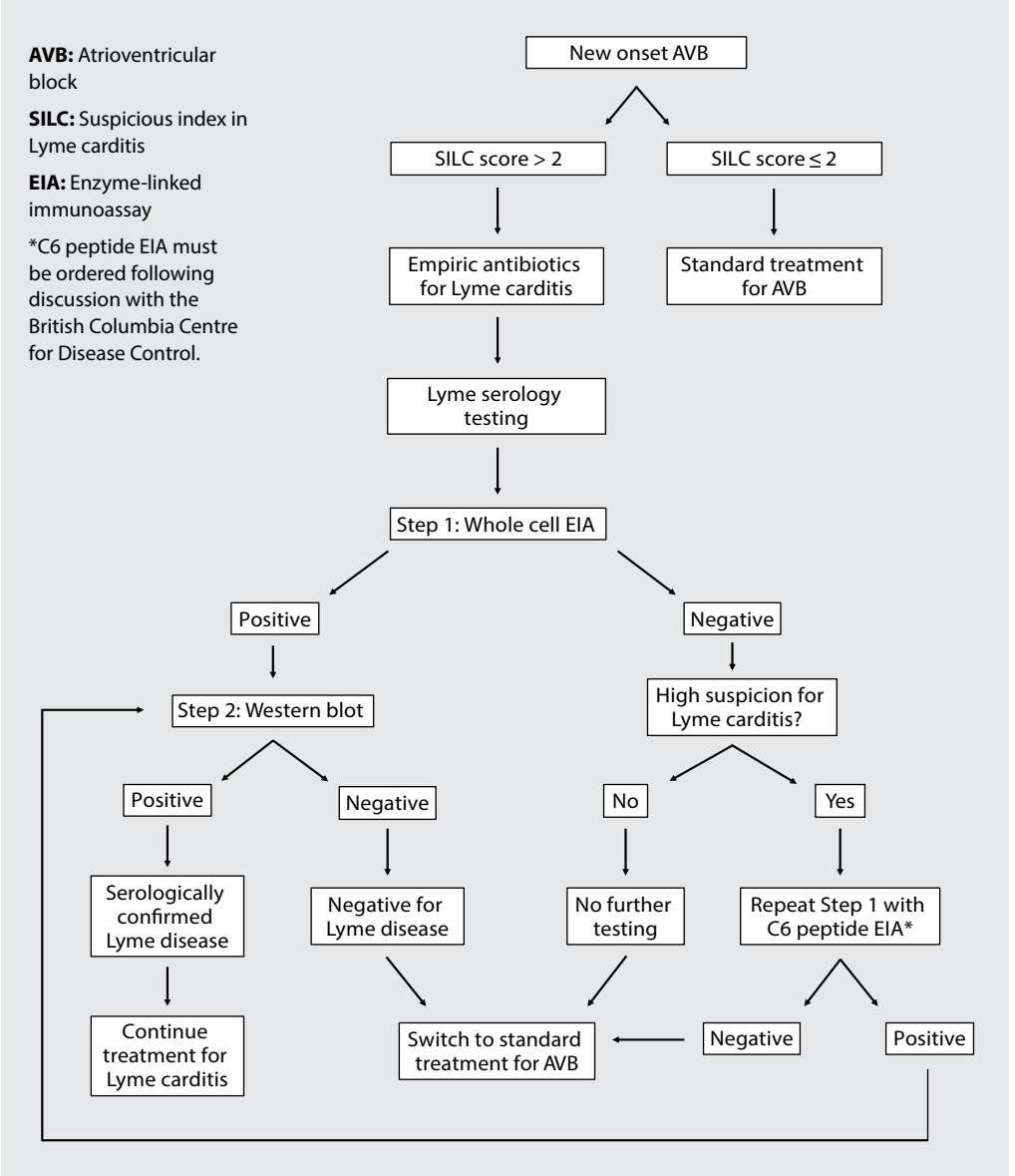


**FIGURE 5.** Proposed diagnostic and treatment algorithm for Lyme carditis.

methodology of whole cell EIA.[16] In BC, most clinicians cannot independently order the C6 peptide EIA test; it must be ordered following discussion with the BC Centre for Disease Control. A positive C6 peptide EIA still needs to be followed by a Western blot for confirmation. Further details on Lyme serology testing can be found in Scheffold and colleagues[9] and Marques.[15]

## Treatment of Lyme carditis

Lyme carditis is fully reversible with timely and appropriate antibiotic therapy: most cases of AVB resolve within the first 10 days of antibiotic administration.[4,9] The choice of antibiotic treatment varies based on the severity of the presentation **[Table 2]**. Treatment should be started immediately after Lyme carditis has been clinically diagnosed. It is especially important not to wait for serology results before initiating antibiotic treatment because increased morbidity and mortality can occur, as seen in a recent case of Lyme carditis in New England.[17]

Because the AVB is fully reversible with appropriate antibiotic therapy, permanent pacemaker placement is usually not indicated for Lyme carditis, though a temporary transvenous pacemaker is required in 33% of cases.[4] The indications for temporary pacing are symptomatic bradycardia, hemodynamic instability, or high-risk features on ECG, such as alternating bundle branch block.[4] With appropriate antibiotic treatment, AV conduction is restored in a stepwise fashion from-third degree AVB **[Figure 1A]**, to second-degree AVB **[Figure 1B, 1C]**, then first-degree AVB **[Figure 1D]**, then back to normal.[4]

Yeung and Baranchuk[4] outlined an excellent pre- and post-discharge cardiac testing protocol for Lyme carditis patients. Once 1:1 AV conduction is restored, the temporary pacemaker can be removed. A predischarge stress test is recommended to assess the stability of the AV conduction and the need for a permanent pacemaker. All Lyme carditis patients should also have an outpatient ECG at 4 to 6 weeks postdischarge to assess for rhythm or conduction abnormalities.

## Summary

Clinicians should consider Lyme carditis in the differential diagnosis of new onset AVB. Clinical clues for diagnosing Lyme carditis include the following: a young patient without a history of cardiovascular disease, presence of flu-like symptoms, history of tick bite and/or travel to an endemic area for Lyme disease 1 to 2 months prior to the onset of AVB, and the presence of EM. Early detection and treatment of Lyme carditis will reduce the incidences of morbidity and mortality from this rare but important manifestation of Lyme disease. ■

**Competing interests**

None declared.

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**TABLE 2. Antibiotic treatment for Lyme carditis.[1,4]**

| Presentation | Line of treatment | Antibiotic | Duration of therapy |
|---|---|---|---|
| 1st degree AVB* | 1st | Doxycycline 100 mg PO BID | 14–21 days |
| | 2nd | Amoxicillin 500 mg PO TID | |
| | 3rd | Cefuroxime 500 mg PO TID | |
| | 4th | Erythromycin 250 mg PO QID | |
| 2nd or 3rd degree AVB | 1st | Ceftriaxone 2 g IV q24h | 10–14 days,† followed by oral antibiotics‡ |
| | 2nd | Cefotaxime 2 g IV q8h | |
| | 3rd | Penicillin G 5 million U IV q6h | |

*AVB: atrioventricular block
†Until 1:1 atrioventricular conduction is restored
‡Combined total course of IV and oral antibiotics should be 14–21 days

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