Lyme disease and the heart in the UK

Heart involvement from Lyme disease is uncommon in the UK but, when it does occur, can be rapidly progressive and require intensive therapy. A history of exposure and frequently a characteristic rash (erythema migrans) are the cardinal features in diagnosis.

Lyme disease is a tick-transmitted infection caused by several genospecies of the spirochaete *Borrelia burgdorferi* (*Figure 1*), which can affect the skin, nervous and musculoskeletal systems and occasionally the heart. Eighteen years ago a commentary in the *British Heart Journal* reported an annual incidence of 200 serologically confirmed cases of Lyme disease in the UK (Hayward et al, 1993). Has the clinical picture changed and was it correct for Hayward et al (1993) to conclude that a 'relentless spread' of Lyme disease was unfounded?

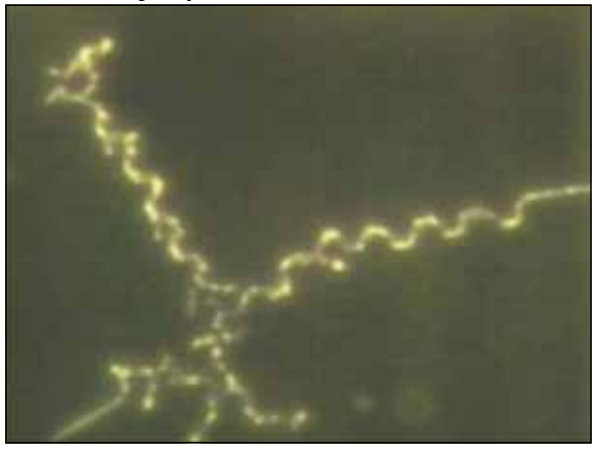
Epidemiology

Well-known UK foci for Lyme disease include the New Forest, Exmoor, Salisbury Plain, the South Downs, rural Wiltshire, Berkshire, Surrey, Sussex, Thetford Forest, north Yorkshire moors, the Lake District, Scottish Highlands and Islands. Other areas with suitable habitat (mixed deciduous woodland and heathland) occur throughout the country, including large urban deer parks such as Richmond and Bushy in London. Countries within Europe with a high incidence of Lyme disease include Slovenia, Sweden (south), Austria, Bulgaria, Estonia, Switzerland, the Czech Republic, Netherlands, Germany and Lithuania (European Concerted Action on Lyme Borreliosis, 2009b).

Reports of serologically confirmed cases probably underestimate the true incidence. In 2009 the Health Protection Agency reported 973 cases of Lyme borreliosis. Of note, 800 of these were indigenous (England and Wales) and 173 people (18%) acquired the infection abroad. The Health Protection Agency (2011) estimate that closer to 3000 cases may occur annually. In 2009, 68% of serologically confirmed cases were diagnosed between July and October, related to peak tick feeding activity in the late spring and early summer. However, only a minority of ticks in the UK carry borreliae (The Deer Initiative, 2007; Health Protection Agency, 2011). The incidence of Lyme disease is influenced by numerous ecological factors affecting tick populations and the small mammal and bird reservoir hosts of *B. burgdorferi*. These include climatic factors and burgeoning deer numbers (European Concerted Action on Lyme Borreliosis, 2009a). Estimates of wild deer populations suggest there are now more in the UK than at any time in the last 1000 years (around 1.15 million red and roe deer and over 300 000 fallow, muntjac and sika species) (The Deer Initiative, 2007). Human residential, recreational and occupational factors are also important.

This article focuses on heart involvement as one of the more sinister and sometimes acute manifestations of this infection. Extensive reviews and position statements on Lyme borreliosis have been published (Map of Medicine, 2010; British Infection Association, 2011; Stanek et al, 2011).

Figure 1. An electron micrograph showing the typical spirochaetes of the* Borrelia *genospecies.



Clinical features

In common with syphilis, another spirochaete infection, Lyme disease can have three clinical phases (*Table 1*). The progression from an early localized phase to a late stage disease occurs in only a small minority of untreated infections, and some infections can be asymptomatic (Stanek and Strie, 2003; Bratton et al, 2008). A greater range of clinical presentations is seen in European-acquired infections compared to American infections, presumably related to the wider range of pathogenic genospecies in Europe. *B. burgdorferi sensu stricto*, the only pathogenic genospecies found in the USA, also occurs in some parts of Europe (Stanek and Strie, 2003). In addition four other pathogenic genospecies, *B. afzelii*, *B. garinii*, *B. bavariensis* and *B. spielmanii* are found in Europe (European Concerted Action on Lyme Borreliosis, 2009b). *B. garinii* predominates in western Europe with

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B. afzelii more prevalent in northern, central and eastern Europe. *B. burgdorferi sensu stricto* is the most acutely pathogenic and the most frequently associated with cardiac complications. In recent years two or three cases with cardiac manifestations have been reported in the UK annually; some were acquired in the USA.

In the early phase (3–30 days post tick bite), erythema migrans, an expanding erythematous rash that can take on an annular 'target-like' appearance (*Figure 2*), develops in around 60–80% of serologically confirmed cases. Many erythema migrans rashes are homogenous; central clearing is a feature arising with duration, although less frequently seen as a result of earlier recognition and treatment. The border can be flat or slightly raised, a feature dependent on the infecting genospecies. The diameter may extend from 5–100 cm (mean 15 cm) (Stanek and Strie, 2003; Bratton et al, 2008). Other features are listed in *Table 1*.

In the second 'early disseminated' phase, cardiac and neurological involvement can occur. Around 10% of untreated people develop late neurological features (*Table 1*).

Cardiac features

In keeping with this infection having a predilection for the nervous system, heart involvement usually presents as varying degrees of atrioventricular block, and appears to be more common in infections acquired in the United States. Bundle–branch block, QT interval prolongation, ST segment (including those associated with pericarditis) and T-wave changes, sinoatrial node dysfunction and sinus node arrest are also reported. Heart block is usually reversible within a few days (median 3 days, range 1–7 days) (Costello et al, 2009). Estimates for the requirement for temporary pacing in the USA range from 'infrequent' (Costello et al, 2009) to over 30% in one study of Lyme carditis patients (Bratton et al, 2008). In an early meta-analysis of 105 American and European patients, the frequency of observed atrioventricular block was similar, with 12% having first degree, 16% second degree and 49% third degree atrioventricular block (Van der Linde et al, 1990). With prompt appropriate antibiotics the development of chronic heart block is an unusual event. However, progression of conduction system involvement may be rapid and can require intensive monitoring in a coronary care unit with facilities for transvenous pacing and haemodynamic support. The long-term prognosis for Lyme carditis with treatment is usually excellent.

Myocarditis, requiring confirmation by endomyocardial biopsy (*Figure 3*), remains unusual in the UK. Histology in these cases shows infiltrates of plasma cells, lymphocytes, macrophages and myocyte necrosis (Van der Linde et al, 1990). Most reported cases are from the United States or mainland Europe, probably reflecting a higher overall incidence of the disease in hyper-endemic areas of these regions (Stanek et al, 2011). European and Scandinavian estimates for heart involvement lie between 1 and 10% of cases of Lyme disease (Groner et al, 1992; Friman et al, 1995), possibly biased by being early tertiary referral reports. In more recent European prospective studies, about 90% of cases presented with erythema migrans and <1% with cardiac involvement (Stanek and Strie, 2003). The aetiology of both myocardial and atrio-

Table 1. Stages and clinical features of Lyme borreliosis

Phase of Lyme disease	Nomenclature	Clinical features
First phase	Early localized	Erythema migrans
		Flu-like symptoms, limited pyrexia
		Headache, myalgia, arthralgia, local lymphadenopathy
		Borrelia lymphocytoma (uncommon and frequently involves earlobe or nipple)
Second phase	Early disseminated	Multiple erythema migrans lesions (<5 cm diameter and unusual in the UK)
		Sweats, myalgia
		Viral-like meningitis
		VII cranial nerve palsy (can be bilateral)
		Other cranial nerve palsies
		Mononeuritis multiplex
		Radiculopathies
		Cardiac conduction disturbances
		Myocarditis
		Pericarditis
		Cardiomyopathy and heart failure (rare)
Third phase	Late disseminated	Oligoarthritis
		Acrodermatitis chronica atrophicans
		Sensory neuropathy
		Encephalomyelitis

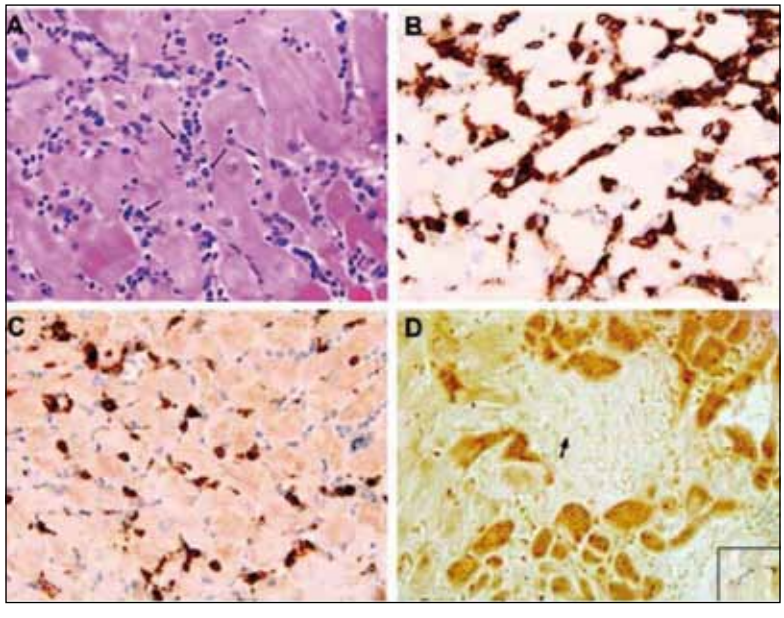
Figure 2. The target lesion of erythema migrans. This classic morphology is more commonly found in Europe than in North America.

ventricular conduction tissue injury is likely to be the result of direct invasion of cardiac tissues by spirochaetes and the resultant inflammatory process (de Koning et al, 1989; Fish et al, 2008).

Clinical evidence of a cardiomyopathy and development of heart failure in association with Lyme disease is very rare in the UK and few cases have been reported in Europe. Cardiac involvement should be considered, in a person likely to have been exposed to ticks, if a patient complains of palpitations, dizziness, becomes breathless, syncopal or develops chest pains and/or has any degree of heart block on his/her electrocardiogram. European Cardiac Society guidelines (Task Force for Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of European Society of Cardiology, 2008) currently include determining borrelia serology status in patients with dilated cardiomyopathy and heart block. However, determining that a patient with dilated cardiomyopathy, is seropositive for borrelia does not confirm Lyme disease as the cause, as background seropositivity can be high (up to 20%) in some European endemic regions (Wilske et al, 2007; Stanek et al, 2011).

A recent case report describes a patient, seen in the UK, who developed a cardiomyopathy (global hypokinesia on echocardiography with an ejection fraction of 35–40%) and severe orthostatic hypotension; the latter likely to be the result of autonomic complications of Lyme neuroborreliosis. The patient had been camping in the Czech republic, a recognized risk area, some months earlier. He reported a typical rash and was found to be strongly positive for borrelia immunoglobulin G in serum and CSF (Burman et al, 2011).

Figure 3. a. Endomyocardial biopsy from a 14-year-old child with Lyme carditis showing an extensive interstitial lymphoplasmacytic infiltrate associated with myocyte damage and necrosis. Arrows indicate plasma cells. b. Interstitial CD20+ B lymphocytes are numerous. c. CD3+ T lymphocytes were also present but in a lesser number than the B lymphocytes. d. A Steiner stain for microorganisms revealed rare interstitial spirochaetes. The spirochaete indicated by the arrow is better seen at higher magnification in the inset. From Costello et al (2009).



In support of *B. burgdorferi* infection as a cause of myocarditis, spirochaetes have been demonstrated in cardiac biopsies (*Figure 3*) and within myocardial capillaries from some seropositive patients (Cary et al, 1990; Stanek et al, 1990). *B. burgdorferi* have also been cultured from hearts of patients with dilated cardiomyopathy (de Koning et al, 1989), although causality cannot be presumed (Stanek et al, 2011).

Only one case of fatal probable Lyme carditis appears in the UK literature; a 31-year-old farm worker dying suddenly with features of an inflammatory pan-carditis and complete heart block (Cary et al, 1990). However, this may have been an incidental seropositive in someone with heavy long-standing tick exposure.

Untreated patients may develop late manifestations of Lyme disease (*Table 1*). Autoimmune processes may contribute to the pathogenesis of these late stage presentations. All stages of active infection will respond to antibiotic therapies but the extent of recovery following treatment of late stage disease will depend on the degree of damage sustained pre-treatment (Stanek and Strie, 2003; Stanek et al, 2011).

Following apparently adequate treatment a small proportion of patients can continue to experience persistent subjective features of fatigue, musculoskeletal pain and neurocognitive symptoms, without laboratory evidence of active infection. This has been termed 'post-Lyme disease syndrome' and appears similar in presentation and incidence to other post-infection syndromes (Map of Medicine, 2010). The prevalence and diagnosis of this aspect of the disease remains a matter of some controversy (Feder et al, 2007). Repeated or prolonged courses of antibiotics have not shown benefit in randomized prospective studies (Stanek et al, 2011).

Diagnosis

Lyme disease should be considered in people who have had contact with ticks and have symptoms and signs suggesting infection. Serological screening tests, demonstrating IgG and IgM antibodies to *B. burgdorferi*, are the usual starting point for laboratory diagnostic support (British Infection Association, 2011; Stanek et al, 2011). However, antibodies may not be detectable in the first 2–4 weeks following infection and a later sample should be tested if there is a high index of suspicion. If positive, the more specific Western blot (immunoblot) test should be used for confirmation, as screening tests have significant risk of false-positive reactions. If a cardiac biopsy is performed, then this can be examined for spirochaetes. Polymerase chain reaction analysis is not useful on blood or urine, because of the lack of target borreliae DNA, but is good using skin or synovium and will be much more effective than culture on cardiac biopsies. In the UK, advice on investigation of suspected patients may be sought from the Lyme Borreliosis Unit in Southampton.

Prevention and treatment

Use of insect repellent and early removal of attached ticks are valuable infection prevention measures (Bratton et al, 2008; European Concerted Action on Lyme Borreliosis, 2009a). The management of adult patients with cardiac involvement not requiring pacing involves the use of oral doxycycline (100 mg twice daily) or amoxicillin (500 mg three times per day) or cefuroxime (500 mg twice daily) for 14–21 days. Late or severe disease requires intravenous antibiotics, usually with ceftriaxone (2 g once daily) for 2–4 weeks (Feder et al, 2007). Cardiac patients would usually finish their course of treatment with oral therapy once pacing or intravenous access is no longer required.

Adults with acute cardiac involvement not requiring pacing should receive oral doxycycline (100 mg twice daily) or amoxicillin (500 mg three times per day) or cefuroxime (500 mg twice daily) for 14–21 days. Patients requiring pacing should initially receive intravenous antibiotics, usually ceftriaxone (2 g once daily), switching to oral antibiotics once pacing or intravenous access is no longer required (Stanek et al, 1990; Fish et al, 2008). Those with late or severe disease should receive ceftriaxone for 2–4 weeks.

Recommended doses for children are: amoxicillin 50 mg/kg/day in three divided doses, cefuroxime 15 mg/kg twice daily, doxycycline 2.5 mg/kg twice daily and ceftriaxone 50–75 mg/kg daily, up to the adult dose recommendations. Doxycycline is not recommended for children aged <8 years (<12 years in the UK).

Conclusions

There has undoubtedly been a significant increase in the number of cases of Lyme disease over the last 20 years even though the disease continues to be under-reported. A strong history of exposure and recognized clinical features (usually erythema migrans) are essential to making the diagnosis. Enquiry into travel is important as many cases are acquired abroad and Lyme disease remains the commonest arthropod-borne disease in the temperate northern hemisphere. Within the UK, the 'relentless spread' of Lyme disease, and particularly Lyme carditis, does not appear to have materialized. **BJHM**

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Conflict of interest: none.

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KEY POINTS

- Lyme disease is a tick-borne disease that affects the skin, musculoskeletal and nervous system and only occasionally the heart.
- The cardinal features are the characteristic rash (erythema migrans) and usually a history of exposure to ticks.
- Heart involvement, while rare in the UK, can be rapid and necessitate temporary cardiac pacing and an intensive care unit environment.
- With appropriate and prompt antibiotics, recovery from Lyme disease is usually complete without long-term sequelae.
- Controversy exists regarding the existence of a specific 'post-Lyme disease' syndrome.