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# A Brief Overview of Lyme disease and One Health Approach for its Control

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**Abstract:** Lyme disease is a complex structured pathogenic infection induced by the bacterium *Borrelia burgdorferi*. The primary dissemination of this infection is by the bite of a contaminated vector (tick). The purpose of this review paper is to signify the various factors that contribute to understanding the spread of Lyme disease globally. Epidemiological studies have shown that Lyme disease is common in shady or grassy areas where the population of ticks is high. The ticks transmit *B. burgdorferi* from the asymptomatic host (rodents) that harbors the pathogens to the human hosts. The incidence rate of Lyme disease is significant in the Arctic region, causing public health infections due to modifications in ecosystems and mandeeds. Symptoms may include fever, flu, dermatitis, and inflammation of the heart and central nervous system in chronic cases. The disease can be diagnosed by performing PCR and serological tests for antibodies averse to *Borrelia burgdorferi*. The treatment includes effective antibiotics like Augmentin, Vibramycin, and Ceftrex depending on the phase of infection and condition of the patient and therapeutic vaccination strategies. The One Health perspective of Lyme disease connects human, animal, and environmental well-being by providing strategies to surveil tick ubiquity, educational public initiative, and collaboration of researchers for vaccine development. This review emphasizes the extensive outline of Lyme disease by discussing the historical background of the disease, clinical representation, interpretation of the pathogen, targeted therapies, and one health outlook for its management.

**Keywords:** History of Lyme disease, pathogenesis, clinical manifestations, prevention, control, treatment, one health approach

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## Introduction

Lyme borreliosis (Lyme disease) is elicit by Borelia burgdorferi, and it is spread by ticks [1]. It happens in moderate areas of the Northern Hemisphere in Asia and Europe mostly [2]. This disease was recognized almost 30 years ago and is increasing due to its agent (Lyme burgdorferi) and is considered a vital emerging infection [3]. Apart from advancements in treatment and prevention, Lyme borreliosis (LB) is the most common arthropod-borne disease [4]. It was first identified in the 1920s but the illness started in 1981 when Willy Burgdorfer discovered a new Borrelia species from ticks [5, 6]. In the last 3 decades, not only has its number been increasing in North America but also there is a rapid increase in its geographical range [7].

According to 2 studies by the US Centre for Disease Control and Prevention, it is estimated that 300,000 new cases appear in the US per year [8]. 85000 cases are recorded annually in Europe according to WHO, and due to incomplete methods, many cases of infections of Lyme disease go unknown [9]. Climate change also had an impact on the incidence of LB disease. The interactions between climate change and humans lead to the spread of new cases and environmental factors such as moisture, temperature, and host availability, have increased tick abundance and their disease-causing ability [10]. The major hosts for Lyme burgdorferi are small mammals (mice) and birds [11].

In Western Europe, the populace-weighted occurrence has been predicted at 22.04 instances in step with 100,000 character years.7 In the UK, Lyme sickness isn't always an apprise sickness, however, laboratory-showed Borrelia spp. are important causation agents [12]. Public Health England (PHE) compiles statistics on laboratory-showed instances of Lyme sickness in England and Wales, which display an upward thrust inside the country-wide occurrence of instances from 0.38 in step with 100,000 populace in 19979 to 1. Ninety-five in step with 100,000 populace in 2016 [13]. The skin lesion factor of Lyme disease was identified in Sweden for the first time in 1909. The major 3 areas famous for the spreading of Lyme disease in the US are Midwest, coastal areas, and Northeast areas [14].

Lyme disease is a multi-system disorder and it has three stages of illness. In the first stage, the patient may develop skin lesions or skin-like diseases. In the second stage, brain and heart abnormalities may occur. In the third stage, arthritis attacks may happen and they can be chronic [15]. Some patients may have symptoms of meningitis. In humans, symptoms of Lyme disease include fever, chills, fatigue, muscle and joint pain, swollen lymph nodes, and skin rash (Erythema migrans (EM). Arthritis, nerve pain, facial paralysis, and dizziness may occur months after a tick bite. In animals, symptoms include loss in appetite, anorexia, kidney problems, lameness occurring frequently, chronic weight loss, and joint swelling. These symptoms may be mild or severe and they appear only for a specific period [16]. If these symptoms are missing, patients may undergo a syndrome in which different organs suffer such as the brain, heart, kidney, and muscles [17].

Lyme disorder Borrelia evolved an uncommon lifestyle wherein they ought to change among vertebrate and arthropod hosts; they may be by no means free-living. Additionally, they are related to a set of rather invasive organisms, the spirochetes, able to invade a couple of tissues in inclined vertebrates and inflict contamination and incarnations for months or maybe years. In this way, contamination with Lyme disorder Borrelia in a few aspects parallels that of any other spirochete, Treponema pallidum subsp. Pallidum, the syphilis-causing agent. Both illnesses showcase local, widely spread, and continual image, and tissue deviations seem to be due on the whole to inflammatory reactions of the host. However, there are critical variations inside the mode of transmission (i.e. vectored via way of means of an inflamed tick vs. human-to-human interaction (direct) [18].

In the case of the pathogenesis of Lyme disease, the killing of bacterial cells occurs by phagocytosis of nonimmune and immune cells. In chronic Lyme disease, autoimmunity may activate [19]. During infection, first bacteria replicate in the tick, then after the tick bites humans, bacteria undergo the skin, then replicate and spread widely in the skin. After that, it undergoes in blood vessels and replication also continues in blood vessels it leads to evasion of innate immunity, differentiation of tissues, and cause facial paralysis, neurological disorders, and carditis. It also affects the central nervous system and joints, muscles, and peripheral nervous system [18]. Once they are inserted into the central nervous system, the borrelia engages immune cells such as

monocytes, macrophages, and dendritic cells [20]. These cells manufacture further cells of cytokines such as Interleukin 8, Interleukin 6, and Interleukin 12. At the same time, chemokines are inducted to approach other immune cells in the inflammatory area [21].

For diagnosis of Lyme disease, serological testing is still confusing for physicians, especially for people who are at minimum risk for the disease. Diagnosing Lyme disease depends on the abundance of disease and the severity like at what stage the infection is present. In the case of erythema migrans, the patients do not require serological testing, they can be recovered with clinical tests [22]. It is diagnosed according to symptoms such as rash and exposure to ticks. Furthermore, immuno-PCR and mass spectrometry can be performed [23]. Laboratory tests for diagnosis may include cerebrospinal fluid, PCR in skin, blood, and cerebrospinal fluid.

Treatment for Lyme disease includes various antibiotics such as doxycycline for patients of 9 years and older (non–pregnant ladies), and amoxicillin for younger patients than 9 years [24]. The period of treatment varies according to the type and severity of the infection. The skin infection treatment lasts for 14 days and for arthritis, approximately 30 to 60 days [25]. Late disease can be connected with the failure of treatment and new treatment may be helpful to cure the disease [26]. Patients with early-stage Lyme disease can be recovered with antibiotic therapy while patients with late-stage Lyme arthritis require different treatment techniques [27]. There aren't any diagnostic checks that could both decide clearance of contamination or expect the achievement of remedy in sufferers with mild Lyme disease (neurological). Determination of neurologic indications is occasionally delayed, and staying power of signs, consisting of facial paralysis, isn’t always denotative of remedy failure. It may also soak up to seven or 8 weeks for complete healing of motor function [28].

Prevention of Lyme disease for humans involves several factors such as wearing full sleeves when encountering ticks or going in areas affected with ticks. Use of insect repellent can also minimize the risk of tick bites use of pesticides to get rid of ticks, and avoid long grasses and bushes while walking in areas where chances of ticks are higher [29]. In the case of animals, it is necessary to vaccinate them against ticks, do daily tick checks, and check for tick habitats in yards. The diseases associated with their vectors can be prevented by two methods, either direct (biological control)

or indirect (migration or changing wildlife populace). If the cases are more in urban areas then removing vegetation is better than burning it [30].

The public health impact of Lyme disease is very critical as it has prolonged symptoms and due to overdiagnosis, some patients are given LB treatment while they are not even affected by it [31]. Vaccines are important tools of public health to deal with disease mortality, morbidity, and occurrence of disease. Successful vaccines are results indicative of the public health community, and health care providers' appropriate approach. Early vaccines for Lyme disease were LYMErix and ImuLyme. Both vaccines have undergone clinical trials to check their effectiveness [32]. It has to be burdened that no matter the intervention, whether or not it's tick manipulate or academic prospectus traversing control partners have to seek advice from and conjoin with journey fitness professionals and public fitness government if we're to make any profits in handling this fitness and protection issue. There is a position for tourism and it's far advocated that tourism collaborators accomplice with suitable groups and companies, emerge as lively in nearby monitoring efforts, and co-broaden academic or different interventions [33].

**Geographical distribution of Lyme disease**

Lyme disease has been reported as a common tick-borne disease in the US and the microorganism that causes this disease is Borrelia burgdorferi. Species such as Borrelia garinii and Borrelia afzelii cause Lyme disease in Asia and Europe [34, 11]. The geographical diversity of various Borrelia species is discussed in Table 1. The only vector of Lyme disease is a hard tick belonging to the Ixodes genus therefore, it is geographically distributed in the region where these ticks are found. This disease is also found in various areas of Latin America, Brazil, and Argentina [35]. It is worth noting that the Schaulenfeld Experiment is the first zoonotic classical pathogen cycle to be stated, specifically for Borrelia burgdorferi in an epidemic among children in Connecticut in 1977. This disease mostly causes infection in the northeastern and mid-Atlantic nations and is also observed in Pennsylvania and Mid-western states [36].

More than 90% of disease incidences occur in northeastern and mid-Atlantic regions. Lyme disease was widespread across North America, Europe, Russia, and Asia in the 20$^{th}$ century. The

most prevalent areas for the illness are central Europe and Scandinavia where they frequently appear. Finnish islands are one of the places where the incidence is the greatest and equals more than 100 cases per 100,000 [37]. The total number of cases reported is about 30,000 annually. Some recent studies showed that almost all the recognized tick bites were not fed for less than 2 days and only a few percent of these bites may progress into Lyme disease and infect a person in native areas [11]. Various extrinsic factors like host specificity, hunting habits, a span of diapause, and intrinsic factors including the variety of vegetation, climatic surroundings, generosity, and efforts of the reservoir to tick species are determined by the capacity of ticks to spread borrelia to several parasites. The maturation, function, and existence of ticks are also affected by environmental factors like temperature, humidity, climate change, and an increase in season length [38].

**Table 1: Geographical diversity, tick vectors, and, reservoir host of various Borrelia specie**

| Borrelia Species | Geographical diversity | Tick vectors | Reservoir host | Reference |
|---|---|---|---|---|
| B. burgdorferi sensu stricto | North America, Europe | Ixodex. pacificus, I. ricinus, I. scapularis | Birds, rodents, mammals, lizards | [92] |
| B. afzelii | Eurasia | Ixodex. ricinus, I. persulcatus | Birds, rodents | [93] |
| B. garinii | Europe, Asia | Ixodex. ricinus, I. persulcatus | Birds, rodents | [94] |
| B. sinicia | China | Ixodex. ovatus, I. granulatus | Wild Rodents, Tick | [95] |

| | | | | |
|---|---|---|---|---|
| B. japonica | Japan | Ixodex. ovatus, I. tanuki | Masked palm civet, racoon | [96] |
| B. Americana | Northeastern US, Southeastern US | Ixodex. minor, I. pacificus | Birds, Rodents | [97] |
| B. bissettiae | USA, Europe | Ixodex. pacificus, I. spinipalpis, I. scapularis | Rodents (mice, squirrels) | [98] |
| B. lusitaniae | Europe, North Africa, | Ixodex. Ricinus | Lizards | [99] |
| B. tanukii | Japan | Ixodex. tanukii | Wild animals | [100] |
| B. valaisiana | Asia, Europe | I. Ricinus | Birds | [101] |

| | | | | |
|---|---|---|---|---|
| B. mayonii | USA | Ixodex. scapularis | Small mammals | [102] |
| B. andersonii | USA | Ixodex. dentatus | Wild birds, Cotton tail rabbits | [103] |
| B. spielmanii | Europe | Ixodex. ricinus | Hedgehogs, garden dormouse | [104],[105] |

**Clinical manifestation**

Lyme disease shows clinical manifestations in three stages. The initial, localized primary stage leads to erythema migrans (Red skin rash) near tick bites that arise in 90% of infected children [39, 40]. The lesion formed is raised, sometimes hardened, and irritating but rarely painful. It occurs after a few days or weeks post-vaccination. The lesion can be detected on the head, neck, or earlobe for very young children and on the extremities in the older ones [41]. Rashes and flue-like symptoms like fever, cold, firm neck, and myalgia appear after tick bites [42]. The second, early disseminated stage results in various lesions such as erythema migrans, carditis, Lyme arthritis, and Lyme neuroborreliosis [43]. It arises several months after manifestation and the patient experiences headache, sleep disturbance, pain in the extremities, mood swings, memory loss, and face paralysis [42]. In the third late disseminated stage, Lyme arthritis and neurological signs are detected and appear years after early infection. It mostly attacks the knees and shoulder with a display of synovitis and pain [43, 42].

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In the United States, two chronic neurologic syndromes associated with Lyme disease include the representative pathophysiology of the dorsal root ganglia, including presenting symptoms such as tingling and demonstration of polyneuropathy axonal electrophysiology and the other one is CNS memory impairment and encephalopathy which are visible [44]. The infrequent dermal symptom of Lyme disease is borrelial lymphocitoma and the site of infection in adults is the nipple and breast [43]. Lyme disease also results in various neurological complications including meningitis (headache,), cranial neuritis (facial weakness), and radiculoneuritis (weakness or pain) [40]. The neurological complications that become apparent are mostly due to unprocessed infection for 3-4 weeks [45].

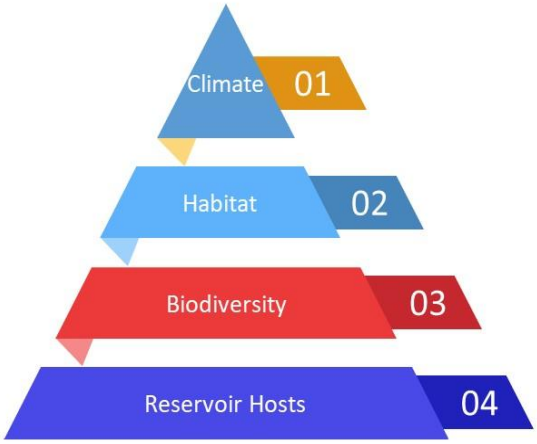


**Fig 1: Contributing Factors of Lyme disease**

**Implications in public health**

Public health scholars should have a great command of Lyme disease and give details and advice about the disease signs and symptoms, and preventive and treatment measures to the citizens [46]. The vaccine plan is an essential public health tool employed to reduce the burden of incidence, morbidity, and mortality. Various agencies including the CDC, the National Institute of Health, and the FDA play important roles in developing vaccines [32]. The licensed LYMErix vaccine

was used as a preventive measure for Lyme disease. Still, many issues were debated regarding the long-term safety and production of auto-immune reactions [47]. In the deficiency of vaccines and other preventive and essential tick control methods, education and guidance on Lyme disease become the only means of diminishing the spread of the infection. This activity should be a foremost part of funding by public health agencies, employers, and other organizations [33]. Lyme disease will continue to be a public health concern worldwide due to the lack of crucial adaptations in the tick ecosystem, lack of surveillance, vaccines, tick control, microbial modification, and human habits [48].

**Diagnostic tests for Lyme disease**

The diagnosis and laboratory testing of Lyme disease mainly depend on the geological area and the medical condition of the patient. The occurrence of Lyme disease relies on the pretest possibility of a disorder. The high pretest likelihood of disease includes those patients who live in the area of epidemic and represent symptoms of Lyme disease. In this case, a negative trial is probably inaccurate. On the other hand, people living in the areas where chances of the disease are low, develop non-specific, systemic manifestations of Lyme disease and as a result, the results of a positive test can create Type I error. Direct and indirect tests can be used for the detection of B.burgdorferi for the diagnosis of Lyme disease. The identification and detection of B.burgdorferi is laborious because of the shortage of specific microorganisms [49],[50],[51],[52]. Although culturing of B.burgdorferi requires long incubation periods and special culture media it is still used as a standard for the diagnosis of Lyme disease. B.burgdorferi shows excellent growth in two media; Barbour-Stoenner-Kelly and modified Kelly-Pettenkofer [53]. The growth of the microbes is visualized by staining with acridine orange under a fluorescent or dark field microscope. The culturing of B.burgdorferi is highly dependent on the phase of infection and the genotype of the organism [54]. To check the sensitivity of B.burgdorferi, PCR is done to check the presence of microorganisms in blood or skin. To get high-quality results, PCR is integrated with mass spectrometry, and a sample of synovial fluid is used. By using this technique, the DNA of B.burgdorferi can be observed in nearly 80% of the patients [55, 56, 57]. Indirect methods of diagnosis disclose the performance of the immune system of the host in response to pathogenic

microorganisms. It is done by checking the antibody titer in the serum against B.burgdorferi. Most antibody assays include whole cell sonicates extracted from B.burgdorferi that can provide false alarms due to the reactive antigens. A lipoprotein, VlsE induces a rapid humoral response during disease and it has a minimum activity in the cultured B.burgdorferi. But when this protein is added to antibody titers, it demonstrates enhanced activity [58]. The sensitivity of the antibody test elevates with the infection until it corresponds with a sufficient amount of antibodies. Serological tests are done in patients in the later stages of Lyme disease.

**One health approach for the control of Lyme disease**

To protect the environment and the health of human beings from zoonotic diseases, we must avoid the spread of infections and conservation of biosphere [59]. With time, the domestication and interaction of animals increases which causes elevated levels of diseases. Nearly 65-70% of human diseases are of animal origin and they disturb the normal balance of the environment [60]. The one-health approach can play a major role in the protection of ecosystems and biodiversity as we are facing various issues associated with zoonotic diseases [61]. It helps in developing a strong among humans, animals, and the environment for the effective management, diagnosis, prevention, and treatment of disease [62]. To deal with Lyme borreliosis, the veterinarians and public should interact and formulate useful policies to preserve nature. They should devise tools that are substantial to implement control measures against Lyme disease [63]. Epidemiologists can control the proliferation of Lyme disease by determining the prevalence, significance, and cost of infection. People must gain education about the severity of disease by participating in the immunization drive and the developed vaccine should be cost-effective to reduce the burden of disease [64]. The protection of ecosystem health is also important to monitor the production and distribution of edibles and water to the infected area and monitoring of disease and ecosystem. The establishment of regional risk plans creates a wonderful coordination between ecology maintenance and public health. Complete safety from zoonotic infections like Lyme borreliosis can be obtained by adequate vaccination and proper control of ticks. Furthermore, future researches mainly aim at the production and administration of booster shots that protect people against Lyme disease [65].

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**Pathogenesis**

At the initial phase of tick feeding (early 24-48 hours), Borrelia remains attached to the tick gut via the interaction of OspA (bacterial surface protein A) with TROSPA (the tick's receptor for this protein) [66]. During the flow of host blood towards the tick gut, multiplication of Borrelia occurs and later disseminates to the tick's salivary glands. Key factors that contribute towards pathogenicity (ability to cause an infection) and virulence of spirochete; Borrelia burgdorferi, include bacterial antigenic variability, persistence inside the host, cytotoxic immune response, agglomeration centers, immunosuppressive nature of tick saliva, and lymphocyte activation by bacteria. Borrelia biofilms trigger chronic infections, and permit bacterial survival for months to years [67]. Furthermore, surface antigenic variability (of protein VIsE) also contributes to the pathogenesis of B. burgdorferi as it protects bacterial membranous proteins from the attack of antibiotics. Infectious nature could be attributed to every Borrelia species extracted from fauna (animals) or ticks while bacterial pathogenicity is host-dependent in many aspects [68]. Borrelia species undergo various alternations in their gene expression so they can easily survive inside the host's cell [69].

For effective colonization or residence inside the dermal layer of the host, Borrelia undergoes strategic adaptations to fluctuating homeostatic pH levels and elevated temperature range, in addition to defense against innate immunity elicited by the host organism. Consequently, bacterial count increases during tick feeding in the midgut (via replication). There is about ~ a 300-fold increase in bacterial numbers [70]. The infection becomes difficult to treat; as Borrelia species show pleomorphism, antimicrobial peptide resistance, and intracellular localization [71].

Once the bacteria enter the host cell, they transit toward different body sites by binding OspC (bacterial outer surface protein) with human plasminogen [72]. It spreads via the bloodstream, lymph, or peripheral nerves. At the tick-bite sites, the manifestation of inflammation; a skin lesion named erythema migrans, is often observed [73]. Hence, it implies that infected tissues show efficient pathogen spread and agglomeration centers are formed; bacterial clusters contribute towards persistent infections.

Recent research has shed light on Borrelia mechanisms to evade the host's immune response. During the early stage of Lyme disease, there is a significant increase in cytokines and TNF-α levels leading to the eosinophils concentrating near the infection site [74]. Another remarkable characteristic of the B. burgdorferi bacterium is its ability to modify organisms' immune response, causing the disturbance in cytokine secretion and forming aggregation with cellular proteins ultimately diminishing the host's phagocytosis ability [75]. Furthermore, cytotoxin efflux into the blood from phagocytic cells decreases the host's phagocytosis ability. Evasion of the host's immune response by spirochete is achieved by regulation of bacterial outer surface proteins, utilization of proteins of tick's saliva, and complement regulators binding (by different bacterial proteins) resulting in disabling of the complement system plays a key role in bacterial survival during infection. The complement system is a cytotoxic biochemical cascade that increases the susceptibility of pathogens toward phagocytes [76]. Salivary proteins of ticks result in poor innate immunity and the immune cells cannot reach infected sites, inducing or enhancing the disease intensity. Upon the lymph node invasion by these spirochete species, the adaptive system of the host is affected together with immunoglobulin class switching and the diminished memory cell level [77]. Borrelia escapes from the host immune responses by hiding in the extracellular matrix, downregulating immunogenic proteins (Osp's), suppressing the host immune system, or inactivating the host's effector mechanisms [78].

B. burgdorferi fuses with dermatan sulfate and heparan sulfate which facilitates the adhesion of bacterium to glial cells and endothelium respectively [79]. Bacterial species, once phagocytosed, are expelled from the patient's body via two major methods named Oxygen-independent and Oxygen-dependent phagocytic methods where different lysosomal hydrolyses, H2O2, and nitrogen compounds are involved. Furthermore, the act of acquisition of host plasmin facilitates penetration of pathogen inside body tissues leading to further pathogenesis of disease [80]. This vector-borne disease reaches its peak level during late summer and spring.

Lyme disease is an invasive, chronic persistent disorder that spreads locally as well as systemically and causes abnormalities such as Erythema migrans (target clearing leison-early stages of infection; <30 days), peripheral neuropathy, Lyme carditis, migratory arthralgias, early and late

neuroborreliosis, arthritis encephalopathy and cardiovascular manifestations. Most of them occur during persistent and disseminated stages of infection [18].

Local immune cells first target bacteria when they reach the central nervous system. These cells include macrophages, dendritic cells, and monocytes which further induce the production of interferons, and cytokines (i.e. IL-8, IL-6, IL-12, and IL-18) [20]. Chemokines are crucial for inflammatory central nervous system reactions. Borrelia after the recognition by host B-cells; B-cells later immigrate into cerebrospinal fluid and mature into plasma cells, destroying the pathogen by antibodies. In this case, bacteria acquire mechanisms that lead to neural dysfunction. The mechanisms include autoimmunity via molecular mimicry, and glial and leukocyte cytotoxic release [81]. The adherence of bacteria to neural and glial cells; particularly of mice or rats, mediated by proteoglycans, bacterial outer surface protein (OpsA) is cytotoxic for the host cells which further can induce apoptosis [82, 19]. Cytokines and tumor necrosis factor (TNF) release during bacterial encounters in glial cells might elicit autoimmune reactions [83]. Cross-reaction of antibodies (against flagellin of Borrelia) with neural antigen plays an important role in host autoimmune mechanisms; highlighting the pathogenesis of Lyme neuroborreliosis, leading towards neural dysfunction [84].

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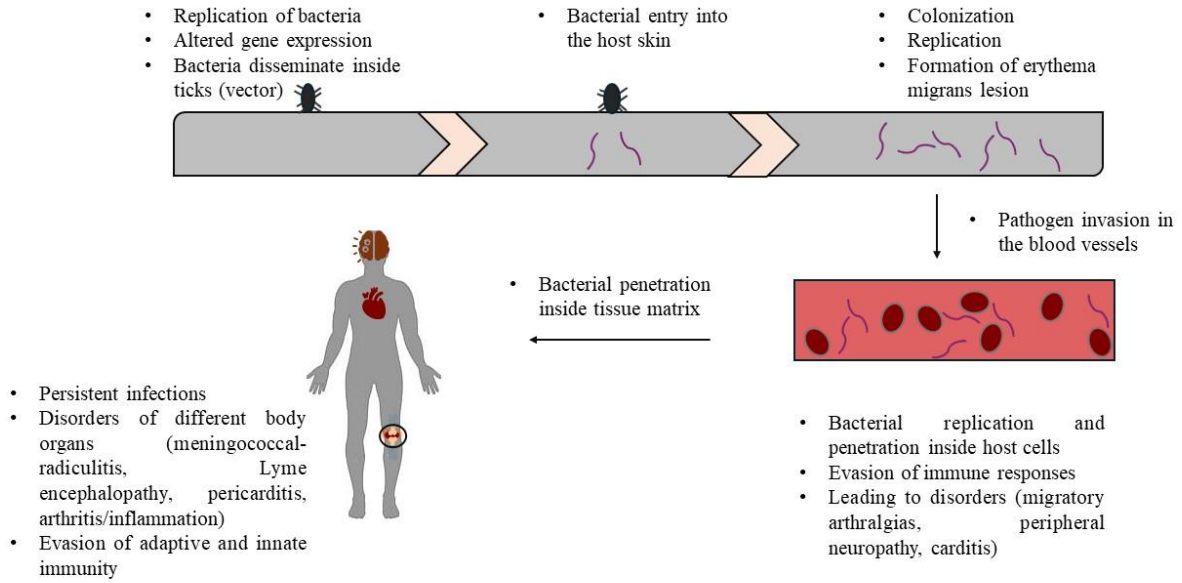


**Fig 2: Pathogenesis of Lyme disease**

**Transmission**

In this transmission type, pathogens are transmitted from vector males to females through co-feeding, instead of systemic transmission before host feeding. These transmission means are essential to ticks, as they remain embedded in the host for multiple days to feed. Unlike other arthropod vectors, ticks adhere to the hosts for several days to extract blood. In co-feeding transmission, the host serves as a fleeting conduit that unites individuals of infected and non-infected ticks at the same time and destination thereby enabling pathogen transmission. What stands, in contrast, is systemic transmission where the infected host acts as a reservoir from which vectors can obtain pathogens for a prolonged period, sometimes even up to a few months just after its host has been infected. Systemic transmission is where the causative pathogen replicates as an incubation period in the host and the host is not in the infectious state to the vectors. However, we can observe that the infection process during co-feeding transmission is quick and sometimes even

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immediate for some of the tickborne viruses [85]. The period of tick attachment is a vital question that determines how dangerous an infected tick is. 6–8 However, before engagement, it feeds and fattens up, which is after the tick exists at the bite by discharging its saliva. The time that would take for B. burgdorferi to migrate from the stomach to the salivary glands of the ticks is about thirty-six to forty-eight hours after the tick's attachment [86].

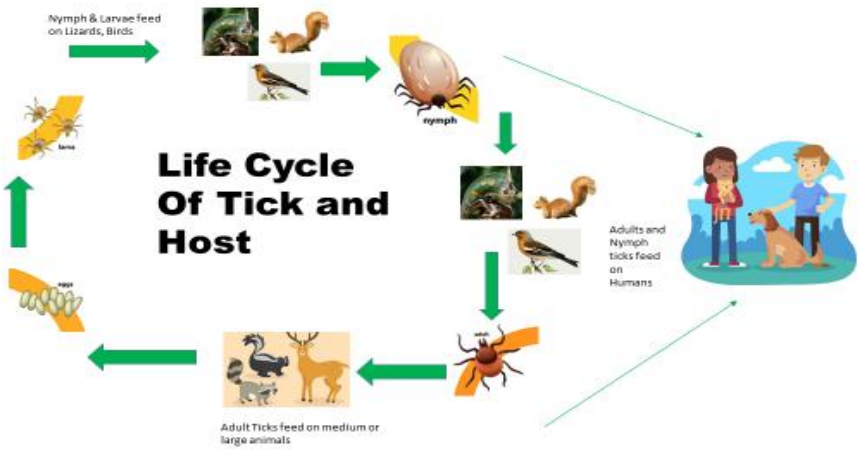


**Fig 3: Life Cycle of Tick in Host**

**Treatment**

The antibiotic treatment for Lyme disease is of two types; the first one is doxycycline for nonpregnant patients who are 9 years and older (100 mg orally, twice daily) or amoxicillin for patients who are younger than 9 years (50 mg/kg per day orally), both of which are usually effective in early disease. Secondary medication for adults is amoxicillin (500 mg orally, 3 times daily) [87]. Macrolide antibiotics are not recommended as first-line therapy for early Lyme disease (E-I). When used, they should be reserved for patients who are intolerant of amoxicillin, doxycycline, and cefuroxime axetil [88]. In vitro, the B. burgdorferi responds negatively to many bacteria-killing drugs, namely tetracyclines, penicillins, and different second and third-generation cephalosporins. Whereas a test of in vitro sensitivity to macrolides such as erythromycin and

azithromycin demonstrates the sensitivity of MRSA to macrolides, these agents are less effective in the real case clinically. On the list of parenteral antibiotics ceftriaxone and cefotaxime are two of the equally effective drugs that are available, however, given the once-daily dosage of ceftriaxone it is much handier, and cheaper, to use [89].

**Table 2: Anti-biotic drug therapies for Lyme Disease**

| Phase of infection | Primary medication | Replacement drugs | Time |
|---|---|---|---|
| Pre-mature confinement | Vibramycin, Streptomycin, Cipazine | Azitrocin, Macladin, Erythrocin | Around 3 weeks |
| Untimely circulization | Monodox, Ampicillin, Cefaxona | Azadose, Klaricid | Around 2-4 weeks |
| Delayed propagation | Benaxona, Benzylpenicillin | Periostat, Tetracycline | Approximately 4 weeks |

**Prevention**

The most developed nowadays way of curbing the infection with B. burgdorferi and other Ixodes-transmitted infections is to stay away from tick-infested areas. If one is bound to be in the I. Scapularis or I. Pacificus ticks' presence, in several ways, may help to the extent that ticks will not attach and thus, will not transmit infection. The use of surgical clothes (shirt tucked into pants and pants tucked into socks) might be a reason for the ticks to be attached to the body for a long time, thus, they can find the exposed skin and remove it easily. Through the use of light-colored clothes (as a background for the tick to contrast), the people in the endemic areas can be the ones to notice (and get rid of) the ticks before they have attached. Every day checkups of the whole body for finding the ticks and then removing them as well as the risk of transmission of infections carried

by ticks are brought out. Attached ones should be extracted right away with fine-toothed forceps, if possible. The repellents for ticks and insects which have been applied on the skin and the clothing give more protection [26].

**Future Directions and Challenges**

Recently, research has focused on the early diagnosis of Lyme disease using Western immunoblotting techniques. Another technique to identify proteins is in the serum of infected patients. In the past decades, essential advancements have been made in terms of the pathogenesis of Lyme disease [90]. Studies have shown the impact of climate change and how it is influencing the spread of disease. Ongoing researchers are working on new vaccines that are ideal for treating Lyme Burgdorferi infections [91]. Public health strategies also play an important role in dealing with diseases such as habitat modification and community-based interventions. It is also necessary to highlight challenges in surveillance such as incomplete or incorrect data and lack of standardization to diagnose disease correctly.

**Conclusion**

This review has supplied us with a brief overview of Lyme disease, highlighting the main points of history, case-control study of the disease, pathophysiology, signs and symptoms, diagnostic tests, and therapy. It also focuses on the prevalence of Lyme disease in areas with a high tick population. Since it is a disease of zoonotic origin, researchers pay attention to control strategies like vaccination and effective management of ticks in the affected areas. Early diagnosis of infection is necessary to negotiate because it is a challenge to protect patients from the early manifestation of Lyme disease. This review also signifies that future research i.e.: immuno-PCR (iPCR) and liquid chromatography are associated with the outbreak of Lyme disease and its consequences. Common people and health care workers should get appropriate knowledge for tick management and deterrence from Lyme disease. The upcoming exploration of Lyme disease should concentrate on the establishment of better treatments to tackle the emerging pathogenic disorder.

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