Lyme borreliosis

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Abstract

Lyme borreliosis is a tick-transmitted spirochaetal infection caused by pathogenic genospecies of *Borrelia burgdorferi* sensu lato. It occurs in wooded and heathland areas of temperate regions of the northern hemisphere. The most common clinical presentation is an erythematous rash slowly spreading from the site of a tick bite. Spirochaetes can spread hamatogenously and affect other organs and tissues, particularly the nervous system and joints. Manifestations of disseminated infection include facial palsy, viral-like meningitis, radiculopathy, meningoencephalitis and arthritis. The infection responds to antibiotic treatment at all stages, but early recognition and treatment is strongly recommended to avoid possible development of complications. Patients with long-standing infection and significant tissue damage can have slow or incomplete recovery. A small minority of appropriately treated patients can have persistent non-specific symptoms, similar to those seen following some other infections. Controlled trials in patients with post-Lyme symptoms have shown no evidence of persistent infection and no sustained benefit from prolonged antibiotic treatment. Prevention measures focus on tick and disease awareness, avoidance of tick-infested areas where possible, use of insect repellents, frequent skin inspections for attached ticks, particularly at the end of the day, as early removal minimizes the risk of infection transmission. No vaccine is available.

Keywords acrodermatitis chronica atrophicans; *Borrelia burgdorferi*; erythema migrans; facial palsy; Lyme arthritis; Lyme borreliosis; meningitis; neuroborreliosis; radiculopathy

What's new?

- An excellent neuroborreliosis treatment trial published in 2008 showed oral doxycycline (200 mg daily for 14 days) to be non-inferior to intravenous ceftriaxone (2 g daily for 14 days)
- Further improvements in diagnostic tests include recombinant and peptide antigen-based antibody tests with greater specificity, and a greater variety of DNA detection methods
- Additional trial data supported findings from earlier studies, showing that patients with post-Lyme syndrome do not gain sustained benefit from prolonged antibiotic treatments, which can cause potentially dangerous adverse events
- Over-diagnosis and mistreatment continue to be major concerns, driven by misinformation, especially on the Internet

Lyme borreliosis (Lyme disease) is caused by the tick-borne spirochaete *Borrelia burgdorferi*. Erythema migrans, an early skin lesion, is the most common clinical presentation. The organism can spread, causing various later manifestations, including facial palsy, viral-like meningitis, radiculitis and arthritis, usually affecting the knee.

Epidemiology and environmental factors

Lyme borreliosis is the most common tick-borne infection in the temperate northern hemisphere. More than 27,000 cases were reported in the USA in 2007, predominantly from northeast and mid-Atlantic seaboard states, north-central and Pacific coast states.[1] There may be over 200,000 European cases annually. The infection is particularly prevalent in parts of southern Scandinavia, Germany, Austria and other Central European countries.[2] In the UK, about 1,000 cases are serologically confirmed annually.[3] Infection can occur at any age, and is most likely in individuals whose residence, or occupational or recreational activities place them at high risk of tick bites.

Ixodid ticks (deer ticks; sheep ticks) (Figure 1) are the vectors of *B. burgdorferi*.[2] They are common in woodland, heath and moorland but can also live in semi-rural areas bordering large population centres. They take a single blood meal in each of the three stages of their 2–3-year life-cycle (Figure 2), attaching themselves to their hosts by barbed mouth-parts. An infected tick can transmit borreliae towards the end of its feed, regurgitating infected saliva into the animal's skin. Reservoir hosts for the spirochaetes include small and medium-sized mammals (e.g. field mice, hares) and birds, including blackbirds and pheasants.[2] Human beings are incidental hosts for ticks, and infections occur mainly in late spring, early summer and autumn — the peak periods for tick feeds.[1–3] The annual incidence of Lyme borreliosis can vary, depending on climatic and other factors affecting tick population density and activity and on human activities in tick habitats.

Nymphal ticks, the main sources for human infection, are very small and can be overlooked. Tick bites are often not recognized because they do not usually cause significant pain, irritation or itch. People exposed to ticks can minimize their risk of infection by wearing protective clothing (light-coloured long-sleeved shirts and long trousers) and using DEET-containing insect repellents. They should check regularly for attached ticks, especially at the end of the day, and remove them gently, preferably using tweezers or a tick hook as close as possible to the skin.[1–3] It is particularly important to check the head and neck areas (including scalps) of young children (Figure 3). Borrelial infection is unlikely to occur when ticks are attached for less than 24 h, so prompt removal is a valuable preventive measure.

Ixodid ticks can also carry other organisms, including ehrlichiae, babesiae, and, in parts of Europe, tick-borne encephalitis virus.[2] Co-infections can occur and can cause atypical presentations.

Pathogenesis

At least four genospecies of *B. burgdorferi* are pathogenic, and borrelial heterogeneity is significant in organotropism and disease presentation. Only one genospecies (*B. burgdorferi* sensu stricto) appears to cause human infection in North America, and

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Figure 1 Ixodid tick.

can cause neurological and arthritic complications.[1] At least two other pathogenic genospecies occur more commonly in Europe — *Borrelia garinii*, which is particularly associated with neurological complications, and *Borrelia afzelii*, associated with later skin manifestations and occasionally with neuroborreliosis.[2] *Borrelia spielmanii* occasionally causes erythema migrans. Antigenic heterogeneity also has implications for vaccine development strategies.

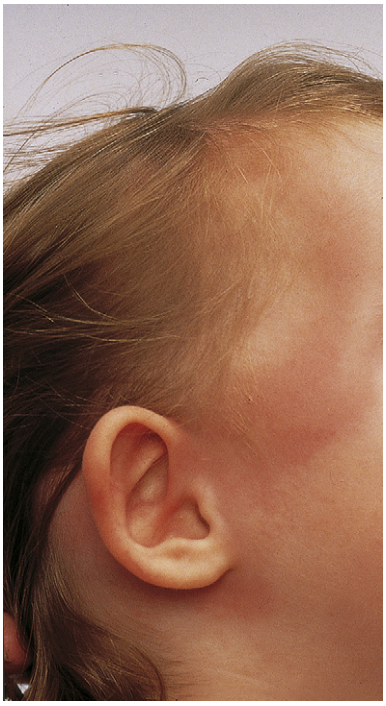

Figure 3 Erythema migrans on face of 2-year-old child who had received a tick bite on her scalp 10 days previously.

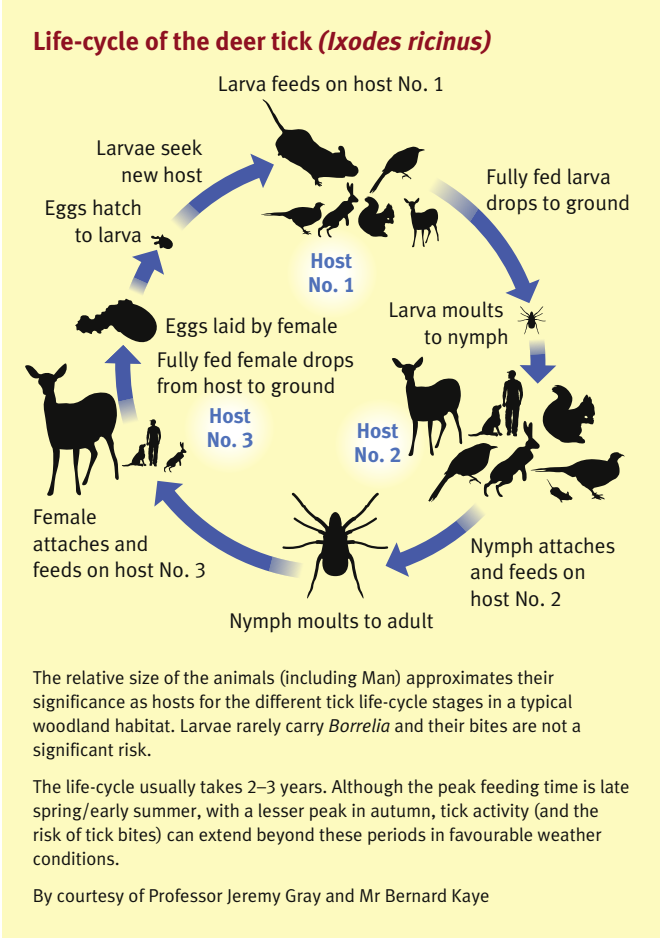

Figure 2

B. burgdorferi can spread directly and via the bloodstream and lymphatics to many tissues, and can migrate through the blood–brain barrier. Changes in outer surface protein (Osp) expression, from OspC in the early stage to others (including OspA and OspB) in established infection, can help the organism evade the host immune response. Spirochaetal invasion and cytokine mediation have been implicated in the pathogenesis of neuroborreliosis. Experimental evidence suggests that borrelial lipoproteins adhere to cells and promote vigorous inflammatory reactions. Antibodies produced in response to spirochaetal antigens may also cross-react with axonal tissue components.[4] Lyme arthritis may be caused partly by cytokine activity, Certain individuals (particularly those with HLA DR4 alleles) can be genetically predisposed to antibiotic-refractory Lyme arthritis, which persists for some time following successful antibiotic treatment of the infection, and can require anti-inflammatory treatments.[5]

Clinical features

Infection can be asymptomatic. Clinically significant disease has been customarily divided into three stages, but the process should be regarded as a continuing pathological evolution rather than having distinct phases. Progression to later-stage disease is not inevitable, even in untreated patients.[6] European experts estimated that late neuroborreliosis occurs in less than one in 1,000 previously untreated patients.

Localized infection: the most common clinical manifestation is erythema migrans, a localized, red or pink rash appearing after 2–30 days (usually 5–15 days) at the site of a bite (Figures 3 and 4).[6,7]

The rash can be faint, with a more pronounced margin that gradually migrates outwards to produce a sizeable lesion. A