Lyme Disease: ecology, epidemiology and prevention

by Edward R Wilson ¹ and Kevin J Smith ²

¹Medical School, University of Sheffield, Beech Hill Road, Sheffield, England S10 2RX.

Corresponding author. Email: mda06erw@sheffield.ac.uk

² Yorkshire and the Humber Specialised Commissioning Group, Hillder House, 49-51 Gawber Road, Barnsley, South Yorkshire, England S75 2PY.

Summary

Lyme disease is caused by the bite of a tick that is infected with spirochete bacteria of the genus *Borrelia*. It has emerged over the past three decades as the most important vector-borne infection in Europe and North America, and is associated with woodland habitats and green space. Those working in and visiting tick areas are most at risk of acquiring the infection. This paper presents an overview of the ecology, epidemiology, clinical presentation and control of Lyme disease. Emphasis is placed on public health aspects of the infection, including raising awareness of the disease, reducing the risk of being bitten and safe removal of ticks.

Introduction

Lyme disease is the most important vector-borne infection in Europe and North America (Steere 2001). It is caused by spirochete bacteria of the genus *Borrelia* which are transferred from infected wildlife species to humans through the bite of a tick. Incidence of Lyme disease has risen dramatically during the past three decades, with more than 100,000 cases now being reported world-wide each year (Steere *et al.* 2004, Lindgren and Jaenson 2006). The disease is associated with north-temperate forests, wooded areas and green spaces where people might come into contact with infected ticks (Steere 2001, Tonks 2007, Ogden *et al.* 2008). Several focal regions for infection have been identified across the northern hemisphere, but there are many more areas, including the United Kingdom, where Lyme disease is becoming increasingly prevalent (HPA 2008, HPS 2009a).

From a clinical perspective, Lyme disease is a potentially complex illness (Steere 2001, Davidson *et al* 2003). If treated early with antibiotics there are usually few complications and most patients make a complete recovery. However, where diagnosis and treatment are delayed, the infection can progress to more serious or life-threatening conditions involving the skin, nervous system, heart and joints (Steere 2001). Lyme disease is a Notifiable Disease in a growing number of jurisdictions and an increasingly high-profile public health issue (Feder *et al.* 2007, Tonks 2007, Ogden *et al.* 2008).

We present an overview of the ecology, epidemiology and clinical features of Lyme disease. Where relevant we include information specific to Scotland and/or the UK. Our overall objective is to promote awareness of Lyme disease and strategies for minimising the risk of infection.

Epidemiology of Lyme disease

In North America, Lyme disease is most prevalent in New England, the Midwest and in northern California/Oregon. These areas account for 15,000 to 20,000 reported cases each year (Steere *et al.* 2004). In Northern Europe, it is endemic to most countries. Highest rates of infection are in Germany, Austria, Slovenia and Sweden. The total number of reported cases exceeds 85,000 each year (Lindgren and Jaenson 2006). Across Asia, regional foci for Lyme disease are located in parts of Russia, China and Japan. Despite its emerging importance, data remains unavailable in some jurisdictions and there is thought to be widespread under-reporting of the disease (Davidson *et al* 2003, Stanek and Strle 2003, WHO 2005, HPA 2008).

The incidence of Lyme disease in Britain has increased over the past decade (Defra 2008). In England and Wales, the number of laboratory reported cases rose from 268 in 2001 to 813 in 2008 (HPA 2009). This corresponds with a rise in mean annual infection rates over the same period from 0.50/100,000 to 1.52/100,000 in the general population. Approximately fifty per cent of cases were located in the southern counties of England, especially the South East and South West health regions (HPA 2009). These include well known regional foci around the New Forest, Salisbury Plain, Exmoor, the South Downs, parts of Wiltshire and Berkshire, and Thetford Forest. Other areas to the north include the North Yorks Moors and the Lake District (Defra 2008). In Scotland, a similar rise in the number of laboratory reported cases has been recorded over the past decade, with 285 laboratory confirmed cases in 2008 (Figure 1) (HPS 2009b). Currently, the annual incidence of Lyme disease in Scotland is 2.08/100,000 but is very much higher in the Scottish Highlands with a rate of 28.0/100,000 (HPS 2009a). Part of the recent rise in number of reported cases may be attributed to heightened public awareness (HPS 2009a). Up to twenty percent of cases each year are acquired abroad, especially among those travelling to and from central and eastern Europe, and southern Scandinavia (HPA 2009).



Figure 1 The number of laboratory confirmed reports for Lyme disease in Scotland between 1999 and 2008 (HPS 2009b).

Ecology of Lyme disease

The rapid spread of Lyme disease in recent decades can be viewed in the context of the epidemiological triangle (*Figure 2*) (Ahrens and Pigeot 2007). This model helps clarify ecological relationships between the causative agent, host species and environmental factors, and the vector for disease transmission:

1. Borrelia - the causative agent. Lyme disease, also called Lyme Borreliosis (LB), was first characterised following a cluster of infections at Old Lyme, Connecticut, in 1975 (Steere et al. 1977). Subsequent research identified the causative agent to be a spirochete bacteria of the Borrelia burgdorferi complex (Burgdorfer et al. 1982, Steere et al. 1983), with three species being responsible for most infections (Table 1). These are highly adaptable corkscrewshaped bacteria, able to shuttle between ticks and a wide variety of vertebrate species, despite significant differences in host immune systems and body temperature (Stanek and Strle 2003). Based on studies of host immunity, it is thought that Borrelia have been endemic to north-temperate forest ecosystems for thousands of years, though infection in human populations has been sporadic up to the late 20th century (Steere et al. 2004).



Figure 2 The epidemiological triangle. Interactions between the agent, host and environment determine changes in the prevalence of disease. A fourth element is the role of the disease vector, which transfers the agent of infection from one host to another.

associate	ted spirochete bacteria in Lyme disease (Steere 2001, Steere <i>et al</i> 2004).		
Region/foci	Ixodes species (vector)	Spirochete bacteria (agent)	
North America			
New England and Midwest	lxodes scapularis ¹	Borrelia burgdorferi	
Northern Calif/Oregon	Ixodes pacificus	Borrelia borgdorferi	
Europe and Scandinavia	Ixodes ricinus	Borrelia afzelii Borrelia garinii Borrelia burgdorferi	
Asia	Ixodes persulcatus	Borrelia afzelii Borrelia garinii	

2. Ticks - vector of infection. Ticks are small, parasitic arthropods, closely related to spiders and mites. Those responsible for Lyme disease are from the Ixodes ricinus complex, commonly known as hard-bodied, deer or woodland ticks (Table 1). Ixodes ticks have three stages in their lifecycle: larval, nymph and adult (Figures 3 and 4). They require a blood-meal at each stage and move as they mature from small mammals, such as mice, to larger mammals, such as deer (Randolph 2004, Dennis and Hayes 2002, Gern and Pierre-Francois 2002). Most ticks complete their lifecycle over two to three years, depending on the local climate and feeding conditions (Gern and Pierre-Francois 2002). Their favoured habitat is ground vegetation in woodlands with high deer populations, but they can also be found in moorland, meadows, parks, and gardens (Randolph 2004, Dennis and Hayes 2002, Gern and Pierre-Francois 2002). Open areas with thick swards of bracken (Pteridium aquilinum) provide an excellent habitat for the tick (Wilson et al. 1998).



3. Transmission route to human hosts. Peak infection times each year are May-July and September-October, though the risk of tick bites remains throughout the growing season (HPA 2008). When ready to feed, a tick climbs onto tall grass or foliage, from where it attaches to mammals and birds that brush past (Randolph 2004, Gern and Pierre-Francois 2002). The tick then seeks a safe location to puncture the skin with its hypostome (a barbed proboscis) and tap a blood vessel; the "bite" is firm but painless. Preferred locations on humans include the armpits, navel, groin and hairline (Stanek and Strle 2003). Once attached, blood is drawn over many hours and the tick's abdomen swells like a coffee bean (Figure 5). It is only during later stages of a blood-meal (usually > 24 hours) that the spirochete, if present, is transferred to the host (Box 1) (Piesman 1993). Nymphs are especially likely to transfer infection due to their ability to evade detection (Piesman 1993).

4. Our changing environment. Change in several environmental factors, including forest cover, wildlife populations, climate and societal trends, are responsible for

the current epidemic (Lindgren and Jaenson 2006, Steere et al. 2004). In New England, large-scale reversion of agricultural land to forest in the late 20th century has provided improved habitat for many woodland species (Dennis and Hayes 2002, Spielman 1994, LoGiudice et al. 2003, Guerra et al. 2002). Tick numbers have increased in tandem with the proliferation of deer and other woodland mammals which act as host pools for the Borrelia (Spielman 1994, LoGiudice et al. 2003, Guerra et al. 2002). In Europe and Canada, the spread of Lyme disease is closely tied with climate change (Gern and Pierre-Francois 2002, WHO 2005, Lindgren and Jaenson 2006). Milder winters and warmer summers have enabled infected ticks to survive at higher elevations and in more northern latitudes, including Canada (Ogden et al. 2008) and the UK (HPA 2008, Smith et al. 2000, O'Connell 1995). With a hot summer predicted for 2009, the continuing rise in infections calls for a high level of awareness (HPS 2009a).

Changes in social behaviour have also had an impact on the increased prevalence of Lyme disease, with increased numbers of people living, working and pursuing leisure activities in woodland settings (Steere *et al.* 2004, Stanek and

Box 1. Four tick facts

- Not all ticks carry the spirochete bacteria. The tick must first have a blood-meal from a previously infected mammal. Complex interactions between ticks and their preferred host species explain regional differences in the risk of infection for humans.
- 2. Ticks feed only once at each stage of development which prevents individual ticks from infecting more than one person. The infection does not pass from person-person (Steere 2001, Stanek and Strle 2003).
- Even if bitten by an infected tick, it takes >24 hours for the spirochete bacteria to be transferred to the host. In one study the frequency of Lyme disease after a confirmed bite was around 1% (Shapiro et al. 1992). Early detection and removal of ticks is, therefore, an important Lyme disease prevention measure.
- 4. *Ixodes* ticks can be carried into the home by other mammals, so regular checks should be made on pet cats and dogs if living close to or visiting a "tick area".

Figure 3 left Ixodes ricinus nymph. Ticks are hardest to detect and most likely to spread infection at this stage of development. Note 4 pairs of legs, as opposed to 3 pairs on insects. (Photo: Edward Wilson 2008)

Figure 4 right Ixodes ricinus adult walking across the upper surface of a finger. The flaccid abdomen (red-brown) and the mouthparts are clearly visible. The hypostome is protected by two lateral palps. (Photo: Edward Wilson 2008)





Figure 5. Ixodes ricinus adult engorged with blood after feeding on a pet dog. In this state the tick resembles a coffee bean. The hypostome is visible between the two palps, and has been slightly damaged during removal of the tick. (Photo: Edward Wilson 2008)

Strle 2003, Dennis and Hayes 2002). Among groups most at risk of infection are forestry workers, wildlife managers, gamekeepers, outdoor educators, hikers, military field personnel, rural residents and visitors to focal regions (Lindgren and Jaenson 2006, Guerra *et al.* 2002). In England and Wales, the highest number of reported cases are in the 25-44 and 45-64 age groups, reflecting the age range of most visitors to areas where infected ticks are endemic (HPA 2009). In Scotland, the peak age group for infection is 60-64 years in both sexes (HPS 2009a). This is likely a reflection of greater exposure among the newly retired age groups. Children are however vulnerable due to their small stature, typical play activities and lack of awareness (Chin 2000, CDC 2002).

Clinical profile – diagnosis of Lyme disease can be tricky

Many early symptoms of Lyme disease are non-specific and overlap with those of other physical and neurological illnesses (Stanek and Strle 2003, Davidson *et al* 2003). A diagnosis of exclusion is required to differentiate Lyme disease from other potentially serious conditions, including meningitis, fibromyalgia and chronic fatigue syndrome (*Table 2*) (eg Chin 2000, Longmore *et al*. 2007). Biochemical differences among species of spirochete bacteria give rise to regional variation in the course of infection, notably between North America and Europe/Asia (Steere 2001). Nevertheless, in general terms Lyme disease can be classified according to three stages of progression: localized, disseminated and persistent infection (Steere *et al*. 2004).

Localized infection. The earliest, most common and sometimes only presenting feature of Lyme disease is a distinctive skin lesion, *erythema migrans* (EM) (*Figure 6*) (HPA 2008). This usually radiates from the site of a bite and expands over a period of 3-30 days. The outer border is usually bright red and inflamed, with partial central clearing. It classically presents as a round, target lesion but different shapes are possible depending on its location in relation to folds in the skin. The lesion can cover an extensive area of skin and is diagnostic when it reaches a diameter of 5 cm (Tibbles and Edlow 2007). In North America it tends to be more intensely coloured, more rapidly expanding and of shorter duration than those in Europe (Steere *et al.* 2004).

Early infection is often accompanied by fatigue, fever, chills, headaches, stiff neck and aches in muscles and joints (Steere 2001, Ogden *et al.* 2008, Wormser 2006). Symptoms may be similar to a flu-like or meningitis-like infection and may last for several weeks. Some patients have only the flu-like symptoms, while others may be asymptomatic (Stanek

(Steere 2001, Ogd	diagnosis of Lyme disease. en <i>et al</i> 2008, Stanek and Strle 2003, HPA 2008, Chin 2000)
Component	Condition or questions
Differential diagnosis - other medical conditions your doctor will want to eliminate during his/her investigations (examples)	 Meningitis Fibromyalgia Chronic fatigue syndrome
Focus questions typically asked in relation to tick bites	 Remember being bitten by a tick? <i>Erythema migrans</i>? Localised or general pain, fatigue or numbness? Previous exposure/treatment for Lyme disease? Leisure pursuits? outdoor activities in woodland settings Occupation? Especially those in forestry, game management, agriculture, outdoor education
Other points the doctor will want to consider	 Recent travel to focal regions? Proximity of home to green space? Pets? Use of protective clothing and preventive measures when outdoors



Figure 6 Characteristic "bull's eye" erythema migrans lesion on the posterior right upper arm of a woman diagnosed with Lyme disease. This is a dramatic presentation of the lesion, which appears in different shapes and forms dependent on the location of the bite. This picture was taken in the US; in Europe the erythema migrans lesions tends to be less intensely coloured and to have a longer duration. (Photo: James Gathany, Centers for Disease Control and Prevention (CDC), reproduced with permission.)

and Strle 2003, Wormser 2006). It is important to note that *erythema migrans* is absent in approximately 20 percent of cases in North America and a higher proportion of those in Europe (Steere *et al.* 2004).

Disseminated infection. In this stage the spirochete disseminates in the blood to specific locations in the body, including the skin, nervous system, heart and/or joints (Steere 2001). This occurs over days to weeks after an untreated infection. Clinical features in the skin often present as a circular or ring-like rash, secondary to the erythema migrans. Early neurological presentations include a severe headache and neck stiffness, Bell's palsy, and radiating pain or abnormal sensations in peripheral nerves (Stanek and Strle 2003). Heart involvement may be indicated by short-term episodes of palpitations or fainting due to heart block (Steere 2001). Muskulo-skeletal symptoms include migratory pain in the joints, tendons, bursae, muscle or bone (Stanek and Strle 2003). Such manifestations of Lyme disease generally resolve after weeks or months, even in untreated patients (Steere 2001).

Persistent infection. More serious complications may appear in untreated patients several months after the initial spirochete infection and will require specialist medical treatment. The most common symptom is chronic arthritis (Chin 2000). This often continues for a period of years as intermittent attacks in one or a few large joints, especially the knee(s). Other potential problems are relatively uncommon and include memory impairment, pain and numbness, and a number of possible heart complications. Some patients are left with debilitating fatigue and other neurological complications even after elimination of the spirochete (Steere 2001, Stanek and Strle 2003, Chin 2000). However, death from complications of Lyme disease is very rare (Steere 2001, CDC 2002).

Testing

Testing for Lyme disease is conducted at specialist labs and generally follows an internationally-agreed protocol (HPA 2008, Wormser *et al.* 2006). The standard blood test measures antibodies for *Borrelia* but is often negative in the first weeks after infection (HPA 2008). A more reliable result is obtained if the test is repeated at a later stage, as the spirochete starts to disseminate. Culture of *Borrelia* has proved ineffective in diagnosis, unless a biopsy sample is taken from the *erythema migrans* at an early stage of infection (Steere 2001). Neurological tests may be required to assess memory impairment and nerve abnormalities, or to exclude other potential diagnoses (Steere 2001).

Treatment

For most patients, antibiotics are the first line of treatment for Lyme disease (Steere 2001, Stanek and Strle 2003, Wormser et al. 2006). For localised or disseminated infection, a course of doxycycline for 14-21 days is recommended in patients over eight years of age, except in pregnant women (Steere 2001, O'Connell 1995, CDC 2002). Lyme arthritis is often treated successfully with oral antibiotics, but a small number of patients require intravenous antibiotic therapy (Steere 2001). In rare cases, Lyme arthritis does not respond to either oral or intravenous antibiotics; in this event anti-inflammatory medications are prescribed (Steere 2001). Neurologic involvement may also require intravenous therapy. Antibiotic therapy for 21 days is usually adequate for early disease but 30 days may be needed in more severe cases or for later manifestations of the disease (Stanek and Strle 2003). As with all infections, the course of treatment will depend on individual patient circumstances.

Public health and prevention

Strategic approaches to minimising infection rates for Lyme disease have focused on reducing tick populations and humantick interactions (Hayes and Piesman 2003). Attempts have been made in some jurisdictions to spray acaricides over areas of vegetation with high tick populations. Other work has been undertaken to target specific host mammals, such as rodents and deer. There have also been attempts to cull deer populations in several areas of New England. In most cases, these efforts have proved expensive and largely ineffective in reducing the population of infected ticks and Lyme disease infection rates (Hayes and Piesman 2003). Of more practical value may be local habitat modification, such as removing vegetation from around buildings, cutting wider paths and clearing tall leafy vegetation from public access areas (CDC 2002, Hayes and Piesman 2003). A vaccine was briefly

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available, but this was withdrawn after 2002 (Steere et al. 2004, HPA 2008).

At the present time, the most effective strategy for avoiding infection in most jurisdictions is public health information that promotes awareness of Lyme disease and provides advice on how to treat tick bites (eg Wilson 2008). Personal preventive measures include avoidance of known tick areas, covering exposed skin, wearing appropriate clothing and use of acaricide sprays (*see Box 2*). If working in or visiting a tick-infested area, regular checks of the total body area are strongly advised. Responsible adults should check for ticks on children; pets should also be checked as they can bring ticks into a vehicle or the home (HPA 2008, CDC 2002). Employers need to be aware of the risk to staff that work in woodlands and green spaces, and should take appropriate actions, such as providing up-to-date health information and training.

In the vast majority of situations if a tick is found attached to the skin, rapid intervention to remove the tick is effective in preventing Lyme disease (*Box 3*) (Steere 2001, Stanek and Strle 2003, Ogden *et al.* 2008). Safe removal can be achieved with a tick removal tool, tweezers or cotton thread (*see Box 3*). Best practice is gentle traction to pull the tick away from the skin without any twisting movement (Chin 2000, CDC 2002, HPA 2008). This minimises the risk of a tick regurgitating its stomach contents into the lesion, or the likelihood that the hypostome might become detached in the wound (Steere 2001, CDC 2002, Steere *et al.* 2004, HPA 2008). Removal of the tick within 24 hours of a bite should prevent transmission of the spirochete from an infected tick (Shapiro et al. 1992).

Several agencies and organisations in Britain now produce leaflets and factsheets about Lyme disease. Examples of good practice include a leaflet published by New Forest District Council (NFDC 2004) and a factsheet by Health Protection Scotland (HPS 2009c), both available online. A leaflet has also been produced by the Forestry Commission, though this is currently only available for members of staff (Forestry Commission 2008). Official sources of online information include the Centers for Disease Control and Prevention (CDC) (US Government), the Health Protection Agency (HPA) and Health Protection Scotland (HPS) (*see Useful Websites*).

As with most emerging infections, significant media coverage has been devoted to Lyme disease in recent years (eg Johnson 2007, Elliott 2008, Howarth 2009). Increasing anxiety about access to green space runs counter to public health messages promoting woodland walks for mental and physical well-being. There is, therefore, a need to target high quality information and educational material, especially in

Box 2. Tick Aware! - a personal protection strategy to minimise the risk of Lyme disease

This box outlines a set of practical measures that minimise the likelihood of being bitten when visiting a tick area. This is the most effective way of avoiding infection.

Prior to your visit:

- Access appropriate public health information to review the current status of ticks and Lyme disease in areas you are working or visiting. For example, update reports and factsheets are produced by public health agencies, such as Health Protection Scotland (eg HPS 2009b,c).
- Purchase and carry a tick removal tool in tick areas (see Box 3).
- Be familiar with the identification features of nymph and adult ticks (Figures 3 and 4).
- Pet dogs can be treated with acaricides (available from vets and pet shops) to reduce the risk of being bitten or bringing a tick home.

During your visit:

- Cover skin, especially in "brushy" areas.
- Wear long trousers rather than shorts or a skirt.
- Favour light coloured clothing to make ticks easier to spot.
- Button up collars and cuffs, wear a hat and tuck socks into trousers.
- Wear boots, not sandals.
- Apply an acaricide (e.g. permethrin) or insect repellent to clothes or exposed skin.
- Be especially vigilant during peak feeding times, May-July and September-October.

After your visit:

- Brush off clothing and check pets before getting into a car and/or returning home.
- Conduct a self-inspection at the earliest opportunity; focus on armpits, the navel, groin and hairline. Remember that early detection is an important strategy for preventing Lyme disease.
- Children should be checked by a responsible adult, with close attention to areas such as the hairline.

Box 3. Safe removal of ticks



• Avoid extraction of ticks with fingernails. This increases the risk of squashing the tick.

focal areas and to those groups of people most at risk of being bitten by an infected tick (Steere *et al.* 2004, Ogden *et al.* 2008, Hayes and Piesman 2003). Reassurance should be given about the overwhelming benefits of exercise, while providing suitable information about prevention of Lyme disease. Travel advice is required for many holiday destinations where Lyme disease is endemic, especially in New England, central Europe and Scandinavia (Steere *et al.* 2004, Hayes and Piesman 2003).

Conclusions

Lyme disease is an increasingly common illness in Europe and North America. In Britain, the number of reported cases has risen rapidly since the late 1990s. It is a potentially complex illness, especially where diagnosis and treatment are delayed. Anyone who becomes ill after being bitten by a tick should immediately seek medical advice. It is helpful to provide the doctor with as much information as possible so that other potential causes of ill-health can be checked and eliminated from investigations. Although the *erythema migrans* rash is a significant feature of the infection, it is not always present. Short-term antibiotic therapy is the mainstay of treatment. Simple preventive measures are effective in minimising the risk of infection. However, a public health approach to managing Lyme disease is warranted so that positive health messages about outdoor exercise can be promoted along with best practice for avoiding possible infection.

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ear	Season	Stage in tick life-cycle	Principal host species	Potential habitat Intervention	Personal precautions ¹
1	Spring	Eggs hatch		Area-wide acaricide and vegetation management	
	Summer	Larvae	Rodents	Area-wide acaricide and vegetation management Rodent targeted acaricides	
	Autumn	Nymph	Rodents		
	Winter	Nymph	Rodents		
2	Spring	Nymph	Rodents Small mammals	Area-wide acaricide and vegetation management Rodent targeted acaricides	Repellent and barriers Tick checks Rapid treatment of tick bite
	Summer	Adult	Rodents Small mammals Deer	Area-wide acaricide and vegetation management Deer targeted acaricides	Repellent and barriers Tick checks Rapid treatment of tick bite
	Autumn	Adult	Small mammals Deer	Elimination/exclusion of deer Deer targeted acaricides	Repellent and barriers Tick checks Rapid treatment of tick bite
	Winter	Eggs laid Adult dies		C C C C C C C C C C C C C C C C C C C	

Table 3. Life-cycle of *Ixodes* ticks and opportunities for primary prevention of Lyme

Medical Advisory

This article provides general information only, with respect to Lyme disease. It is meant to promote awareness and is not a substitute for professional medical advice. Anyone developing symptoms of Lyme disease following a tick bite should immediately consult their GP.

Useful Websites

Health Protection Agency (UK): www.hpa.org.uk (search under A-Z topics for Lyme disease) (comprehensive coverage of biology, diagnosis, testing and treatment of Lyme disease).

Health Protection Scotland (HPS): www.hps.scot.nhs.uk/ giz/lymedisease.aspx (latest information on the status of Lyme disease in Scotland).

European Concerted Action on Lyme Borreliosis (EUCALB): http://meduni09.edis.at/eucalb (up-to-date information on Lyme disease in Europe in the form of short reviews and latest publications; open access but mainly targeted at health-care professionals/researchers).

Centers for Disease Control and Prevention (CDC) (US Government): www.cdc.gov/ncidod/dvbid/Lyme (leading centre for information on Lyme disease; focus on conditions in USA).

National Institute for Occupational Safety and Health (NIOSH) (US Government): www.cdc.gov/niosh/topics/lyme/ (information for employers and employees).

General References

Hayes, E. B., and J. Piesman. 2003. How can we prevent Lyme disease? N Eng J Med 348: 2424-2430.

Kahl, O., J. S. Gray, R. S. Lane and G. Stanek (editors). Lyme borreliosis: biology, epidemiology and control. CABI Publishing. Oxford, United Kingdom. 480 pp.

Stanek, G., and F. Strle. 2003. Lyme borreliosis. Lancet 362(9396): 1639-1647.

Steere, A.C. 2001. Lyme disease. N Eng J Med 345: 115-125.

Steere, A. C., J. Coburn and L. Glickstein. 2004. The emergence of Lyme disease. J Clin Invest 113: 1093-1101.

Centers for Disease Control (CDC). 2002. Lyme disease: a public health guide. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), Fort Collins, CO. 12 pp.

Literature cited

Ahrens, W., and I. Pigeot (editors). 2007. Handbook of Epidemiology. Springer, Berlin. 1639 pp.

Burgdorfer W., A. G. Barbour, S. F. Hayes, J. L. Benach, E. Grunwaldt, J. P. Davis. 1982. Lyme disease – a tick-borne spirochetosis? Science 216: 1317-9.

Centers for Disease Control (CDC). 2002. Lyme disease: a public health guide. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), Fort Collins, CO. 12 pp.

Chin, J. (editor) 2000. Control of communicable diseases manual. 17th edition. American Public Health Association, Washington, DC 624 pp.

Davidson, M. M., R. Evans and D. O. Ho-Yen. 2003. Lyme disease: gold for Scotland and bronze for USA. Scottish Medical Journal 48(1): 6-9.

Defra. 2008. Zoonoses Report, United Kingdom 2007. Department for Environment, Food and Rural Affairs (Defra), London. 88 pp.

Dennis, D.T., and E.B. Hayes. 2002. Epidemiology of Lyme Borreliosis. p. 251–280 published in O. Kahl, J. S. Gray, R. S. Lane and G. Stanek (editors). Lyme borreliosis: biology, epidemiology and control. CABI Publishing. Oxford, United Kingdom. 480 pp.

Elliott, J. 2008. 'I found my own diagnosis on the net' [online]. BBC News. URL: news.bbc.co.uk/1/hi/health/7461617.stm. Last accessed: 17 June 2009.

Feder, H. M., B. J. B. Johnson, S. O'Connell, E. D. Shapiro, A. C. Steere, G. P. Wormser and Ad Hoc International Lyme Disease Group. 2007. A critical appraisal of "chronic Lyme disease". N Engl J Med 357(14): 1422-1430.

Forestry Commission. 2008. Lyme disease: information and advice for Forestry Commission staff. [leaflet] FCMS021/FC-GB(ECD)/ZCard-5K/May 2008. Forestry Commission, Edinburgh.

Gern, L., and H. Pierre-Francois. 2002. Ecology of *Borrelia burgdorferi* sensu lato in Europe. In O. Kahl, J. S. Gray, R. S. Lane and G. Stanek (editors). Lyme borreliosis: biology, epidemiology and control. CABI Publishing. Oxford, United Kingdom. 149–174.

Guerra, M., *et al.* 2002. Predicting the risk of Lyme disease: habitat suitability for *Ixodes scapularis* in the north central United States. Emerg Infect Dis 8: 289–297.

Hayes, E. B., and J. Piesman. 2003. How can we prevent Lyme disease? N Eng J Med 348: 2424-2430.

Health Protection Agency (HPA). 2008. Lyme borreliosis/Lyme disease [online]. Health Protection Agency, England. URL: www.hpa.org.uk; last accessed 29 March 2009.

Health Protection Agency (HPA). 2009. Epidemiology of Lyme borreliosis in the UK (26/05/09)[online]. Health Protection Agency, Lyme Borreliosis Unit, Southampton, England. URL: www.hpa.org.uk; last accessed 17 June 2009.

Health Protection Scotland (HPS). 2009a. Epidemiology and risks of tick-borne Lyme borreliosis. HPS Weekly Report 2009/21 ((27 May 2009) 43: 213-214 [available online at: www.hps.scot.nhs.uk]

Health Protection Scotland (HPS). 2009b. Lyme disease [online]. URL: www.hps.scot.nhs.uk. Last accessed: 17 June 2009.

Health Protection Scotland (HPS). 2009c. What do I need to know about ticks and tick borne diseases? HPS Factsheet (April 2009). Health Protection Scotland, Glasgow. 2 pp. (available online at: www.documents.hps.scot.nhs.uk/giz/general/tickfactsheet-2009-04.pdf)

Howarth, A. 2009. Campers warned over tick bites as Lyme disease soars. The Scotsman, 3 June 2009.

Johnson, I. 2007. Alert over rise of 'killer' ticks in Scottish cities. The Scotsman, 11 May 2007.

Lindgren, E., and T.G.T Jaenson. 2006. Lyme borreliosis in Europe: influences of climate and climate change, epidemiology, ecology and adaptation measures. CCASHH Project Report, EUR/04/5046250. WHO Regional Office for Europe, Copenhagen. 34 pp.

LoGiudice, K., R. S. Ostfeld, K. A. Schmidt and F. Keesing. 2003. The ecology of infectious disease: effects of host diversity and community composition on Lyme disease risk. Proc Natl Acad Sci 100: 567–571.

Longmore, M., I. Wilkinson, T. Turmezei and C. K. Cheung. 2007. Oxford handbook of clinical medicine. 7th edition. Oxford University Press, Oxford. 841 pp.

O'Connell, S. 1995. Lyme disease in the United Kingdom. BMJ 310: 303-308

Ogden, N. H., H. Artsob, L. R. Lindsay and P. N. Sockett. 2008. Lyme disease: a zoonotic disease of increasing importance to Canadians. Canadian Family Physician 54: 1381-1384.

New Forest District Council (NFDC). 2004. Just a tick ... Tick bites and Lyme disease. [leaflet] NFDC Environmental Health, Lymington, Hampshire. (available online at: www.nfdc.gov.uk)

Piesman, J. 1993. Dynamics of *Borrelia burgdorferi* transmission by nymphal *Ixodes dammini* ticks. J Infect Dis 167:1082-1085.

Randolph, S. E. 2004. Tick ecology: processes and patterns behind the epidemiological risk posed by ixodid ticks as vectors. Parasitology 129: S37-S65.

Shapiro, E. D., M. A. Gerber, N. B. Holabird, *et al.* 1992. A controlled trial of antimicrobial prophylaxis for Lyme disease after deer-tick bites. N Eng J Med 327: 1769-1773

Smith, R., S. O'Connell and S. Palmer. 2000. Lyme disease surveillance in England and Wales, 1986-1998. Emerging Infectious Diseases 6(4): 404-407

Spielman, A. 1994. The emergence of Lyme disease and human babesiosis in a changing environment. Ann NY Acad Sci 740: 146–156.

Stanek, G., and F. Strle. 2003. Lyme borreliosis. Lancet 362(9396): 1639-1647.

Steere, A.C. 2001. Lyme disease. N Eng J Med 345: 115-125.

Steere A.C., S. E. Malawista, D. R. Snydman, *et al.* 1977. Lyme arthritis: an epidemic of oligoarticular arthritis in children and adults in three Connecticut communities. Arthritis Rheum 20:7-17.

Steere A. C., R. L. Grodzicki, A. N. Kornblatt, *et al.* 1983. The spirochetal etiology of Lyme disease. N Engl J Med 308:733-40.

Steere, A. C., J. Coburn and L. Glickstein. 2004. The emergence of Lyme disease. J Clin Invest 113: 1093-1101.

Tibbles, C. D. and J. A. Edlow. 2007. Does this patient have

erythema migrans? *JAMA* 297(23): 2617-2627. Tonks, A. 2007. Lyme wars. BMJ 339: 910-912.

Wilson, E. 2008. Lyme disease in British woodlands. Quarterly Journal of Forestry 102: 209-212.

Wilson, D., L. J. Donaldson and O. Sepai. 1998. Should we be frightened of bracken? A review of the evidence. Journal of Epidemiology and Community Health 52: 812–817

World Health Organisation (WHO). 2005. Impact of climate change on health: how to address new threats now. Factsheet EURO/15/5. WHO Regional Office for Europe, Rome. 4 pp.

Wormser, G. P. 2006. Early Lyme disease. N Engl J Med 354: 2794-2801.

Wormser, G. P., R. J. Dattwyler, E. D. Shapiro, J. J. Halperin, A. C. Steere, M. S. Klempner, *et al.* 2006. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 43: 1089-1134.