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Lyme disease often under diagnosed says HPSC

Introduction

Lyme disease is an infection caused by various genospecies of the spirochete, *Borrelia burgdorferi*¹ and transmitted to humans by the bite of an infected tick. The clinical course is generally mild and affects only the skin. Occasionally, however, it can be more severe, leading to extensive, systemic involvement of the nervous system and heart.

The causative agent was first identified in 1982, following identification of a cluster of cases of an atypical juvenile arthritis, thought initially to be autoimmune in nature and centred on the town of Lyme, Connecticut seven years earlier. Cases of Lyme disease are common in North America and in Northern and Central (and to a lesser extent in Western) Europe. Lyme disease is the commonest cause of tick-borne infection in Europe.²

Campers, walkers and certain occupational groups such as forestry workers, conservation workers, deer cullers and farmers would appear to be at particular risk of exposure. The ticks responsible are generally hard-bodied ticks (*Ixodidae*). Ixodes ticks are hosted by a wide range of mammals including deer, sheep and cows; their tiny size (less than 2mm unfed) means they can remain undetected for long periods. Transmission of spirochetes tends to occur late in a feed and is unlikely if the tick has been attached for less than 18-24 hours. They tend to gravitate towards areas with thinnest skin; the groin and armpit. Risk of infection is greatest in late spring and early summer.

Since first being described, more than 150,000 cases have been reported in the US with highest incidence rates being seen in New England; US State Epidemiology Departments reported 28,921 confirmed cases and 6,277 probable cases of Lyme disease to the Centers for Disease Control and Prevention (CDC) in 2008.³

In Europe, similarly high rates are seen in Germany, but forested regions of Austria, Sweden and Slovenia frequently report cases as well. In England, Lyme disease is considered to be endemic in the New Forest area of Hampshire.

Incidence

Lyme disease is notifiable in neither Ireland nor in England and Wales (there is no statutory responsibility on clinicians to report cases) and estimates of the true level of the disease are difficult to determine. The latest available figures from the Health Protection agency in London indicate that in 2008, there were 813 reported cases of the disease in England and Wales, a slight increase on the 794 cases reported in 2007.⁴

It is estimated that the true figure in England and Wales may be considerably higher. In Scotland, where there is a responsibility on clinicians to report disease, the number of reported cases has risen over the last

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few years; from 28 in 2001, to over 285 in 2008.⁵

In 2007, 71 specimens, referred to the HPA's Lyme Borreliosis Unit in Southampton from Irish hospital laboratories, were confirmed positive for Lyme borreliosis, suggesting a crude incidence rate of 1.67 per 100,000 for Lyme borreliosis in Ireland that year (Dr. Sue O Connell, HPA UK, and Dr. Robert Smith, Public Health Wales, personal communication). However, a recent study in the west of Ireland reported by Moloney & colleagues at GUH suggests that the disease incidence may be higher in the Galway area.⁶

Clinical Features

Lyme disease is a diagnosis that is often overlooked by clinicians. Anecdotal evidence suggests that individuals displaying symptoms are much more likely to be tested for Lyme disease, in Ireland, if they give a history of recent travel to the north-eastern United States, despite the fact that there is considerable evidence that a significant proportion of cases seen in Ireland have been exposed locally.

The earliest, and often only, manifestation of Lyme borelliosis is the pathognomonic erythema migrans (a circular erythematous rash spreading peripherally from the central site of a tick bite, often taking on a "bull's-eye" appearance – see Figure 1 below). This is seen in 70-80% of infections and develops between 3 and 30 days following a tick bite. Because of this Lyme disease is primarily a clinical diagnosis. In the US, Lyme diagnosis is based on symptoms, objective physical findings (for example erythema migrans, facial palsy, or arthritis), and a history of possible exposure to ticks. Laboratory testing in the US tends to be used as an adjunct, especially when a patient presents with obvious erythema migrans.

Figure 1. Erythema migrans following tick bite on medial surface upper arm, showing classical "bulls-eye" appearance. (Photo courtesy of CDC/ James Gathany)



Complications

A minority of patients may complain of nonspecific 'flu-like symptoms with headache, malaise and myalgia. Neuroborreliosis tends to be the commonest serious complication in Europe, leading to facial palsy, meningitis, peripheral motor and sensory manifestations including paraesthesiae and weakness. Other complications including Lyme arthritis, myocarditis and ocular Lyme are rare in Europe but seen more commonly in the US. Some authorities use staging regimes to categorise clinical cases.²

More serious complications involve:

- Joints: arthritis which can recur over many years
- Heart: myocarditis with irregularities of heart rhythm
- Eye: conjunctivitis and eye pain.

- Nervous System: numbness and weakness, meningitis/encephalitis and Bell's palsy (facial paralysis).

A small proportion of patients may go on to develop a post infection syndrome resembling chronic fatigue syndrome, termed 'post-Lyme syndrome'. Similar symptoms can be triggered by other infectious and non-infectious conditions. The frequency of serious complications varies. Cases contracted in North America tend to be more severe in every sense than those contracted in Europe. Between 10% and 20% of untreated cases will go on to develop nervous system symptoms. Arthritis will develop in about half of untreated cases, while cardiac complications will occur in fewer than 10% of subjects not receiving antibiotics. There is currently no effective human vaccine to protect against Lyme disease, and little sign that one can be expected soon.⁷

Diagnosis

As culture of *Borrelia* from body fluids is such a challenging and specialised process, testing for Lyme borelliosis commonly relies on identification of *Borrelia*-specific antibodies. CDC recommends a two-step process when testing for evidence of Lyme disease – initial ELISA or IFA test followed by confirmatory Western immunoblot if the initial test is positive.⁸ This system is the one currently most recommended by European authorities. The antibody response takes several weeks to reach a detectable level, so antibody tests in the first few weeks of infection may be negative. It is very uncommon for patients to have negative antibody tests in longstanding infections.⁸

Lyme disease is not currently one of the notifiable diseases stipulated in S.I. No. 707 of 2003. When there is not the legal onus on practitioners to report cases of an infectious disease, the knowledge we have about such disease is, accordingly, incomplete. Notification allows identification in a more systematic way, and facilitates following trends in the disease over time.

Treatment

Lyme disease can be very successfully treated using common antibiotics. These antibiotics are effective at clearing the rash and helping to prevent the development of complications. Antibiotics are generally given for up to three weeks. If complications develop, intravenous antibiotics may be considered.

In Ireland, treatment by most clinicians is based on that laid out in evidence-based guidelines for the management of patients with Lyme disease, human granulocytic anaplasmosis (formerly known as human granulocytic ehrlichiosis), and babesiosis published by the Infectious Diseases Society of America (IDSA) in 2006.⁹ This pharmacological regime can be summarised thus:

- Doxycycline, amoxicillin or cefuroxime for the treatment of adults with early localized or early disseminated Lyme disease associated with erythema migrans, in the absence of specific neurologic manifestations (ceftriaxone in early Lyme disease for adults with acute neurologic disease manifested by meningitis or radiculopathy)
- Doxycycline, amoxicillin, or cefuroxime for adults with Lyme arthritis but without clinical evidence of neurologic disease
- For late neurological disease in adults - intravenous ceftriaxone, cefotaxime or Penicillin G.

In 2008, controversy arose around these guidelines in that the Connecticut Attorney General accused the IDSA of harbouring conflicts of interest, and launched an investigation under antitrust statutes, claiming that the IDSA monopolised treatment standards. Under an agreement struck between the Attorney General of Connecticut and IDSA, the guidelines for the management of patients with Lyme disease remain in effect.

These guidelines have been endorsed by the Health Protection Agency in London who considered that the IDSA Guidelines “continue to represent the best available synthesis of the medical literature on the diagnosis and treatment of Lyme disease available in the English language, and they are in keeping with European expert recommendations”.¹⁰

Prevention

The main method of prevention of Lyme disease is avoidance of tick bites. Information for walkers and others whose work or leisure may take them through habitats where contact with ticks is likely is available on the [HPSC's website](#).

The principal advice for people who may be at risk involves advising them to:

1. Walk in the middle of paths/trails; avoid sitting on logs or leaning against trees.
2. Wear a hat and tuck in hair if possible.
3. Wear a long sleeved shirt fitted at the wrist.
4. Wear shoes, not sandals or bare feet.
5. Wear long trousers tucked into socks or boots.
6. Consider using an insect repellent containing DEET (N,N-Diethyl-meta-toluamide). Follow the manufacturers' application guidelines.
7. Wear white or light coloured clothing to make ticks more visible and inspect clothes every 3-4 hours.
8. At the end of your day out, check yourself (and your children) for ticks. Check both skin and hair, paying particular attention to warm moist areas such as the groin, backs of knees, armpits and neck.
9. If you find a tick, remove it as described [here](#) and consult your GP if symptoms develop.
10. Check your pets for ticks following outdoor activities

Dr Paul McKeown and Dr Patricia Garvey HPSC

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