Lyme Disease

Lyme Borreliosis,
Lyme Arthritis,
Erythema Migrans
with Polyarthritis

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Importance

Lyme disease is a tickborne illness caused by members of the *Borrelia burgdorferi* sensu lato complex. These organisms are maintained in wildlife, but most reported illnesses are in humans, with occasional cases in domestic animals, particularly dogs. Lyme disease was first recognized in the 1970s, when a cluster of juvenile arthritis cases was investigated in the U.S.; however, the causative organisms are now known to be relatively widespread and have been found in Europe as well as parts of Asia, Canada and South America. Clinical cases in humans are readily cured with antibiotics during the initial stage of the illness, when an unusual rash often aids disease recognition. However, people whose infections remain untreated during this early stage sometimes develop other syndromes, such as arthritis or neurological signs, which can be more difficult to diagnose. Lyme disease in animals is still incompletely understood.

Etiology

Lyme disease is caused by members of the *Borrelia burgdorferi* sensu lato complex, in the family Spirochaetaceae. A very similar disease in Brazil is sometimes called Lyme-like disease or Baggio-Yoshinari syndrome. There are about 20 recognized genospecies (genomic groups) in the *B. burgdorferi* s.l. complex, of which approximately half have been reported in humans. The organisms found most often in clinical cases are *B. burgdorferi* sensu stricto (*B. burgdorferi* s.s.), *B. garinii, B. bavariensis* (formerly *B. garinii* OspA serotype 4), *B. afzelii,* and to a lesser extent, *B. mayonii* and *B. spielmanii*. *B. bissetii, B. valaisiana* and *B. lusitaniae* have been reported in rare cases, while *B. americana* and *B. andersonii* were each found in the blood of a single person in North America. Little is known about the specific organisms in domestic animals, but *B. burgdorferi* s.s. is presumed to be the agent in North America, and *B. afzelii* and *B. garinii* might also play a role in other parts of the world. Other *B. burgdorferi* s.l. complex members (e.g., *B. lusitaniae*) have only been found in healthy animals, to date.

Species Affected

Reservoir hosts

Mammals, birds and reptiles can serve as reservoir hosts for the members of the *B. burgdorferi* s.l. complex. Most of the clinically important organisms are maintained in rodents, insectivores (e.g., shrews) or other small mammals. The white-footed mouse (*Peromyscus leucopus*) is the primary reservoir host for *B. burgdorferi* s.s. in the eastern U.S., but various chipmunks, squirrels, mice, voles and shrews may be important in some other parts of North America. *P. leucopus* has also been suggested as a maintenance hosts for *B. mayonii*. Yellow-necked mice (*Apodemus flavicollis*), striped field mice (*A. agrarius*), wood mice (*A. sylvaticus*), and the voles *Clethrionomys glareolus* and *Microtus agrestis*, are among the reservoir hosts for *B. burgdorferi* s.l. complex members (e.g., *B. afzelii, B. bavariensis, B. lusitaniae*) in Europe and Asia. Other possible hosts include European hedgehogs (*Erinaceus europaeus*), and lagomorphs, particularly the brown hare (*Lepus europaeus*) and the varying hare (*L. timidus*). Capybaras (*Hydrochoerus hydrochaeris*) are thought to be maintenance hosts in Brazil. Cervids are important in providing blood meals to ticks, but they do not play a role in amplifying or maintaining the members of the *B. burgdorferi* s.l. complex.

Birds are thought to maintain *B. garinii*, which causes some cases of Lyme disease in people, as well as *B. valaisiana* and *B. turdi. B. garinii* occurs in seabirds as well as terrestrial species such as pheasants (*Phasianus colchicus*) and some passerines. Certain lizards appear to be reservoir hosts for *B. lusitaniae.* However, the complement proteins in the blood of many lizards are highly lytic for some members of the *B. burgdorferi* s.l., complex, and may reduce their prevalence in ticks.

Incidental hosts

Evidence for *B. burgdorferi* sensu lato infections has been found in many domestic animals and some free-living wildlife, including large mammals such as

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wild carnivores. Most surveys have examined mammals, but some organisms, including *B. lusitaniae* and *B. burgdorferi* s.s., have been detected occasionally in birds. Clinical cases have mainly been reported in domestic animals, particularly dogs and horses, with a few putative cases in cats, ruminants and a captive chimpanzee (*Pan troglodytes*). Dogs, horses, cats, rabbits, mice, hamsters, gerbils and guinea pigs have been infected experimentally.

Some incidental hosts, such as dogs, may occasionally transmit *B. burgdorferi* s.l. to ticks, but they are not thought to be significant in maintaining these organisms.

Zoonotic potential

Organisms known to affect people include *B. burgdorferi* s.s., *B. garinii*, *B. bavariensis*, *B. afzelii*, *B. mayonii*, *B. spielmanii*, *B. bissetii*, *B. valaisiana* and *B. lusitaniae*. *B. americana* and *B. andersonii* were each detected in the blood of a single person in North America. Other genospecies might also be zoonotic but appear to be rare in humans.

Geographic Distribution

As of 2020, Lyme disease is known to occur in parts of North and South America, Europe and Asia. There are reports of a Lyme-like disease in Australia; however, researchers have been unable to find evidence for any *B. burgdorferi* s.l. members in his location, suggesting that the Australian cases might either be another disease or acquired elsewhere. Most members of the *B. burgdorferi* s.l complex are limited to temperate areas where their vectors, *Ixodes* ticks, can survive. *B. garinii*, which can be spread by seabirds and their cold-resistant ticks, can be found even in polar regions, where it has been detected in seabird colonies. Migratory birds sometimes distribute infected ticks beyond their usual locations, but the organisms do not necessarily persist long-term.

Different genospecies can cause Lyme disease in different locations. In North America, this disease is usually caused by *B. burgdorferi* s.s., though *B. mayonii* has been responsible for some cases in the Upper Midwest. The major endemic foci are in the northeastern, mid-Atlantic and north-central U.S., and along the Pacific coast, though cases can occur elsewhere, including parts of Canada. *B. garinii* has been found in seabird colonies in a few North American locations including Alaska and Gull Island, Newfoundland, but there have been no human cases attributed to this organism in the Western Hemisphere. In South America, Lyme disease or a similar illness has been documented in Brazil, where it is thought to be caused by *B. burgdorferi* s.s. Members of the *B. burgdorferi* s.l. complex have also been reported from Uruguay, Argentina and Chile, with the latter two reports describing the species as *B. chilensis*.

Organisms found in Europe include *B. garinii*, *B. bavariensis*, *B. afzelii*, *B. burgdorferi* s.s., *B. spielmanii*, *B. valaisiana* and *B. lusitaniae*. Some of these agents, such as *B. lusitaniae*, seem to occur in limited locations. *B. garinii* and *B. afzelii* are thought to be the most important genospecies in Asia, but *B. burgdorferi* s.s. has been detected in a few countries (e.g., Taiwan), and recent research suggests that *B. bavariensis* is widespread. *B. lusitaniae* and either *B. valaisiana* or a related species have also been documented in some parts of Asia.

Transmission

Members of the *B. burgdorferi* s.l. complex are usually transmitted by ticks in the genus *Ixodes;* however, other tick genera, including *Amblyomma* and *Rhipicephalus*, were proposed as important vectors in Brazil. *Ixodes scapularis* is the major vector for *B. burgdorferi* s.s. in eastern North America and the Midwest, while *I. pacificus* transmits this organism on the Pacific coast. *B. mayonii* is also thought to be transmitted by *I. scapularis*. *I. ricinus* and *I. persulcatus* are the primary vectors for *B. burgdorferi* s.l. complex members in Europe and Asia, though other *Ixodes* ticks may be important locally. The cold-tolerant seabird tick *I. uriae* can transmit *B. garinii* in polar regions. Infrequently, *I. uriae* has been found to carry other organisms such as *B. bavariensis*, *B. lusitaniae* and *B. burgdorferi* s.s.

Successful transmission of *B. burgdorferi* s.l. to a new host requires that an infected tick remain attached for at least a day or two, though certain circumstances (e.g., bites from partially fed ticks or bites from multiple infected ticks) may shorten this period. The minimum attachment time seems to vary with the organism. *B. burgdorferi* s.s. and *B. mayonii* are not usually acquired with attachment times of less than 48 hours, while *B. afzelii* could infect some mice by 48 hours but not before 24 hours. Transstadial transmission has been demonstrated in some tick species, but transovarial transmission seems to be insignificant.

B. burgdorferi s.l. does not spread directly between infected vertebrates to any significant extent, although there are a few research reports of organisms (or their nucleic acids) occasionally being detected in body fluids such as urine, the breast milk of humans with erythema migrans, and colostrum or milk from cattle. One report described transmission from an experimentally infected dog, which excreted spirochetes in its urine, to a control animal. However, another study found that susceptible dogs co-housed with infected dogs for a year did not seroconvert. Possible transplacental and sexual transmission have been proposed in humans, but definitive evidence to support either route is currently lacking. There are no known cases of Lyme disease resulting from a blood transfusion, though transfusion-acquired disease is theoretically possible and it has been demonstrated in experimentally infected mice.

Disinfection

Borrelia burgdorferi sensu lato does not survive well outside the body, but if necessary it can be inactivated by 1% sodium hypochlorite or 70% ethanol. It is also sensitive to heat and ultraviolet light.

Infections in Animals

Incubation Period

There is limited information about the incubation period in animals, but some experimentally infected dogs developed arthritis in 2-5 months.

Clinical Signs

Most infections in animals seem to be asymptomatic. The range of clinical syndromes is not completely understood, but they are assumed to be similar to those in humans, with most reports describing arthritis, neurological signs, ocular disease and/or cardiac signs. A possible link with nephritis has also been proposed in dogs. Erythema migrans, a common initial sign in humans, has rarely been documented in animals.

Dogs

Arthritis is the most commonly described syndrome in dogs and can affect one to a few joints, especially the carpal joints. The joints may or may not be swollen. The resulting lameness may be intermittent or shift from leg to leg. Nonspecific signs including fever, anorexia, lethargy or lymphadenitis, particularly of the prescapular or popliteal nodes, may be seen concurrently in some animals. Arthritis is the only syndrome that has been reproduced in experimentally infected dogs. In one experiment, it was most likely to occur in younger puppies, transient (1-2 days) in older puppies, and absent in adults, which seroconverted without clinical signs. Arthritis was self-limited in this report, though younger animals sometimes had a few recurrent episodes. However, subsequent studies have suggested that severe arthritis is possible in some animals.

Cardiac dysfunction (myocarditis or conduction abnormalities with bradycardia) and neurological signs (e.g., facial paralysis, seizures, aggression) have been attributed to *B. burgdorferi* in a small number of naturally infected dogs. Some of these animals had a history of arthritis. Based on immunostaining for *Borrelia* antigens, Lyme disease was also proposed to cause a syndrome of acute or chronic nephritis with protein-losing nephropathy and immune-mediated glomerulonephritis. Most affected dogs had signs of renal failure, which often progressed rapidly. The association of this condition with Lyme disease is considered unconfirmed, as it has not been reproduced experimentally, and immunostaining could result from cross-reactivity.

Dogs referred to specialists for Lyme disease that is unresponsive to antibiotics often have other illnesses.

Cats

Very little is known about the consequences of infection in cats. While significant numbers of cats are seropositive in some surveys, reports of naturally occurring disease are rare, and definitive attribution of the clinical signs to *B. burgdorferi* is difficult. Most suspected cases have involved lameness or intermittent lameness, with or without fever, that improved after treatment with antibiotics effective for *Borrelia*. There have also been cases submitted for Lyme disease serology with neurological signs (e.g., hind leg paresis, ataxia, trembling). Two cases of bradydysrhythmia in asymptomatic cats were recently attributed to this disease. One cat had a structurally normal heart, with a previous history of an erythema migrans-like lesion on its abdomen. The arhythmia resolved after treatment with doxycycline. The other cat had both dilated cardiomyopathy and arhythmia, and eventually developed congestive heart failure.

Conflicting results have been seen in experimentally infected cats. In one study, the animals remained asymptomatic; in another, they developed fever, lethargy and arthritis with intermittent stiffness.

Horses

The prevalence of Lyme disease in horses remains controversial. Currently, the syndromes with the most evidence for *B. burgdorferi* in a causative role are uveitis, which is often severe and sometimes progresses to blindness; neurological signs (e.g., meningitis, dysphagia, laryngeal dysfunction, facial paresis, neck and back stiffness, progressive ataxia, encephalitis); and cutaneous pseudolymphoma. Cutaneous pseudolymphomas are papular to nodular lesions that occur at the site of a tick bite. They have been documented in experimentally infected as well as naturally infected horses.

Arthritis, cardiac arhythmias and myocarditis have also been attributed to Lyme disease in horses. A few reports of arthritis supported the diagnosis with evidence for *B. burgdorferi* infection, and documented lymphoplasmacytic synovitis with marked fluid distention of the joints or tendon sheaths. However, most horses with presumed but unconfirmed cases have not had joint swelling. There are also diverse unconfirmed and often anecdotal syndromes attributed to Lyme disease, including rare reports of conditions such as laminitis, hepatitis or nephritis, as well as nonspecific signs (e.g., low grade fever) or multisystemic syndromes.

Other species

Clinical signs that have been attributed to Lyme disease in cattle include fever, lameness/ stiffness with or without joint swelling, uveitis, skin lesions (erythema, warmth, swelling and hypersensitivity of the skin on the ventral udder, developing into dark sloughing scabs) and nonspecific signs such as chronic weight loss and abortions. In one study, calves inoculated with the three European genospecies remained asymptomatic. One presumptive case was reported in a captive chimpanzee that had recurrent episodes of illness with nonspecific signs and shifting leg lameness. This animal had elevated antibody titers to *B. burgdorferi* at the time of diagnosis, and responded to doxycycline, with subsequent decrease in titers. Erythema migrans skin lesions, polyarthritis and carditis have been reported in experimentally infected rabbits.

Post Mortem Lesions

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The predominant lesions attributed to Lyme disease are nonerosive arthritis, uveitis, myocarditis and lesions in the central nervous system (CNS). Neurological involvement has been described as neutrophilic or lymphoplasmacytic, histiocytic, perivascular to diffuse inflammation that affects the meninges, ganglia, and cranial and spinal nerve roots, with variable necrosis, fibrosis and neuroparenchymal invasion. Some horses with neuroborreliosis may have visible lesions in the meninges, including opacification, yellowish discoloration and hyperemia, with injected vessels and plaques of edema. Nephritis and various lesions associated with uremia were attributed to Lyme disease in some dogs.

Diagnostic Tests

Antemortem diagnosis of Lyme disease is typically based on a combination of the clinical signs, epidemiology (i.e., a history of exposure to ticks in an endemic area), elimination of other diseases, laboratory data and response to antibiotics. It is most often presumptive, as laboratory confirmation is usually limited to serology. *B. burgdorferi* s.l. is rarely found in blood; however, organisms, nucleic acids or antigens may be detected occasionally in affected tissues, particularly the joints (especially synovium), meninges, cerebrospinal fluid (CSF), ocular fluid or cardiac muscle. Histopathology may be helpful in some instances, particularly at necropsy.

Antibody titers can often be detected within 3-8 weeks of exposure in dogs and horses, depending on the assay. Commonly used serological tests include various ELISAs, line immunoassays (LIA), fluorescent bead-based multiplex assays and immunoblotting. Most tests were developed for dogs; however, some are also used in other species. Indirect immunofluorescence assays (IFA) were employed in the past, but some sources no longer recommend them due to their low specificity. Screening tests such as ELISAs can be confirmed by immunoblotting, but a single C6-peptide-based assay is sometimes used in place of this two-tier testing in dogs. Serological diagnosis is complicated by the long incubation period, prevalence of asymptomatic infections in healthy animals, cross-reactions with some other organisms, and persistence of titers for months or years. Some assays (e.g., immunoblotting, the C6-peptide-based ELISA) can distinguish vaccinated dogs from those that are infected.

PCR is used most often to detect the organism directly, but there are occasional research reports of antigen detection by immunohistochemistry, often postmortem. Whenever possible, PCR or antigen testing should be interpreted in conjunction with histopathology, as nucleic acids or antigens may be present without being the cause of the disease, and cross-reactivity may be an issue with antigen tests. Isolation of *B. burgdorferi* s.l. is uncommonly attempted and often unsuccessful. The organisms in this complex are fastidious and microaerophilic, and must be cultured on enriched bacteriologic media such as Barbour-Stoenner-Kelly (BSK) or modified Kelly-Pettenkofer (MKP) media. Recovered organisms (Gram negative, motile spirochetes) can be visualized with dark-field or phase-contrast microscopy, immunofluorescent microscopy, silver stains, Giemsa, or acridine orange stain. They can be confirmed as members of the *B. burgdorferi* s.l. complex with specific monoclonal antibodies or by PCR.

The genospecies is rarely identified in clinical cases. If necessary, this can be done with molecular methods such as large restriction fragment pattern (LRFP) analysis plus plasmid profiling, PCR-based typing methods that target single genes, PCR-based restriction fragment length polymorphism (RFLP) analysis, MLST of house-keeping genes or whole genome sequencing. Distinguishing some closely-related organisms, such as *B. garinii* and *B. bavariensis*, is impractical outside a specialized facility that can do multilocus genotyping.

Treatment

Lyme disease is usually treated with antibiotics, often beta-lactam drugs (e.g., amoxicillin) or tetracyclines (e.g., doxycycline). Steroids are employed in immune-mediated polyarthropathy in dogs. Oral antibiotic treatment of horses with neurological signs is often unsuccessful, and some sources suggest that parenteral treatment focusing on adequate drug concentrations in the target organ might be more effective.

Control

Disease reporting

Veterinarians who encounter or suspect an infection with *B. burgdorferi* sensu lato should follow their national and/or local guidelines for disease reporting. Although Lyme disease in humans is nationally reportable in the U.S., this is not the case for animals. State authorities should be consulted for any reporting requirements.

Prevention

Acaricides (e.g., pour-on preparations) and tick repellents can help prevent tick bites. Animals should also be checked frequently (at least daily) for ticks, which should be removed as soon as possible. Avoidance of habitats where ticks are more common, such as the woods, reduces exposure. Environmental modifications such as excluding deer (which provide blood meals to sustain ticks) and removing debris or other features that may shelter ticks and rodents, may be helpful, but most of these measures have not been extensively evaluated. The efficacy of some measures, such as attempts to reduce tick populations on wildlife with acaricides, is inconclusive and the cost-benefit unclear.

Several different types of Lyme disease vaccines are currently available for dogs, but their use is controversial, with varying estimates of efficacy. Canine vaccines have sometimes been used off-label in horses, though responses seem to be inconsistent.

Morbidity and Mortality

In endemic areas, antibodies to *B. burgdorferi* sensu lato have been detected in 5-50% or more of healthy dogs, cats, horses and some ruminants, as well as wildlife. Some studies have found that dogs are more likely to be seropositive than cats. Most infections in animals are thought to be subclinical, with epidemiological studies suggesting that approximately 5% or less of all infected dogs in endemic areas develop Lyme disease. Clinical cases seem to be uncommon in horses and have been rarely reported in other species, but lack of awareness and diagnostic uncertainties might play a role. The consequences of infection vary with the syndrome. Neurological cases in horses typically have a poor prognosis, and vision may not improve in horses with uveitis.

Infections in Humans

Incubation Period

Erythema migrans rashes can appear from a few days to a month after exposure, with most cases becoming apparent within a week or two. The incubation period for borrelial lymphocytoma ranges from 10 days to several weeks or more. If Lyme disease is not treated in the early stages, additional signs may be observed weeks to years later.

Clinical Signs

Most, though not all, people with early Lyme disease develop a distinctive skin lesion called erythema migrans, which may or may not be accompanied by a flu-like, sometimes febrile, illness. Erythema migrans typically originates as a macule or papule, which widens into a red or bluish-red rash with distinct and often intensely colored (e.g., bright red), but not raised, borders. The rash, which is usually painless, expands over days or weeks. It often develops a "bullseye" appearance with central clearing. This central area may occasionally have vesicular or necrotic lesions. Secondary erythema migrans lesions can occasionally appear on other parts of the body. A small number of people with Lyme disease develop a painless bluish-red or reddish-purple nodule or plaque on the skin, which called a borrelial lymphocytoma. Borrelial lymphocytomas often occur on the ear, nipple or scrotum; are most common in children; can accompany or follow erythema migrans; and tend to be caused by *B. afzelii* or *B. garinii/ B. bavariensis*. They are rare in North America, where these genospecies are absent. Atypical rashes have been reported occasionally in Lyme disease patients, including a diffuse macular rash in some people infected with *B. mayonii*.

Without treatment, the initial symptoms of Lyme disease usually last a few weeks (untreated borrelial lymphocytoma may persist for months) and may recur, but eventually disappear. Some of these patients can later develop arthritis, neurological signs, or other syndromes. Arthritis, which appears to be particularly common in North America, usually appears as intermittent pain affecting one or a few joints, with or without swelling. Large, weight-bearing joints such as the knee are affected most often. The arthritis may be recurrent or long lasting, persisting for months or possibly years. It usually responds well to antibiotics, but a small proportion of nonresponsive cases are thought to be caused by an autoimmune reaction.

Neurological syndromes, which seem to be especially common with *B. garinii/ B. bavariensis*, can include meningitis, facial palsy, radiculitis (pain or discomfort associated with nerve inflammation) or lymphocytic meningoradiculitis with or without paresis, as well as less common or rare conditions such as myelitis, cranial neuritis, chorea or encephalitis. Acute syndromes such as facial nerve palsy are usually self-limiting, but some signs can persist for months, and sequelae are possible. Occasional cardiac complications tend to be transient atrioventricular blocks of varying severity, but other arhythmias, myocarditis, endocarditis or pericarditis are also possible. Rarely, there may be ocular signs including conjunctivitis during the early stages, and uveitis, keratitis, optic nerve involvement (e.g., optic neuritis, papilledema secondary to elevated intracranial pressure, neuroretinitis) and other conditions late.

Late stage complications occur in some untreated patients months or years after the tick bite, and can include acrodermatitis chronica atrophicans, rare incidents of neurological involvement (e.g., chronic progressive meningoencephalitis, multifocal cerebral vasculitis) and chronic arthritis. Acrodermatitis chronica atrophicans is a skin condition often associated with *B. afzelii*, though it can be caused by other genospecies. It usually affects older adults, is uncommon in children, and occurs most often on the limbs. The typical presentation is an area of red or bluish-red cutaneous discoloration, often accompanied by doughy swelling, which is followed by slow, progressive skin atrophy that eventually results in an area of parchment-like skin with prominent veins. The skin lesions may be accompanied by pain, pruritus, hyperesthesia or paresthesia. Acrodermatitis chronica atrophicans can be treated successfully in the initial stages, but skin atrophy and neuropathy are often irreversible. Likewise, other late stage Lyme disease complications may result in residual neurological deficits or arthritis, especially if treatment is delayed until the signs are advanced.

Co-infection with another tick-borne disease, especially human granulocytic anaplasmosis or babesiosis, can alter the clinical signs and response to treatment.

Chronic Lyme disease and post-Lyme disease syndrome

"Chronic Lyme disease" has been used to describe several different groups of patients, including untreated or inadequately treated patients with persistent objective signs of Lyme disease (e.g., acrodermatitis chronica atrophicans) and people with post-Lyme disease syndrome. Patients with post-Lyme disease syndrome complain of persistent or relapsing nonspecific symptoms such as fatigue, headache,

sleep disorders, myalgia, arthralgia, paresthesias, or difficulty with memory or concentration after they have been treated for Lyme disease. Possible causes include slow resolution after treatment, autoimmune reactions, post-infective fatigue syndrome (which also occurs after a variety of other infections), and concurrent diseases or conditions. There is no evidence that *B. burgdorferi* persists in this syndrome. The number of patients reporting symptoms decreases over time.

Some practitioners have also applied the term "chronic Lyme disease" to a group of people with vague, nonspecific illnesses and positive serology but no response to antibiotics or other evidence that *B. burgdorferi* s.l. is causing their symptoms.

Diagnostic Tests

As in animals, human Lyme disease is usually diagnosed by the clinical signs, together with a history of exposure to ticks and supportive evidence from laboratory tests. The diagnosis is typically based on symptoms alone in people with erythema migrans, as this rash usually develops before antibodies can be found. While PCR can often detect nucleic acids in a skin biopsy at this stage, testing is normally done only for atypical lesions. It should be noted that, while erythema migrans lesions are usually caused by Lyme disease, it is possible for other diseases to cause a similar rash.

The diagnosis in other syndromes is most often supported by serology. Patients can be screened with various enzyme immunoassays (e.g., ELISAs, enzyme-linked fluorescent assays, chemiluminescence immunoassays), and positive or indeterminate samples are confirmed by immunoblotting. A second ELISA is now considered acceptable for confirmation in some countries. Serology must be interpreted with caution and in conjunction with the clinical signs, as antibodies to *B. burgdorferi* are very common in the human population, including healthy people. The CSF/serum antibody index is helpful in the diagnosis of neurological disease, together with signs of inflammation in the CSF.

PCR is sometimes useful for conditions such as acrodermatitis chronica atrophicans, or on synovial tissue or fluid in arthritis. Although PCR may detect nucleic acids in the CSF of patients with neurological conditions, it is not very sensitive in this syndrome. Culture is rarely attempted.

Treatment

Early treatment with antibiotics reduces the duration of erythema migrans and prevents later complications such as arthritis. Anti-inflammatory drugs are employed in cases of Lyme arthritis thought to be caused by an autoimmune reaction. Treatment failures are rare with the currently recommended regimens; however, patients treated later in the course of the disease may recover more slowly, and acrodermatitis chronica atrophicans can require several weeks of treatment. Studies have found no benefit to prolonged antibiotic treatment in post-Lyme disease syndrome.

Prevention

Lyme disease prevention consists of avoiding tick-infested locations and/or preventing tick bites with protective footwear, clothing (e.g., long pants tucked into the boots, and shirts tucked into the trousers) and tick repellents. Ticks may be more visible on light-colored clothing. People who enter tick habitats should check frequently for ticks and remove them as soon as possible. Gloves are recommended during tick removal. One study found that showering soon after exposure to a tick-infested area was also helpful. Environmental modifications to decrease tick exposure (see Prevention section for animals, above) are more common in North America, where people are often exposed around their homes, than in Europe, where exposure tends to be occupational or recreational.

Postexposure antimicrobial prophylaxis (a single dose of doxycycline within 72 hours) is sometimes given in parts of North America where the risk of infection is high and the tick has been attached for at least 36 hours. Prophylactic treatment is not usually employed in Europe, but some studies suggest there may be a benefit. There is currently no vaccine for humans; a vaccine licensed in the U.S. was withdrawn from the market by the manufacturer in 2002.

Morbidity and Mortality

In the Northern Hemisphere, most cases of Lyme disease are seen from late spring to summer, when ticks are most active and more people are outdoors. People can become reinfected, usually with a different strain. The reported incidence of Lyme disease is approximately 7-10 cases per 100,000 population in the U.S., where exposure around the home is common in some rural and suburban areas. In Europe, infections tend to result from occupational exposure to ticks or recreation in tick habitats, and the estimated incidence in various countries ranges from < 1 to > 100 cases per 100,000 population. The precise number of Lyme disease cases in both North America and Europe is unclear, as some authors feel that significant numbers of cases might be missed, while others suggest that the reliance on serology leads to overdiagnosis and confusion with other conditions. Many patients with chronic conditions seen at Lyme disease referral centers do not have this disease.

How many infected people become ill is uncertain, with estimates ranging from 5% to 50%. In Europe, 3-6% of people have been estimated to seroconvert after a tick bite, with overt clinical signs developing in 0.3% to 1.4%. In one study, 61% of Lyme disease patients with erythema migrans developed neurological, articular or cardiac symptoms. Fatalities appear to be very rare, with only one human death attributed to Lyme disease,

Internet Resources

Centers for Disease Control and Prevention (CDC)

European Centre for Disease Prevention and Control. Borreliosis

Public Health Agency of Canada. Pathogen Safety Data Sheets

The Merck Manual

The Merck Veterinary Manual

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